DISSERTATION ZUR ERLANGUNG DES DOKTORGRADES

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DER LUDWIG-MAXIMILIANS-UNIVERSITÄT MÜNCHEN

TOTAL SYNTHESES OF *GANODERMA* MEROTERPENOIDS

VON

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AUS NOWOTROIZKOJE, KASACHSTAN

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Erklärung

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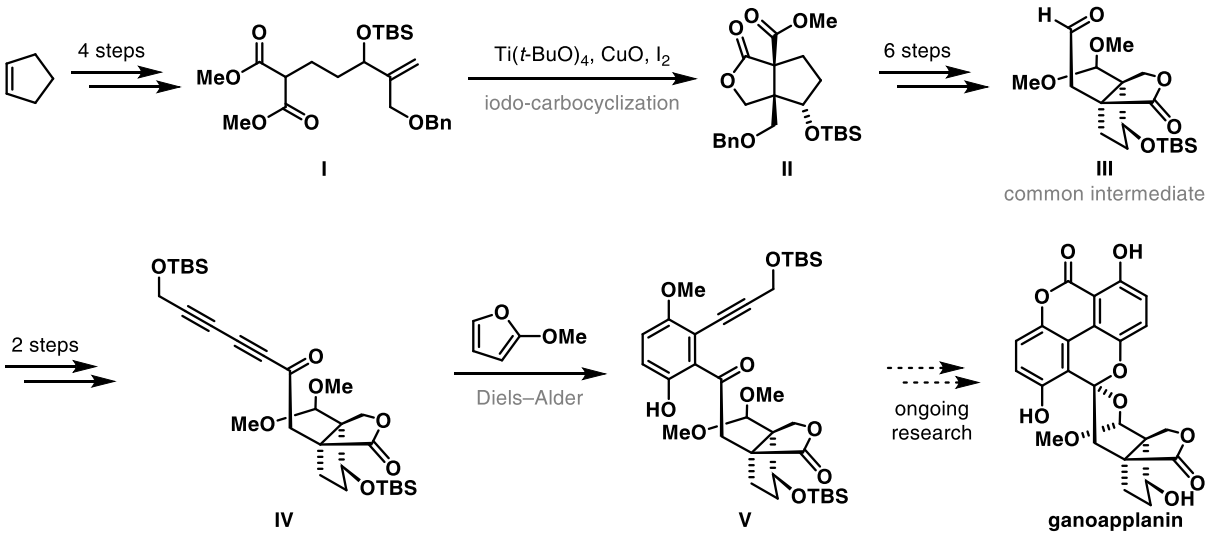
– To my parents, and my sister –

for their love and support

ABSTRACT

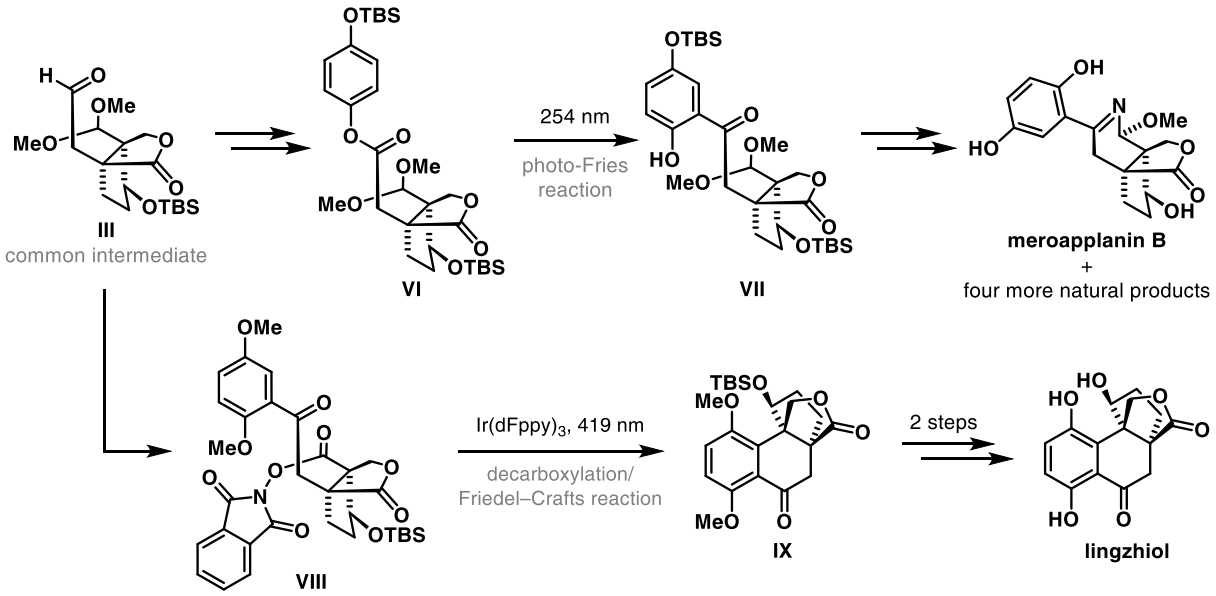
Ganoderma meroterpenoids, medicinally highly valued in Asia as traditional folk medicine, are a hybrid natural product class containing a 1,2,4-trisubstituted benzene ring and a polyunsaturated terpenoid part. The secondary metabolite ganoapplanin, that was isolated from the fungus *Ganoderma* applanatum, was found to act as a selective inhibitor for T-type voltage-gated Calcium channels, which makes it a potential agent to treat neurodegenerative diseases such as epilepsy or Parkinson's disease. In addition to this bioactivity, ganoapplanin is a structurally fascinating natural product possessing a dioxyspirocycle which is built up from a northern tetracyclic hemisphere and southern tricyclododecane moiety. From the same *Ganoderma* genus, several highly related congeners of ganoapplanin were isolated. The meroterpenoid family of applanatumol, lingzhilactone, the recently isolated meroapplanin and lingzhiol natural products share the same bicyclic lactone moiety as ganoapplanin as well as a trisubstituted benzene moiety.

This Ph.D. thesis describes the evolution of a strategy for the collective synthesis of the *Ganoderma* natural product family. The synthesis commenced with the functionalization of cyclopentene in four steps to malonate **I** that was reacted in an orchestrated and highly diastereoselective iodo-carbocyclization to **II** (Scheme A). Elaboration of the bicyclic lactone in a few steps gave access to aldehyde **III** that serves as a pivotal intermediate for the synthesis of ganoapplanin as well as its congeners. We relied on a Diels–Alder reaction of 2-methoxyfuran with a diyne as part of our studies towards the synthesis of ganoapplanin.



Scheme A: Studies towards the total synthesis of ganoapplanin.

A rare photo-Fries rearrangement is at the heart of the synthesis of the applanatumol natural products as well as lingzhilactone B and meroapplanin B (Scheme B). In addition to the photo-Fries reaction, we unveiled an oxidative decarboxylation / Friedel–Crafts sequence as a possible biomimetic transformation to access lingzhiol.



Scheme B: Total syntheses of meroapplanin B and lingzhiol.

ACKNOWLEDGEMENTS

The time as a PhD student has definitely been an interesting and unforgettable time in my life that has been marked by a lot of ups and downs. This journey would not have been possible without the help and support of many people. I am grateful to everyone that stood by my side and made this time even more valuable. Some of the people I want to thank were involved inside the laboratory where I spent an incredible amount of time to enjoy my passion for chemistry and to realize my ideas. I am also thankful for all the people that enriched my life outside of the laboratory that oftentimes had to deal with my chemistry-related mood changes.

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Lastly, I would like to thank my family for their exceptional support and all their love. Thanks mom and dad for all you have given me. I cannot thank you enough. Thanks to my loving sister Irina and the newest member of our family, my nephew Maximilian. I am grateful to my wonderful girlfriend Andrea for her endless support. We have already had so many unforgettable moments and I am looking forward to more to come.

All things considered, I am thankful for the possibility that I was given to carry out a PhD, as this is a chance that often comes only once in the life and I am looking forward to the opportunities that will open in the future.

LIST OF ABBVREVIATIONS

Ac	acetyl
AIBN	azoisobutyronitrile
Ar	undefined aryl substituent
Bn	benzyl
Br	broad (NMR spectroscopy, IR spectroscopy)
Bu	butyl
calc.	calculated
CDI	1,1'-carbonyldiimidazole
COSY	homonuclear correlation spectroscopy
Cp	cyclopentadienyl
CSA	camphorsulfonic acid
d	doublet (NMR spectroscopy)
d.r.	diastereomeric ratio
dba	dibenzylideneacetone
DBU	1,8-diazabicyclo[5.4.0]undec-7-ene
DCC	*N*,*N*'-dicyclohexylcarbodiimide
DCHT	dicyclohexyl tartrate
DDQ	2,3-dichloro-4,5-dicyano-1,3-benzoquinone
DIBAL-H	diisobutylaluminum hydride
DIPA	*N*,*N*-diisopropylamine
DIPEA	*N*,*N*-diisopropylethylamine (Hünig's base)
DIPT	diisopropyl tartrate
DMAP	4-(dimethylamino)pyridine
DMF	*N*,*N*-dimethylformamide
DMP	Dess–Martin periodinane
DMSO	dimethylsulfoxide
ee	enantiomeric excess
EDCI	*N*-(3-dimethylaminopropyl)-*N'*-ethyl-carbodiimid-hydrochlorid
e.g.	exempli gratia
EI	electron impact ionization (mass spectrometry)
equiv	equivalent(s)
ESI	electron spray ionization (mass spectrometry)
Et	ethyl
FDA	U. S. Food and Drug Administration
FGI	functional group interconversion
FTIR	Fourier-transform infrared spectroscopy
g	gram(s)
GM	*Ganoderma* meroterpenoid
h	hour(s)
HFIP	1,1,1,3,3,3-hexafluoro-2-propanol
HMPA	hexamethylphosphoramide
HPLC	high-performance liquid chromatography
HSQC	heteronuclear single quantum coherence
Hz	Hertz (frequency)
i	*iso* (isomer)
IBX	2-iodoxybenzoic acid
IC_{50}	half maximal inhibitory concentration
imH	imidazole
IPr	1,3-bis(2,6-diisopropylphenyl) imidazole-2-ylidene
IR	infrared

$Ir(dFppy)_3$	(tris[2-(2,4-difluorophenyl)pyridine]-iridium(III))
HMDS	hexamethyldisilazide
HVA	high voltage-activated
LDA	lithium *N*,*N*-diisopropylamide
L_n	ligand(s)
LVA	low voltage-activated
m	medium (IR spectroscopy)
m	multiplet (NMR spectroscopy)
m-CPBA	*meta*-chloroperbenzoic acid
Me	methyl
min	minute(s)
mL	milliliter
mmol	millimole
MOM	methoxymethyl
MS	mass spectrometry
Ms	methanesulfonyl
n	normal (unbranched isomer)
NBS	*N*-bromosuccinimide
NMO	*N*-methylmorpholine-*N*-oxide
NMR	nuclear magnetic resonance
NOESY	nuclear Overhauser effect correlation spectroscopy
Nu	nucleophile
o	*ortho* (isomer)
p	*para* (isomer)
PCC	pyridinium chlorochromate
PDC	pyridinium dichromate
Ph	phenyl
PIFA	[bis(trifluoroacetoxy)iodo]-benzene
pin	pinacol
PMB	*para*-methoxybenzyl
PMP	*para*-methoxyphenyl
ppm	parts per million
PPTS	pyridinium *para*-toluenesulfonate
p-TsOH	*para*-toluenesulfonic acid
py	pyridine
q	quartet (NMR spectroscopy)
R	undefined substituent
R_f	retardation factor
Rh_2esp_2	Bis[rhodium(α,α,α′,α′-tetramethyl-1,3-benzenedipropionic acid)]
s	strong (IR spectroscopy)
s	singlet (NMR spectroscopy)
SM	starting material
Sudan III	benzolazo-4-benzolazo-1-(2-naphthol)
T	temperature
t	triplet (NMR spectroscopy)
t	(*tert*-) tertiary (isomer)
TBAF	tetrabutylammonium fluoride
TBAI	tetrabutylammonium iodide
TBDPS	*tert*-butyldiphenylsilyl
TBHP	*tert*-butyl hydroperoxide
TBS	*tert*-butyldimethylsilyl
TC	thiophene-2-carboxylate
TMEDA	*N*,*N*,*N'*,*N'*-tetramethylethylenediamine
TMP	2,2,6,6-tetramethylpiperidine
Tf	trifluoromethanesulfonyl
TFAA	trifluoroacetic anhydride
TFA	trifluoroacetic acid
THF	tetrahydrofuran
TLC	thin layer chromatography
TMS	trimethylsilyl
tol	tolyl
Tr	trityl
Ts	*para*-toluenesulfonyl
w	weak (IR spectroscopy)

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THEORETICAL SECTION

1. Fungal Natural Products as a Source for new Drugs

The growth of the human population, which is estimated to reach 9.8 billion by 2050[1] and higher life expectancies pose great challenge to serve mankind with appropriate medical care. For the most time of human existence, plants, fungi and extracts thereof served the early human population as a source of medication. As the understanding of these complex extracts grew, predictive assumptions about their curative power became more precise, which culminated in the traditional Chinese medicine. Thanks to accurate chemical analyses of these extracts in the late 20th century, we know today that natural products are key active ingredients.[2] Besides plants as a vast natural resource for natural products, fungi have historically played a significant role for treatment of diseases.

The earliest record of medicinal use of fungi dates from around the year 800. Chinese cultivated the yeast *Monascus purpurea* in rice to give a pharmaceutically active medication which was used to treat cardiovascular problems.[3] A detailed chemical analysis of its composition revealed a mixture of organic compounds belonging to the class of statins (Figure 1).

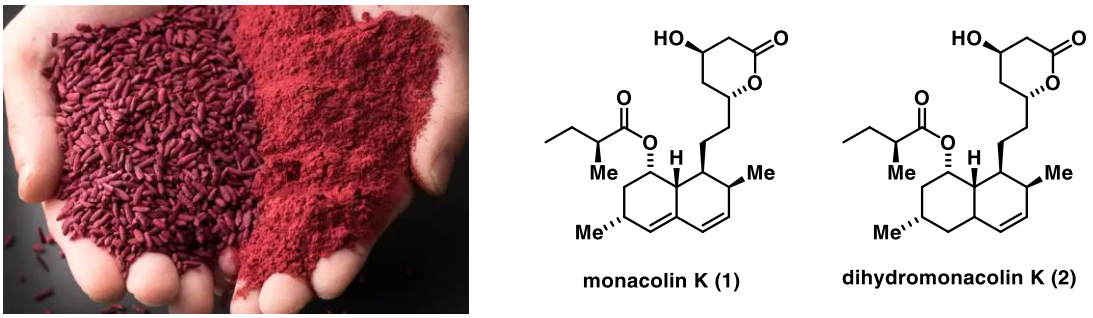


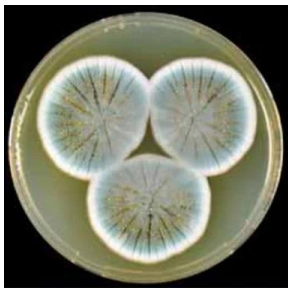
Figure 1: Red yeast rice[4] and selected statins isolated from it.

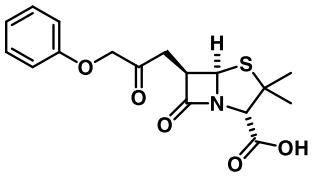
Clinical evaluation of red yeast rice approximately 1200 years later confirmed the early discovery of the traditional Chinese medicine by showing its ability to lower blood cholesterol levels.[5] Notably, the natural product monacolin K (**1**) is marketed as Mecavor® and approved by the FDA in 1987 in the United States to treat high blood cholesterol level and lower the risk of cardiovascular diseases.[6] Today,

[1] https://www.un.org/development/desa/en/news/population/world-population-prospects-2017.html accessed on 02.12.2020 at 16:51 o'clock.
[2] H. Müller, O. Brackhagen, R. Brunne, T. Henkel, F. Reichel, in *The Role of Natural Products in Drug Discovery* (Ed.: J. Mulzer, R. Bohlmann), Springer Berlin Heidelberg, Berlin, Heidelberg, **2000**, pp. 205-216.
[3] J. Ma, Y. Li, Q. Ye, J. Li, Y. Hua, D. Ju, D. Zhang, R. Cooper, M. Chang, *J. Agric. Food Chem.* **2000**, *48*, 5220–5225.
[4] https://www.bakerandflavoristkl.com/red-yeast-rice-malaysia/ accessed on 08.11.2020 at 17:10 o'clock.
[5] D. Heber, I. Yip, J. M. Ashley, D. A. Elashoff, R. M. Elashoff, V. L. W. Go, *Am. J. Clin. Nutr.* **1999**, *69*, 231–236.
[6] https://www.accessdata.fda.gov/drugsatfda_docs/label/2014/019643s088lbl.pdf accessed on 08.11.2020 at 18:16 o'clock.

the cholesterol lowering group of statins constitute the most successful medication measured by the number of prescriptions filled and revenues generated.[7]

In 1928 a landmark discovery has been achieved by the physician Alexander Fleming. He accidently observed a blue-green mold growing on a Petri dish with the bacterial culture *Staphylococcus aureus*.[8] This mold, later identified as *Penicillium notatum*, inhibited the growth of adjacent bacterial colonies. Edward Abraham and Ernst Chain were the first to propose the structure of penicillin in 1943 to contain a novel β-lactam which was later confirmed in 1945 using X-ray crystallography (Figure 2).[9] These findings led to the discovery of the first β-lactam antibiotics that were mainly active against Gram-positive bacteria. In the upcoming Second World War, penicillin played an important role in saving soldier's life by preventing the infection of wounds that oftentimes was more life threatening than the wound itself.[10]





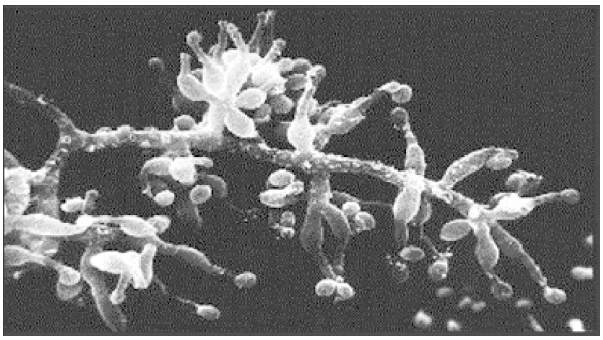
penicillin V (3)

Figure 2: *Penicillium notatum* on a Petri dish[11] and penicillin V (**3**), the first member of the penicillin family to be discovered.

Since Fleming's discovery, a lot of effort has been devoted to identify novel drug leads from microfungi. Even nowadays, penicillin remains a blockbuster drug. However, emerging cases of bacterial resistances towards existing antibiotics call for an awareness for antibiotic research.

With the discovery of the cyclic peptide cyclosporine (**4**) in 1971 a revolution in immunopharmacology was initiated. Cyclosporine (**4**) was isolated from the fungus *Tolypocladium inflatum* found in a soil sample by Sandoz scientists (figure 3).[12] Researchers found the remarkable immunologic properties of cyclosporine (**4**) which made it an important candidate for immunosuppression during solid organ transplants.

[7] J. P. A. Ioannidis, *JAMA* **2014**, *311*.
[8] A. Fleming, *Br. J. Exp. Pathol.* **1929**, *10*, 226–236.
[9] E. Abraham, *BioEssays* **1990**, *12*, 601–606.
[10] R. Quinn, *Am. J. Public Health* **2013**, *103*, 426–434.
[11] https://upload.wikimedia.org/wikipedia/commons/6/62/Penicillium_rubens_%28Fleming%27s_strain%29.png accessed on 08.11.2020 at 19:23 o'clock.
[12] J. F. Borel, C. Feurer, C. Magnée, H. Stähelin, *Immunology* **1977**, *32*, 1017–1025.



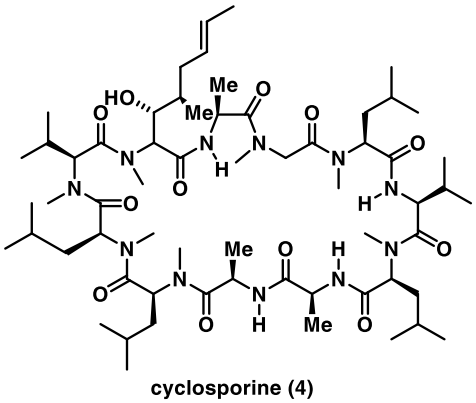


Figure 3: The fungus *Tolypocladium inflatum*[13] and the immunosuppressant cyclic peptide cyclosporine (**4**).

The mode of action of cyclosporine lies in decreasing T-cell functioning which are a type of lymphocyte that play a crucial role in the immune response.

Despite tremendous efforts in isolating novel active pharmaceutical ingredients from fungi, yet unexplored species have the potential to provide the next blockbuster drug which is particularly important facing the rising cases of unknown upcoming diseases.

[13] G. Pasero, M. Piero, *Reumatismo* **2012**, *64*, 44–54.

2. Importance of Voltage-gated Ca^{2+} Channels in Neuropathy

2.1. Overview of Voltage-gated Ca^{2+} Channels

Calcium ions are critical for cellular functioning due to their ability to induce changes in membrane potential as well as their function as ubiquitous intracellular second messengers.[14] Normally, intracellular calcium ion concentration is maintained at a low level (100 nM) through regulatory mechanisms such as Ca^{2+}-selective binding proteins, plasma membrane calcium exchanger pumps and intracellular organelles (including the endoplasmic reticulum and the mitochondria).[15] However, cytoplasmic concentration of calcium may rise transiently by virtue of calcium release from intracellular calcium stores and / or extracellular influx of Ca^{2+} through open ligand-gated and voltage-gated calcium channels facilitated by the 20,000-fold gradient of Ca^{2+} between the extracellular space and the cytoplasm.[16]

Voltage-gated calcium channels are membrane proteins that are key mediators of calcium entry into the cell. They activate upon membrane depolarization in response to action potentials. Once activated, they open and mediate influx of calcium ions along its electrochemical gradient. These channels are heteromultimers comprising of the pore forming α_1 subunit which assembles with the α_2, β, γ and δ subunits to form a functional calcium channel protein (Figure 4).[17] The subsequent increase in free intracellular calcium is linked to various physiological responses, including muscle contraction,[18] secretion of hormones and neurotransmitters,[19] enzyme activity and activation of gene transcription.[20, 21]

Historically, based on their voltage dependent activation, calcium channels are classified into high voltage-activated (HVA) and low voltage-activated (LVA) channels, with the latter being activated at low membrane depolarizations compared to HVA channels. These channels are further subdivided with respect to their pharmacological and biophysical properties into L("long-lasting")-, P/Q("Purkinje")-, N("neuronal", "non-L")-, and R("residual")-types which form the HVA channels and into a T("tiny")-type channel which forms the LVA channels.[22]

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[14] G. W. Zamponi, *Nat. Rev. Drug Discovery* **2016**, *15*, 19–34.
[15] M. Brini, E. Carafoli, *Cell. Mol. Life Sci.* **2000**, *57*, 354–370.
[16] G. M. Joseph, *CNS Neurol. Disord. Drug Targets* **2006**, *5*, 587–603.
[17] M. Iftinca, *J. Med. Life* **2011**, *4*, 126–138.
[18] T. Tanabe, K. G. Beam, B. A. Adams, T. Niidome, S. Numa, *Nature* **1990**, *346*, 567–569.
[19] D. Wheeler, A. Randall, R. Tsien, *Science* **1994**, *264*, 107–111.
[20] D. G. Wheeler, R. D. Groth, H. Ma, C. F. Barrett, S. F. Owen, P. Safa, R. W. Tsien, *Cell* **2012**, *149*, 1112–1124.
[21] D. E. Clapham, *Cell* **2007**, *131*, 1047–1058.
[22] B. P. Bean, *Annu. Rev. Physiol.* **1989**, *51*, 367–384.

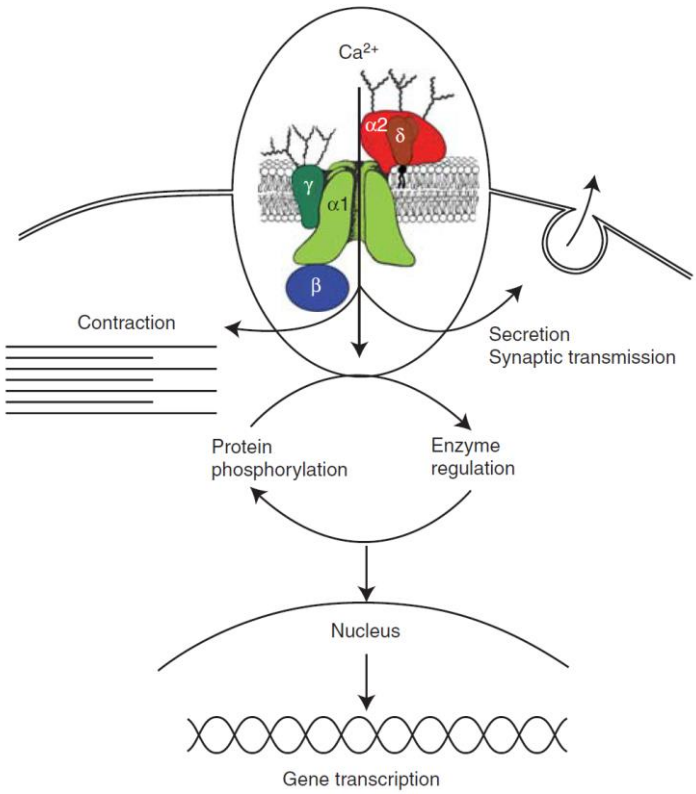


Figure 4: Structure of voltage-gated calcium channels and cellular events activated by free intracellular calcium.[23]

The pore forming α_1 subunit attracts special interest, since it forms the gateway for Ca^{2+} influx and poses a prominent site for drug interaction. Structurally, the α_1 subunit is an amino acid sequence organized in a repetitive array of six transmembrane helices forming in total four hydrophobic domains I-IV (Figure 5). The fourth helix in each domain contains positively-charged amino acid residues at physiologic pH (highlighted in yellow) which forms a voltage sensor that reacts in response to membrane depolarization. In addition, between the fifth and sixth helix a hydrophobic pore loop (highlighted in green) composes the permeation pathway of calcium ions and the selectivity filter, that blocks other ions from entering.[24]

[23] W. A. Catterall, *Cold Spring Harb. Perspect. Biol.* **2011**, *3*, a003947.
[24] T. P. Snutch, J. Peloquin, E. Mathews, J. E. McRory, in *Voltage-Gated Calcium Channels*, Springer US, Boston, MA, **2005**, pp. 61–94.

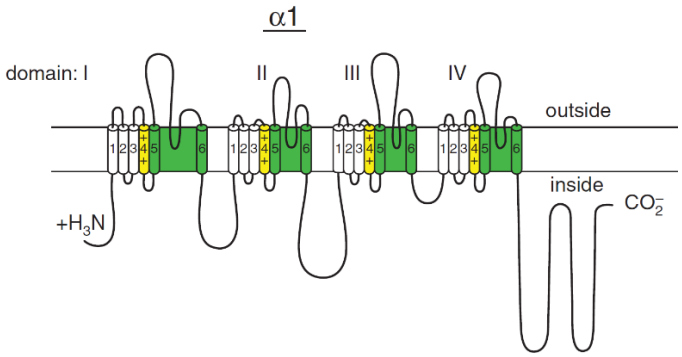


Figure 5: Pore-forming α_1 subunit structure.[23]

It becomes evident, that disturbances in this highly regulated and orchestrated interplay between membrane potential and intracellular calcium concentrations can have detrimental effects on neuronal signaling. In fact, calcium channel dysregulations are linked to various central nervous system disorders such as Alzheimer's disease,[25] Parkinson's disease and epilepsy.[26] Thus, treatments based on reactions at calcium channels provide a wide range of different curing possibilities, especially for neural diseases.

2.2. T-type Ca^{2+} Channels in Central Nervous System Disorders and Pharmacology

T-type calcium channels are broadly expressed in the central nervous system and are linked to various central nervous system disorders. Potential treatments of these disorders were already found in the past, however, investigations towards novel T-type calcium channel inhibitors are still ongoing and object of ongoing research. Challenges for the discovery of novel drugs are well established and enclose 1) high affinity to the target, 2) high selectivity, 3) metabolic stability, 4) non-toxicity and 5) effective crossing of the blood-brain barrier. However, designing an appropriate drug candidate for voltage-gated calcium challenge poses an additional challenge: To avoid side effects, one has to overcome the high sequence conservation among different calcium channel subtypes in addition to substantial similarities to other members of voltage-gated ion channels (such as voltage-gated sodium and potassium channels).[14]

The thalamus is a centrally-located part of the human brain. It is also known as "the gate to consciousness" as is relays incoming neuronal information to the cerebral cortex (outer layer of the brain) where the information is processed. Voltage-gated T-type channels are abundantly expressed in this part of the central nervous system. Animal models of absence epilepsy show increased T-type channel activity in thalamic neurons.[27] Epilepsy is a central nervous system disorder characterized by recurrent uncontrollable epileptic seizures resulting from neuronal hyperactivity in combination with asynchrony of neurons. In patients with childhood absence epilepsy and idiopathic epilepsy, mutations

[25] M. W. Bondi, E. C. Edmonds, D. P. Salmon, *J. Int. Neuropsychol. Soc.* **2017**, *23*, 818–831.
[26] Brett A. Simms, Gerald W. Zamponi, *Neuron* **2014**, *82*, 24–45.
[27] K.-H. Choi, *Expert Opin. Drug Discov.* **2013**, *8*, 919–931.

of voltage-gated T-type calcium channels were found.[28,29] These mutant T-type channels increase the surface expression in the thalamus causing hyperactivity in neurons.[30] Enhanced thalamic T-type calcium channel expression as well as hyperactivity increase the probability for seizures and could lead to epilepsy.

A selective inhibition of thalamic neuronal activity by T-type calcium channel inhibition has proven to be a successful treatment of epilepsy. Ethosuximide (**5**, marketed as Zarontin® by Pfizer, Figure 6) is a drug for generalized absence epilepsy treatment which acts by inhibition of T-type calcium channels, especially T-type currents are inhibited in the thalamus.[31] Together with other antiepileptic drugs such as methsuximide (**6**, marketed as Celontin® by Pfizer), the pyrimidinamine sipatrigine (**7**), the pyridylamide TTA-A2 (**8**) and the piperidine Z944 (**9**), ethosuximide selectively inhibits T-type channels other HVA calcium channels in the thalamus.

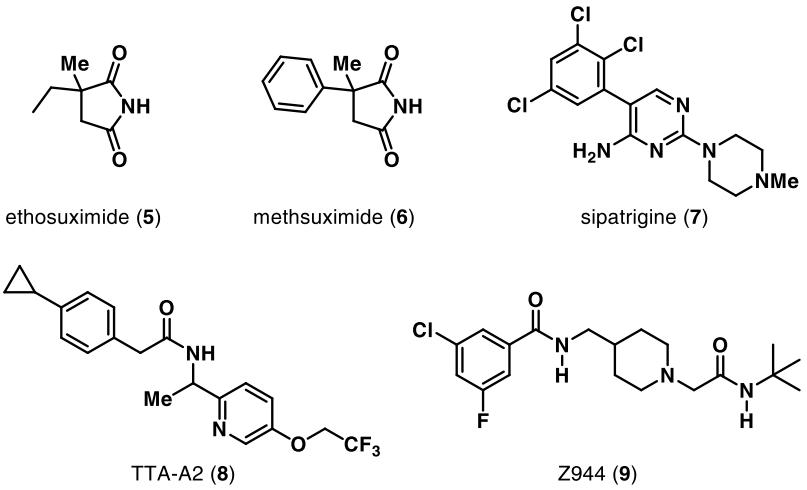


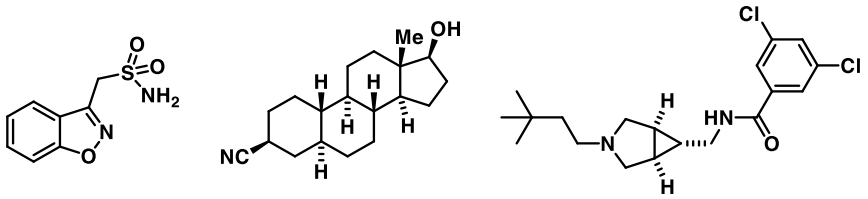
Figure 6: Ethosuximide (**5**), methsuximide (**6**), sipatrigine (**7**), TTA-A2 (**8**) and Z944 (**9**) constitute selective T-type calcium channel inhibitors for the treatment of epilepsy.

Besides the thalamus, T-type calcium channels are also highly expressed in the inferior olive, a structure found in the brainstem. Characteristic repetitive neuronal bursting and hyperactivity mediated by T-type calcium channels in the thalamus and the inferior olive, are related to tremor-related neuronal activities.[32] Parkinson's disease, the most common neurodegenerative disorder, is characterized by involuntary movements and reduction of motor skills, leading to tremor. Knockout mice lacking T-type

[28] Y. Chen, J. Lu, H. Pan, Y. Zhang, H. Wu, K. Xu, X. Liu, Y. Jiang, X. Bao, Z. Yao, K. Ding, W. H. Y. Lo, B. Qiang, P. Chan, Y. Shen, X. Wu, *Ann. Neurol.* **2003**, *54*, 239–243.
[29] S. E. Heron, H. Khosravani, D. Varela, C. Bladen, T. C. Williams, M. R. Newman, I. E. Scheffer, S. F. Berkovic, J. C. Mulley, G. W. Zamponi, *Ann. Neurol.* **2007**, *62*, 560–568.
[30] I. Vitko, I. Bidaud, J. M. Arias, A. Mezghrani, P. Lory, E. Perez-Reyes, *J. Neurosci.* **2007**, *27*, 322–330.
[31] V. Crunelli, N. Leresche, *Epilepsy Curr.* **2002**, *2*, 53–56.
[32] H. Miwa, T. Kondo, *Cerebellum (London, England)* **2011**, *10*, 563–569.

channels in the inferior olive did not exhibit harmaline-induced (harmaline is a tremor inducing drug) tremor, indicating the connection of Parkinson's disease to voltage-gated T-type calcium channels.[33]

T-type calcium channel inhibitors that readily pass the blood-brain barrier have proven to effectively reduce tremor in various models and possibly could become valid drugs for the treatment of Parkinson's disease.[34] These include ethosuximide (**6**, Figure 6), zonisamide (**10**, already used to treat symptoms of epilepsy and Parkinson's disease, marketed as Zonegran®, Figure 7), the steroid (+)-ECN (**11**) and the benzamide ML218 (**12**).



zonisamide (**10**) (+)-ECN (**11**) ML218 (**12**)

Figure 7: T-type calcium channel inhibitors that exhibit anti-tremor efficacy to possibly treat Parkinson's disease.

[33] Y.-G. Park, H.-Y. Park, C. J. Lee, S. Choi, S. Jo, H. Choi, Y.-H. Kim, H.-S. Shin, R. R. Llinas, D. Kim, *Proc. Natl. Acad. Sci. U.S.A.* **2010**, *107*, 10731–10736.
[34] H. Miwa, J. Koh, Y. Kajimoto, T. Kondo, *Pharmacol. Biochem. Behav.* **2011**, *97*, 656–659.

3. Ganoderma Meroterpenoids

3.1. Overview and Introduction

Ganoderma meroterpenoids (GMs) are a hybrid natural product class consisting of a 1,2,4-trisubstituted benzene ring connected to a polyunsaturated side chain.[35] Ganomycin A (**13**) (Figure 8) was the first member of the *Ganoderma* natural product family to be isolated in the year 2000.[36] Since then, more than 100 members of this natural product class were isolated. The most recent member ganodermaone A was isolated in July 2020[37] (four months before the preparation of this manuscript) emphasizing the current relevance of these natural products and ongoing efforts in isolating novel congeners of this interesting molecules.

Ganoderma meroterpenoids can be classified into three groups regarding their structural composition and biosynthetic origin: linear, polycyclic and dimeric GMs. Linear GMs contain a 1,2,4-trisubstituted phenyl residue bound to either a C10 or C15 terpenoid chain. Oxidations can easily occur on the allylic positions to give alcohols, aldehydes or carboxylic acids which in turn can cyclize to form ethers or lactones as seen in the structure of lucidulactone B (**14**). When the cyclization occurs forming carbon-carbon bonds along the polyunsaturated chain (presumably occurring by cationic or radical pathways under the influence of acid, light or heating) polycyclic GMs are generated. Compared to linear GMs this process builds higher complexity resulting in natural products such as cochlearol B (**15**), genodermaone A (**16**), applanatumol B (**17**) and applanatumol E (**18**). In contrast to these intramolecular reactions, dimeric GMs arise from an intramolecular cyclization. In the case of ganoapplanin (**19**), it is hypothesized that applanatumol E (**18**) reacted with 2,4-dihydroxy benzoic acid[38] and applanatumin A (**20**) arose from a heterodimerization through a Diels–Alder reaction.[39] Additionally, dimeric GMs often possess unprecedented structural motifs making them invaluable candidates for bioassays and attractive targets for total synthesis. In this respect, ganoapplanin (**19**) contains a highly decorated core dioxaspirocycle. Applanatumin A (**20**) is featuring a spirobenzofuran-cyclopentane motif embedded in a new hexacyclic skeleton.

[35] X. Peng, M. Qiu, *Nat. Prod. Bioprospect.* **2018**, *8*, 137–149.
[36] R. A. A. Mothana, R. Jansen, W.-D. Jülich, U. Lindequist, *J. Nat. Prod.* **2000**, *63*, 416–418.
[37] J.-J. Zhang, F.-Y. Qin, X.-H. Meng, Y.-M. Yan, Y.-X. Cheng, *Bioorg. Chem.* **2020**, *100*, 103930.
[38] L. Li, H. Li, X.-R. Peng, B. Hou, M.-Y. Yu, J.-R. Dong, X.-N. Li, L. Zhou, J. Yang, M.-H. Qiu, *Org. Lett.* **2016**, *18*, 6078–6081.
[39] Q. Luo, L. Di, W.-F. Dai, Q. Lu, Y.-M. Yan, Z.-L. Yang, R.-T. Li, Y.-X. Cheng, *Org. Lett.* **2015**, *17*, 1110–1113.

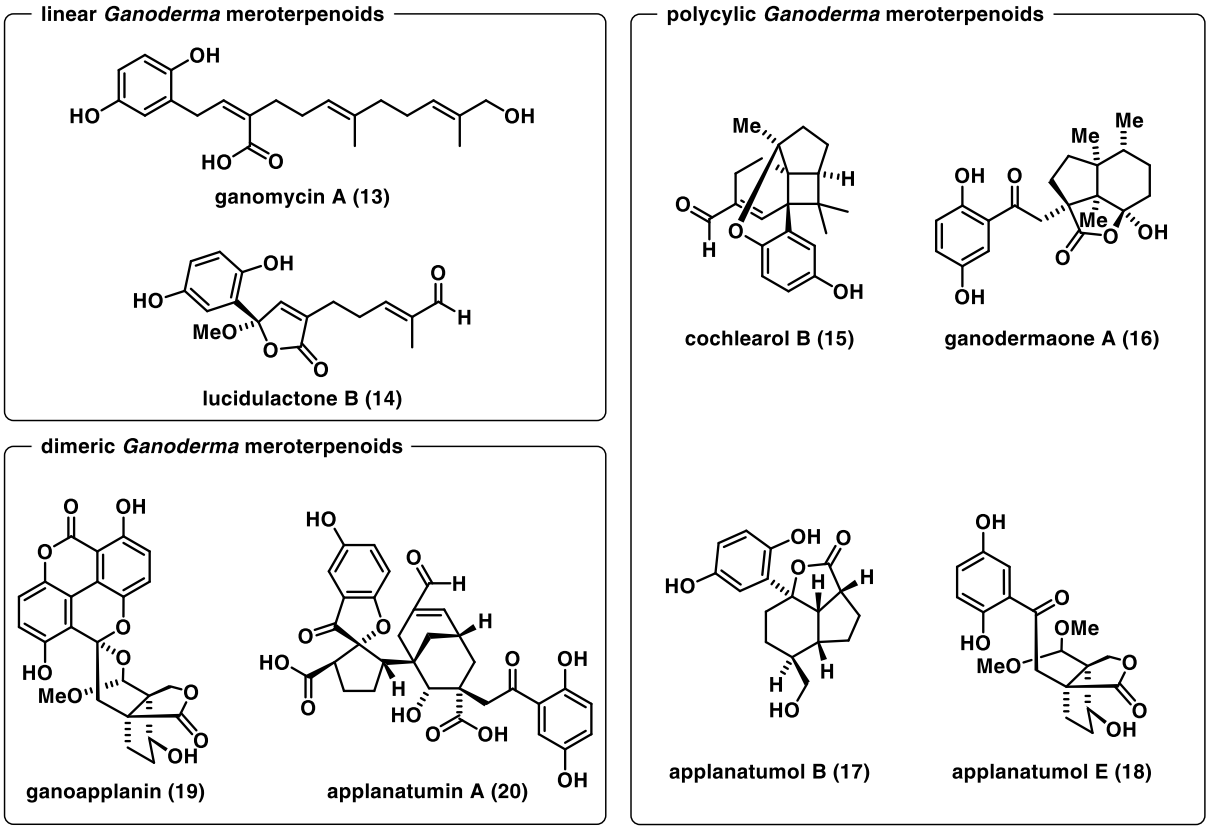


Figure 8: Different classes of Ganoderma meroterpenoids: linear, polycyclic or dimeric.

3.2. Isolation and Biological Activity of *Ganoderma Meroterpenoids*

Ganoderma is a wood decay fungus usually growing on trees having a cosmopolitan distribution. In Japan, South Korea and in the traditional Chinese medicine this fungus is medicinally highly valued. From the *Ganoderma* genus more than 78 species are known in traditional folk medicines and the species *Ganoderma lucidum* and *Ganoderma sinense* are even recorded in the Chinese Pharmacopoeia, a Chinese handbook of drugs covering traditional Chinese and western medicine.[35]

The secondary metabolites from the *Ganoderma* fungus cover the classes of polysaccharides, terpenoids, steroids and fatty acids of which polysaccharides were found to be the main bioactive component. However, their structural complexity and molecular weight hindered the general use of polysaccharides in drugs. Thus, a lot of effort has been devoted to isolate and identify bioactive aromatic meroterpenoids from *Ganoderma* species which were found to exhibit e.g., antioxidant,[40] antifibrotic[41] and antimicrobial bioactivity.[36]

[40] X. Peng, J. Liu, C. Wang, Z. Han, Y. Shu, X. Li, L. Zhou, M. Qiu, *Food Chem.* **2015**, *171*, 251–257.
[41] S. Z. Huang, B. H. Cheng, Q. Y. Ma, Q. Wang, F. D. Kong, H. F. Dai, S. Q. Qiu, P. Y. Zheng, Z. Q. Liu, Y.-X. Zhao, *RSC Advances* **2016**, *6*, 21139–21147.

The polycyclic meroterpenoid ganoapplanin (**19**) was isolated in 2016 by Li and co-workers from *Ganoderma applanatum* (Figure 9).[38] The natural product was obtained in racemic form as a white solid that was suitable for structure validation by X-ray crystallography.

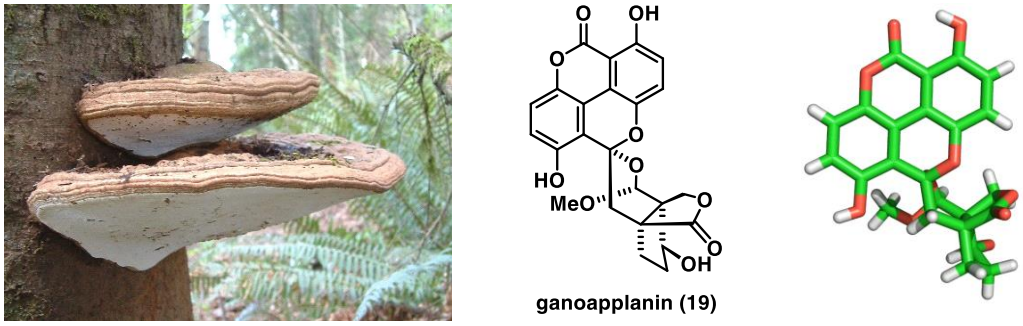


Figure 9: The fungus *Ganoderma applanatum*[42] and the natural product ganoapplanin together with its crystal structure.

Since the extracts from *G. applanatum* are well known in traditional Chinese medicine as an adjuvant in central nervous system diseases,[43] ganoapplanin (**19**) was tested for its neuroprotective properties. In general, voltage-gated calcium channels play an important role in neural disorders and especially the T-type calcium channels are widely expressed in the central part of the brain. Abnormally high activity of these T-type voltage-gated calcium channels can cause disorders such as epilepsy or Parkinson's disease. In this respect, effects of ganoapplanin (**19**) on T-type calcium channels were investigated and indeed, Li found a selective inhibition of these channels with a inhibitory concentration of IC_{50} = 36.6 µM for the racemic sample.[38]

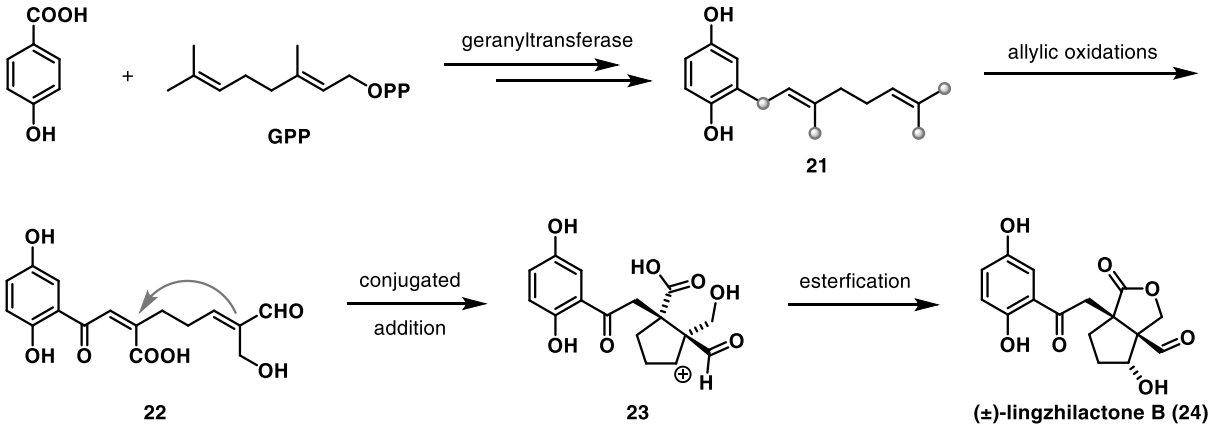
3.3. Proposed Biosynthesis of Ganoapplanin

Considering the biosynthesis of *Ganoderma* meroterpenoids, their complex structure can be broken down to an aromatic moiety and a terpenoid part. Mechanisms like the prenylation of aromatic compounds are often found in nature that increase the molecular complexity and bioactivity of natural products. An analysis of the genome of the species *Ganoderma lucidum* revealed carbohydrate-active and ligninolytic enzymes that are active in wood degradation.[44] It is thus hypothesized, that this degradation delivers the starting materials for the fungus to synthesize the aromatic moiety through a shikimic acid pathway and the terpenoid residue through a mevalonate pathway which are subsequently assembled by prenyltransferase.

The biosynthesis of the dimeric GM ganoapplanin (**19**) goes through the intermediate of the natural product lingzhilactone B (**24**, Scheme 1). 4-Hydroxybenzoic acid is attached to the monoterpene geranyl diphosphate (GPP) via geranyltransferase and the so-formed intermediate **21** is oxidized at the

[42] http://www.scmsfungi.org/fungi/ganoderma_applanatum.htm accessed on 13.11.2020 at 08:21 o'clock.
[43] R. R. M. Paterson, *Phytochemistry* **2006**, *67*, 1985–2001.
[44] D. Liu, J. Gong, W. Dai, X. Kang, Z. Huang, H.-M. Zhang, W. Liu, L. Liu, J. Ma, Z. Xia, Y. Chen, Y. Chen, D. Wang, P. Ni, A.-Y. Guo, X. Xiong, *PLoS One* **2012**, *7*, e36146.

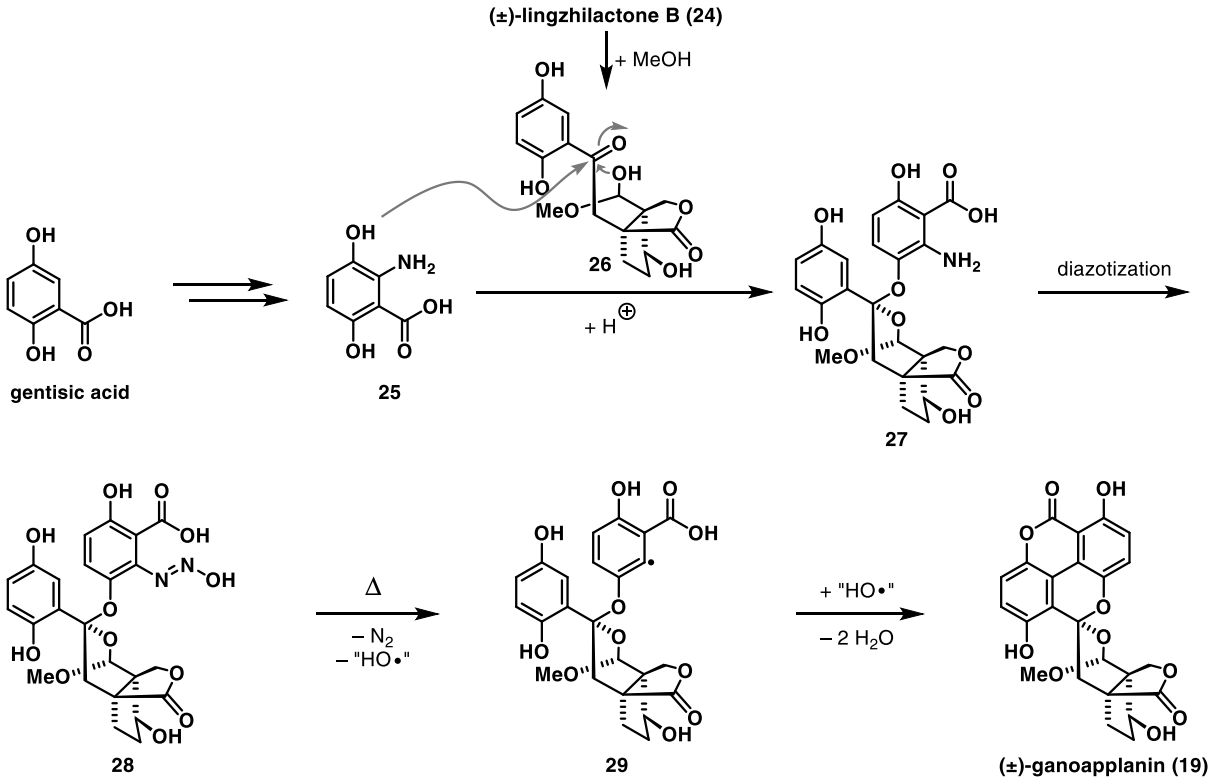
highlighted allylic positions to give the linear cyclization precursor **22**.[45] A conjugated addition gives the cyclopentane ring of **23** which was further reacted in an esterification to the bicyclic lactone moiety of lingzhilactone B (**24**).



Scheme 1: Proposed biosynthesis of lingzhilactone B (**24**).

In a second phase of the ganoapplanin biosynthesis, gentisic acid is reacted to anthranilic acid **25** (Scheme 2). Methanol addition to lingzhilactone B forms the hemiacetal group **26**. An acid catalyzed cyclization reaction of anthranilic acid **25** with intermediate **26** gives the tetrahydropyran moiety **27** of ganoapplanin (**19**). A diazotization of the aniline followed by a Gomberg–Bachmann radical cyclization[46,47] and lactonization forms the tetracyclic northern hemisphere together with the core dioxaspirocyclic skeleton of the natural product ganoapplanin (**19**), which is synthesized by the fungus in racemic form.

[45] Q. Luo, L. Tian, L. Di, Y.-M. Yan, X.-Y. Wei, X.-F. Wang, Y.-X. Cheng, *Org. Lett.* **2015**, *17*, 1565–1568.
[46] M. Gomberg, W. E. Bachmann, *J. Am. Chem. Soc.* **1924**, *46*, 2339–2343.
[47] C. Rüchardt, E. Merz, *Tetrahedron Lett.* **1964**, *5*, 2431–2436.



Scheme 2: Proposed biosynthesis of ganoapplanin.

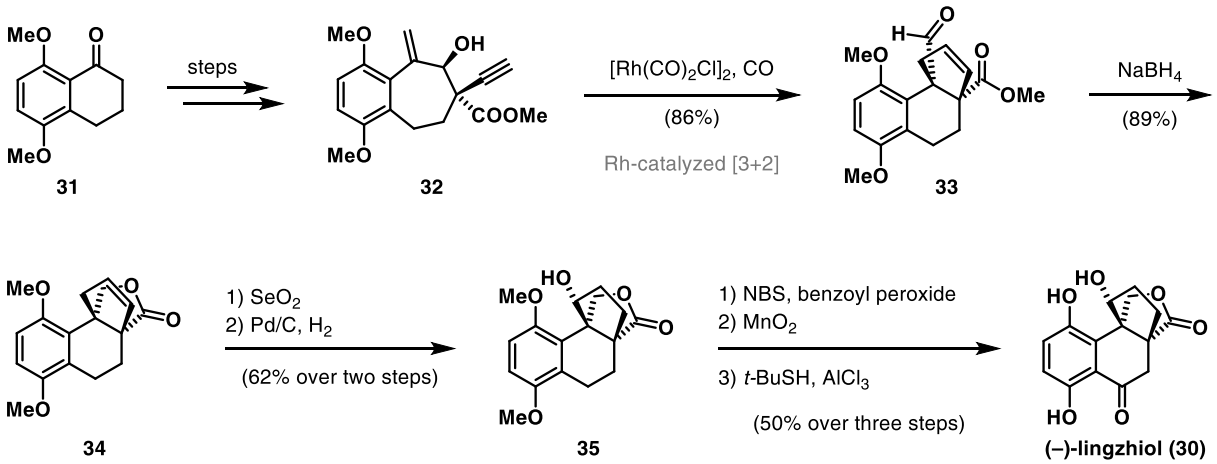
3.4. Previous Syntheses of *Ganoderma* Meroterpenoids

The manifold structures of *Ganoderma* meroterpenoids in combination with their relevant bioactivity for the human body have attracted the attention of synthetic chemists culminating in various total syntheses of GMs. Herein, we would like to summarize the key strategies and reactions towards selected members of this natural product class.

The first total synthesis of lingzhiol (**30**) was achieved by the group of Yang (Scheme 3) in 2014.[48] The methodology-based access to the natural product was furnished by a [3+2] cycloaddition between an enal and an alleno rhodium species to give the GM in an asymmetric fashion. Starting from commercially available tetralone **31** Yang and co-workers synthesized the key-step precursor **32** asymmetrically in a few steps. By employing the $[Rh(CO)_2Cl]$ catalyst and an atmosphere of carbon monoxide they initiated a skeletal rearrangement yielding the hydrindane structure of **33** (86%, vide infra for the mechanism). A subsequent reduction of aldehyde **33** with sodium borohydride also formed the propellane structure of **34** (89%). The secondary alcohol was installed through an allylic oxidation with selenium dioxide followed by reduction of the double bond under classical hydrogenation conditions (H_2, Pd/C) giving the late-stage intermediate **35** in 62% over two steps. The benzylic ketone was synthesized through a benzylic oxidation involving the reaction with NBS and benzoyl peroxide followed by a subsequent oxidation with manganese dioxide. *Tert*-butyl thiol in combination with

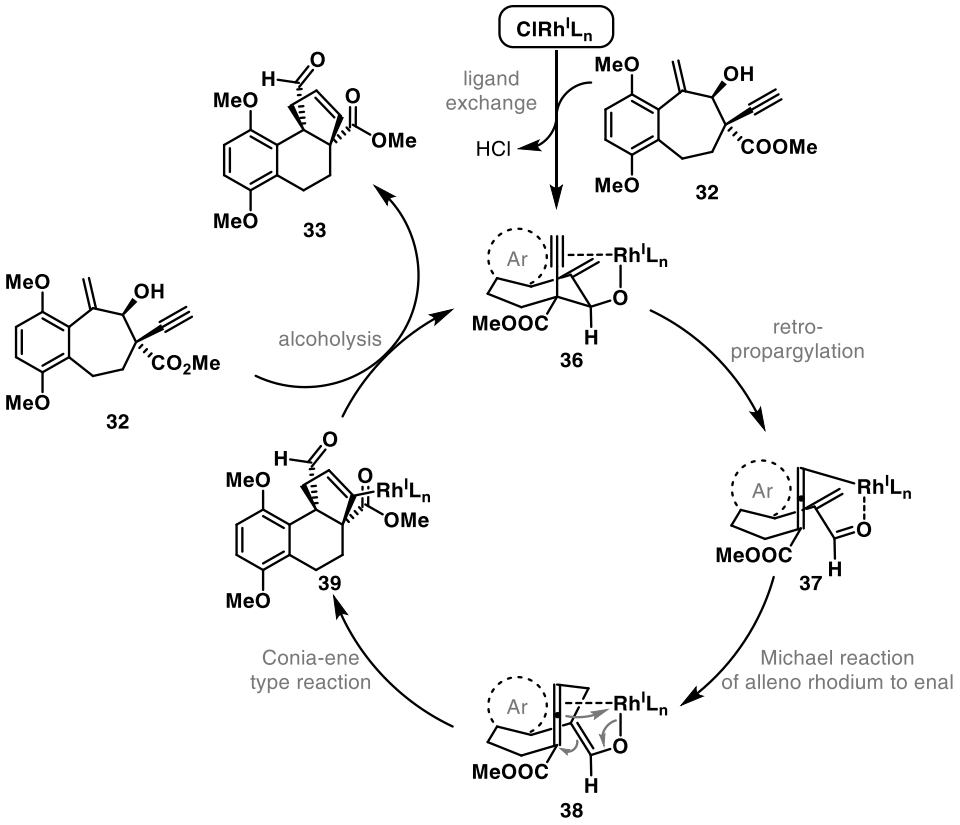
[48] R. Long, J. Huang, W. Shao, S. Liu, Y. Lan, J. Gong, Z. Yang, *Nat. Commun.* **2014**, *5*, 5707.

aluminum trichloride removed the methyl protecting groups of the hydroquinone moiety to furnish (–)-lingzhiol (**30**) in 50% over three steps.



Scheme 3: Asymmetric total synthesis of lingzhiol (**30**) by Yang.

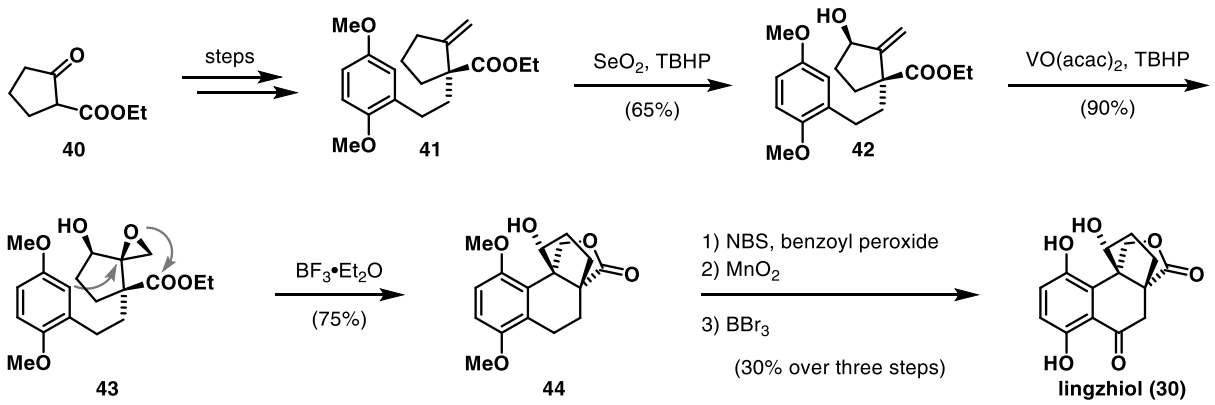
The complexity of the key [3+2] cycloaddition deserves special attention. Mechanistically, the authors propose an initial ligand exchange of the $[Rh(CO)_2Cl]$ complex with the alcohol **32** to give an oxygen bound rhodium complex **36** (Scheme 4). A retro-propargylation breaks a C–C bond forming an alleno rhodium species and an enal **37** that react in a subsequent step via a Michael reaction to afford complex **38**. The next step is regarded as a Conia-ene type reaction between the rhodium enolate and the allene to give complex **39** which reacts to the product through an alcoholysis with the starting material recycling the initial intermediate **36**.



Scheme 4: Proposed mechanism of the formal rhodium catalyzed [3+2] cycloaddition.

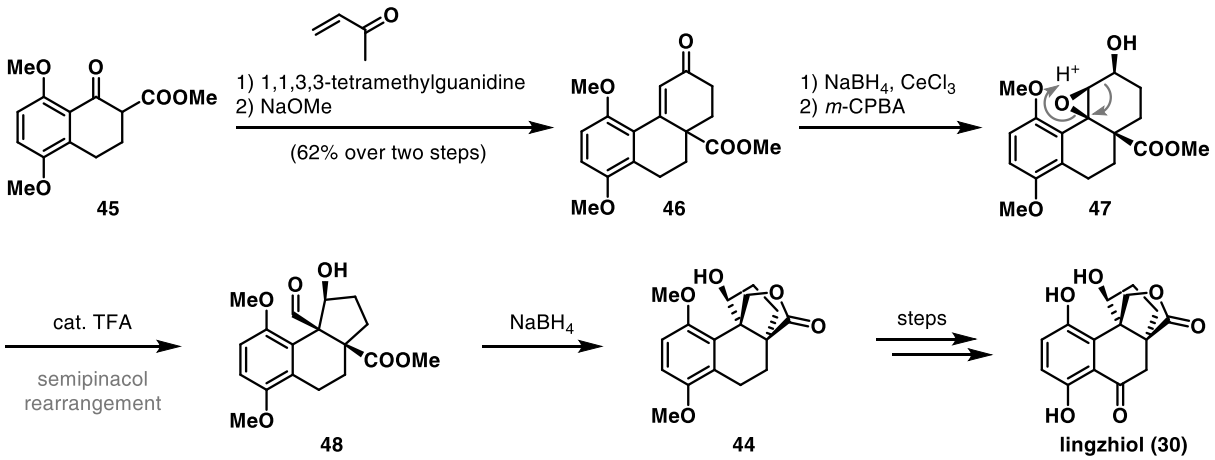
In 2015 the group of Qin realized a racemic synthesis of lingzhiol (**30**) in eight steps based on an epoxy-arene cyclization (Scheme 5).[49] Ethyl 2-oxocyclopentanecarboxylate **40** was converted in three steps to *exo*-methylene **41** which was reacted to allylic alcohol **42** by treatment with catalytic amounts of selenium dioxide and excess of the terminal oxidant TBHP (65%). The diastereoselectivity is attributed to a coordinating effect of the ester moiety. An alcohol directed epoxidation of the double bond with $VO(acac)_2$ and TBHP set the stage for the key epoxy-arene cyclization (90%). Upon treatment of **43** with BF_3•OEt_2, a Lewis acid mediated opening of the epoxide followed by a Friedel–Crafts reaction and lactonization furnished the 5/5/6/6 skeleton **44** of the natural product in one step (75%). In analogy to the synthesis by Yang, the benzylic oxidation was carried out in two steps (NBS, benzoyl peroxide and then MnO_2) followed by demethylation with BBr_3 to yield lingzhiol (**30**) in 30% over three steps.

[49] D. Chen, H.-M. Liu, M.-M. Li, Y.-M. Yan, W.-D. Xu, X.-N. Li, Y.-X. Cheng, H.-B. Qin, *Chem. Commun.* **2015**, *51*, 14594-14596.



Scheme 5: Total synthesis of lingzhiol (**30**) by Qin.

Based on the proposed biosynthesis of lingzhiol (**30**), Birman and co-workers have synthesized the natural product in a concise manner featuring a biogenetically inspired Brønsted acid catalyzed semipinacol rearrangement to install the core hydrindane scaffold (Scheme 6).[50] Known ketoester **45** was converted in a two-step Robinson annulation with methyl vinyl ketone to enone **46** (62% over two steps). The ketone was further reduced with good diastereoselectivity in a Luche reduction ($NaBH_4$ and $CeCl_3$). With *m*-CPBA a hydroxyl directed epoxidation was carried out to afford **47**. Employing catalytic amounts of trifluoroacetic acid initiated a semipinacol rearrangement to aldehyde **48**. Interestingly, this transformation was also oberserved in the presence of residual amounts of acids found in the epoxidation step with *m*-CPBA or when deuterated chloroform was used. A reduction of aldehyde **48** with $NaBH_4$ led to known intermediate **44** which concluded the formal synthesis. Similar approaches for the synthesis of lingzhiol (**30**) have been also undertaken by the group of Xie,[51] Schindler[52] and Qin.[53]

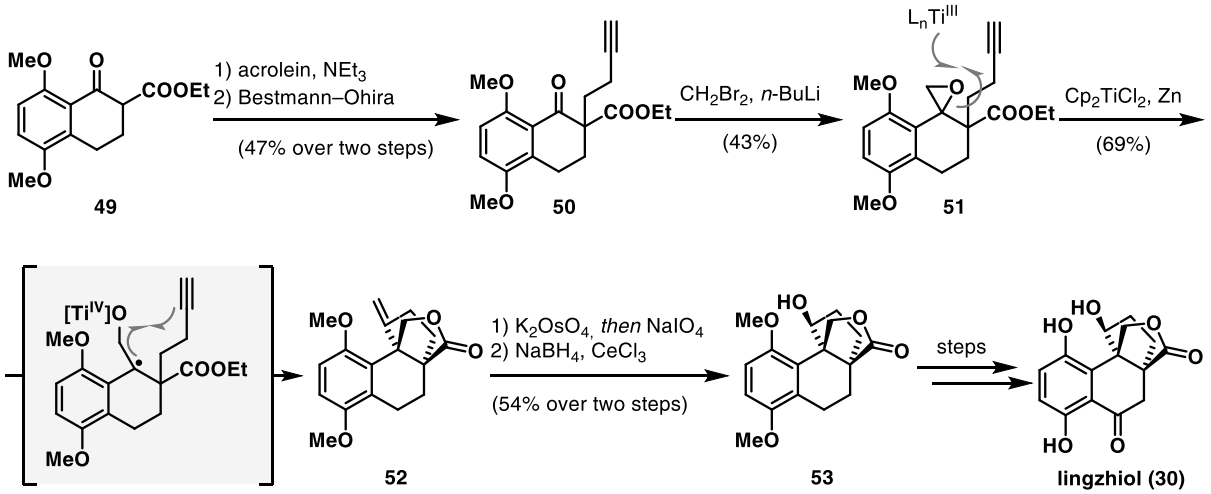


Scheme 6: Total synthesis of lingzhiol (**30**) by Birman.

A novel approach to lingzhiol (**30**) was presented by Maier applying a radical cyclization of a benzyl radical with a triple bond to install the tetralone structure (Scheme 7).[54] The starting material **50** for this

[50] K. Sharmah Gautam, V. B. Birman, *Org. Lett.* **2016**, *18*, 1499–1501.
[51] X. Li, X. Liu, X. Jiao, H. Yang, Y. Yao, P. Xie, *Org. Lett.* **2016**, *18*, 1944–1946.
[52] P. S. Riehl, A. D. Richardson, T. Sakamoto, C. S. Schindler, *Org. Lett.* **2020**, *22*, 290–294.
[53] D.-W. Zhang, H.-L. Fan, W. Zhang, C.-J. Li, S. Luo, H.-B. Qin, *Chem. Commun.* **2020**, *56*, 10066–10069.
[54] L.-M. Mehl, M. E. Maier, *J. Org. Chem.* **2017**, *82*, 9844–9850.

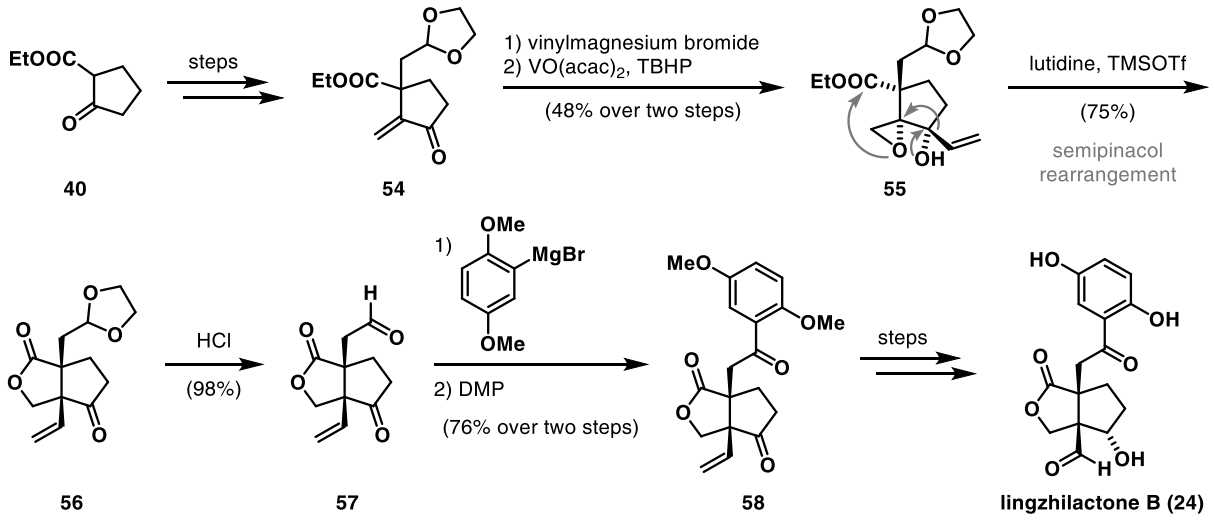
transformation was prepared in three steps from tetralone **49**. To this end, alkyne **50** was synthesized through a Michael reaction of β-ketoester **49** with acrolein followed by a Bestmann–Ohira reaction (47% over two steps). Dibromomethane and *n*-BuLi subsequently installed the epoxide **51** (43%). By employing titanocene and zinc, a radical opening of the epoxide with an in situ formed L_nTi^{III} species was initiated. The so-formed benzylic radical then undergoes a 5-*exo*-dig cyclization with the alkyne to furnish the carbon skeleton **52** of lingzhiol in 69% yield. The secondary *endo*-alcohol **53** was installed through a dihydroxylation / diol cleavage procedure that followed a reduction with $NaBH_4$ and $CeCl_3$ (54% over two steps) completing the formal synthesis of lingzhiol (**30**).



Scheme 7: Total synthesis of lingzhiol (**30**) by Maier.

Besides lingzhiol (**30**), lingzhilactone B (**24**) has also attracted the attention of the synthetic community. The first total synthesis was reported in 2016 by the group of Qin yielding the racemic natural product in 13 steps.[55] Ethyl 2-oxo cyclopentanecarboxylate (**40**) was first converted in three steps to ketone **54**. Qin performed a vinyl Grignard addition to the ketone followed by a hydroxyl directed epoxidation of the double bond with $VO(acac)_2$ and TBHP (48% over two steps). By subjecting the Lewis acid TMSOTf to epoxide **55**, a semipinacol rearrangement was initiated forging the bicyclic lactone **56** with the vicinal quaternary stereocenters (75%). Under acidic conditions, the dioxolane protecting group was removed to yield aldehyde **57** (98%). Afterwards, the 2,5-dimethoxy phenyl magnesium bromide Grignard was added to **57** and the so-formed secondary alcohol was oxidized with DMP (76 % yield over two steps). Three more steps from **58** revealed the natural product lingzhilactone B (**24**).

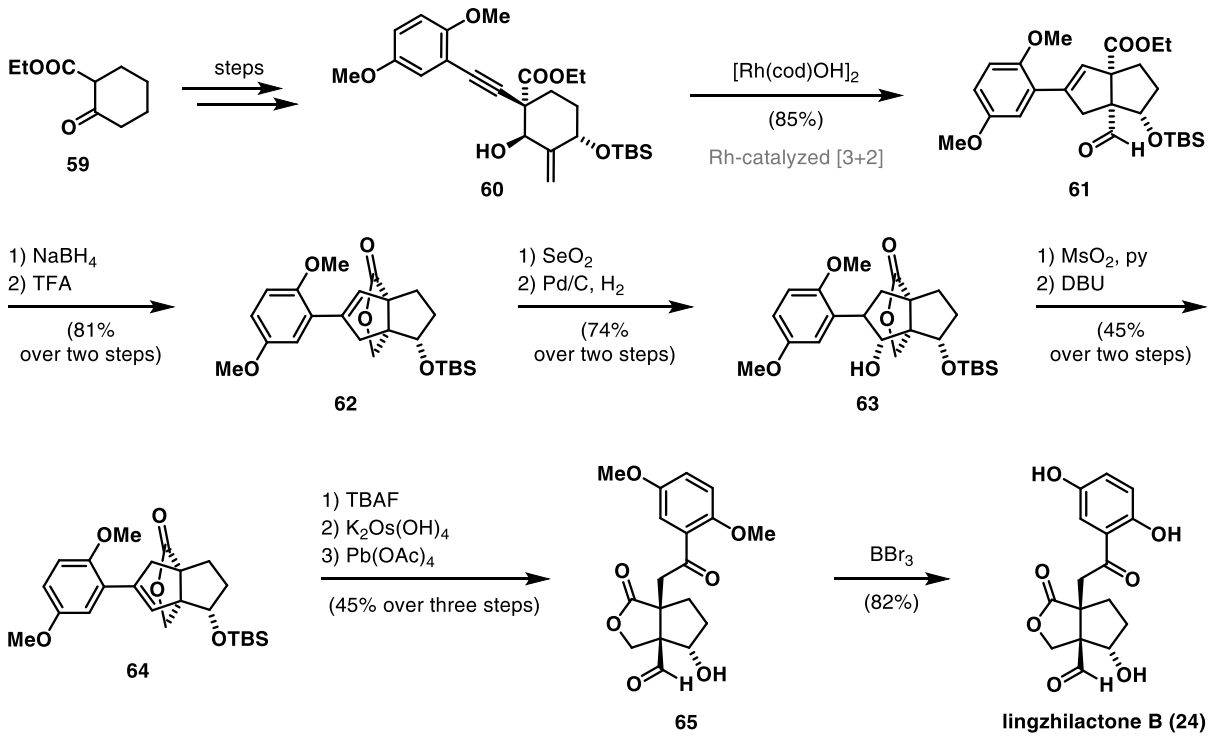
[55] D. Chen, X.-M. Li, H.-M. Liu, M.-M. Li, Y.-X. Cheng, H.-B. Qin, *Tetrahedron Lett.* **2016**, *57*, 2877–2879.



Scheme 8: Total synthesis of lingzhilactone B (**24**) by Qin.

After the successful synthesis of lingzhiol (**30**), the Yang group also implemented their formal rhodium catalyzed [3+2] cycloaddition methodology for the synthesis of lingzhilactone B (**24**).[56] Cyclohexanone **59** was elaborated in several steps to the densely functionalized cyclohexane **60** (Scheme 9). That intermediate served as the starting material for the [3+2] cycloaddition of the in situ formed alleno rhodium species with an enal. The catalyst $[Rh(cod)OH]_2$ smoothly converted **60** into bicycle **61** which was obtained as a single diastereomer in 85% yield. Sodium borohydride selectively reduced aldehyde **61** to the corresponding alcohol and a subsequent acid-mediated lactone closure with trifluoro acetic acid afforded **62** (81% over two steps). Isomerization of the double bond was carried out in a rather lengthy process and involved an allylic oxidation of **62** with selenium dioxide followed by a hydrogenation to give **63**. A mesylation (Ms_2O, py) of the secondary alcohol and elimination of the mesylate with DBU yielded the correct double bond isomer **64** (45% over two steps). The silyl protecting group was removed with tetrabutylammonium fluoride and the bicyclic lactone was revealed through a dihydroxylation ($K_2Os(OH)_4$) and cleavage of the so-obtained diol ($Pb(OAc)_4$) to provide the vicinal quaternary stereo center of **65** (45% over three steps). Finally, demethylation with BBr_3 delivered lingzhilactone B (**24**) in 82% yield.

[56] W. Shao, J. Huang, K. Guo, J. Gong, Z. Yang, *Org. Lett.* **2018**, *20*, 1857–1860.



Scheme 9: Total synthesis of lingzhilactone B (**24**) by Yang.

4. Results and Discussion

4.1. Nucleophilic Addition / Spiroacetalization Approach

The first retrosynthesis of ganoapplanin (**19**) was based on a disconnection that resulted in a symmetric 6/6/6/6 flat tetracycle **66** and a structurally elaborated bicyclo[3.3.0]octane **67** (Figure 10). Retrosynthetically, the free phenolic hydroxyl groups might arise from a deprotection of a benzyl group. For the synthesis of the core dioxaspirocycle we envisioned a nucleophilic addition of an organometallic species derived from iodide **67** to the tetracycle **66**. In the following paragraphs we are going to focus on the synthesis of the northern tetracycle **66** and following that, we will disclose our attempts towards the bicyclic lactone **67**.

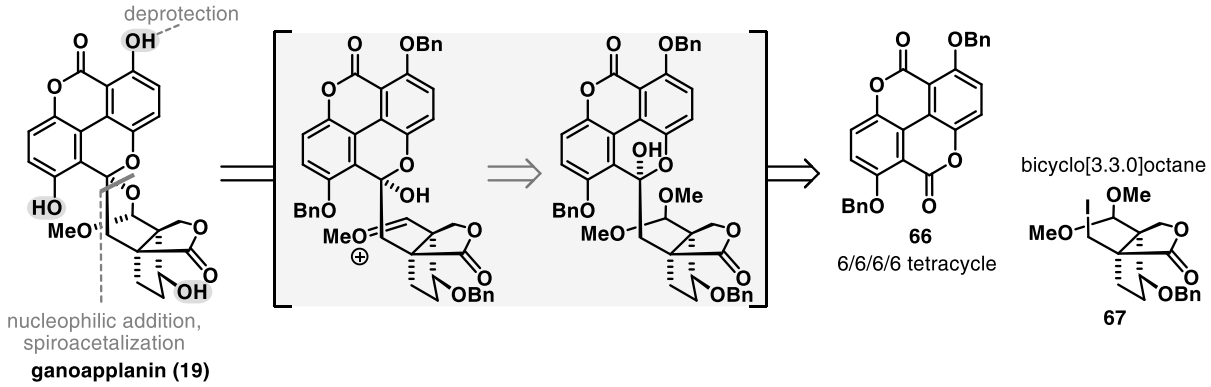


Figure 10: Retrosynthetic analysis based on a nucleophilic addition of the bicyclo[3.3.0]octane **67** to the symmetric tetracycle **66**.

A retrosynthetic analysis of tetracycle **68** revealed a possible Buchwald coupling for the hydroxyl groups that could be taken back to the corresponding aryl chlorides **69** (Figure 11). Further C–O disconnections give rise to chlorobenzoate **70**. Thus, **70** could arise from a ring opening of chlorocyclopropane **71** that is in line with our previous ring-expansion methodology[57] to access highly substituted benzoates. Finally, a dimerization reaction of known 2-iodo-2-cyclopentenone **72** followed by a cyclopropanation might yield the chlorocyclopropane **71**.

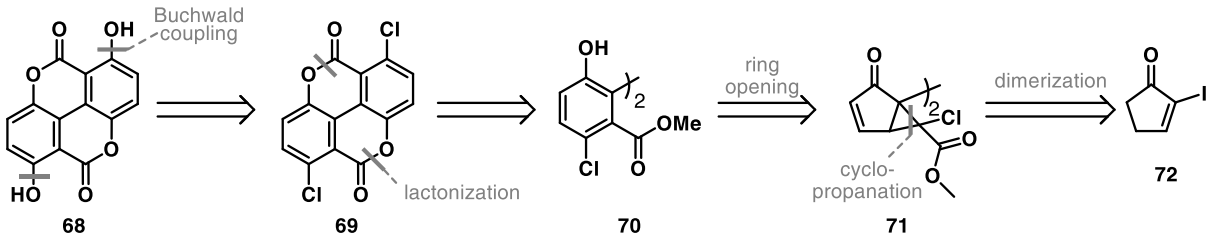
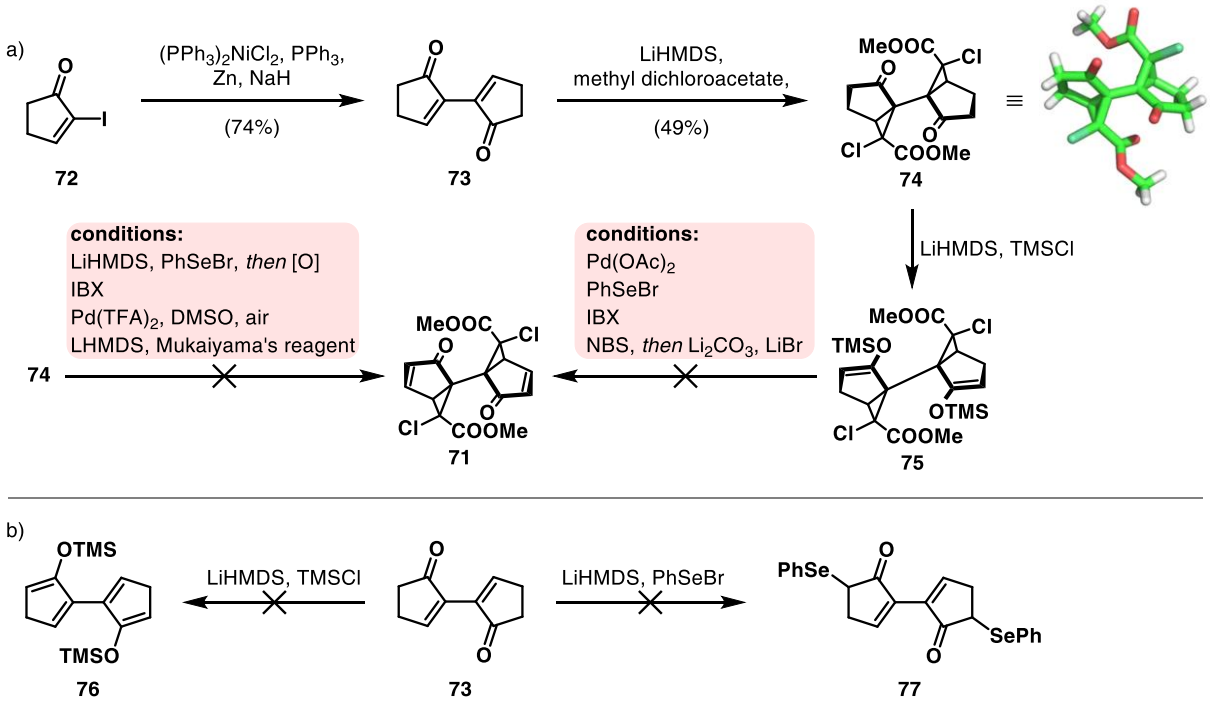


Figure 11: Retrosynthetic analysis of 6/6/6/6 tetracycle **68**.

[57] J. Feierfeil, A. Grossmann, T. Magauer, *Angew. Chem. Int. Ed.* **2015**, *54*, 11835–11838.

Our synthesis towards the tetracycle **68** commenced with a Nickel catalyzed dimerization of 2-iodo-2-cyclopentenone **72** based on the methodology by Hong to furnish dimer **73** (74%, Scheme 10a).[58] The synthetic plan called for a cyclopropanation that we carried out with LiHMDS and methyl dichloroacetate to yield chlorocyclopropane **74** (49%) and the structure was confirmed via X-ray crystallography. In the following steps, we needed to dehydrogenate **74** to enone **71** but a direct conversion failed under several conditions: selenoxide elimination,[59] Nicolaou's dehydrogenation with IBX,[60] palladium catalyzed aerobic oxidation by Stahl[61] or dehydrogenation using Mukaiyama's reagent.[62] We attempted to overcome this issue by a two-step protocol. First, we prepared silyl enol ether **75** from ketone **74** with LiHMDS and TMSCl and planned to oxidize this intermediate to enone **71**. However, this route was also met with failure under several conditions: Saegusa–Ito oxidation with $Pd(OAc)_2$,[63] selenylation with PhSeBr, Nicolaou's dehydrogenation[60] with IBX or alpha bromination with NBS followed by bromide elimination with Li_2CO_3 and LiBr.

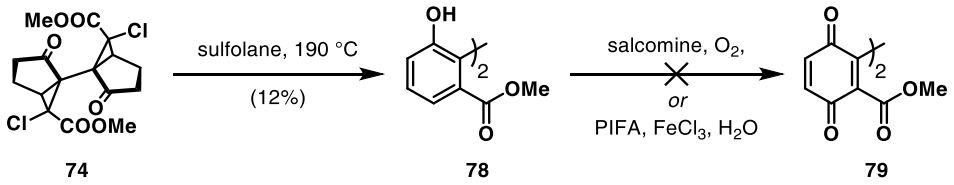
An alternative route that relied on installing the prerequisite enone at an earlier stage was unsuccessful, as dimer **73** proved to be reluctant to functionalization either by reaction with LiHMDS and TMSCl or with LiHMDS and PhSeBr (Scheme 10b).



Scheme 10: Synthesis towards dimer **71** (a) an attempted functionalization of **73** (b).

[58] G.-q. Lin, R. Hong, *J. Org. Chem.* **2001**, *66*, 2877–2880.
[59] H. J. Reich, I. L. Reich, J. M. Renga, *J. Am. Chem. Soc.* **1973**, *95*, 5813–5815.
[60] K. C. Nicolaou, Y. L. Zhong, P. S. Baran, *J. Am. Chem. Soc.* **2000**, *122*, 7596–7597.
[61] T. Diao, S. S. Stahl, *J. Am. Chem. Soc.* **2011**, *133*, 14566–14569.
[62] M. Teruaki, M. Jun-ichi, K. Hideo, *Chem. Lett.* **2000**, *29*, 1250–1251.
[63] Y. Ito, T. Hirao, T. Saegusa, *J. Org. Chem.* **1978**, *43*, 1011–1013.

Therefore, we focused on the ring-expansion of chlorocyclopropane **74** that proceeded at 190 °C in sulfolane to afford dimeric benzoate **78** (12%, Scheme 11). Notably, the bromo derivative of **74** fragmented at 100 °C but gave the benzoate in 10% yield (not shown). At this juncture, we needed to convert **78** to a hydroquinone or quinone derivative. However, our attempts to oxidize **78** to quinone **79** either with salcomine and oxygen or with a combination of PIFA and $FeCl_3$ in the presence of water led to decomposition.[64]



Scheme 11: Ring-expansion to afford **78** and unsuccessful synthesis of quinone **79**.

Since the installation of the enone moiety posed significant problems, we elaborated the idea to mask the enone as a norbornene Diels–Alder retron **80a** or **80b**, that in a forward sense might be unmasked in a retro-Diels–Alder reaction under extrusion of cyclopentadiene (Figure 12).

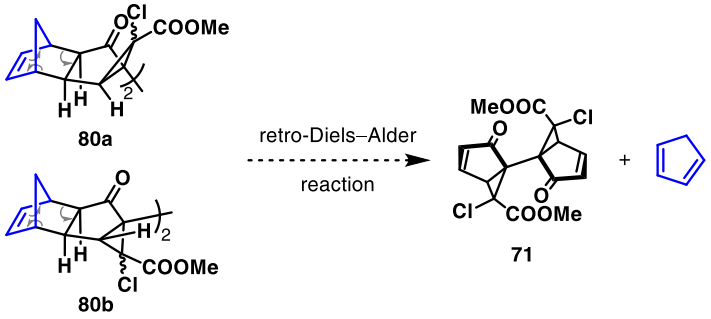
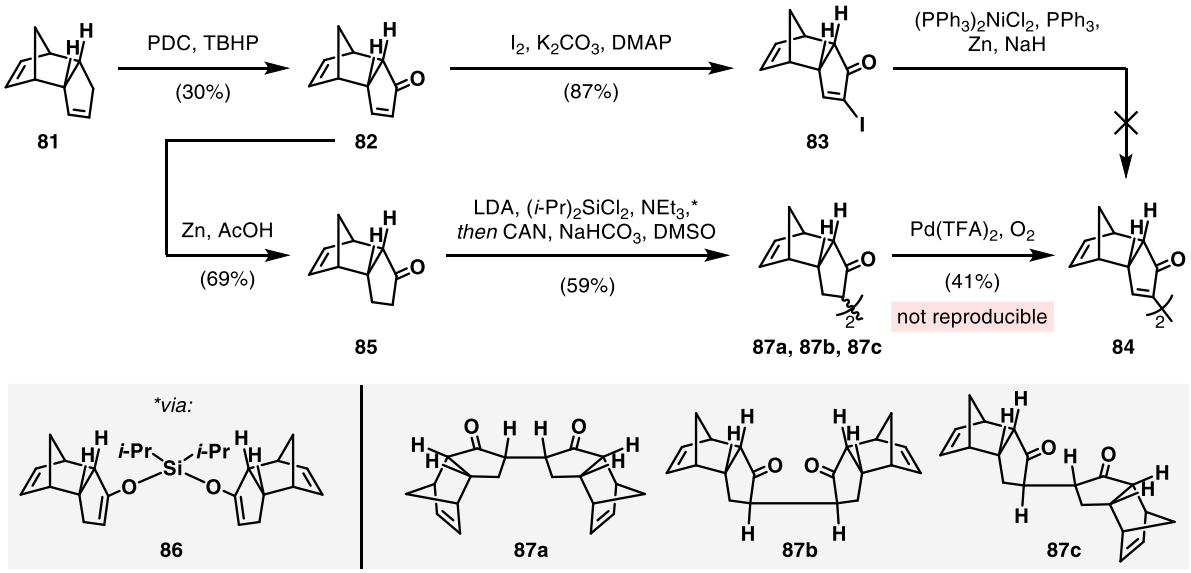


Figure 12: A retro-Diels–Alder reaction of norbornene **80a** or **80b** might reveal a masked enone moiety in **71**.

Starting from commercially available dicyclopentadiene **81**, we performed an allylic oxidation to access enone **82** employing an equimolar ratio of PDC and TBHP (30%, Scheme 12)[65]. Subsequent iodination with I_2, K_2CO_3 and DMAP furnished α-iodo enone **83** in 87% yield. With **83** in hand, we opted for the nickel catalyzed dimerization[58] that was successfully applied for the dimerization of **72**. However, for **83** no product was formed. We rationalized, that the norbornene moiety serves as a strongly coordinating ligand for nickel and is further inhibiting the desired reaction pathway. Surprisingly, increasing the catalyst loading from 50 mol% to 150 mol% did not change the reaction outcome. On these grounds, we reduced enone **82** with zinc in acetic acid to ketone **85** (69%) and resorted to an oxidative carbon-carbon bond formation via a silyl bis-enol ether.[66] Following the synthesis of the bridged silyl bis-enol ether **86** with LDA, NEt_3 and $(i\text{-Pr})_2SiCl_2$, the oxidative coupling was initiated with CAN to give a mixture of **87a**, **87b**, and **87c** in 59% yield. We had an initial moment of success with oxidation

[64] Elias A. Couladouros, Alexandros T. Strongilos, *Eur. J. Org. Chem.* **2002**, 3341–3350.
[65] N. Chidambaram, S. Chandrasekaran, *J. Org. Chem.* **1987**, *52*, 5048–5051.
[66] C. T. Avetta, L. C. Konkol, C. N. Taylor, K. C. Dugan, C. L. Stern, R. J. Thomson, *Org. Lett.* **2008**, *10*, 5621–5624.

conditions reported by Stahl[61] ($Pd(TFA)_2$, O_2) for the conversion of **87a-c** to enone **84** but this reaction proved to be unreproducible in our hands. Other ways to realize this transformation (IBX, Saegusa–Ito or selenoxide elimination) were also met with failure and only starting material was recovered.



Scheme 12: Conversion of dicyclopentadiene to dimer **84** via an oxidative carbon-carbon bond formation.

Chlorocyclopropane **80a** or **80b** is an ideal precursor for the northern hemisphere. A retrosynthetic analysis revealed that it could be accessed through a symmetric Pauson–Khand reaction of simple building blocks such as norbornadiene, carbon monoxide and butadiyne (Figure 13).

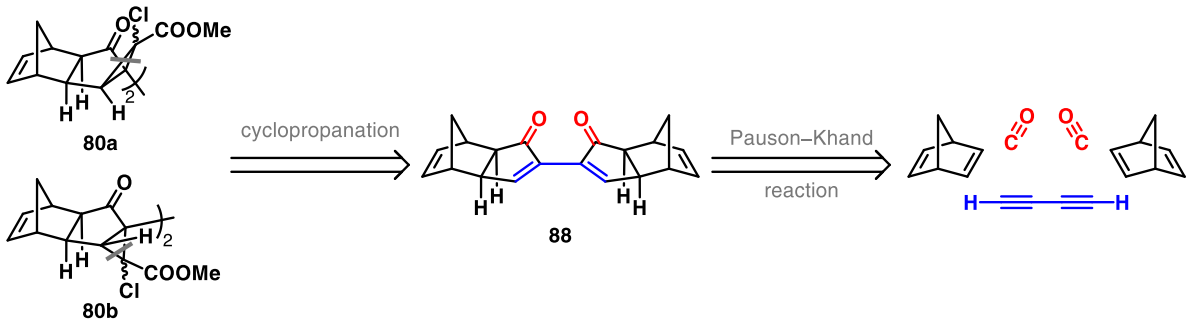
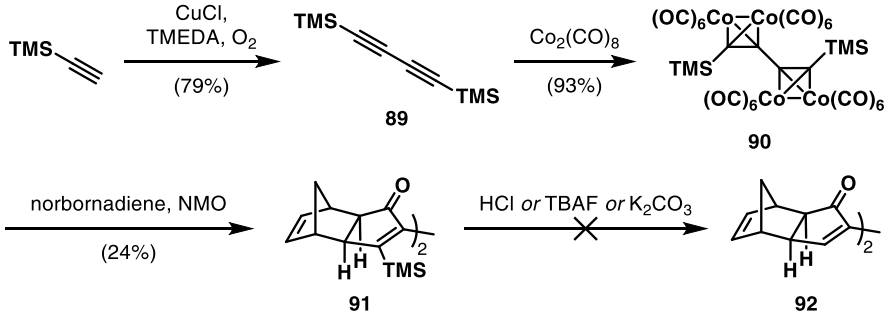


Figure 13: Retrosynthetic analysis of norbornene **88** based on a Pauson–Khand approach.

To test this approach, we started with the Hay dimerization of trimethylsilylacetylene[67] (which is a variant of the Glaser coupling[68]) with the in situ formed CuCl•TMEDA complex and oxygen to form diyne **89** in 79% yield (Scheme 13). For practical reasons, we replaced butadiyne (a gas) with trimethylsilylacetylene. Complexation of diyne **89** with $[Co_2(CO)_8]$ yielded **90** in 93% which served as the starting material for the upcoming Pauson–Khand reaction.[69] Gratifyingly, subjecting complex **90** to

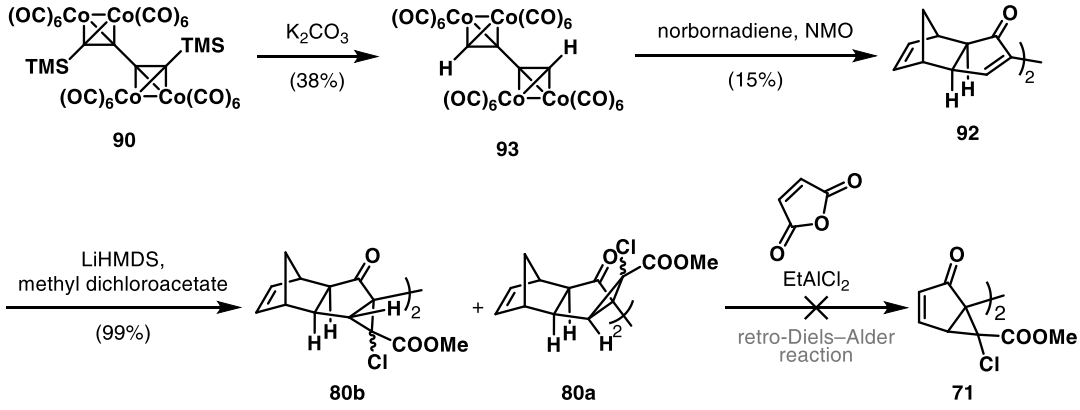
[67] A. S. Hay, *J. Org. Chem.* **1962**, *27*, 3320–3321.
[68] C. Glaser, *Ann. Chem. Pharm.* **1870**, *154*, 137–171.
[69] I. U. Khand, G. R. Knox, P. L. Pauson, W. E. Watts, *J. Chem. Soc. D* **1971**, 36a–36a.

norbornadiene and NMO delivered enone dimer **91** (24%). However, **91** was reluctant to desilylation either under acidic (HCl) or basic conditions (TBAF, or K_2CO_3 in methanol).



Scheme 13: Pauson–Khand reaction of complex **90**.

For this reason, we performed the TMS removal already on the stage of cobalt alkyne complex **90** with K_2CO_3 in methanol to yield complex **93** (38%, Scheme 14). A subsequent Pauson–Khand reaction furnished norbornene **92** (15%). This reaction proved to be the bottleneck of the reaction sequence and was difficult to optimize due to the low solubility of complex **93**. Pleasingly, the cyclopropanation of **92** with LiHMDS and methyl dichloroacetate yielded almost quantitatively chlorocyclopropane **80a** and **80b** as a mixture of four diastereomers. Unfortunately, treatment of **80a** and **80b** with maleic anhydride (which served as the competing dienophile) and ethyl aluminium dichloride did not elicit the envisioned retro-Diels–Alder reaction at elevated temperatures (70 °C). Notably, the corresponding chlorobenzoate which derives from the ring-expansion was also not observed.



Scheme 14: Unsuccessful retro-Diels–Alder reaction of **80a** and **80b** prepared through a Pauson–Khand reaction of complex **93** followed by a cyclopropanation.

Because of these drawbacks, we resorted to a novel synthetic approach for the 6/6/6/6 tetracycle based on an Ullmann dimerization (Figure 14). This disconnection revealed bromobenzoate **96** which is literature known and can be synthesized through a Diels–Alder reaction of bromoalkyne **97** with 2-methoxyfuran.

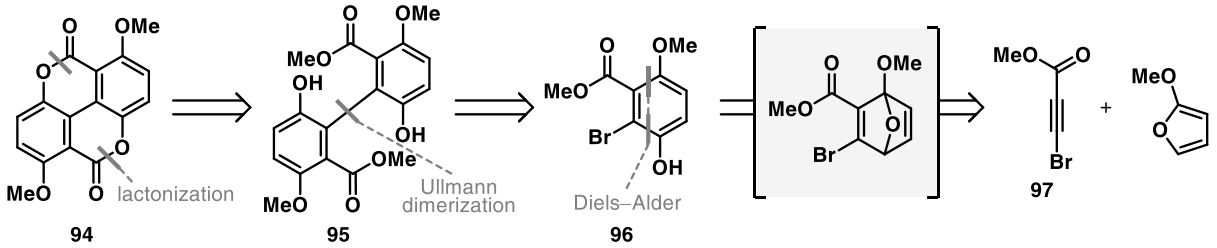
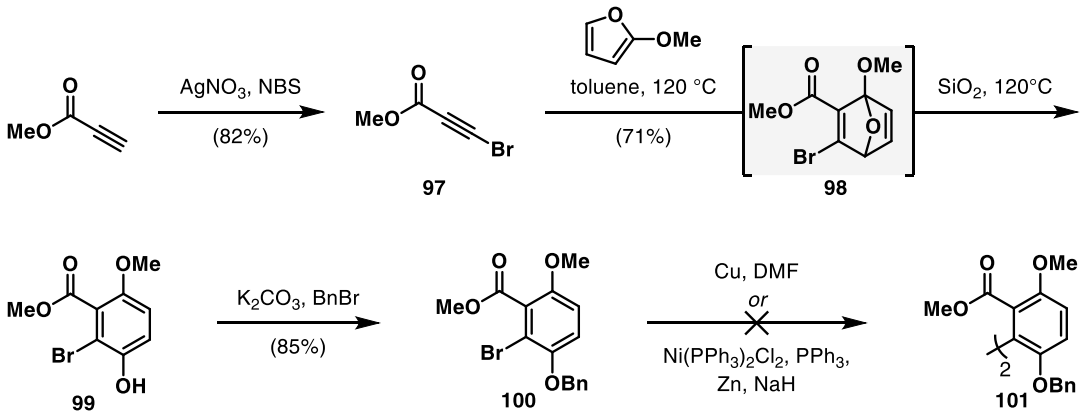


Figure 14: Retrosynthesis of tetracycle **94** based on an Ullmann dimerization and Diels–Alder sequence.

We commenced our studies with the conversion of propiolic acid into bromo alkyne **97** with silver nitrate and NBS (82%, Scheme 15). Following the precedent of Ogawa,[70] treatment of **97** with 2-methoxyfuran furnished the Diels–Alder adduct **98** which was aromatized in situ by adding silica gel to the hot reaction mixture to provide **99**. The hydroxyl group of **99** was further protected with BnBr and K_2CO_3 to give Ullmann precursor **100** in 85% yield. Subjecting **100** to Ullmann conditions[71] (activated copper in DMF) did not furnish biaryl **101**. A Nickel catalyzed reductive dimerization[58] did not show any conversion to the product. While similar substrates are known to undergo reductive couplings, we rationalized that the steric encumbrance around the aryl bromide bond hampered the reaction.



Scheme 15: Ullmann based dimerization approach towards biaryl **101**.

Due to this unexpected drawback, we intended to change the starting material for the Ullmann coupling. We envisioned tetracycle **66** could be traced back to biaryl **102** or **103** that might be synthesized from **104** either through a directed α-oxidation or an electrophilic aromatic bromination (Figure 15). Intermediate **105** can be synthesized via an Ullmann dimerization of iodobenzaldehyde **106**.

[70] H. Shinohara, M. Sonoda, N. Hayagane, S. Kita, S. Tanimori, A. Ogawa, *Tetrahedron Lett.* **2014**, *55*, 5302–5305.
[71] F. Ullmann, J. Bielecki, *Ber. Dtsch. Chem. Ges.* **1901**, *34*, 2174–2185.

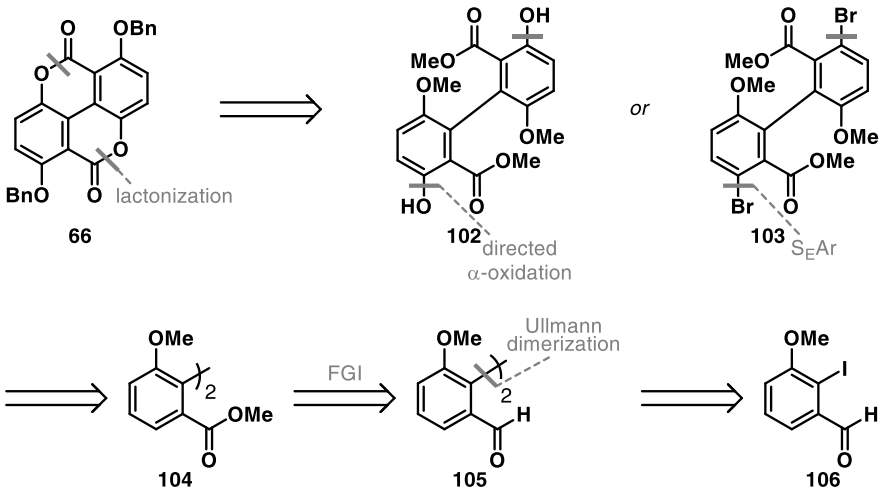
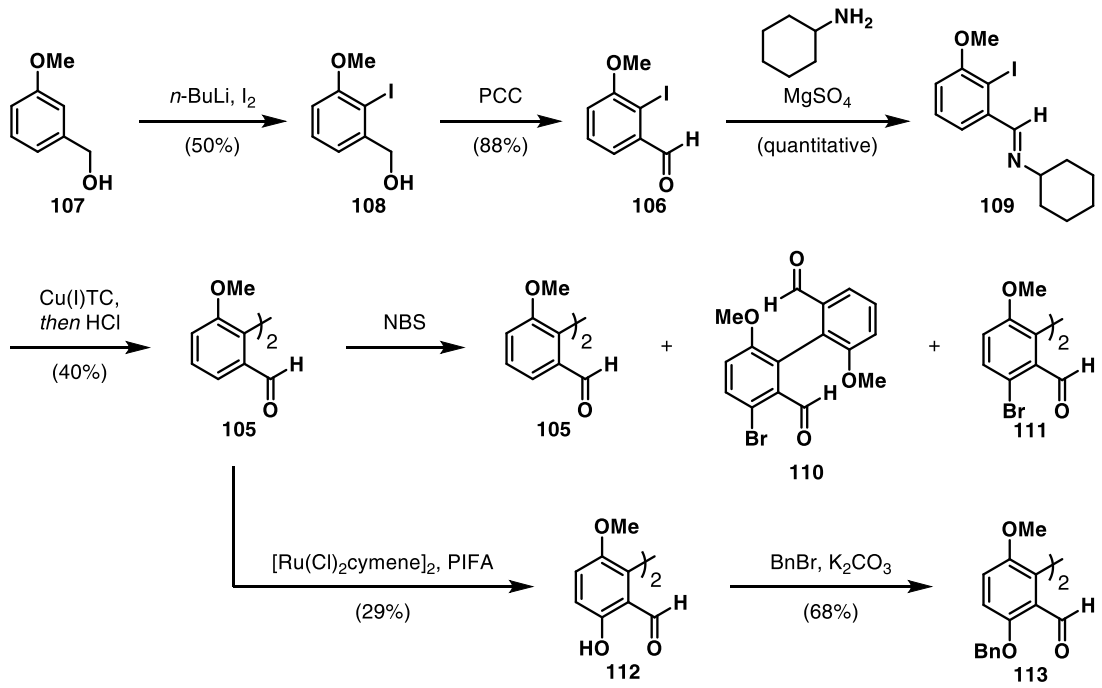


Figure 15: Retrosynthesis of tetracycle **66** based on a directed α-oxidation of benzoate **104** or an aromatic bromination.

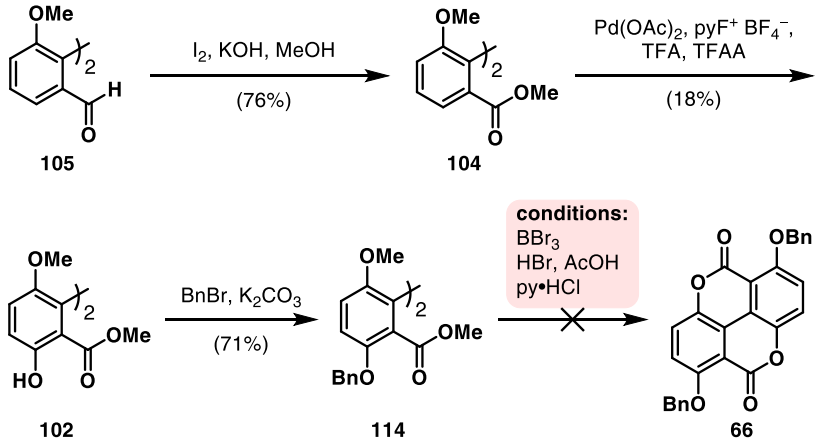
In analogy to the synthesis reported by Schmalz,[72] we performed a hydroxyl directed iodination of benzyl alcohol **107** to aryl iodide **108** (50%) which was further elaborated in an oxidation with PCC to benzaldehyde **106** (88%). A quantitative imine formation with cyclohexylamine set the stage for a copper(I) thiophene-2-carboxylate mediated Ullmann dimerization that proceeded in moderate yield (40%).[73] The anticipated bromination with NBS gave a mixture of starting material **105**, mono bromination **110** and the desired bromoarene **111** that were not separable. Longer reaction times and an excess of NBS did not increase the conversion to the product **111**. With **105** in hand, we opted for a aldehyde directed α-oxidation of the benzene ring employing $[Ru(Cl)_2cymene]_2$ in combination with PIFA to furnish salicylic aldehyde **112** in 29% yield.[74] A subsequent benzylation (BnBr, K_2CO_3) provided **113** (68%).

[72] S. Neufeind, N. Hülsken, J.-M. Neudörfl, N. Schlörer, H.-G. Schmalz, *Chem. Eur. J.* **2011**, *17*, 2633–2641.
[73] S. Reichert, B. Breit, *Org. Lett.* **2007**, *9*, 899–902.
[74] F. Yang, K. Rauch, K. Kettelhoit, L. Ackermann, *Angew. Chem. Int. Ed.* **2014**, *53*, 11285–11288.



Scheme 16: Synthesis of biaryl **105** through a Cu(I)TC mediated Ullmann dimerization and further elaboration via a ruthenium(II) catalyzed directed α-oxidation.

With these promising results in hand, we applied the same directed α-oxidation logic to benzoate **104** that was obtained through an oxidation of aldehyde **105** with iodine in the presence of methanol (76%, Scheme 17). Exposure of **104** to $Pd(OAc)_2$ catalyst in combination with 1-fluoropyridinium tetrafluoroborate, acetic acid and acetic anhydride[75] yielded the desired hydroquinone **102** in poor yield (18%). We were able to access enough material to prepare benzyl ether **114** from **102** (BnBr, K_2CO_3, 71%) and to test the double lactonization to give tetracycle **66**. Typical reaction conditions for this transformation such as BBr_3, HBr and acetic acid or pyridinium chloride did not furnish the desired product and only starting material was recovered.



Scheme 17: Directed palladium(II) catalyzed α-oxidation of **104** and attempted synthesis of tetracycle **66**.

[75] G. Shan, X. Yang, L. Ma, Y. Rao, *Angew. Chem. Int. Ed.* **2012**, *51*, 13070–13074.

As an alternative, we identified two complementary approaches that rely on a carboxyl radical addition (Figure 16a) or a Friedel–Crafts disconnection (Figure 16b). For the former approach, benzoic acid dimer **115** had to be prepared through an oxidative dimerization of 2-methoxybenzoic acid and for the latter approach an oxidative dimerization of 4-methoxyphenol would give the starting material for the Friedel–Crafts reaction **116**.

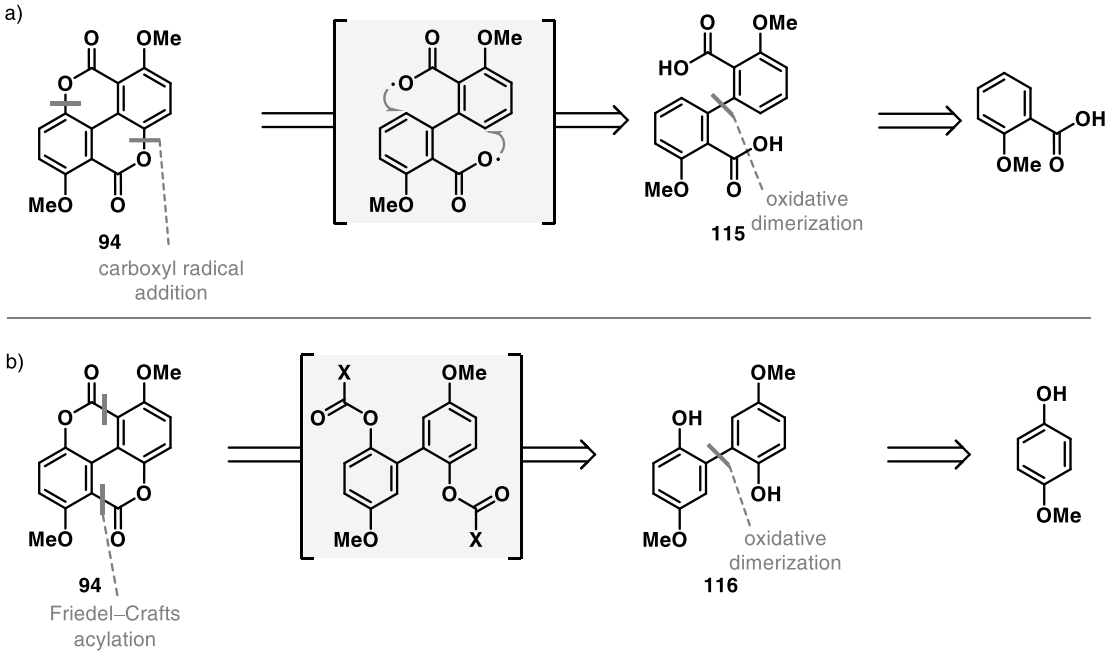
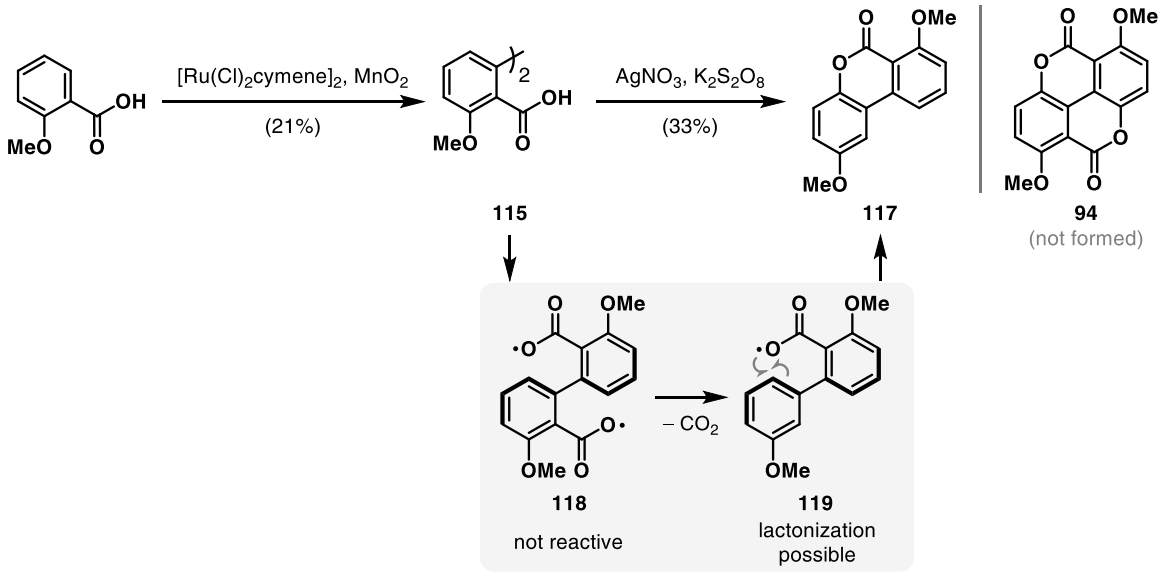


Figure 16: Retrosynthesis of tetracycle **94** based on an intramolecular carboxyl radical addition (a) and a Friedel–Crafts acylation (b), respectively.

We were inspired by the work of Gevorgyan that reported the lactonization of benzoic acids through a radical mechanism induced by potassium persulfate.[76] Even though the formation of a tetracycle through this method is not described, we thought it was still a method worthwhile to pursue. Benzoic acid dimer **115** was synthesized via a rhodium(I) catalyzed dimerization of 2-methoxybenzoic acid according to Li (21%, Scheme 18).[77] When applying Gevorgyan's conditions, the desired tetracyclic lactone was not formed but we observed the formation of tricycle **117** (33%). We hypothesized that the rotation around the biaryl bond in **118** is hindered even under the elevated temperatures of the reaction conditions (80 °C). As a consequence, carboxylic radical **118** cannot undergo a double lactonization. A subsequent monodecarboxylation formed **119** which then reacted to tricycle **117**.

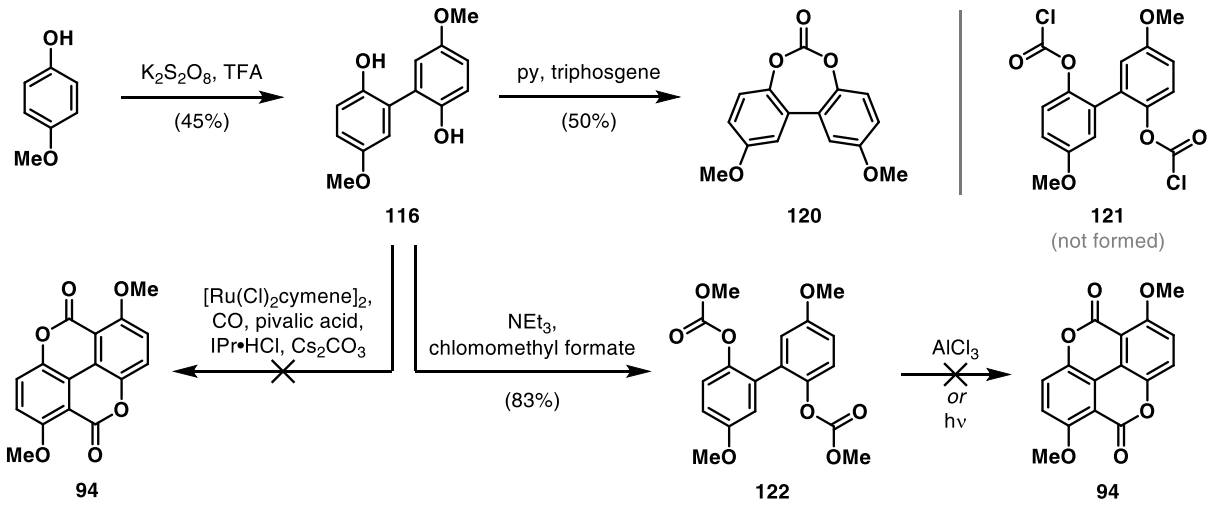
[76] Y. Wang, A. V. Gulevich, V. Gevorgyan, *Chem. Eur. J.* **2013**, *19*, 15836–15840.
[77] H. Gong, H. Zeng, F. Zhou, C.-J. Li, *Angew. Chem. Int. Ed.* **2015**, *54*, 5718–5721.



Scheme 18: Regioselective dimerization of 2-methoxybenzoic acid and potassium persulfate induced radical lactonization of benzoic acid dimer **115**.

Next, we focused on the functionalization of the phenol dimer **116** that was accessible via an oxidative dimerization of 4-methoxyphenol with potassium persulfate in 45% yield (Scheme 19).[78] Based on a communication stating that carbonates react to lactones under irradiation with UV light,[79] we prepared carbonate **122** by reaction of **116** with chloromethyl formate and triethylamine. Unfortunately, no reaction occurred when we irradiated the reaction mixture with a Hanovia lamp or the Rayonet photo set-up at 254 nm. When Lewis acid conditions ($AlCl_3$) were employed to realize this transformation, only **116** was recovered. We also aimed to prepare chloroformate **121** from **116** by reaction with triphosgene to have a better leaving group for the intramolecular Friedel–Crafts acylation. However, we obtained the cyclic carbonate **120** under the reaction conditions (50%). Unfortunately, a direct conversion of **116** to the tetracycle **94** by means of a ruthenium(II) catalyzed carbonylative cyclization ($[Ru(Cl)_2cymene]_2$, CO, pivalic acid)[80] was also unsuccessful.

[78] N. Y. More, M. Jeganmohan, *Org. Lett.* **2015**, *17*, 3042–3045.
[79] N. C. Yang, A. Shani, G. R. Lenz, *J. Am. Chem. Soc.* **1966**, *88*, 5369–5369.
[80] K. Inamoto, J. Kadokawa, Y. Kondo, *Org. Lett.* **2013**, *15*, 3962–3965.



Scheme 19: Attempted synthesis of tetracycle **94** either through an intramolecular Friedel–Crafts acylation or a ruthenium(II) catalyzed carbonylative cyclization.

As outlined in Figure 17, the retrosynthesis of southern hemisphere of ganoapplanin revealed bicyclic lactone **67**. The dimethyl acetal might arise from an ozonolysis of **123** followed by a protection of the corresponding aldehyde. For intermediate **123**, we envisioned a 1,4-addition of vinyl cuprate to enone **124** and trapping the enolate with diiodomethane. Thus, **124** could arise from a regioselective dehydrogenation of bicyclic lactone **125**. For this intermediate we identified a diastereoselective iodo-carbocyclization of malonate **126** reported by Taguchi.[81,82,83,84] In line with this precedent, the linear cyclization precursor **126** arose from a nucleophilic substitution of dimethyl malonate with the mesylate of the primary alcohol **127** which can be prepared enantioselectively through a kinetic resolution. A functional group interconversion traces **127** back to ester **128** that can be synthesized from a 1,2-addition of ethyl acetate to acrolein.

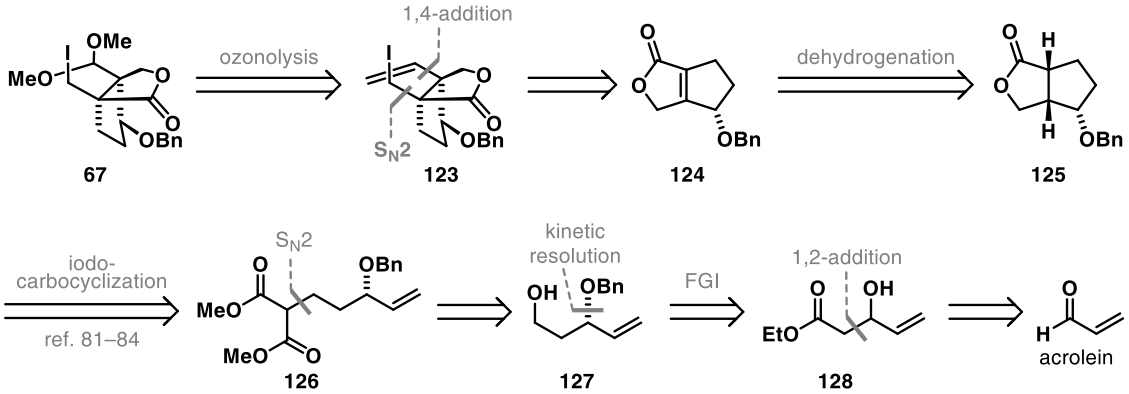
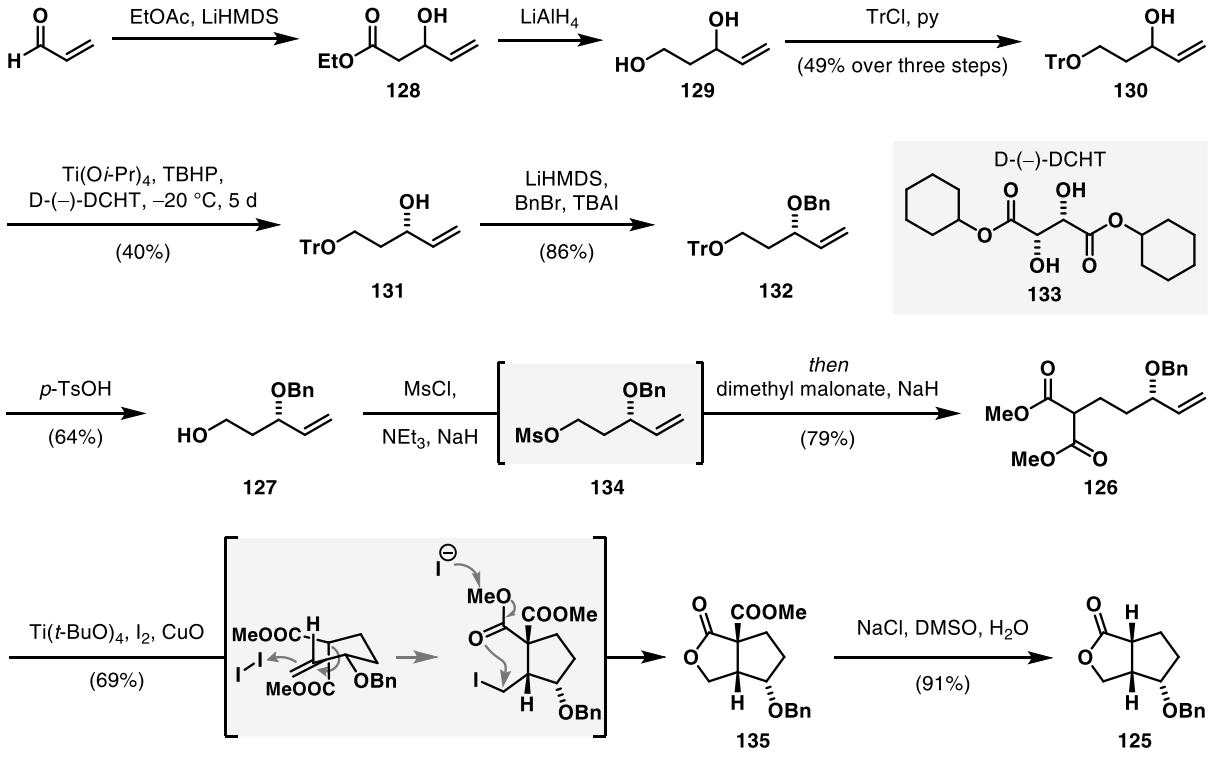


Figure 17: Retrosynthetic analysis of bicyclo[3.3.0]octane (**67**).

Our synthesis commenced with a 1,2-addition of ethyl acetate to acrolein to yield β-hydroxy ester **128** that was reduced with $LiAlH_4$ to 1,3-diol **129** (Scheme 20). A selective protection of the primary alcohol

[81] O. Kitagawa, T. Inoue, T. Taguchi, *Tetrahedron Lett.* **1994**, *35*, 1059–1062.
[82] T. Inoue, O. Kitagawa, Y. Oda, T. Taguchi, *J. Org. Chem.* **1996**, *61*, 8256–8263.
[83] T. Inoue, O. Kitagawa, A. Saito, T. Taguchi, *J. Org. Chem.* **1997**, *62*, 7384–7389.
[84] O. Kitagawa, T. Taguchi, *Synlett* **1999**, *1999*, 1191–1199.

yielded triphenylmethyl ether **30** in 49% over three steps. The synthesis was rendered enantioselective via a kinetic resolution of allylic alcohol **130** through a Sharpless asymmetric epoxidation[85] that afforded chiral allylic alcohol **131** in 40% yield (enantiomeric access was not determined at this point but the literature reported >99%ee). The employed dicyclohexyl tartrate (DCHT) ligand is known to deliver better enantioselectivity compared to the more common diisopropyl tartrate (DIPT).[85] A benzylation of the allylic alcohol (BnBr, LiHMDS, 86%) was carried out followed by the removal of the trityl protecting group under acidic conditions with *p*-TsOH (64%). We prepared the linear cyclization precursor **126** by mesylation of the primary alcohol that was directly displaced by dimethyl malonate in 79% yield. The iodo-carbocyclization occured in an orchestrated and diastereoselective manner to react malonate **126** to bicycle **135** in good yield (69%). Mechanistically, Ti(*t*-BuO)$_4$ complexes the malonate moiety, while iodine is activating the double bond. Through a conformer of malonate **126** where the benzyl ether adopts an axial position, the cyclopentane ring is formed via a 5-*exo*-trig cyclization. The bicyclic lactone is further completed through an in situ iodolactonization. Following the cyclization, a Krapcho decarboxylation[86] with NaCl in wet DMSO removed the ester group to furnish **125** (91%) that served as a functional handle for the cyclization reaction.

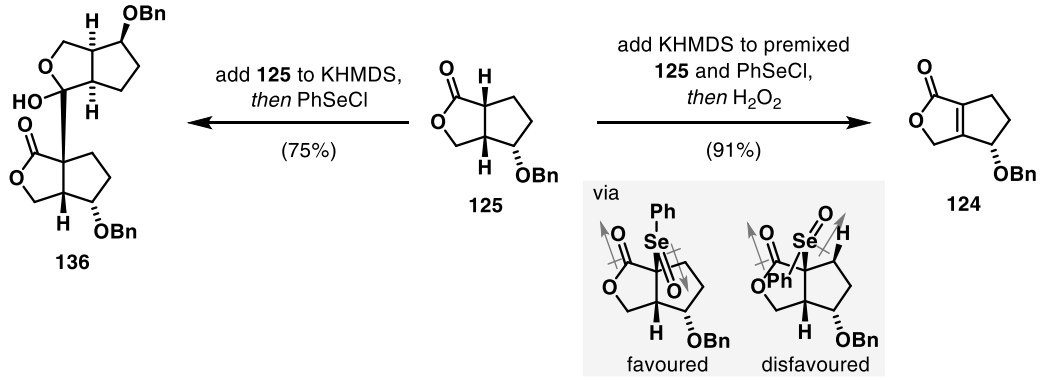


Scheme 20: Synthesis of bicycle **125** via an iodo-carbocyclization as the key step.

According to our synthetic plan, we investigated a selenoxide mediated dehydrogenation of bicycle **125** (Scheme 21). To this end, **125** was first treated with the KHMDS followed by addition of PhSeCl. Surprisingly, a Claisen-type dimerization occurred to give hemiacetal **136**. Based on this finding, we

[85] Y. Gao, J. M. Klunder, R. M. Hanson, H. Masamune, S. Y. Ko, K. B. Sharpless, *J. Am. Chem. Soc.* **1987**, *109*, 5765–5780
[86] A. P. Krapcho, B. P. Mundy, *Tetrahedron* **1970**, *26*, 5437–5446.

found that the order of addition was crucial for the reaction outcome. Premixing the starting material with PhSeCl and then adding KHMDS to the reaction mixture cleanly afforded the selenylated product that was in situ oxidized with hydrogen peroxide to the desired enone **124** in very good yield (91%). The preference for the endocyclic dehydrogenation might be rationalized by the dipole minimization of the lactone and the strong selenoxide dipole.[87]



136 **125** **124**

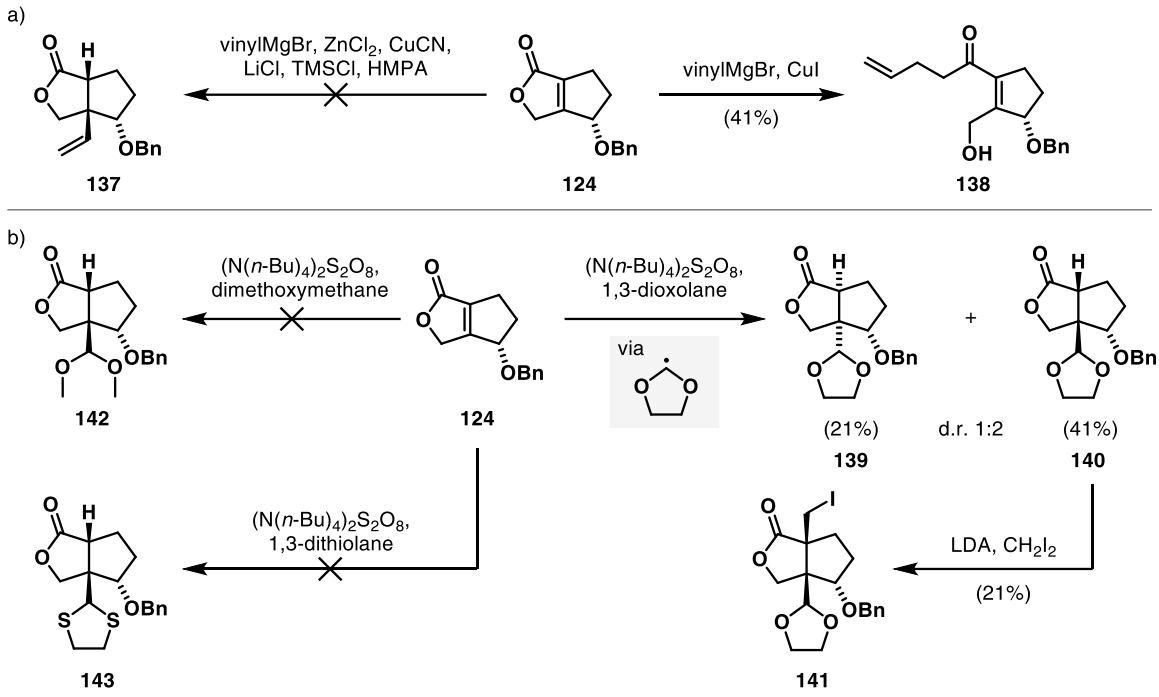
Scheme 21: Selenoxide mediated dehydrogenation of bicycle **125**.

Following the synthesis of enone **124**, we aimed at an anionic functionalization via a cuprate addition. The mixture containing vinylMgBr, $ZnCl_2$, CuCN, LiCl, TMSCl and HMPA is especially known for the addition of cuprates to hindered systems.[88] In our case no conversion was observed (Scheme 22a). Employing a Normant cuprate derived from vinylMgBr and CuI, the lactone moiety proved to be too reactive and nucleophilic opening of the lactone occurred followed by vinylcuprate 1,4-addition to furnish ketone **138** in 41% yield.

At this stage, we turned our attention to a radical functionalization of the enone. We hypothesized that radical reaction on sterically hindered systems might have an advantage over anionic functionalization where the nucleophile is usually complexed by solvent molecules (e.g. THF) shielding it from interacting with the electrophile. We took advantage of a masked formylation protocol that describes a radical 1,4-addition of 1,3-dioxolane to electron deficient olefins utilizing (*n*-butyl)ammonium peroxydisulfate.[89] Implementing this procedure, the desired lactone **140** was obtained as the major product, however, in a poor diastereomeric ratio of 2:1 (Scheme 22b). We assumed that the benzylether did not provide enough steric bias for high diastereoselectivity. With lactone **140** in hand, we focused on the introduction of the last residue of the bicylcooctane motif. **140** was subjected to an S_N2-type alkylation with diiodomethane. We soon realized that the intended alkylation is difficult and no reaction took place at ambient temperature. Heating the reaction mixture at 40 °C over the course of four hours afforded iodide **141** in 21% yield which reflects the steric encumbrance of the so formed vicinal

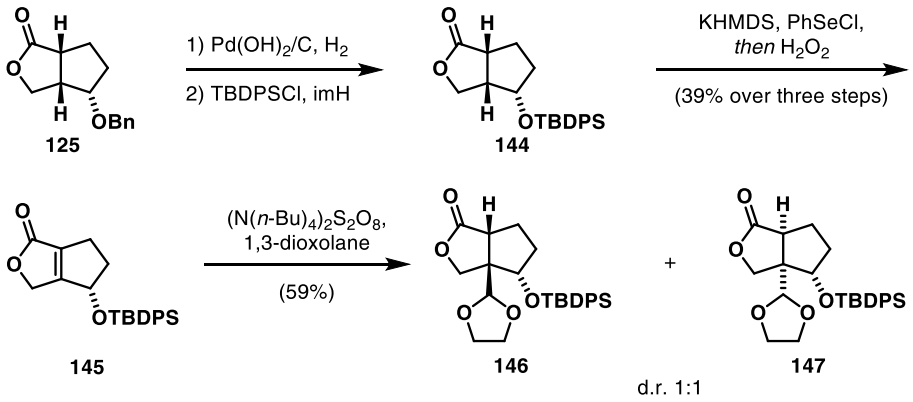
[87] H. Reich, S. Wollowitz, in *Organic Reactions, Vol. 44* (Ed.: L. Paquette), John Wiley & Sons, **1993**, pp. 1–296.
[88] B. H. Lipshutz, S. Sengupta, in *Organic Reactions, Vol. 41* (Ed.: L. Paquette), John Wiley & Sons, **1992**, pp. 135–631.
[89] J. C. Jung, Y. H. Kim, K. Lee, *Tetrahedron Lett.* **2011**, *52*, 4662–4664.

quaternary centers. Surprisingly, neither the introduction of dimethoxymethane or 1,3-dithiolane under otherwise same reaction conditions was successful.



Scheme 22: Anionic (a) and radical (b) functionalization of enone **124**.

In order to increase the diastereoselectivity of the dioxolane addition, we reasoned that a sterically demanding protecting group on the secondary alcohol would direct the dioxolane addition to selectively occur from one side. We synthesized the TBDPS protected α,β-unsaturated lactone **145** starting from the lactone **125** in three steps that span a debenzylation ($Pd(OH)_2/C$, H_2), TBDPS protection of the secondary alcohol and dehydrogenation (KHMDS, PhSeCl, *then* H_2O_2, Scheme 23). Surprisingly, the crucial dioxolane addition occurred in even lower selectivity of 1:1.



Scheme 23: Radical 1,4-addition of 1,3-dioxolane to bicycle **145**.

4.2. Cationic Cyclization Approach

With the knowledge that we gained from our first approach, we intended to make crucial adjustments to the next retrosynthetic analysis. As outlined in Figure 18, we envisioned a late-stage Lewis or Brønsted acid mediated cationic cyclization cascade from intermediate **148** to construct the core dioxaspirocycle. Thus, **148** could arise from an alkylation of **150** with tricycle **149**. This strategy allowed us to us to use the same iodo-carbocyclization strategy for the bicycle and disconnected the northern hemisphere of ganoapplanin to a structurally simpler tricycle.

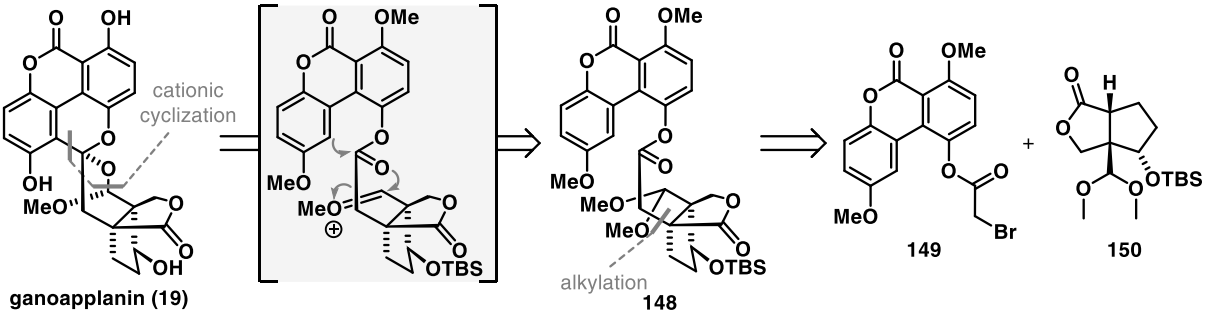


Figure 18: The cationic cyclization disconnection of ganoapplanin (**19**).

β-Bromoester **149** could be traced back to tricycle **151** through a Buchwald disconnection and an esterification (Figure 19). Tricycle **151** can be seen as a chlorinated benzoate and thus, the ring-expansion strategy developed in our laboratory could be applied to chlorocyclopropane **152**. For **152** we envisioned an intramolecular cyclopropanation of α-dichloroester with the enone moiety of **153**. The double bond of **152** which is crucial for the ring-expansion reaction would arise from an oxidation. **153** in turn, could be synthesized in an esterification and a Suzuki coupling reaction.

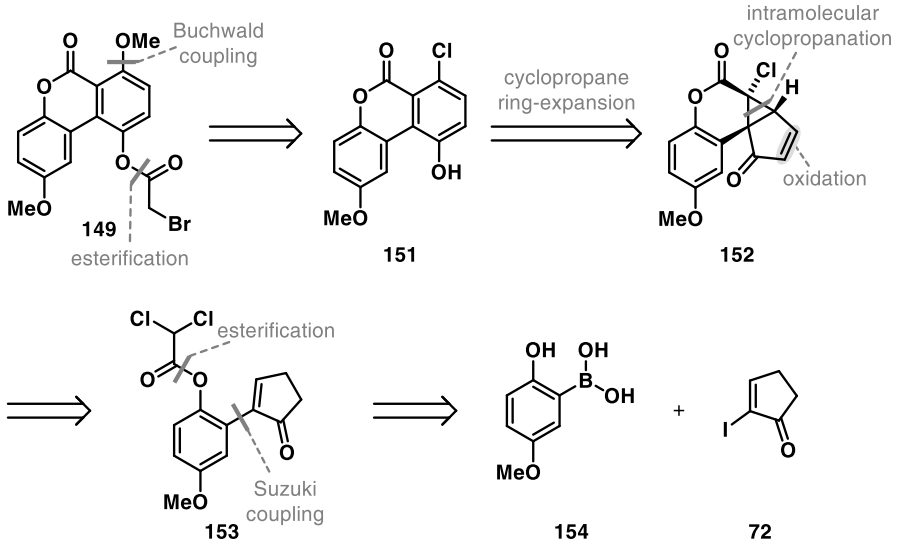
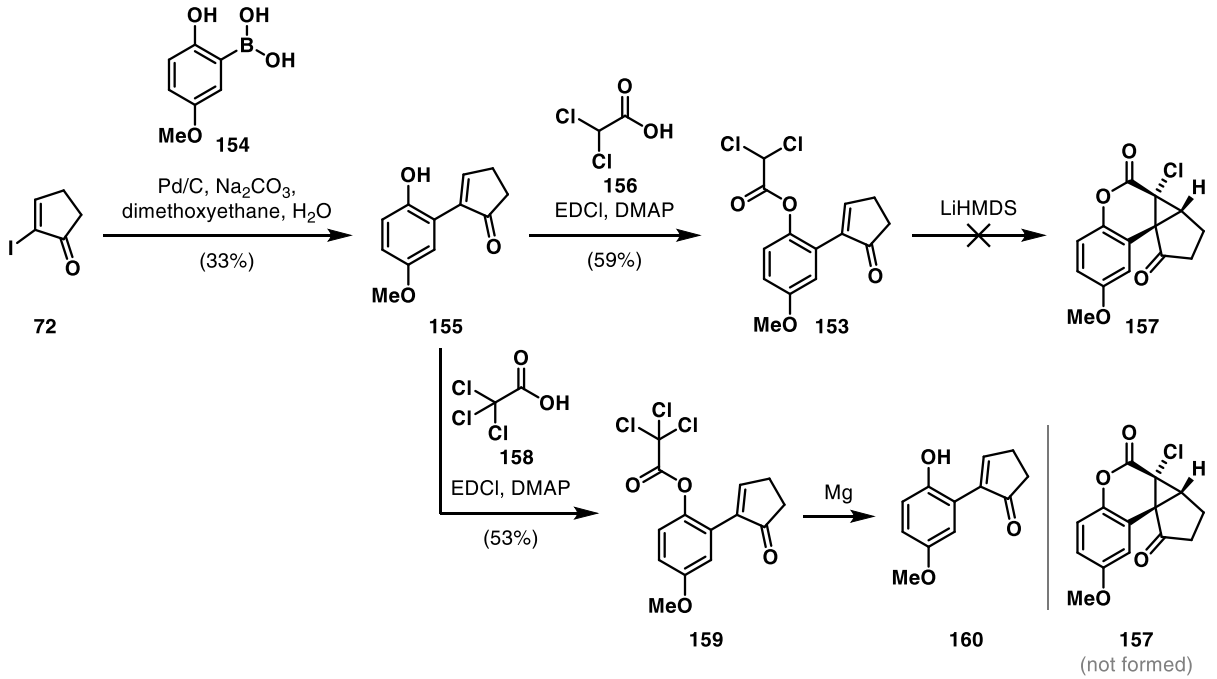


Figure 19: Retrosynthesis of β-bromoester (**149**) through an intramolecular cyclization and ring-expansion strategy.

The starting material for our attempted intramolecular cyclopropanation was accessible in two steps. The esters **153** and **159** were obtained via Suzuki cross-coupling of α-iodocyclopentenone **72** with

boronic acid **154** (33%, main by-product comes from protodeboronation of **154**) followed by EDCI promoted esterification of phenol **155** with acid **156** (59%) or **158** (53%), respectively (Scheme 24). The attempted intramolecular cyclopropanation of **153** mediated by LiHMDS did not furnish the desired chlorocyclopropane **157** and phenol **155** was recovered. Similarly, the conversion of trichloro ester **159** to **157** only gave phenol **155**. For both reactions, we assumed the formation of a ketene under basic conditions from the esters **153** and **159** where phenol **155** served as a leaving group.



Scheme 24: Failed intramolecular cyclopropanation of **153** and **159**.

To overcome this problem, we focused on the synthesis of tricycle **161** via a C–H activation or Ullmann coupling approach (Figure 20). Retrosynthetically, ester **162** could be synthesized through esterification of bromobenzoate **99** that is literature known and accessible through a Diels–Alder reaction of 2-methoxyfuran with bromoalkyne **97**.

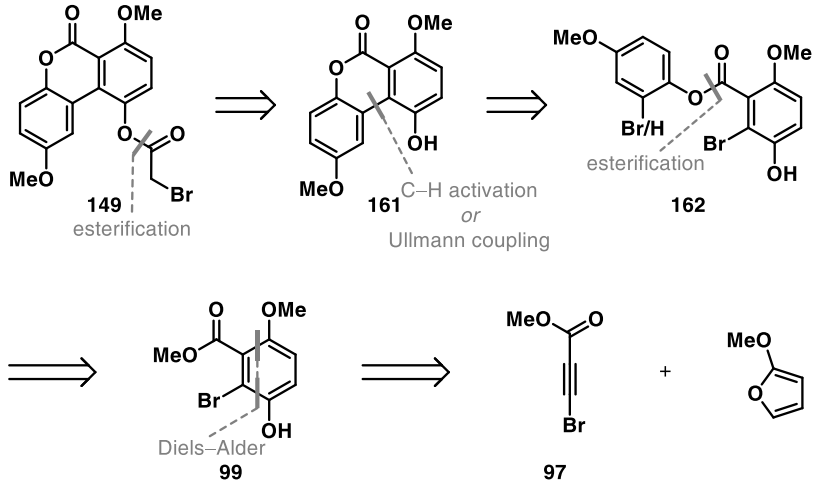
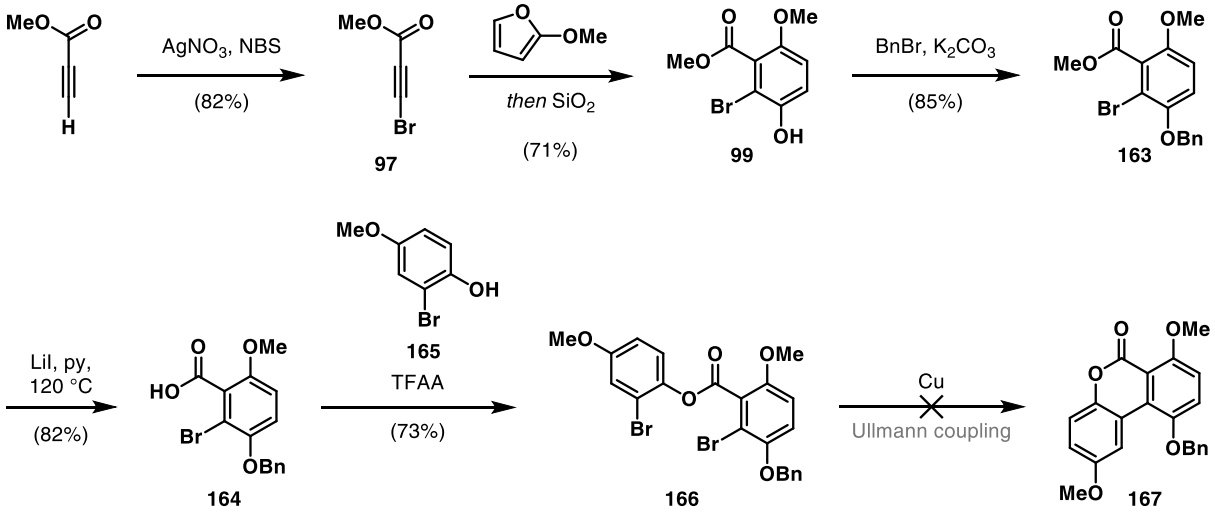


Figure 20: Approach to tricycle **161** based on a C–H activation or Ullmann coupling approach.

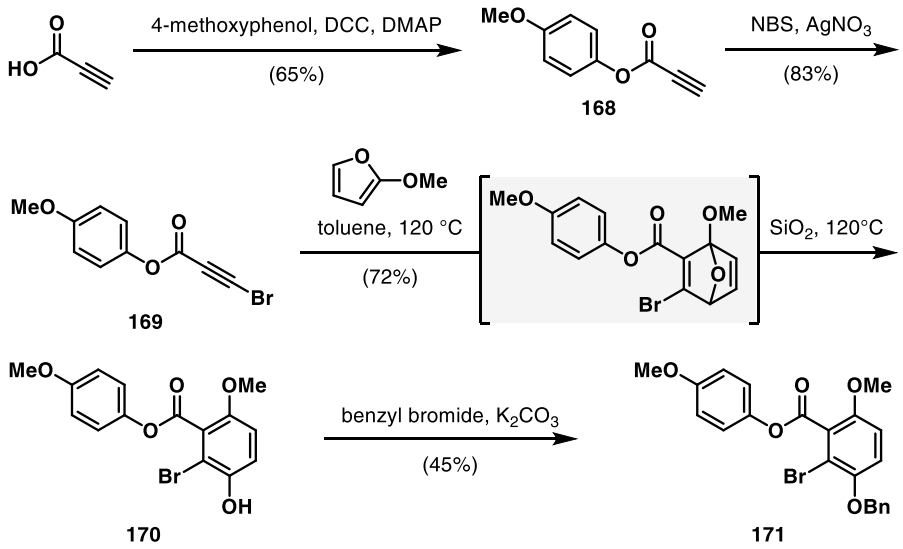
Methylpropiolate was converted to bromoalkyne **97** with silver nitrate and NBS (82%) and then reacted in a Diels–Alder reaction with 2-methoxyfuran following the precedent of Ogawa (71%, Scheme 25).[70] A benzylation was carried out (BnBr, K_2CO_3, 85%) and the benzoate **163** was converted into benzoic acid **164** by a nucleophilic saponification with lithium iodide at 120 °C (82%). Standard saponification (NaOH in THF) did not give any conversion to the product presumably due to steric hindrance provided by two ortho substituents. We accessed the Ullmann precursor **166** through an esterification with bromophenol **165** and trifluoroacetic anhydride (73%). Unfortunately, standard Ullmann coupling procedures led to no reaction. Dehalogenation prevailed when activated copper was used (prepared in situ from CuI and potassium by a Rieke procedure[90]). Switching to a nickel catalyst system to forge the biaryl bond did not change the outcome and only starting material was recovered. We assumed the steric hindrance around the aryl bromide was too high to get sufficient reactivity for this transformation.



Scheme 25: Attempted intramolecular Ullmann coupling to synthesize tricycle **167**.

Since Ullmann coupling approaches remained unsuccessful in our hands, we turned our attention to palladium catalyzed C–H activation protocols. For this purpose, we slightly modified our Diels–Alder reagents to make the route more step efficient. The esterification was carried out in the first step. Propiolic acid was reacted with 4-methoxyphenol and DCC to ester **168** (65%) and the alkyne was subsequently brominated at the terminal position with silver nitrate and NBS to provide the Diels–Alder precursor **169** in 83% yield (Scheme 26). The attempted reaction of the alkyne moiety with 2-methoxyfuran proceeded smoothly to give an isolable cycloaddition adduct which was converted in situ to bromobenzoate **170** upon exposure to silica gel (72%). The free hydroxyl group was protected as the benzyl ether to afford **171** (BnBr, K_2CO_3, 45%).

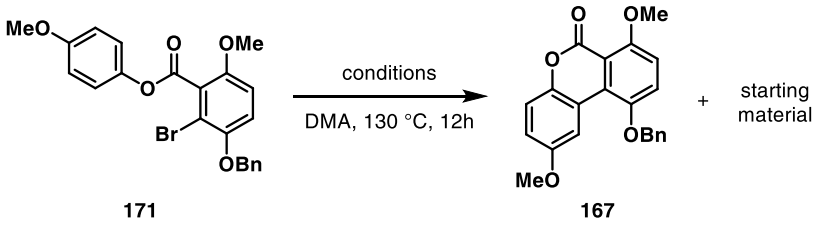
[90] R. D. Rieke, L. D. Rhyne, *J. Org. Chem.* **1979**, *44*, 3445–3446.



Scheme 26: Diels–Alder reaction of bromoalkyne **169** with 2-methoxyfuran to access cyclization precursor **171**.

We screened several conditions to forge the tricycle through C–H activation methods. To have comparable results, all reactions were carried out in *N*,*N*-dimethylacetamide at 130 °C for 12 hours using a catalyst loading of 10 mol%. We commenced with $Pd(PPh_3)_2Cl_2$ catalyst in combination with PPh_3 and sodium acetate as the base. This combination provided a good starting point for further investigations since we obtained 23% of product **167** along with 30% of recovered starting material (Table 1, entry 1). Other Pd(II) sources such as $Pd(OAc)_2$ in combination with sodium acetate or $Pd(OAc)_2$ in combination with P(*n*-Bu)$_3$ and silver(I)oxide (entry 2 and 3) only gave traces of the product. Similarly, $Pd_2(dba)_3$ with sodium acetate proved to be ineffective and no reaction was observed (entry 4). Switching to $Pd(PPh_3)_4$ with silver(I)oxide as the base gave product **167** in 12% yield (entry 5). A significant improvement was obtained when sodium acetate was used instead of silver(I)oxide without changing the catalyst (41%, entry 6). Interestingly, increasing the catalyst loading to 100 mol%, we only observed decomposition (entry 7).

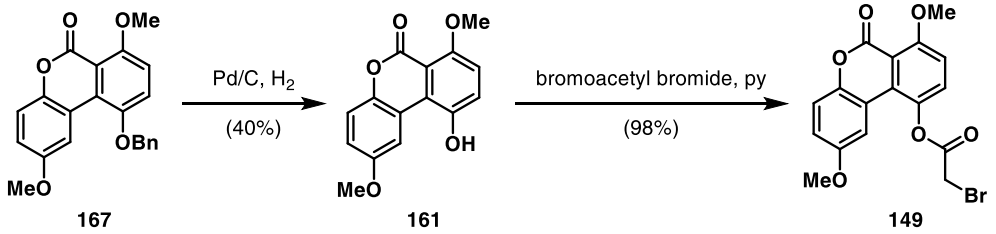
Table 1: Optimization of palladium catalyzed C–H activation.



171 167

entry	catalyst system	base	result
1	$Pd(PPh_3)_2Cl_2$ (10 mol%), PPh_3	NaOAc	product (23%) + starting material (30%)
2	$Pd(OAc)_2$ (10 mol%)	NaOAc	trace of product + starting material
3	$Pd(OAc)_2$ (10 mol%), P(*n*-Bu)$_3$	Ag_2O	trace of product + starting material
4	$Pd_2(dba)_3$ (10 mol%)	NaOAc	no reaction
5	$Pd(PPh_3)_4$ (10 mol%)	Ag_2O	product (12%)
6	$Pd(PPh_3)_4$ (10 mol%)	NaOAc	product (41%)
7	$Pd(PPh_3)_4$ (100 mol%)	NaOAc	decomposition

We continued our synthetic endeavors by hydrogenolysis of the benzyl protecting group (Pd/C, H_2, 40%) followed by esterification of phenol **161** with bromoacetyl bromide to give the northern tricyclic fragment **149** (Scheme 27).



167 161 149

Scheme 27: Completed synthesis of the northern tricycle **149**.

As outlined in the retrosynthesis (Figure 18), we envisioned a modified iodo-carbocyclization to access bicyclic lactone **150** from the cyclization precursor **172** (Figure 21). Key to the proposed synthesis is the utility of a disubstituted double bond that would give the desired substitution pattern. Malonate **172** might arise from an acylation of ester **173**, that in turn could be synthesized through a 1,2-addition of a vinyl lithium species to aldehyde **174**. Aldehyde **174** is known to be accessible through an ozonolysis of cyclopentene.

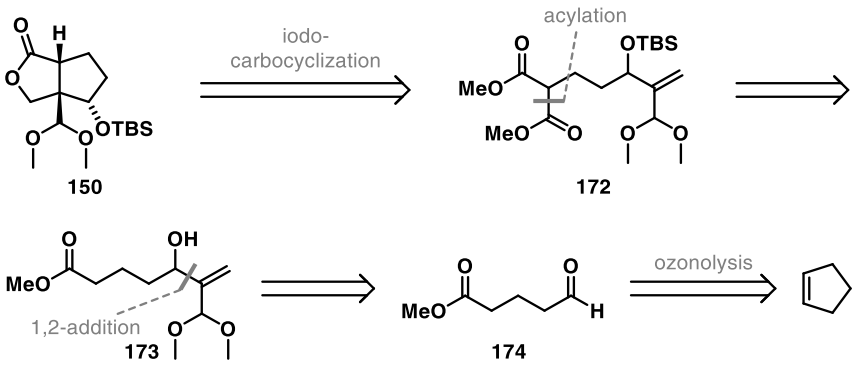
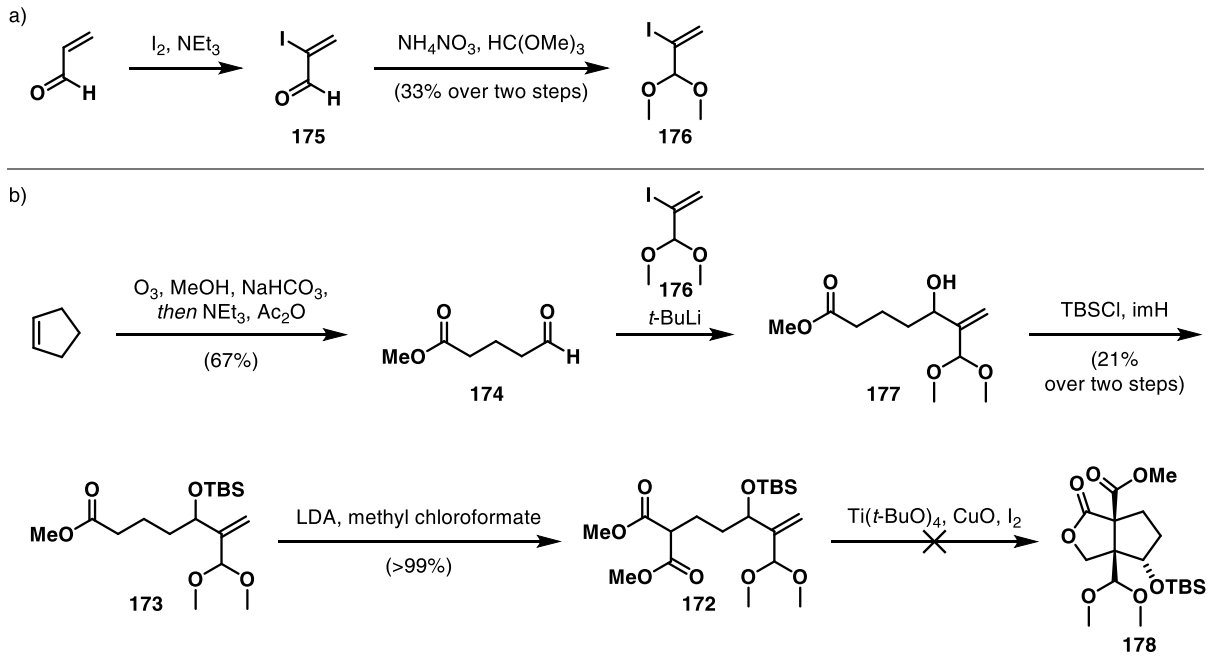


Figure 21: Iodo-carbocyclization of malonate **172** to install the correct substitution pattern of bicycle **150**.

The dimethyl acetal group should be introduced at an early stage. Thus, we commenced with the synthesis of vinyl iodide **176** bearing the dimethyl acetal moiety. **176** was synthesized in two steps from acrolein through iodination (I_2, NEt_3) followed by acetal installation with trimethyl orthoformate and ammonium nitrate (33% over two steps, Scheme 28a).

The ozonolysis of cyclopentene in methanol afforded aldehyde **174** in 67% yield[91]. A 1,2-addition with a vinyl lithium species, derived from halogen lithium exchange of **176** with *t*-BuLi, gave allylic alcohol **177** (Scheme 28b). **177** proved to be slightly unstable upon silica gel purification and was therefore used without further purification in the following TBS protection to furnish silyl ether **173** in 21% yield over two steps. Despite the low yield for the addition reaction, we did not observe any major side product derived from intramolecular lactonization. Next, the acylation of ester **173** was carried out with methyl chloroformate and LDA to give cyclization precursor **172** in excellent yield (>99%). Unfortunately, for the upcoming cyclization reaction, decomposition prevailed under the reaction conditions (Ti(*t*-BuO)$_4$, CuO, I_2) that we attributed to the instability of the acetyl moiety under Lewis acidic conditions.

[91] K. Griesbaum, J. Neumeister, *Chem. Ber.* **1982**, 115, 2697–2706.

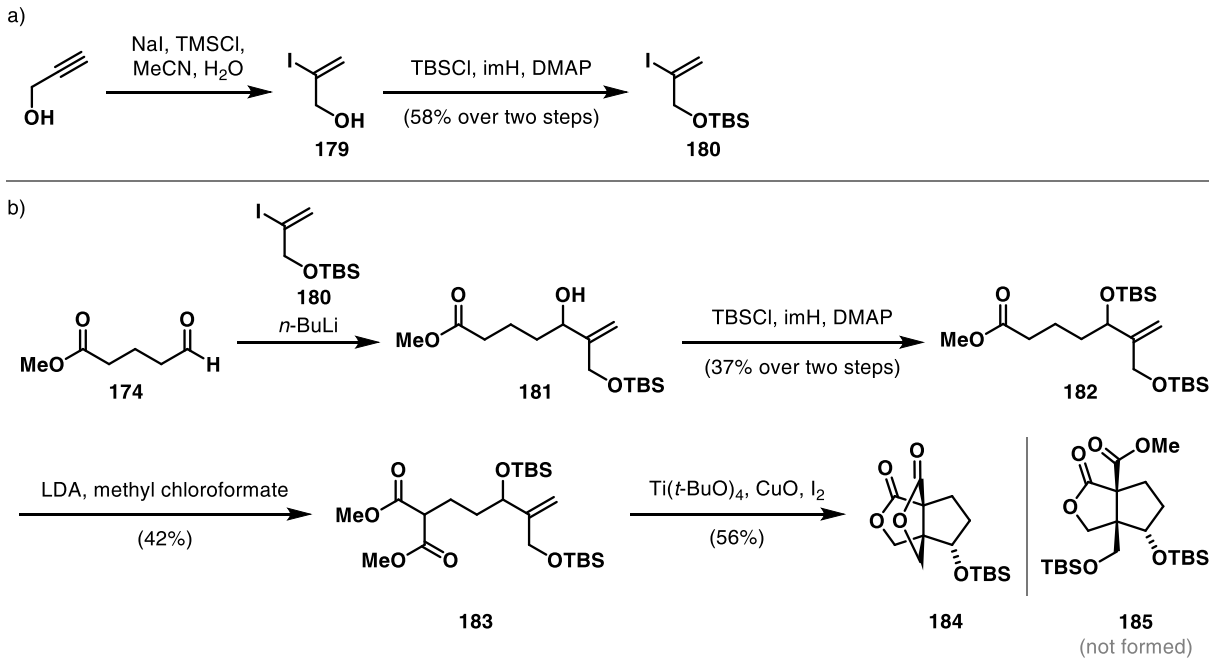


Scheme 28: Synthesis of vinyl iodide **176** (a) and attempted iodo-carbocyclization to access bicycle **178** (b).

Since the acetal proved to be too labile, we assumed that a protected alcohol in place of the acetal group could increase the chance for a successful cyclization. To this end, we synthesized vinyl iodide **180** (Scheme 29a) in two steps from a regioselective addition of hydrogen iodide (formed in situ from NaI, TMSCl and H_2O)[92] to propargyl alcohol followed by a silylation with TBSCl (58% over two steps).

In analogy to the previous synthesis, a 1,2-addition was followed by a TBS protection of allylic alcohol **181** (35% over two steps, Scheme 29b). The acylation with methyl chloroformate performed worse (42%) but gave enough material for the upcoming reaction. We tested malonate **183** in the cyclization reaction but only observed the formation of propellane **184** (56%) instead of bicycle **185**. The use of Lewis acidic conditions (that presumably removed the silyl protecting group) in combination with the geometrically proximity of the primary alcohol and the methyl ester led to the formation of **184**. Even though structurally interesting, further functionalization of **184** was not carried out due to foreseen chemoselectivity issues.

[92] J.-L. Gras, Y. Y. K. W. Chang, M. Bertrand, *Tetrahedron Lett.* **1982**, *23*, 3571–3572.

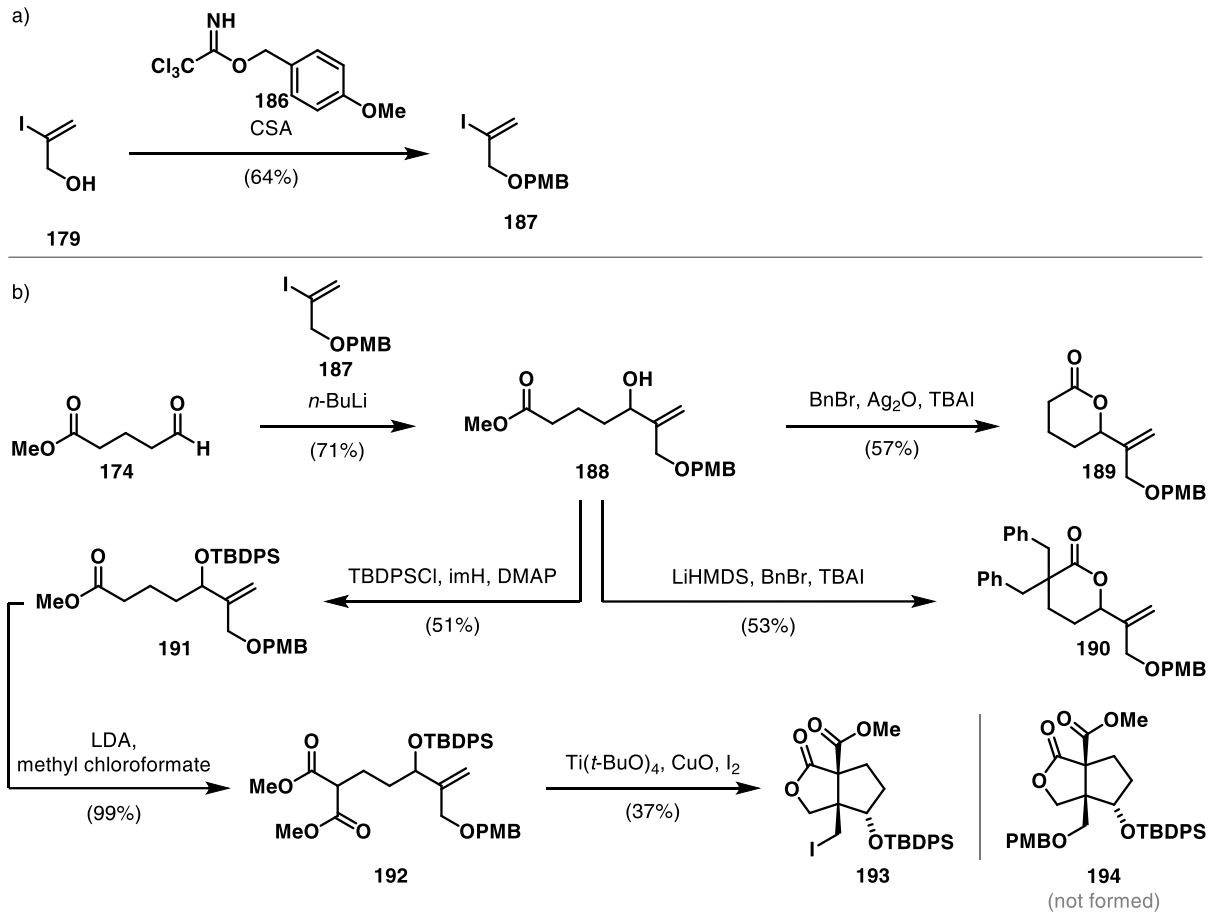


Scheme 29: Iodo-carbocyclization of malonate **183** formed propellane **184**.

We assumed that the combination of a PMB ether on the primary alcohol and a benzyl protecting group on the secondary alcohol would be an ideal choice since they can be removed orthogonally and are stable under acidic conditions. The PMB protected allylic alcohol **187** was synthesized from **179** with Bundle's reagent under acidic conditions (CSA, 64%, Scheme 30a)[93] and the 1,2-addition proceeded smoothly to give allylic alcohol **188** in 71% yield (Scheme 30b). In our hands, the benzylation of allylic alcohol **188** proved to be unsuccessful. Under the conditions shown (BnBr, Ag_2O and TBAI) either no reaction took place or competing lactonization to **189** occurred (57%). When an excess of LiHMDS and BnBr were applied, alpha dibenzylated lactone **190** was isolated (53%). Since we were able to protect the secondary allylic alcohol with a silicon protecting group, we introduced the TBDPS ether which should withstand slightly acidic conditions. The desired silyl ether **191** was obtained in moderate yields from **188** by reaction with TBDPSCl and imidazole (51%). **191** was then acylated under standard conidtions to give **192** (99%). The iodo-carbocyclization reaction gave 5/5-lactone **193** but surprisingly the PMB ether was displaced by iodide. Presumably, CuO that is used as a scavenger for hydrogen iodide also acts as an oxidant for the PMB ether. The intermediate oxonium ion that results from this oxidation is likely to be displaced by iodide (not shown).

Due to this unforeseen outcome of the cyclization reaction, we aimed at switching the PMB group to the benzyl protecting group (vide infra).

[93] T. Iversen, D. R. Bundle, *J. Chem. Soc., Chem. Commun.* **1981**, 1240–1241.

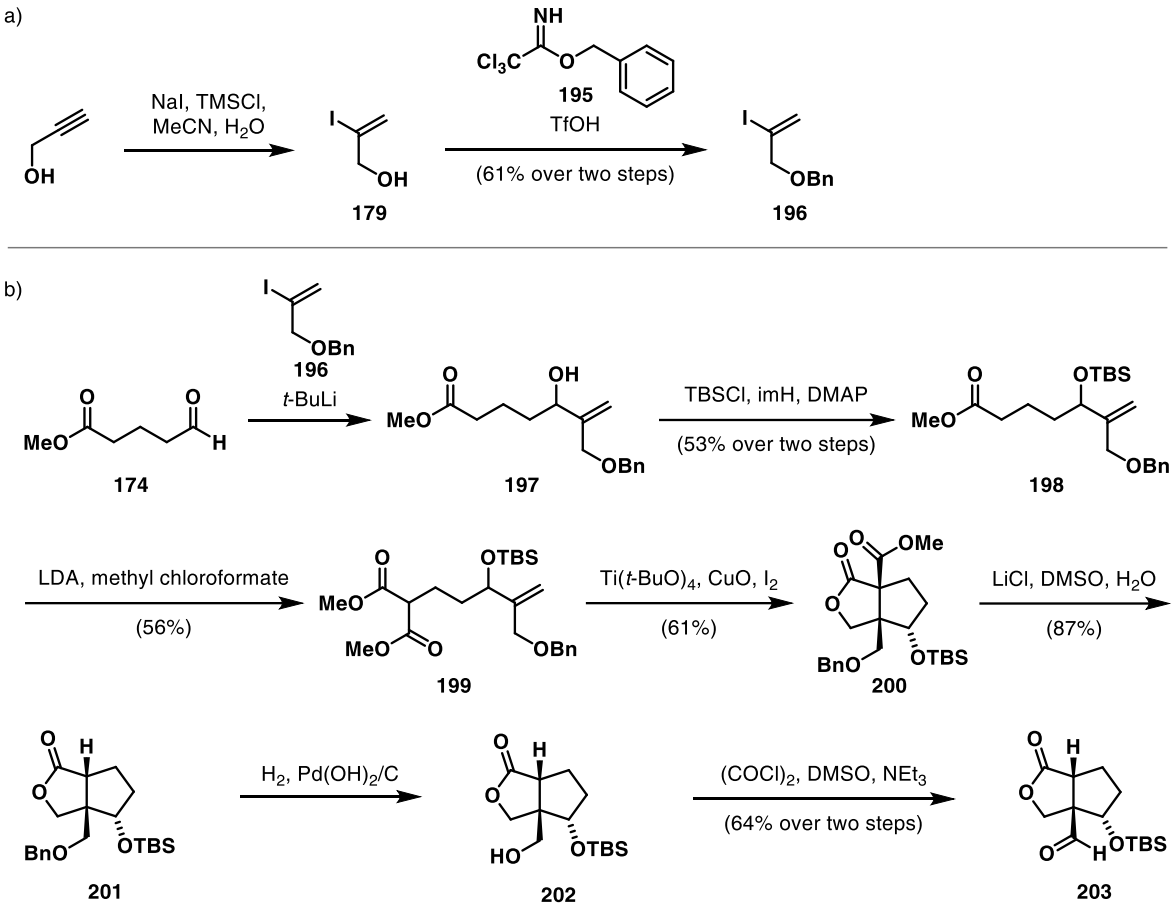


Scheme 30: Synthesis of vinyliodide **187** (a) and bicyclic lactone **193** (b).

We surmised that the benzyl group on the primary alcohol should be stable under the Lewis acidic reaction conditions of the iodo-carbocyclization. Vinyl iodide **196** was prepared in two steps from propargyl alcohol in 61% yield (Scheme 31a).

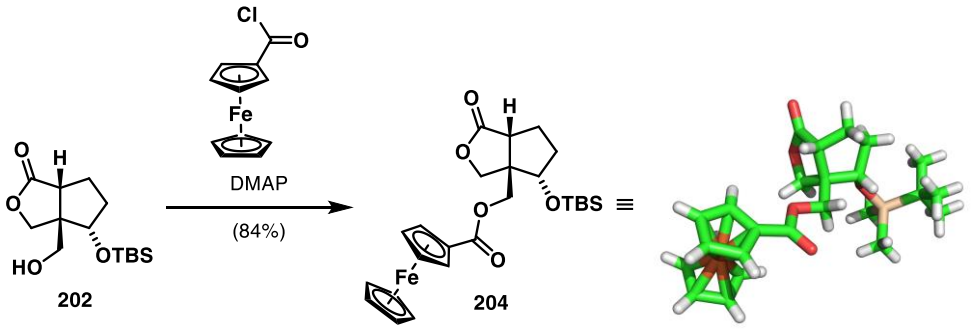
In analogy to the beforementioned synthesis, a 1,2-addition was carried out, followed by TBS protection of allylic alcohol **197** (Scheme 31b). The acylation of ester **198** with LDA and methyl chloroformate yielded malonate **199** (56%). Pleasingly, the cyclization proceeded in 61% yield giving **200** as one diastereomer. The methyl ester, that served as a functional handle for the iodo-carbocyclization, was cleaved using Krapcho decarboxylation conditions (LiCl in wet DMSO at 140 °C)[86] to give bicyclic lactone **201** in 87% yield. To overcome the lack of reactivity that was observed in the debenzylation of **201** under standard hydrogenolysis conditions (Pd/C and atmospheric pressure of hydrogen gas), we had to employ a hydrogen pressure of 40 bar and resort to the more reactive Pearlman's catalyst.[94] A subsequent Swern oxidation[95] resulted in the formation of aldehyde **203** in 64% yield over two steps.

[94] W. M. Pearlman, *Tetrahedron Lett.* **1967**, *8*, 1663–1664.
[95] K. Omura, D. Swern, *Tetrahedron* **1978**, *34*, 1651–1660.



Scheme 31: Successful synthesis of bicyclic lactone **203**.

At this stage, we wanted to verify if the key iodo-carbocyclization reaction provided indeed the correct diastereomer. Liquid intermediates hampered the structural elucidation via X-ray crystallography. Primary alcohol **202** was an ideal intermediate for further derivatization. We prepared ferrocenecarboxylic ester **204** from **202** that was a yellow solid (84%, Scheme 32). We were able to grow crystals that were suitable for X-ray crystallography and verified the relative configuration of ester **204**.

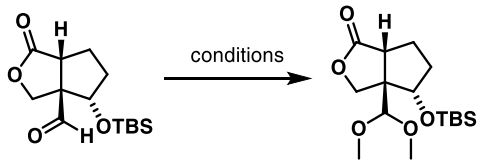


Scheme 32: Verification of the relative configuration of ferrocenecarboxylic ester **204** via X-ray crystallography.

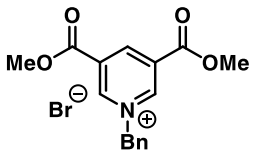
With aldehyde **203** in hand, we opted for the protection as the dimethyl acetal. To our surprise, this protection proved to be more challenging than expected and standard conditions that use Brønsted or

Lewis acids in combination with methanol led either to decomposition (Table 2, entry 1) or no reaction (entry 2 and 3). We resorted to a relatively new method for visible-light-induced acetalization of aldehydes that required the use of the photocatalyst eosin Y.[96] It is hypothesized that upon irradiation with light, a photogenerated acidic species from eosin Y is formed that eventually catalyzes the acetalization. However, also this method failed for aldehyde **203** (entry 4). Another way to catalytically generate an acid in situ represents the combination of the pyridinium salt shown in entry 5 and methanol.[97] Unfortunately, this combination did not promote the acetalization in our case and only starting material was recovered. To our delight, the use of the acidic resin Dowex 50WX4 in combination with trimethyl orthoformate afforded the product in 81% yield (entry 6). Remarkably, while the use of *p*-TsOH resulted in decomposition, the immobilized sulfonic acid groups on the resin of Dowex gave clean conversion to the product highlighting that marginally different reagents could have significantly different reaction outcomes.

Table 2: Screening of the acetalization conditions to furnish aldehyde **150**.



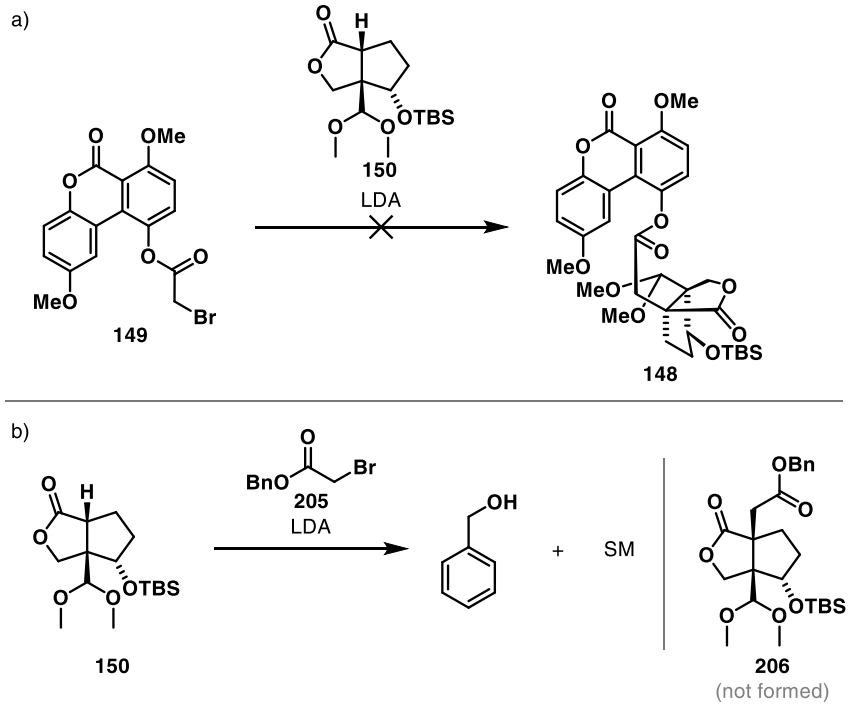
203 **150**

entry	conditions	result
1	*p*-TsOH, MeOH	decomposition
2	$TiCl_4$, MeOH, NEt_3	no reaction
3	NH_4NO_3, MeOH	no reaction
4	Eosin Y, MeCN/ MeOH green LEDs	no reaction
5	 + MeOH	no reaction
6	Dowex 50WX4, $HC(OMe)_3$	81%

The attempted alkylation of lactone **150** with α-bromoester **149** did not occur (Scheme 33). While **150** was recovered from the reaction mixture, α-bromoester **149** decomposed under the reaction conditions. Presumably, **149** is more acidic than **150** and hence gets deprotonated by the enolate derived from lactone **150** and LDA. The so formed anion might eliminate phenol **161** and form a ketene which could engage in decomposition pathways. To verify this hypothesis, we attempted the alkylation of bicycle **150** with α-bromoester **205**. Under similar reaction conditions using LDA as the base, we were able to

[96] H. Yi, L. Niu, S. Wang, T. Liu, A. K. Singh, A. Lei, *Org. Lett.* **2017**, *19*, 122–125.
[97] B. Procuranti, S. J. Connon, *Org. Lett.* **2008**, *10*, 4935–4938.

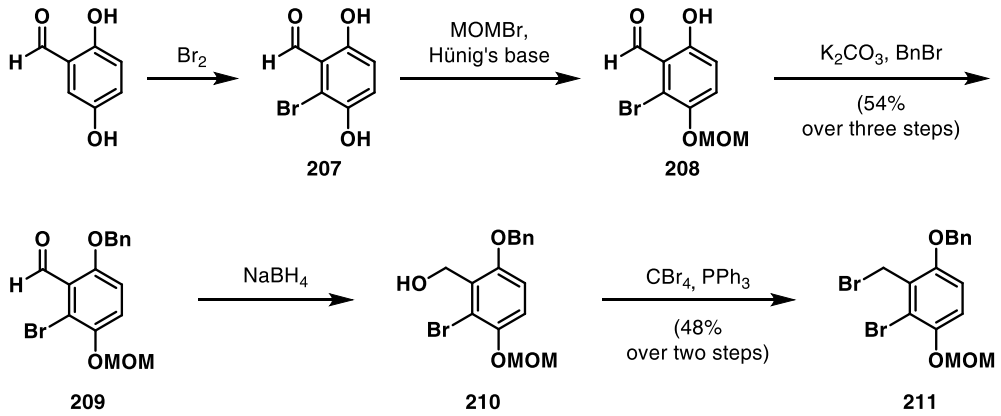
recover **150** together with benzyl alcohol that indeed could arise from an elimination in course of a ketene formation.



Scheme 33: Attempted alkylation of northern tricycle **149** with southern lactone **150** (a) and a control experiment of an alkylation of **150** with α-bromoester **205** (b).

Besides the intramolecular C–H activation to forge the tricycle, we also investigated a copper mediated reductive biaryl coupling (vide infra). To this end, we prepared benzyl bromide **211** from commercially available and inexpensive 2,5-dihydroxybenzaldehyde in five steps (Scheme 34). A regioselective bromination gave bromobenzaldehyde **207** that was treated with MOMBr and Hünig's base to chemoselectively protect one hydroxyl group. A discrimination between the hydroxyl groups is possible due to intramolecular hydrogen bonding of one OH group to the aldehyde moiety. Subsequently, the remaining hydroxy functionality of **208** was protected orthogonal to the MOM group as the benzyl ether to give **209** (54% over three steps). Aldehyde **209** was reduced with sodium borohydride to benzyl alcohol **210**. An Appel bromination[98] of the benzylic alcohol furnished benzyl bromide **211** in 48% yield over two steps.

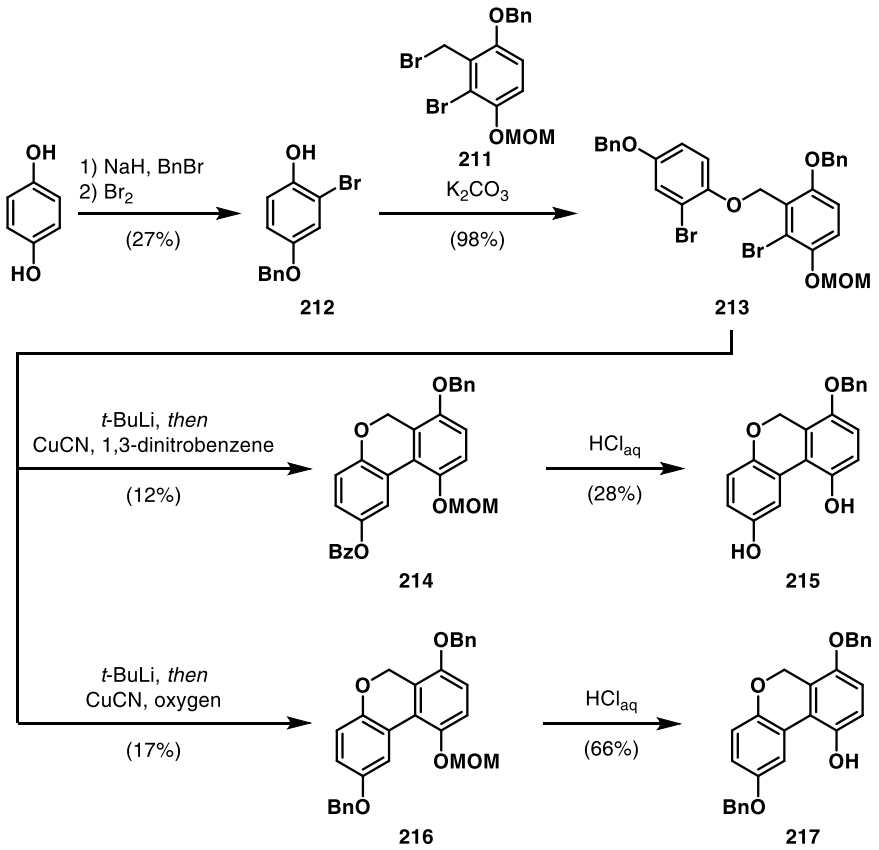
[98] R. Appel, *Angew. Chem. Int. Ed.* **1975**, *14*, 801–811.



Scheme 34: Synthesis of benzyl bromide **211** that serves as a reactant for a copper mediated reductive biaryl coupling.

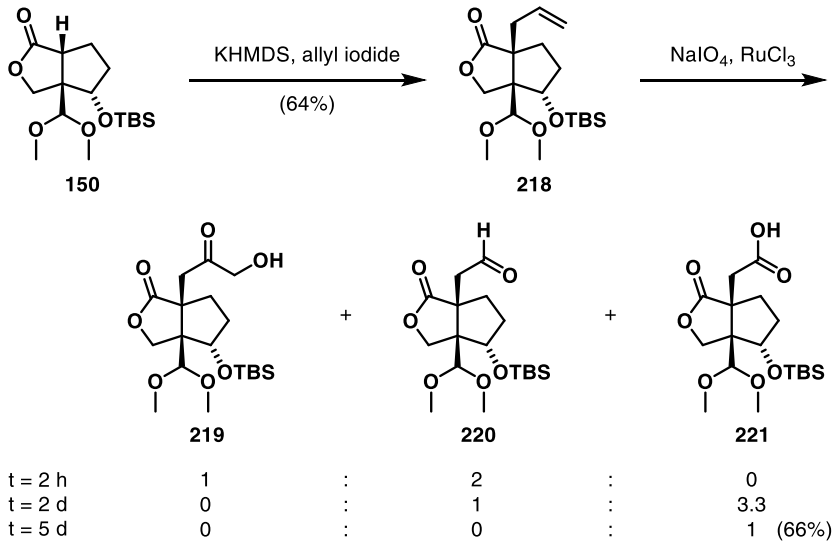
Bromophenol **212** was synthesized from hydroquinone by benzylation followed by bromination (27%, Scheme 35). Cyclization precursor **213** was obtained in almost quantitative yield via a reaction of **212** with benzyl bromide **211** (98%). Employing conditions reported by Schreiber[99] for the copper mediated reductive coupling (a methodology initially introduced by Lipshutz[100]), we observed the formation of the desired tricycle **214** in poor yield (12%). Notably, a concomitant oxidation of a benzyl protecting group to the benzoate was observed. Treatment of **214** with aqueous hydrochloric acid afforded tricycle **215** (28%). We assumed that the oxidant 1,3-dinitrobenzol initiated the reductive coupling of an intermediate organocuprate and also oxidized the benzylic position. Therefore, switching to a milder oxidant in the reductive coupling step could avoid the undesired oxidation. In fact, employing oxygen gas as the oxidant suppressed the oxidation of the benzyl group and slightly improved the yield (17%). Aqueous hydrochloric acid removed the MOM ether to give tricycle **217** (66%).

[99] D. R. Spring, S. Krishnan, S. L. Schreiber, *J. Am. Chem. Soc.* **2000**, *122*, 5656–5657.
[100] B. H. Lipshutz, K. Siegmann, E. Garcia, *J. Am. Chem. Soc.* **1991**, *113*, 8161–8162.



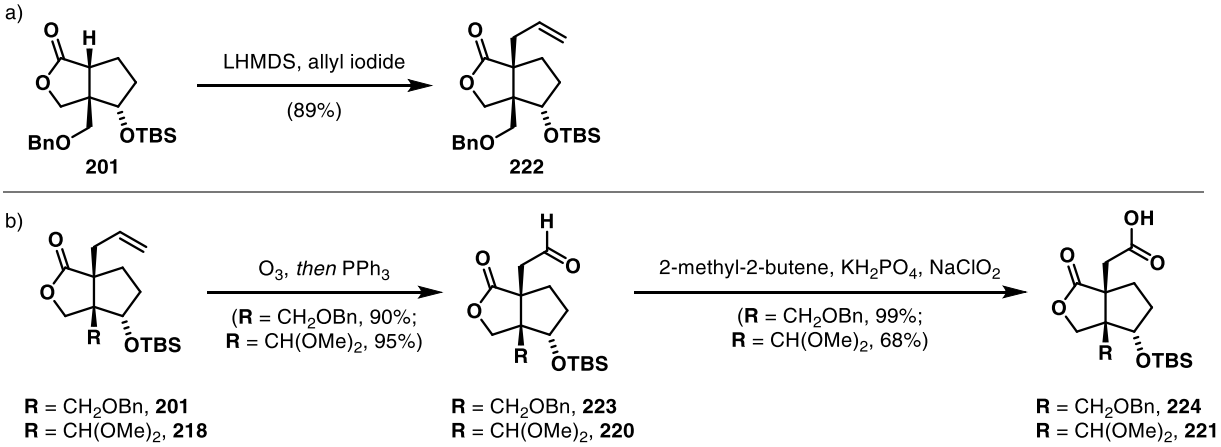
Scheme 35: Synthesis of tricycles **215** and **217** via a copper mediated reductive coupling.

Merging of the northern with the southern hemisphere failed through an alkylation. Next, we attempted to connect both fragments through an esterification. With the northern tricyclic phenol **217** already in hand, we focused on the synthesis of acid **221**. To this end, bicyclic lactone **150** was first allylated with (KHMDS, allyl iodide) to yield **218** (64%, Scheme 36). The alkylation had to be carried out at 23 °C since typical cryogenic conditions (–78 °C) did not give any conversion presumably due to steric reasons at the neopentyl position. Afterwards, the allyl group was oxidatively cleaved using $RuCl_3$ as the catalyst and sodium periodate as the stochiometric co-oxidant. Reaction times were crucial for the outcome of the oxidation. Full conversion of **218** was already achieved after two hours but the products obtained were alpha hydroxy ketone **219** and aldehyde **220**. Only after a prolonged reaction times (five days) we were able to solely obtain the desired acid **221** (66%).



Scheme 36: Allylation of lactone **150** followed by an oxidative degradation of the double bond.

The direct conversion of the double bond to the carboxylic acid **221** had two drawbacks. The long reaction times made the scale-up of **221** very tedious. Furthermore, while the deconstructive oxidation of the double bond with $RuCl_3$ and $NaIO_4$ proceeded smoothly on small scale (≤ 5 mg, 66%), yields dropped significantly when the reaction scale was increased (10 mg to 20 mg, 24%). For this reason, we carried out the oxidation of **218** and **201** (synthesized through an allylation, Scheme 37a) to their corresponding acids **221** and **224** through a more conservative two step protocol: ozonolysis to the aldehyde followed by Pinnick–Lindgren–Kraus oxidation[101] to the acid (Scheme 37b). The yields of these reactions proved to be consistently good, operationally simple and the reaction also proceeded faster than the previous one-step oxidation.

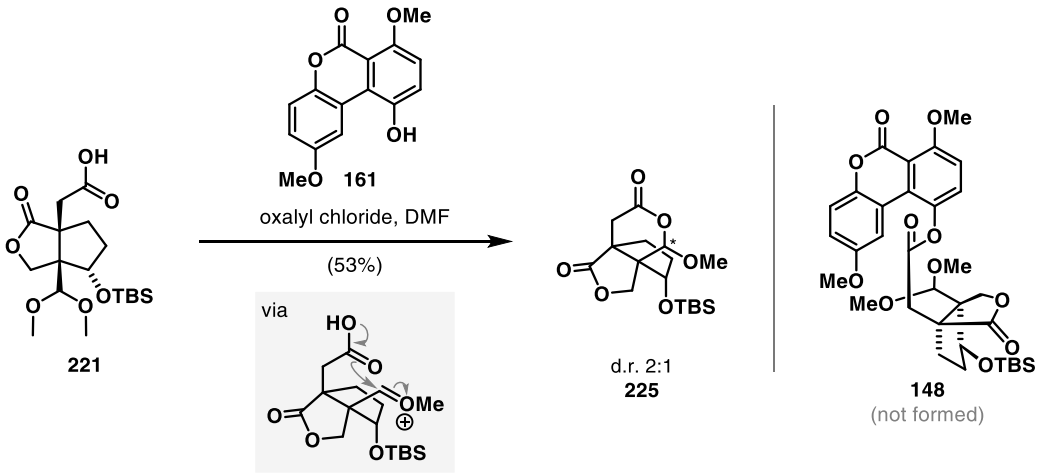


Scheme 37: Allylation of **201** to form bicyclic lactone **222** (a). Oxidation of the double bond to the corresponding carboxylic acid through an ozonolysis and Pinnick–Lindgren–Kraus reaction (b).

With both building blocks in hand, we attempted to merge them through an esterification via an acid chloride (Scheme 38). Acid **221** was treated with oxalyl chloride. Adding phenol **161** to this intermediate, however, did not furnish the desired ester **148** but instead gave lactone acetal **225**

[101] B. O. Lindgren, T. Nilsson, *Acta. Chem. Scand.* **1973**, *27*, 888–890.

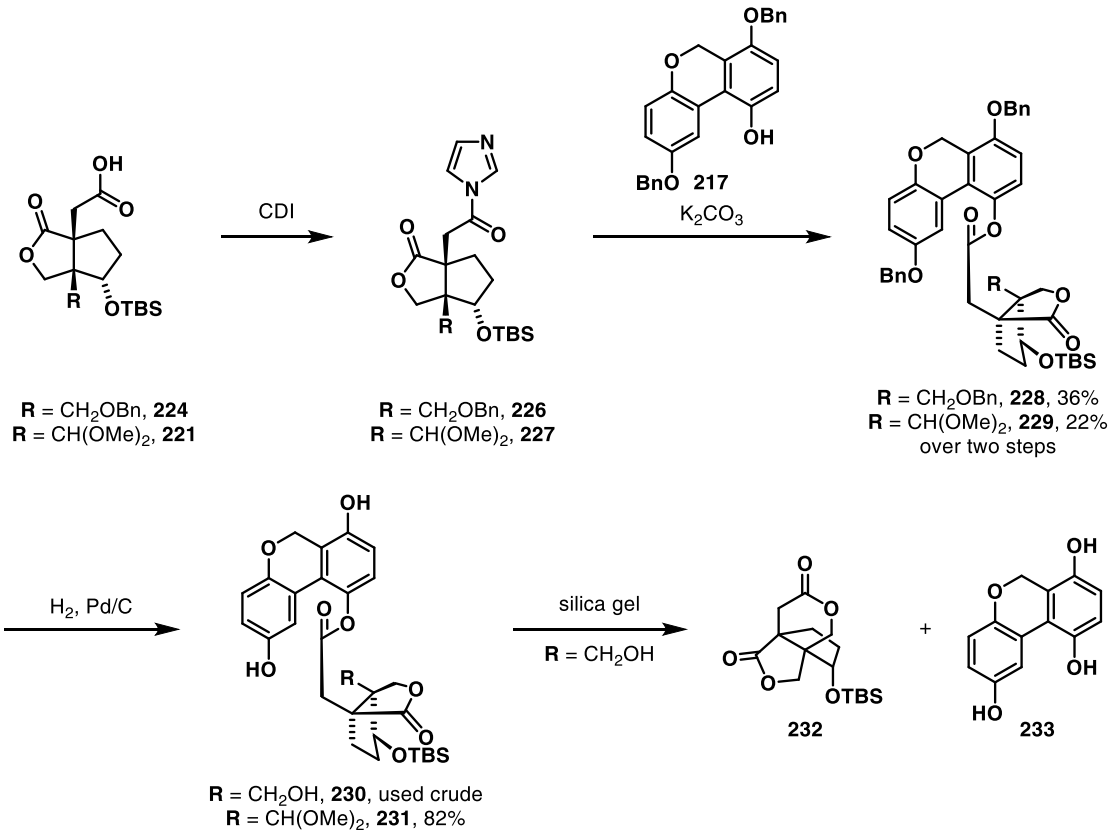
(d.r. = 2:1, 53%). Phenol **161** was recovered from the reaction mixture. We surmised that under the reaction conditions small amounts of hydrochloric acid are being formed which trigger the formation of an oxonium ion from the dimethyl acetal which is than intramolecularly trapped by the carboxylic acid. This assumption was tested by reacting acid **221** with oxalyl chloride and DMF without the presence of phenol **161**. In this case we observed the formation of lactone acetal **225** as well.



Scheme 38: Synthesis of lactone acetal **225** via an oxonium intermediate.

To avoid the detrimental effect of acid in the reaction mixture, we decided to use CDI (Staab's reagent[102]) to activate the acid moiety under basic conditions (Scheme 39). Clean and isolable carbonylimidazoles **226** and **227** were obtained by reaction of **224** and **221** with CDI. These intermediates were subjected to esterification with tricycle **217** to furnish ester **228** (36%) and **229** (22%). Debenzylation took place under hydrogenolysis with Pd/C to give **230** (used crude) and **231** (82%). Ester **230** had to be used without the advantage of silica gel purification as it readily formed lactone **232** and tricycle **233** under slightly acidic conditions.

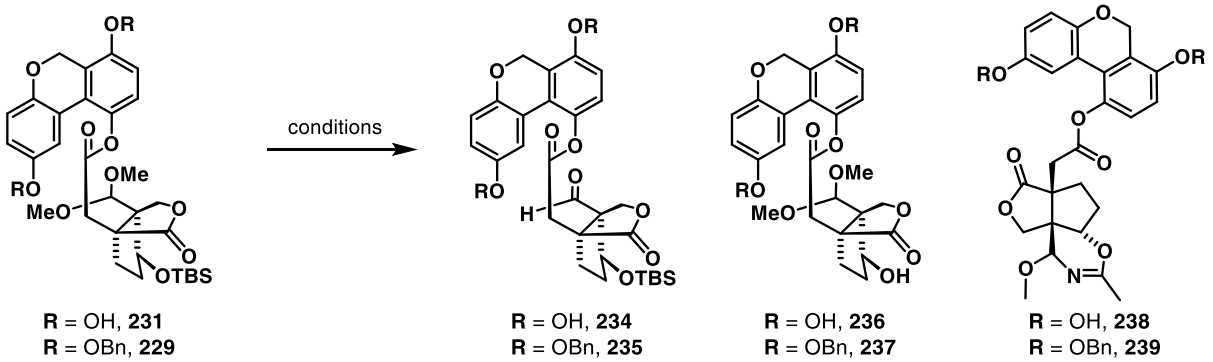
[102] H. A. Staab, *Angew. Chem. Int. Ed.* **1962**, *1*, 351–367.



Scheme 39: Merging of the southern bicyclic lactone fragment with the northern tricyclic moiety **217** to afford esters **228** and **229** that were further debenzylated.

With the cyclization precursor in hand, we applied several Lewis and Brønsted acids to initiate a cationic cyclization as outlined in the retrosynthesis. We only observed deprotection of the acetal and desilylation applying various acids. This outcome was independent of the residue on the hydroxyl groups (Table 3, entry 1 to 5). Remarkably, amidate **239** was formed when **231** was treated with boron trifluoride in acetonitrile. We assumed that the formation of the amidate arose from a nucleophilic addition of acetonitrile to the in situ formed oxonium ion and further cyclization with the secondary alcohol (derived from desilylation).

Table 3: Conditions tested for the attended cationic cyclization.



entry	residue, **R** =	conditions	result
1	Bn	$SnCl_4$, DCM, –78 °C to 23 °C	starting material + **234** + **236**
2	Bn	*p*-TsOH, MeOH, 0 °C to 23 °C	starting material + **236**
3	Bn	TMSCl, NaI, MeCN, 23 °C	**234**
4	H	*p*-TsOH, HFIP, 23 °C	complex mixture
5	H	HCl, MeOH, 0 °C to 23 °C	starting material + **237**
6	H	BF_3•OEt_2, MeCN, –78 °C	**239**

Compared to the cationic cyclization approach, a retrosynthetic analysis based on a Fries rearrangement would give the same intermediate **148** that might serve as the starting material to build the core dioxaspirocycle of ganoapplanin (**19**) (Figure 22). Importantly, the regioselectivity of the radical recombination might hamper the success of the reaction outcome.

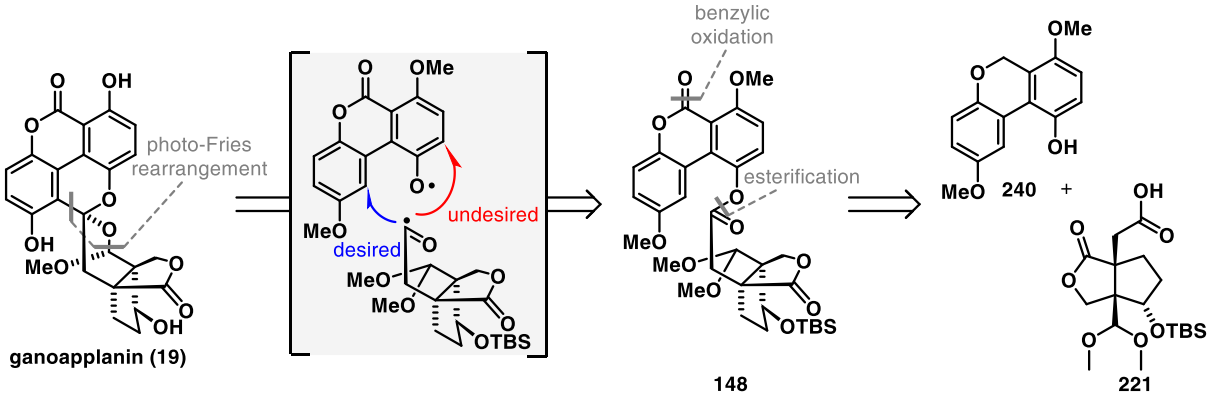
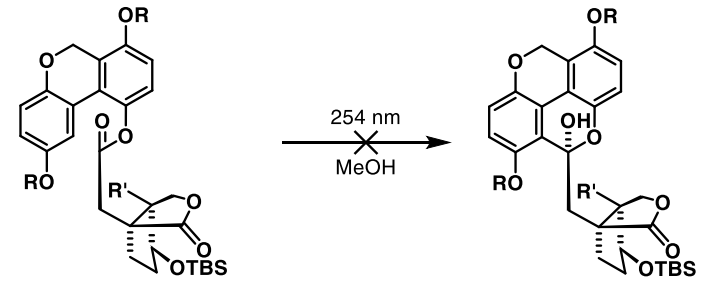


Figure 22: Retrosynthesis of ganoapplanin (**19**) based on a Fries rearrangement disconnection.

As depicted in Scheme 40, we irradiated various esters that differ in the presence of protecting groups on the phenolic hydroxy moiety and in the residue R' that was either a primary benzyl ether or a dimethyl acetal. Since typical Fries rearrangements require the use of strong Lewis acids in combination with high temperatures ($AlCl_3$ and around 140 °C)[103] we opted for the photochemical Fries variant that

[103] K. Fries, G. Finck, *Ber. Dtsch. Chem. Ges.* **1908**, *41*, 4271–4284.

usually takes place under UV light irradiation.[104] Unfortunately, when esters **230**, **228** and **231** were irradiated at 254 nm, rapid decomposition was observed.



R = H, **R'** = CH_2OBn, **230**
R = Bn, **R'** = CH_2OBn, **228**
R = H, **R'** = $CH(OMe)_2$, **231**

Scheme 40: Attempted photo-Fries rearrangement to access tetracycle of ganoapplanin (**19**).

4.3. Diels–Alder Approach

Since previous attempts to access ganoapplanin failed, we designed a new synthetic approach that disconnected the northern hemisphere differently but still utilized the bicyclic lactone motif that we have already successfully synthesized. We realized that the core dioxaspirocycle as well as the tetracyclic northern hemisphere with a tetrasubstituted biaryl bond would pose a significant synthetic challenge. In a first step, we envisioned to disconnect the C–O bonds of the tetracyclic northern framework giving the tetrasubstituted biaryl **241** (Figure 23). A retrosynthetic analysis of biaryl **241** revealed a possible Diels–Alder retron arising from the reaction of 2-methoxyfuran with alkyne **242** or **243**. We reasoned that the regioselectivity for the cycloaddition could be mainly governed by an electronical match of the partial negative charge on 2-methoxyfuran and the partial positive charge on the dienophile. The ketones **242** or **243** would arise from an addition of phenylacetylene **244** or diyne **245** to aldehyde **220** followed by an oxidation. Aldehyde **220** was already prepared by an iodo-carbocyclization reaction.

[104] J. C. Anderson, C. B. Reese, *Proc. Chem. Soc.* **1960**, 217.

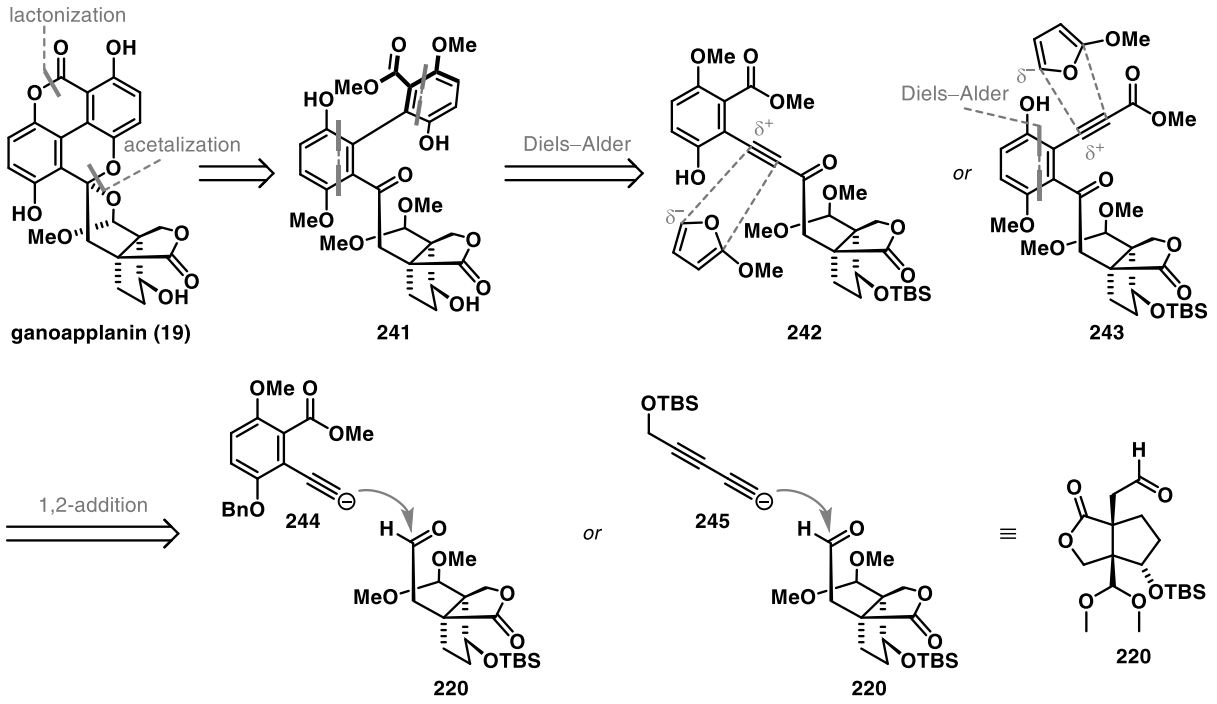


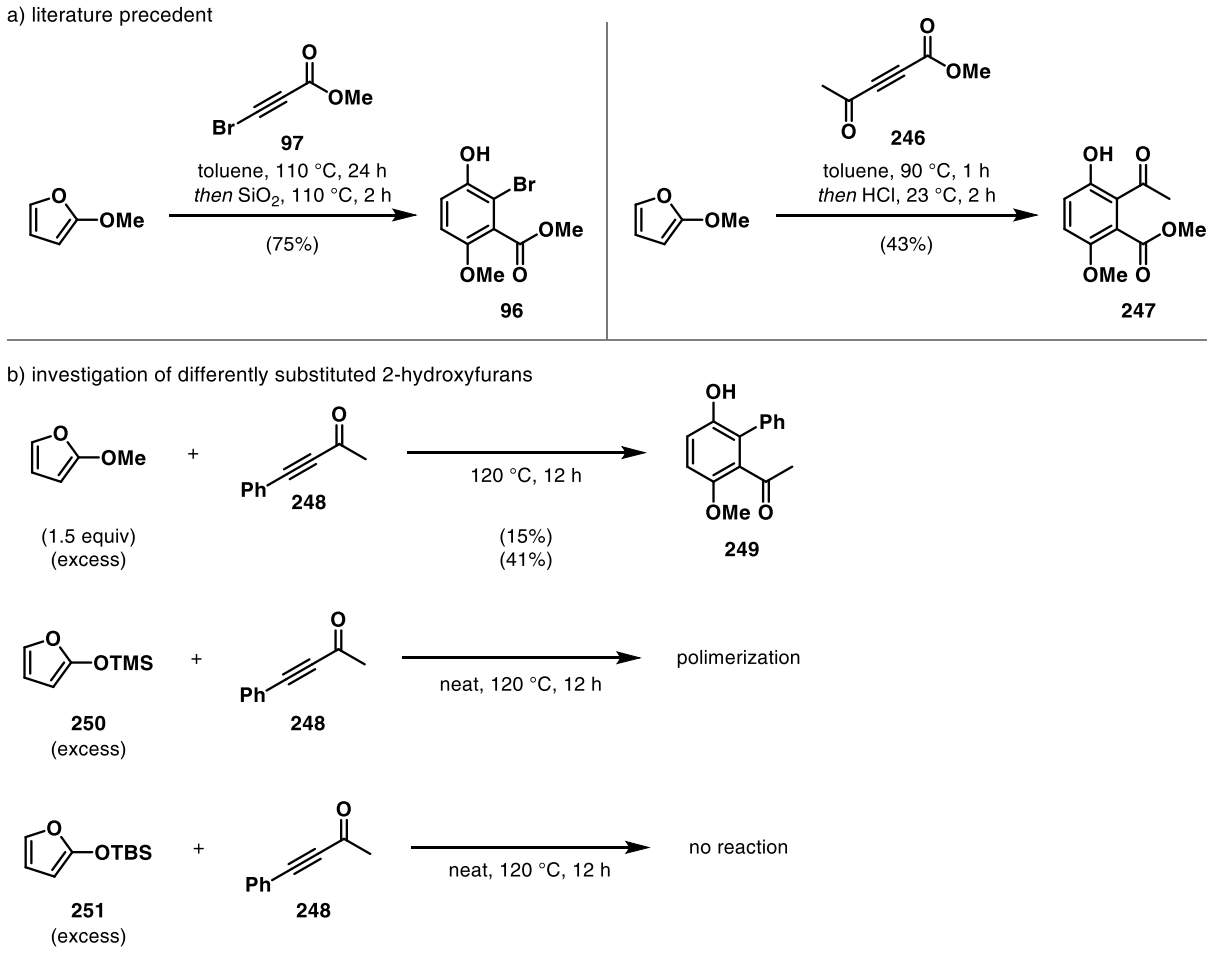
Figure 23: Retrosynthesis of ganoapplanin (19) based on a Diels–Alder reaction of 2-methoxyfuran with an alkyne.

Cycloadditions of 2-methoxyfuran with triple bonds are scarce in the literature and are limited to arynes[105,106] or highly activated alkynes.[107,108,109] To the best of our knowledge, a Diels–Alder reaction of this kind has never been applied to structurally complex molecules in total synthesis. Representative examples that closely relate to our total synthesis include the cycloaddition of 2-methoxyfuran with bromoalkyne **97**[70] or with alkyne **246**[110] that readily form hydroquinone moieties in good to moderate yields (Scheme 41a).

In this context, we aimed for a cycloaddition of 2-methoxyfuran with alkyne **248** that served as a model system as it reflected the electronical and steric properties of substrate **242** or **243**. An initial attempt proved to be successful and reacted 2-methoxyfuran (1.50 equiv) with alkyne **248** in toluene at 120 °C to hydroquinone **249** in 15% yield (Scheme 41b). Notably, no additional aromatization step with an acid was required to yield the hydroquinone. When performing the reaction neat with an excess of 2-methoxyfuran we were able to increase the yield to 41%. In addition to 2-methoxyfuran, we also investigated TMS and TBS protected 2-hydroxyfuran **250** and **251** in their cycloaddition behaviour with alkyne **248**. Surprisingly, both diynes did not undergo cycloadditions. TMS 2-hydroxyfuran **250** was

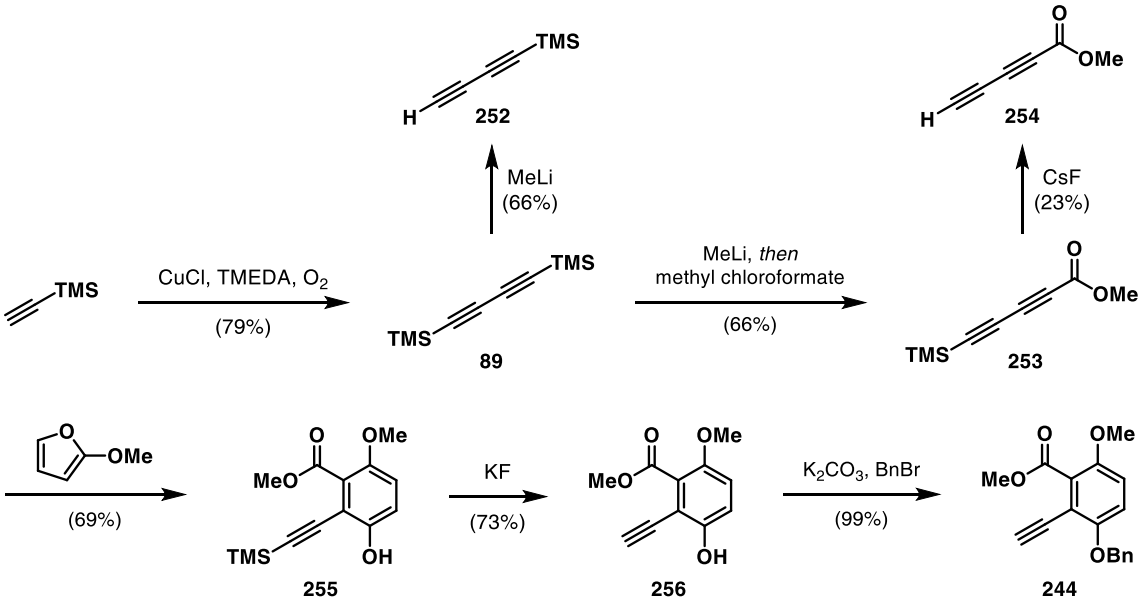
[105] G. E. Collis, A. K. Burrell, *Tetrahedron Lett.* **2005**, *46*, 3653–3656.
[106] M.-X. Zhang, W. Shan, Z. Chen, J. Yin, G.-A. Yu, S. H. Liu, *Tetrahedron Lett.* **2015**, *56*, 6833–6838.
[107] G.-D. Zhu, M. A. Staeger, S. A. Boyd, *Org. Lett.* **2000**, *2*, 3345–3348.
[108] A. Moreno, M. V. Gómez, E. Vázquez, A. de la Hoz, A. Díaz-Ortiz, P. Prieto, J. A. Mayoral, E. Pires, *Synlett* **2004**, *2004*, 1259–1263.
[109] H. Shinohara, M. Sonoda, N. Hayagane, S. Kita, S. Tanimori, A. Ogawa, *Tetrahedron Lett.* **2014**, *55*, 5302–5305.
[110] A. Nawrotek, S. Benabdi, S. Niyomchon, M.-H. Kryszke, C. Ginestier, T. Cañeque, L. Tepshi, A. Mariani, R. P. St.Onge, G. Giaever, C. Nislow, E. Charafe-Jauffret, R. Rodriguez, M. Zeghouf, J. Cherfils, *Nat. Chem. Biol.* **2019**, *15*, 358–366 (see supporting information of the reference).

prone to polymerization under the reaction conditions while the TBS 2-hydroxyfuran did not show any reaction with **248**.



Scheme 41: Literature known cycloadditions of 2-methoxyfuran (a) and investigation of the Diels–Alder reaction of 2-hydroxyfurans with alkyne **248** (b).

With these optimized reaction conditions in hand, we prepared diynes **252** and **254** as well as phenylacetylene **244** that we opted to react with the aldehyde moiety of our bicyclic lactone **220**. Diyne **89** was prepared by a Hay dimerization[67] of trimethylsilylacetylene in 79% yield (Scheme 42). Treatment of **89** with methyllithium followed by an aqueous work-up gave the first diyne **252** in 66% yield. When the intermediate lithium acetylide was quenched with methyl chloroformate **253** was obtained (66%). Transformation to the second diyne **254** was accomplished by desilylation with CsF (27%). To access phenylacetylene **244**, we performed a first Diels–Alder between **253** and 2-methoxyfuran to give hydroquinone **255** in good yield (69%). Finally, the removal of the TMS protecting group with KF followed by a benzylation of the hydroxy moiety yielded phenylacetylene **244** (BnBr, K_2CO_3, 99%).



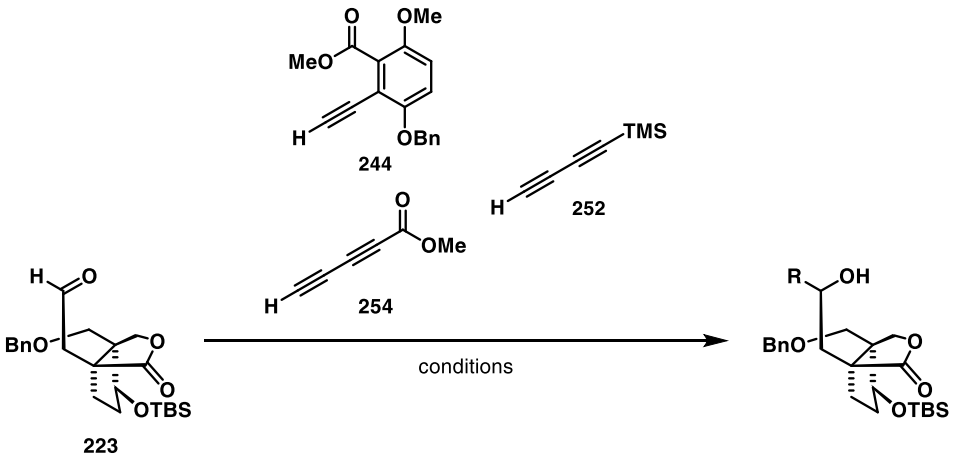
Scheme 42: Synthesis of various alkynes and diynes for the addition to the bicyclic southern fragment.

The synthetic planned called for a 1,2-addition of alkynes **252**, **254** or **244** to the aldehyde of bicycle **223**. We started our investigation with the addition of phenylacetylene **244** employing conditions reported by Carreira ($Zn(OTf)_2$ and triethylamine)[111] that however led to decomposition of the reactants (Table 4, entry 1). A deprotonation of the alkyne with LDA did not yield any addition product (entry 2). Noteworthy, addition of deuterium oxide revealed a deuterium incorporation alpha to the aldehyde group indicating that an enolization of the carbonyl moiety under the influence of the organometallic species occurred. To overcome the basicity of the lithium acetylide, we added cerium trichloride to the reaction mixture to conduct a transmetalation forming a more nucleophilic and less basic organocerium species.[112] Unfortunately, this did not have the desired reaction outcome and no conversion was observed (entry 3). Changing the base from LDA to *n*-BuLi did not change the reaction outcome (entry 4). Based on the lack of reactivity of phenylacetylene **244**, we focused on diyne **254**. Initial attempts to add diyne **254** to the aldehyde by a deprotonation with LDA led to decomposition of the diyne presumably due to reaction of the lithium acetylide with the carbonyl moiety of another diyne **254** molecule (entry 5). Using the less reactive zinc acetylide species (formed by diethyl zinc) did not give any addition product either (entry 6). Eventually, we concentrated on diyne **252** that did not have the reactive carbonyl moiety. Employing diethyl zinc in the deprotonation of diyne **252** did not result in the formation of the desired product (entry 7). Notably, the combination of LDA with $CeCl_3$ yielded traces of product with diyne **252** (entry 8). We hypothesized that diisopropylamine (the corresponding acid of LDA) that arose from the deprotonation of the alkyne with LDA is responsible for the enolization of the aldehyde and thus only a small amount of the product was isolated. These results imply that, using

[111] D. E. Frantz, R. Fässler, E. M. Carreira, *J. Am. Chem. Soc.* **2000**, *122*, 1806–1807.
[112] T. Imamoto, T. Kusumoto, Y. Tawarayama, Y. Sugiura, T. Mita, Y. Hatanaka, M. Yokoyama, *J. Org. Chem.* **1984**, *49*, 3904–3912.

the base *n*-Buli (that has a gaseous corresponding acid: butane), no enolization of aldehyde **223** should occur. As predicted, using *n*-Buli to deprotonate diyne **252** followed by transmetalation with $CeCl_3$ gave the 1,2-addition product **257** in 85% yield in a diastereomeric ratio of 1:1.9 (entry 9).

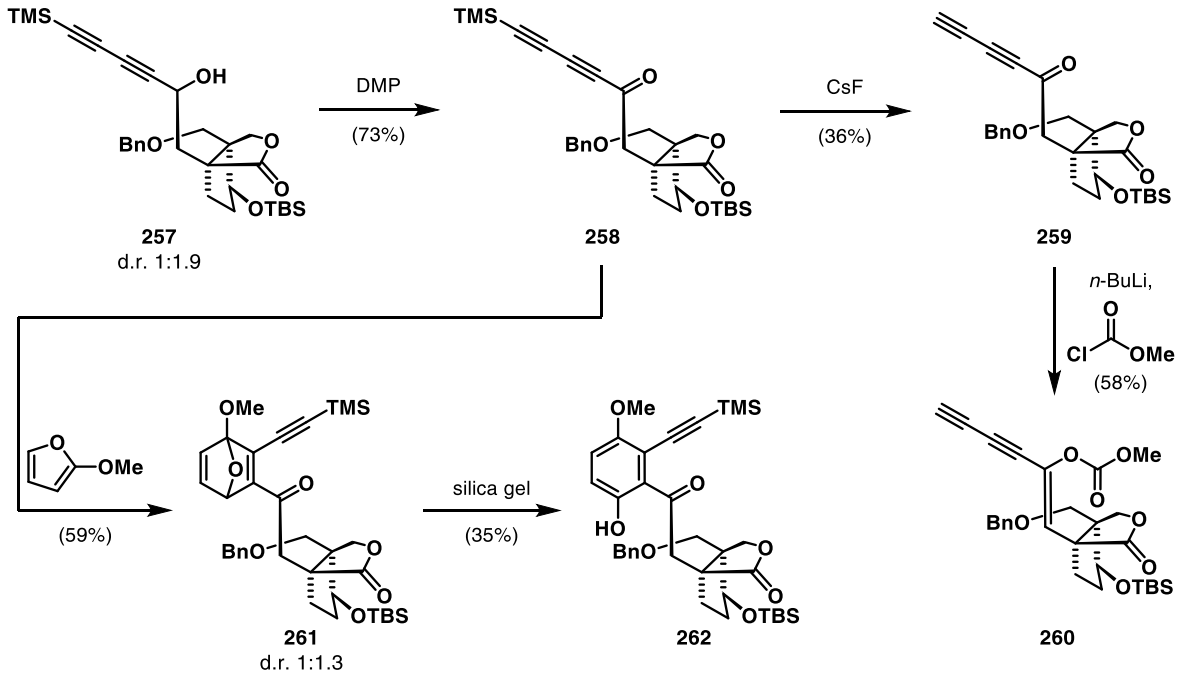
Table 4: Screening of alkyne additions to aldehyde **223**.



entry	conditions	result
1	**244**, $Zn(OTf)_2$, NEt_3, 60 °C	decomposition
2	**244**, LDA	no reaction[1)]
3	**244**, LDA, $CeCl_3$	no reaction
4	**244**, *n*-BuLi, $CeCl_3$	no reaction
5	**254**, LDA	decomposition of **254**
6	**254**, diethyl zinc	no reaction
7	**252**, diethyl zinc	no reaction
8	**252**, LDA, $CeCl_3$	traces of the product
9	**252**, *n*-BuLi, $CeCl_3$	**257**, 85% yield, d.r. 1:1.9

[1)] addition of D_2O only showed deprotonation of the aldehyde

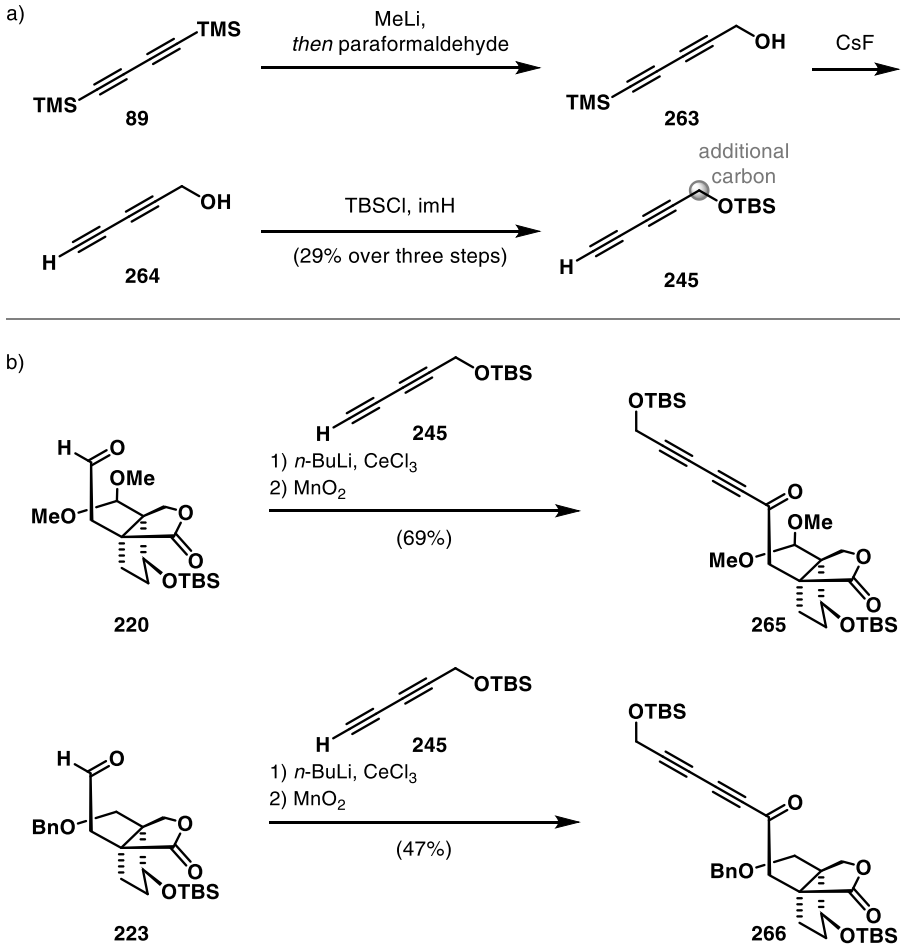
We oxidized propargyl alcohol **257** with DMP to ketone **258** in 73% yield (Scheme 43). In order to further activate the triple bond for the upcoming Diels–Alder reaction, we intended to install an electron-withdrawing group on the terminal alkyne position. Therefore, we removed the TMS protecting group with CsF to yield **259** (36%) that was subsequently treated with *n*-BuLi and methyl chloroformate. Instead of the expected methyl ester, we obtained vinyl carbonate **260** in 58% yield emphasizing again the acidity of the methylene group alpha to the carbonyl moiety. Independently from this reaction outcome, we tested the Diels–Alder reaction of 2-methoxyfuran with diyne **258** and were pleased to isolate the cycloaddition adduct **261** (59%, d.r. = 1:1.3) that was converted to hydroquinone **262** by treatment with silica gel (35%).



Scheme 43: Synthesis of hydroquinone **261** via a Diels–Alder reaction of diyne **258** with 2-methoxyfuran.

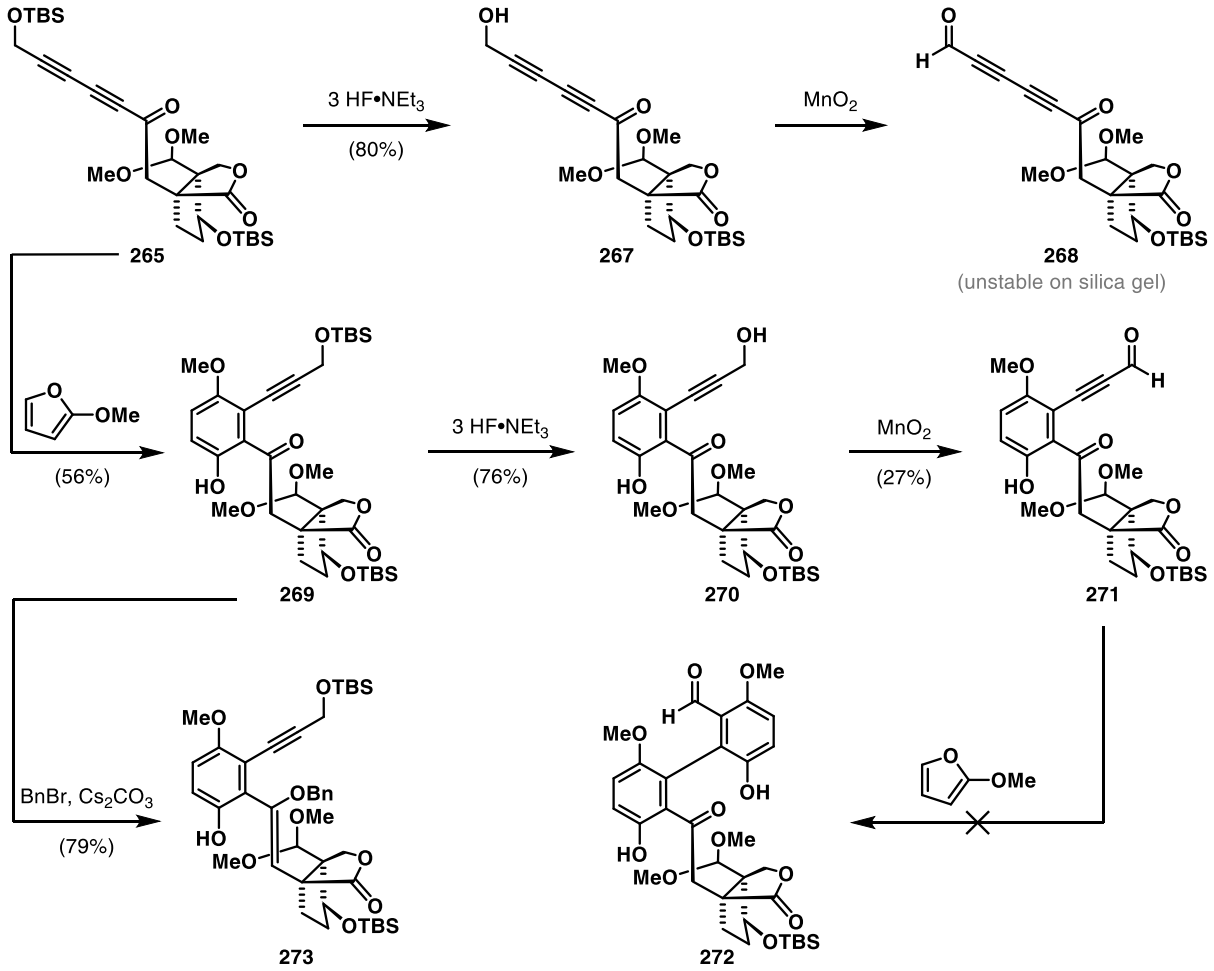
To overcome the problem of the readily enolizable carbonyl group, we prepared diyne **245** that, compared to the previous diyne **252**, contained an additional carbon atom (Scheme 44a). TMS alkyne dimer **89** was treated with methyllithium followed by paraformaldehyde to give propargyl alcohol **263**. Desilylation was carried out with CsF to yield **264** and addition of TBSCl gave diyne **245** in 29% over three steps.

With the optimized procedure for a 1,2-addition in hand (Table 4), an addition and oxidation sequence of diyne **245** with aldehyde **220** and **223** was carried out to obtain the corresponding ketones **265** (69%) and **266** (47%, Scheme 44b).



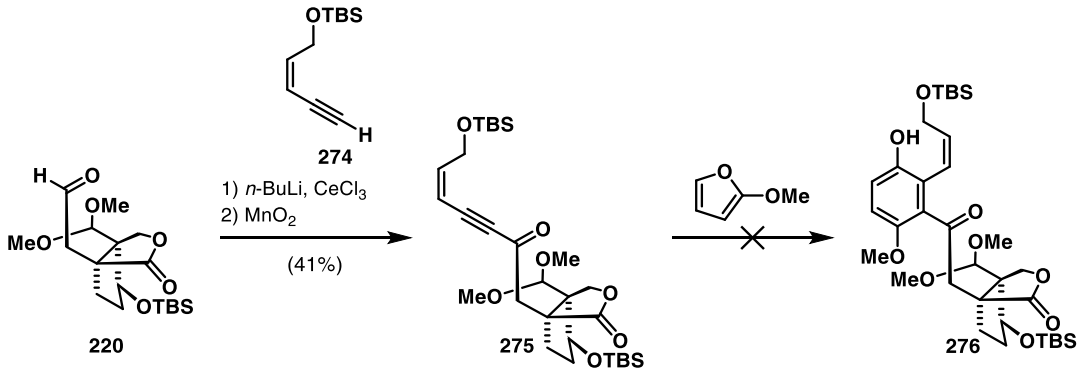
Scheme 44: Synthesis of improved diyne **245** bearing an additional carbon atom and the 1,2-addition of this diyne to aldehyde **220** and **223**.

With ketone **265** in hand, the crucial phase of our synthesis approached: the key Diels–Alder reaction (Scheme 45). For this purpose, the silyl protecting group on the propargyl alcohol was removed chemoselectively over the TBS group on the secondary alcohol with 3 HF•NEt_3 to furnish propargyl alcohol **267** in 80% yield. With the subsequent MnO_2 oxidation to aldehyde **268** we intended to activate the diyne for the Diels–Alder reaction but this compound proved to be unstable and purification on silica gel was impossible. Thus, we performed the cycloaddition with 2-methoxyfuran at the stage of **265** that pleasingly afforded hydroquinone **269** in 56% yield. Employing TMS or TBS 2-hydroxyfuran **250** and **251** in the cycloaddition proved to be unsuccessful and only starting material was recovered. 3 HF•NEt_3 was again used in the desilylation (76%) and the so-obtained propargylic alcohol **270** was oxidized with MnO_2. Aldehyde **271** was unstable, hence the low yield in the oxidation step. However, we were able to use **217** without the benefit of purification on silica gel. For the upcoming key Diels–Alder reaction of **271** with 2-methoxyfuran we employed several conditions including using an excess of diene at elevated temperature (60 °C) or applying a pressure of 14 kbar but all attempts resulted in decomposition. Furthermore, an attempt to protect the phenolic hydroxy group with BnBr solely yielded benzyl enol ether **273** (79%).



Scheme 45: Cycloaddition of 2-methoxyfuran to yield hydroquinone **269** and failed attempt to install a second aromatic core through a Diels–Alder reaction.

Noteworthy, a Diels–Alder reaction of 2-methoxyfuran with enyne **275**, obtained from a 1,2-addition and oxidation sequence (Scheme 46), resulted in no reaction. Because of the structural similarity of **275** compared to **265** this outcome was surprising. A possible explanation for the failed cycloaddition could be increased steric hindrance of the dienophile.



Scheme 46: Preparation of enyne **275** and unsuccessful cycloaddition with 2-methoxyfuran.

Building on the ease of the alkyne 1,2-addition and the first Diels–Alder reaction, we envisioned a retrosynthesis of ganoapplanin (**19**) through an intramolecular Stille coupling (Figure 24). The

bromohydroquinone moiety of **277** could arise from a cycloaddition of 2-methoxyfuran with bromoalkyne **278** that in turn might arise from a 1,2-addition of an alkyne to aldehyde **220**.

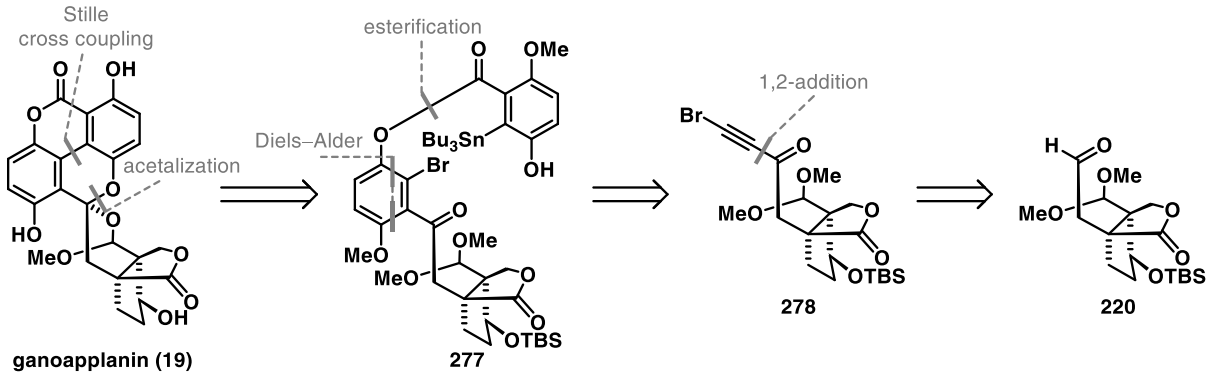
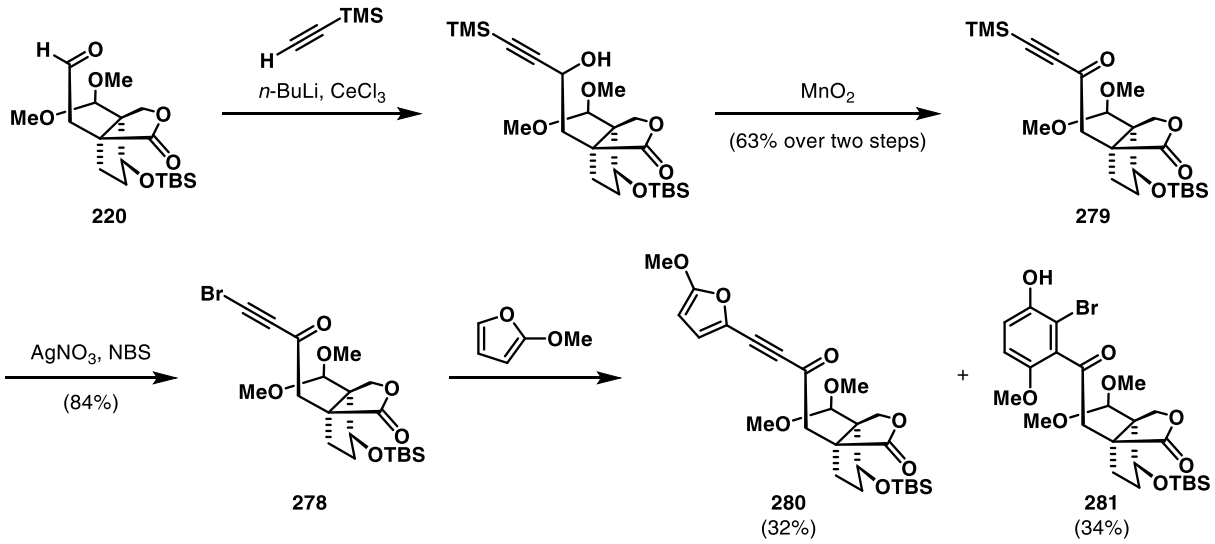


Figure 24: Proposed intramolecular Stille cross coupling to form the tetracycle of ganoapplanin (**19**).

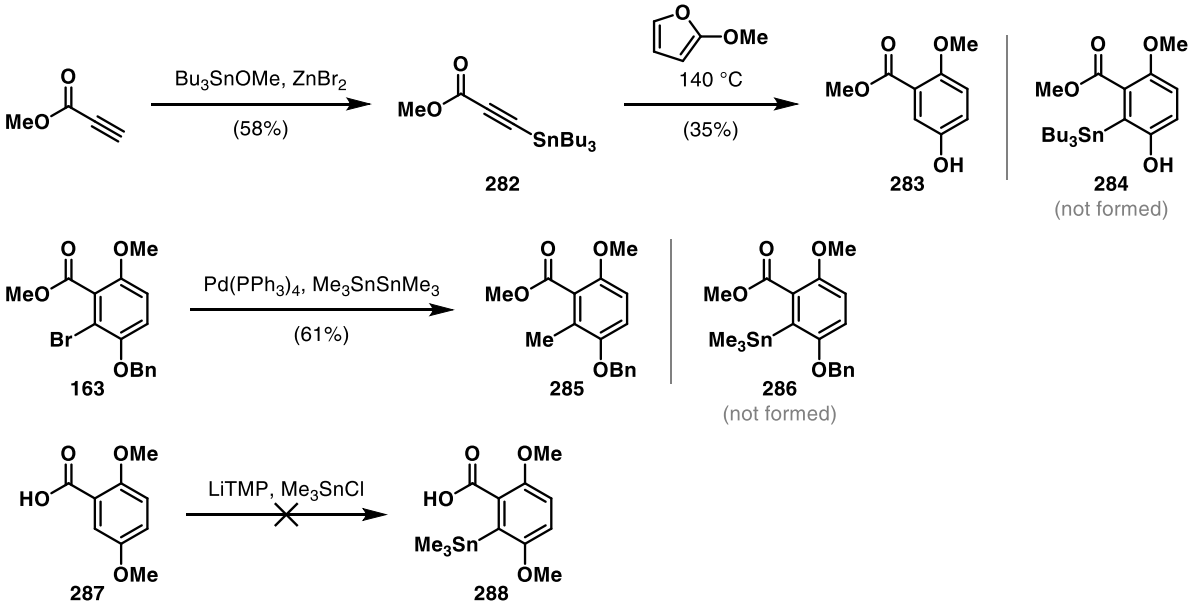
As outlined in Scheme 47, we started to investigate this proposed route with a 1,2-addition of trimethylsilylalkyne to aldehyde **220**. The so-formed propargyl alcohol was oxidized by reaction with MnO_2 to ketone **279** (63% over two steps). A combination of silver nitrate and NBS directly converted **279** to bromoalkyne **278** in 84% yield. To our surprise, the Diels–Alder reaction of bromoalkyne **278** with 2-methoxyfuran gave two products in nearly equal amounts. Furan **280** is the outcome of a 1,4-addition of 2-methoxyfuran to bromoalkyne **278** followed by bromide elimination (32%). The anticipated bromohydroquinone **281** was isolated in 34% yield.



Scheme 47: Cycloaddition of 2-methoxyfuran with bromoalkyne **278** to yield furan **280** and bromohydroquinone **281**.

For the intramolecular Stille cross-coupling we had to synthesize the corresponding benzoic acid bearing an aryltin moiety (Scheme 48). The substitution pattern of aryltin **284** was reminiscent of our Diels–Alder reaction of an alkyne with 2-methoxyfuran. To this end, we prepared alkynyl tin **282** from methyl propiolate by reaction with tributyltin methoxide and zinc bromide (58%). We subsequently reacted **282** with 2-methoxyfuran and indeed obtained a cycloaddition product. However, under the elevated reaction

temperature (140 °C) a protodestannylation occurred giving hydroquinone **283** in 35% yield instead of the desired aryl tin **284**. An anticipated Stille cross-coupling[113] of bromohydroquinone **163** with hexamethylditin also did not furnish aryl tin **286**. Instead, the methylated hydroquinone **285** was isolated as the sole product (61%). According to a procedure of Pronin,[114] we attempted to synthesize aryl tin **288** through a carboxylic acid directed deprotonation with LiTMP followed by quenching the anion with Me_3SnCl. Surprisingly, in our hands this literature known reaction did not give any conversion.

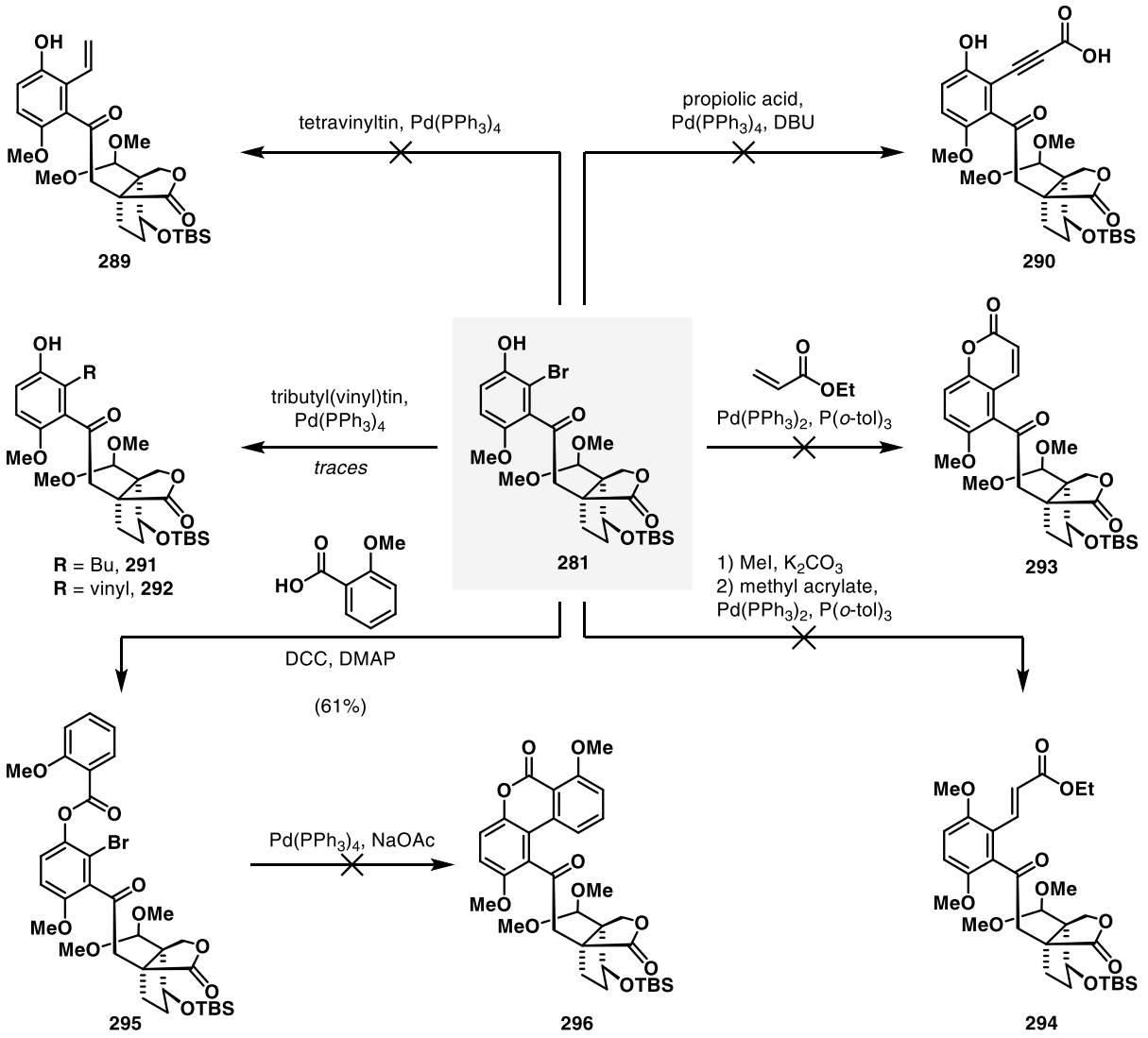


Scheme 48: Various attempts to access aryltin species **284**, **286** or **288**.

Since we were not able to test an intramolecular Stille cross-coupling, we focused on the functionalization of bromohydroquinone **281** (Scheme 49). We realized that the steric encumbrance of the aryl bromide rendered a functionalization very difficult. A palladium catalyzed vinylation to access **289** failed as did a Sonogashira cross-coupling[115] of bromohydroquinone with propiolic acid. The attempt to introduce a vinyl group via a Stille cross-coupling of **281** with tributyl(vinyl)tin resulted in the isolation of traces of vinyl hydroquinone **292** and butyl hydroquinone **291**. Inspired by the work of Hertweck,[116] we attempted a Heck reaction[117,118] of **281** with ethyl acrylate to directly form lactone **293**. However, in our case no reaction occurred. We assumed that the phenolic hydroxyl group might interfere in the Heck reaction. Thus, we methylated the OH-group (MeI, K_2CO_3). Nevertheless, no conversion was observed for the Heck reaction to form **294**. As a last resort, we performed an esterification of

[113] D. Milstein, J. K. Stille, *J. Am. Chem. Soc.* **1979**, *101*, 4992–4998.
[114] S. D. Holmbo, S. V. Pronin, *J. Am. Chem. Soc.* **2018**, *140*, 5065–5068.
[115] K. Sonogashira, Y. Tohda, N. Hagihara, *Tetrahedron Lett.* **1975**, *16*, 4467–4470.
[116] N. Ueberschaar, Z. Xu, K. Scherlach, M. Metsä-Ketelä, T. Bretschneider, H.-M. Dahse, H. Görls, C. Hertweck, *J. Am. Chem. Soc.* **2013**, *135*, 17408–17416.
[117] M. Tsutomu, M. Kunio, O. Atsumu, *Bull. Chem. Soc. Jpn.* **1971**, *44*, 581–581.
[118] R. F. Heck, J. P. Nolley, *J. Org. Chem.* **1972**, *37*, 2320–2322.

bromohydroquinone **281** with 2-methoxybenzoic acid (61%) in an attempt to forge the tricyclic moiety **296** in a palladium catalyzed C–H activation which, unfortunately, resulted in decomposition.



Scheme 49: Functionalization of bromohydroquinone **281**.

4.4. Total Syntheses of Ganoapplanin Congeners

Besides ganoapplanin (**19**), we had a special interest in the *Ganoderma* meroterpenoids applanatumol H (**297**), E (**18**), I (**298**) and lingzhilactone B (**24**) (that only differ in the oxidation state of the residue R), meroapplanin B (**299**) as well as lingzhiol (**30**). These natural products are highly structural related (Figure 25) and have a 1,2,4-trisubstituted benzene ring (highlighted in red) and a bicyclic lactone moiety (highlighted in blue) in common. The structural resemblance prompted us to come up with a collective synthesis of the GMs. In addition to the interesting synthetic challenge these natural products pose, they were also found to exhibit interesting bioactivity. Lingzhilactone B (**24**) and lingzhiol (**30**)

are reported to protect against renal injuries by increasing the activity of antioxidants and hence might be beneficial for anti-kidney disease drug design.[119,120]

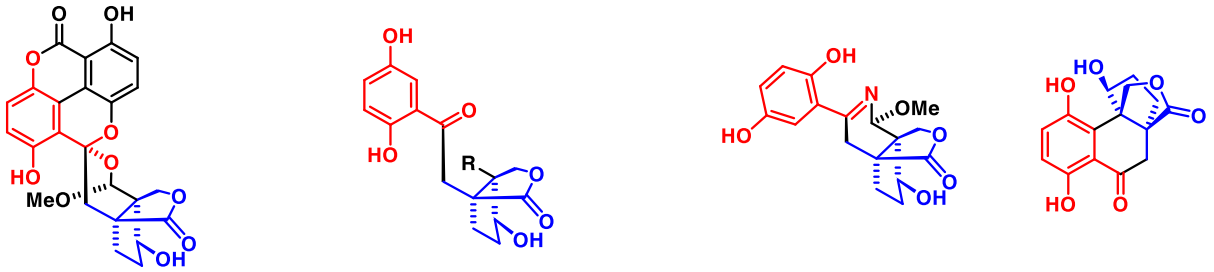


Figure 25: Structurally related Ganoderma meroterpenoids.

A first retrosynthetic analysis of lingzhilactone B (**24**) was based on a late-stage introduction of the benzylic ketone through a benzylic oxidation of **301** or through an ozonolysis of **300** (Figure 26). These intermediates might be prepared via an alkylation of bicyclic lactone **150**.

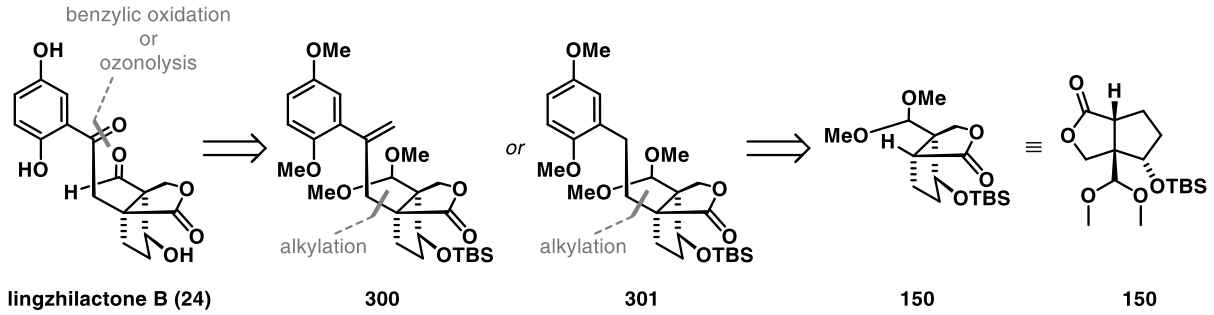
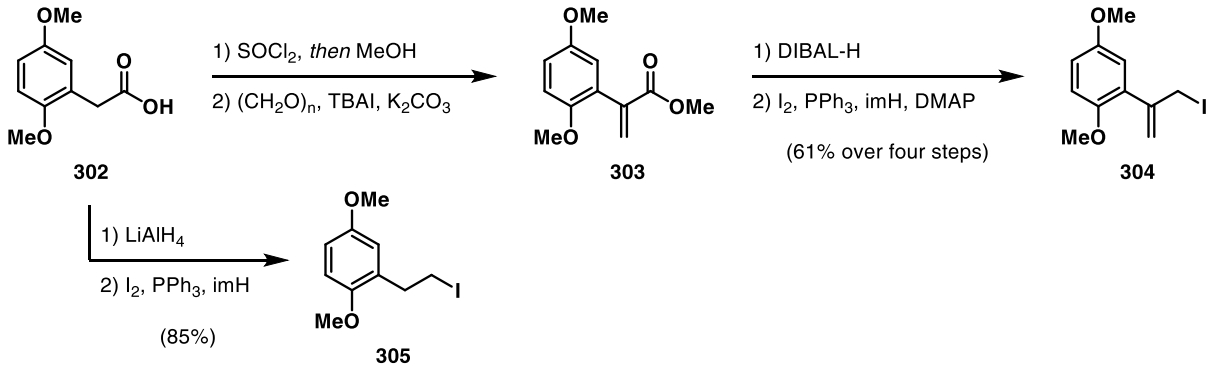


Figure 26: Proposed synthesis of lingzhilactone B (**24**) through a late-stage oxidation and alkylation of bicycle **150**.

We commenced with the preparation of alkyl iodides **304** and **305** starting from carboxylic acid **302**. Following a protocol by Baran,[121] acid **302** was converted to its corresponding methyl ester (thionyl chloride and methanol) followed by a methylenation with paraformaldehyde under basic conditions giving **303**. Upon treatment with DIBAl-H, ester **303** was reduced to the corresponding allylic alcohol that was further converted in an Appel reaction to allyl iodide **304** (61% over four steps). Alkyl iodide **305** was obtained from **302** by reduction with $LiAlH_4$ followed by an Appel reaction in 85% yield.

[119] Y.-M. Yan, X.-L. Wang, L.-L. Zhou, F.-J. Zhou, R. Li, Y. Tian, Z.-L. Zuo, P. Fang, A. C. K. Chung, F.-F. Hou, Y.-X. Cheng, *J. Ethnopharmacol.* **2015**, *176*, 385–393.
[120] Y.-M. Yan, J. Ai, L. L. Zhou, A. C. K. Chung, R. Li, J. Nie, P. Fang, X.-L. Wang, J. Luo, Q. Hu, F.-F. Hou, Y.-X. Cheng, *Org. Lett.* **2013**, *15*, 5488–5491.
[121] P. S. Baran, N. Z. Burns, *J. Am. Chem. Soc.* **2006**, *128*, 3908–3909.

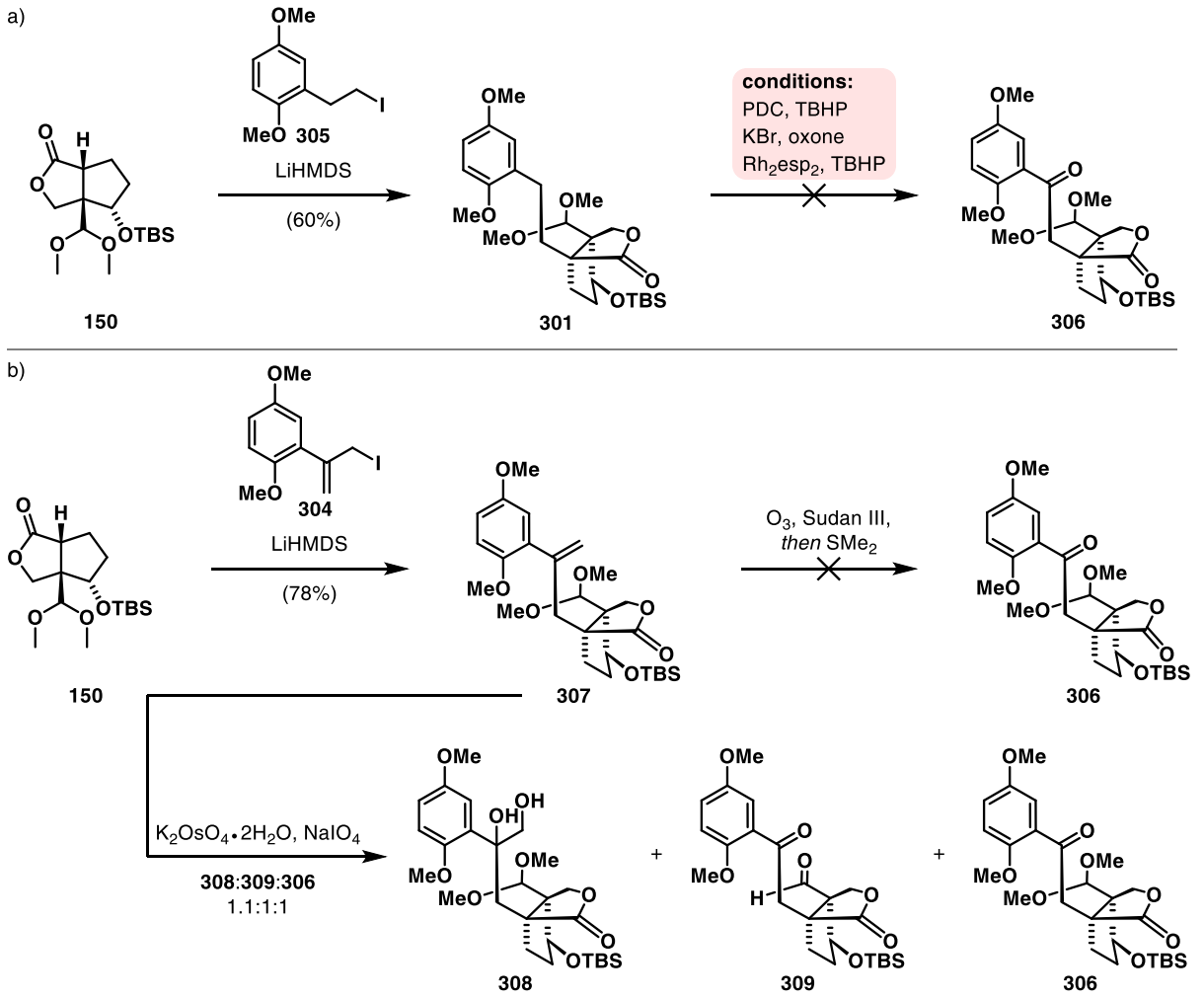


Scheme 50: Synthesis of alkyl iodides **304** and **305**.

With the electrophiles in hand, we tested the proposed alkylation and further functionalization towards lingzhilactone B (**24**). We were able to alkylate lactone **150** with **305** in 60% yield (Scheme 51a). Unfortunately, conditions to oxidize the benzylic position of **301** to the ketone failed. While PDC in combination with TBHP resulted in no conversion, the use of KBr and oxone (which generates bromide radicals)[122] removed the acetal protecting group without any oxidation. Using a combination of Rh_2esp_2 catalyst and TBHP resulted in decomposition.

Next, we examined the alkylation with allyl iodide **304** that proceeded in 78% yield. Unfortunately, conversion of the *exo*-methylene unit to its corresponding ketone via ozonolysis resulted in decomposition. We were aware that the electron-rich 2,5-dimethoxybenzene residue could react with ozone as well. For that reason, we added the diazo dye Sudan III to the reaction mixture which is known to suppress undesired oxidation of sensitive reaction sites.[123] However, in our hands the reaction in presence of Sudan III was not successful proving that the electron-rich aromatic residue is not compatible with ozone. In contrast, a mixture of catalytic amounts of $K_2Os_4•2H_2O$ and stochiometric $NaIO_4$ yielded a mixture of three different oxidation products in a ratio of 1.1:1:1. Among them, the desired ketone **306** was detected together with diol **308**. Another product **309** was formed in equal amounts where the acetal protecting group was removed and the double bond was oxidized to the ketone.

[122] K. Moriyama, M. Takemura, H. Togo, *Org. Lett.* **2012**, *14*, 2414–2417.
[123] T. Veysoglu, L. A. Mitscher, J. K. Swayze, *Synthesis* **1980**, *1980*, 807–810.



Scheme 51: Alkylation of bicycle **150** with iodide **305** and attempted benzylic oxidation (a). Alkylation with allyl iodide **304** followed by an oxidative cleavage of the double bond to a mixture of products (b).

To overcome the sluggish oxidation of the *exo*-methylene group, we planned to resort to the photo-Fries reaction that we tried to implement during our synthetic studies of ganoapplanin. Based on this key-step, lingzhilactone B (**24**) could be traced back to ester **310** that might be accessible from carboxylic acid **221** (Figure 27). Thus, **221** could arise from a Pinnick oxidation of aldehyde **220** which represents a common intermediate for the synthesis of ganoapplanin (**19**) as well as other congeners of the *Ganoderma* meroterpenoid family.

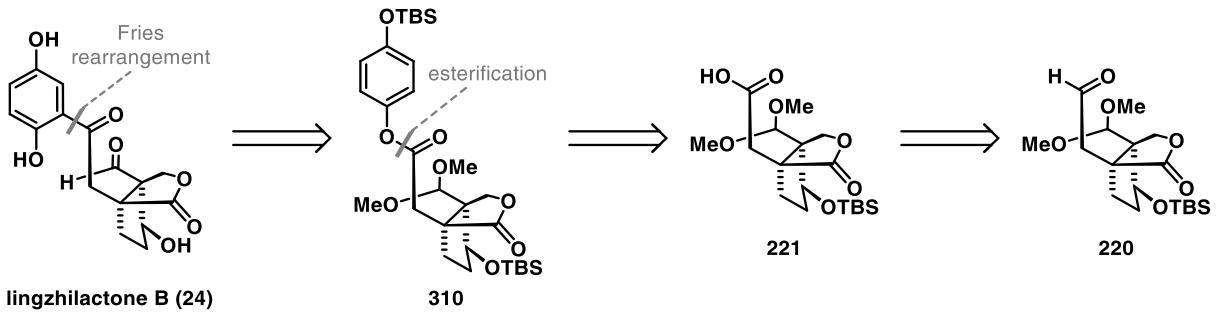
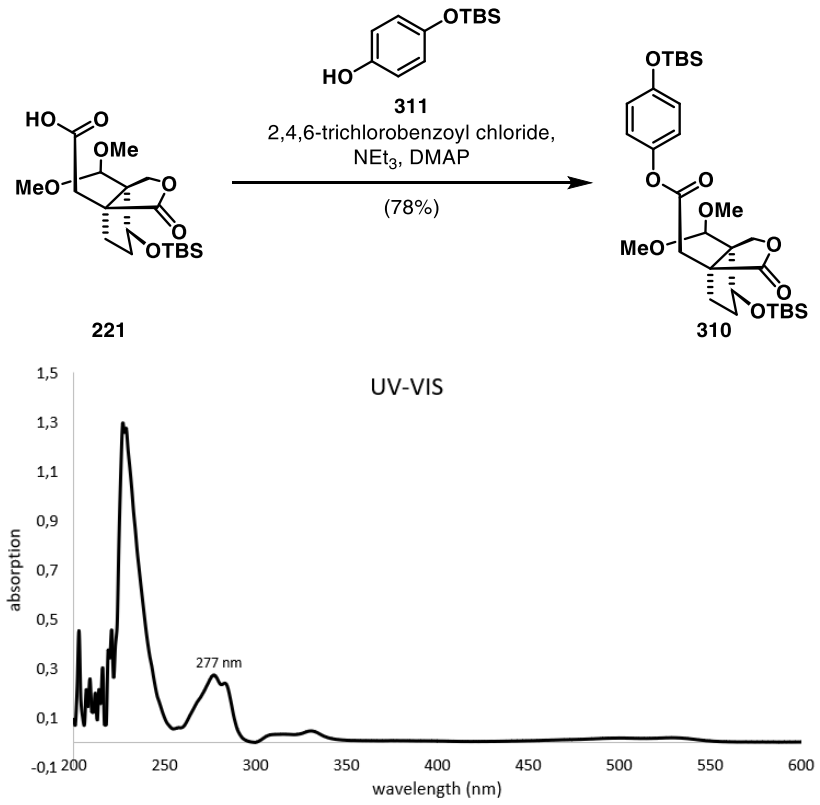


Figure 27: Proposed photo-Fries rearrangement from ester **310** to access lingzhilactone B (**24**).

Before we started with the photo-Fries reaction, we synthesized Fries precursor **310** through esterification of acid **221** with phenol **311** (78%) to study its photochemical absorption (Scheme 52). An UV-VIS spectrum of **310** recorded in methanol revealed a local absorption maximum at 277 nm that constitutes the ideal wavelength for irradiation.



Scheme 52: Synthesis of photo-Fries precursor **310** and UV-VIS spectrum of **310** recorded in methanol.

Additionally, we have also prepared several precursors for the photo-Fries rearrangement by variation of the substitution of the phenol and the residue R' on the lactone moiety (primary benzyl ether or dimethyl acetal). These esters were prepared in analogy to **310** and were investigated in their behavior upon irradiation with UV light. Giving the available photochemistry set-up and the absorption maximum of a representative Fries ester **310**, we utilized a Rayonet apparatus to irradiate at 254 nm or 300 nm or resorted to a broad emission spectrum respectively, provided by a Xenon lamp. The number of solvents were limited based on their cut-off wavelengths: acetonitrile (190 nm), *n*-hexane (195 nm) and methanol (205 nm)[124] were used.

Surprisingly, irradiation of ester **312** at 254 nm containing the primary benzyl ether (R') and an unsubstituted phenol group resulted in decomposition (Table 5, entry 1). Similarly, ester **313** that contained a 4-hydroxyphenol moiety (entry 2) decomposed under irradiation. Regarding a 4-benzyloxyphenol residue on ester **314** (entry 3), we were only able to isolate 4-benzyloxyphenol from the reaction mixture indicating that the desired homolytic cleavage occurred but the radical

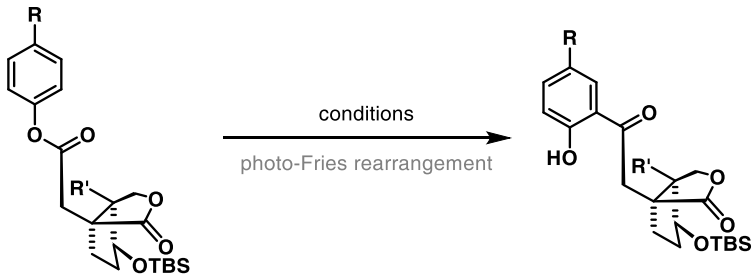
[124] C. Reichardt, T. Welton, in *Solvents and Solvent Effects in Organic Chemistry*, *4th edition*, Wiley-VCH, **2010**, pp. 549–586.

recombination was hampered. Remarkably, the 4-methoxyphenol ester **315** behaved completely different and the desired photo-Fries product was obtained in 47% yield (along with isolated 4-methoxyphenol) when the irradiation was carried out at 254 nm (entry 4) and in 31% when the irradiation was carried out at 300 nm (entry 5). The broad emission spectrum of the Xenon lamp used in entry 6 proved to be detrimental to the reaction time and the yield. The best results for the substrate containing the primary benzyl ether were obtained with the 4-(*tert*-butyldimethylsilyl)phenol residue (**316**) when the photo-Fries rearrangement was conducted in *n*-hexane at 254 nm (47%). This substrate would be ideal for the synthesis of applanatumol H (**297**).

Taking these results into account, ester **310** bearing a dimethyl acetal group was solely irradiated in methanol and *n*-hexane. Better results were found for the reaction in *n*-hexane (50%) while the reaction in methanol yielded the product in 42% and 4-(*tert*-butyldimethylsiloxy)phenol was isolated from the reaction mixture.

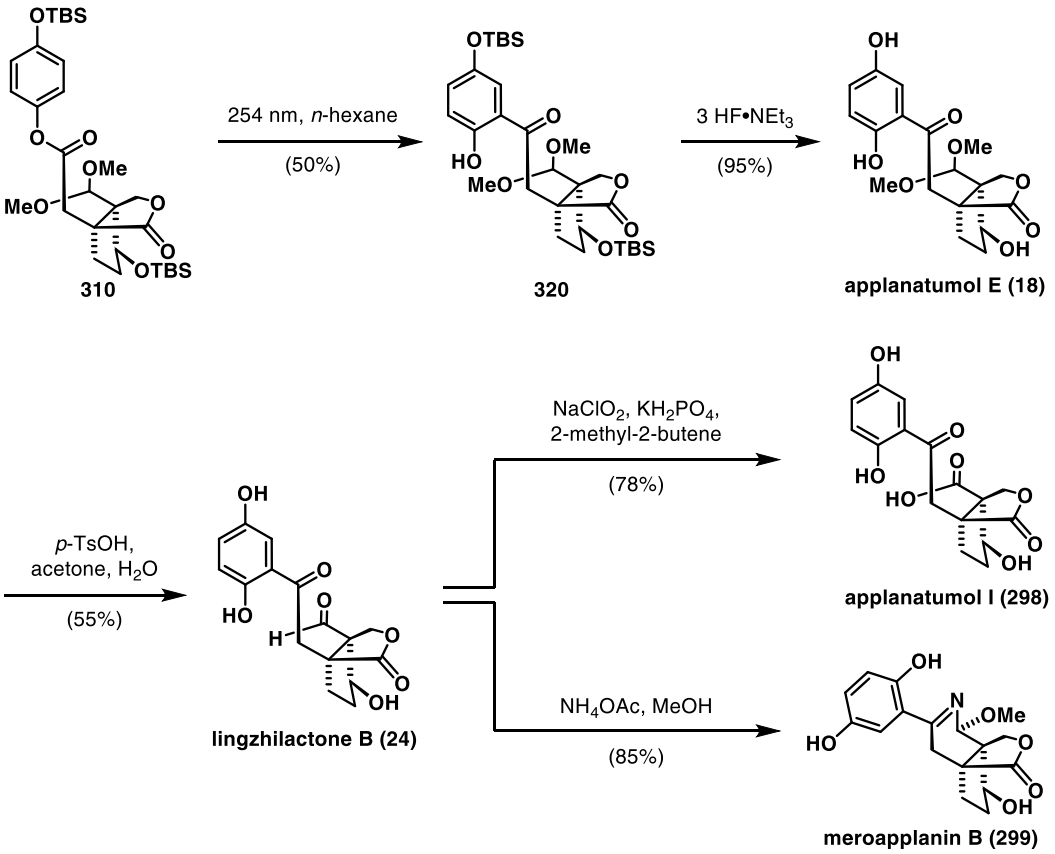
To conclude, the Fries rearrangement performed best at 254 nm (Rayonet) using esters containing no additional chromophores (additional benzyl ethers compromise the yield) in *n*-hexane (in methanol we always isolated the cleaved phenol moiety of the Fries precursor).

Table 5: Optimization of the photo-Fries rearrangement.



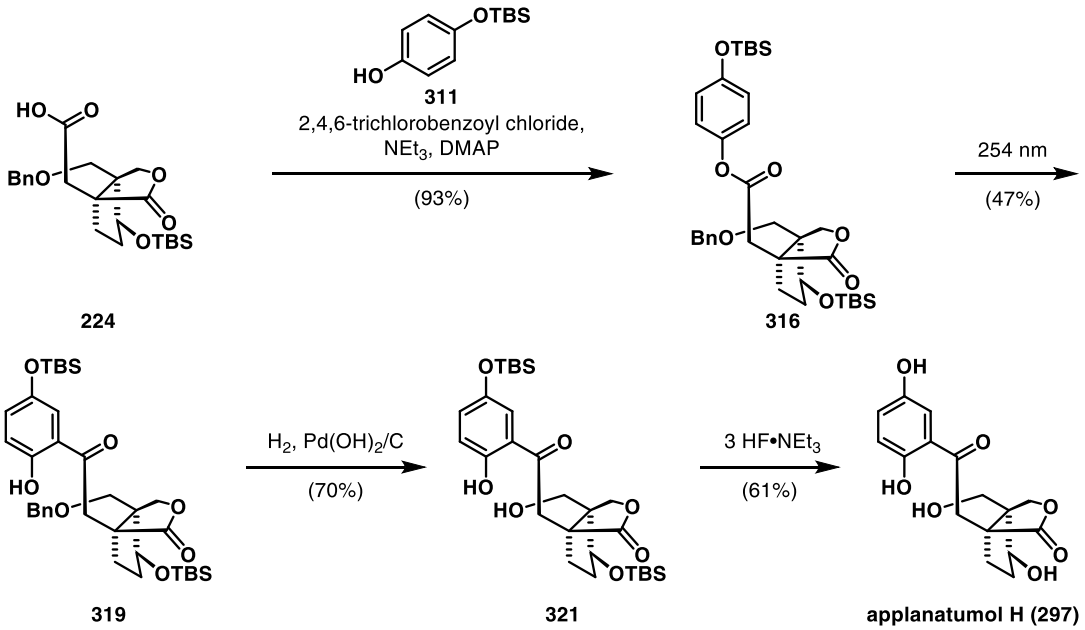
entry	compound	**R** =	**R'** =	conditions	result
1	**312**	**H**	**CH_2OBn**	methanol, 254 nm (Rayonet)	decomposition
2	**313**	**OH**	**CH_2OBn**	methanol, 254 nm (Rayonet)	decomposition
3	**314**	**OBn**	**CH_2OBn**	acetonitrile, 254 nm (Rayonet)	decomposition + isolation of 4-benzyloxyphenol
4	**315**	**OMe**	**CH_2OBn**	methanol, 254 nm (Rayonet)	**317**, 36% + isolation of 4-methoxyphenol
5	**315**	**OMe**	**CH_2OBn**	methanol, 300 nm (Rayonet)	**318**, 31%
6	**315**	**OMe**	**CH_2OBn**	*n*-hexane, 50 °C (Xenon lamp)	very slow conversion
7	**316**	**OTBS**	**CH_2OBn**	*n*-hexane, 254 nm (Rayonet)	**319**, 47%
8	**310**	**OTBS**	**$CH(OMe)_2$**	methanol, 254 nm (Rayonet)	**320**, 42% + isolation of 4-(*tert*-butyldimethylsiloxy)phenol
9	**310**	**OTBS**	**$CH(OMe)_2$**	*n*-hexane, 254 nm (Rayonet)	**320**, 50%

As shown in Table 5, irradiation of **310** at 254 nm in *n*-hexane afforded photo-Fries product **320** in 50 % yield (Scheme 53). To complete the synthesis of applanatumol E (**18**), **320** was treated with 3 HF•NEt_3 (95%). We were able to convert **18** to lingzhilactone B (**24**) by means of acetal removal with *p*-TsOH in 55% yield. Moreover, lingzhilactone B (**24**) served as a starting point for two more natural products. Pinnick oxidation delivered applanatumol I (**298**, 78%) and finally, **24** was treated with NH_4OAc in methanol at 50 °C to elicit the transformation to meroapplanin B (**299**) in 85% yield.



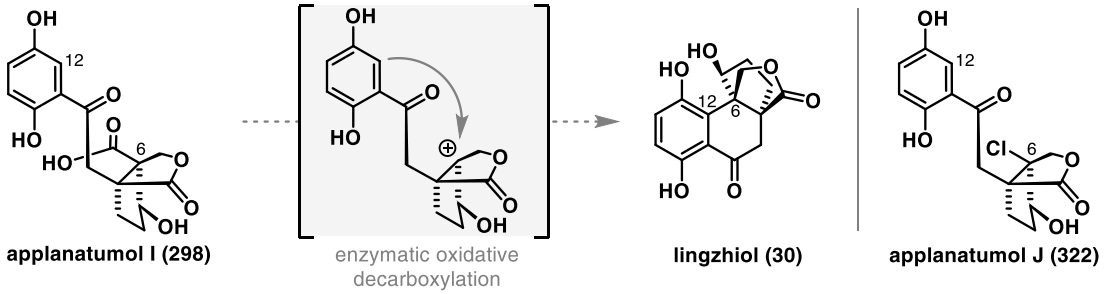
Scheme 53: Total syntheses of applanatumol E (**18**) and I (**298**), lingzhilactone B (**24**) and meroapplanin B (**299**).

Similarly, applanatumol H (**297**) was synthesized from carboxylic acid **224** benefitting from the already established conditions (Scheme 54). Thus, **224** was converted to ester **316** in 93% yield comprising an esterification with **311** utilizing Yamaguchi's reagent. The remaining steps span a photo-Fries rearrangement (47%, see Table 5, entry 7), followed by a debenzylation (70%) and global desilylation (61%) to give applanatumol H (**297**).



Scheme 54: Total synthesis of applanatumol H (**297**).

For the synthesis of the *Ganoderma* meroterpenoid lingzhiol (**30**) we were seeking for a direct conversion of applanatumol I (**298**) to **30**. From the *Ganoderma* fungus was also isolated the natural product applanatumol J (**322**) (Scheme 55). Compared to the acid applanatumol I (**298**) a decarboxylation and chlorination (a formal Hunsdiecker reaction[125]) took place to furnish **322**. The carbon atom 6 bearing a C–Cl bond in **322** is oxidized compared to the same atom in applanatumol I (**298**). We hypothesized that this enzymatic oxidative decarboxylation to access applanatumol J (**322**) from applanatumol I (**298**) might also be used by the fungus to access lingzhiol (**30**). In this respect, an intermediate carbocation that might arise from the oxidative decarboxylation could be intercepted by the electron-rich hydroquinone moiety in form of a Friedel–Crafts reaction to give **30**.

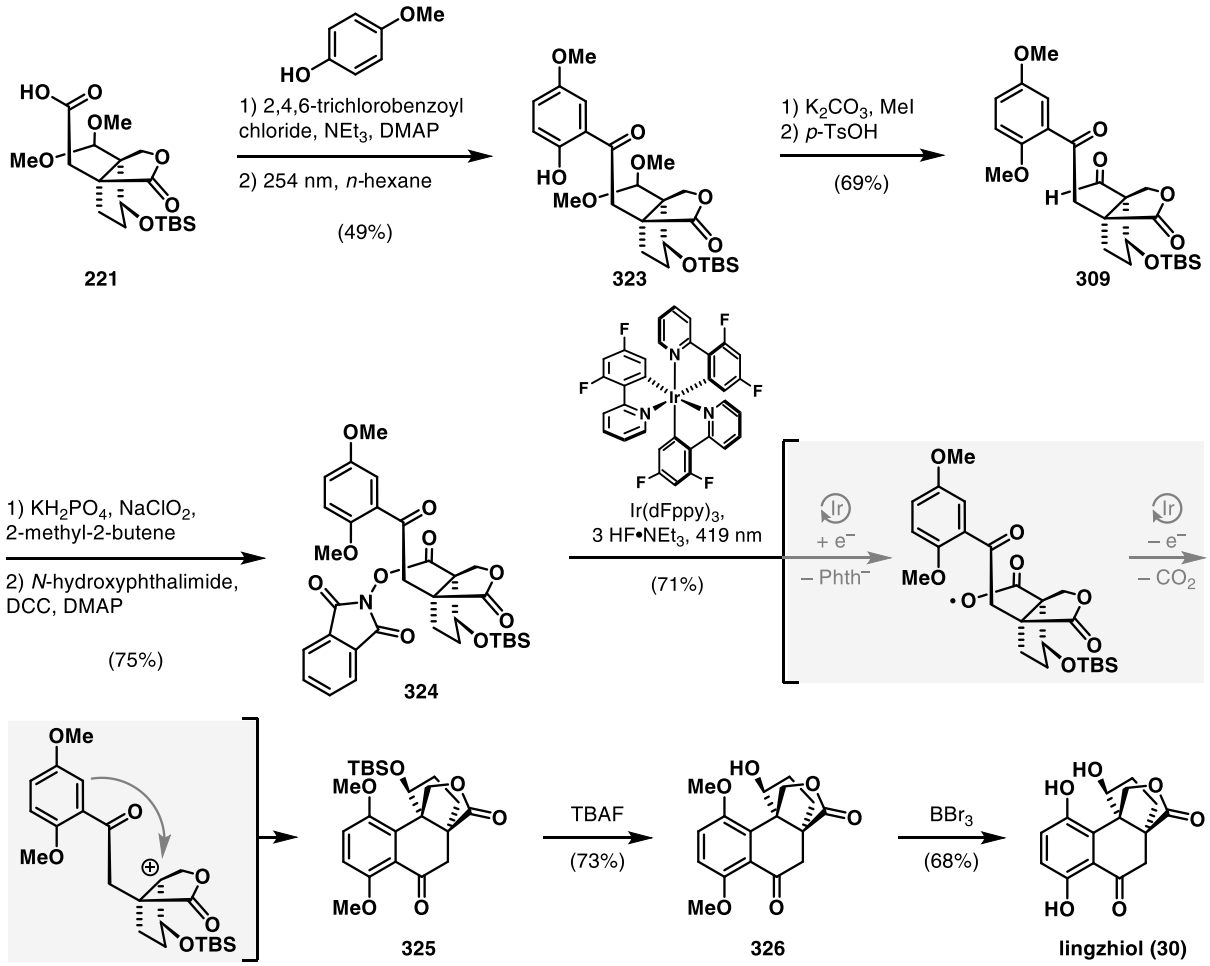


Scheme 55: Proposed biosynthetic conversion of applanatumol I (**298**) to lingzhiol (**30**) through an oxidative decarboxylation / Friedel–crafts sequence and applanatumol J (**322**) which might be formed via the same process.

In order to test the feasibility of this proposed biosynthetic reaction, we first synthesized a redox-active erster **324** as a precursor for the intended oxidative decarboxylation. Starting from acid **221**, we accessed *o*-acyl phenol **323** through the well-established esterification / photo-Fries sequence (Scheme 56, 49% over two steps). In order to make the delicate hydroquinone moiety less prone to oxidation in the

[125] H. Hunsdiecker, C. Hunsdiecker, *Ber. Dtsch. Chem. Ges.* **1942**, *75*, 291–297.

upcoming oxidative key-step we had to protect the phenolic hydroxy group as a methyl ether (K_2CO_3 and MeI, 96%). Acetal removal with *p*-TsOH gave aldehyde **309** which was further oxidized via a Pinnick oxidation (81%). The obtained acid was converted to the prerequisite redox-active *N*-hydroxyphthalimide ester **324** (92%) for the anticipated biomimetic oxidative decarboxylation / Friedel–Crafts sequence. Pleasingly, by employing $Ir(dFppy)_3$ catalyst in combination with catalytic amounts of 3 HF•NEt_3 at 419 nm (blue light), conditions recently reported by the group of Doyle,[126] cleanly converted **324** to the tetralone structure of **325** in 71% yield. As mechanistically proposed, a sequential single electron reduction by the iridium catalyst (Ir(III) to Ir(IV)) followed by an elimination of the phthalimide anion forms a carboxyl radical. Following the extrusion of carbon dioxide and a single electron oxidation (Ir(IV) to Ir(III), regenerating the iridium catalyst) a stabilized tertiary carbocation is formed that can subsequently undergo a Friedel–Crafts reaction. Global deprotection of the silyl protecting group (TBAF, 73%) and the methyl ethers (BBr_3, 68%) afforded the natural product lingzhiol (**30**).



Scheme 56: Total synthesis of lingzhiol (**30**)

[126] E. W. Webb, J. B. Park, E. L. Cole, D. J. Donnelly, S. J. Bonacorsi, W. R. Ewing, A. G. Doyle, *J. Am. Chem. Soc.* **2020**, *142*, 9493–9500.

4.5. Conversion of Applanatumol H to Ganoapplanin

With applanatumol E (**18**) in hand, we envisioned a synthetic route to convert this natural product to ganoapplanin employing the ring-expansion methodology developed in our laboratory. In analogy to the Diels–Alder approach (chapter 4.3.), ganoapplanin (**19**) was traced back to tetrasubstituted biaryl **327**, that could be synthesized through a ring-expansion of chlorocyclopropane **328** (Figure 28). Ideally, the double bond of enone **328** is introduced via a retro-Diels–Alder reaction of a norbornene. Thus, **329** could arise from a 1,4-addition of a nucleophile derived from iodocyclopropane **330** to quinone **331**. Finally, quinone **331** might be accessed from applanatumol E (**18**) through an oxidation and **330** could be synthesized via a cyclopropanation of the corresponding enone.

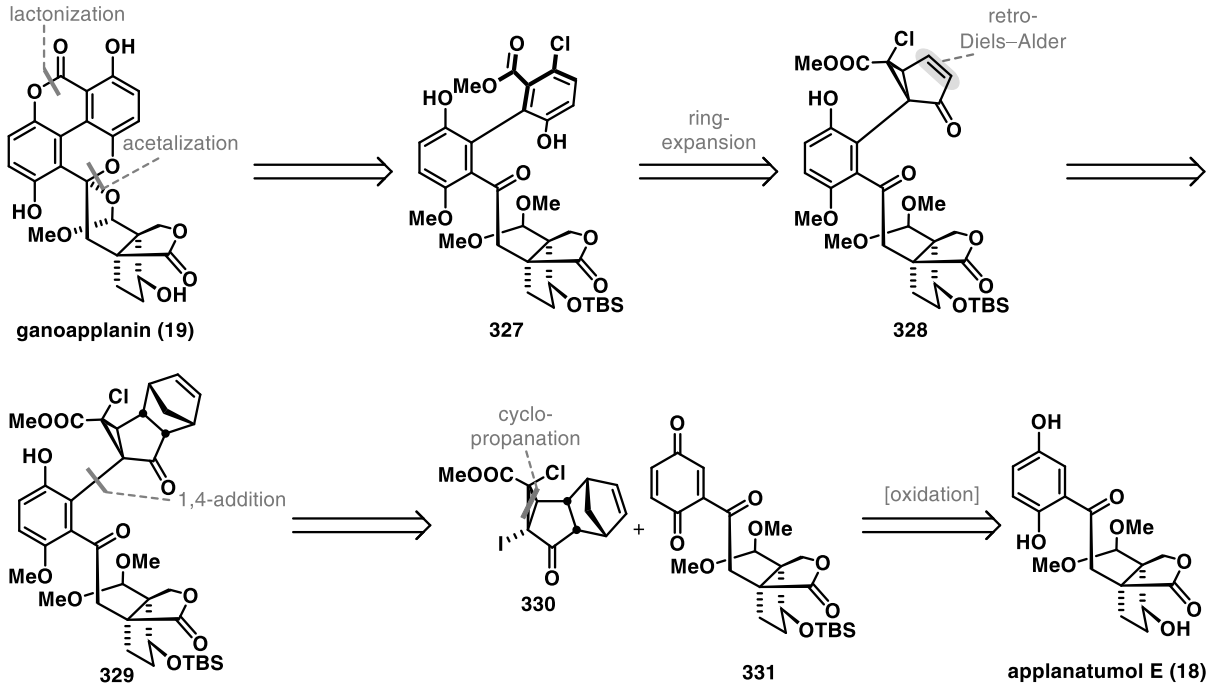
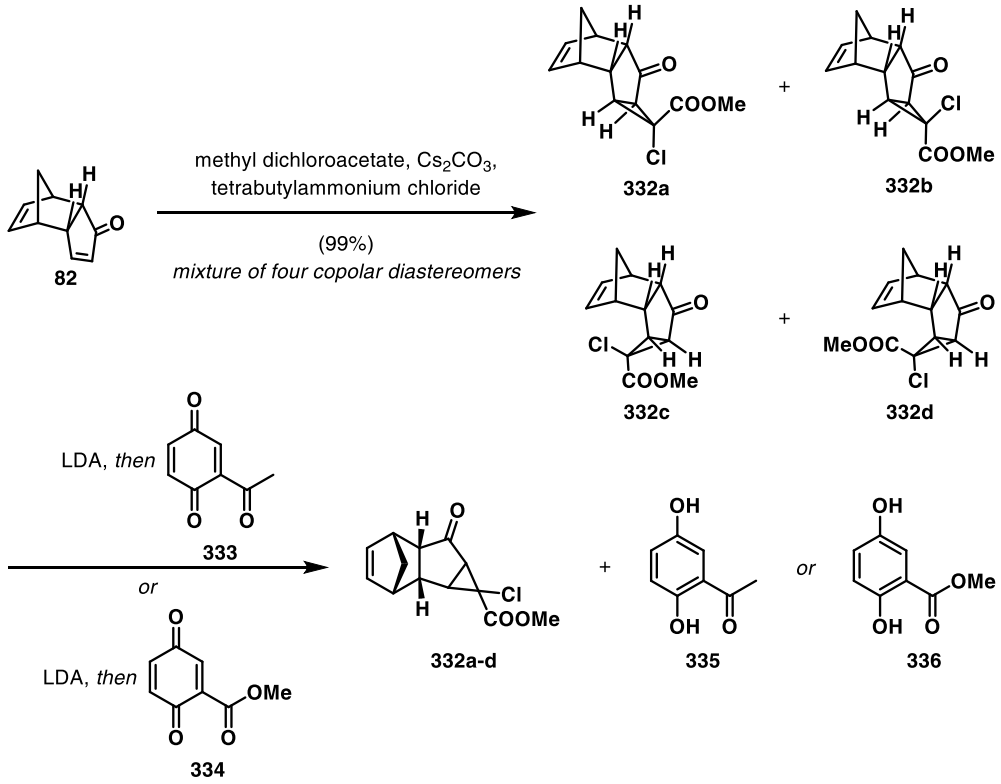


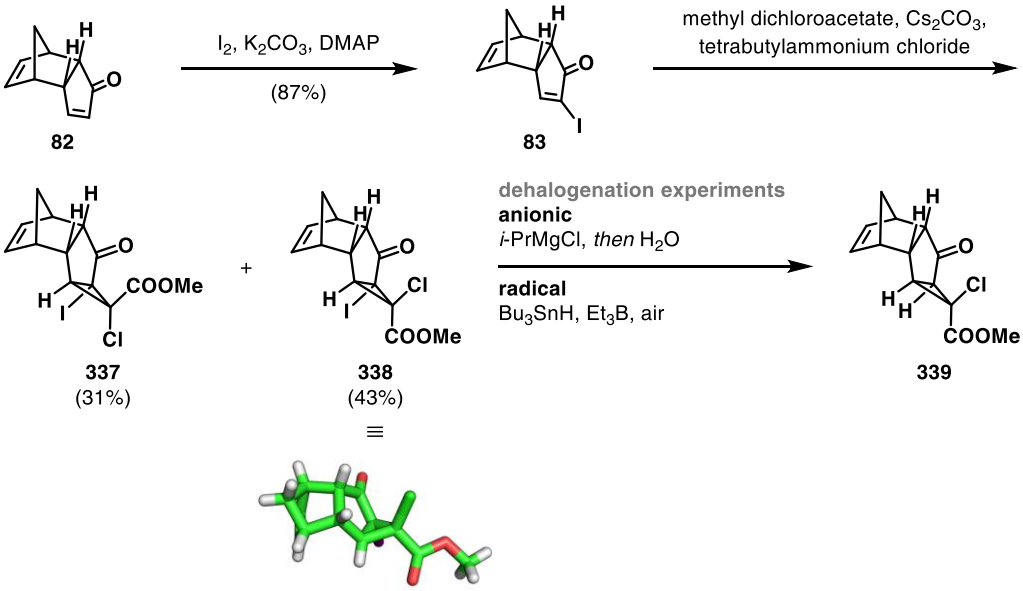
Figure 28: Proposed synthesis of ganoapplanin (**19**) from applanatumol E (**18**) through a ring-expansion of chlorocyclopropane **328**.

On these grounds, we converted enone **82** in a cyclopropanation with methyl dichloroacetate, Cs_2CO_3 and catalytic amounts of tetrabutylammonium chloride in almost quantitative yield to a mixture of four copolar diastereomers of chlorocyclopropanes **332a-d** (99%, Scheme 57). Unfortunately, attempts to realize a 1,4-addition to model quinones **333** or **334** failed. LDA was used to deprotonate the position alpha to the ketone. We isolated non-reacted chlorocyclopropanes **332a-d** along with hydroquinones **335** and **336** from the reaction mixture that resulted from an in situ reduction of the respective quinones.



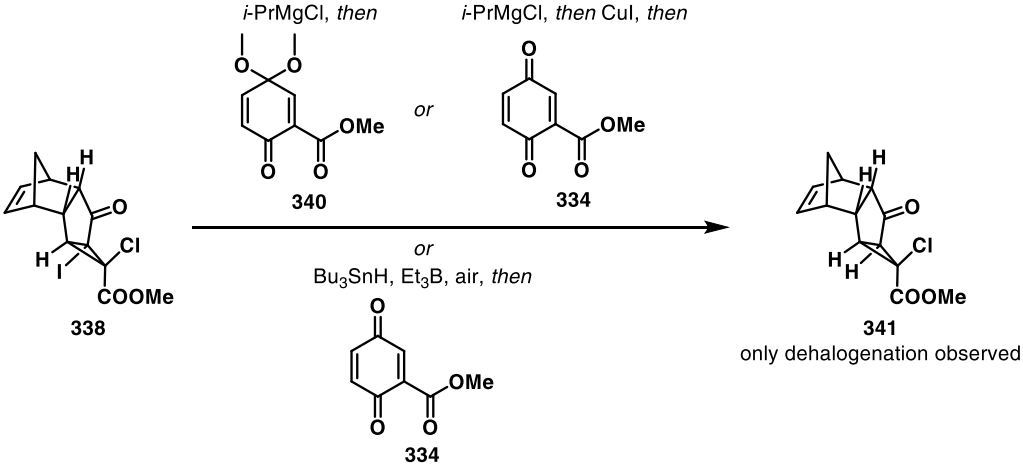
Scheme 57: Synthesis of chlorocyclopropanes **332** and attempted Michael addition to quinones **333** and **334**.

Instead of deprotonation, a halogen metal exchange would be an alternative to generate an anion alpha to the ketone. To this end, we iodinated **82** to afford iodocyclopentene **83** in good yields (87%, Scheme 58). Cyclopropanation gave separable diastereomers of iodochlorocyclopopane **337** (31%) and **338** (43%). We were able to identify the major diastereomer via X-ray crystallography to be the *endo*-diastereomer (in respect to the chloro substituent). Next, we tested if the iodide **338** could be transformed to an anion or a radical through either iodide magnesium exchange with *i*-PrMgCl or radical generation with Bu_3SnH, Et_3B and air. In both cases we observed dehalogenation of the iodide meaning that this position is accessible for further functionalization.



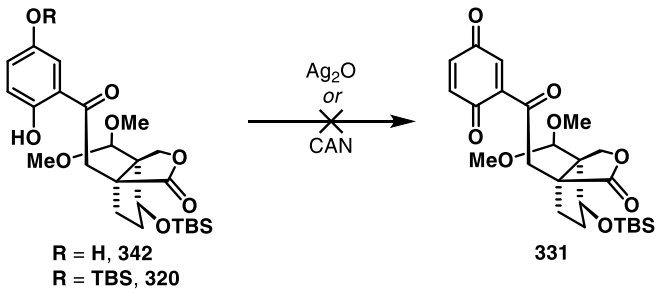
Scheme 58: Synthesis of iodochlorocyclopropane **337** and **338** from enone **83** and anionic and radical dehalogenation experiments.

Since the iodide group in **338** was easily accessible either through anionic or radical conditions, we were surprised to see that a Michael reaction of **338** to quinones **340** or **334** failed turning the iodide to organomagnesium, organocuprate or radical nucleophiles (Scheme 59). Under the conditions shown in Scheme 59, only dehalogenation of the C-I bond was observed.



Scheme 59: Failed 1,4-addition of **338** to quinones **340** or **334** through organomagnesium, organocuprate or radical addition.

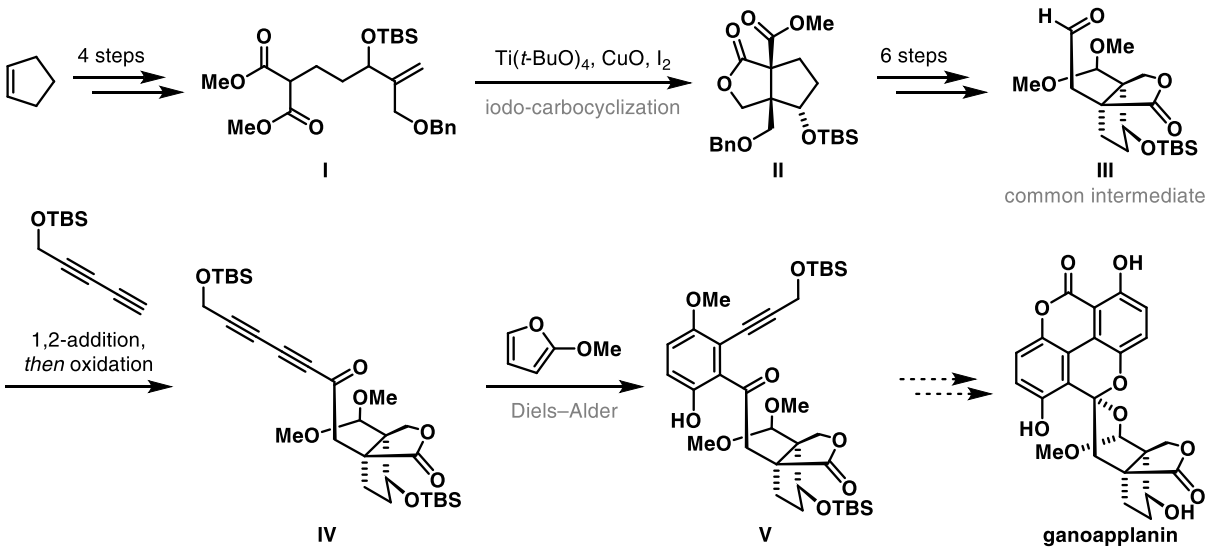
Additionally, the anticipated oxidation of the hydroquinone moiety of an applanatumol E derivative (**342** or **320**) to its corresponding quinone **331** led to decomposition by reaction with Ag_2O or with CAN (Scheme 60) eventually bringing this approach to an end.



Scheme 60: Attempted oxidation of hydroquinone **342** or **320** to quinone **331**.

5. Conclusion and Outlook

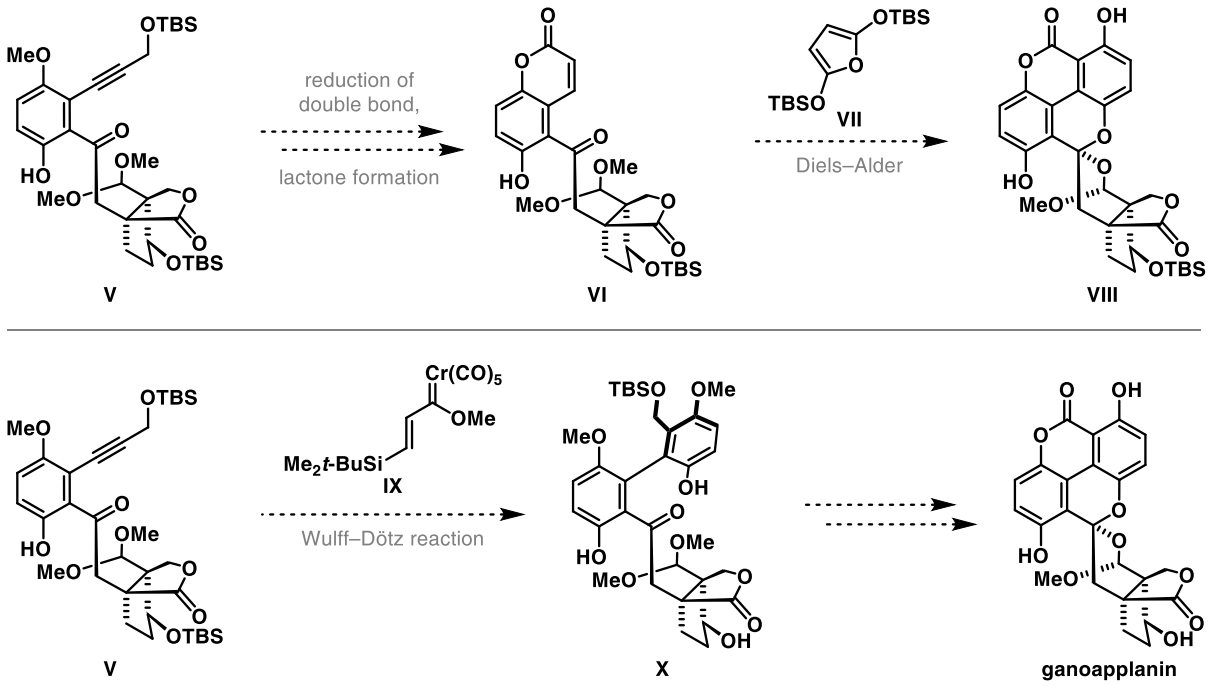
In summary, our efforts towards the first total synthesis of ganoapplanin culminated in a late-stage intermediate **V** which was synthesized in 16 steps (Scheme W). Our synthetic route commenced with the functionalization of cyclopentene to malonate **I** that served as a precursor for a diastereoselective iodo-carbocyclization to yield bicyclic lactone **II**. In six more steps, the lactone skeleton was further elaborated to give aldehyde **III** that poses as a pivotal intermediate for the synthesis of ganoapplanin and for the total syntheses of six more *Ganoderma* meroterpenoids. With **III** in hand, a 1,2-addition of a diyne followed by a propargylic oxidation furnished ketone **IV**. The aromatic moiety was assembled through a Diels–Alder reaction of 2-methoxyfuran with the diyne moiety. The work presented in my thesis brought the total synthesis to the late-stage intermediate **V** and conversion of it to ganoapplanin is currently the subject of ongoing research.



Scheme W: Our synthetic effort towards the Ganoderma meroterpenoid ganoapplanin.

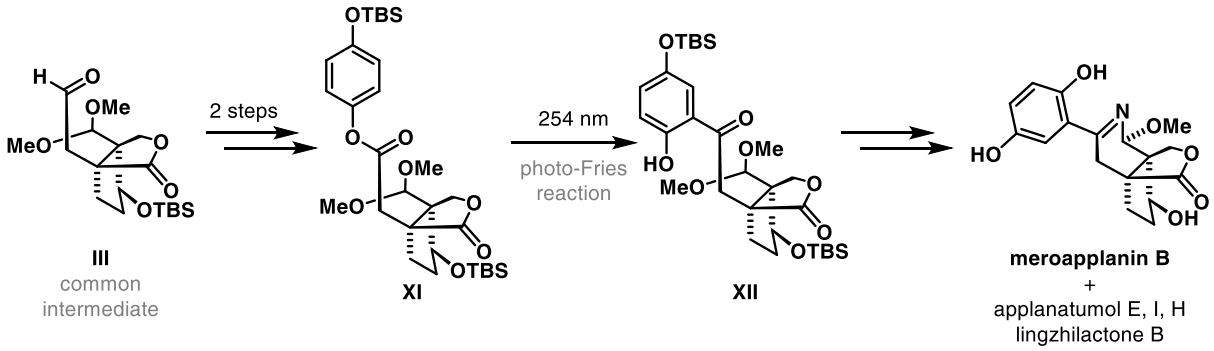
In the future, we envisioned that **V** could be converted to lactone **VI** by means of a reduction of the triple bond (e.g. Lindlar reduction, hydroboration/protodeboronation or hydrosilylation/protodesilylation) followed by a Diels–Alder reaction of the unsaturated enone with known furan **VII** (Scheme X).[127] Additionally, the late-stage intermediate **V** could serve as a substrate for a Wulff–Dötz benzannulation[128] with literature known Fischer-carbene **IX**[129] to furnish biaryl **X** that might be transformed into ganoapplanin in a few steps. This synthetic approach is complementary to the Diels–Alder route as an electronically activated triple bond is not required for the Wulff–Dötz reaction.

[127] I. Dissanayake, J. D. Hart, E. C. Becroft, C. J. Sumby, C. G. Newton, *J. Am. Chem. Soc.* **2020**, *142*, 13328–13333.
[128] K. H. Dötz, *Angew. Chem. Int. Ed.* **1975**, *14*, 644.
[129] S. Chamberlin, W. D. Wulff, *J. Org. Chem.* **1994**, *59*, 3047–3054.



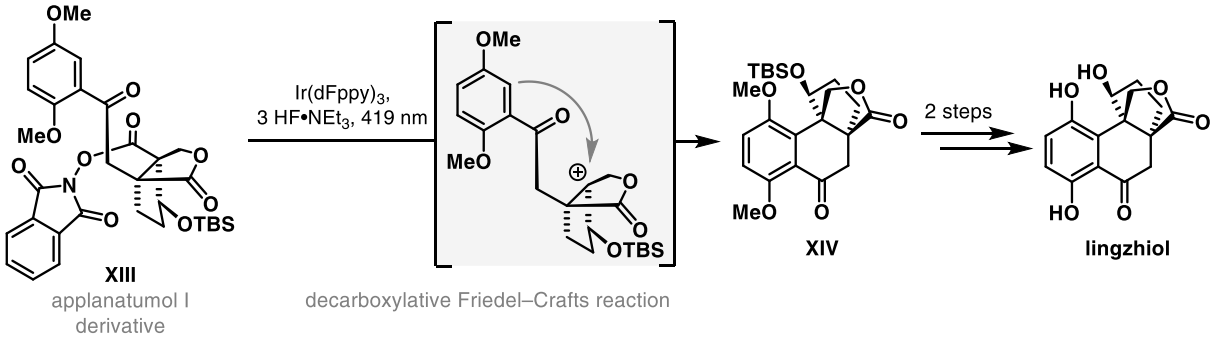
Scheme X: Proposed synthesis of ganoapplanin from late-stage intermediate **V** through a Diels–Alder reaction or via a Wulff–Dötz benzannulation.

Furthermore, we were able to synthesize five more congeners of ganoapplanin in a divergent manner starting from common intermediate **III** (Scheme Y). The meroterpenoids meroapplanin B, applanatumol E, I, H and lingzhilactone B were accessed using a powerful, yet rare photo-Fries rearrangement to build up the 1,2,4-trisubstituted benzene ring—a characteristic common in the *Ganoderma* meroterpenoid family. Notably, we accomplished the total synthesis of meroapplanin B two months after its structure has been reported in the literature for the first time.



Scheme Y: Total syntheses of meroapplanin B, applanatumol E, I, H and lingzhilactone B enabled through a rare photo-Fries rearrangement.

Lingzhiol was synthesized using an innovative oxidative decarboxylation / Friedel–Crafts sequence that converted applanatumol I derivative **XIII** to lingzhiol precursor **XIV** (Scheme Z). This transformation might be used by *Ganoderma* enzymes to convert applanatumol I to lingzhiol.



Scheme Z: Total synthesis of lingzhiol through a photoredox enabled decarboxylation / Friedel–Crafts sequence.

EXPERIMENTAL SECTION

6. General Experimental Details

6.1. General Working Methods

All reactions were carried out with magnetic stirring and, if moisture or air sensitive, under nitrogen or argon atmosphere using standard Schlenk techniques in oven-dried glassware (130 °C oven temperature). If required glassware was further dried under vacuum (0.1 mmHg) with a heat-gun at 650 °C. External bath thermometers were used to record all reaction temperatures. Low temperature reactions were carried out in a Dewar vessel filled with acetone and dry ice (–78 °C) or equipped with an electronically regulated cryostat in acetone (between –78 °C and 0 °C) or with distilled water and ice (0 °C). High temperature reactions were conducted in reaction vessels equipped with a reflux condenser or in a pressure tube using a heated silicon oil bath or a metal block. The reactions were magnetically stirred and monitored by NMR spectroscopy or analytical thin-layer chromatography (TLC), using aluminum plates percolated with silica gel (0.25 mm, 60-Å pore size, *Merck*) impregnated with a fluorescent indicator (254 nm). TLC plates were visualized by exposure to ultraviolet light (UV) at 254 nm, were stained by submersion in aqueous potassium permanganate solution ($KMnO_4$) or ceric ammonium molybdate solution (CAM) and were developed by heating with a heat-gun. Flash column chromatography (FCC) was performed as described by Still employing silica gel (60 Å, 40–63 μm, *Merck KGaA*).[130] The yields refer to chromatographically and spectroscopically (^{1}H and ^{13}C NMR) pure material, unless otherwise specified.

6.2. Materials

Tetrahydrofuran (THF) and diethyl ether (Et_2O) were purchased from Merck as "anhydrous" and dried over molecular sieves (4 Å) prior to use. All other solvents were purchased from Acros Organics as 'extra dry' reagents. If required solvents were degassed by freeze-pump-thaw under vacuum (0.1 mmHg). All other reagents with a purity > 95% were obtained from commercial sources (Sigma Aldrich, TCI, Acros Organics, Alfa Aesar, Strem Chemicals, ABCR and others) and used without further purification unless otherwise stated. Solvents for extraction, crystallization and flash column chromatography were purchased in technical grade and distilled under reduced pressure prior to use. Lithium chloride was dried at 100 °C under vacuum (0.1 mmHg) for 12 h and stored in a drying oven at 150 °C (760 mmHg); the hot, dried solid was flame dried under vacuum (0.1 mmHg) for 4−5 min immediately prior to use. The molarity of *n*-butyllithium and *t*-butyllithium solutions was determined by titration against diphenylacetic acid as an indicator (average of three determinations).[131] The concentration of freshly prepared dimethyldioxirane solutions[175] was determined by iodometric titration as follows: A 20 mM aqueous stock solution of sodium thiosulfate pentahydrate (124 mg $Na_2S_2O_3 \cdot 5\ H_2O$ in 25 mL H_2O) was prepared in a 25 mL graduated cylinder. A 100 mL flask was charged with water

[130] W.C. Still, M. Kahn, A. J. Mitra, *Org. Chem.***1978**, *43*, 2923.
[131] W. G. Kofron, L. M. Baclawski, *J. Org. Chem.* **1976**, *41*, 1879.

(30 mL), sodium iodide (2.00 g) and glacial acetic acid (1 mL), whereupon the dimethyldioxirane solution (2 mL) was added. The resulting brown mixture was rapidly titrated with the sodium thiosulfate stock solution until disappearance of the yellow iodine color occurred. The concentration of the dimethyldioxirane solution was calculated according to the following equation:

$$c(DMDO) = \frac{M(titrant)\ x\ V(titrant)}{V(DMDO)\ x\ 2}$$

and was generally in the range of 40.0 mM to 60.0 mM.

6.3. NMR Spectroscopy

NMR spectra (^{1}H NMR and ^{13}C NMR) were recorded in deuterated chloroform (chloroform-*d*), deuterated benzene (benzene-d_6), deuterated dichloromethane (dichloromethane-d_2) or deuterated pyridine (pyridine-d_5) on a Bruker Avance III HD 400 MHz spectrometer equipped with a CryoProbe™, a Bruker Avance Neo 400 MHz spectrometer, Bruker AXR300 spectrometer, Varian VXR400 S spectrometer, JOEL ECX400 spectrometer, Bruker AMX600 spectrometer, a Bruker Avance II 600 MHz spectrometer, Bruker Avance HD 800 spectrometer and are reported as follows: chemical shift δ in ppm (multiplicity, coupling constant *J* in Hz, number of protons) for ^{1}H NMR spectra and chemical shift δ in ppm for ^{13}C NMR spectra. Multiplicities are abbreviated as follows: s = singlet, d = doublet, t = triplet, q = quartet, p = quintet, br = broad, m = multiplet, or combinations thereof. For ^{1}H NMR the residual protic solvent peak served as internal reference (chloroform-*d*: 7.26 ppm, benzene-d_6: 7.16 ppm, dichloromethane-d_2: 5.32 ppm, pyridine-d_5: 8.74 ppm for the signal with the highest shift, acetone-d_6: 2.05 ppm). For ^{13}C NMR the central carbon resonance of chloroform-*d* (77.16 ppm or 77.00 ppm for comparison of synthetic and isolated natural products), benzene-d_6 (128.06 ppm), dichloromethane-d_2 (54.00 ppm), pyridine-d_5 (150.35 ppm for the signal with the highest shift) or acetone-d_6 (29.84 ppm) served as internal reference. NMR spectra were assigned using information ascertained from homonuclear correlation spectroscopy (COSY), heteronuclear multiple bond coherence (HMBC), heteronuclear single quantum coherence (HSQC) and nuclear Overhauser enhancement spectroscopy (NOESY) experiments.

6.4. Mass Spectrometry

High resolution mass spectra (HRMS) were recorded on a MAT 95 spectrometer and MAT 90 spectrometer from Thermo Finnigan GmbH or MS-700 spectrometer from JOEL by the analytic section of the Department of Chemistry, Ludwig-Maximilians-Universität München.

High resolution mass spectra were recorded on a Thermo Scientific™ LTQ Orbitrap XL™ Hybrid Ion Trap-Orbitrap Mass spectrometer at the Institute of Organic Chemistry and Center for Molecular Biosciences, University of Innsbruck.

6.5. IR Spectroscopy

Infrared spectra (IR) were recorded from 4000 cm^{-1} to 450 cm^{-1} on a Bruker™ ALPHA FT-IR Spectrometer from Bruker or on a PerkinElmer Spectrum BX II FT-IR system. Samples were prepared as a neat film or a film by evaporation of a solution in Chloroform-*d*, Benzene-d_6 or dichloromethane. IR data in frequency of absorption (cm^{-1}) is reported as follows: *w* = weak, *m* = medium, *s* = strong, *br* = broad or combinations thereof.

6.6. Optical Rotation

Optical rotation values were recorded on a PerkinElmer 241 polarimeter, a Anton Paar MCP 200 polarimeter or a Schmidt+Haensch UniPol L1000 Peltier polarimeter. The specific rotation is calculated as follows:

$$[\alpha]_{\lambda}^{\varphi} = \frac{[\alpha] \cdot 100}{c \cdot d}$$

Thereby, the wave length λ is reported in nm and the measuring temperature ϕ in °C. α represents the recorded optical rotation at the apparatus, *c* the concentration of the analyte in 10 mg/mL and *d* the length of the cuvette in dm. Thus, the specific rotation is given in 10^{-1}·deg·cm^2·g^{-1}. Usage of the sodium D line (λ = 589 nm) is indicated by D instead of the wavelength in nm. The respective concentration as well as the solvent is reported at the relevant section of the experimental section.

6.7. Melting Points

Melting points were determined on a B-450 melting point apparatus from BÜCHI Labortechnik AG or an SRS MPA120 EZ-Melt melting point apparatus in open glass capillaries and are uncorrected.

6.8. X-Ray Diffraction Analysis

X-Ray diffraction analysis was carried out by Dr. Klaus Wurst at the Institute of Inorganic and Theoretical Chemistry and Center for Molecular Biosciences, University of Innsbruck. The data collections were performed on a Bruker D8 Quest diffractometer (Photon 100 detector) equipped with a microfocus source generator (Incoatec GmbH, Geesthacht, Germany) combined with multi-layer optics (monochromatized Mo *Kα* radiation, λ = 71.073 pm). The Bruker Apex III software was applied for the integration, scaling and multi-scan absorption correction of the data. The structure was solved with SHELXS (version 2013/1).[132] Structure refinement (full-matrix least-squares against F^2) with SHELXL (version 2014/7).[133]

X-ray diffraction analysis was carried out by Dr. Peter Mayer (Ludwig-Maximilians-Universität München). The data collections were performed either on an Oxford Diffraction Xcalibur diffractometer, on a Bruker D8Quest diffractometer or on a Bruker D8Venture diffractometer using Mo *Kα*-radiation (λ = 0.71073 Å, graphite monochromator). The CrysAlisPro software (version

[132] G. M. Sheldrick, *Acta Crystallogr. Sect. Found. Adv.* **2015**, *71*, 3–8.
[133] G. M. Sheldrick, *Acta Crystallogr. Sect. C Struct. Chem.* **2015**, *71*, 3–8.

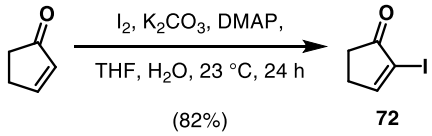
1.171.33.41) was applied for the integration, scaling and multi-scan absorption correction of the data. The structures were solved by direct methods with SIR9713[134] and refined by least-squares methods against F^2 with SHELXL-97.14.[133]

All non-hydrogen atoms were refined anisotropically. The hydrogen atoms were placed in ideal geometry riding on their parent atoms. Further details are summarized in the tables at the different sections. Plotting of thermal ellipsoids in this document was carried out using MERCURY for Windows at 50% probability level.

[134] A. Altomare, M. C. Burla, M. Camalli, G. L. Cascarano, C. Giacovazzo, A. Guagliardi, A. G. G. Moliterni, G. Polidori, R. Spagna, *J. Appl. Crystallogr.* **1999**, *32*, 115–119.

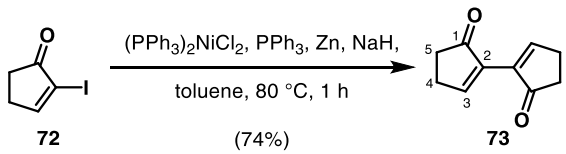
7. Experimental Procedures, X-Ray Crystallographic and Spectroscopic Data

7.1. Experimental Procedures



Cyclopentenone iodide 72

To a solution of 2-cyclopenten-1-one (2.00 g, 24.4 mmol, 1 equiv) in tetrahydrofuran (50 mL) and water (50 mL) was successively added potassium carbonate (4.04 g, 29.2 mmol, 1.20 equiv), iodine (9.37 g, 36.5 mmol, 1.50 equiv) and 4-dimethylaminopyridine (601 mg, 4.87 mmol, 0.20 equiv) at 23 °C. After 24 hours, ethyl acetate (50 mL) was added to the reaction mixture and the layers were separated. The organic layer was washed twice with an ice-cold saturated aqueous solution of sodium thiosulfate (2 × 25 mL). The washed solution was dried over sodium sulfate. The dried solution was filtered and the filtrate was concentrated. The residue was purified by flash column chromatography on silica gel (20% ethyl acetate in cyclohexane) to give cyclopentenone iodide **72** (4.14 g, 19.9 mmol, 82%) as a colourless solid. The obtained analytical data were in full agreement with those reported in the literature.[135]



Cyclopentenone dimer 73

A Schlenk-flask was charged with iodo cyclopentenone **72** (100 mg, 481 µmol, 1 equiv), bis(triphenylphosphine)nickel(II) dichloride (157 mg, 240 µmol, 0.500 equiv), triphenylphosphine (126 mg, 481 µmol, 1 equiv), zinc (94.3 mg, 1.44 mmol, 3.00 equiv) and sodium hydride (92.4 mg, 3.85 mmol, 8.00 equiv). The flask was evacuated and back-filled with nitrogen (3 cycles) and then toluene (2 mL) was added and the reaction mixture was heated to 80 °C. After one hour, the reaction mixture was allowed to cool to 23 °C and then an aqueous solution of hydrochloric acid (1 M, 2 mL) was added. The layers were separated, the aqueous layer was extracted with ethyl acetate (3 × 1 mL) and the combined organic layers were dried over sodium sulfate. The dried solution was filtered through a pad of Celite, the filter cake was washed with ethyl acetate (5 mL) and the filtrate was concentrated.

[135] H. Lin, L.-J. Xiao, M.-J. Zhou, H.-M. Yu, J.-H. Xie, Q.-L. Zhou, *Org. Lett.* **2016**, *18*, 1434–1437.

The residue was purified by flash column chromatography on silica gel (30% ethyl acetate in cyclohexane) to yield cyclopentenone dimer **73** (28.9 mg, 178 µmol, 74%) as a colourless solid.

TLC (30% ethyl acetate in cyclohexane): R_f = 0.32 ($KMnO_4$).

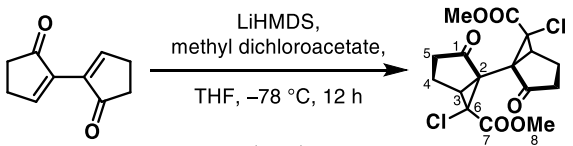
mp: (134-135) °C

^{1}H NMR (400 MHz, chloroform-*d*) δ 8.57 – 8.53 (m, 2H, 3-H), 2.74 – 2.70 (m, 4H, 4-H), 2.46 – 2.43 (m, 4H, 5-H).

^{13}C NMR (101 MHz, chloroform-*d*) δ 208.9 (C-1), 161.5 (C-3), 134.2 (C-2), 34.5 (C-5), 27.2 (C-4).

IR (Diamond-ATR, neat) $\tilde{\upsilon}_{max}$: 2919 (w), 1711 (s), 1568 (w), 1445 (w), 1417 (w), 1390 (w), 1271 (m), 1234 (m), 1156 (m), 1010 (w), 996 (w), 932 (w), 870 (w), 782 (m), 754 (w), 722 (w) cm^{-1}.

HRMS (EI) calc. for $C_{10}H_{10}O_2$ $[M]^{\bullet+}$: 162.0675 found: 162.0677.



73 **74**

Cyclopropane dimer 74

To a solution of lithium bis(trimethylsilyl)amide (1.00 M in tetrahydrofuran, 2.84 mL, 2.84 mmol, 2.10 equiv) was added methyl dichloroacetate (308 µL, 2.97 mmol, 2.20 equiv) at –78 °C. After 30 minutes, a solution of cyclopentenone dimer **73** (219 mg, 1.35 mmol, 1 equiv) in tetrahydrofuran (10 mL) was added dropwise at –78 °C. After one hour, the reaction mixture was allowed to warm to 23 °C. After 11 hours at 23 °C, to the brown solution was added a saturated aqueous solution of ammonium chloride (10 mL) and ethyl acetate (10 mL). The layers were separated and the aqueous layer was extracted with ethyl acetate (3 × 3 mL), the combined organic layers were dried over sodium sulfate. The dried solution was filtered and the filtrate was concentrated. The residue was purified by flash column chromatography on silica gel (30% ethyl acetate in cyclohexane) to yield cyclopropane dimer **74** (247 mg, 658 µmol, 49%) as an orange solid.

TLC (30% ethyl acetate in cyclohexane): R_f = 0.27 ($KMnO_4$, UV).

mp: *decomposition before melting point was reached*

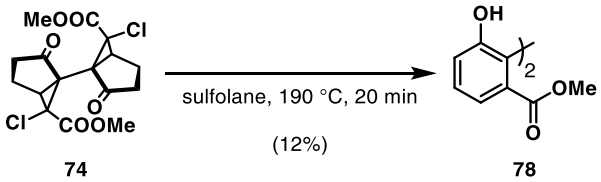
^{1}H NMR (400 MHz, chloroform-*d*) δ 3.74 (s, 6H, 8-H), 2.71 (d, *J* = 6.1 Hz, 2H, 3-H), 2.52 – 2.43 (m, 2H, 4-H), 2.40 – 2.31 (m, 2H, 5-H), 2.19 – 2.12 (m, 2H, 4-H), 2.12 – 2.03 (m, 2H, 5-H).

^{13}C NMR (101 MHz, chloroform-*d*) δ 209.7 (C-1), 169.0 (C-7), 54.0 (C-8), 51.3 (C-6), 48.7 (C-2), 42.7 (C-3), 37.0 (C-5), 20.1 (C-4).

IR (Diamond-ATR, neat) $\tilde{\upsilon}_{max}$: 2954 (w), 1737 (s), 1718 (s), 1436 (m), 1273 (s), 1236 (m), 1215 (m), 1190 (m), 1064 (w), 955 (w), 744 (w), 735 (w) cm^{-1}.

HRMS (ESI) calc. for $C_{16}H_{20}Cl_2NO_6$ $[M+NH_4]^+$: 392.0662 found: 392.0665.

Crystal structure: *see chapter 7.2. for more details*



74 **78**

Phenol dimer 78

A flask containing a solution of cyclopropane dimer **74** (111 mg, 296 µmol, 1 equiv) in sulfolane (3 mL) was submerged in a preheated oil bath at 190 °C. After 20 minutes, the reaction mixture was allowed to cool to 23 °C and then water (5 mL) was added to the solution and the layers were separated. The aqueous layer was extracted with diethyl ether (3 × 2 mL) and the combined organic layers were dried over sodium sulfate. The dried solution was filtered and the filtrate was concentrated. The residue was purified by flash column chromatography on silica gel (20% grading to 30% ethyl acetate in cyclohexane) to yield phenol dimer **78** (11.0 mg, 36.0 µmol, 12%) as a colourless solid.

TLC (20% ethyl acetate in cyclohexane): R_f = 0.38 ($KMnO_4$, UV).

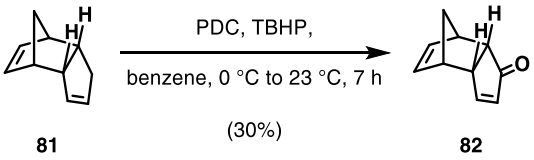
mp: (215-216) °C

^{1}H NMR (200 MHz, chloroform-*d*) δ 7.83 – 7.67 (m, 4H), 7.60 – 7.47 (m, 2H), 3.93 (s, 6H).

^{13}C NMR (101 MHz, chloroform-*d*) δ 168.6, 157.0, 128.6, 127.5, 124.9, 121.4, 115.4, 52.5.

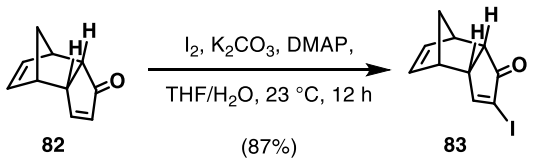
IR (Diamond-ATR, neat) $\tilde{\upsilon}_{max}$: 2925 (w), 2851 (w), 2362 (w), 1724 (s), 1430 (w), 1321 (m), 1291 (m), 1197 (m), 1135 (m), 994 (w), 810 (w), 755 (m) cm^{-1}.

HRMS (EI) calc. for $C_{16}H_{12}O_5$ $[M–H_2O]^{\bullet+}$: 284.0679 found: 284.0678.



Enone 82

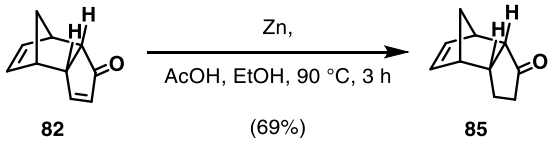
Following a literature precedent,[136] to a solution of dicyclopentadiene **81** (516 mg, 3.90 mmol, 1 equiv) in benzene (12 mL) was added Celite (2.50 g) and pyridinium dichromate (2.94 g, 7.81 mmol, 2.00 equiv) and the suspension was cooled to 0 °C. A solution of *tert*-butyl hydroperoxide (5.50 M in nonane, 1.42 mL, 7.81 mmol, 2.00 equiv) was added to the suspension and the reaction mixture was allowed to warm to 23 °C. After seven hours at 23 °C, the mixture was diluted with diethyl ether (30 mL) and filtered through a pad of Celite. The filter cake was washed with diethyl ether (30 mL) and the filtrate was concentrated. The residue was purified by flash column chromatography on silica gel (20% ethyl acetate in cyclohexane) to yield enone **82** (171 mg, 1.17 mmol, 30%) as a slightly yellow oil. The obtained analytical data were in full agreement with those reported in the literature.



Iodo enone 83

To a solution of enone **82** (676 mg, 4.62 mmol, 1 equiv) in tetrahydrofuran (10 mL) and water (10 mL) was added potassium carbonate (767 mg, 5.55 mmol, 1.20 equiv), iodine (1.76 g, 6.94 mmol, 1.50 equiv) and 4-dimethylaminopyridine (114 mg, 925 µmol, 0.200 equiv) in sequence at 23 °C. After 12 hours, water (50 mL) and ethyl acetate (50 mL) were added to the reaction mixture. The layers were separated and the aqueous layer was extracted with ethyl acetate (3 × 20 mL). The combined organic layers were washed with a saturated aqueous solution of sodium thiosulfate (30 mL) and with a saturated aqueous solution of sodium chloride (30 mL). The washed solution was dried over sodium sulfate. The dried solution was filtered and the filtrate was concentrated. The residue was purified by flash column chromatography on silica gel (30% ethyl acetate in cyclohexane) to yield iodo enone **83** (1.10 g, 4.04 mmol, 87%) as a slightly yellow oil. The obtained analytical data were in full agreement with those reported in the literature.[137]

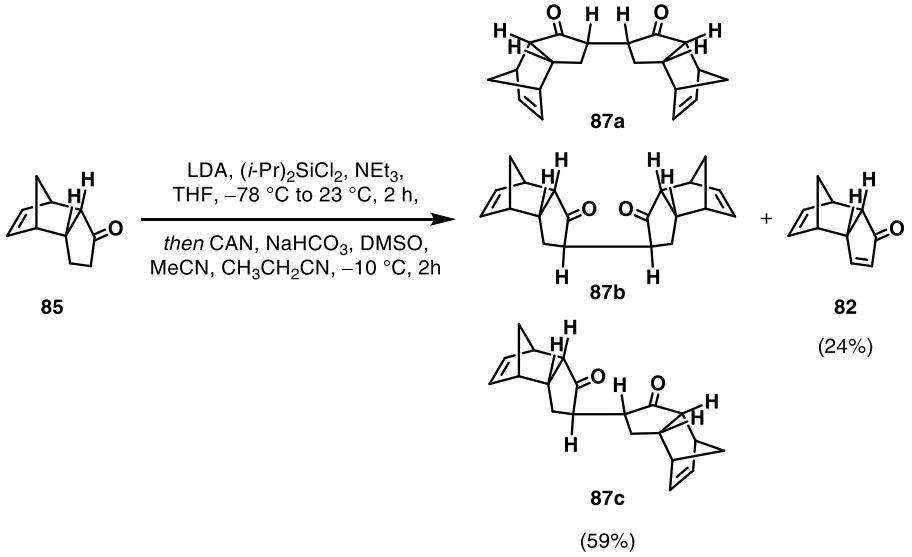
[136] N. Chidambaram, S. Chandrasekaran, *J. Org. Chem.* **1987**, *52*, 5048–5051.
[137] S. Lal, A. Chowdhury, I. N. N. Namboothiri, *Tetrahedron* **2017**, *73*, 1297–1305.



82 85

Ketone 85

To a solution of enone **82** (953 mg, 6.52 mmol, 1 equiv) in acetic acid (7.5 mL) and ethanol (22.5 mL) was added zinc (2.13 g, 32.6 mmol, 5.00 equiv) and the mixture was heated to 90 °C in a pressure tube. After three hours at 90 °C, the reaction mixture was allowed to cool to 23 °C, then filtered through a pad of Celite and the filter cake was washed with diethyl ether (20 mL). The filtrate was concentrated and the residue was purified by flash column chromatography on silica gel (15% ethyl acetate in cyclohexane) to yield ketone **85** (662 mg, 4.47 mmol, 69%) as a colourless solid. The obtained analytical data were in full agreement with those reported in the literature.[138]



Norbornene dimer 87

To a solution of lithium diisopropylamide (prepared from *n*-butyllithium (1.29 mL, 2.50 M, 3.22 mmol, 1.10 equiv) and diisopropylamine (497 µL, 3.51 mmol, 1.20 equiv)) in tetrahydrofuran (15 mL) was added a solution of cyclopentanone **85** (434 mg, 2.93 mmol, 1 equiv) in tetrahydrofuran (10 mL) dropwise over the course of 30 minutes at –78 °C. 30 minutes after the addition of cyclopentanone **85** was completed, dichlorodiisopropylsilane (317 µL, 1.76 mmol, 0.60 equiv) and triethylamine (244 µL, 1.76 mmol, 0.600 equiv) were added in sequence at –78 °C. After one hour, the solution was allowed to warm to 23 °C. After 15 minutes at 23 °C, a neutral aqueous phosphate buffer (pH = 7, 30 mL) and diethyl ether (30 mL) were added to the reaction mixture. The layers were separated and the aqueous layer was extracted with diethyl ether (3 × 10 mL), the combined organic layers were dried over sodium

[138] S. Takano, T. Kamikubo, M. Moriya, K. Ogasawara, *Synthesis* **1994**, *1994*, 601–604.

sulfate. The dried solution was filtered and the filtrate was concentrated. The residue was dissolved in propionitrile (10 mL) and the resulting solution was added to a suspension of ammonium cerium(IV) nitrate (3.53 g, 6.44 mmol, 2.20 equiv), sodium bicarbonate (1.62 g, 19.3 mmol, 6.60 equiv) and dimethyl sulfoxide (416 µL, 5.86 mmol, 2.00 equiv) in acetonitrile (20 mL) dropwise over the course of 30 minutes at –10 °C. Two hours after the addition was completed, a saturated aqueous solution of sodium bicarbonate (30 mL) and ethyl acetate (30 mL) were added to the reaction mixture. The layers were separated and the aqueous layer was extracted with ethyl acetate (3 × 10 mL). The combined organic layers were dried over sodium sulfate. The dried solution was filtered and the filtrate was concentrated. The residue was purified by flash column chromatography on silica gel (15% ethyl acetate in cyclohexane) to yield a mixture of norbornene dimer **87** (254 mg, 863 µmol, 59%) as a colourless oil (in a 1:3.0:4.2 mixture of diastereomers) and cyclopentenone **82** (101 mg, 691 µmol, 24%).

TLC (30% ethyl acetate in cyclohexane): R_f = 0.50 ($KMnO_4$, UV).

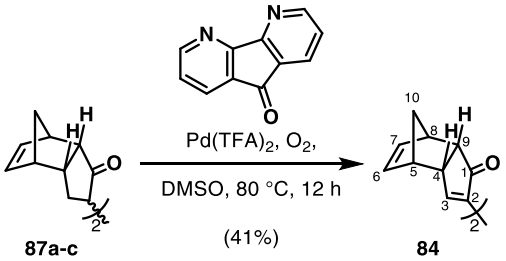
^{1}H NMR (600 MHz, chloroform-*d*) δ *complex mixture of signals arising from different diastereomers in a ratio of 1:3.0:4.2*

^{13}C NMR (151 MHz, chloroform-*d*) δ 137.4, 136.6, 136.4, 136.3, 136.1, 135.6, 135.4, 135.3, 135.0, 134.9, 55.0, 54.9, 54.8, 54.5, 53.6, 53.2, 52.7, 52.4, 52.4, 52.3, 52.2, 50.8, 49.2, 48.1, 48.0, 47.9, 47.7, 47.7, 47.2, 46.6, 44.4, 41.4, 40.7, 39.5, 39.4, 39.3, 38.6, 27.7, 25.9, 25.8, 25.4, 22.8.

Note: The signals arise from a mixture of diastereomers.

IR (Diamond-ATR, neat) $\tilde{\nu}_{max}$: 2964 (w), 2866 (w), 1725 (s), 1342 (w), 1227 (w), 1173 (w), 733 (w) cm^{-1}.

HRMS (EI) calc. for $C_{20}H_{22}O_2$ $[M]^{\bullet+}$: 294.1614 found: 294.1614.



Enone dimer 84

To a solution of norbornene dimer **87a-c** (18.0 mg, 61.0 µmol, 1 equiv) in dimethyl sulfoxide (600 µL) was added palladium(II) trifluoroacetate (8.13 mg, 24.5 µmol, 0.400 equiv) and 4,5-diazafluoren-9-one (4.46 mg, 24.5 µmol, 0.400 equiv) at 23 °C. An atmosphere of oxygen was maintained by sparging with a stream of pure oxygen gas through a stainless-steel needle for five minutes. Vigorous stirring of the suspension was then continued under oxygen atmosphere at 80 °C. After 12 hours, water (5 mL) and

diethyl ether (5 mL) were added to the reaction mixture and the layers were separated. The aqueous layer was extracted with diethyl ether (3 × 2 mL), the combined organic layers were dried over sodium sulfate. The dried solution was filtered and the filtrate was concentrated. The residue was purified by flash column chromatography on silica gel (20% ethyl acetate in cyclohexane) to yield enone dimer **84** (7.20 mg, 24.8 µmol, 41%) as a colourless oil.

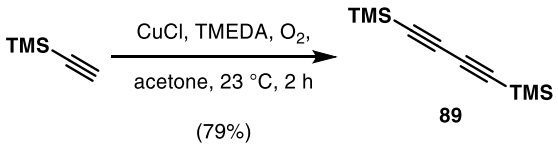
TLC (20% ethyl acetate in cyclohexane): R_f = 0.26 ($KMnO_4$, UV).

^{1}H NMR (400 MHz, chloroform-*d*) δ 8.15 – 8.13 (m, 2H, 3-H), 5.84 (dd, *J* = 5.6, 2.9 Hz, 2H, 7-H), 5.75 – 5.72 (m, 2H, 6-H), 3.38 – 3.35 (m, 2H, 4-H), 3.24 – 3.22 (m, 2H, 8-H), 2.99 (ddd, *J* = 3.1, 2.2, 1.0 Hz, 2H, 5-H), 2.83 – 2.80 (m, 2H, 9-H), 1.75 – 1.72 (m, 2H, 10-H), 1.64 – 1.61 (m, 2H, 10-H).

^{13}C NMR (101 MHz, chloroform-*d*) δ 209.1 (C-1), 161.3 (C-3), 136.5 (C-2), 133.0 (C-6), 132.2 (C-7), 52.9 (C-10), 50.6 (C-9), 46.2 (C-4), 45.5 (C-8), 44.7 (C-5).

IR (Diamond-ATR, neat) $\tilde{\upsilon}_{max}$: 2942 (s), 2866 (s), 1696 (s), 1632 (w), 1464 (w), 1270 (w), 1088 (m), 1058 (m), 885 (m), 684 (w) cm^{-1}.

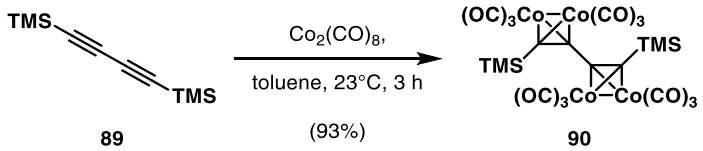
HRMS (ESI) calc. for $C_{20}H_{19}O_2$ $[M+H]^+$: 291.1380 found: 291.1381



Alkyne dimer 89

To a suspension of cuprous chloride (500 mg, 5.05 mmol, 0.100 equiv) in acetone (9 mL) was added *N*,*N*,*N'*,*N'*-tetramethylethylenediamine (250 µL, 1.64 mmol, 0.0320 equiv) upon which the reaction mixture became homogenous and turned from bright blue to turquoise. After 30 minutes, the supernatant solution of the freshly prepared Cu(I)Cl-TMEDA complex was added to a solution of trimethylsilylacetylene (5.00 g, 50.9 mmol, 1 equiv) in acetone (30 mL) dropwise over the course of ten minutes at 0 °C while an atmosphere of oxygen was maintained by sparging with a stream of pure oxygen gas through a stainless-steel needle for 20 minutes. Vigorous stirring of the suspension was then continued under oxygen atmosphere at 23 °C. After 90 minutes, the reaction mixture was concentrated, then cyclohexane was added (100 mL) and the organic layer was washed with an aqueous solution of hydrochloric acid (2 M in water, 50 mL). The layers were separated and the aqueous layer was extracted with ethyl acetate (3 × 20 mL), the combined organic layers were dried over sodium sulfate. The dried solution was filtered and the filtrate was concentrated. The residue was purified by flash column chromatography on silica gel (cyclohexane) to yield alkyne dimer **89** (3.91 g, 20.1 mmol, 79%) as a

colourless solid. The obtained analytical data were in full agreement with those reported in the literature.[139]



Cobalt alkyne complex 90

To a solution of dicobalt octacarbonyl (1.15 g, 3.18 mmol, 2.05 equiv) in toluene (4 mL) was added a solution of alkyne dimer **89** (302 mg, 1.55 mmol, 1 equiv) in toluene (4 mL) dropwise over the course of 5 minutes at 23 °C. Three hours after the addition of the alkyne was completed, the reaction mixture was concentrated and the residue was purified by flash column chromatography on silica gel (cyclohexane) to yield cobalt alkyne complex **90** (1.12 g, 1.44 mmol, 93%) as a dark green, nearly black solid.

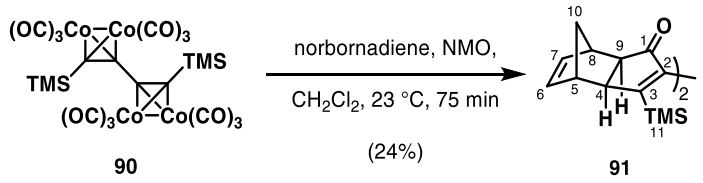
TLC (cyclohexane): R_f = 0.57 ($KMnO_4$, UV).

mp: decomposition at 142 °C

^{1}H NMR (400 MHz, chloroform-*d*) δ 0.40 (s, 18H).

^{13}C NMR (101 MHz, chloroform-*d*) δ 199.8, 1.1.

IR (Diamond-ATR, neat) $\tilde{\upsilon}_{max}$: 2074 (m), 2048 (m), 2034 (s), 2015 (m), 2000 (m), 1475 (w), 1251 (w), 837 (w), 510 (w), 491 (w) cm^{-1}.



Norbornene dimer 91

To a solution of cobalt alkyne complex **90** (341 mg, 438 µmol, 1 equiv) in dichloromethane (4 mL) was added norbornadiene (98.0 µl, 964 µmol, 2.20 equiv) dropwise at 23 °C. After 15 minutes, a solution of 4-methylmorpholine *N*-oxide (616 mg, 5.26 mmol, 12.0 equiv) in dichloromethane (2 mL) was added to the reaction mixture dropwise upon which the colour changed from dark green to dark brown. After one hour, the reaction mixture was filtered through a pad of silica gel and the pad was washed with diethyl ether (20 mL). The filtrate was concentrated and the residue was purified by flash column

[139] G. E. Jones, D. A. Kendrick, A. B. Holmes, *Org. Synth.* **1987**, *65*, 52.

chromatography on silica gel (0% grading to 5% ethyl acetate in cyclohexane) to yield cobalt norbornene dimer **91** (46.0 mg, 106 µmol, 24%) as a slightly brownish oil.

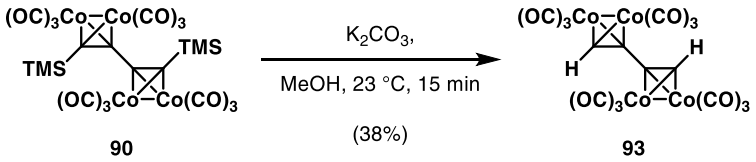
TLC (5% ethyl acetate in cyclohexane): R_f = 0.43 ($KMnO_4$, UV).

^{1}H NMR (300 MHz, chloroform-*d*) δ 6.29 – 6.20 (m, 4H, 6-H, 7-H), 2.95 – 2.91 (m, 4H, 5-H, 8-H), 2.80 (d, *J* = 5.6 Hz, 2H, 4-H), 2.34 – 2.29 (m, 2H, 9-H), 1.43 – 1.39 (m, 2H, 10-H), 1.21 (d, *J* = 9.1 Hz, 2H, 10-H), 0.25 (s, 18H, 11-H).

^{13}C NMR (101 MHz, chloroform-*d*) δ 213.3 (C-1), 164.4 (C-3), 153.4 (C-2), 138.3 (C-6 or C-7), 138.0 (C-6 or C-7), 55.8 (C-4), 53.7 (C-9), 44.8 (C-5 or C-8), 43.6 (C-5 or C-8), 41.9 (C-10), –0.4 (C-11), –1.1 (C-11).

IR (Diamond-ATR, neat) $\tilde{\upsilon}_{max}$: 2956 (w), 1688 (m), 1547 (w), 1250 (m), 843 (s), 761 (w) cm^{-1}.

HRMS (ESI) calc. for $C_{26}H_{34}NaO_2Si_2$ $[M+Na]^+$: 457.1990 found: 457.1984.



Cobalt alkyne complex 93

To a solution of cobalt complex dimer **90** (72.0 mg, 93.0 µmol, 1 equiv) in methanol (2 mL) was added potassium carbonate (128 mg, 925 µmol, 10.0 equiv) at 23 °C, upon which the reaction mixture turned from green to brown. After 15 minutes, the reaction mixture was filtered through a pad of Celite and the pad was washed with dichloromethane (5 mL). The filtrate was concentrated to yield cobalt alkyne complex **93** (22.0 mg, 35.0 µmol, 38%) as a brownish solid.

*Note: Cobalt alkyne complex **93** is instable on silica gel and was therefore used without further purification in the next reaction.*

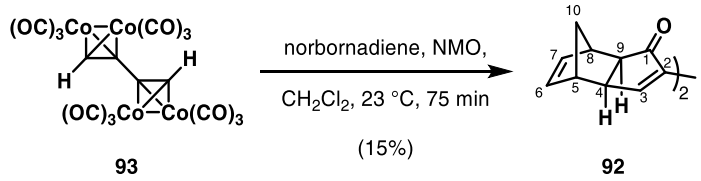
TLC (cyclohexane): R_f = 0.57 ($KMnO_4$, UV).

mp: decomposition at 113 °C

^{1}H NMR (400 MHz, chloroform-*d*) δ 6.46 (s, 2H)

^{13}C NMR (101 MHz, chloroform-*d*) δ 200.0.

IR (Diamond-ATR, neat) $\tilde{\upsilon}_{max}$: 2078 (m), 2040 (s), 2006 (s) cm^{-1}.



Norbornene dimer 92

To a solution of cobalt alkyne complex **93** (209 mg, 330 µmol, 1 equiv) in dichloromethane (6 mL) was added norbornadiene (76.0 µl, 726 µmol, 2.20 equiv) dropwise at 23 °C. After 15 minutes, a solution of 4-methylmorpholine *N*-oxide (464 mg, 3.96 mmol, 12.0 equiv) in dichloromethane (3 mL) was added to the reaction mixture dropwise. After one hour, the reaction mixture was filtered through a combined pad of silica gel and Celite and the pad was washed with diethyl ether (20 mL). The filtrate was concentrated and the residue was purified by flash column chromatography on silica gel (0% grading to 5% ethyl acetate in cyclohexane) to yield cobalt norbornene dimer **92** (14.0 mg, 48.0 µmol, 15%) as a colourless solid.

TLC (5% ethyl acetate in cyclohexane): R_f = 0.21 ($KMnO_4$, UV).

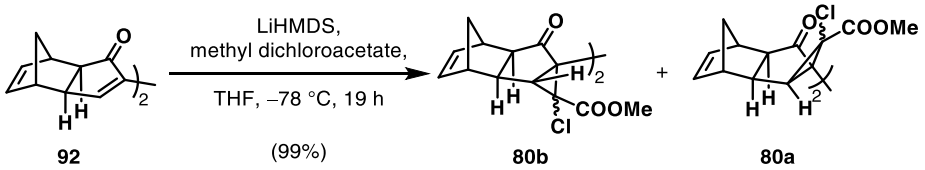
mp: (152-153) °C

^{1}H NMR (600 MHz, chloroform-*d*) δ 8.44 (d, *J* = 2.7 Hz, 2H, 3-H), 6.32 (dd, *J* = 5.6, 3.1 Hz, 2H, 6-H), 6.22 (dd, *J* = 5.6, 3.0 Hz, 2H, 7-H), 2.95 (d, *J* = 3.0 Hz, 2H, 8-H), 2.86 (dd, *J* = 5.8, 2.6 Hz, 2H, 4-H), 2.79 – 2.77 (m, 2H, 5-H), 2.31 (dt, *J* = 5.1, 1.4 Hz, 2H, 9-H), 1.38 (dt, *J* = 9.7, 1.7 Hz, 2H, 10-H), 1.19 (dt, *J* = 9.5, 1.5 Hz, 2H, 10-H).

^{13}C NMR (151 MHz, chloroform-*d*) δ 209.1 (C-1), 163.0 (C-3), 138.8 (C-6), 137.7 (C-2), 137.2 (C-7), 52.4 (C-9), 48.6 (C-4), 44.1 (C-8), 43.4 (C-5), 41.6 (C-10).

IR (Diamond-ATR, neat) $\tilde{\upsilon}_{max}$: 2973 (w), 1695 (s), 1256 (w), 1164 (w), 853 (w), 715 (w) cm^{-1}.

HRMS (ESI) calc. for $C_{20}H_{18}NaO_2$ $[M+Na]^+$: 313.1199 found: 313.1170.



Cyclopropane dimer 80

To a solution of lithium bis(trimethylsilyl)amide (1.00 M in tetrahydrofuran, 121 µL, 121 µmol, 2.50 equiv) in tetrahydrofuran (200 µL) was added methyl dichloroacetate (13.5 µL, 130 µmol, 2.70 equiv) at –78 °C. After 30 minutes, a solution of norbornene dimer **92** (14.0 mg, 48.0 µmol, 1 equiv) in tetrahydrofuran (1 mL) was added dropwise at –78 °C. After 90 minutes, the reaction mixture was allowed to warm to 23 °C. After 18 hours at 23 °C, a saturated aqueous solution of

ammonium chloride (5 mL) and ethyl acetate (5 mL) were added to the brown reaction mixture. The layers were separated and the aqueous layer was extracted with ethyl acetate (3 × 2 mL), the combined organic layers were dried over sodium sulfate. The dried solution was filtered and the filtrate was concentrated. The residue was purified by flash column chromatography on silica gel (30% ethyl acetate in cyclohexane) to yield a mixture of cyclopropane dimer **80** (24.0 mg, 48.0 µmol, 99%) as a colourless oil.

Note: The product was obtained as a mixture of diastereomers. In total four diastereomers can be obtained. Due to the complexity of the NMR spectra analysis of the product was carried out by HRMS.

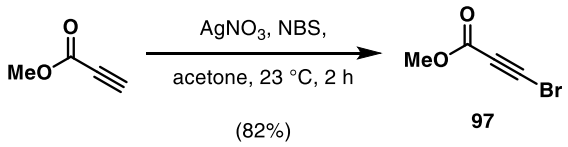
TLC (20% ethyl acetate in cyclohexane): R_f = 0.28 ($KMnO_4$, UV).

^{1}H NMR (300 MHz, chloroform-*d*) δ *complex mixture of signals arising from four diastereomers*

^{13}C NMR (75 MHz, chloroform-*d*) δ *complex mixture of signals arising from four diastereomers*

IR (Diamond-ATR, neat) $\tilde{\upsilon}_{max}$: 2973(w), 1731 (s), 1702 (s), 1436 (w), 1273 (m), 1205 (m), 718 (w), 668 (w) cm^{-1}.

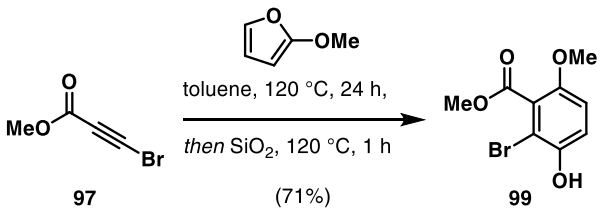
HRMS (ESI) calc. for $C_{26}H_{24}Cl_2NaO_6$ $[M+Na]^+$: 525.0842 found: 525.0774; calc. for $C_{26}H_{24}Cl_2KO_6$ $[M+K]^+$: 541.0582 found: 541.0512.



Bromopropiolate 97

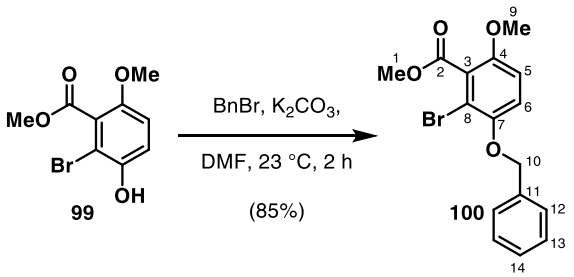
To a solution of methyl propiolate (3.00 mL, 33.0 mmol, 1 equiv) in acetone (100 mL) was added silver nitrate (561 mg, 3.30 mmol, 0.100 equiv) at 23 °C. After five minutes, *N*-bromosuccinimide (6.83 g, 38.0 mmol, 1.15 equiv) was added to the suspension. After two hours, the reaction mixture was filtered through a pad of Celite and the pad was washed with acetone (30 mL). The filtrate was concentrated (16 mbar, 20 °C) and the residue was purified by bulb-to-bulb distillation (0.1 mmHg, 75 °C, the product was collected in a flask cooled to –78 °C) to yield bromopopiolate **97** (4.44 g, 27.2 mmol, 82%) as a yellow oil. The obtained analytical data were in full agreement with those reported in the literature.[140]

[140] J. Leroy, *Synth. Commun.* **1992**, *22*, 567–572.



Bromomethoxybenzoate 99

To a solution of bromopropiolate **97** (2.15 g, 13.2 mmol, 1 equiv) in toluene (40 mL) was added 2-methoxyfuran (1.49 mL, 15.8 mmol, 1.20 equiv) and the reaction mixture was heated to 120 °C in a pressure tube. After 24 hours, the reaction mixture was allowed to cool to 23 °C and then silica gel (4 g) was added to the solution. The suspension was heated to 120 °C. After one hour, the reaction mixture was allowed to cool to 23 °C, then filtered through a pad of Celite and the pad was washed with toluene (10 mL). The filtrate was concentrated and the residue was purified by flash column chromatography on silica gel (30% ethyl acetate in cyclohexane) to yield bromomethoxybenzoate **99** (2.43 g, 9.31 mmol, 71%) as a yellow oil. The obtained analytical data were in full agreement with those reported in the literature.[141]



Bromomethoxybenzoate 100

To a solution of bromomethoxybenzoate **99** (1.02 g, 3.90 mmol, 1 equiv) in *N*,*N*-dimethylformamide (20 mL) was added potassium carbonate (1.62 g, 11.7 mmol, 3.00 equiv) and benzyl bromide (524 µL, 4.29 mmol, 1.10 equiv) at 23 °C. After two hours, water (20 mL) and diethyl ether (20 mL) were added to the reaction mixture and the layers were separated. The aqueous layer was extracted with diethyl ether (3 × 10 mL), the combined organic layers were washed with a 10% aqueous solution of lithium chloride (20 mL) and the washed organic layers were dried over sodium sulfate. The dried solution was filtered and the filtrate was concentrated. The residue was purified by flash column chromatography on silica gel (20% ethyl acetate in cyclohexane) to yield bromomethoxybenzoate **100** (1.17 g, 3.32 mmol, 85%) as a yellow solid.

TLC (20% ethyl acetate in cyclohexane): R_f = 0.38 ($KMnO_4$, UV).

mp: (80-81) °C

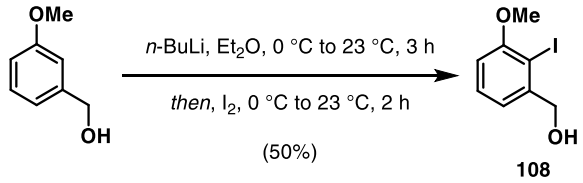
[141] H. Shinohara, M. Sonoda, N. Hayagane, S. Kita, S. Tanimori, A. Ogawa, *Tetrahedron Lett.* **2014**, *55*, 5302–5305.

^{1}H NMR (400 MHz, chloroform-*d*) δ 7.46 – 7.43 (m, 2H, 12-H), 7.41 – 7.36 (m, 2H, 13-H), 7.35 – 7.29 (m, 1H, 14-H), 6.91 (d, *J* = 9.1 Hz, 1H, 5-H), 6.79 (d, *J* = 9.1 Hz, 1H, 6-H), 5.10 (s, 2H, 10-H), 3.96 (s, 3H, 1-H), 3.78 (s, 3H, 9-H).

^{13}C NMR (101 MHz, chloroform-*d*) δ 166.6 (C-2), 151.3 (C-4), 149.5 (C-7), 136.6 (C-11), 128.7 (C-13), 128.2 (C-14), 127.6 (C-3), 127.3 (C-12), 115.7 (C-5), 111.2 (C-8), 111.0 (C-6), 72.1 (C-10), 56.7 (C-9), 52.9 (C-1).

IR (Diamond-ATR, neat) $\tilde{\upsilon}_{max}$: 2950 (w), 1736 (s), 1574 (w), 1478 (s), 1435 (s), 1381 (w), 1281 (s), 1261 (s), 1115 (m), 1036 (s), 800 (w), 738 (m), 697 (w) cm^{-1}.

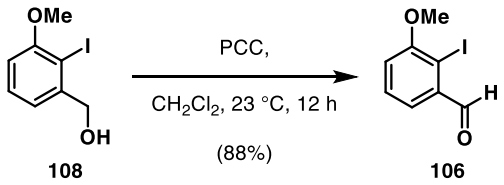
HRMS (ESI) calc. for $C_{16}H_{15}BrNaO_4$ $[M+Na]^+$: 373.0046, 375.0025 found: 373.0021, 375.0000.



Iodobenzene 108

To a solution of *m*-anisyl alcohol (2.22 g, 16.1 mmol, 1 equiv) in diethyl ether (100 mL) was added a solution of *n*-butyllithium (2.44 M in hexanes, 13.8 mL, 33.7 mmol, 2.10 equiv) over the course of one hour at 0 °C. After the addition was completed, the orange reaction mixture was allowed to warm to 23 °C. After two hours at 23 °C, the reaction mixture was cooled to 0 °C and a solution of iodine (4.53 g, 17.7 mmol, 1.10 equiv) in diethyl ether (30 mL) was added to the reaction mixture over the course of 30 minutes. After the addition of iodine was completed, the red mixture was allowed to warm to 23 °C. After two hours at 23 °C, a saturated aqueous solution of sodium thiosulfate (50 mL) was added to the reaction mixture and the layers were separated. The aqueous layer was extracted with diethyl ether (3 × 30 mL) and the combined organic layers were dried over sodium sulfate. The dried solution was filtered and the filtrate was concentrated. The residue was purified by flash column chromatography on silica gel (20% ethyl acetate in hexanes) to yield iodobenzene **108** (2.12 g, 8.04 mmol, 50%) as a colourless solid. The obtained analytical data were in full agreement with those reported in the literature.[142]

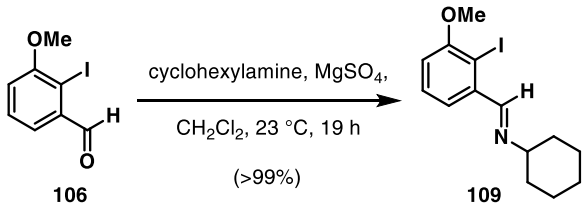
[142] S. Neufeind, N. Hülsken, J.-M. Neudörfl, N. Schlörer, H.-G. Schmalz, *Chem. Eur. J.* **2011**, *17*, 2633–2641.



108 106

Benzaldehyde 106

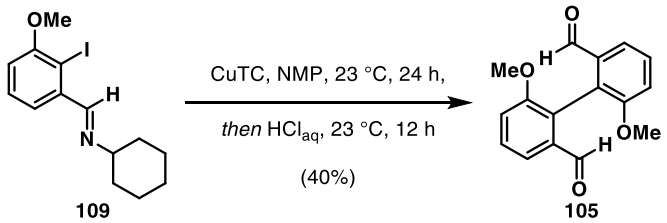
To a solution of iodobenzene **108** (2.12 g, 8.04 mmol, 1 equiv) in dichloromethane (30 mL) was added a pyridinium chlorochromate (3.19 g, 14.5 mmol, 1.80 equiv) at 23 °C. After 12 hours, Celite (5 g) was added to the reaction mixture and after 15 minutes, the suspension was filtered through a pad of Celite. The filtrate was concentrated and residue was purified by flash column chromatography on silica gel (10% ethyl acetate in hexanes) to yield benzaldehyde **106** (1.86 g, 7.09 mmol, 88%) as a colourless solid. The obtained analytical data were in full agreement with those reported in the literature.[143]



106 109

Cyclohexylimine 109

To a solution of benzaldehyde **106** (1.86 g, 7.09 mmol, 1 equiv) in dichloromethane (20 mL) was added cyclohexylamine (1.23 mL, 10.6 mmol, 1.50 equiv) and magnesium sulfate (2.00 g) at 23 °C. After 19 hours, the reaction mixture was filtered through a pad of Celite and the filtrate was concentrated to yield cyclohexylamine **109** (2.45 g, 7.09 mmol, >99%) as a colourless solid. The obtained analytical data were in full agreement with those reported in the literature.[144]



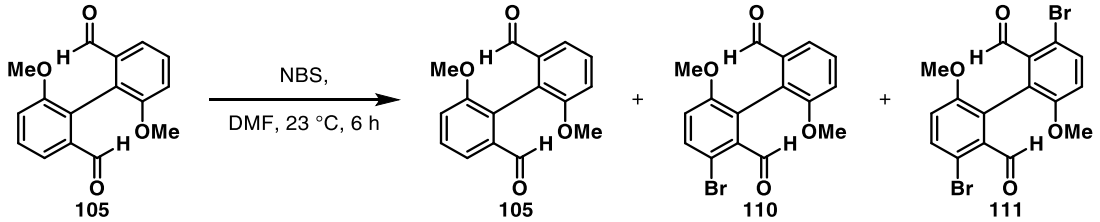
109 105

Benzaldehyde dimer 105

To a solution of cyclohexylimine **109** (445 mg, 1.30 mmol, 1 equiv) in 1-methyl-2-pyrrolidinone (2.6 mL) was added copper(I) thiophene-2-carboxylate (618 mg, 3.24 mmol, 2.50 equiv) at 23 °C and the reaction mixture was protected from light. After 24 hours, ammonia solution (25% in water, 10 mL) was added. After ten minutes, ethyl acetate (5 mL) was added to the reaction mixture and the layers were separated. The aqueous layer was extracted with ethyl acetate (4 × 3 mL) and the combined organic layers were washed with ammonia solution (25% in water, 2 × 3 mL) and brine (2 × 3 mL). The washed

[143] Y. C. Fan, O. Kwon, *Org. Lett.* **2015**, *17*, 2058–2061.
[144] P. Zhang, J. Yu, F. Peng, X. Wu, J. Jie, C. Liu, H. Tian, H. Yang, H. Fu, *Chem. Eur. J.* **2016**, *22*, 17477–17484.

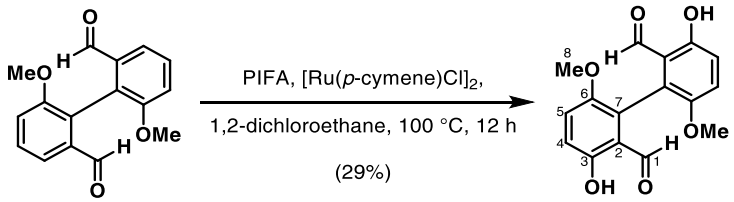
solution was dried over sodium sulfate, the dried solution was filtered through a pad of Celite and the filtrate was concentrated. The residual orange oil was dissolved in dichloromethane (3 mL) and to the resulting solution was added an aqueous solution of hydrochloric acid (6 M in water, 1 mL). After 12 hours, the layers were separated and the aqueous layer was extracted with dichloromethane (1 × 1 mL). The combined organic layers were dried over sodium sulfate and the dried solution was filtered. The filtrate was concentrated and the residue was purified by flash column chromatography on silica gel (30% ethyl acetate in hexanes) to yield benzaldehyde dimer **105** (70.0 mg, 259 µmol, 40%) as an off-white solid. The obtained analytical data were in full agreement with those reported in the literature.[145]



105 105 110 111

Bromobenzene dimer 110 and 111

To a solution of benzaldehyde dimer **105** (11.0 mg, 41.0 µmol, 1 equiv) in *N*,*N*-dimethylformamide (0.4 mL) was added *N*-bromosuccinimide (22.0 mg, 122 µmol, 3.00 equiv) at 23 °C. After six hours, a saturated aqueous solution of lithium chloride (5 mL) and ethyl acetate (5 mL) were added to the reaction mixture. The layers were separated and the aqueous layer was extracted with ethyl acetate (3 × 2 mL) and the combined organic layers were dried over sodium sulfate and the dried solution was filtered. The filtrate was concentrated and the residue was purified by flash column chromatography on silica gel (30% ethyl acetate in hexanes) to yield an inseparable mixture of starting material **105**, bromobenzene **110** and **111** as a slightly yellow solid.



105 112

Salicylaldehyde dimer 112

A pressure tube was charged with aldehyde dimer **105** (20.0 mg, 74.0 µmol, 1 equiv), [bis(trifluoroacetoxy)iodo]benzene (98.4 mg, 222 µmol, 3.00 equiv) and dichloro(*p*-cymene)ruthenium(II) dimer (4.77 mg, 7.40 µmol, 0.10 equiv). The pressure tube was evacuated and back-filled with nitrogen (three cycles) and then 1,2-dichloroethane (400 µL) was added and the reaction mixture was heated to 100 °C. After 12 hours, the reaction mixture was allowed to cool to 23 °C and then an aqueous solution of hydrochloric acid (2 M in water, 5 mL) was added to the reaction mixture.

[145] S. Reichert, B. Breit, *Org. Lett.* **2007**, *9*, 899–902.

After 30 minutes, dichloromethane (5 mL) was added and the layers were separated. The aqueous layer was extracted with dichloromethane (3 × 2 mL) and the combined organic layers were dried over sodium sulfate. The dried solution was filtered and the filtrate was concentrated. The residue was purified by flash column chromatography on silica gel (30% ethyl acetate in cyclohexane) to yield salicylaldehyde dimer **112** (6.4 mg, 21.2 µmol, 29%) as a slightly yellow oil.

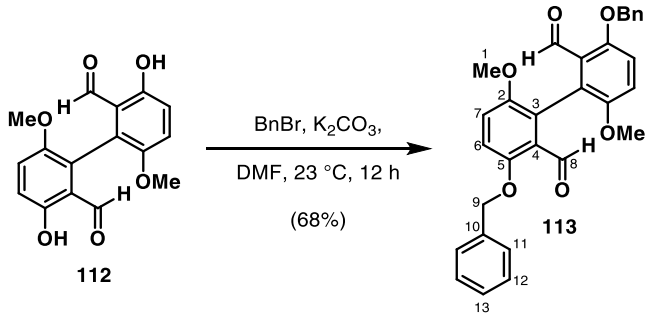
TLC (30% ethyl acetate in cyclohexane): R_f = 0.39 (CAM, UV).

^{1}H NMR (600 MHz, chloroform-*d*) δ 11.28 (s, 2H, 3-OH), 9.51 (s, 2H, 1-H), 7.25 (d, *J* = 9.2 Hz, 2H, 4-H), 7.07 (d, *J* = 9.2 Hz, 2H, 5-H), 3.68 (s, 6H, 8-H).

^{13}C NMR (151 MHz, chloroform-*d*) δ 196.8 (C-1), 156.8 (C-2), 149.6 (C-6), 124.5 (C-4), 121.5 (C-4), 119.1 (C-5), 119.0 (C-3), 56.8 (C-8).

IR (Diamond-ATR, neat) $\tilde{\upsilon}_{max}$: 3458 (br,w), 2955 (w), 1765 (s), 1606 (m), 1487 (m), 1284 (s), 1220 (s), 1185 (w), 1076 (m), 1053 (m), 876 (w) cm^{-1}.

HRMS (ESI) calc. for $C_{16}H_{14}NaO_6$ $[M+Na]^+$: 325.0683 found: 325.0688.



Aldehyde dimer 113

To a solution of salicylaldehyde dimer **112** (6.00 mg, 19.8 µmol, 1 equiv) in *N*,*N*-dimethylformamide (300 µL) was added benzyl bromide (7.20 µL, 59.5 µmol, 3.00 equiv) and potassium carbonate (8.2 mg, 59.5 µmol, 3.00 equiv) at 23 °C. After 12 hours, water (5 mL) was added to the reaction mixture and the layers were separated. The aqueous layer was extracted with diethyl ether (3 × 2 mL), the combined organic layers were washed with a 10% aqueous solution of lithium chloride (5 mL) and the washed organic layers were dried over sodium sulfate. The dried solution was filtered and the filtrate was concentrated. The residue was purified by flash column chromatography on silica gel (10% ethyl acetate in cyclohexane) to yield aldehyde dimer **113** (6.50 mg, 13.5 µmol, 68%) as a slightly yellow oil.

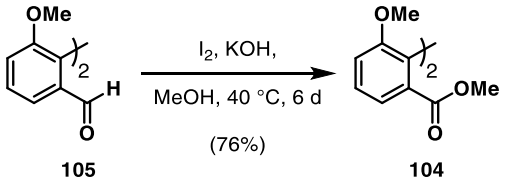
TLC (30% ethyl acetate in cyclohexane): R_f = 0.20 ($KMnO_4$, UV).

^{1}H NMR (600 MHz, chloroform-*d*) δ 10.31 (s, 2H, 8-H), 7.48 – 7.45 (m, 4H, 11-H), 7.42 – 7.37 (m, 4H, 12-H), 7.36 – 7.31 (m, 2H, 13-H), 7.11 (d, *J* = 9.1 Hz, 2H, 6-H), 7.06 (d, *J* = 9.1 Hz, 2H, 7-H), 5.16 (s, 4H, 9-H), 3.64 (s, 6H, 1-H).

^{13}C NMR (151 MHz, chloroform-*d*) δ 190.7 (C-8), 155.4 (C-5), 151.1 (C-2), 136.7 (C-10), 128.8 (C-12), 128.2 (C-13), 125.6 (C-3), 127.6 (C-11), 124.7 (C-4), 117.4 (C-6), 113.2 (C-7), 71.3 (C-9), 56.8 (C-1).

IR (Diamond-ATR, neat) $\tilde{\upsilon}_{max}$: 2962 (w), 1767 (s), 1615 (m), 1573 (w) 1434 (m), 1285 (s), 1239 (s), 1216 (s), 1183 (m), 1137 (m), 1042 (w), 1001 (w), 876 (w), 781 (w) cm^{-1}.

HRMS (ESI) calc. for $C_{30}H_{26}NaO_6$ $[M+Na]^+$: 505.1622 found: 505.1628.



105 104

Methyl benzoate dimer 104

To a solution of benzaldehyde dimer **105** (42.0 mg, 155 µmol, 1 equiv) in methanol (1.5 mL) was added potassium hydroxide (52.3 mg, 932 µmol, 6.00 equiv) and iodine (120 mg, 466 µmol, 3.00 equiv) at 40 °C. After six days, a saturated aqueous solution of sodium thiosulfate (5 mL) and ethyl acetate (5 mL) were added to the reaction mixture. The layers were separated and the aqueous layer was extracted with ethyl acetate (3 × 2 mL) and the combined organic layers were dried over sodium sulfate and the dried solution was filtered. The filtrate was concentrated and the residue was purified by flash column chromatography on silica gel (30% ethyl acetate in hexanes) to yield methyl benzoate dimer **104** (39.0 mg, 118 µmol, 76%) as a colourless oil.

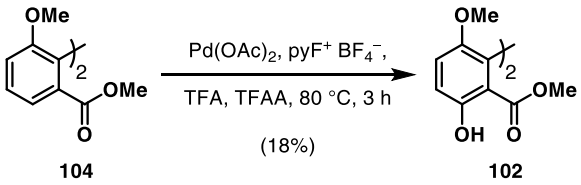
TLC (30% ethyl acetate in cyclohexane): R_f = 0.38 (CAM, UV).

^{1}H NMR (400 MHz, chloroform-*d*) δ 7.49 (d, *J* = 2.7 Hz, 2H), 7.11 (dd, *J* = 8.4, 0.5 Hz, 2H), 7.06 (dd, *J* = 8.5, 2.7 Hz, 2H), 3.88 (s, 4H), 3.63 (s, 6H).

^{13}C NMR (101 MHz, chloroform-*d*) δ 167.6, 158.5, 135.4, 131.9, 130.8, 117.7, 114.6, 55.6, 52.0.

IR (Diamond-ATR, neat) $\tilde{\upsilon}_{max}$: 2951 (w), 1727 (s), 1606 (m), 1574 (w), 1484 (m), 1434 (m), 1285 (s), 1243 (s), 1215 (s), 1183 (m), 1137 (w), 1075 (m), 1047 (m), 1000 (w), 874 (w), 825 (w), 791 (w) cm^{-1}.

HRMS (ESI) calc. for $C_{18}H_{18}NaO_6$ $[M+Na]^+$: 353.0996 found: 353.0981.

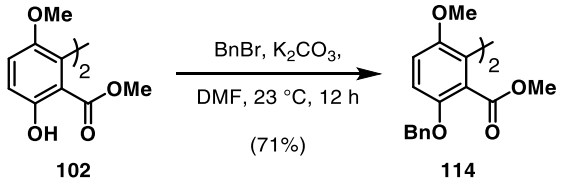


Phenol dimer 102

To a solution of methyl benzoate dimer **104** (38.0 mg, 115 µmol, 1 equiv) in a mixture of trifluoroacetic acid and trifluoroacetic anhydride (9:1, 1.2 mL) was added palladium(II) acetate (10.3 mg, 46.0 µmol, 0.400 equiv) and 1-fluoropyridinium tetrafluoroborate (89.6 mg, 460 µmol, 4.00 equiv) at 23 °C. The reaction mixture was heated in a pressure tube to 80 °C. After three hours, the reaction mixture was allowed to cool to 23 °C and then a saturated aqueous solution of sodium bicarbonate (5 mL) and dichloromethane (5 mL) were added to the mixture. The layers were separated and the aqueous layer was extracted with dichloromethane (3 × 2 mL) and the combined organic layers were dried over sodium sulfate and the dried solution was filtered through a pad of Celite. The filtrate was concentrated and the residue was purified by flash column chromatography on silica gel (20% ethyl acetate in hexanes) to yield phenol dimer **102** (7.50 mg, 21.0 µmol, 18%) as a colourless solid.

TLC (30% ethyl acetate in cyclohexane): R_f = 0.34 (KMnO4, UV).

^{1}H NMR (400 MHz, chloroform-*d*) δ 10.50 (s, 2H), 7.11 (d, *J* = 9.1 Hz, 2H), 6.98 (d, *J* = 9.0 Hz, 2H), 3.58 (s, 6H), 3.47 (s, 6H).



Benzyl ether dimer 114

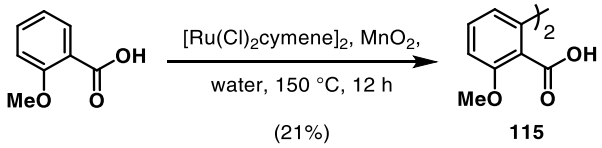
To a solution of phenol dimer **102** (7.50 mg, 21.0 µmol, 1 equiv) in *N*,*N*-dimethylformamide (200 µL) was added potassium carbonate (22.9 mg, 166 µmol, 8.00 equiv) and benzyl bromide (20.0 µL, 166 µmol, 8.00 equiv) at 23 °C. After 12 hours, a saturated aqueous solution of lithium chloride (5 mL) and ethyl acetate (5 mL) were added to the reaction mixture. The layers were separated and the aqueous layer was extracted with ethyl acetate (3 × 2 mL) and the combined organic layers were dried over sodium sulfate and the dried solution was filtered. The filtrate was concentrated and the residue was purified by flash column chromatography on silica gel (10% ethyl acetate in hexanes) to yield benzyl ether dimer **114** (8.00 mg, 15.0 µmol, 71%) as a colourless oil.

TLC (30% ethyl acetate in cyclohexane): R_f = 0.20 (KMnO4, UV).

^{1}H NMR (400 MHz, chloroform-*d*) δ 7.43 – 7.39 (m, 4H), 7.37 – 7.33 (m, 4H), 7.31 – 7.27 (m, 2H), 6.93 (s, 4H), 3.56 (s, 6H), 5.09 (s, 4H), 3.70 (s, 6H).

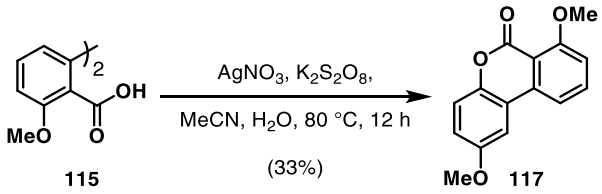
IR (Diamond-ATR, neat) $\tilde{\upsilon}_{max}$: 2924 (s), 2852 (m), 1692 (w), 1465 (m), 1260 (m), 1056 (w) cm^{-1}.

HRMS (ESI) calc. for $C_{30}H_{26}NaO_6$ $[M+Na]^+$: 505.1622 found: 505.1602.



Anisic acid dimer 115

A mixture of *o*-anisic acid (300 mg, 1.95 mmol, 1 equiv), manganese dioxide (566 mg, 5.86 mmol, 3.00 equiv) and chloronorbornadiene rhodium(I) dimer (45.4 mg, 98.0 µmol, 0.0500 equiv) in water (5 mL) was heated to 150 °C in a pressure tube. After 12 hours, an aqueous solution of hydrochloric acid (2 M, 5 mL) and ethyl acetate (5 mL) were added to the reaction mixture. The layers were separated, the aqueous layer was extracted with ethyl acetate (3 × 1 mL) and the combined organic layers were dried over sodium sulfate. The dried solution was filtered through a pad of Celite and the filtrate was concentrated. The residue was purified by flash column chromatography on silica gel (50% ethyl acetate and 10% formic acid in cyclohexane) to yield anisic acid dimer **115** (62.0 mg, 205 µmol, 21%) as an off-white solid. The obtained analytical data were in full agreement with those reported in the literature.[146]



Tricycle 117

To a solution of anisic acid dimer **115** (33.0 mg, 109 µmol, 1 equiv) in a mixture of acetonitrile and water (1:1, 0.1 mL) was added silver nitrate (3.71 mg, 22.0 µmol, 0.20 equiv) and potassium persulfate (177 mg, 655 µmol, 6.00 equiv) and the mixture was heated to 80 °C. After 12 hours, the reaction mixture was allowed to cool to 23 °C and then an aqueous solution of sodium hydroxide (2 M, 5 mL) and ethyl acetate (5 mL) were added. The layers were separated, the aqueous layer was extracted with ethyl acetate (3 × 1 mL) and the combined organic layers were dried over sodium sulfate. The dried solution was filtered through a pad of Celite, the filter cake was washed with ethyl acetate (3 mL) and the filtrate was concentrated. The residue was purified by flash column chromatography on silica gel (1% methanol in dichloromethane) to yield tricycle **117** (9.20 mg, 36.0 µmol, 33%) as a yellow solid.

[146] H. Gong, H. Zeng, F. Zhou, C.-J. Li, *Angew. Chem. Int. Ed.* **2015**, *54*, 5718–5721.

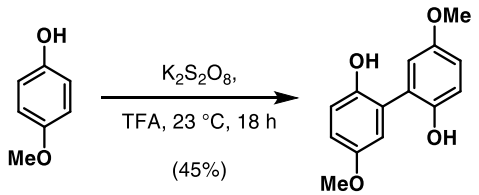
TLC (1% methanol in dichloromethane): R_f = 0.18 ($KMnO_4$, UV).

mp: (186-187) °C

^{1}H NMR (400 MHz, methanol-d_4) δ 7.89 – 7.88 (m, 1H), 7.87 (d, *J* = 5.0 Hz, 1H), 7.77 (dd, *J* = 8.2, 1.3 Hz, 1H), 7.32 (d, *J* = 8.2 Hz, 1H), 7.29 – 7.27 (m, 1H), 7.20 (dd, *J* = 8.1, 1.3 Hz, 1H), 4.03 (s, 3H), 3.98 (s, 3H)

IR (Diamond-ATR, neat) $\tilde{\upsilon}_{max}$: 2952 (w), 2856 (w), 1736 (s), 1597 (w), 1482 (m), 1454 (w), 1346 (m), 1272 (s), 1259 (s), 1106 (w), 1010 (w), 807 (w), 762 (w) cm^{-1}.

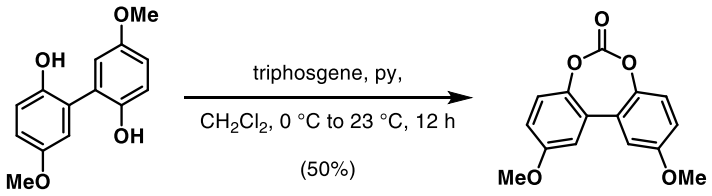
HRMS (ESI) calc. for $C_{15}H_{12}NaO_4$ $[M+Na]^+$: 279.0628 found: 279.0630.



116

Methoxyphenol dimer 116

To a solution of 4-methoxyphenol (1.00 g, 7.25 mmol, 1 equiv) in trifluoroacetic acid (20 mL) was added potassium persulfate at 23 °C. After 18 hours, the reaction mixture was concentrated and the residue was purified by flash column chromatography on silica gel (30% ethyl acetate in cyclohexane) to yield methoxyphenol dimer **116** (399 mg, 1.62 mmol, 45%) as a brown oil. The obtained analytical data were in full agreement with those reported in the literature.[147]



116 **120**

Carbonate 120

To a solution of methoxyphenol dimer **116** (300 mg, 1.22 mmol, 1 equiv) and triphosgene (253 mg, 853 µmol, 0.700 equiv) in dichloromethane (10 mL) was added pyridine (197 µL, 2.44 mmol, 2.00 equiv) at 0 °C. After the addition of pyridine, the reaction mixture was allowed to warm to 23 °C and was stirred at that temperature for 12 hours. An aqueous solution of hydrochloric acid (1 M, 10 mL) was added to the reaction mixture and the layers were separated. The aqueous layer was extracted with dichloromethane (3 × 3 mL) and the combined organic layers were dried over sodium sulfate. The dried

[147] S. V. Mulay, R. A. Fernandes, *Chem. Eur. J.* **2015**, *21*, 4842–4852.

solution was filtered and the filtrate was concentrated to yield carbonate **120** (224 mg, 603 µmol, 50%) as a colourless solid.

TLC (20% ethyl acetate in cyclohexane): R_f = 0.38 ($KMnO_4$, UV).

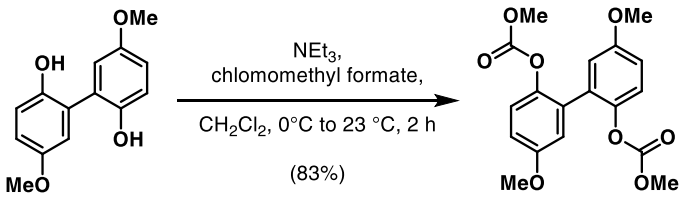
mp: (137-138) °C

^{1}H NMR (400 MHz, chloroform-*d*) δ 7.15 (d, *J* = 8.8 Hz, 2H), 6.98 (d, *J* = 3.0 Hz, 2H), 6.86 (dd, *J* = 8.9, 3.0 Hz, 2H), 3.76 (s, 6H).

^{13}C NMR (101 MHz, chloroform-*d*) δ 158.2, 152.8, 143.9, 128.2, 122.3, 115.4, 112.7, 55.9.

IR (Diamond-ATR, neat) $\tilde{\upsilon}_{max}$: 3400 (br,w), 2938 (w), 1784 (m), 1497 (s), 1464 (m), 1420 (m), 1345 (m), 1205 (s), 1159 (s), 1037 (m), 871 (w), 824 (w) cm^{-1}.

HRMS (ESI) calc. for $C_{15}H_{12}NaO_5$ $[M+Na]^+$: 295.0577 found: 295.0573.



116 122

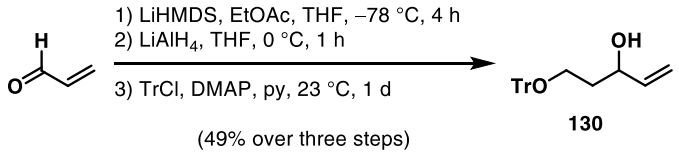
Carbonate 122

To a solution of methoxyphenol dimer **116** (22.0 mg, 89.0 µmol, 1 equiv) in dichloromethane (1 mL) was added triethylamine (14.9 µL, 107 µmol, 1.20 equiv) and methyl chloroformate (8.50 µL, 107 µmol, 1.20 equiv) in sequence at 0 °C. After ten minutes, the reaction mixture was allowed to warm to 23 °C. After two hours, water (5 mL) was added to the reaction mixture and the layers were separated. The aqueous layer was extracted with dichloromethane (3 × 2 mL) and the combined organic layers were dried over sodium sulfate. The dried solution was filtered and the filtrate was purified by flash column chromatography on silica gel (10% ethyl acetate in cyclohexane) to yield carbonate **122** (27.0 mg, 75.0 µmol, 83%) as a colourless oil.

TLC (10% ethyl acetate in cyclohexane): R_f = 0.23 ($KMnO_4$, UV).

^{1}H NMR (300 MHz, chloroform-*d*) δ 7.16 (d, *J* = 9.0 Hz, 2H), 6.92 (dd, *J* = 9.0, 2.8 Hz, 2H), 6.84 (d, *J* = 3.0 Hz, 2H), 3.80 (s, 6H), 3.74 (s, 6H).

HRMS (ESI) calc. for $C_{18}H_{18}NaO_8$ $[M+Na]^+$: 385,0894 found 385.0895.



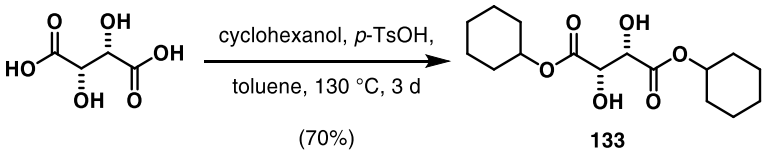
Trityl ether 130

To a solution of ethyl acetate (3.09 mL, 31.7 mmol, 1 equiv) in tetrahydrofuran (50 mL) was added a solution of lithium bis(trimethylsilyl)amide (1.00 M in tetrahydrofuran, 38.0 mL, 38.0 mmol, 1.20 equiv) at –78 °C. After 1 hour, acrolein (2.12 mL, 31.7 mmol, 1 equiv) was added dropwise at –78 °C. After three hours, a saturated aqueous solution of ammonium chloride (100 mL) and ethyl acetate (50 mL) were added to the reaction mixture and the layers were separated. The aqueous layer was extracted with ethyl acetate (3 × 20 mL) and the combined organic layers were dried over sodium sulfate. The dried solution was filtered and the filtrate was concentrated to yield the crude β-hydroxy ester (4.17 g, 28.9 mmol) as a colourless oil.

To a suspension of lithium aluminium hydride (1.32 g, 34.7 mmol, 1.20 equiv) in tetrahydrofuran (150 mL) was added a solution of the crude β-hydroxy ester (4.17 g, 28.9 mmol, 1 equiv) in tetrahydrofuran (50 mL) at 0 °C. After one hour, an aqueous solution of sodium hydroxide (15wt%, 10 mL) was added to the reaction mixture at 0 °C and the mixture was then allowed to warm to 23 °C. After one hour at 23 °C, sodium sulfate was added and the mixture was filtered through a pad of Celite. The filtrate was concentrated to yield the crude diol (3.08 g, 30.2 mmol) as a colourless oil.

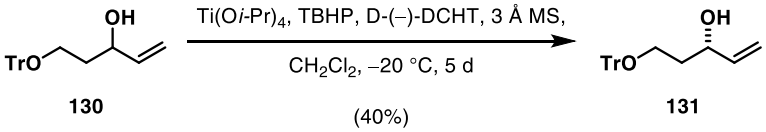
To a solution of the crude diol (3.08 g, 30.2 mmol, 1 equiv) in pyridine (80 mL) was added 4-dimethylaminopyridine (359 mg, 2.94 mmol, 0.10 equiv) and trityl chloride (9.42 g, 33.8 mmol, 1.15 equiv) at 23 °C. After one day, ice-cold water (300 mL), an aqueous solution of citric acid (15wt%, 200 mL) and diethyl ether (100 mL) were added to the reaction mixture. The layers were separated and the aqueous layer was extracted with diethyl ether (3 × 20 mL) and the combined organic layers were washed with a saturated aqueous solution of copper sulfate (50 mL), water (50 mL) and a saturated aqueous solution of sodium chloride (50 mL). The washed organic layer was dried over sodium sulfate. The dried solution was filtered and the filtrate was purified by flash column chromatography on silica gel to yield trityl ether **130** (5.31 g, 15.4 mmol, 49% over three steps) as a slightly yellow oil. The obtained analytical data were in full agreement with those reported in the literature.[148]

[148] T. Inoue, O. Kitagawa, Y. Oda, T. Taguchi, *J. Org. Chem.* **1996**, *61*, 8256–8263.



D-(–)-DCHT 133

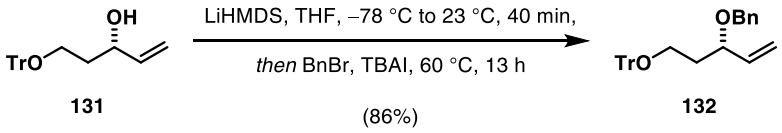
To a solution of D-(–)-tartaric acid (7.50 g, 50.0 mmol, 1 equiv) in toluene (50 mL) was added cyclohexanol (12.5 g, 125 mmol, 2.50 equiv) and *p*-toluenesulfonic acid monohydrate (500 mg, 2.63 mmol, 0.0500 equiv) at 23 °C and the mixture was heated to 130 °C. The during the reaction formed water was removed with a Dean–Stark apparatus. After three days, the reaction mixture was allowed to cool to 23 °C and the mixture was concentrated. The residual cyclohexanol was removed under vacuum (0.1 mmHg) and trapping the reagent in flask cooled in liquid nitrogen (–196 °C). The residue was purified by flash column chromatography on silica gel (15% grading to 20% ethyl acetate in cyclohexane) to yield tartaric ester **133** (11.0 g, 34.9 mmol, 70%) as a colourless solid. The obtained analytical data were in full agreement with those reported in the literature.[149]



Allyl alcohol 131

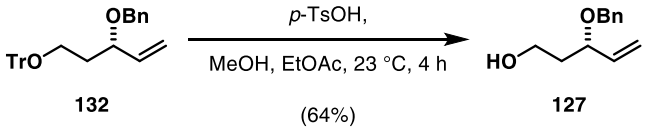
To a suspension of allyl alcohol **130** (1.00 g, 2.90 mmol, 1 equiv) and crushed molecular sieves (3 Å, 300 mg) in dichloromethane (10 mL) was added titanium(IV) *iso*-propoxide (87.0 µL, 290 µmol, 0.100 equiv) and D-(–)-DCHT **133** (137 mg, 435 µmol, 0.150 equiv) at –20 °C. After one hour, to the suspension was added a solution of *tert*-butyl hydroperoxide (5.50 M in nonane, 0.369 mL, 2.03 mmol, 0.700 equiv). After five days, a solution of iron(II) sulfate (3.30 g) and citric acid (1.10 g) in water (10 mL) were added to the reaction mixture at –20 °C and then the mixture was allowed to warm to 23 °C. Water (20 mL) and ethyl acetate (20 mL) were added to the reaction mixture and the layers were separated. The aqueous layer was extracted with ethyl acetate (3 × 5 mL) and the combined organic layers were dried over sodium sulfate. The dried solution was filtered and the filtrate was concentrated. The residue was purified by flash column chromatography on silica gel (15% grading to 20% ethyl acetate in cyclohexane) to yield allyl alcohol **131** (398 mg, 1.16 mmol, 40%) as a colourless oil. The obtained analytical data were in full agreement with those reported in the literature.[148]

[149] Y. Gao, J. M. Klunder, R. M. Hanson, H. Masamune, S. Y. Ko, K. B. Sharpless, *J. Am. Chem. Soc.* **1987**, *109*, 5765–5780.



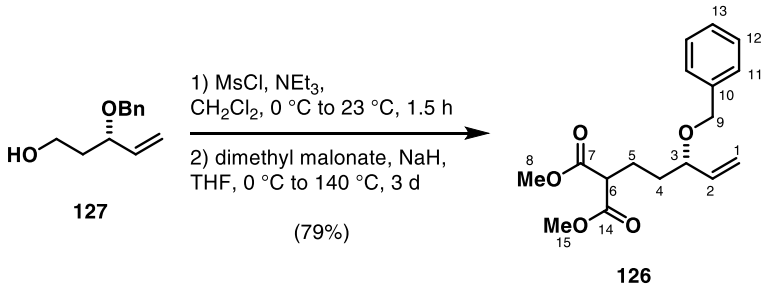
Benzyl ether 132

To a solution of allylic alcohol **131** (4.87 g, 14.1 mmol, 1 equiv) in tetrahydrofuran (140 mL) was added a solution of lithium bis(trimethylsilyl)amide (1.00 M in tetrahydrofuran, 18.4 mL, 18.4 mmol, 1.30 equiv) at –78 °C. After 30 minutes, the solution was allowed to warm to 23 °C. After ten minutes at 23 °C, benzyl bromide (2.37 mL, 19.8 mmol, 1.40 equiv) and tetrabutylammonium iodide (7.31 g, 19.8 mmol, 1.40 equiv) were added to the reaction mixture and the solution was heated to 60 °C. After 13 hours, the solution was allowed to cool to 23 °C and then a saturated aqueous solution of ammonium chloride (200 mL) and diethyl ether (100 mL) were added. The layers were separated and the aqueous layer was extracted with diethyl ether (3 × 30 mL) and the combined organic layers were dried over sodium sulfate. The dried solution was filtered and the filtrate was concentrated. The residue was purified by flash column chromatography on silica gel (0% grading to 5% ethyl acetate in cyclohexane) to yield benzyl ether **132** (5.31 g, 12.2 mmol, 86%) as a colourless oil. The obtained analytical data were in full agreement with those reported in the literature.[148]



Alcohol 127

To a solution of benzyl ether **132** (210 mg, 483 µmol, 1 equiv) in a mixture of methanol and ethyl acetate (1:1, 5 mL) was added *p*-toluenesulfonic acid monohydrate (184 mg, 966 µmol, 2.00 equiv) at 23 °C. After four hours, a saturated aqueous solution of sodium hydrogen carbonate (10 mL) was added to the reaction mixture and the layers were separated. The aqueous layer was extracted with ethyl acetate (3 × 3 mL) and the combined organic layers were dried over sodium sulfate. The dried solution was filtered and the filtrate was concentrated. The residue was purified by flash column chromatography on silica gel (20% grading to 30% ethyl acetate in cyclohexane) to yield alcohol **127** (59.0 mg, 307 µmol, 64%) as a colourless oil. The obtained analytical data were in full agreement with those reported in the literature.[148]



Malonate 126

To a solution of alcohol **127** (127 mg, 661 µmol, 1 equiv) in dichloromethane (3 mL) was added triethylamine (119 µL, 859 µmol, 1.30 equiv) and methanesulfonyl chloride (67.0 µL, 859 µmol, 1.30 equiv) at 0 °C. After 15 minutes, the solution was allowed to warm to 23 °C. After one hour at 23 °C, a saturated aqueous solution of ammonium chloride (10 mL) and dichloromethane (5 mL) were added to the reaction mixture. The layers were separated, the aqueous layer was extracted with dichloromethane (3 × 3 mL) and the combined organic layers were dried over sodium sulfate. The dried solution was filtered and the filtrate was concentrated to yield the crude mesylate as a colourless oil.

To a suspension of sodium hydride (31.7 mg, 1.32 mmol, 2.00 equiv) in tetrahydrofuran (4 mL) was added dimethyl malonate (189 µL, 1.65 mmol, 2.50 equiv) dropwise at 0 °C. After 30 minutes, the solution was allowed to warm to 23 °C. A solution of the crude mesylate in tetrahydrofuran (1 mL) was added to the mixture and the solution was heated to 140 °C in a pressure tube. After three days, the solution was allowed to cool to 23 °C and was then poured into a solution of hydrochloric acid (2 M in water, 10 mL) and ethyl acetate (5 mL) was added. The layers were separated, the aqueous layer was extracted with ethyl acetate (3 × 3 mL) and the combined organic layers were dried over sodium sulfate. The dried solution was filtered and the filtrate was concentrated. The residue was purified by flash column chromatography on silica gel (20% ethyl acetate in cyclohexane) to yield malonate **126** (159 mg, 519 µmol, 79% over two steps) as a colourless oil. The obtained analytical data were in full agreement with those reported in the literature.[148]

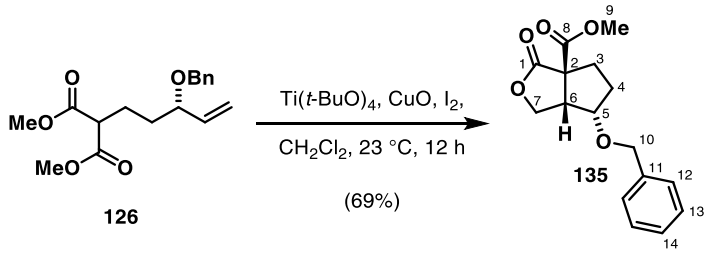
TLC (30% ethyl acetate in cyclohexane): R_f = 0.56 ($KMnO_4$).

^{1}H NMR (400 MHz, chloroform-*d*) δ 7.36 – 7.27 (m, 5H, 11-H, 12-H, 13-H), 5.72 (ddd, *J* = 17.6, 10.5, 7.7 Hz, 1H, 2-H), 5.28 – 5.21 (m, 2H, 1-H), 4.58 (d, *J* = 11.8 Hz, 1H, 9-H), 4.34 (d, *J* = 11.8 Hz, 1H, 9-H), 3.77 – 3.72 (m, 7H, 3-H, 8-H, 15-H), 3.36 (t, *J* = 7.6 Hz, 1H, 6-H), 2.05 – 1.99 (m, 1H, 5-H), 1.98 – 1.93 (m, 1H, 5-H), 1.68 – 1.62 (m, 1H, 4-H), 1.55 – 1.50 (m, 1H, 4-H).

^{13}C NMR (101 MHz, chloroform-*d*) δ 169.9 (C-1 or C-14), 169.9 (C-1 or C-14), 138.6 (C-10), 138.4 (C-2), 128.5 (C-12), 127.9 (C-11), 127.6 (C-13), 118.0 (C-1), 80.0 (C-3), 70.2 (C-9), 52.6 (C-8, C-15), 51.6 (C-6), 33.1 (C-4), 25.0 (C-5).

IR (Diamond-ATR, neat) $\tilde{\upsilon}_{max}$: 3030 (w), 2953 (w), 2859 (w), 1753 (s), 1735 (s), 1454 (m), 1436 (m), 1227 (m), 1156 (m), 1069 (m), 931 (w), 739 (w), 700 (w) cm^{-1}.

HRMS (ESI) calc. for $C_{17}H_{26}NO_5$ $[M+NH_4]^+$: 324.1805 found: 324.1803.



Ester 135

To a solution of malonate **126** (51.1 mg, 167 µmol, 1 equiv) in dichloromethane (1.5 mL) was added Ti(*t*-BuO)$_4$ (57.0 µL, 167 µmol, 1 equiv) at 23 °C. After 15 minutes, iodine (50.8 mg, 200 µmol, 1.20 equiv) and cupric oxide (15.9 mg, 200 µmol, 1.20 equiv) were added. After 12 hours, a saturated aqueous solution of sodium thiosulfate (10 mL), dichloromethane (5 mL) was added to the reaction mixture and the layers were separated. The aqueous layer was extracted with dichloromethane (3 × 5 mL) and the combined organic layers were dried over sodium sulfate. The dried solution was filtered over a pad of Celite and the filtrate was concentrated. The residue was purified by flash column chromatography on silica gel (20% ethyl acetate in cyclohexane) to yield ester **135** (33.4 mg, 115 µmol, 69%) as a colourless oil. The obtained analytical data were in full agreement with those reported in the literature.[148]

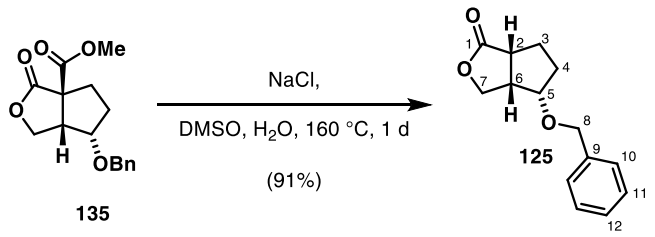
TLC (30% ethyl acetate in cyclohexane): R_f = 0.38 (CAM).

^{1}H NMR (400 MHz, chloroform-*d*) δ 7.38 – 7.27 (m, 5H, 12-H, 13-H, 14-H), 4.64 (dd, *J* = 9.3, 2.5 Hz, 1H, 7-H), 4.59 (d, *J* = 12.0 Hz, 1H, 10-H), 4.42 (d, *J* = 12.0 Hz, 1H, 10-H), 4.33 (dd, *J* = 9.3, 8.1 Hz, 1H, 7-H), 4.07 (td, *J* = 7.0, 4.9 Hz, 1H, 5-H), 3.78 (s, 3H, 9-H), 3.17 (td, *J* = 7.5, 2.5 Hz, 1H, 6-H), 2.40 – 2.27 (m, 2H, 3-H), 2.02 – 1.94 (m, 1H, 4-H), 1.83 – 1.73 (m, 1H, 4-H).

^{13}C NMR (101 MHz, chloroform-*d*) δ 176.1 (C-1), 170.4 (C-8), 137.7 (C-11), 128.5 (C-13), 127.9 (C-14), 127.4 (C-12), 80.2 (C-5), 71.5 (C-10), 66.1 (C-7), 59.9 (C-2), 53.2 (C-9), 48.1 (C-6), 30.8 (C-4), 30.4 (C-3).

IR (Diamond-ATR, neat) $\tilde{\upsilon}_{max}$: 3030 (w), 2957 (w), 1770 (s), 1740 (s), 1454 (w), 1380 (w), 1268 (m), 1250 (m), 1157 (m), 1055 (m), 989 (m), 738 (w), 699 (m) cm^{-1}.

HRMS (ESI) calc. for $C_{16}H_{22}NO_5$ $[M+NH_4]^+$: 308.1498 found: 308.1492.



Lactone 125

To solution of ester **135** (880 mg, 3.03 mmol, 1 equiv) in dimethyl sulfoxide (8 mL) was added water (1.75 mL, 97.0 mmol, 32.0 equiv) and sodium chloride (709 mg, 12.1 mmol, 4.00 equiv) and the mixture was heated to 160 °C. After one day, the mixture was allowed to cool to 23 °C and water (20 mL) and ethyl acetate (20 mL) were added. The layers were separated, the aqueous layer was extracted with ethyl acetate (3 × 5 mL) and the combined organic layers were dried over sodium sulfate. The dried solution was filtered and the filtrate was concentrated. The residue was purified by flash column chromatography on silica gel (30% ethyl acetate in cyclohexane) to yield lactone **125** (643 mg, 2.77 mmol, 91%) as a colourless oil. The obtained analytical data were in full agreement with those reported in the literature.[148]

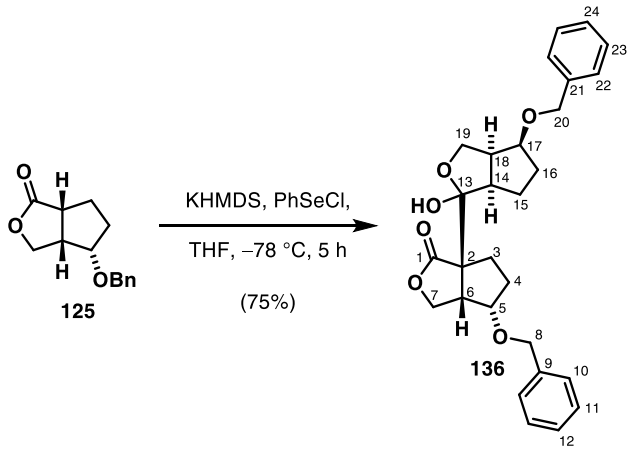
TLC (30% ethyl acetate in cyclohexane): R_f = 0.16 (CAM).

^{1}H NMR (400 MHz, chloroform-*d*) δ 7.38 – 7.27 (m, 5H, 10-H, 11-H, 12-H), 4.61 – 4.56 (m, 2H, 7-H, 8-H), 4.43 (d, *J* = 12.0 Hz, 1H, 8-H), 4.27 – 4.20 (m, 1H, 7-H), 4.03 – 3.97 (m, 1H, 5-H), 3.05 – 2.97 (m, 2H, 2-H, 6-H), 2.13 – 2.05 (m, 1H, 3-H), 1.96 – 1.87 (m, 2H, 3-H, 4-H), 1.73 – 1.64 (m, 1H, 4-H).

^{13}C NMR (201 MHz, chloroform-*d*) δ 180.9 (C-1), 138.1 (C-9), 128.6 (C-11), 127.9 (C-12), 127.6 (C-10), 81.1 (C-5), 71.7 (C-8), 67.0 (C-7), 43.0 (C-2), 41.6 (C-6), 30.3 (C-4), 26.5 (C-3).

IR (Diamond-ATR, neat) $\tilde{\upsilon}_{max}$: 2964 (w), 1764 (s), 1454 (w), 1377 (w), 1166 (m), 1114 (m), 1030 (m), 985 (m), 739 (w), 699 (w) cm^{-1}.

HRMS (ESI) calc. for $C_{14}H_{16}NaO_3$ $[M+Na]^+$: 255.0992 found: 255.0976.



Lactone dimer 136

To a solution of potassium bis(trimethylsilyl)amide (1.00 M in tetrahydrofuran, 38.7 µL, 39.0 µmol, 1.50 equiv) was added a solution of lactone **125** (6.00 mg, 26.0 µmol, 1 equiv) in tetrahydrofuran (400 µL) at –78 °C. After one hour, a solution of phenylselenyl chloride (7.92 mg, 41.0 µmol, 1.60 equiv) in tetrahydrofuran (300 µL) was added at –78 °C. After four hours, water (5 mL) and ethyl acetate (5 mL) were added to the reaction mixture. The layers were separated, the aqueous layer was extracted with ethyl acetate (3 × 2 mL) and the combined organic layers were dried over sodium sulfate. The dried solution was filtered and the filtrate was concentrated. The residue was purified by flash column chromatography on silica gel (20% grading to 30% ethyl acetate in cyclohexane) to yield lactone dimer **136** (9.00 mg, 19.0 µmol, 75%) as a colourless oil.

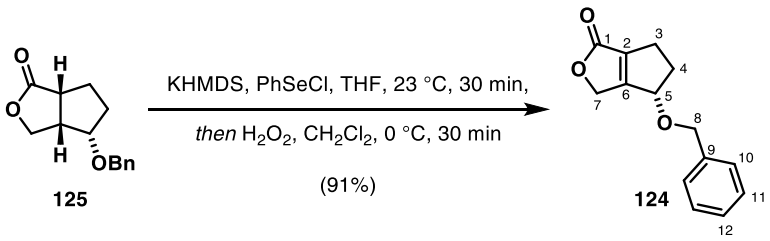
TLC (20% ethyl acetate in cyclohexane): R_f = 0.52 (CAM).

^{1}H NMR (400 MHz, chloroform-*d*) δ 7.37 – 7.28 (m, 10H, aromatic), 5.22 (s, 1H, 13-OH), 4.71 (d, *J* = 11.9 Hz, 1H, 20-H), 4.53 – 4.45 (m, 3H, 7-H, 8-H), 4.41 (d, *J* = 11.9 Hz, 1H, 20-H), 4.23 (t, *J* = 8.8 Hz, 1H, 7-H), 4.06 – 3.99 (m, 2H, 5-H, 19-H), 3.85 (d, *J* = 8.9 Hz, 1H, 19-H), 3.82 – 3.79 (m, 1H, 17-H), 3.75 – 3.68 (m, 1H, 14-H), 3.46 – 3.41 (m, 1H, 6-H), 2.88 – 2.81 (m, 1H, 18-H), 2.29 – 2.23 (m, 1H, 16-H), 2.00 – 1.95 (m, 1H, 3-H), 1.93 – 1.89 (m, 1H, 4-H), 1.86 – 1.82 (m, 1H, 15-H), 1.79 – 1.73 (m, 1H, 3-H), 1.70 – 1.63 (m, 1H, 16-H), 1.62 – 1.56 (m, 1H, 4-H).

^{13}C NMR (201 MHz, chloroform-*d*) δ 180.3 (C-1), 138.3 (C-9), 137.1 (C-21), 128.8 (aromatic), 128.6 (aromatic), 128.3 (aromatic), 128.1 (aromatic), 127.8 (aromatic), 127.5 (aromatic), 105.3 (C-13), 81.2 (C-5), 79.7 (C-17), 71.6 (C-8), 71.0 (C-20), 65.9 (C-7), 64.6 (C-19), 61.1 (C-2), 50.1 (C-18), 47.2 (C-14), 43.4 (C-6), 34.4 (C-16), 30.9 (C-4), 29.1 (C-3), 23.4 (C-15).

IR (Diamond-ATR, neat) $\tilde{\upsilon}_{max}$: 2926 (m), 2855 (w), 1737 (s), 1459 (w), 1370 (m), 1218 (s), 1049 (m), 605 (w) cm^{-1}.

HRMS (ESI) calc. for $C_{28}H_{36}NO_6$ $[M+NH_4]^+$: 482.2537 found: 482.2541.



Lactone 124

To a solution of the lactone **125** (23.0 mg, 99.0 µmol, 1 equiv) in tetrahydrofuran (1 mL) was added phenylselenyl chloride (80.1 mg, 410 µmol, 3.00 equiv) and then a solution of potassium bis(trimethylsilyl)amide (1.00 M in tetrahydrofuran, 119 µL, 119 µmol. 1.20 equiv) dropwise over the course of 20 minutes at 23 °C. 30 minutes after the addition was completed, a solution of hydrochloric acid (2 M in water, 5 mL) and ethyl acetate (5 mL) were added to the reaction mixture. The layers were separated and the aqueous layer was extracted with ethyl acetate (3 × 2 mL), the combined organic layers were dried over sodium sulfate. The dried solution was filtered and the filtrate was concentrated to yield the crude phenyl selenyl ether. The residue was dissolved in dichloromethane (1 mL) and to the resulting solution was added a solution of hydrogen peroxide (30% in water, 1 mL) at 0 °C. After 30 minutes, a saturated aqueous solution of sodium hydrogen carbonate (5 mL) and dichloromethane (5 mL) were added to the reaction mixture and the layers were separated. The aqueous layer was extracted with dichloromethane (3 × 2 mL), the combined organic layers were dried over sodium sulfate. The dried solution was filtered and the filtrate was concentrated. The filtrate was purified by flash column chromatography on silica gel (40% ethyl acetate in cyclohexane) to yield lactone **124** (20.7 mg, 90.0 µmol, 91%) as a colourless solid.

TLC (30% ethyl acetate in cyclohexane): R_f = 0.23 ($KMnO_4$).

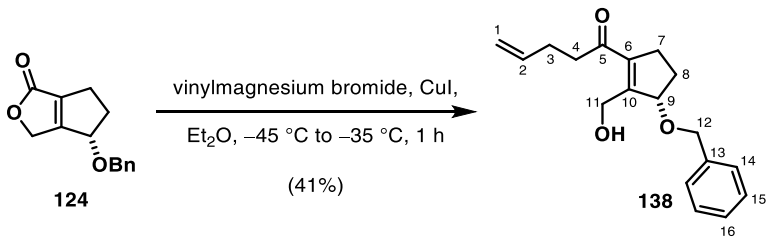
mp: (76-77) °C

^{1}H NMR (400 MHz, chloroform-*d*) δ 7.40 – 7.30 (m, 5H, 10-H, 11-H, 12-H), 4.87 (t, *J* = 5.3 Hz, 1H, 5-H), 4.81 – 4.65 (m, 2H, 7-ßH), 4.62 (d, *J* = 11.7 Hz, 1H, 8-H), 4.49 (d, *J* = 11.7 Hz, 1H, 8-H), 2.83 – 2.74 (m, 1H, 4-H), 2.68 – 2.60 (m, 1H, 3-H), 2.49 – 2.39 (m, 2H, 3-H, 4-H).

^{13}C NMR (101 MHz, chloroform-*d*) δ 171.2 (C-6), 169.6 (C-1), 140.0 (C-2), 137.5 (C-9), 128.8 (C-10), 128.4 (C-12), 128.1 (C-11), 79.5 (C-5), 72.4 (C-8), 68.5 (C-7), 36.7 (C-4), 23.7 (C-3).

IR (Diamond-ATR, neat) $\tilde{\upsilon}_{max}$: 2930 (w), 2862 (w), 1753 (s), 1454 (w), 1348 (w), 1206 (w), 1091 (m), 1039 (m), 986 (m), 752 (m), 699 (w) cm^{-1}.

HRMS (ESI) calc. for $C_{14}H_{18}NO_3$ $[M+NH_4]^+$: 248.1281 found: 248.1283.



Enone 138

To a suspension of cuprous iodide (42.7 mg, 224 µmol, 4.00 equiv) in diethyl ether (0.5 mL) was added a solution of vinylmagnesium bromide (700 mM in tetrahydrofuran, 640 µL, 448 µmol, 8.00 equiv) at 0 °C upon which the reaction mixture turned grey. After ten minutes, the mixture was cooled to –45 °C and then a solution of lactone **124** (12.9 mmol, 56.0 µmol, 1 equiv) in diethyl ether (0.8 mL) was added. The reaction mixture was allowed to warm to –35 °C over the course of 50 minutes and then a saturated aqueous solution of ammonium chloride (10 mL) and ethyl acetate (5 mL) were added to the solution and then the layers were separated. The aqueous layer was extracted with ethyl acetate (3 × 2 mL), the combined organic layers were dried over sodium sulfate. The dried solution was filtered and the filtrate was concentrated. The residue was purified by flash column chromatography on silica gel (20% ethyl acetate in cyclohexane) to yield enone **138** (6.50 mg, 23.0 µmol, 41%) as a colourless oil.

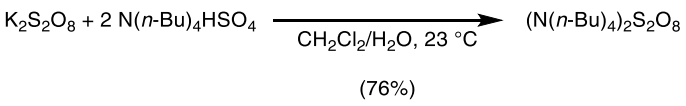
TLC (30% ethyl acetate in cyclohexane): R_f = 0.35 (UV, $KMnO_4$).

^{1}H NMR (400 MHz, chloroform-*d*) δ 7.30 – 7.24 (m, 5H, 14-H, 15-H, 16-H), 5.81 – 5.71 (m, 1H, 2-H), 5.01 – 4.91 (m, 2H, 1-H), 4.69 (t, *J* = 6.5 Hz, 1H, 9-H), 4.57 (d, *J* = 11.5 Hz, 1H, 12-H), 4.43 (d, *J* = 11.5 Hz, 1H, 12-H), 4.38 – 4.27 (m, 2H, 11-H), 3.71 (t, *J* = 6.8 Hz, 1H, 11-OH), 2.82 – 2.74 (m, 1H, 7-H), 2.62 – 2.51 (m, 3H, 4-H, 7-H), 2.29 (q, *J* = 7.0 Hz, 2H, 3-H), 2.23 – 2.16 (m, 1H, 8-H), 1.91 – 1.83 (m, 1H, 8-H).

^{13}C NMR (101 MHz, chloroform-*d*) δ 201.7 (C-5), 155.1 (C-10), 138.9 (C-6), 137.9 (C-13), 137.1 (C-2), 128.7 (C-15), 128.1 (C-14, C-16), 115.6 (C-1), 86.0 (C-9), 71.6 (C-12), 59.1 (C-11), 41.2 (C-4), 31.6 (C-7), 29.0 (C-8), 27.4 (C-3).

IR (Diamond-ATR, neat) $\tilde{\upsilon}_{max}$: 3438 (w, br), 2918 (s), 2850 (m), 1718 (m), 1454 (m), 1261 (m), 1094 (s), 916 (m), 804 (w), 738 (w), 698 (m) cm^{-1}.

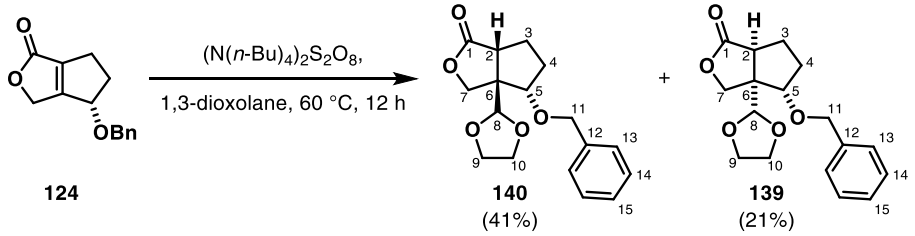
HRMS (ESI) calc. for $C_{18}H_{26}NO_3$ $[M+NH_4]^+$: 304.1907 found: 304.1908.



***n*-Tetrabutylammonium peroxydisulfate**

Following a literature precedent, to a separatory funnel filled with water (100 mL) was added potassium persulfate (1.39 g, 5.14 mmol, 1 equiv) and tetrabutylammonium hydrogensulfate (3.49 g, 10.3 mmol,

2.00 equiv). Dichloromethane (30 mL) was added to the solution and the layers were separated. The aqueous layer was extracted with dichloromethane (3 × 20 mL), the combined organic layers were dried over sodium sulfate. The dried solution was filtered and the filtrate was concentrated. The residual white solid was washed with water (3 × 20 mL) on a glass filter to yield *n*-tetrabutylammonium peroxydisulfate (2.63 g, 3.89 mmol, 76%) as a white solid after drying under vacuum (0.1 mmHg) for 12 hours.



Dioxolane 140 and 139

To a solution of lactone **124** (85.0 mg, 369 µmol, 1 equiv) in 1,3-dioxolane (3.6 mL) was added tetrabutylammonium peroxydisulfate (500 mg, 738 µmol, 2.00 equiv) and the reaction mixture was heated to 60 °C. After 12 hours, the reaction mixture was allowed to cool to 23 °C and was then concentrated. The residue was partitioned between ethyl acetate (10 mL) and water (10 mL) and the layers were separated. The aqueous layer was extracted with ethyl acetate (3 × 5 mL) and the combined organic layers were dried over sodium sulfate. The dried solution was filtered and the filtrate was concentrated. The residue was purified by flash column chromatography on silica gel (20% ethyl acetate in cyclohexane) to yield dioxolane **140** (46.0 mg, 0.151 mmol, 41%) and dioxolane **139** (23.0 mg, 76.0 µmol, 21%) as colourless oils.

Dioxolane 140

TLC (40% ethyl acetate in cyclohexane): R_f = 0.34 ($KMnO_4$).

^{1}H NMR (600 MHz, chloroform-*d*) δ 7.36 – 7.28 (m, 5H, 13-H, 14-H, 15-H), 4.89 (s, 1H, 8-H), 4.66 (d, *J* = 9.8 Hz, 1H, 7-H), 4.58 (d, *J* = 12.0 Hz, 1H, 11-H), 4.53 (d, *J* = 12.0 Hz, 1H, 11-H), 4.23 (d, *J* = 9.8 Hz, 1H, 7-H), 4.06 (dd, *J* = 9.5, 5.9 Hz, 1H, 5-H), 4.00 – 3.90 (m, 4H, 9-H, 10-H), 2.94 (dd, *J* = 9.5, 2.1 Hz, 1H, 2-H), 2.11 – 2.04 (m, 2H, 3-H, 4-H), 1.89 – 1.82 (m, 1H, 3-H), 1.63 – 1.57 (m, 1H, 4-H).

^{13}C NMR (151 MHz, chloroform-*d*) δ 180.1 (C-1), 138.3 (C-12), 128.5 (C-14), 127.8 (C-15), 127.5 (C-13), 105.1 (C-8), 82.0 (C-5), 72.1 (C-11), 68.1 (C-7), 65.7 (C-9 or C-10), 65.6 (C-9 or C-10), 56.0 (C-6), 45.2 (C-2), 31.1 (C-4), 26.3 (C-3).

IR (Diamond-ATR, neat) $\tilde{\upsilon}_{max}$: 2924 (m), 1768 (s), 1166 (s), 1022 (s), 804 (m), 737 (m), 698 (m) cm^{-1}.

HRMS (ESI) calc. for $C_{17}H_{24}NO_5$ $[M+NH_4]^+$: 322.1649 found: 322.1647.

Dioxolane 139

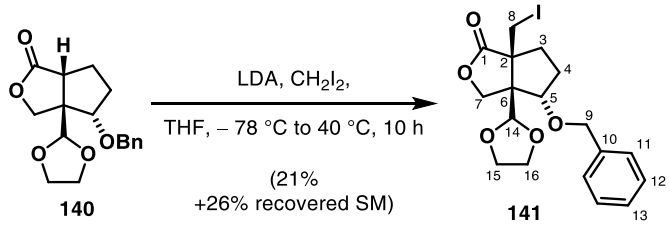
TLC (40% ethyl acetate in cyclohexane): R_f = 0.41 ($KMnO_4$).

^{1}H NMR (600 MHz, chloroform-*d*) δ 7.36 – 7.29 (m, 5H, 13-H, 14-H, 15-H), 5.22 (s, 1H, 8-H), 4.58 (d, *J* = 11.8 Hz, 1H, 11-H), 4.52 – 4.47 (m, 2H, 7-H, 11-H), 4.06 – 4.03 (m, 2H, 9-H or 10-H), 3.99 – 3.96 (m, 1H, 5-H), 3.92 – 3.90 (m, 2H, 9-H or 10-H), 3.65 (d, *J* = 9.9 Hz, 1H, 7-H), 3.05 (dd, *J* = 10.4, 1.9 Hz, 1H, 2-H), 2.39 – 2.32 (m, 1H, 3-H), 2.08 – 2.02 (m, 2H, 3-H, 4-H), 1.72 – 1.66 (m, 1H, 4-H).

^{13}C NMR (151 MHz, chloroform-*d*) δ 180.2 (C-1), 138.3 (C-12), 128.5 (C-14), 127.8 (C-15), 127.6 (C-13), 103.7 (C-8), 86.1 (C-5), 71.7 (C-11), 71.2 (C-7), 66.0 (C-9 or C-10), 65.4 (C-9 or C-10), 57.6 (C-6), 46.0 (C-2), 30.2 (C-4), 28.8 (C-3).

IR (Diamond-ATR, neat) $\tilde{\upsilon}_{max}$: 2917 (m), 1769 (s), 1454 (w), 1201 (w), 1149 (m), 1121 (m), 1028 (m), 741 (w), 699 (w) cm^{-1}.

HRMS (ESI) calc. for $C_{17}H_{24}NO_5$ $[M+NH_4]^+$: 322.1649 found: 322.1647.



Iodide 141

To a solution of lithium diisopropylamide (250 mM in tetrahydrofuran, 248 µL, 62.0 µmol, 1.20 equiv) was added a solution of dioxolane **140** (15.7 mg, 52.0 µmol, 1 equiv) in tetrahydrofuran (300 µL) dropwise of the course of 15 minutes at –78 °C. 30 minutes after the addition of **140** was completed, diiodomethane (8.00 µL, 103 µmol, 2.00 equiv) was added to the solution at –78 °C. After three hours, the solution was allowed to warm to 23 °C. After two hours at 23 °C, the reaction mixture was heated to 40 °C. After four hours at 40 °C, the solution was allowed to cool to 23 °C. Water (5 mL) and ethyl acetate (5 mL) were added to the reaction mixture and the layers were separated. The aqueous layer was extracted with ethyl acetate (3 × 2 mL), the combined organic layers were dried over sodium sulfate. The dried solution was filtered and the filtrate was concentrated. The residue was purified by flash column chromatography on silica gel (20% ethyl acetate in cyclohexane) to yield iodide **141** (4.70 mg, 11.0 µmol, 21%) along with recovered starting material **140** (5.70 mg, 19.0 µmol, 36%) as colourless oils.

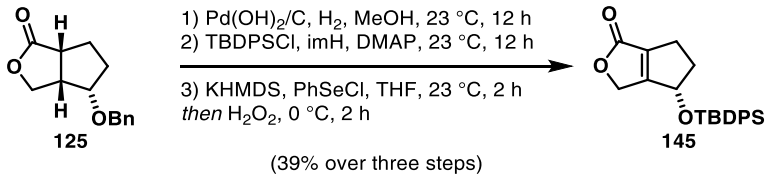
TLC (20% ethyl acetate in cyclohexane): R_f = 0.34 (CAM).

^{1}H NMR (600 MHz, chloroform-*d*) δ 7.34 – 7.27 (m, 5H, 11-H, 12-H, 13-H), 5.37 (s, 1H, 14-H), 4.73 (d, *J* = 9.5 Hz, 1H, 7-H), 4.56 (d, *J* = 6.6 Hz, 2H, 9-H), 4.25 (d, *J* = 9.5 Hz, 1H, 7-H), 4.09 (dd, *J* = 9.7, 7.1 Hz, 1H, 5-H), 3.96 – 3.91 (m, 2H, 15-H or 16-H), 3.88 – 3.83 (m, 2H, 15-H or 16-H), 3.49 – 3.43 (m, 2H, 8-H), 2.21 – 2.17 (m, 1H, 3-H), 2.09 (dt, *J* = 13.2, 6.9 Hz, 1H, 4-H), 1.64 (td, *J* = 12.9, 6.7 Hz, 1H, 3-H), 1.48 – 1.42 (m, 1H, 4-H).

^{13}C NMR (151 MHz, chloroform-*d*) δ 178.8 (C-1), 138.0 (C-10), 128.1 (C-12), 127.4 (C-13), 127.4 (C-11), 103.5 (C-14), 79.7 (C-5), 71.7 (C-9), 67.4 (C-7), 65.3 (C-15 or C-16), 65.0 (C-15 or C-16), 57.9 (C-2), 55.8 (C-6), 35.7 (C-3), 30.8 (C-4), 3.6 (C-8).

IR (Diamond-ATR, neat) $\tilde{\nu}_{max}$: 2919 (w), 1770 (s), 1109 (m), 1019 (s), 981 (w), 944 (w), 738 (w), 699 (w) cm^{-1}.

HRMS (ESI) calc. for $C_{18}H_{25}INO_5$ $[M+NH_4]^+$: 462.0772 found: 462.07741.



125 145

Lactone 145

To a solution of lactone **125** (24.3 mg, 105 µmol, 1 equiv) in methanol (0.5 mL) was added palladium hydroxide on activated charcoal (20 wt%, 7.35 mg, 11.0 µmol, 0.100 equiv) at 23 °C. An atmosphere of hydrogen was maintained by sparging with a stream of pure hydrogen gas through a stainless-steel needle for five minutes and vigorous stirring of the suspension was then continued under hydrogen atmosphere at 23 °C. After 12 hours, the reaction mixture was filtered through a pad of Celite, the filter cake was washed with dichloromethane (5 mL) and the filtrate was concentrated to yield the crude secondary alcohol (14.7 mg, 0.103 mmol) as a colourless oil.

To a solution of the crude alcohol (14.7 mg, 103 µmol, 1 equiv) in dichloromethane (1 mL) was added *tert*-butyldiphenylchlorosilane (37.6 mg, 134 µmol, 1.30 equiv), imidazole (9.21 mg, 134 µmol, 1.30 equiv) and 4-dimethylaminopyridine (1.27 mg, 10.0 µmol, 0.100 equiv) at 23 °C. After 12 hours, water (5 mL) was added to the reaction mixture and the layers were separated. The aqueous layer was extracted with dichloromethane (3 × 3 mL), the combined organic layers were dried over sodium sulfate. The dried solution was filtered and the filtrate was concentrated to yield the crude silyl ether (52.0 mg, 137 µmol) as a colourless oil.

To a solution of the crude silyl ether (52.0 mg, 137 µmol, 1 equiv) in tetrahydrofuran (1.4 mL) was added phenylselenyl chloride (80.1 mg, 410 µmol, 3.00 equiv) and then a solution of potassium bis(trimethylsilyl)amide (1.00 M in tetrahydrofuran, 410 µL, 410 µmol. 3.00 equiv) was added dropwise

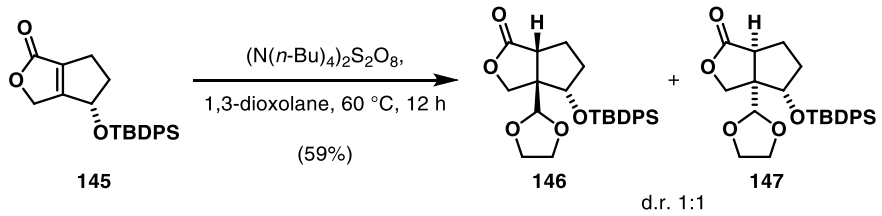
over the course of 20 minutes at 23 °C. Two hours after the addition was completed, the solution was cooled to 0 °C and a solution of hydrogen peroxide (30% in water, 400 µL) was added. After two hours, added a saturated aqueous solution of sodium hydrogen carbonate (5 mL) and diethyl ether (5 mL) were added to the reaction mixture and the layers were separated. The aqueous layer was extracted with diethyl ether (3 × 2 mL), the combined organic layers were dried over sodium sulfate. The dried solution was filtered and the filtrate was concentrated. The filtrate was purified by flash column chromatography on silica gel (5% grading to 10% ethyl acetate in cyclohexane) to yield lactone **145** (20.0 mg, 53.0 µmol, 39% over three steps) as a colourless oil.

TLC (20% ethyl acetate in cyclohexane): R_f = 0.37 ($KMnO_4$).

^{1}H NMR (300 MHz, chloroform-*d*) δ 7.67 – 7.60 (m, 5H), 7.45 – 7.39 (m, 5H), 5.17 – 5.09 (m, 1H), 4.50 – 4.43 (m, 1H), 4.09 – 4.02 (m, 1H), 2.72 – 2.58 (m, 2H), 2.49 – 2.42 (m, 1H), 2.34 – 2.26 (m, 1H), 1.08 (s, 9H).

IR (Diamond-ATR, neat) $\tilde{\upsilon}_{max}$: 2932 (w), 2858 (w), 1760 (s), 1428 (w), 1106 (m), 1037 (m), 971 (w), 822 (w), 743 (w), 702 (s), 504 (m) cm^{-1}.

HRMS (ESI) calc. for $C_{23}H_{27}O_3Si$ $[M+H]^+$: 379.1724 found: 379.1702, calc. for $C_{23}H_{30}NO_3Si$ $[M+NH_4]^+$: 396.1989 found: 396.1990.



Dioxolane 146 and 147

To a solution of lactone **145** (9.10 mg, 24.0 µmol, 1 equiv) in 1,3-dioxolane (300 µL) was added tetrabutylammonium peroxydisulfate (32.6 mg, 48.0 µmol, 2.00 equiv) and the reaction mixture was heated to 60 °C. After 12 hours, the reaction mixture was allowed to cool to 23 °C and was then concentrated. The residue was partitioned between ethyl acetate (5 mL) and water (5 mL) and the layers were separated. The aqueous layer was extracted with ethyl acetate (3 × 2 mL), the combined organic layers were dried over sodium sulfate. The dried solution was filtered and the filtrate was concentrated. The residue was purified by flash column chromatography on silica gel (20% ethyl acetate in cyclohexane) to yield dioxolane **146** and **147** (6.40 mg, 14.0 µmol, 59%) as colourless oils.

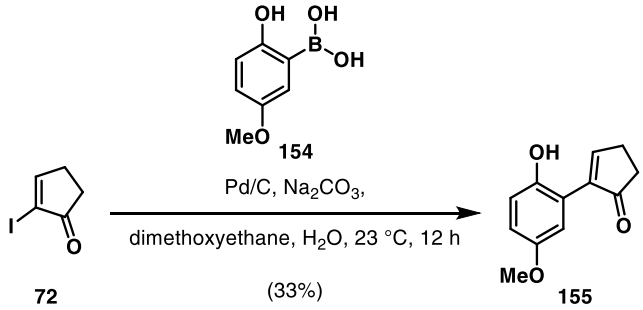
TLC (30% ethyl acetate in cyclohexane): R_f = 0.34 and 0.41 ($KMnO_4$).

^{1}H NMR (300 MHz, chloroform-*d*) *complex mixture of signals arising from two diastereomers in a ratio of 1:1*

^{13}C NMR (75 MHz, chloroform-*d*) *complex mixture of signals arising from two diastereomers in a ratio of 1:1*

IR (Diamond-ATR, neat) $\tilde{\upsilon}_{max}$: 2925 (m), 2855 (m), 1765 (s), 1456 (w), 1318 (w), 1121 (s), 1020 (s), 817 (w), 737 (m), 701 (w) cm^{-1}.

HRMS (ESI) calc. for $C_{26}H_{33}O_5Si$ $[M+H]^+$: 453.2092 found: 453.2096.



Phenol 155

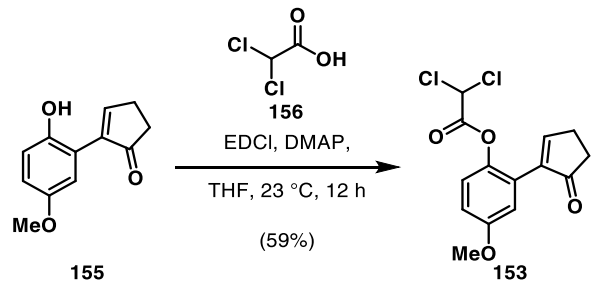
To a mixture of cyclopentenone iodide **72** (131 mg, 627 µmol, 1 equiv) in degassed dimethoxyethane (3 mL) and degassed water (3 mL) was added boronic acid **154**[150] (137 mg, 816 µmol, 1.30 equiv), sodium carbonate (86.5 mg, 816 µmol, 1.30 equiv) and palladium on activated charcoal (10 wt%, 66.8 mg, 63.0 µmol, 0.100 equiv) at 23 °C. After 12 hours, water (10 mL) and ethyl acetate (10 mL) were added to the reaction mixture and the layers were separated. The aqueous layer was extracted with ethyl acetate (3 × 3 mL) and the combined organic layers were dried over sodium sulfate. The dried solution was filtered through a pad of Celite and the filtrate was concentrated. The residue was purified by flash column chromatography on silica gel (20% ethyl acetate in cyclohexane) to yield phenol **155** (42.0 mg, 206 µmol, 33%) as a yellow oil.

TLC (30% ethyl acetate in cyclohexane): R_f = 0.22 (CAM, UV).

^{1}H NMR (300 MHz, chloroform-*d*) δ 8.87 (s, 1H), 7.91 (dd, *J* = 3.7, 2.3 Hz, 1H), 7.02 – 6.76 (m, 2H), 3.78 (s, 3H), 2.90 – 2.83 (m, 2H), 2.76 – 2.68 (m, 2H).

HRMS (ESI) calc. for $C_{12}H_{12}NaO_3$ $[M+Na]^+$: 227.0679 found: 227.0683.

[150] E. Z. Oblak, M. D. VanHeyst, J. Li, A. J. Wiemer, D. L. Wright, *J. Am. Chem. Soc.* **2014**, *136*, 4309–4315.

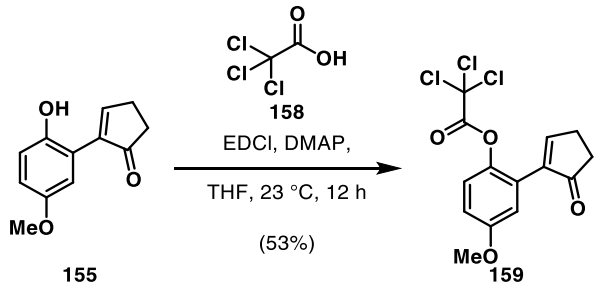


Dichloroacetic acid ester 153

To a solution of phenol **155** (17.7 mg, 87.0 µmol, 1 equiv) in tetrahydrofuran (1 mL) was added dichloroacetic acid (8.60 µL, 104 µmol, 1.20 equiv), 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (22.0 mg, 113 µmol, 1.30 equiv) and 4-dimethylaminopyridine (1.07 mg, 9.00 µmol, 0.100 equiv) at 23 °C. After 12 hours, a saturated aqueous solution of ammonium chloride (10 mL) and ethyl acetate (10 mL) were added to the reaction mixture and the layers were separated. The aqueous layer was extracted with ethyl acetate (3 × 3 mL) and the combined organic layers were dried over sodium sulfate. The dried solution was filtered and the filtrate was concentrated. The residue was purified by flash column chromatography on silica gel (20% ethyl acetate in cyclohexane) to yield dichloroacetic acid ester **153** (16.0 mg, 51.0 µmol, 59%) as a colourless oil.

TLC (20% ethyl acetate in cyclohexane): R_f = 0.26 (CAM, UV).

^{1}H NMR (300 MHz, chloroform-*d*) δ 7.78 (t, *J* = 2.8 Hz, 1H), 7.10 (d, *J* = 8.9 Hz, 1H), 6.99 – 6.88 (m, 1H), 6.09 (s, 1H), 3.82 (s, 3H), 2.74 (dt, *J* = 4.7, 2.3 Hz, 2H), 2.59 – 2.52 (m, 2H).



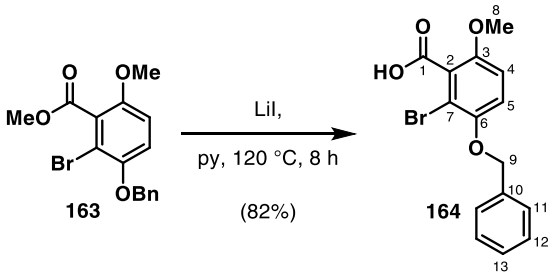
Trichloroacetic acid ester 159

To a solution of phenol **155** (19.5 mg, 96.0 µmol, 1 equiv) in tetrahydrofuran (1 mL) was added trichloroacetic acid **158** (20.3 mg, 124 µmol, 1.30 equiv), 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (24.3 mg, 124 µmol, 1.30 equiv) and 4-dimethylaminopyridine (1.18 mg, 10.0 µmol, 0.100 equiv) at 23 °C. After 12 hours, a saturated aqueous solution of ammonium chloride (10 mL) and ethyl acetate (10 mL) were added to the reaction mixture and the layers were separated. The aqueous layer was extracted with ethyl acetate (3 × 3 mL) and the combined organic layers were dried over sodium sulfate. The dried solution was filtered and the filtrate was concentrated.

The residue was purified by flash column chromatography on silica gel (30% ethyl acetate in cyclohexane) to yield dichloroacetic acid ester **159** (17.7 mg, 51.0 µmol, 53%) as a colourless oil.

TLC (40% ethyl acetate in cyclohexane): R_f = 0.28 (CAM, UV).

^{1}H NMR (300 MHz, chloroform-*d*) δ 7.82 – 7.80 (m, 1H), 7.15 (d, *J* = 8.9 Hz, 1H), 7.01 (d, *J* = 2.9 Hz, 1H), 6.92 (dd, *J* = 9.0, 3.1 Hz, 1H), 3.83 (s, 3H), 2.76 – 2.71 (m, 2H), 2.57 – 2.53 (m, 2H).



Acid 164

To a solution of bromomethoxybenzoate **163** (916 mg, 2.61 mmol, 1 equiv) in pyridine (26 mL) was added lithium iodide (2.67 g, 19.6 mmol, 7.50 equiv) and the suspension was heated to 120 °C. After eight hours, the reaction mixture was allowed to cool to 23 °C and an aqueous solution of hydrochloric acid (6 M in water, 10 mL) and ethyl acetate (10 mL) were added to the suspension and the layers were separated. The aqueous layer was extracted with ethyl acetate (3 × 10 mL), the combined organic layers were dried over sodium sulfate. The dried solution was filtered and the filtrate was concentrated to yield acid **164** (879 mg, 2.15 mmol, 82%) as a colourless solid.

TLC (5% methanol in dichloromethane): R_f = 0.12 ($KMnO_4$, UV).

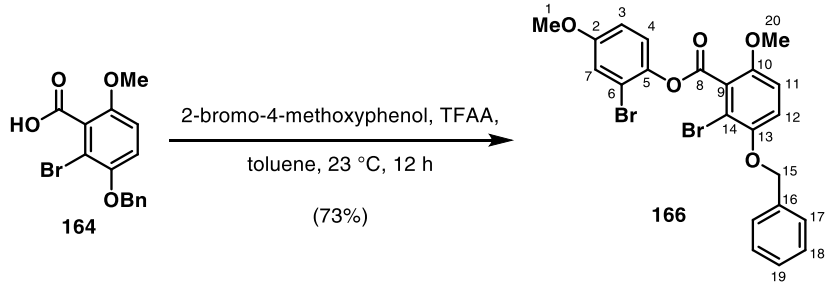
mp: (189-191) °C

^{1}H NMR (400 MHz, methanol-d_4) δ 7.49 – 7.45 (m, 2H, 11-H), 7.39 – 7.34 (m, 2H, 12-H), 7.33 – 7.28 (m, 1H, 13-H), 7.09 (d, *J* = 9.1 Hz, 1H, 4-H), 6.99 (d, *J* = 9.1 Hz, 1H, 5-H), 5.12 (s, 2H, 9-H), 3.80 (s, 3H, 8-H).

^{13}C NMR (101 MHz, methanol-d_4) δ 169.5 (C-1), 152.0 (C-3), 150.6 (C-6), 138.2 (C-10), 130.0 (C-2), 129.5 (C-12), 129.0 (C-13), 128.5 (C-11), 116.3 (C-4), 112.4 (C-5), 110.6 (C-7), 72.7 (C-9), 57.1 (C-8).

IR (Diamond-ATR, neat) $\tilde{\upsilon}_{max}$: 2935 (br, w), 1710 (s), 1575 (w), 1478 (s), 1436 (m), 1381 (w), 1265 (s), 1036 (s), 802 (w), 737 (m), 696 (w) cm^{-1}.

HRMS (ESI) calc. for $C_{15}H_{14}BrO_4$ $[M+H]^+$: 337.0070 found: 337.0052.



Ester 166

To a solution of acid **164** (37.0 mg, 110 µmol, 1 equiv) in toluene (1 mL) was added trifluoroacetic anhydride (0.25 mL) at 23 °C. After 12 hours, the reaction mixture was concentrated and the residue was purified by flash column chromatography on silica gel (20% ethyl acetate in cyclohexane) to yield ester **166** (42.0 mg, 80.0 µmol, 73%) as a colourless oil.

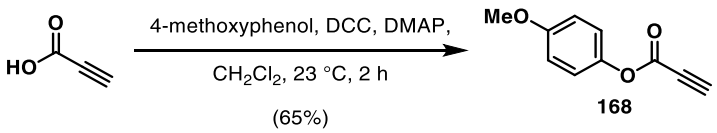
TLC (30% ethyl acetate in cyclohexane): R_f = 0.39 ($KMnO_4$, UV).

^{1}H NMR (600 MHz, chloroform-*d*) δ 7.48 – 7.46 (m, 2H, 17-H), 7.41 – 7.38 (m, 2H, 18-H), 7.35 – 7.32 (m, 1H, 19-H), 7.30 (d, *J* = 8.9 Hz, 1H, 4-H), 7.18 (d, *J* = 2.9 Hz, 1H, 7-H), 6.97 (d, *J* = 9.0 Hz, 1H, 11-H), 6.92 (dd, *J* = 8.9, 2.9 Hz, 1H, 3-H), 6.86 (d, *J* = 9.0 Hz, 1H, 12-H), 5.13 (s, 2H, 15-H), 3.86 (s, 3H, 20-H), 3.82 (s, 3H, 1-H).

^{13}C NMR (151 MHz, chloroform-*d*) δ 164.2 (C-8), 158.1 (C-2), 151.8 (C-10), 149.6 (C-13), 141.8 (C-5), 136.6 (C-16), 128.8 (C-18), 128.2 (C-19), 127.3 (C-17), 126.6 (C-14), 124.2 (C-4), 118.4 (C-7), 116.3 (C-11), 116.1 (C-6), 114.5 (C-3), 111.2 (C-12), 72.2 (C-15), 56.8 (C-20), 56.0 (C-1).

IR (Diamond-ATR, neat) $\tilde{\upsilon}_{max}$: 2918 (w), 2850 (w), 1761 (m), 1579 (w), 1489 (s), 1438 (w), 1271 (s), 1221 (w), 1195 (s), 1095 (w), 1037 (s), 860 (w), 799 (w), 736 (m), 697 (w) cm^{-1}.

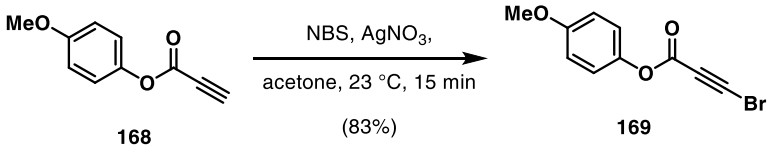
HRMS (ESI) calc. for $C_{22}H_{18}Br_2NaO_5$ $[M+Na]^+$: 544.9393, 542.9413, 546.9372, 545.9426 found: 544.9368, 542.9389, 546.9347, 545.9402.



Ester 168

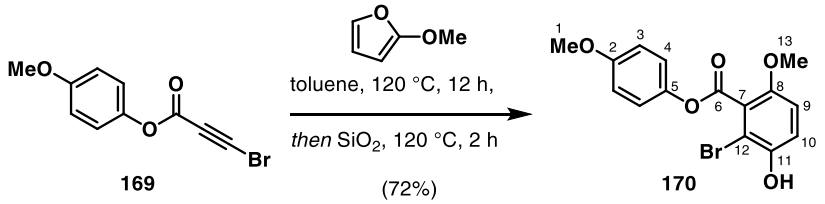
To a solution of propiolic acid (1.00 g, 13.6 mmol, 1.20 equiv) in dichloromethane (50 mL) was added *N*,*N*′-dicyclohexylcarbodiimide (3.53 g, 17.0 mmol, 1.50 equiv) at 0 °C. After five minutes, 4-methoxyphenol (1.56 g, 11.3 mmol, 1 equiv) and a solution of 4-(dimethylamino)pyridine (139 mg, 1.13 mmol, 0.100 equiv) in dichloromethane (3 mL) were added in sequence to the reaction mixture. After two hours at 0 °C, the reaction mixture was filtered through a pad of Celite and the filter cake was washed with dichloromethane (20 mL). The filtrate was concentrated and the residue was purified by

flash column chromatography on silica gel (15% diethyl ether in cyclohexane) to yield ester **168** (1.30 g, 7.38 mmol, 65%) as a slightly yellow oil. The obtained analytical data were in full agreement with those reported in the literature.[151]



Bromo alkyne 169

To a solution of ester **168** (1.30 g, 7.38 mmol, 1 equiv) in acetone (15 mL) was added silver nitrate (125 mg, 738 µmol, 0.100 equiv) and *N*-bromosuccinimide (1.46 g, 8.12 mmol, 1.10 equiv) in sequence at 23 °C. During the reaction, a colourless precipitate formed and the reaction mixture turned yellow. After 15 minutes, the reaction mixture was filtered through a pad of Celite and the filter cake was washed with acetone (10 mL). The filtrate was concentrated and the residue was purified by flash column chromatography on silica gel (15% diethyl ether in cyclohexane) to yield bromo alkyne **169** (1.57 g, 6.16 mmol, 83%) as a yellow oil. The obtained analytical data were in full agreement with those reported in the literature.[151]



Bromophenol 170

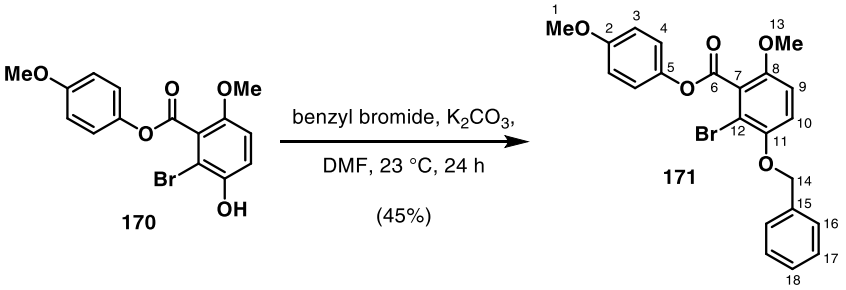
To a solution of bromo alkyne **169** (1.04 g, 4.08 mmol, 1 equiv) in toluene (15 mL) was added 2-methoxyfuran (465 µL, 4.89 mmol, 1.20 equiv) and the reaction mixture was heated to 120 °C in a pressure tube. After 12 hours, the reaction mixture was allowed to cool to 23 °C and then silica gel (2 g) was added to the solution. The suspension was heated to 120 °C. After two hours, the reaction mixture was allowed to cool to 23 °C and then filtered through a pad of Celite and the pad was washed with toluene (10 mL). The filtrate was concentrated and the residue was purified by flash column chromatography on silica gel (40% ethyl acetate in cyclohexane) to yield bromophenol **170** (1.04 g, 2.94 mmol, 72%) as a yellow oil.

TLC (30% ethyl acetate in cyclohexane): R_f = 0.23 ($KMnO_4$, UV).

^{1}H NMR (400 MHz, chloroform-*d*) δ 7.20 (d, *J* = 9.1 Hz, 2H, 4-H), 7.08 (d, *J* = 9.0 Hz, 1H, 10-H), 6.94 (d, *J* = 9.1 Hz, 2H, 3-H), 6.91 (d, *J* = 9.1 Hz, 1H, 9-H), 3.87 (s, 3H, 13-H), 3.82 (s, 3H, 1-H).

[151] M. D. Aparece, P. A. Vadola, *Org. Lett.* **2014**, *16*, 6008–6011.

HRMS (ESI) calc. for $C_{15}H_{13}BrNaO_5$ $[M+Na]^+$: 374.9839 found: 374.9842.



Benzyl ether 171

To a solution of bromophenol **170** (53.0 mg, 150 µmol, 1 equiv) in *N*,*N*-dimethylformamide (2 mL) was added potassium carbonate (62.2 mg, 450 µmol, 3.00 equiv) and benzyl bromide (21.8 µL, 180 µmol, 1.20 equiv) at 23 °C. After 24 hours, water (5 mL) was added to the reaction mixture and the layers were separated. The aqueous layer was extracted with diethyl ether (3 × 3 mL), the combined organic layers were washed with a 10% aqueous solution of lithium chloride (5 mL) and the washed organic layers were dried over sodium sulfate. The dried solution was filtered and the filtrate was concentrated. The residue was purified by flash column chromatography on silica gel (20% ethyl acetate in cyclohexane) to yield benzyl ether **171** (30.0 mg, 68.0 µmol, 45%) as a colourless solid.

TLC (30% ethyl acetate in cyclohexane): R_f = 0.31 ($KMnO_4$, UV).

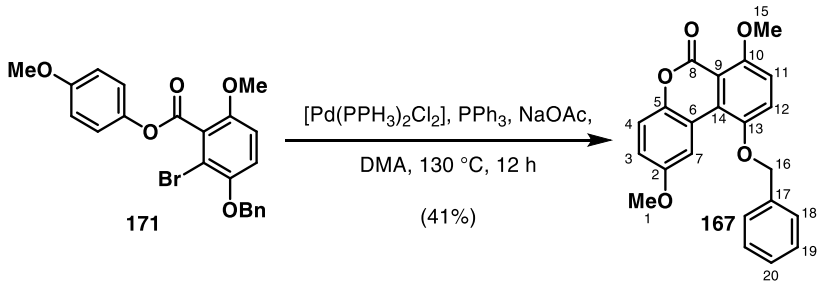
mp: (148-149) °C

^{1}H NMR (400 MHz, chloroform-*d*) δ 7.51 (d, *J* = 6.9 Hz, 2H, 16-H), 7.46 – 7.41 (m, 2H, 17-H), 7.41 – 7.36 (m, 1H, 18-H), 7.30 – 7.26 (m, 2H, 4-H), 7.01 – 6.98 (m, 2H, 3-H, 9-H), 6.89 (d, *J* = 9.1 Hz, 1H, 10-H), 5.17 (s, 2H, 14-H), 3.89 (s, 3H, 13-H), 3.86 (s, 3H, 1-H).

^{13}C NMR (101 MHz, chloroform-*d*) δ 164.9 (C-6), 157.7 (C-2), 151.5 (C-8), 149.5 (C-11), 144.4 (C-5), 136.6 (C-15), 128.8 (C-17), 128.2 (C-18), 127.3 (C-16), 127.1, 122.5 (C-4), 116.1 (C-9), 114.7 (C-3), 111.2 (C-10), 111.2, 72.1 (C-14), 56.9 (C-13), 55.8 (C-1).

IR (Diamond-ATR, neat) $\tilde{\upsilon}_{max}$: 2941 (w), 1754 (m), 1505 (s), 1478 (m), 1439 (w), 1276 (s), 1225 (m), 1188 (s), 1100 (w), 1036 (s), 739 (w) cm^{-1}.

HRMS (ESI) calc. for $C_{50}H_{54}NaO_9Si$ $[M+Na]^+$: 849.3429 found: 849.3444.



Tricyclic lactone 167

To a solution of benzyl ether **171** (65.0 mg, 147 µmol, 1 equiv) in *N*,*N*-dimethylacetamide (3 mL) was added bis(triphenylphosphine)palladium(II) dichloride (10.4 mg, 15.0 µmol, 0.100 equiv), triphenylphosphine (7.77 mg, 29.0 µmol, 0.200 equiv) and sodium acetate (24.1 mg, 293 µmol, 2.00 equiv). Nitrogen was sparged through the reaction mixture for 5 minutes and then the mixture was heated to 130 °C. After 12 hours, the reaction mixture was allowed to cool to 23 °C and then ethyl acetate (5 mL) and an aqueous solution of hydrochloric acid (2 M, 5 mL) was added. The layers were separated, the aqueous layer was extracted with ethyl acetate (3 × 3 mL), the combined organic layers were dried over sodium sulfate. The dried solution was filtered through a pad of Celite, the pad was washed with ethyl acetate (5 mL) and the filtrate was concentrated. The residue was purified by flash column chromatography on silica gel (40% ethyl acetate in cyclohexane) to yield tricyclic lactone **167** (22.0 mg, 61.0 µmol, 41%) as a colourless solid.

TLC (40% ethyl acetate in cyclohexane): R_f = 0.21 ($KMnO_4$, UV).

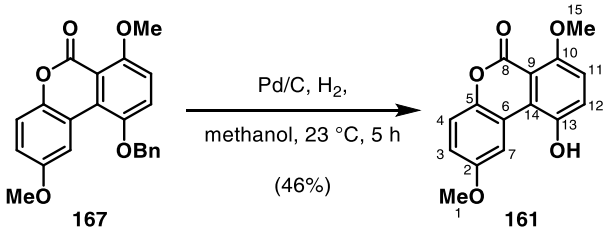
mp: (189-190) °C

^{1}H NMR (400 MHz, chloroform-*d*) δ 8.49 (d, *J* = 3.0 Hz, 1H, 7-H), 7.54 – 7.39 (m, 6H, 11-H, 18-H, 19-H, 20-H), 7.21 (d, *J* = 8.9 Hz, 1H, 4-H), 7.07 (d, *J* = 9.3 Hz, 1H, 12-H), 6.96 (dd, *J* = 9.0, 3.0 Hz, 1H, 3-H), 5.18 (s, 2H, 16-H), 4.00 (s, 3H, 15-H), 3.30 (s, 3H, 1-H).

^{13}C NMR (101 MHz, chloroform-*d*) δ 158.3 (C-8), 156.6 (C-10), 155.6 (C-2), 150.0 (C-13), 145.6 (C-5), 136.0 (C-17), 129.0 (C-18 or C-19), 128.9 (C-20), 128.8 (C-18 or C-19), 126.4 (C-6), 120.0 (C-11), 118.3 (C-3), 117.8 (C-9), 117.6 (C-4), 112.2 (C-12), 111.8 (C-14), 111.2 (C-7), 72.3 (C-16), 57.0 (C-15), 55.2 (C-1).

IR (Diamond-ATR, neat) $\tilde{\upsilon}_{max}$: 2918 (s), 2850 (m), 1732 (m), 1506 (w), 1465 (w), 1197 (w), 1030 (w) cm^{-1}.

HRMS (ESI) calc. for $C_{22}H_{18}NaO_5$ $[M+Na]^+$: 385.1046 found: 385.1027.



Tricyclic phenol 161

To a solution of tricyclic lactone **167** (16.0 mg, 44.0 mol, 1 equiv) in methanol (1 mL) was added palladium on activated charcoal (10 wt%, 9.40 mg, 0.200 equiv) at 23 °C. An atmosphere of hydrogen was maintained by sparging with a stream of pure hydrogen gas through a stainless-steel needle for five minutes and vigorous stirring of the suspension was then continued under hydrogen atmosphere at 23 °C. After five hours, the reaction mixture was filtered through a pad of Celite and the pad was washed with dichloromethane (5 mL). The filtrate was concentrated and the residue was purified by flash column chromatography on silica gel (5% methanol in dichloromethane) to yield tricyclic phenol **161** (5.50 mg, 20.0 µmol, 46%) as a colourless solid.

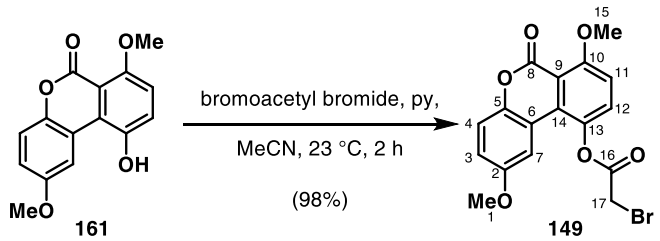
TLC (5% methanol in dichloromethane): R_f = 0.35 ($KMnO_4$, UV).

mp: *decomposition before melting point was reached*

^{1}H NMR (400 MHz, methanol-d_4) δ 8.84 (d, *J* = 3.0 Hz, 1H, 13-OH), 7.35 (d, *J* = 9.1 Hz, 1H, 3-H or 4-H), 7.20 (d, *J* = 9.0 Hz, 1H, 3-H or 4-H), 7.17 (d, *J* = 9.1 Hz, 1H, 11-H), 7.06 (dd, *J* = 8.9, 3.0 Hz, 1H, 12-H), 3.92 (s, 3H, 1-H or 15-H), 3.85 (s, 3H, 1-H or 15-H).

IR (Diamond-ATR, neat) $\tilde{\upsilon}_{max}$: 3314 (br, w), 2921 (w), 1694 (s), 1584 (m), 1479 (m), 1390 (m), 1290 (m), 1259 (s), 1200 (s), 1074 (m), 1024 (m), 808 (w), 779 (m) cm^{-1}.

HRMS (ESI) calc. for $C_{15}H_{12}NaO_5$ $[M+Na]^+$: 295.0577 found: 295.0572.



Bromoketone 149

To a solution of tricyclic phenol **161** (5.00 mg, 18.0 µmol, 1 equiv) in acetonitrile (300 µL) was added pyridine (8.90 µL, 110 µmol, 6.00 equiv) and bromoacetyl bromide (6.40 µL, 74.0 µmol, 4.00 equiv) at 23 °C. After two hours, the reaction mixture was concentrated and the residue was purified by flash

column chromatography on silica gel (30% ethyl acetate in cyclohexane) to yield bromoketone **149** (7.10 mg, 18.0 µmol, 98%) as a colourless solid.

TLC (40% ethyl acetate in cyclohexane): R_f = 0.27 ($KMnO_4$, UV).

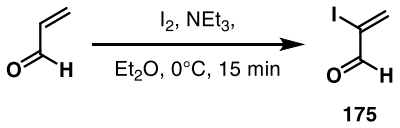
mp: (176-177) °C

^{1}H NMR (600 MHz, chloroform-*d*) δ 7.96 (d, *J* = 2.9 Hz, 1H, 7-H), 7.48 (d, *J* = 9.1 Hz, 1H, 11-H or 12-H), 7.28 (d, *J* = 9.0 Hz, 1H, 4-H), 7.12 (d, *J* = 9.2 Hz, 1H, 11-H or 12-H), 7.08 – 7.06 (m, 1H, 13-H), 4.20 (s, 2H, 17-H), 4.06 (s, 3H, 15-H), 3.87 (s, 3H, 1-H).

^{13}C NMR (151 MHz, chloroform-*d*) δ 165.8 (C-16), 160.8 (C-10), 157.4 (C-2), 156.0, 145.8, 139.6, 130.8, 129.4, 118.3 (C-4), 116.9 (C-3), 116.5, 111.9 (C-7), 111.9, 111.5, 57.0 (C-15), 56.1 (C-1), 25.3 (C-17).

IR (Diamond-ATR, neat) $\tilde{\upsilon}_{max}$: 2918 (w), 1695 (s), 1579 (m), 1462 (m), 1265 (m), 1259 (s), 1208 (s), 1079 (w), 1026 (m), 813 (w), 771 (w) cm^{-1}.

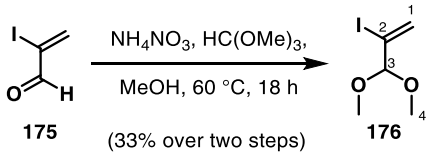
HRMS (ESI) calc. for $C_{17}H_{13}BrNaO_6$ $[M+Na]^+$: 414.9788 found: 414.9790.



175

Aldehyde 175

To a solution of acrolein (2.00 g, 35.7 mmol, 2.00 equiv) in diethyl ether (50 mL) was added triethylamine (2.48 mL, 17.8 mmol, 1 equiv) at 0 °C. Iodine (4.57 g, 17.8 mmol, 1 equiv) was added portion wise to the solution at 0 °C. After 15 minutes, the reaction mixture was filtered through a pad of Celite and the pad was washed with diethyl ether (20 mL). The filtrate was concentrated at 23 °C to yield aldehyde **175** (2.18 g, 12.0 mmol) as a slightly yellow oil. The crude product was used in the next step without further purification. The obtained analytical data were in full agreement with those reported in the literature.[152]



175 **176**

Acetal 176

[152] B. V. D. Vijaykumar, P. Mallesham, S. Chandrasekhar, *Eur. J. Org. Chem.* **2012**, *2012*, 988–994.

To a solution of aldehyde **175** (2.18 g, 12.0 mmol, 1 equiv) in methanol (3 mL) was added ammonium nitrate (47.9 mg, 599 µmol, 0.0500 equiv) and trimethyl orthoformate (1.34 mL, 12.0 mmol, 1 equiv) and the reaction mixture was heated to 60 °C. After 18 hours, the reaction mixture was allowed to cool to 23 °C and was then concentrated. Sodium carbonate (0.5 g) was added to the residue and the mixture was purified by bulb-to-bulb distillation (0.1 mmHg, 125 °C, the product was collected in a flask cooled to –78 °C and protected from light) to yield acetal **176** (1.35 g, 5.92 mmol, 33% over two steps) as a slightly yellow oil.

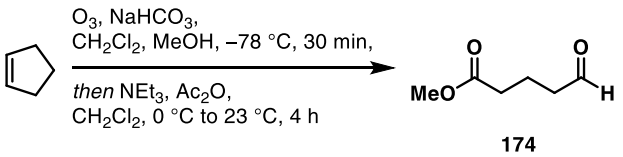
TLC (20% ethyl acetate in cyclohexane): R_f = 0.58 ($KMnO_4$).

^{1}H NMR (400 MHz, chloroform-*d*) δ 6.57 (dd, *J* = 1.5, 1.1 Hz, 1H, 1-H), 6.09 (dd, *J* = 1.5, 0.6 Hz, 1H, 1-H), 4.38 (t, *J* = 0.9 Hz, 1H, 3-H), 3.35 (s, 6H, 4-H).

^{13}C NMR (101 MHz, chloroform-*d*) δ 128.9 (C-1), 107.9 (C-2), 105.4 (C-3), 53.6 (C-4).

IR (Diamond-ATR, neat) $\tilde{\upsilon}_{max}$: 2929 (s), 2865 (m), 1698 (m), 1464 (w), 1090 (m), 884 (w), 860 (w), 572 (w), 542 (w) cm^{-1}.

HRMS (ESI) no mass found.



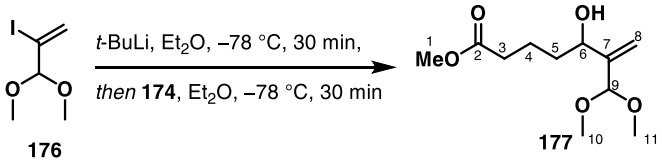
174

(67%)

Aldehyde 174

To a solution of cyclopentene (6.60 mL, 72.0 mmol, 1 equiv) in dichloromethane (250 ml) and methanol (50 mL) was added sodium bicarbonate (1.94 g, 23.0 mmol, 0.320 equiv) and the mixture was cooled to −78 °C. Ozone was sparged through the reaction mixture until a blue colour appeared. After 30 minutes, oxygen was sparged through the mixture until the blue colour disappeared. The reaction mixture was filtered and to the filtrate was added benzene (80 mL). The solution was concentrated until approximately 50 mL of solvent remained. Dichloromethane (250 mL) was added and the mixture was cooled to 0 °C. To the ice-cold mixture was added triethylamine (15.0 mL, 108 mmol, 1.50 equiv) and acetic anhydride (22.1 g, 216 mmol, 3.00 equiv). After 15 minutes, the reaction mixture was allowed to warm to 23 °C. After four hours at 23 °C, aqueous hydrochloric acid (0.1 M, 500 mL) was added to the reaction mixture and the layers were separated. The aqueous layer was extracted with ethyl acetate (3 × 150 mL) and the combined organic layers were dried over sodium sulfate. The dried solution was filtered and the filtrate was concentrated. The residue was purified by flash column chromatography on

silica gel (15% ethyl acetate in hexanes) to yield aldehyde **174** (6.30 g, 48.4 mmol, 67%) as a colourless liquid. The obtained analytical data were in full agreement with those reported in the literature.[153]



Allyl alcohol 177

To a solution of *tert*-butyllithium (1.50 M in pentane, 1.11 mL, 1.67 mmol, 2.40 equiv) in diethyl ether (2 mL) was added a solution of vinyl iodide **176** (190 mg, 835 µmol, 1.20 equiv) in diethyl ether (2 mL) dropwise over the course of 15 minutes at −78 °C. 30 minutes after the addition of **176** was completed, a solution of aldehyde **174** (90.6 mg, 696 µmol, 1 equiv) in diethyl ether (2 mL) was added to the yellow mixture over the course of ten minutes. 15 minutes after the addition of **174** was completed, saturated aqueous solution of ammonium chloride (20 mL) was added to the reaction mixture and the solution was allowed to warm to 23 °C. The layers were separated and the aqueous layer was extracted with ethyl acetate (3 × 10 mL). The combined organic layers were dried over sodium sulfate, the dried solution was filtered and the filtrate was concentrated to obtain **177** as a colourless oil (88 mg). The residue was used crude in the next reaction.

Note: The allylic alcohol is slightly unstable on silica gel. A small sample was purified on silica gel (30% ethyl acetate in cyclohexane) to obtain an analytical clean product.

TLC (30% ethyl acetate in cyclohexane): R_f = 0.11 ($KMnO_4$).

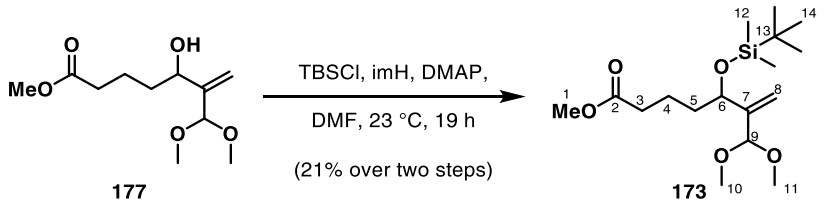
^{1}H NMR (400 MHz, chloroform-*d*) δ 5.27 – 5.23 (m, 2H, 8-H), 4.72 (s, 1H, 9-H), 4.17 – 4.12 (m, 1H, 6-H), 3.62 (s, 3H, 1-H), 3.32 – 3.27 (m, 6H, 10-H, 11-H), 2.65 (d, *J* = 4.7 Hz, 1H, 6-OH), 2.33 – 2.28 (m, 2H, 3-H), 1.77 – 1.70 (m, 1H, 5-H), 1.66 – 1.58 (m, 3H, 4-H, 5-H).

^{13}C NMR (101 MHz, chloroform-*d*) δ 174.1 (C-2), 146.2 (C-7), 114.6 (C-8), 104.7 (C-9), 71.2 (C-6), 54.0 (C-10 or C-11), 53.6 (C-10 or C-11), 51.5 (C-1), 35.0 (C-4), 33.8 (C-3), 21.3 (C-5).

IR (Diamond-ATR, neat) $\tilde{\nu}_{max}$: 3485 (br, w), 2929 (m), 1737 (s), 1438 (m), 1367 (w), 1195 (m), 1112 (m), 1074 (m), 983 (w) cm^{-1}.

HRMS (ESI) calc. for $C_{11}H_{20}NaO_5$ $[M+Na]^+$: 255.1203 found: 255.1198; calc. for $C_{11}H_{20}KO_5$ $[M+K]^+$: 271.0942 found: 271.0937.

[153] J. Chen, J. Chen, Y. Xie, H. Zhang, *Angew. Chem. Int. Ed.* **2012**, *51*, 1024–1027.



177 173

Silyl ether 173

To a solution of crude allyl alcohol **177** (88.0 mg, 379 µmol, 1 equiv) in *N*,*N*-dimethylformamide (3 mL) was added *tert*-butyldimethylchlorosilane (68.5 mg, 455 µmol, 1.20 equiv), imidazole (61.9 mg, 909 µmol, 2.40 equiv) and 4-(dimethylamino)pyridine (4.68 mg, 38.0 µmol, 0.100 equiv) at 23 °C. After 19 hours, water (5 mL) and diethyl ether (5 mL) were added to the reaction mixture and the layers were separated. The aqueous layer was extracted with diethyl ether (3 × 3 mL), the combined organic layers were washed with an aqueous solution of lithium chloride (10%, 5 mL) and the washed organic layers were dried over sodium sulfate. The dried solution was filtered and the filtrate was concentrated. The residue was purified by flash column chromatography on silica gel (10% ethyl acetate in cyclohexane) to yield silyl ether **173** (50.5 mg, 146 µmol, 21% over two steps) as a colourless oil.

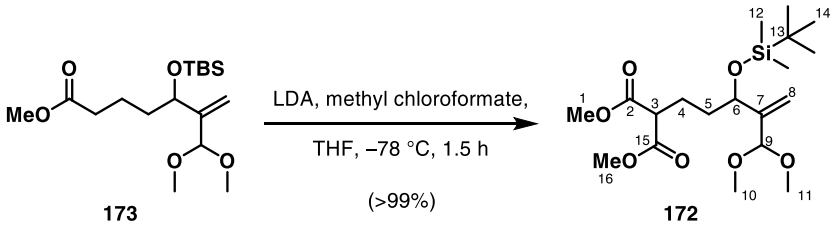
TLC (20% ethyl acetate in cyclohexane): R_f = 0.24 ($KMnO_4$).

^{1}H NMR (600 MHz, chloroform-*d*) δ 5.35 (t, *J* = 1.7 Hz, 1H, 8-H), 5.29 – 5.26 (m, 1H, 8-H), 4.70 (s, 1H, 9-H), 4.25 – 4.21 (m, 1H, 6-H), 3.66 (s, 3H, 1-H), 3.34 (s, 3H, 10-H or 11-H), 3.25 (s, 3H, 10-H or 11-H), 2.33 – 2.27 (m, 2H, 3-H), 1.68 – 1.57 (m, 3H, 4-H, 5-H), 1.55 – 1.49 (m, 1H, 5-H), 0.90 (s, 9H, 14-H), 0.06 – –0.01 (m, 6H, 12-H).

^{13}C NMR (151 MHz, chloroform-*d*) δ 174.3 (C-2), 147.0 (C-7), 113.9 (C-8), 103.2 (C-9), 71.5 (C-6), 54.4 (C-10 or C-11), 52.4 (C-10 or C-11), 51.6 (C-1), 36.5 (C-5), 34.2 (C-3), 26.0 (C-14), 20.5 (C-4), 18.3 (C-13), –4.5 (C-12), –4.9 (C-12).

IR (Diamond-ATR, neat) $\tilde{\upsilon}_{max}$: 2953 (m), 2930 (m), 2857 (w), 1741 (s), 1463 (w), 1253 (m), 1193 (w), 1091 (s), 994 (w), 837 (m), 776 (m) cm^{-1}.

HRMS (ESI) calc. for $C_{17}H_{34}NaO_5Si$ $[M+Na]^+$: 369.2068 found: 369.2061.



Malonate 172

To a solution of silyl ether **173** (30.0 mg, 87.0 µmol, 1 equiv) in THF (0.8 mL) was added dropwise a solution of lithium diisopropylamide (500 mM in tetrahydrofuran, 173 µL, 87.0 µmol, 1 equiv) at −78 °C. After 30 minutes, to the yellow mixture was added a solution of lithium diisopropylamide (500 mM in tetrahydrofuran, 190 µL, 95.0 µmol, 1.10 equiv). After 15 minutes, methyl chloroformate (14 µL, 173 µmol, 2.00 equiv) was added to the reaction mixture. After one hour, a saturated aqueous solution of ammonium chloride (5 mL) and diethyl ether (5 mL) were added to the reaction mixture and the layers were separated. The aqueous layer was extracted with diethyl ether (3 × 3 mL), the combined organic layers were dried over sodium sulfate. The dried solution was filtered and the filtrate was concentrated to yield malonate **172** (41.0 mg, 101 µmol, >99%) as a colourless oil. The crude reaction mixture was used in the next step without further purification.

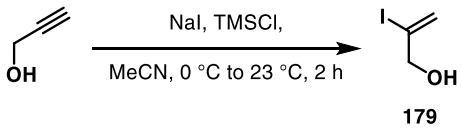
TLC (30% ethyl acetate in cyclohexane): R_f = 0.26 ($KMnO_4$).

^{1}H NMR (700 MHz, chloroform-*d*) δ 5.36 – 5.35 (m, 1H, 8-H), 5.28 (dt, *J* = 2.0, 1.0 Hz, 1H, 8-H), 4.67 (s, 1H, 9-H), 4.27 – 4.24 (m, 1H, 6-H), 3.71 (m, 6H, 10-H, 11-H), 3.36 (t, *J* = 7.6 Hz, 1H, 3-H), 3.33 (s, 3H, 1-H or 16-H), 3.24 (s, 3H, 1-H or 16-H), 1.92 (ddt, *J* = 9.8, 7.4, 5.4 Hz, 2H, 4-H), 1.64 – 1.58 (m, 1H, 5-H), 1.57 – 1.52 (m, 1H, 5-H), 0.90 (s, 9H, 14-H), 0.05 – –0.02 (m, 6H, 12-H).

^{13}C NMR (176 MHz, chloroform-*d*) δ 170.1 (C-2 or C-15), 170.0 (C-2 or C-15), 146.6 (C-7), 114.3 (C-8), 103.3 (C-9), 71.0 (C-6), 54.4 (C-9 or C-10), 52.6 (OMe), 52.5 (OMe), 52.5 (OMe), 51.7 (C-3), 34.3 (C-5), 26.0 (C-14), 24.2 (C-4), 18.3 (C-13), –4.6 (C-12), –4.9 (C-12).

IR (Diamond-ATR, neat) $\tilde{\upsilon}_{max}$: 2954 (m), 2930 (m), 2857 (w), 1739 (s), 1437 (w), 1254 (m), 1156 (m), 1092 (s), 991 (w), 836 (m), 777 (m) cm^{-1}.

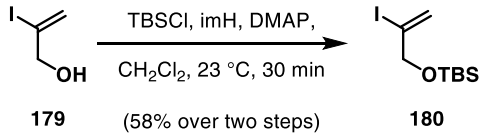
HRMS (ESI) calc. for $C_{19}H_{36}NaO_7Si$ $[M+Na]^+$: 427.2123 found: 427.2113.



Vinyl iodide 179

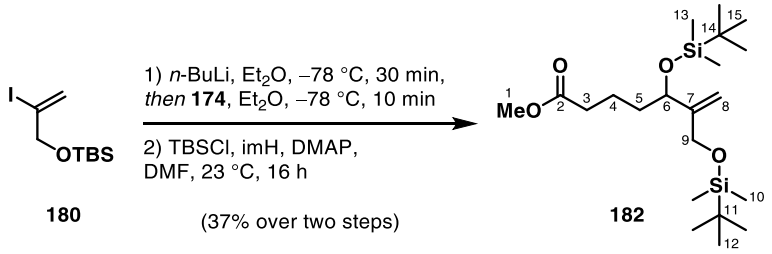
To a suspension of sodium iodide (121 g, 804 mmol, 1.20 equiv) in acetonitrile (1 L) was added trimethylsilyl chloride (105 mL, 804 mmol, 1.20 equiv) at 0 °C. After 15 minutes, water (7.25 mL,

402 mmol, 0.60 equiv) and propargyl alcohol (30 mL, 503 mmol, 1 equiv) were added and the reaction was allowed to warm to 23 °C. After two hours at 23 °C, a saturated aqueous solution of sodium hydrogen carbonate (1 L) was added to the reaction mixture and the layers were separated. The aqueous layer was extracted with ethyl acetate (3 × 300 mL). The combined organic layers were washed with a saturated aqueous solution of sodium thiosulfate (500 mL) and a saturated aqueous solution of sodium chloride (500 mL) in sequence. The washed organic layers were dried over sodium sulfate. The dried solution was filtered and the filtrate was concentrated to yield vinyliodide **179** (123 g, 670 mmol) as a slightly yellow liquid. The crude reaction mixture was used in the next step without further purification. The obtained analytical data were in full agreement with those reported in the literature.[154]



Vinyl iodide 180

To a solution of crude vinyl iodide **179** (3.04 g, 16.5 mmol, 1 equiv) in dichloromethane (160 mL) was added *tert*-butyldimethylchlorosilane (3.05 g, 19.8 mmol, 1.20 equiv), imidazole (1.36 g, 19.8 mmol, 1.20 equiv) and 4-dimethylaminopyridine (204 mg, 1.65 mmol, 0.100 equiv) at 23 °C. After 30 minutes, water (100 mL) was added to the reaction mixture and the layers were separated. The aqueous layer was extracted with dichloromethane (3 × 30 mL), the combined organic layers were dried over sodium sulfate. The dried solution was filtered and the filtrate was concentrated. The residue was purified by flash column chromatography on silica gel (cyclohexane) to yield vinyl iodide **180** (2.87 g, 9.62 mmol, 58% over two steps) as a colourless oil. The obtained analytical data were in full agreement with those reported in the literature.[155]



Silyl ether 182

To a solution of *n*-butyllithium (2.44 M in hexane, 1.05 mL, 2.57 mmol, 1.15 equiv) in diethyl ether (7 mL) was added a solution of vinyl iodide **180** (767 mg, 2.57 mmol, 1.15 equiv) in diethyl ether (4 mL) dropwise over the course of 30 minutes at −78 °C. 30 minutes after the addition of **180** was completed, a solution of aldehyde **174** (291 mg, 2.24 mmol, 1 equiv) in diethyl ether (2 mL) was added to the

[154] M. Kurosu, M.-H. Lin, Y. Kishi, *J. Am. Chem. Soc.* **2004**, *126*, 12248–12249.
[155] T. Smeilus, F. Mousavizadeh, J. Krieger, X. Tu, M. Kaiser, A. Giannis, *Beilstein J. Org. Chem.* **2019**, *15*, 567–570.

reaction mixture over the course of ten minutes. 30 minutes after the addition of **174** was completed, a saturated aqueous solution of ammonium chloride (20 mL) was added to the mixture and the solution was allowed to warm to 23 °C. The layers were separated and the aqueous layer was extracted with ethyl acetate (3 × 10 mL). The combined organic layers were dried over sodium sulfate, the dried solution was filtered and the filtrate was concentrated to yield the allylic alcohol (291 mg, 962 µmol) as a colourless oil.

To a solution of the crude allylic alcohol (291 mg, 962 µmol, 1 equiv) in *N*,*N*-dimethylformamide (10 mL) was added *tert*-butyldimethylchlorosilane (222 mg, 1.44 mmol, 1.50 equiv), imidazole (99.2 mg, 1.44 mmol, 1.50 equiv) and 4-(dimethylamino)pyridine (11.9 mg, 96.0 µmol, 0.10 equiv) at 23 °C. After six hours, water (20 mL) and diethyl ether (20 mL) were added to the reaction mixture and the layers were separated. The aqueous layer was extracted with diethyl ether (3 × 10 mL), the combined organic layers were washed with a 10% aqueous solution of lithium chloride (20 mL) and the washed organic layers were dried over sodium sulfate. The dried solution was filtered and the filtrate was concentrated. The residue was purified by flash column chromatography on silica gel (4% grading to 10% ethyl acetate in cyclohexane) to yield silyl ether **182** (349 mg, 837 µmol, 37% over two steps) as a colourless oil.

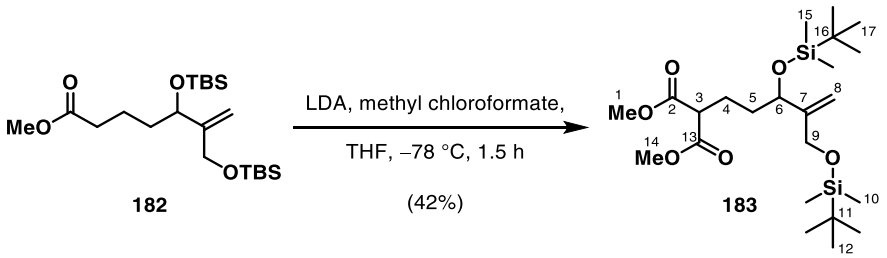
TLC (10% ethyl acetate in cyclohexane): R_f = 0.56 (CAM).

^{1}H NMR (400 MHz, chloroform-*d*) δ 5.11 – 5.07 (m, 1H, 8-H), 5.03 – 5.00 (m, 1H, 8-H), 4.20 (t, *J* = 5.8 Hz, 1H, 6-H), 4.18 – 4.11 (m, 2H, 9-H), 3.66 (s, 3H, 1-H), 2.30 (t, *J* = 7.3 Hz, 2H, 3-H), 1.71 – 1.63 (m, 1H, 5-H), 1.62 – 1.50 (m, 3H, 5-H, 4-H), 0.92 – 0.87 (m, 18H, 12-H, 15-H), 0.06 (s, 6H, 10-H or 13-H), 0.05 – 0.00 (m, 6H, 10-H or 13-H).

^{13}C NMR (101 MHz, chloroform-*d*) δ174.2 (C-2), 150.6 (C-7), 109.6 (C-8), 74.0 (C-6), 62.8 (C-9), 51.6 (C-1), 36.4 (C-4), 34.1 (C-3), 26.1 (C-12 or C-15), 26.0 (C-12 or C-15), 21.1 (C-5), 18.5 (C-11 or C-14), 18.3 (C-11 or C-14), –4.6 (C-10 or C-13), –4.9 (C-10 or C-13), –5.2 (C-10 or C-13), –5.3 (C-10 or C-13).

IR (Diamond-ATR, neat) $\tilde{\upsilon}_{max}$: 2954 (m), 2930 (m), 2857 (m), 1743 (m), 1463 (w), 1253 (m), 1158 (w), 1079 (m), 1005 (m), 836 (s), 776 (s).

HRMS (ESI) calc. for $C_{21}H_{44}NaO_4Si_2$ $[M+Na]^+$: 439.2670 found: 439.2648.



Malonate 183

To a solution of silyl ether **182** (349 mg, 837 µmol, 1 equiv) in tetrahydrofuran (8 mL) was added dropwise a solution of lithium diisopropylamide (1.00 M in tetrahydrofuran, 837 µL, 837 µmol, 1.00 equiv) at −78 °C. After 30 minutes, a solution of lithium diisopropylamide (1 M in tetrahydrofuran, 921 µL, 921 µmol, 1.10 equiv) was added to the yellow mixture. After ten minutes, methyl chloroformate (132 µL, 1.67 mmol, 2.00 equiv) was added to the reaction mixture. After one hour, a saturated aqueous solution of ammonium chloride (20 mL) was added to the reaction mixture and the layers were separated. The aqueous layer was extracted with diethyl ether (3 × 10 mL), the combined organic layers were dried over sodium sulfate. The dried solution was filtered and the filtrate was concentrated. The residue was purified by flash column chromatography on silica gel (3% ethyl acetate in cyclohexane) to yield malonate **183** (165 mg, 348 µmol, 42%) as a slightly yellow oil.

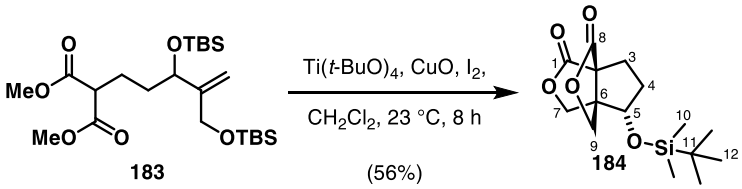
TLC (3% ethyl acetate in cyclohexane): R_f = 0.16 (CAM).

^{1}H NMR (600 MHz, chloroform-*d*) δ 5.11 – 5.09 (m, 1H, 8-H), 5.05 – 5.03 (m, 1H, 8-H), 4.23 (t, *J* = 5.9 Hz, 1H, 6-H), 4.14 (dt, *J* = 8.7, 1.6 Hz, 2H, 9-H), 3.73 (s, 6H, 1-H, 14-H), 3.36 (t, *J* = 7.5 Hz, 1H, 3-H), 1.97 – 1.91 (m, 1H, 4-H), 1.90 – 1.84 (m, 1H, 4-H), 1.55 – 1.54 (m, 2H, 5-H), 0.91 (s, 9H, 12-H or 17-H), 0.89 (s, 9H, 12-H or 17-H), 0.06 (s, 6H, 10-H or 15-H), 0.04 – 0.01 (m, 6H, 10-H or 15-H).

^{13}C NMR (151 MHz, chloroform-*d*) δ 170.0 (C-2, C-13), 169.9 (C-7), 150.1 (C-8), 110.0 (C-6), 73.5 (C-9), 62.8 (C-1 or C-14), 52.6 (C-1 or C-14), 51.7 (C-9), 34.3 (C-5), 26.1 (C-12 or C-17), 26.0 (C-12 or C-17), 24.9 (C-4), 18.5 (C-11 or C-16), 18.3 (C-11 or C-16), –4.6 (C-10 or C-15), –5.0 (C-10 or C-15), –5.2 (C-10 or C-15), –5.3 (C-10 or C-15).

IR (Diamond-ATR, neat) $\tilde{\upsilon}_{max}$: 2930 (m), 2857 (m), 1739 (m), 1463 (w), 1252 (m), 1152 (m), 1079 (m), 1006 (w), 834 (s), 774 (s) cm^{-1}.

HRMS (ESI) calc. for $C_{23}H_{46}NaO_6Si_2$ $[M+Na]^+$: 497.2725 found: 497.2718.



Dilactone 184

To a solution of malonate **183** (42.0 mg, 89.0 µmol, 1 equiv) in dichloromethane (1 mL) was added Ti(*t*-BuO)$_4$ (41.0 µL, 106 µmol, 1 equiv) at 23 °C. After 15 minutes, iodine (90.7 mg, 354 µmol, 4.00 equiv) and cupric oxide (10.1 g, 124 µmol, 1.40 equiv) were added. After eight hours, a saturated aqueous solution of sodium thiosulfate (5 mL) was added to the red suspension and the layers were separated. The aqueous layer was extracted with dichloromethane (3 × 2 mL) and the combined organic layers were dried over sodium sulfate. The dried solution was filtered over a pad of Celite and the filtrate was concentrated. The residue was purified by flash column chromatography on silica gel (40% ethyl acetate in cyclohexane) to yield dilactone **184** (15.5 mg, 50.0 µmol, 56%) as a slightly yellow oil.

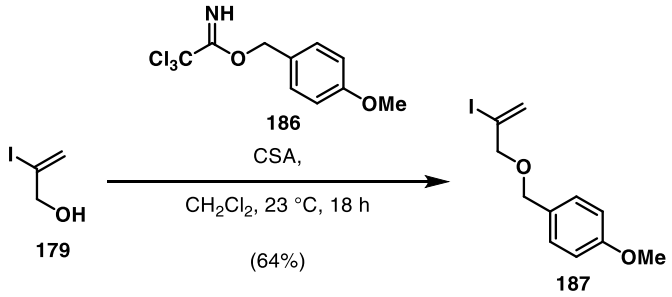
TLC (50% ethyl acetate in cyclohexane): R_f = 0.32 (CAM).

^{1}H NMR (600 MHz, chloroform-*d*) δ 4.75 (d, *J* = 9.8 Hz, 1H, 7-H or 9-H), 4.40 (d, *J* = 10.1 Hz, 1H, 7-H or 9-H), 4.26 (t, *J* = 4.3 Hz, 1H, 5-H), 4.21 (d, *J* = 9.8 Hz, 1H, 7-H or 9-H), 4.13 (d, *J* = 10.1 Hz, 1H, 7-H or 9-H), 2.53 – 2.48 (m, 1H, 3-H), 2.39 – 2.35 (m, 1H, 3-H), 2.06 – 2.03 (m, 1H, 4-H), 1.98 – 1.94 (m, 1H, 4-H), 0.88 (s, 9H, 12-H), 0.10 (s, 6H, 10-H).

^{13}C NMR (151 MHz, chloroform-*d*) δ 172.0 (C-1 or C-8), 171.9 (C-1 or C-8), 78.8 (C-5), 74.5 (C-7 or C-9), 71.5 (C-7 or C-9), 60.8 (C-2, C-6), 36.0 (C-4), 32.3 (C-3), 25.7 (C-12), 18.0 (C-11), –4.3 (C-10), –4.9 (C-10).

IR (Diamond-ATR, neat) $\tilde{\upsilon}_{max}$: 2955 (w), 2929 (w), 2856 (w), 1782 (s), 1746 (m), 1254 (m), 1206 (m), 1143 (m), 1071 (w), 1020 (m), 836 (m), 778 (m) cm^{-1}.

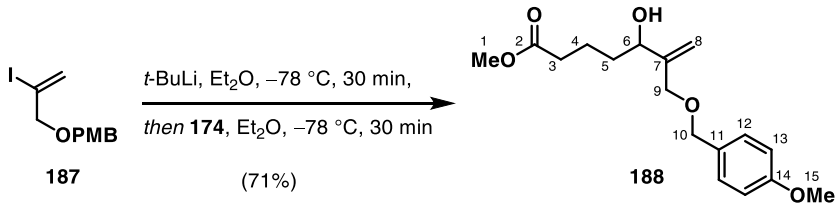
HRMS (ESI) calc. for $C_{15}H_{24}NaO_5Si$ $[M+Na]^+$: 335.1285 found: 335.1282.



Benzyl ether 187

To a solution of vinyl iodide **179** (224 mg, 1.22 mmol, 1 equiv) in dichloromethane (8 mL) was added Bundle´s reagent **186** (1.03 g, 3.65 mmol, 3.00 equiv) and (1*S*)-(+)-10-camphorsulfonic acid (28.9 mg,

122 µmol, 0.100 equiv) at 23 °C. After 18 hours, the reaction mixture was concentrated and the residue was purified by flash column chromatography on silica gel (5% ethyl acetate in cyclohexane) to yield benzyl ether **187** (237 mg, 779 µmol, 64%) as a slightly yellow oil. The obtained analytical data were in full agreement with those reported in the literature.[156]



Allyl alcohol 188

To a solution of *tert*-butyllithium (1.64 M in pentane, 2.01 mL, 3.29 mmol, 2.20 equiv) in diethyl ether (9 mL) was added a solution of vinyl iodide **187** (501 mg, 1.65 mmol, 1.10 equiv) in diethyl ether (3 mL) dropwise over the course of ten minutes at −78 °C. 30 minutes after the addition of **187** was completed, a solution of aldehyde **174** (195 mg, 1.50 mmol, 1 equiv) in diethyl ether (3 mL) was added to the yellow solution over the course of ten minutes. 30 minutes after the addition of **174** was completed, a saturated aqueous solution of ammonium chloride (20 mL) was added to the reaction mixture and the solution was allowed to warm to 23 °C. The layers were separated and the aqueous layer was extracted with ethyl acetate (3 × 5 mL). The combined organic layers were dried over sodium sulfate, the dried solution was filtered and the filtrate was concentrated. The residue was purified by flash column chromatography on silica gel (30% ethyl acetate in cyclohexane) to yield allyl alcohol **188** (295 mg, 1.06 mmol) as a yellow oil.

TLC (40% ethyl acetate in cyclohexane): R_f = 0.29 (CAM).

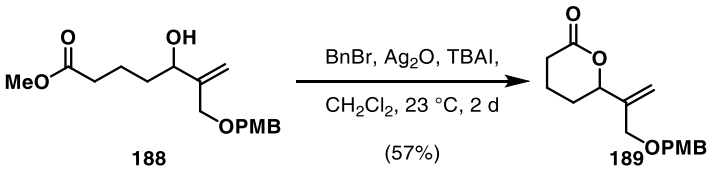
^{1}H NMR (600 MHz, chloroform-*d*): δ 7.26 – 7.25 (m, 2H, 12-H or 13-H), 6.93 – 6.92 (m, 2H, 12-H or 13-H), 5.17 (s, 1H, 8-H), 5.14 (s, 1H, 8-H), 4.46 (s, 2H, 10-H), 4.20 – 4.16 (m, 1H, 6-H), 4.12 (d, 1H, *J* = 11.9 Hz, 9-H), 4.02 (d, 1H, *J* = 11.9 Hz, 9-H), 3.81 (s, 3H, 15-H), 3.66 (s, 3H, 1-H), 2.36 – 2.33 (m, 2H, 3-H), 1.76 – 1.73 (m, 1H, 4-H), 1.64 – 1.63 (m, 1H, 4-H), 1.55 – 1.52 (m, 2H, 5-H).

^{13}C NMR (151 MHz, chloroform-*d*): δ 174.2 (C-2), 159.5 (C-14), 147.1 (C-7), 130.0 (C-11), 129.6 (C-12 or C-13), 128.8 (C-12 or C-13), 114.0 (C-8), 73.9 (C-6), 72.4 (C-10), 71.4 (C-9), 55.5 (C-15), 51.7 (C-1), 35.1 (C-5), 33.9 (C-3), 21.3 (C-4).

IR (Diamond-ATR, neat) $\tilde{\upsilon}_{max}$: 3502 (br, w), 2933 (w), 2853 (w), 1736 (m), 1613 (m), 1513 (s), 1248 (s), 1174 (w), 1077 (w), 1034 (m), 822 (w) cm^{-1}.

[156] M. T. Riaz, I. Pohorilets, J. J. Hernandez, J. Rios, N. I. Totah, *Tetrahedron Lett.* **2018**, *59*, 2809–2812.

HRMS (ESI) calc. for $C_{17}H_{24}KO_5$ $[M+K]^+$: 347.1255 found: 347.1255.



Lactone 189

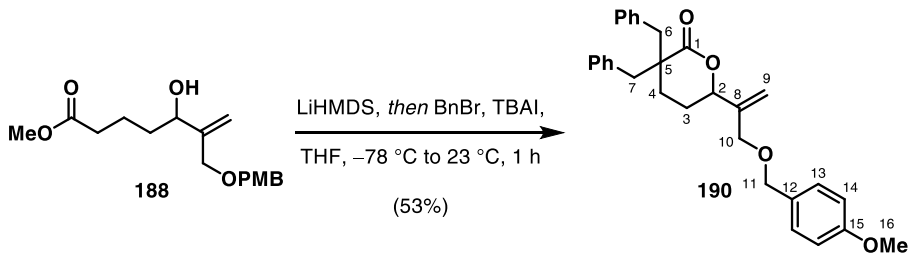
To a solution of allyl alcohol **188** (19.5 mg, 63.0 µmol, 1 equiv) in dichloromethane (700 µL) was added benzyl bromide (15 µL, 126 µmol, 2.00 equiv), silver(I) oxide (29.6 mg, 126 µmol, 2.00 equiv) and tetrabutylammonium iodide (2.38 mg, 6.32 µmol, 0.100 equiv) at 23 °C. After two days, the reaction mixture was filtered through a pad of Celite and the pad was washed with dichloromethane (5 mL). The filtrate was concentrated and the residue was purified by flash column chromatography on silica gel (30% ethyl acetate in cyclohexane) to yield lactone **189** (10.0 mg, 36.0 µmol, 57%) as a colourless oil.

TLC (40% ethyl acetate in cyclohexane): R_f = 0.26 (CAM, UV).

^{1}H NMR (400 MHz, chloroform-*d*): δ 7.26 – 7.22 (m, 2H), 6.90 – 6.87 (m, 2H), 5.32 – 5.28 (m, 2H), 4.90 (dd, *J* = 9.9, 3.5 Hz, 1H), 4.46 – 4.42 (m, 2H), 4.10 – 4.01 (m, 2H), 3.81 (s, 3H), 2.64 – 2.56 (m, 1H), 2.53 – 2.44 (m, 1H), 2.09 – 2.02 (m, 1H), 1.98 – 1.89 (m, 1H), 1.89 – 1.81 (m, 1H), 1.80 – 1.74 (m, 1H).

IR (Diamond-ATR, neat) $\tilde{\nu}_{max}$: 2908 (w), 2864 (w), 1735 (s), 1612 (w), 1513 (s), 1457 (w), 1301 (w), 1248 (s), 1173 (m), 1076 (m), 1033 (m), 925 (w), 821 (w) cm^{-1}.

HRMS (ESI) calc. for $C_{26}H_{31}IKO_5Si$ $[M+K]^+$: 347.1255 found: 347.1255.



Lactone 190

To a solution of allyl alcohol **188** (25.5 mg, 83.0 µmol, 1 equiv) in tetrahydrofuran (1 mL) was added a solution of lithium bis(trimethylsilyl)amide (1.00 M in tetrahydrofuran, 198 µL, 198 µmol, 2.40 equiv) at –78 °C. After 30 minutes, benzyl bromide (14.0 µL, 116 µmol, 1.40 equiv) and tetrabutylammonium iodide (43.6 mg, 116 µmol, 1.40 equiv) were added to the solution and after the addition, the reaction

mixture was allowed to warm to 23 °C. After 30 minutes at 23 °C, a saturated aqueous solution of ammonium chloride (5 mL) and diethyl ether (5 mL) were added to the reaction mixture and the layers were separated. The aqueous layer was extracted with diethyl ether (3 × 2 mL), the combined organic layers were dried over sodium sulfate. The dried solution was filtered and the filtrate was concentrated. The residue was purified by flash column chromatography on silica gel (5% ethyl acetate in cyclohexane) to yield lactone **190** (20.0 mg, 44.0 µmol, 53%) as a colourless oil.

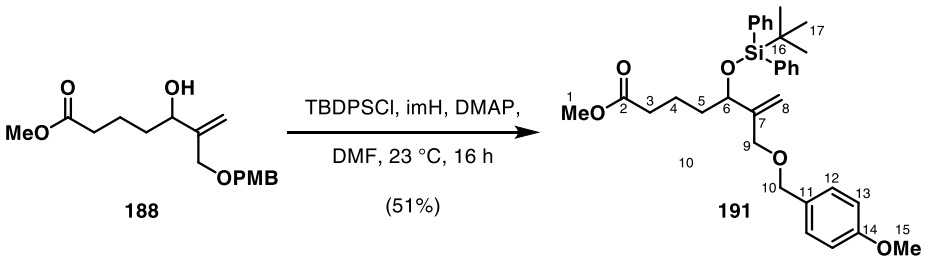
TLC (30% ethyl acetate in cyclohexane): R_f = 0.56 (CAM, UV).

^{1}H NMR (400 MHz, chloroform-*d*) δ 7.31 – 7.27 (m, 2H, aromatic), 7.25 – 7.14 (m, 8H, aromatic), 6.88 – 6.84 (m, 2H, 13-H, 14-H), 5.05 – 5.02 (m, 1H, 9-H), 4.92 – 4.88 (m, 1H, 9-H), 4.28 (q, *J* = 11.4 Hz, 2H, 11-H), 4.21 (dd, *J* = 10.4, 3.2 Hz, 1H, 2-H), 3.80 (s, 3H, 16-H), 3.78 (s, 2H, 10-H), 3.45 (dd, *J* = 17.6, 13.2 Hz, 2H, 6-H or 7-H), 2.71 (d, *J* = 13.1 Hz, 1H, 6-H or 7-H), 2.60 (d, *J* = 13.2 Hz, 1H, 6-H or 7-H), 1.84 – 1.75 (m, 2H, 4-H), 1.59 – 1.54 (m, 1H, 3-H), 1.20 – 1.08 (m, 1H, 3-H).

^{13}C NMR (101 MHz, chloroform-*d*) δ 175.8 (C-1), 159.4 (C-15), 143.4 (C-8), 137.1, 137.0, 130.8, 130.7, 130.2, 129.5, 128.6, 128.5, 127.1, 127.1, 114.8 (C-9), 113.9, 81.1 (C-2), 71.8 (C-11), 69.7 (C-10), 55.4 (C-16), 48.9 (C-5), 47.1 (C-6 or C-7), 46.1 (C-6 or C-7), 26.5 (C-4), 25.7 (C-3).

IR (Diamond-ATR, neat) $\tilde{\upsilon}_{max}$: 2924 (m), 1720 (s), 1612 (w), 1513 (s), 1496 (m), 1455 (m), 1248 (s), 1174 (s), 1089 (m), 1033 (m), 820 (w), 759 (w), 704 (s) cm^{-1}.

HRMS (ESI) calc. for $C_{30}H_{32}NaO_4$ $[M+Na]^+$: 479.2193 found: 479.2180.



Silyl ether 191

To a solution of allyl alcohol **188** (145 mg, 470 µmol, 1 equiv) in *N*,*N*-dimethylformamide (4 mL) was added *tert*-butyldiphenylchlorosilane (171 mg, 611 µmol, 1.30 equiv), imidazole (42.0 mg, 611 µmol, 1.30 equiv) and 4-(dimethylamino)pyridine (5.80 mg, 47.0 µmol, 0.100 equiv) at 23 °C. After 16 hours, water (5 mL) and diethyl ether (5 mL) were added to the reaction mixture and the layers were separated. The aqueous layer was extracted with diethyl ether (3 × 2 mL), the combined organic layers were washed with a 10% aqueous solution of lithium chloride (5 mL) and the washed organic layers were dried over sodium sulfate. The dried solution was filtered and the filtrate was concentrated. The residue

was purified by flash column chromatography on silica gel (5% ethyl acetate in cyclohexane) to yield silyl ether **191** (131 mg, 240 µmol, 51%) as a slightly yellow oil.

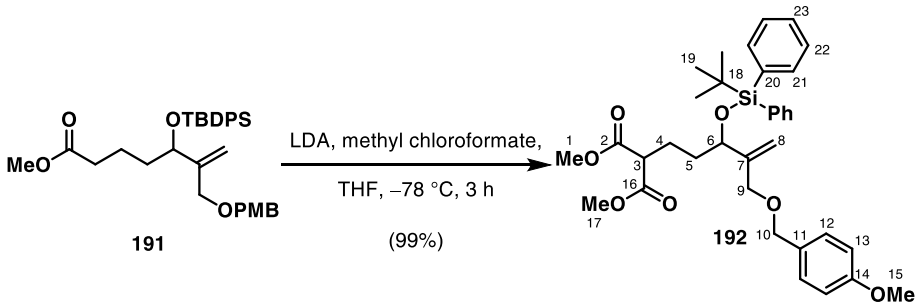
TLC (10% ethyl acetate in cyclohexane): R_f = 0.42 (CAM, UV).

^{1}H NMR (400 MHz, chloroform-*d*) δ 7.64 (ddt, *J* = 13.6, 6.6, 1.5 Hz, 4H, Ph), 7.44 – 7.32 (m, 6H, Ph), 7.22 – 7.14 (m, 2H, 13-H), 6.93 – 6.81 (m, 2H, 12-H), 5.19 – 5.11 (m, 2H, 8-H), 4.39 – 4.26 (m, 3H, 10-H, 6-H), 4.03 – 3.89 (m, 2H, 9-H), 3.80 (s, 3H, 15-H), 3.60 (s, 3H, 1-H), 2.16 – 2.08 (m, 2H, 3-H), 1.56 – 1.42 (m, 4H, 4-H, 5-H), 1.06 (s, 9H).

^{13}C NMR (101 MHz, chloroform-*d*) δ 174.1 (C-2), 159.2 (C-14), 146.6 (Ph), 136.1 (Ph), 136.1 (Ph), 134.4 (Ph), 130.6 (Ph), 129.8 (Ph), 129.7 (C-11), 129.4 (C-13), 127.7 (Ph), 127.6 (Ph), 113.9 (C-12), 113.1 (C-8), 74.5 (C-6), 71.8 (C-10), 69.7 (C-9), 55.4 (C-15), 51.5 (C-1), 35.1 (C-5), 34.0 (C-3), 27.2 (C-17), 19.9 (C-4), 19.5 (C-16).

IR (Diamond-ATR, neat) $\tilde{\upsilon}_{max}$: 2932 (m), 2857 (m), 1738 (s), 1613 (w), 1513 (m), 1428 (m), 1361 (w), 1302 (w), 1248 (s), 1173 (m), 1110 (s), 1037 (m), 822 (m), 741 (m), 703 (s), 612 (w), 505 (m) cm^{-1}.

HRMS (EI) calc. for $C_{33}H_{42}NaO_5Si$ $[M+Na]^+$: 569.2694 found: 569.2665.



Malonate 192

To a solution of silyl ether **191** (119 mg, 218 µmol, 1 equiv) in THF (2 mL) was added dropwise a solution of lithium diisopropylamide (1.00 M in tetrahydrofuran, 218 µL, 218 µmol, 1.00 equiv) at −78 °C. After 30 minutes, a solution of lithium diisopropylamide (1.00 M in tetrahydrofuran, 239 µL, 239 µmol, 1.10 equiv) was added to the yellow mixture. After 30 minutes, methyl chloroformate (435 µmol, 34.3 µL, 2.00 equiv) was added to the reaction mixture. After two hours, a saturated aqueous solution of ammonium chloride (5 mL) and ethyl acetate (5 mL) were added to the reaction mixture and the layers were separated. The aqueous layer was extracted with ethyl acetate (3 × 2 mL), the combined organic layers were dried over sodium sulfate. The dried solution was filtered and the filtrate was concentrated. The residue was purified by flash column chromatography on silica gel (20% ethyl acetate in cyclohexane) to yield malonate **192** (130 mg, 215 µmol, 99%) as a colourless oil.

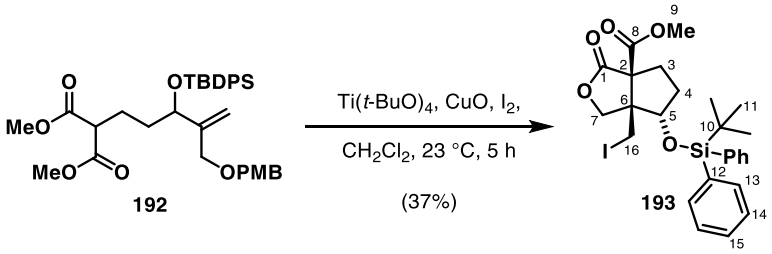
TLC (30% ethyl acetate in cyclohexane): R_f = 0.50 (CAM, UV).

^{1}H NMR (400 MHz, chloroform-*d*) δ 7.67 – 7.61 (m, 4H, 21-H), 7.43 – 7.31 (m, 6H, 22-H, 23-H), 7.18 – 7.14 (m, 2H, 13-H), 6.86 – 6.82 (m, 2H, 12-H), 5.21 – 5.15 (m, 2H, 8-H), 4.36 – 4.26 (m, 3H, 6-H, 10-H), 3.99 – 3.87 (m, 2H, 9-H), 3.80 (s, 3H, 15-H), 3.67 (s, 3H, 1-H), 3.65 (s, 3H, 17-H), 3.16 (t, *J* = 7.5 Hz, 1H, 3-H), 1.89 – 1.79 (m, 1H, 4-H), 1.79 – 1.68 (m, 1H, 4-H), 1.54 – 1.43 (m, 2H, 5-H), 1.07 (s, 9H, 19-H).

^{13}C NMR (101 MHz, chloroform-*d*) δ 169.8 (C-2, C-16), 159.3 (C-14), 146.3 (C-7), 136.1 (C-21), 136.1 (C-21), 129.8 (C-23), 129.8 (C-23), 129.3 (C-13), 127.7 (C-22), 127.6 (C-22), 113.9 (C-12), 113.5 (C-8), 74.0 (C-6), 71.8 (C-10), 69.8 (C-9), 55.4 (C-15), 52.5 (C-1), 52.5 (C-17), 51.6 (C-13), 33.1 (C-5), 27.2 (C-19), 23.7 (C-4), 19.5 (C-18).

IR (Diamond-ATR, neat) $\tilde{\upsilon}_{max}$: 2953 (w), 2857 (w), 1736 (s), 1612 (w), 1513 (m), 1429 (w), 1248 (s), 1158 (m), 1110 (s), 1036 (m), 821 (w), 742 (w), 704 (m), 611 (w), 506 (m) cm^{-1}.

HRMS (ESI) calc. for $C_{35}H_{44}NaO_7Si$ $[M+Na]^+$: 627.2749 found: 627.2742.



Ester 193

To a solution of malonate **192** (13.4 mg, 22.0 µmol, 1 equiv) in dichloromethane (0.5 mL) was added titanium(IV) *tert*-butoxide (10.0 µL, 26.0 µmol, 1.20 equiv) at 23 °C. After 15 minutes, iodine (22.7 mg, 89.0 µmol, 4.00 equiv) and cupric oxide (2.52 mg, 31.0 µmol, 1.40 equiv) were added. After five hours, a saturated aqueous solution of sodium thiosulfate (5 mL) and dichloromethane (5 mL) were added to the red suspension and the layers were separated. The aqueous layer was extracted with dichloromethane (3 × 2 mL) and the combined organic layers were dried over sodium sulfate. The dried solution was filtered over a pad of Celite and the filtrate was concentrated. The residue was purified by flash column chromatography on silica gel (20% ethyl acetate in cyclohexane) to yield ester **193** (4.80 mg, 8.30 µmol, 37%) as a colourless oil.

TLC (30% ethyl acetate in cyclohexane): R_f = 0.38 (CAM, UV).

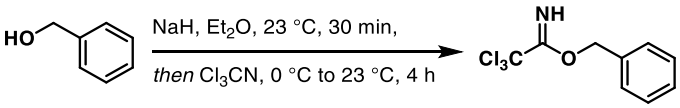
^{1}H NMR (600 MHz, chloroform-*d*) δ 7.73 – 7.71 (m, 2H, aromatic), 7.67 – 7.64 (m, 2H, aromatic), 7.48 – 7.40 (m, 6H, aromatic), 4.81 (d, *J* = 9.3 Hz, 1H, 7-H), 4.42 (t, *J* = 4.9 Hz, 1H, 5-H), 4.04 (d, *J* = 9.3 Hz, 1H, 7-H), 3.05 (d, *J* = 10.4 Hz, 1H, 16-H), 3.01 (d, *J* = 10.4 Hz, 1H, 16-H), 2.43 – 2.38 (m, 1H, 3-H),

2.30 (dt, *J* = 14.0, 7.2 Hz, 1H, 3-H), 1.75 – 1.70 (m, 1H, 4-H), 1.58 – 1.54 (m, 1H, 4-H), 1.09 (s, 9H, 11-H).

^{13}C NMR (151 MHz, chloroform-*d*) δ 176.0 (C-1), 168.6 (C-8), 136.1 (C-13 or C-14), 135.9 (C-13 or C-14), 130.2 (C-15), 130.1 (C-15), 128.0 (C-13 or C-14), 127.8 (C-13 or C-14), 80.8 (C-5), 72.8 (C-7), 64.0 (C-6), 58.3 (C-2), 33.1 (C-4), 29.9 (C-3), 26.9 (C-14), 19.3 (C-10), 7.5 (C-16).

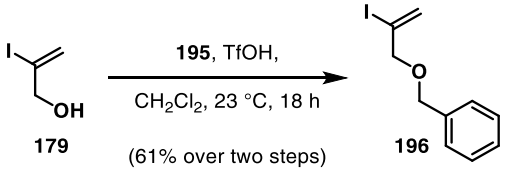
IR (Diamond-ATR, neat) $\tilde{\upsilon}_{max}$: 2931 (w), 1732 (m), 1106 (m), 820 (m), 738 (m), 699 (s), 608 (m), 503 (s) cm^{-1}.

HRMS (ESI) calc. for $C_{26}H_{31}INaO_5Si$ $[M+Na]^+$: 601.0878 found: 601.0910; calc. for $C_{26}H_{31}IKO_5Si$ $[M+K]^+$: 617.0617 found: 617.0652.



Bundle's reagent 195

To a solution of benzyl alcohol (24.7 mL, 238 mmol, 1 equiv) in diethyl ether (500 mL) was added sodium hydride (6.41 g, 262 mmol, 1.10 equiv) at 23 °C. After 30 minutes, the reaction mixture was cooled to 0 °C and trichloroacetonitrile (26.8 mL, 262 mmol, 1.10 equiv) was added to the solution. After 15 minutes, the reaction mixture was allowed to warm to 23 °C. After four hours at 23 °C, water (500 mL) was slowly added to the reaction mixture and the layers were separated. The aqueous layer was extracted with diethyl ether (3 × 150 mL) and the combined organic layers were dried over sodium sulfate. The dried solution was filtered and the filtrate was concentrated to yield Bundle's reagent **195** (54.4 g, 215 mmol, 91%) as a brownish oil. The obtained analytical data were in full agreement with those reported in the literature.[157]

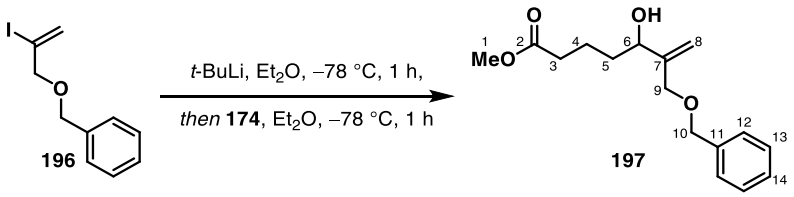


Benzyl ether 196

To a solution of crude vinyl iodide **179** (37.4 g, 203 mmol, 1 equiv) in dichloromethane (500 mL) was added Bundle´s reagent **195** (56.5 g, 224 mmol, 1.10 equiv) at 23 °C. To this reaction mixture was added trifluoromethanesulfonic acid (1.81 mL, 20.3 mmol, 0.100 equiv). After 18 hours, a saturated aqueous solution of sodium bicarbonate (500 mL) was added to the reaction mixture and the layers were

[157] C. Li, W. Li, J. Wang, *Tetrahedron Lett.* **2009**, *50*, 2533–2535.

separated. The aqueous layer was extracted with diethyl ether (3 × 150 mL) and the combined organic layers were dried over sodium sulfate. The dried solution was filtered and the filtrate was concentrated. The residue was purified by flash column chromatography on silica gel (10% grading to 20% ethyl acetate in cyclohexane) to yield benzyl ether **196** (33.8 g, 123 mmol, 61% over two steps) as a slightly yellow oil. The obtained analytical data were in full agreement with those reported in the literature.[158]



Allyl alcohol 197

To a solution of *tert*-butyllithium (1.60 M in pentane, 63.1 mL, 97.8 mmol, 2.00 equiv) in diethyl ether (400 mL) was added a solution of vinyl iodide **196** (13.4 g, 48.9 mmol, 1 equiv) in diethyl ether (100 mL) dropwise over the course of 30 minutes at −78 °C. 30 minutes after the addition of **196** was completed, a solution of aldehyde **174** (6.36 g, 48.9 mmol, 1 equiv) in diethyl ether (100 mL) was added to the yellow solution over the course of 30 minutes. 30 minutes after the addition of **174** was completed, a saturated aqueous solution of ammonium chloride (600 mL) was added to the reaction mixture and the solution was allowed to warm to 23 °C. The layers were separated and the aqueous layer was extracted with ethyl acetate (3 × 200 mL). The combined organic layers were dried over sodium sulfate, the dried solution was filtered and the filtrate was concentrated to yield allyl alcohol **197** (13.6 g, 48.9 mmol) as a colourless oil. The crude reaction mixture was used in the next step without further purification. To obtain analytical data a small aliquot of the crude reaction mixture was purified by flash column chromatography on silica gel (30% ethyl acetate in cyclohexane).

TLC (30% ethyl acetate in cyclohexanes): R_f = 0.29 (CAM).

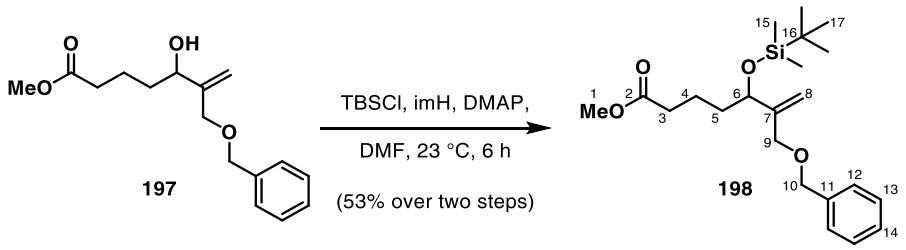
^{1}H NMR (400 MHz, chloroform-*d*) δ 7.37 – 7.31 (m, 4H, 12-H, 13-H, 14-H), 5.19 (t, *J* = 1.2 Hz, 1H, 8-H), 5.16 – 5.15 (m, 1H, 8-H), 4.52 (s, 2H, 10-H), 4.19 (t, *J* = 6.1 Hz, 1H, 6-H), 4.16 – 4.12 (m, 1H, 9-H), 4.08 – 4.03 (m, 1H, 9-H), 3.66 (s, 3H, 1-H), 2.36 – 2.32 (m, 2H, 4-H), 1.79 – 1.72 (m, 1H, 5-H), 1.68 – 1.59 (m, 3H, 5-H, 3-H).

^{13}C NMR (101 MHz, chloroform-*d*) δ 174.2 (C-2), 147.1 (C-7), 137.9 (C-11), 128.6 (C-13), 127.9 (C-12), 127.9 (C-14), 114.1 (C-8), 73.7 (C-6), 72.6 (C-10), 71.5 (C-9), 51.6 (C-1), 35.1 (C-3), 33.9 (C-4), 21.2 (C-5).

IR (Diamond-ATR, neat) $\tilde{\upsilon}_{max}$: 3468 (br, w), 2950 (w), 1735 (s), 1454 (w), 1365 (w), 1241 (m), 1072 (m), 738 (w), 699 (w) cm^{-1}.

[158] M. T. Riaz, I. Pohorilets, J. J. Hernandez, J. Rios, N. I. Totah, *Tetrahedron Lett.* **2018**, *59*, 2809–2812.

HRMS (ESI) calc. for $C_{16}H_{22}NaO_4$ $[M+Na]^+$: 301.1410 found: 301.1391.



Silyl ether 198

To a solution of crude allyl alcohol **197** (25.0 g, 89.8 mmol, 1 equiv) in *N*,*N*-dimethylformamide (900 mL) was added *tert*-butyldimethylsilyl chloride (14.9 g, 98.8 mmol, 1.10 equiv), imidazole (7.41 g, 108 mmol, 1.20 equiv) and 4-(dimethylamino)pyridine (1.11 g, 8.98 mmol, 0.100 equiv) at 23 °C. After six hours, water (450 mL) and diethyl ether (100 mL) was added to the reaction mixture and the layers were separated. The aqueous layer was extracted with diethyl ether (3 × 300 mL), the combined organic layers were washed with a 10% aqueous solution of lithium chloride (300 mL) and the washed organic layers were dried over sodium sulfate. The dried solution was filtered and the filtrate was concentrated. The residue was purified by flash column chromatography on silica gel (4% grading to 10% ethyl acetate in cyclohexane) to yield silyl ether **198** (18.7 g, 47.6 mmol, 53% over two steps) as a slightly yellow oil.

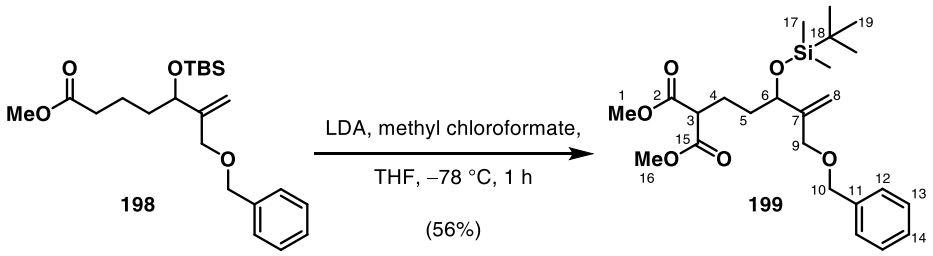
TLC (10% ethyl acetate in cyclohexane): R_f = 0.38 (CAM).

^{1}H NMR (400 MHz, chloroform-*d*) δ 7.37 – 7.33 (m, 5H, 12-H, 13-H, 14-H), 5.18 – 5.15 (m, 2H, 8-H), 4.54 – 4.47 (m, 2H, 10-H), 4.23 (t, *J* = 5.6 Hz, 1H, 6-H), 4.07 – 3.97 (m, 2H, 9-H), 3.66 (s, 3H, 1-H), 2.29 (t, *J* = 7.2 Hz, 2H, 3-H), 1.70 – 1.60 (m, 2H, 4-H), 1.58 – 1.54 (m, 2H, 5-H), 0.88 (s, 9H, 17-H), 0.05 – 0.00 (m, 6H, 15-H).

^{13}C NMR (101 MHz, chloroform-*d*) δ 174.2 (C-2), 147.9 (C-7), 138.6 (C-11), 128.5 (C-13), 127.7 (C-12), 127.7 (C-14), 112.3 (C-8), 73.9 (C-6), 72.3 (C-10), 70.0 (C-9), 51.6 (C-1), 36.1 (C-5), 34.1 (C-3), 26.0 (C-17), 20.9 (C-4), 18.3 (C-16), –4.6 (C-15), –4.9 (C-15).

IR (Diamond-ATR, neat) $\tilde{\upsilon}_{max}$: 2953 (w), 2929 (w), 2856 (w), 1739 (s), 1454 (w), 1251 (m), 1087 (s), 835 (s), 776 (s), 698 (m) cm^{-1}.

HRMS (ESI) calc. for $C_{22}H_{36}NaO_4Si$ $[M+Na]^+$: 415.2275 found: 415.2250.



Malonate 199

To a solution of silyl ether **198** (18.7 g, 47.6 mmol, 1 equiv) in THF (150 mL) was added dropwise a solution of lithium diisopropylamide (1.00 M in tetrahydrofuran, 47.6 mL, 47.6 mmol, 1.00 equiv) at −78 °C over the course of 30 minutes. 30 minutes after the addition of the solution of lithium diisopropylamide was completed, a solution of lithium diisopropylamide (1.00 M in tetrahydrofuran, 52.4 mL, 52.4 mmol, 1.10 equiv) was added to the yellow mixture over the course of five minutes. Ten minutes after the addition of the lithium diisopropylamide solution was completed, methyl chloroformate (95.3 mmol, 7.36 mL, 2.00 equiv) was added to the reaction mixture. After one hour, a saturated aqueous solution of ammonium chloride (200 mL) was added to the reaction mixture and the layers were separated. The aqueous layer was extracted with diethyl ether (3 × 100 mL), the combined organic layers were dried over sodium sulfate. The dried solution was filtered and the filtrate was concentrated. The residue was purified by flash column chromatography on silica gel (10% ethyl acetate in cyclohexane) to yield malonate **199** (13.2 g, 29.3 mmol, 56%) as a slightly yellow oil.

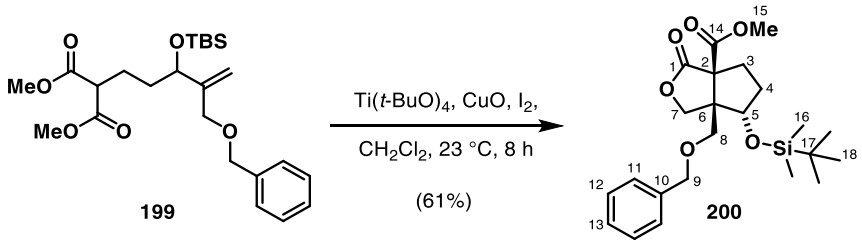
TLC (30% ethyl acetate in cyclohexane): R_f = 0.50 (CAM).

^{1}H NMR (400 MHz, chloroform-*d*) δ 7.38 – 7.30 (m, 5H, 12-H, 13-H, 14-H), 5.21 – 5.15 (m, 2H, 8-H), 4.56 – 4.44 (m, 2H, 10-H), 4.26 (t, *J* = 5.7 Hz, 1H, 6-H), 4.07 – 3.96 (m, 2H, 9-H), 3.71 (s, 6H, 1-H, 16-H), 3.35 (t, *J* = 7.5 Hz, 1H, 13-H), 1.98 – 1.84 (m, 2H, 4-H), 1.59 – 1.53 (m, 2H, 5-H), 0.89 (s, 9H, 19-H), 0.06 – 0.00 (m, 6H, 17-H).

^{13}C NMR (101 MHz, chloroform-*d*) δ 169.9, 169.9, 147.4, 138.4, 128.5, 127.7, 127.6, 112.8, 73.4, 72.3, 70.1, 52.5, 52.5, 51.6, 34.0, 26.0, 25.9, 24.6, 18.3, –4.6, –5.0.

IR (Diamond-ATR, neat) $\tilde{\upsilon}_{max}$: 2953 (w), 2929 (w), 2856 (w), 1737 (s), 1435 (w), 1251 (s), 1073 (s), 835 (s), 775 (s), 698 (m) cm^{-1}.

HRMS (ESI) calc. for $C_{24}H_{38}NaO_6Si$ $[M+Na]^+$: 473.2330 found: 473.2297.



Ester 200

To a solution of malonate **199** (13.2 g, 29.3 mmol, 1 equiv) in dichloromethane (300 mL) was added titanium(IV) *tert*-butoxide (12.3 mL, 32.2 mmol, 1.10 equiv) at 23 °C. After 15 minutes, iodine (29.7 g, 117 mmol, 4.00 equiv) and cupric oxide (2.85 g, 35.1 mmol, 1.20 equiv) were added. After eight hours, a saturated aqueous solution of sodium thiosulfate (200 mL) was added to the red suspension and the layers were separated. The aqueous layer was extracted with dichloromethane (3 × 100 mL) and the combined organic layers were dried over sodium sulfate. The dried solution was filtered over a pad of Celite and the filtrate was concentrated. The residue was purified by flash column chromatography on silica gel (10% ethyl acetate in cyclohexane) to yield ester **200** (7.72 g, 17.8 mmol, 61%) as a slightly yellow oil.

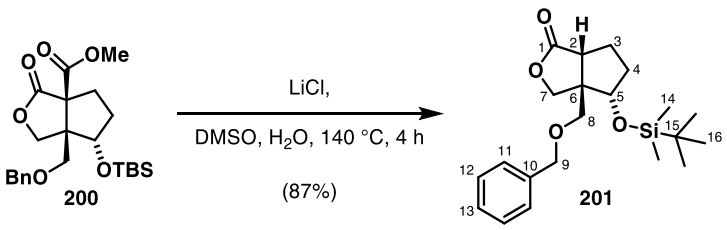
TLC (30% ethyl acetate in cyclohexane): R_f = 0.50 (CAM).

^{1}H NMR (600 MHz, chloroform-*d*) δ 7.36 – 7.33 (m, 2H, 12-H), 7.31 – 7.28 (m, 1H, 13-H), 7.26 – 7.24 (m, 2H, 11-H), 4.63 (d, *J* = 9.3 Hz, 1H, 7-H), 4.45 – 4.39 (m, 2H, 9-H), 4.22 (dd, *J* = 8.5, 5.7 Hz, 1H, 5-H), 4.01 (d, *J* = 9.3 Hz, 1H, 7-H), 3.59 (s, 3H, 15-H), 3.48 (d, *J* = 9.3 Hz, 1H, 8-H), 3.35 (d, *J* = 9.2 Hz, 1H, 8-H), 2.39 (ddd, *J* = 13.4, 11.4, 6.9 Hz, 1H, 3-H), 2.24 (ddd, *J* = 13.5, 6.9, 3.3 Hz, 1H, 3-H), 1.99 (dddd, *J* = 12.7, 6.8, 5.7, 3.3 Hz, 1H, 4-H), 1.49 (dddd, *J* = 12.7, 11.3, 8.5, 6.9 Hz, 1H, 4-H), 0.86 (s, 9H, 18-H), 0.05 – 0.00 (m, 6H, 16-H).

^{13}C NMR (151 MHz, chloroform-*d*) δ 176.9 (C-1), 169.2 (C-14), 137.3 (C-10), 128.4 (C-12), 127.9 (C-13), 127.6 (C-14), 76.0 (C-5), 73.5 (C-9), 69.8 (C-8), 68.7 (C-7), 61.3 (C-2), 58.0 (C-6), 52.7 (C-15), 32.7 (C-4), 30.3 (C-3), 25.6 (C-18), 17.9 (C-17), –4.5 (C-16), –5.1 (C-16).

IR (Diamond-ATR, neat) $\tilde{\upsilon}_{max}$: 2954 (w), 2929 (w), 2856 (w), 1778 (s), 1743 (m), 1252 (m), 1147 (m), 1036 (m), 838 (m), 778 (w) cm^{-1}.

HRMS (ESI) calc. for $C_{23}H_{34}KO_6Si$ $[M+K]^+$: 473.1756 found: 473.2299.



Lactone 201

To a solution of ester **200** (7.60 g, 17.5 mmol, 1 equiv) in dimethyl sulfoxide (70 mL) was added lithium chloride (5.99 g, 140 mmol, 8.00 equiv) and water (2.52 mL, 140 mmol, 8.00 equiv). The suspension was heated to 140 °C. After four hours, the reaction mixture was allowed to cool to 23 °C. When 23 °C was reached, water (70 mL) and diethyl ether (70 mL) were added to the reaction mixture and the layers were separated. The aqueous layer was extracted with diethyl ether (3 × 25 mL) and the combined organic layers were dried over sodium sulfate. The dried solution was filtered and the filtrate was concentrated. The residue was purified by flash column chromatography on silica gel (20% ethyl acetate in cyclohexane) to yield lactone **201** (5.72 g, 15.2 mmol, 87%) as a colourless oil.

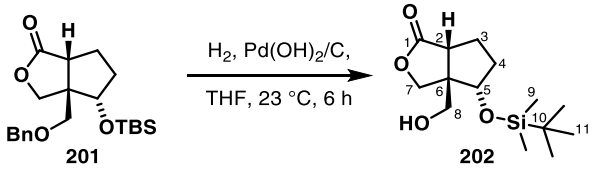
TLC (20% ethyl acetate in cyclohexane): R_f = 0.26 (CAM).

^{1}H NMR (400 MHz, chloroform-*d*) δ 7.40 – 7.28 (m, 5H, 11-H, 12-H, 13-H), 4.55 (d, *J* = 9.7 Hz, 1H, 7-H), 4.53 (s, 2H, 9-H), 4.15 (dd, *J* = 9.1, 5.3 Hz, 1H, 5-H), 3.92 (d, *J* = 9.7 Hz, 1H, 7-H), 3.42 – 3.37 (m, 2H, 8-H), 2.88 – 2.84 (m, 1H, 2-H), 2.07 – 1.99 (m, 1H, 3-H), 1.96 – 1.85 (m, 2H, 3-H, 4-H), 1.64 – 1.57 (m, 1H, 4-H), 0.86 (s, 9H, 16-H), 0.05 – 0.01 (m, 6H, 14-H).

^{13}C NMR (101 MHz, chloroform-*d*) δ 180.8 (C-1), 137.8 (C-10), 128.6 (C-12), 128.0 (C-13), 127.8 (C-11), 76.1 (C-5), 73.6 (C-9), 72.3 (C-8), 69.9 (C-7), 54.3 (C-6), 46.0 (C-2), 33.7 (C-4), 26.1 (C-3), 25.8 (C-16), 18.0 (C-15), –4.4 (C-14), –5.0 (C-14).

IR (Diamond-ATR, neat) $\tilde{\nu}_{max}$: 2954 (w), 2929 (w), 2856 (w), 1770 (s), 1463 (w), 1362 (w), 1253 (m), 1147 (m), 1113 (s), 1028 (m), 866 (m), 837 (m), 777 (m), 698 (m) cm^{-1}.

HRMS (ESI) calc. for $C_{21}H_{32}NaO_4Si$ $[M+Na]^+$: 399.1962 found: 399.1934.



Alcohol 202

To a solution of lactone **201** (5.68 g, 15.1 mmol, 1 equiv) in tetrahydrofuran (16 mL) was added $Pd(OH)_2$/C (20 wt%, 5.30 g, 7.54 mmol, 0.500 equiv). The reaction vessel was placed in a high-pressure

autoclave and exposed to hydrogen pressure of 40 bar. After six hours, the gas was released and the autoclave was purged with nitrogen for one minute. The reaction mixture was filtered through a pad of Celite and the pad washed with dichloromethane (20 mL). The filtrate was concentrated to yield alcohol **202** (4.43 g, 15.5 mmol) as a colourless oil. The crude reaction mixture was used in the next step without further purification. To obtain analytical data a small aliquot of the crude reaction mixture was purified by flash column chromatography on silica gel (50% ethyl acetate in cyclohexane).

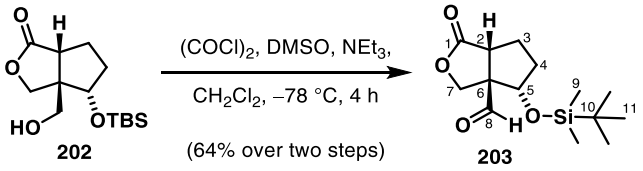
TLC (50% ethyl acetate in cyclohexane): R_f = 0.29 (CAM).

^{1}H NMR (600 MHz, chloroform-*d*) δ 4.57 (d, *J* = 9.8 Hz, 1H, 7-H), 4.14 (dd, *J* = 9.1, 5.3 Hz, 1H, 5-H), 4.00 (d, *J* = 9.8 Hz, 1H, 7-H), 3.69 – 3.62 (m, 2H, 8-H), 2.85 – 2.80 (m, 1H, 2-H), 2.07 – 2.02 (m, 1H, 3-H), 1.96 – 1.90 (m, 2H, 3-H, 4-H), 1.78 (t, *J* = 4.6 Hz, 1H, 8-OH), 1.63 – 1.58 (m, 1H, 4-H), 0.87 (s, 9H, 11-H), 0.08 – 0.05 (m, 6H, 9-H).

^{13}C NMR (151 MHz, chloroform-*d*) δ 180.8 (C-1), 76.3 (C-5), 69.7 (C-7), 65.3 (C-8), 55.0 (C-6), 45.4 (C-2), 33.6 (C-4), 26.1 (C-3), 25.8 (C-11), –4.3 (C-9), –5.0 (C-9).

IR (Diamond-ATR, neat) $\tilde{\nu}_{max}$: 3478 (br, w), 2955 (m), 2930 (m), 2858 (m), 1752 (s), 1471 (w), 1254 (m), 1197 (m), 1149 (m), 1112 (m), 1031 (m), 865 (s), 838 (s), 778 (m) cm^{-1}.

HRMS (ESI) calc. for $C_{14}H_{26}NaO_4Si$ $[M+Na]^+$: 309.1493 found: 309.1469.



Aldehyde 203

To a solution of oxalylchloride (1.65 mL, 17.0 mmol, 1.10 equiv) in dichloromethane (100 mL) was added dimethyl sulfoxide (2.42 mL, 34.0 mmol, 2.20 equiv) at −78 °C. After ten minutes, a solution of crude alcohol **202** (4.43 g, 15.5 mmol, 1 equiv) in dichloromethane (40 mL) was added dropwise to the reaction mixture over the course of five minutes. Ten minutes after the addition of the alcohol **202** was completed, triethylamine (10.7 mL, 77.3 mmol, 5.00 equiv) was added to the reaction mixture. After 20 minutes, the reaction mixture was allowed to warm to 23 °C. After four hours at 23 °C, water (150 mL) was added to the reaction mixture and the layers were separated. The aqueous layer was extracted with dichloromethane (3 × 50 mL) and the combined organic layers were dried over sodium sulfate. The dried solution was filtered and the filtrate was concentrated. The residue was purified by flash column chromatography on silica gel (30% ethyl acetate in cyclohexane) to yield aldehyde **203** (2.80 g, 9.84 mmol, 64% over two steps) as a colourless oil.

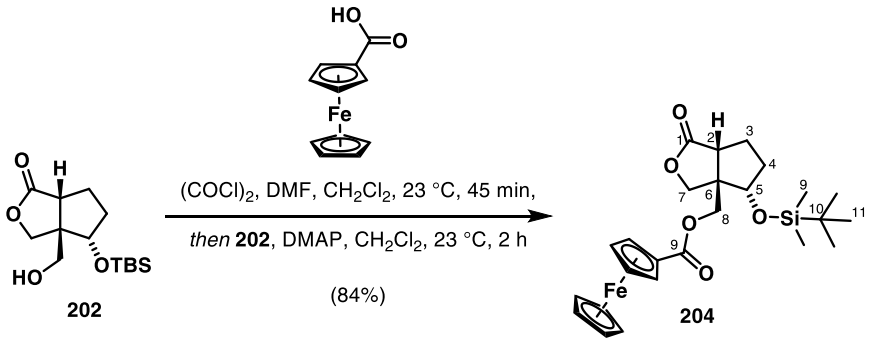
TLC (30% ethyl acetate in cyclohexane): R_f = 0.22 (CAM).

^{1}H NMR (600 MHz, chloroform-*d*) δ 9.67 (s, 1H, 8-H), 4.63 (dd, *J* = 10.2, 1.1 Hz, 1H, 7-H), 4.57 – 4.53 (m, 2H, 7-H, 5-H), 3.11 (dt, *J* = 8.6, 1.9 Hz, 1H, 2-H), 2.19 – 2.15 (m, 1H, 3-H), 2.04 – 1.98 (m, 2H, 3-H, 4-H), 1.73 – 1.66 (m, 1H, 4-H), 0.86 (s, 9H, 11-H), 0.08 – 0.03 (m, 6H, 9-H).

^{13}C NMR (151 MHz, chloroform-*d*) δ 198.6 (C-8), 178.2 (C-1), 75.7 (C-5), 65.6 (C-7), 64.6 (C-6), 45.5 (C-2), 34.1 (C-4), 26.5 (C-3), 25.7 (C-11), 18.0 (C-10), –4.5 (C-9), –5.0 (C-9).

IR (Diamond-ATR, neat) $\tilde{\upsilon}_{max}$: 3010 (br, w), 2955 (m), 2931 (m), 2887 (w), 2858 (m), 1777 (s), 1745 (s), 1471 (w), 1387 (w), 1254 (m), 1198 (m), 1129 (m), 1028 (m), 861 (s), 839 (s), 779 (m) cm^{-1}.

HRMS (ESI) calc. for $C_{14}H_{24}NaO_4Si$ $[M+Na]^+$: 307.1336 found: 307.1314.



Ferrocene ester 204

To suspension of ferrocene carboxylic acid (8.25 mg, 35.0 µmol, 2.00 equiv) in dichloromethane (800 µL) was added a solution of oxalyl chloride (2.00 M, 19.1 µL, 38.0 µmol, 2.20 equiv) followed by a microsyringe drop of *N*,*N*-dimethylformamide at 23 °C upon which gas formation was observed. The reaction mixture turned red. After 45 minutes, toluene (800 µL) was added and the mixture was concentrated. To a solution of alcohol **202** (4.98 mg, 17.4 µmol, 1 equiv) and 4-dimethylaminopyridine (21.5 mg, 174 µmol, 10.0 equiv) in dichloromethane (300 µL) was added a solution of the freshly prepared ferrocene acid chloride in dichloromethane (300 µL) at 23 °C. After 2 hours, the reaction mixture was concentrated and the residue was purified by flash column chromatography on silica gel (10% ethyl acetate in cyclohexane) to yield ferrocene ester **204** (7.30 mg, 15.0 µmol, 84%) as a yellow solid.

TLC (10% ethyl acetate in cyclohexane): R_f = 0.20 (CAM, UV).

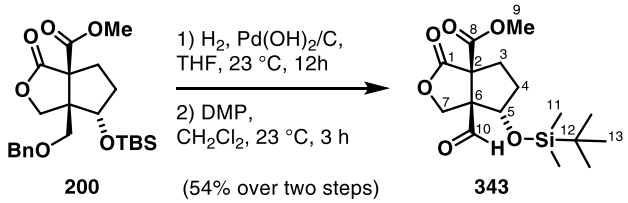
^{1}H NMR (400 MHz, chloroform-*d*) δ 4.79 – 4.76 (m, 2H, Cp), 4.66 (d, *J* = 9.9 Hz, 1H, 7-H), 4.45 – 4.42 (m, 2H, Cp), 4.28 (d, *J* = 11.1 Hz, 1H, 8-H), 4.22 – 4.19 (m, 5H, Cp), 4.16 – 4.11 (m, 2H, 8-H, 5-H), 4.08 (d, *J* = 9.9 Hz, 1H, 7-H), 2.91 – 2.86 (m, 1H, 2-H), 2.18 – 2.09 (m, 1H, 3-H), 2.06 – 1.96 (m, 2H, 3-H, 4-H), 1.76 – 1.64 (m, 1H, 4-H), 0.90 (s, 9H, 12-H), 0.11 – 0.07 (m, 6H, 10-H).

^{13}C NMR (101 MHz, chloroform-*d*) δ 180.1 (C-1), 171.8 (C-9), 76.6 (C-5), 71.9 (Cp), 70.3 (Cp), 70.2 (Cp), 70.2 (Cp), 70.0 (Cp), 69.8 (C-7), 66.6 (C-8), 53.7 (C-6), 46.1 (C-2), 33.6 (C-4), 26.0 (C-3), 25.8 (C-12), 18.0 (C-11), –4.2 (C-10), –4.9 (C-10).

IR (Diamond-ATR, neat) $\tilde{\upsilon}_{max}$: 2955 (w), 2857 (w), 1773 (s), 1717 (s), 1460 (w), 1385 (s), 1273 (s), 1212 (w), 1132 (s), 1028 (m), 1002 (w), 864 (m), 838 (m), 776 (m) cm^{-1}.

HRMS (ESI) calc. for $C_{25}H_{34}FeNaO_5Si$ $[M+Na]^+$: 521.1417 found: 521.1394.

Crystal structure: *see chapter 7.2. for more details*



200 **343**

Aldehyde 343

To a solution of ester **200** (7.60 mg, 18.0 µmol, 1 equiv) in tetrahydrofuran (2 mL) was added palladium hydroxide on activated charcoal (20 wt%, 24.6 mg, 35.0 µmol, 2.00 equiv). The reaction vessel was placed in a high-pressure autoclave and exposed to hydrogen pressure of 40.0 bar. After 12 hours, the gas was released and the autoclave was purged with nitrogen for one min. The reaction mixture was filtered through a pad of Celite. The pad was washed with dichloromethane (5 mL) and the filtrate was concentrated to yield the primary alcohol (6.00 mg, 17.0 µmol) as a colourless oil.

To a solution of the crude alcohol in dichloromethane (1 mL) was added Dess-Martin periodinane (36.9 mg, 87.0 µmol, 5.00 equiv) at 23 °C. After three hours, the reaction mixture was concentrated and the residue was purified by flash column chromatography on silica gel (30% ethyl acetate in cyclohexane) to yield aldehyde **343** (3.20 mg, 9.34 µmol, 54% over two steps) as a colourless oil.

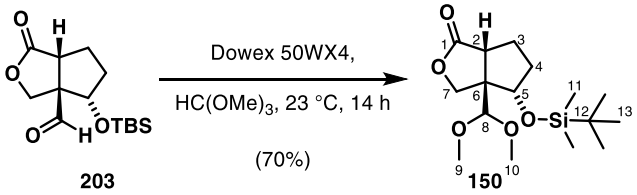
TLC (30% ethyl acetate in cyclohexane): R_f = 0.21 (CAM).

^{1}H NMR (600 MHz, chloroform-*d*) δ 9.50 (s, 1H, 10-H), 4.73 – 4.69 (m, 2H, 7-H), 4.50 (dd, *J* = 8.8, 5.6 Hz, 1H, 5-H), 3.75 (s, 3H, 9-H), 2.48 (ddd, *J* = 13.8, 11.7, 6.8 Hz, 1H, 3-H), 2.38 (ddd, *J* = 10.7, 6.9, 3.4 Hz, 1H, 3-H), 2.15 (ddt, *J* = 12.7, 6.5, 3.2 Hz, 1H, 4-H), 1.66 (dddd, *J* = 11.7, 8.8, 4.9, 2.0 Hz, 1H, 4-H), 0.86 (s, 9H, 13-H), 0.07 – 0.02 (m, 6H, 11-H).

^{13}C NMR (151 MHz, chloroform-*d*) δ 197.0 (C-10), 174.5 (C-1), 167.6 (C-8), 75.9 (C-5), 66.7 (C-6), 65.6 (C-7), 63.5 (C-2), 53.6 (C-9), 33.7 (C-4), 30.4 (C-3), 25.7 (C-13), 18.0 (C-12), –4.5 (C-11), –5.0 (C-11).

IR (Diamond-ATR, neat) $\tilde{\upsilon}_{max}$: 2986 (m), 2834 (w), 1760 (s), 1712 (s), 1560 (w), 1450 (m), 1248 (m), 1133 (s), 1025 (m), 860 (s), 587 (w) cm^{-1}.

HRMS (ESI) calc. for $C_{16}H_{26}KO_6Si$ $[M+K]^+$: 381.1130 found: 381.1111.



Acetal 150

To a solution of aldehyde **203** (2.80 g. 9.84 mmol, 1 equiv) in trimethyl orthoformate (18 mL) was added Dowex 50WX4 (4.20 g) at 23 °C. After 14 hours, the reaction mixture was filtered through a pad of Celite and the pad was washed with ethyl acetate (20 mL). The filtrate was concentrated and the residue was purified by flash column chromatography on silica gel (20% ethyl acetate in cyclohexane) to yield acetal **150** (2.26 g, 6.84 mmol, 70%) as a colourless oil.

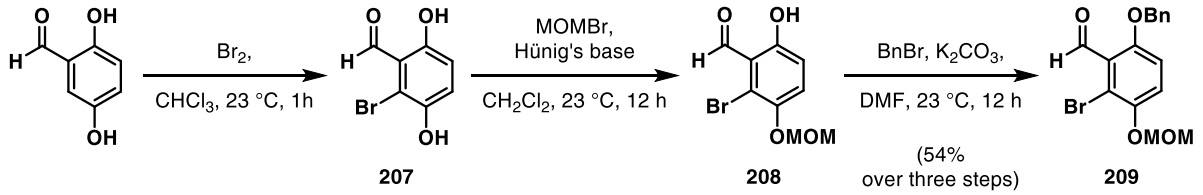
TLC (20% ethyl acetate in cyclohexane): R_f = 0.26 (CAM).

^{1}H NMR (600 MHz, chloroform-*d*) δ 4.53 (d, *J* = 9.6 Hz, 1H, 7-H), 4.27 (dd, *J* = 9.1, 5.7 Hz, 1H, 5-H), 4.20 (s, 1H, 8-H), 4.09 (d, *J* = 9.7 Hz, 1H, 7-H), 3.52 – 3.49 (m, 6H, 9-H, 10-H), 2.92 (dd, *J* = 9.6, 1.8 Hz, 1H, 2-H), 2.02 – 1.98 (m, 1H, 3-H), 1.94 – 1.90 (m, 1H, 4-H), 1.89 – 1.82 (m, 1H, 3-H), 1.52 (tdd, *J* = 11.1, 6.6, 4.0 Hz, 1H, 4-H), 0.87 (s, 9H, 13-H), 0.06 – 0.04 (m, 6H, 11-H).

^{13}C NMR (151 MHz, chloroform-*d*) δ 180.8 (C-1), 108.3 (C-8), 75.9 (C-5), 68.8 (C-7), 58.8 (C-6), 58.2 (C-9, C-10), 44.8 (C-2), 34.0 (C-4), 26.3 (C-3), 25.8 (C-13), 18.0 (C-12), –4.3 (C-11), –5.0 (C-11).

IR (Diamond-ATR, neat) $\tilde{\upsilon}_{max}$: 2954 (m), 2930 (m), 2857 (m), 1770 (s), 1471 (w), 1385 (w), 1253 (m), 1195 (m), 1150 (m), 1073 (s), 1029 (m), 867 (m), 837 (s), 777 (m), 673 (w) cm^{-1}.

HRMS (ESI) calc. for $C_{16}H_{30}NaO_5Si$ $[M+Na]^+$: 353.1755 found: 353.1753.



Benzyl ether 209

To a solution of 2,5-dihydroxybenzaldehyde (5.08 g, 36.4 mmol, 1 equiv) in chloroform (150 mL) was added bromine (1.96 ml, 38.2 mmol, 1.05 equiv) dropwise at 23 °C. After one hour, an aqueous solution

of sodium thiosulfate (100 mL) was added to the reaction mixture and the layers were separated. The aqueous layer was extracted with dichloromethane (3 × 30 mL) the combined organic layers were washed with a saturated aqueous solution of sodium thiosulfate (50 mL) and the washed solution was dried over sodium sulfate. The dried solution was filtered and the filtrate was concentrated to yield crude bromobenzaldehyde **207** (5.28 g, 24.3 mmol) as a yellow solid. The obtained analytical data were in full agreement with those reported in the literature.[159]

To a solution of crude bromobenzaldehyde **207** (5.28 g, 24.3 mmol, 1 equiv) in dichloromethane (120 mL) was added *N*,*N*-diisopropylethylamine (4.68 mL, 26.8 mmol, 1.10 equiv) and bromomethyl methyl ether (2.32 mL, 25.5 mmol, 1.05 equiv) in sequence at 23 °C. After 12 hours, water (100 mL) was added to the reaction mixture and the layers were separated. The aqueous layer was extracted with dichloromethane (3 × 30 mL) and the combined organic layers were dried over sodium sulfate. The dried solution was filtered and the filtrate was concentrated to yield crude MOM-ether **208** (6.47 g, 24.8 mmol) as a yellow solid.

To a solution of crude MOM-ether **208** (6.47 g, 24.8 mmol, 1 equiv) in *N*,*N*-dimethylformamide (80 mL) was added potassium carbonate (6.85 g, 49.6 mmol, 2.00 equiv) and benzyl bromide (3.59 mL, 29.7 mmol, 1.20 equiv) in sequence at 23 °C. After 12 hours, water (100 mL), diethyl ether (100 mL) was added to the reaction mixture and the layers were separated. The aqueous layer was extracted with diethyl ether (3 × 30 mL), the combined organic layers were washed with an aqueous solution of lithium chloride (10%, 300 mL) and the washed organic layers were dried over sodium sulfate. The dried solution was filtered and the filtrate was concentrated. The residue was purified by flash column chromatography on silica gel (30% ethyl acetate in cyclohexane) to yield benzyl ether **209** (4.73 g, 13.5 mmol, 54% over three steps) as a dark yellow solid.

TLC (30% ethyl acetate in cyclohexane): R_f = 0.32 ($KMnO_4$, UV).

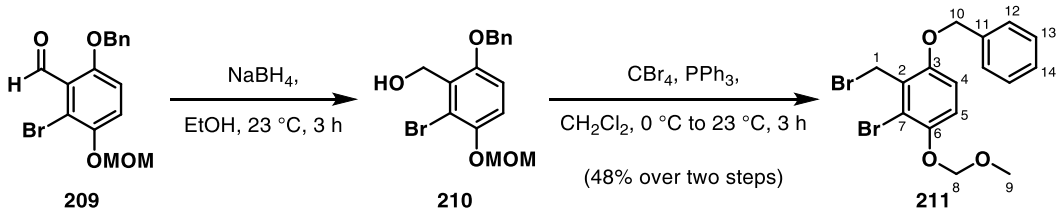
^{1}H NMR (400 MHz, chloroform-*d*) δ 10.46 (s, 1H), 7.42 – 7.32 (m, 6H), 6.95 (d, *J* = 9.2 Hz, 1H), 5.19 (s, 2H), 5.15 (s, 2H), 3.53 (s, 3H).

^{13}C NMR (101 MHz, chloroform-*d*) δ 190.6, 157.4, 153.6, 136.1, 131.4, 128.9, 128.4, 127.3, 122.0, 115.7, 113.6, 96.2, 71.7, 56.7.

IR (Diamond-ATR, neat) $\tilde{\upsilon}_{max}$: 2978 (m), 2925 (m), 2876 (w), 1764 (s), 1750 (s), 1388 (w), 1259 (m), 1210 (m), 1129 (m), 1028 (m), 869 (s), 844 (s), 753 (m), 512 (w) cm^{-1}.

HRMS (ESI) calc. for $C_{16}H_{15}BrNaO_4$ $[M+Na]^+$: 373.0046, 375.0025 found: 373.0028, 375.0006.

[159] J. L. Carr, D. A. Offermann, M. D. Holdom, P. Dusart, A. J. P. White, A. J. Beavil, R. J. Leatherbarrow, S. D. Lindell, B. J. Sutton, A. C. Spivey, *Chem. Commun. (Cambridge, U. K.)* **2010**, *46*, 1824–1826.



Benzyl bromide 211

To a solution of benzyl ether **209** (7.53 g, 21.4 mmol, 1 equiv) in ethanol (105 mL) was added sodium borohydride (828 mg, 21.4 mmol, 1 equiv) at 23 °C. After three hours, the reaction mixture was concentrated and a saturated aqueous solution of ammonium chloride (100 mL) and diethyl ether (100 mL) were added to the residue. The layers were separated and the aqueous layer was extracted with diethyl ether (3 × 30 mL) and the combined organic layers were dried over sodium sulfate. The dried solution was filtered and the filtrate was concentrated to yield crude benzyl alcohol **210** (6.93 g, 19.6 mmol) as yellow solid.

To a solution of crude benzyl alcohol **210** (6.64 g, 18.8 mmol, 1 equiv) in dichloromethane (90 mL) was added carbon tetrabromide (6.30 g, 18.8 mmol, 1 equiv) and triphenylphosphine (5.48 g, 20.7 mmol, 1.10 equiv) at 0 °C. After 30 minutes, the reaction mixture was allowed to warm to 23 °C. After 2.5 hours at 23 °C, the reaction mixture was concentrated and the residue was purified by flash column chromatography on silica gel (100% cyclohexane grading to 10% ethyl acetate in cyclohexane) to yield benzyl bromide **211** (3.76 g, 9.04 mmol, 48% over two steps) as a yellow oil.

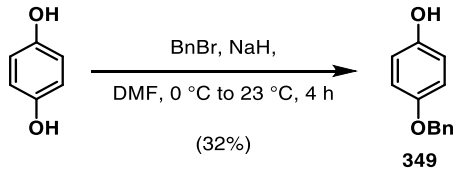
TLC (30% ethyl acetate in cyclohexane): R_f = 0.45 ($KMnO_4$, UV).

^{1}H NMR (400 MHz, chloroform-*d*) δ 7.49 – 7.46 (m, 2H, 12-H), 7.42 – 7.35 (m, 3H, 13-H, 14-H), 7.07 (d, *J* = 9.1 Hz, 1H, 4-H), 6.83 (d, *J* = 9.1 Hz, 1H, 5-H), 5.17 (s, 2H, 8-H), 5.13 (s, 2H, 10-H), 4.82 (s, 2H, 1-H), 3.52 (s, 3H, 9-H).

^{13}C NMR (101 MHz, chloroform-*d*) δ 152.6 (C-3), 148.6 (C-6), 136.7 (C-11), 128.8 (C-13), 128.2 (C-14), 127.9 (C-7), 127.4 (C-12), 117.4 (C-2, C-4), 112.0 (C-5), 96.1 (C-8), 71.2 (C-10), 56.6 (C-9), 28.8 (C-1).

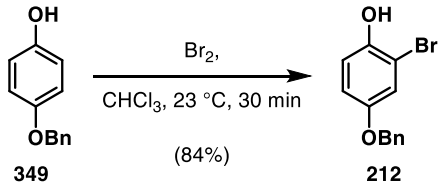
IR (Diamond-ATR, neat) $\tilde{\upsilon}_{max}$: 2918 (m), 2850 (w), 1574 (w), 1475 (s), 1379 (w), 1259 (s), 1220 (w), 1153 (m), 1086 (w), 1026 (s), 933 (m), 803 (w), 734 (m), 696 (m) cm^{-1}.

HRMS (ESI) calc. for $C_{16}H_{16}Br_2NaO_3$ $[M+Na]^+$: 436.9358 found: 436.9528.



Benzyl ether 352

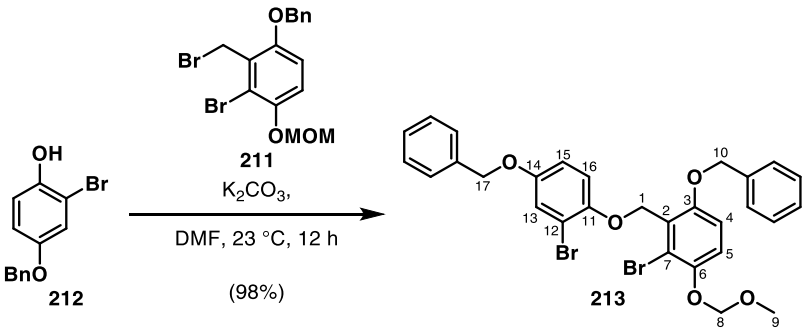
To a solution of hydroquinone (2.00 g, 18.0 mmol, 1 equiv) in *N*,*N*-dimethylformamide (45 mL) was added sodium hydride (60% dispersion in paraffin liquid, 719 mg, 18.0 mmol, 1 equiv) at 0 °C. After 15 minutes, benzyl bromide (2.39 mL, 19.8 mmol, 1.10 equiv) was added to the reaction mixture at 0 °C and then the mixture was allowed to warm to 23 °C. After four hours, water (50 mL) and diethyl ether (50 mL) were added to the reaction mixture and the layers were separated. The aqueous layer was extracted with diethyl ether (3 × 10 mL), the combined organic layers were washed with an aqueous solution of lithium chloride (10%, 30 mL) and the washed organic layers were dried over sodium sulfate. The dried solution was filtered and the filtrate was concentrated. The residue was purified by flash column chromatography on silica gel (10% ethyl acetate in cyclohexane) to yield benzyl ether **352** (1.15 g, 5.74 mmol, 32%) as a colourless solid. The obtained analytical data were in full agreement with those reported in the literature.[160]



Bromophenol 212

To a solution of benzyl ether **352** (1.15 g, 5.74 mmol, 1 equiv) in chloroform (60 mL) was added bromine (309 µL, 6.03 mmol, 1.05 equiv) at 23 °C. After 30 minutes, a saturated aqueous solution of sodium thiosulfate (50 mL) was added to the reaction mixture and the layers were separated. The aqueous layer was extracted with chloroform (3 × 10 mL) and the combined organic layers were dried over sodium sulfate. The dried solution was filtered and the filtrate was concentrated. The residue was purified by flash column chromatography on silica gel (10% ethyl acetate in cyclohexane) to yield bromophenol **212** (1.35 g, 4.84 mmol, 84%) as a colourless solid. The obtained analytical data were in full agreement with those reported in the literature.[161]

[160] T. F. Al-Azemi, M. Vinodh, F. H. Alipour, A. A. Mohamod, *RSC Advances* **2019**, *9*, 23295–23301.
[161] R. Kranich, K. Eis, O. Geis, S. Mühle, J. W. Bats, H.-G. Schmalz, *Chem. Eur. J.* **2000**, *6*, 2874–2894.



Benzyl aryl ether 213

To a solution of bromophenol **212** (1.05 g, 3.77 mmol, 1 equiv) and benzyl bromide **211** (1.57 g, 3.77 mmol, 1 equiv) in *N*,*N*-dimethylformamide (40 mL) was added potassium carbonate (1.04 g, 7.54 mmol, 2.00 equiv) at 23 °C. After 12 hours, water (50 mL) and diethyl ether (50 mL) were added to the reaction mixture and the layers were separated. The aqueous layer was extracted with diethyl ether (3 × 10 mL), the combined organic layers were washed with an aqueous solution of lithium chloride (10%, 30 mL) and the washed organic layers were dried over sodium sulfate. The dried solution was filtered and the filtrate was concentrated. The residue was purified by flash column chromatography on silica gel (10% ethyl acetate in cyclohexane) to yield benzyl aryl ether **213** (2.26 g, 3.68 mmol, 98%) as a yellow oil.

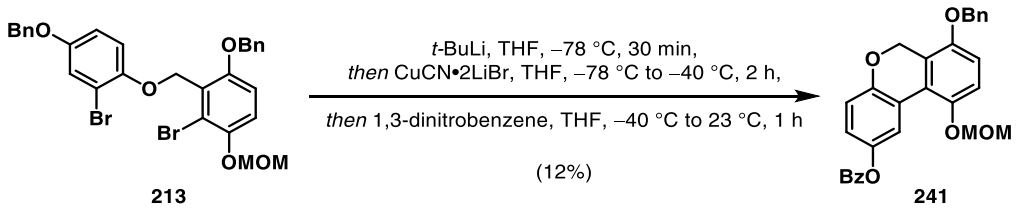
TLC (30% ethyl acetate in cyclohexane): R_f = 0.43 ($KMnO_4$, UV).

^{1}H NMR (400 MHz, chloroform-*d*) δ 7.41 – 7.32 (m, 10H, Ph), 7.17 (d, *J* = 3.0 Hz, 1H, 13-H), 7.12 (d, *J* = 9.1 Hz, 1H, 4-H), 7.00 (d, *J* = 9.0 Hz, 1H, 16-H), 6.86 (d, *J* = 9.1 Hz, 1H, 5-H), 6.80 (dd, *J* = 8.9, 3.0 Hz, 1H, 15-H), 5.29 (s, 2H, 1-H), 5.18 (s, 2H, 8-H), 5.06 (s, 2H, 17-H), 4.99 (s, 2H, 10-H), 3.53 (s, 3H, 9-H).

^{13}C NMR (101 MHz, chloroform-*d*) δ 154.0 (C-3), 153.6 (C-11), 150.3 (C-14), 148.6 (C-6), 136.9 (Ph), 136.8 (Ph), 128.8 (Ph), 128.7 (Ph), 128.2 (Ph), 128.1 (Ph), 127.6 (Ph), 127.5 (Ph), 126.6 (C-7), 119.8 (Ph), 118.8 (C-2), 117.9 (Ph), 117.7 (Ph), 114.9 (Ph), 114.2 (C-12), 112.6 (Ph), 96.2 (C-8), 71.6 (C-17), 70.9 (C-10), 67.7 (C-1), 56.5 (C-9).

IR (Diamond-ATR, neat) $\tilde{\upsilon}_{max}$: 2918 (m), 2850 (w), 1598 (w), 1490 (s), 1461 (m), 1379 (w), 1258 (s), 1204 (s), 1154 (m), 1087 (w), 1038 (s), 936 (w), 803 (w), 736 (m), 697 (m) cm^{-1}.

HRMS (ESI) calc. for $C_{29}H_{26}Br_2NaO_5$ $[M+Na]^+$: 635.0039 found: 635.0056.



Tricyclic benzoate 214

To a solution of benzyl aryl ether **213** (225 mg, 366 µmol, 1 equiv) in tetrahydrofuran (7 mL) was added a solution of *tert*-butyllithium (1.84 M in pentane, 796 µl, 1.47 mmol, 4.00 equiv) at –78 °C. After 30 minutes, a solution of CuCN•2LiBr complex (freshly prepared from copper (I) cyanide (33.5 mg, 366 µmol, 1.00 equiv) and lithium bromide (64.3 mg, 733 µmol, 2.00 equiv) in tetrahydrofuran (700 µL) at 23 °C) was added to the clear brown solution at –78 °C. The greenish reaction mixture was allowed to warm to –40 °C over the course of two hours. When –40 °C was reached, a solution of 1,3-dinitrobenzene (249 mg, 1.47 mmol, 4.00 equiv) in tetrahydrofuran (1 mL) was added and the mixture was allowed to warm to 23 °C over the course of one hour. A saturated aqueous solution of ammonium chloride (10 mL) and dichloromethane (10 mL) were added to the reaction mixture and the layers were separated. The aqueous layer was extracted with dichloromethane (3 × 2 mL), the combined organic layers were washed with an aqueous solution of hydrochloric acid (2 M, 5 mL) and the washed organic layers were dried over sodium sulfate. The dried solution was filtered and the filtrate was concentrated. The residue was purified by flash column chromatography on silica gel (20% ethyl acetate in cyclohexane) to yield tricyclic benzoate **214** (21.0 mg, 45.0 µmol, 12%) as a yellow oil.

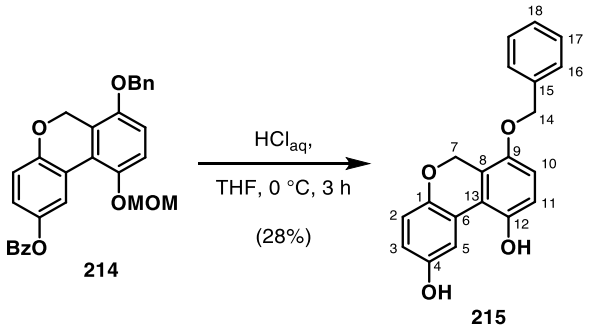
TLC (30% ethyl acetate in cyclohexane): R_f = 0.22 ($KMnO_4$, UV).

^{1}H NMR (600 MHz, chloroform-*d*) δ 7.91 (d, *J* = 3.0 Hz, 1H), 7.43 – 7.31 (m, 10H), 7.10 (d, *J* = 9.0 Hz, 1H), 6.90 (d, *J* = 8.6 Hz, 1H), 6.85 (d, *J* = 9.0 Hz, 1H), 6.72 (dd, *J* = 8.6, 3.0 Hz, 1H), 5.19 (s, 2H), 5.10 (s, 2H), 5.07 (s, 2H), 3.49 (s, 3H).

^{13}C NMR (151 MHz, chloroform-*d*) δ 149.9, 149.5, 149.0, 148.6, 137.1, 128.7, 128.6, 128.1, 127.4, 123.9, 122.8, 121.0, 117.6, 115.9, 115.8, 115.2, 112.5, 95.7, 71.0, 63.5, 56.4.

IR (Diamond-ATR, neat) $\tilde{\upsilon}_{max}$: 3004 (w), 2978 (w), 1515 (s), 1132 (m), 1008 (w), 869 (m), 735 (w), 463 (w) cm^{-1}.

HRMS (ESI) calc. for $C_{29}H_{24}NaO_6$ $[M+Na]^+$: 491.1465 found: 491.1463.



Tricyclic phenol 215

To a solution of tricyclic benzoate **215** (21.0 mg, 45.0 µmol, 1 equiv) in tetrahydrofuran (200 µL) was added an aqueous solution of hydrochloric acid (37% solution in water, 200 µL) at 0 °C. After three hours, water (5 mL) and dichloromethane (5 mL) were added to the reaction mixture and the layers were separated. The aqueous layer was extracted with dichloromethane (3 × 1 mL) and the combined organic layers were washed with a saturated aqueous solution of sodium bicarbonate (3 mL). The washed solution was dried over sodium sulfate, the dried solution was filtered and the filtrate was concentrated. The residue was purified by flash column chromatography on silica gel (30% ethyl acetate in cyclohexane) to yield tricyclic phenol **215** (4.00 mg, 13.0 µmol, 28%) as an orange solid.

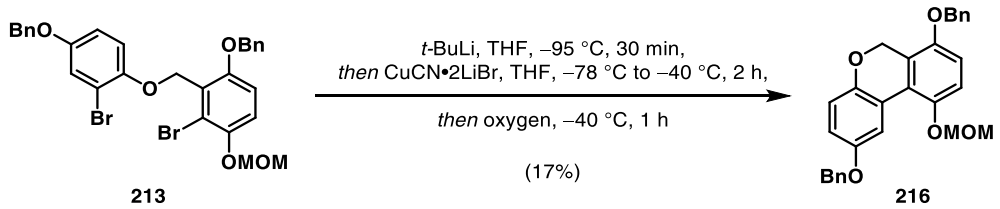
TLC (40% ethyl acetate in cyclohexane): R_f = 0.28 (CAM, UV).

^{1}H NMR (400 MHz, methanol-d_4) δ 8.02 (d, *J* = 2.9 Hz, 1H, 5-H), 7.43 – 7.41 (m, 2H, 16-H), 7.39 – 7.35 (m, 2H, 17-H), 7.33 – 7.29 (m, 1H, 18-H), 6.86 (d, *J* = 8.9 Hz, 1H, 10-H), 6.78 – 6.74 (m, 2H, 11-H, 2-H), 6.62 (dd, *J* = 8.6, 3.0 Hz, 1H, 3-H), 5.04 (s, 2H, 14-H), 4.97 (s, 2H, 7-H).

^{13}C NMR (101 MHz, methanol-d_4) δ 152.4, 150.0, 149.4, 148.2, 138.9, 129.5, 128.9, 128.6, 124.7, 124.4, 119.2, 117.7, 116.6, 116.3, 115.9, 114.6, 72.4 (C-14), 64.3 (C-7).

IR (Diamond-ATR, neat) $\tilde{\upsilon}_{max}$: 3356 (br, w), 3019 (w), 2985 (w), 1502 (s), 1425 (m), 1218 (s), 1056 (m), 1005 (w), 775 (w), 512 (w) cm^{-1}.

HRMS (ESI) calc. for $C_{20}H_{15}O_4$ $[M–H]^-$: 319.0976 found: 319.0991.



Tricyclic ether 216

To a solution of benzyl aryl ether **213** (333 mg, 542 µmol, 1 equiv) in tetrahydrofuran (9 mL) was added a solution of *tert*-butyllithium (1.84 M in pentane, 1.18 mL, 2.17 mmol, 4.00 equiv) at –95 °C. After 30 minutes, a solution of CuCN•2LiBr complex (freshly prepared from copper(I) cyanide (49.5 mg,

542 µmol, 1.00 equiv) and lithium bromide (95.1 mg, 1.08 mmol, 2.00 equiv) in tetrahydrofuran (700 µL) at 23 °C) was added to the clear green solution at –78 °C. The greenish reaction mixture was allowed to warm to –40 °C over the course of two hours. When –40 °C was reached, the reaction mixture was sparged with oxygen upon which the solution immediately turned first yellow, then orange and finally dark brown. After one hour, methanol (2 mL), a saturated aqueous solution of sodium bisulfite (10 mL) and diethyl ether (10 mL) were added in sequence to the reaction mixture at –40 °C and the mixture was allowed to warm to 23 °C. The layers were separated and the aqueous layer was extracted with diethyl ether (3 × 2 mL), the combined organic layers were washed with an aqueous solution of hydrochloric acid (2 M, 5 mL) and the washed organic layers were dried over sodium sulfate. The dried solution was filtered and the filtrate was concentrated. The residue was purified by flash column chromatography on silica gel (10% ethyl acetate in cyclohexane) to yield tricyclic ether **216** (42.0 mg, 92.0 µmol, 17%) as a colourless oil.

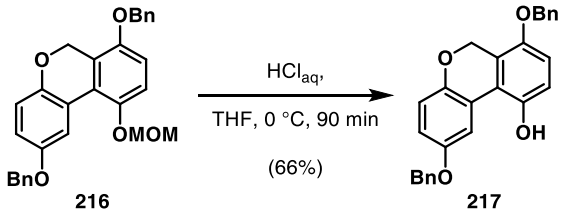
TLC (30% ethyl acetate in cyclohexane): R_f = 0.43 ($KMnO_4$, UV).

^{1}H NMR (400 MHz, chloroform-*d*) δ 7.95 (d, *J* = 2.9 Hz, 1H), 7.38 – 7.26 (m, 10H), 7.01 (d, *J* = 9.0 Hz, 1H), 6.87 (d, *J* = 8.8 Hz, 1H), 6.80 (dd, *J* = 8.8, 3.0 Hz, 1H), 6.76 (d, *J* = 9.0 Hz, 1H), 5.03 (d, *J* = 1.2 Hz, 4H), 4.99 (d, *J* = 1.0 Hz, 4H), 3.36 (s, 3H).

^{13}C NMR (151 MHz, chloroform-*d*) δ 153.4, 149.7, 148.6, 137.2, 128.8, 128.7, 128.7, 128.1, 128.0, 128.0, 127.6, 127.5, 127.4, 127.4, 117.5, 116.1, 116.1, 116.0, 115.9, 114.9, 71.0, 70.8, 65.9, 63.5, 56.3.

IR (Diamond-ATR, neat) $\tilde{\upsilon}_{max}$: 2935 (w), 1721 (w), 1573 (w), 1505 (s), 1463 (s), 1379 (w), 1250 (s), 1152 (m), 1079 (w), 1042 (s), 1023 (s), 922 (w), 736 (m), 696 (m), 516 (w) cm^{-1}.

HRMS (ESI) calc. for $C_{29}H_{26}NaO_5$ $[M+Na]^+$: 477.1672 found: 477.1652.



216 217

Tricyclic phenol 217

To a solution of tricyclic ether **216** (42.0 mg, 92.0 µmol, 1 equiv) in tetrahydrofuran (700 µL) was added an aqueous solution of hydrochloric acid (37% solution in water, 300 µL) at 0 °C. After 90 minutes, water (5 mL) and dichloromethane (5 mL) were added to the reaction mixture and the layers were separated. The aqueous layer was extracted with dichloromethane (3 × 1 mL) and the combined organic layers were washed with a saturated aqueous solution of sodium bicarbonate (3 mL). The washed solution was dried over sodium sulfate, the dried solution was filtered and the filtrate was concentrated.

The residue was purified by flash column chromatography on silica gel (30% ethyl acetate in cyclohexane) to yield tricyclic phenol **217** (25.0 mg, 61.0 µmol, 66%) as a yellow solid.

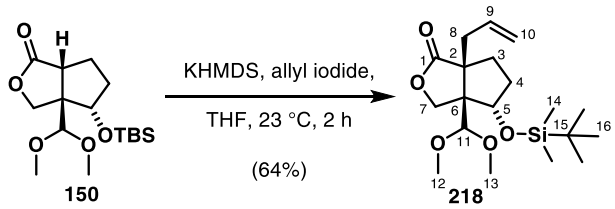
TLC (30% ethyl acetate in cyclohexane): R_f = 0.30 (CAM, UV).

^{1}H NMR (600 MHz, chloroform-*d*) δ 7.86 (d, *J* = 3.0 Hz, 1H), 7.36 (d, *J* = 7.5 Hz, 2H), 7.32 – 7.27 (m, 6H), 7.23 (dd, *J* = 7.2, 5.3 Hz, 2H), 6.85 (d, *J* = 8.8 Hz, 1H), 6.77 (dd, *J* = 8.8, 3.0 Hz, 1H), 6.69 (d, *J* = 8.7 Hz, 1H), 6.62 (d, *J* = 8.8 Hz, 1H), 4.99 (s, 2H), 4.98 (s, 2H), 4.96 (s, 2H), 4.65 (s, 1H).

^{13}C NMR (151 MHz, chloroform-*d*) δ 153.7, 149.7, 148.3, 137.5, 137.2, 128.8, 128.7, 128.2, 128.0, 127.7, 127.5, 125.0, 124.1, 122.6, 118.8, 117.7, 116.3, 115.9, 114.3, 113.1, 71.4, 70.9, 63.7.

IR (Diamond-ATR, neat) $\tilde{\upsilon}_{max}$: 3008 (w), 2974 (w), 1505 (s), 1454 (w), 1380 (w), 1209 (s), 1026 (m), 824 (w), 736 (w), 697 (w), 465 (w) cm^{-1}.

HRMS (ESI) calc. for $C_{27}H_{21}O_4$ $[M–H]^-$: 409.1445 found: 409.1446.



Lactone 218

To a solution of acetal **150** (2.26 g, 6.84 mmol, 1 equiv) and allyl iodide (2.60 mL, 27.9 mmol, 4.00 equiv) in tetrahydrofuran (70 mL) was added a potassium bis(trimethylsilyl)amide solution (1.00 M in tetrahydrofuran, 13.7 mL, 13.7 mmol, 2.00 equiv) at 23 °C. After two hours, water (70 mL) was added to the reaction mixture and the layers were separated. The aqueous layer was extracted with diethyl ether (3 × 20 mL) and the combined organic layers were dried over sodium sulfate. The dried solution was filtered and the filtrate was concentrated. The residue was purified by flash column chromatography on silica gel (10% ethyl acetate in cyclohexane) to yield lactone **218** (1.63 g, 4.40 mmol, 64%) as a colourless oil.

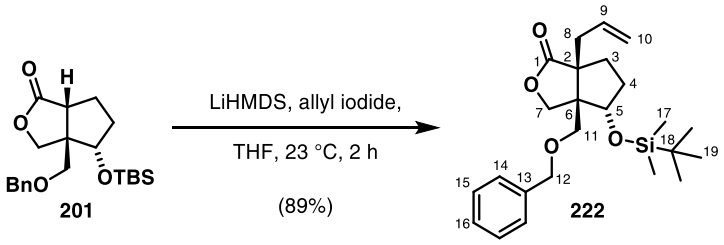
TLC (30% ethyl acetate in cyclohexane): R_f = 0.49 (CAM).

^{1}H NMR (400 MHz, chloroform-*d*) δ 5.89 (ddt, *J* = 17.4, 10.4, 7.3 Hz, 1H, 9-H), 5.18 – 5.10 (m, 2H, 10-H), 4.61 (d, *J* = 9.2 Hz, 1H, 7-H), 4.55 (dd, *J* = 8.2, 6.7 Hz, 1H, 5-H), 4.47 (s, 1H, 11-H), 3.84 (d, *J* = 9.2 Hz, 1H, 7-H), 3.52 – 3.47 (m, 6H, 12-H, 13-H), 2.47 (dd, *J* = 7.2, 1.5 Hz, 2H, 8-H), 2.07 – 1.96 (m, 2H, 3-H, 4-H), 1.61 – 1.55 (m, 1H, 3-H), 1.35 – 1.28 (m, 1H, 4-H), 0.87 (s, 9H, 16-H), 0.06 – 0.03 (m, 6H, 14-H).

^{13}C NMR (151 MHz, chloroform-*d*) δ 181.9 (C-1), 134.1 (C-9), 118.6 (C-10), 108.5 (C-11), 74.7 (C-5), 68.0 (C-7), 59.3 (C-6), 59.0 (C-12 or C-13), 57.4 (C-12 or C-13), 56.2 (C-2), 37.4 (C-8), 34.0 (C-4), 33.5 (C-3), 25.9 (C-16), 18.1 (C-15), –4.4 (C-14), –5.0 (C-14).

IR (Diamond-ATR, neat) $\tilde{\upsilon}_{max}$: 2954 (m), 2930 (m), 2856 (m), 1768 (s), 1471 (w), 1362 (w), 1251 (m), 1149 (s), 1107 (s), 1070 (s), 1027 (s), 866 (m), 837 (s), 777 (m) cm^{-1}.

HRMS (ESI) calc. for $C_{19}H_{34}NaO_5Si$ $[M+Na]^+$: 393.2068 found: 393.2060.



Lactone 222

To a solution of lactone **201** (442 mg, 1.17 mmol, 1 equiv) and allyl iodide (1.10 mL, 11.7 mmol, 10.0 equiv) in tetrahydrofuran (12 mL) was added a lithium bis(trimethylsilyl)amide solution (1.00 M in tetrahydrofuran, 3.52 mL, 3.52 mmol, 3.00 equiv) at 23 °C. After two hours, water (20 mL) was added to the reaction mixture and the layers were separated. The aqueous layer was extracted with diethyl ether (3 × 10 mL) and the combined organic layers were dried over sodium sulfate. The dried solution was filtered and the filtrate was concentrated. The residue was purified by flash column chromatography on silica gel (5% ethyl acetate in cyclohexane) to yield lactone **222** (435 mg, 1.04 mmol, 89%) as a slightly yellow oil.

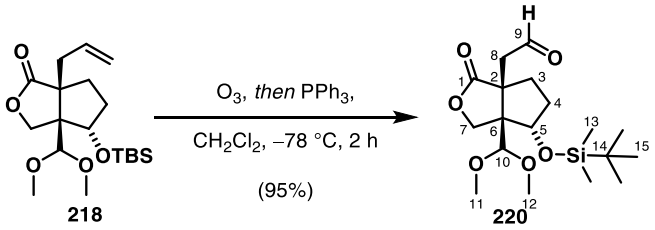
TLC (30% ethyl acetate in cyclohexane): R_f = 0.65 (CAM).

^{1}H NMR (600 MHz, chloroform-*d*) δ 7.36 (dd, *J* = 8.3, 6.2 Hz, 2H, 14-H), 7.33 – 7.28 (m, 3H, 15-H, 16-H), 5.87 (ddt, *J* = 17.2, 10.2, 7.2 Hz, 1H, 9-H), 5.08 – 5.03 (m, 2H, 10-H), 4.56 (d, *J* = 9.4 Hz, 1H, 7-H), 4.49 (s, 2H, 12-H), 4.27 (dd, *J* = 9.0, 6.2 Hz, 1H, 5-H), 3.75 (d, *J* = 9.4 Hz, 1H, 7-H), 3.52 (d, *J* = 9.4 Hz, 1H, 11-H), 3.41 (d, *J* = 9.4 Hz, 1H, 11-H), 2.55 (dd, *J* = 14.4, 7.4 Hz, 1H, 8-H), 2.44 (ddt, *J* = 14.4, 7.1, 1.7 Hz, 1H, 8-H), 2.07 (ddd, *J* = 13.2, 7.3, 2.5 Hz, 1H, 3-H), 1.91 (dtd, *J* = 13.0, 6.6, 2.5 Hz, 1H, 4-H), 1.62 (ddd, *J* = 13.2, 11.6, 6.8 Hz, 1H, 3-H), 1.46 – 1.39 (m, 1H, 4-H), 0.87 – 0.83 (m, 9H, 19-H), 0.03 – 0.01 (m, 6H, 17-H).

^{13}C NMR (151 MHz, chloroform-*d*) δ 182.2 (C-1), 137.7 (C-13), 133.9 (C-9), 128.6 (C-14), 128.0 (C-16), 127.9 (C-15), 118.5 (C-10), 76.3 (C-5), 73.6 (C-12), 70.3 (C-11), 68.6 (C-7), 55.2 (C-6), 54.3 (C-2), 37.3 (C-8), 33.5 (C-3), 32.6 (C-4), 25.8 (C-19), 18.0 (C-18), –4.3 (C-17), –5.0 (C-17).

IR (Diamond-ATR, neat) $\tilde{\upsilon}_{max}$: 2954 (w), 2929 (w), 2856 (w), 1765 (s), 1463 (w), 1362 (w), 1252 (m), 1144 (s), 1124 (s), 1029 (m), 837 (s), 698 (m), 673 (m) cm^{-1}.

HRMS (ESI) calc. for $C_{24}H_{36}NaO_4Si$ $[M+Na]^+$: 439.2275 found: 439.2240.



Aldehyde 220

Through a solution of lactone **218** (1.63 g, 4.40 mmol, 1 equiv) in dichloromethane (44 mL) was sparged a stream of ozone at −78 °C. After ten minutes, the reaction mixture turned blue and then oxygen was sparged through the blue reaction mixture until the colour disappeared. Triphenylphosphine (3.50 g, 13.2 mmol, 3.00 equiv) was added to the reaction mixture. The reaction mixture was allowed to warm to 23° C. After two hours at 23 °C, the mixture was concentrated and the residue was purified by flash column chromatography on silica gel (30% ethyl acetate in cyclohexane) to yield aldehyde **220** (1.55 g, 4.16 mmol, 95%) as a colourless solid.

TLC (40% ethyl acetate in cyclohexane): R_f = 0.35 (CAM).

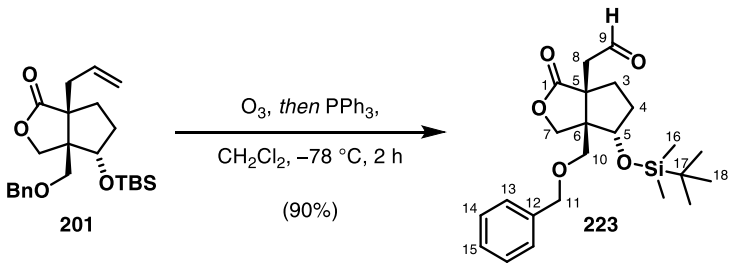
mp: (63-64) °C

^{1}H NMR (600 MHz, chloroform-*d*) δ 9.67 (dd, *J* = 1.9, 0.9 Hz, 1H, 9-H), 4.71 (d, *J* = 9.2 Hz, 1H, 7-H), 4.48 (dd, *J* = 9.8, 6.6 Hz, 1H, 5-H), 4.17 (s, 1H, 10-H), 4.09 (d, *J* = 9.2 Hz, 1H, 7-H), 3.47 – 3.44 (m, 6H, 11-H, 12-H), 2.97 (dd, *J* = 18.2, 1.9 Hz, 1H, 8-H), 2.86 (dd, *J* = 18.1, 1.0 Hz, 1H, 8-H), 2.08 (ddd, *J* = 13.1, 7.2, 1.8 Hz, 1H, 3-H), 1.98 – 1.93 (m, 1H, 4-H), 1.69 (td, *J* = 12.9, 6.6 Hz, 1H, 3-H), 1.46 – 1.40 (m, 1H, 4-H), 0.89 (s, 9H, 15-H), 0.06 (s, 6H, 13-H).

^{13}C NMR (151 MHz, chloroform-*d*) δ 200.2 (C-9), 181.8 (C-1), 108.6 (C-10), 75.3 (C-5), 68.4 (C-7), 59.1 (C-11 or C-12), 58.8 (C-6), 57.9 (C-11 or C-12), 51.8 (C-2), 47.6 (C-8), 34.7 (C-3), 32.6 (C-4), 25.9 (C-15), 18.1 (C-14), –4.2 (C-13), –4.9 (C-13).

IR (Diamond-ATR, neat) $\tilde{\upsilon}_{max}$: 2955 (m), 2930 (m), 2957 (m), 1766 (s), 1724 (m), 1471 (w), 1388 (w), 1253 (m), 1188 (m), 1152 (m), 1114 (s), 1071 (s), 1028 (s), 870 (m), 837 (m), 777 (m), 670 (w) cm^{-1}.

HRMS (ESI) calc. for $C_{18}H_{32}NaO_6Si$ $[M+Na]^+$: 395.1860 found: 395.1852.



Aldehyde 223

Through a solution of lactone **201** (342 mg, 821 µmol, 1 equiv) in dichloromethane (8 mL) was sparged a stream of ozone at −78 °C. After ten minutes, the reaction mixture turned blue and then oxygen was sparged through the blue reaction mixture until the blue colour disappeared. Triphenylphosphine (652 mg, 2.46 mmol, 3.00 equiv) was added to the reaction mixture. The reaction mixture was allowed to warm to 23° C. After two hours at 23 °C, the mixture was concentrated and the residue was purified by flash column chromatography on silica gel (10% ethyl acetate in cyclohexane) to yield aldehyde **223** (308 mg, 736 µmol, 90%) as a colourless solid.

TLC (30% ethyl acetate in cyclohexane): R_f = 0.38 (CAM).

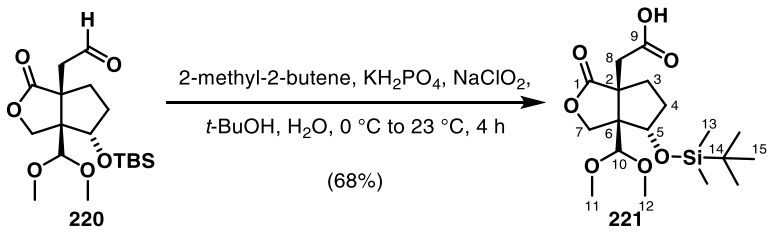
mp: (111-114) °C

^{1}H NMR (600 MHz, chloroform-*d*) δ 9.52 (s, 1H, 9-H), 7.38 – 7.34 (m, 2H, 13-H), 7.33 – 7.31 (m, 1H, 15-H), 7.28 – 7.26 (m, 2H, 14-H), 4.66 (d, *J* = 9.4 Hz, 1H, 7-H), 4.46 (d, *J* = 11.7 Hz, 1H, 11-H), 4.35 (dd, *J* = 11.1, 6.2 Hz, 2H, 11-H, 5-H), 3.82 (d, *J* = 9.4 Hz, 1H, 7-H), 3.35 (d, *J* = 9.7 Hz, 1H, 10-H), 3.29 (d, *J* = 9.7 Hz, 1H, 10-H), 3.08 (dd, *J* = 18.7, 1.1 Hz, 1H, 8-H), 2.90 (d, *J* = 18.7 Hz, 1H, 8-H), 2.06 (dd, *J* = 13.0, 6.8 Hz, 1H, 3-H), 1.91 – 1.86 (m, 1H, 4-H), 1.64 (td, *J* = 13.2, 6.2 Hz, 1H, 3-H), 1.50 – 1.43 (m, 1H, 4-H), 0.87 (s, 9H, 18-H), 0.06 – 0.01 (m, 6H, 16-H).

^{13}C NMR (151 MHz, chloroform-*d*) δ 199.9 (C-9), 182.2 (C-1), 137.3 (C-12), 128.7 (C-13), 128.3 (C-15), 128.2 (C-14), 75.3 (C-5), 73.7 (C-11), 69.7 (C-10), 68.5 (C-7), 54.0 (C-6), 51.0 (C-2), 48.2 (C-8), 34.6 (C-3), 31.5 (C-4), 25.9 (C-18), 18.1 (C-17), –4.3 (C-16), –5.0 (C-16).

IR (Diamond-ATR, neat) $\tilde{\upsilon}_{max}$: 2954 (w), 2928 (w), 2855 (w), 1765 (s), 1721 (m), 1386 (w), 1252 (m), 1153 (m), 1130 (m), 1034 (m), 871 (m), 837 (s), 777 (m), 699 (m) cm^{-1}.

HRMS (ESI) calc. for $C_{23}H_{34}NaO_5Si$ $[M+Na]^+$: 441.2068 found: 441.2080.



Acid 221

To a solution of aldehyde **220** (209 mg, 561 µmol, 1 equiv) and potassium dihydrogen phosphate (153 mg, 1.12 mmol, 2.00 equiv) in *tert*-butanol (3 mL), 2-methyl-2-butene (1 mL) and water (1 mL) was added sodium chlorite (190 mg, 1.68 mmol, 3.00 equiv) at 0 °C. After four hours, saturated aqueous solution of ammonium chloride (10 mL) and ethyl acetate (5 mL) were added to the reaction mixture and the layers were separated. The aqueous layer was extracted with ethyl acetate (3 × 5 mL) and the combined organic layers were dried over sodium sulfate. The dried solution was filtered and the filtrate was concentrated to yield acid **221** (271 mg, 697 µmol) as a colourless solid. The crude reaction mixture was used in the next step without further purification. To obtain analytical data a small aliquot of the crude reaction mixture was purified by flash column chromatography on silica gel (5% methanol in dichloromethane).

TLC (5% methanol in dichloromethane): R_f = 0.18 (CAM).

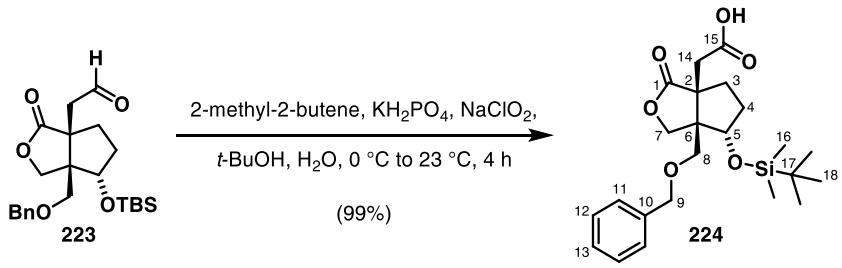
mp: (89-91) °C

^{1}H NMR (600 MHz, chloroform-*d*) δ 4.76 (d, *J* = 8.9 Hz, 1H, 7-H), 4.51 (dd, *J* = 9.8, 6.7 Hz, 1H, 5-H), 4.26 (s, 1H, 10-H), 4.07 (d, *J* = 9.0 Hz, 1H, 7-H), 3.49 – 3.47 (m, 6H, 11-H, 12-H), 2.91 (q, *J* = 17.7 Hz, 2H, 8-H), 2.03 – 1.98 (m, 1H, 3-H), 1.96 – 1.91 (m, 1H, 4-H), 1.65 – 1.61 (m, 1H, 3-H), 1.36 (ddt, *J* = 12.5, 5.7, 2.8 Hz, 1H, 4-H), 0.88 (s, 9H, 15-H), 0.06 (s, 6H, 13-H).

^{13}C NMR (151 MHz, chloroform-*d*) δ 182.6 (C-1), 176.4 (C-9), 108.5 (C-10), 75.1 (C-5), 68.6 (C-7), 59.1 (C-11 or C-12), 58.3 (C-6), 57.7 (C-11 or C-12), 52.9 (C-2), 38.3 (C-8), 34.7 (C-3), 32.7 (C-4), 25.9 (C-15), 18.1 (C-14), –4.3 (C-13), –5.0 (C-13).

IR (Diamond-ATR, neat) $\tilde{\upsilon}_{max}$: 3011 (br, w), 2955 (m), 2929 (m), 2856 (m), 1767 (m), 1739 (s), 1390 (m), 1362 (m), 1253 (m), 1186 (m), 1153 (s), 1135 (s), 1116 (s), 1070 (s), 1026 (s), 906 (m), 865 (m), 837 (s), 776 (m), 724 (w) cm^{-1}.

HRMS (ESI) calc. for $C_{18}H_{32}NaO_7Si$ $[M+Na]^+$: 411.1810 found: 411.1817, calc. for $C_{18}H_{31}O_7Si$ $[M–H]^–$: 387.1845 found: 387.1842.



Acid 224

To a solution of aldehyde **223** (221 mg, 528 µmol, 1 equiv) and potassium dihydrogen phosphate (144 mg, 1.06 mmol, 2.00 equiv) in *tert*-butanol (3 mL), 2-methyl-2-butene (1 mL) and water (1 mL) was added sodium chlorite (179 mg, 1.58 mmol, 3.00 equiv) at 0 °C. After four hours, a saturated aqueous solution of ammonium chloride (10 mL) and ethyl acetate (5 mL) were added to the reaction mixture and the layers were separated. The aqueous layer was extracted with ethyl acetate (3 × 5 mL) and the combined organic layers were dried over sodium sulfate. The dried solution was filtered and the filtrate was concentrated. The residue was purified by flash column chromatography on silica gel (5% methanol in dichloromethane) to yield acid **224** (228 mg, 525 µmol, 99 %) as a colourless solid.

TLC (3% methanol in dichloromethane): R_f = 0.24 (CAM).

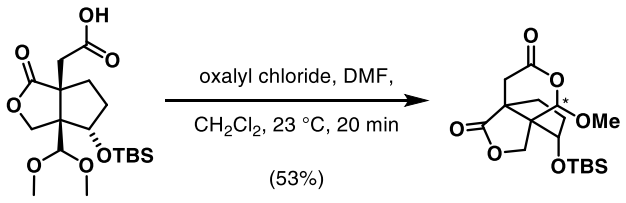
mp: (100-101) °C

^{1}H NMR (400 MHz, chloroform-*d*) δ 7.37 – 7.28 (m, 5H, 11-H, 12-H, 13-H), 4.68 (d, *J* = 9.3 Hz, 1H, 7-H), 4.48 – 4.42 (m, 2H, 9-H), 4.35 (dd, *J* = 10.7, 6.3 Hz, 1H, 5-H), 3.78 (d, *J* = 9.4 Hz, 1H, 7-H), 3.50 (d, *J* = 9.8 Hz, 1H, 8-H), 3.35 (d, *J* = 9.8 Hz, 1H, 8-H), 3.08 (d, *J* = 17.8 Hz, 1H, 14-H), 2.90 (d, *J* = 17.8 Hz, 1H, 14-H), 2.07 (dd, *J* = 12.9, 6.7 Hz, 1H, 3-H), 1.88 (dt, *J* = 12.2, 6.1 Hz, 1H, 4-H), 1.65 (dt, *J* = 13.2, 6.7 Hz, 1H, 3-H), 1.51 – 1.42 (m, 1H, 4-H), 0.86 (s, 9H, 18-H), 0.06 – 0.00 (m, 6H, 16-H).

^{13}C NMR (151 MHz, chloroform-*d*) δ 183.0 (C-1), 174.5 (C-15), 137.3 (C-10), 128.7 (C-12), 128.2 (C-11, C-13), 75.1 (C-5), 73.9 (C-9), 69.6 (C-8), 68.8 (C-7), 53.9 (C-6), 51.7 (C-2), 38.0 (C-14), 34.6 (C-3), 31.4 (C-4), 25.8 (C-18), 18.1 (C-17), –4.3 (C-16), –5.0 (C-16).

IR (Diamond-ATR, neat) $\tilde{\upsilon}_{max}$: 3008 (br, w), 2927 (m), 2855 (m), 1769 (s), 1743 (s), 1463 (w), 1362 (w), 1252 (m), 1154 (s), 1132 (s), 1034 (s), 894 (m), 862 (m), 837 (m), 777 (m), 699 (w) cm^{-1}.

HRMS (ESI) calc. for $C_{23}H_{33}O_6Si$ $[M–H]^-$: 433.2052 found: 433.2056.



221 **225**

Tricyclic lactone 225

To a solution of acid **221** (4.50 mg, 12.0 µmol, 1 equiv) in dichloromethane (300 µL) was added a solution of oxalyl chloride (2.00 M in dichloromethane, 23.0 µL, 46.0 µmol, 4.00 equiv) and a microsyringe drop of *N*,*N*-dimethylformamide at 23 °C. After 20 minutes, the reaction mixture was concentrated and the residue was purified by flash column chromatography on silica gel (30% ethyl acetate in cyclohexane) to yield tricyclic lactone **225** (2:1 ratio of diastereomers, 2.20 mg, 6.00 µmol, 53%) as a colourless oil.

TLC (30% ethyl acetate in cyclohexane): R_f = 0.30 (double spot) (CAM, UV).

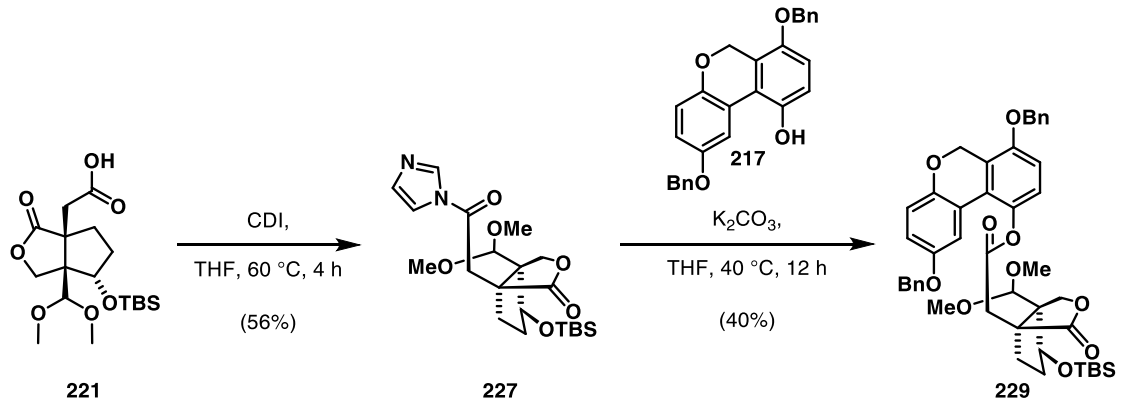
Product was obtained in a diastereomeric ratio of 2:1. The ^{1}H and ^{13}C NMR signals are shown for the major diastereomer.

^{1}H NMR (600 MHz, chloroform-*d*) δ 5.05 (d, *J* = 5.0 Hz, 1H), 4.57 (d, *J* = 10.1 Hz, 1H), 4.31 (d, *J* = 10.1 Hz, 1H), 4.23 – 4.18 (m, 1H), 3.57 (s, 3H), 2.90 (d, *J* = 15.7 Hz, 1H), 2.69 (d, *J* = 15.7 Hz, 1H), 2.29 – 2.26 (m, 1H), 1.95 – 1.91 (m, 1H), 1.62 – 1.58 (m, 2H), 0.88 (s, 9H), 0.08 (s, 6H).

^{13}C NMR (151 MHz, chloroform-*d*) δ 179.9, 168.4, 103.9, 76.3, 67.5, 57.8, 55.6, 48.8, 36.7, 34.1, 31.8, 25.7, 18.0, –4.3, –4.9.

IR (Diamond-ATR, neat) $\tilde{\upsilon}_{max}$: 2957 (w), 2929 (w), 2856 (w), 1782 (s), 1748 (w), 1463 (w), 1397 (w), 1256 (m), 1206 (m), 1166 (m), 1142 (m), 1071 (m), 1047 (m), 1021 (m), 988 (m), 902 (w), 838 (m), 778 (m) cm^{-1}.

HRMS (ESI) calc. for $C_{17}H_{28}NaO_6Si$ $[M+Na]^+$: 379.1547 found: 379.1522.



221 227 229

Amide 227

To a solution of acid **221** (7.10 mg, 18.0 µmol, 1 equiv) in tetrahydrofuran (300 µL) was added 1,1′-carbonyldiimidazole (3.67 mg, 22.0 µmol, 1.20 equiv) and the reaction mixture was heated to 60 °C. After four hours, the reaction mixture was allowed to cool to 23 °C and when 23 °C was reached, the reaction mixture was concentrated. The residue was purified by flash column chromatography on silica gel (5% methanol in dichloromethane) to yield amide **227** (4.90 mg, 10.0 µmol, 56%) as a colourless oil.

TLC (5% methanol in dichloromethane): R_f = 0.26 ($KMnO_4$, UV).

^{1}H NMR (400 MHz, chloroform-*d*) δ 8.15 (t, *J* = 1.1 Hz, 1H), 7.47 (t, *J* = 1.5 Hz, 1H), 7.11 (dd, *J* = 1.7, 0.8 Hz, 1H), 4.75 (d, *J* = 9.0 Hz, 1H), 4.53 – 4.47 (m, 1H), 4.17 (s, 1H), 4.12 (d, *J* = 9.0 Hz, 1H), 3.51 (d, *J* = 17.7 Hz, 1H), 3.39 (s, 3H), 3.32 (d, *J* = 17.7 Hz, 1H), 3.28 (s, 3H), 2.10 (ddd, *J* = 12.8, 7.3, 1.8 Hz, 1H), 2.02 (ddd, *J* = 12.6, 6.7, 1.7 Hz, 1H), 1.87 (td, *J* = 12.6, 6.5 Hz, 1H), 1.53 – 1.44 (m, 1H), 0.90 (s, 9H), 0.11 – 0.04 (m, 6H).

HRMS (ESI) calc. for $C_{21}H_{34}N_2NaO_6Si$ $[M+Na]^+$: 461.2078 found: 461.2080.

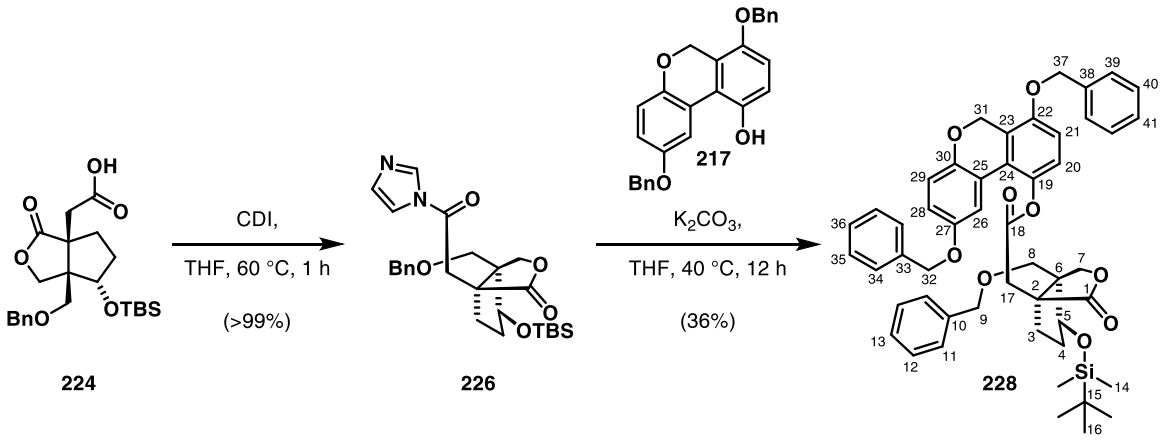
Ester 229

To a solution of amide **227** (4.90 mg, 10.0 µmol 1 equiv) in tetrahydrofuran (300 µL) was added tricyclic phenol **217** (5.00 mg, 12.0 µmol, 1.20 equiv) and potassium carbonate (2.81 mg, 20.0 µmol, 2.00 equiv) and the reaction mixture was heated to 40 °C. After 12 hours, the reaction mixture was allowed to cool to 23 °C and was then concentrated. The residue was purified by flash column chromatography on silica gel (10% ethyl acetate in cyclohexane) to yield ester **229** (3.20 mg, 4.10 µmol, 40%) as a colourless oil.

TLC (30% ethyl acetate in cyclohexane): R_f = 0.30 (double spot) (CAM, UV).

^{1}H NMR (400 MHz, chloroform-*d*) δ 7.69 (d, *J* = 2.9 Hz, 1H), 7.48 – 7.33 (m, 10H), 7.07 (d, *J* = 9.0 Hz, 1H), 6.95 (d, *J* = 8.8 Hz, 1H), 6.91 (d, *J* = 9.0 Hz, 1H), 6.87 (dd, *J* = 8.8, 2.9 Hz, 1H), 5.24 (d, *J* = 13.7 Hz, 1H), 5.11 (s, 2H), 5.07 (s, 2H), 4.97 (d, *J* = 13.7 Hz, 1H), 4.70 (d, *J* = 9.0 Hz, 1H), 4.52 (dd, *J* = 9.7, 6.8 Hz, 1H), 4.18 (s, 1H), 4.07 (d, *J* = 8.9 Hz, 1H), 3.29 (s, 3H), 3.21 (s, 3H), 3.20 (s, 2H), 2.06 (dd, *J* = 12.9, 7.0 Hz, 1H), 1.96 (dt, *J* = 13.1, 6.6 Hz, 1H), 1.73 (td, *J* = 12.7, 6.6 Hz, 1H), 1.43 – 1.34 (m, 1H), 0.87 (s, 9H), 0.05 – 0.02 (m, 6H).

HRMS (ESI) calc. for $C_{45}H_{52}NaO_{10}Si$ $[M+Na]^+$: 803.3222 found: 803.3175.



Amide 226

To a solution of acid **224** (4.80 mg, 11.0 µmol, 1 equiv) in tetrahydrofuran (300 µL) was added 1,1′-carbonyldiimidazole (2.22 mg, 13.0 µmol, 1.20 equiv) and the reaction mixture was heated to 60 °C. After one hour, the reaction mixture was allowed to cool to 23 °C and when 23 °C was reached, the reaction mixture was concentrated. The residue was purified by flash column chromatography on silica gel (3% methanol in dichloromethane) to yield amide **226** (5.40 mg, 11.0 µmol, >99%) as a colourless oil.

TLC (5% methanol in dichloromethane): R_f = 0.40 (CAM, UV).

^{1}H NMR (400 MHz, chloroform-*d*) δ 7.31 (t, *J* = 1.5 Hz, 1H), 7.22 – 7.16 (m, 3H), 7.11 – 7.10 (m, 1H), 7.09 – 7.07 (m, 1H), 7.06 – 7.01 (m, 2H), 4.73 (d, *J* = 9.4 Hz, 1H), 4.45 (dd, *J* = 11.0, 6.2 Hz, 1H), 4.38 (d, *J* = 11.5 Hz, 1H), 4.13 (d, *J* = 11.5 Hz, 1H), 3.81 (d, *J* = 9.4 Hz, 1H), 3.58 (d, *J* = 18.2 Hz, 1H), 3.48 (d, *J* = 9.8 Hz, 1H), 3.38 – 3.32 (m, 2H), 2.09 (dd, *J* = 12.9, 6.6 Hz, 1H), 1.92 (dt, *J* = 12.2, 6.1 Hz, 1H), 1.71 (td, *J* = 13.3, 6.0 Hz, 1H), 1.55 – 1.45 (m, 1H), 0.89 (s, 9H), 0.10 – 0.04 (m, 6H).

Ester 228

To a solution of amide **226** (5.40 mg, 11.0 µmol, 1 equiv) in tetrahydrofuran (300 µL) was added tricyclic phenol **217** (5.40 mg, 13.0 µmol, 1.20 equiv) and potassium carbonate (2.29 mg, 16.0 µmol,

1.50 equiv) and the reaction mixture was heated to 40 °C. After 12 hours, the reaction mixture was allowed to cool to 23 °C and was then concentrated. The residue was purified by flash column chromatography on silica gel (10% ethyl acetate in cyclohexane) to yield ester **228** (3.30 mg, 3.99 µmol, 36%) as a colourless oil.

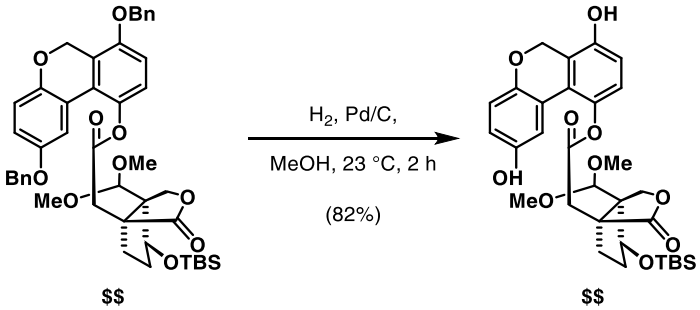
TLC (5% ethyl acetate in cyclohexane): R_f = 0.13 (CAM, UV).

^{1}H NMR (600 MHz, chloroform-*d*) δ 7.66 (d, *J* = 2.9 Hz, 1H, 26-H), 7.44 – 7.34 (m, 10H), 7.33 – 7.30 (m, 1H), 7.26 – 7.23 (m, 3H), 7.18 – 7.15 (m, 2H), 6.95 (dd, *J* = 8.9, 3.4 Hz, 2H), 6.88 – 6.84 (m, 2H), 5.22 (d, *J* = 13.7 Hz, 1H, benzylic), 5.11 (s, 2H, benzylic), 5.03 (s, 2H, benzylic), 4.99 (d, *J* = 13.7 Hz, 1H, benzylic), 4.63 (d, *J* = 9.2 Hz, 1H, 7-H), 4.38 – 4.33 (m, 2H, 5-H, benzylic), 4.21 (d, *J* = 12.0 Hz, 1H, benzylic), 3.77 (d, *J* = 9.2 Hz, 1H, 7-H), 3.41 (d, *J* = 9.8 Hz, 1H, 8-H), 3.35 – 3.29 (m, 2H, 8-H, 17-H), 3.23 (d, *J* = 18.0 Hz, 1H, 17-H), 2.08 (dd, *J* = 13.1, 6.7 Hz, 1H, 3-H), 1.89 – 1.84 (m, 1H, 4-H), 1.70 (td, *J* = 13.1, 6.2 Hz, 1H, 3-H), 1.46 – 1.41 (m, 1H, 4-H), 0.82 (s, 9H, 16-H), 0.02 – –0.06 (m, 6H, 14-H).

^{13}C NMR (151 MHz, chloroform-*d*) δ 182.0 (C-1), 170.8 (C-18), 153.8, 151.9, 150.0, 140.5, 137.4, 136.7, 128.8, 128.7, 128.7, 128.6, 128.3, 128.0, 128.0, 127.6, 127.4, 124.0, 123.8, 123.4, 121.6, 118.2, 116.6 (C-28), 113.6 (C-26), 111.7, 75.5 (C-5), 73.6, 70.9, 70.9, 69.8 (C-8), 68.5 (C-7), 63.5, 53.8 (C-6), 52.3 (C-2), 38.6 (C-17), 34.6 (C-3), 31.7 (C-4), 25.8 (C-16), 18.0 (C-15), –4.3 (C-14), –5.0 (C-14).

IR (Diamond-ATR, neat) $\tilde{\upsilon}_{max}$: 2856 (w), 1760 (m), 1460 (m), 1249 (m), 1135 (s), 1206 (s), 836 (m), 776 (m), 733 (s), 696 (s) cm^{-1}.

HRMS (ESI) calc. for $C_{50}H_{54}NaO_9Si$ $[M+Na]^+$: 849.3429 found: 849.3444.



Ester 231

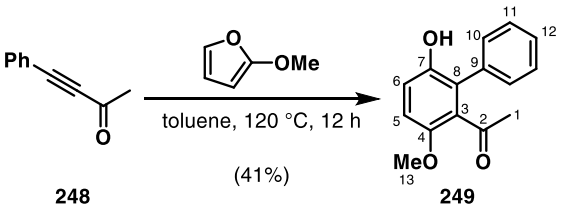
To a solution of ester **229** (2.70 mg, 3.46 µmol, 1 equiv) in methanol (300 µL) was added palladium on activated charcoal (10 wt%, 1.84 mg, 0.500 equiv) at 23 °C. An atmosphere of hydrogen was maintained by sparging with a stream of pure hydrogen gas through a stainless-steel needle for five minutes and vigorous stirring of the suspension was then continued under hydrogen atmosphere at 23 °C. After two hours, the reaction mixture was filtered through a pad of Celite and the pad was washed with dichloromethane (5 mL). The filtrate was concentrated and the residue was purified by flash column

chromatography on silica gel (30% ethyl acetate in cyclohexane) to yield ester **231** (1.70 mg, 2.83 µmol, 82%) as a colourless solid.

TLC (30% ethyl acetate in cyclohexane): R_f = 0.11 (CAM, UV).

^{1}H NMR (400 MHz, chloroform-*d*) δ 7.16 (d, *J* = 2.9 Hz, 1H), 6.91 (d, *J* = 8.6 Hz, 1H), 6.84 (d, *J* = 8.6 Hz, 1H), 6.80 (dd, *J* = 8.6, 2.9 Hz, 1H), 6.70 (d, *J* = 8.6 Hz, 1H), 6.52 (s, 1H), 5.26 (d, *J* = 13.5 Hz, 1H), 4.87 (d, *J* = 9.0 Hz, 1H), 4.82 (d, *J* = 13.4 Hz, 1H), 4.60 (dd, *J* = 9.8, 6.6 Hz, 1H), 4.54 (s, 1H), 4.25 (d, *J* = 9.1 Hz, 1H), 3.49 – 3.46 (m, 6H), 3.21 (d, *J* = 5.5 Hz, 2H), 2.12 (dd, *J* = 12.6, 6.4 Hz, 1H), 1.98 (dd, *J* = 12.7, 6.4 Hz, 1H), 1.70 (td, *J* = 12.8, 6.4 Hz, 1H), 1.29 – 1.23 (m, 1H), 0.89 (s, 9H), 0.10 – 0.05 (m, 6H).

HRMS (ESI) calc. for $C_{31}H_{40}NaO_{10}Si$ $[M+Na]^+$: 623.2283 found: 623.2284.



248 249

Acetophenone 249

A solution of alkyne **248**[162] (101 mg, 701 µmol, 1 equiv) in 2-methoxyfuran (0.4 mL) was heated to 120 °C in a pressure tube. After 12 hours, the reaction mixture was allowed to cool to 23 °C and was then concentrated. The residue was purified by flash column chromatography on silica gel (20% ethyl acetate in cyclohexane) to yield acetophenone **249** (69.0 mg, 285 µmol, 41%) as a yellow solid.

TLC (30% ethyl acetate in cyclohexane): R_f = 0.31 (double spot) (CAM, UV).

mp: (189-190) °C

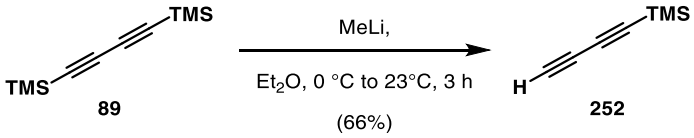
^{1}H NMR (400 MHz, chloroform-*d*) δ 7.48 – 7.40 (m, 3H, Ph), 7.32 – 7.29 (m, 2H, Ph), 6.97 (d, *J* = 9.0 Hz, 1H, 5-H), 6.87 (d, *J* = 8.9 Hz, 1H, 6-H), 4.75 (s, 1H, 7-OH), 3.81 (s, 3H, 13-H), 2.13 (s, 3H, 1-H).

^{13}C NMR (101 MHz, chloroform-*d*) δ 203.9 (C-2), 149.5 (C-4), 146.8 (C-7), 133.5 (C-9), 132.4 (C-8), 130.3 (C-11), 129.6 (C-10), 128.9 (C-12), 125.6 (C-3), 116.4 (C-5), 112.4 (C-6), 56.6 (C-13), 32.5 (C-1).

IR (Diamond-ATR, neat) $\tilde{\upsilon}_{max}$: 3389 (br, w), 2952 (w), 1702 (s), 1597 (w), 1483 (m), 1435 (m), 1351 (m), 1281 (s), 1259 (s), 1100 (m), 1020 (m), 812 (w), 755 (w), 723 (m), 702 (m) cm^{-1}.

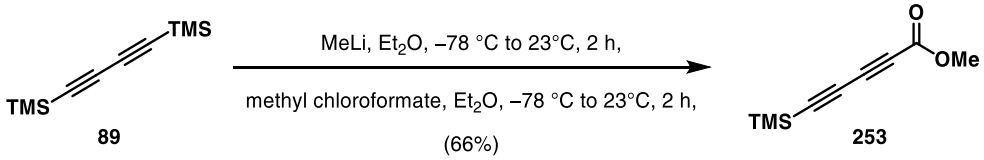
[162] Y. Sadamitsu, K. Komatsuki, K. Saito, T. Yamada, *Org. Lett.* **2017**, *19*, 3191–3194.

HRMS (ESI) calc. for $C_{15}H_{13}O_3$ $[M–H]^-$: 241.0870 found: 241.0864.



Dialkyne 252

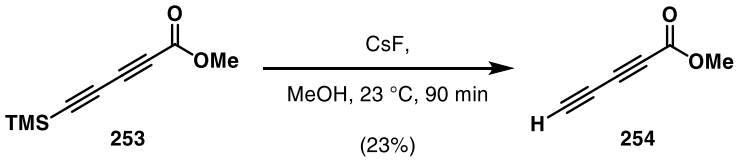
To a solution of dialkyne **89** (1.82 g, 9.36 mmol, 1 equiv) in diethyl ether (20 mL) was added a solution of methyllithium (1.60 M in diethyl ether, 7.02 mL, 11.2 mmol, 1.20 equiv) at 0 °C and then the mixture was allowed to warm to 23 °C. After three hours, a saturated aqueous solution of ammonium chloride (10 mL) was added to the reaction mixture and the layers were separated. The aqueous layer was extracted with diethyl ether (3 × 3 mL), the combined organic layers were dried over sodium sulfate, the dried solution was filtered and the filtrate was concentrated at 23 °C. The residue was purified by distillation (60 °C, 60 mbar) to yield dialkyne **252** (756 mg, 6.18 mmol, 66 %) as a slightly yellow oil. The obtained analytical data were in full agreement with those reported in the literature.[163]



Methyl ester 253

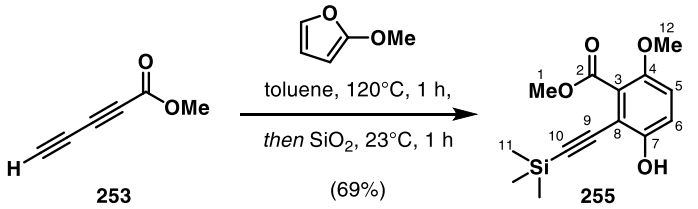
To a solution of dialkyne **89** (500 mg, 2.57 mmol, 1 equiv) in diethyl ether (20 mL) was added a solution of methyllithium (1.60 M in diethyl ether, 4.82 mL, 7.72 mmol, 3.00 equiv) at –78 °C and then the mixture was allowed to warm to 23 °C. After two hours, methyl chloroformate (795 µL, 10.3 mmol, 4.00 equiv) was added to the reaction mixture at –78 °C and then the mixture was allowed to warm to 23 °C. After two hours, water (10 mL) was added and the layers were separated. The aqueous layer was extracted with diethyl ether (3 × 3 mL) and the combined organic layers were dried over sodium sulfate. The dried solution was filtered and the filtrate was concentrated. The residue was purified by flash column chromatography on silica gel (4% ethyl acetate in cyclohexane) to yield methyl ester **253** (304 mg, 1.69 mmol, 66%) as a brown oil. The obtained analytical data were in full agreement with those reported in the literature.[164]

[163] F. Ungeheuer, A. Fürstner, *Chem. Eur. J.* **2015**, *21*, 11387-11392.
[164] N. Kerisit, L. Toupet, Y. Trolez, J.-C. Guillemin, *Chem. Eur. J.* **2013**, *19*, 17683–17686.



Methyl ester 254

To a solution of methyl ester **253** (1.02 g, 5.66 mmol, 1 equiv) in methanol (25 mL) was added cesium fluoride (1.82 g, 11.9 mmol, 2.10 equiv) at 23 °C. After 90 minutes, water (30 mL) and dichloromethane (30 mL) were added to the reaction mixutre and the layers were separated. The aqueous layer was extracted with dichloromethane (3 × 5 mL) and the combined organic layers were dried over sodium sulfate. The dried solution was filtered and the filtrate was concentrated. The residue was purified by flash column chromatography on silica gel (5% ethyl acetate in cyclohexane) to yield methyl ester **254** (142 mg, 1.31 mmol, 23%) as a brown liquid. The obtained analytical data were in full agreement with those reported in the literature.[165]



Methyl benzoate 255

To a solution of methyl ester **253** (1.26 g, 6.99 mmol, 1 equiv) and 2-methoxyfuran (848 mg, 8.39 mmol, 1.20 equiv) in toluene (15 mL) was heated to 120 °C in a pressure tube. After one hour, the reaction mixture was allowed to cool to 23 °C. When 23 °C was reached, silica gel (2 g) was added to the reaction mixture. After one hour, the suspension was filtered and the filtrate was concentrated. The residue was purified by flash column chromatography on silica gel (10% ethyl acetate in cyclohexane) to yield methyl ester **255** (1.35 g, 4.85 mmol, 69%) as a brown oil.

TLC (10% ethyl acetate in cyclohexane): R_f = 0.27 ($KMnO_4$, UV).

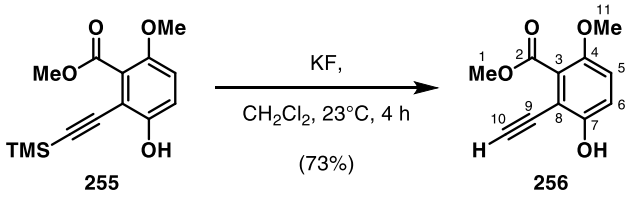
^{1}H NMR (700 MHz, chloroform-*d*) δ 10.73 (s, 1H, 7-OH), 7.07 (d, *J* = 9.1 Hz, 1H, 6-H), 6.94 (d, *J* = 9.1 Hz, 1H, 5-H), 3.96 (s, 3H, 1-H), 3.85 (s, 3H, 12-H), 0.28 (s, 9H, 11-H).

^{13}C NMR (176 MHz, chloroform-*d*) δ 170.8 (C-2), 156.1 (C-4 or C-7), 155.6 (C-4 or C-7), 119.8 (C-6), 118.9 (C-5), 114.1 (C-3), 112.5 (C-8), 105.7 (C-9), 99.3 (C-10), 57.5 (C-12), 52.1 (C-1), 0.2 (C-11).

IR (Diamond-ATR, neat) $\tilde{\upsilon}_{max}$: 2954 (w), 2152 (w), 1737 (m), 1589 (w), 1480 (m), 1439 (m), 1286 (s), 1251 (s), 1145 (w), 1063 (s), 845 (m), 738 (w), 698 (w) cm^{-1}.

HRMS (ESI) calc. for $C_{14}H_{17}O_4Si$ $[M–H]^-$: 277.0902 found: 277.0903.

[165] J.-C. Deng, C.-W. Kuo, S.-C. Chuang, *Chem. Commun.* **2014**, *50*, 10580–10583.



Aryl alkyne 256

To a solution of methyl benzoate **255** (1.35 g, 4.85 mmol, 1 equiv) in dichloromethane (50 mL) was added potassium fluoride (1.99 g, 33.9 mmol, 7.00 equiv) at 23 °C. After four hours, a saturated aqueous solution of ammonium fluoride (30 mL) was added to the reaction mixture and the layers were separated. The aqueous layer was extracted with dichloromethane (3 × 5 mL), the combined organic layers were dried over sodium sulfate, the dried solution was filtered and the filtrate was concentrated. The residue was purified by flash column chromatography on silica gel (100% ethyl acetate) to yield aryl alkyne **256** (728 mg, 3.53 mmol, 73%) as a brownish oil.

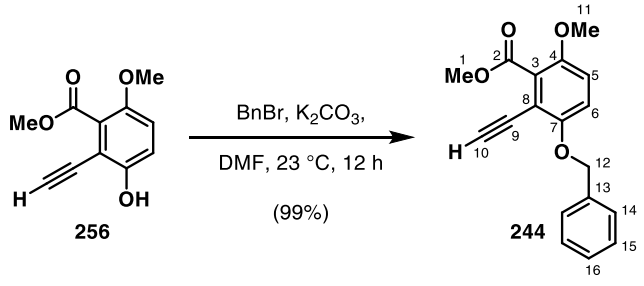
TLC (100% ethyl acetate): R_f = 0.26 (CAM, UV).

^{1}H NMR (400 MHz, chloroform-*d*) δ 10.68 (s, 1H, 7-OH), 7.11 (d, *J* = 9.2 Hz, 1H, 6-H), 7.00 (d, *J* = 9.2 Hz, 1H, 5-H), 3.98 (s, 3H, 1-H), 3.88 (s, 3H, 11-H), 3.63 (s, 1H, 10-H).

^{13}C NMR (101 MHz, chloroform-*d*) δ 170.8 (C-2), 156.1 (C-4 or C-7), 155.6 (C-4 or C-7), 119.3 (C-5 or C-6), 119.1 (C-3), 118.9 (C-4 or C-7), 114.1 (C-8), 99.3 (C-9), 87.4 (C-10), 57.2 (C-1), 52.3 (C-11).

IR (Diamond-ATR, neat) $\tilde{\upsilon}_{max}$: 2956 (w), 1738 (m), 1671 (w), 1594 (w), 1471 (m), 1439 (m), 1330 (w), 1270 (m), 1249 (s), 1221 (w), 1068 (m), 1026 (w), 845 (m), 758 (w) cm^{-1}.

HRMS (ESI) calc. for $C_{11}H_9O_4$ $[M–H]^-$: 205.0506 found: 204.0499.



Benzyl ether 244

To a solution of aryl alkyne **256** (44.0 mg, 213 µmol, 1 equiv) in *N*,*N*-dimethylformamide (2 mL) was added potassium carbonate (88.5 mg, 640 µmol, 3.00 equiv) at 23 °C. After 12 hours, water (10 mL) and diethyl ether (10 mL) were added to the reaction mixture and the layers were separated. The aqueous layer was extracted with diethyl ether (3 × 3 mL), the combined organic layers were washed with a 10% aqueous solution of lithium chloride (5 mL) and the washed organic layers were dried over sodium

sulfate. The dried solution was filtered and the filtrate was concentrated. The residue was purified by flash column chromatography on silica gel (20% ethyl acetate in cyclohexane) to yield benzyl ether **244** (63.2 mg, 213 µmol, 99%) as a colourless solid.

TLC (20% ethyl acetate): R_f = 0.08 ($KMnO_4$, UV).

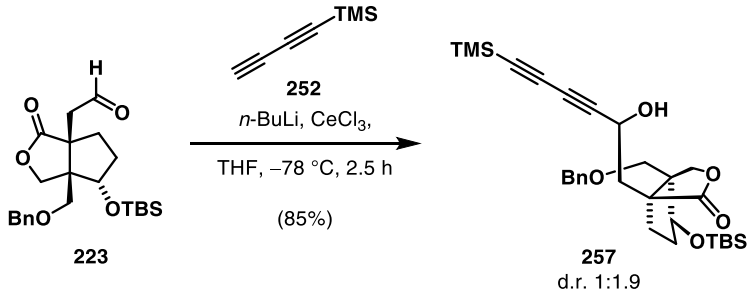
mp: (99-100) °C

^{1}H NMR (400 MHz, chloroform-*d*) δ 7.39 – 7.29 (m, 5H, Ph), 6.92 (d, *J* = 9.1 Hz, 1H, 5-H), 6.83 (d, *J* = 9.1 Hz, 1H, 6-H), 5.07 (s, 2H, 12-H), 3.92 (s, 3H, 1-H), 3.86 (s, 3H, 11-H), 3.42 (s, 1H, 10-H).

^{13}C NMR (151 MHz, chloroform-*d*) δ 167.0 (C-2), 155.3 (C-4), 149.0 (C-7), 136.8 (C-13), 129.4 (C-8), 128.7 (C-14 or C-15), 128.1 (C-16), 127.2 (C-14 or C-15), 115.7 (C-5), 112.7 (C-6), 110.3 (C-3), 85.1 (C-10), 71.7 (C-12), 56.7 (C-11), 52.8 (C-1).

IR (Diamond-ATR, neat) $\tilde{\upsilon}_{max}$: 3281 (w), 2985 (w), 1734 (m), 1589 (w), 1481 (m), 1439 (m), 1287 (s), 1144 (w), 1061 (s), 807 (w), 741 (w), 697 (w) cm^{-1}.

HRMS (ESI) calc. for $C_{18}H_{16}NaO_4$ $[M+Na]^+$: 319.0941 found: 319.0932.



Propargyl alcohol 257

Cerium(III) chloride (29.6 mg, 119 µmol, 5.00 equiv) was suspended in tetrahydrofuran (100 µL). In another flask, a solution of *n*-butyllithium (400 mM in hexane, 99.0 µL, 119 µmol, 5.00 equiv) was added to a solution of dialkyne **252** (14.6 mg, 119 µmol, 5.00 equiv) in tetrahydrofuran (50 µL) at –78 °C. After one hour, the cerium(III) chloride suspension was cooled to –78 °C and then the lithium acetylide was added to the suspension at –78 °C and the transfer was quantified with tetrahydrofuran (50 µL). After one hour, a solution of aldehyde **223** (10.0 mg, 24.0 µmol, 1 equiv) in tetrahydrofuran (200 µL) was added to the organocerium species at –78 °C. After 30 minutes, a saturated aqueous solution of ammonium chloride (5 mL) was added to the reaction mixture and the layers were separated. The aqueous layer was extracted with diethyl ether (3 × 3 mL) and the combined organic layers were dried over sodium sulfate. The dried solution was filtered through a pad of Celite, the filtrate concentrated and the residue was purified by flash column chromatography on silica gel (10% ethyl acetate in cyclohexane) to yield TMS dialkyne **257** (d.r. = 1.9:1, 11.0 mg, 20.0 µmol, 85%) as a colourless solid.

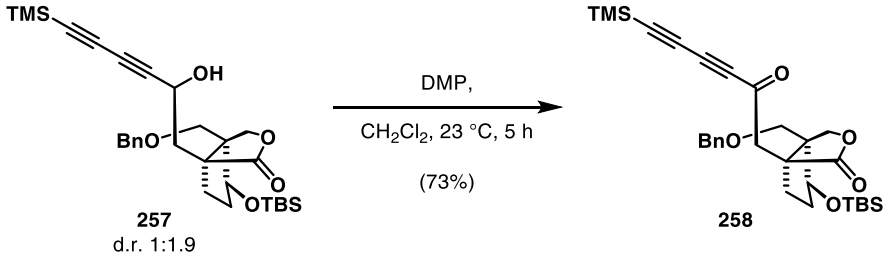
TLC (30% ethyl acetate in cyclohexane): R_f = 0.53 (CAM, UV).

^{1}H NMR (400 MHz, chloroform-*d*) *complex signals arising from a diastereomeric ratio of 1.2:1*

^{13}C NMR (151 MHz, chloroform-*d*) *complex signals arising from a diastereomeric ratio of 1.2:1*

IR (Diamond-ATR, neat) $\tilde{\upsilon}_{max}$: 2930 (m), 2857 (m), 2235 (w), 2147 (w), 1760 (s), 1676 (m), 1471 (m), 1379 (m), 1152 (m), 1092 (s), 1027 (m), 834 (m), 776 (w) cm^{-1}.

HRMS (ESI) calc. for $C_{30}H_{44}NaO_5Si_2$ $[M+Na]^+$: 563.2619 found: 563.2622.

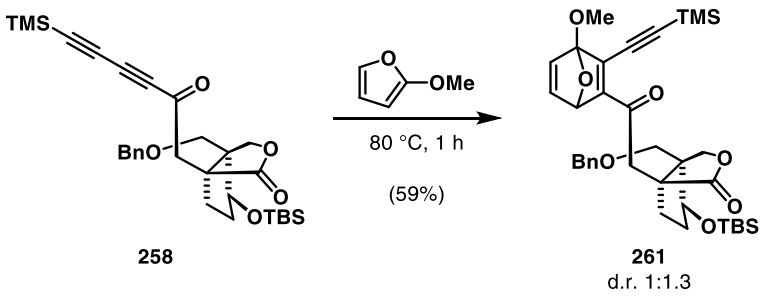


Ketone 258

To a solution of propargyl alcohol **257** (11.0 mg, 20.0 µmol, 1 equiv) in dichloromethane (300 µL) was added Dess–Martin periodinane (10.7 mg, 24.0 µmol, 1.20 equiv) at 23 °C. After five hours, the reaction mixture was filtered through a pad of Celite and the pad was washed with dichloromethane (3 mL). The filtrate was concentrated and the residue was purified by flash column chromatography on silica gel (10% ethyl acetate in cyclohexane) to yield benzyl ether **258** (8.00 mg, 15.0 µmol, 73%) as a slightly yellow solid.

TLC (30% ethyl acetate in cyclohexane): R_f = 0.61 (CAM, UV).

HRMS (ESI) calc. for $C_{30}H_{42}NaO_5Si_2$ $[M+Na]^+$: 561.2463 found: 561.2458.



Bridged ether 261

A solution of ketone **258** (3.00 mg, 5.57 µmol, 1 equiv) in 2-methoxyfuran (50 µL) was heated to 80 °C. After one hour, the reaction mixture was allowed to cool to 23 °C and then the solution was concentrated. The residue was purified by flash column chromatography on silica gel (10% ethyl acetate in

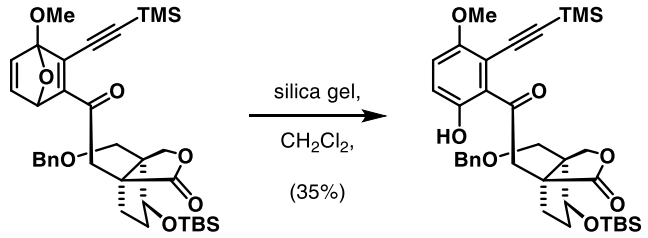
cyclohexane) to yield bridged ether **261** (diastereomeric ratio of 1.3:1, 2.10 mg, 3.30 µmol, 59%) as a colourless oil.

TLC (30% ethyl acetate in cyclohexane): R_f = 0.50 (CAM, UV).

^{1}H NMR (400 MHz, chloroform-*d*) *complex signals arising from a diastereomeric ratio of 1.3:1*
^{13}C NMR (151 MHz, chloroform-*d*) *complex signals arising from a diastereomeric ratio of 1.3:1*

IR (Diamond-ATR, neat) $\tilde{\upsilon}_{max}$: 2927 (s), 2853 (m), 1766 (m), 1523 (w), 1463 (m), 1385 (w), 1285 (m), 1145 (s), 1083 (m), 893 (m), 777 (m) cm^{-1}.

HRMS (ESI) calc. for $C_{35}H_{48}NaO_7Si_2$ $[M+Na]^+$: 659.2831 found: 659.2845.



Hydroquinone 262

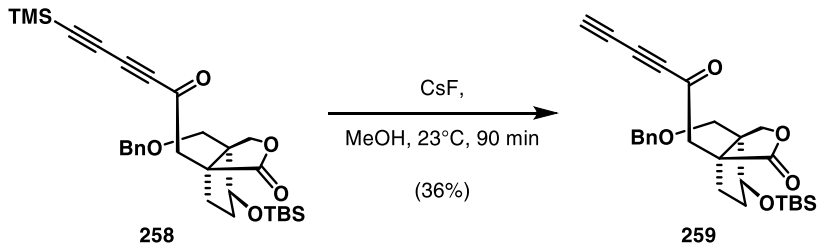
To a solution of bridged ether **261** (2.10 mg, 3.30 µmol, 1 equiv) in dichloromethane (200 µL) was added silica gel (50 mg) at 23 °C. After 12 hours, the reaction mixture was filtered and the filtrate was concentrated. The residue was purified by flash column chromatography on silica gel (10% ethyl acetate in cyclohexane) to yield hydroquinone **262** (0.700 mg, 1.00 µmol, 35%) as a yellow oil.

TLC (30% ethyl acetate in cyclohexane): R_f = 0.35 (CAM, UV).

^{1}H NMR (400 MHz, chloroform-*d*) δ 11.95 (s, 1H), 7.17 – 7.13 (m, 3H), 7.11 (d, *J* = 9.2 Hz, 1H), 7.07 – 7.03 (m, 2H), 6.95 (d, *J* = 9.2 Hz, 1H), 4.74 (d, *J* = 9.1 Hz, 1H), 4.39 (dd, *J* = 11.0, 6.1 Hz, 1H), 4.33 (d, *J* = 19.3 Hz, 1H), 4.23 (d, *J* = 11.6 Hz, 1H), 4.07 (d, *J* = 11.6 Hz, 1H), 3.98 (d, *J* = 19.4 Hz, 1H), 3.86 (s, 3H), 3.78 (d, *J* = 9.1 Hz, 1H), 3.74 (d, *J* = 6.6 Hz, 1H), 3.22 (s, 2H), 2.09 (dd, *J* = 12.6, 6.2 Hz, 1H), 1.85 (dt, *J* = 11.8, 5.8 Hz, 1H), 1.66 (td, *J* = 13.2, 5.6 Hz, 1H), 1.46 (ddd, *J* = 25.4, 11.3, 6.2 Hz, 1H), 0.87 (s, 9H), 0.27 (s, 9H), 0.06 – –0.01 (m, 6H).

IR (Diamond-ATR, neat) $\tilde{\upsilon}_{max}$: 3450 (br, w), 2929 (s), 2849 (m), 1770 (m), 1555 (w), 1463 (m), 1385 (w), 1278 (m), 1150 (s), 1079 (m), 1033 (m), 893 (m), 777 (m), 698 (w) cm^{-1}.

HRMS (ESI) calc. for $C_{35}H_{48}NaO_7Si_2$ $[M+Na]^+$: 659.2831 found: 659.2845.



258 **259**

Dialkyne 259

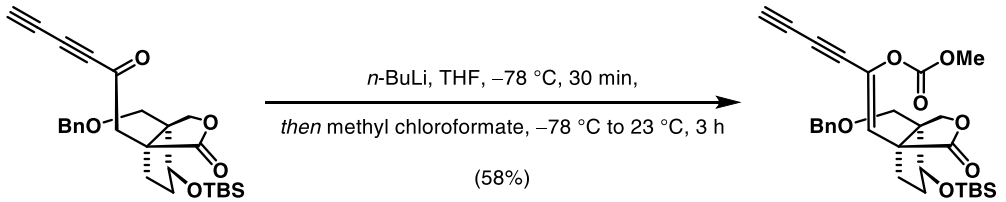
To a solution of ketone **258** (5.50 mg, 10.0 µmol, 1 equiv) in methanol (200 µL) was added cesium fluoride (1.72 mg, 11.0 µmol, 1.10 equiv) at 23 °C. After 90 minutes, water (5 mL) and dichloromethane (5 mL) were added to the reaction mixture and the layers were separated. The aqueous layer was extracted with dichloromethane (3 × 1 mL) and the combined organic layers were dried over sodium sulfate. The dried solution was filtered and the filtrate was concentrated. The residue was purified by flash column chromatography on silica gel (10% ethyl acetate in cyclohexane) to yield dialkyne **259** (1.70 mg, 3.60 µmol, 36%) as a colourless oil.

TLC (20% ethyl acetate in cyclohexane): R_f = 0.50 (CAM, UV).

^{1}H NMR (400 MHz, chloroform-*d*) δ 7.40 – 7.27 (m, 5H), 4.66 (d, *J* = 9.3 Hz, 1H), 4.46 – 4.35 (m, 3H), 3.73 (d, *J* = 9.4 Hz, 1H), 3.40 (d, *J* = 19.4 Hz, 1H), 3.34 – 3.27 (m, 2H), 3.16 (d, *J* = 19.3 Hz, 1H), 2.69 (s, 1H), 1.99 (dd, *J* = 12.8, 6.5 Hz, 1H), 1.84 (dt, *J* = 12.0, 5.9 Hz, 1H), 1.63 – 1.55 (m, 1H), 1.48 – 1.39 (m, 1H), 0.86 (s, 9H), 0.06 – 0.00 (m, 6H).

IR (Diamond-ATR, neat) $\tilde{\nu}_{max}$: 2966 (s), 2929 (s), 2228 (w), 1759 (s), 1667 (m), 1354 (m), 1253 (m), 1132 (m), 1027 (m), 834 (s), 777 (m) cm^{-1}.

HRMS (ESI) calc. for $C_{27}H_{35}O_5Si$ $[M+H]^+$: 467.2248 found: 467.2243.



259 **260**

Carbonate 260

To a solution of dialkyne **259** (1.70 mg, 3.36 µmol, 1 equiv) in tetrahydrofuran (50 µL) was added a solution of *n*-butyllithium (20.0 mM in hexanes, 200 µL, 4.01 µmol, 1.10 equiv) at –78 °C. After 30 minutes, methyl chloroformate (3.70 µL, 4.74 µmol, 1.30 equiv) was added to the solution at –78 °C. After one hour, the reaction mixture was allowed to warm to 23 °C over the course of two hours. Then, the mixture was concentrated and the residue was purified by flash column chromatography on silica

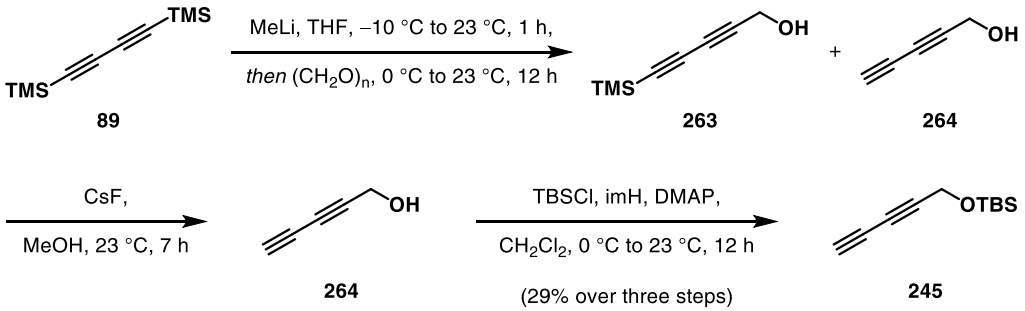
gel (20% ethyl acetate in cyclohexane) to yield carbonate **260** (1.10 mg, 2.10 µmol, 58%) as a colourless oil.

TLC (30% ethyl acetate in cyclohexane): R_f = 0.41 (CAM, UV).

^{1}H NMR (400 MHz, chloroform-*d*) δ 7.36 – 7.24 (m, 5H), 5.73 (s, 1H), 4.63 (d, *J* = 9.2 Hz, 1H), 4.42 (s, 2H), 4.40 – 4.33 (m, 1H), 3.82 (s, 3H), 3.62 (d, *J* = 9.4 Hz, 1H), 3.26 (d, *J* = 2.2 Hz, 2H), 2.50 (s, 1H), 2.31 – 2.21 (m, 1H), 1.90 (ddd, *J* = 18.6, 12.8, 6.5 Hz, 1H), 1.71 (td, *J* = 13.1, 6.2 Hz, 1H), 1.44 – 1.38 (m, 1H), 0.82 (s, 9H), 0.01 – –0.05 (m, 6H).

IR (Diamond-ATR, neat) $\tilde{\upsilon}_{max}$: 2954 (m), 2930 (w), 2232 (w), 1736 (s), 1667 (m), 1439 (w), 1356 (w), 1253 (w), 1128 (m), 1022 (w), 986 (m), 834 (m), 805 (w), 777 (w) cm^{-1}.

HRMS (ESI) calc. for $C_{29}H_{36}NaO_7Si$ $[M+Na]^+$: 547.2123 found: 547.2129.



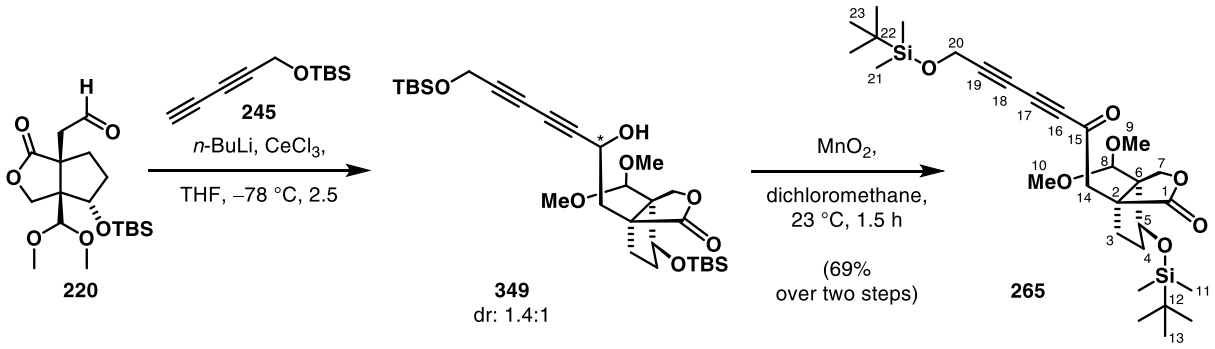
Propargyl alcohol 245

To a solution of dialkyne **89** (6.04 g, 31.1 mmol, 1 equiv) in tetrahydrofuran (80 mL) was added a solution of methyllithium (1.55 M in diethyl ether, 25.1 mL, 38.8 mmol, 1.25 equiv) at –10 °C over the course of 15 minutes. After the addition was completed, the reaction mixture was allowed to warm to 23 °C. After one hour at 23 °C, a suspension of paraformaldehyde (1.77 g, 55.9 mmol, 1.80 equiv) was added to the brown solution at 0 °C over the course of 15 minutes. After the addition was completed, the mixture was allowed to warm to 23 °C. After 12 hours, a saturated aqueous solution of ammonium chloride (50 mL) and diethyl ether (50 mL) were added to the reaction mixture and the layers were separated. The aqueous layer was extracted with diethyl ether (3 × 30 mL) and the combined organic layers were dried over sodium sulfate. The dried solution was filtered and the filtrate was concentrated to yield a mixture of silylated and desilylated propargyl alcohol **263** and **264** (4.03 g) as a colourless oil which was used in the next step without further purification.

To a solution of the crude mixture of propargyl alcohol **263** and **264** (4.03 g, 26.5 mmol, 1 equiv based on **263**) in methanol (100 mL) was added cesium fluoride (8.53 g, 55.6 mmol, 2.10 equiv based on **263**) at 23 °C. After seven hours, the reaction mixture was concentrated and the residue was partitioned between water (50 mL) and diethyl ether (50 mL). The layers were separated and the aqueous layer was extracted with diethyl ether (3 × 10 mL) and the combined organic layers were dried over sodium

sulfate. The dried solution was filtered and the filtrate was concentrated to yield crude propargyl alcohol **264** as a yellow oil. The obtained analytical data were in full agreement with those reported in the literature.[166]

To a solution of crude propargyl alcohol **264** (2.07 g, 25.8 mmol, 1 equiv) in dichloromethane (100 mL) was added imidazole (5.28 g, 77.5 mmol, 3.00 equiv) and 4-dimethylaminopyridine (319 mg, 2.58 mmol, 0.100 equiv) in sequence at 0 °C. After 15 minutes, *tert*-butyldimethylchlorosilane (4.87 g, 32.3 mmol, 1.25 equiv) was added to the solution at 0 °C and then the mixture was allowed to warm to 23 °C. After 12 hours at 23 °C, water (100 mL) was added to the reaction mixture and the layers were separated. The aqueous layer was extracted with dichloromethane (3 × 20 mL) and the combined organic layers were dried over sodium sulfate. The dried solution was filtered and the filtrate was concentrated. The residue was purified by flash column chromatography on silica gel (1% ethyl acetate in cyclohexane) to yield propargyl alcohol **245** (1.10 g, 2.10 mmol, 58%) as a yellow oil. The obtained analytical data were in full agreement with those reported in the literature.[167]



Ketone 265

Cerium(III) chloride (92.9 mg, 375 µmol, 3.00 equiv) was suspended in tetrahydrofuran (0.5 mL). In another flask, a solution of *n*-butyllithium (800 mM in hexane, 469 µL, 375 µmol, 3.00 equiv) was added to a solution of dialkyne **245** (72.9 mg, 375 µmol, 3.00 equiv) in tetrahydrofuran (0.3 mL) at –78 °C. After one hour, the cerium(III) chloride suspension was cooled to –78 °C and then the lithium acetylide was added to the suspension at –78 °C and the transfer was quantified with tetrahydrofuran (0.5 mL). After one hour, a solution of aldehyde **220** (46.6 mg, 125 µmol, 1 equiv) in tetrahydrofuran (0.5 mL) was added to the organocerium species at –78 °C. After 30 minutes, a saturated aqueous solution of ammonium chloride (10 mL) was added to the reaction mixture and the layers were separated. The aqueous layer was extracted with diethyl ether (3 × 3 mL) and the combined organic layers were dried over sodium sulfate. The dried solution was filtered through a pad of Celite and the filtrate was concentrated to yield crude propargyl alcohol **349** in a diastereomeric ratio of 1.4:1 (71.0 mg, 125 µmol) as an orange oil.

[166] X. Ouyang, F. W. Fowler, J. W. Lauher, *J. Am. Chem. Soc.* **2003**, *125*, 12400-12401.
[167] P. Gangadhar, A. Sathish Reddy, P. Srihari, *Tetrahedron* **2016**, *72*, 5807-5817.

To a solution of crude alcohol **349** (71.0 mg, 125 µmol, 1 equiv) in dichloromethane (2 mL) was added manganese dioxide (109 mg, 1.25 mmol, 10.0 equiv) at 23 °C. After 30 minutes, another portion of manganese dioxide (218 mg, 2.50 mmol, 20.0 equiv) was added to the mixture. After one hour, the reaction mixture was filtered through a pad of Celite and the pad was washed with dichloromethane (5 mL). The filtrate was concentrated and the residue was purified by flash column chromatography on silica gel (5% ethyl acetate in cyclohexane) to yield TMS alkyne **265** (49.0 mg, 87.0 µmol, 69%) as a slightly yellow oil.

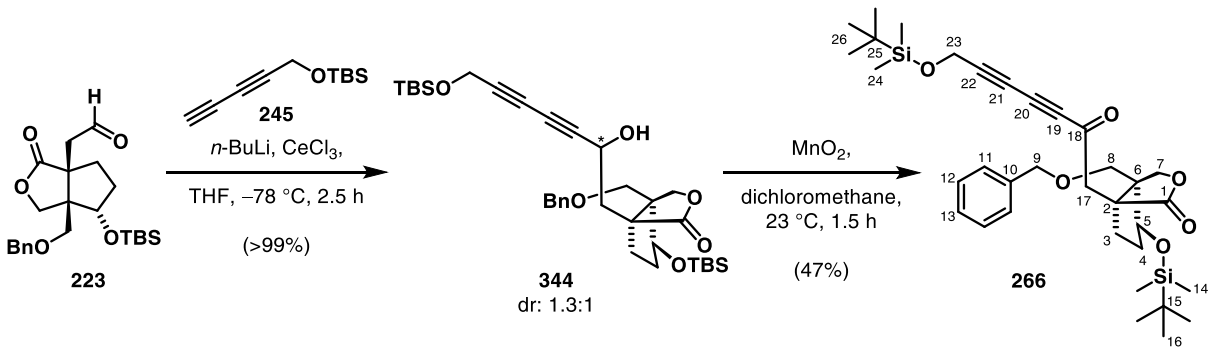
TLC (30% ethyl acetate in cyclohexane): R_f = 0.60 (CAM, UV).

^{1}H NMR (600 MHz, chloroform-*d*) δ 4.76 (d, *J* = 8.9 Hz, 1H, 7-H), 4.49 (dd, *J* = 9.7, 6.6 Hz, 1H, 5-H), 4.44 (s, 2H, 20-H), 4.14 – 4.12 (m, 1H, 8-H), 4.08 (d, *J* = 8.9 Hz, 1H, 7-H), 3.47 – 3.45 (m, 6H, 9-H, 10-H), 3.22 (d, *J* = 19.0 Hz, 1H, 14-H), 3.15 (d, *J* = 19.0 Hz, 1H, 14-H), 1.98 – 1.90 (m, 2H, 3-H, 4-H), 1.61 (td, *J* = 12.7, 6.3 Hz, 1H, 3-H), 1.37 (ddt, *J* = 12.7, 9.8, 6.2 Hz, 1H, 4-H), 0.91 – 0.87 (m, 18H, 13-H, 23-H), 0.13 (s, 6H, 11-H or 21-H), 0.05 (s, 6H, 11-H, 21-H).

^{13}C NMR (151 MHz, chloroform-*d*) δ 184.4 (C-15), 181.7 (C-1), 108.6 (C-8), 87.1 (C-19), 75.4 (C-17), 75.2 (C-5), 74.5 (C-16), 68.2 (C-7), 67.9 (C-18), 59.2 (C-9 or C-10), 58.2 (C-6), 57.6 (C-9 or C-10), 52.7 (C-2), 52.3 (C-20), 49.6 (C-14), 34.7 (C-3), 32.7 (C-4), 25.9 (C-13 or C-23), 25.8 (C-13 or C-23), 18.4 (C-12 or C-22), 18.1 (C-12 or C-22), –4.3 (C-11 or C-21), –5.0 (C-11 or C-21), –5.1 (C-11 or C-21).

IR (Diamond-ATR, neat) $\tilde{\upsilon}_{max}$: 2955 (s), 2929 (s), 2857 (m), 2233 (w), 2149 (w), 1767 (s), 1676 (m), 1471 (w), 1361 (w), 1253 (m), 1152 (m), 1092 (s), 1027 (m), 900 (w), 834 (s), 777 (m) cm^{-1}.

HRMS (ESI) calc. for $C_{29}H_{48}NaO_7Si_2$ $[M+Na]^+$: 587.2831 found: 587.2858.



Propargyl alcohol 344

Cerium(III) chloride (92.3 mg, 373 µmol, 3.00 equiv) was suspended in tetrahydrofuran (0.5 mL). In another flask, a solution of *n*-butyllithium (800 mM in hexane, 466 µL, 373 µmol, 3.00 equiv) was added to a solution of dialkyne **245** (72.4 mg, 373 µmol, 3.00 equiv) in tetrahydrofuran (0.3 mL) at –78 °C. After one hour, the cerium(III) chloride suspension was cooled to –78 °C and then the lithium acetylide

was added to the suspension at –78 °C and the transfer was quantified with tetrahydrofuran (0.5 mL). After one hour, a solution of aldehyde **223** (52.0 mg, 124 µmol, 1 equiv) in tetrahydrofuran (0.5 mL) was added to the organocerium species at –78 °C. After 30 minutes, a saturated aqueous solution of ammonium chloride (10 mL) was added to the reaction mixture and the layers were separated. The aqueous layer was extracted with diethyl ether (3 × 3 mL) and the combined organic layers were dried over sodium sulfate. The dried solution was filtered through a pad of Celite and the filtrate was concentrated. The residue was purified by flash column chromatography on silica gel (10% ethyl acetate in cyclohexane) to yield the propargyl alcohol **344** in a diastereomeric ratio of 1.3:1 (79.0 mg, 129 µmol, >99%) as an orange oil.

TLC (10% ethyl acetate in cyclohexane): R_f = 0.14 and 0.22 (CAM, UV).

^{1}H NMR (400 MHz, chloroform-*d*) *complex mixture of signals arising from different diastereomers in a ratio of 1.3:1*

^{13}C NMR (151 MHz, chloroform-*d*) *complex mixture of signals arising from different diastereomers in a ratio of 1.3:1*

IR (Diamond-ATR, neat) $\tilde{\upsilon}_{max}$: 3398 (br, w), 2954 (w), 2929 (w), 2857 (w), 1761 (w), 1471 (w), 1362 (w), 1254 (m), 1089 (s), 836 (s), 778 (m), 699 (w) cm^{-1}.

HRMS (ESI) calc. for $C_{34}H_{50}NaO_6Si_2$ $[M+Na]^+$: 633.3038 found: 633.3024.

Ketone 266

To a solution of alcohol **344** (77.0 mg, 126 µmol, 1 equiv) in dichloromethane (2 mL) was added manganese dioxide (109 mg, 1.25 mmol, 20.0 equiv) at 23 °C. After 1.5 hours, the reaction mixture was filtered through a pad of Celite and the pad was washed with dichloromethane (5 mL). The filtrate was concentrated and the residue was purified by flash column chromatography on silica gel (5% ethyl acetate in cyclohexane) to yield ketone **266** (49.0 mg, 87.0 µmol, 69%) as a slightly yellow oil.

TLC (30% ethyl acetate in cyclohexane): R_f = 0.59 (CAM, UV).

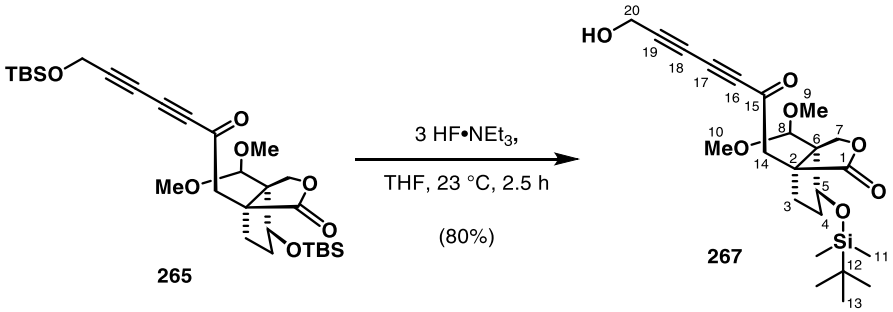
^{1}H NMR (400 MHz, chloroform-*d*) δ 7.24 – 7.15 (m, 5H, 11-H, 12-H, 13-H), 4.52 (d, *J* = 9.3 Hz, 1H, 7-H), 4.32 (s, 2H, 23-H), 4.29 – 4.24 (m, 3H, 9-H, 5-H), 3.60 (d, *J* = 9.3 Hz, 1H, 7-H), 3.27 (d, *J* = 19.3 Hz, 1H, 17-H), 3.20 – 3.15 (m, 2H, 8-H), 3.03 (d, *J* = 19.3 Hz, 1H, 17-H), 1.88 – 1.82 (m, 1H, 3-H), 1.74 – 1.68 (m, 1H, 4-H), 1.48 – 1.41 (m, 1H, 3-H), 1.34 – 1.26 (m, 1H, 4-H), 0.78 – 0.73 (m, 18H, 16-H, 26-H), 0.00 (s, 6H, 14-H or 24-H), –0.09 – –0.13 (m, 6H, 14-H or 24-H).

^{13}C NMR (101 MHz, chloroform-*d*) δ 184.5 (C-18), 182.1 (C-1), 137.3 (C-10), 128.7 (C-12), 128.3 (C-11), 128.2 (C-13), 87.3 (C-22), 75.9 (C-20), 75.0 (C-5), 74.4 (C-19), 73.9 (C-9), 69.8 (C-8), 68.3 (C-7), 67.8 (C-21), 53.6 (C-6), 52.3 (C-23), 51.6 (C-2), 50.1 (C-17), 34.6 (C-3), 31.2 (C-4), 25.8 (C-16, C-26),

18.4 (C-15 or C-25), 18.0 (C-15 or C-25), –4.3 (C-11 or C-21), –5.0 (C-11 or C-21), –5.1 (C-11 or C-21).

IR (Diamond-ATR, neat) $\tilde{\upsilon}_{max}$: 2954 (w), 2929 (w), 2857 (w), 2233 (w), 2149 (w), 1769 (m), 1675 (w), 1474 (w), 1361 (w), 1253 (m), 1153 (m), 1091 (s), 1031 (m), 891 (w), 835 (s), 778 (m) cm^{-1}.

HRMS (ESI) calc. for $C_{34}H_{50}NaO_6Si_2$ $[M+Na]^+$: 633.3038 found: 633.3024.



Propargylic alcohol 267

To a solution of ketone **265** (11.0 mg, 19.5 µmol, 1 equiv) in tetrahydrofuran (500 µL) was added hydrogen fluoride triethylamine (32.0 µL, 195 µmol, 10.0 equiv) at 23 °C. After 2.5 hours, a saturated aqueous solution of sodium bicarbonate (5 mL) and ethyl acetate (5 mL) were added to the reaction mixture and the layers were separated. The aqueous layer was extracted with ethyl acetate (3 × 5 mL) and the combined organic layers were dried over sodium sulfate. The dried solution was filtered and the filtrate was concentrated. The residue was purified by flash column chromatography on silica gel (50% ethyl acetate in cyclohexane) to yield propargylic alcohol **267** (7.00 mg, 15.5 µmol, 80%) as a yellow oil.

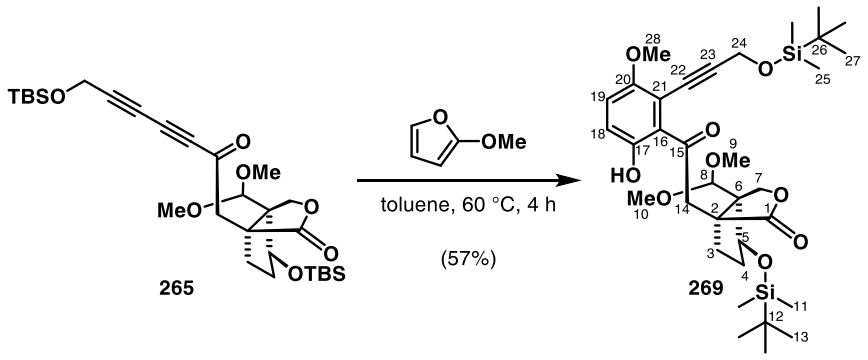
TLC (50% ethyl acetate in cyclohexane): R_f = 0.33 (CAM, UV).

^{1}H NMR (400 MHz, chloroform-*d*) δ 4.76 (d, *J* = 8.9 Hz, 1H, 7-H), 4.49 (dd, *J* = 9.7, 6.5 Hz, 1H, 5-H), 4.42 (s, 2H, 20-H), 4.13 (s, 1H, 8-H), 4.07 (d, *J* = 8.9 Hz, 1H, 7-H), 3.47 – 3.45 (m, 6H, 9-H, 10-H), 3.23 (d, *J* = 19.0 Hz, 1H, 14-H), 3.14 (d, *J* = 19.0 Hz, 1H, 14-H), 1.99 – 1.90 (m, 2H, 3-H, 4-H), 1.67 – 1.59 (m, 1H, 3-H), 1.41 – 1.33 (m, 1H, 4-H), 0.88 (s, 9H, 13-H), 0.05 (s, 6H. 11-H).

^{13}C NMR (101 MHz, chloroform-*d*) δ 184.2 (C-15), 181.8 (C-1), 108.6 (C-8), 86.2 (C-19), 75.2 (C-5), 74.9 (C-16 or C-17), 74.9 (C-16 or C-17), 68.7 (C-18), 68.2 (C-7), 59.2 (C-9 or C-10), 58.3 (C-6), 57.6 (C-9 or C-10), 52.6 (C-2), 51.6 (C-20), 49.5 (C-14), 34.7 (C-3), 32.7 (C-4), 25.9 (C-13), 18.1 (C-12), –4.3 (C-11), –5.0 (C-11).

IR (Diamond-ATR, neat) $\tilde{\upsilon}_{max}$: 3418 (br, w), 2955 (w), 2929 (w), 2856 (w), 2231 (w), 2149 (w), 1766 (m), 1675 (m), 1471 (w), 1360 (w), 1252 (m), 1153 (m), 1106 (m), 1069 (s), 1026 (m), 838 (m), 777 (w) cm^{-1}.

HRMS (ESI) calc. for $C_{23}H_{34}NaO_7Si$ [M+Na]$^+$: 473.1966 found: 473.1975.



Phenol 269

To a solution of ketone **265** (15.0 mg, 26.6 µmol, 1 equiv) and 2-methoxyfuran (12.6 µL, 133 µmol, 5.00 equiv) in toluene (300 µL) was heated to 60 °C. After four hours, the reaction mixture was allowed to cool to 23 °C and the solution was concentrated. The residue was purified by flash column chromatography on silica gel (10% ethyl acetate in cyclohexane) to yield phenol **269** (10.0 mg, 15.1 µmol, 57%) as a yellow oil.

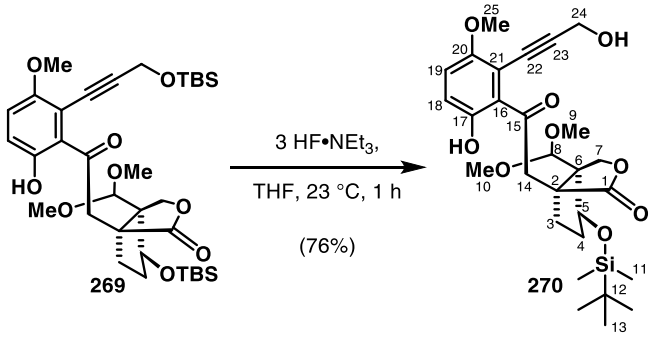
TLC (30% ethyl acetate in cyclohexane): R_f = 0.30 (CAM, UV).

^{1}H NMR (400 MHz, chloroform-*d*) δ 8.30 (s, 1H, 20-OH), 6.95 (d, *J* = 9.0 Hz, 1H, 19-H), 6.75 (d, *J* = 9.0 Hz, 1H, 18-H), 5.11 (s, 2H, 24-H), 4.81 (d, *J* = 8.9 Hz, 1H, 7-H), 4.56 (dd, *J* = 9.7, 6.6 Hz, 1H, 5-H), 4.22 (s, 1H, 8-H), 4.15 (d, *J* = 8.9 Hz, 1H, 7-H), 3.83 (s, 3H, 28-H), 3.48 (s, 3H, 9-H or 10-H), 3.46 (s, 3H, 9-H or 10-H), 3.30 (d, *J* = 1.6 Hz, 2H, 14-H), 2.00 (ddd, *J* = 12.5, 6.7, 1.8 Hz, 1H, 3-H), 1.92 (ddd, *J* = 12.6, 6.3, 1.9 Hz, 1H, 4-H), 1.62 (td, *J* = 12.7, 6.2 Hz, 1H, 3-H), 1.39 (ddd, *J* = 12.6, 6.4, 3.4 Hz, 1H, 4-H), 0.93 (s, 9H, 13-H or 27-H), 0.89 (s, 9H, 13-H or 27-H), 0.17 (s, 6H, 11-H or 25-H), 0.06 (s, 6H, 11-H or 25-H).

^{13}C NMR (101 MHz, chloroform-*d*) δ 185.0 (C-15), 182.0 (C-1), 155.9 (C-17), 150.8 (C-20), 127.5 (C-16), 121.0 (C-19), 111.3 (C-18), 108.9 (C-8), 106.2 (C-21), 96.1 (C-23), 86.2 (C-22), 75.0 (C-5), 68.3 (C-7), 64.1 (C-24), 59.2 (C-9 or C-10), 57.9 (C-6), 57.4 (C-9 or C-10), 56.5 (C-28), 53.0 (C-2), 50.0 (C-14), 34.8 (C-3), 32.9 (C-4), 25.9 (C-13 or C-27), 25.8 (C-13 or C-27), 18.3 (C-12 or C-26), 18.1 (C-12 or C-26), –4.4 (C-11 or C-25), –5.0 (C-11 or C-25), –5.4 (C-11 or C-25).

IR (Diamond-ATR, neat) $\tilde{\upsilon}_{max}$: 3342 (br, w), 2954 (br, w), 2930 (m), 2857 (w), 2189 (w), 1768 (m), 1671 (w), 1471 (m), 1258 (m), 1185 (m), 1116 (s), 1072 (s), 837 (s), 779 (m) cm^{-1}.

HRMS (ESI) calc. for $C_{34}H_{54}NaO_9Si_2$ [M+Na]$^+$: 685.3199 found: 685.3182.



Propargyl alcohol 270

To a solution of phenol **269** (8.00 mg, 12.1 µmol, 1 equiv) in tetrahydrofuran (300 µL) was added triethylamine trihydrofluoride (20.1 µL, 121 µmol, 10.0 equiv) at 23 °C. After one hour, a saturated aqueous solution of sodium bicarbonate (5 mL) and dichloromethane (5 mL) were added to the reaction mixture and the layers were separated. The aqueous layer was extracted with dichloromethane (3 × 2 mL) and the combined organic layers were dried over sodium sulfate. The dried solution was filtered and the filtrate was concentrated. The residue was purified by flash column chromatography on silica gel (40% ethyl acetate in cyclohexane) to yield propargyl alcohol **270** (5.00 mg, 9.11 µmol, 76%) as a yellow oil.

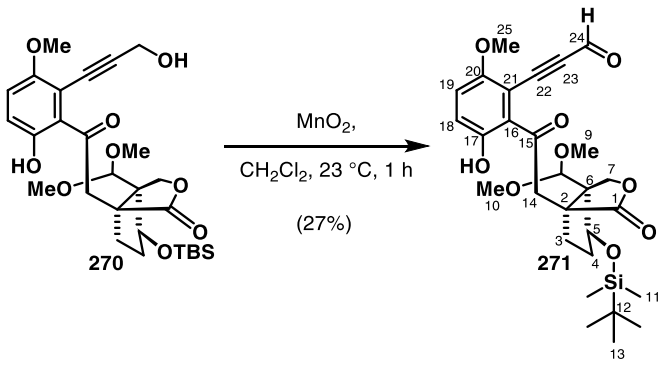
TLC (50% ethyl acetate in cyclohexane): R_f = 0.28 (CAM, UV).

^{1}H NMR (400 MHz, chloroform-*d*) δ 7.75 (s, 1H, 17-OH), 6.97 (d, *J* = 9.0 Hz, 1H, 19-H), 6.77 (d, *J* = 9.1 Hz, 1H, 18-H), 5.14 – 5.06 (m, 2H, 24-H), 4.81 (d, *J* = 8.9 Hz, 1H, 7-H), 4.56 (dd, *J* = 9.7, 6.6 Hz, 1H, 5-H), 4.24 (s, 1H, 8-H), 4.14 (d, *J* = 8.9 Hz, 1H, 7-H), 3.83 (s, 3H, 25-H), 3.49 – 3.46 (m, 6H, 9-H, 10-H), 3.29 (s, 2H, 14-H), 2.03 – 1.97 (m, 1H, 3-H), 1.93 (ddd, *J* = 12.7, 6.4, 1.9 Hz, 1H, 4-H), 1.64 (td, *J* = 12.6, 6.2 Hz, 1H, 3-H), 1.41 – 1.33 (m, 1H, 4-H), 0.88 (s, 9H, 13-H), 0.06 (s, 6H, 11-H).

^{13}C NMR (101 MHz, chloroform-*d*) δ 185.4 (C-15), 182.3 (C-1), 156.1 (C-20), 150.5 (C-17), 128.0 (C-16), 121.1 (C-19), 111.6 (C-18), 108.8 (C-8), 107.0 (C-21), 95.8 (C-23), 86.5 (C-22), 75.0 (C-5), 68.5 (C-7), 62.7 (C-24), 59.3 (C-9 or C-10), 58.0 (C-6), 57.4 (C-9 or C-10), 56.5 (C-25), 53.2 (C-2), 49.9 (C-14), 34.9 (C-3), 32.9 (C-4), 25.9 (C-13), 18.1 (C-12), –4.4 (C-11), –5.0 (C-11).

IR (Diamond-ATR, neat) $\tilde{\upsilon}_{max}$: 3324 (br, w), 2954 (w), 2855 (w), 2186 (w), 1737 (m), 1666 (m), 1462 (m), 1440 (w), 1270 (m), 1186 (m), 1153 (m), 1116 (s), 1069 (s), 1026 (s), 902 (m), 864 (m), 837 (m), 776 (m) cm^{-1}.

HRMS (ESI) calc. for $C_{28}H_{40}NaO_9Si$ $[M+Na]^+$: 571.2334 found: 571.2318.



Propargyl aldehyde 271

To a solution of propargyl alcohol **270** (5.90 mg, 10.8 µmol, 1 equiv) in dichloromethane (300 µL) was added manganese dioxide (18.7 mg, 215 µmol, 20.0 equiv) at 23 °C. After one hour, the suspension was filtered through a pad of Celite and the filtrate was concentrated to yield propargyl aldehyde **271** (1.60 mg, 2.93 mmol, 27%) as a yellow oil.

Note: The product is instable on silica gel and was used crude for further reactions.

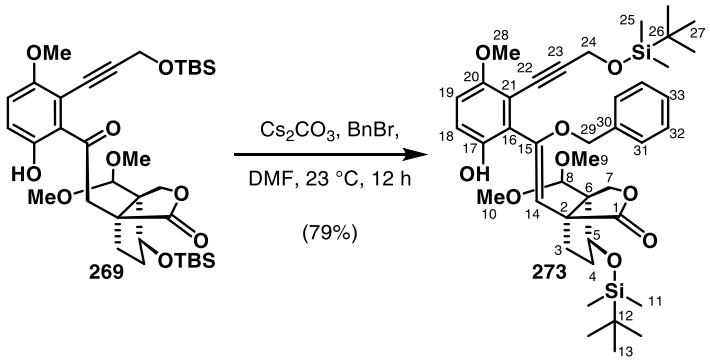
TLC (30% ethyl acetate in cyclohexane): R_f = 0.26 (CAM, UV).

^{1}H NMR (600 MHz, chloroform-*d*) δ 11.23 (s, 1H, 17-OH), 10.40 (s, 1H, 24-H), 7.20 (d, *J* = 9.3 Hz, 1H, 18-H), 7.10 (d, *J* = 9.3 Hz, 1H, 19-H), 4.80 (d, *J* = 8.9 Hz, 1H, 7-H), 4.55 (dd, *J* = 9.7, 6.6 Hz, 1H, 5-H), 4.22 (s, 1H, 8-H), 4.15 (d, *J* = 9.0 Hz, 1H, 7-H), 3.91 (s, 3H, 25-H), 3.48 (s, 6H, 9-H, 10-H), 3.33 (d, *J* = 7.2 Hz, 2H, 14-H), 2.01 (ddd, *J* = 12.6, 6.8, 1.9 Hz, 1H, 3-H), 1.95 (dtd, *J* = 12.9, 6.5, 1.9 Hz, 1H, 4-H), 1.67 (td, *J* = 12.7, 6.4 Hz, 1H, 3-H), 1.42 – 1.36 (m, 1H, 4-H), 0.89 (s, 9H, 13-H), 0.07 – 0.06 (m, 6H, 11-H).

^{13}C NMR (151 MHz, chloroform-*d*) δ 195.9 (C-24), 184.8 (C-15), 181.9 (C-1), 156.5 (C-20), 156.0 (C-17), 144.3 (C-16), 122.2 (C-19), 121.1 (C-18), 119.6 (C-21), 108.8 (C-8), 95.9 (C-23), 82.7 (C-22), 75.1 (C-5), 68.3 (C-7), 59.3 (C-9 or C-10), 58.2 (C-6), 57.5 (C-9 or C-10), 57.0 (C-25), 52.9 (C-2), 49.8 (C-14), 34.8 (C-3), 32.8 (C-4), 25.9 (C-13), 18.1 (C-12), –4.3 (C-11), –4.9 (C-11).

IR (Diamond-ATR, neat) $\tilde{\upsilon}_{max}$: 2958 (m), 2929 (m), 2854 (w), 2195 (m), 2181 (m), 1765 (s), 1657 (m), 1474 (m), 1293 (w), 1271 (m), 1152 (m), 1118 (s), 1071 (m), 1027 (m), 1006 (m), 900 (m), 838 (m), 777 (w) cm^{-1}.

HRMS (ESI) calc. for $C_{28}H_{38}NaO_9Si$ $[M+Na]^+$: 569.2177 found: 569.2161.



Benzyl enol ether 273

To a solution of phenol **269** (2.00 mg, 3.02 µmol, 1 equiv) in *N*-*N*-dimethylformamide (100 µL) was added cesium carbonate (3.97 mg, 12.1 µmol, 4.00 equiv) and benzyl bromide (0.700 µL, 6.03 µmol, 2.00 equiv) at 23 °C. After 12 hours, water (5 mL) and diethyl ether (5 mL) were added to the reaction mixture and the layers were separated. The aqueous layer was extracted with diethyl ether (3 × 2 mL), the combined organic layers were washed with a 10% aqueous solution of lithium chloride (5 mL) and the washed organic layers were dried over sodium sulfate. The dried solution was filtered and the filtrate was concentrated. The residue was purified by flash column chromatography on silica gel (20% ethyl acetate in cyclohexane) to yield benzyl enol ether **273** (1.80 mg, 2.39 µmol, 79%) as a yellow oil.

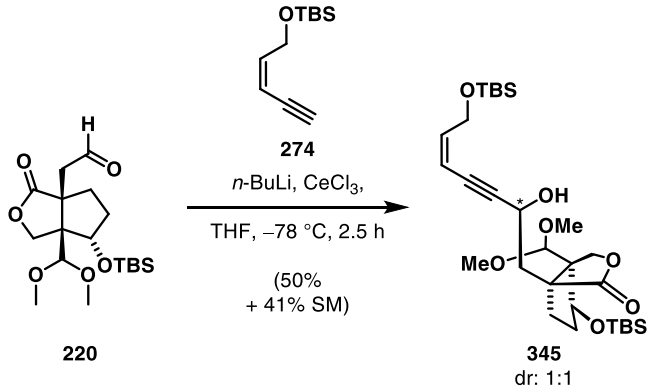
TLC (30% ethyl acetate in cyclohexane): R_f = 0.38 (CAM, UV).

^{1}H NMR (400 MHz, chloroform-*d*) δ 7.52 – 7.49 (m, 2H, 31-H), 7.40 – 7.34 (m, 3H, 32-H, 33-H), 7.04 (d, *J* = 8.9 Hz, 1H, 18-H), 6.84 (d, *J* = 9.0 Hz, 1H, 19-H), 5.33 (d, *J* = 11.3 Hz, 1H, 29-H), 5.05 (s, 1H, 14-H), 4.92 (d, *J* = 11.2 Hz, 1H, 29-H), 4.78 (d, *J* = 0.9 Hz, 2H, 24-H), 4.63 (d, *J* = 8.9 Hz, 1H, 7-H), 4.55 (dd, *J* = 9.6, 6.7 Hz, 1H, 5-H), 4.07 (s, 1H, 8-H), 3.83 (s, 3H, 28-H), 3.77 (d, *J* = 8.8 Hz, 1H, 7-H), 3.46 (s, 3H, 9-H or 10-H), 3.24 (s, 3H, 9-H or10-H), 2.23 (q, *J* = 6.1 Hz, 1H, 3-H), 1.94 (dt, *J* = 12.6, 6.3 Hz, 1H, 4-H), 1.65 (td, *J* = 12.9, 6.0 Hz, 1H, 3-H), 1.37 – 1.32 (m, 1H, 4-H), 0.88 (s, 9H, 13-H or 27-H), 0.85 (s, 9H, 13-H or 27-H), 0.07 – 0.06 (m, 6H, 11-H or 25-H), 0.03 – 0.00 (m, 6H, 11-H or 25-H).

^{13}C NMR (151 MHz, chloroform-*d*) δ 181.5 (C-1), 158.7 (C-17), 143.3 (C-20), 138.3 (C-15), 136.9 (C-30), 135.2 (C-16), 129.1 (C-31), 128.6 (C-32), 128.4 (C-33), 124.5 (C-18), 118.0 (C-14), 112.4 (C-21), 110.5 (C-19), 109.9 (C-8), 91.2 (C-23), 86.9 (C-22), 73.4 (C-5), 71.7 (C-29), 68.4 (C-7), 60.6 (C-6), 59.8 (C-24), 58.9 (C-9 or C-10), 58.0 (C-9 or C-10), 56.3 (C-2), 56.2 (C-28), 35.8 (C-3), 34.1 (C-4), 26.1 (C-13 or C-27), 25.9 (C-13 or C-27), 18.5 (C-12 or C-26), 18.2 (C-12 or C-26), –4.6 (C-11 or C-25), –5.0 (C-11 or C-25).

IR (Diamond-ATR, neat) $\tilde{\upsilon}_{max}$: 3400 (br, w), 2927 (s), 2854 (m), 1765 (m), 1736 (m), 1460 (m), 1386 (m), 1255 (m), 1149 (m), 1069 (m), 1029 (m), 974 (m), 877 (m), 837 (m), 778 (m), 699 (w), 448 (w), 414 (w) cm^{-1}.

HRMS (ESI) calc. for $C_{41}H_{60}NaO_9Si_2$ $[M+Na]^+$: 775.3668 found: 775.3691.



Propargyl alcohol 345

Cerium(III) chloride (45.9 mg, 185 µmol, 3.00 equiv) was suspended in tetrahydrofuran (0.5 mL). In another flask, a solution of *n*-butyllithium (800 mM in hexane, 232 µL, 185 µmol, 3.00 equiv) was added to a solution of enyne **274**[168] (36.4 mg, 185 µmol, 3.00 equiv) in tetrahydrofuran (0.3 mL) at –78 °C. After one hour, the cerium(III) chloride suspension was cooled to –78 °C and then the lithium acetylide was added to the suspension at –78 °C and the transfer was quantified with tetrahydrofuran (0.3 mL). After one hour, a solution of aldehyde **220** (23.0 mg, 62.0 µmol, 1 equiv) in tetrahydrofuran (0.5 mL) was added to the organocerium species at –78 °C. After 30 minutes, a saturated aqueous solution of ammonium chloride (10 mL) was added to the reaction mixture and the layers were separated. The aqueous layer was extracted with diethyl ether (3 × 3 mL) and the combined organic layers were dried over sodium sulfate. The dried solution was filtered through a pad of Celite and the filtrate was concentrated. The residue was purified by flash column chromatography on silica gel (10% grading to 20% ethyl acetate in cyclohexane) to yield the propargyl alcohol **345** in a diastereomeric ratio of 1:1 (17.5 mg, 31.0 µmol, 50%) as a colourless oil together with reisolated starting material (9.40 mg, 25.0 µmol, 41%).

TLC (30% ethyl acetate in cyclohexane): R_f = 0.43 (CAM, UV).

^{1}H NMR (400 MHz, chloroform-*d*) δ 6.01 (dtd, *J* = 10.9, 6.2, 1.9 Hz, 1H), 5.56 – 5.47 (m, 1H), 4.95 – 4.87 (m, 0.5H), 4.82 (dtd, *J* = 9.2, 3.5, 1.8 Hz, 0.5H), 4.64 (dd, *J* = 14.4, 9.3 Hz, 1H), 4.49 (ddd, *J* = 8.3, 6.8, 4.2 Hz, 1H), 4.43 (s, 0.5H), 4.41 (dt, *J* = 6.2, 1.8 Hz, 2H), 4.32 (s, 0.5H), 4.04 (d, *J* = 9.2 Hz, 0.5H), 3.95 (d, *J* = 9.4 Hz, 0.5H), 3.53 – 3.50 (m, 6H), 2.25 – 2.20 (m, 1H), 2.05 – 1.96 (m, 1H), 1.81 (ddd, *J* = 13.1, 11.6, 7.2 Hz, 0.5H), 1.69 (td, *J* = 12.6, 6.8 Hz, 0.5H), 1.36 (dddd, *J* = 12.4, 8.0, 4.5, 2.6 Hz, 1H), 0.90 (s, 9H), 0.87 (s, 9H), 0.08 (s, 6H), 0.06 – 0.05 (m, 6H).

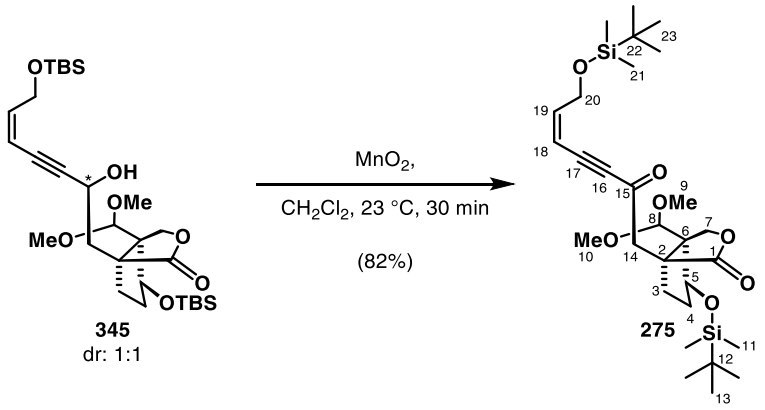
[168] I. V. Hartung, U. Eggert, L. O. Haustedt, B. Niess, P. M. Schäfer, H. M. R. Hoffmann, *Synthesis* **2003**, *2003*, 1844–1850.

^{13}C NMR (101 MHz, chloroform-*d*) δ 183.3, 182.2, 143.3, 143.2, 108.9, 108.8, 108.7, 108.6, 96.1, 95.9, 80.5, 80.3, 74.6, 74.5, 68.6, 68.2, 61.8, 61.8, 60.6, 60.3, 60.1, 59.7, 59.2, 59.0, 58.0, 57.9, 54.7, 54.5, 40.2, 40.2, 34.2, 34.0, 33.8, 33.5, 27.1, 26.1, 25.9, 25.8, 18.5, 18.1, –4.3, –5.0, –5.0.

Note: The signals arise from a mixture of diastereomers.

IR (Diamond-ATR, neat) $\tilde{\upsilon}_{max}$: 3439 (br, w), 2955 (m), 2929 (m), 2857 (m), 1761 (m), 1472 (w), 1254 (w), 1095 (s), 837 (s), 777 (m) cm^{-1}.

HRMS (ESI) calc. for $C_{29}H_{52}NaO_7Si_2$ $[M+Na]^+$: 591.3144 found: 591.3132.



Ketone 275

To a solution of propargyl alcohol **345** (17.5 mg, 31.0 µmol, 1 equiv) in dichloromethane (400 µL) was added manganese dioxide (60.8 mg, 615 µmol, 20.0 equiv) at 23 °C. After 30 minutes, the suspension was filtered through a pad of Celite, the filter cake was washed with dichloromethane (5 mL), the filtrate was concentrated. The filtrate was concentrated and the residue was purified by flash column chromatography on silica gel (10% ethyl acetate in cyclohexane) to yield ketone **275** (14.3 mg, 25.0 µmol, 82%) as a colourless oil.

TLC (30% ethyl acetate in cyclohexane): R_f = 0.58 (CAM, UV).

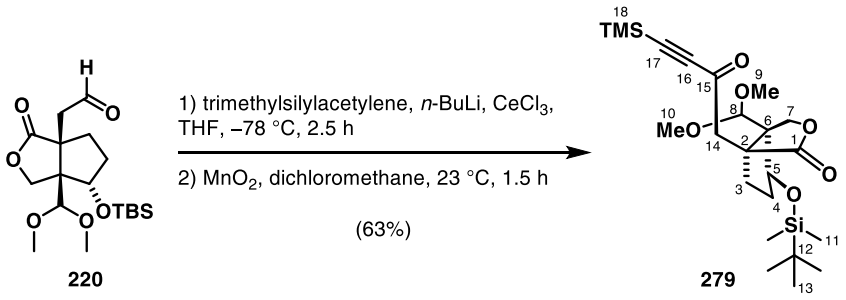
^{1}H NMR (600 MHz, chloroform-*d*) δ 6.36 (dt, *J* = 11.1, 6.1 Hz, 1H, 19-H), 5.63 (dt, *J* = 11.1, 1.8 Hz, 1H, 18-H), 4.79 (d, *J* = 8.8 Hz, 1H, 7-H), 4.53 (dd, *J* = 9.8, 6.6 Hz, 1H, 5-H), 4.45 (dd, *J* = 6.1, 1.7 Hz, 2H, 20-H), 4.17 (s, 1H, 8-H), 4.12 (d, *J* = 8.9 Hz, 1H, 7-H), 3.47 – 3.44 (m, 6H, 9-H, 10-H), 3.24 – 3.16 (m, 2H, 14-H), 1.97 (ddd, *J* = 12.6, 6.8, 1.8 Hz, 1H, 3-H), 1.91 (dtd, *J* = 12.8, 6.4, 1.8 Hz, 1H, 4-H), 1.60 (dt, *J* = 12.8, 6.4 Hz, 1H, 3-H), 1.36 (tdd, *J* = 12.8, 9.7, 6.8 Hz, 1H, 4-H), 0.91 (s, 9H, 13-H or 23-H), 0.88 (s, 9H, 13-H or 23-H), 0.09 (s, 6H, 11-H or 21-H), 0.05 (s, 6H, 11-H or 21-H).

^{13}C NMR (151 MHz, chloroform-*d*) δ 185.1 (C-15), 182.0 (C-1), 150.2 (C-19), 108.8 (C-8), 106.4 (C-18), 92.5 (C-17), 87.0 (C-16), 75.0 (C-5), 68.3 (C-7), 61.9 (C-20), 59.3 (C-9 or C-10), 58.0 (C-6), 57.4 (C-9 or C-10), 52.8 (C-2), 49.9 (C-14), 34.8 (C-3), 32.8 (C-4), 26.0 (C-13 or C-23), 25.9 (C-13 or C-

23), 18.4 (C-12 or C-22), 18.1 (C-12 or C-22), –4.4 (C-11 or C-21), –5.0 (C-11 or C-21), –5.0 (C-11 or C-21), –5.0 (C-11 or C-21).

IR (Diamond-ATR, neat) $\tilde{\upsilon}_{max}$: 2955 (m), 2930 (m), 2857 (w), 2188 (w), 1769 (m), 1673 (m), 1471 (w), 1254 (m), 1153 (m), 1102 (s), 1073 (m), 901 (w), 837 (s), 778 (m) cm^{-1}.

HRMS (ESI) calc. for $C_{29}H_{50}NaO_7Si_2$ $[M+Na]^+$: 589.2987 found: 589.2977.



TMS alkyne 279

Cerium(III) chloride (49.9 mg, 201 µmol, 5.00 equiv) was suspended in tetrahydrofuran (0.5 mL). In another flask, a solution of *n*-butyllithium (800 mM in hexane, 252 µL, 201 µmol, 5.00 equiv) was added to a solution of trimethylsilylacetylene (28.7 µL, 201 µmol, 5.00 equiv) in tetrahydrofuran (0.3 mL) at –78 °C. After one hour, the cerium(III) chloride suspension was cooled to –78 °C and then the lithium acetylide was added to the suspension at –78 °C and the transfer was quantified with tetrahydrofuran (0.5 mL). After one hour, a solution of aldehyde **220** (15.0 mg, 40.0 µmol, 1 equiv) in tetrahydrofuran (0.5 mL) was added to the organocerium species at –78 °C. After 30 minutes, a saturated aqueous solution of ammonium chloride (5 mL) was added to the reaction mixture and the layers were separated. The aqueous layer was extracted with diethyl ether (3 × 3 mL) and the combined organic layers were dried over sodium sulfate. The dried solution was filtered through a pad of Celite and the filtrate was concentrated to yield the propargylic alcohol (19.0 mg, 40.0 µmol) as a colourless oil.

To a solution of the crude alcohol (19.0 mg, 40.0 µmol, 1 equiv) in dichloromethane (1 mL) was added manganese dioxide (39.9 mg, 404 µmol, 10.0 equiv) at 23 °C. After 30 minutes, another portion of manganese dioxide (79.7 mg, 807 µmol, 20.0 equiv) was added. After one hour, the reaction mixture was filtered through a pad of Celite and the pad was washed with dichloromethane (5 mL). The filtrate was concentrated and the residue was purified by flash column chromatography on silica gel (5% ethyl acetate in cyclohexane) to yield TMS alkyne **279** (12.0 mg, 26.0 µmol, 63%) as a colourless solid.

TLC (30% ethyl acetate in cyclohexane): R_f = 0.41 (CAM, UV).

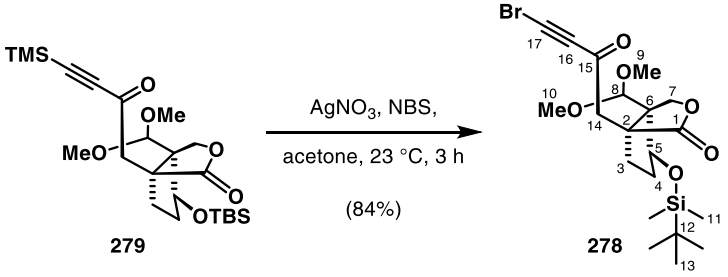
mp: (115-117) °C

^{1}H NMR (400 MHz, chloroform-*d*) δ 4.78 (d, *J* = 8.9 Hz, 1H, 7-H), 4.52 (dd, *J* = 9.7, 6.6 Hz, 1H, 5-H), 4.16 (s, 1H, 8-H), 4.11 (d, *J* = 8.9 Hz, 1H, 7-H), 3.46 – 3.45 (m, 6H, 9-H, 10-H), 3.18 (s, 2H, 14-H), 1.98 – 1.88 (m, 2H, 3-H, 4-H), 1.60 (dt, *J* = 12.8, 6.4 Hz, 1H, 3-H), 1.35 (tdd, *J* = 12.8, 10.0, 6.9 Hz, 1H, 4-H), 0.88 (s, 9H, 18-H), 0.24 (s, 9H, 13-H), 0.05 (s, 6H, 11-H).

^{13}C NMR (101 MHz, chloroform-*d*) δ 185.3 (C-15), 181.9 (C-1), 108.8 (C-8), 101.5 (C-16 or C-17), 99.1 (C-16 or C-17), 75.0 (C-5), 68.3 (C-7), 59.2 (C-9 or C-10), 58.0 (C-6), 57.3 (C-9 or C-10), 52.9 (C-2), 49.7 (C-14), 34.7 (C-3), 32.8 (C-4), 25.9 (C-13), 18.1 (C-12), –0.7 (C-18), –4.4 (C-11), –5.0 (C-11).

IR (Diamond-ATR, neat) $\tilde{\upsilon}_{max}$: 2957 (m), 2167 (w), 2036 (w), 1769 (s), 1680 (m), 1465 (w), 1253 (m), 1117 (s), 1073 (m), 843 (s), 779 (w) cm^{-1}.

HRMS (ESI) calc. for $C_{23}H_{41}O_6Si_2$ $[M+H]^+$: 469.2436 found: 469.2424; calc. for $C_{23}H_{40}NaO_6Si_2$ $[M+Na]^+$: 491,2256 found: 491.2242.



Bromoalkyne 278

To a solution of TMS alkyne **279** (11.1 mg, 24.0 µmol, 1 equiv) in acetone (500 µL) was added silver nitrate (2.01 mg, 12.0 µmol, 0.500 equiv) at 23 °C. After five minutes, *N*-bromosuccinimide (4.68 mg, 26.0 µmol, 1.10 equiv) was added to the suspension. After three hours, the reaction mixture was filtered through a pad of Celite and the pad was washed with acetone (3 mL). The filtrate was concentrated and the residue was purified by flash column chromatography on silica gel (10% ethyl acetate in cyclohexane) to yield bromoalkyne **278** (9.40 mg, 20.0 µmol, 84%) as a colourless oil.

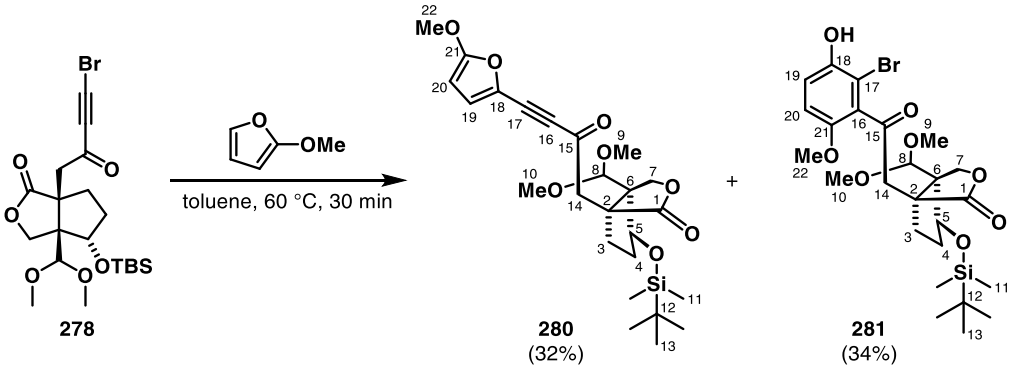
TLC (30% ethyl acetate in cyclohexane): R_f = 0.36 (CAM, UV).

^{1}H NMR (400 MHz, chloroform-*d*) δ 4.76 (d, *J* = 8.9 Hz, 1H, 7-H), 4.50 (dd, *J* = 9.7, 6.6 Hz, 1H, 5-H), 4.14 (s, 1H, 8-H), 4.08 (d, *J* = 8.9 Hz, 1H, 7-H), 3.47 – 3.45 (m, 6H, 9-H, 10-H), 3.24 – 3.11 (m, 2H, 14-H), 1.94 (dddd, *J* = 19.0, 12.7, 6.7, 1.8 Hz, 2H, 3-H, 4-H), 1.62 (dt, *J* = 12.8, 6.4 Hz, 1H, 3-H), 1.40 – 1.31 (m, 1H, 4-H), 0.88 (s, 9H, 13-H), 0.05 (s, 6H, 11-H).

^{13}C NMR (101 MHz, chloroform-*d*) δ 183.9 (C-15), 181.7 (C-1), 108.7 (C-8), 79.6 (C-17), 77.4 (C-16), 75.2 (C-5), 68.2 (C-7), 59.2 (C-9 or C-10), 58.2 (C-6), 57.6 (C-9 or C-10), 52.6 (C-2), 49.6 (C-14), 34.7 (C-3), 32.7 (C-4), 25.9 (C-13), 18.1 (C-12), –4.3 (C-11), –5.0 (C-11).

IR (Diamond-ATR, neat) $\tilde{\upsilon}_{max}$: 2955 (m), 2930 (m), 2856 (w), 2174 (m), 1766 (s), 1682 (m), 1471 (w), 1361 (w), 1253 (m), 1153 (s), 1129 (s), 1072 (m), 1027 (m), 900 (m), 838 (m), 776 (m) cm^{-1}.

HRMS (ESI) calc. for $C_{20}H_{31}BrNaO_6Si$ $[M+Na]^+$: 497.0965, 499.0945 found: 497.0952, 499.0931.



Furan 280 and Bromophenol 281

To a solution of bromoalkyne **278** (4.90 mg, 10.0 µmol, 1 equiv) in toluene (300 µL) was added 2-methoxyfuran (10.0 µL, 103 µmol, 10.0 equiv) and the reaction mixture was heated to 60 °C. After 30 minutes at 60 °C, the reaction mixture was allowed to cool to 23 °C and when 23 °C was reached, the solution was concentrated. The residue was purified by flash column chromatography on silica gel (20% ethyl acetate in cyclohexane) to yield furan **280** (1.60 mg, 3.25 µmol, 32%) and bromophenol **281** (2.00 mg, 3.49 µmol, 34%) as yellow solids.

Furan 280:

TLC (30% ethyl acetate in cyclohexane): R_f = 0.24 (CAM, UV).

mp: (77-79) °C

^{1}H NMR (600 MHz, chloroform-*d*) δ 6.90 (d, *J* = 3.6 Hz, 1H, 19-H), 5.26 (d, *J* = 3.6 Hz, 1H, 20-H), 4.74 (d, *J* = 8.9 Hz, 1H, 7-H), 4.50 (dd, *J* = 9.6, 6.7 Hz, 1H, 5-H), 4.18 (s, 1H, 8-H), 4.07 (d, *J* = 8.9 Hz, 1H, 7-H), 3.89 (s, 3H, 22-H), 3.41 – 3.39 (m, 6H, 9-H, 10-H), 3.17 (s, 2H, 14-H), 1.94 – 1.91 (m, 1H, 3-H), 1.86 (ddd, *J* = 12.6, 6.5, 4.7 Hz, 1H, 4-H), 1.57 – 1.53 (m, 1H, 3-H), 1.33 – 1.29 (m, 1H, 4-H), 0.83 (s, 9H, 13-H), 0.00 (s, 6H, 11-H).

^{13}C NMR (151 MHz, chloroform-*d*) δ 184.2 (C-15), 182.0 (C-1), 163.8 (C-21), 126.5 (C-19), 125.3 (C-18), 108.9 (C-8), 94.9 (C-17), 84.3 (C-16), 84.0 (C-20), 75.0 (C-5), 68.3 (C-7), 59.3 (C-9 or C-10), 58.1 (C-9 or C-10), 58.0 (C-6), 57.4 (C-22), 53.1 (C-2), 49.1 (C-14), 34.9 (C-3), 32.9 (C-4), 25.9 (C-13) 18.2 (C-12), –4.4 (C-11), –4.9 (C-11).

IR (Diamond-ATR, neat) $\tilde{\upsilon}_{max}$: 3379 (br, w), 2929 (s), 2855 (m), 2019 (w), 1739 (s), 1713 (m), 1471 (m), 1264 (s), 1186 (s), 1152 (s), 1115 (s), 1074 (s), 1027 (s), 865 (m), 837 (m), 778 (m) cm^{-1}.

HRMS (ESI) calc. for $C_{25}H_{37}O_8Si$ $[M+H]^+$: 493.2252 found: 493.2236.

Bromophenol 281:

TLC (30% ethyl acetate in cyclohexane): R_f = 0.11 (CAM, UV).

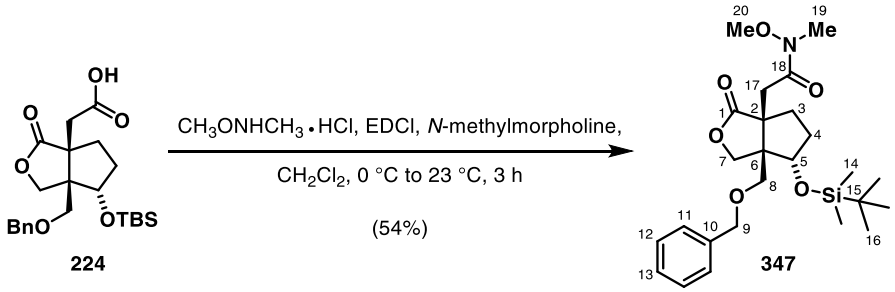
mp: (98-100) °C

^{1}H NMR (600 MHz, chloroform-*d*) δ 7.02 (dd, *J* = 9.0, 1.5 Hz, 1H, 19-H), 6.85 (dd, *J* = 9.0, 1.5 Hz, 1H, 20-H), 5.32 (s, 1H, 18-OH), 4.91 – 4.88 (m, 1H, 7-H), 4.73 – 4.69 (m, 1H, 5-H), 4.52 (d, *J* = 1.6 Hz, 1H, 8-H), 4.42 – 4.40 (m, 1H, 7-H), 3.80 (s, 3H, 22-H), 3.55 – 3.51 (m, 4H, 9-H or 10-H, 14-H), 3.46 (s, 3H, 9-H or 10-H), 3.39 – 3.35 (m, 1H, 14-H), 1.99 – 1.96 (m, 1H, 3-H), 1.95 – 1.90 (m, 1H, 4-H), 1.57 – 1.54 (m, 1H, 3-H), 1.40 – 1.36 (m, 1H, 4-H), 0.90 (s, 9H, 13-H), 0.08 – 0.07 (m, 6H, 11-H).

^{13}C NMR (151 MHz, chloroform-*d*) δ 202.3 (C-15), 182.0 (C-1), 150.4 (C-21), 147.1 (C-18), 131.1 (C-16), 116.9 (C-19), 112.8 (C-20), 108.6 (C-8), 107.0 (C-17), 74.4 (C-5), 68.4 (C-7), 59.8 (C-22), 57.4 (C-6), 56.9 (C-9 or C-10), 56.0 (C-9 or C-10), 53.2 (C-2), 48.7 (C-14), 34.9 (C-3), 33.2 (C-4), 25.9 (C-13), 18.2 (C-12), –4.4 (C-11), –4.9 (C-11).

IR (Diamond-ATR, neat) $\tilde{\upsilon}_{max}$: 2955 (m), 2929 (m), 2856 (w), 2170 (s), 1767 (s), 1661 (w), 1593 (s), 1541 (s), 1433 (w), 1253 (w), 1153 (m), 1113 (s), 1072 (m), 1024 (s), 901 (w), 838 (m), 777 (w) cm^{-1}.

HRMS (ESI) calc. for $C_{25}H_{37}BrNaO_8Si$ $[M+Na]^+$: 595.1333, 597.1313 found: 595.1308, 597.1286.



Amide 347

To a solution of acid **224** (27.2 mg, 63.0 µmol, 1 equiv) in dichloromethane (630 µL) was added *N*-methylmorpholine (35.1 µL, 313 µmol, 5.00 equiv), *N*,*O*-dimethylhydroxylamine hydrochloride (7.48 mg, 75.0 µmol, 1.20 equiv) and *N*-(3-dimethylaminopropyl)-*N*′-ethylcarbodiimide hydrochloride (14.4 mg, 75.0 µmol, 1.20 equiv) in sequence at 0 °C. After five minutes, the reaction mixture was allowed to warm to 23 °C. After three hours at 23 °C, a saturated aqueous solution of ammonium chloride (5 mL) was added to the reaction mixture and the layers were separated. The aqueous layer was

extracted with dichloromethane (3 × 5 mL) and the combined organic layers were dried over sodium sulfate. The dried solution was filtered and the filtrate was concentrated. The residue was purified by flash column chromatography on silica gel (30% ethyl acetate in cyclohexane) to yield amide **347** (16.1 mg, 34.0 µmol, 54%) as a slightly yellow solid.

TLC (40% ethyl acetate in cyclohexane): R_f = 0.36 (CAM, UV).

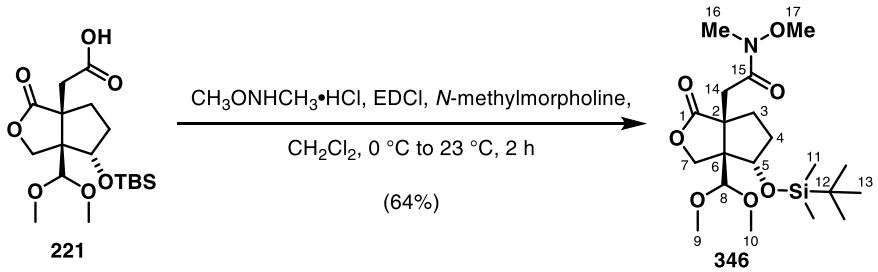
mp: (78-79) °C

^{1}H NMR (600 MHz, chloroform-*d*) δ 7.28 (dd, *J* = 8.0, 6.4 Hz, 2H, 12-H), 7.26 – 7.23 (m, 1H, 13-H), 7.23 – 7.21 (m, 2H, 11-H), 4.64 (d, *J* = 8.9 Hz, 1H, 7-H), 4.43 (dd, *J* = 11.1, 6.2 Hz, 1H, 5-H), 4.40 – 4.34 (m, 2H, 9-H), 3.70 (d, *J* = 9.0 Hz, 1H, 7-H), 3.56 – 3.51 (m, 4H, 20-H, 8-H), 3.25 (d, *J* = 9.4 Hz, 1H, 8-H), 3.24 – 3.19 (m, 1H, 17-H), 3.06 (s, 3H, 19-H), 2.93 (d, *J* = 18.1 Hz, 1H, 17-H), 1.96 (dd, *J* = 12.8, 6.4 Hz, 1H, 3-H), 1.78 (dt, *J* = 12.0, 5.9 Hz, 1H, 4-H), 1.58 (td, *J* = 13.3, 5.8 Hz, 1H, 3-H), 1.41 – 1.35 (m, 1H, 4-H), 0.82 (s, 9H, 16-H), 0.00 – –0.05 (m, 6H, 14-H).

^{13}C NMR (151 MHz, chloroform-*d*) δ 183.4 (C-1), 172.6 (C-18), 137.8 (C-10), 128.6 (C-12), 127.9 (C-13), 127.8 (C-11), 74.9 (C-5), 73.8 (C-9), 69.9 (C-8), 68.2 (C-7), 61.1 (C-20), 53.3 (C-6), 52.1 (C-2), 37.4 (C-17), 35.0 (C-3), 32.3 (C-19), 31.3 (C-4), 25.9 (C-16), 18.1 (C-15), –4.3 (C-14), –4.9 (C-14).

IR (Diamond-ATR, neat) $\tilde{\upsilon}_{max}$: 2955 (w), 2856 (w), 1766 (s), 1663 (m), 1463 (w), 1252 (w), 1152 (m), 1110 (m), 1036 (m), 894 (m), 862 (m), 777 (m), 699 (w) cm^{-1}.

HRMS (ESI) calc. for $C_{25}H_{39}NNaO_6Si$ $[M+Na]^+$: 500.2439 found: 500.2445.



Amide 346

To a solution of acid **221** (11.5 mg, 30.0 µmol, 1 equiv) in dichloromethane (500 µL) was added *N*-methylmorpholine (16.0 µL, 148 µmol, 5.00 equiv), *N*,*O*-dimethylhydroxylamine hydrochloride (3.54 mg, 36.0 µmol, 1.20 equiv) and *N*-(3-dimethylaminopropyl)-*N*′-ethylcarbodiimide hydrochloride (6.81 mg, 36.0 µmol, 1.20 equiv) in sequence at 0 °C. After five minutes, the reaction mixture was allowed to warm to 23 °C. After two hours at 23 °C, a saturated aqueous solution of ammonium chloride (5 mL) was added to the reaction mixture and the layers were separated. The aqueous layer was extracted with dichloromethane (3 × 5 mL) and the combined organic layers were dried over sodium sulfate. The

dried solution was filtered and the filtrate was concentrated. The residue was purified by flash column chromatography on silica gel (40% ethyl acetate in cyclohexane) to yield amide **346** (8.20 mg, 19.0 µmol, 54%) as a colourless solid.

TLC (30% ethyl acetate in cyclohexane): R_f = 0.16 (CAM, UV).

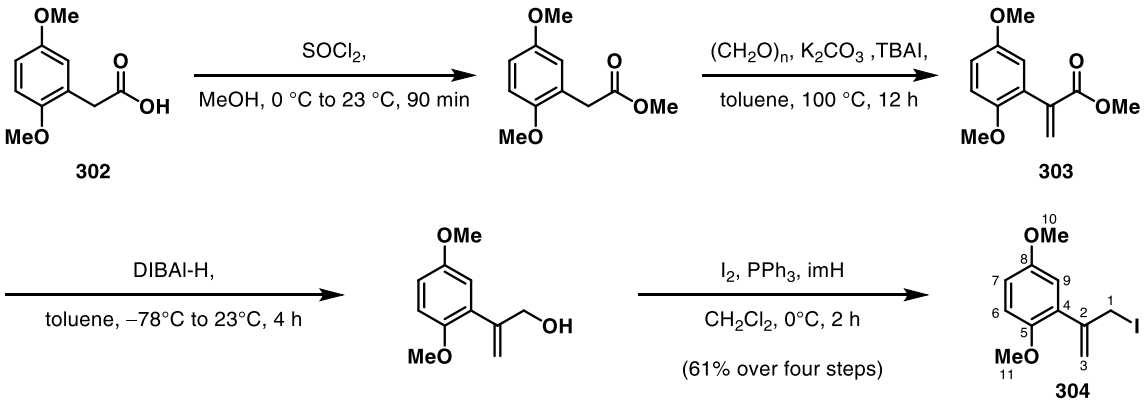
mp: (117-118) °C

^{1}H NMR (600 MHz, chloroform-*d*) δ 4.82 (d, *J* = 8.6 Hz, 1H, 7-H), 4.58 (dd, *J* = 9.9, 6.6 Hz, 1H, 5-H), 4.37 (s, 1H, 8-H), 4.19 (d, *J* = 8.6 Hz, 1H, 7-H), 3.70 (s, 3H, 17-H), 3.47 – 3.43 (m, 6H, 9-H, 10-H), 3.17 (s, 3H, 16-H), 3.09 – 2.96 (m, 2H, 14-H), 1.96 (ddd, *J* = 12.5, 6.5, 1.7 Hz, 1H, 3-H), 1.87 (ddd, *J* = 10.9, 7.2, 5.5 Hz, 1H, 4-H), 1.58 (dd, *J* = 13.0, 6.2 Hz, 1H, 3-H), 1.35 (tdd, *J* = 12.9, 8.2, 4.9 Hz, 1H, 4-H), 0.88 (s, 9H, 13-H), 0.05 (s, 6H, 11-H).

^{13}C NMR (151 MHz, chloroform-*d*) δ 183.0 (C-1), 172.5 (C-15), 109.2 (C-8), 74.7 (C-5), 68.5 (C-7), 61.3 (C-17), 59.5 (C-9 or C-10), 57.2 (C-6), 57.0 (C-9 or C-10), 53.4 (C-2), 37.2 (C-14), 35.3 (C-3), 32.9 (C-4), 32.4 (C-16), 25.9 (C-13), 18.2 (C-12), –4.4 (C-11), –5.0 (C-11).

IR (Diamond-ATR, neat) $\tilde{\upsilon}_{max}$: 2954 (m), 2857 (m), 1764 (s), 1659 (m), 1465 (w), 1391 (w), 1256 (m), 1154 (m), 1113 (m), 1073 (m), 1028 (m), 907 (w), 868 (w), 836 (w), 774 (w) cm^{-1}.

HRMS (ESI) calc. for $C_{20}H_{37}NNaO_7Si$ $[M+Na]^+$: 454.2232 found: 454.2242.



Allyl iodide 304

To a solution of (2,5-dimethoxyphenyl)acetic acid (524 mg, 2.64 mmol, 1 equiv) in methanol (5 mL) was added thionyl chloride (291 µL, 3.97 mmol, 1.50 equiv) at 0 °C. After one hour, the solution was allowed to warm to 23 °C over the course of 30 minutes. Then, the mixture was concentrated to yield the crude methyl ester (556 mg, 2.64 mmol) as a colourless oil. The obtained analytical data were in full agreement with those reported in the literature.[169]

[169] P. Pahari, U. P. Saikia, T. P. Das, C. Damodaran, J. Rohr, *Tetrahedron* **2016**, *72*, 3324–3334.

To a solution of the crude methyl ester (555 mg, 2.64 mmol, 1 equiv) in toluene (26 mL) was added tetrabutylammonium iodide (995 mg, 2.64 mmol, 1 equiv), potassium carbonate (730 mg, 5.28 mmol, 2.00 equiv) and paraformaldehyde (417 mg, 13.2 mmol, 5.00 equiv) in sequence and the mixture was heated to 100 °C. After 12 hours, the mixture was allowed to cool to 23 °C and was then filtered through a pad of Celite and the pad was washed with ethyl acetate (10 mL). The filtrate was washed with water (30 mL) and the washed solution was dried over sodium sulfate. The dried solution was concentrated to yield crude acrylate **303** (458 mg, 2.06 mmol) as a yellow oil. The obtained analytical data were in full agreement with those reported in the literature.[170]

To a solution of crude acrylate **303** (458 mg, 2.06 mmol, 1 equiv) in toluene (20 mL) was added a solution of diisobutylaluminium hydride (1.00 M in hexanes, 6.18 mL, 6.18 mmol, 3.00 equiv) at –78 °C. After 30 minutes, the solution was allowed to warm to 23 °C. After 3.5 hours at 23 °C, ethyl acetate (10 mL) and methanol (10 mL) and a saturated aqueous solution of potassium sodium tartrate (30 mL) were added to the reaction mixture. After one hour of vigorous stirring, the layers were separated. The aqueous layer was extracted with dichloromethane (3 × 10 mL) and the combined organic layers were dried over sodium sulfate. The dried solution was filtered through a pad of Celite and the filtrate was concentrated to yield the crude allylic alcohol (408 mg, 2.10 mmol) as a colourless oil.

To a solution of the crude allylic alcohol (408 mg, 2.10 mmol, 1 equiv) in dichloromethane (10 mL) was added triphenylphosphine (723 mg, 2.73 mmol, 1.30 equiv), imidazole (202 mg, 2.94 mmol, 1.40 equiv) and iodine (727 mg, 2.84 mmol, 1.35 equiv) in sequence at 0 °C. After two hours at 0 °C, a saturated aqueous solution of sodium thiosulfate (10 mL) was added to the solution and the layers were separated. The aqueous layer was extracted with dichloromethane (3 × 3 mL) and the combined organic layers were dried over sodium sulfate. The dried solution was filtered and the filtrate was concentrated. The residue was purified by flash column chromatography on silica gel (10% ethyl acetate in cyclohexane) to yield allyl iodide **304** (392 mg, 1.29 mmol, 61% over four steps) as a slightly yellow oil. The obtained analytical data were in full agreement with those reported in the literature.

TLC (30% ethyl acetate in cyclohexane): R_f = 0.53 ($KMnO_4$, UV).

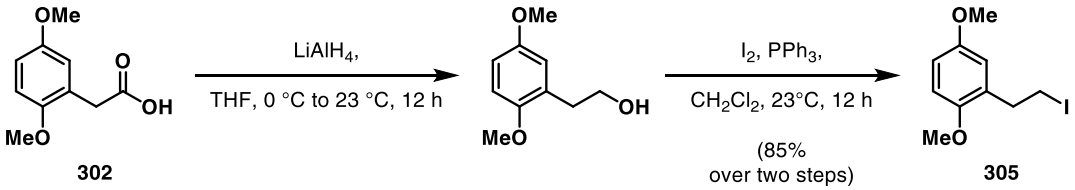
^{1}H NMR (400 MHz, chloroform-*d*) δ 6.84 – 6.79 (m, 3H, 6-H, 7-H, 9-H), 5.53 (q, *J* = 1.0 Hz, 1H, 3-H), 5.19 (d, *J* = 1.3 Hz, 1H, 3-H), 4.42 (d, *J* = 0.8 Hz, 2H, 1-H), 3.79 (s, 6H, 10-H, 11-H).

^{13}C NMR (101 MHz, chloroform-*d*) δ 153.7 (C-5 or C-8), 151.0 (C-5 or C-8), 146.3 (C-4), 129.8 (C-2), 118.4 (C-3), 117.3 (C-6 or C-7 or C-9), 113.9 (C-6 or C-7 or C-9), 112.0 (C-6 or C-7 or C-9), 56.3 (C-10 or C-11), 56.0 (C-10 or C-11), 10.2 (C-1).

[170] F.-X. Felpin, K. Miqueu, J.-M. Sotiropoulos, E. Fouquet, O. Ibarguren, J. Laudien, *Chem. Eur. J.* **2010**, *16*, 5191–5204.

IR (Diamond-ATR, neat) $\tilde{\upsilon}_{max}$: 2951 (w), 2832 (w), 1495 (s), 1463 (w), 1422 (w), 1265 (w), 1219 (s), 1180 (w), 1046 (m), 803 (w) cm^{-1}.

HRMS (ESI) calc. for $C_{11}H_{13}INaO_2$ $[M+Na]^+$: 326.9852 found: 326.9860.

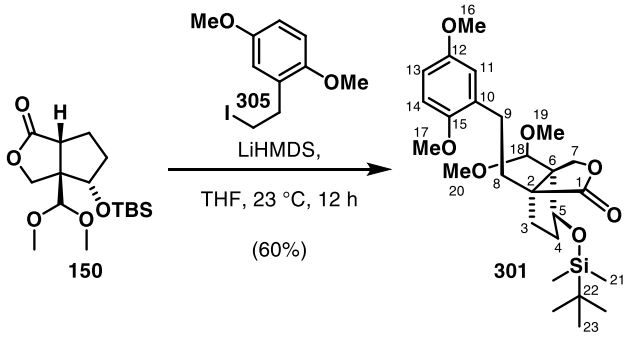


Alkyl iodide 305

To a solution of (2,5-dimethoxyphenyl)acetic acid (1.00 g, 5.05 mmol, 1 equiv) in tetrahydrofuran (30 mL) was added lithium aluminium hydride (504 mg, 12.6 mmol, 2.50 equiv) portionwise at 0 °C. After 30 min, the reaction mixture was allowed to warm to 23 °C and was stirred at that temperature for 12 hours. A saturated aqueous solution of potassium sodium tartrate (50 mL) was added to the solution at 0 °C and the mixture was allowed to warm to 23 °C. After 45 min at 23 °C, dichloromethane (50 mL) was added to the mixture and the layers were separated. The aqueous layer was extracted with dichloromethane (3 × 10 mL) and the combined organic layers were dried over sodium sulfate. The dried solution was filtered through a pad of Celite and the filtrate was concentrated to yield the crude alcohol (922 mg, 5.06 mmol) as a colourless oil. The obtained analytical data were in full agreement with those reported in the literature.[171]

To a solution of triphenylphosphine (1.74 g, 6.58 mmol, 1.30 equiv) in dichloromethane (20 mL) was added iodine (1.69 g, 6.58 mmol, 1.30 equiv) at 23 °C. After 30 minutes, a solution of the crude alcohol (922 mg, 5.06 mmol, 1 equiv) in dichloromethane (5 mL) was added at 23 °C and the reaction mixture was protected from light. After 12 hours, a saturated aqueous solution of sodium thiosulfate (40 mL) was added to the solution and the layers were separated. The aqueous layer was extracted with dichloromethane (3 × 10 mL) and the combined organic layers were dried over sodium sulfate. The dried solution was filtered and the filtrate was concentrated. The residue was purified by flash column chromatography on silica gel (10% ethyl acetate in cyclohexane) to yield alkyl iodide **305** (1.25 g, 4.28 mmol, 85%) as a colourless oil. The obtained analytical data were in full agreement with those reported in the literature.[172]

[171] D. Kim, A. Nash, J. De Brabander, U. K. Tambar, *Tetrahedron* **2018**, *74*, 3787–3790.
[172] D. Chen, H.-M. Liu, M.-M. Li, Y.-M. Yan, W.-D. Xu, X.-N. Li, Y.-X. Cheng, H.-B. Qin, *Chem. Commun.* **2015**, *51*, 14594–14596.



Lactone 301

To a solution of lactone **150** (10.5 mg, 31.8 µmol, 1 equiv) in tetrahydrofuran (300 µL) was added alkyl iodide **305** (55.7 mg, 191 µmol, 6.00 equiv) and a solution of lithium bis(trimethylsilyl)amide (1.00 M in tetrahydrofuran, 95.3 µL, 95.3 µmol, 3.00 equiv) in sequence at 23 °C. After 12 hours, water (5 mL) and dichloromethane (5 mL) were added to the mixture and the layers were separated. The aqueous layer was extracted with dichloromethane (3 × 5 mL) and the combined organic layers were dried over sodium sulfate. The dried solution was filtered and the filtrate was concentrated. The residue was purified by flash column chromatography on silica gel (10% ethyl acetate in cyclohexane) to yield lactone **301** (9.50 mg, 19.2 µmol, 60%) as a colourless oil.

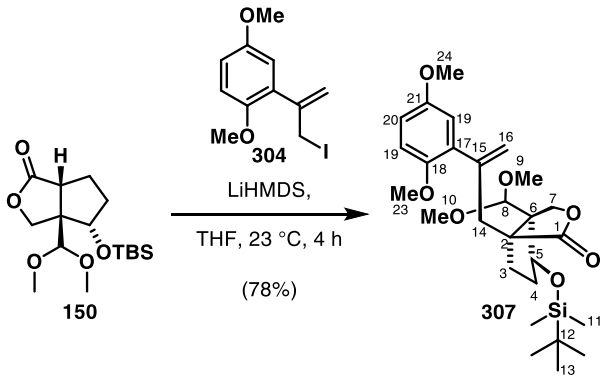
TLC (20% ethyl acetate in cyclohexane): R_f = 0.43 (CAM, UV).

^{1}H NMR (400 MHz, chloroform-*d*) δ 6.77 (dd, *J* = 8.3, 0.9 Hz, 1H, 14-H), 6.73 – 6.68 (m, 2H, 11-H, 13-H), 4.65 (d, *J* = 9.2 Hz, 1H, 7-H), 4.62 – 4.58 (m, 1H, 5-H), 4.49 (s, 1H, 18-H), 3.90 (d, *J* = 9.2 Hz, 1H, 7-H), 3.79 (s, 3H, 17-H), 3.75 (s, 3H, 16-H), 3.50 – 3.48 (m, 6H, 19-H, 20-H), 2.89 – 2.81 (m, 1H, 9-H), 2.63 – 2.54 (m, 1H, 9-H), 2.15 (ddd, *J* = 12.5, 7.3, 2.2 Hz, 1H, 3-H), 2.08 – 2.01 (m, 1H, 4-H), 1.89 – 1.80 (m, 2H, 8-H), 1.63 – 1.56 (m, 1H, 3-H), 1.37 – 1.30 (m, 1H, 4-H), 0.88 (s, 9H, 23-H), 0.07 – 0.05 (m, 6H, 21-H).

^{13}C NMR (101 MHz, chloroform-*d*) δ 181.9 (C-1), 153.8 (C-12), 151.6 (C-15), 131.6 (C-10), 116.2 (C-11), 111.7 (C-13), 111.4 (C-14), 108.7 (C-18), 74.4 (C-5), 68.2 (C-7), 59.4 (C-6), 58.9 (C-19 or C-20), 57.5 (C-19 or C-20), 56.6 (C-2), 55.9 (C-17), 55.9 (C-16), 34.6 (C-4), 33.1 (C-8, C-3), 26.6 (C-9), 25.9 (C-23), 18.1 (C-22), –4.4 (C-21), –5.0 (C-21).

IR (Diamond-ATR, neat) $\tilde{\upsilon}_{max}$: 2953 (m), 2857 (w), 1765 (s), 1501 (s), 1465 (m), 1222 (s), 1147 (s), 1112 (s), 1070 (s), 1026 (s), 872 (m), 837 (m), 778 (m) cm^{-1}.

HRMS (ESI) calc. for $C_{26}H_{42}NaO_7Si$ $[M+Na]^+$: 517.2592 found: 517.2569.



***Exo*-methylene 307**

To a solution of lactone **150** (10.0 mg, 30.0 µmol, 1 equiv) and allyl iodide **304** (55.2 mg, 182 µmol, 6.00 equiv) in tetrahydrofuran (300 µL) was added a solution of lithium bis(trimethylsilyl)amide (1.00 M in tetrahydrofuran, 91.0 µL, 91.0 µmol, 3.00 equiv) at 23 °C. After four hours, water (5 mL) and diethyl ether (5 mL) were added to the solution and the layers were separated. The aqueous layer was extracted with diethyl ether (3 × 1 mL) and the combined organic layers were dried over sodium sulfate. The dried solution was filtered and the filtrate was concentrated. The residue was purified by flash column chromatography on silica gel (10% ethyl acetate in cyclohexane) to yield *exo*-methylene **307** (12.0 mg, 24.0 µmol, 78%) as a colourless oil.

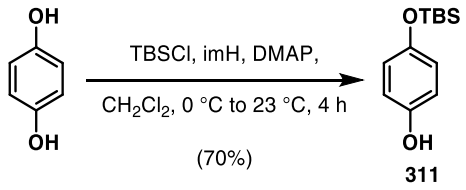
TLC (30% ethyl acetate in cyclohexane): R_f = 0.38 (CAM, UV).

^{1}H NMR (400 MHz, chloroform-*d*) δ 6.87 (dd, *J* = 2.5, 1.1 Hz, 1H, 22-H), 6.82 – 6.78 (m, 2H, 19-H, 20-H), 5.28 (t, *J* = 1.4 Hz, 1H, 16-H), 5.21 – 5.16 (m, 1H, 16-H), 4.52 (d, *J* = 9.0 Hz, 1H, 7-H), 4.50 – 4.46 (m, 1H, 5-H), 4.10 (s, 1H, 8-H), 3.79 (s, 3H, 23-H or 24-H), 3.78 (s, 3H, 23-H or 24-H), 3.74 (d, *J* = 9.0 Hz, 1H, 7-H), 3.31 (s, 3H, 9-H or 10-H), 3.24 (s, 3H, 9-H or 10-H), 3.06 (d, *J* = 14.1 Hz, 1H, 14-H), 2.80 (d, *J* = 14.1 Hz, 1H, 3-H), 1.96 – 1.84 (m, 2H, 3-H, 4-H), 1.44 – 1.34 (m, 1H, 3-H), 1.26 – 1.16 (m, 1H, 4-H), 0.84 (s, 9H, 13-H), 0.02 – –0.03 (m, 6H, 11-H).

^{13}C NMR (101 MHz, chloroform-*d*) δ 181.1 (C-1), 153.9 (C-18), 150.8 (C-21), 144.1 (C-17), 133.5 (C-15), 120.9 (C-16), 116.8 (C-22), 113.5 (C-19 or C-20), 112.0 (C-19 or C-20), 108.5 (C-8), 74.0 (C-5), 67.6 (C-7), 59.0 (C-6), 59.0 (C-2), 58.4 (C-9 or C-10), 56.6 (C-9 or C-10), 56.1 (C-23 or C-24), 56.0 (C-23 or C-24), 38.2 (C-14), 34.5 (C-3 or C-4), 34.2 (C-3 or C-4), 25.8 (C-13), 18.1 (C-12), –4.5 (C-11), –5.0 (C-11).

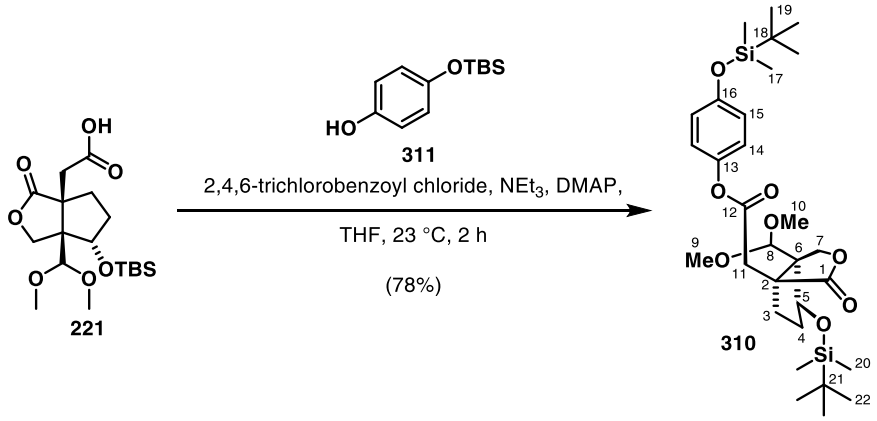
IR (Diamond-ATR, neat) $\tilde{\upsilon}_{max}$: 2955 (m), 2855 (w), 1768 (s), 1493 (m), 1464 (m), 1252 (m), 1219 (s), 1181 (m), 1148 (m), 1070 (m), 1026 (m), 867 (m), 838 (m), 778 (m) cm^{-1}.

HRMS (ESI) calc. for $C_{27}H_{42}NaO_7Si$ $[M+Na]^+$: 529.2592 found: 529.2597.



Phenol 311

To a solution of hydroquinone (581 mg, 5.22 mmol, 1 equiv) in dichloromethane (52 mL) was added imidazole (898 mg, 13.1 mmol, 2.50 equiv) and *tert*-butyldimethylsilyl chloride (956 mg, 6.22 mmol, 1.20 equiv) at 23 °C. After four hours, the solution was concentrated and the residue was purified by flash column chromatography on silica gel (10% ethyl acetate in cyclohexane) to yield phenol **311** (821 mg, 3.66 mmol, 70%) as a slightly yellow oil. The obtained analytical data were in full agreement with those reported in the literature.[173]



Ester 310

To a solution of acid **221** (271 mg, 698 µmol, 1 equiv) and phenol **311** (203 mg, 907 µmol, 1.30 equiv) in tetrahydrofuran (7 mL) was added triethylamine (776 µl, 5.58 mmol, 8.00 equiv) followed by 2,4,6-trichlorobenzoyl chloride (556 µl, 3.49 mmol, 5.00 equiv) at 23 °C. After 15 minutes, 4-(dimethylamino)pyridine (8.61 mg, 70.0 µmol, 0.100 equiv) was added. After two hours, the mixture was concentrated and the residue was purified by flash column chromatography on silica gel (5% ethyl acetate in cyclohexane) to yield ester **310** (325 mg, 546 µmol, 78%) as a colourless solid.

TLC (10% ethyl acetate in cyclohexane): R_f = 0.37 (CAM, UV).

mp: (95-96) °C

^{1}H NMR (600 MHz, chloroform-*d*) δ 6.96 – 6.93 (m, 2H, 14-H or 15-H), 6.81 – 6.78 (m, 2H, 14-H or 15-H), 4.76 (d, *J* = 8.9 Hz, 1H, 7-H), 4.55 (dd, *J* = 9.8, 6.7 Hz, 1H, 5-H), 4.34 (s, 1H, 8-H), 4.10 (d, *J* = 9.0 Hz, 1H, 7-H), 3.51 – 3.48 (m, 6H, 9-H, 10-H), 3.11 – 3.03 (m, 2H, 11-H), 2.06 (ddd, *J* = 12.7,

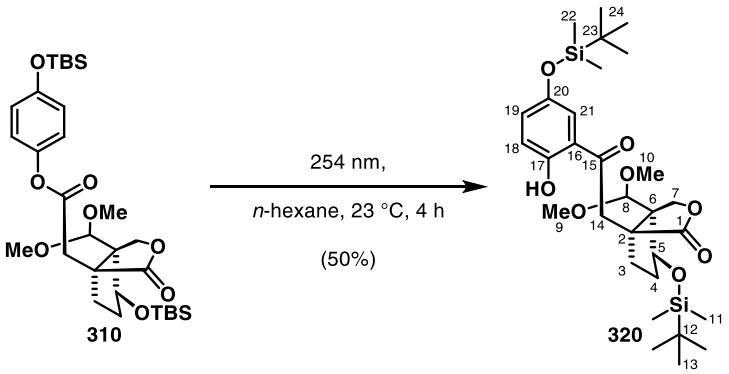
[173] W. Li, Y. Gao, Q. Li, Z.-J. Li, *Org. Biomol. Chem.* **2018**, *16*, 4720–4727.

7.0, 1.7 Hz, 1H, 3-H), 1.95 (ddd, *J* = 11.3, 7.4, 5.7 Hz, 1H, 4-H), 1.70 (td, *J* = 12.9, 6.5 Hz, 1H, 3-H), 1.41 – 1.35 (m, 1H, 4-H), 0.97 (s, 9H, 19-H or 22-H), 0.88 (s, 9H, 19-H or 22-H), 0.18 (s, 6H, 17-H or 20-H), 0.06 (s, 6H, 17-H or 20-H).

^{13}C NMR (151 MHz, chloroform-*d*) δ 181.8 (C-1), 170.5 (C-12), 153.5 (C-13 or C-16), 144.5 (C-13 or C-16), 122.1 (C-14 or C-15), 120.6 (C-14 or C-15), 108.8 (C-8), 75.2 (C-5), 68.1 (C-7), 59.2 (C-9 or C-10), 58.2 (C-6), 57.7 (C-9 or C-10), 53.2 (C-2), 38.4 (C-11), 34.9 (C-3), 32.8 (C-4), 25.9 (C-19 or C-22), 25.8 (C-19 or C-22), 18.3 (C-18 or C-21), 18.1 (C-18 or C-21), –4.3 (C-17 or C20), –4.4 (C-17 or C20), –5.0 (C-17 or C20).

IR (Diamond-ATR, neat) $\tilde{\upsilon}_{max}$: 2930 (w), 2857 (w), 1765 (m), 1502 (s), 1471 (w), 1254 (m), 1188 (m), 1145 (m), 1069 (m), 1027 (m), 906 (s), 835 (s), 776 (s), 733 (w), 670 (w), 526 (w) cm^{-1}.

HRMS (ESI) calc. for $C_{30}H_{50}NaO_8Si_2$ $[M+Na]^+$: 617.2936 found: 617.2958, calc. for $C_{30}H_{50}KO_8Si_2$ $[M+K]^+$: 633.2676 found: 633.2669.



Ketone 320

A solution of ester **310** (60.0 mg, 101 µmol, 1 equiv) in degassed hexane (6 ml) was irradiated at 254 nm in a quartz tube. *Note: The reaction was set up in three parallel batches (20.0 mg and 2 ml n-hexane each) and irradiated at the same time.* After four hours, the reaction mixture was concentrated and the residue was purified by flash column chromatography on silica gel (5% ethyl acetate in cyclohexane) to yield ketone **320** (30.2 mg, 51.0 µmol, 50%) as a slightly yellow solid.

TLC (20% ethyl acetate in cyclohexane): R_f = 0.49 (CAM, UV).

mp: (160-161) °C

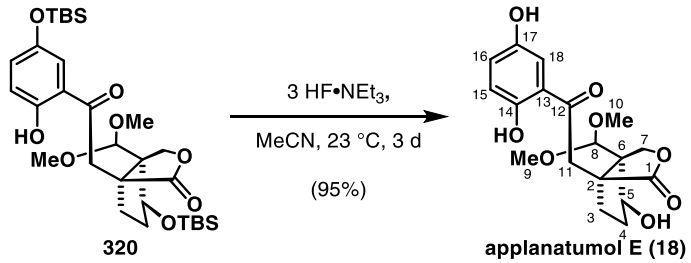
^{1}H NMR (600 MHz, chloroform-*d*) δ 11.51 (s, 1H, 17-OH), 7.13 (d, *J* = 2.9 Hz, 1H, 21-H), 7.02 (dd, *J* = 8.9, 2.9 Hz, 1H, 19-H), 6.87 (d, *J* = 8.9 Hz, 1H, 18-H), 4.87 (d, *J* = 8.8 Hz, 1H, 7-H), 4.55 (dd, *J* = 10.1, 6.6 Hz, 1H, 5-H), 4.19 (d, *J* = 8.8 Hz, 1H, 7-H), 4.11 (s, 1H, 8-H), 3.69 (d, *J* = 18.6 Hz, 1H, 14-H), 3.42 (d, *J* = 18.6 Hz, 1H, 14-H), 3.38 (s, 3H, 9-H or 10-H), 3.25 (s, 3H, 9-H or 10-H), 2.07 – 2.03 (m, 1H, 3-H), 1.94 (ddd, *J* = 12.6, 6.3, 4.7 Hz, 1H, 4-H), 1.71 (dt, *J* = 12.8, 6.4 Hz, 1H, 3-H), 1.42

(ddd, *J* = 13.0, 6.4, 3.7 Hz, 1H, 4-H), 0.99 (s, 9H, 13-H or 24-H), 0.90 (s, 9H, 13-H or 24-H), 0.20 – 0.18 (m, 6H, 11-H or 24-H), 0.07 – 0.06 (m, 6H, 11-H or 24-H).

^{13}C NMR (151 MHz, chloroform-*d*) δ 203.6 (C-15), 182.5 (C-1), 157.0 (C-16), 147.4 (C-20), 129.7 (C-19), 119.3 (C-18), 118.9 (C-21), 118.5 (C-17), 108.7 (C-8), 75.0 (C-5), 68.1 (C-7), 59.3 (C-9 or C-10), 57.6 (C-2), 57.2 (C-9 or C-10), 52.5 (C-6), 43.3 (C-14), 35.1 (C-3), 32.5 (C-4), 25.8 (C-13 or C-24), 25.7 (C-13 or C-24), 18.2 (C-12 or C-23), 18.0 (C-12 or C-23), –4.4 (C-11 or C-22), –4.4 (C-11 or C-22), –4.5 (C-11 or C-22), –5.1 (C-11 or C-22).

IR (Diamond-ATR, neat) $\tilde{\upsilon}_{max}$: 2928 (m), 2857 (w), 1769 (s), 1640 (w), 1481 (m), 1388 (m), 1278 (m), 1174 (m), 1149 (m), 1115 (m), 1077 (m), 1003 (m), 947 (m), 886 (m), 836 (s), 783 (m), 642 (w) cm^{-1}.

HRMS (ESI) calc. for $C_{30}H_{50}NaO_8Si_2$ $[M+Na]^+$: 617.2936 found: 617.2958, calc. for $C_{30}H_{50}KO_8Si_2$ $[M+K]^+$: 633.2676 found: 633.2669.



Applanatumol E (18)

To a solution of ketone **320** (57.4 mg, 97.0 µmol, 1 equiv) in acetonitrile (650 µL) was added hydrogen fluoride triethylamine (802 µL, 4.82 mmol, 50.0 equiv) at 23 °C. After three days, a saturated aqueous solution of sodium bicarbonate (5 mL) and ethyl acetate (5 mL) were added to the reaction mixture and the layers were separated. The aqueous layer was extracted with ethyl acetate (3 × 5 mL), the combined organic layers were dried over sodium sulfate. The dried solution was filtered and the filtrate was concentrated. The residue was purified by flash column chromatography on silica gel (5% methanol in dichloromethane) to yield applanatumol E (**18**) (33.4 mg, 91.2 µmol, 95%) as a yellow solid.

TLC (5% methanol in dichloromethane): R_f = 0.33 (CAM, UV).

mp: (130-133) °C

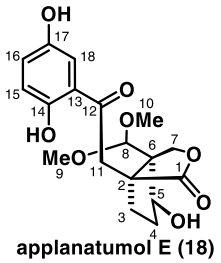
^{1}H NMR (600 MHz, acetone-d_6) δ 11.30 (s, 1H, 14-OH), 8.21 (s, 1H, 17-OH), 7.38 (d, *J* = 2.9 Hz, 1H, 18-H), 7.12 (dd, *J* = 8.9, 3.0 Hz, 1H, 16-H), 6.84 (d, *J* = 8.9 Hz, 1H, 15-H), 4.81 (d, *J* = 8.8 Hz, 1H, 7-H), 4.59 (t, *J* = 8.2 Hz, 1H, 5-H), 4.39 (s, 1H, 8-H), 4.22 (d, *J* = 8.8 Hz, 1H, 7-H), 3.84 (d, *J* = 19.0 Hz, 1H, 11-H), 3.68 (d, *J* = 3.9 Hz, 1H, 5-OH), 3.48 (d, *J* = 19.0 Hz, 1H, 11-H), 3.43 (s, 3H, 10-H), 3.34 (s, 3H, 9-H), 1.97 – 1.88 (m, 2H, 3-H, 4-H), 1.79 – 1.71 (m, 1H, 3-H), 1.31 (dddd, *J* = 14.0, 12.2, 10.9, 6.6 Hz, 1H, 4-H).

^{13}C NMR (151 MHz, acetone-d_6) δ 205.2 (C-12), 182.4 (C-1), 156.5 (C-14), 150.3 (C-17), 126.2 (C-16), 119.7 (C-15), 119.6 (C-13), 115.3 (C-18), 110.2 (C-8), 75.4 (C-5), 68.0 (C-7), 59.4 (C-9), 57.8 (C-10), 57.4 (C-6), 53.5 (C-2), 44.3 (C-11), 35.7 (C-3), 31.6 (C-4).

IR (Diamond-ATR, neat) $\tilde{\upsilon}_{max}$: 3389 (br, w), 2963 (w), 2834 (w), 1743 (m), 1662 (m), 1485 (m), 1280 (m), 1235 (m), 1177 (s), 1093 (m), 1066 (s), 1027 (m), 785 (m), 647 (m) cm^{-1}.

HRMS (ESI) calc. for $C_{18}H_{22}NaO_8$ $[M+Na]^+$: 389.1207 found: 389.1206.

Table 6: Comparison of ^{1}H-NMR shifts for natural[174] and synthetic applanatumol E.



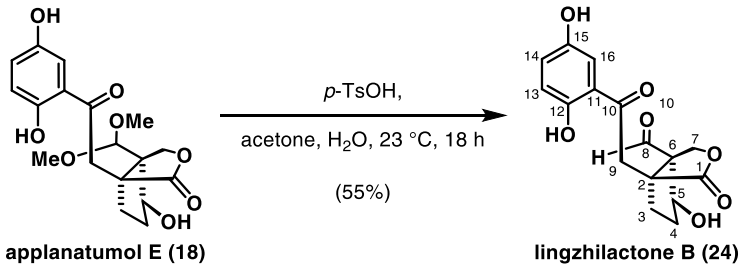
applanatumol E (18)

No	^{1}H-NMR (400 MHz, acetone-d_6) isolated applanatumol E **ppm**	^{1}H-NMR (600 MHz, acetone-d_6) synthetic applanatumol E **ppm**	Δ ppm
1	-	-	-
2	-	-	-
3	1.89 (overlap)	1.97 – 1.88 (m, overlap)	+0.04
	1.72 (m)	1.79 – 1.71 (m)	+0.03
4	1.89 (overlap)	1.97 – 1.88 (m, overlap)	+0.04
	1.28 (m)	1.31 (dddd, *J* = 14.0, 12.2, 10.9, 6.6 Hz)	+0.03
5	4.55 (dd, *J* = 10.3, 6.6 Hz)	4.59 (t, *J* = 8.2 Hz)	+0.04
5-OH	3.68 (s)	3.68 (d, *J* = 3.9 Hz)	±0
6	-	-	-
7	4.78 (d, *J* = 8.8 Hz)	4.81 (d, *J* = 8.8 Hz)	+0.03
	4.19 (d, *J* = 8.8 Hz)	4.22 (d, *J* = 8.8 Hz)	+0.03
8	4.36 (s)	4.39 (s)	+0.03
9	3.39 (s)	3.34 (s)	–0.05
10	3.31 (s)	3.43 (s)	+0.12
11	3.77 (d, *J* = 18.9 Hz)	3.84 (d, *J* = 19.0 Hz)	+0.07
	3.45 (d, *J* = 18.9 Hz)	3.48 (d, *J* = 19.0 Hz)	+0.03
12	-	-	-
13	-	-	-
14-OH	11.26 (s)	11.30 (s)	+0.04
15	6.81 (d, *J* = 8.9 Hz)	6.84 (d, *J* = 8.9 Hz)	+0.03
16	7.10 (dd, *J* = 8.9, 2.9 Hz)	7.12 (dd, *J* = 8.9, 3.0 Hz)	+0.02
17-OH	8.19 (br, s)	8.21 (s)	+0.02
18	7.34 (d, *J* = 2.9 Hz)	7.38 (d, *J* = 2.9 Hz)	+0.04

[174] Q. Luo, X.-H. Yang, Z.-L. Yang, Z.-C. Tu, Y.-X. Cheng, *Tetrahedron* **2016**, *72*, 4564–4574.

Table 7: Comparison of ^{13}C-NMR shifts for natural and synthetic applanatumol E.

No	^{13}C-NMR (150 MHz, acetone-d_6) isolated applanatumol E **ppm**	^{13}C-NMR (151 MHz, acetone-d_6) synthetic applanatumol E **ppm**	Δ ppm
1	182.4	182.4	±0
2	53.4	53.5	–0.1
3	35.7	35.7	±0
4	31.5	31.6	+0.1
5	75.2	75.4	+0.2
6	57.4	57.4	±0
7	68.0	68.0	±0
8	110.2	110.2	±0
9	59.3	59.4	+0.1
10	57.8	57.8	±0
11	44.3	44.3	±0
12	205.1	205.2	+0.1
13	119.5	119.6	+0.1
14	156.1	156.5	+0.4
15	119.6	119.7	+0.1
16	126.0	126.2	+0.2
17	150.3	150.3	±0
18	115.3	115.3	±0



Lingzhilactone B (24)

To a solution of applanatumol E (**18**) (4.60 mg, 12.6 µmol, 1 equiv) in acetone (100 µL) was added water (1 µL) and *p*-toluenesulfonic acid monohydrate (0.200 mg, 1.26 µmol, 0.100 equiv) at 23 °C. After 18 hours, the reaction mixture was concentrated and the residue was purified by flash column chromatography (5% methanol in dichloromethane) to yield lingzhilactone B (**24**) (2.20 mg, 6.87 µmol, 55%) as a slightly yellow oil.

TLC (5% methanol in dichloromethane): R_f = 0.17 (CAM, UV).

mp: (138-139) °C

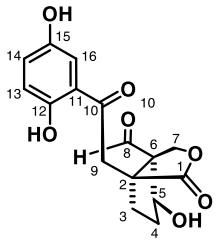
^{1}H NMR (400 MHz, acetone-d_6) δ 10.99 (s, 1H, 12-OH), 9.68 (s, 1H, 8-H), 7.33 (d, *J* = 2.9 Hz, 1H, 16-H), 7.12 (dd, *J* = 9.0, 3.0 Hz, 1H, 14-H), 6.81 (d, *J* = 9.0 Hz, 1H, 13-H), 4.94 (d, *J* = 9.7 Hz, 1H, 7-H), 4.89 (d, *J* = 9.7 Hz, 1H, 7-H), 4.83 – 4.70 (m, 1H, 5-OH), 4.69 – 4.64 (m, 1H, 5-H), 3.78 (s, 2H, 9-H), 2.04 – 1.97 (m, 3H, 3-H, 4-H), 1.65 – 1.55 (m, 1H, 4-H).

^{13}C NMR (101 MHz, acetone-d_6) δ 205.2 (C-10), 203.2 (C-8), 181.2 (C-1), 156.4 (C-12), 150.4 (C-15), 126.7 (C-13), 119.7 (C-14), 119.4 (C-11), 115.4 (C-16), 77.9 (C-5), 66.9 (C-7), 63.7 (C-6), 54.4 (C-2), 44.5 (C-9), 35.5 (C-3), 32.0 (C-4).

IR (Diamond-ATR, neat) $\tilde{\upsilon}_{max}$: 3414 (br, m), 2965 (br, w), 1747 (s), 1719 (m), 1642 (m), 1621 (m), 1485 (m), 1383 (m), 1278 (s), 1174 (s), 1032 (m) cm^{-1}.

HRMS (ESI) calc. for $C_{16}H_{15}O_7$ $[M–H]^-$: 319.0823 found: 319.0823.

Table 8: Comparison of ^{1}H-NMR shifts for natural[119] and synthetic lingzhilactone B.

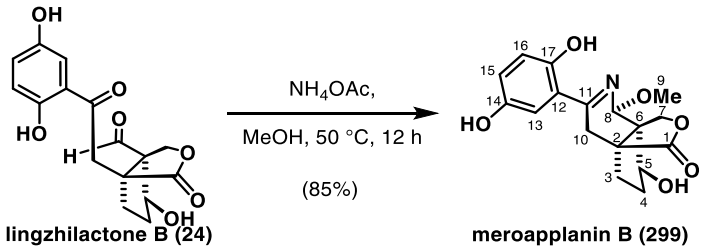


lingzhilactone B (24)

No	^{1}H-NMR (600 MHz, acetone-d_6) <u>isolated</u> lingzhilactone B **ppm**	^{1}H-NMR (400 MHz, acetone-d_6) <u>synthetic</u> lingzhilactone B **ppm**	Δ ppm
1	-	-	-
2	-	-	-
3	2.03 (m)	2.04 – 1.97 (m)	+0.01
4	2.06 (overlap)	2.04 – 1.97 (m)	–0.02
	1.58 (m)	1.65 – 1.55 (m)	–0.03
5	4.66 (dd, *J* = 11.0, 5.4 Hz)	4.69 – 4.64 (m)	–0.02
5-OH	-	4.83 – 4.70 (m)	-
6	-	-	-
7	4.94 (d, *J* = 9.7 Hz)	4.94 (d, *J* = 9.7 Hz)	±0
	4.88 (d, *J* = 9.7 Hz)	4.89 (d, *J* = 9.7 Hz)	+0.01
8	9.68 (s)	9.68 (s)	±0
9	3.77 (s)	3.78 (s)	+0.01
10	-	-	-
11	-	-	-
12-OH	11.00 (s)	10.99 (s)	–0.01
13	6.81 (d, *J* = 8.9 Hz)	6.81 (d, *J* = 9.0 Hz)	±0
14	7.12 (dd, *J* = 8.9, 2.9 Hz)	7.12 (dd, *J* = 9.0, 3.0 Hz)	±0
15-OH	8.35 (br, s)	-	-
16	7.33 (d, *J* = 2.9 Hz)	7.33 (d, *J* = 2.9 Hz)	±0

Table 9: Comparison of ^{13}C-NMR shifts for natural and synthetic lingzhilactone B.

No	^{13}C-NMR (150 MHz, acetone-d_6) <u>isolated</u> lingzhilactone B **ppm**	^{13}C-NMR (100 MHz, acetone-d_6) <u>synthetic</u> lingzhilactone B **ppm**	Δ ppm
1	181.2	181.2	±0
2	54.3	54.4	+0.1
3	35.4	35.5	+0.1
4	31.9	32.0	+0.1
5	77.8	77.9	+0.1
6	63.6	63.7	+0.1
7	66.9	66.9	±0
8	203.3	203.2	–0.1
9	44.4	44.5	+0.1
10	205.2	205.2	±0
11	119.4	119.4	±0
12	156.3	156.4	+0.1
13	126.7	126.7	±0
14	119.7	119.7	±0
15	150.4	150.4	±0
16	115.3	115.4	+0.1



Meroapplanin B (299)

To a solution of lingzhilactone B (**24**) (12.0 mg, 38.0 µmol, 1 equiv) in methanol (100 µL) was added ammonium acetate (14.4 mg, 187 µmol, 5.00 equiv) and the mixture was heated to 50 °C. After 12 hours, the reaction mixture was allowed to cool to 23 °C and then the mixture was concentrated. The residue was purified by flash column chromatography (3% methanol in dichloromethane) to yield meroapplanin B (**299**) (10.6 mg, 32.0 µmol, 85%) as a slightly yellow solid.

TLC (3% methanol in dichloromethane): R_f = 0.31 (CAM, UV).

mp: (134-135) °C

^{1}H NMR (400 MHz, pyridine-d_5) δ 13.82 (s, 1H, 17-OH), 7.71 (d, J = 2.9 Hz, 1H, 13-H), 7.31 (dd, J = 8.8, 2.8 Hz, 1H, 16-H), 7.19 (d, J = 8.8 Hz, 2H, 15-H), 5.16 (d, J = 9.8 Hz, 1H, 7-H), 4.71 (s, 1H, 8-

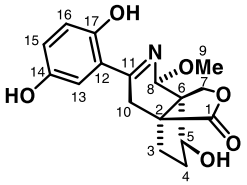
H), 4.63 (dd, *J* = 7.1, 5.0 Hz, 1H, 5-H), 4.47 (d, *J* = 9.8 Hz, 1H, 7-H), 3.95 (d, *J* = 15.4 Hz, 1H, 10-H), 3.51 (s, 3H, 9-H), 2.51 – 2.46 (m, 1H, 3-H), 2.40 (d, *J* = 15.4 Hz, 1H, 10-H), 2.14 – 2.08 (m, 1H, 4-H), 1.91 – 1.85 (m, 1H, 3-H), 1.84 – 1.78 (m, 1H, 4-H).

^{13}C NMR (151 MHz, pyridine-d_5) δ 182.1 (C-1), 173.6 (C-11), 155.8 (C-17), 151.4 (C-14), 123.1 (C-15), 119.6 (C-16), 119.2 (C-12), 115.3 (C-13), 95.1 (C-8), 78.1 (C-5), 68.3 (C-7), 58.3 (C-2), 56.8 (C-9), 54.0 (C-6), 36.0 (C-3), 34.3 (C-4), 33.3 (C-10).

IR (Diamond-ATR, neat) $\tilde{\upsilon}_{max}$: 3420 (br, w), 2924 (s), 2853 (m), 1744 (s), 1575 (w), 1456 (w), 1375 (m), 1221 (s), 1178 (m), 1051 (m), 1018 (m) cm^{-1}.

HRMS (ESI) calc. for $C_{17}H_{20}NO_6$ $[M+H]^+$: 334.1285 found: 334.1269; calc. for $C_{17}H_{19}NNaO_6$ $[M+Na]^+$: 356.1105 found: 356.1088; calc. for $C_{17}H_{19}KNO_6$ $[M+K]^+$: 372.0844 found: 372.0827.

Table 10: Comparison of ^{1}H-NMR shifts for natural[174] and synthetic meroapplanin B.

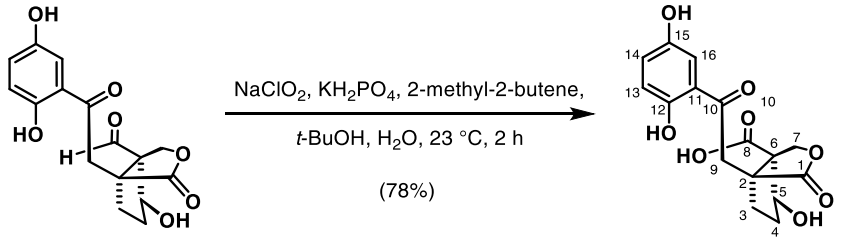


meroapplanin B (299)

No	^{1}H-NMR (600 MHz, pyridine-d_5) <u>isolated</u> meroapplanin B **ppm**	^{1}H-NMR (400 MHz, pyridine-d_5) <u>synthetic</u> meroapplanin B **ppm**	Δ ppm
1	-	-	-
2	-	-	-
3	2.44 (m)	2.51 – 2.46 (m)	+0.02
	1.78 (m)	1.91 – 1.85 (m)	+0.07
4	2.05 (m)	2.14 – 2.08 (m)	+0.03
	1.81 (m)	1.84 – 1.78 (m)	+0.03
5	4.59 (br, s)	4.63 (dd, *J* = 7.1, 5.0 Hz)	+0.04
5-OH	-	-	-
6	-	-	-
7	5.13 (d, *J* = 9.9 Hz)	5.16 (d, *J* = 9.8 Hz)	+0.03
	4.44 (d, *J* = 9.9 Hz)	4.47 (d, *J* = 9.8 Hz)	+0.03
8	4.68 (s)	4.71 (s)	+0.04
9	3.48 (s)	3.51 (s)	+0.03
10	3.92 (d, *J* = 15.4 Hz)	3.95 (d, *J* = 15.4 Hz)	+0.03
	2.34 (d, *J* = 15.4 Hz)	2.40 (d, *J* = 15.4 Hz)	+0.06
11	-	-	-
12	-	-	-
13	7.68 (d, *J* = 2.8 Hz)	7.71 (d, *J* = 2.9 Hz)	+0.03
14-OH	-	-	-
15	7.15 (d, *J* = 8.8 Hz)	7.19 (d, *J* = 8.8 Hz)	+0.04
16	7.28 (dd, *J* = 8.8, 2.8 Hz)	7.31 (dd, *J* = 8.8, 2.8 Hz)	+0.03
17-OH	-	13.82 (s)	-

Table 11: Comparison of ^{13}C-NMR shifts for natural and synthetic meroapplanin B.

No	^{13}C-NMR (150 MHz, pyridine-d_5) isolated meroapplanin B ppm	^{13}C-NMR (150 MHz, pyridine-d_5) synthetic meroapplanin B ppm	Δ ppm
1	181.5	182.1	+0.6
2	57.6	58.3	+0.7
3	35.4	36.0	+0.6
4	33.7	34.3	+0.6
5	77.5	78.1	+0.6
6	53.4	54.0	+0.6
7	67.7	68.3	+0.6
8	94.5	95.1	+0.6
9	56.2	56.8	+0.6
10	32.7	33.3	+0.6
11	173.0	173.6	+0.6
12	118.6	119.2	+0.6
13	114.6	115.3	+0.7
14	150.8	151.4	+0.6
15	122.5	123.1	+0.6
16	119.0	119.6	+0.6
17	155.2	155.8	+0.6



Applanatumol I (298)

To a solution of lingzhilactone B (**24**) (2.20 mg, 6.87 µmol, 1 equiv) and potassium dihydrogen phosphate (1.87 mg, 13.7 µmol, 2.00 equiv) in *tert*-butanol (180 µL), 2-methyl-2-butene (60 µL) and water (60 µL) was added sodium chlorite (2.33 mg, 20.6 µmol, 3.00 equiv) at 0 °C. After one hour, the reaction mixture was allowed to warm to 23 °C. After one hour at 23 °C, a saturated aqueous solution of ammonium chloride (5 mL) and ethyl acetate (5 mL) were added to the reaction mixture and the layers were separated. The aqueous layer was extracted with ethyl acetate (3 × 2 mL) and the combined organic layers were dried over sodium sulfate. The dried solution was filtered and the filtrate was concentrated to yield applanatumol I (**298**) (1.80 mg, 5.35 µmol, 78%) as a colourless solid.

Note: The product is instable on silica gel and analytical data of crude applanatumol I were obtained.

TLC (20% methanol in dichloromethane): R_f = 0.20 (CAM).

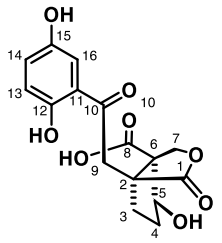
^{1}H NMR (600 MHz, methanol-d_4) δ 7.23 (d, *J* = 3.0, Hz, 1H, 16-H), 7.01 (dd, *J* = 9.0, 2.9 Hz, 1H, 14-H), 6.78 (d, *J* = 9.0 Hz, 1H, 13-H), 4.93 (d, *J* = 9.7 Hz, 1H, 7-H), 4.83 (d, *J* = 9.7 Hz, 1H, 7-H), 4.54 (dd, *J* = 11.2, 5.8 Hz, 1H, 5-H), 4.06 (d, *J* = 18.8 Hz, 1H, 9-H), 3.59 (d, *J* = 18.8 Hz, 1H, 9-H), 2.07 – 2.03 (m, 1H, 3-H), 2.03 – 1.99 (m, 1H, 4-H), 1.94 (td, *J* = 12.8, 5.4 Hz, 1H, 3-H), 1.55 – 1.46 (m, 1H, 4-H).

^{13}C NMR (151 MHz, methanol-d_4) δ 205.2 (C-10), 184.0 (C-1), 176.2 (C-8), 156.5 (C-12), 150.8 (C-15), 126.4 (C-14), 120.0 (C-11), 119.8 (C-13), 115.3 (C-16), 80.9 (C-5), 68.8 (C-7), 60.4 (C-6), 55.3 (C-2), 46.3 (C-9), 36.0 (C-3), 32.1 (C-4).

IR (Diamond-ATR, neat) $\tilde{\upsilon}_{max}$: 3381 (br, w), 2927 (m), 2856 (w), 1734 (s), 1643 (m), 1485 (w), 1381 (m), 1227 (s), 1178 (m), 1098 (w), 1023 (m), 834 (w), 782 (w) cm^{-1}.

HRMS (ESI) calc. for $C_{16}H_{16}NaO_8$ $[M+Na]^+$: 359.0737 found: 359.0728.

Table 12: Comparison of ^{1}H-NMR shifts for natural[174] and synthetic applanatumol I.

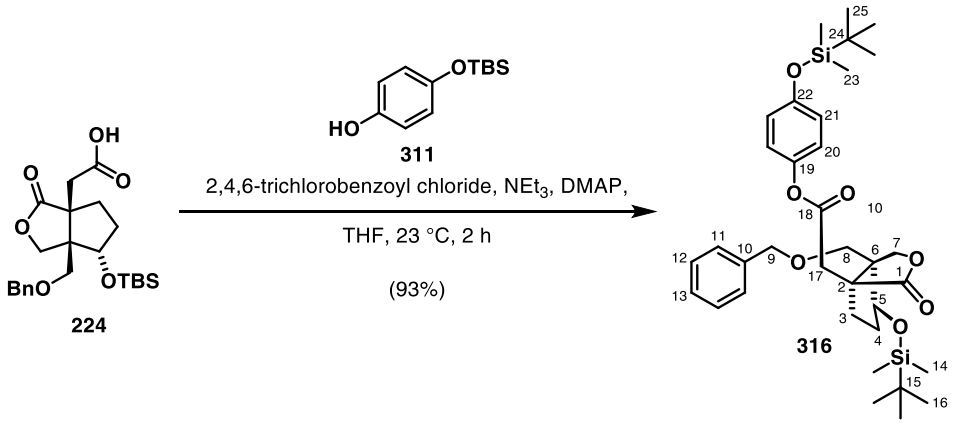


lingzhilactone I (298)

No	^{1}H-NMR (600 MHz, methanol-d_4) <u>isolated</u> applanatumol I **ppm**	^{1}H-NMR (600 MHz, methanol-d_4) <u>synthetic</u> applanatumol I **ppm**	Δ ppm
1	-	-	-
2	-	-	-
3	2.06 (m)	2.07 – 2.03 (m)	–0.1
	1.96 (m)	1.94 (td, *J* = 12.8, 5.4 Hz)	–0.2
4	2.02 (m)	2.03 – 1.99 (m)	–0.1
	1.51 (m)	1.55 – 1.46 (m)	–0.1
5	4.54 (dd, *J* = 11.2, 5.8 Hz)	4.54 (dd, *J* = 11.2, 5.8 Hz)	±0
5-OH	-	-	-
6	-	-	-
7	4.93 (d, *J* = 9.7 Hz)	4.93 (d, *J* = 9.7 Hz)	±0
	4.83 (d, *J* = 9.7 Hz)	4.83 (d, *J* = 9.7 Hz)	±0
8	-	-	-
9	4.05 (d, *J* = 18.8 Hz)	4.06 (d, *J* = 18.8 Hz)	+0.1
	3.60 (d, *J* = 18.8 Hz)	3.59 (d, *J* = 18.8 Hz)	–0.1
10	-	-	-
11	-	-	-
12-OH	-	-	-
13	6.79 (d, *J* = 8.9 Hz)	6.78 (d, *J* = 9.0 Hz)	–0.1
14	7.02 (dd, *J* = 8.9, 2.9 Hz)	7.01 (dd, *J* = 9.0, 3.0 Hz)	–0.1
15-OH	-	-	-
16	7.24 (d, *J* = 2.9 Hz)	7.23 (d, *J* = 3.0 Hz)	–0.1

Table 13: Comparison of ^{13}C-NMR shifts for natural and synthetic applanatumol I.

No	^{13}C-NMR (150 MHz, methanol-d_4) isolated applanatumol I **ppm**	^{13}C-NMR (151 MHz, methanol-d_4) synthetic applanatumol I **ppm**	Δ ppm
1	183.9	184.0	+0.1
2	55.3	55.3	±0
3	36.0	36.0	±0
4	32.0	32.1	+0.1
5	80.8	80.9	+0.1
6	60.4	60.4	±0
7	68.7	68.8	+0.1
8	176.1	176.2	+0.1
9	46.3	46.3	±0
10	205.1	205.2	+0.1
11	119.9	120.0	+0.1
12	156.5	156.5	±0
13	119.8	119.8	±0
14	126.4	126.4	±0
15	150.8	150.8	±0
16	115.3	115.3	±0



Ester 316

To a solution of acid **224** (66 mg, 152 µmol, 1 equiv) and phenol **311** (44.3 mg, 197 µmol, 1.30 equiv) in tetrahydrofuran (1.5 mL) was added triethylamine (169 µl, 1.21 mmol, 8.00 equiv) followed by 2,4,6-trichlorobenzoyl chloride (121 µl, 759 µmol, 5.00 equiv) at 23 °C. After 15 minutes, 4-(dimethylamino)pyridine (1.87 mg, 15.0 µmol, 0.100 equiv) was added. After two hours, the reaction mixture was concentrated and the residue was purified by flash column chromatography on silica gel (10% ethyl acetate in cyclohexane) to yield ester **316** (90.0 mg, 140 µmol, 93%) as a colourless solid.

TLC (30% ethyl acetate in cyclohexane): R_f = 0.62 (CAM, UV).

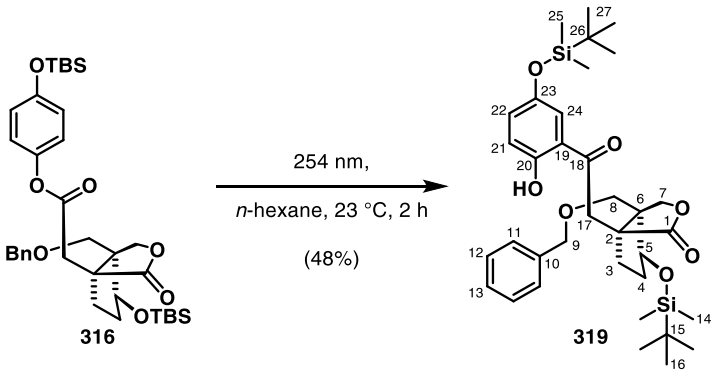
mp: (78-79) °C

^{1}H NMR (400 MHz, chloroform-*d*) δ 7.41 – 7.31 (m, 5H, 11-H, 12-H, 13-H), 6.86 – 6.82 (m, 2H, 20-H or 21-H), 6.79 – 6.74 (m, 2H, 20-H or 21-H), 4.68 (d, *J* = 9.3 Hz, 1H, 7-H), 4.50 – 4.46 (m, 2H, 9-H), 4.43 (dd, *J* = 10.9, 6.3 Hz, 1H, 5-H), 3.75 (d, *J* = 9.3 Hz, 1H, 7-H), 3.57 (d, *J* = 9.8 Hz, 1H, 8-H), 3.39 (d, *J* = 9.8 Hz, 1H, 8-H), 3.26 (d, *J* = 18.0 Hz, 1H, 17-H), 3.13 (d, *J* = 18.0 Hz, 1H, 17-H), 2.10 (dd, *J* = 12.9, 6.5 Hz, 1H, 3-H), 1.88 (dt, *J* = 12.0, 6.0 Hz, 1H, 4-H), 1.69 (td, *J* = 13.2, 6.0 Hz, 1H, 3-H), 1.51 – 1.40 (m, 1H, 4-H), 0.97 (s, 9H, 16-H or 25-H), 0.87 (s, 9H, 16-H or 25-H), 0.18 (s, 6H, 14-H or 23-H), 0.06 – 0.01 (m, 6H, 14-H or 23-H).

^{13}C NMR (101 MHz, chloroform-*d*) δ 182.3 (C-1), 153.5 (C-18), 144.4 (C-22), 137.5 (C-19), 128.8 (C-10), 128.5 (C-12), 128.2 (C-13), 128.1 (C-11), 122.2 (C-20 or C-21), 120.6 (C-20 or C-21), 75.2 (C-5), 74.0 (C-9), 69.9 (C-8), 68.3 (C-7), 53.6 (C-6, C-2), 38.5 (C-17), 34.8 (C-3), 31.4 (C-4), 25.9 (C-16 or C-25), 25.8 (C-16 or C-25), 18.1 (C-15, C-24), –4.3 (C-14 or C-23), –4.3 (C-14 or C-23), –5.0 (C-14 or C-23).

IR (Diamond-ATR, neat) $\tilde{\upsilon}_{max}$: 2955 (w), 2929 (w), 2857 (w), 1767 (m), 1502 (s), 1254 (m), 1189 (m), 1145 (s), 1035 (m), 913 (m), 837 (s), 778 (s), 698 (w) cm^{-1}.

HRMS (ESI) calc. for $C_{35}H_{52}NaO_7Si_2$ $[M+Na]^+$: 663.3144 found: 663.3157.



Ketone 319

A solution of ester **316** (93.9 mg, 146 µmol, 1 equiv) in degassed *n*-hexane (6 mL) was irradiated at 254 nm in a quartz tube. *Note: The reaction was set up in three parallel batches (31.3 mg and 2 mL n-hexane each) and irradiated at the same time.* After two hours, the reaction mixture was concentrated and the residue was purified by flash column chromatography on silica gel (5% ethyl acetate in cyclohexane) to yield ketone **319** (45.0 mg, 70.0 µmol, 48%) as a slightly yellow solid.

TLC (10% ethyl acetate in cyclohexane): R_f = 0.39 (CAM, UV).

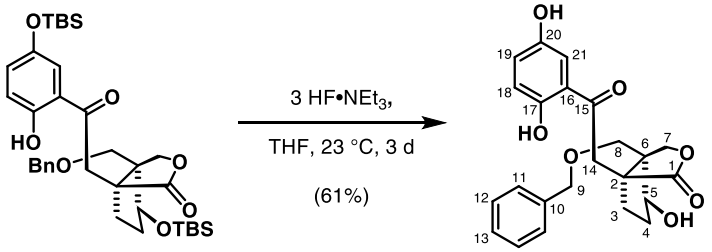
mp: (78-79) °C

^{1}H NMR (400 MHz, chloroform-*d*) δ 11.39 (s, 1H, 20-OH), 7.20 – 7.14 (m, 3H, aromatic), 7.07 – 7.01 (m, 4H, aromatic), 6.87 (d, *J* = 8.8 Hz, 1H, 21-H), 4.75 (d, *J* = 9.2 Hz, 1H, 7-H), 4.46 (dd, *J* = 11.1, 6.1 Hz, 1H, 5-H), 4.29 (d, *J* = 11.5 Hz, 1H, 9-H), 4.13 (d, *J* = 11.5 Hz, 1H, 9-H), 3.87 – 3.78 (m, 2H, 7-H, 17-H), 3.47 (d, *J* = 18.8 Hz, 1H, 17-H), 3.36 (d, *J* = 9.7 Hz, 1H, 8-H), 3.27 (d, *J* = 9.7 Hz, 1H, 8-H), 2.07 (dd, *J* = 12.8, 6.3 Hz, 1H, 3-H), 1.88 (dt, *J* = 11.9, 5.9 Hz, 1H, 4-H), 1.72 (td, *J* = 13.3, 5.8 Hz, 1H, 3-H), 1.54 – 1.45 (m, 1H, 4-H), 0.99 (s, 9H, 16-H or 27-H), 0.89 (s, 9H, 16-H or 27-H), 0.17 (s, 6H, 14-H or 25-H), 0.08 – 0.01 (m, 6H, 14-H or 25-H).

^{13}C NMR (101 MHz, chloroform-*d*) δ 203.7 (C-18), 183.0 (C-1), 157.2 (aromatic), 147.5 (aromatic), 137.0 (aromatic), 129.8 (aromatic), 128.6 (aromatic), 128.1 (aromatic), 119.5 (aromatic), 119.2 (aromatic), 118.6 (aromatic), 75.0 (C-5), 73.9 (C-9), 69.8 (C-8), 68.4 (C-7), 53.4 (C-6), 51.5 (C-2), 43.9 (C-17), 35.1 (C-3), 31.1 (C-4), 25.9 (C-16 or C-27), 25.8 (C-16 or C-27), 18.3 (C-15 or C-26), 18.1 (C-15 or C-26), –4.2 (C-14 or C-25), –4.3 (C-14 or C-25), –4.9 (C-14 or C-25).

IR (Diamond-ATR, neat) $\tilde{\upsilon}_{max}$: 2955 (m), 2930 (m), 2857 (m), 1768 (s), 1644 (w), 1614 (w), 1483 (s), 1363 (w), 1275 (m), 1255 (s), 1176 (m), 1154 (m), 1132 (m), 1037 (m), 953 (m), 839 (s), 752 (m), 699 (w) cm^{-1}.

HRMS (ESI) calc. for $C_{35}H_{52}NaO_7Si_2$ $[M+Na]^+$: 663.3144 found: 663.3157.



319 **348**

Hydroquinone 348

To a solution of ketone **319** (16.7 mg, 26.1 µmol, 1 equiv) in tetrahydrofuran (200 µL) was added hydrogen fluoride triethylamine (217 µL, 1.30 mmol, 50.0 equiv) at 23 °C. After three days, a saturated aqueous solution of sodium bicarbonate (5 mL) and ethyl acetate (5 mL) were added to the reaction mixture and the layers were separated. The aqueous layer was extracted with ethyl acetate (3 × 2 mL), the combined organic layers were dried over sodium sulfate. The dried solution was filtered and the filtrate was concentrated. The residue was purified by flash column chromatography on silica gel (5% methanol in dichloromethane) to yield hydroquinone **348** (6.60 mg, 16.0 µmol, 61%) as a yellow oil.

TLC (5% methanol in dichloromethane): R_f = 0.35 (CAM, UV).

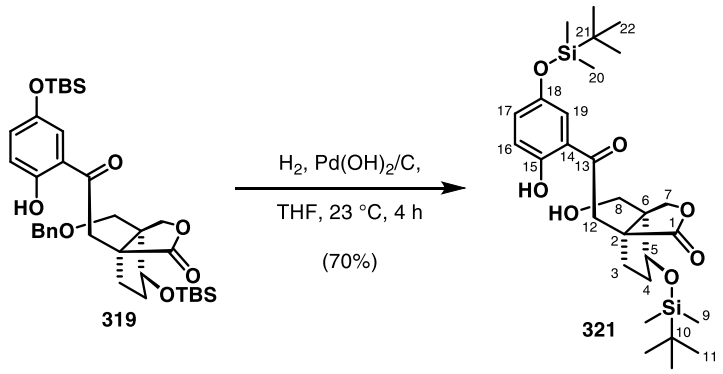
^{1}H NMR (400 MHz, methanol-d_4) δ 7.08 – 7.04 (m, 4H, aromatic), 7.00 – 6.97 (m, 2H, aromatic), 6.98 – 6.94 (m, 1H, 19-H), 6.72 (d, *J* = 9.0 Hz, 1H, 18-H), 4.65 (d, *J* = 9.2 Hz, 1H, 7-H), 4.34 – 4.27 (m, 2H,

5-H, 9-H), 4.08 (d, *J* = 11.6 Hz, 1H, 9-H), 3.88 (d, *J* = 9.2 Hz, 1H, 7-H), 3.80 (d, *J* = 19.0 Hz, 1H, 14-H), 3.38 (d, *J* = 19.1 Hz, 1H, 14-H), 3.30 (s, 2H, 8-H), 1.93 – 1.84 (m, 2H, 3-H, 4-H), 1.73 – 1.63 (m, 1H, 3-H), 1.40 – 1.31 (m, 1H, 4-H).

^{13}C NMR (101 MHz, methanol-d_4) δ 205.0 (C-15), 185.8 (C-1), 156.5 (C-20), 150.8 (C-14), 138.6 (C-10), 129.3 (C-11 or C-12), 129.1 (C-11 or C-12), 128.8 (C-13), 126.3 (C-19), 120.0 (C-16), 119.9 (C-18), 115.4 (C-21), 75.9 (C-5), 74.7 (C-9), 71.0 (C-8), 69.6 (C-7), 54.0 (C-2 or C-6), 53.7 (C-2 or C-6), 45.2 (C-14), 35.9 (C-3), 31.5 (C-4).

IR (Diamond-ATR, neat) $\tilde{\upsilon}_{max}$: 3354 (br,w), 2958 (w), 2871 (w), 1739 (s), 1642 (m), 1484 (m), 1453 (m), 1278 (m), 1234 (m), 1174 (s), 1100 (m), 1027 (m) cm^{-1}.

HRMS (ESI) calc. for $C_{23}H_{24}NaO_7$ $[M+Na]^+$: 435.1414 found: 435.1403.



Alcohol 321

To a solution of ketone **319** (43.0 mg, 67.0 µmol, 1 equiv) in tetrahydrofuran (4 mL) was added $Pd(OH)_2/C$ (20 wt%, 31.4 mg, 34.0 µmol, 0.500 equiv). The reaction vessel was placed in a high-pressure autoclave and exposed to hydrogen pressure of 40.0 bar. After four hours, the gas was released and the autoclave was purged with nitrogen for one minute. The reaction mixture was filtered through a pad of Celite and the pad washed with dichloromethane (5 mL). The filtrate was concentrated and the residue was purified by flash column chromatography on silica gel (5% grading to 20% ethyl acetate in cyclohexane) to yield alcohol **321** (26.0 mg, 47.0 µmol, 70%) as a colourless solid.

TLC (20% ethyl acetate in cyclohexane): R_f = 0.20 (CAM, UV).

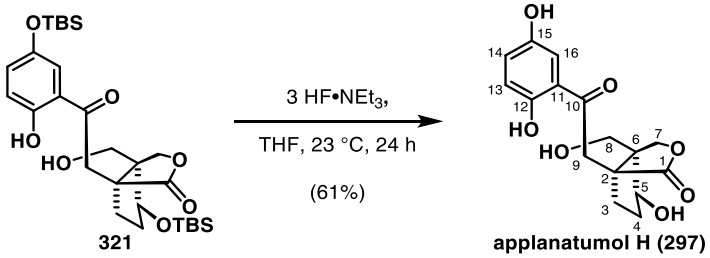
mp: (169-170) °C

^{1}H NMR (600 MHz, chloroform-*d*) δ 11.43 (s, 1H, 15-OH), 7.14 (d, *J* = 2.9 Hz, 1H, 19-H), 7.02 (dd, *J* = 9.0, 2.9 Hz, 1H, 17-H), 6.86 (d, *J* = 8.9 Hz, 1H, 16-H), 4.77 (d, *J* = 9.3 Hz, 1H, 7-H), 4.45 (dd, *J* = 11.1, 6.1 Hz, 1H, 5-H), 3.89 – 3.84 (m, 2H, 7-H, 12-H), 3.62 (dd, *J* = 10.5, 3.0 Hz, 1H, 8-H), 3.55 – 3.49 (m, 2H, 8-H, 12-H), 2.11 (dd, *J* = 12.8, 6.4 Hz, 1H, 3-H), 1.92 (dt, *J* = 12.0, 5.9 Hz, 1H, 4-H), 1.75 (td, *J* = 13.3, 5.8 Hz, 1H, 3-H), 1.54 – 1.49 (m, 1H, 4-H), 0.99 (s, 9H, 11-H or 22-H), 0.90 (s, 9H, 11-H or 22-H), 0.19 – 0.18 (m, 6H, 9-H or 20-H), 0.10 – 0.07 (m, 6H, 9-H or 20-H).

^{13}C NMR (151 MHz, chloroform-*d*) δ 204.0 (C-13), 183.0 (C-1), 157.2 (C-15), 147.5 (C-18), 130.0 (C-17), 119.5 (C-16), 119.3 (C-19), 118.7 (C-14), 75.1 (C-5), 68.4 (C-7), 62.8 (C-8), 53.8 (C-6), 51.5 (C-2), 43.6 (C-12), 35.1 (C-3), 31.2 (C-4), 25.9 (C-11 or C-22), 25.8 (C-11 or C-22), 18.3 (C-10 or C-21), 18.1 (C-10 or C-21), –4.2 (C-9 or C-20), –4.3 (C-9 or C-20), –4.3 (C-9 or C-20), –4.9 (C-9 or C-20).

IR (Diamond-ATR, neat) $\tilde{\upsilon}_{max}$: 3457 (br, w), 2955 (m), 2929 (m), 2858 (m), 1747 (s), 1484 (s), 1255 (s), 1174 (m), 954 (m), 838 (s), 778 (m), 728 (w) cm^{-1}.

HRMS (ESI) calc. for $C_{28}H_{46}NaO_7Si_2$ $[M+Na]^+$: 573.2674 found: 573.2665.



Applanatumol H (297)

To a solution of alcohol **321** (7.80 mg, 14.0 µmol, 1 equiv) in tetrahydrofuran (100 µL) was added hydrogen fluoride triethylamine (118 µL, 708 µmol, 50.0 equiv) at 23 °C. After 24 hours, a saturated aqueous solution of sodium bicarbonate (5 mL) and ethyl acetate (5 mL) were added to the reaction mixture and the layers were separated. The aqueous layer was extracted with ethyl acetate (3 × 2 mL) and the combined organic layers were dried over sodium sulfate. The dried solution was filtered and the filtrate was concentrated. The residue was purified by flash column chromatography on silica gel (5% grading to 20% methanol in dichloromethane) to yield applanatumol H (**297**) (2.80 mg, 8.69 µmol, 61%) as a colourless solid.

TLC (10% methanol in dichloromethane): R_f = 0.33 (CAM, UV).

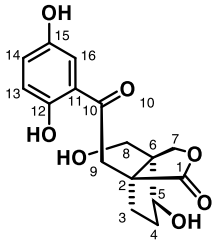
^{1}H NMR (400 MHz, methanol-d_4) δ 7.24 (d, *J* = 2.9 Hz, 1H, 16-H), 7.02 (dd, *J* = 8.9, 2.9 Hz, 1H), 6.80 (d, *J* = 9.0 Hz, 1H), 4.75 (d, *J* = 9.0 Hz, 1H), 4.38 (dd, *J* = 11.0, 6.2 Hz, 1H), 4.01 – 3.95 (m, 2H, 7-H, 9-H), 3.53 – 3.47 (m, 3H, 8-H, 9-H), 2.03 – 1.94 (m, 2H, 3-H, 4-H), 1.79 (td, *J* = 13.1, 5.8 Hz, 1H, 3-H), 1.42 (dddd, *J* = 15.8, 13.3, 11.4, 6.6 Hz, 1H).

^{13}C NMR (151 MHz, methanol-d_4) δ 205.5 (C-10), 186.1 (C-1), 156.5 (C-12), 150.8 (C-15), 126.3 (C-14), 120.2 (C-11), 119.8 (C-13), 115.5 (C-16), 75.9 (C-5), 70.0 (C-7), 63.2 (C-8), 54.3 (C-6), 53.7 (C-2), 44.6 (C-9), 35.8 (C-3), 31.8 (C-4).

IR (Diamond-ATR, neat) $\tilde{\upsilon}_{max}$: 3389 (br, m), 2956 (m), 2921 (s), 2852 (m), 1739 (s), 1486 (m), 1277 (s), 1174 (s), 1020 (m), 783 (w) cm^{-1}.

HRMS (ESI) calc. for $C_{16}H_{18}NaO_7$ $[M+Na]^+$: 345.0945 found: 345.0933.

Table 14: Comparison of ^{1}H-NMR shifts for natural[174] and synthetic applanatumol H.

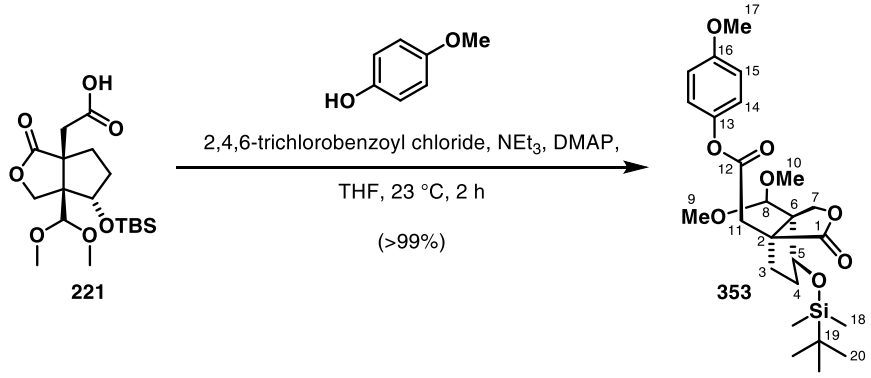


applanatumol H (297)

No	^{1}H-NMR (600 MHz, methanol-d_4) <u>isolated</u> applanatumol H **ppm**	^{1}H-NMR (400 MHz, methanol-d_4) <u>synthetic</u> applanatumol H **ppm**	Δ ppm
1	-	-	-
2	-	-	-
3	1.98 (overlap)	2.03 – 1.94 (m, overlap)	+0.01
	1.78 (m)	1.79 (td, *J* = 13.1, 5.8 Hz)	+0.01
4	1.98 (overlap)	2.03 – 1.94 (m, overlap)	+0.01
	1.42 (m)	1.42 (dddd, *J* = 15.8, 13.3, 11.4, 6.6 Hz)	±0
5	4.38 (dd, *J* = 10.8, 6.1 Hz)	4.38 (dd, *J* = 11.0, 6.2 Hz)	±0
5-OH	-	-	-
6	-	-	-
7	4.75 (d, *J* = 9.1 Hz)	4.75 (d, *J* = 9.0 Hz)	±0
	4.00 (d, *J* = 9.1 Hz)	4.01 – 3.95 (m, overlap)	–0.02
8	3.51 (s)	3.53 – 3.47 (m, overlap)	–0.01
9	3.97 (d, *J* = 15.9 Hz)	4.01 – 3.95 (m, overlap)	+0.01
	3.48 (d, *J* = 15.9 Hz)	3.53 – 3.47 (m, overlap)	+0.02
10	-	-	-
11	-	-	-
12-OH	-	-	-
13	6.80 (d, *J* = 8.9 Hz)	6.80 (d, *J* = 9.0 Hz)	±0
14	7.02 (dd, *J* = 8.9, 2.9 Hz)	7.02 (dd, *J* = 8.9, 2.9 Hz)	±0
15-OH	-	-	-
16	7.24 (d, *J* = 2.9 Hz)	7.24 (d, *J* = 2.9 Hz)	±0

Table 15: Comparison of ^{13}C-NMR shifts for natural and synthetic applanatumol H.

No	^{13}C-NMR (150 MHz, methanol-d_4) isolated applanatumol H **ppm**	^{13}C-NMR (151 MHz, methanol-d_4) synthetic applanatumol H **ppm**	Δ ppm
1	186.1	186.1	±0
2	53.8	53.7	–0.1
3	35.8	35.8	±0
4	31.7	31.8	+0.1
5	76.0	75.9	–0.1
6	54.3	54.3	±0
7	70.0	70.0	±0
8	63.2	63.2	±0
9	44.8	44.6 (low intensity due to deuteration in methanol-d_4)	–0.2
10	205.4	205.5	+0.1
11	120.0	120.2	+0.2
12	156.4	156.5	+0.1
13	119.8	119.8	±0
14	126.3	126.3	±0
15	150.6	150.8	+0.2
16	115.4	115.5	+0.1



Ester 353

To a solution of acid **221** (97.4 mg, 251 µmol, 1 equiv) and 4-methoxyphenol (45.0 mg, 326 µmol, 1.30 equiv) in tetrahydrofuran (2.5 mL) was added triethylamine (279 µl, 2.01 mmol, 8.00 equiv) followed by 2,4,6-trichlorobenzoyl chloride (200 µl, 1.25 mmol, 5.00 equiv) at 23 °C. After 15 minutes, 4-(dimethylamino)pyridine (3.09 mg, 25.0 µmol, 0.100 equiv) was added. After two hours, the reaction mixture was concentrated and the residue was purified by flash column chromatography on silica gel (5% ethyl acetate in cyclohexane) to yield ester **353** (124 mg, 251 µmol, >99%) as a colourless solid.

TLC (20% ethyl acetate in cyclohexane): R_f = 0.28 (CAM, UV).

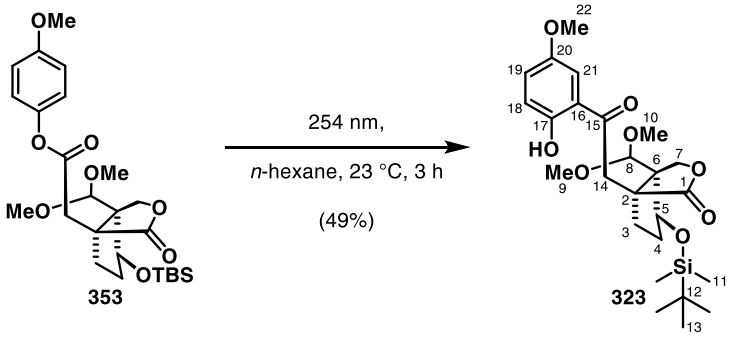
mp: (123-124) °C

^{1}H NMR (700 MHz, chloroform-*d*) δ 7.01 (d, *J* = 9.1 Hz, 1H, 18-H), 6.88 (d, *J* = 9.1 Hz, 1H, 17-H), 4.76 (d, *J* = 9.0 Hz, 1H, 7-H), 4.55 (dd, *J* = 9.7, 6.7 Hz, 1H, 5-H), 4.34 (s, 1H, 8-H), 4.10 (d, *J* = 9.0 Hz, 1H, 7-H), 3.79 (s, 3H, 20-H), 3.51 (s, 3H, 9-H or 10-H), 3.49 (s, 3H, 9-H or 10-H), 3.13 – 3.04 (m, 2H, 14-H), 2.09 – 2.05 (m, 1H, 3-H), 1.96 (dtd, *J* = 12.8, 6.6, 1.7 Hz, 1H, 4-H), 1.71 (td, *J* = 12.9, 6.5 Hz, 1H, 3-H), 1.41 – 1.37 (m, 1H, 4-H).

^{13}C NMR (176 MHz, chloroform-*d*) δ 181.8 (C-15), 170.7 (C-1), 157.5 (C-19), 144.1 (C-16), 122.3 (C-18), 114.6 (C-17), 108.8 (C-8), 75.2 (C-5), 68.2 (C-7), 59.2 (C-9 or C-10), 58.2 (C-6), 57.7 (C-9 or C-10), 55.8 (C-20), 53.3 (C-2), 38.4 (C-14), 34.9 (C-3), 32.9 (C-4), 25.9 (C-13), 18.1 (C-12), –4.3 (C-11), –4.9 (C-11).

IR (Diamond-ATR, neat) $\tilde{\upsilon}_{max}$: 2955 (m), 2929 (m), 2855 (w), 1767 (s), 1506 (s), 1251 (m), 1195 (s), 1149 (s), 1070 (m), 1028 (m), 839 (m), 777 (w) cm^{-1}.

HRMS (ESI) calc. for $C_{25}H_{38}NaO_8Si$ $[M+Na]^+$: 517.2228 found: 517.2226.



Ketone 323

A solution of ester **353** (100 mg, 202 µmol, 1 equiv) in degassed *n*-hexane (12 mL) was irradiated at 254 nm (23 °C) in a quartz tube. *Note: The reaction was set up in three parallel batches (33.3 mg and 4 mL n-hexane each) and irradiated at the same time.* After three hours, the reaction mixture was concentrated and the residue was purified by flash column chromatography on silica gel (5% ethyl acetate in cyclohexane) to yield ketone **323** (49.0 mg, 99.0 µmol, 49%) as a slightly yellow solid.

TLC (20% ethyl acetate in cyclohexane): R_f = 0.29 (CAM, UV).

mp: (158-159) °C

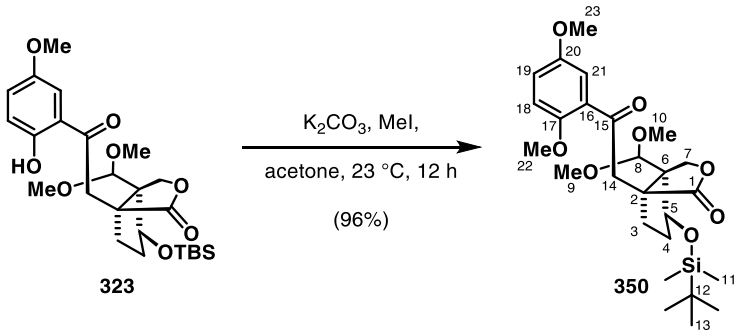
^{1}H NMR (700 MHz, chloroform-*d*) δ 11.53 (s, 1H, 17-OH), 7.16 (d, *J* = 3.0 Hz, 1H, 21-H), 7.13 (dd, *J* = 9.0, 3.0 Hz, 1H, 19-H), 6.94 (d, *J* = 9.1 Hz, 1H, 18-H), 4.87 (d, *J* = 8.8 Hz, 1H, 7-H), 4.55 (dd, *J* = 10.0, 6.6 Hz, 1H, 5-H), 4.20 (d, *J* = 8.8 Hz, 1H, 7-H), 4.13 (s, 1H, 8-H), 3.81 (s, 3H, 22-H), 3.72 (d,

J = 18.6 Hz, 1H, 14-H), 3.49 (d, *J* = 18.6 Hz, 1H, 14-H), 3.38 (s, 3H, 9-H or 10-H), 3.25 (s, 3H, 9-H or 10-H), 2.05 (ddd, *J* = 12.6, 6.6, 1.7 Hz, 1H, 3-H), 1.95 (ddd, *J* = 12.7, 6.3, 1.7 Hz, 1H, 4-H), 1.70 (td, *J* = 12.8, 6.2 Hz, 1H, 3-H), 1.45 – 1.40 (m, 1H, 4-H), 0.90 (s, 9H, 13-H), 0.07 – 0.06 (m, 6H, 11-H).

^{13}C NMR (176 MHz, chloroform-*d*) δ 203.8 (C-15), 182.6 (C-1), 156.9 (C-20), 151.9 (C-17), 124.5 (C-19), 119.7 (C-18), 118.5 (C-16), 112.6 (C-21), 108.9 (C-8), 75.2 (C-5), 68.3 (C-7), 59.4 (C-9 or C-10), 57.8 (C-6), 57.3 (C-9 or C-10), 56.3 (C-22), 52.7 (C-2), 43.4 (C-14), 35.3 (C-3), 32.7 (C-4), 25.9 (C-13), 18.2 (C-12), –4.3 (C-11), –5.0 (C-11).

IR (Diamond-ATR, neat) $\tilde{\upsilon}_{max}$: 2955 (m), 2849 (w), 1759 (s), 1676 (w), 1500 (s), 1393 (w), 1258 (m), 1185 (s), 1032 (s), 837 (m), 720 (w) cm^{-1}.

HRMS (ESI) calc. for $C_{25}H_{38}NaO_8Si$ $[M+Na]^+$: 517.2228 found: 517.2226.



1,4-Dimethylhydroquinone 350

To a solution of ketone **323** (39.0 mg, 79.0 µmol, 1 equiv) in acetone (1 mL) was added potassium carbonate (21.8 mg, 158 µmol, 2.00 equiv) and iodomethane (6.00 µL, 95.0 µmol, 1.20 equiv) in sequence at 23 °C. After 12 hours, the mixture was filtered and the filtrate was concentrated. The residue was purified by flash column chromatography on silica gel (20% ethyl acetate in cyclohexane) to yield 1,4-dimethylhydroquinone **350** (38.3 mg, 75.0 µmol, 96%) as a slightly yellow solid.

TLC (10% ethyl acetate in cyclohexane): R_f = 0.11 (CAM, UV).

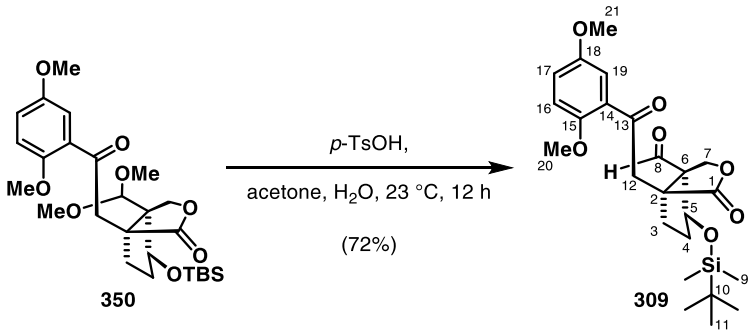
mp: (127-128) °C

^{1}H NMR (400 MHz, chloroform-*d*) δ 7.33 (d, *J* = 3.3 Hz, 1H, 21-H), 7.05 (dd, *J* = 9.0, 3.3 Hz, 1H, 19-H), 6.92 (d, *J* = 9.0 Hz, 1H, 18-H), 4.90 (d, *J* = 8.7 Hz, 1H, 7-H), 4.61 (dd, *J* = 10.0, 6.5 Hz, 1H, 5-H), 4.28 (d, *J* = 8.7 Hz, 1H, 7-H), 4.20 (s, 1H, 8-H), 3.89 (s, 3H, 22-H or 23-H), 3.81 – 3.74 (m, 4H, 22-H or 23-H, 14-H), 3.52 (d, *J* = 19.8 Hz, 1H, 14-H), 3.40 (s, 3H, 9-H or 10-H), 3.33 (s, 3H, 9-H or 10-H), 1.99 (ddd, *J* = 12.3, 6.5, 1.6 Hz, 1H, 3-H), 1.89 (dtd, *J* = 12.4, 6.2, 1.5 Hz, 1H, 4-H), 1.61 (ddd, *J* = 13.4, 12.5, 5.9 Hz, 1H, 3-H), 1.42 – 1.32 (m, 1H, 4-H), 0.89 (d, *J* = 3.2 Hz, 9H, 13-H), 0.06 (s, 6H, 11-H).

^{13}C NMR (101 MHz, chloroform-*d*) δ 199.9 (C-15), 183.2 (C-1), 153.7 (C-20), 127.0 (C-17), 121.5 (C-19), 113.8 (C-21), 113.4 (C-18), 109.4 (C-8), 74.7 (C-5), 68.5 (C-7), 59.4 (C-9 or C-10), 57.3 (C-6), 57.1 (C-9 or C-10), 56.2 (C-22 or C-23), 56.0 (C-22 or C-23), 53.6 (C-2), 49.5 (C-14), 35.2 (C-3), 32.9 (C-4), 25.9 (C-13), 18.2 (C-12), –4.4 (C-11), –5.0 (C-11).

IR (Diamond-ATR, neat) $\tilde{\upsilon}_{max}$: 2955 (m), 2929 (m), 2855 (w), 1764 (s), 1670 (w), 1496 (s), 1465 (m), 1278 (m), 1255 (m), 1152 (s), 1028 (s), 905 (w), 837 (m), 721 (w) cm^{-1}.

HRMS (ESI) calc. for $C_{26}H_{40}NaO_8Si$ $[M+Na]^+$: 531.2385 found: 531.2378.



Aldehyde 309

To a solution of 1,4-dimethylhydroquinone **350** (38.0 mg, 75.0 µmol, 1 equiv) in acetone (1 mL) was added *p*-toluenesulfonic acid monohydrate (1.42 mg, 7.00 µmol, 0.100 equiv) at 23 °C. After 12 hours, the reaction mixture was concentrated and the residue was purified by flash column chromatography (10% ethyl acetate in cyclohexane) to yield aldehyde **309** (24.9 mg, 54.0 µmol, 72%) as slightly yellow oil.

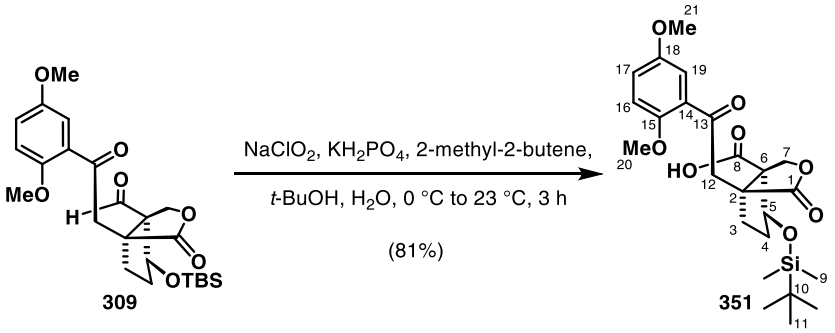
TLC (20% ethyl acetate in cyclohexane): R_f = 0.50 (CAM, UV).

^{1}H NMR (400 MHz, chloroform-*d*) δ 9.59 (s, 1H, 8-H), 7.28 (d, *J* = 3.3 Hz, 1H, 19-H), 7.05 (dd, *J* = 9.0, 3.3 Hz, 1H, 17-H), 6.89 (d, *J* = 9.1 Hz, 1H, 16-H), 5.04 – 4.97 (m, 2H, 7-H), 4.62 (dd, *J* = 11.1, 5.9 Hz, 1H, 5-H), 3.87 (s, 3H, 21-H), 3.76 (s, 3H, 20-H), 3.72 (d, *J* = 19.6 Hz, 1H, 12-H), 3.44 (d, *J* = 19.6 Hz, 1H, 12-H), 2.12 (dd, *J* = 13.2, 6.6 Hz, 1H, 3-H), 1.94 (dt, *J* = 11.9, 5.8 Hz, 1H, 4-H), 1.78 (dd, *J* = 13.4, 5.9 Hz, 1H, 3-H), 1.60 (m, 1H, 4-H), 0.85 (s, 9H, 11-H), 0.01 (m, 6H, 9-H).

^{13}C NMR (101 MHz, chloroform-*d*) δ 203.5 (C-8), 199.4 (C-13), 181.3 (C-1), 154.4 (C-18), 153.6 (C-15), 125.7 (C-14), 122.5 (C-17), 113.5 (C-16 or C-19), 113.3 (C-16 or C-19), 78.8 (C-5), 67.5 (C-7), 63.7 (C-6), 56.1 (C-20 or C-21), 55.9 (C-20 or C-21), 54.7 (C-2), 49.6 (C-12), 34.8 (C-3), 31.9 (C-4), 25.7 (C-11), 18.0 (C-10) –4.5 (C-9), –5.0 (C-9).

IR (Diamond-ATR, neat) $\tilde{\upsilon}_{max}$: 2954 (m), 2930 (m), 2857 (w), 1765 (s), 1720 (m), 1661 (w), 1496 (s), 1464 (m), 1254 (m), 1154 (s), 1133 (s), 1035 (m), 838 (m), 779 (m), 725 (w) cm^{-1}.

HRMS (ESI) calc. for $C_{24}H_{34}NaO_7Si$ $[M+Na]^+$: 485.1966 found: 485.1956.



Acid 351

To a solution of aldehyde **309** (24.0 mg, 52.0 µmol, 1 equiv) and potassium dihydrogen phosphate (14.1 mg, 104 µmol, 2.00 equiv) in *tert*-butanol (600 µL), 2-methyl-2-butene (200 µL) and water (200 µL) was added sodium chlorite (17.6 mg, 156 µmol, 3.00 equiv) at 0 °C. After one hour, the mixture was allowed to warm to 23 °C. After two hours at 23 °C, a saturated aqueous solution of ammonium chloride (5 mL) and ethyl acetate (5 mL) were added to the reaction mixture and the layers were separated. The aqueous layer was extracted with ethyl acetate (3 × 2 mL) and the combined organic layers were dried over sodium sulfate. The dried solution was filtered and the filtrate was concentrated. The residue was purified by flash column chromatography on silica gel (30% ethyl acetate in hexane) to yield acid **351** (20.0 mg, 42.0 µmol, 81%) as a colourless solid.

TLC (30% ethyl acetate in cyclohexane): R_f = 0.14 (CAM, UV).

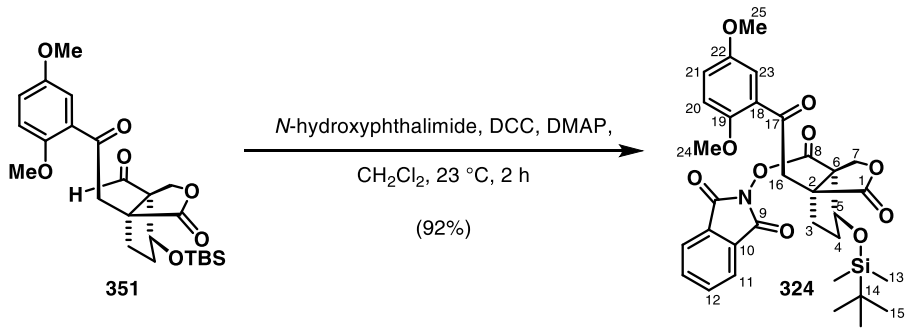
mp: (207-208) °C

^{1}H NMR (400 MHz, chloroform-*d*) δ 7.27 (d, *J* = 3.3 Hz, 1H, 19-H), 7.01 (dd, *J* = 9.0, 3.3 Hz, 1H, 17-H), 6.87 (d, *J* = 9.0 Hz, 1H, 16-H), 4.97 (d, *J* = 9.7 Hz, 1H, 7-H), 4.83 (d, *J* = 9.7 Hz, 1H, 7-H), 4.43 (dd, *J* = 11.0, 5.7 Hz, 1H, 5-H), 3.92 (d, *J* = 19.5 Hz, 1H, 12-H), 3.87 (s, 3H, 21-H), 3.74 (s, 3H, 20-H), 3.66 (d, *J* = 19.5 Hz, 1H, 12-H), 2.10 (dd, *J* = 12.7, 6.3 Hz, 1H, 3-H), 1.92 – 1.85 (m, 1H, 4-H), 1.79 (dd, *J* = 13.3, 5.7 Hz, 1H, 3-H), 1.52 (dtd, *J* = 12.7, 11.3, 10.9, 6.1 Hz, 1H, 4-H), 0.77 (s, 9H, 11-H), –0.15 (m, 6H, 9-H).

^{13}C NMR (101 MHz, chloroform-*d*) δ 199.0 (C-13), 181.4 (C-1, C-8), 154.3 (C-18), 153.5 (C-15), 126.2 (C-14), 121.9 (C-17), 113.8 (C-16 or C-19), 113.3 (C-16 or C-19), 81.1 (C-5), 66.9 (C-7), 56.2 (C-6), 55.9 (C-20 or C-21), 54.4 (C-20 or C-21), 50.1 (C-2), 34.9 (C-12), 31.9 (C-3), 25.9 (C-4), 25.6 (C-11), 17.9 (C-10), –5.0 (C-9), –5.3 (C-9).

IR (Diamond-ATR, neat) $\tilde{\upsilon}_{max}$: 3000 (br, w), 2930 (m), 2857 (m), 1767 (s), 1741 (s), 1702 (s), 1496 (s), 1465 (m), 1278 (s), 1223 (s), 1166 (s), 1127 (s), 1029 (m), 839 (s), 779 (m) cm^{-1}.

HRMS (ESI) calc. for $C_{24}H_{33}O_8Si$ [M–H]$^-$: 477.1950 found: 477.1941.



***N*-(Acyloxy)phthalimide 324**

To a solution of acid **351** (20.0 mg, 42.0 µmol, 1 equiv) in dichloromethane (200 µL) was added 4-(dimethylamino)pyridine (0.500 mg, 4.18 µmol, 0.100 equiv), *N*-hydroxyphthalimide (9.14 mg, 54.0 µmol, 1.30 equiv) and a solution of *N*,*N*'-dicyclohexylcarbodiimide (9.58 mg, 46.0 µmol, 1.10 equiv) in dichloromethane (100 µL) in sequence at 23 °C. After two hours, the mixture was diluted with diethyl ether (2 mL) and filtered through a pad of Celite, the filter cake was washed with diethyl ether (2 mL) and the filtrated was concentrated. The residue was purified by flash column chromatography on silica gel (30% ethyl acetate in hexane) to yield *N*-(acyloxy)phthalimide **324** (24.0 mg, 39.0 µmol, 92%) as a colourless solid.

TLC (30% ethyl acetate in cyclohexane): R_f = 0.17 (CAM, UV).

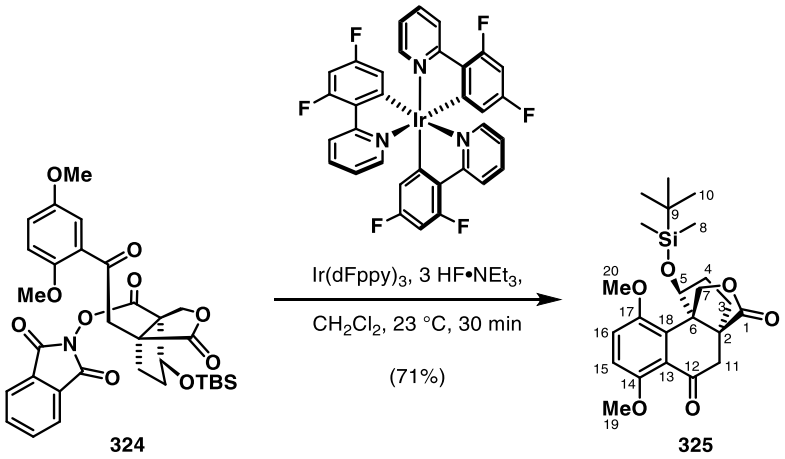
mp: (177-178) °C

^{1}H NMR (400 MHz, chloroform-*d*) δ 7.80 – 7.77 (m, 2H, 11-H), 7.73 (dd, *J* = 5.5, 3.1 Hz, 2H, 12-H), 7.46 (d, *J* = 3.3 Hz, 1H, 23-H), 7.04 (dd, *J* = 9.0, 3.3 Hz, 1H, 21-H), 6.89 (d, *J* = 9.0 Hz, 1H, 20-H), 5.19 – 5.10 (m, 2H, 7-H), 4.78 (dd, *J* = 10.5, 5.9 Hz, 1H, 5-H), 4.00 – 3.88 (m, 2H, 16-H), 3.87 (s, 3H, 25-H), 3.82 (s, 3H, 24-H), 2.28 – 2.20 (m, 1H, 3-H), 2.10 – 2.02 (m, 1H, 4-H), 1.94 (dd, *J* = 13.3, 5.9 Hz, 1H, 3-H), 1.63 – 1.59 (m, 1H, 4-H), 0.93 (s, 9H, 15-H), 0.19 – 0.16 (m, 6H, 13-H).

^{13}C NMR (101 MHz, chloroform-*d*) δ 198.6 (C-17), 180.8 (C-1), 169.3 (C-8), 161.3 (C-9), 154.4 (C-22), 153.5 (C-19), 134.9 (C-12), 129.0 (C-10), 126.3 (C-18), 124.1 (C-11), 122.3 (C-21), 113.8 (C-23), 113.3 (C-20), 80.6 (C-5), 66.5 (C-7), 59.3 (C-6), 56.2 (C-2), 56.0 (C-24 or C-25), 55.3 (C-24 or C-25), 50.6 (C-16), 35.2 (C-3), 32.9 (C-4), 25.9 (C-15), 18.1 (C-14), –4.5 (C-13), –5.1 (C-13).

IR (Diamond-ATR, neat) $\tilde{\upsilon}_{max}$: 2929 (w), 2856 (w), 1769 (m), 1746 (s), 1496 (w), 1184 (m), 1048 (m), 877 (m), 696 (m) cm^{-1}.

HRMS (ESI) calc. for $C_{32}H_{37}NNaO_{10}Si$ [M+Na]$^+$: 646.2079 found: 646.2067.



Tetralone 325

A solution of *N*-(acyloxy)phthalimide **324** (5.90 mg, 9.46 µmol, 1 equiv), tris[2-(2,4-difluorophenyl)pyridine]iridium(III) (0.700 mg, 0.946 µmol, 0.100 equiv) and hydrogen fluoride triethylamine (1.50 µL, 0.946 µmol, 0.100 equiv) in degassed dichloromethane (300 µL) was irradiated at 419 nm at 23 °C. After 30 minutes, the mixture was concentrated and the residue was purified by flash column chromatography on silica gel (20% grading to 30% ethyl acetate in hexane) to yield tetralone **325** (2.90 mg, 6.70 µmol, 71%) as a yellow solid.

TLC (30% ethyl acetate in cyclohexane): R_f = 0.17 (CAM, UV).

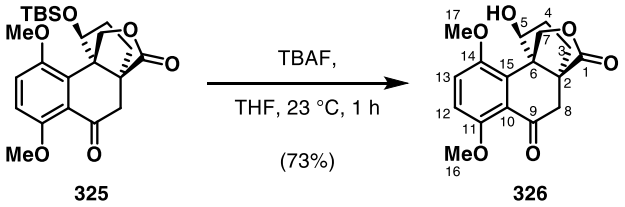
mp: (192-193) °C

^{1}H NMR (600 MHz, chloroform-*d*) δ 7.06 (d, *J* = 9.1 Hz, 1H, 16-H), 6.89 (d, *J* = 9.1 Hz, 1H, 15-H), 5.07 (d, *J* = 9.7 Hz, 1H, 7-H), 4.39 (d, *J* = 2.7 Hz, 1H, 5-H), 4.24 (d, *J* = 9.7 Hz, 1H, 7-H), 3.86 – 3.83 (m, 6H, 19-H, 20-H), 2.87 – 2.77 (m, 2H, 11-H), 2.57 – 2.50 (m, 1H, 3-H), 1.91 (dd, *J* = 13.8, 9.2 Hz, 1H, 3-H), 1.62 (dd, *J* = 13.4, 7.8 Hz, 1H, 4-H), 1.40 (dddd, *J* = 13.5, 12.1, 9.4, 2.9 Hz, 1H, 4-JH), 0.92 (s, 9H, 10-H), 0.18 – 0.05 (m, 6H, 8-H).

^{13}C NMR (151 MHz, chloroform-*d*) δ 195.2 (C-12), 180.0 (C-1), 152.3 (C-17), 150.2 (C-14), 131.7 (C-18), 123.7 (C-13), 116.7 (C-16), 112.0 (C-15), 80.3 (C-5), 71.7 (C-7), 57.5 (C-6), 56.6 (C-19 or C-20), 55.8 (C-19 or C-20), 52.2 (C-2), 45.3 (C-11), 34.3 (C-4), 32.1 (C-3), 25.7 (C-10), 18.0 (C-9), –4.4 (C-8), –4.9 (C-8).

IR (Diamond-ATR, neat) $\tilde{\upsilon}_{max}$: 2927 (s), 2854 (m), 1771 (m), 1701 (m), 1464 (m), 1272 (m), 1181 (w), 1107 (m), 1018 (m), 834 (m), 777 (w) cm^{-1}.

HRMS (ESI) calc. for $C_{23}H_{32}NaO_6Si$ $[M+Na]^+$: 455.1860 found: 455.1855.



Alcohol 326

To a solution of tetralone **325** (8.60 mg, 20.0 µmol, 1 equiv) in tetrahydrofuran (200 µL) was added a solution of tetrabutylammonium fluoride (1.00 M in tetrahydrofuran, 9.94 µL, 9.94 µmol, 5.00 equiv) at 23 °C. After one hour, a saturated aqueous solution of sodium bicarbonate (5 mL) and ethyl acetate (5 mL) were added to the reaction mixture and the layers were separated. The aqueous layer was extracted with ethyl acetate (3 × 2 mL) and the combined organic layers were dried over sodium sulfate. The dried solution was filtered and the filtrate was concentrated. The residue was purified by flash column chromatography on silica gel (30% ethyl acetate in cyclohexane to 5% methanol in dichloromethane) to yield alcohol **326** (4.60 mg, 15.0 µmol, 73%) as a colourless oil.

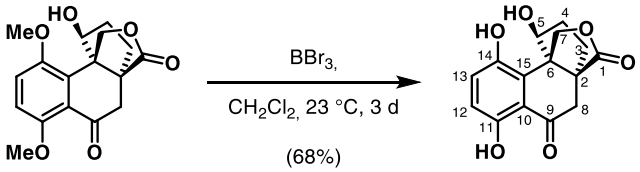
TLC (5% methanol in dichloromethane): R_f = 0.31 (CAM, UV).

^{1}H NMR (600 MHz, chloroform-*d*) δ 7.10 (d, *J* = 9.1 Hz, 1H, 13-H), 6.89 (d, *J* = 9.2 Hz, 1H, 12-H), 5.31 (d, *J* = 9.9 Hz, 1H, 7-H), 4.26 (d, *J* = 9.9 Hz, 1H, 7-H), 4.23 (dd, *J* = 7.5, 5.8 Hz, 1H, 5-H), 3.88 (s, 3H, 16-H), 3.85 (s, 3H, 17-H), 2.87 (d, *J* = 13.1 Hz, 1H, 8-H), 2.80 (d, *J* = 13.1 Hz, 1H, 8-H), 2.68 (s, 1H, 5-OH), 2.38 (ddd, *J* = 13.5, 7.0, 4.3 Hz, 1H, 3-H), 1.93 (dddd, *J* = 13.1, 7.1, 5.7, 4.2 Hz, 1H, 4-H), 1.79 (ddd, *J* = 13.4, 10.0, 7.1 Hz, 1H, 3-H), 1.58 – 1.51 (m, 1H, 4-H).

^{13}C NMR (151 MHz, chloroform-*d*) δ 194.9 (C-9), 179.7 (C-1), 152.7 (C-14), 150.3 (C-11), 134.2 (C-15), 122.6 (C-10), 117.1 (C-13), 111.7 (C-12), 81.8 (C-5), 70.3 (C-7), 56.7 (C-17), 56.5 (C-16), 53.6 (C-2 or C-6), 53.6 (C-2 or C-6), 44.3 (C-8), 32.4 (C-4), 31.6 (C-3).

IR (Diamond-ATR, neat) $\tilde{\upsilon}_{max}$: 3476 (br, w), 2925 (m), 2853 (w), 1747 (s), 1694 (m), 1585 (w), 1476 (m), 1270 (s), 1180 (m), 1107 (m), 1013 (s), 814 (w) cm^{-1}.

HRMS (ESI) calc. for $C_{23}H_{32}NaO_6Si$ $[M+Na]^+$: 455.1860 found: 455.1855.



326 **lingzhiol (30)**

Lingzhiol (30)

To a solution of alcohol **326** (4.10 mg, 13.0 µmol, 1 equiv) in dichloromethane (0.5 mL) was added a solution of boron tribromide (1.00 M in dichloromethane, 64.0 µL, 64.0 µmol, 5.00 equiv) at 23 °C upon which the solution turned quickly dark brown. After three days, a saturated aqueous solution of sodium bicarbonate (5 mL) and dichloromethane (5 mL) were added to the reaction mixture and the layers were separated. The aqueous layer was extracted with dichloromethane (3 × 2 mL) and the combined organic layers were dried over sodium sulfate. The dried solution was filtered and the filtrate was concentrated. The residue was purified by flash column chromatography on silica gel (60% ethyl acetate in cyclohexane) to yield lingzhiol (**30**) (2.55 mg, 8.78 µmol, 68%) as a slightly yellow solid.

TLC (60% ethyl acetate in cyclohexane): R_f = 0.14 (CAM, UV).

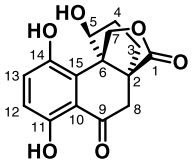
^{1}H NMR (700 MHz, acetone-d_6) δ 7.22 (d, *J* = 8.9 Hz, 1H, 13-H), 6.77 (d, *J* = 8.9 Hz, 1H, 12-H), 5.22 (d, *J* = 9.6 Hz, 1H, 7-H), 4.63 (m, 1H, 5-H), 4.45 (d, *J* = 9.6 Hz, 1H, 7-H), 3.09 (d, *J* = 16.0 Hz, 1H, 8-H), 2.81 – 2.78 (m, 1H, 8-H), 2.47 – 2.44 (m, 1H, 3-H), 1.85 – 1.82 (m, 1H, 4-H), 1.80 – 1.76 (m, 1H, 3-H), 1.72 – 1.69 (m, 1H, 4-H).

^{13}C NMR (176 MHz, acetone-d_6) δ 202.4 (C-9), 180.2 (C-1), 156.5 (C-11), 148.1 (C-14), 129.8 (C-15), 127.7 (C-13), 118.0 (C-12), 116.6 (C-10), 80.8 (C-5), 71.0 (C-7), 56.2 (C-6), 52.6 (C-2), 42.4 (C-8), 33.9 (C-4), 33.4 (C-3).

IR (Diamond-ATR, neat) $\tilde{\upsilon}_{max}$: 3298 (br, w), 2926 (m), 2856 (w), 1768 (m), 1650 (m), 1465 (s), 1332 (m), 1220 (m), 1181 (m), 1103 (w), 1014 (w) cm^{-1}.

HRMS (ESI) calc. for $C_{15}H_{14}NaO_6$ $(M+Na)^+$: 313.0683 found: 313.0680.

Table 16: Comparison of ^{1}H-NMR shifts for natural[120] and synthetic lingzhiol.

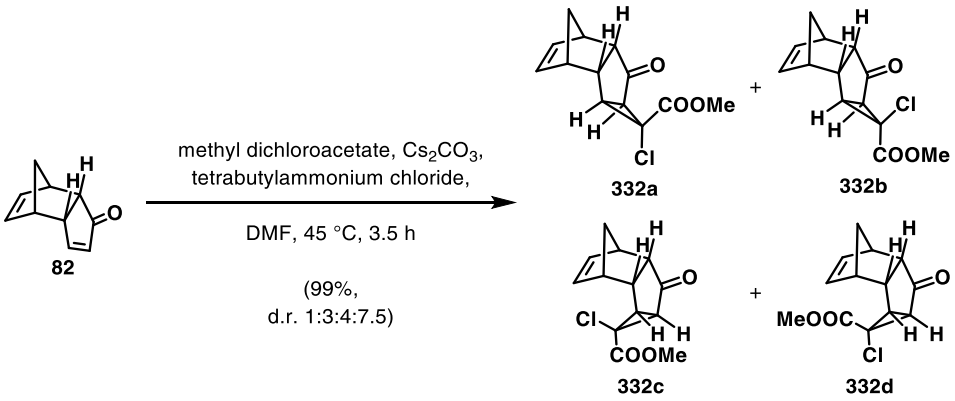


lingzhiol (30)

No	^{1}H-NMR (400 MHz, acetone-d_6) <u>isolated</u> lingzhiol **ppm**	^{1}H-NMR (700 MHz, acetone-d_6) <u>synthetic</u> lingzhiol **ppm**	Δ ppm
1	-	-	-
2	-	-	-
3	2.44 (m)	2.47 – 2.44 (m)	+0.02
	1.78 (m)	1.80 – 1.76 (m)	±0
4	1.83 (m)	1.85 – 1.82 (m)	+0.01
	1.70 (m)	1.72 – 1.69 (m)	+0.01
5	4.63 (t, *J* = 4.5 Hz)	4.63 (m)	±0
6	-	-	-
7	5.22 (d, *J* = 9.6 Hz)	5.22 (d, *J* = 9.6 Hz)	±0
	4.45 (d, *J* = 9.6 Hz)	4.45 (d, *J* = 9.6 Hz)	±0
8	3.09 (d, *J* = 16.0 Hz)	3.09 (d, *J* = 16.0 Hz)	±0
	2.79 (d, *J* = 16.0 Hz)	2.81 – 2.78 (m, overlap)	±0
9	-	-	-
10	-	-	-
11	-	-	-
12	6.77 (d, *J* = 8.9 Hz)	6.77 (d, *J* = 8.9 Hz)	±0
13	7.22 (d, *J* = 8.9 Hz)	7.22 (d, *J* = 8.9 Hz)	±0
14	-	-	-
15	-	-	-

Table 17: Comparison of ^{13}C-NMR shifts for natural and synthetic lingzhiol.

No	^{13}C-NMR (100 MHz, acetone-d_6) isolated lingzhiol **ppm**	^{13}C-NMR (176 MHz, acetone-d_6) synthetic lingzhiol **ppm**	Δ ppm
1	180.1	180.2	+0.1
2	52.5	52.6	+0.1
3	33.3	33.4	+0.1
4	33.7	33.9	+0.2
5	80.6	80.8	+0.2
6	56.1	56.2	+0.1
7	70.9	71.0	+0.1
8	42.3	42.4	+0.1
9	202.3	202.4	+0.1
10	116.4	116.6	+0.2
11	156.3	156.5	+0.2
12	117.9	118.0	+0.1
13	127.5	127.7	+0.2
14	147.9	148.1 (low intensity)	+0.2
15	129.1	129.8 (low intensity)	+0.7



Chlorocyclopropane 332

To a suspension of cesium carbonate (2.13 g, 6.46 mmol, 5.00 equiv) and tetrabutylammonium chloride (37.0 mg, 129 µmol, 0.100 equiv) in *N*,*N*-dimethylformamide (4 mL) was added a solution of enone **82** (189 mg, 1.29 mmol, 1 equiv) and methyl dichloroacetate (924 mg, 6.46 mmol, 5.00 equiv) in *N*,*N*-dimethylformamide (8 mL) over the course of 30 minutes at 45 °C. After the addition was completed, the reaction mixture was stirred at 45 °C for three hours and was then allowed to cool to 23 °C. A saturated aqueous solution of ammonium chloride (10 mL) and diethyl ether (10 mL) were added to the reaction mixture. The layers were separated and the aqueous layer was extracted with diethyl ether (3 × 2 mL) and the combined organic layers were dried over sodium sulfate. The dried solution was filtered and the filtrate was concentrated. The residue was purified by flash column chromatography on

silica gel (20% ethyl acetate in cyclohexane) to yield chlorocyclopropane **332** as a mixture of four inseparable diastereomers in a ratio of 1:3:4:7.5 (338 mg, 1.27 mmol, 99%) as a yellow oil.
Note: The product was obtained as a mixture of four diastereomers. Due to the complexity of the NMR spectra analysis of the product was carried out by HRMS.

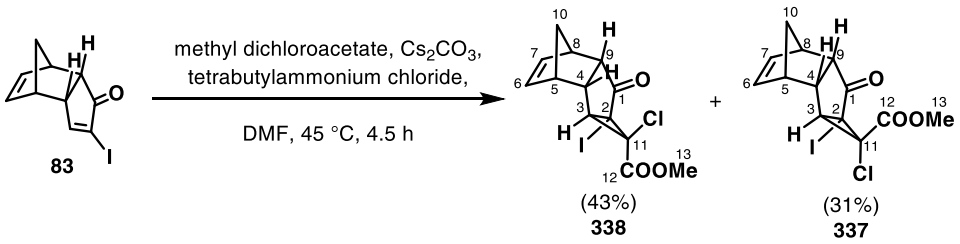
TLC (30% ethyl acetate in cyclohexane): R_f = 0.42 (CAM).

^{1}H NMR (400 MHz, chloroform-*d*) *complex signals due to four diastereomers in a ratio of 1:3:4:7.5*

^{13}C NMR (75 MHz, chloroform-*d*) δ 210.4, 209.9, 168.4, 167.8, 135.3, 135.2, 134.3, 133.8, 56.0, 55.3, 54.9, 54.2, 54.0, 53.9, 51.2, 51.1, 48.8, 48.3, 48.1, 47.2, 46.9, 46.8, 46.7, 46.4, 46.0, 44.5, 44.4, 44.0, 43.5, 42.4, 41.5, 40.6, 39.2, 36.5, 28.5. *complex signals due to four diastereomers in a ratio of 1:3:4:7.5*

IR (Diamond-ATR, neat) $\tilde{\upsilon}_{max}$: 2957 (w), 1725 (s), 1437 (m), 1257 (s), 1182 (m), 1126 (w), 1096 (w), 1027 (w), 985 (w), 909 (w), 848 (w), 736 (w), 693 (w) cm^{-1}.

HRMS (ESI) calc. for $C_{13}H_{13}ClNaO_3$ $[M+Na]^+$: 275.0445 found: 275.0400.



Chloroiodocyclopropane 338 and 337

To a suspension of cesium carbonate (212 mg, 643 µmol, 5.00 equiv) and tetrabutylammonium chloride (3.70 mg, 13.0 µmol, 0.100 equiv) in *N*,*N*-dimethylformamide (1 mL) was added a solution of iodoenone **83** (35.0 mg, 129 µmol, 1 equiv) and methyl dichloroacetate (66.0 µL, 643 µmol, 5.00 equiv) in *N*,*N*-dimethylformamide (1 mL) over the course of 30 minutes at 45 °C. After the addition was completed, the reaction mixture was stirred at 45 °C for four hours and was then allowed to cool to 23 °C. A saturated aqueous solution of ammonium chloride (10 mL) and diethyl ether (10 mL) were added to the reaction mixure. The layers were separated and the aqueous layer was extracted with diethyl ether (3 × 2 mL) and the combined organic layers were dried over sodium sulfate. The dried solution was filtered and the filtrate was concentrated. The residue was purified by flash column chromatography on silica gel (20% ethyl acetate in cyclohexane) to yield chloroiodocyclopropane **338** (21.0 mg, 56.0 µmol, 43%) and **337** (15.0 mg, 40.0 µmol, 31%) as colourless oils.

Chloroiodocyclopropane 338

TLC (30% ethyl acetate in cyclohexane): R_f = 0.50 (CAM).

^{1}H NMR (400 MHz, chloroform-*d*) δ 6.23 – 6.18 (m, 1H, 6-H or 7-H), 6.14 – 6.09 (m, 1H, 6-H or 7-H), 3.85 (s, 3H, 13-H), 3.28 – 3.22 (m, 2H, 5-H, 8-H), 3.17 – 3.11 (m, 1H, 9-H), 3.01 – 2.95 (m, 1H, 4-H), 2.66 (s, 1H, 3-H), 1.63 (dt, *J* = 8.7, 1.7 Hz, 1H, 10-H), 1.56 – 1.53 (m, 1H, 10-H).

^{13}C NMR (101 MHz, chloroform-*d*) δ 206.0 (C-1), 165.7 (C-12), 135.7 (C-6 or C-7), 135.3 (C-6 or C-7), 54.2 (C-13), 54.0 (C-4 or C-9), 52.2 (C-5 or C-8), 50.1 (C-5 or C-8), 47.0 (C-10), 46.0 (C-11), 43.8 (C-3), 42.8 (C-4 or C-9), 24.0 (C-2).

IR (Diamond-ATR, neat) $\tilde{\upsilon}_{max}$: 2975 (w), 1738 (s), 1436 (w), 1284 (m), 1181 (w), 1071 (w), 1030 (w), 698 (w) cm^{-1}.

HRMS (ESI) calc. for $C_{13}H_{12}ClINaO_3$ $[M+Na]^+$: 400.9412, 402.9382 found: 400.9386, 402.9355.

Crystal structure: *see chapter 7.2. for more details*

Chloroiodocyclopropane 337

TLC (30% ethyl acetate in cyclohexane): R_f = 0.50 (CAM).

^{1}H NMR (400 MHz, chloroform-*d*) δ 6.23 – 6.18 (m, 1H, 6-H or 7-H), 6.17 – 6.13 (m, 1H, 6-H or 7-H), 3.80 (s, 3H, 13-H), 3.28 – 3.23 (m, 1H, 5-H or 8-H), 3.20 – 3.16 (m, 1H, 5-H or 8-H), 3.08 – 3.01 (m, 2H, 4-H, 9-H), 2.13 (s, 1H, 3-H), 1.59 (dt, *J* = 8.8, 1.8 Hz, 1H, 10-H), 1.47 (dt, *J* = 8.7, 1.6 Hz, 1H, 10-H).

^{13}C NMR (101 MHz, chloroform-*d*) δ 206.5 (C-1), 166.0 (C-12), 136.0 (C-6 or C-7), 134.9 (C-6 or C-7), 54.4 (C-13), 54.2 (C-4 or C-9), 51.5 (C-5 or C-8), 51.1 (C-5 or C-8), 50.1 (C-10), 47.4 (C-11), 46.8 (C-3), 42.8 (C-4 or C-9), 32.2 (C-2).

IR (Diamond-ATR, neat) $\tilde{\upsilon}_{max}$: 2953 (w), 1735 (s), 1435 (w), 1271 (m), 1198 (w), 1166 (m), 1123 (w), 1072 (w), 1015 (w), 736 (w), 700 (w) cm^{-1}.

HRMS (ESI) calc. for $C_{13}H_{12}ClINaO_3$ $[M+Na]^+$: 400.9412, 402.9382 found: 400.9386, 402.9355.

7.2. X-Ray Crystallographic Data

Dicyclopropane 74

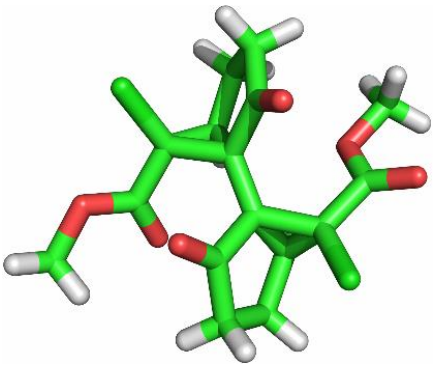


Table 18: Data for dicyclopropane **74**.

net formula	$C_{16}H_{16}Cl_2O_6$
M_r/g mol^{-1}	375.19
crystal size/mm	0.100 × 0.090 × 0.040
T/K	100.(2)
radiation	MoKα
diffractometer	'Bruker D8 Venture TXS'
crystal system	orthorhombic
space group	'P 21 21 21'
a/Å	6.5930(2)
b/Å	15.1450(5)
c/Å	15.9502(6)
α/°	90
β/°	90
γ/°	90
V/Å^3	1592.64(9)
Z	4
calc. density/g cm^{-3}	1.565
μ/mm^{-1}	0.438
absorption correction	Multi-Scan
transmission factor range	0.8791–0.9705
refls. measured	19093
R_{int}	0.0323
mean σ(I)/I	0.0228
θ range	3.344–26.370
observed refls.	3162
x, y (weighting scheme)	0.0209, 0.5306
hydrogen refinement	constr
Flack parameter	0.019(17)
refls in refinement	3249
parameters	219
restraints	0
$R(F_{obs})$	0.0208
$R_w(F^2)$	0.0519
S	1.073
shift/error$_{max}$	0.001
max electron density/e Å^{-3}	0.238
min electron density/e Å^{-3}	−0.141

Ferrocenecarboxylate ester 204

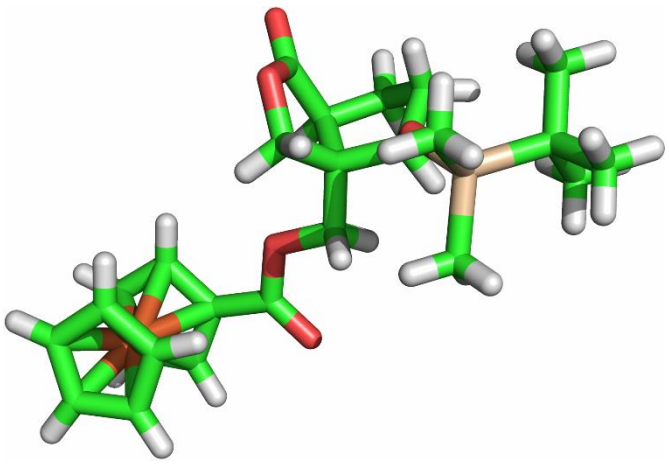


Table 19: Ferrocenecarboxylate ester **204**.

Empirical formula	$C_{25}H_{34}FeO_5Si$	
Formula weight	262.29	
Temperature	193(2) K	
Wavelength	0.71073 Å	
Crystal system	Monoclinic	
Space group	$P2_1/c$ (no. 14)	
Unit cell dimensions	a = 6.3861(4) Å	α = 90°
	b = 12.7167(8) Å	β = 95.450(2)°
	c = 29.8799(18) Å	γ = 90°
Volume	2415.6(3) $Å^3$	
Z	4	
Density (calculated)	1.371 mg/m^3	
Absorption coefficient	0.707 mm^{-1}	
F(000)	1056	
Crystal size	0.160 x 0.110 x 0.060 mm^3	
Theta range for data collection	2.107 to 25.999°	
Index ranges	-7<=h<=7, -15<=k<=15, -36<=l<=36	
Reflections collected	30466	
Independent reflections	4752 [R(int) = 0.0260]	
Completeness to theta = 25.242°	100.0%	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.942 and 0.896	
Refinement method	Full-matrix least-squares on F2	
Data / restraints / parameters	4752 / 0 / 289	
Goodness-of-fit on F^2	1.075	
Final R indices [I>2sigma(I)]	R1 = 0.0280, wR2 = 0.0682	
R indices (all data)	R1 = 0.0321, wR2 = 0.0700	
Extinction coefficient	n/a	
Largest diff. peak and hole	0.267 and -0.360 $e.Å^{-3}$	

Iodocyclopropane 338

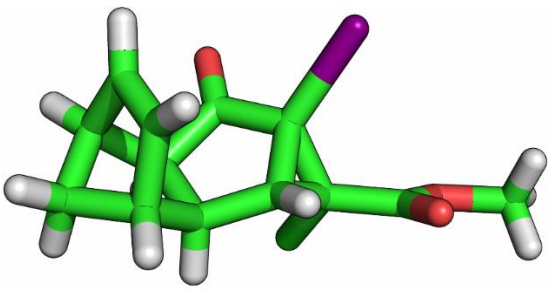
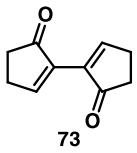


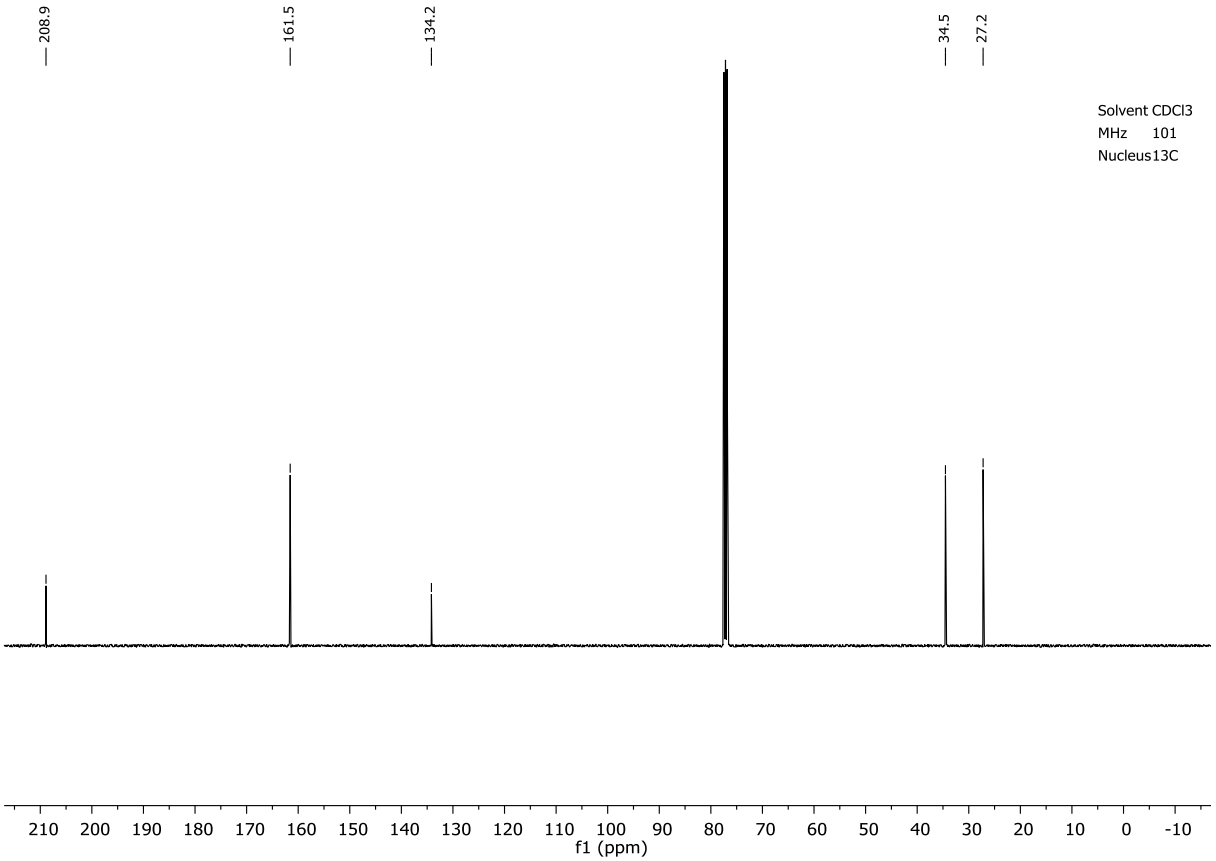
Table 20: Iodocyclopropane **338**.

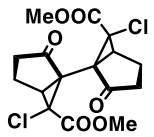
Empirical formula	C_{13} HClIO_3	
Formula weight	378.58	
Temperature	173(2) K	
Wavelength	0.71073 Å	
Crystal system	Monoclinic	
Space group	$P2_1/n$ (no. 14)	
Unit cell dimensions	a = 6.4305(3) Å	α = 90°
	b = 24.3810(14) Å	β = 105.841(2)°.
	c = 8.8313(5) Å	γ = 90°
Volume	1332.01(12) $Å^3$	
Z	4	
Density (calculated)	1.888 mg/m^3	
Absorption coefficient	2.601 mm^{-1}	
F(000)	736	
Crystal size	0.220 x 0.200 x 0.180 mm^3	
Theta range for data collection	2.539 to 26.998°.	
Index ranges	-8<=h<=8, -31<=k<=31, -11<=l<=11	
Reflections collected	19426	
Independent reflections	2901 [R(int) = 0.0262]	
Completeness to theta = 25.242°	99.8%	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.491 and 0.408	
Refinement method	Full-matrix least-squares on F2	
Data / restraints / parameters	2901 / 1 / 168	
Goodness-of-fit on F^2	1.373	
Final R indices [I>2sigma(I)]	R1 = 0.0290, wR2 = 0.0637	
R indices (all data)	R1 = 0.0303, wR2 = 0.0641	
Extinction coefficient	0.0062(5)	
Largest diff. peak and hole	0.758 and -0.566 $e.Å^{-3}$	

7.3. ^{1}H and ^{13}C NMR Spectra

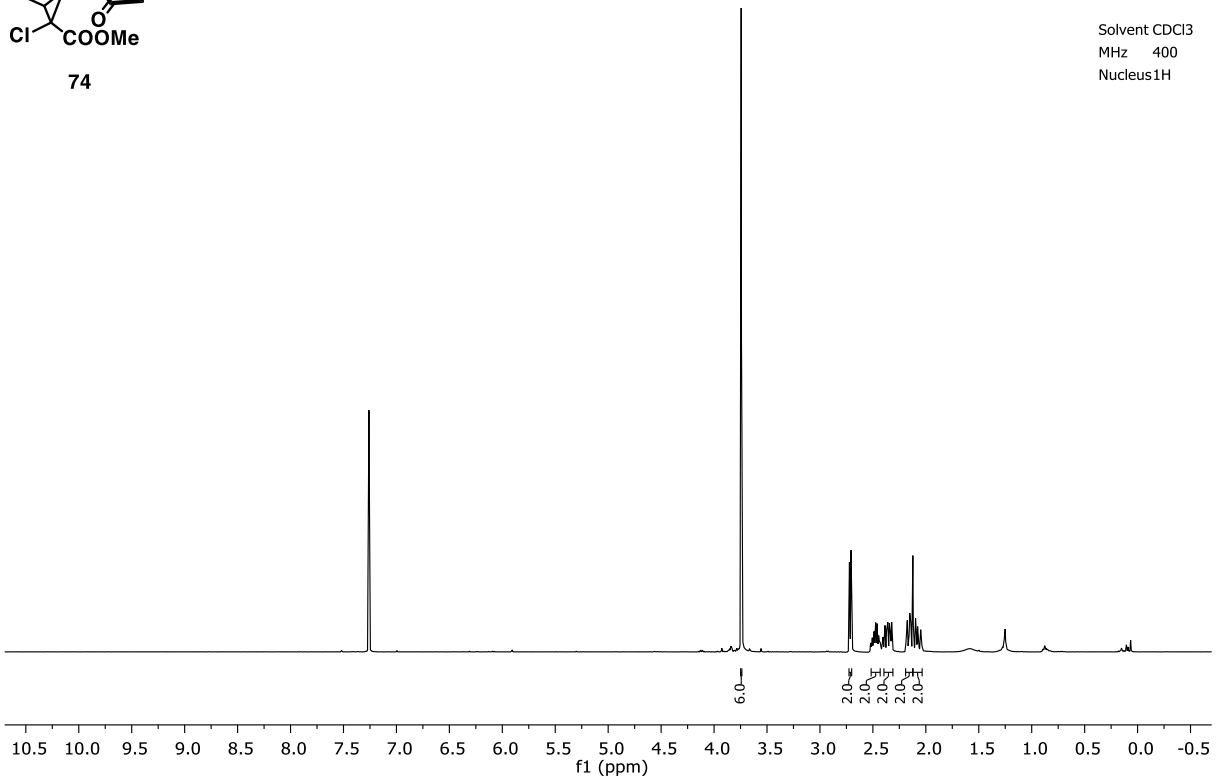


73




MeOOC
Cl
O
O
Cl
COOMe

74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MHz 400
Nucleus1H
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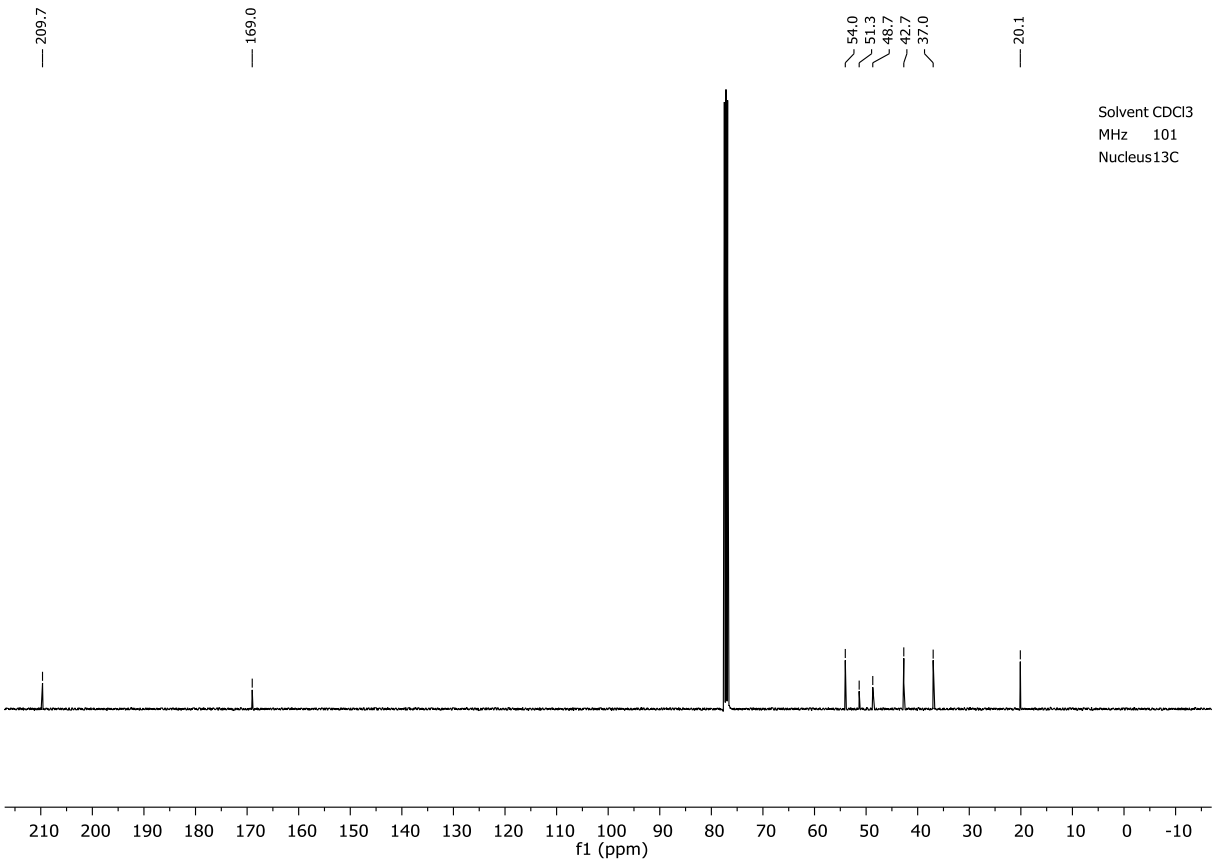
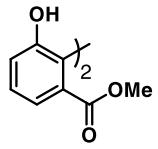
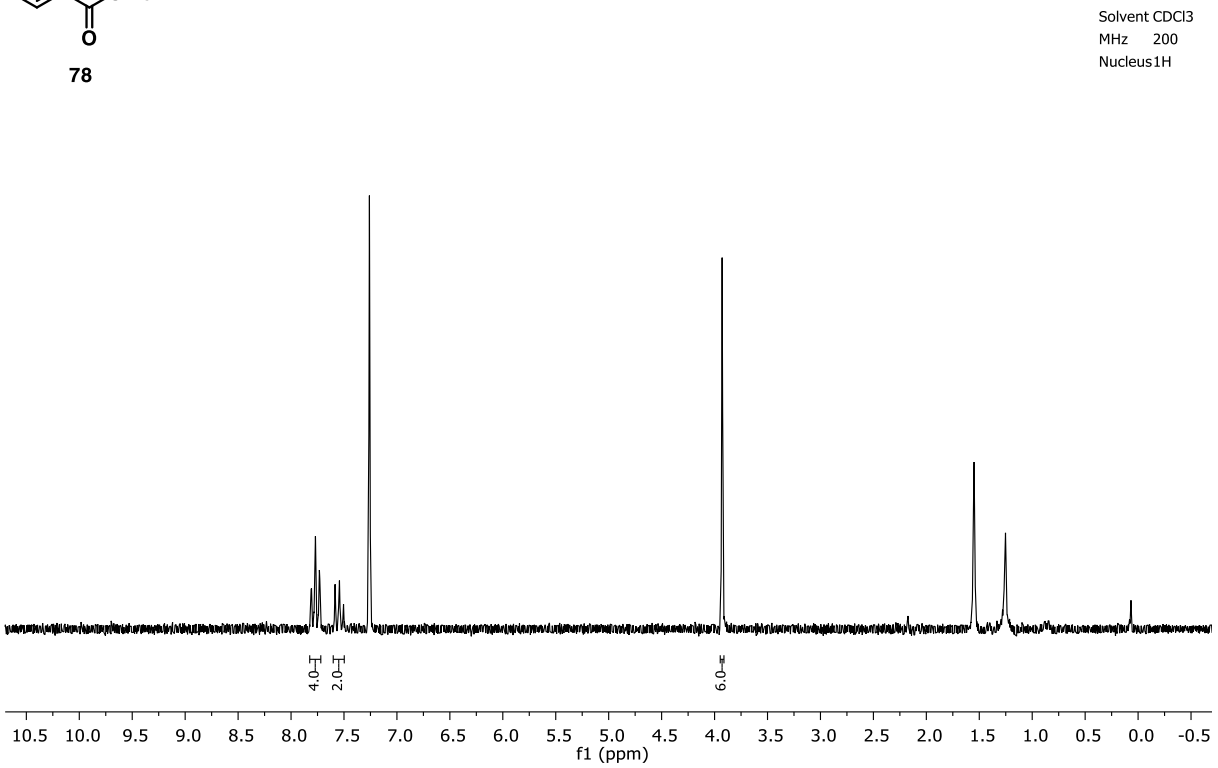
2.0
2.0
2.0
2.0
2.0
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)


209.7
169.0
54.0
51.3
48.7
42.7
37.0
20.1
Solvent CDCl3
MHz 101
Nucleus13C
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


OH
2
OMe
O

78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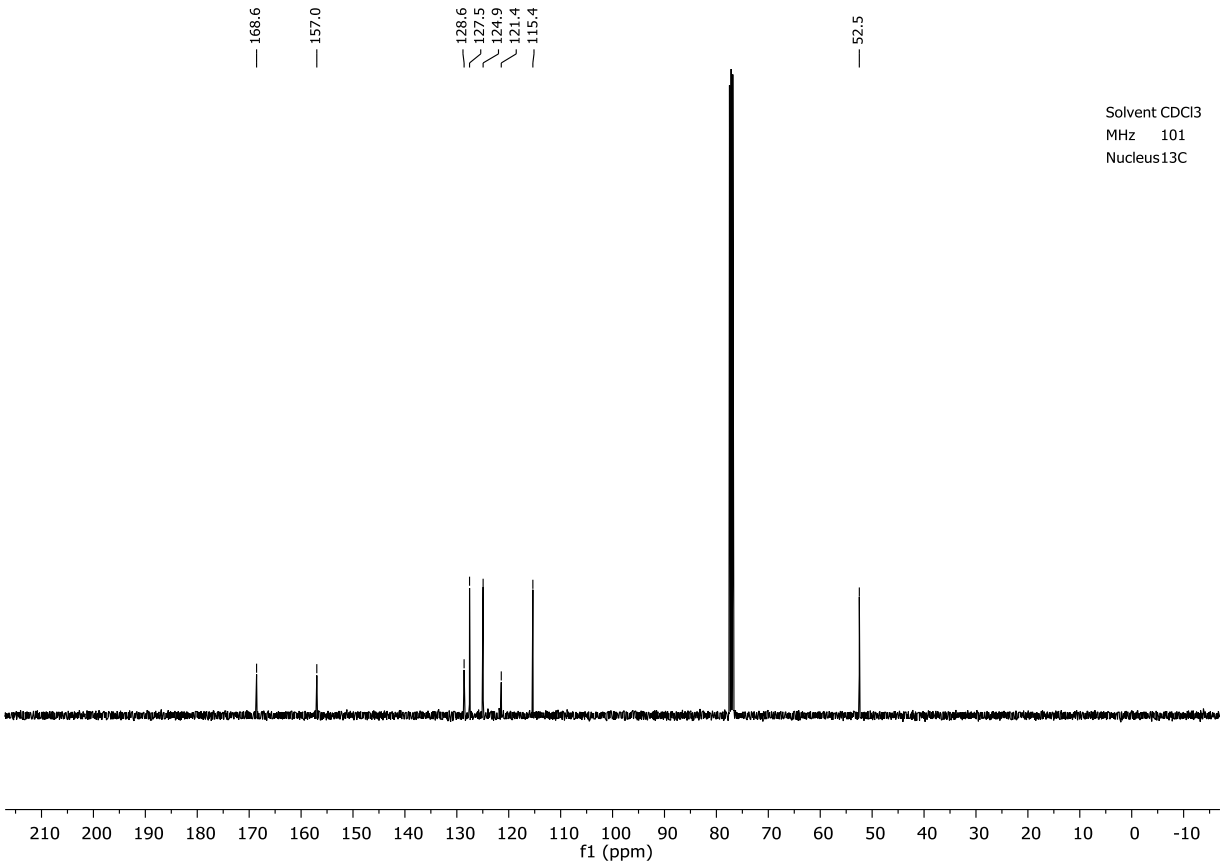
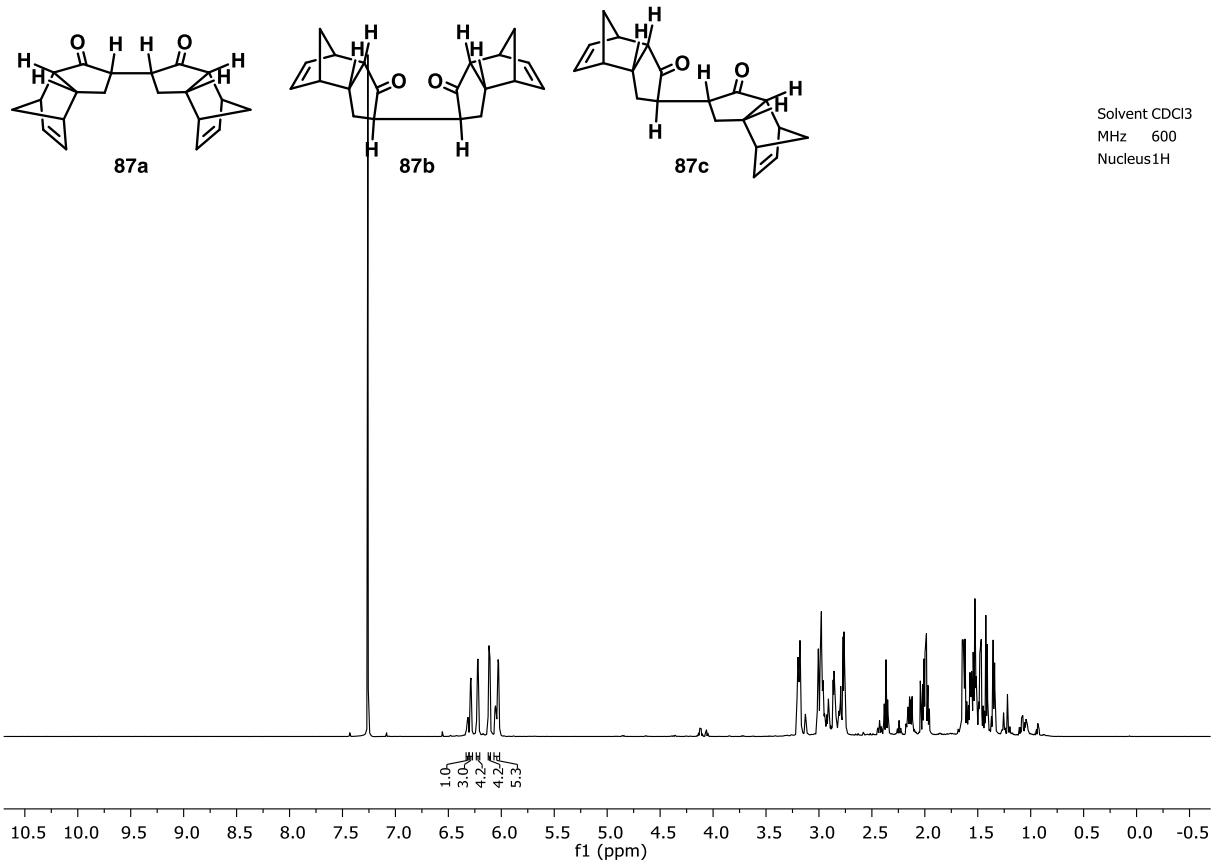
MHz 200
Nucleus1H
4.0
2.0
6.0
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)


168.6
157.0
128.6
127.5
124.9
121.4
115.4
52.5
Solvent CDCl3
MHz 101
Nucleus13C
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


87a
87b
87c
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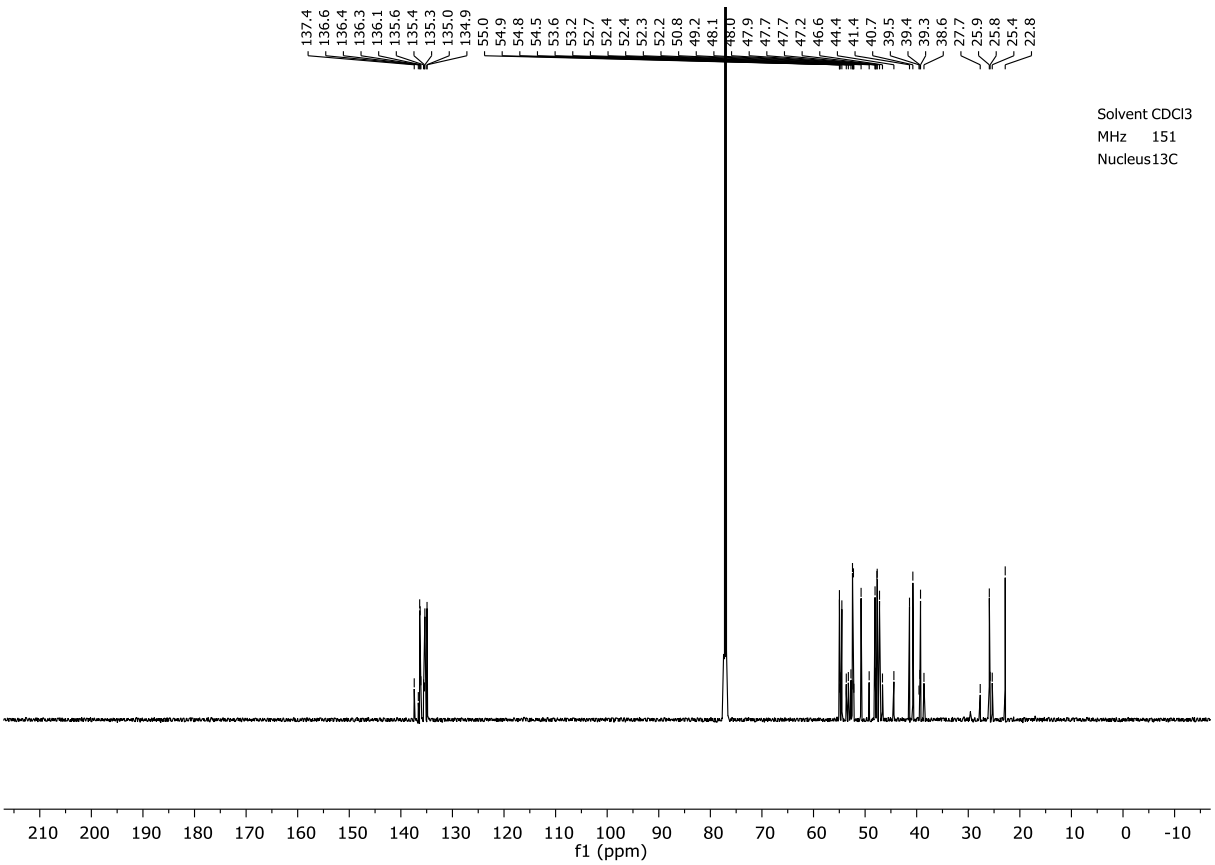
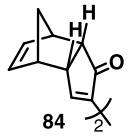
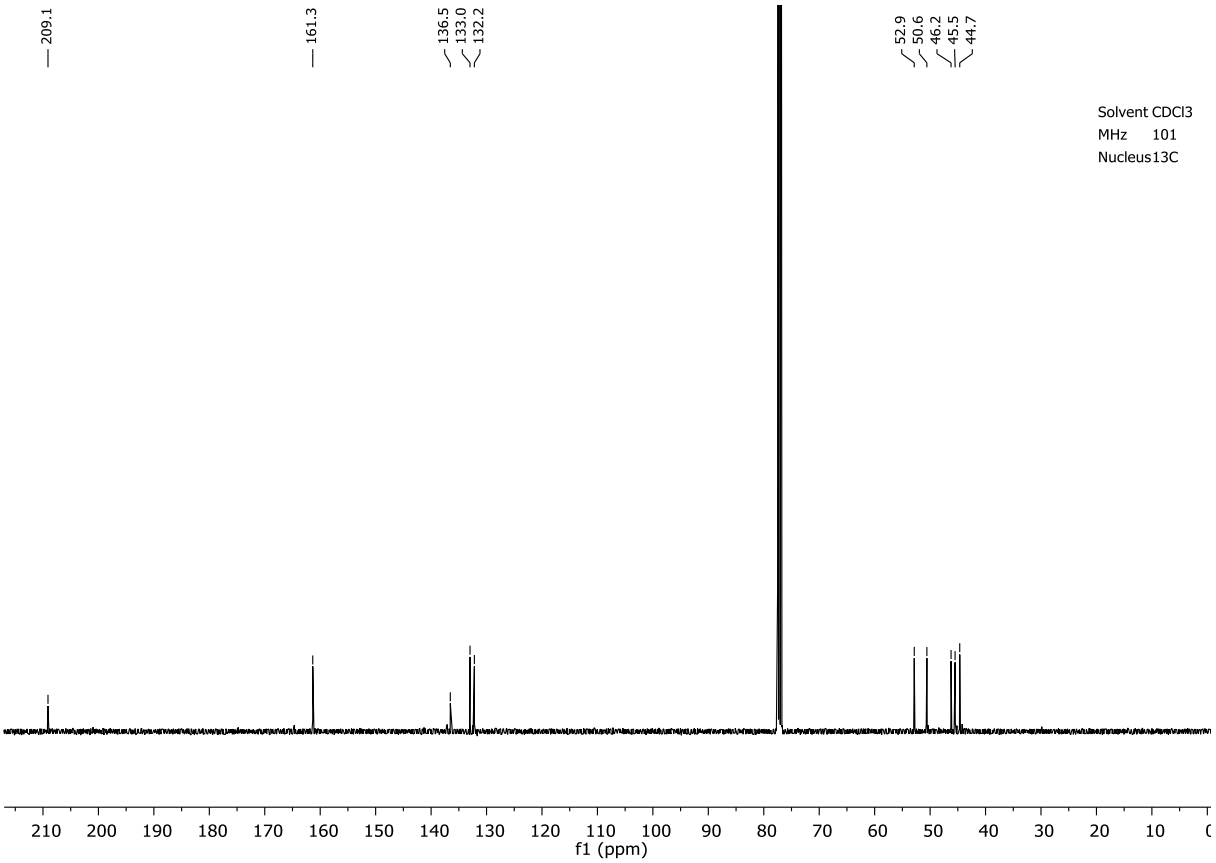
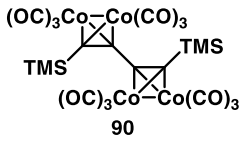
MHz 600
Nucleus1H
1.0
3.0
4.2
4.2
5.3
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)


137.4
136.6
136.4
136.3
136.1
135.6
135.4
135.3
135.0
134.9
55.0
54.9
54.8
54.5
53.6
53.2
52.7
52.4
52.4
52.3
52.2
50.8
49.2
48.1
48.0
47.9
47.7
47.7
47.2
46.6
44.4
41.4
40.7
39.5
39.4
39.3
38.6
27.7
25.9
25.8
25.4
22.8
Solvent CDCl3
MHz 151
Nucleus13C
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


H
H
O
84
2

Solvent CDCl3
MHz 400
Nucleus1H
2.0
2.0
2.0
2.0
2.0
2.0
2.0
2.0
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)


209.1
161.3
136.5
133.0
132.2
52.9
50.6
46.2
45.5
44.7
Solvent CDCl3
MHz 101
Nucleus13C
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
f1 (ppm)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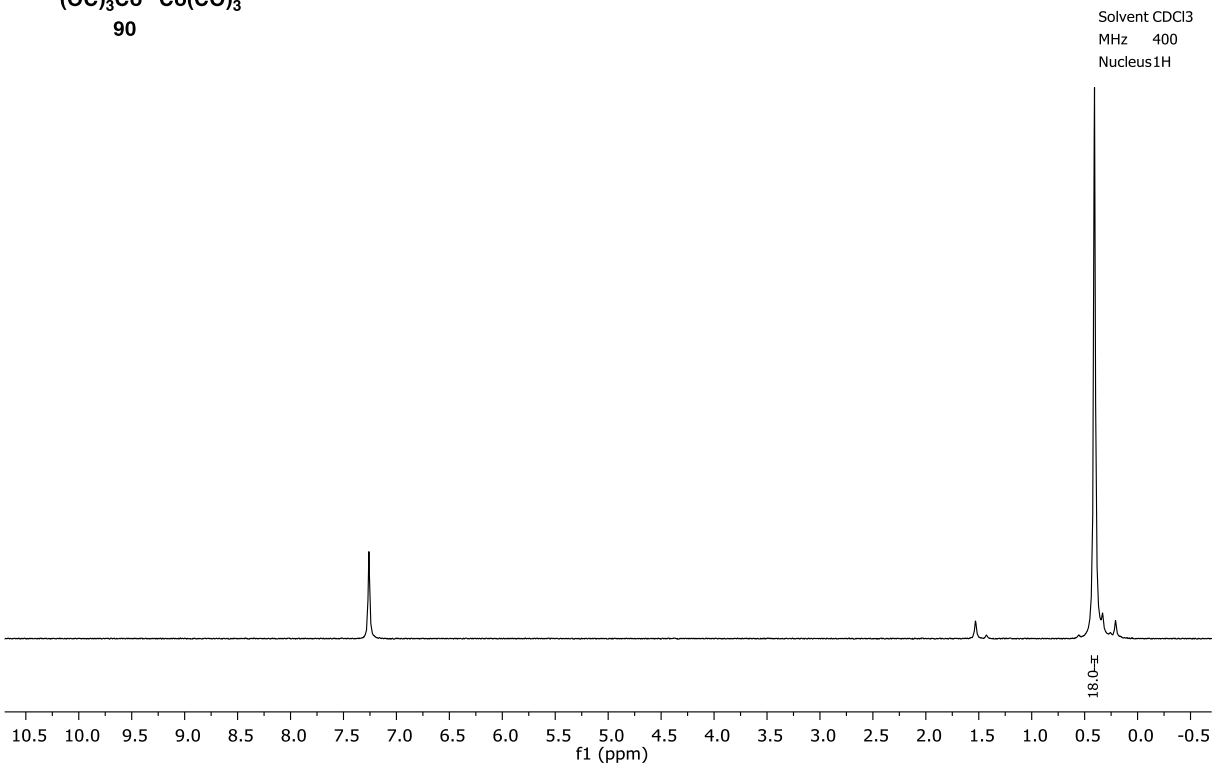
TMS
TMS
(OC)3Co–Co(CO)3

90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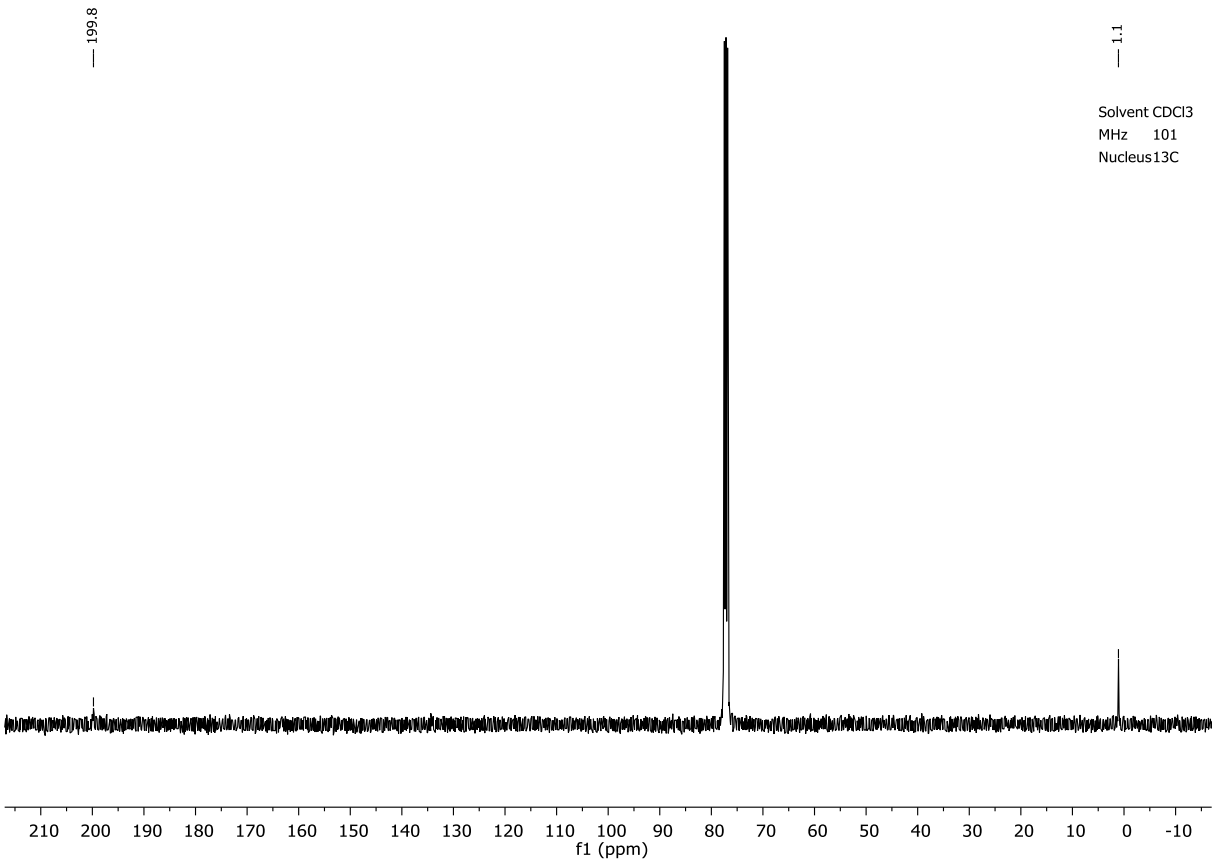
MHz 400
Nucleus1H
18.0
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)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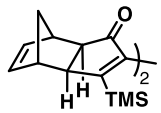
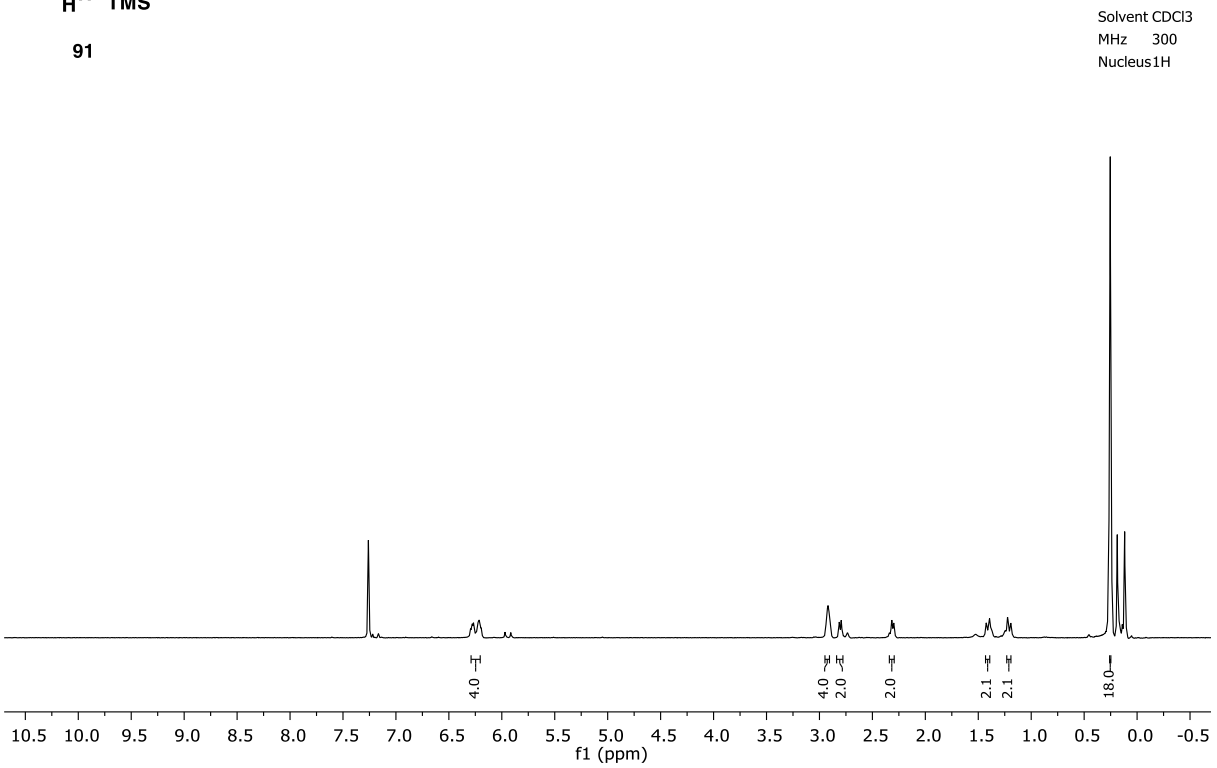
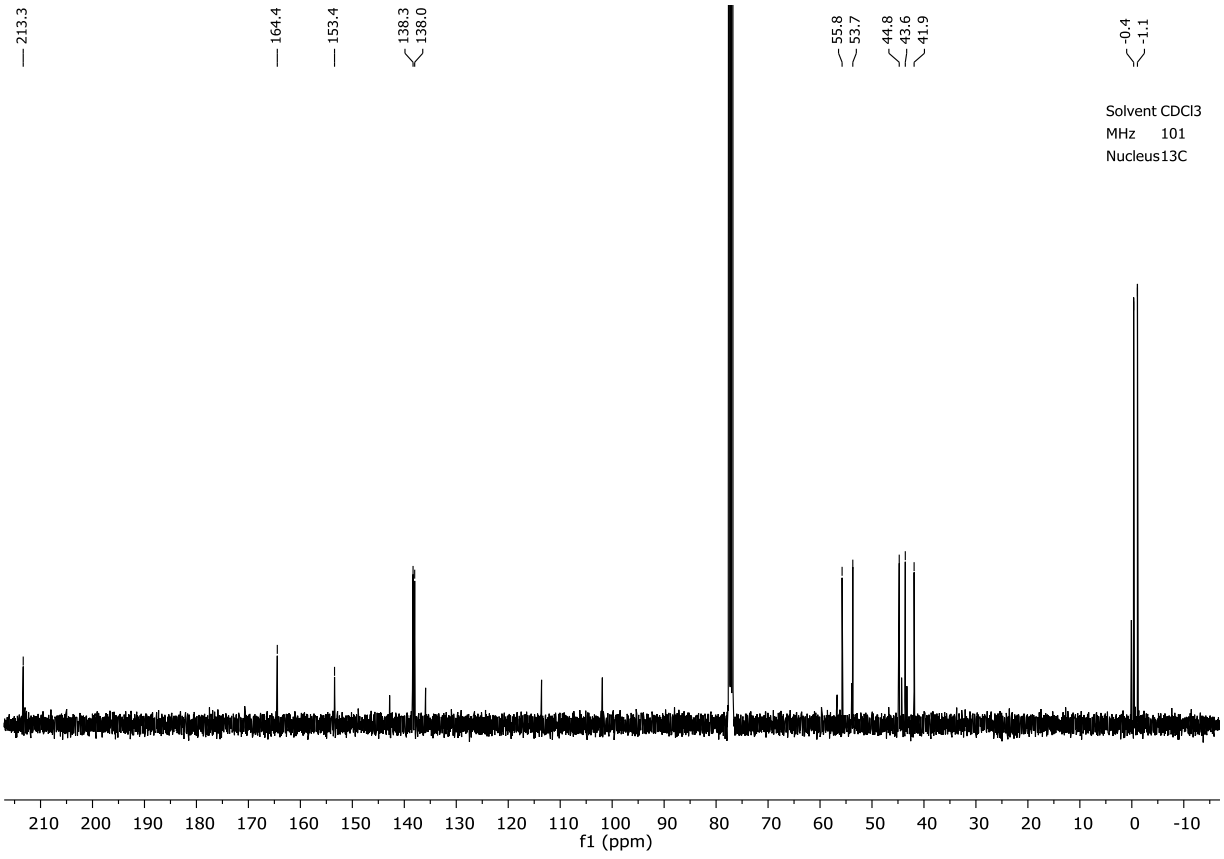
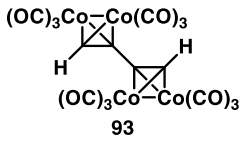
1.1
Solvent CDCl3
MHz 101
Nucleus13C
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


O
H
H
TMS
2

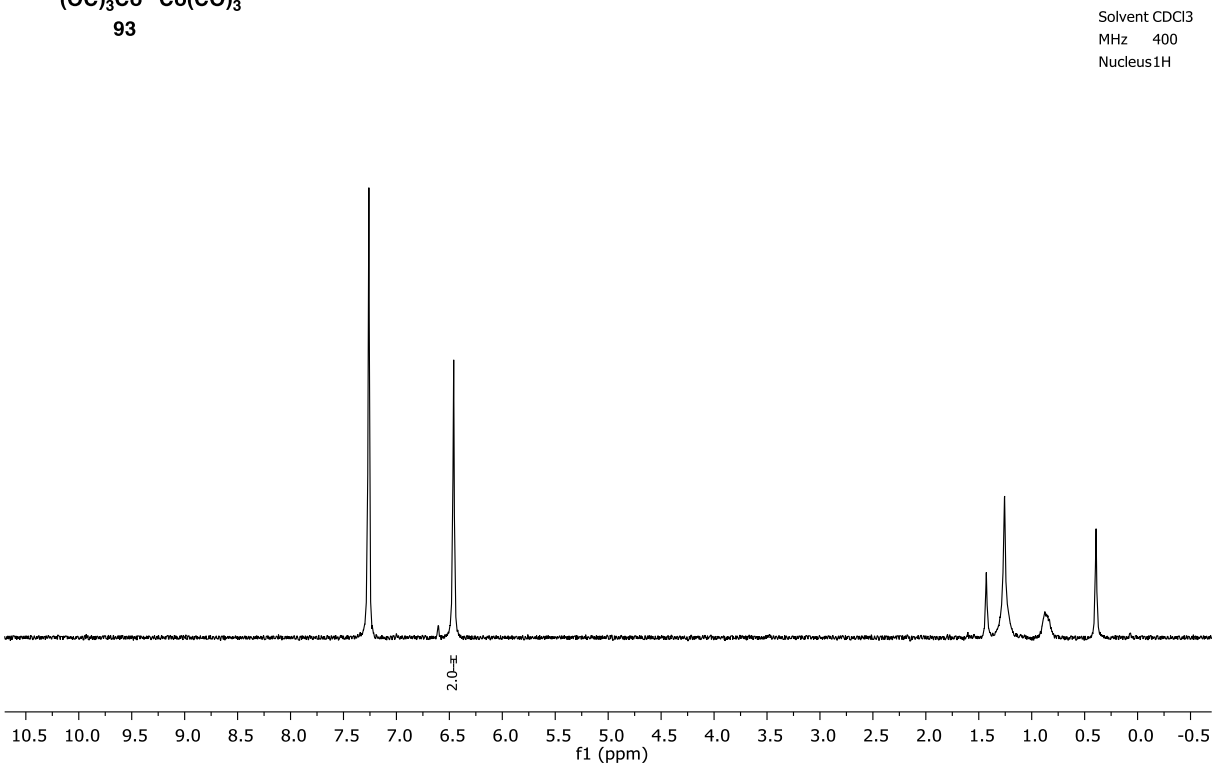
91

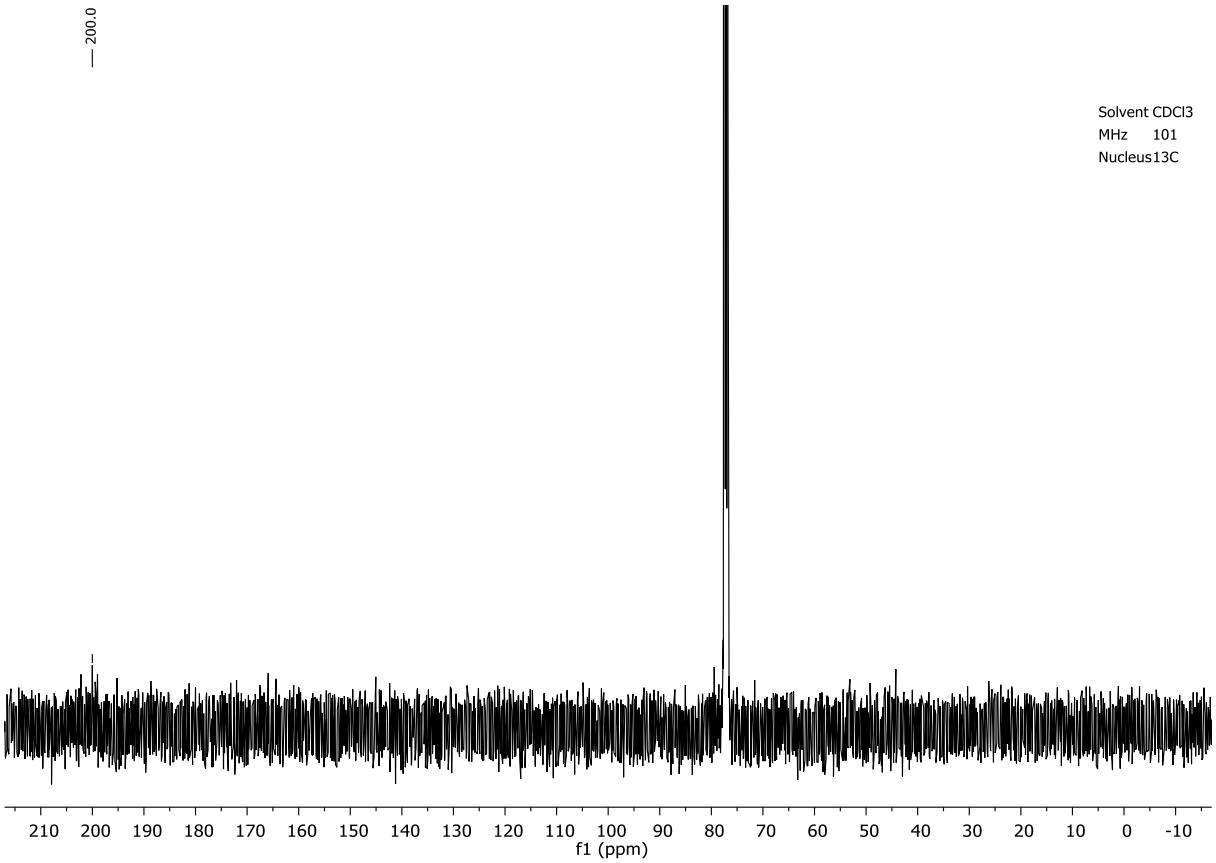

Solvent CDCl3
MHz 300
Nucleus1H
4.0
4.0
2.0
2.0
2.1
2.1
18.0
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

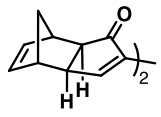

213.3
164.4
153.4
138.3
138.0
55.8
53.7
44.8
43.6
41.9
-0.4
-1.1
Solvent CDCl3
MHz 101
Nucleus13C
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


(OC)3Co–Co(CO)3
H
H
(OC)3Co–Co(CO)3

93

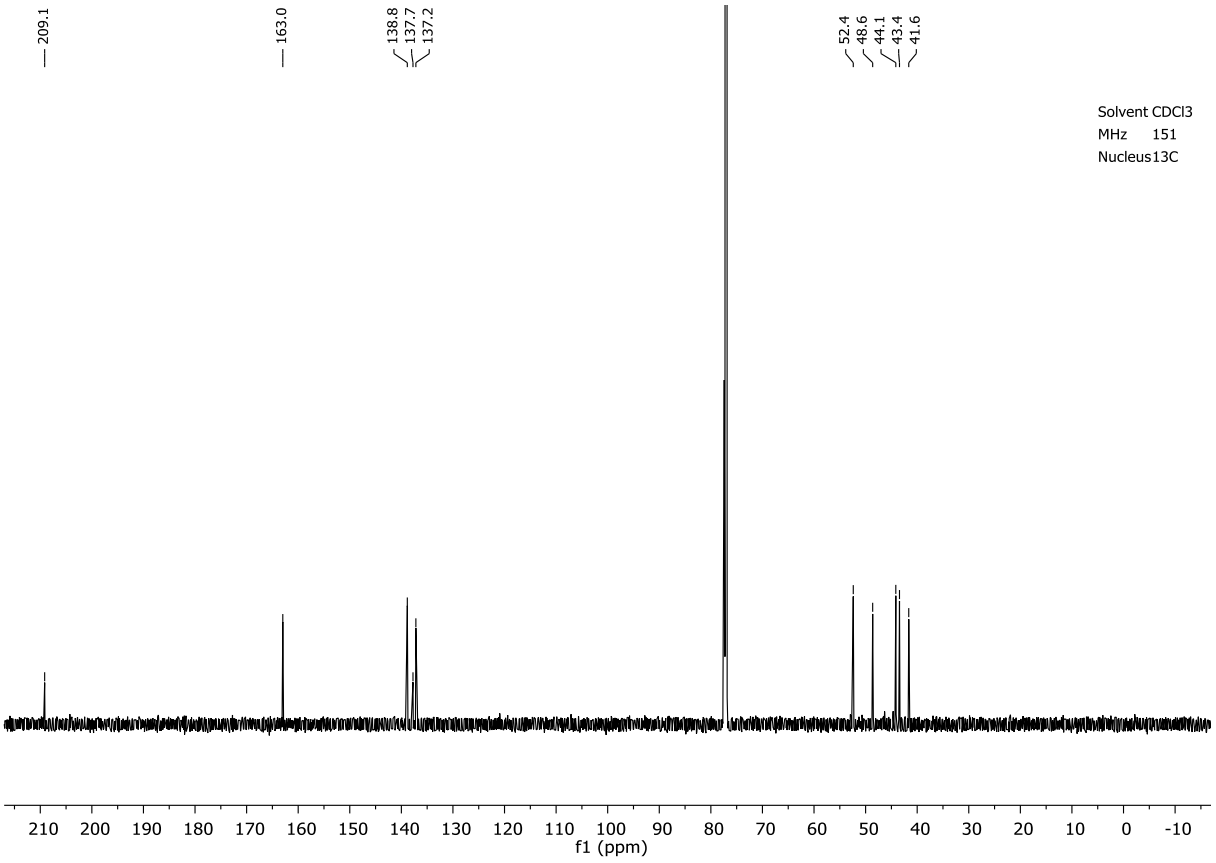

Solvent CDCl3
MHz 400
Nucleus1H
2.0
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

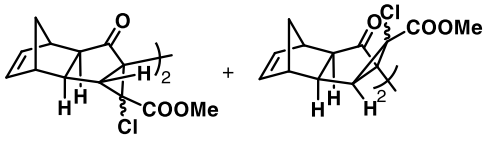

200.0
Solvent CDCl3
MHz 101
Nucleus13C
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)



92

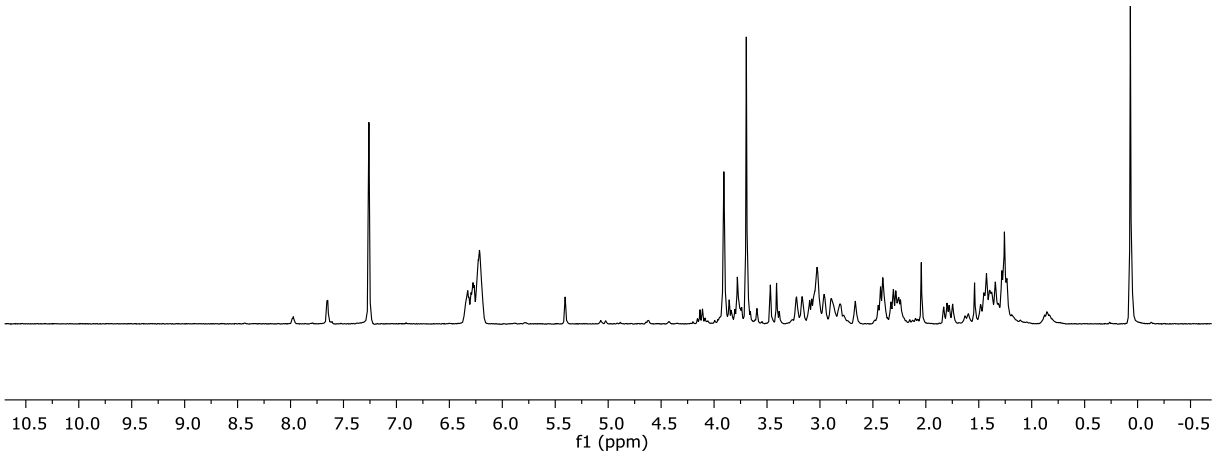
Solvent CDCl3
MHz 600
Nucleus1H
2.0
2.0
2.0
2.0
2.0
2.0
2.0
2.0
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

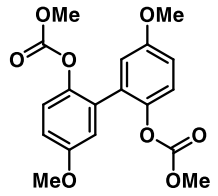

209.1
163.0
138.8
137.7
137.2
52.4
48.6
44.1
43.4
41.6
Solvent CDCl3
MHz 151
Nucleus13C
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)



80b **80a**

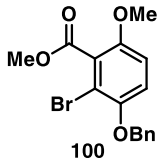
Solvent CDCl3
MHz 300
Nucleus1H



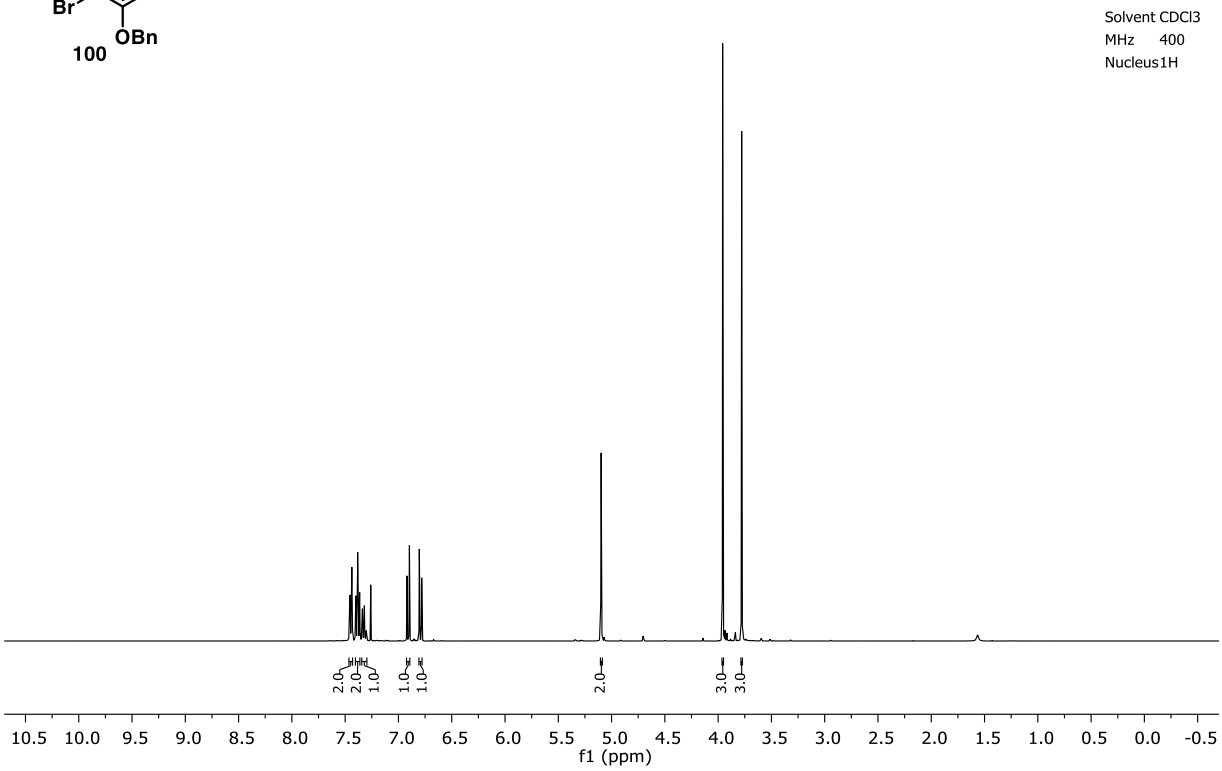


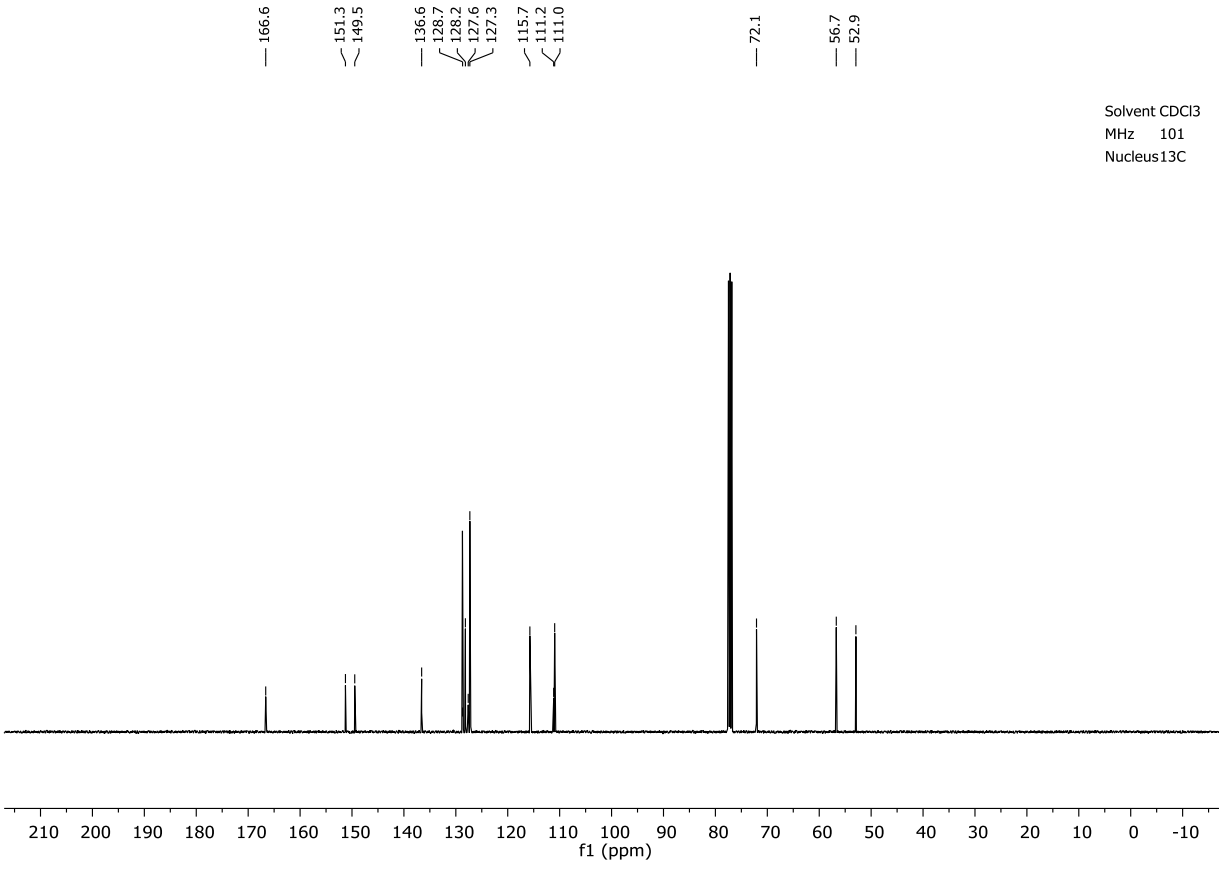
122

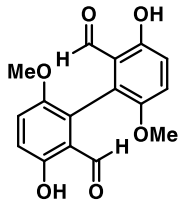
Solvent CDCl3
MHz 300
Nucleus1H


O
OMe
MeO
Br
OBn

100

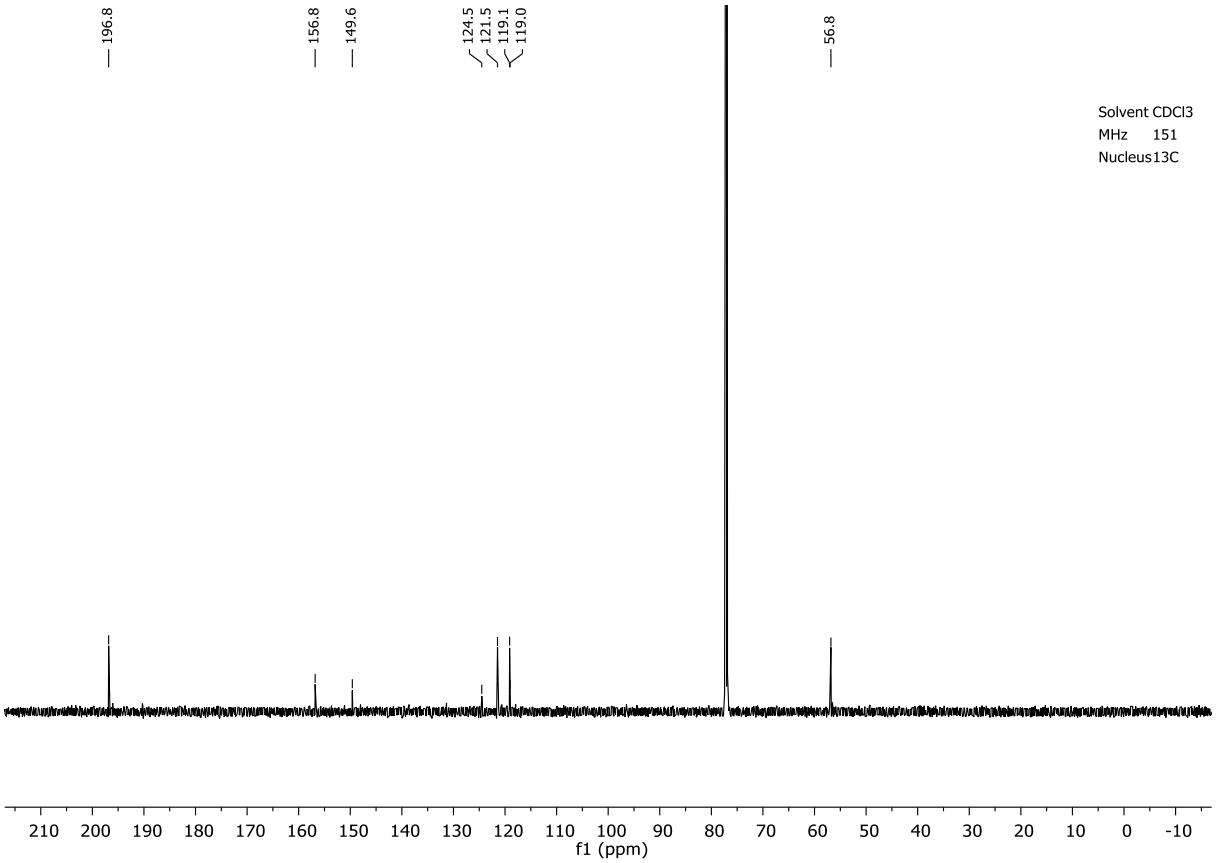

Solvent CDCl3
MHz 400
Nucleus1H
2.0
2.0
1.0
1.0
1.0
2.0
3.0
3.0
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

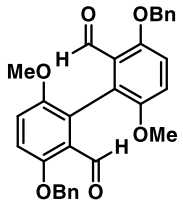

166.6
151.3
149.5
136.6
128.7
128.2
127.6
127.3
115.7
111.2
111.0
72.1
56.7
52.9
Solvent CDCl3
MHz 101
Nucleus13C
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


O
OH
H
MeO
OMe
H
OH
O

105

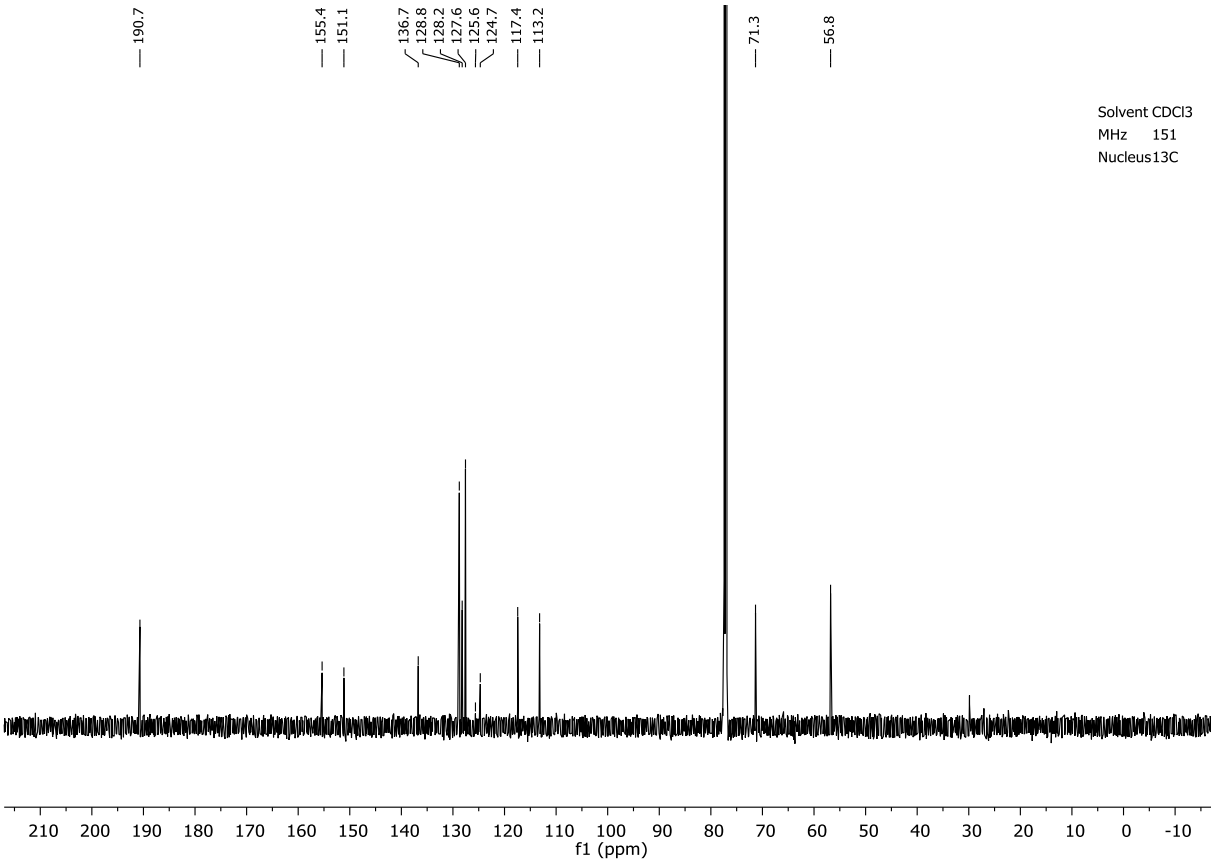
Solvent CDCl3
MHz 600
Nucleus1H
2.0
2.0
2.0
6.0
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

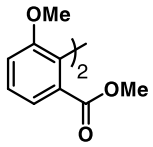

196.8
156.8
149.6
124.5
121.5
119.1
119.0
56.8
Solvent CDCl3
MHz 151
Nucleus13C
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


O
OBn
MeO
H
OMe
H
OBn
O

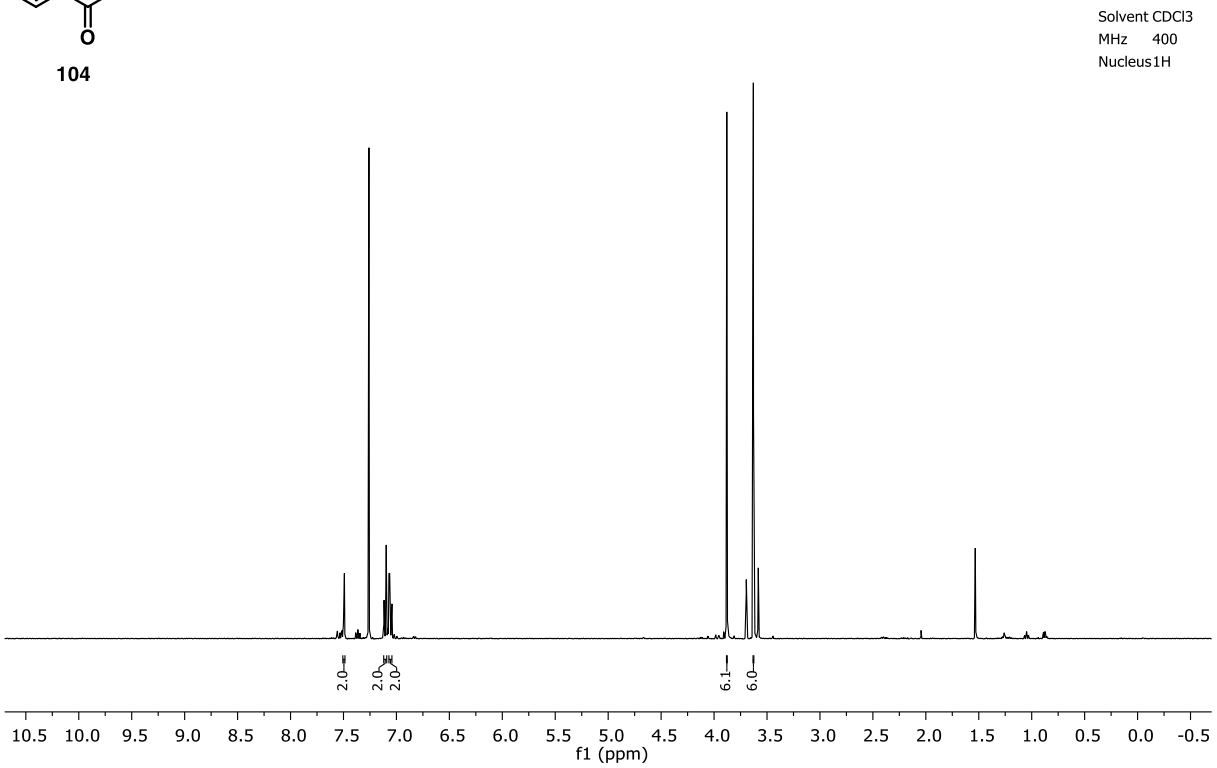
113

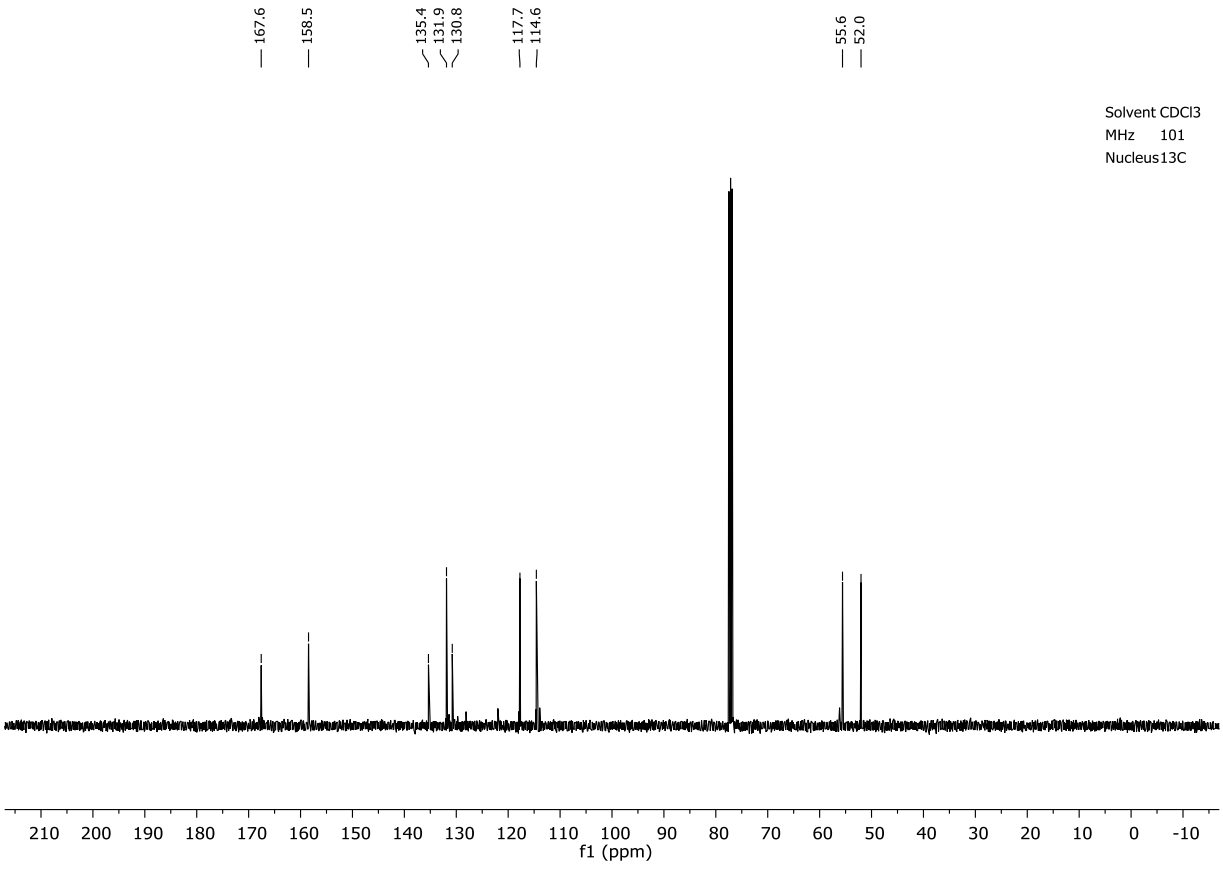
Solvent CDCl3
MHz 400
Nucleus1H
2.0
4.0
4.0
2.0
2.0
4.0
6.0
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

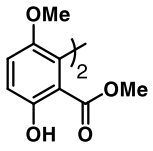

190.7
155.4
151.1
136.7
128.8
128.2
127.6
125.6
124.7
117.4
113.2
71.3
56.8
Solvent CDCl3
MHz 151
Nucleus13C
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


OMe
2
OMe
O

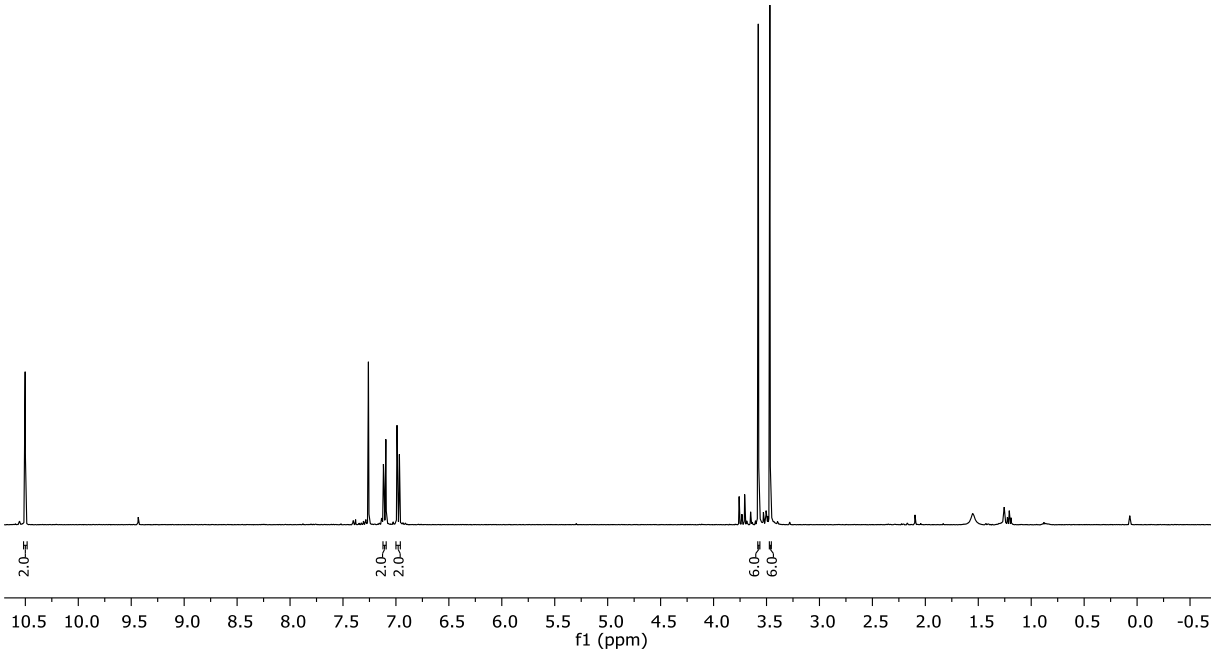
104

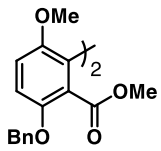

Solvent CDCl3
MHz 400
Nucleus1H
2.0
2.0
2.0
6.1
6.0
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)


167.6
158.5
135.4
131.9
130.8
117.7
114.6
55.6
52.0
Solvent CDCl3
MHz 101
Nucleus13C
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

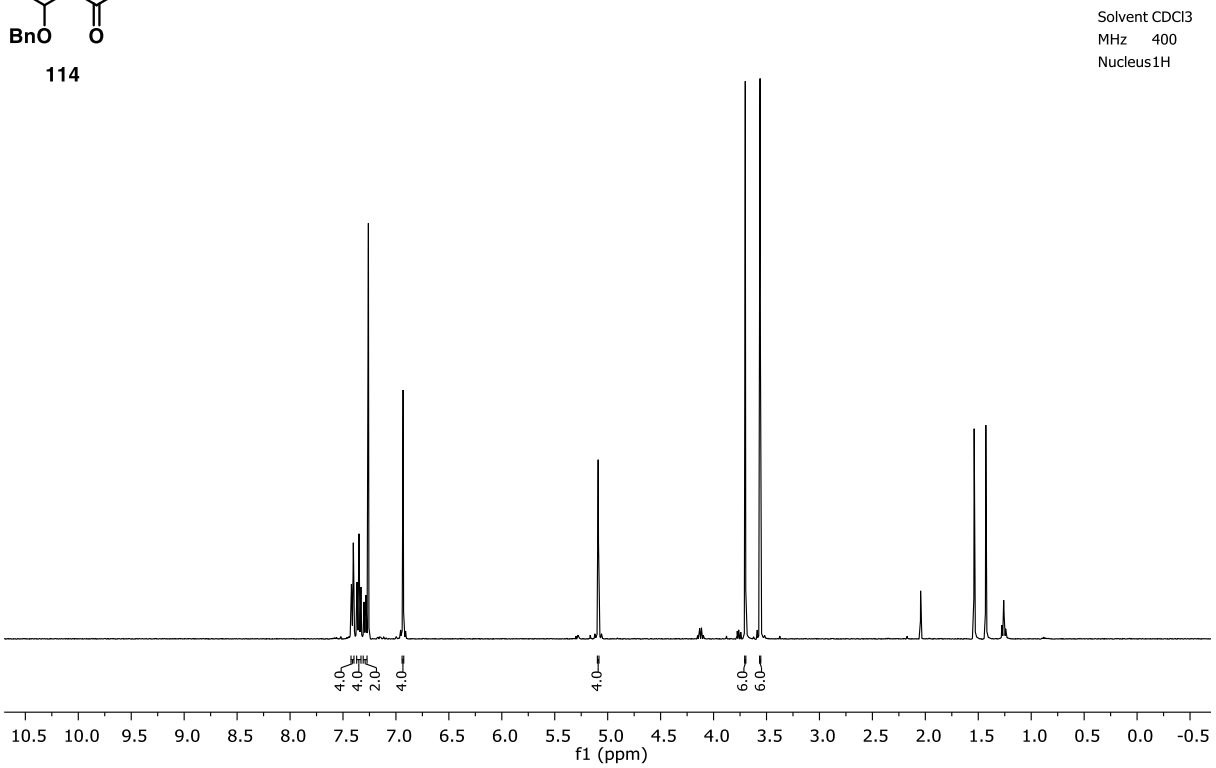

OMe
2
OMe
OH
O

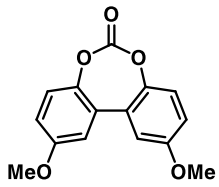
102


Solvent CDCl3
MHz 400
Nucleus1H
2.0
2.0
2.0
6.0
6.0
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

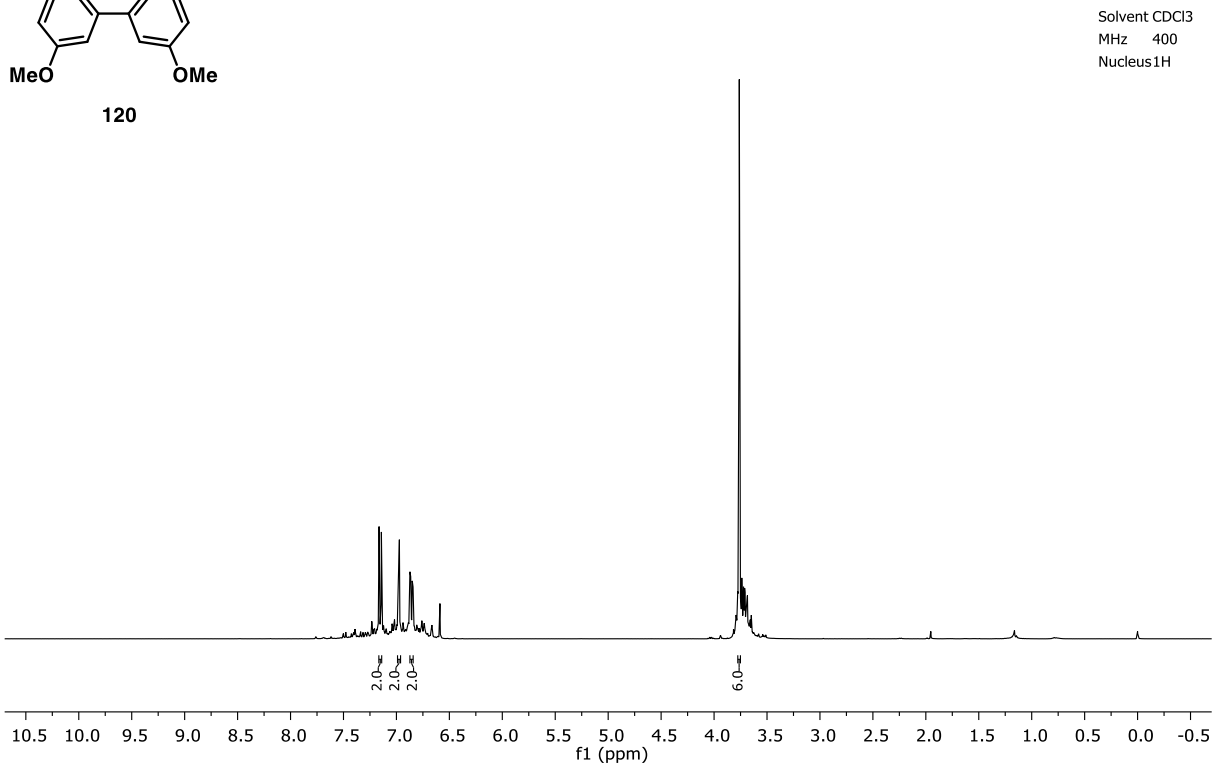

OMe
2
OMe
BnO
O

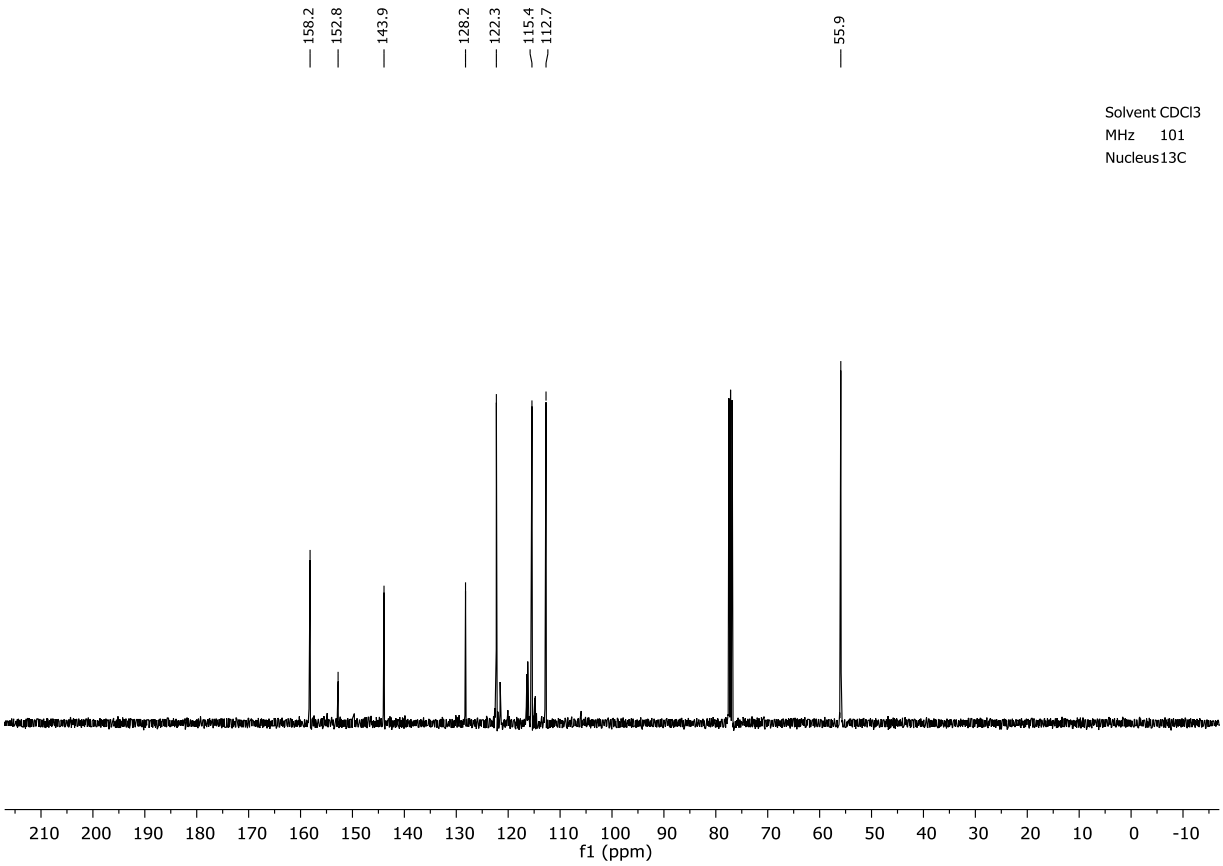
114

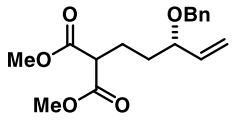

Solvent CDCl3
MHz 400
Nucleus1H
4.0
4.0
2.0
4.0
4.0
6.0
6.0
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)


O
O
O
MeO
OMe

120

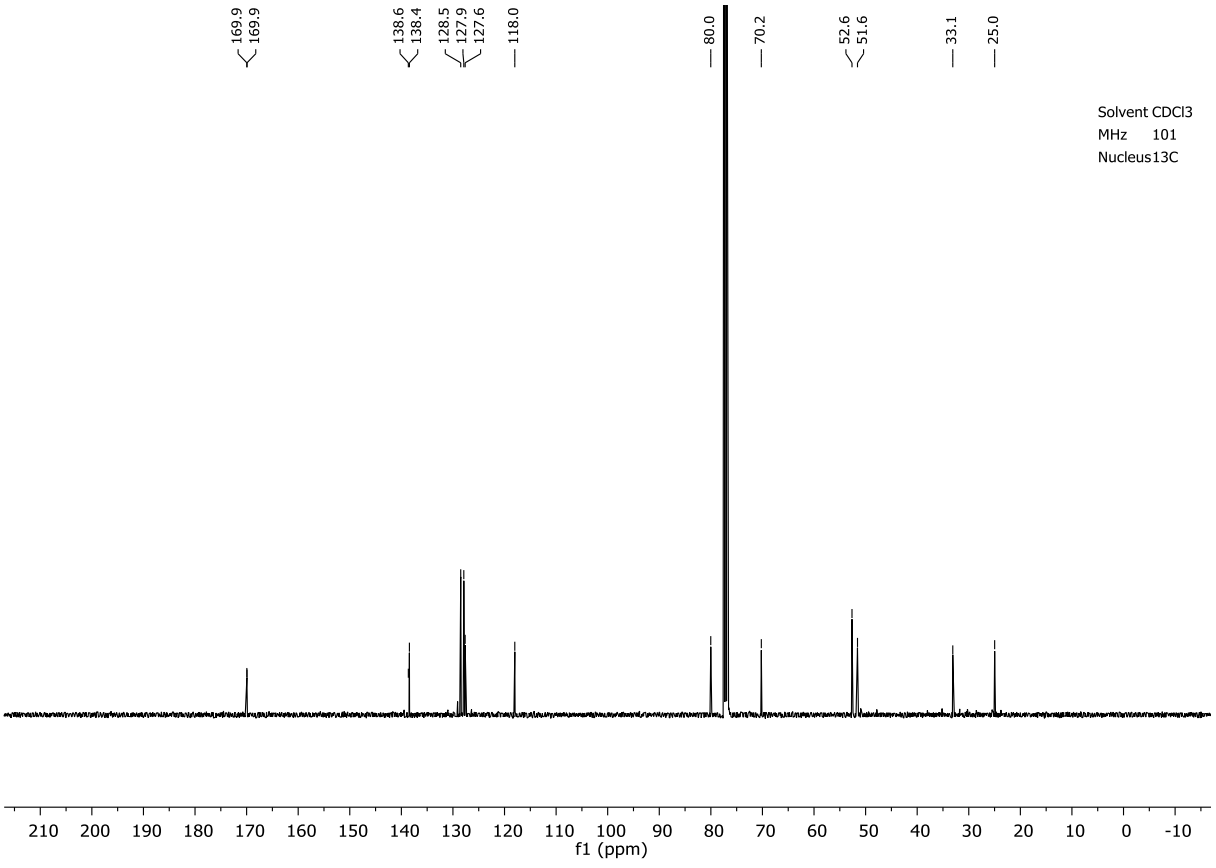

Solvent CDCl3
MHz 400
Nucleus1H
2.0
2.0
2.0
6.0
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

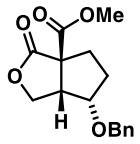

158.2
152.8
143.9
128.2
122.3
115.4
112.7
55.9
Solvent CDCl3
MHz 101
Nucleus13C
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


O
OBn
MeO
MeO
O

126

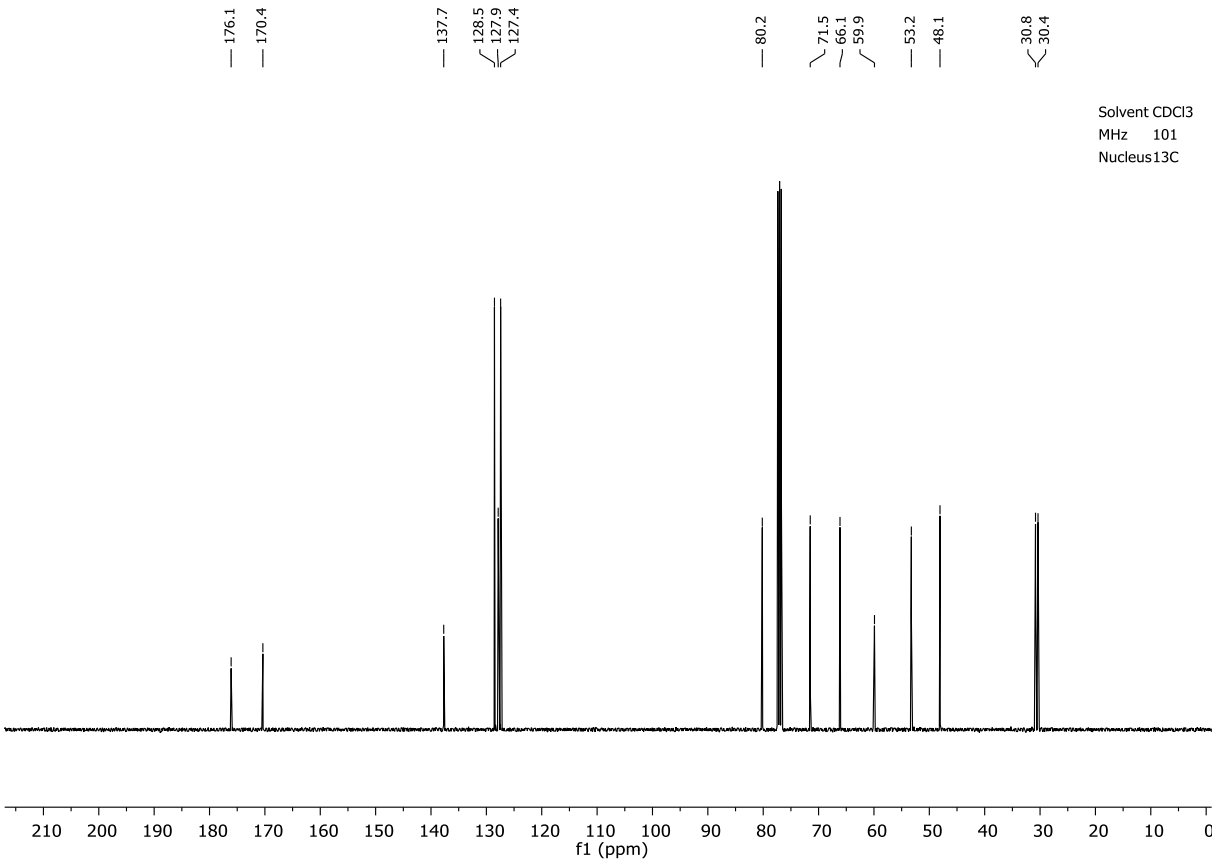
Solvent CDCl3
MHz 400
Nucleus1H
5.0
1.0
2.0
1.0
1.0
7.0
1.0
1.0
1.0
1.0
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

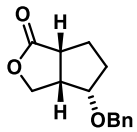

169.9
169.9
138.6
138.4
128.5
127.9
127.6
118.0
80.0
70.2
52.6
51.6
33.1
25.0
Solvent CDCl3
MHz 101
Nucleus13C
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


O
O
OMe
O
H
OBn

135

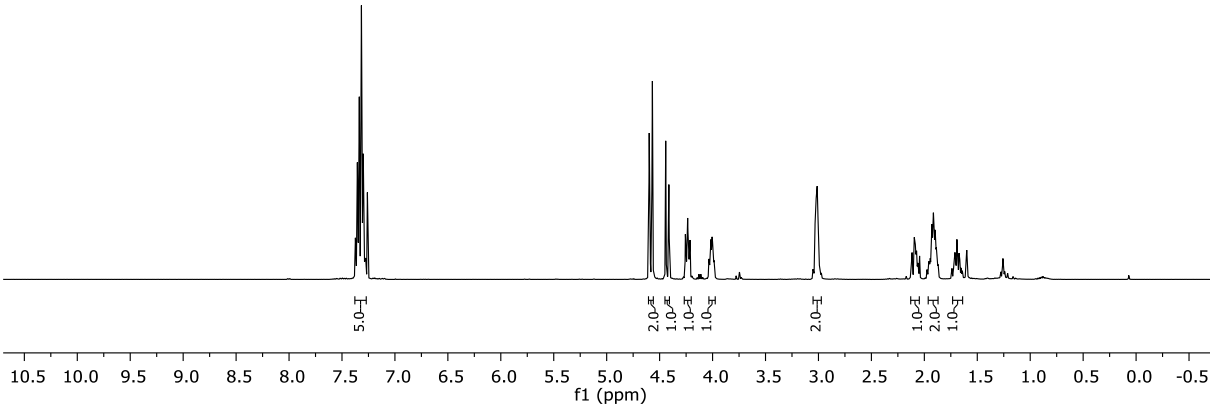
Solvent CDCl3
MHz 400
Nucleus1H
5.0
1.0
1.0
1.0
1.0
1.0
3.0
1.0
2.0
1.0
1.0
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

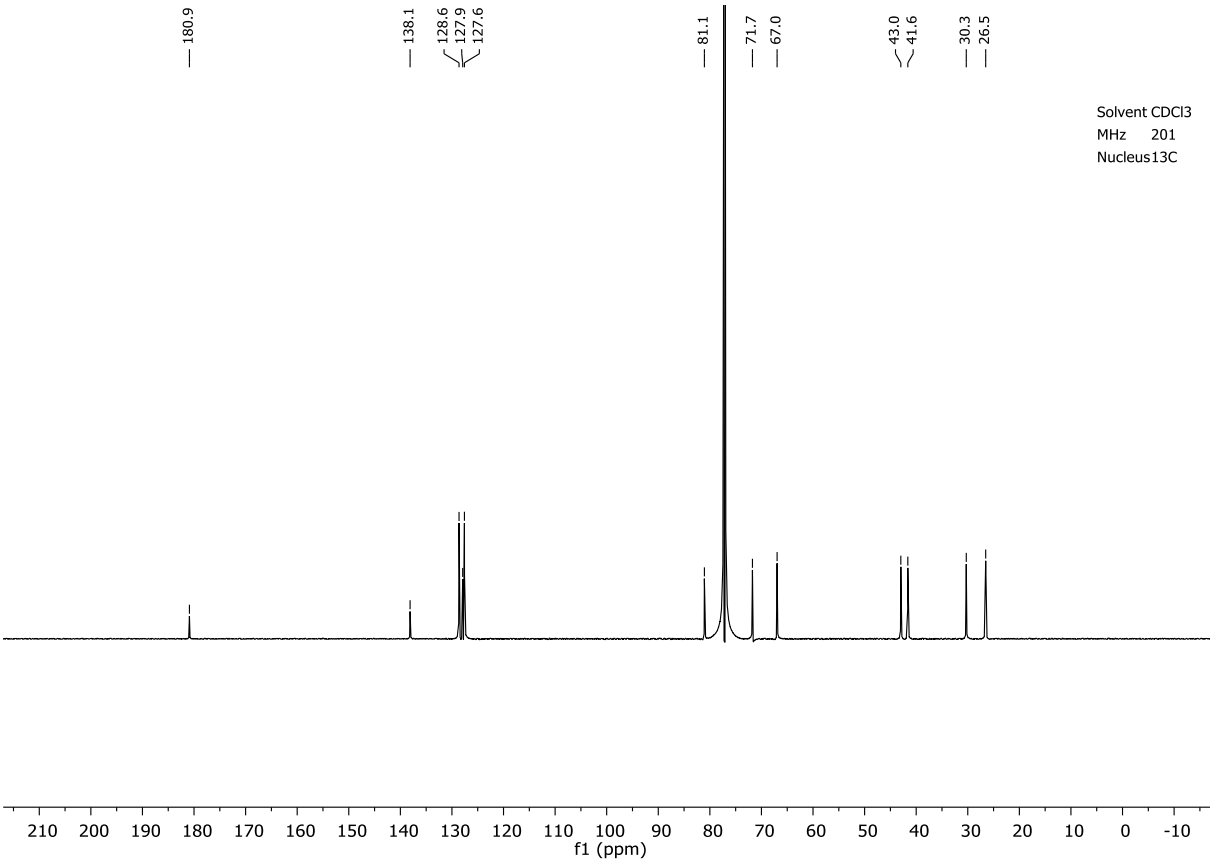

176.1
170.4
137.7
128.5
127.9
127.4
80.2
71.5
66.1
59.9
53.2
48.1
30.8
30.4
Solvent CDCl3
MHz 101
Nucleus13C
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

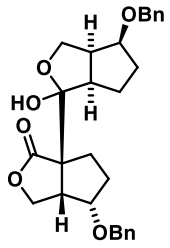


125

Solvent CDCl3
MHz 400
Nucleus1H

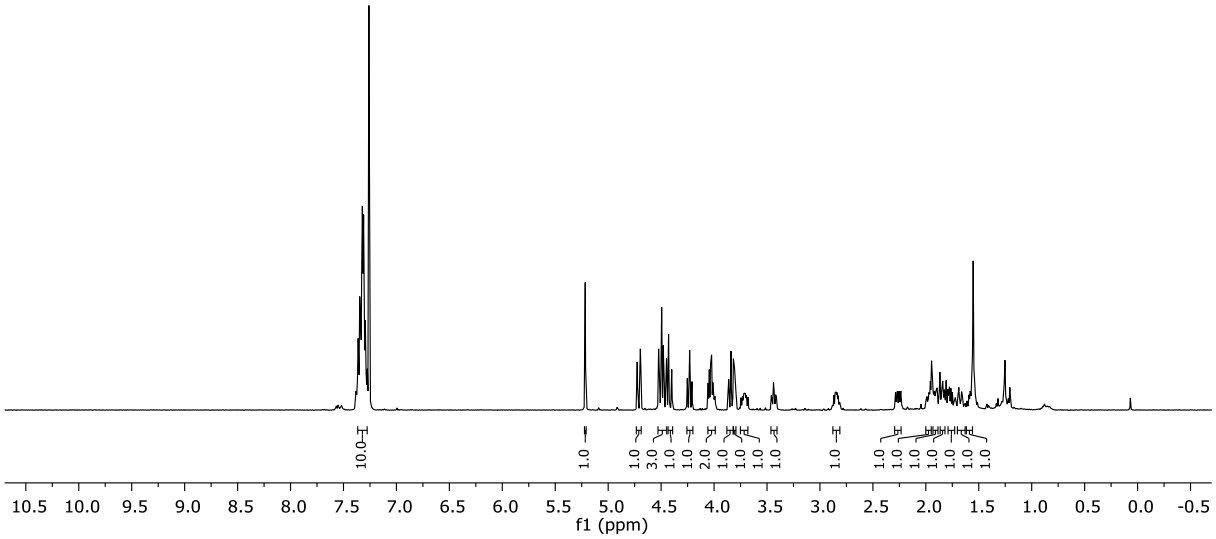


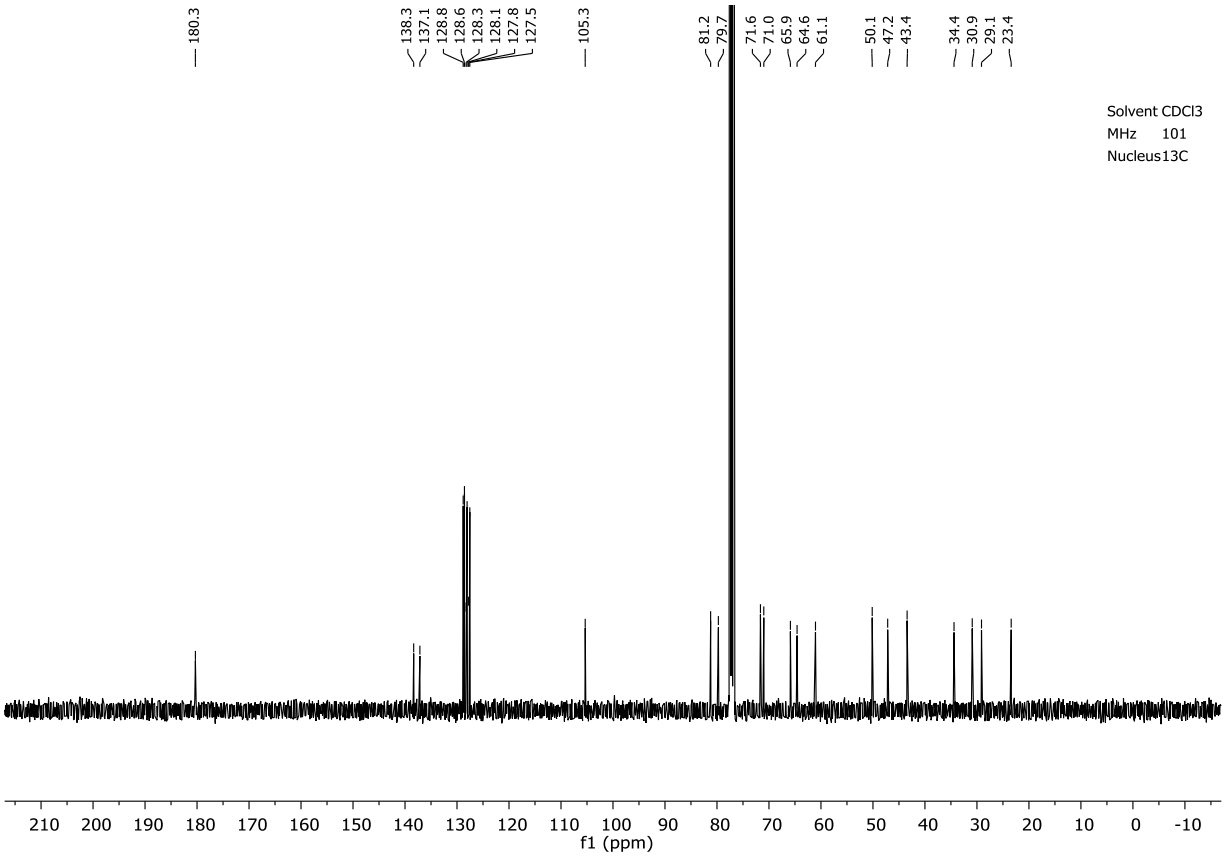


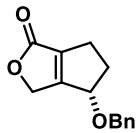


136

Solvent CDCl3
MHz 400
Nucleus1H

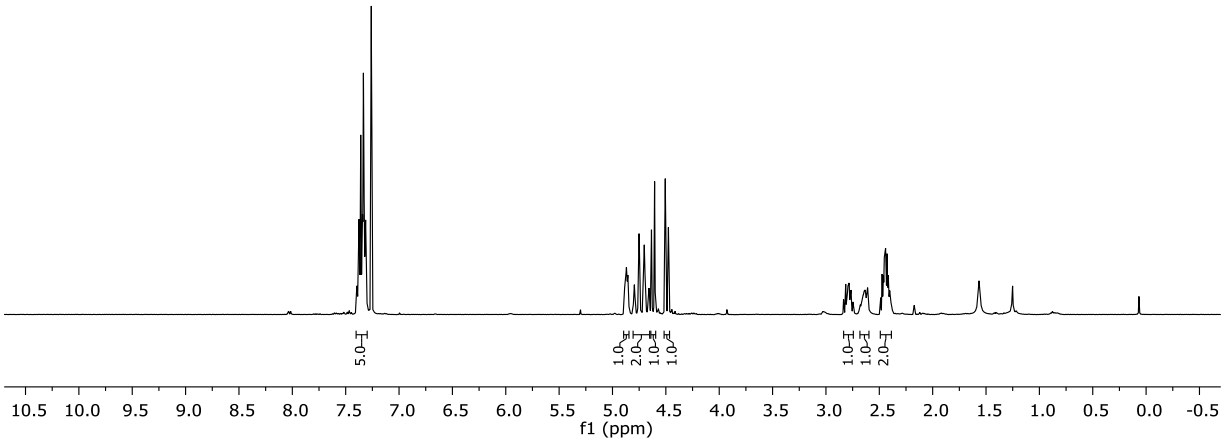


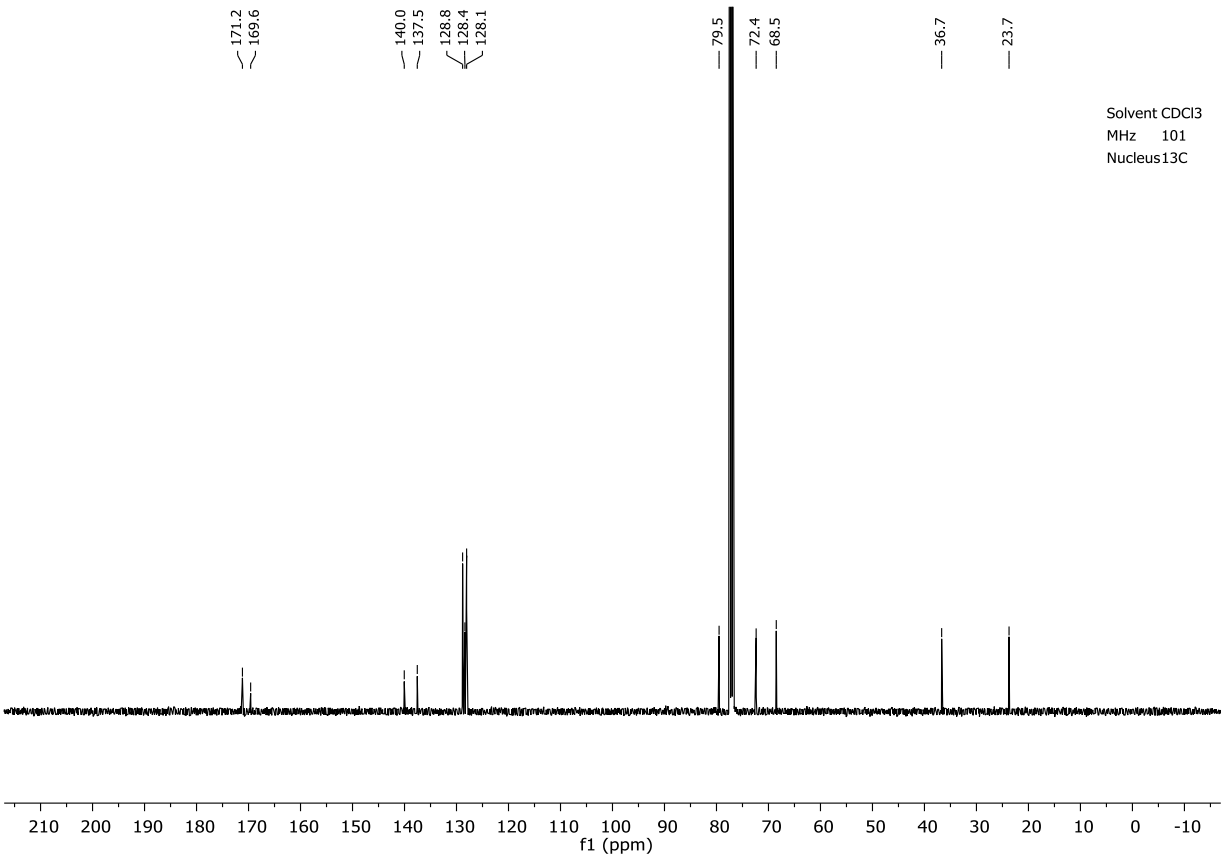


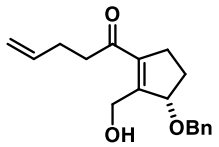


124

Solvent CDCl3
MHz 400
Nucleus1H

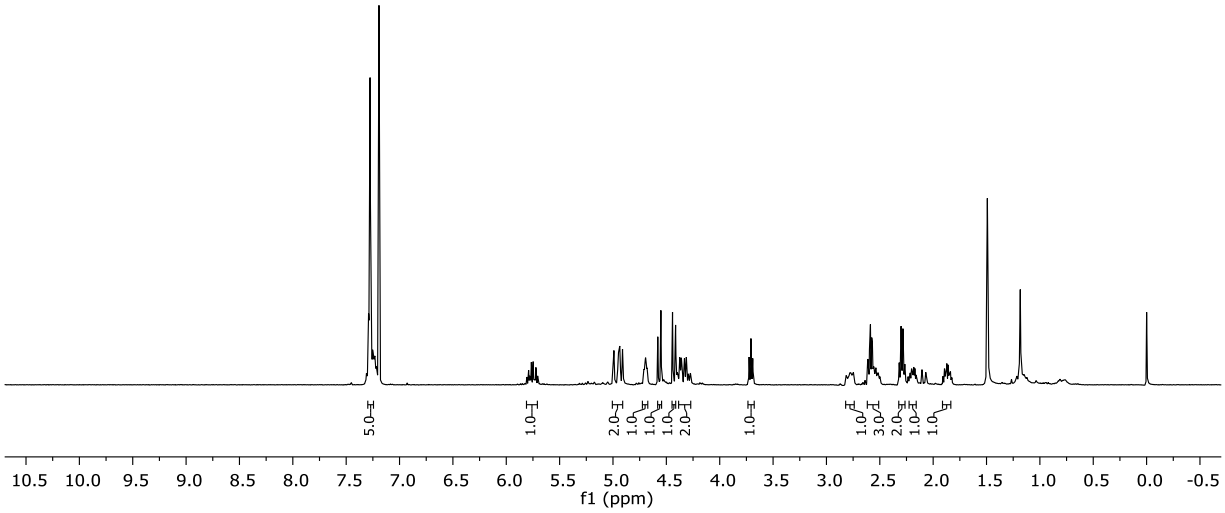


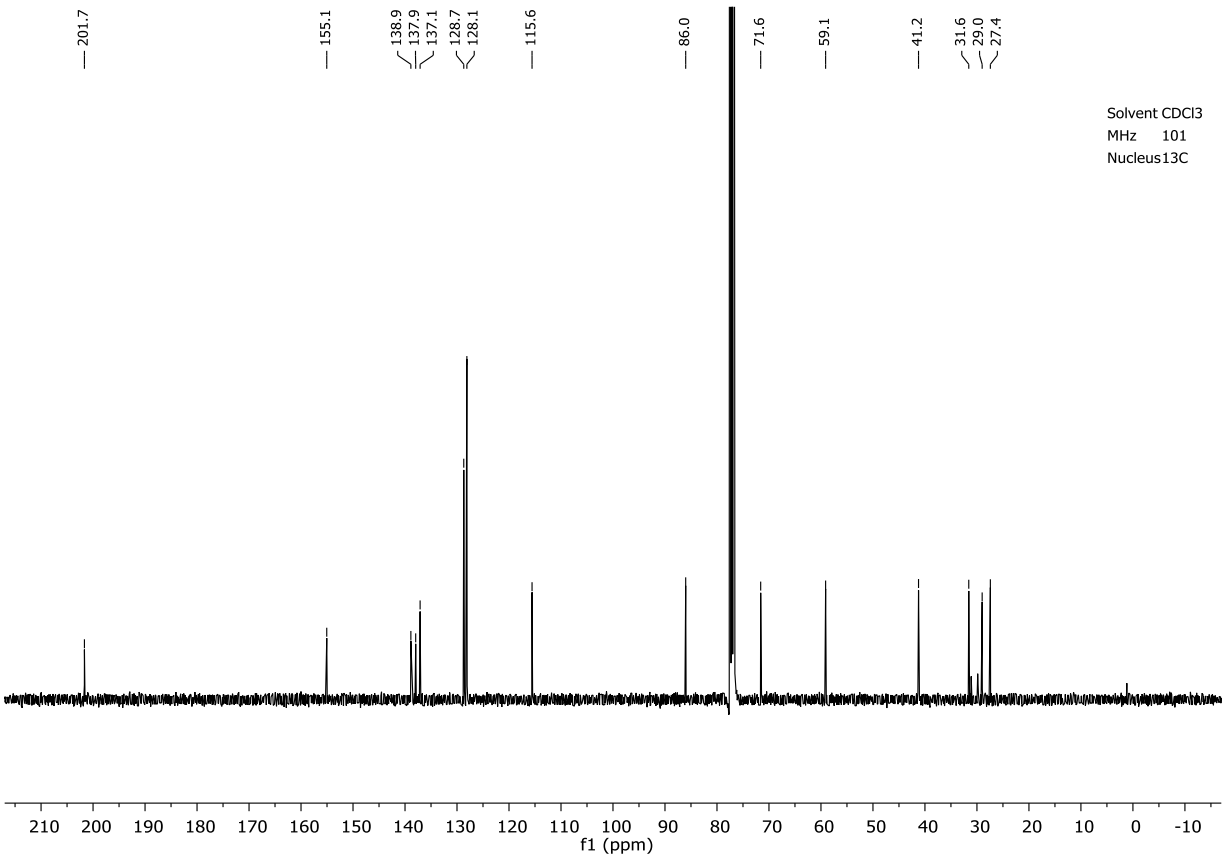


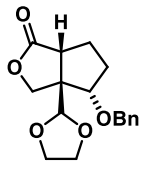


138

Solvent CDCl3
MHz 400
Nucleus1H

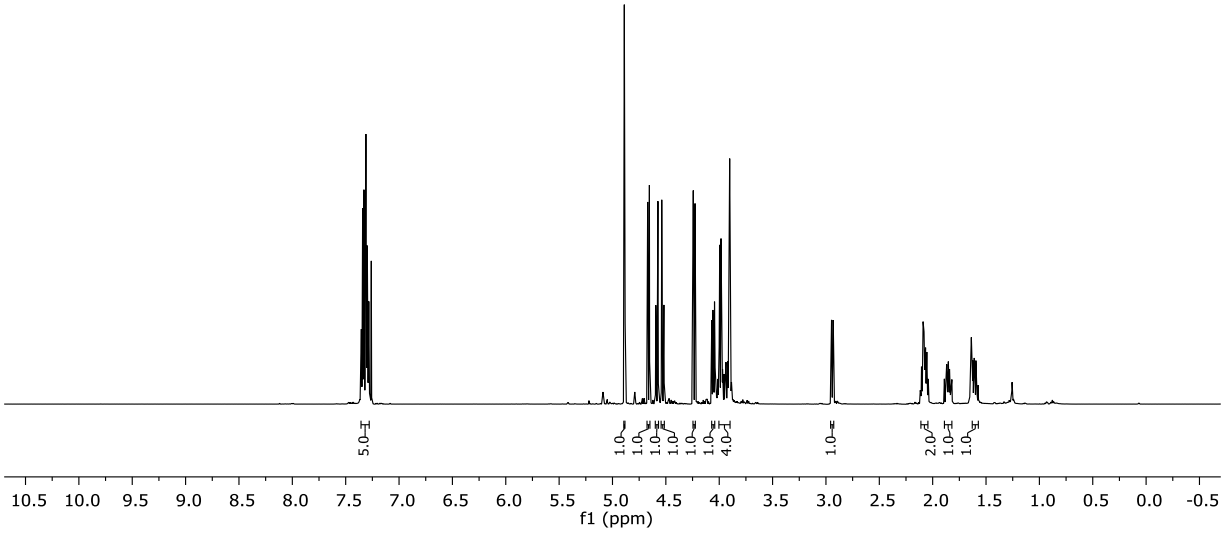




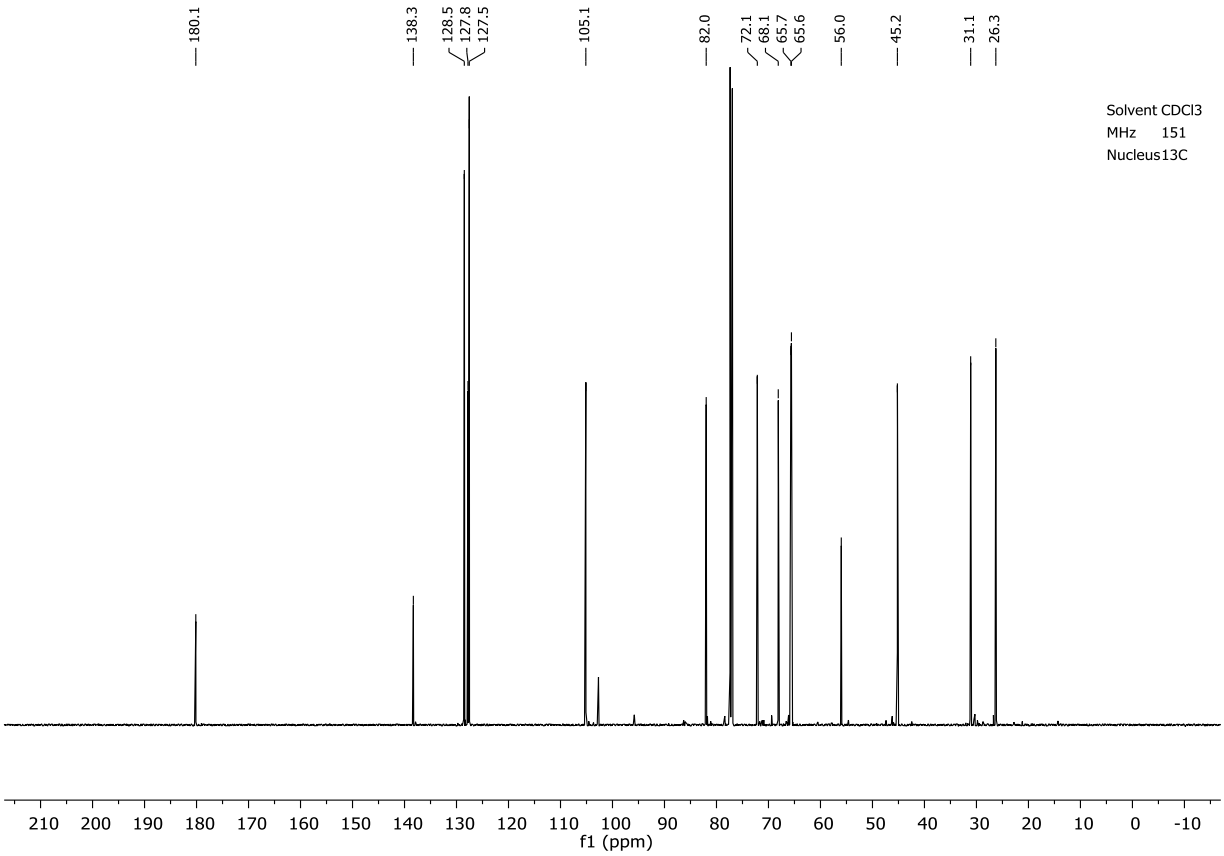


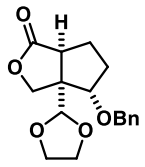
140

Solvent CDCl3
MHz 600
Nucleus1H

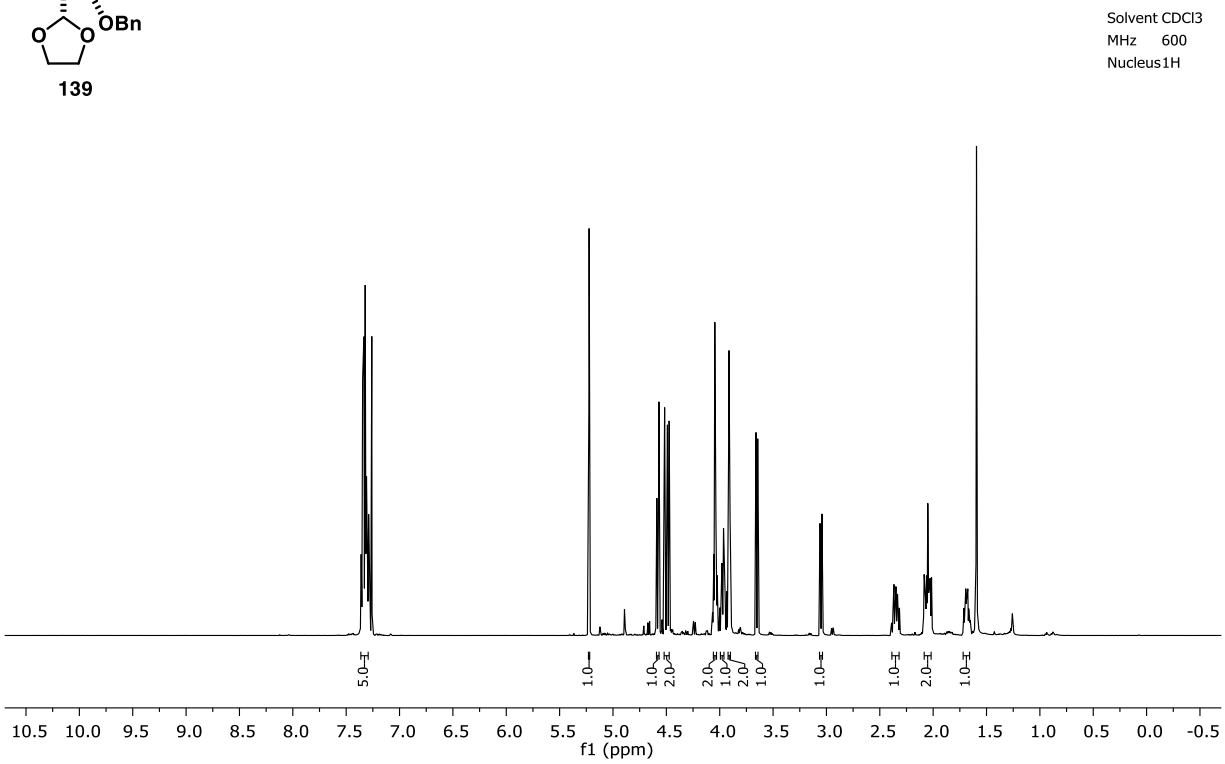


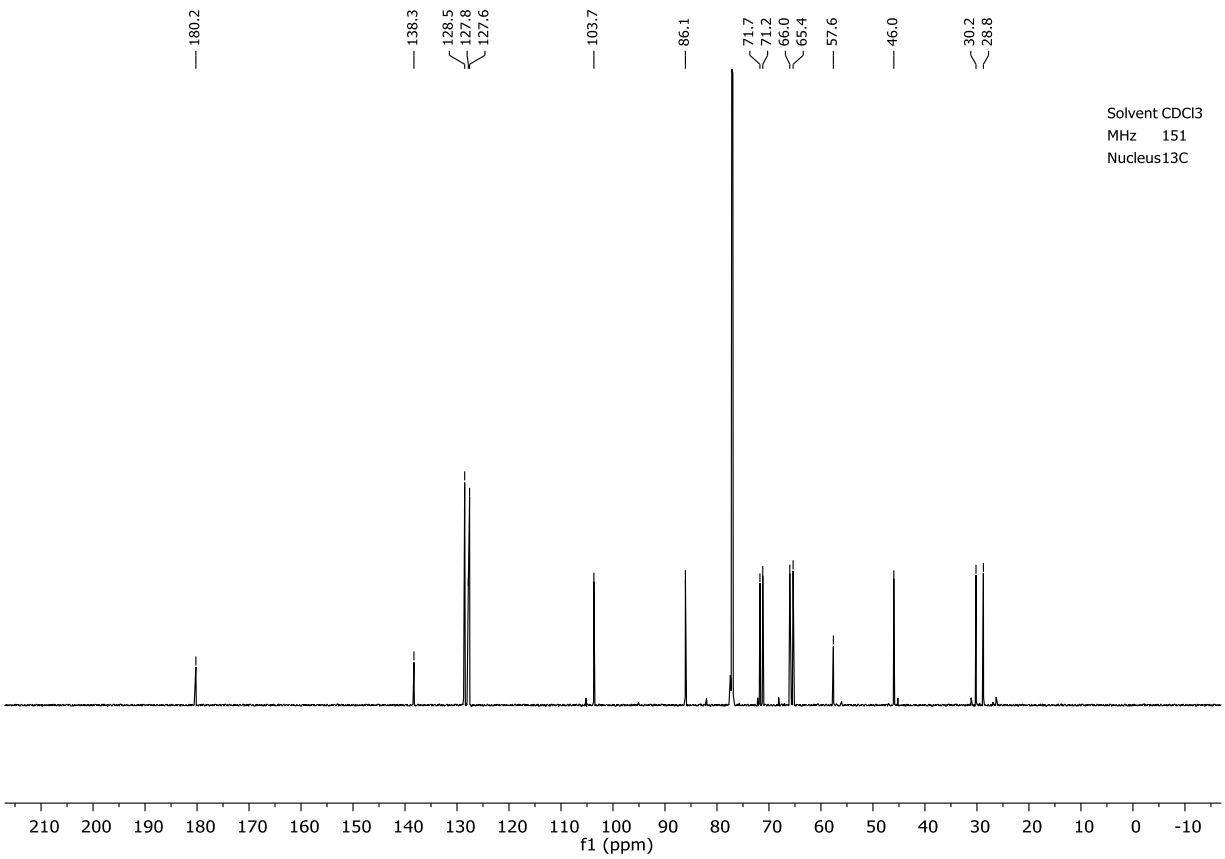
Solvent CDCl3
MHz 151
Nucleus13C

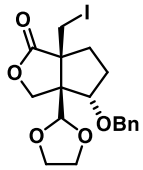



O
H
O
OBn
O
O

139

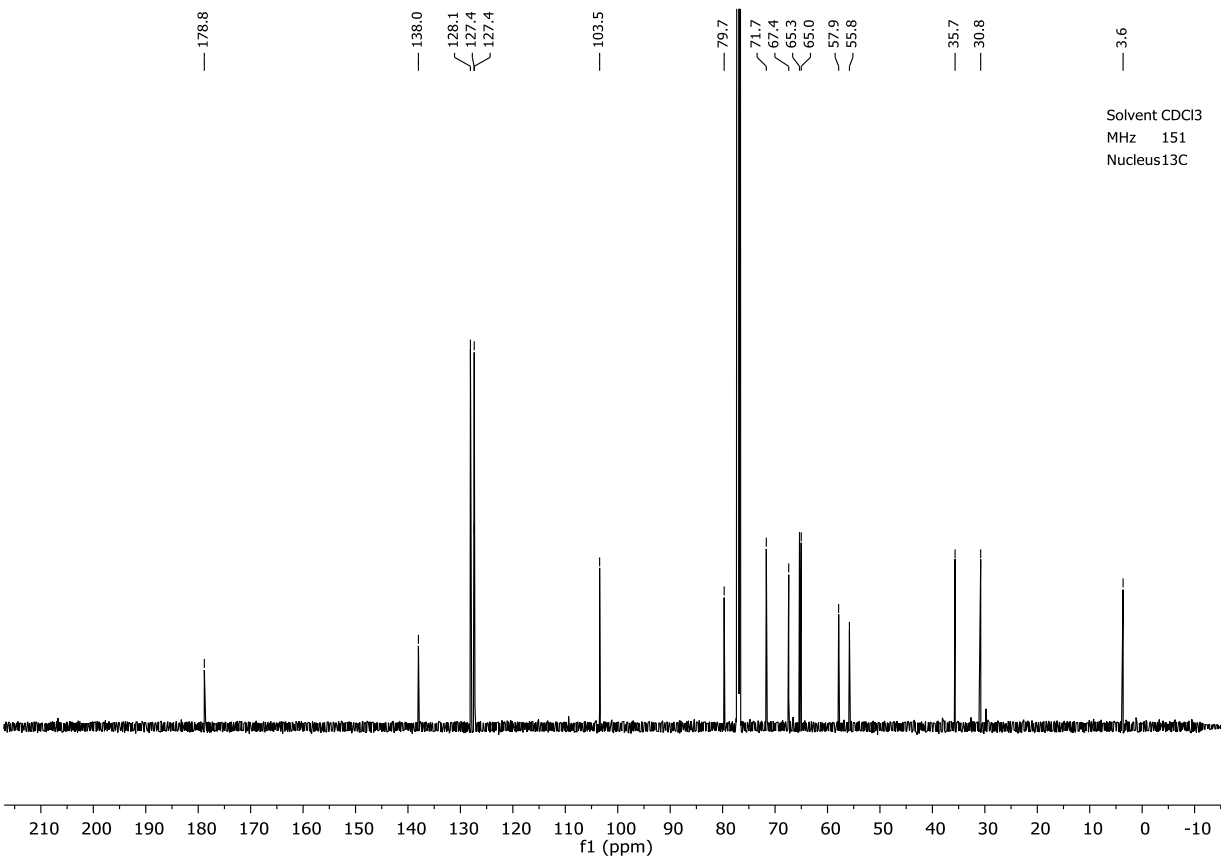

Solvent CDCl3
MHz 600
Nucleus1H
5.0
1.0
1.0
2.0
2.0
1.0
2.0
1.0
1.0
1.0
2.0
1.0
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

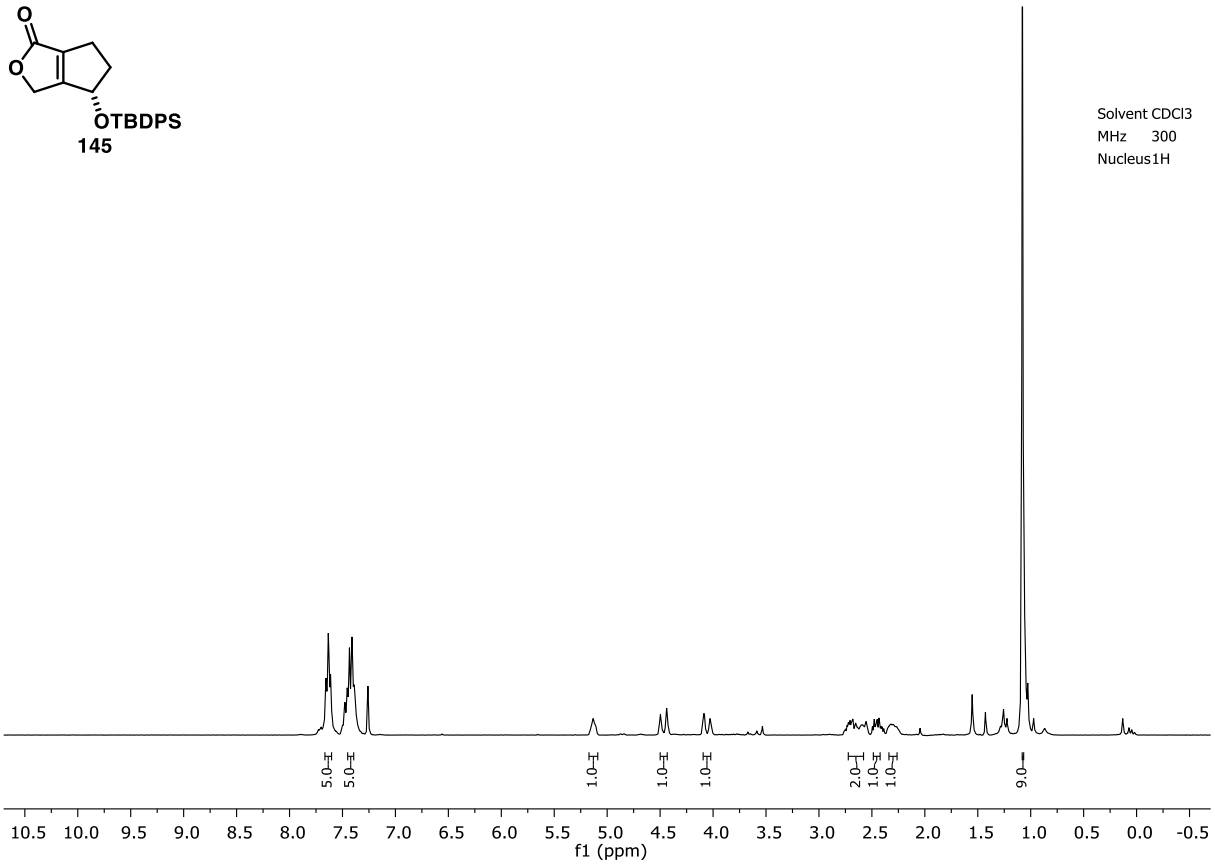

180.2
138.3
128.5
127.8
127.6
103.7
86.1
71.7
71.2
66.0
65.4
57.6
46.0
30.2
28.8
Solvent CDCl3
MHz 151
Nucleus13C
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

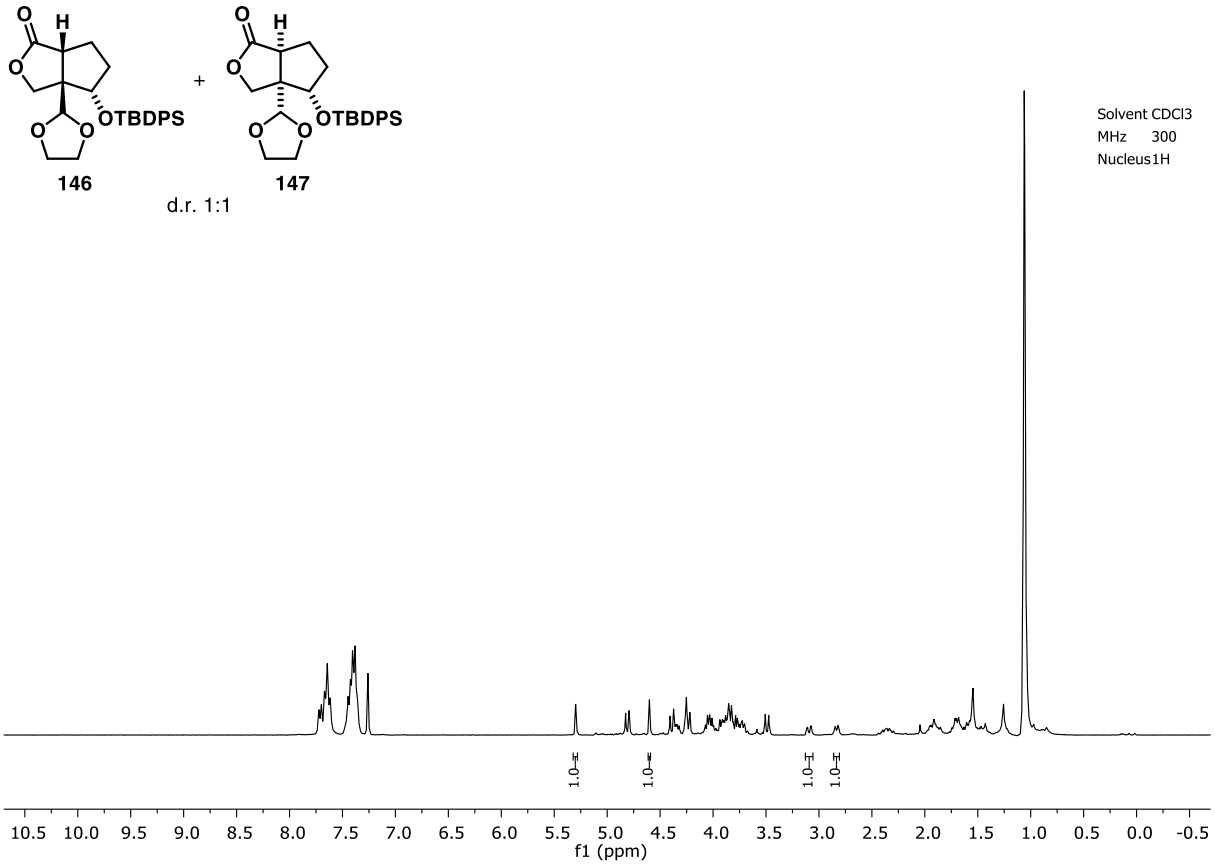

O
I
O
OBn
O
O

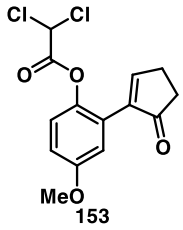
141

Solvent CDCl3
MHz 600
Nucleus1H
5.0
1.0
1.0
2.0
1.0
1.0
2.0
2.0
2.0
1.0
1.0
1.0
1.0
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)


178.8
138.0
128.1
127.4
127.4
103.5
79.7
71.7
67.4
65.3
65.0
57.9
55.8
35.7
30.8
3.6
Solvent CDCl3
MHz 151
Nucleus13C
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

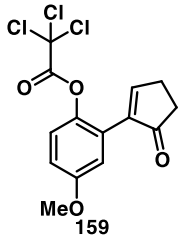

OTBDPS
145
Solvent CDCl3
MHz 300
Nucleus1H
5.0
5.0
1.0
1.0
1.0
2.0
1.0
1.0
9.0
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)


OTBDPS
146
+
OTBDPS
147
d.r. 1:1
Solvent CDCl3
MHz 300
Nucleus1H
1.0
1.0
1.0
1.0
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)


Cl
Cl
O
O
O
MeO

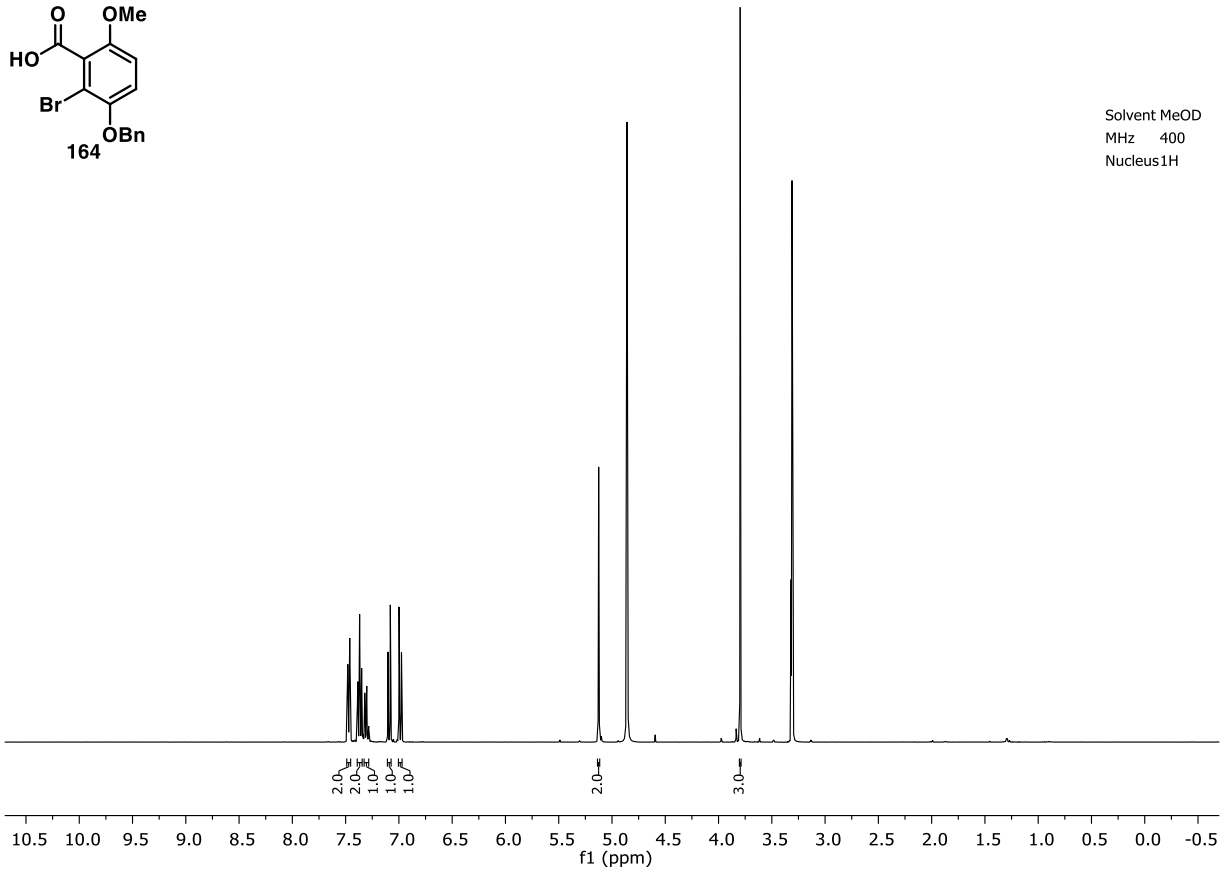
153

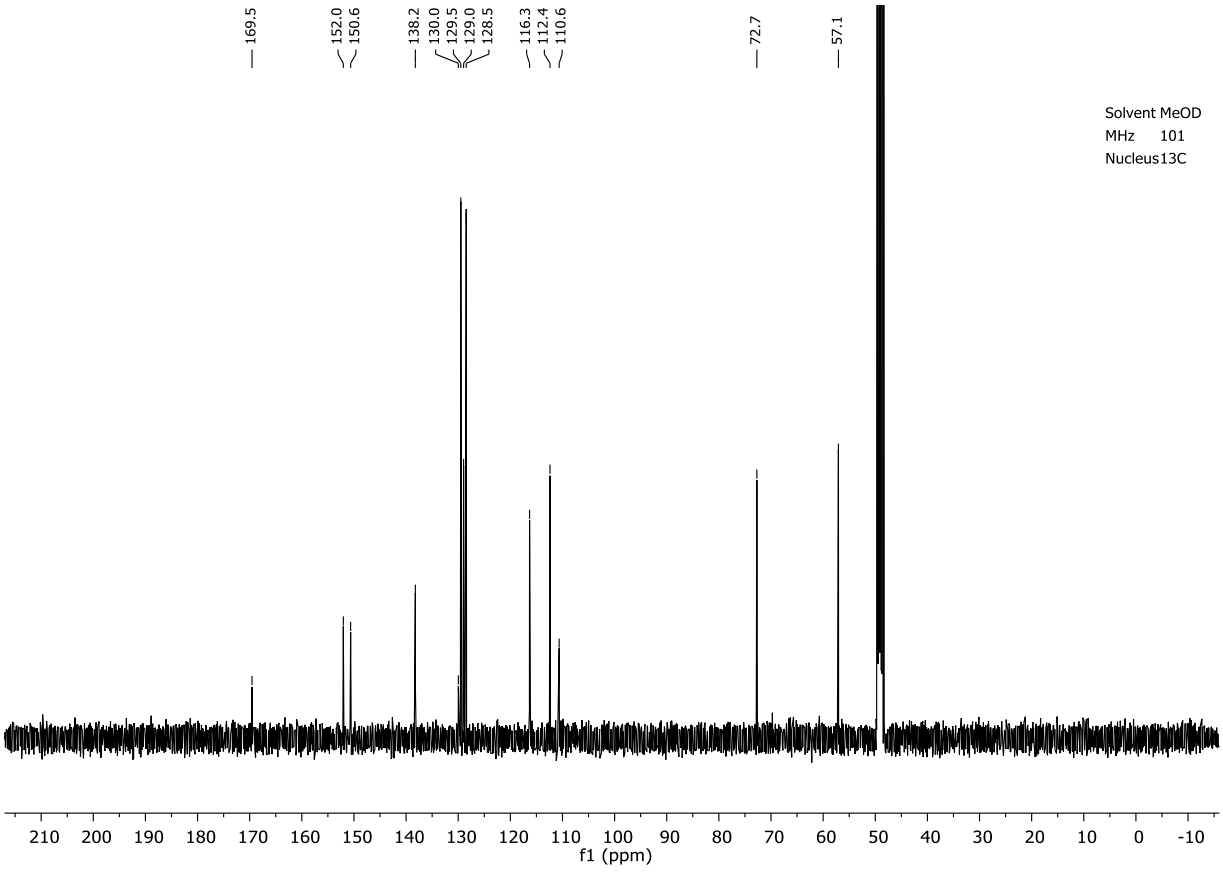
Solvent CDCl3
MHz 300
Nucleus1H
1.0
1.0
2.0
0.7
3.0
2.0
2.0

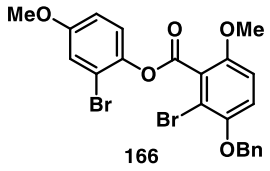

Cl
Cl
Cl
O
O
O
MeO

159

Solvent CDCl3
MHz 300
Nucleus1H
1.0
1.0
1.0
1.0
3.0
2.0
2.0

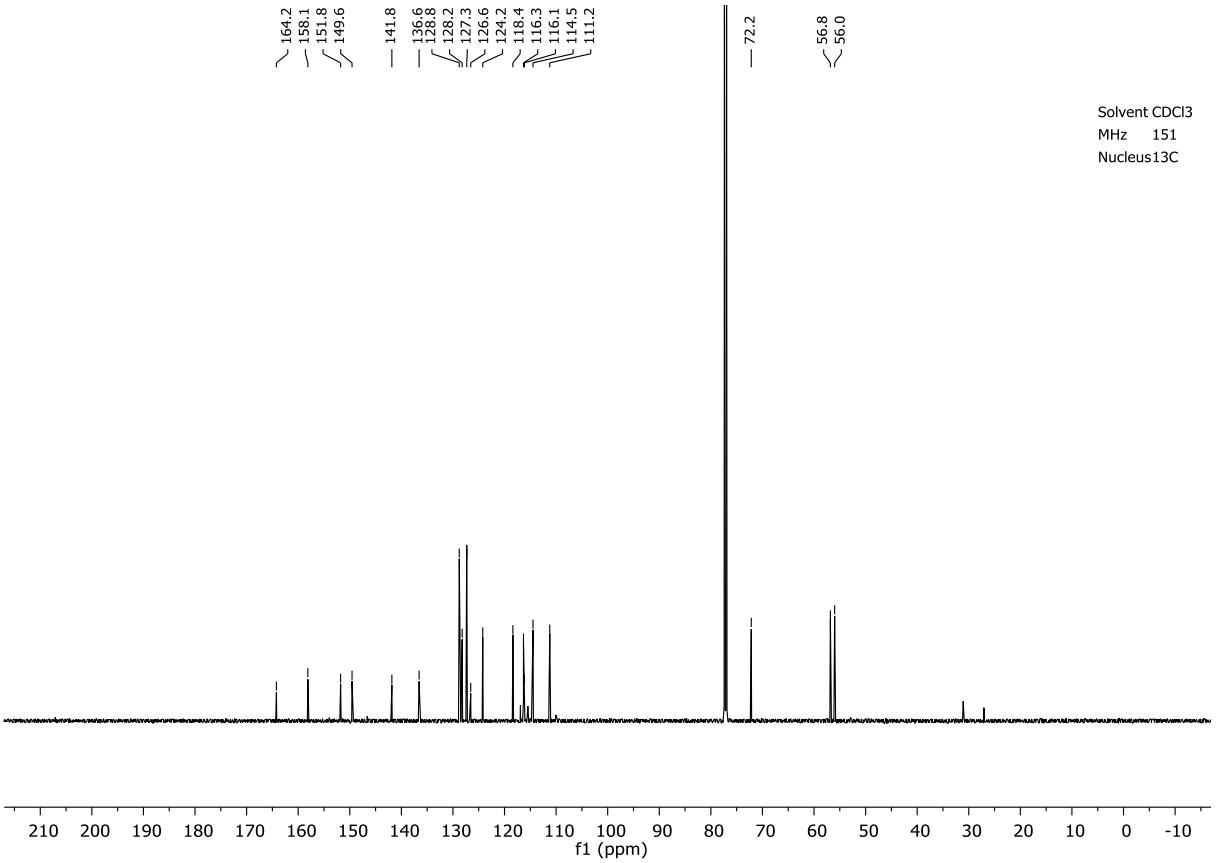

O
OMe
HO
Br
OBn
164
Solvent MeOD
MHz 400
Nucleus1H
2.0
2.0
1.0
1.0
2.0
3.0
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

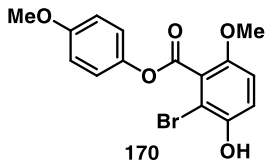

169.5
152.0
150.6
138.2
130.0
129.5
129.0
128.5
116.3
112.4
110.6
72.7
57.1
Solvent MeOD
MHz 101
Nucleus13C
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


MeO
O
OMe
O
Br
Br
OBn

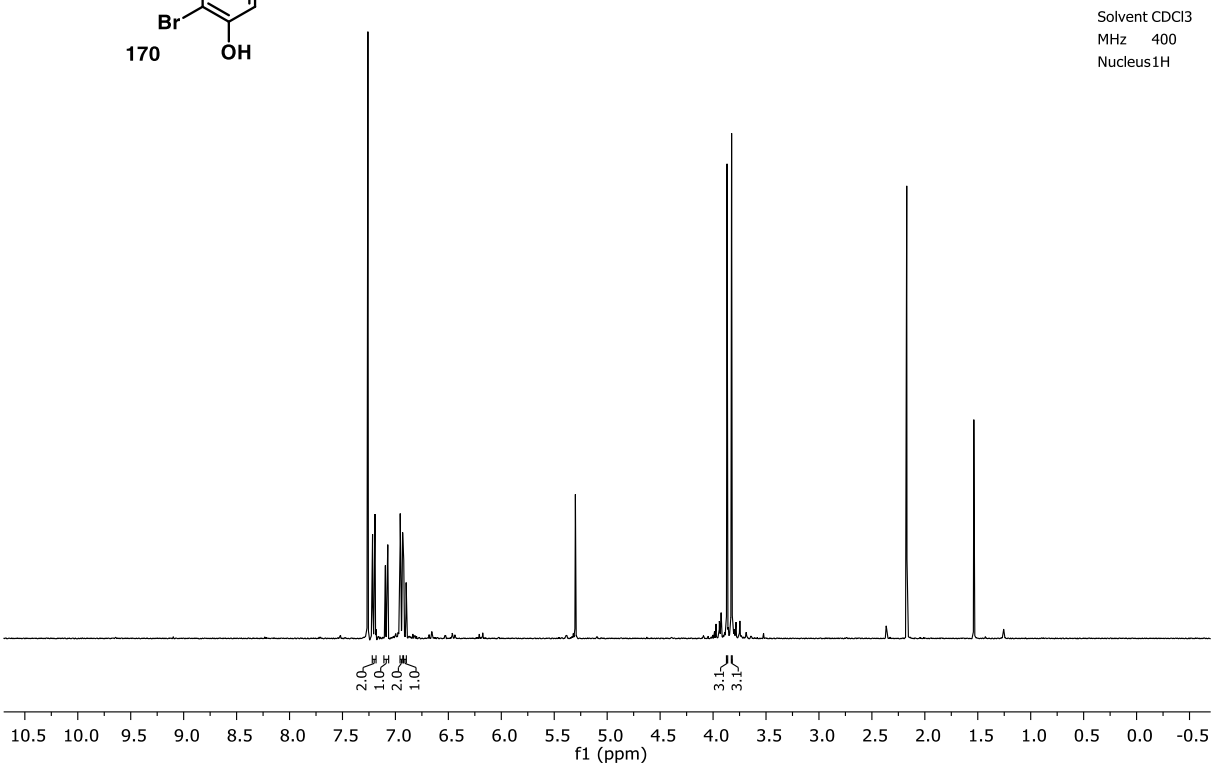
166

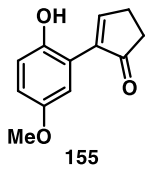
Solvent CDCl3
MHz 600
Nucleus1H
2.0
2.0
1.0
1.0
1.0
1.0
1.0
2.0
3.0
3.0
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)


164.2
158.1
151.8
149.6
141.8
136.6
128.8
128.2
127.3
126.6
124.2
118.4
116.3
116.1
114.5
111.2
72.2
56.8
56.0
Solvent CDCl3
MHz 151
Nucleus13C
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

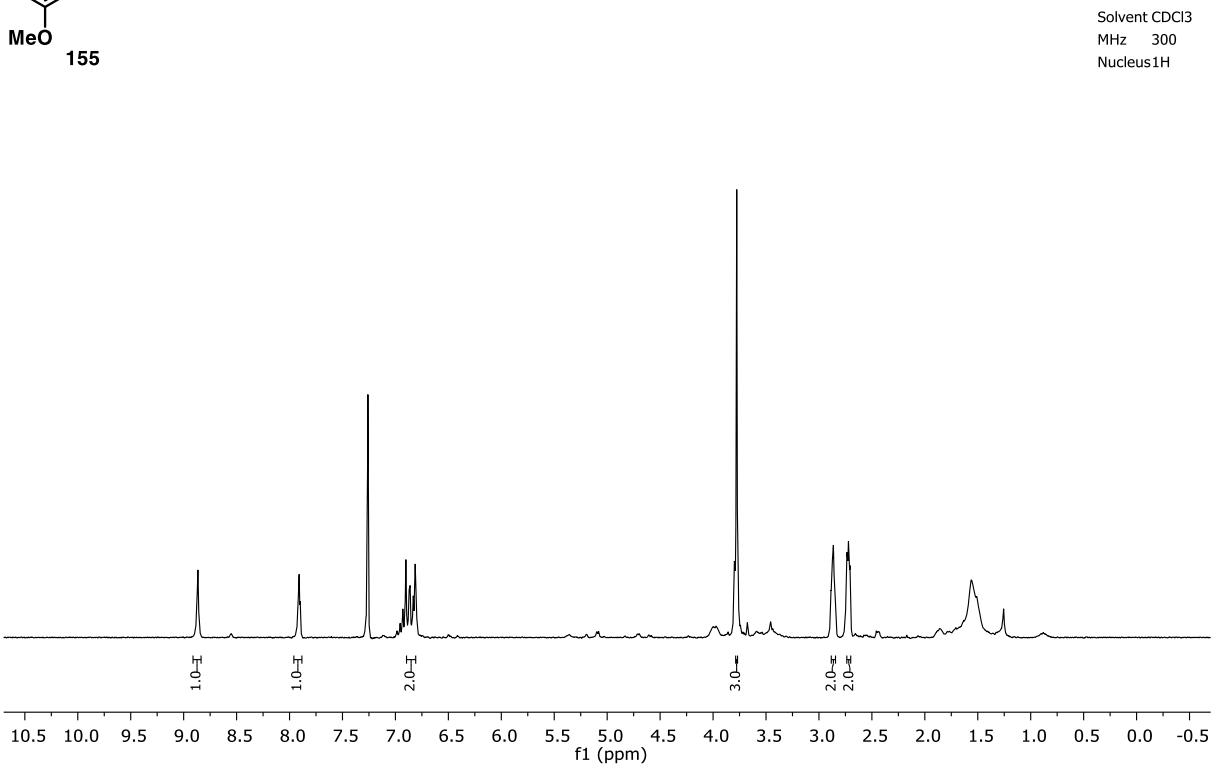

MeO
O
OMe
O
Br
OH

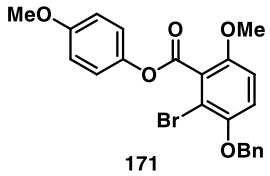
170


Solvent CDCl3
MHz 400
Nucleus1H
2.0
1.0
2.0
1.0
3.1
3.1
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)


OH
O
MeO

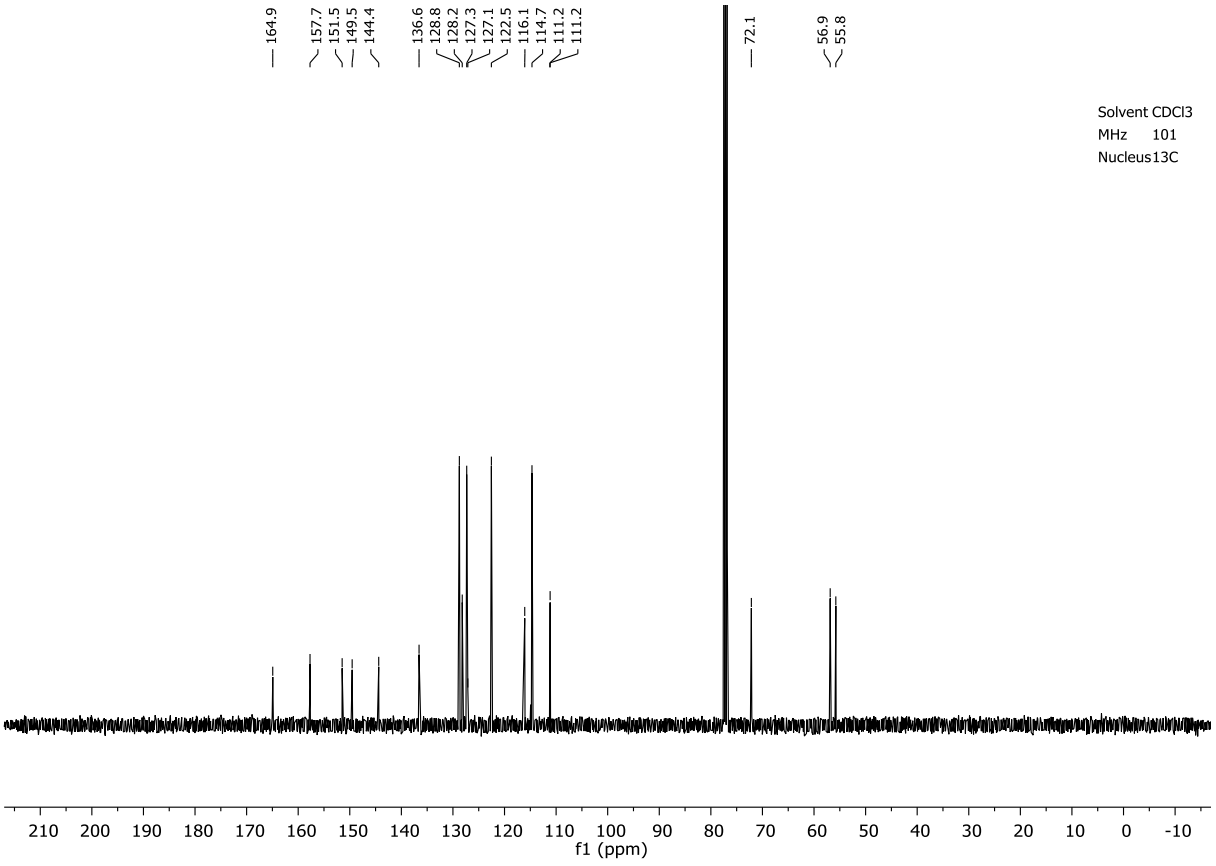
155

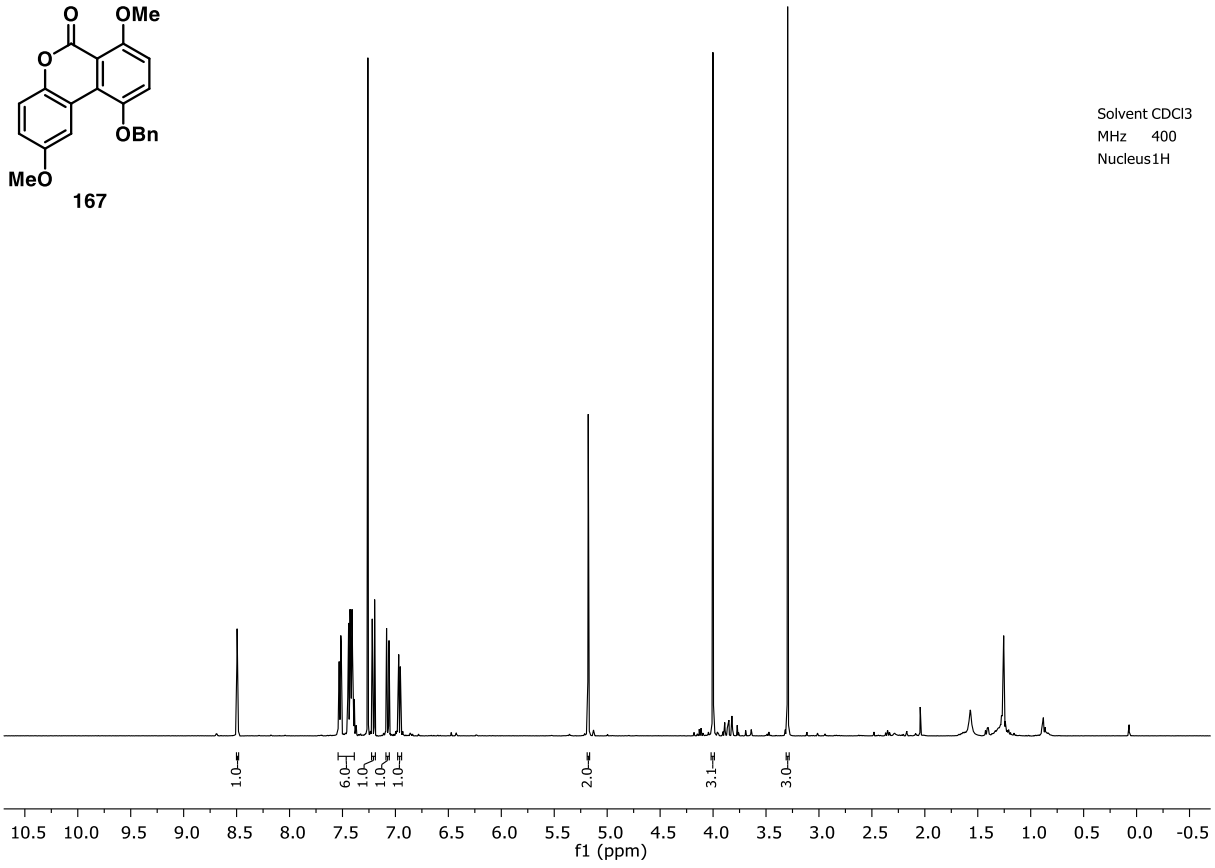

Solvent CDCl3
MHz 300
Nucleus1H
1.0
1.0
2.0
3.0
2.0
2.0
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

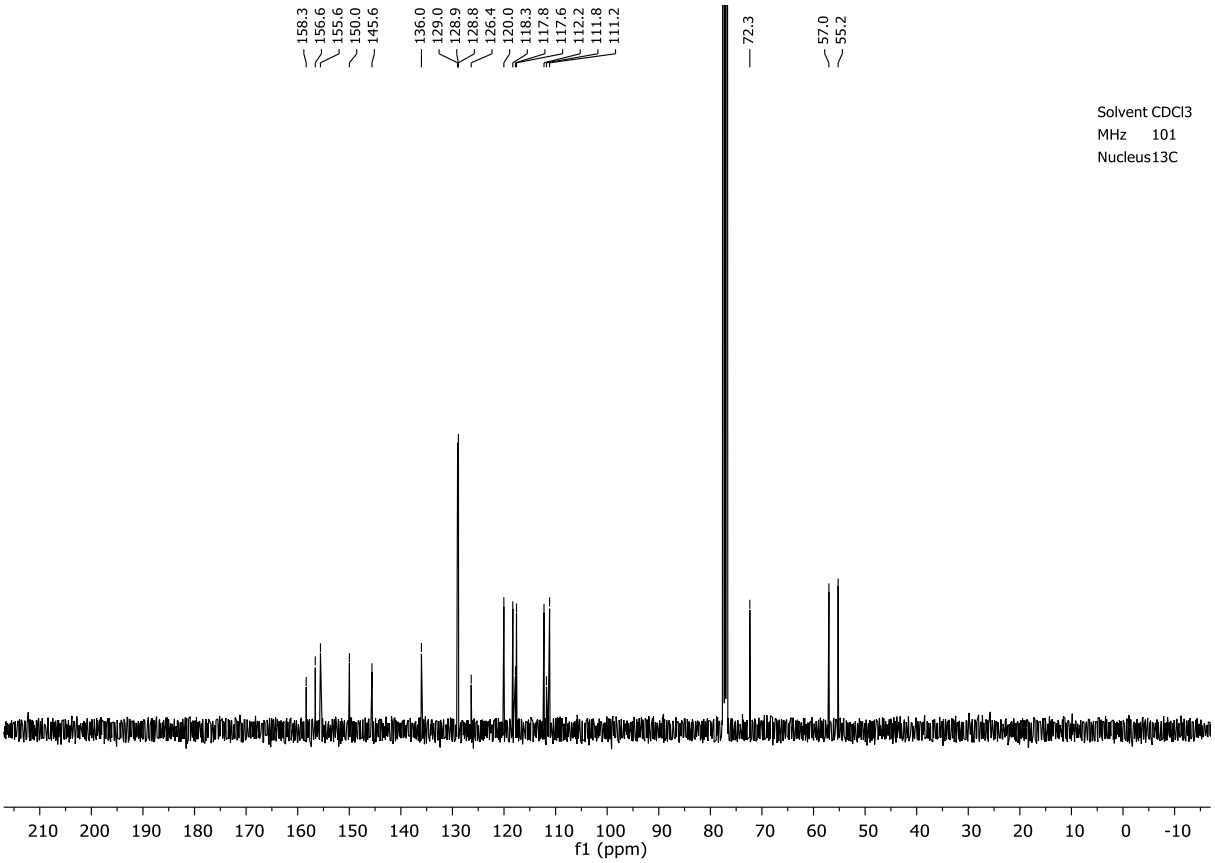

MeO
O
OMe
O
Br
OBn

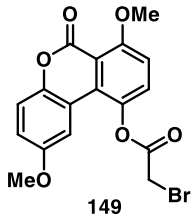
171

Solvent CDCl3
MHz 400
Nucleus1H
2.0
2.0
1.0
2.0
2.0
1.0
2.0
3.0
3.0
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)


164.9
157.7
151.5
149.5
144.4
136.6
128.8
128.2
127.3
127.1
122.5
116.1
114.7
111.2
111.2
72.1
56.9
55.8
Solvent CDCl3
MHz 101
Nucleus13C
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

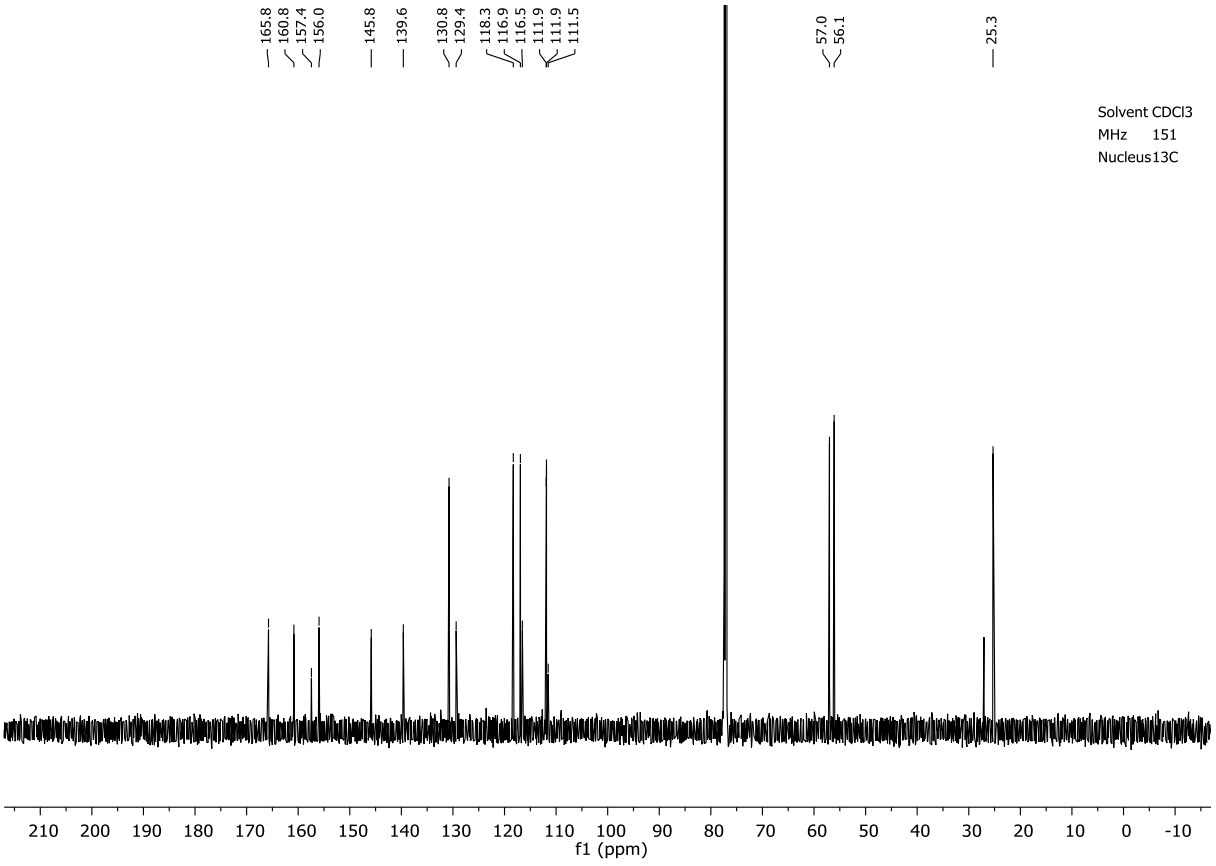

O
OMe
O
OBn
MeO
167
Solvent CDCl3
MHz 400
Nucleus1H
1.0
6.0
1.0
1.0
1.0
2.0
3.1
3.0
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

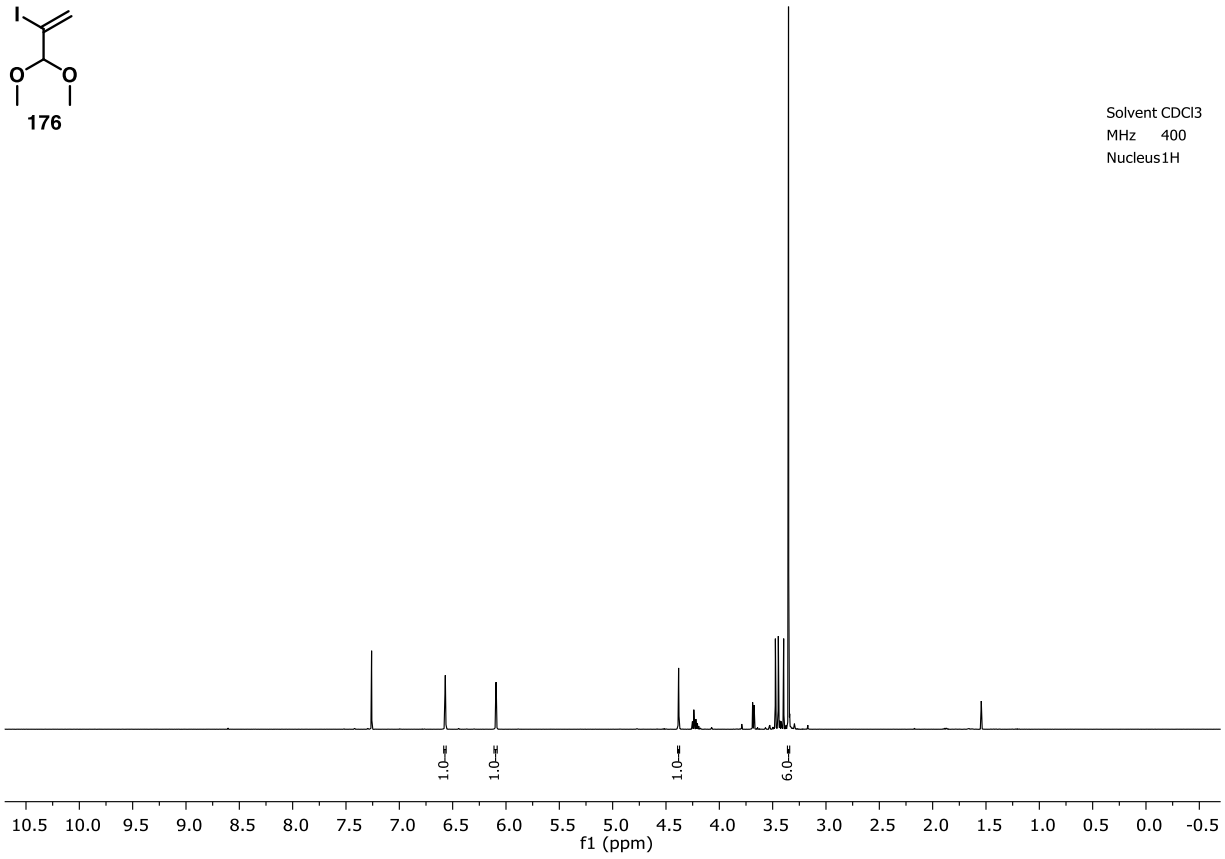

158.3
156.6
155.6
150.0
145.6
136.0
129.0
128.9
128.8
126.4
120.0
118.3
117.8
117.6
112.2
111.8
111.2
72.3
57.0
55.2
Solvent CDCl3
MHz 101
Nucleus13C
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

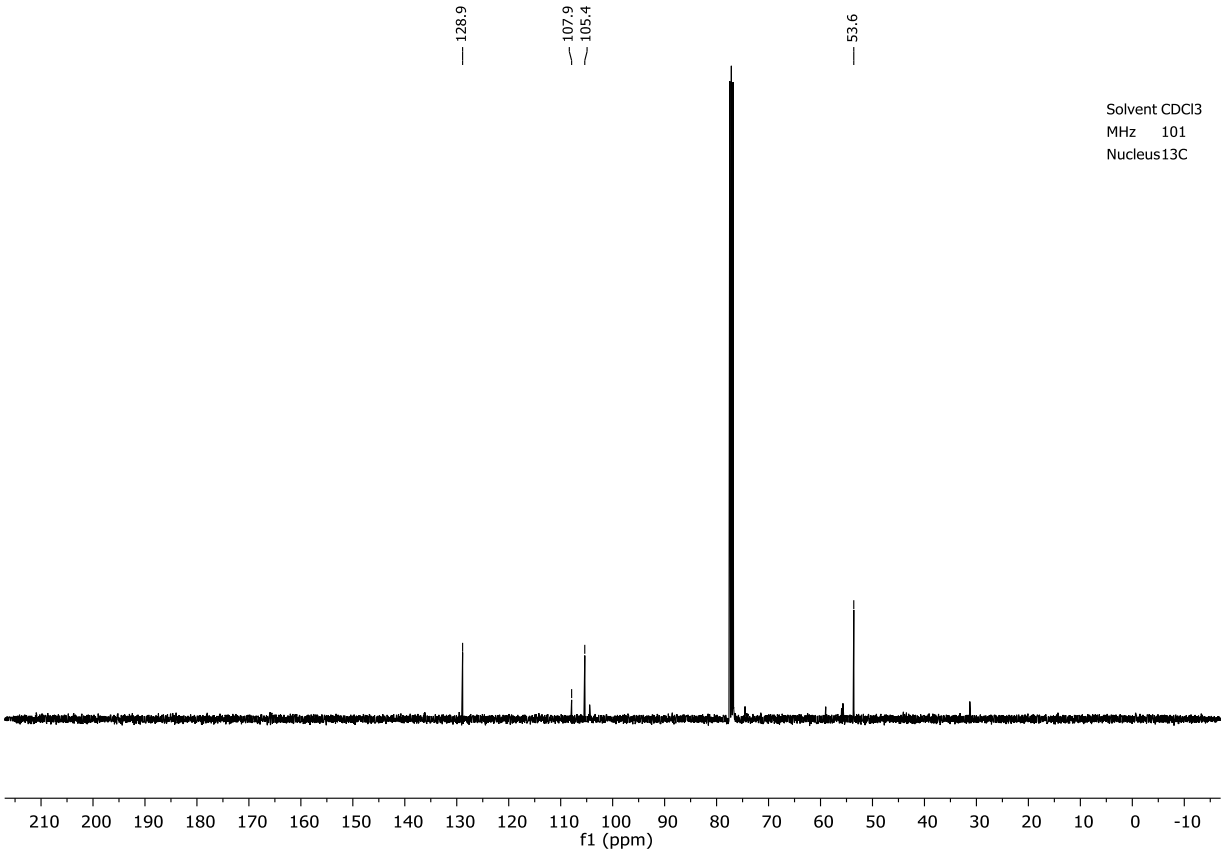

O
OMe
O
O
O
MeO
Br

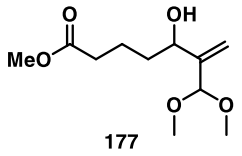
149

Solvent CDCl3
MHz 600
Nucleus1H
1.0
1.1
1.0
1.1
1.0
2.0
3.0
3.0
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)


165.8
160.8
157.4
156.0
145.8
139.6
130.8
129.4
118.3
116.9
116.5
111.9
111.9
111.5
57.0
56.1
25.3
Solvent CDCl3
MHz 151
Nucleus13C
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

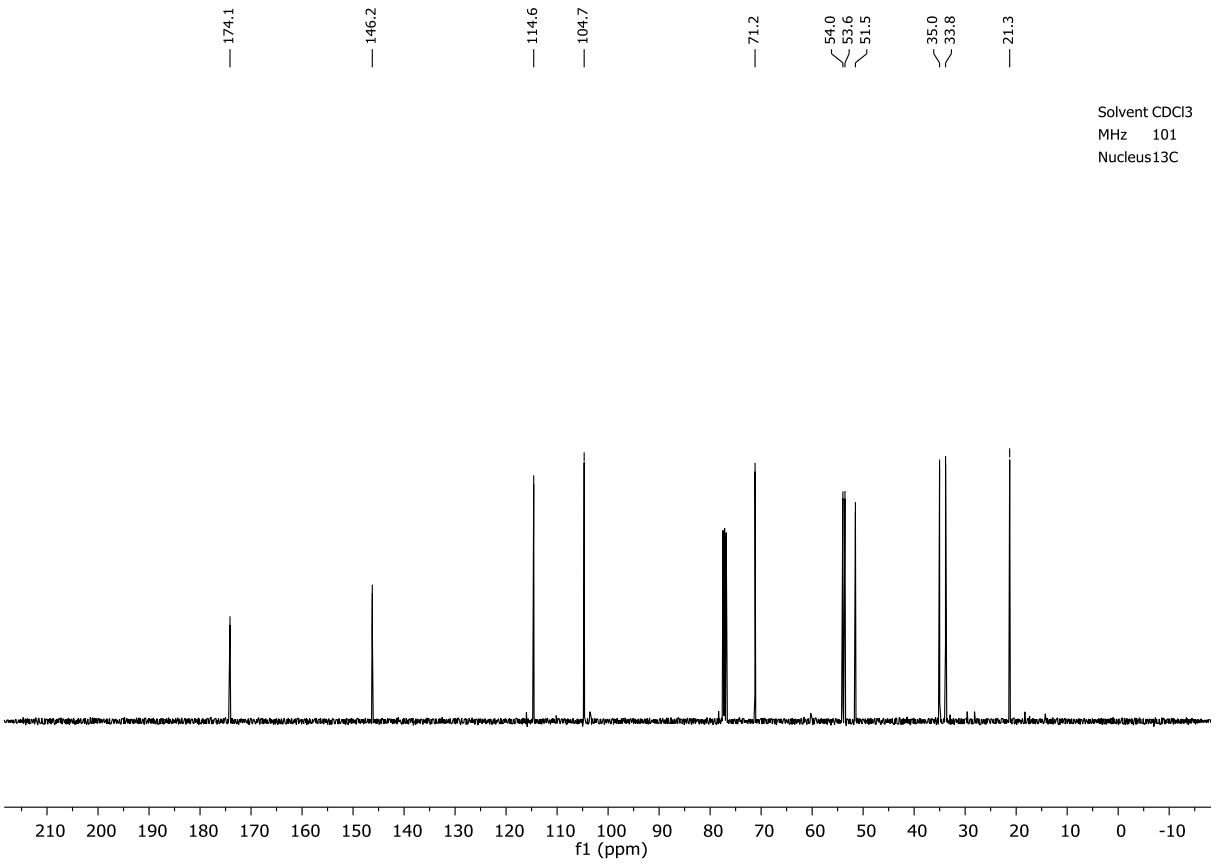

I
O
O
176
Solvent CDCl3
MHz 400
Nucleus1H
1.0
1.0
1.0
6.0
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

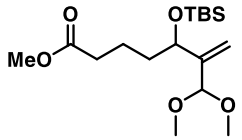

128.9
107.9
105.4
53.6
Solvent CDCl3
MHz 101
Nucleus13C
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


O
OH
MeO
O
O

177

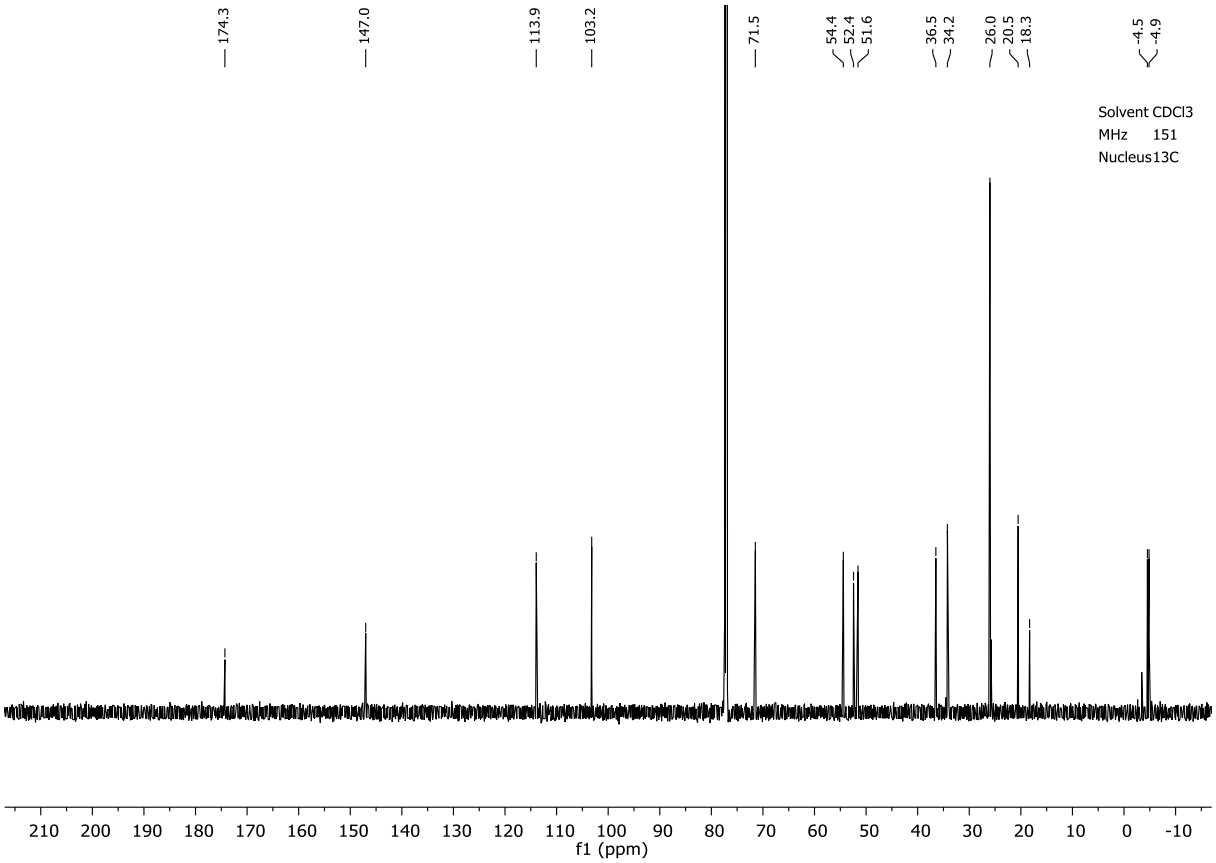
Solvent CDCl3
MHz 400
Nucleus1H
2.0
1.0
1.0
3.0
6.0
1.0
2.0
1.0
3.0
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

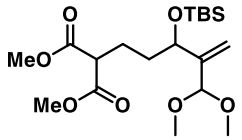

174.1
146.2
114.6
104.7
71.2
54.0
53.6
51.5
35.0
33.8
21.3
Solvent CDCl3
MHz 101
Nucleus13C
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


O
OTBS
MeO
O
O

173

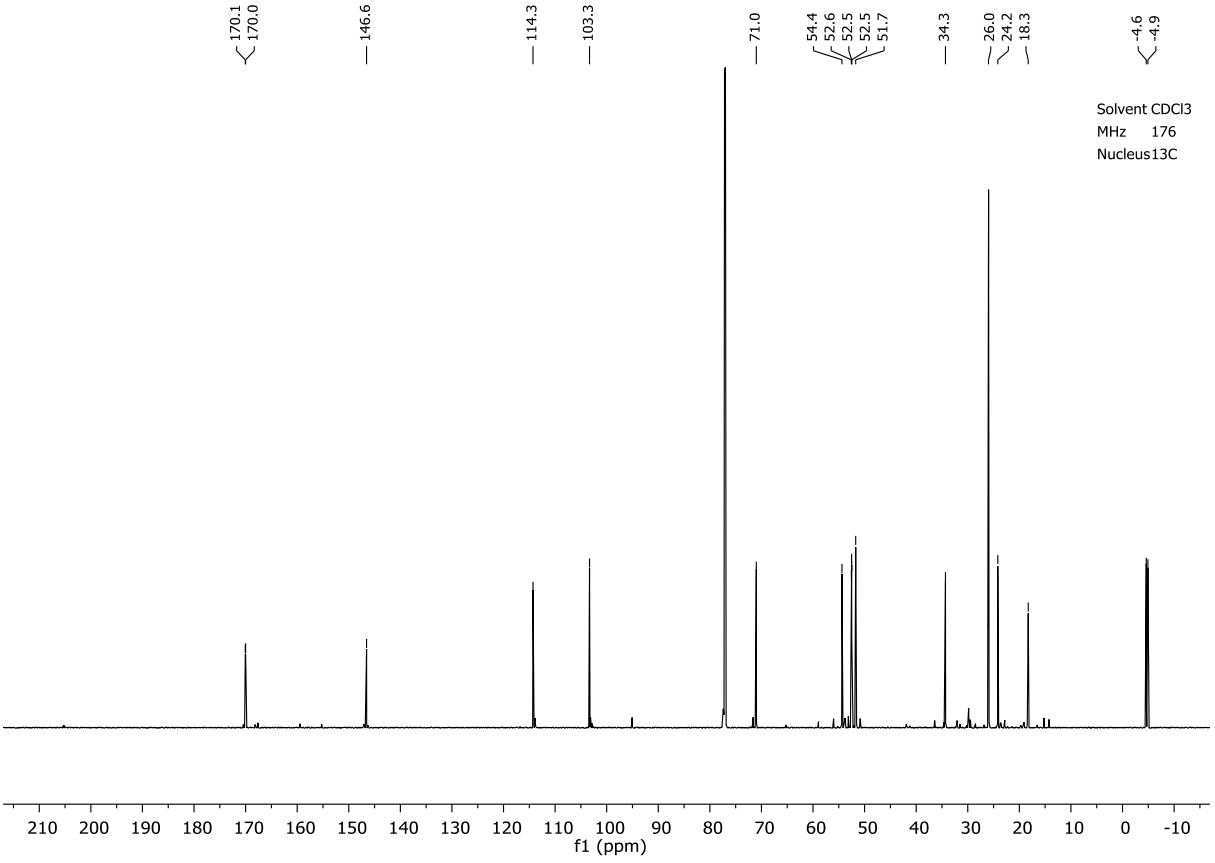
Solvent CDCl3
MHz 600
Nucleus1H
1.0
1.0
1.0
1.0
3.0
3.0
3.0
2.0
3.0
1.0
9.0
6.0
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

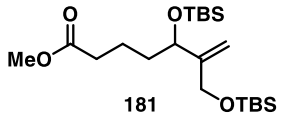

174.3
147.0
113.9
103.2
71.5
54.4
52.4
51.6
36.5
34.2
26.0
20.5
18.3
-4.5
-4.9
Solvent CDCl3
MHz 151
Nucleus13C
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


O
OTBS
MeO
MeO
O
O
O

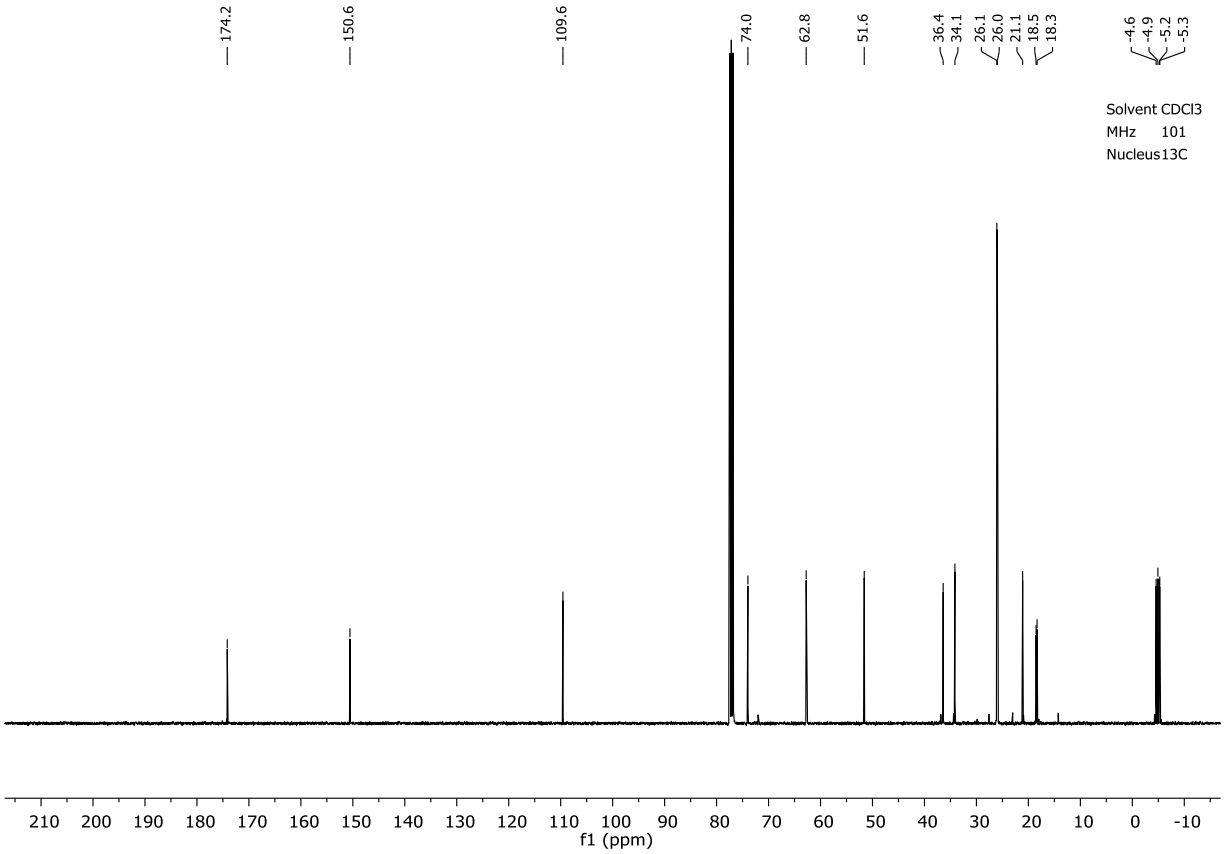
172

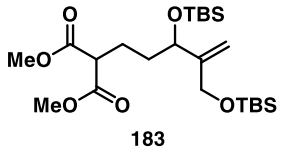
Solvent CDCl3
MHz 700
Nucleus1H
1.0
1.0
1.0
1.0
6.0
1.0
3.0
3.0
2.0
1.0
1.0
9.0
6.0
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)


170.1
170.0
146.6
114.3
103.3
71.0
54.4
52.6
52.5
52.5
51.7
34.3
26.0
24.2
18.3
-4.6
-4.9
Solvent CDCl3
MHz 176
Nucleus13C
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


O
OTBS
MeO
181
OTBS

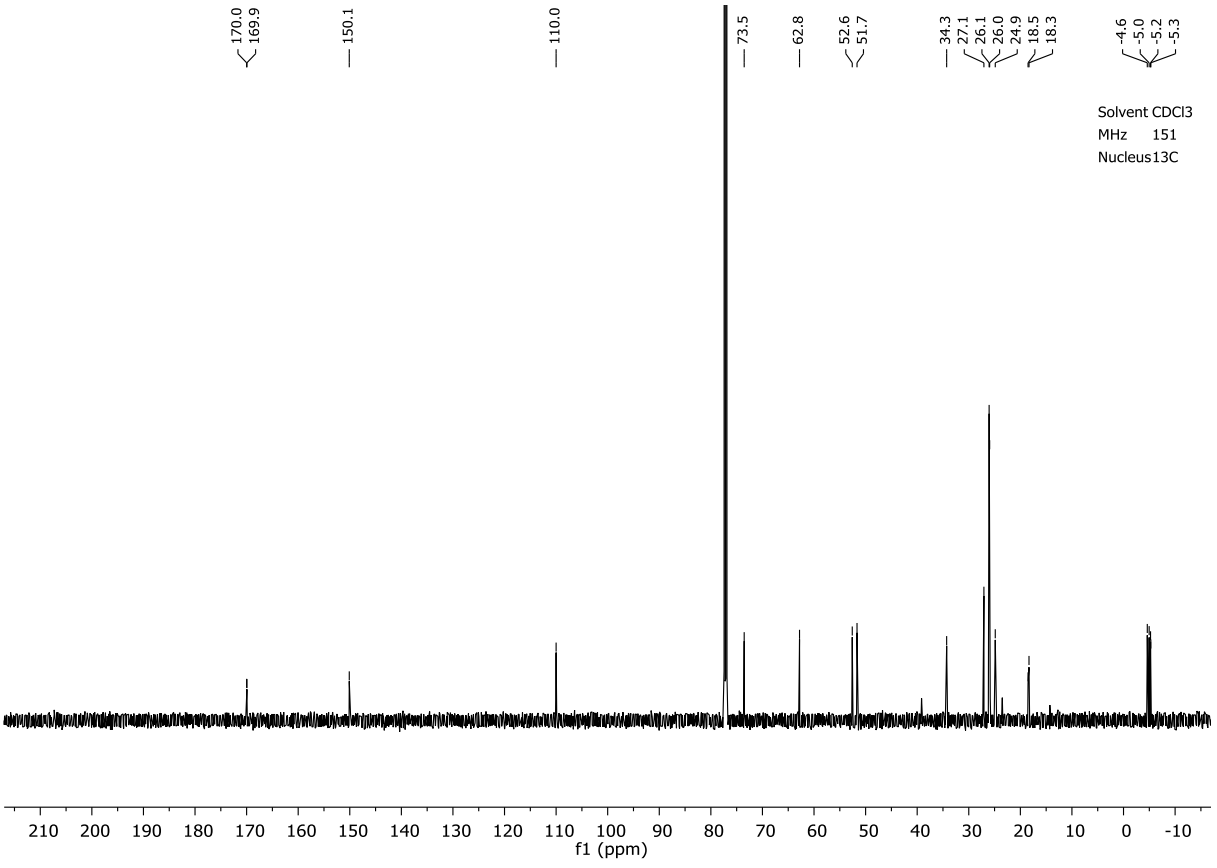
Solvent CDCl3
MHz 400
Nucleus1H
1.0
1.0
1.0
2.0
3.0
2.0
1.0
3.0
18.0
6.0
6.0
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

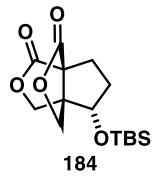

174.2
150.6
109.6
74.0
62.8
51.6
36.4
34.1
26.1
26.0
21.1
18.5
18.3
-4.6
-4.9
-5.2
-5.3
Solvent CDCl3
MHz 101
Nucleus13C
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


O
OTBS
MeO
MeO
O
OTBS

183

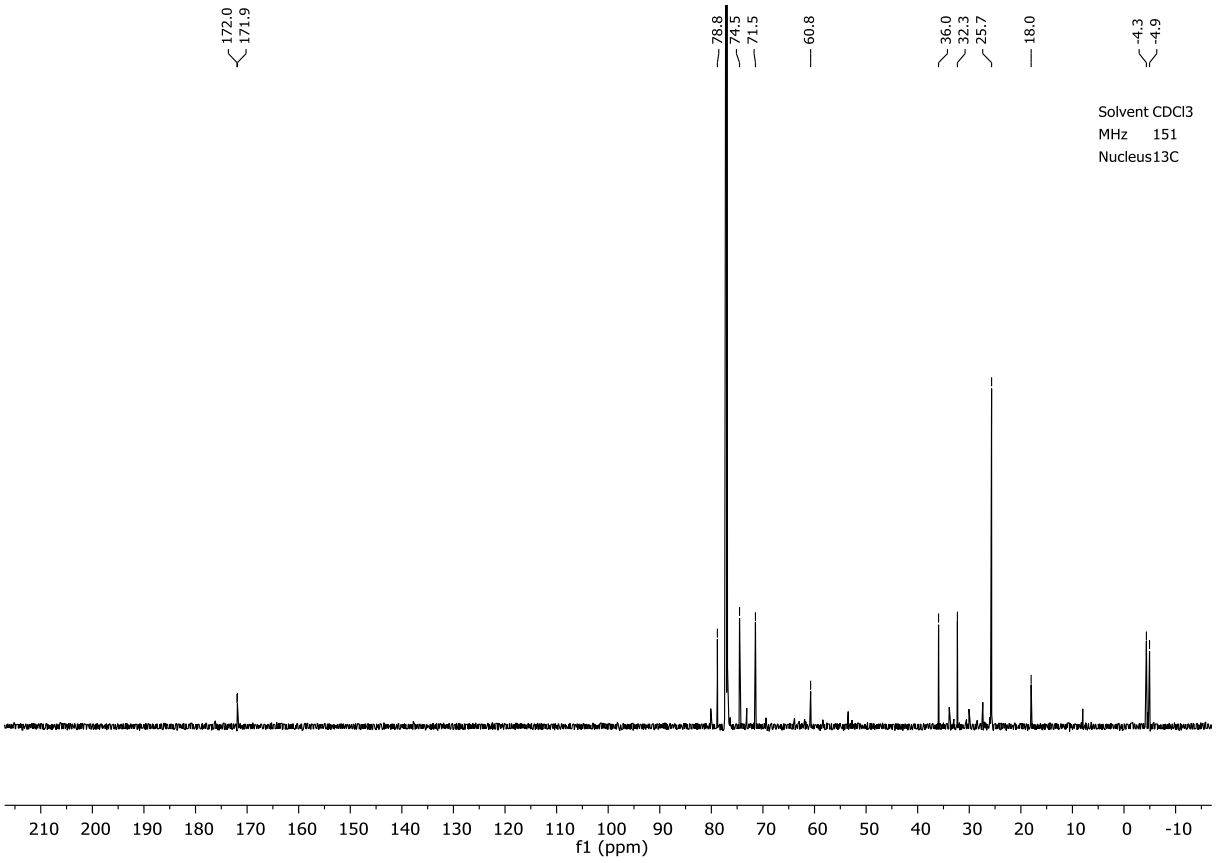
Solvent CDCl3
MHz 600
Nucleus1H
1.0
1.0
1.0
2.0
6.1
1.0
1.0
1.0
2.0
9.1
9.1
6.0
6.1
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

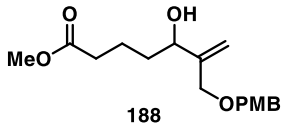

170.0
169.9
150.1
110.0
73.5
62.8
52.6
51.7
34.3
27.1
26.1
26.0
24.9
18.5
18.3
-4.6
-5.0
-5.2
-5.3
Solvent CDCl3
MHz 151
Nucleus13C
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


O
O
O
O
OTBS

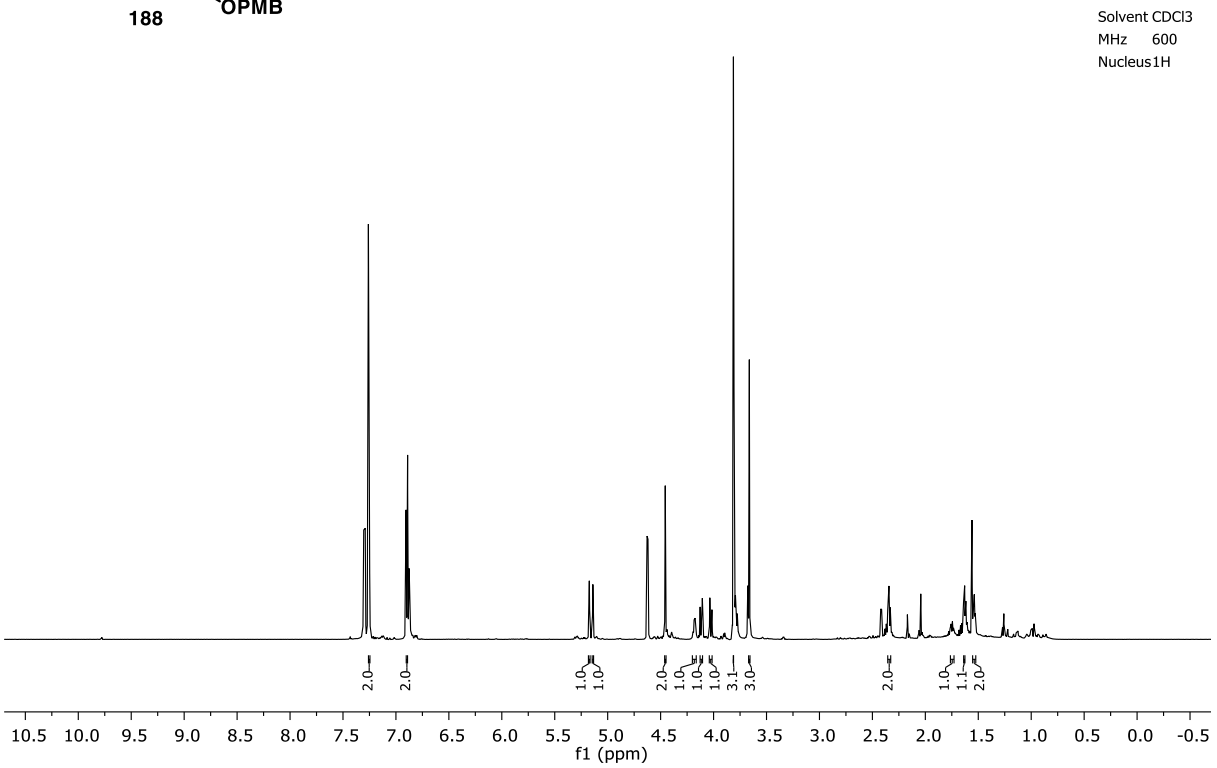
184

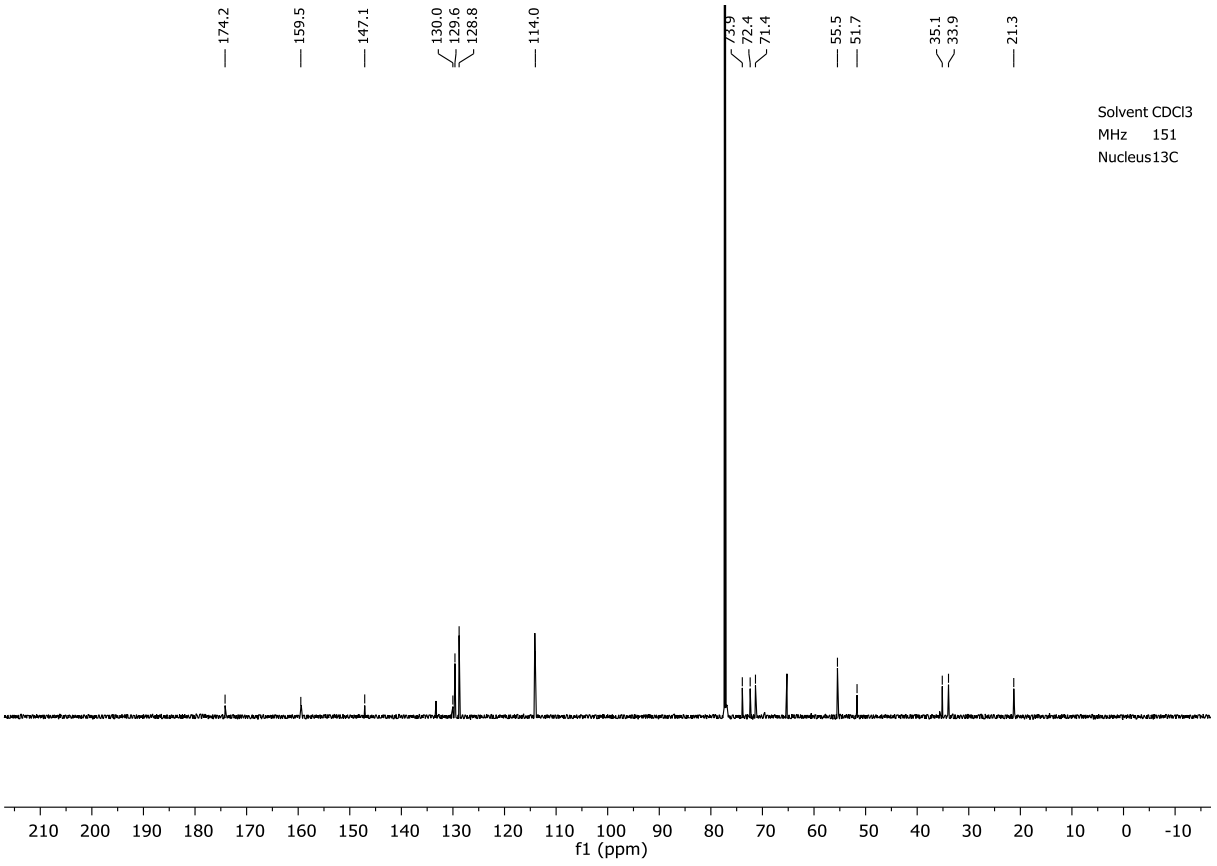
Solvent CDCl3
MHz 600
Nucleus1H
1.0
1.0
1.0
1.0
1.0
1.0
1.0
1.0
9.1
6.0
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

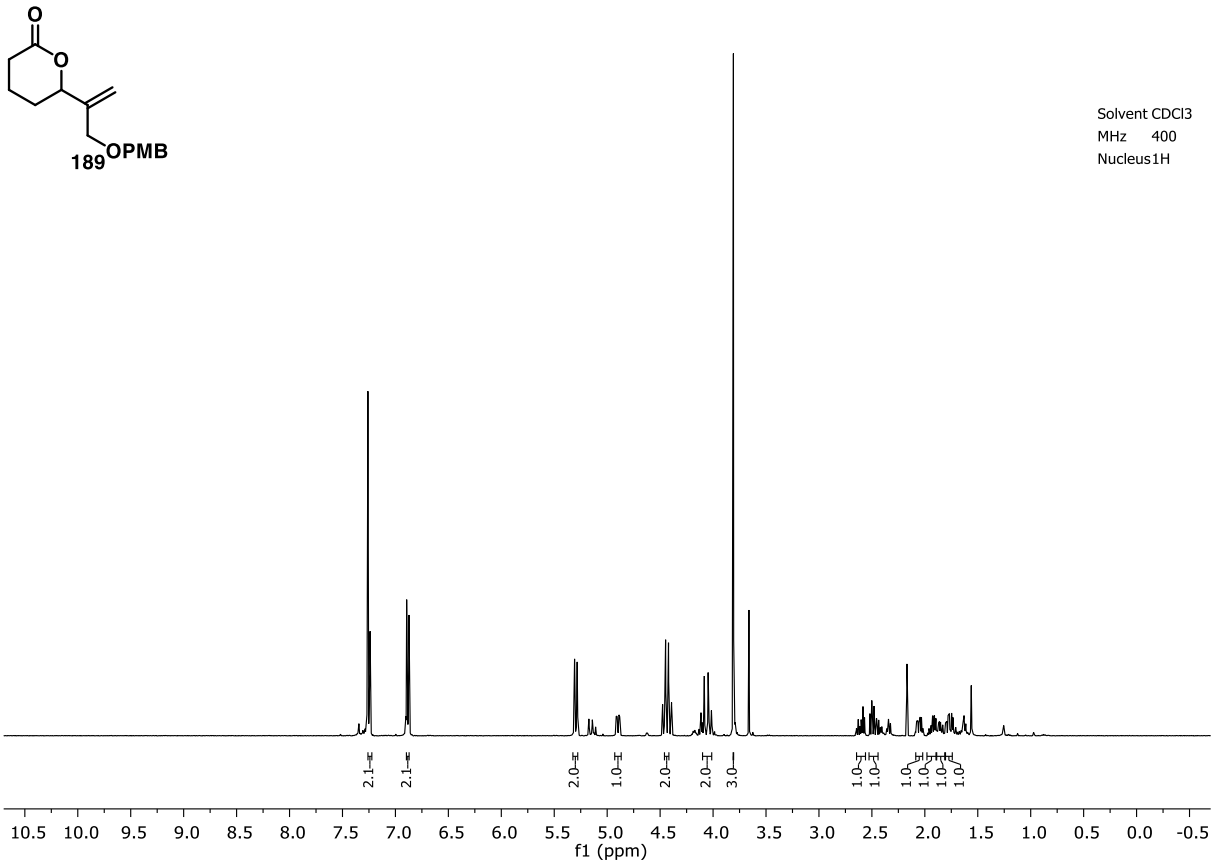

172.0
171.9
78.8
74.5
71.5
60.8
36.0
32.3
25.7
18.0
-4.3
-4.9
Solvent CDCl3
MHz 151
Nucleus13C
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

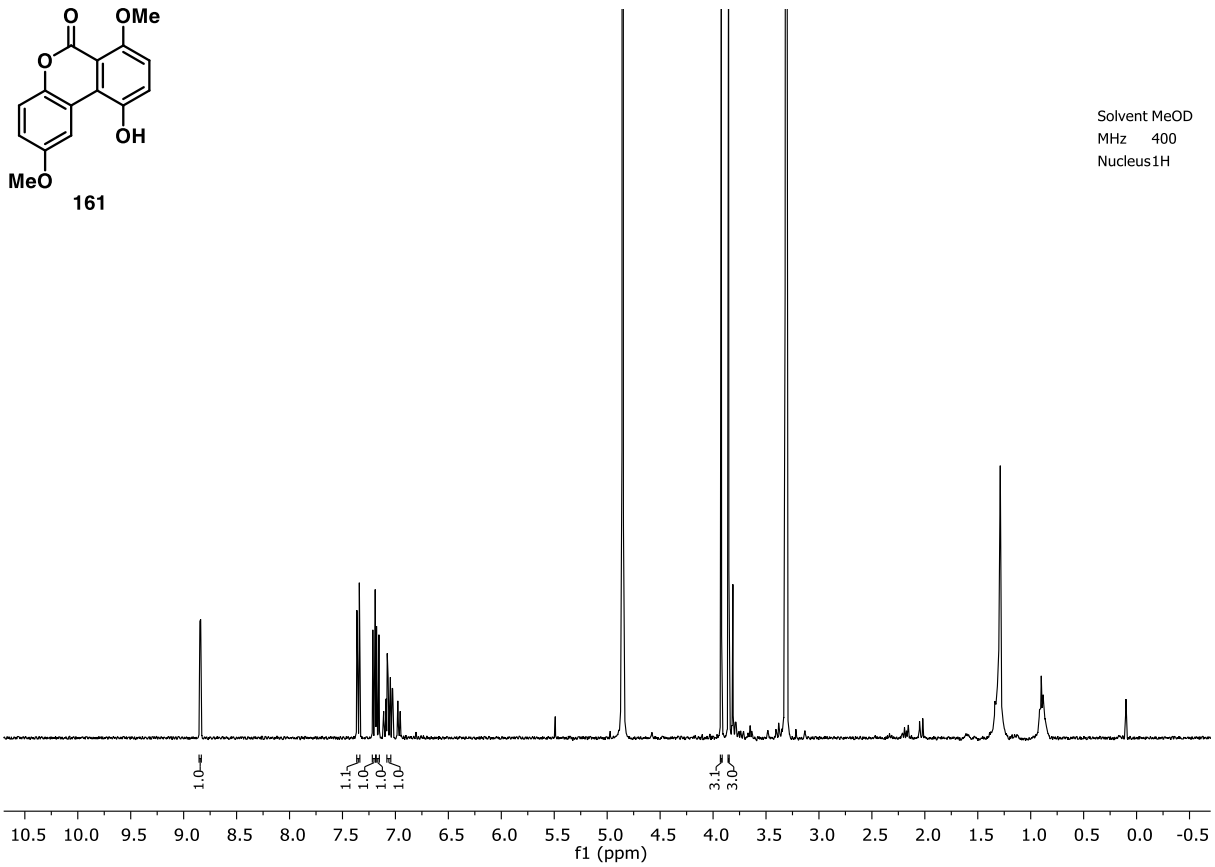

O
OH
MeO
OPMB

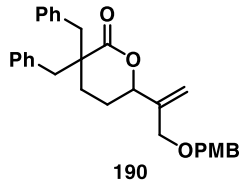
188


Solvent CDCl3
MHz 600
Nucleus1H
2.0
2.0
1.0
1.0
2.0
1.0
1.0
1.0
3.1
3.0
2.0
1.0
1.1
2.0
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)


174.2
159.5
147.1
130.0
129.6
128.8
114.0
73.9
72.4
71.4
55.5
51.7
35.1
33.9
21.3
Solvent CDCl3
MHz 151
Nucleus13C
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

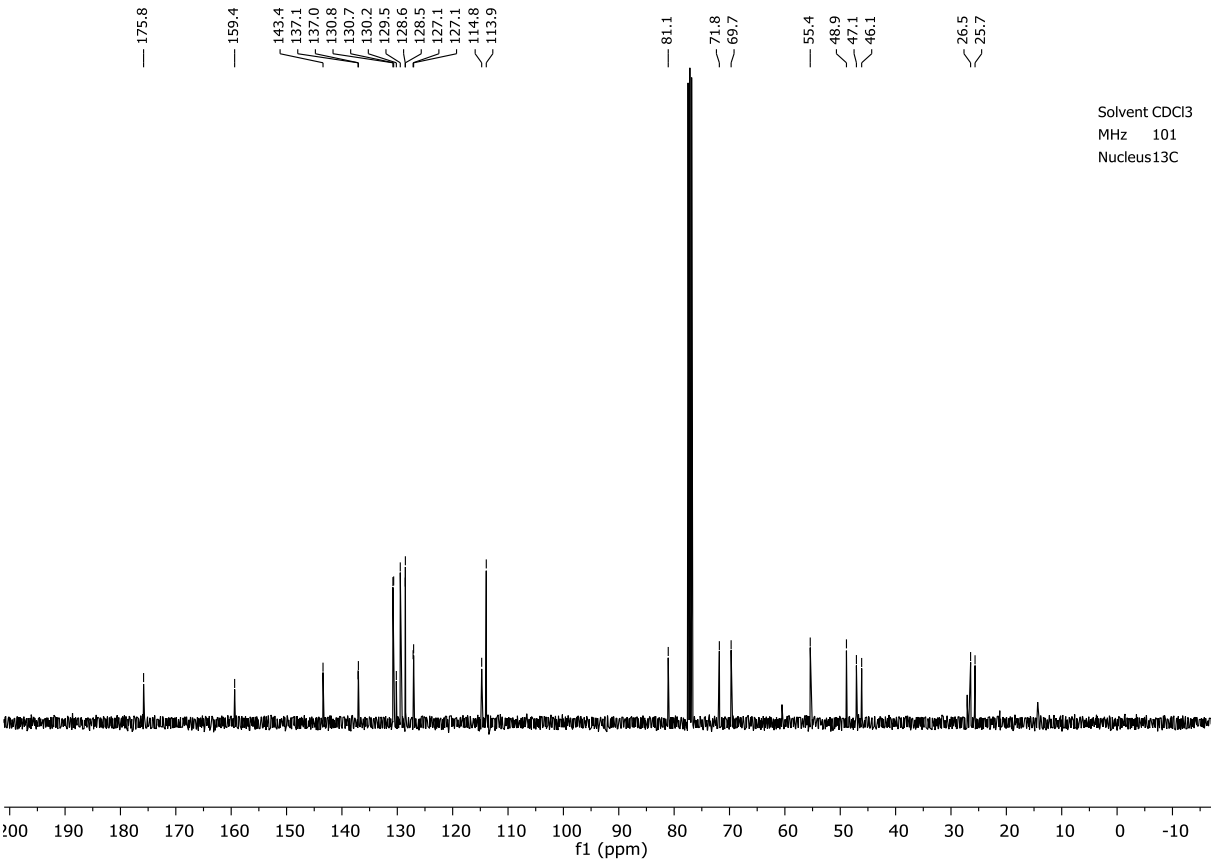

O
O
OPMB
189
Solvent CDCl3
MHz 400
Nucleus1H
2.1
2.1
2.0
1.0
2.0
2.0
3.0
1.0
1.0
1.0
1.0
1.0
1.0
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

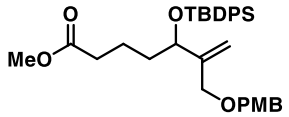

O
OMe
O
OH
MeO
161
Solvent MeOD
MHz 400
Nucleus1H
1.0
1.1
1.0
1.0
1.0
3.1
3.0
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)


Ph
O
Ph
O
OPMB

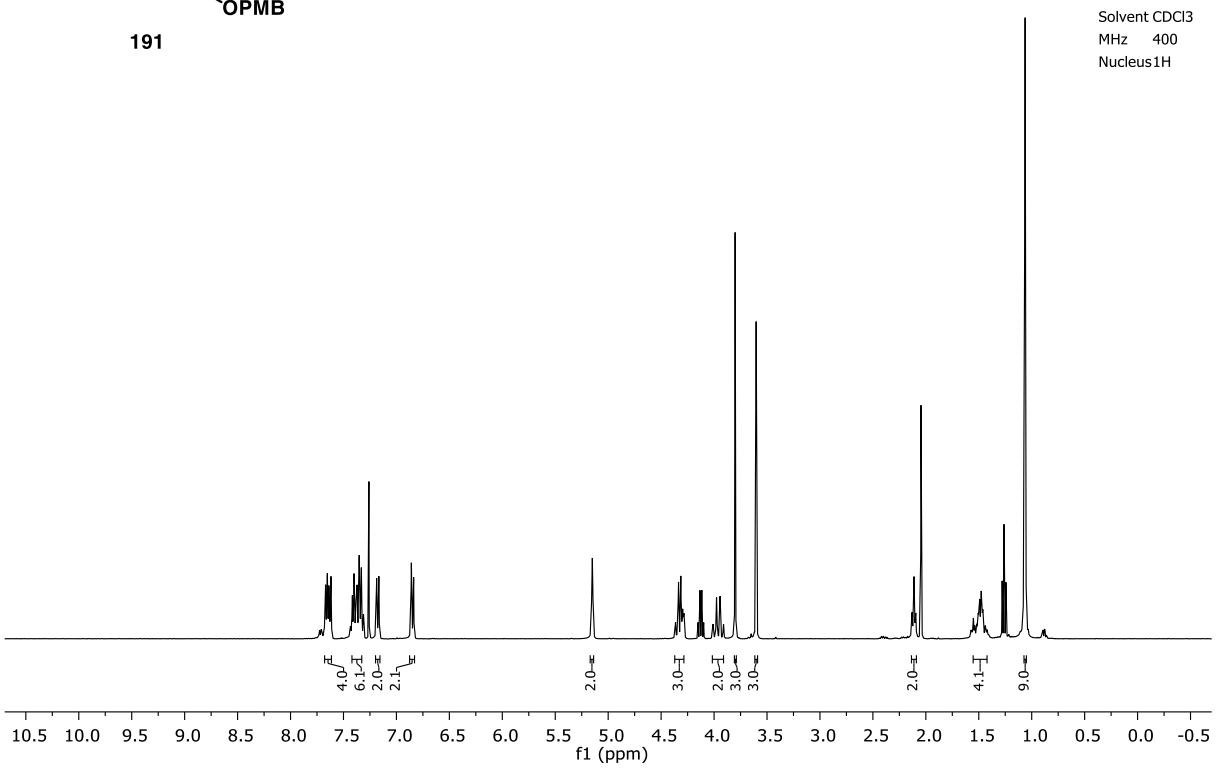
190

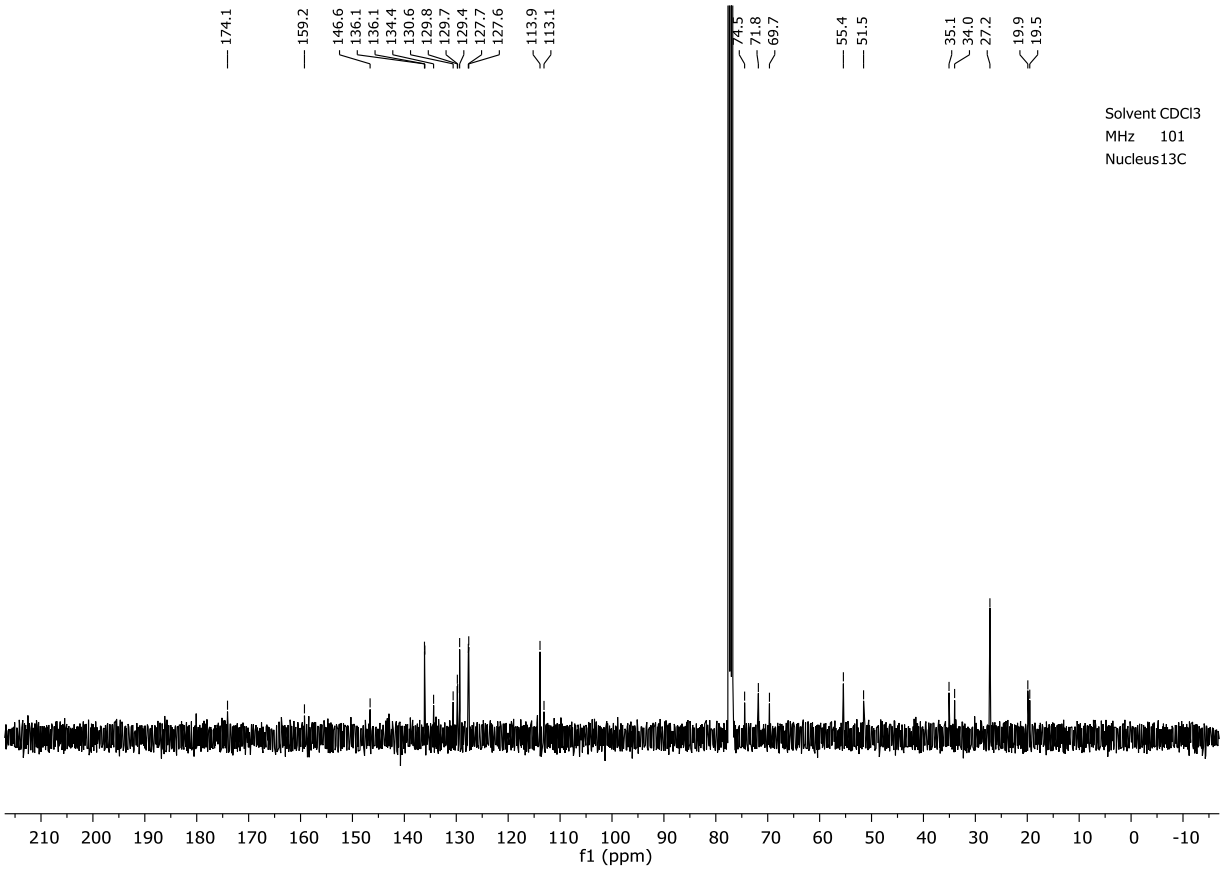
Solvent CDCl3
MHz 400
Nucleus1H
2.0 8.0 2.0 1.0 1.0 2.0 1.0 3.0 2.0 2.0 1.0 1.0 2.0 1.1 1.0
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

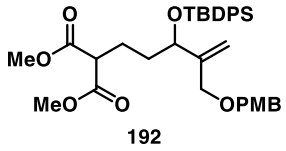

175.8
159.4
143.4
137.1
137.0
130.8
130.7
130.2
129.5
128.6
128.5
127.1
127.1
114.8
113.9
81.1
71.8
69.7
55.4
48.9
47.1
46.1
26.5
25.7
Solvent CDCl3
MHz 101
Nucleus13C
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


O
OTBDPS
MeO
OPMB

191

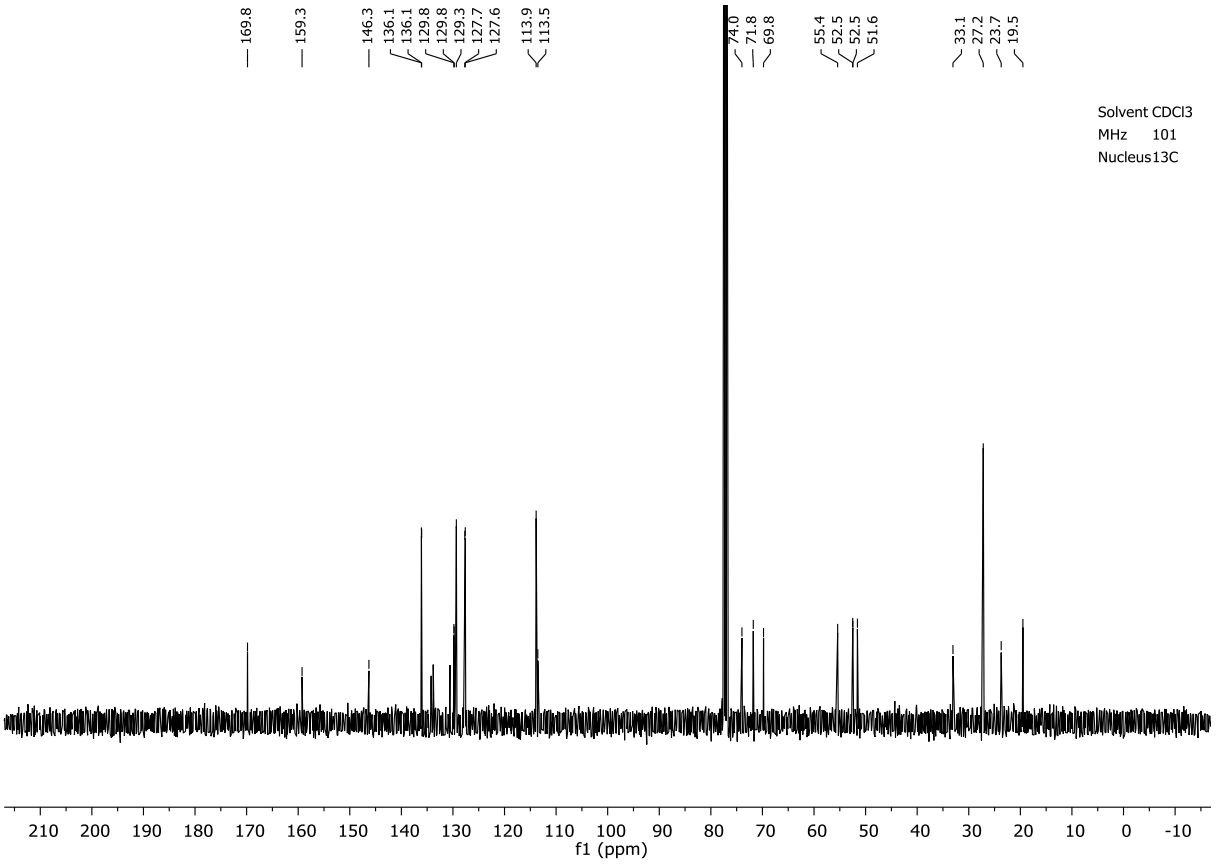

Solvent CDCl3
MHz 400
Nucleus1H
4.0
6.1
2.0
2.1
2.0
3.0
2.0
3.0
3.0
2.0
4.1
9.0
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

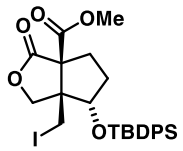

174.1
159.2
146.6
136.1
136.1
134.4
130.6
129.8
129.7
129.4
127.7
127.6
113.9
113.1
74.5
71.8
69.7
55.4
51.5
35.1
34.0
27.2
19.9
19.5
Solvent CDCl3
MHz 101
Nucleus13C
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


O
OTBDPS
MeO
MeO
O
OPMB

192

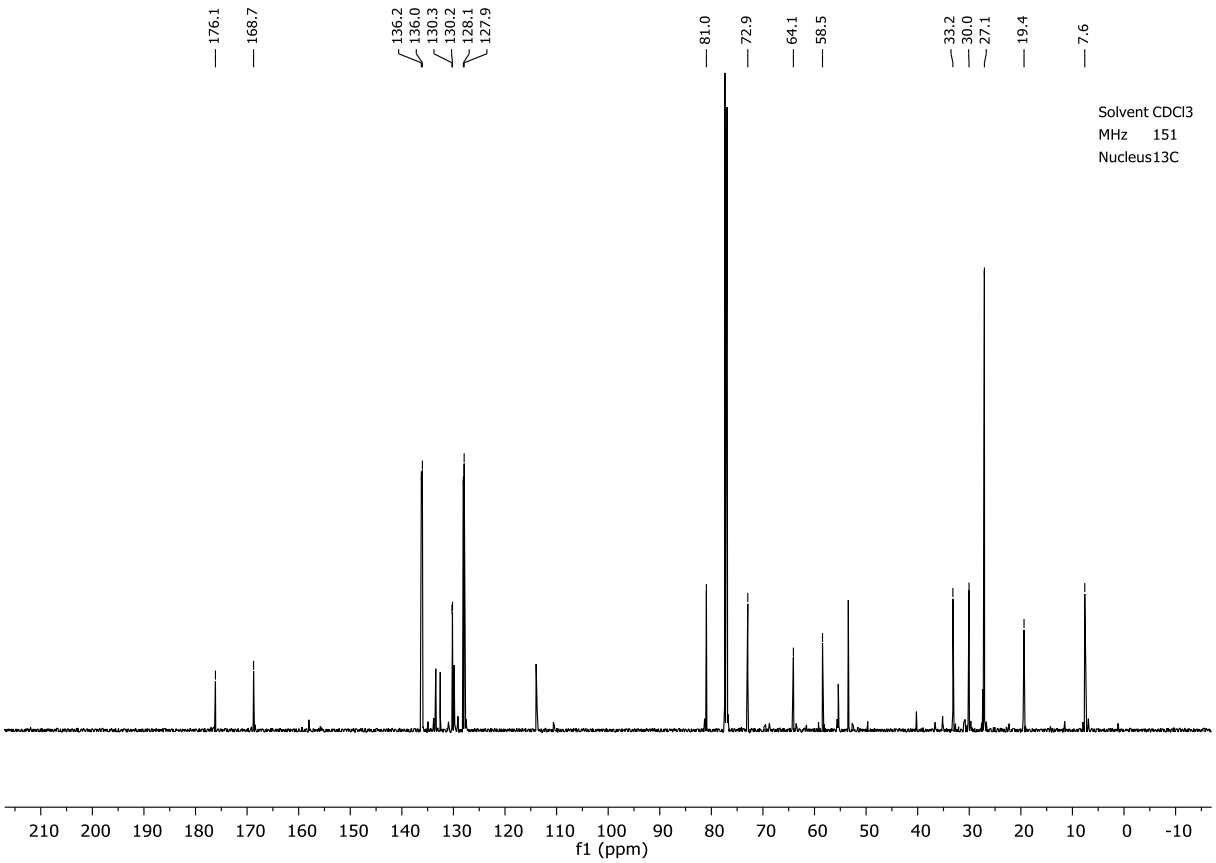
Solvent CDCl3
MHz 400
Nucleus1H
4.0
6.0
2.0
2.0
2.0
3.0
2.1
3.0
3.0
3.0
1.0
1.0
1.0
2.0
9.1
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

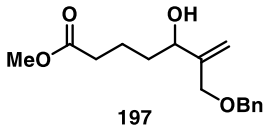

169.8
159.3
146.3
136.1
136.1
129.8
129.8
129.3
127.7
127.6
113.9
113.5
74.0
71.8
69.8
55.4
52.5
52.5
51.6
33.1
27.2
23.7
19.5
Solvent CDCl3
MHz 101
Nucleus13C
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


O
O
OMe
O
I
OTBDPS

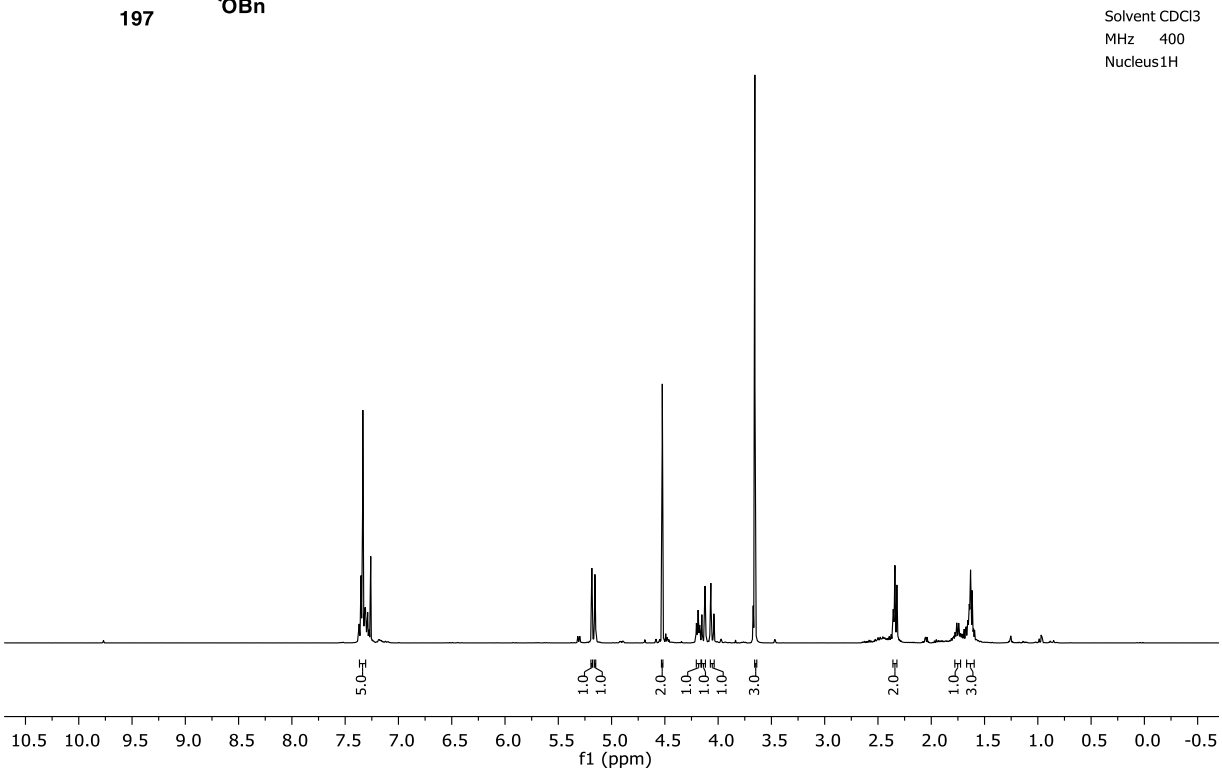
193

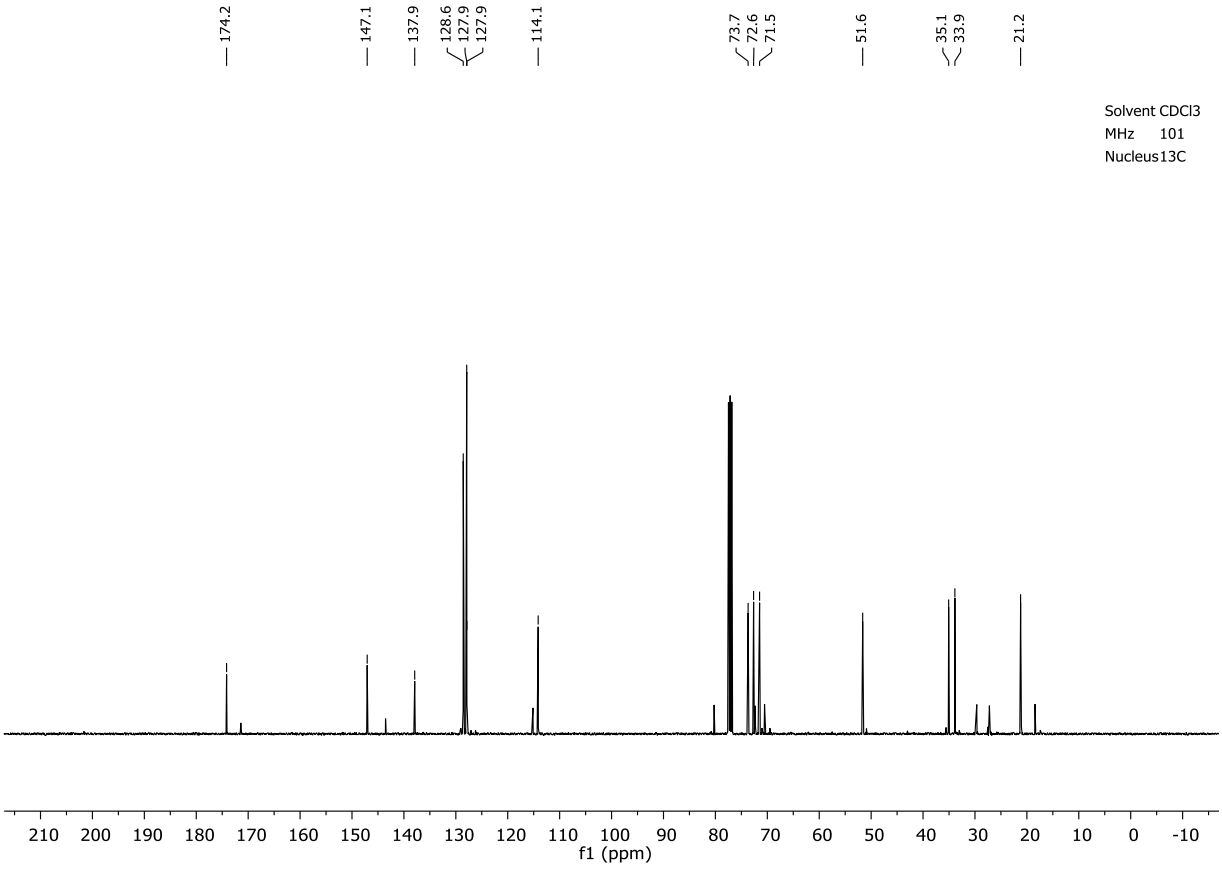
Solvent CDCl3
MHz 600
Nucleus1H
2.0
2.0
6.1
1.0
1.0
1.0
1.0
1.0
1.0
1.0
1.1
1.1
9.0
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

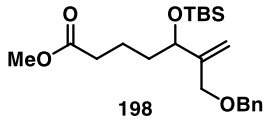

176.1
168.7
136.2
136.0
130.3
130.2
128.1
127.9
81.0
72.9
64.1
58.5
33.2
30.0
27.1
19.4
7.6
Solvent CDCl3
MHz 151
Nucleus13C
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


O
OH
MeO
OBn

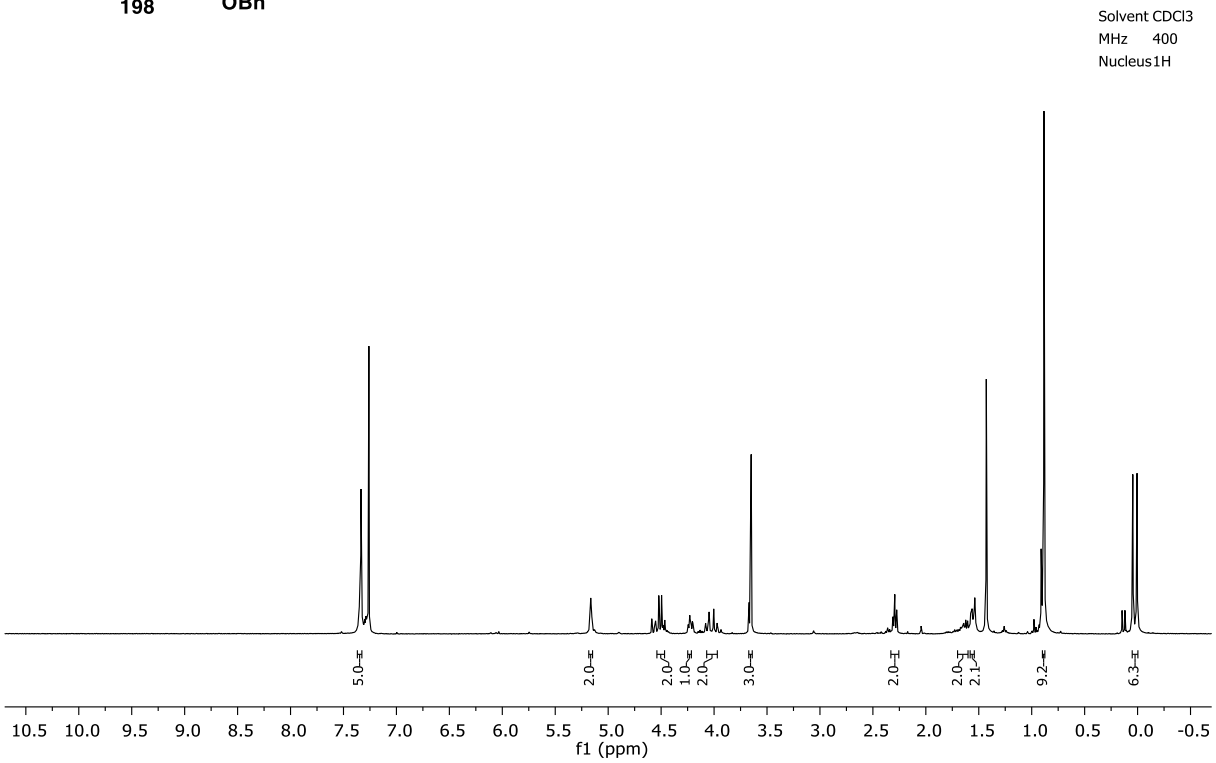
197

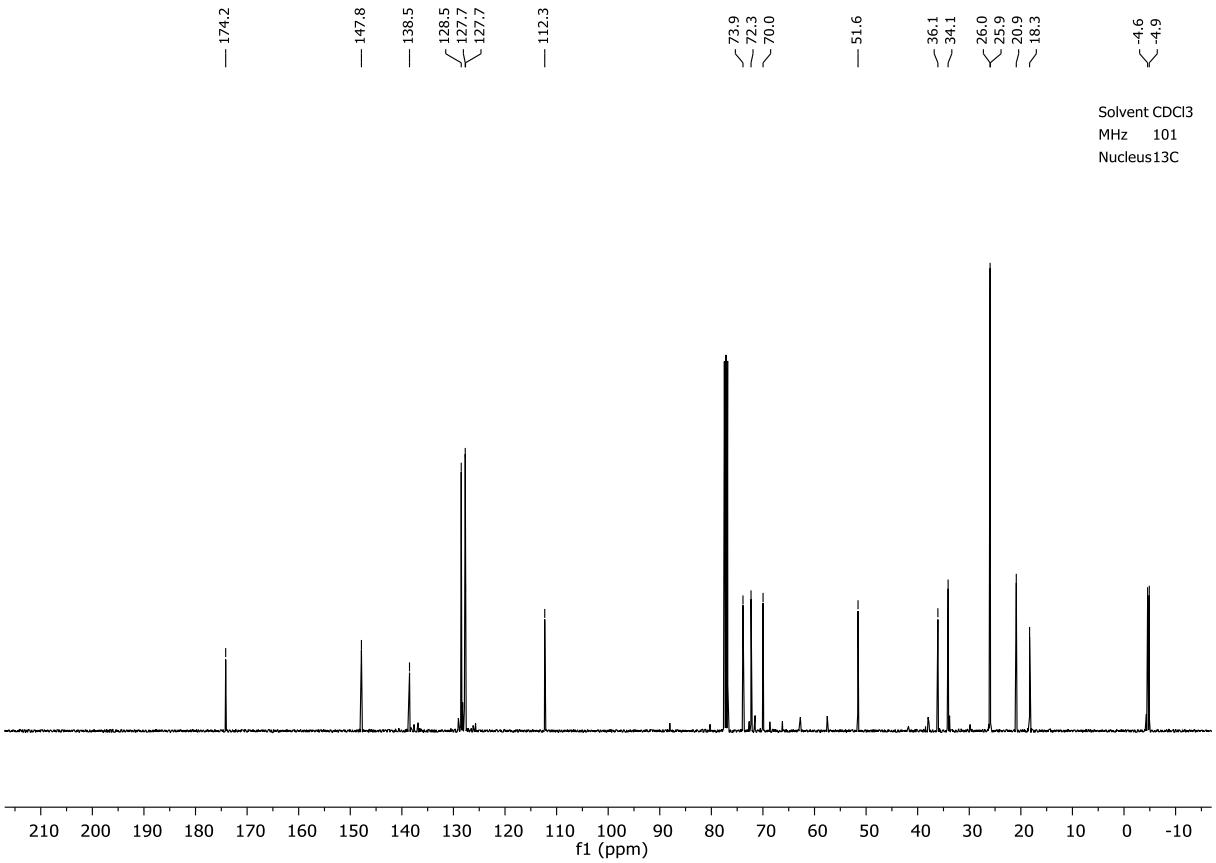

Solvent CDCl3
MHz 400
Nucleus1H
5.0
1.0
1.0
2.0
1.0
1.0
1.0
3.0
2.0
1.0
3.0
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

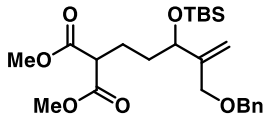

174.2
147.1
137.9
128.6
127.9
127.9
114.1
73.7
72.6
71.5
51.6
35.1
33.9
21.2
Solvent CDCl3
MHz 101
Nucleus13C
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


O
OTBS
MeO
OBn

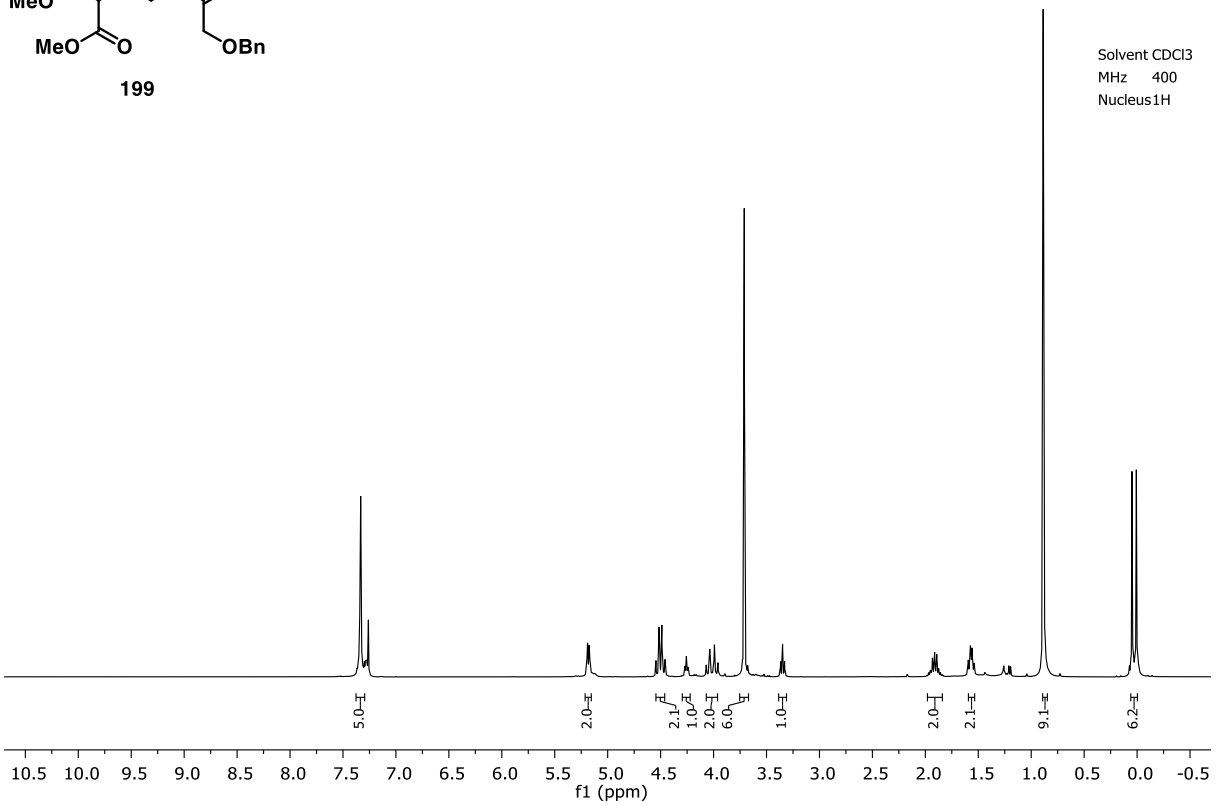
198

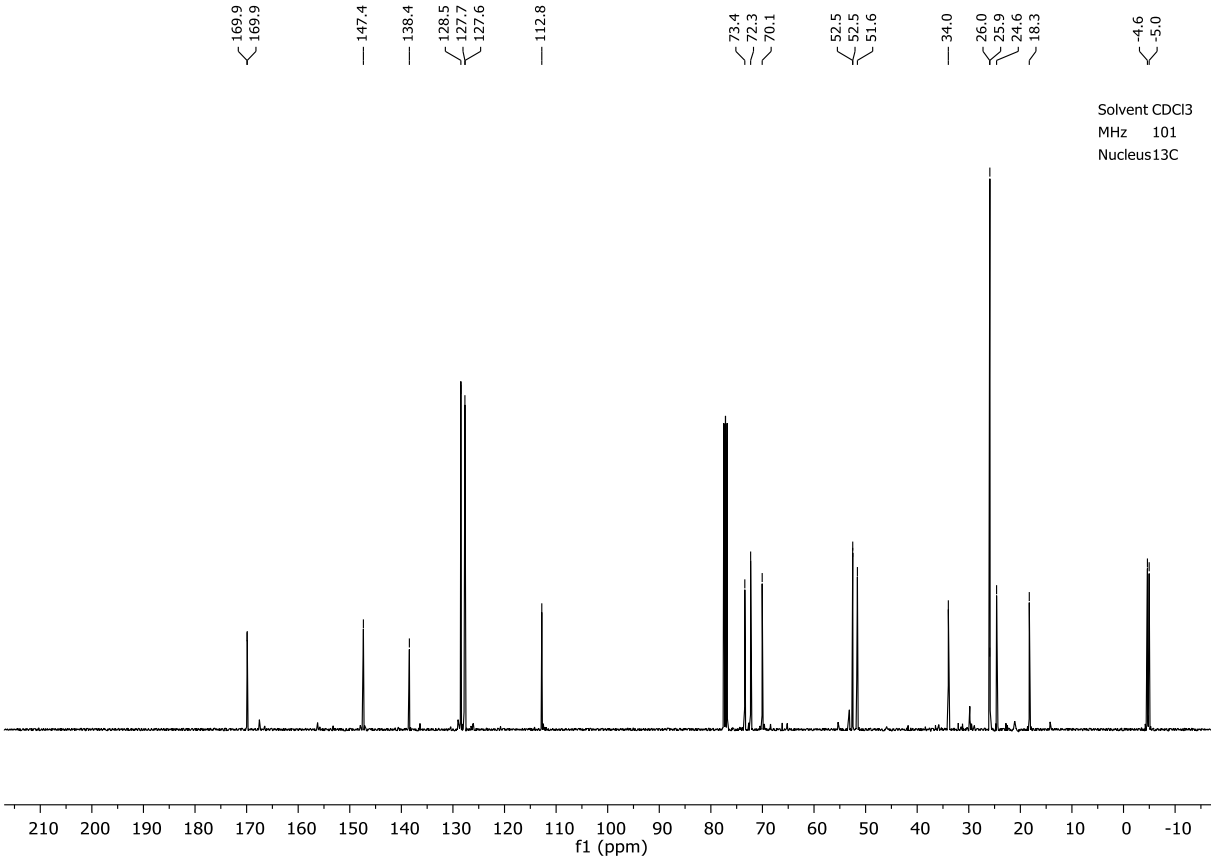

Solvent CDCl3
MHz 400
Nucleus1H
5.0
2.0
2.0
1.0
2.0
3.0
2.0
2.0
2.1
9.2
6.3
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

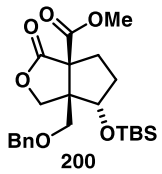

174.2
147.8
138.5
128.5
127.7
127.7
112.3
73.9
72.3
70.0
51.6
36.1
34.1
26.0
25.9
20.9
18.3
-4.6
-4.9
Solvent CDCl3
MHz 101
Nucleus13C
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


O
OTBS
MeO
MeO
O
OBn

199

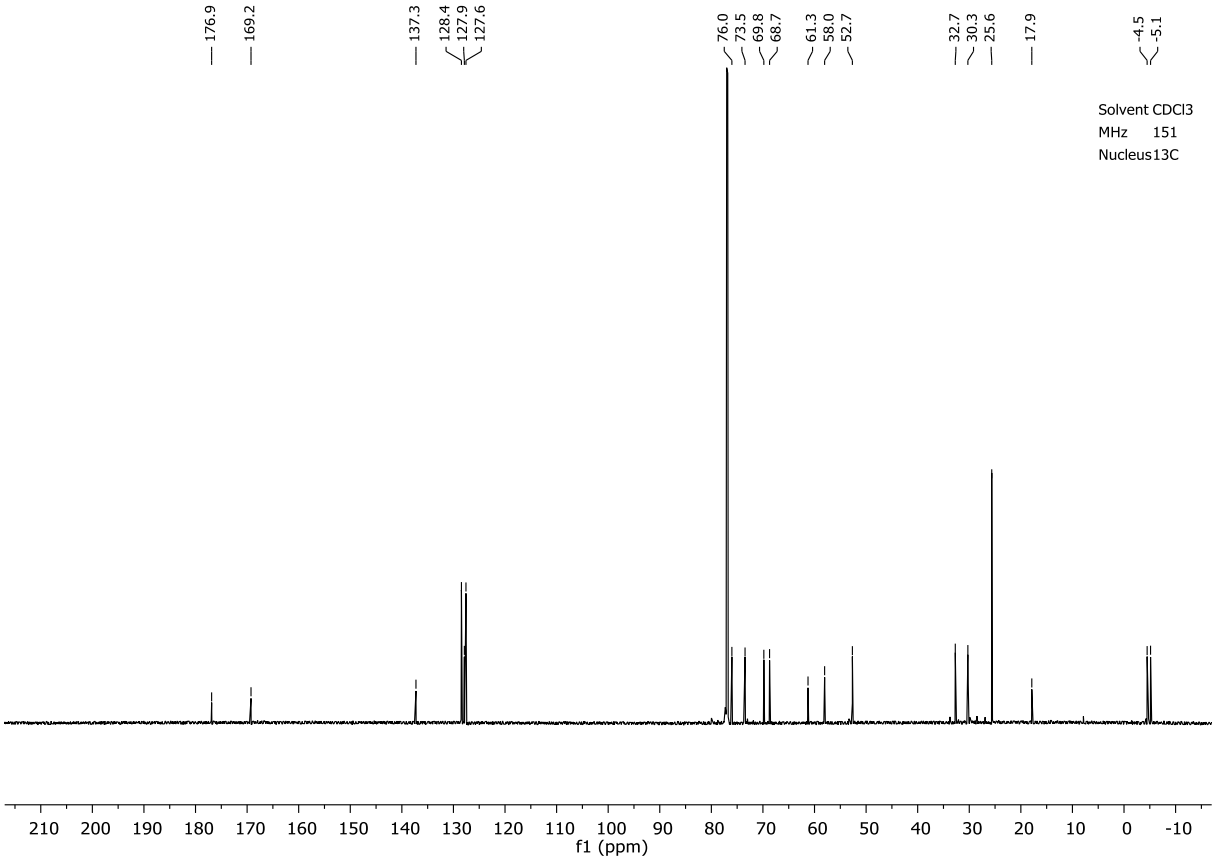

Solvent CDCl3
MHz 400
Nucleus1H
5.0
2.0
2.1
1.0
2.0
6.0
1.0
2.0
2.1
9.1
6.2
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

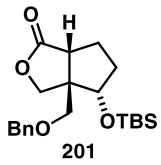

169.9
169.9
147.4
138.4
128.5
127.7
127.6
112.8
73.4
72.3
70.1
52.5
52.5
51.6
34.0
26.0
25.9
24.6
18.3
-4.6
-5.0
Solvent CDCl3
MHz 101
Nucleus13C
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


O
OMe
O
O
BnO
OTBS

200

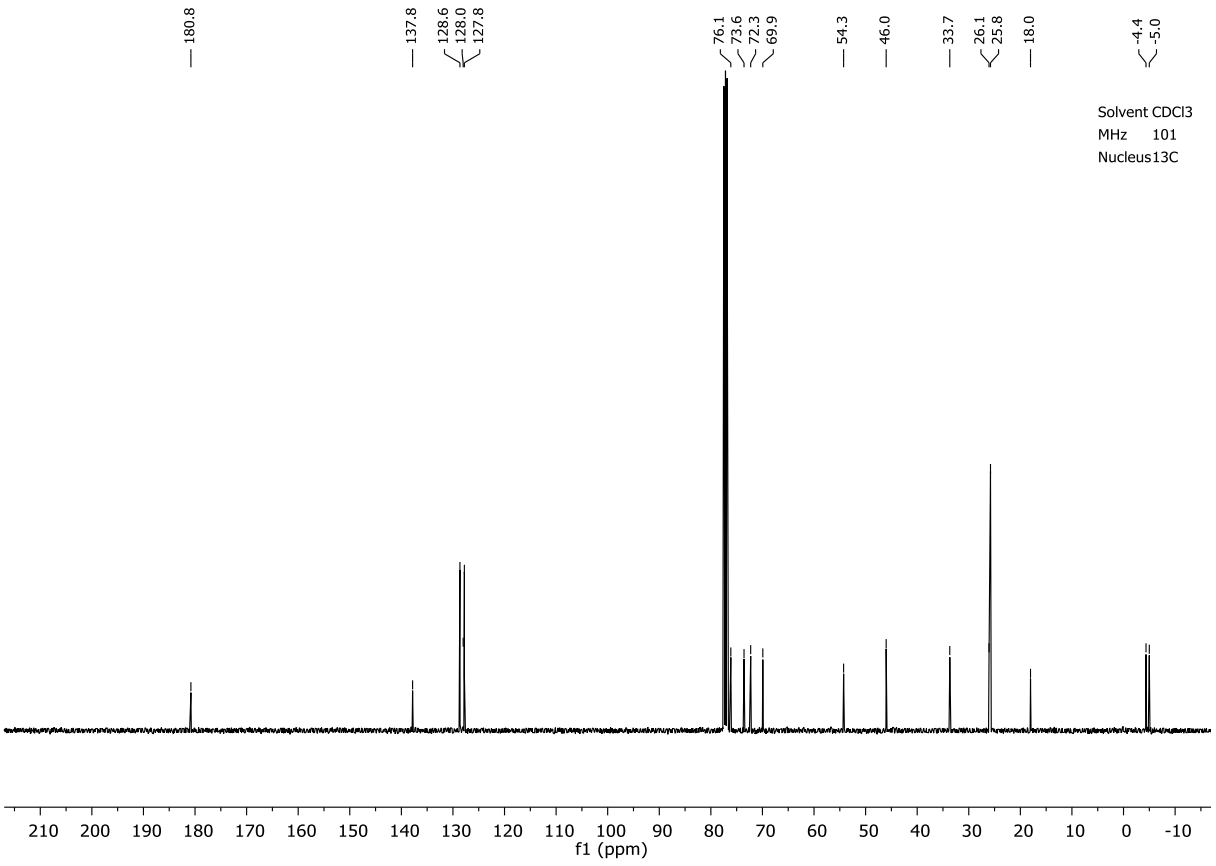
Solvent CDCl3
MHz 600
Nucleus1H
2.0
1.0
2.1
1.0
2.0
1.0
1.0
3.0
1.0
1.0
1.0
1.0
1.0
1.1
9.1
6.0
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

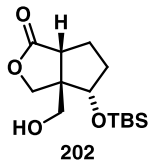

176.9
169.2
137.3
128.4
127.9
127.6
76.0
73.5
69.8
68.7
61.3
58.0
52.7
32.7
30.3
25.6
17.9
-4.5
-5.1
Solvent CDCl3
MHz 151
Nucleus13C
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


O
H
O
BnO
OTBS

201

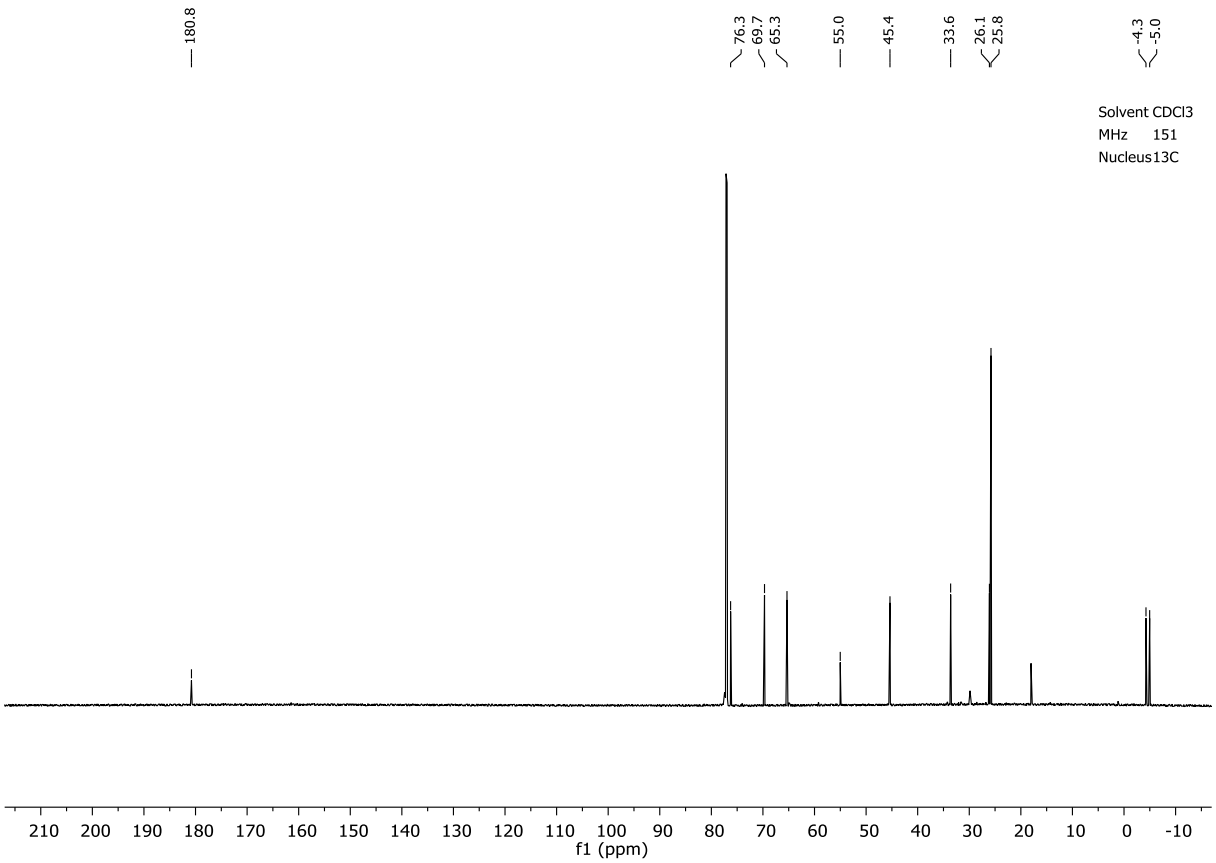
Solvent CDCl3
MHz 400
Nucleus1H
5.0
1.0
2.0
1.0
1.0
2.0
1.0
1.0
2.0
1.0
9.0
6.1
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

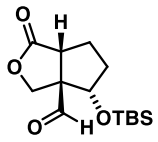

180.8
137.8
128.6
128.0
127.8
76.1
73.6
72.3
69.9
54.3
46.0
33.7
26.1
25.8
18.0
-4.4
-5.0
Solvent CDCl3
MHz 101
Nucleus13C
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


O
H
O
HO
OTBS

202

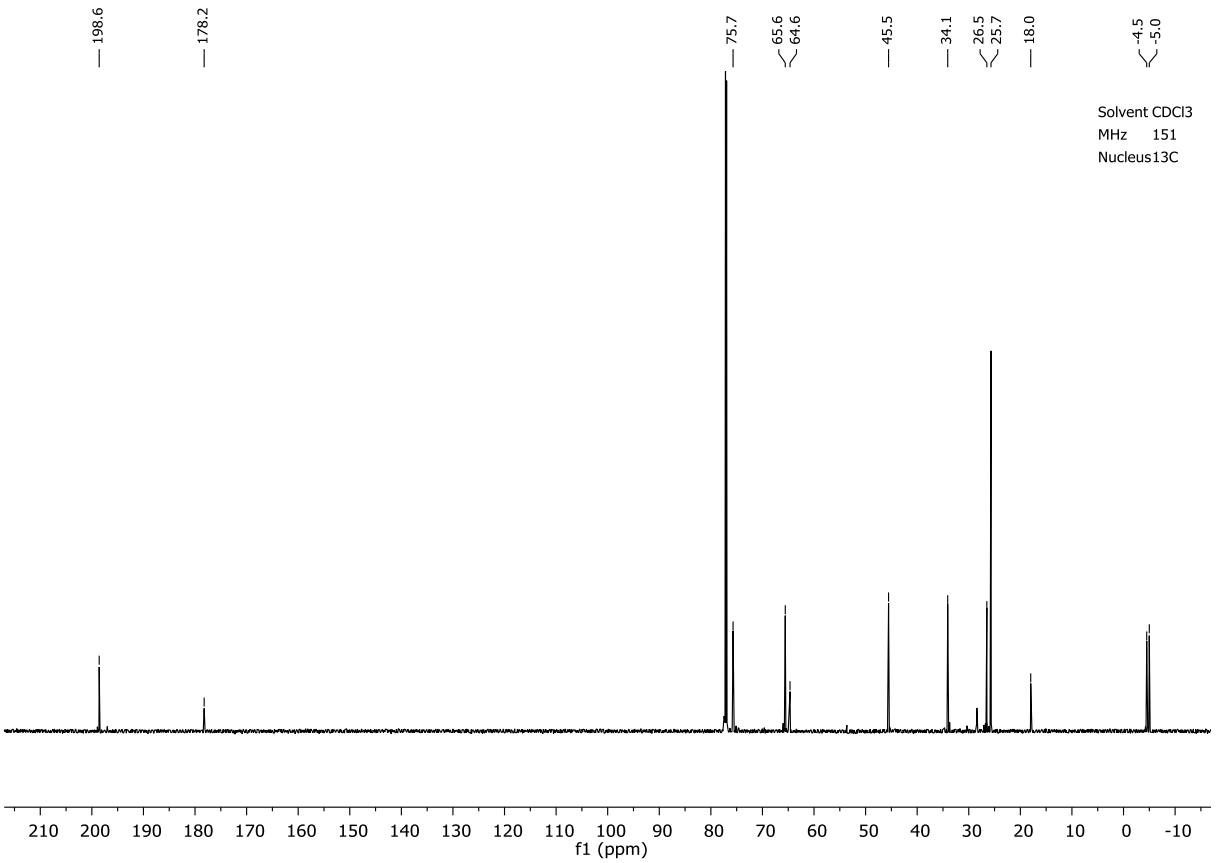
Solvent CDCl3
MHz 600
Nucleus1H
1.0
1.0
1.0
2.0
1.0
1.0
2.0
1.0
1.0
9.0
6.0
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

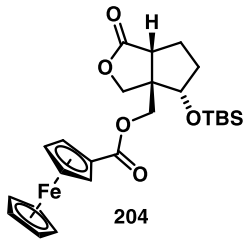

180.8
76.3
69.7
65.3
55.0
45.4
33.6
26.1
25.8
-4.3
-5.0
Solvent CDCl3
MHz 151
Nucleus13C
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


O
H
O
OTBS
H
O

203

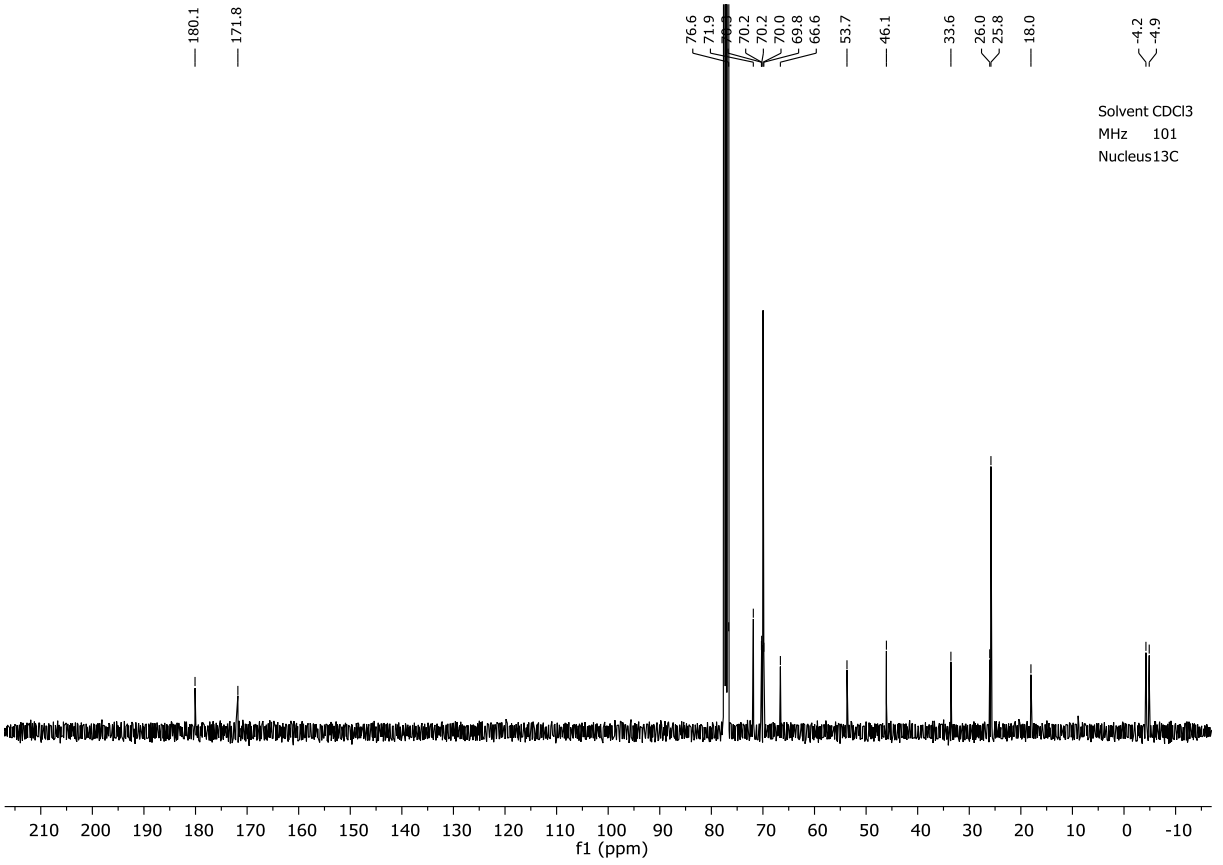
Solvent CDCl3
MHz 600
Nucleus1H
1.0
1.0
2.0
1.0
1.0
2.0
1.0
9.0
6.0
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

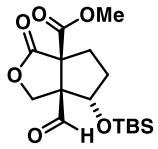

198.6
178.2
75.7
65.6
64.6
45.5
34.1
26.5
25.7
18.0
-4.5
-5.0
Solvent CDCl3
MHz 151
Nucleus13C
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


O
H
O
O
OTBS
O
O
Fe

204

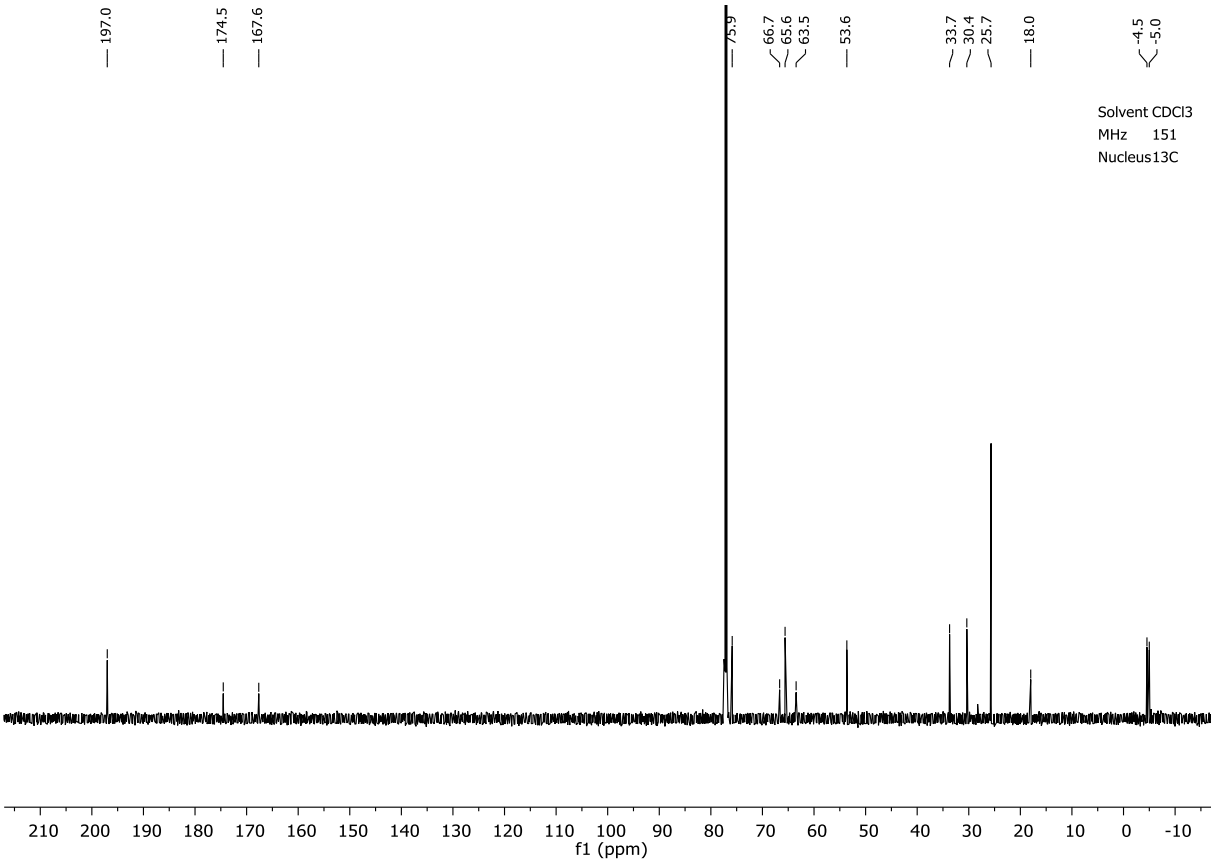
Solvent CDCl3
MHz 400
Nucleus1H
2.0
1.0
2.0
1.0
5.0
2.0
1.0
1.0
1.0
2.0
1.0
9.0
6.0
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

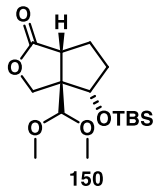

180.1
171.8
76.6
71.9
70.3
70.2
70.2
70.0
69.8
66.6
53.7
46.1
33.6
26.0
25.8
18.0
-4.2
-4.9
Solvent CDCl3
MHz 101
Nucleus13C
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


OMe
OTBS
H

343

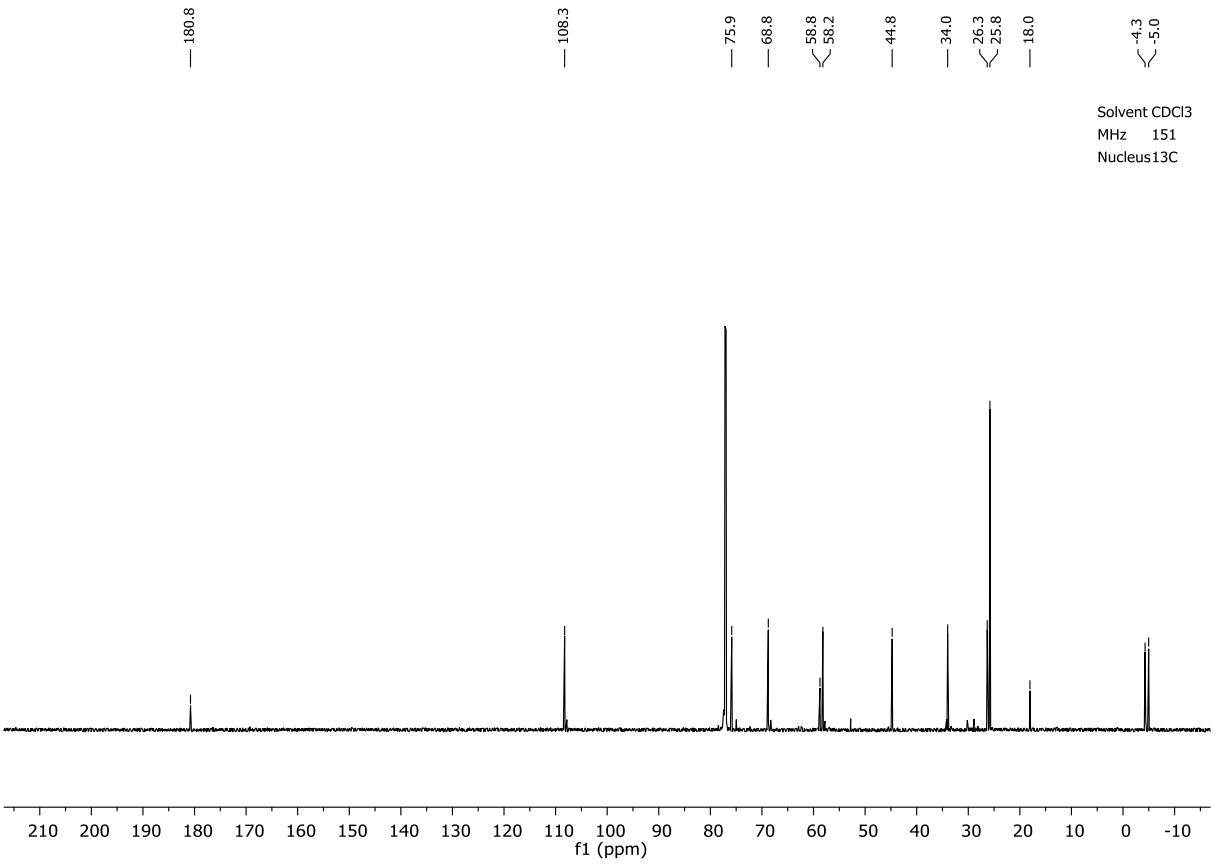
Solvent CDCl3
MHz 600
Nucleus1H
1.0
2.0
1.0
3.0
1.0
1.0
1.0
1.0
9.1
6.1
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

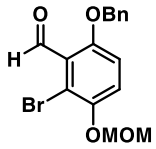

197.0
174.5
167.6
75.9
66.7
65.6
63.5
53.6
33.7
30.4
25.7
18.0
-4.5
-5.0
Solvent CDCl3
MHz 151
Nucleus13C
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


O
H
O
OTBS
O
O

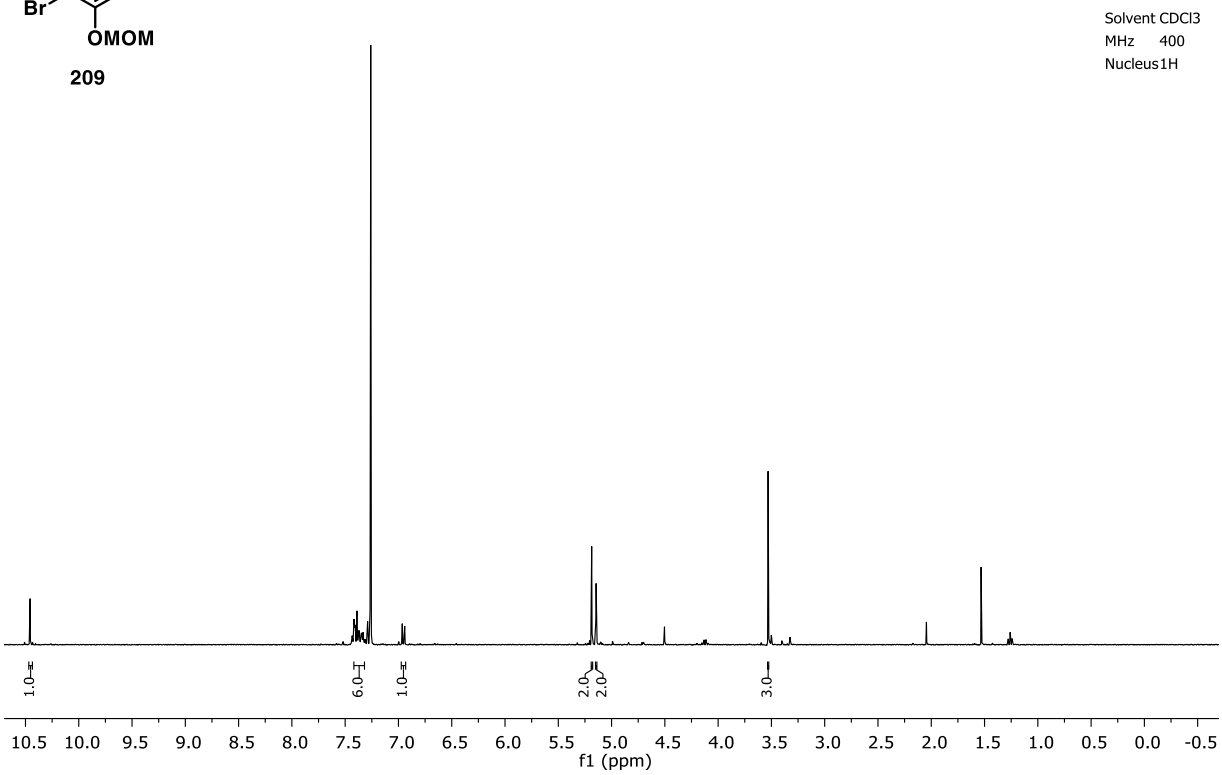
150

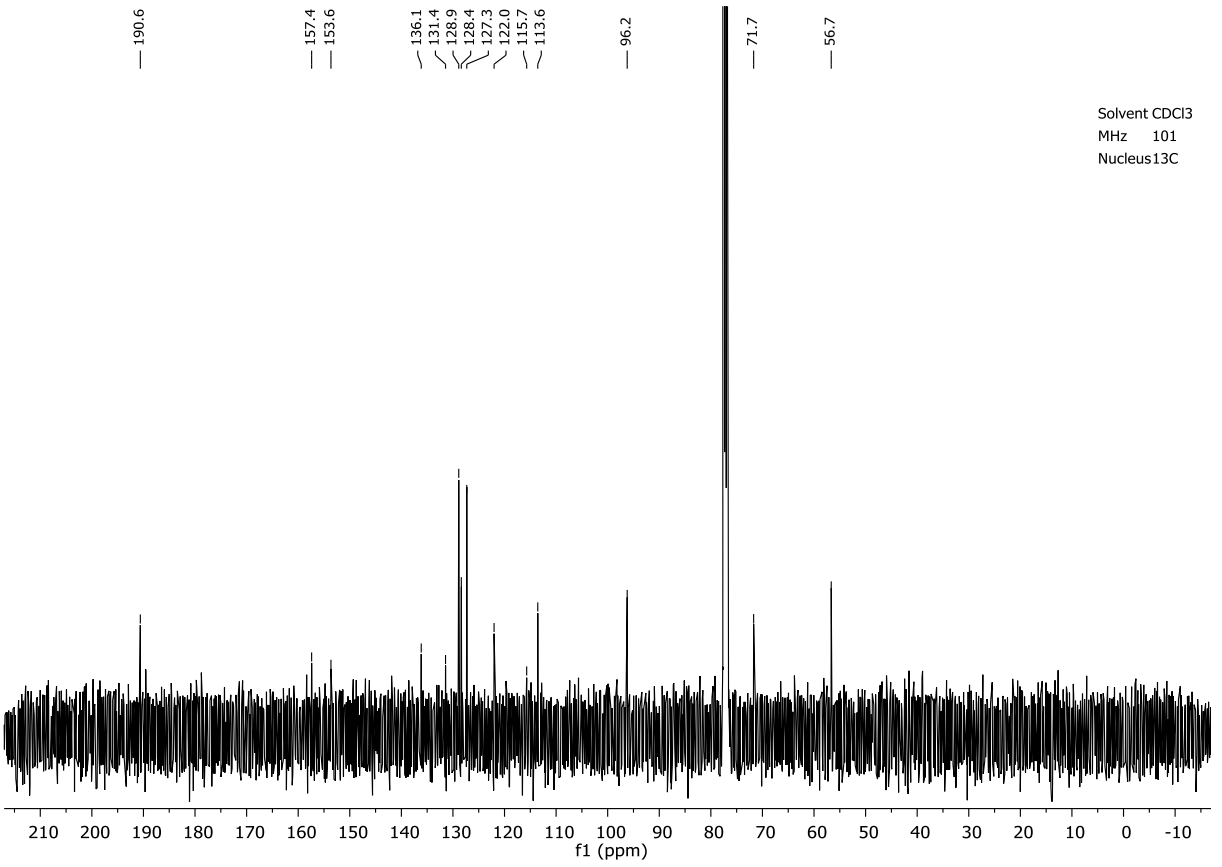
Solvent CDCl3
MHz 600
Nucleus1H
1.0
1.0
1.0
1.0
6.0
1.0
1.0
1.0
1.0
1.0
9.2
6.1
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

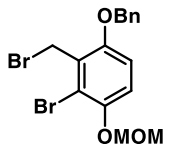

180.8
108.3
75.9
68.8
58.8
58.2
44.8
34.0
26.3
25.8
18.0
-4.3
-5.0
Solvent CDCl3
MHz 151
Nucleus13C
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


O
OBn
H
Br
OMOM

209

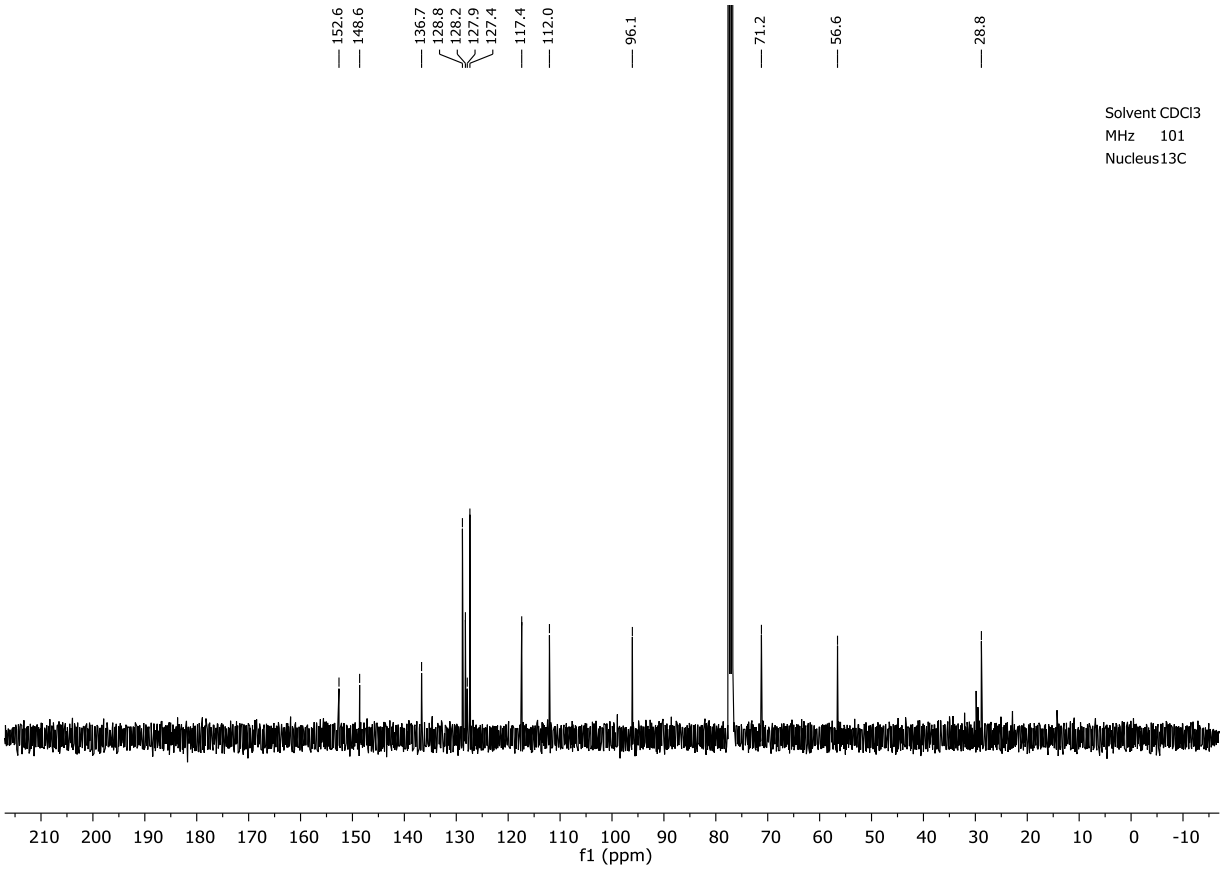

Solvent CDCl3
MHz 400
Nucleus1H
1.0
6.0
1.0
2.0
2.0
3.0
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

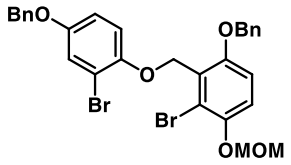

190.6
157.4
153.6
136.1
131.4
128.9
128.4
127.3
122.0
115.7
113.6
96.2
71.7
56.7
Solvent CDCl3
MHz 101
Nucleus13C
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


OBn
Br
Br
OMOM

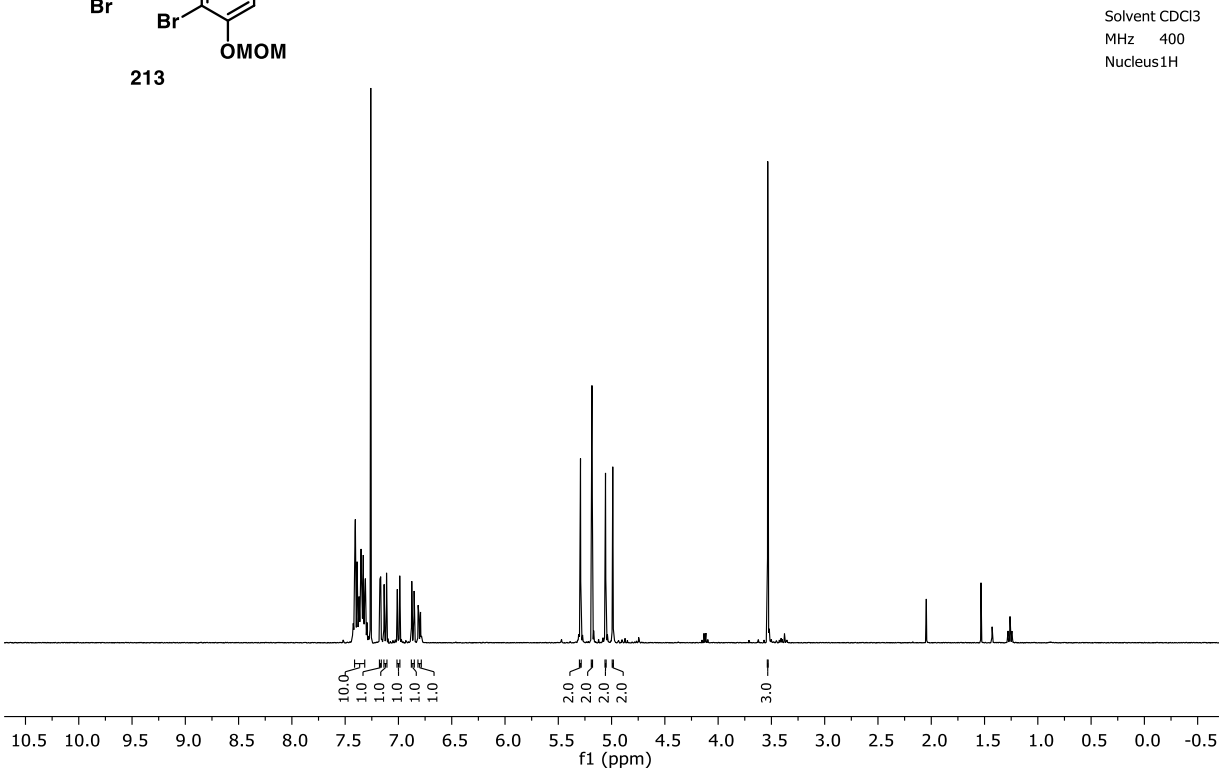
211

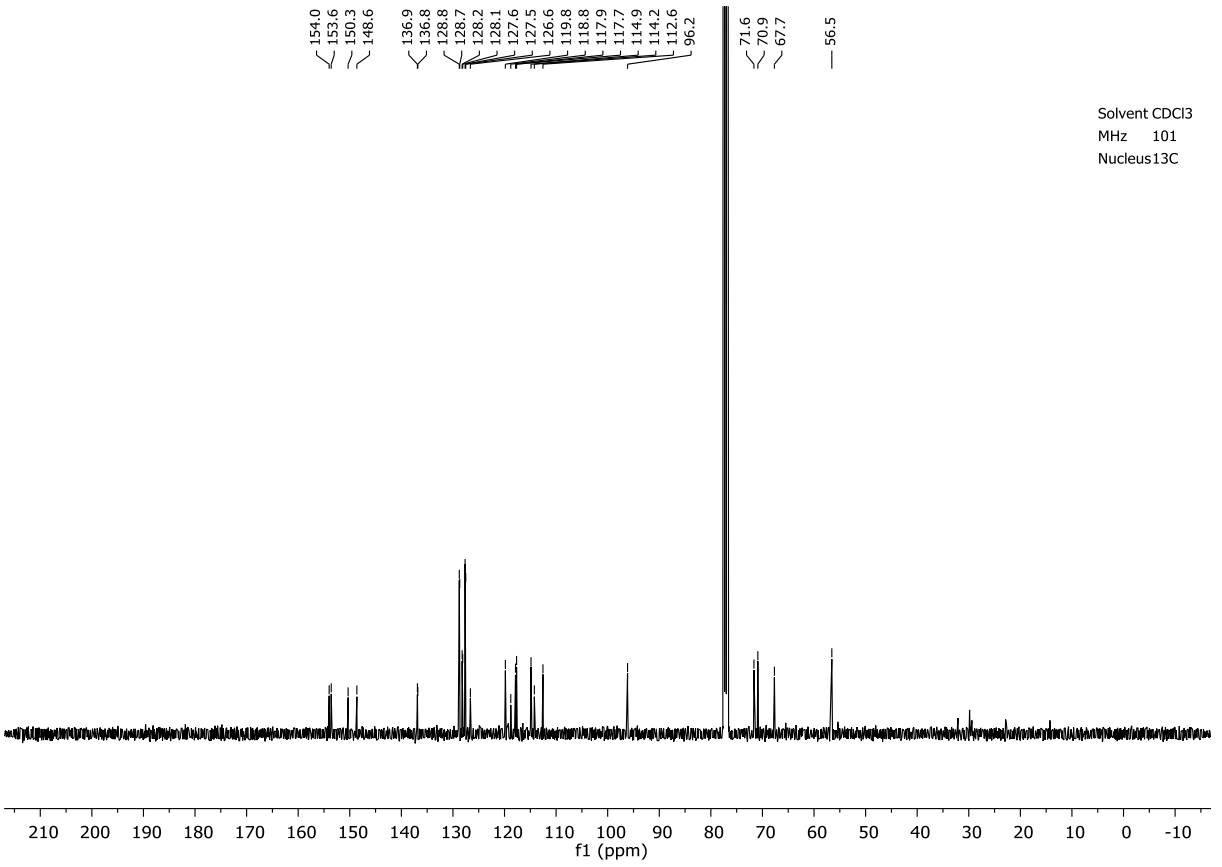
Solvent CDCl3
MHz 400
Nucleus1H
2.0
3.0
1.0
1.0
2.0
2.0
2.0
3.0
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

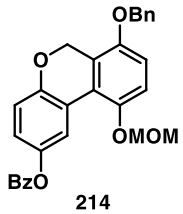

152.6
148.6
136.7
128.8
128.2
127.9
127.4
117.4
112.0
96.1
71.2
56.6
28.8
Solvent CDCl3
MHz 101
Nucleus13C
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


BnO
OBn
O
Br
Br
OMOM

213

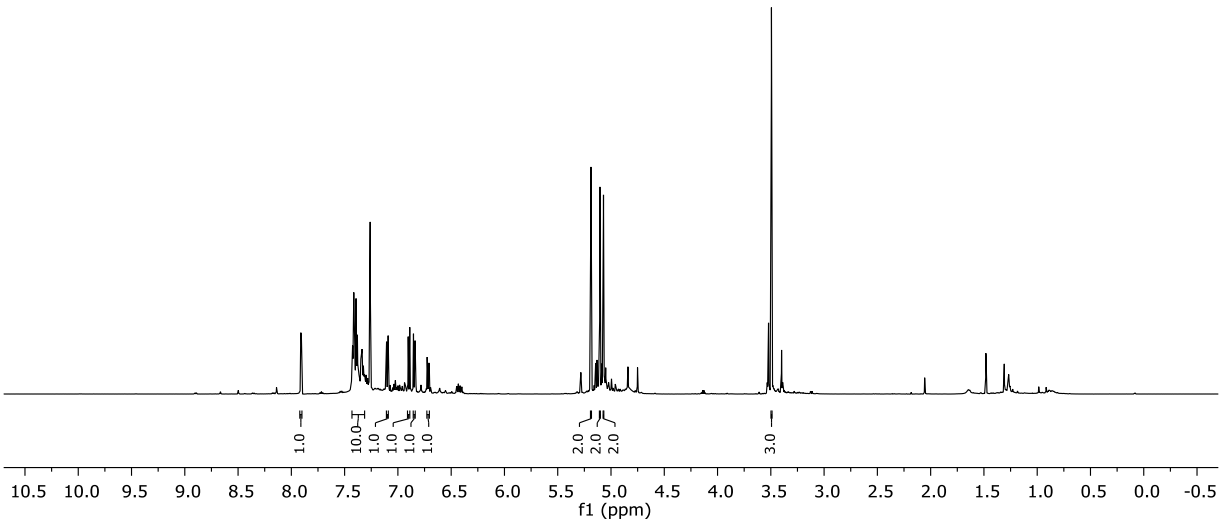

Solvent CDCl3
MHz 400
Nucleus1H
10.0
1.0
1.0
1.0
1.0
1.0
2.0
2.0
2.0
2.0
3.0
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

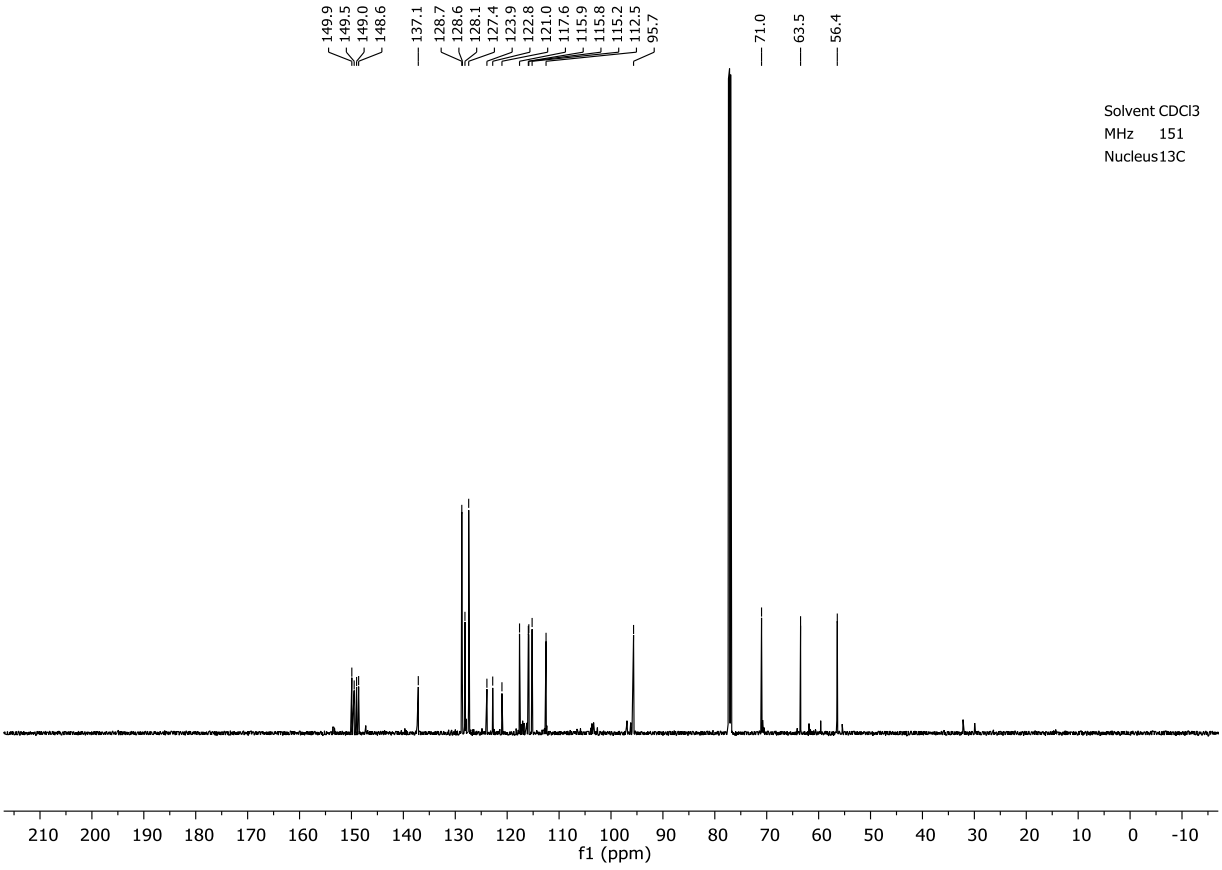

154.0
153.6
150.3
148.6
136.9
136.8
128.8
128.7
128.2
128.1
127.6
127.5
126.6
119.8
118.8
117.9
117.7
114.9
114.2
112.6
96.2
71.6
70.9
67.7
56.5
Solvent CDCl3
MHz 101
Nucleus13C
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

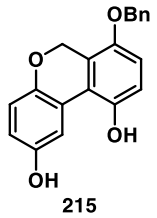


214

Solvent CDCl3
MHz 600
Nucleus1H

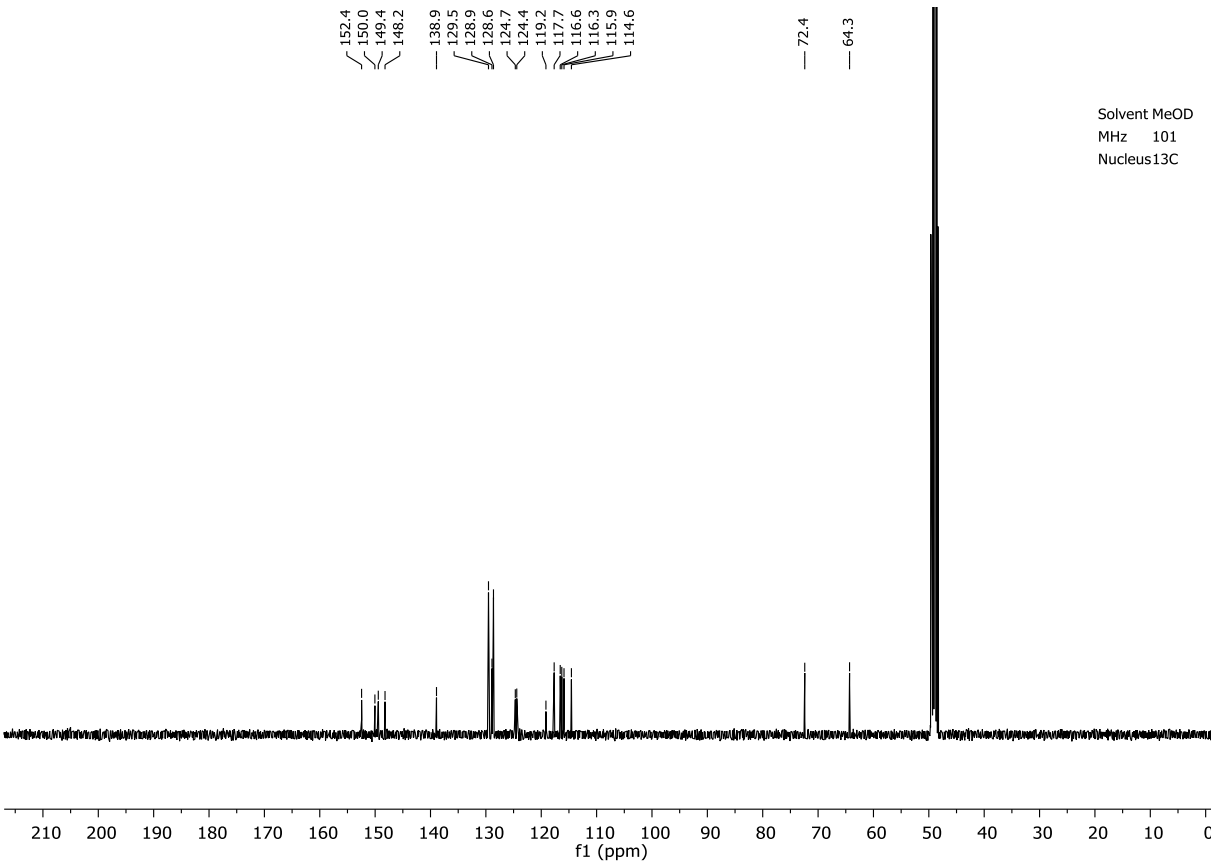


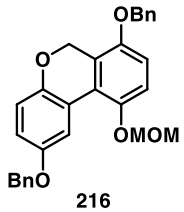



OBn
O
OH
OH

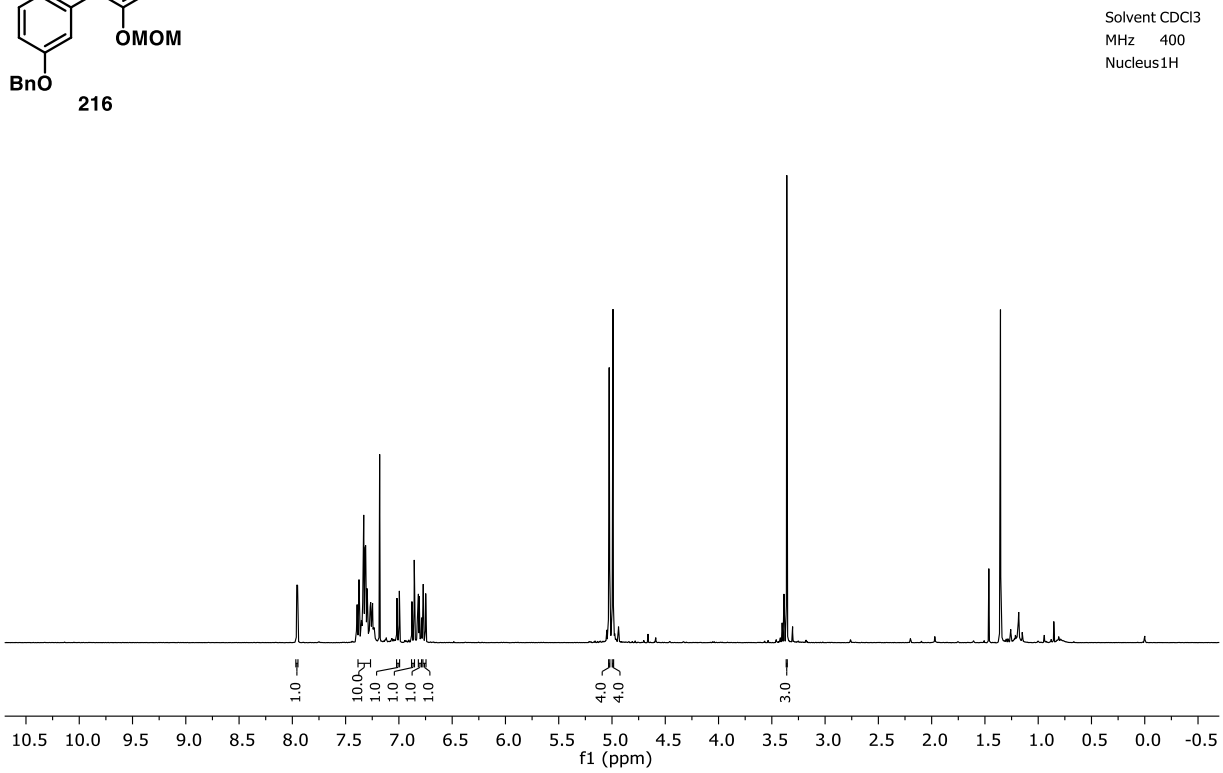
215

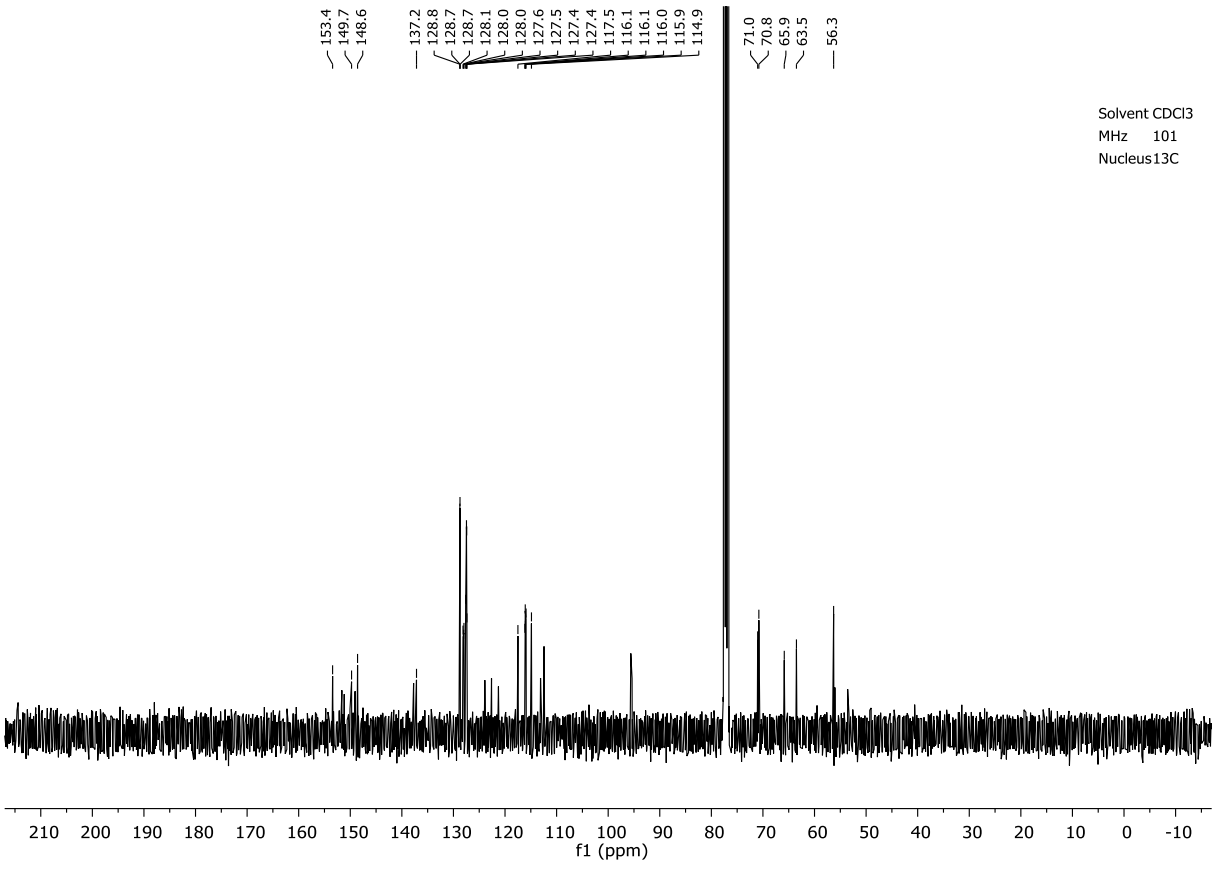
Solvent MeOD
MHz 400
Nucleus1H
1.0
2.0
2.0
1.0
1.0
2.0
1.0
2.0
2.0
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

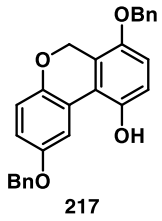

152.4
150.0
149.4
148.2
138.9
129.5
128.9
128.6
124.7
124.4
119.2
117.7
116.6
116.3
115.9
114.6
72.4
64.3
Solvent MeOD
MHz 101
Nucleus13C
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
f1 (ppm)


OBn
O
OMOM
BnO

216

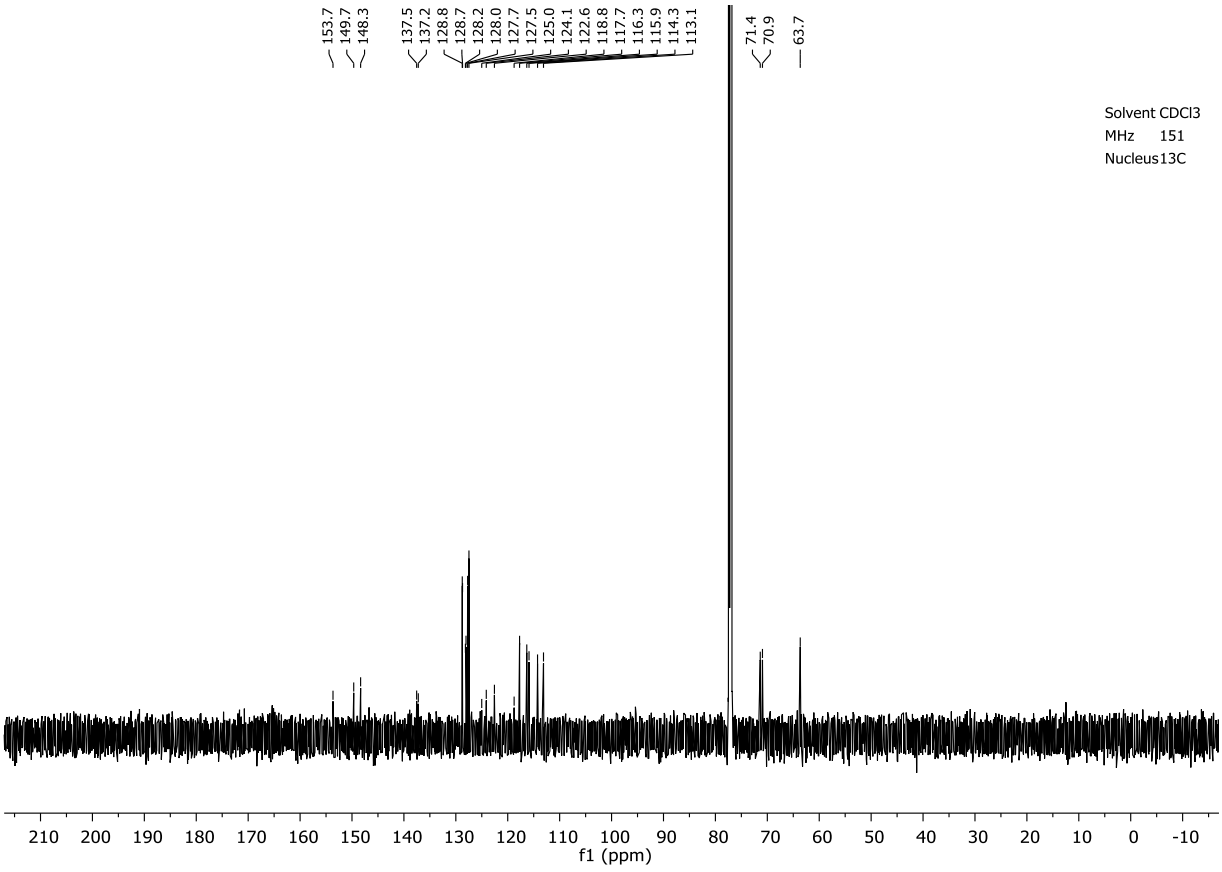

Solvent CDCl3
MHz 400
Nucleus1H
1.0
10.0
1.0
1.0
1.0
1.0
4.0
4.0
3.0
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

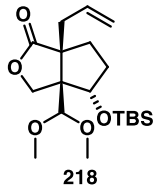

153.4
149.7
148.6
137.2
128.8
128.7
128.7
128.1
128.0
128.0
127.6
127.5
127.4
127.4
117.5
116.1
116.1
116.0
115.9
114.9
71.0
70.8
65.9
63.5
56.3
Solvent CDCl3
MHz 101
Nucleus13C
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


OBn
O
OH
BnO

217

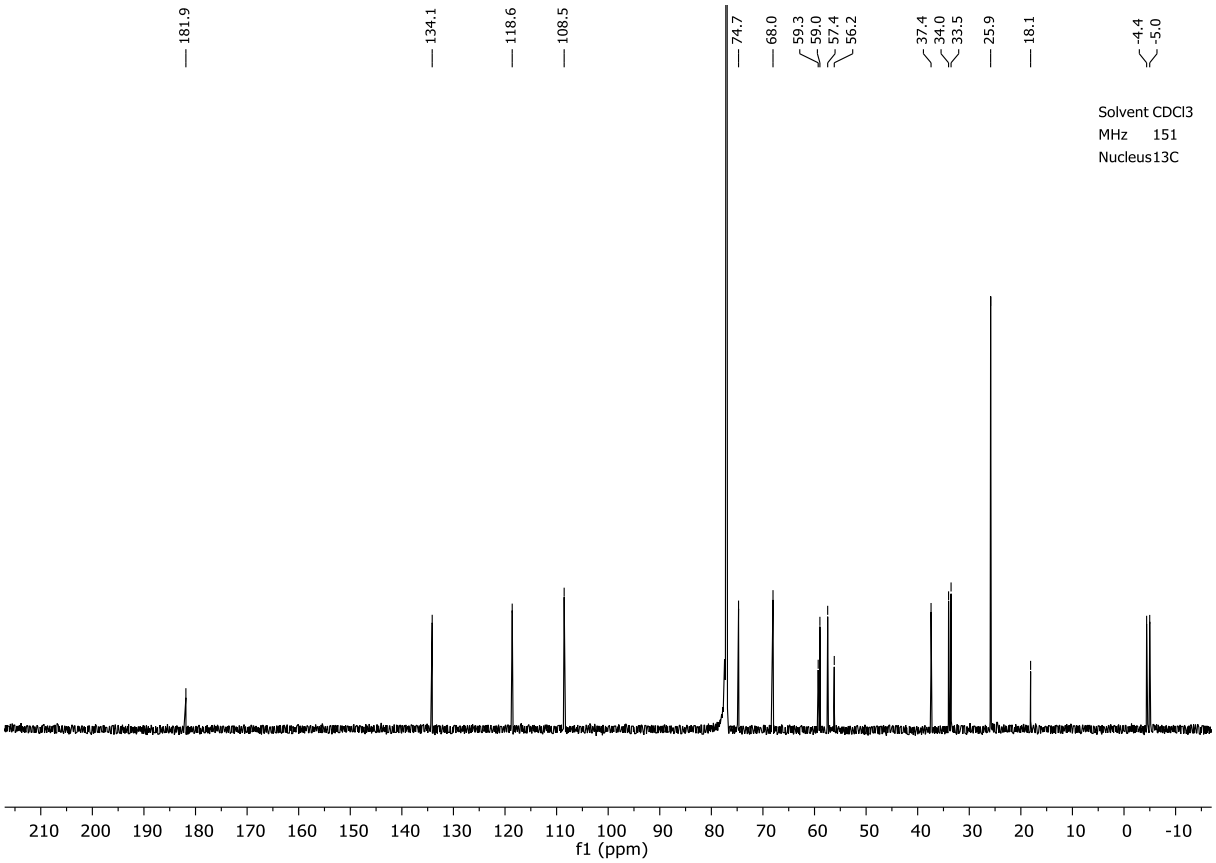
Solvent CDCl3
MHz 600
Nucleus1H
1.0
2.0
6.0
2.0
1.0
1.0
1.0
1.0
2.0
2.0
2.0
1.0
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

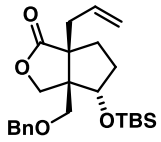

153.7
149.7
148.3
137.5
137.2
128.8
128.7
128.2
128.0
127.7
127.5
125.0
124.1
122.6
118.8
117.7
116.3
115.9
114.3
113.1
71.4
70.9
63.7
Solvent CDCl3
MHz 151
Nucleus13C
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


O
O
OTBS
O
O

218

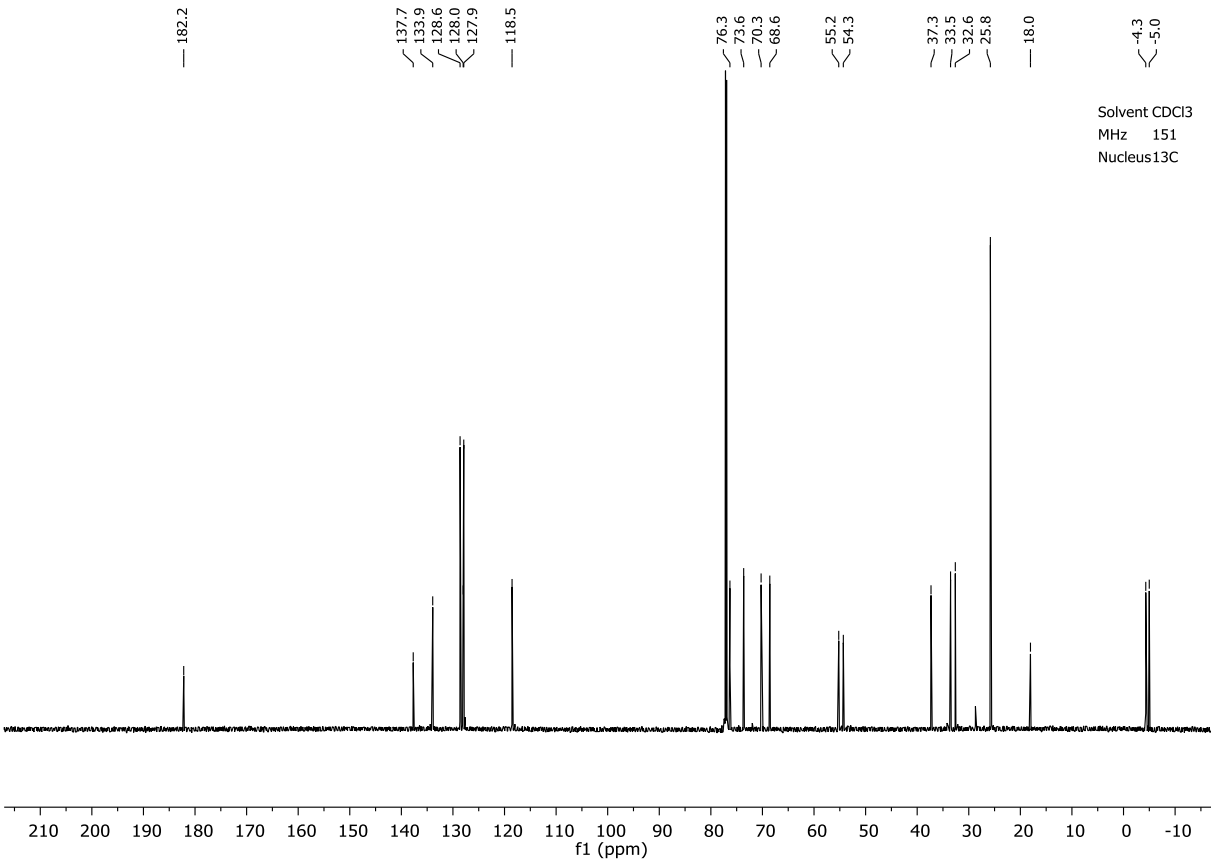
Solvent CDCl3
MHz 400
Nucleus1H
1.0
2.0
1.0
1.0
1.0
1.0
6.0
2.0
2.0
1.0
1.0
9.0
6.0
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

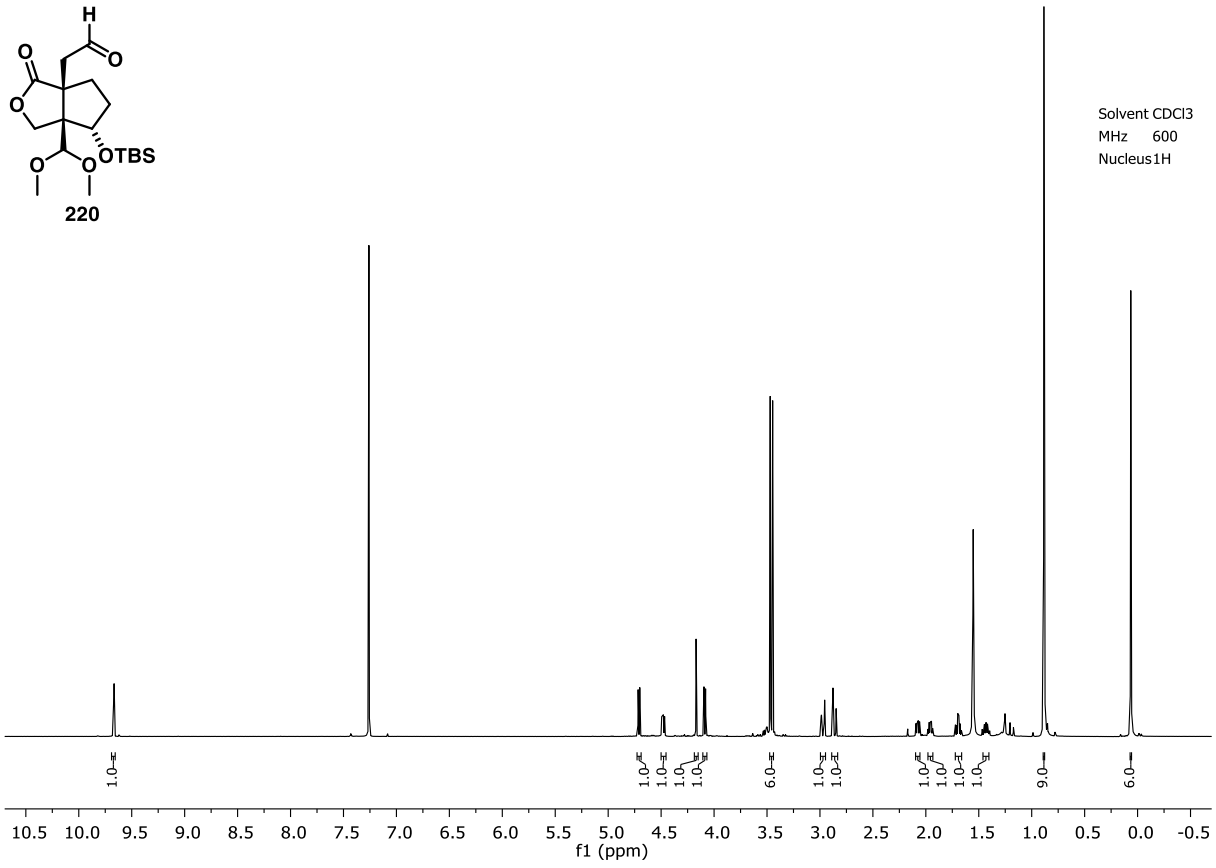

181.9
134.1
118.6
108.5
74.7
68.0
59.3
59.0
57.4
56.2
37.4
34.0
33.5
25.9
18.1
-4.4
-5.0
Solvent CDCl3
MHz 151
Nucleus13C
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

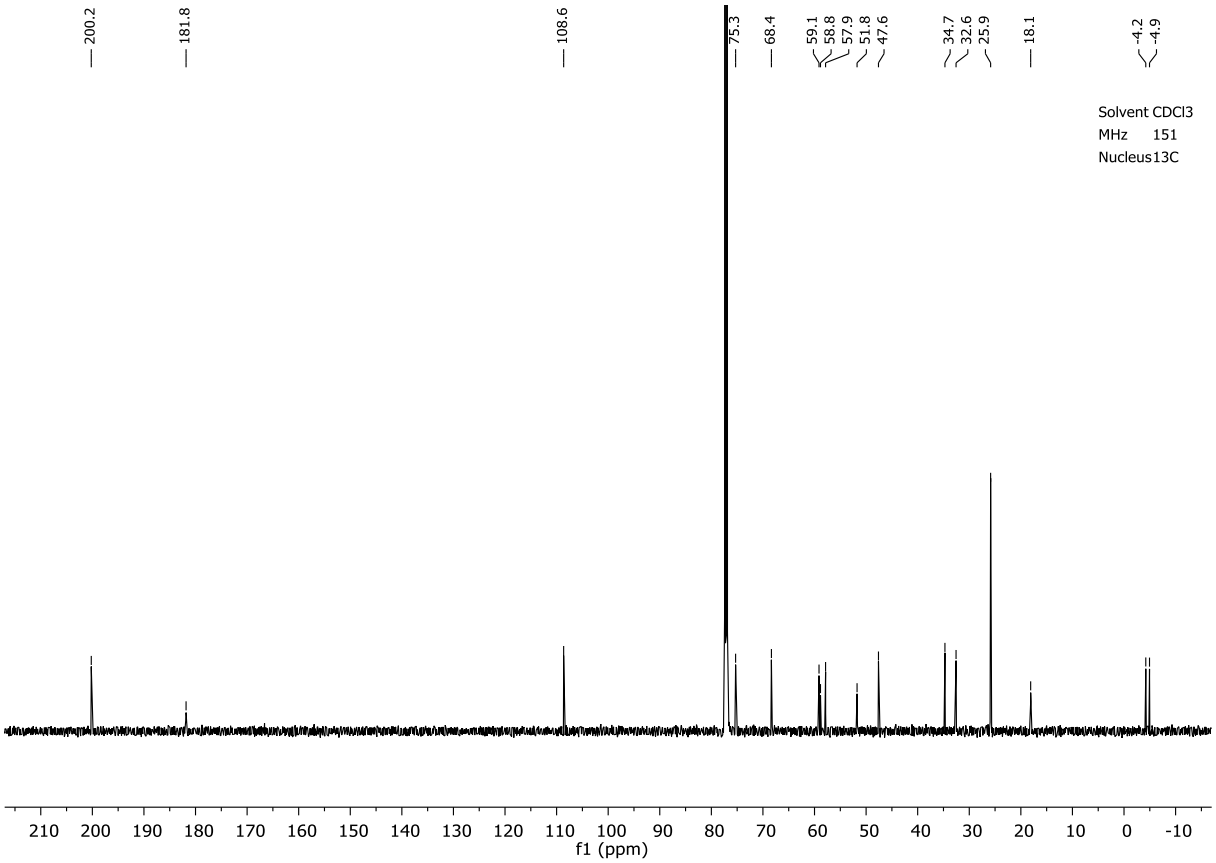

O
O
BnO
OTBS

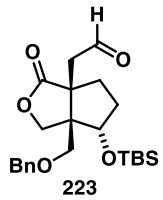
222

Solvent CDCl3
MHz 600
Nucleus1H
2.0
3.0
1.0
2.0
1.0
2.0
1.0
1.0
1.0
1.0
1.0
1.0
1.0
1.0
1.0
9.0
6.0
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)


182.2
137.7
133.9
128.6
128.0
127.9
118.5
76.3
73.6
70.3
68.6
55.2
54.3
37.3
33.5
32.6
25.8
18.0
-4.3
-5.0
Solvent CDCl3
MHz 151
Nucleus13C
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

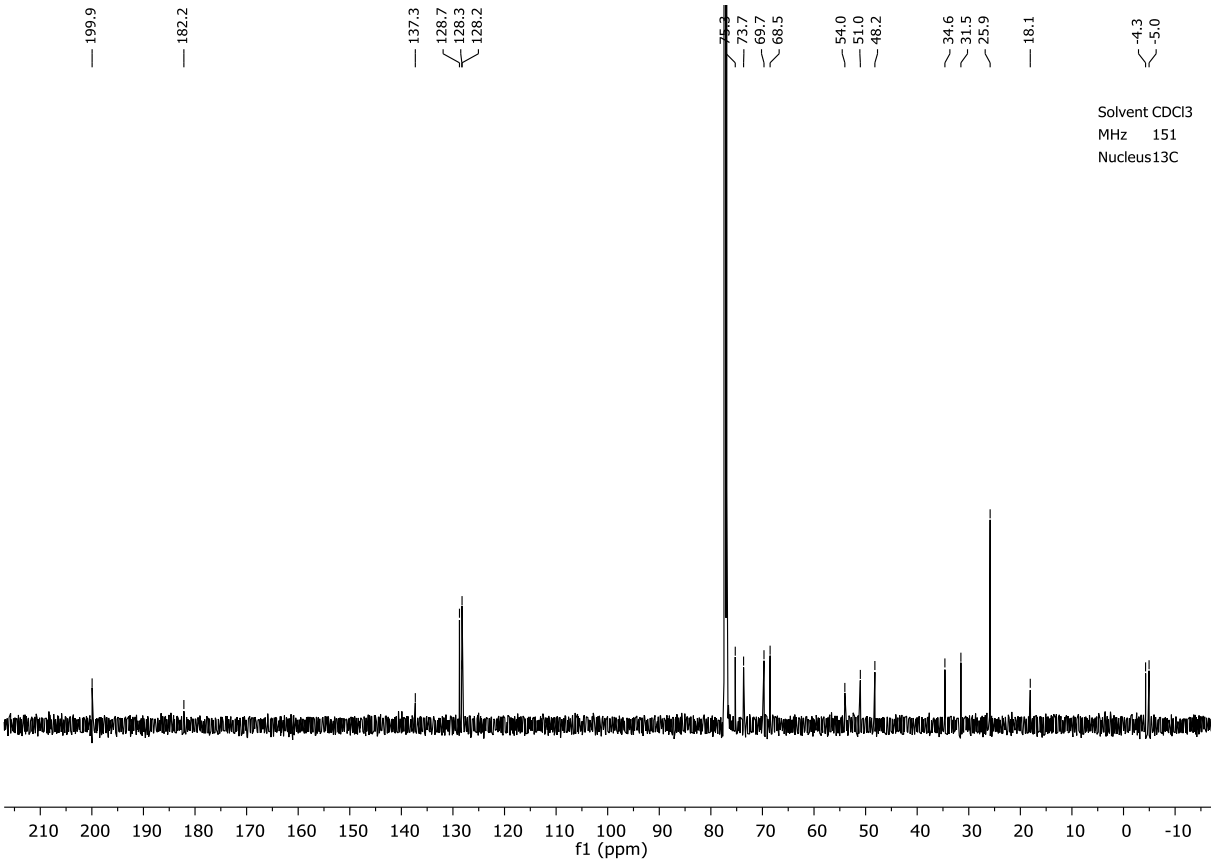

H
O
O
O
O
O
OTBS
220
Solvent CDCl3
MHz 600
Nucleus1H
1.0
1.0
1.0
1.0
6.0
1.0
1.0
1.0
1.0
1.0
1.0
9.0
6.0
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

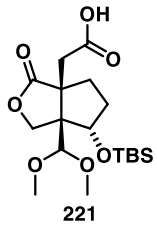

200.2
181.8
108.6
75.3
68.4
59.1
58.8
57.9
51.8
47.6
34.7
32.6
25.9
18.1
-4.2
-4.9
Solvent CDCl3
MHz 151
Nucleus13C
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


H
O
O
O
BnO
OTBS

223

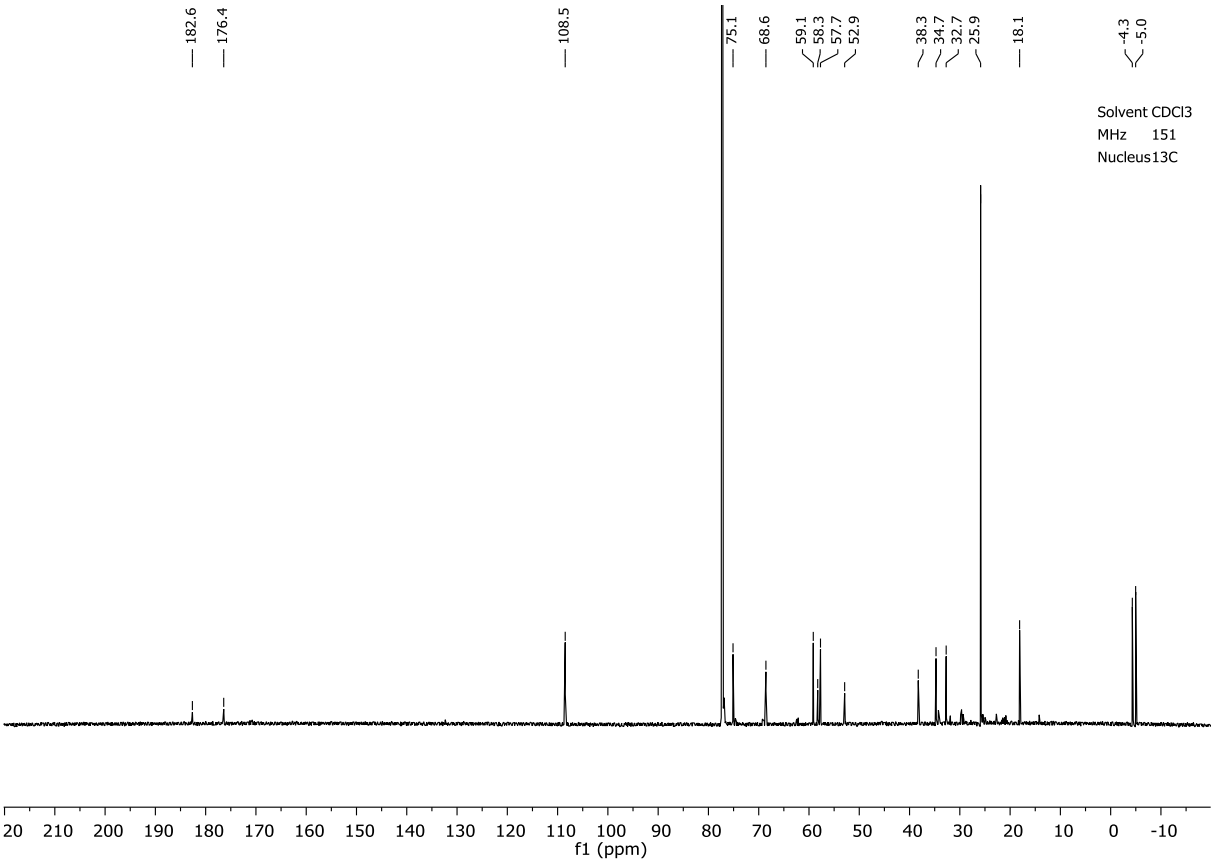
Solvent CDCl3
MHz 600
Nucleus1H
1.0
2.1
1.0
2.0
1.0
1.1
2.1
1.1
1.0
1.0
1.1
1.1
1.1
1.0
1.1
1.1
9.0
6.1
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

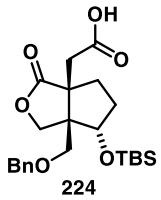

199.9
182.2
137.3
128.7
128.3
128.2
76.3
73.7
69.7
68.5
54.0
51.0
48.2
34.6
31.5
25.9
18.1
-4.3
-5.0
Solvent CDCl3
MHz 151
Nucleus13C
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


OH
O
O
O
O
O
OTBS

221

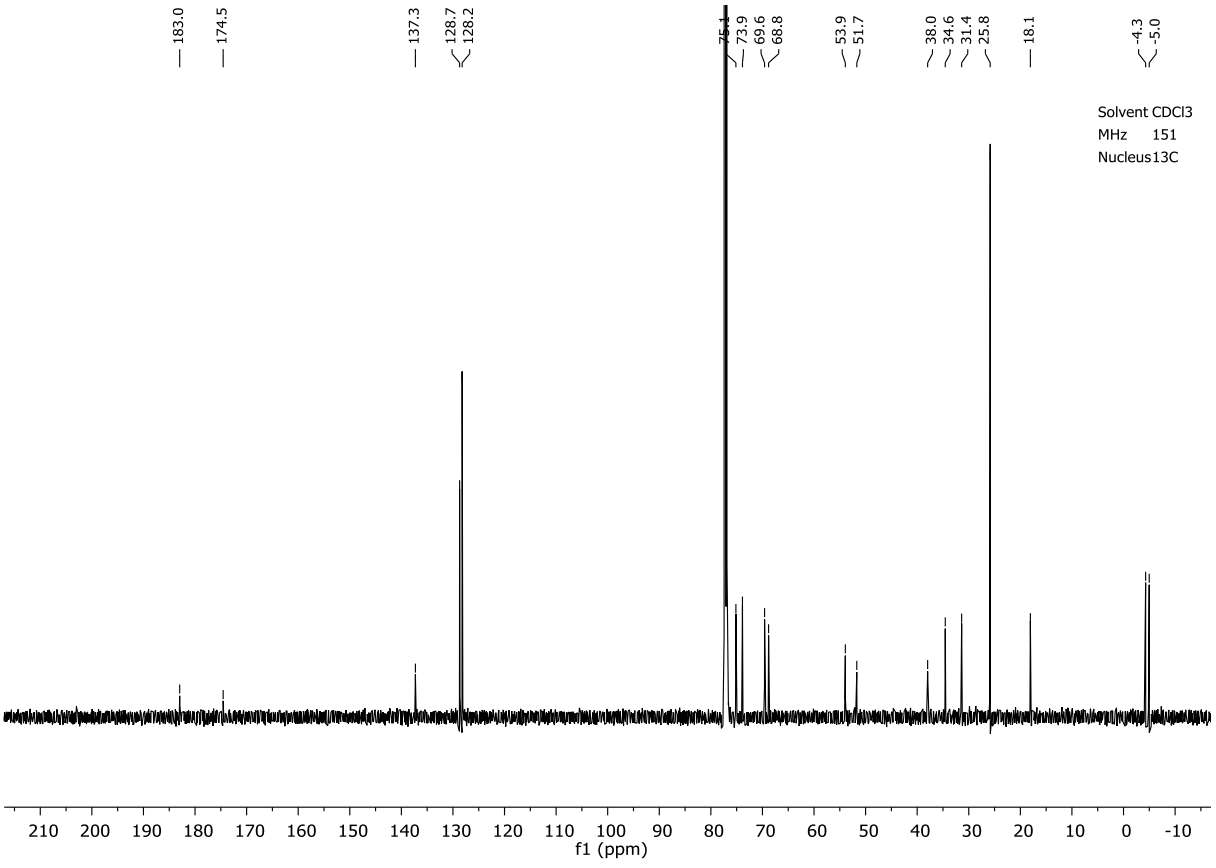
Solvent CDCl3
MHz 600
Nucleus1H
1.0
1.0
1.0
1.0
6.0
2.0
1.0
1.0
1.0
1.0
9.0
6.0
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

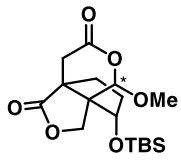

182.6
176.4
108.5
75.1
68.6
59.1
58.3
57.7
52.9
38.3
34.7
32.7
25.9
18.1
-4.3
-5.0
Solvent CDCl3
MHz 151
Nucleus13C
20 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


OH
O
O
O
BnO
OTBS

224

Solvent CDCl3
MHz 400
Nucleus1H
5.0
1.0
2.0
1.0
1.0
1.0
1.0
1.0
1.0
1.0
1.0
1.0
9.0
6.0
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

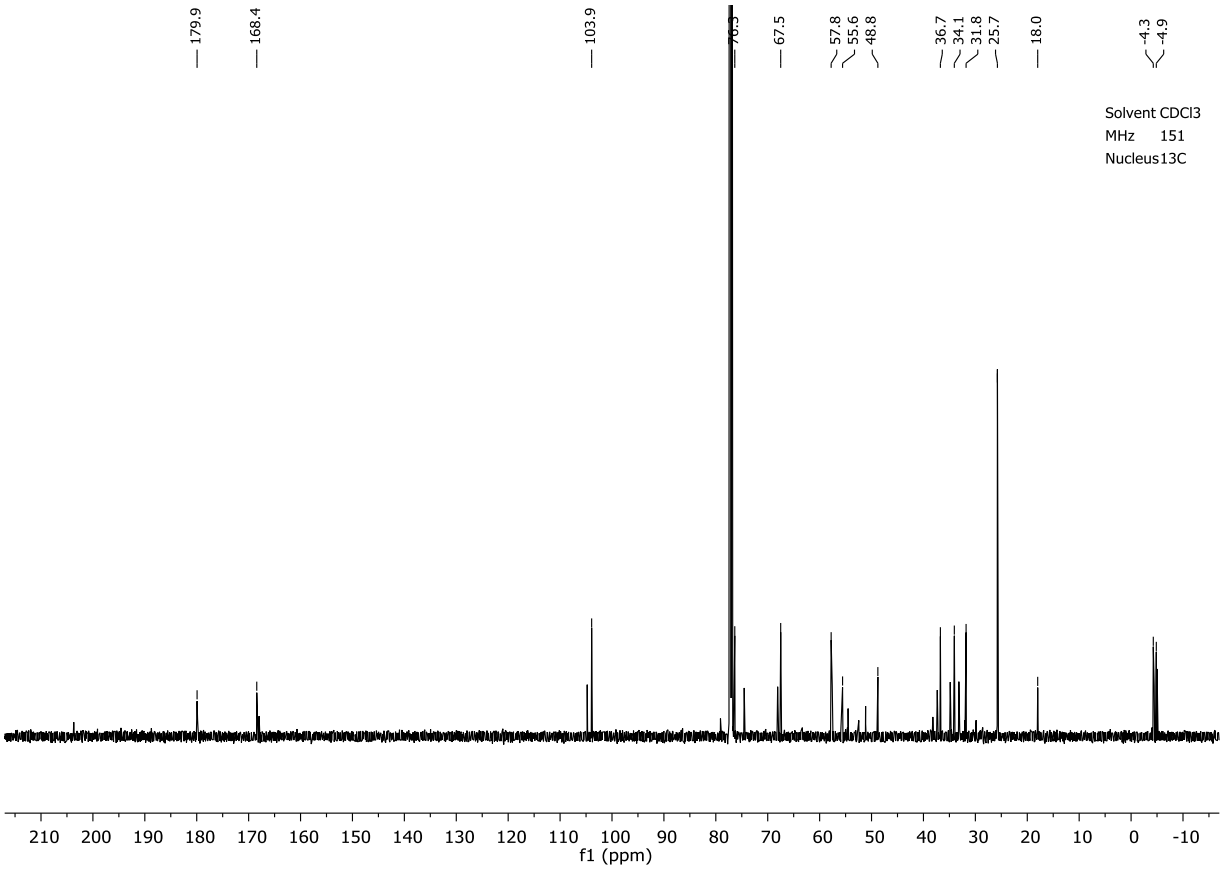

183.0
174.5
137.3
128.7
128.2
75.1
73.9
69.6
68.8
53.9
51.7
38.0
34.6
31.4
25.8
18.1
-4.3
-5.0
Solvent CDCl3
MHz 151
Nucleus13C
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

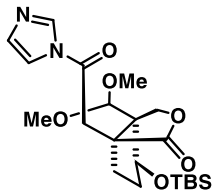

O
O
O
O
*
OMe
OTBS

d.r. 2:1

225

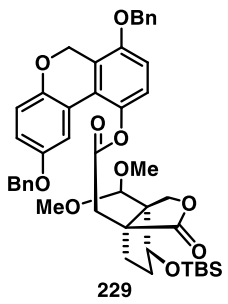
Solvent CDCl3
MHz 600
Nucleus1H
1.0
1.0
1.0
1.0
3.0
1.0
1.0
1.0
1.0
2.0
9.0
6.0
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)


179.9
168.4
103.9
76.3
67.5
57.8
55.6
48.8
36.7
34.1
31.8
25.7
18.0
-4.3
-4.9
Solvent CDCl3
MHz 151
Nucleus13C
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


N
N
O
OMe
MeO
O
O
OTBS

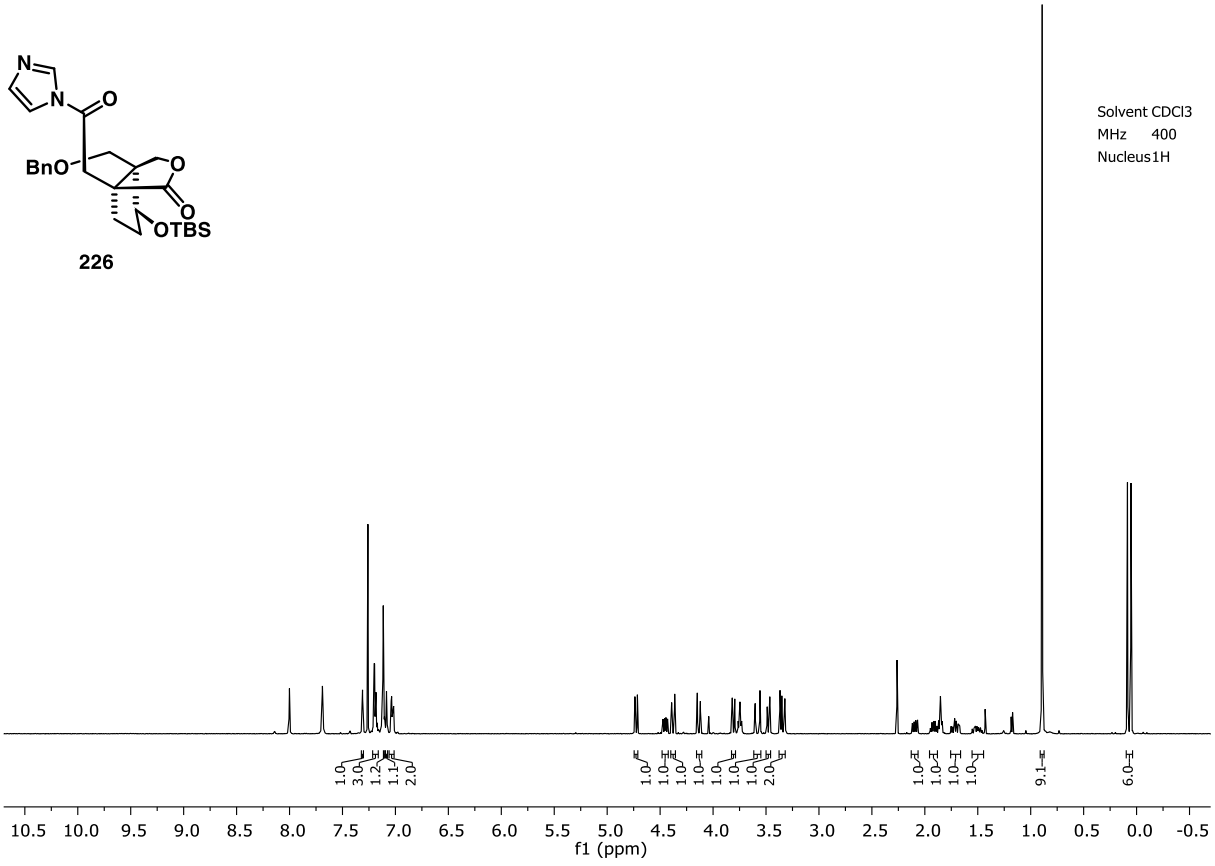
227

Solvent CDCl3
MHz 400
Nucleus1H
1.0
1.0
1.0
1.0
1.0
1.0
1.0
3.0
1.0
3.0
1.0
1.0
1.0
1.0
9.0
6.0
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

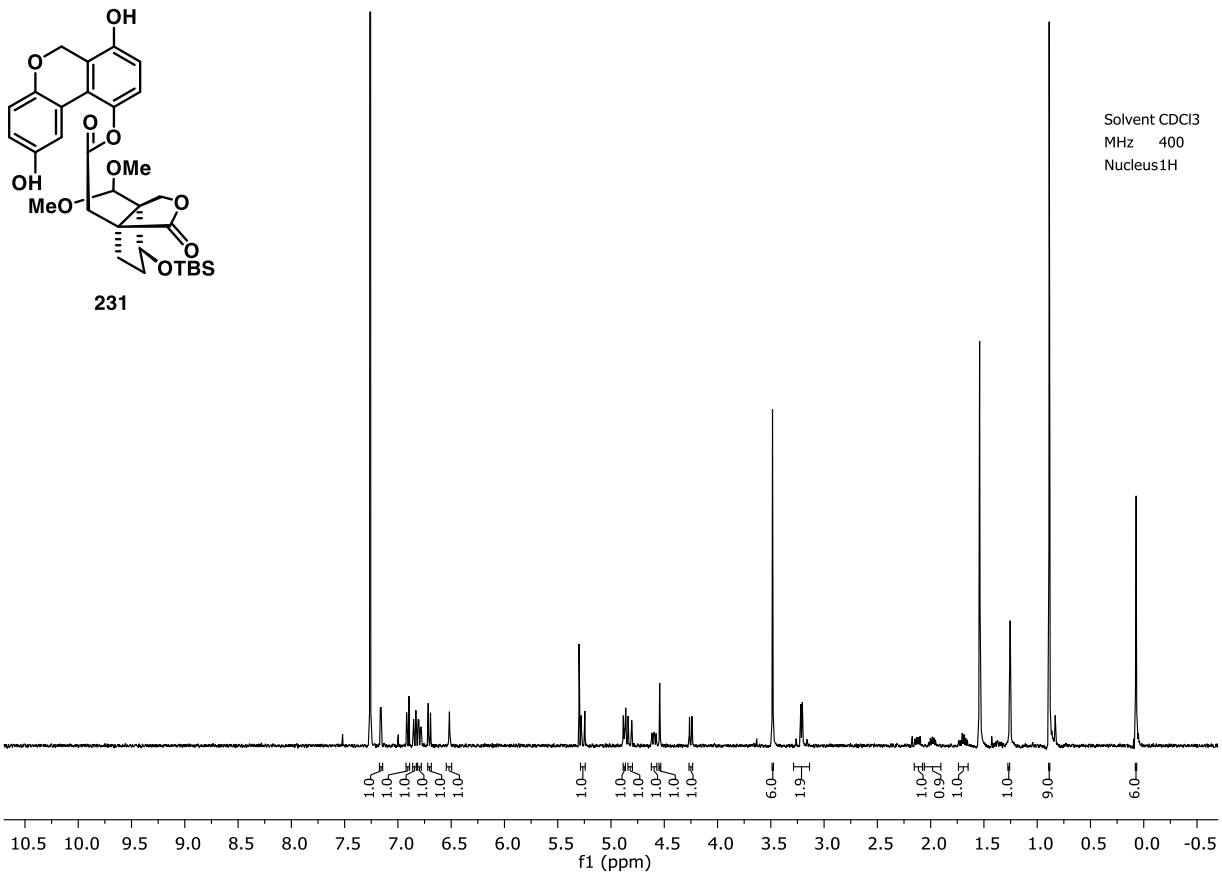

OBn
O
O
O
BnO
OMe
MeO
O
O
OTBS

229

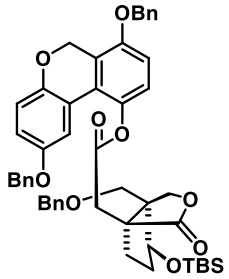
Solvent CDCl3
MHz 400
Nucleus1H
1.0
10.0
1.0
1.0
1.0
1.0
2.0
2.0
1.0
1.0
1.0
3.0
3.0
2.0
1.0
1.0
1.0
1.0
9.0
6.0
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)


Solvent CDCl3
MHz 400
Nucleus1H
f1 (ppm)

226

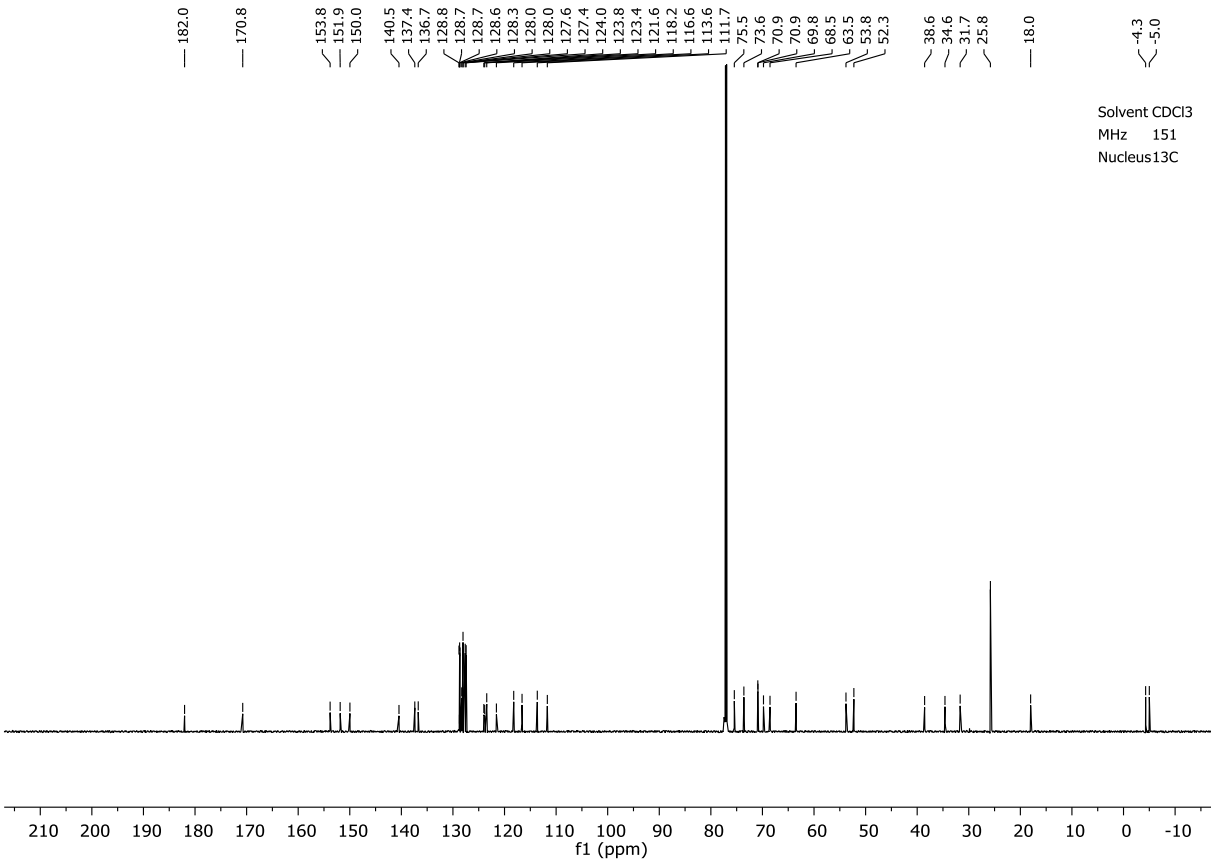

Solvent CDCl3
MHz 400
Nucleus1H
f1 (ppm)

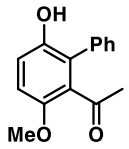
231


OBn
O
O
O
BnO
BnO
O
O
OTBS

228

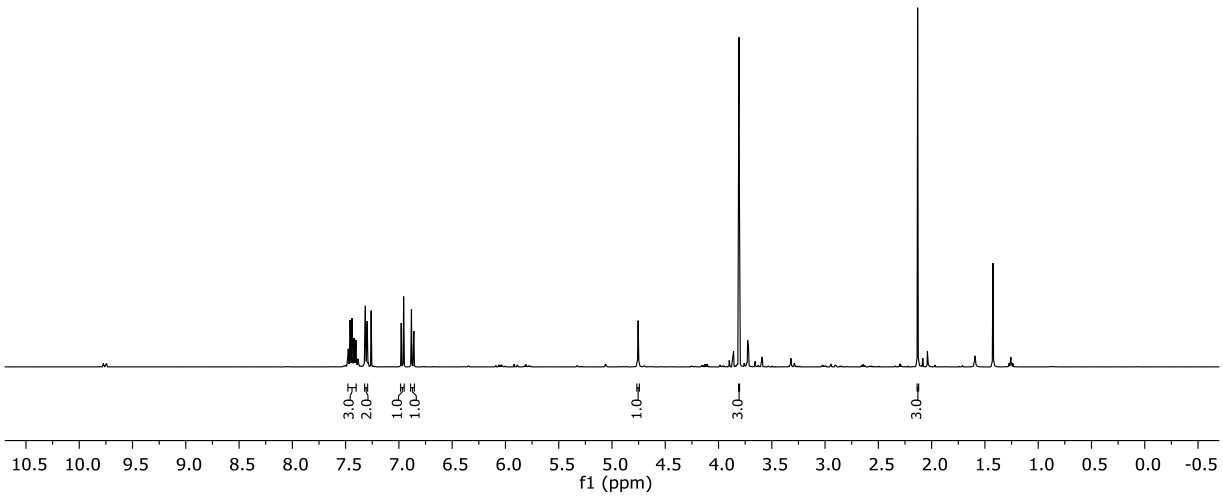
Solvent CDCl3
MHz 600
Nucleus1H
1.0 10.2 1.0 3.1 2.0 2.0 2.0 1.0 2.0 2.0 1.1 1.0 2.0 1.0 1.0 1.0 2.0 1.1 1.0 1.0 1.0 1.0 9.0 6.0
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

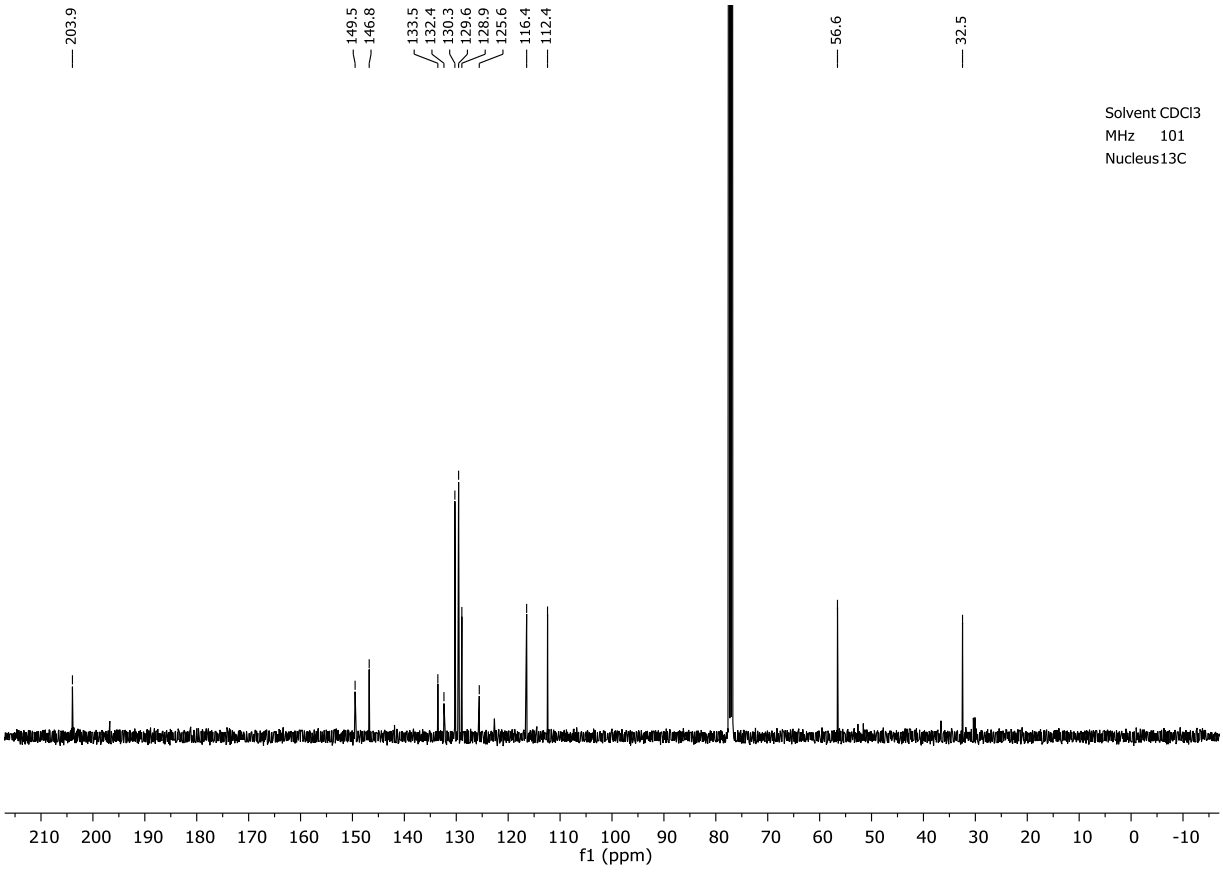

182.0 170.8 153.8 151.9 150.0 140.5 137.4 136.7 128.8 128.7 128.7 128.6 128.3 128.0 128.0 127.6 127.4 124.0 123.8 123.4 121.6 118.2 116.6 113.6 111.7 75.5 73.6 70.9 70.9 69.8 68.5 63.5 53.8 52.3 38.6 34.6 31.7 25.8 18.0 -4.3 -5.0
Solvent CDCl3
MHz 151
Nucleus13C
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

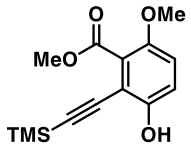


249

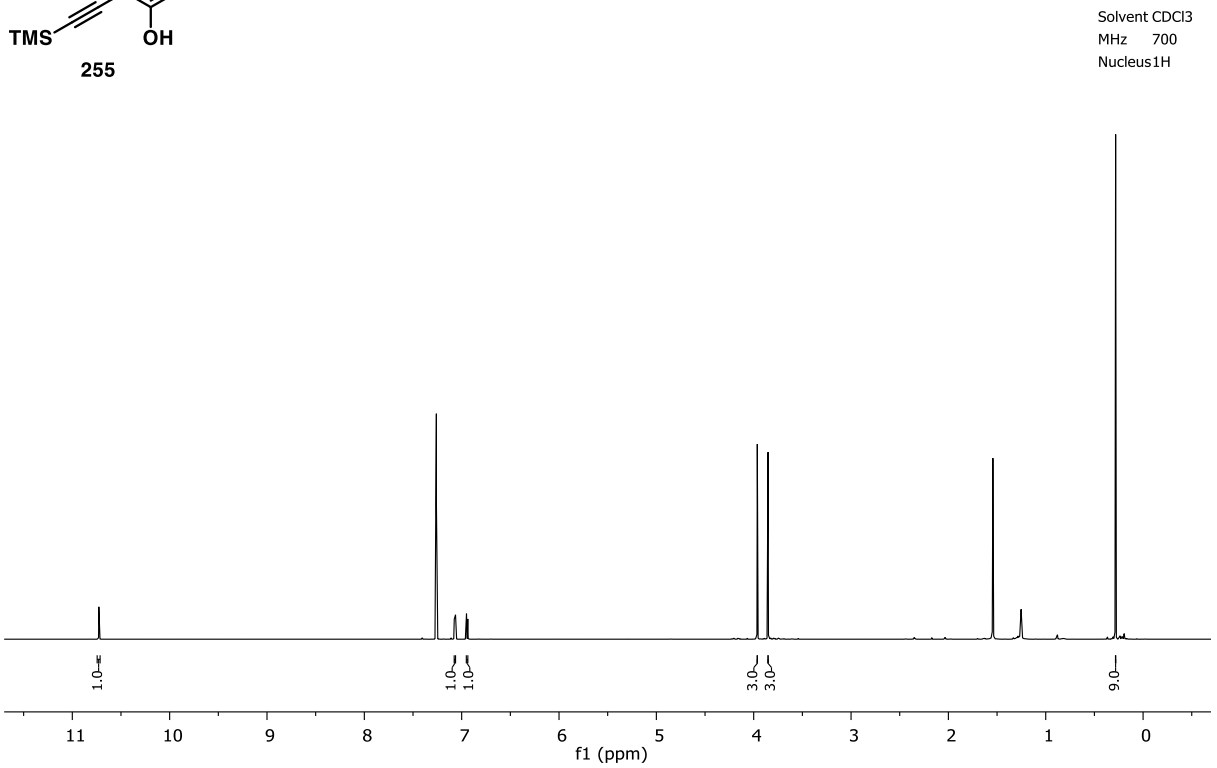
Solvent CDCl3
MHz 400
Nucleus1H

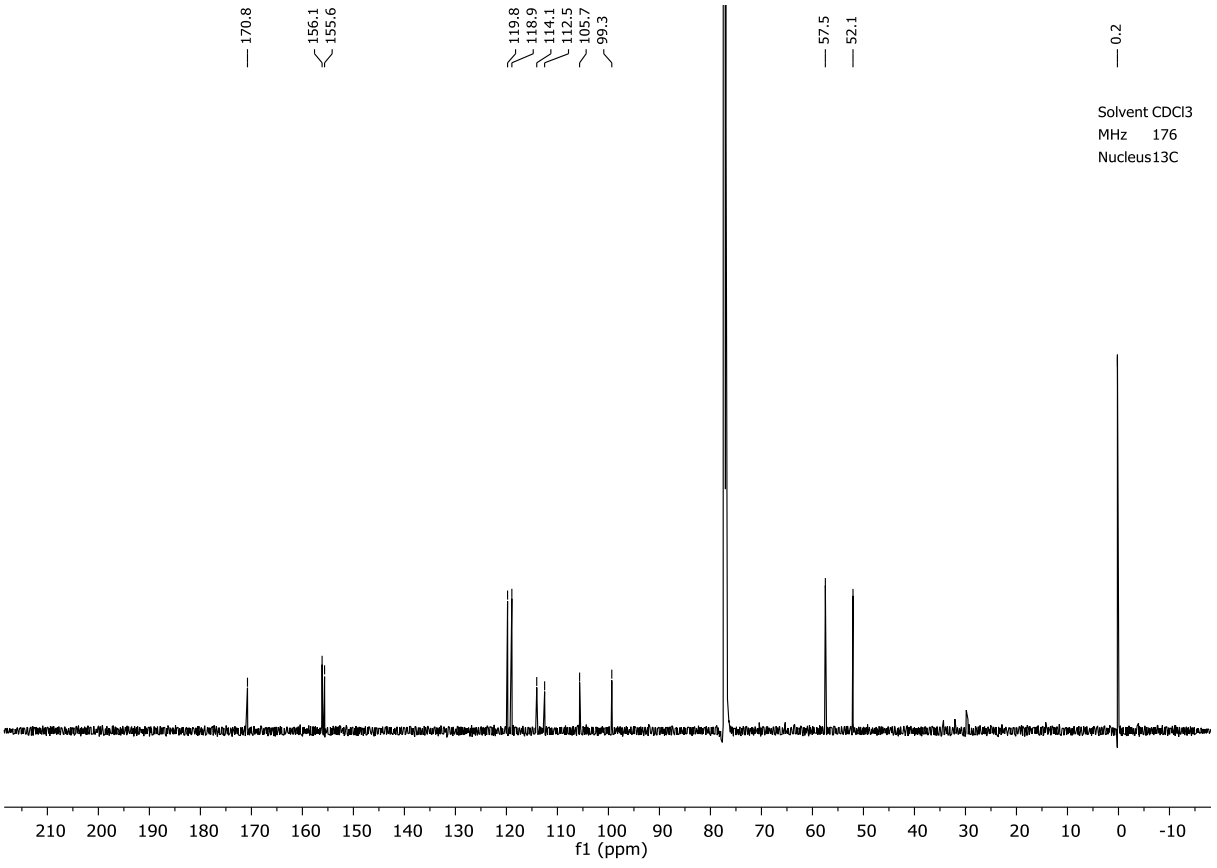


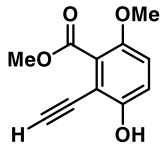



O
OMe
MeO
TMS
OH

255

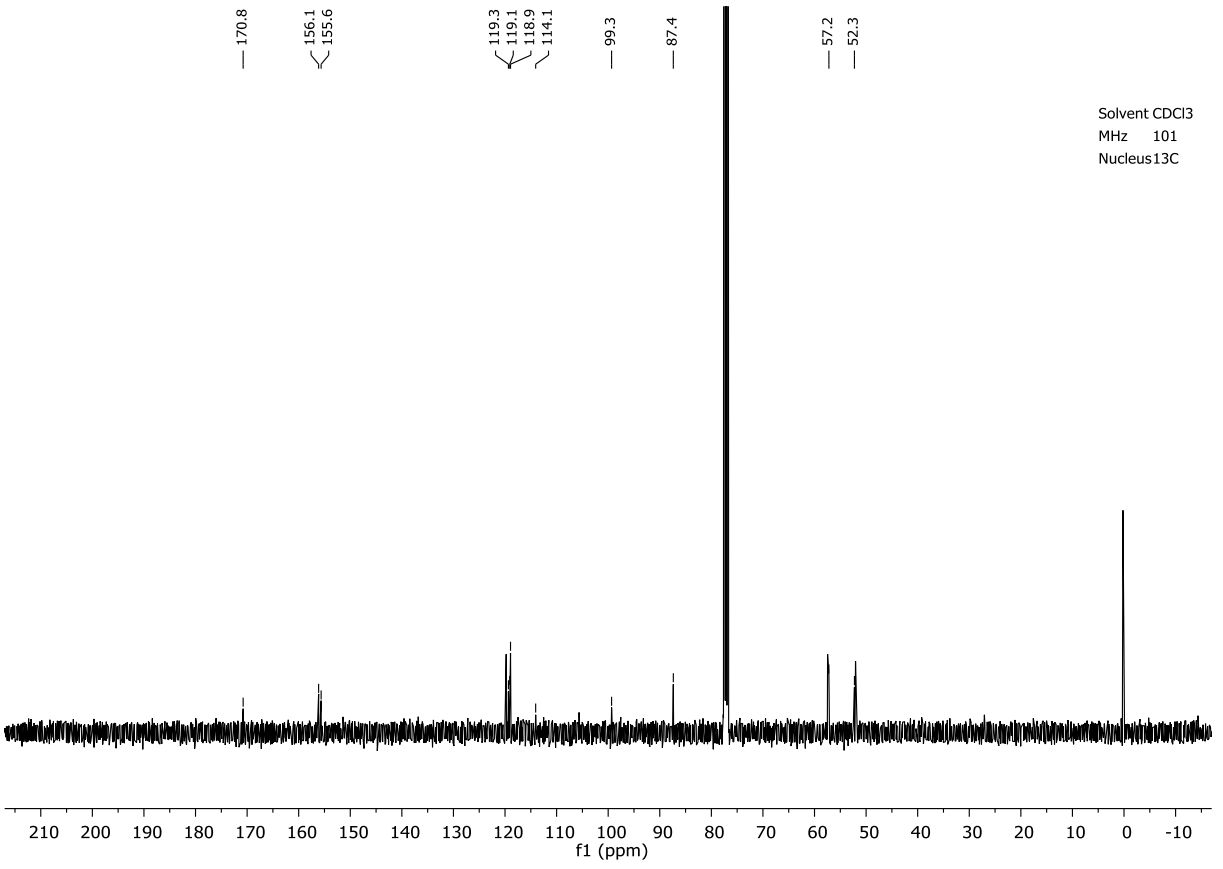

Solvent CDCl3
MHz 700
Nucleus1H
1.0
1.0
1.0
3.0
3.0
9.0
11 10 9 8 7 6 5 4 3 2 1 0
f1 (ppm)

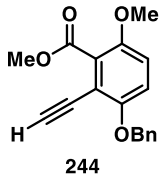

170.8
156.1
155.6
119.8
118.9
114.1
112.5
105.7
99.3
57.5
52.1
0.2
Solvent CDCl3
MHz 176
Nucleus13C
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


O
OMe
MeO
H
OH

256

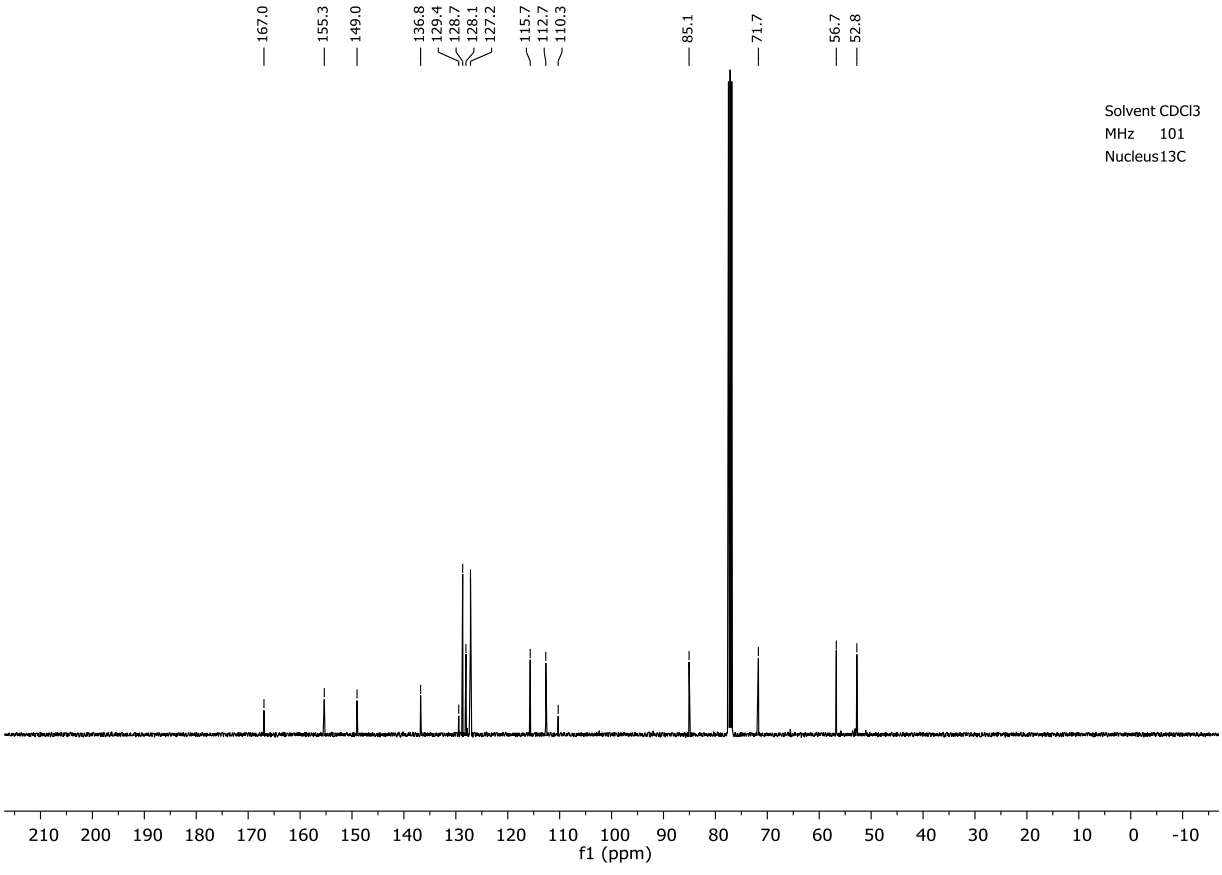
Solvent CDCl3
MHz 400
Nucleus1H
1.0
1.0
1.0
3.0
3.0
1.0
11 10 9 8 7 6 5 4 3 2 1 0
f1 (ppm)

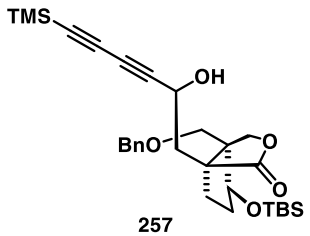

170.8
156.1
155.6
119.3
119.1
118.9
114.1
99.3
87.4
57.2
52.3
Solvent CDCl3
MHz 101
Nucleus13C
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


O
OMe
MeO
H
OBn

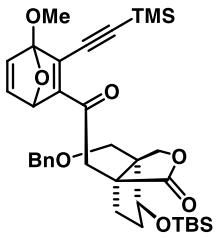
244

Solvent CDCl3
MHz 400
Nucleus1H
5.0
1.0
1.0
2.0
3.0
3.0
0.9
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

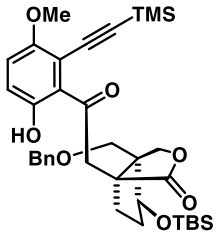

167.0
155.3
149.0
136.8
129.4
128.7
128.1
127.2
115.7
112.7
110.3
85.1
71.7
56.7
52.8
Solvent CDCl3
MHz 101
Nucleus13C
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)



257
d.r. 1:1.9

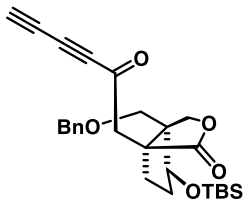


261
d.r. 1:1.3


OMe
TMS
O
HO
BnO
O
O
OTBS

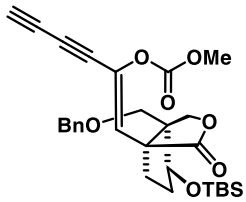
262

Solvent CDCl3
MHz 400
Nucleus1H
f1 (ppm)

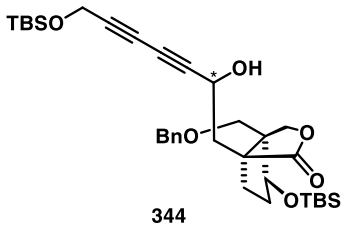

O
BnO
O
O
OTBS

259

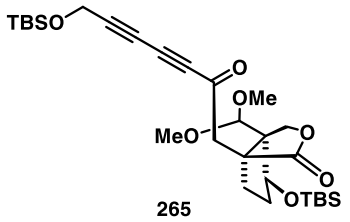
Solvent CDCl3
MHz 400
Nucleus1H
f1 (ppm)



260

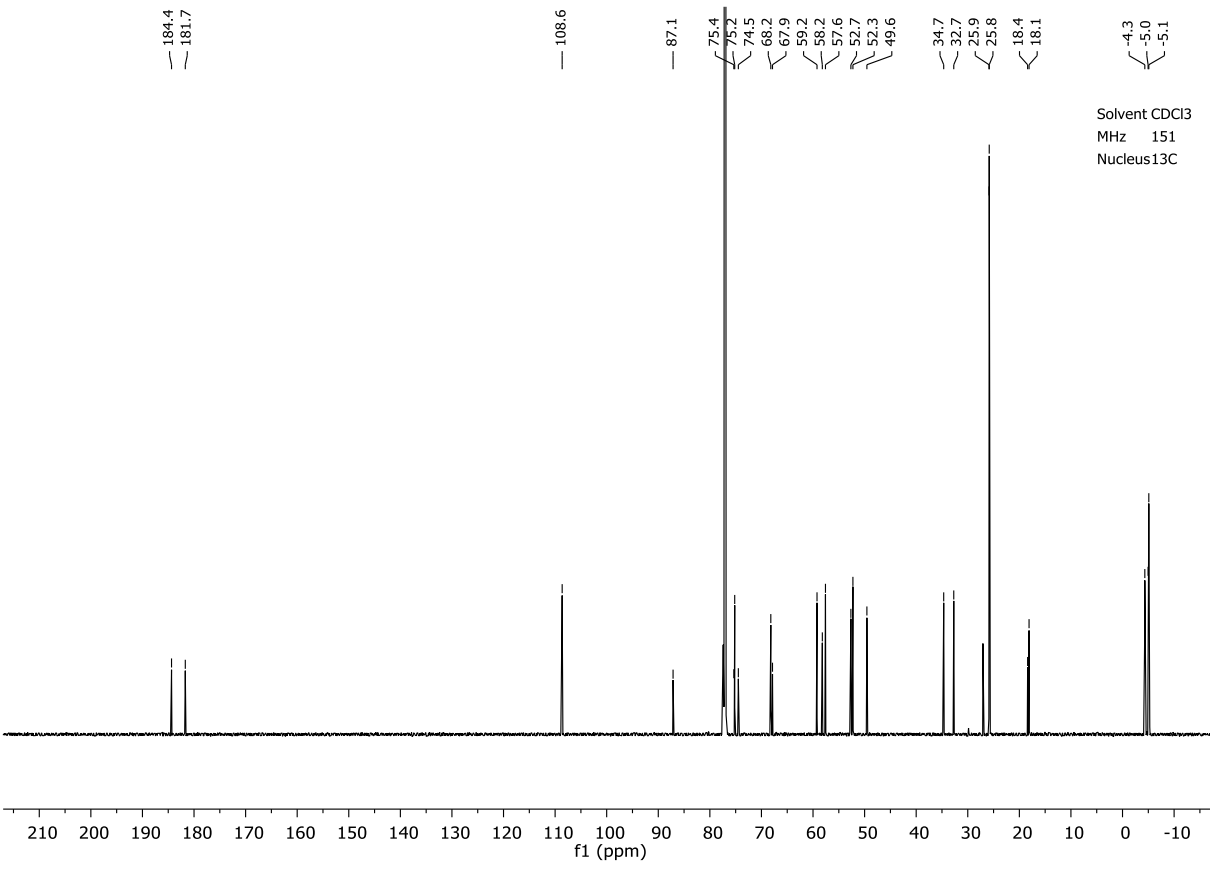


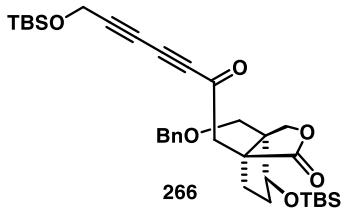
344
dr: 1.3:1


TBSO
O
OMe
MeO
O
O
OTBS

265

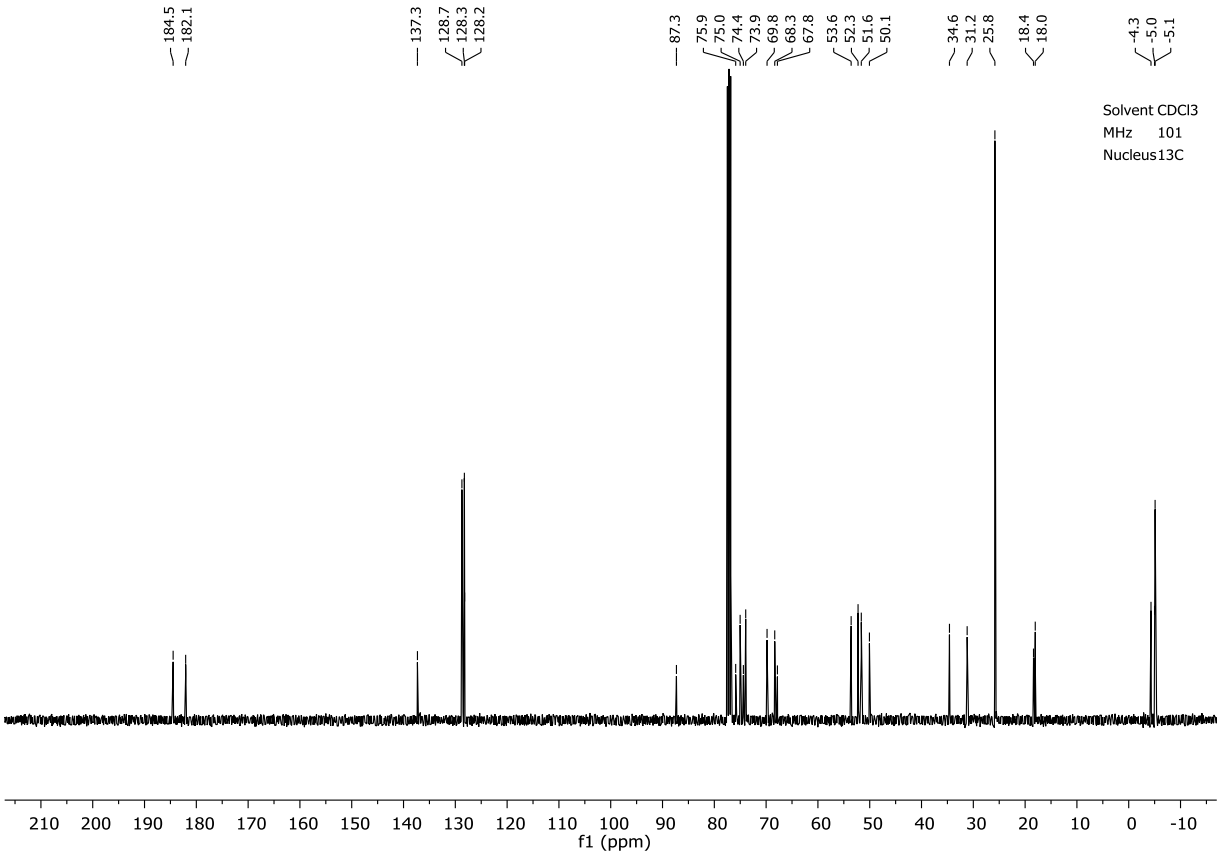
Solvent CDCl3
MHz 600
Nucleus1H
1.0
1.0
2.0
1.0
1.0
6.0
1.0
1.0
2.0
1.0
1.0
18.1
6.0
6.0
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

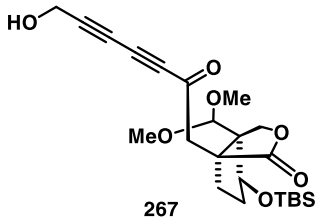

184.4
181.7
108.6
87.1
75.4
75.2
74.5
68.2
67.9
59.2
58.2
57.6
52.7
52.3
49.6
34.7
32.7
25.9
25.8
18.4
18.1
-4.3
-5.0
-5.1
Solvent CDCl3
MHz 151
Nucleus13C
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


TBSO
O
BnO
O
O
OTBS

266

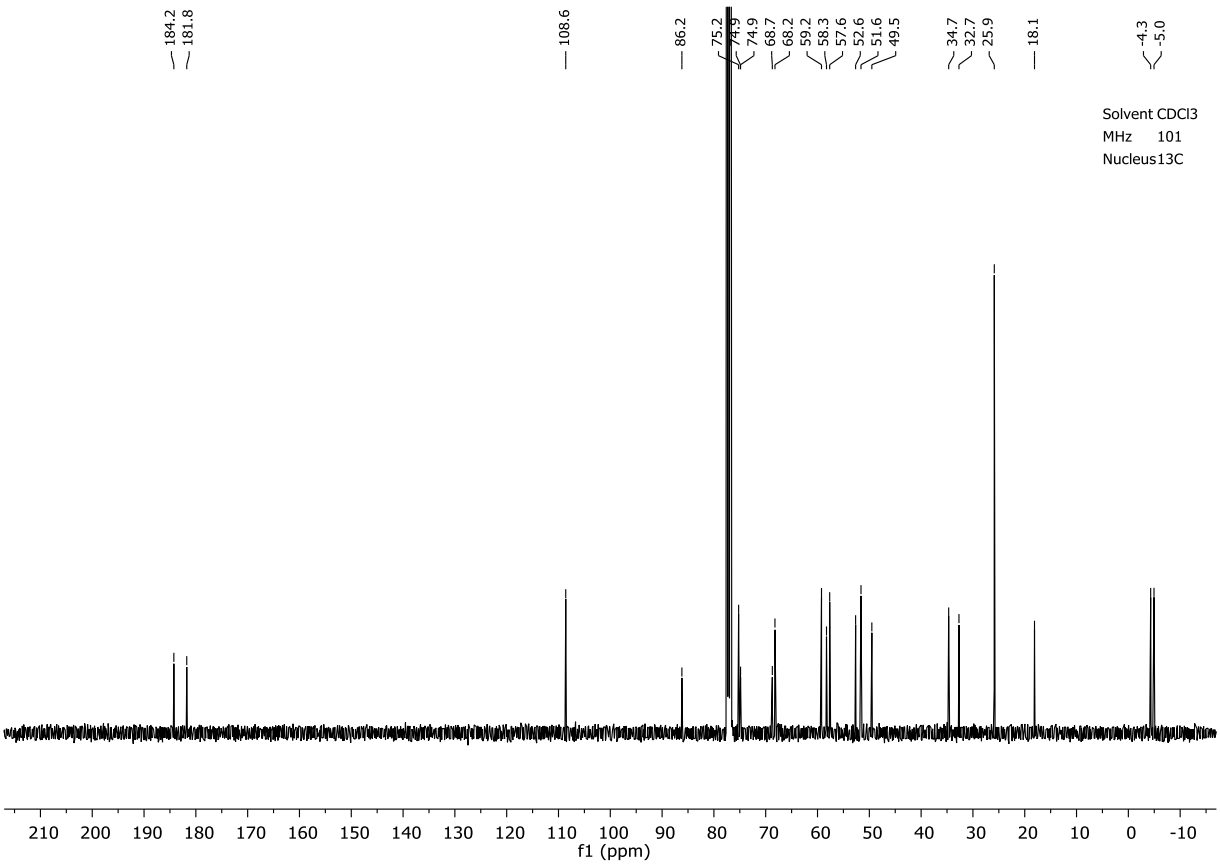
Solvent CDCl3
MHz 400
Nucleus1H
5.1
1.0
2.0
3.0
1.0
1.0
2.0
1.0
1.0
1.0
1.1
1.0
18.1
6.1
6.0
f1 (ppm)

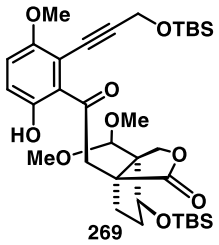

184.5
182.1
137.3
128.7
128.3
128.2
87.3
75.9
75.0
74.4
73.9
69.8
68.3
67.8
53.6
52.3
51.6
50.1
34.6
31.2
25.8
18.4
18.0
-4.3
-5.0
-5.1
Solvent CDCl3
MHz 101
Nucleus13C
f1 (ppm)


HO
O
OMe
MeO
O
O
OTBS

267

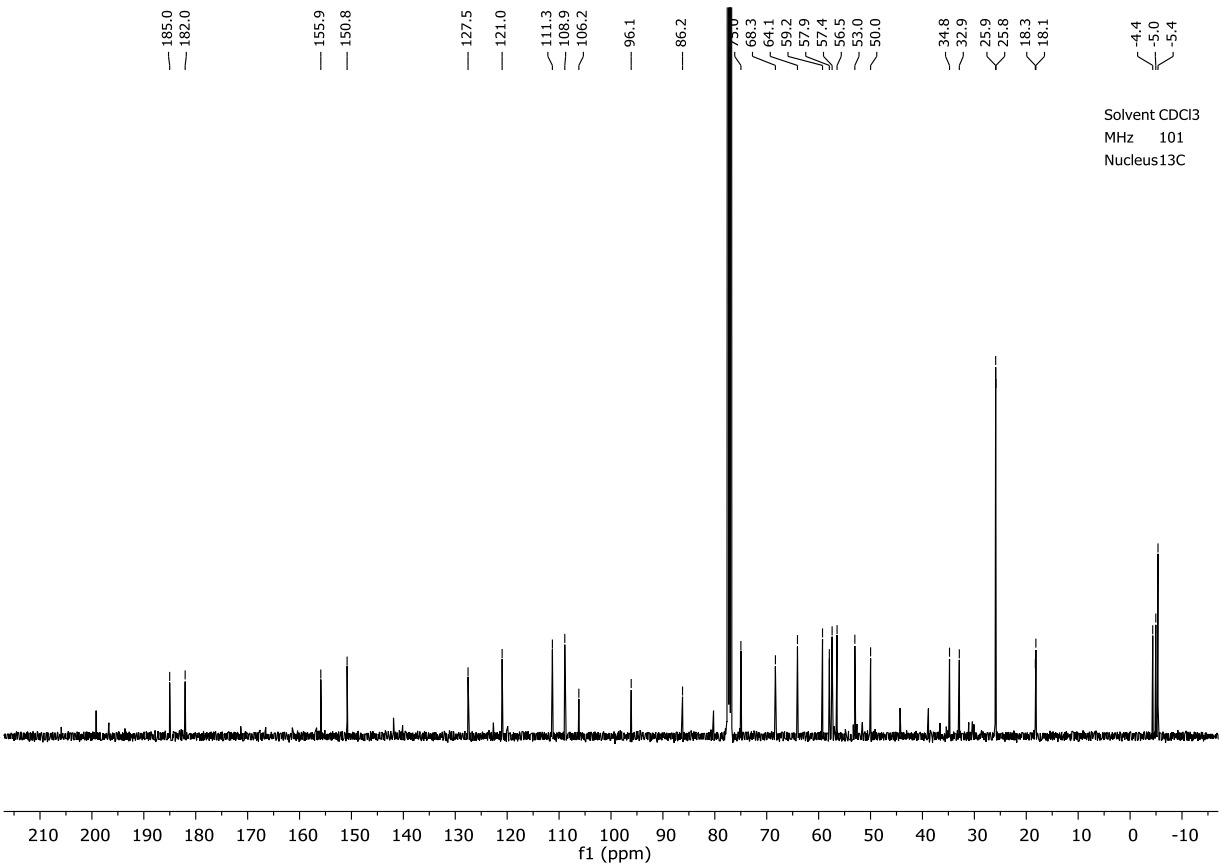
Solvent CDCl3
MHz 400
Nucleus1H
1.0
1.0
2.0
1.0
1.0
6.0
1.0
1.0
2.1
1.0
1.0
9.0
6.0
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

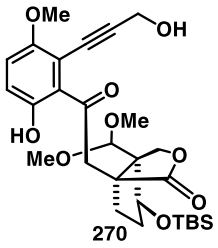

184.2
181.8
108.6
86.2
75.2
74.9
74.9
68.7
68.2
59.2
58.3
57.6
52.6
51.6
49.5
34.7
32.7
25.9
18.1
-4.3
-5.0
Solvent CDCl3
MHz 101
Nucleus13C
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


OMe
OTBS
O
OMe
HO
MeO
O
O
OTBS

269

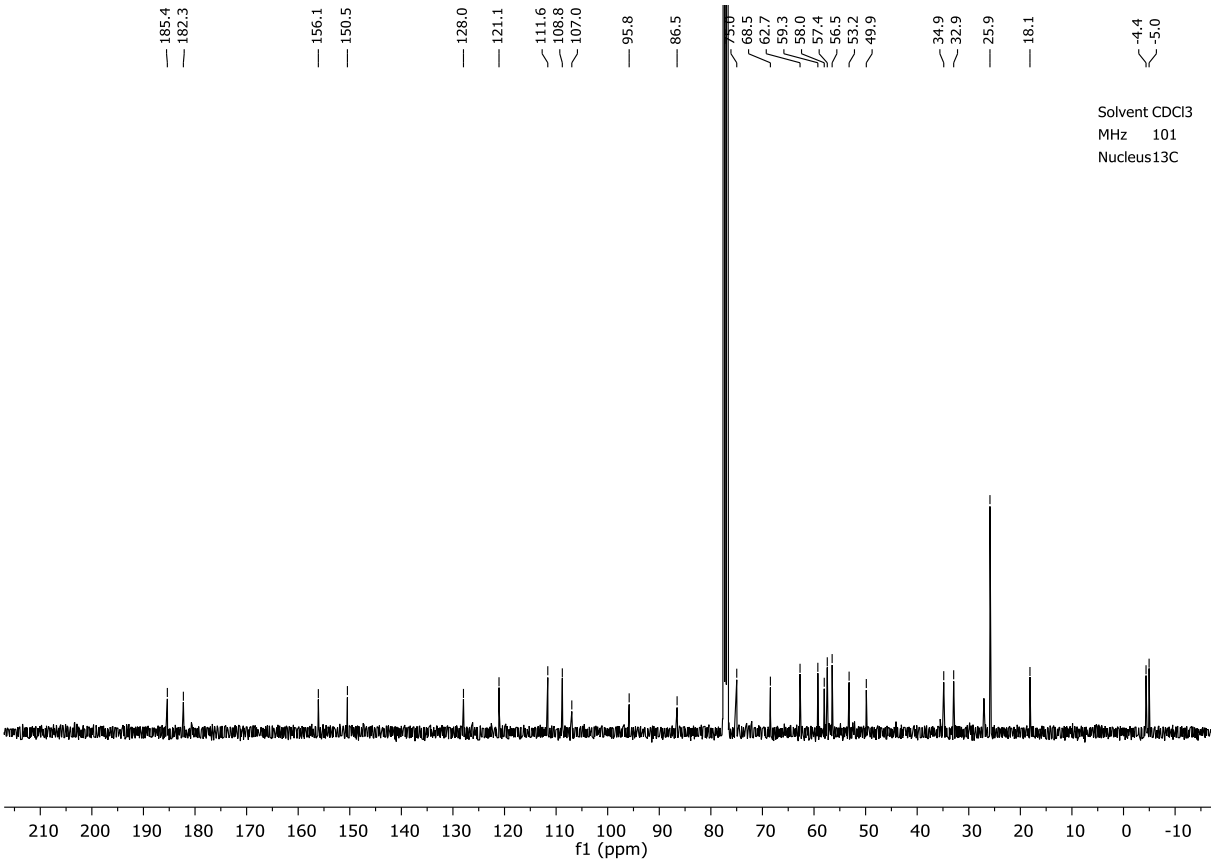
Solvent CDCl3
MHz 400
Nucleus1H
1.0
1.0
1.0
2.0
1.0
1.0
1.0
3.0
3.0
3.0
2.0
1.0
1.0
1.0
1.0
9.0
9.0
6.0
6.0
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

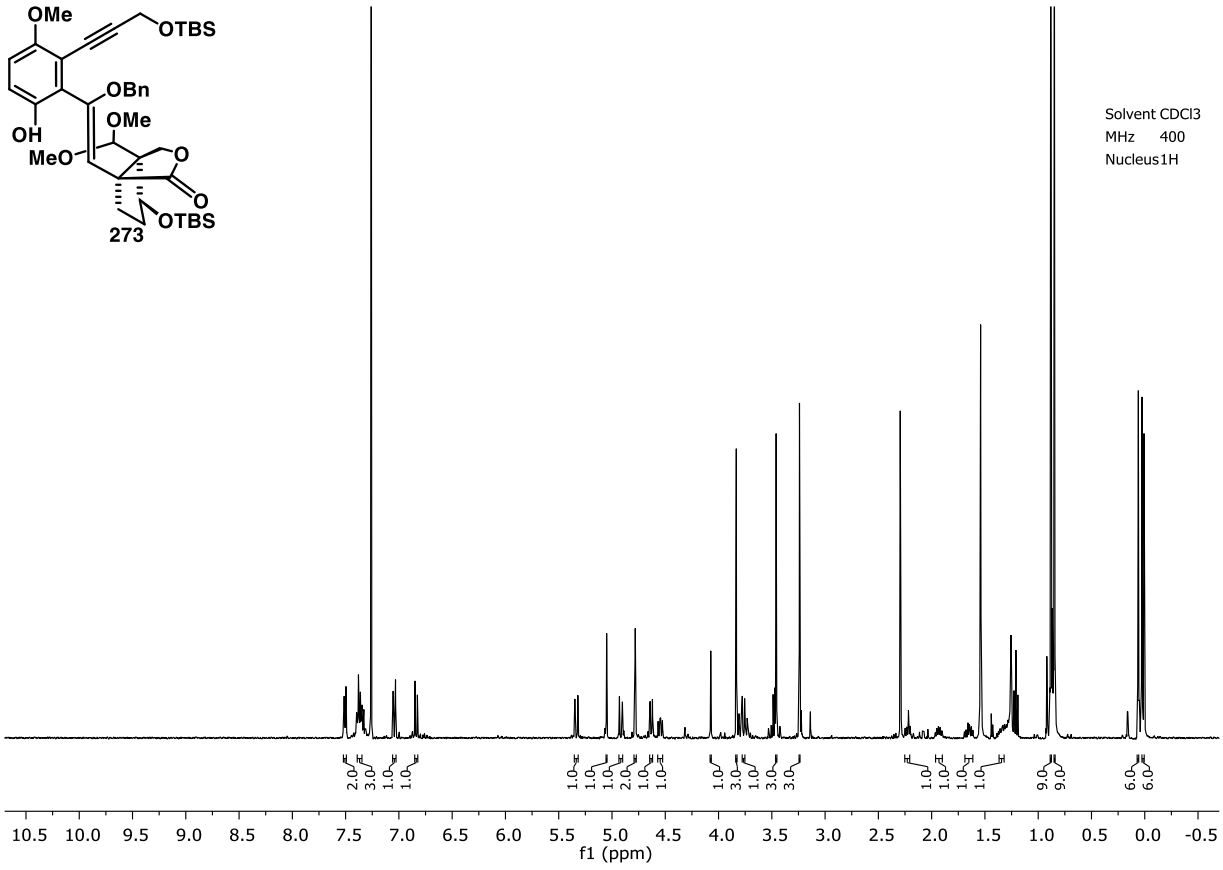

185.0
182.0
155.9
150.8
127.5
121.0
111.3
108.9
106.2
96.1
86.2
75.0
68.3
64.1
59.2
57.9
57.4
56.5
53.0
50.0
34.8
32.9
25.9
25.8
18.3
18.1
-4.4
-5.0
-5.4
Solvent CDCl3
MHz 101
Nucleus13C
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

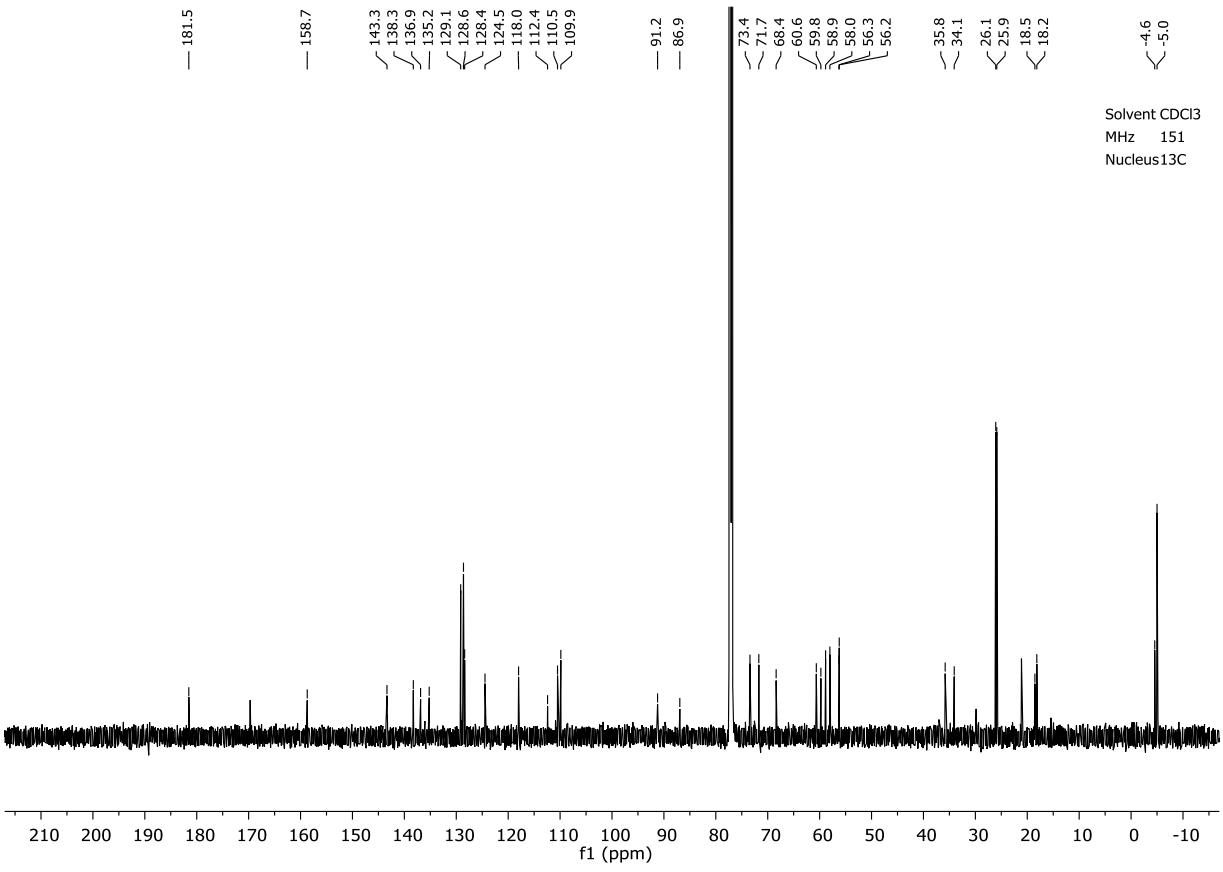

OMe
OH
O
OMe
HO
MeO
O
O
OTBS

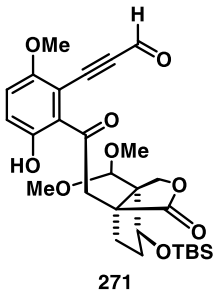
270

Solvent CDCl3
MHz 400
Nucleus1H
1.0 1.0 1.0 2.0 1.0 1.0 1.0 3.0 6.0 2.0 1.0 1.0 1.0 9.0 6.0
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)


185.4
182.3
156.1
150.5
128.0
121.1
111.6
108.8
107.0
95.8
86.5
75.0
68.5
62.7
59.3
58.0
57.4
56.5
53.2
49.9
34.9
32.9
25.9
18.1
-4.4
-5.0
Solvent CDCl3
MHz 101
Nucleus13C
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

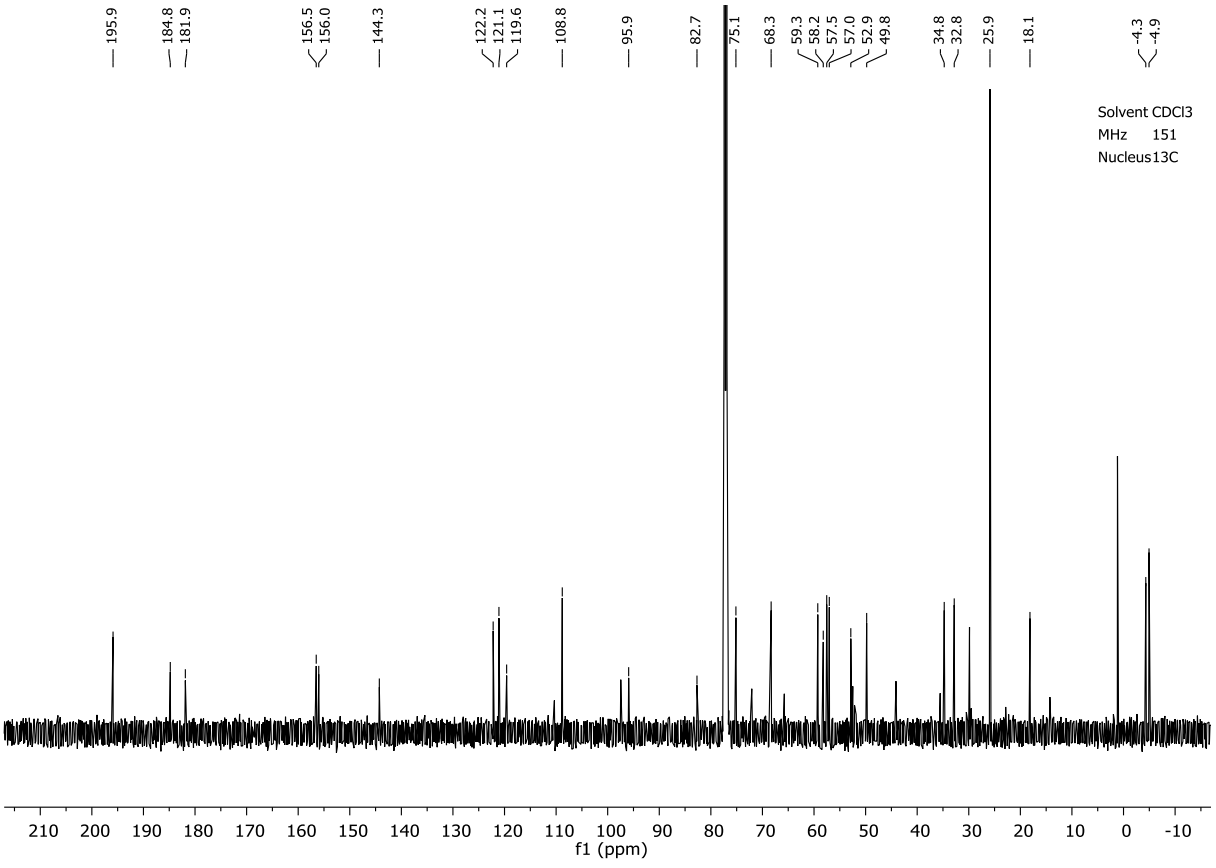

OMe
OTBS
OBn
OMe
OH
MeO
O
O
OTBS
273
Solvent CDCl3
MHz 400
Nucleus1H
f1 (ppm)

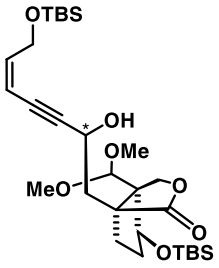

181.5
158.7
143.3
138.3
136.9
135.2
129.1
128.6
128.4
124.5
118.0
112.4
110.5
109.9
91.2
86.9
73.4
71.7
68.4
60.6
59.8
58.9
58.0
56.3
56.2
35.8
34.1
26.1
25.9
18.5
18.2
-4.6
-5.0
Solvent CDCl3
MHz 151
Nucleus13C
f1 (ppm)


H
OMe
O
O
OMe
HO
MeO
O
O
OTBS

271

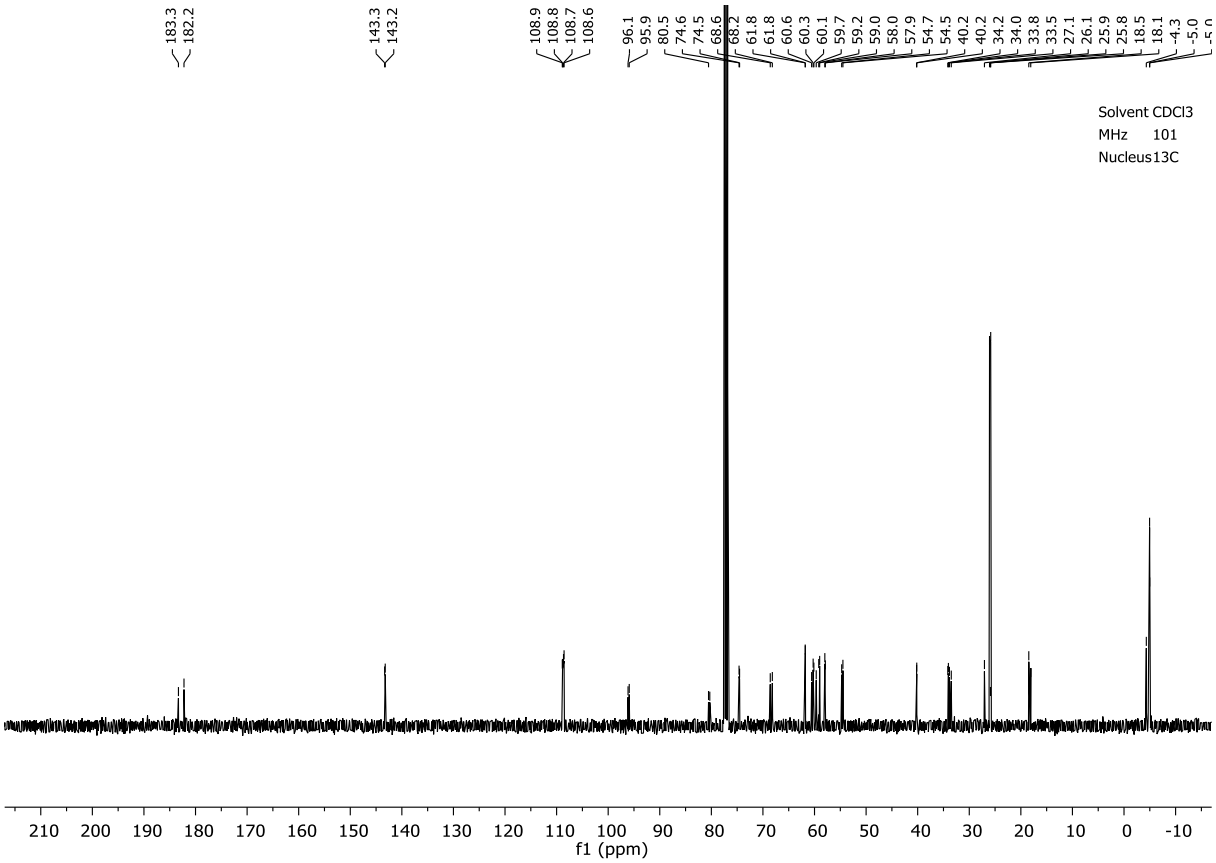
Solvent CDCl3
MHz 600
Nucleus1H
1.0
1.0
1.0
1.0
1.0
1.0
1.0
3.0
6.0
2.0
1.0
1.0
1.0
9.0
12.0
11
10
9
8
7
6
5
4
3
2
1
0
f1 (ppm)

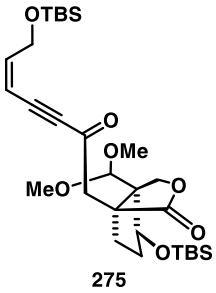

195.9
184.8
181.9
156.5
156.0
144.3
122.2
121.1
119.6
108.8
95.9
82.7
75.1
68.3
59.3
58.2
57.5
57.0
52.9
49.8
34.8
32.8
25.9
18.1
-4.3
-4.9
Solvent CDCl3
MHz 151
Nucleus13C
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)


OTBS
OH
OMe
MeO
O
O
OTBS

345
dr: 1:1

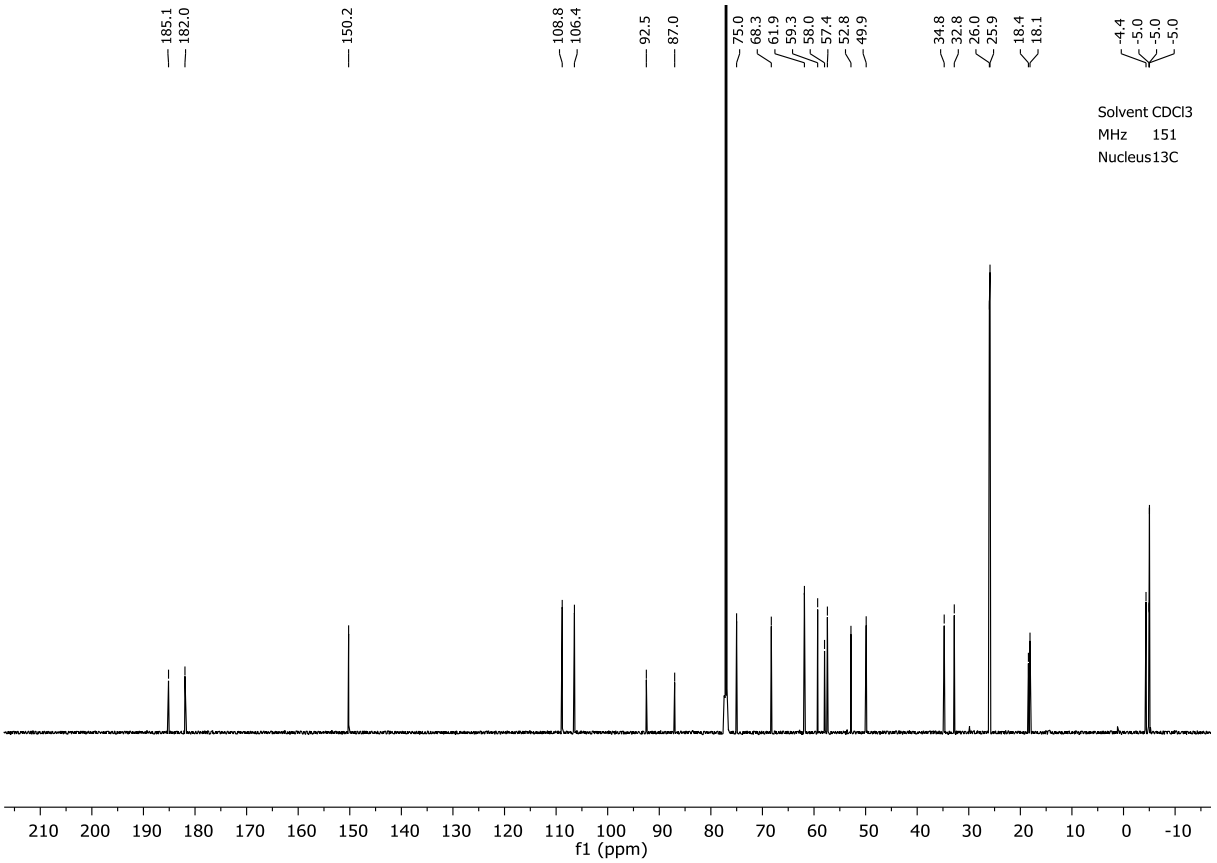
Solvent CDCl3
MHz 400
Nucleus1H
f1 (ppm)

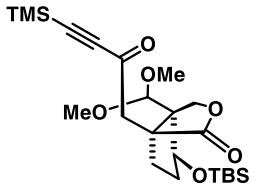

Solvent CDCl3
MHz 101
Nucleus13C
f1 (ppm)


OTBS
O
OMe
MeO
O
O
OTBS

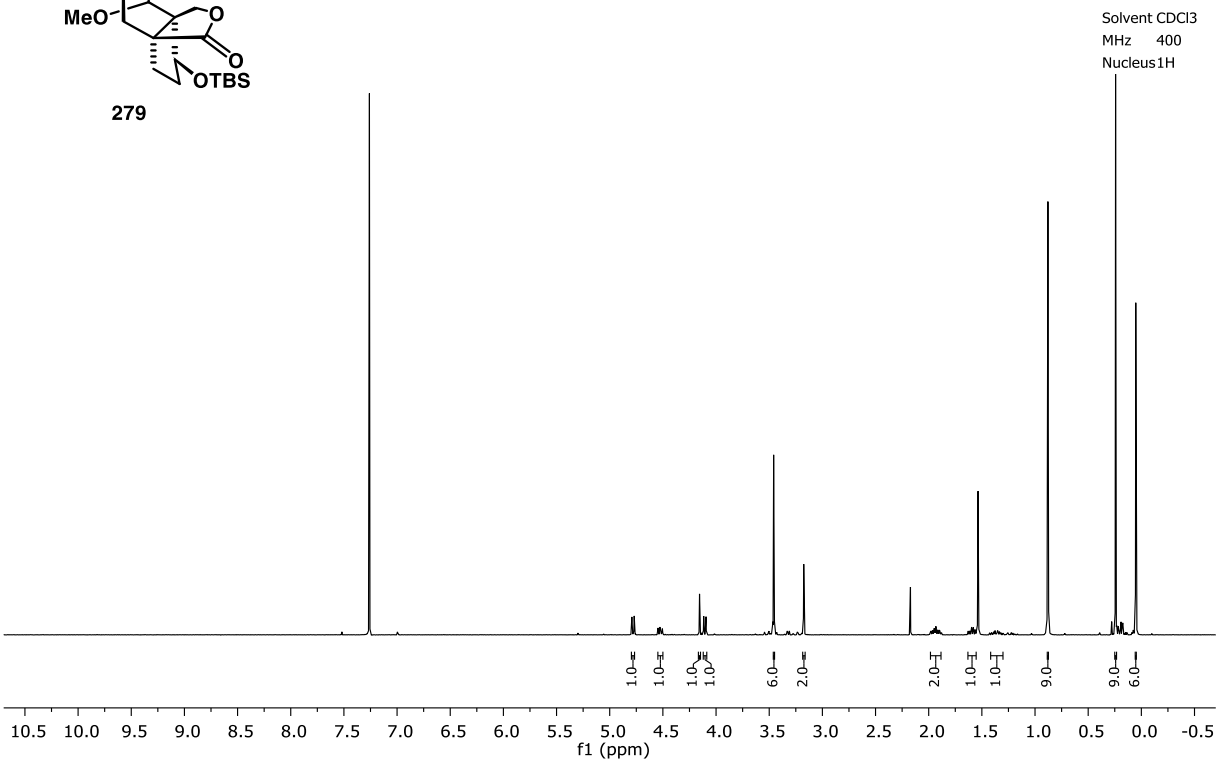
275

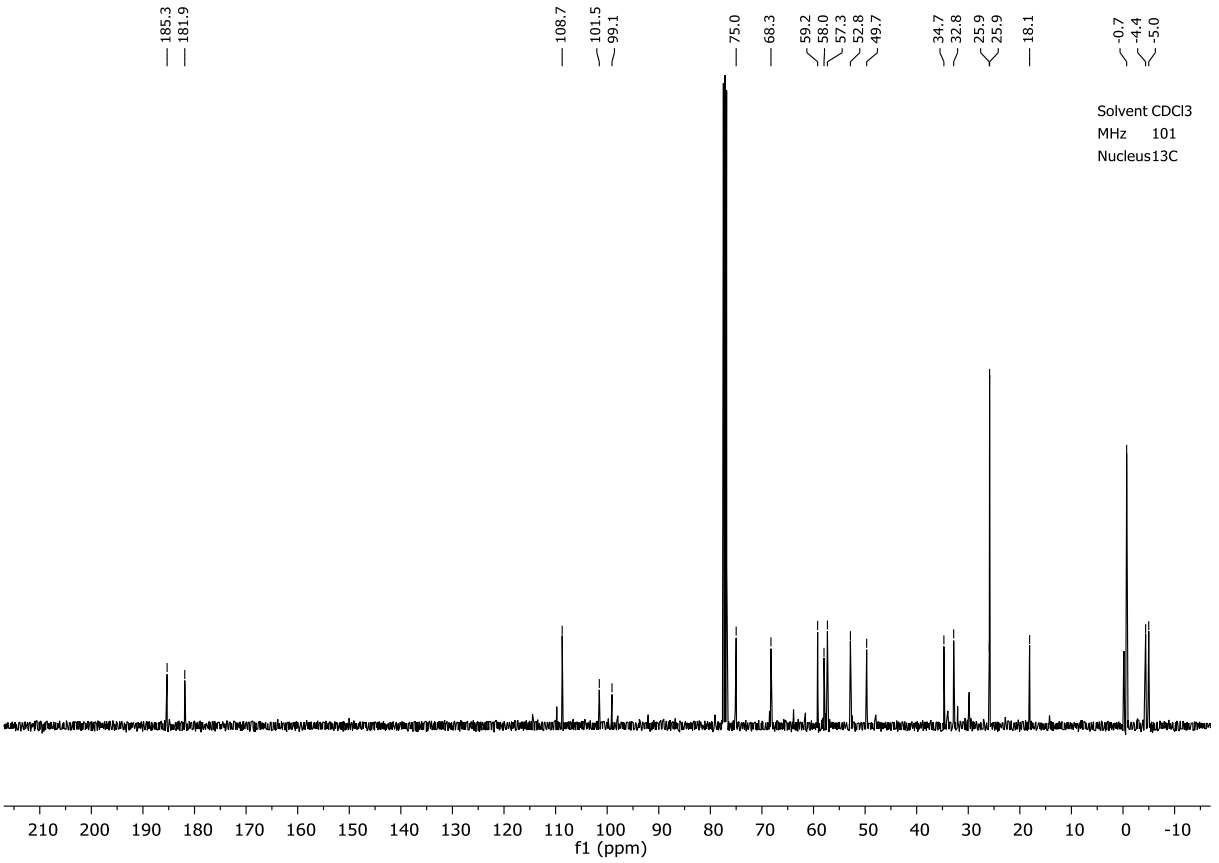
Solvent CDCl3
MHz 600
Nucleus1H
1.0 1.0 1.0 1.0 2.0 1.0 1.0 6.0 2.0 1.0 1.0 1.0 9.0 9.0 6.0 6.0
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

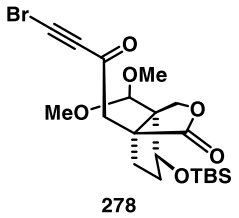

185.1
182.0
150.2
108.8
106.4
92.5
87.0
75.0
68.3
61.9
59.3
58.0
57.4
52.8
49.9
34.8
32.8
26.0
25.9
18.4
18.1
-4.4
-5.0
-5.0
-5.0
Solvent CDCl3
MHz 151
Nucleus13C
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


TMS
O
OMe
MeO
O
O
OTBS

279

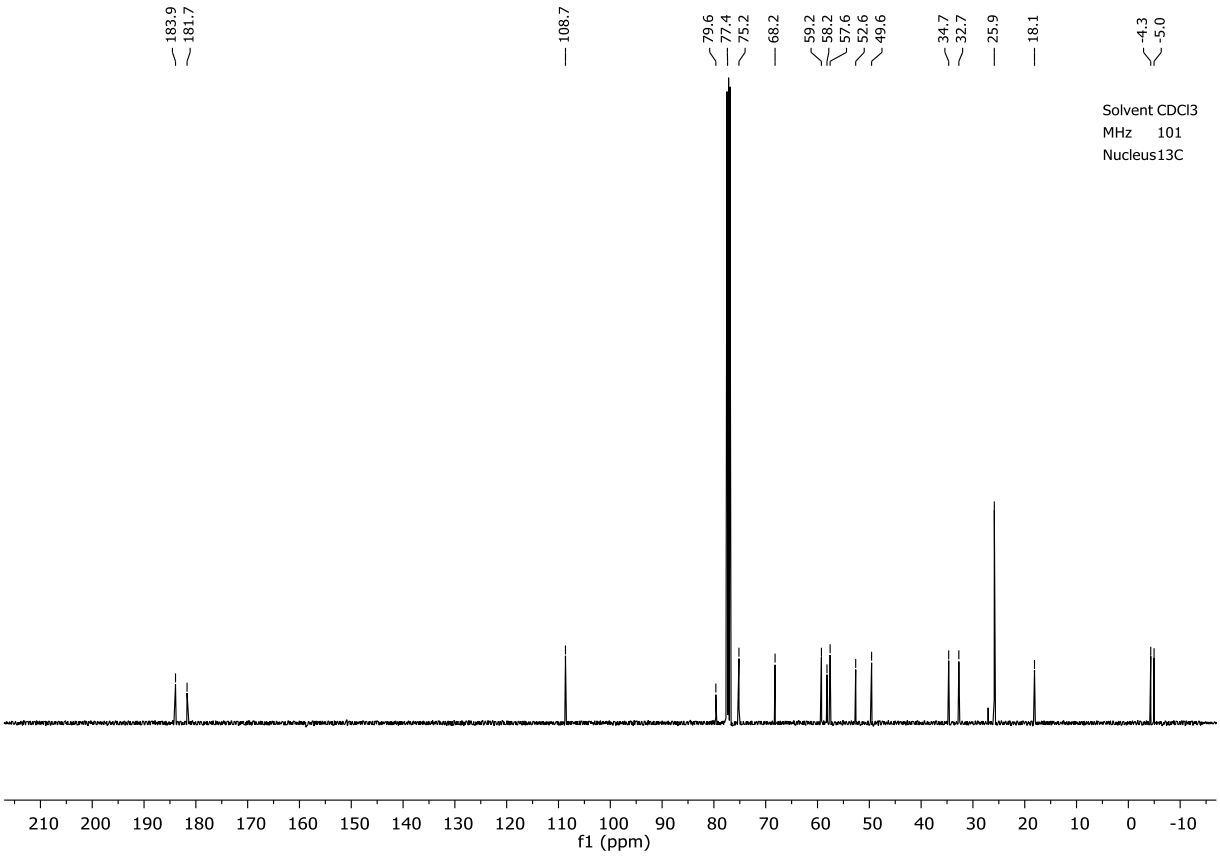

Solvent CDCl3
MHz 400
Nucleus1H
1.0
1.0
1.0
1.0
6.0
2.0
2.0
1.0
1.0
9.0
9.0
6.0
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

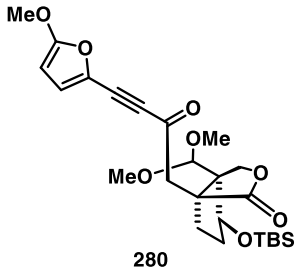

185.3
181.9
108.7
101.5
99.1
75.0
68.3
59.2
58.0
57.3
52.8
49.7
34.7
32.8
25.9
25.9
18.1
-0.7
-4.4
-5.0
Solvent CDCl3
MHz 101
Nucleus13C
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


Br
O
OMe
MeO
O
O
OTBS

278

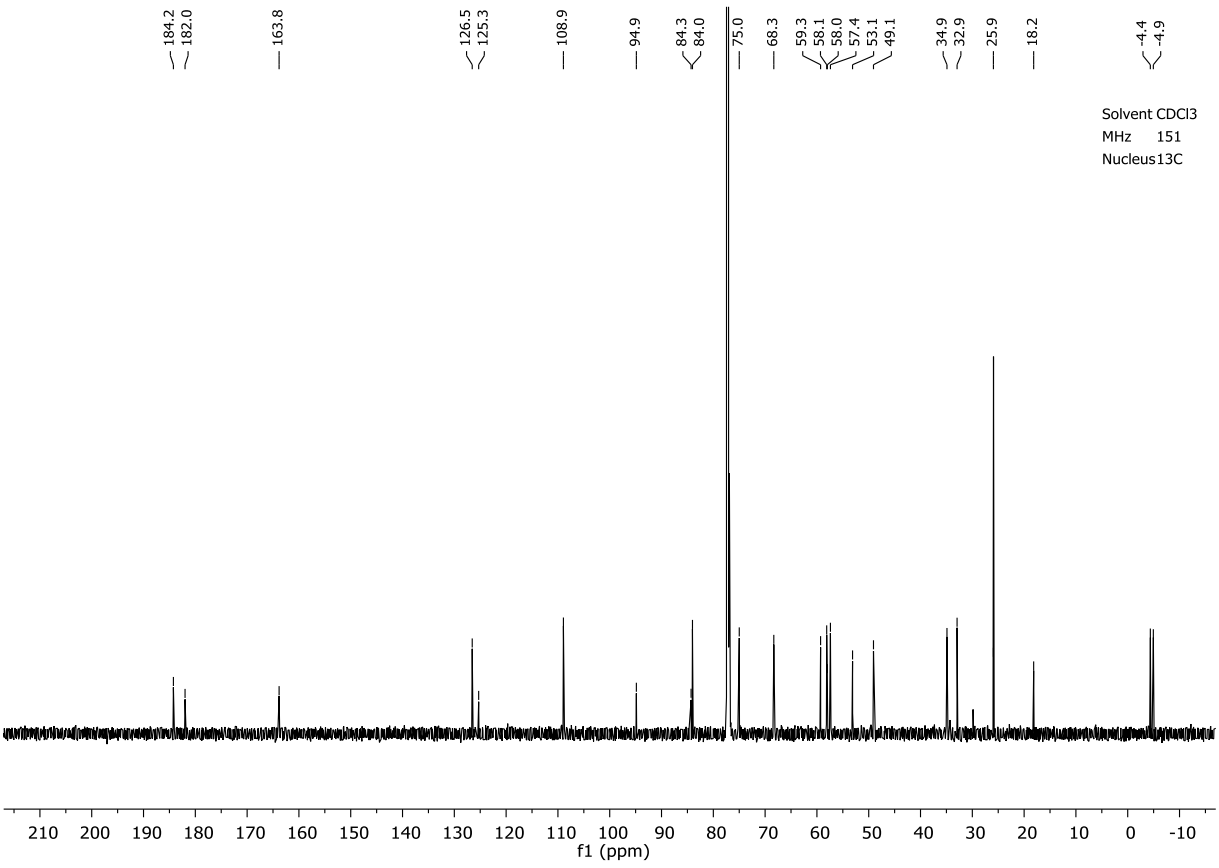
Solvent CDCl3
MHz 400
Nucleus1H
1.0
1.0
1.0
1.0
6.1
2.1
2.1
1.0
1.0
9.0
6.0
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

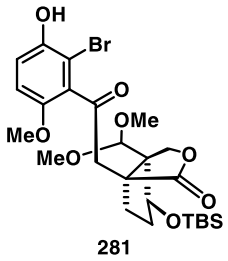

183.9
181.7
108.7
79.6
77.4
75.2
68.2
59.2
58.2
57.6
52.6
49.6
34.7
32.7
25.9
18.1
-4.3
-5.0
Solvent CDCl3
MHz 101
Nucleus13C
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


MeO
O
O
OMe
MeO
O
O
OTBS

280

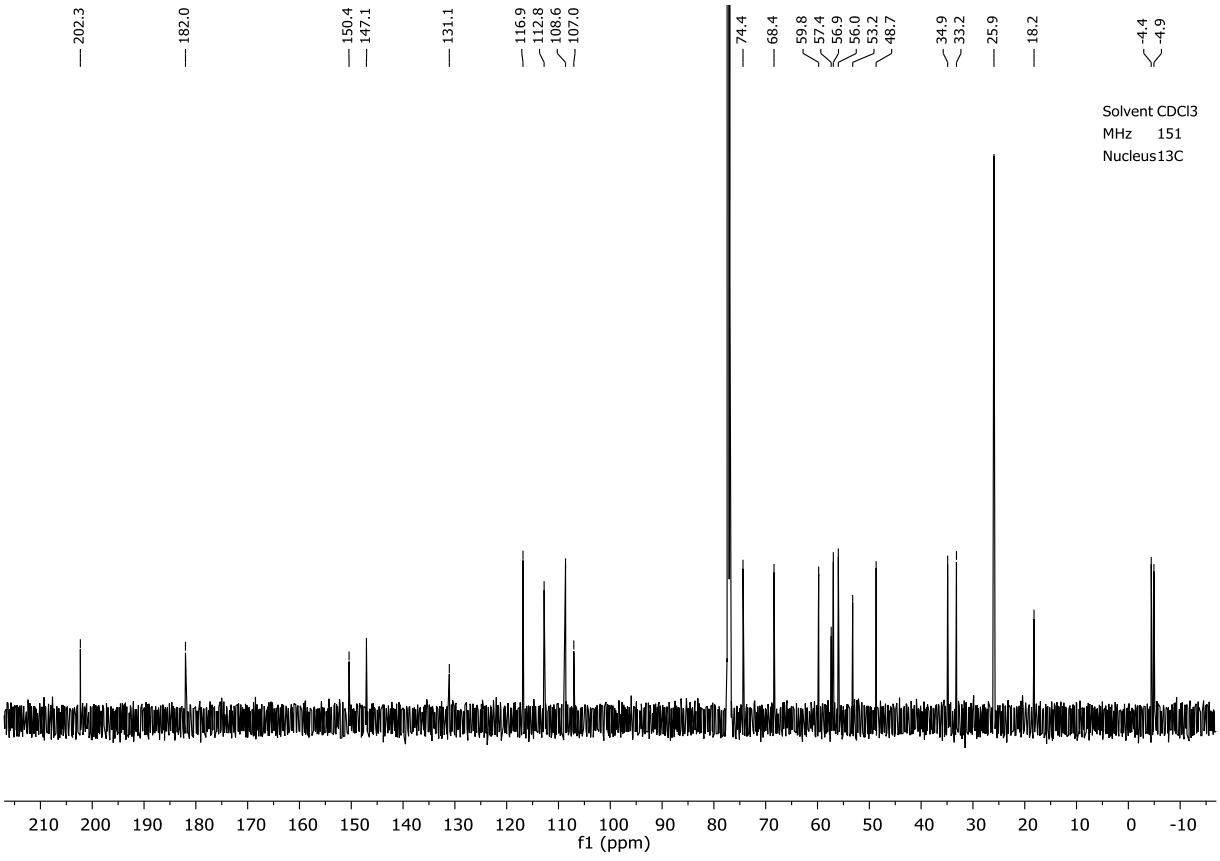
Solvent CDCl3
MHz 600
Nucleus1H
1.0
1.0
1.0
1.1
1.1
1.0
3.0
6.1
2.0
1.0
1.0
1.1
1.0
9.1
6.1
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

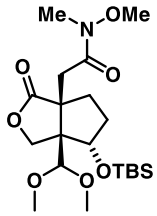

184.2
182.0
163.8
126.5
125.3
108.9
94.9
84.3
84.0
75.0
68.3
59.3
58.1
58.0
57.4
53.1
49.1
34.9
32.9
25.9
18.2
-4.4
-4.9
Solvent CDCl3
MHz 151
Nucleus13C
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


OH
Br
O
OMe
MeO
MeO
O
O
OTBS

281

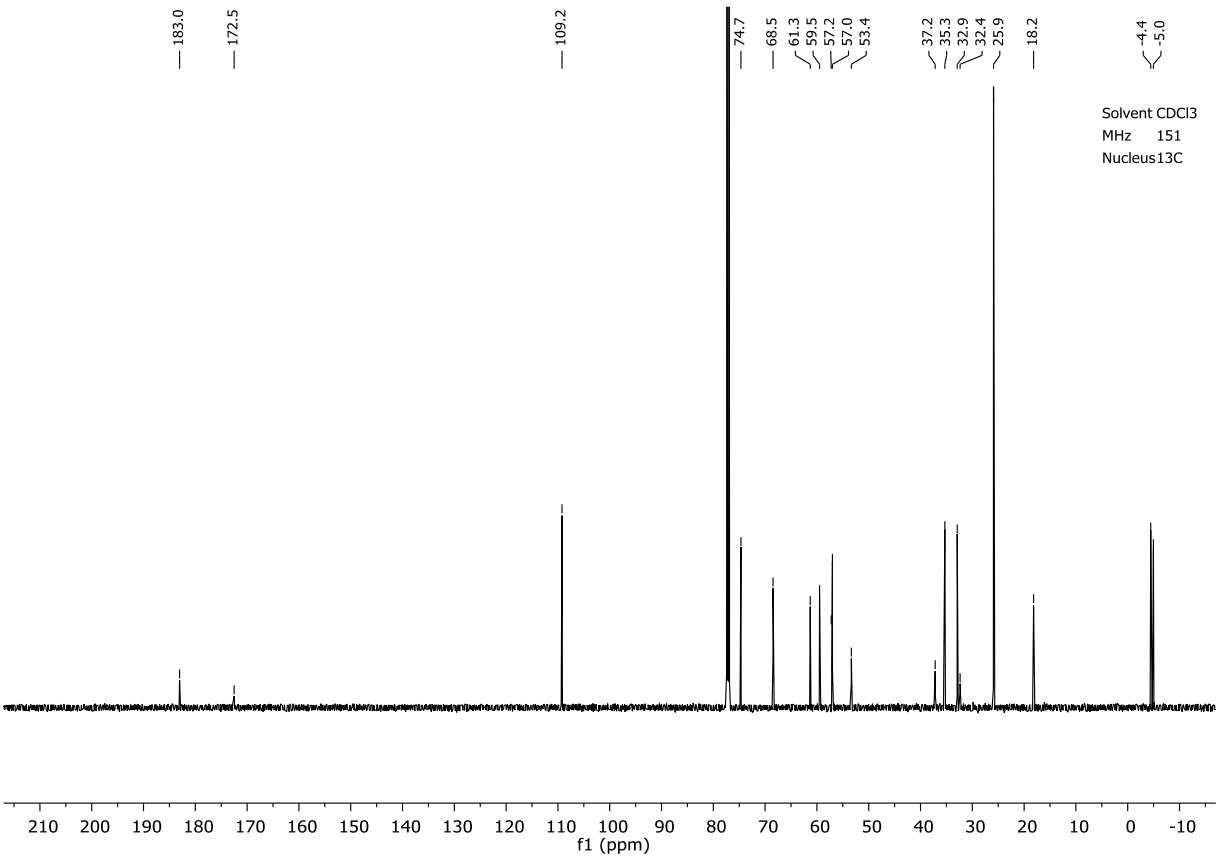
Solvent CDCl3
MHz 600
Nucleus1H
1.0 1.0 1.0 1.1 1.1 1.1 1.0 3.0 4.1 3.0 1.0 1.0 1.0 1.0 1.0 9.0 6.1
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

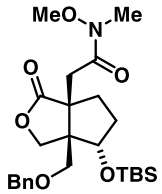

202.3
182.0
150.4
147.1
131.1
116.9
112.8
108.6
107.0
74.4
68.4
59.8
57.4
56.9
56.0
53.2
48.7
34.9
33.2
25.9
18.2
-4.4
-4.9
Solvent CDCl3
MHz 151
Nucleus13C
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


Me
N
OMe
O
O
O
O
O
O
OTBS

346

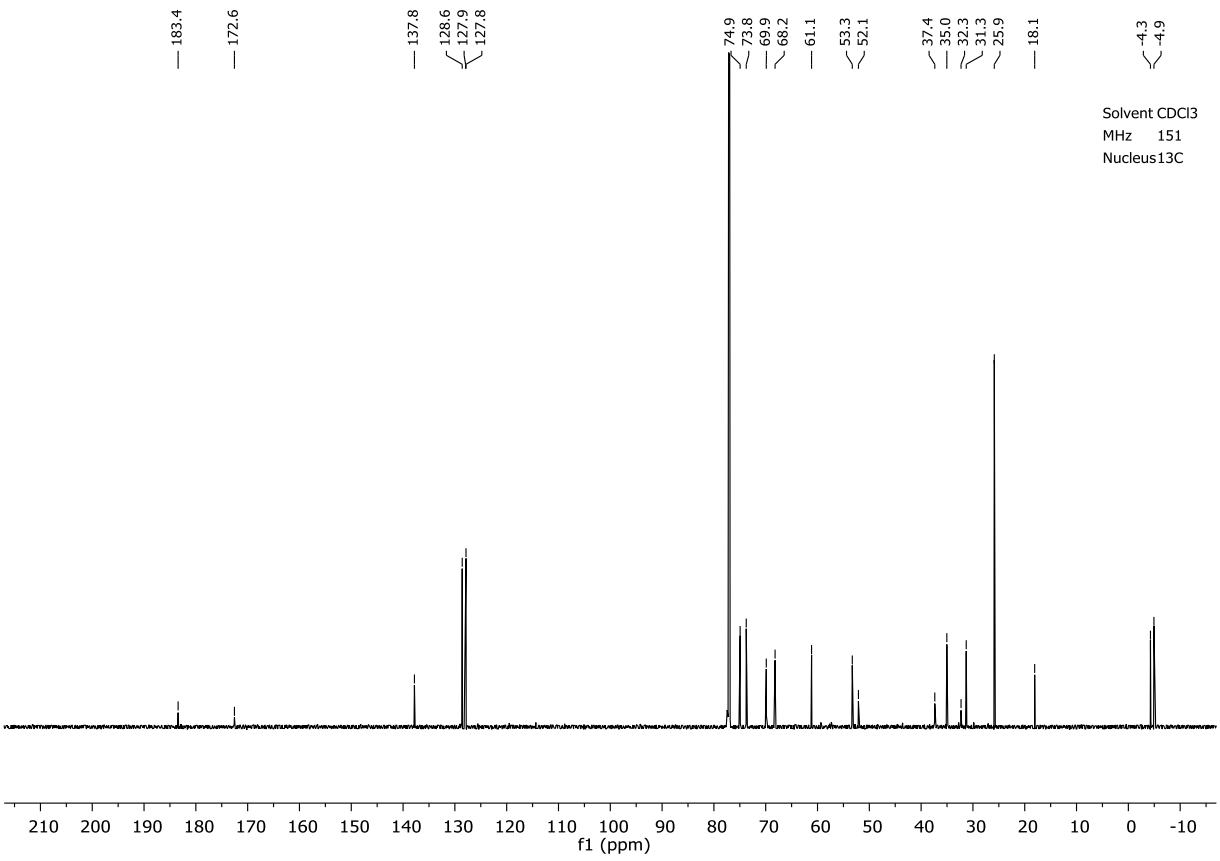
Solvent CDCl3
MHz 600
Nucleus1H
1.0
1.0
1.0
1.0
3.0
6.2
3.0
2.0
1.0
1.0
1.1
1.1
9.2
6.2
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

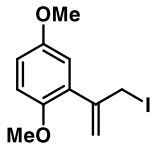

183.0
172.5
109.2
74.7
68.5
61.3
59.5
57.2
57.0
53.4
37.2
35.3
32.9
32.4
25.9
18.2
-4.4
-5.0
Solvent CDCl3
MHz 151
Nucleus13C
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


MeO
N
Me
O
O
O
BnO
OTBS

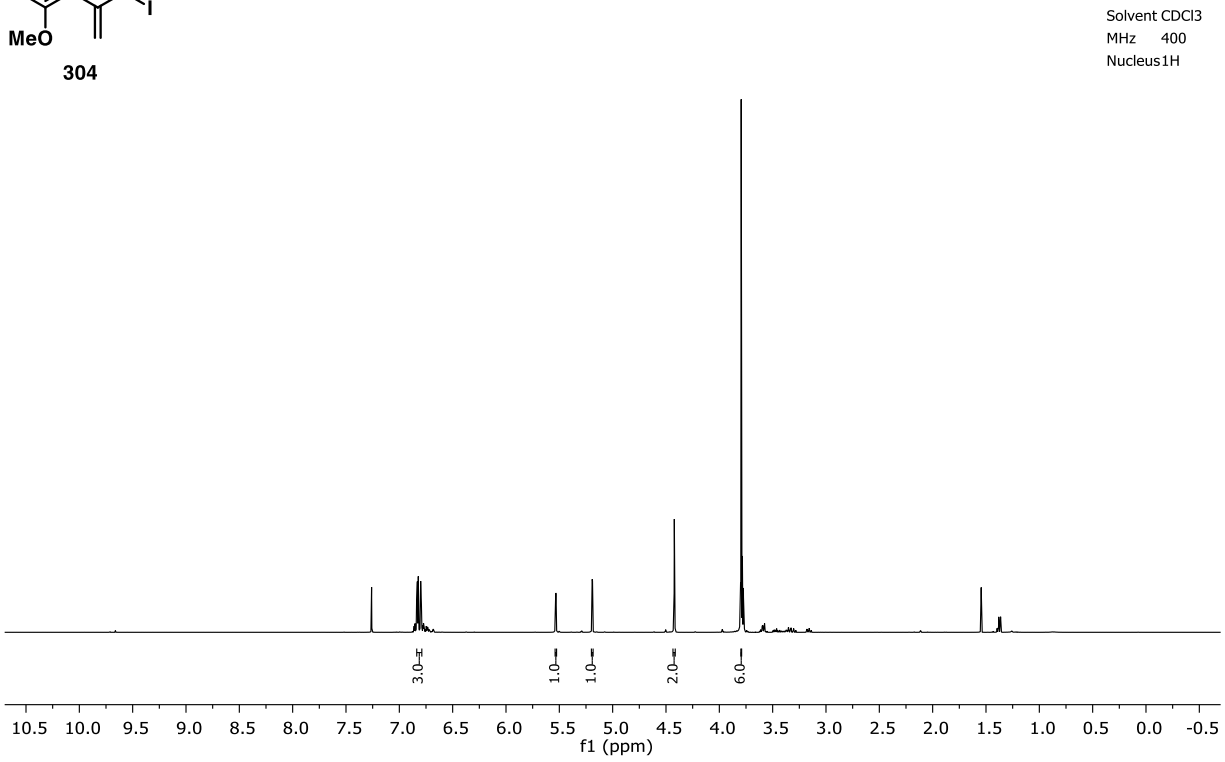
347

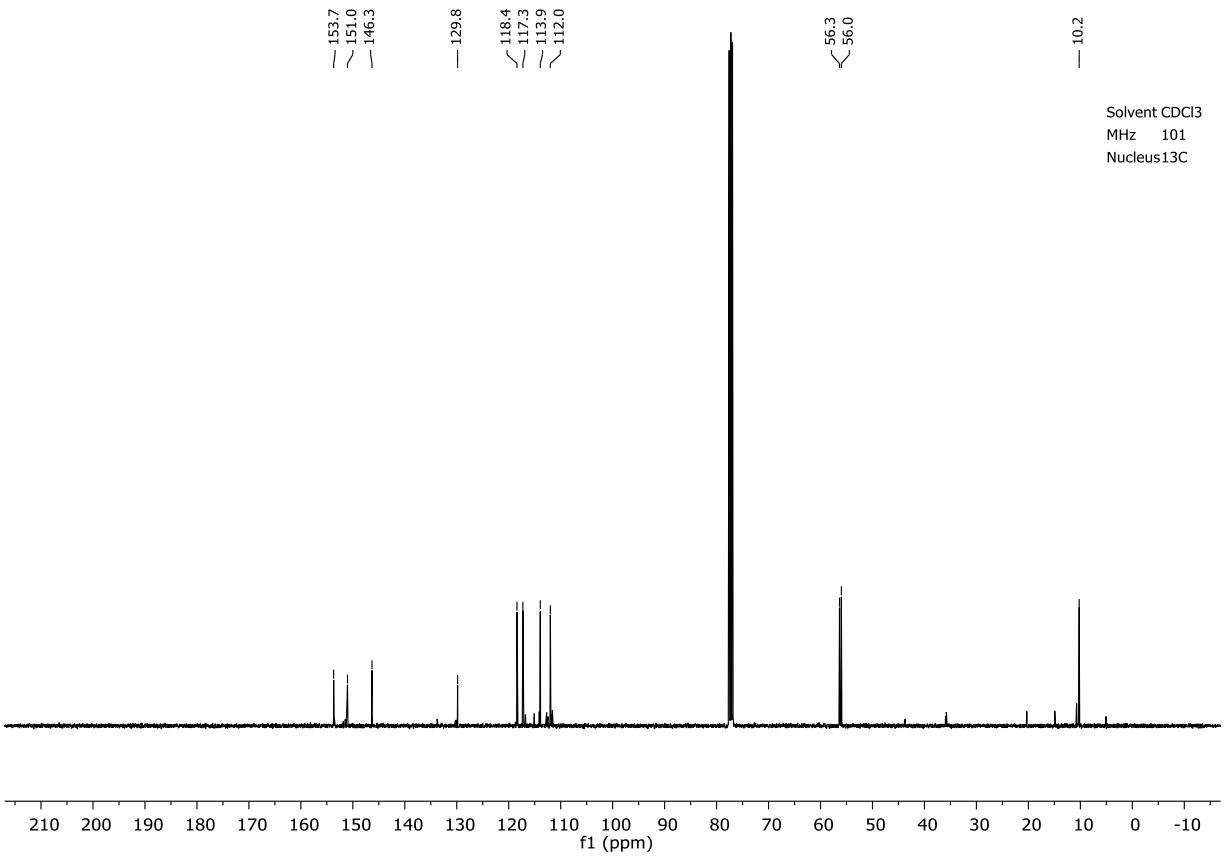
Solvent CDCl3
MHz 600
Nucleus1H
2.0
1.0
2.0
1.0
1.0
2.0
1.0
4.0
1.0
1.0
3.0
1.0
1.0
1.0
1.0
1.1
9.1
6.0
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

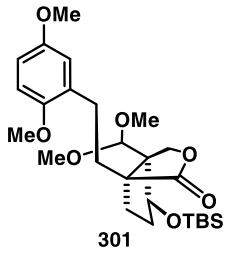

183.4
172.6
137.8
128.6
127.9
127.8
74.9
73.8
69.9
68.2
61.1
53.3
52.1
37.4
35.0
32.3
31.3
25.9
18.1
-4.3
-4.9
Solvent CDCl3
MHz 151
Nucleus13C
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


OMe
I
MeO

304

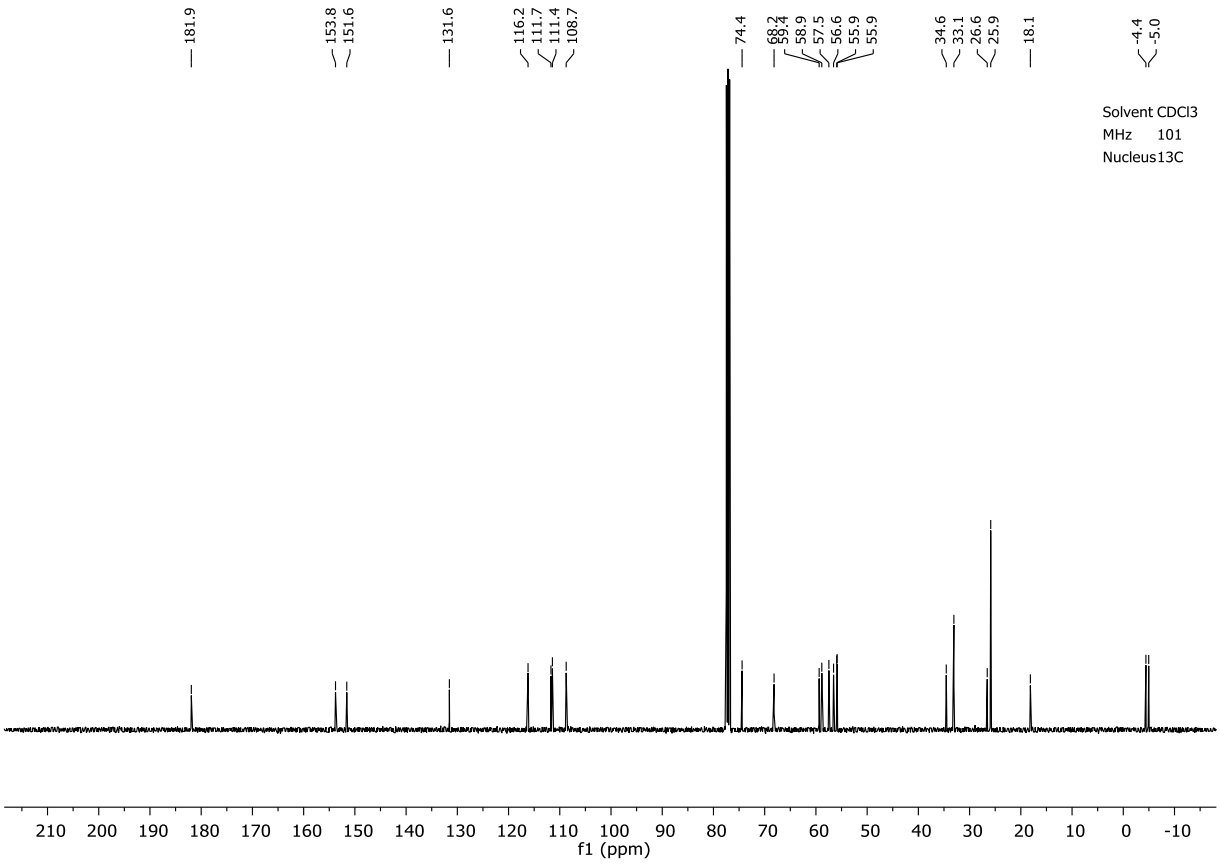

Solvent CDCl3
MHz 400
Nucleus1H
3.0
1.0
1.0
2.0
6.0
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

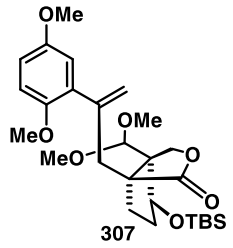

153.7
151.0
146.3
129.8
118.4
117.3
113.9
112.0
56.3
56.0
10.2
Solvent CDCl3
MHz 101
Nucleus13C
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


OMe
MeO
OMe
MeO
O
O
OTBS

301

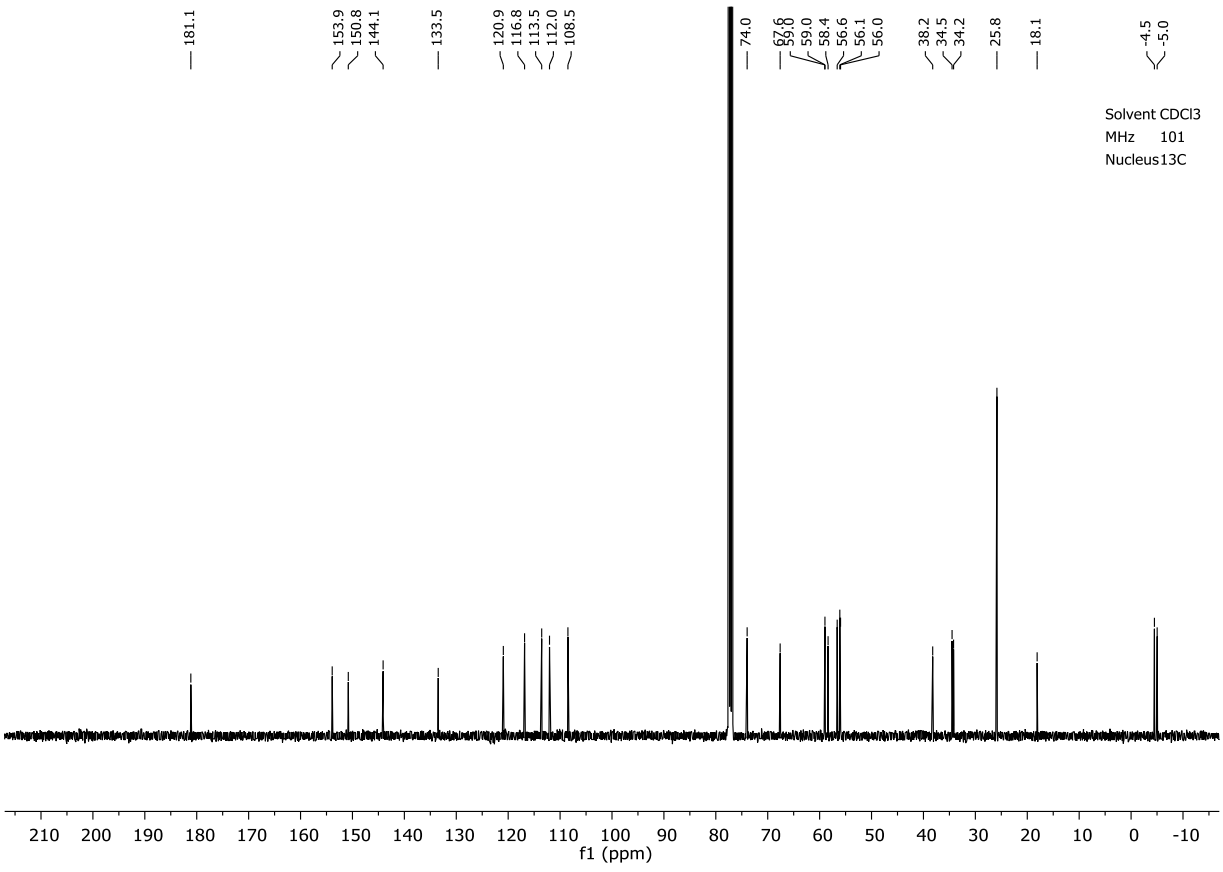
Solvent CDCl3
MHz 400
Nucleus1H
1.0
2.0
1.0
1.0
1.0
1.0
3.0
3.0
6.0
1.0
1.0
1.0
2.0
1.1
1.0
9.1
6.0
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

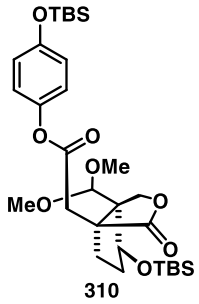

181.9
153.8
151.6
131.6
116.2
111.7
111.4
108.7
74.4
68.2
59.4
58.9
57.5
56.6
55.9
55.9
34.6
33.1
26.6
25.9
18.1
-4.4
-5.0
Solvent CDCl3
MHz 101
Nucleus13C
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


OMe
MeO
OMe
MeO
O
O
OTBS

307

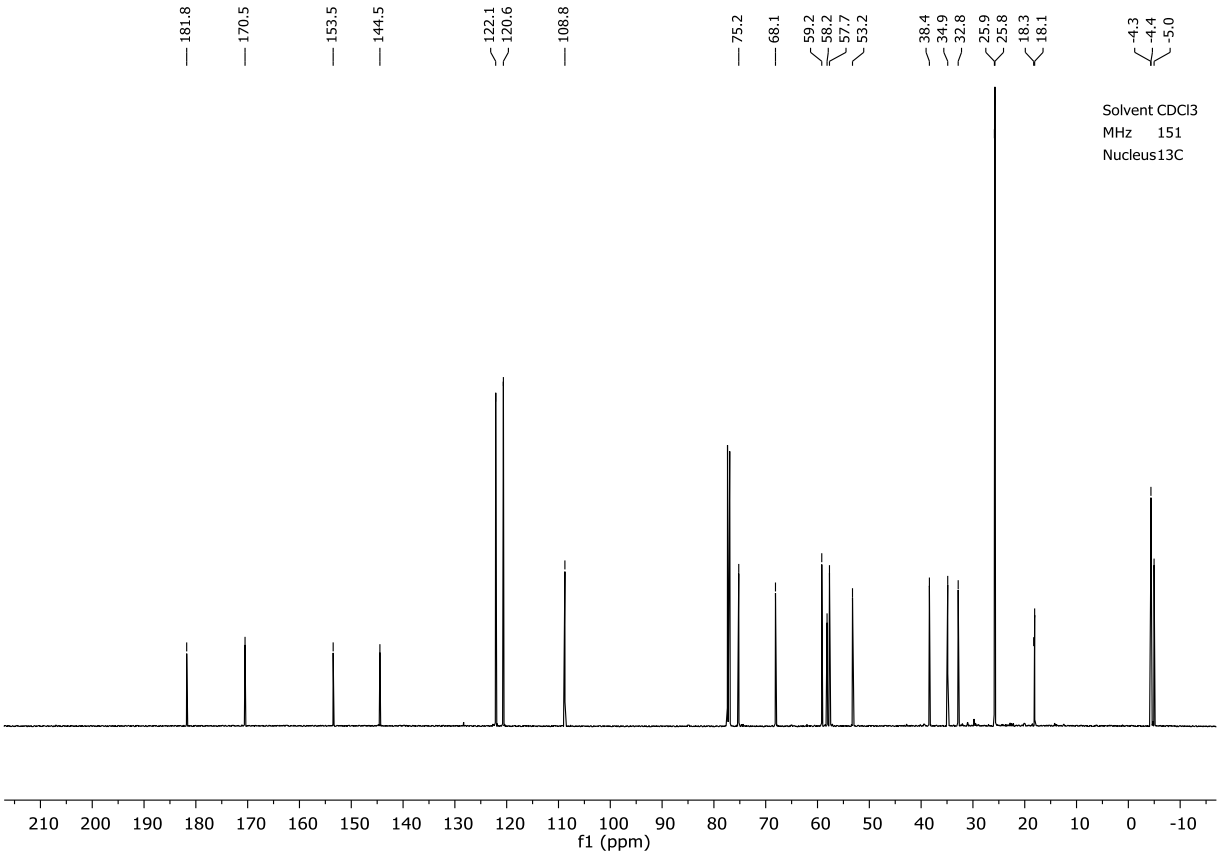
Solvent CDCl3
MHz 400
Nucleus1H
f1 (ppm)

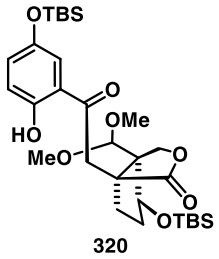

181.1
153.9
150.8
144.1
133.5
120.9
116.8
113.5
112.0
108.5
74.0
67.6
59.0
58.4
56.6
56.1
56.0
38.2
34.5
34.2
25.8
18.1
-4.5
-5.0
Solvent CDCl3
MHz 101
Nucleus13C
f1 (ppm)


OTBS
O
O
OMe
MeO
O
O
OTBS

310

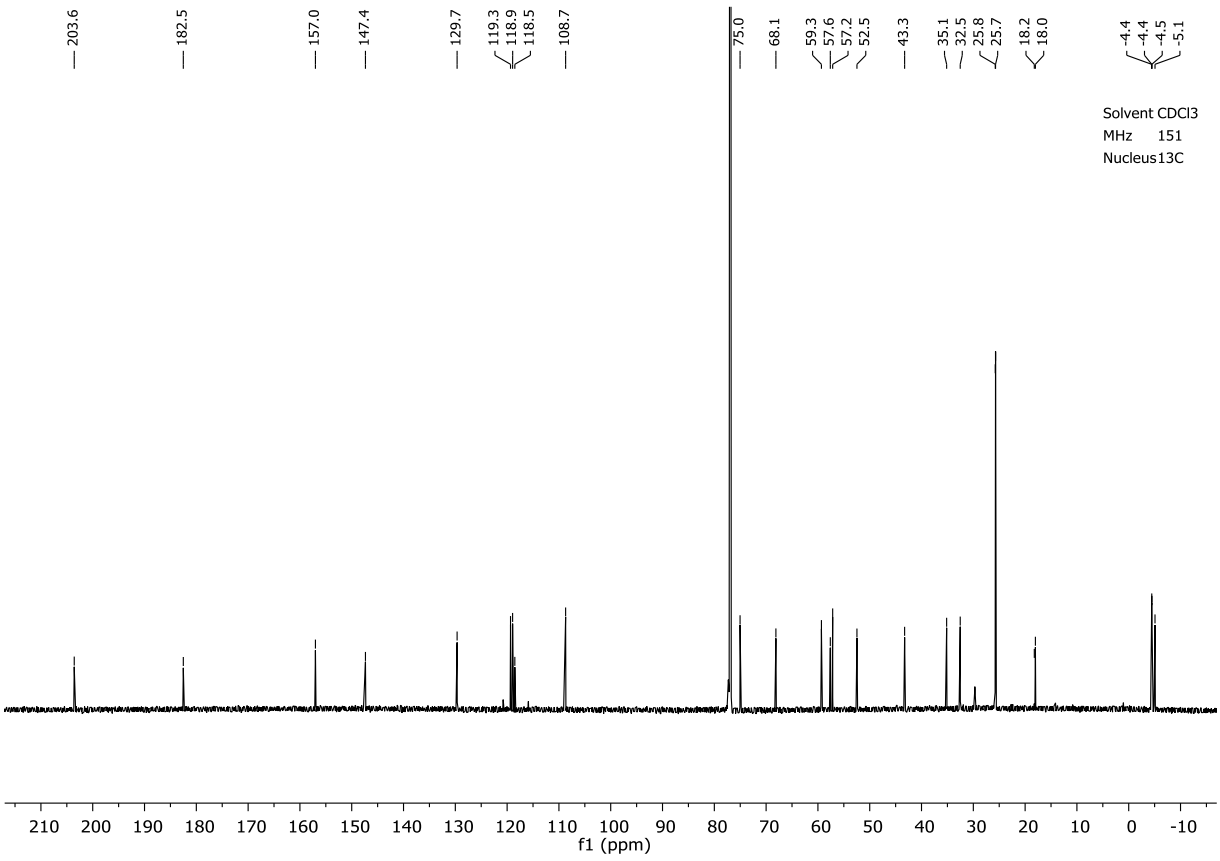
Solvent CDCl3
MHz 600
Nucleus 1H
2.0
2.0
1.0
1.0
1.0
1.0
6.0
2.0
1.0
1.0
1.0
1.0
9.0
9.0
6.0
6.0
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

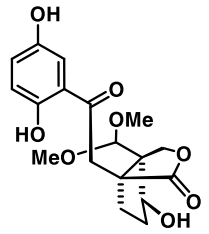

181.8
170.5
153.5
144.5
122.1
120.6
108.8
75.2
68.1
59.2
58.2
57.7
53.2
38.4
34.9
32.8
25.9
25.8
18.3
18.1
-4.3
-4.4
-5.0
Solvent CDCl3
MHz 151
Nucleus 13C
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


OTBS
O
OMe
HO
MeO
O
O
OTBS

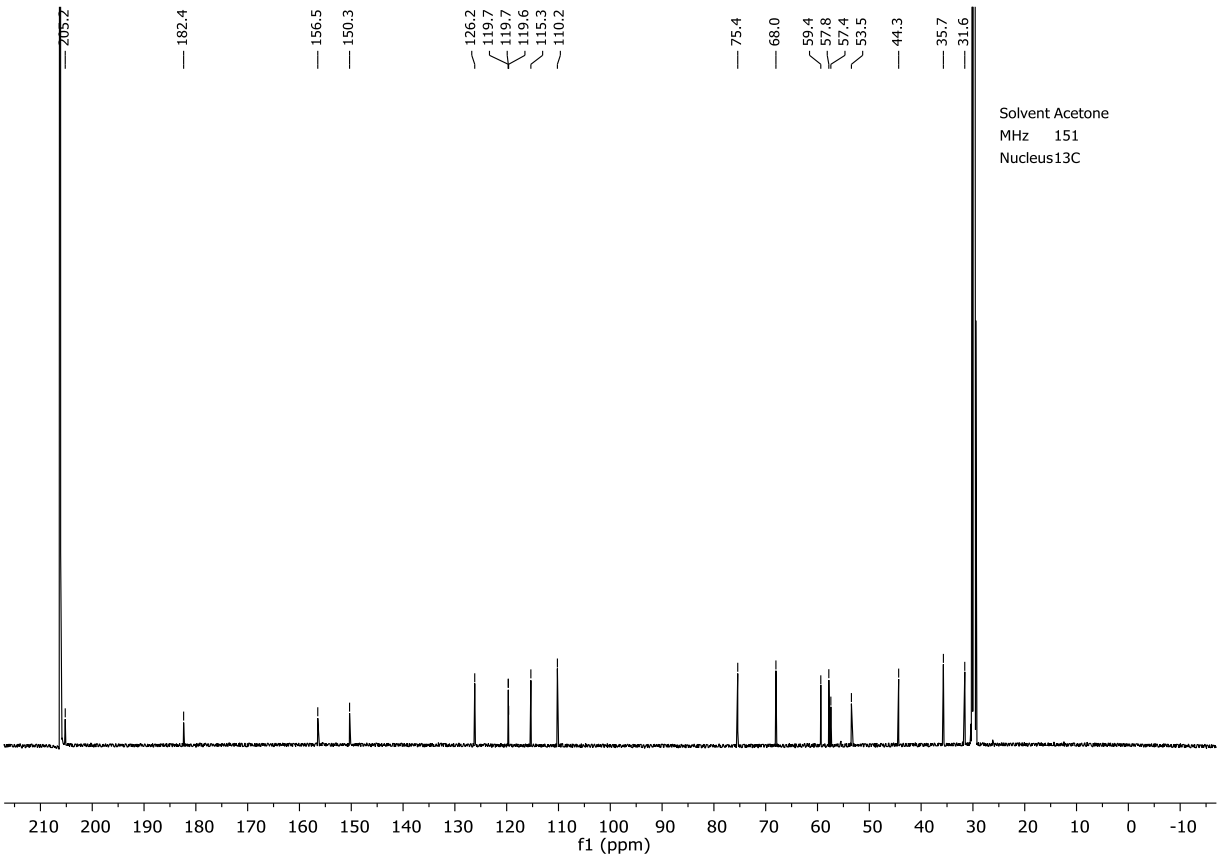
320

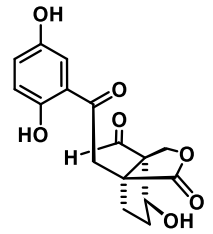
Solvent CDCl3
MHz 600
Nucleus1H
12 11 10 9 8 7 6 5 4 3 2 1 0
f1 (ppm)


203.6
182.5
157.0
147.4
129.7
119.3
118.9
118.5
108.7
75.0
68.1
59.3
57.6
57.2
52.5
43.3
35.1
32.5
25.8
25.7
18.2
18.0
-4.4
-4.4
-4.5
-5.1
Solvent CDCl3
MHz 151
Nucleus13C
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

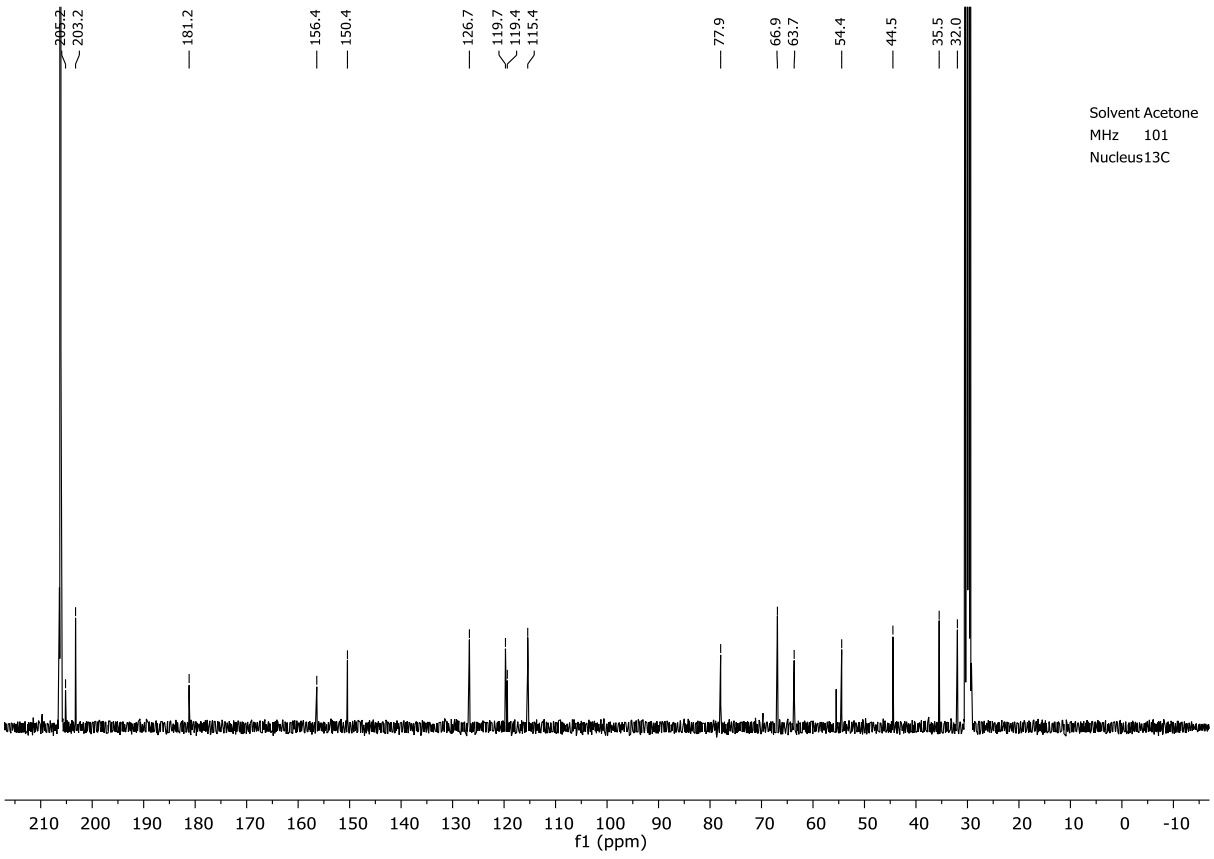


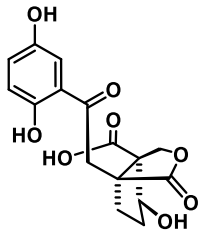
applanatumol E (18)



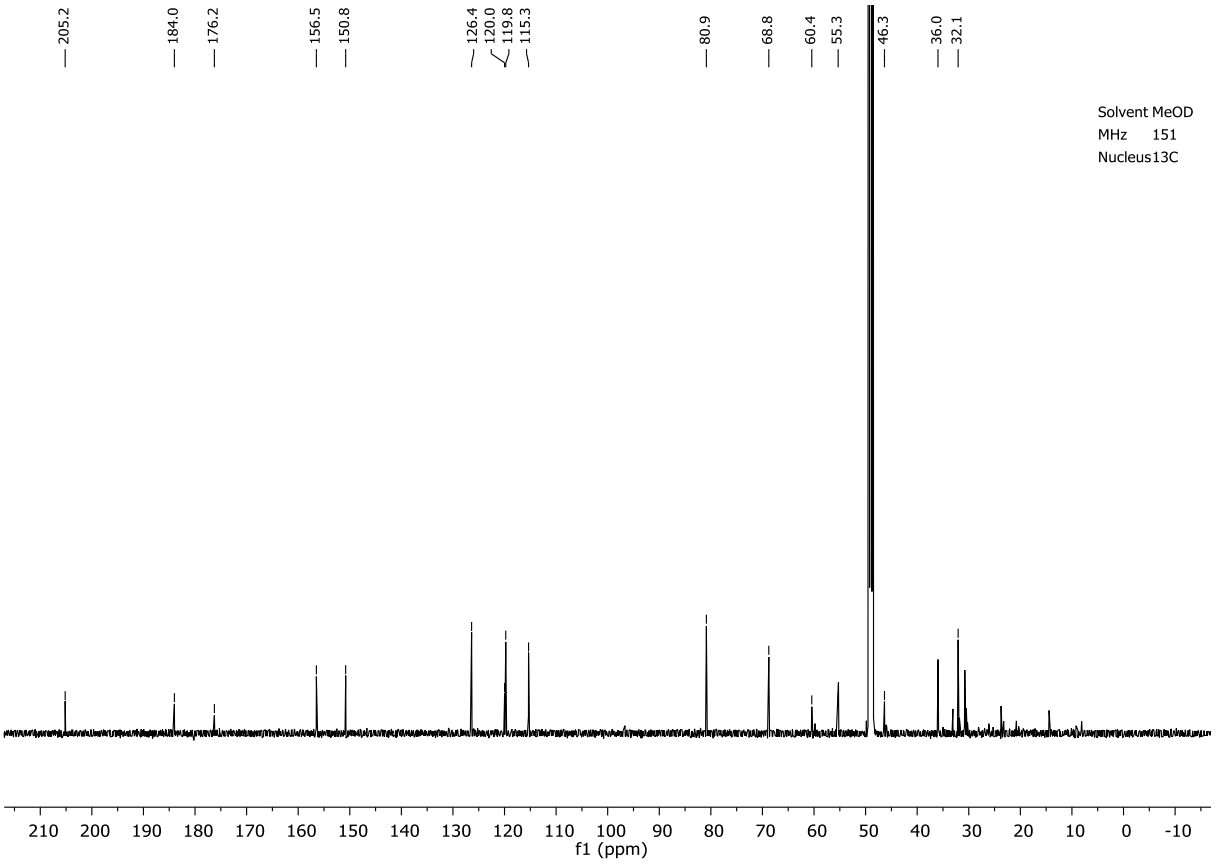


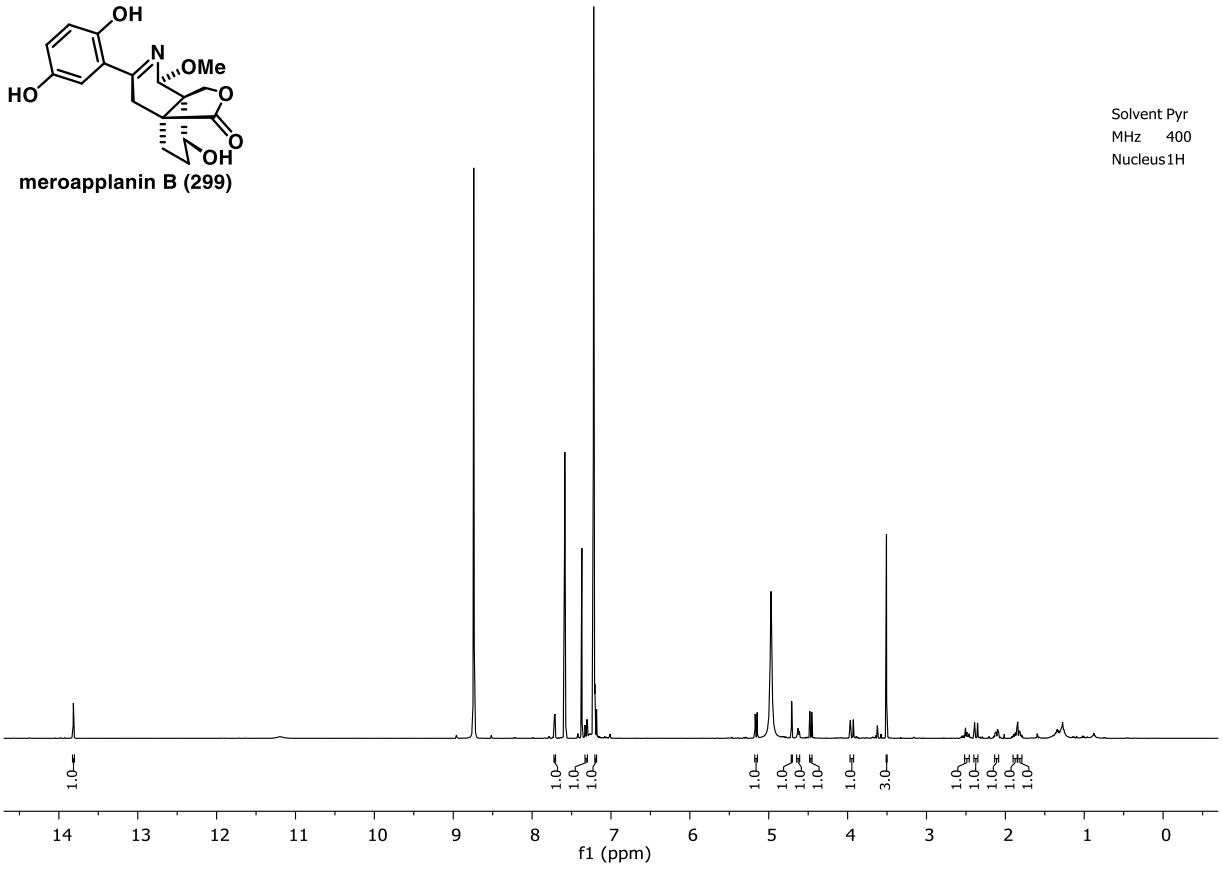
lingzhilactone B (24)

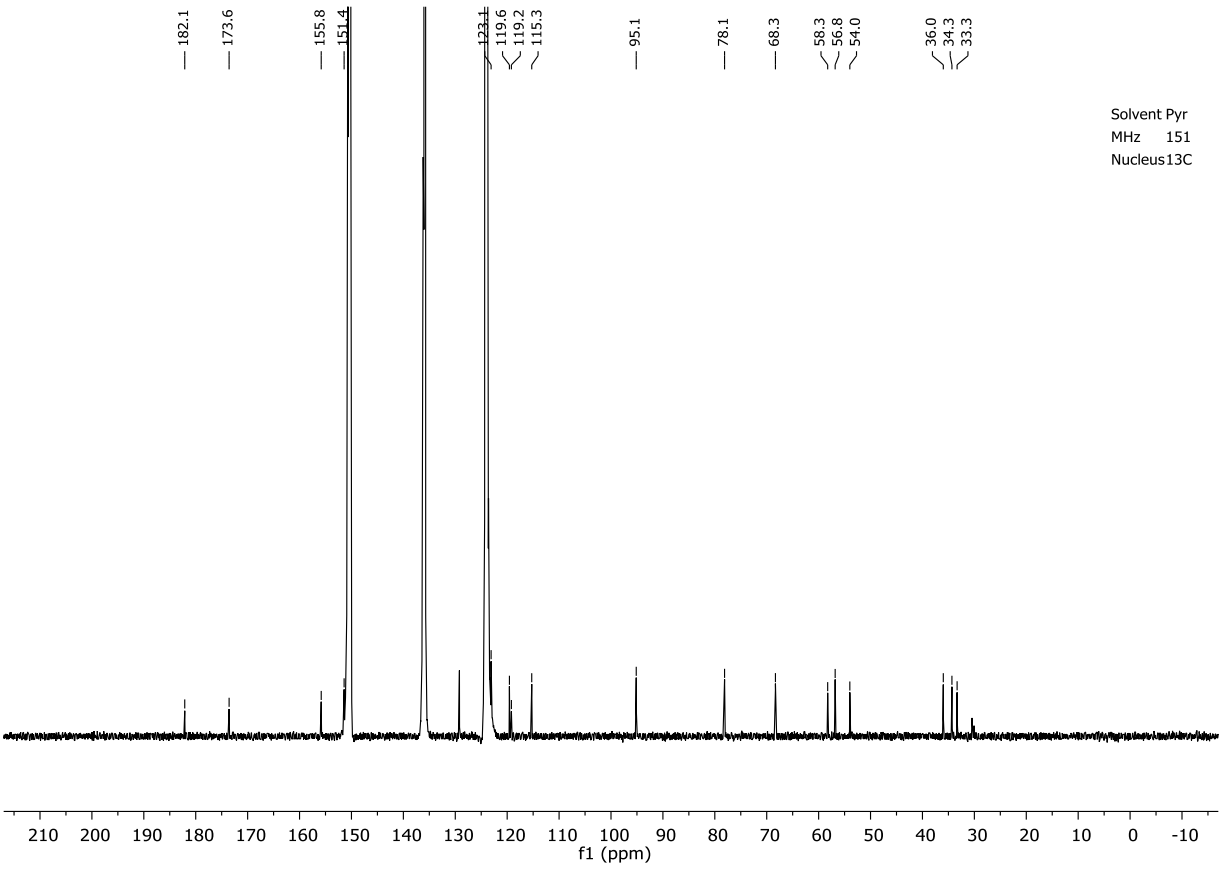


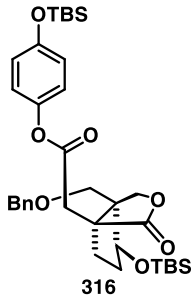


applanatumol I (298)



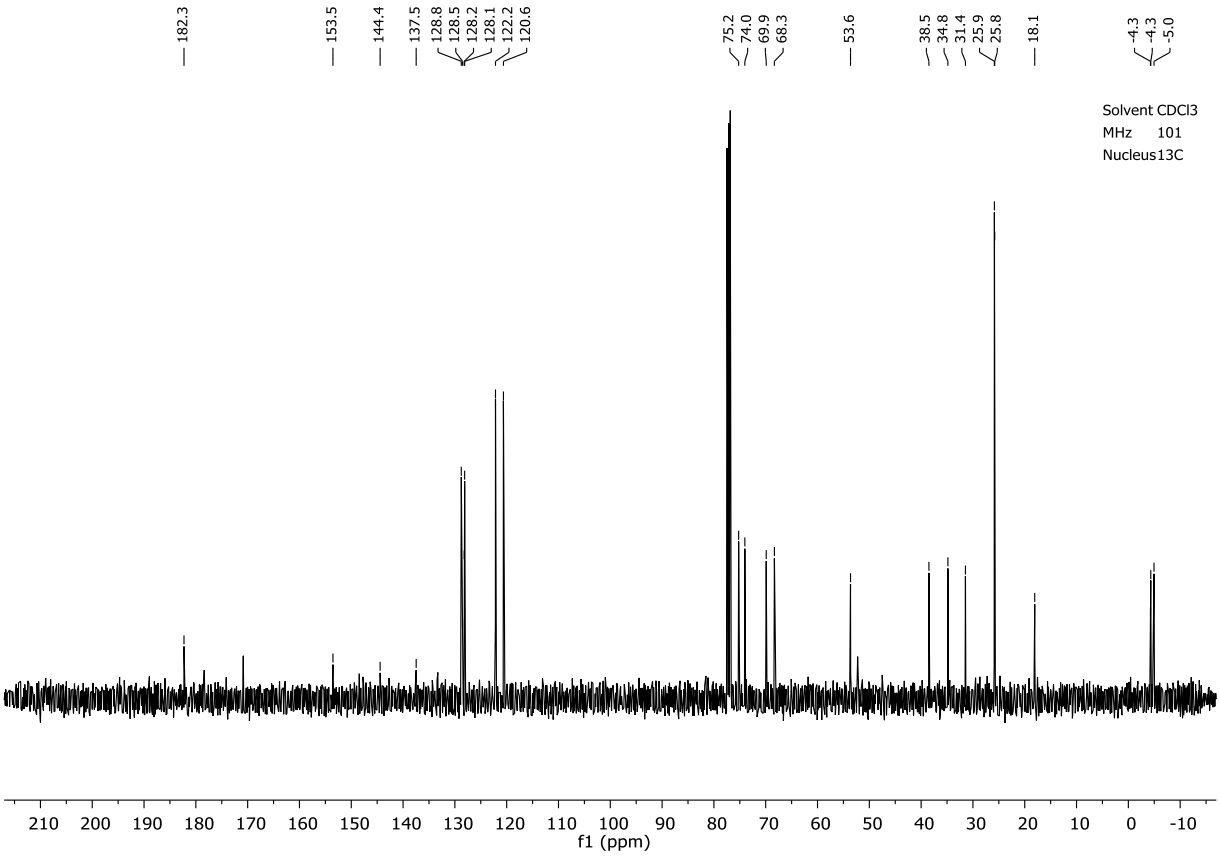

OH
N
OMe
HO
O
O
OH
meroapplanin B (299)
Solvent Pyr
MHz 400
Nucleus1H
1.0
1.0
1.0
1.0
1.0
1.0
1.0
1.0
3.0
1.0
1.0
1.0
1.0
14 13 12 11 10 9 8 7 6 5 4 3 2 1 0
f1 (ppm)

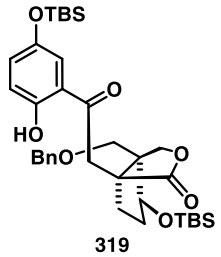

182.1
173.6
155.8
151.4
123.1
119.6
119.2
115.3
95.1
78.1
68.3
58.3
56.8
54.0
36.0
34.3
33.3
Solvent Pyr
MHz 151
Nucleus13C
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


OTBS
O
O
BnO
O
O
OTBS

316

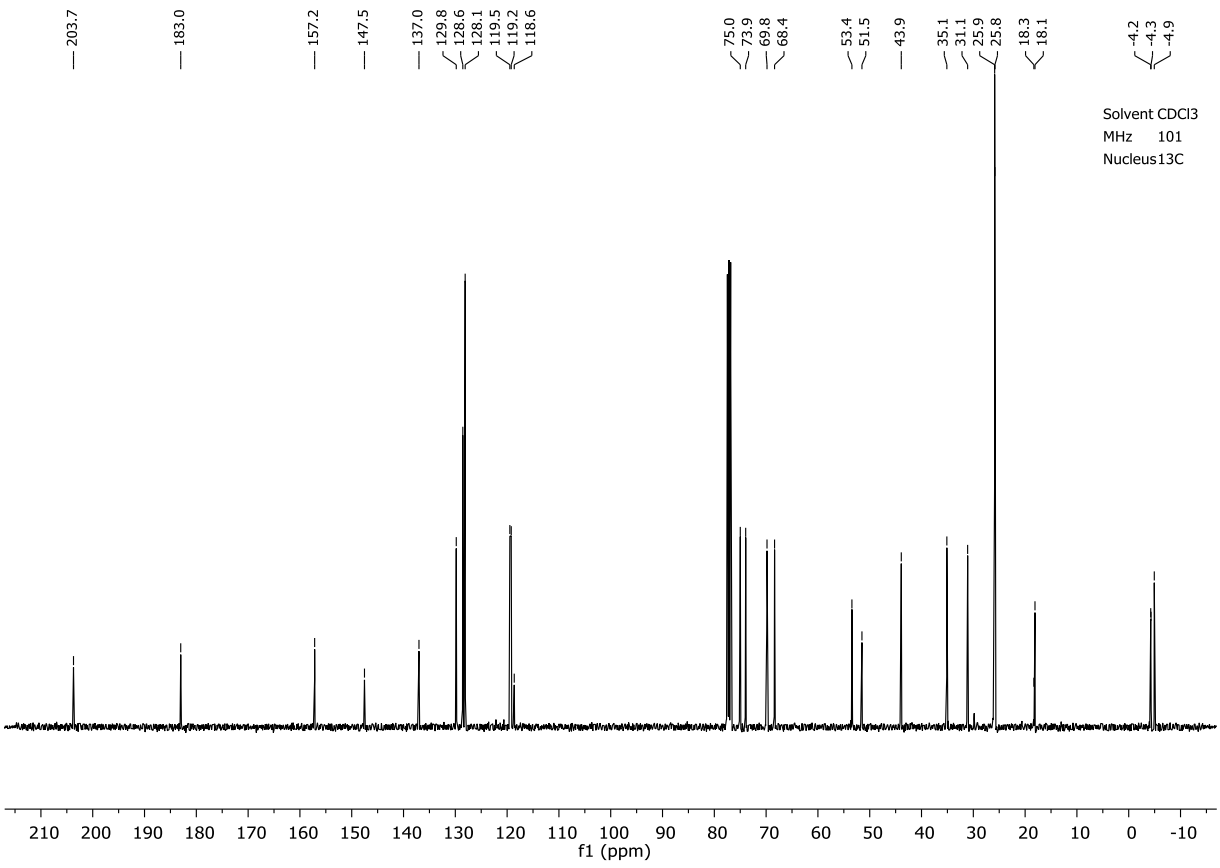
Solvent CDCl3
MHz 400
Nucleus1H
5.0
2.0
2.0
1.0
2.0
1.1
1.0
1.0
1.0
1.0
1.0
1.0
1.0
1.0
9.1
9.1
6.1
6.0
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

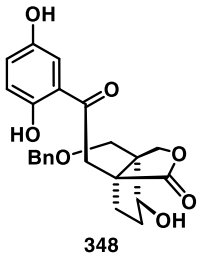

182.3
153.5
144.4
137.5
128.8
128.5
128.2
128.1
122.2
120.6
75.2
74.0
69.9
68.3
53.6
38.5
34.8
31.4
25.9
25.8
18.1
-4.3
-4.3
-5.0
Solvent CDCl3
MHz 101
Nucleus13C
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


OTBS
O
HO
BnO
O
O
OTBS

319

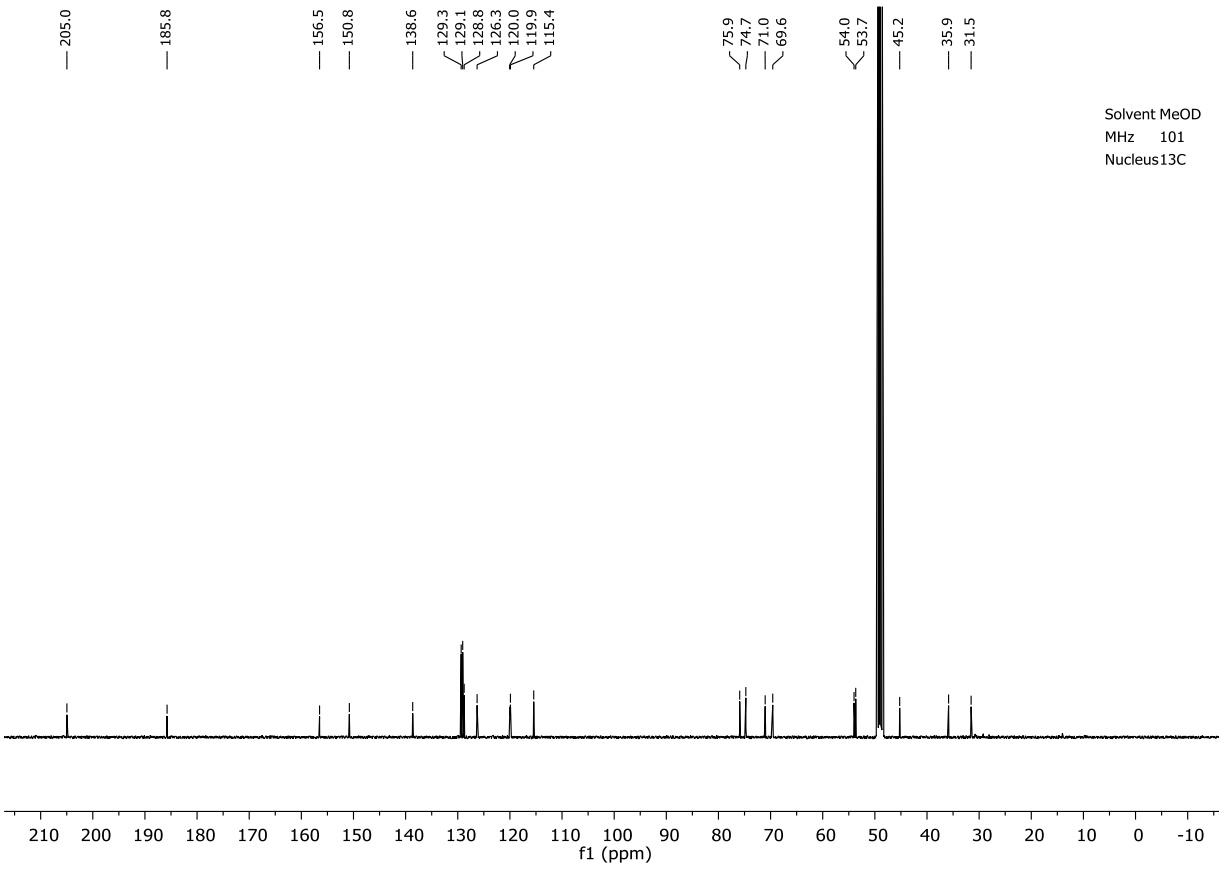
Solvent CDCl3
MHz 400
Nucleus1H
1.0
3.0
4.0
1.0
1.0
1.0
1.0
2.0
1.0
1.0
1.0
1.0
1.1
1.0
9.1
9.0
6.0
3.0
3.0
11 10 9 8 7 6 5 4 3 2 1 0
f1 (ppm)

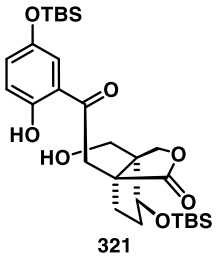

203.7
183.0
157.2
147.5
137.0
129.8
128.6
128.1
119.5
119.2
118.6
75.0
73.9
69.8
68.4
53.4
51.5
43.9
35.1
31.1
25.9
25.8
18.3
18.1
-4.2
-4.3
-4.9
Solvent CDCl3
MHz 101
Nucleus13C
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


OH
O
HO
BnO
O
O
OH

348

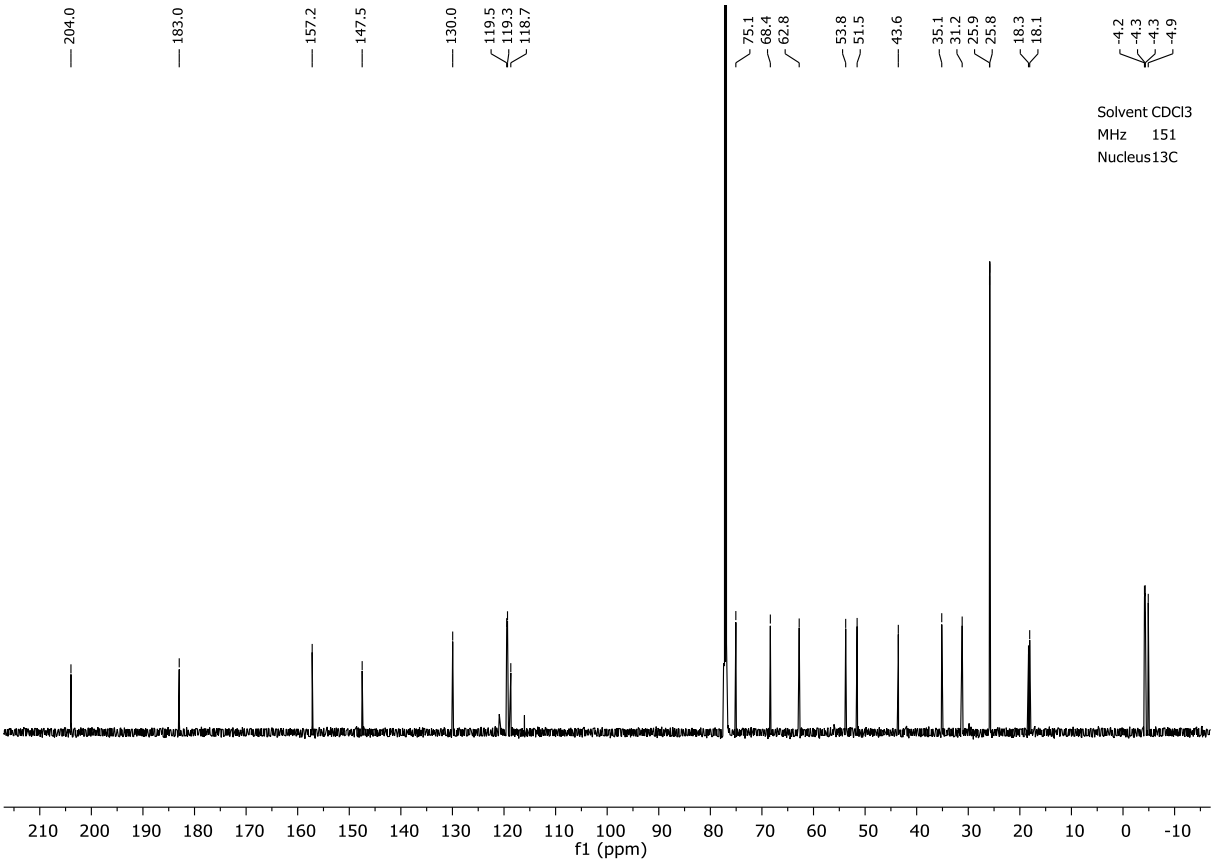
Solvent MeOD
MHz 400
Nucleus1H
4.0
2.0
1.0
1.0
1.0
2.0
1.0
1.0
1.0
1.0
2.0
2.0
1.0
1.0
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

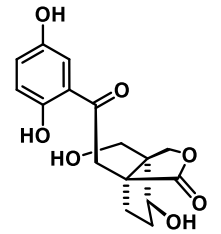

205.0
185.8
156.5
150.8
138.6
129.3
129.1
128.8
126.3
120.0
119.9
115.4
75.9
74.7
71.0
69.6
54.0
53.7
45.2
35.9
31.5
Solvent MeOD
MHz 101
Nucleus13C
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


OTBS
O
HO
HO
O
O
OTBS

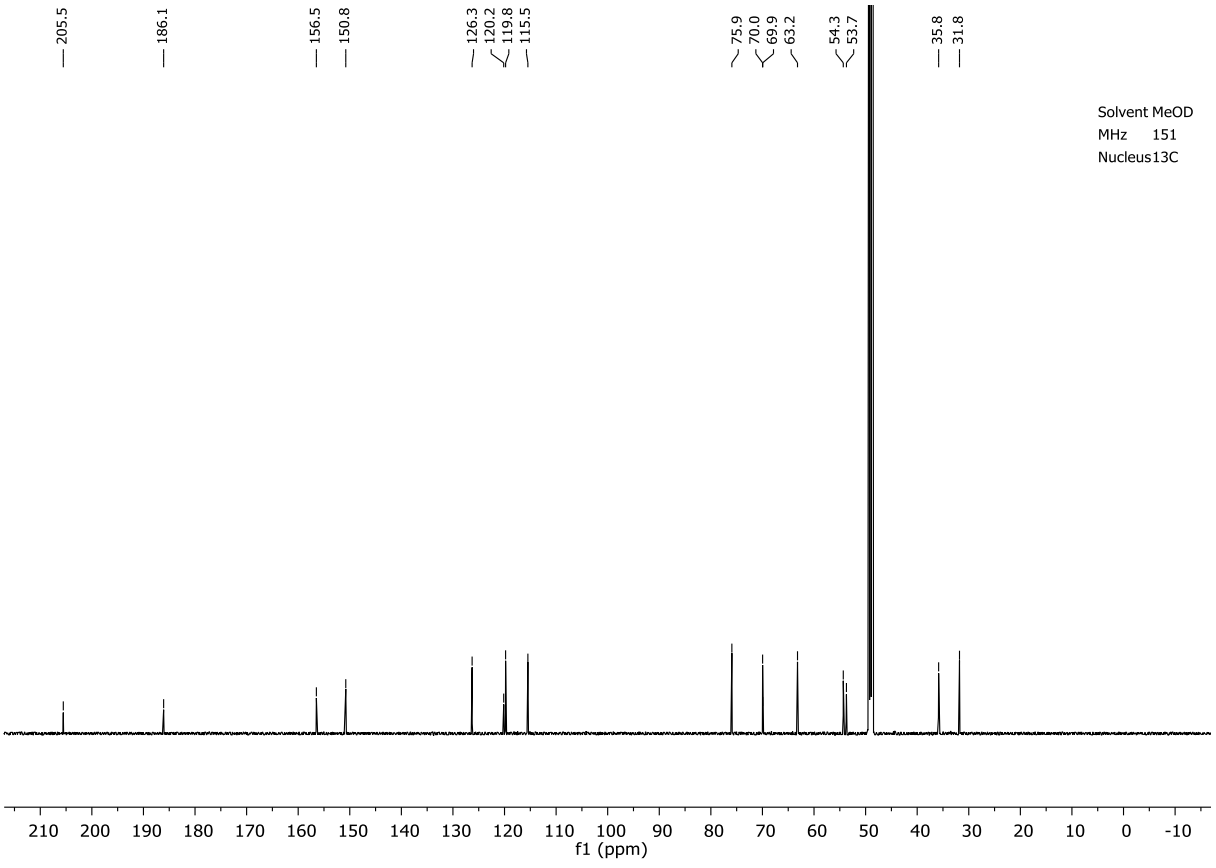
321

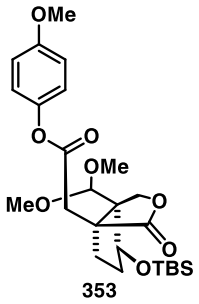
Solvent CDCl3
MHz 600
Nucleus1H
1.0 1.0 1.0 1.0 1.0 2.0 1.0 2.0 1.0 1.0 1.0 1.0 9.0 9.0 6.0 6.0
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)


204.0
183.0
157.2
147.5
130.0
119.5
119.3
118.7
75.1
68.4
62.8
53.8
51.5
43.6
35.1
31.2
25.9
25.8
18.3
18.1
-4.2
-4.3
-4.3
-4.9
Solvent CDCl3
MHz 151
Nucleus13C
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)



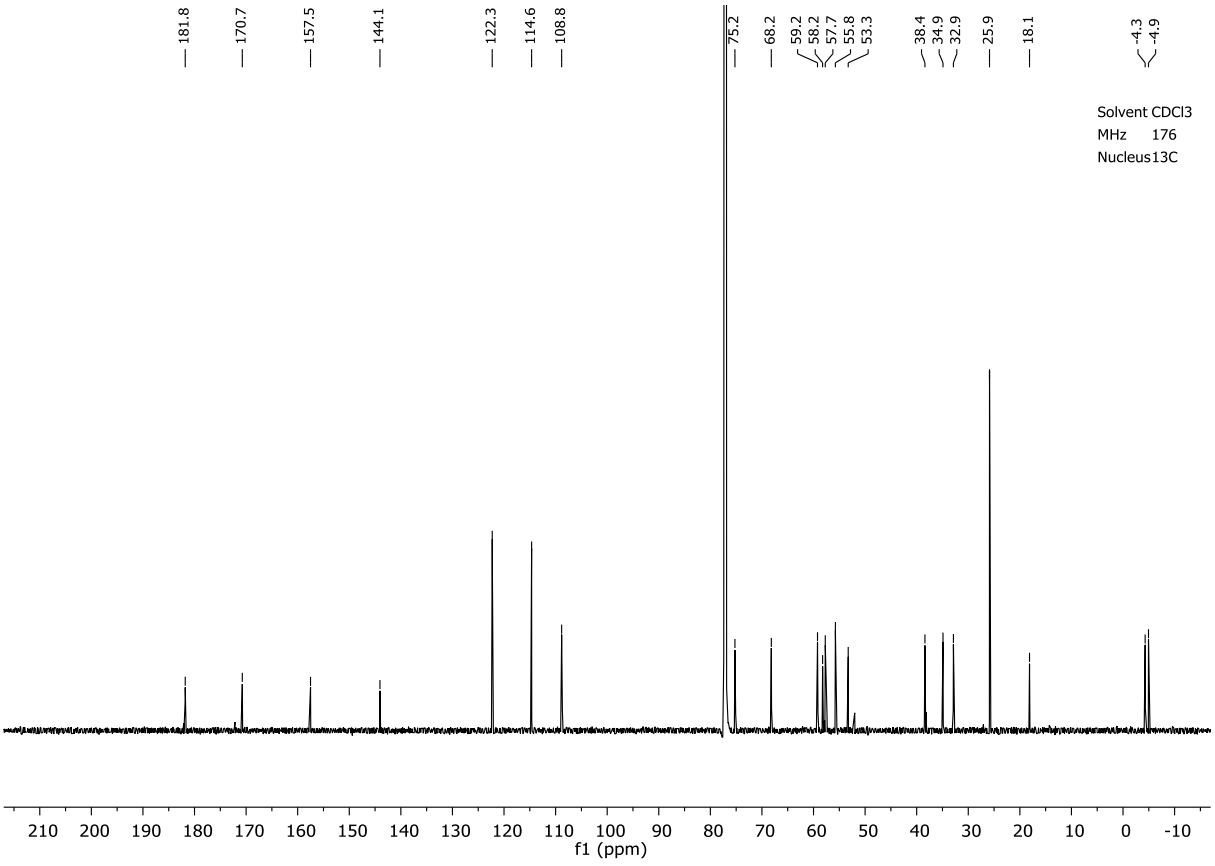
applanatumol H (297)

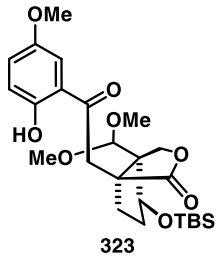



OMe
O
O
OMe
MeO
O
O
OTBS

353

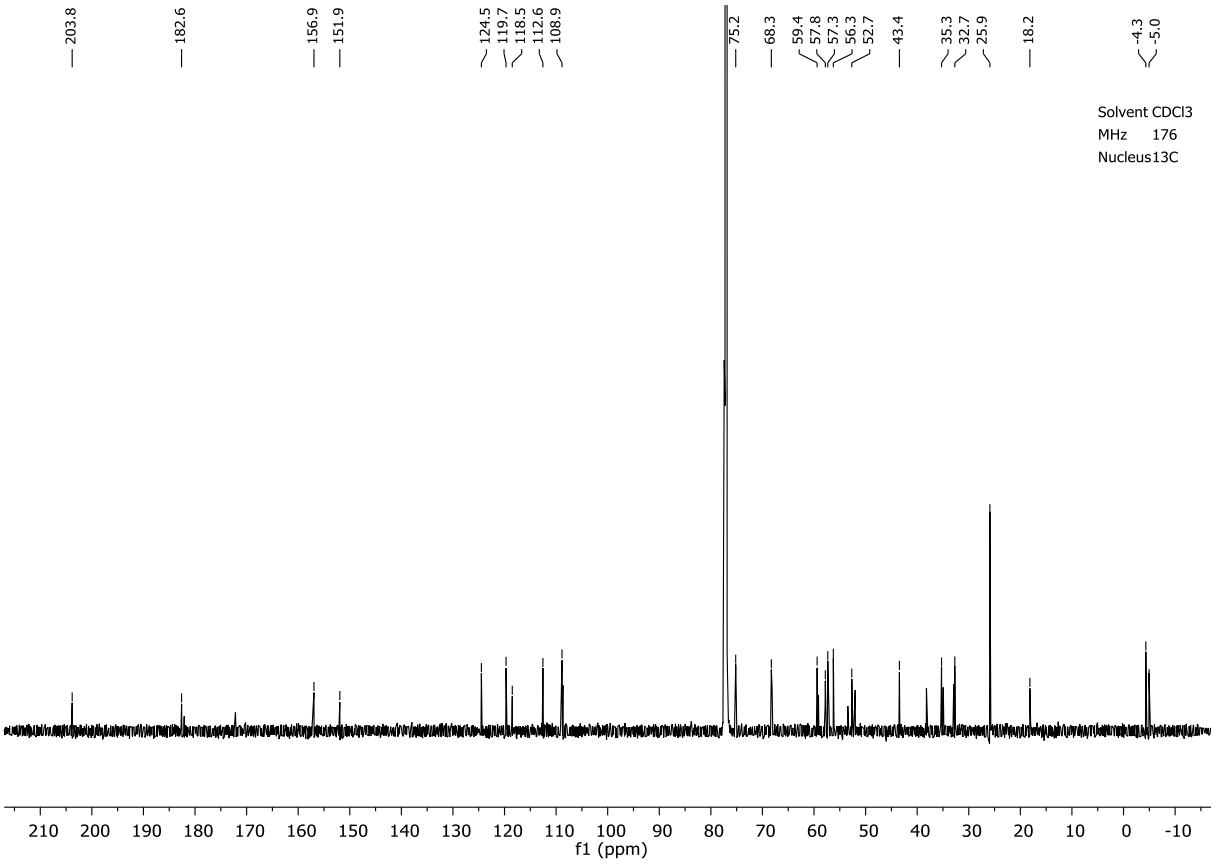
Solvent CDCl3
MHz 700
Nucleus1H
1.0
1.0
1.0
1.0
1.0
3.0
3.0
3.0
2.0
1.0
1.0
1.0
1.0
9.0
6.0
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

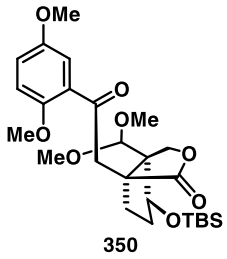

181.8
170.7
157.5
144.1
122.3
114.6
108.8
75.2
68.2
59.2
58.2
57.7
55.8
53.3
38.4
34.9
32.9
25.9
18.1
-4.3
-4.9
Solvent CDCl3
MHz 176
Nucleus13C
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


OMe
O
OMe
HO
MeO
O
O
OTBS

323

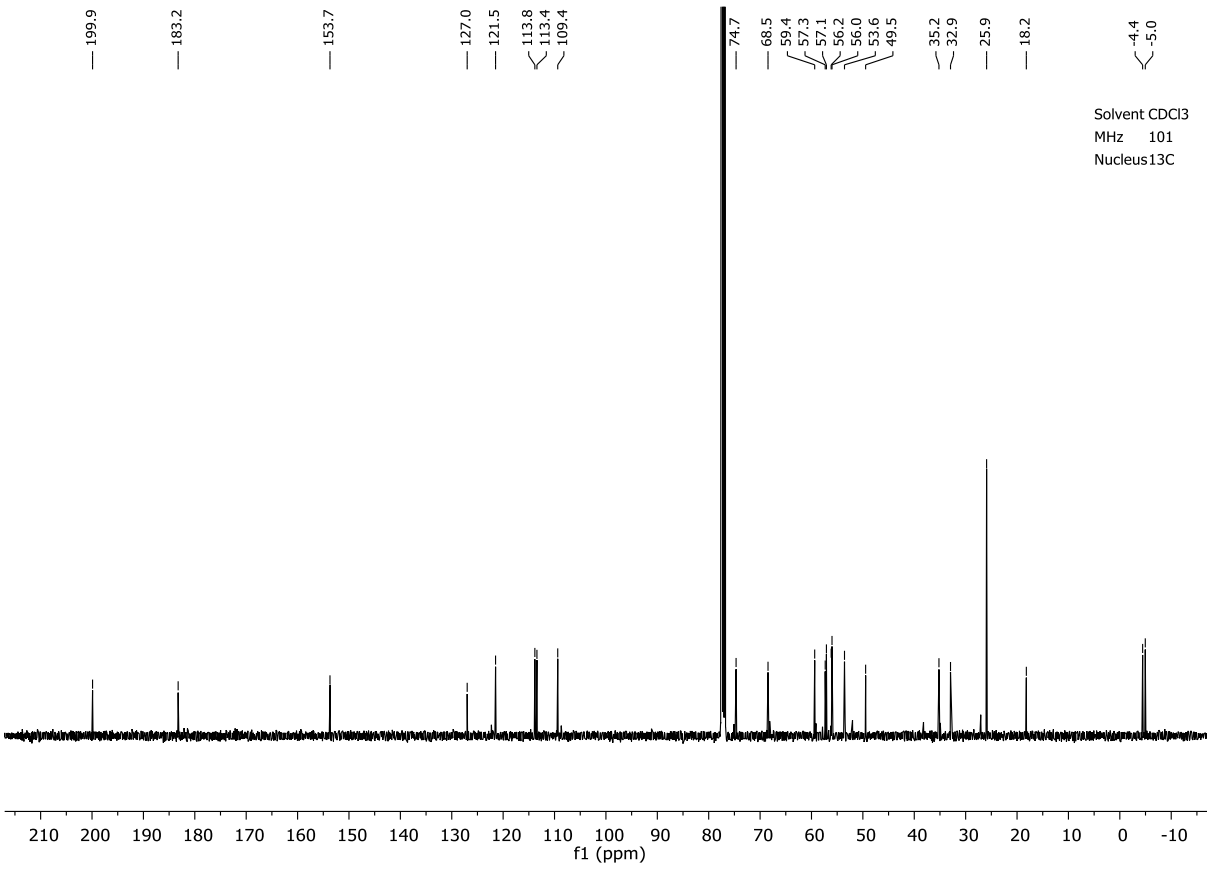
Solvent CDCl3
MHz 700
Nucleus1H
1.0
1.0
1.0
1.0
1.0
1.0
3.0
1.0
3.0
3.0
1.0
1.0
1.0
1.0
9.0
6.0
12
11
10
9
8
7
6
5
4
3
2
1
0
f1 (ppm)

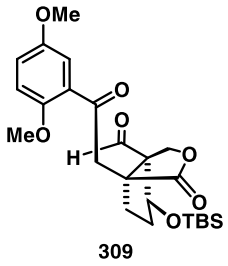

203.8
182.6
156.9
151.9
124.5
119.7
118.5
112.6
108.9
75.2
68.3
59.4
57.8
57.3
56.3
52.7
43.4
35.3
32.7
25.9
18.2
-4.3
-5.0
Solvent CDCl3
MHz 176
Nucleus13C
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)


OMe
O
OMe
MeO
MeO
O
O
OTBS

350

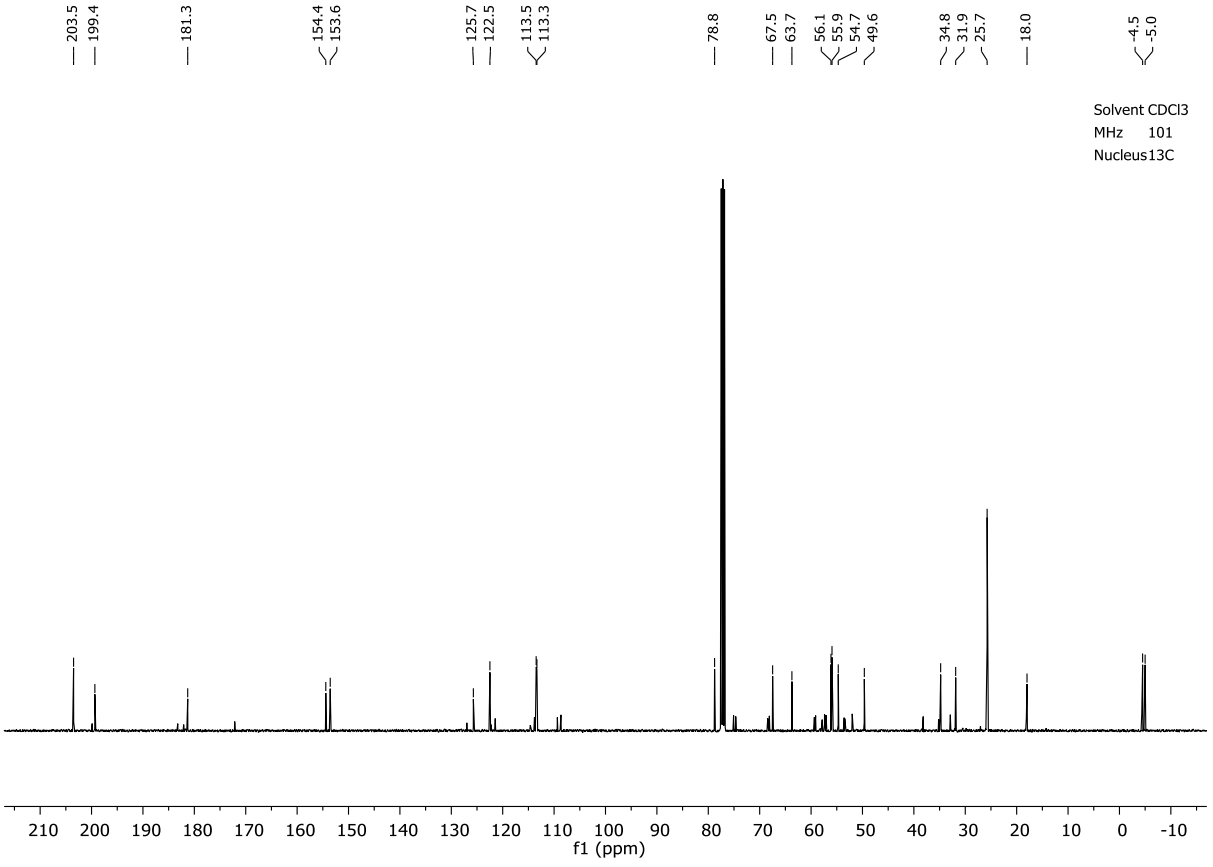
Solvent CDCl3
MHz 400
Nucleus1H
1.0
1.0
1.0
1.0
1.0
1.0
3.0
4.0
1.0
3.0
3.0
1.0
1.0
1.0
1.0
9.0
6.0
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

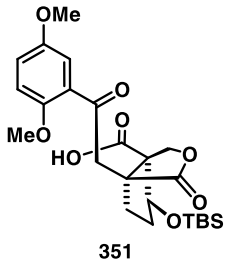

199.9
183.2
153.7
127.0
121.5
113.8
113.4
109.4
74.7
68.5
59.4
57.3
57.1
56.2
56.0
53.6
49.5
35.2
32.9
25.9
18.2
-4.4
-5.0
Solvent CDCl3
MHz 101
Nucleus13C
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


OMe
MeO
O
O
H
O
O
OTBS

309

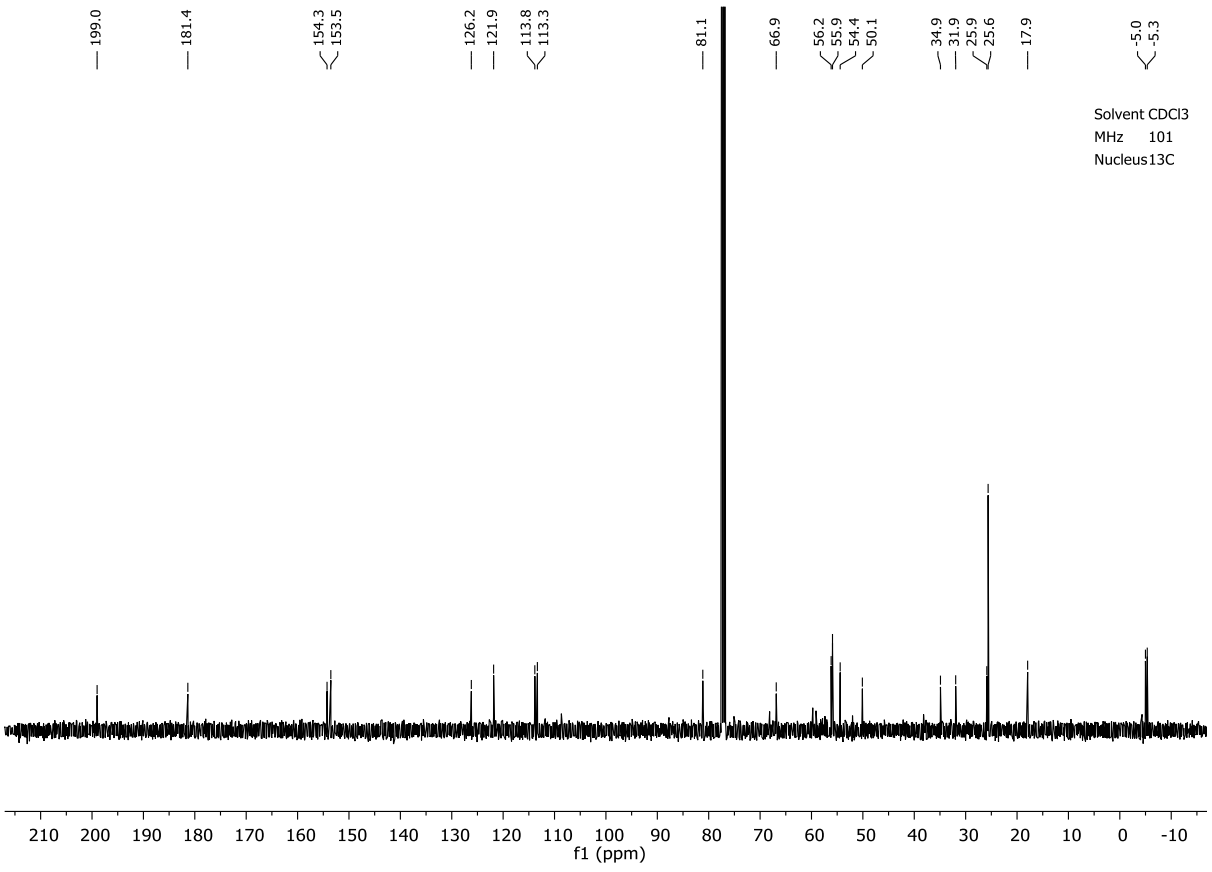
Solvent CDCl3
MHz 400
Nucleus1H
1.0
1.0
1.0
1.0
2.0
1.0
3.0
3.0
1.0
1.0
1.0
1.0
1.0
1.0
9.0
6.0
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

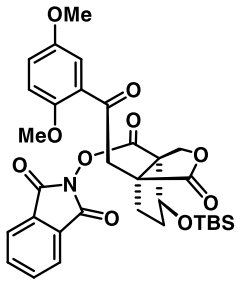

203.5
199.4
181.3
154.4
153.6
125.7
122.5
113.5
113.3
78.8
67.5
63.7
56.1
55.9
54.7
49.6
34.8
31.9
25.7
18.0
-4.5
-5.0
Solvent CDCl3
MHz 101
Nucleus13C
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


OMe
MeO
HO
O
O
O
O
OTBS

351

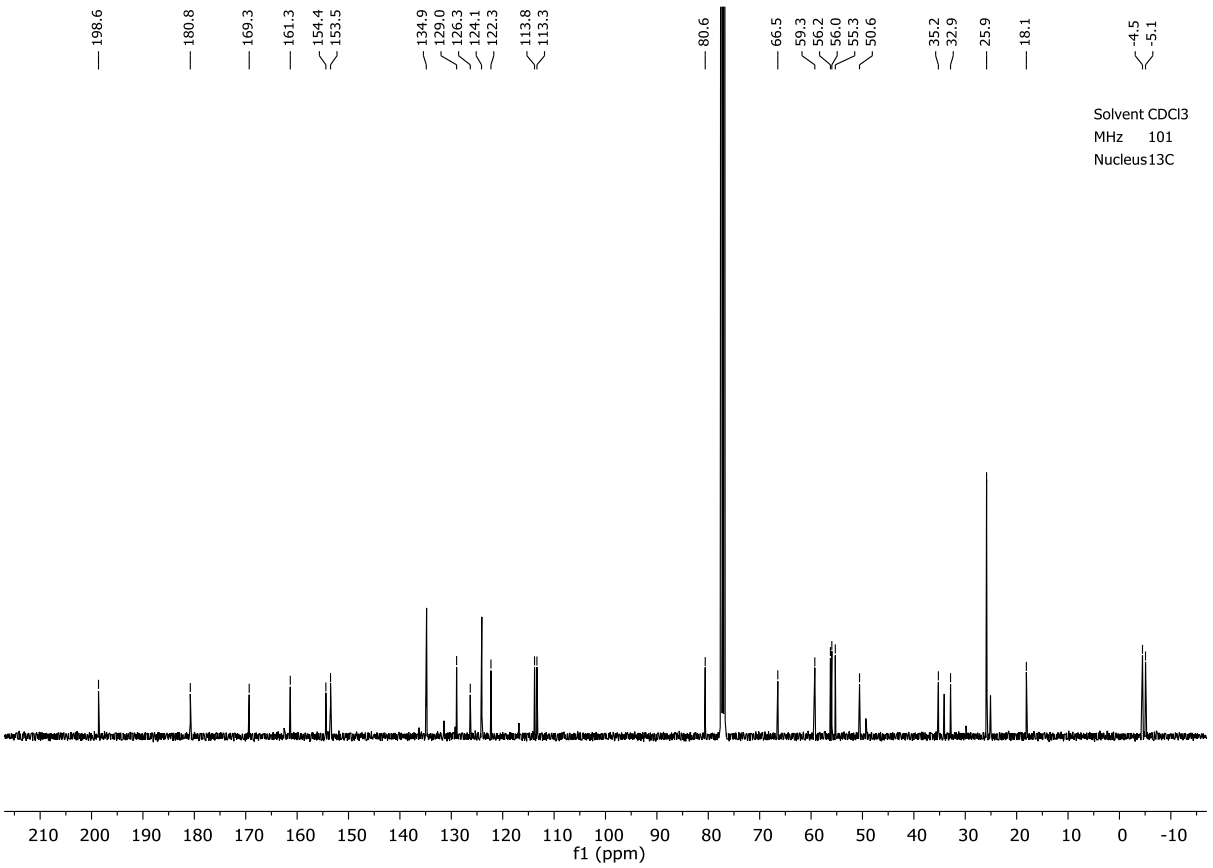
Solvent CDCl3
MHz 400
Nucleus1H
1.0 1.0 1.0 1.0 1.0 1.0 1.0 3.0 3.0 1.0 1.0 1.0 1.0 9.0 6.0
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

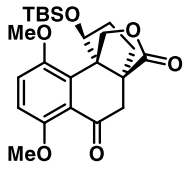

199.0
181.4
154.3
153.5
126.2
121.9
113.8
113.3
81.1
66.9
56.2
55.9
54.4
50.1
34.9
31.9
25.9
25.6
17.9
-5.0
-5.3
Solvent CDCl3
MHz 101
Nucleus13C
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


OMe
MeO
O
O
O
O
N
O
O
O
O
OTBS

324

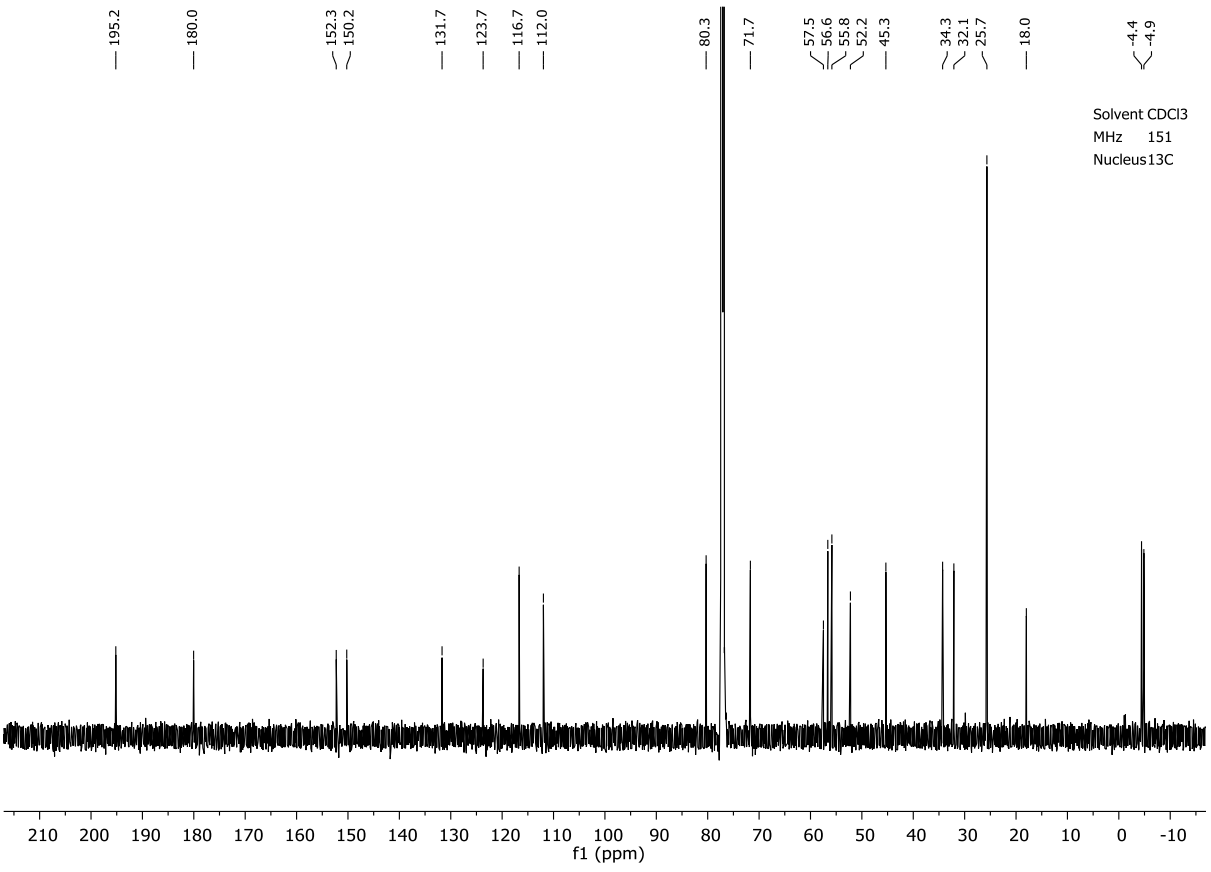
Solvent CDCl3
MHz 400
Nucleus1H
2.0 2.0 1.0 1.0 1.0 2.0 1.0 2.0 3.0 3.0 1.0 1.0 1.0 1.0 9.0 6.0
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

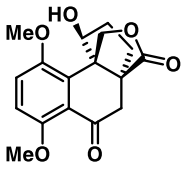

198.6
180.8
169.3
161.3
154.4
153.5
134.9
129.0
126.3
124.1
122.3
113.8
113.3
80.6
66.5
59.3
56.2
56.0
55.3
50.6
35.2
32.9
25.9
18.1
-4.5
-5.1
Solvent CDCl3
MHz 101
Nucleus13C
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


TBSO
MeO
O
O
MeO
O

325

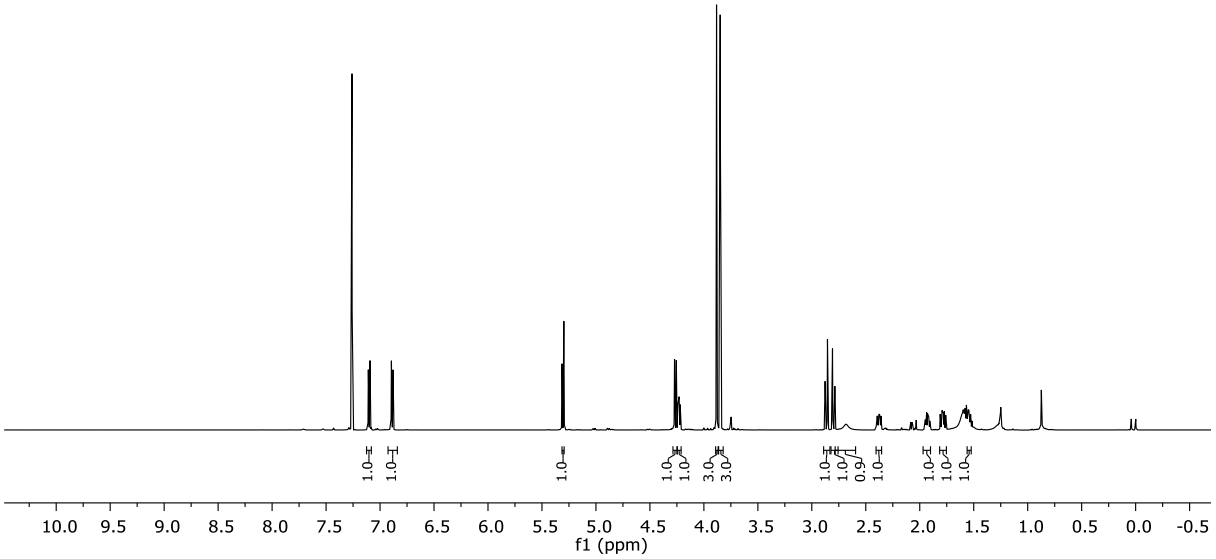
Solvent CDCl3
MHz 600
Nucleus1H
1.0
1.0
1.0
1.0
1.0
6.0
1.0
1.0
1.0
1.0
1.0
9.0
6.0
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

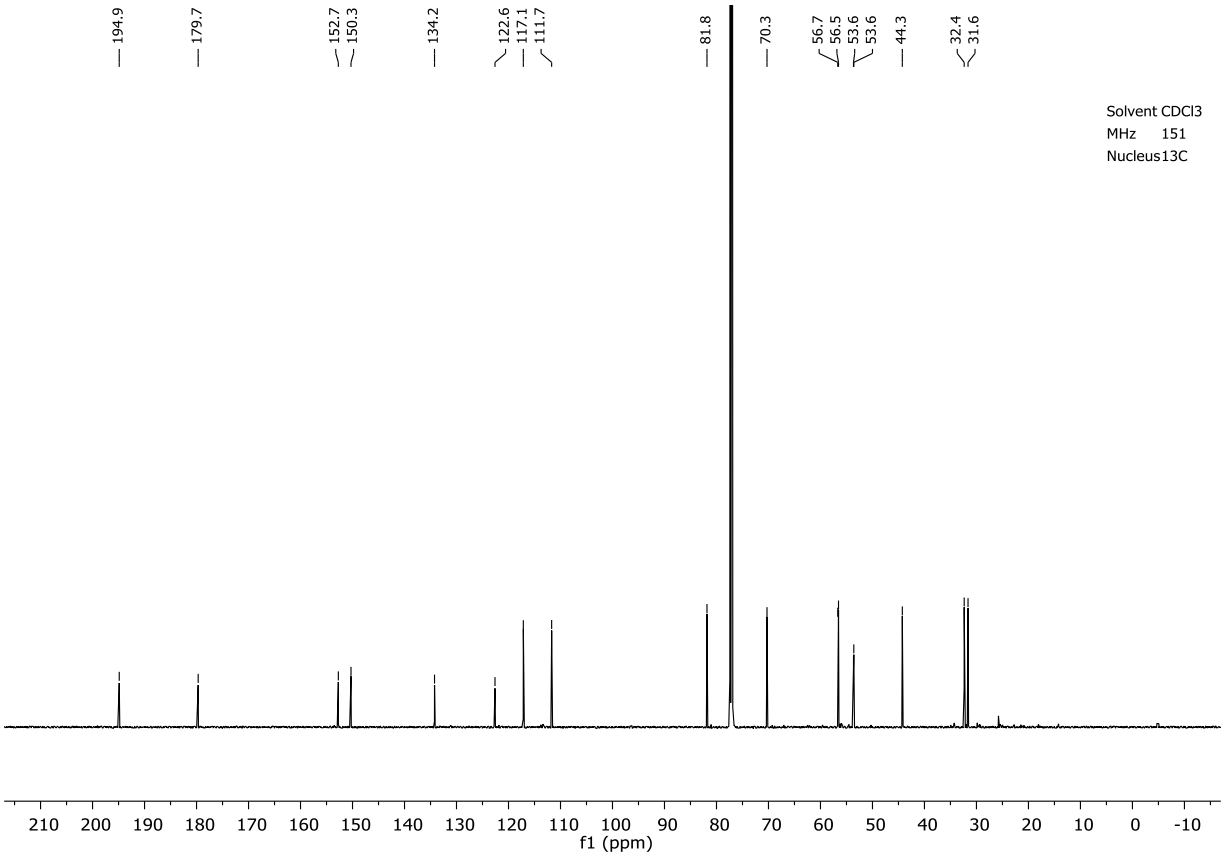

195.2
180.0
152.3
150.2
131.7
123.7
116.7
112.0
80.3
71.7
57.5
56.6
55.8
52.2
45.3
34.3
32.1
25.7
18.0
-4.4
-4.9
Solvent CDCl3
MHz 151
Nucleus13C
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

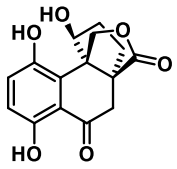


326

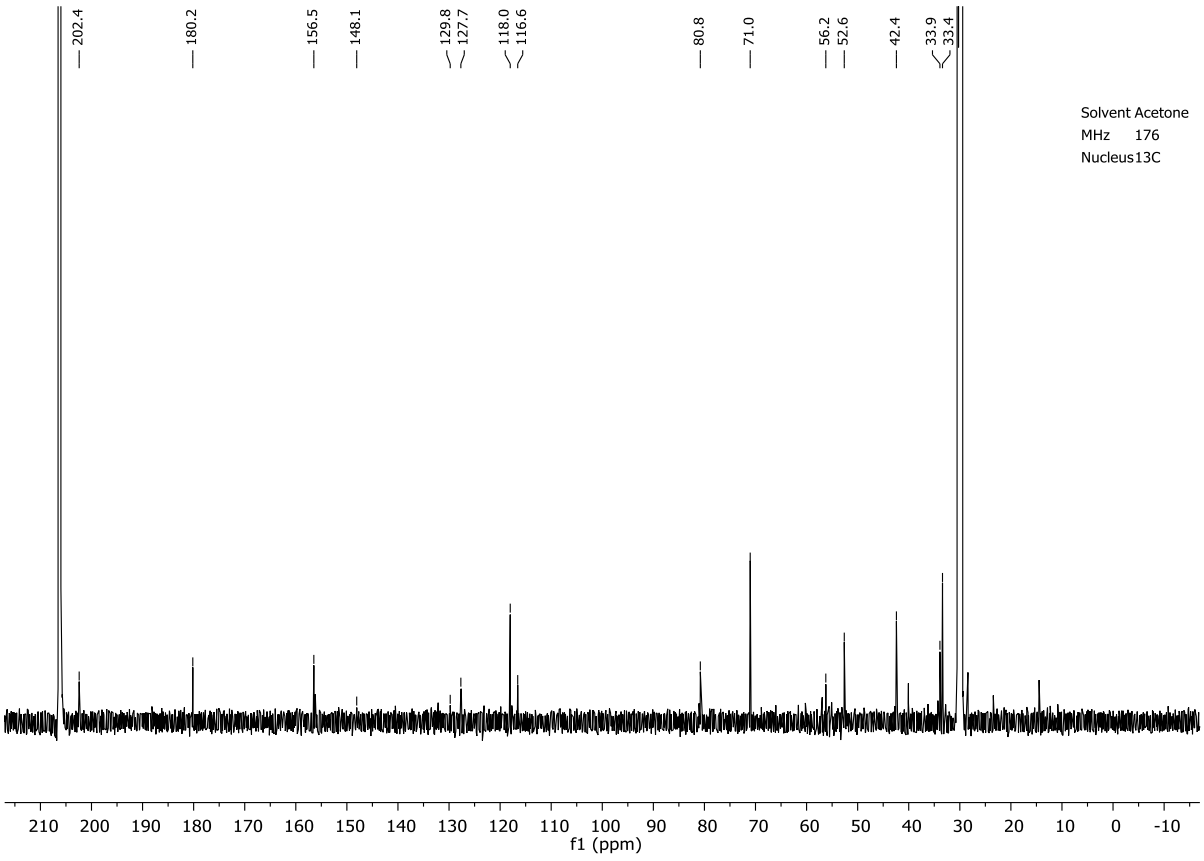
Solvent CDCl3
MHz 600
Nucleus1H

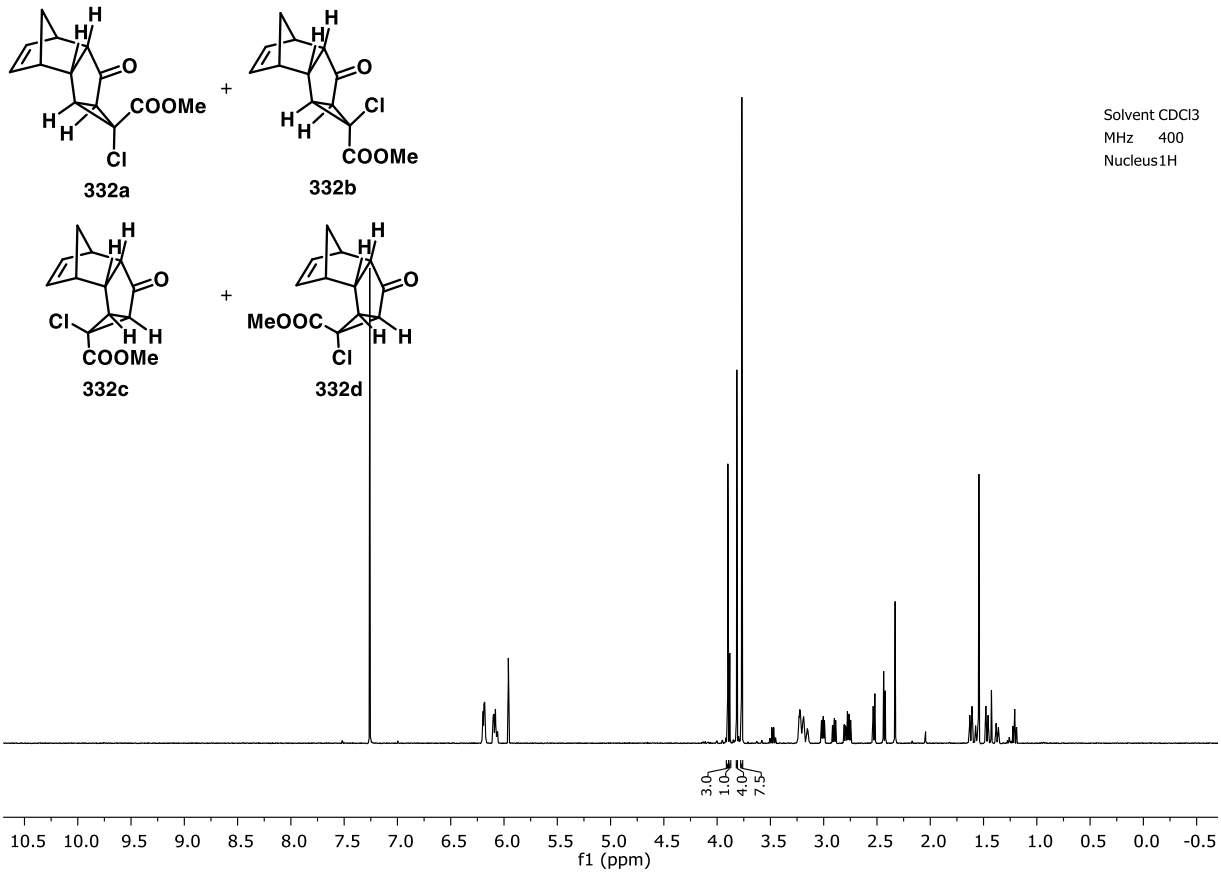


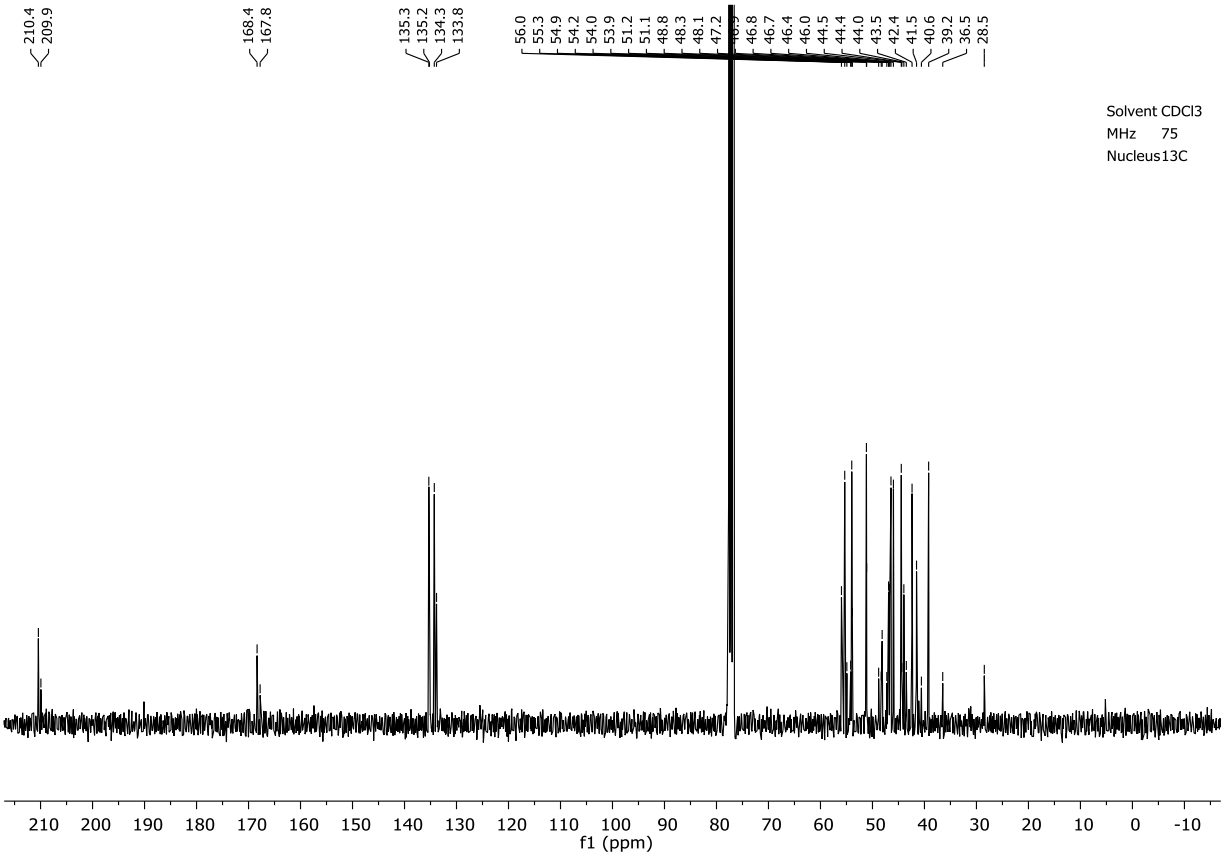


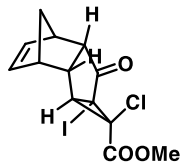


lingzhiol (30)



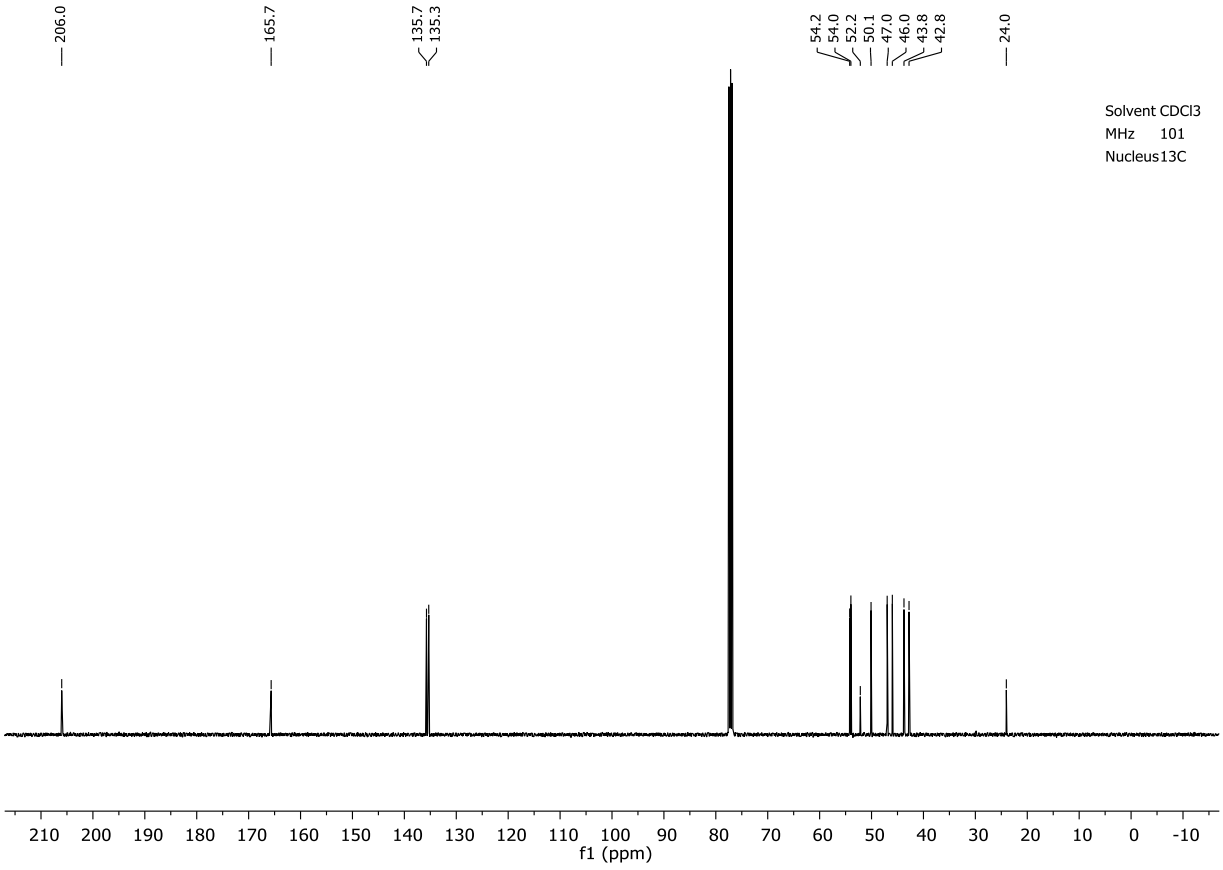

332a
332b
332c
332d
Solvent CDCl3
MHz 400
Nucleus1H
3.0
1.0
4.0
7.5
f1 (ppm)

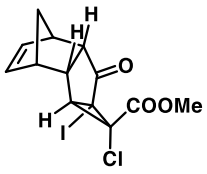

210.4
209.9
168.4
167.8
135.3
135.2
134.3
133.8
56.0
55.3
54.9
54.2
54.0
53.9
51.2
51.1
48.8
48.3
48.1
47.2
46.8
46.7
46.4
46.0
44.5
44.4
44.0
43.5
42.4
41.5
40.6
39.2
36.5
28.5
Solvent CDCl3
MHz 75
Nucleus13C
f1 (ppm)


H
H
O
Cl
H
I
COOMe

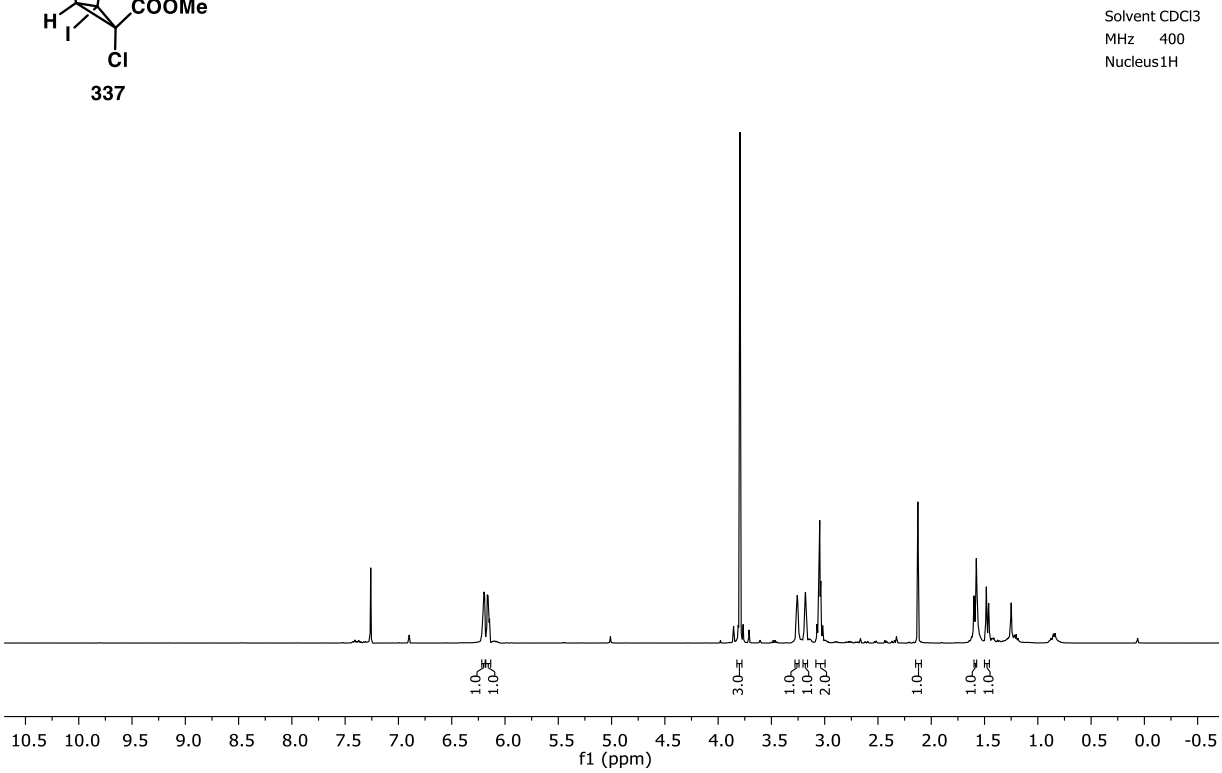
338

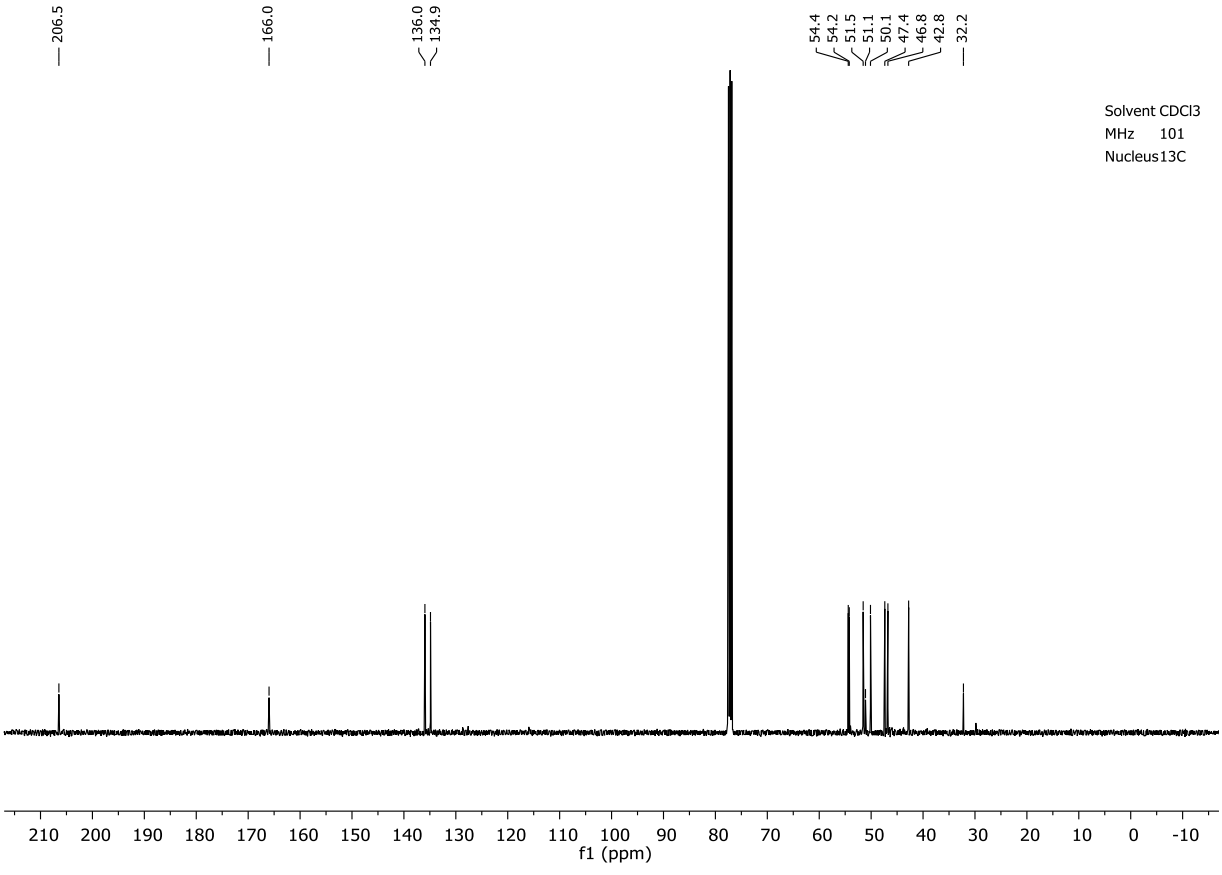
Solvent CDCl3
MHz 400
Nucleus1H
1.0
1.0
3.0
2.0
1.0
1.0
1.0
1.0
1.0
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)


206.0
165.7
135.7
135.3
54.2
54.0
52.2
50.1
47.0
46.0
43.8
42.8
24.0
Solvent CDCl3
MHz 101
Nucleus13C
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


H
H
O
COOMe
H
I
Cl

337


Solvent CDCl3
MHz 400
Nucleus1H
1.0
1.0
3.0
1.0
1.0
2.0
1.0
1.0
1.0
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)


206.5
166.0
136.0
134.9
54.4
54.2
51.5
51.1
50.1
47.4
46.8
42.8
32.2
Solvent CDCl3
MHz 101
Nucleus13C
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)