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Synthesis of New Functionalized Organocopper Reagents *via* a Halogen-Copper Exchange Reaction

Von

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Erklärung

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Ehrenwörtliche Versicherung

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Part of this Ph. D. Thesis have been published:

1. Xiaoyin Yang, Thomas Rotter, Claudia Piazza, Paul Knochel, "Successive Iodine-Magnesium or -Copper Exchange Reactions for the Selective Functionalization of Polyhalogenated Aromatics" *Organic Letters* **2003**, *8*, 1229-1231.

2. Xiaoyin Yang, Paul Knochel, "Preparation and Reactions of Polyfunctional Magnesium Arylcuprates Obtained by an Iodine-Copper Exchange" *Synlett* **2004**, *1*, 81-84.

3. M. Isabel Calaza, Xiaoyin Yang, Darunee Soorukram, Paul Knochel, "Stereoselective S_N2-Substitutions using Polyfunctional Lithium Arylcuprates Prepared by an Iodine-Copper Exchange" *Organic Letters* **2004**, *8*, 1229-1231.

4. Xiaoyin Yang, Andreas Althammer, Paul Knochel, "Selective Functionalized in Position 2 and 3 of Indole *via* an Iodine-Copper Exchange Reaction" *Organic Letters* **2004**, *6*, 1665-1667.

5. Xiaoyin Yang, Paul Knochel, "Preparation and Acylation of Polyfunctional Copper Derivatives of 3-Iodoindazoles Leading to Polyfunctional 3-Acylindazoles" *Synlett*. **2004**, *13*, 2303-2306.

6. Paul Knochel, Xiaoyin Yang, Nina Gommermann, "Polyfunctional Organocopper Reagents for Organic Synthesis" in P. Knochel (Ed.) *Handbook of Functionalized Organometallics*, Wiley-VCH, Weinheim, **2005**.

To Yin, with love

THEORETICAL PART

Abbreviations

Ac	acetyl
approx.	approximately
Bn	benzyl
Boc	*tert*-butoxycarbonyl
br	broad
Bu	butyl
c	concentration
Calcd.	calculated
cat.	catalytic
conc.	concentrated
c-Hex	*cyclo*-hexyl
c-Pent	*cyclo*-pentyl
d	doublet
dr	diastereomeric ratio
DBE	dibromoethane
DMAP	4-dimethylaminopyridine
DMF	dimethylformamide
DMSO	dimethylsulfoxide
ee	enantiomeric excess
equiv	equivalent
E^+	electrophile
EI	electron ionisation
Et	ethyl
EtOAc	ethyl acetate
FAB	fast-atom bombardment
FG	functional group
GC	gas chromatography
h	hour
HMPA	hexamethylphosphorous triamide
HRMS	high resolution mass spectroscopy
i-Bu	*iso*-butyl
i-Pr	*iso*-propyl
IR	infrared spectroscopy
J	coupling constant
LDA	lithiumdiisopropylamine
LG	leaving group
m	multiplett
M	molar
Me	methyl
min	minute
mp.	melting point
MS	mass spectroscopy
NMP	*N*-methyl-pyrrolidinone
NMR	nuclear magnetic resonance
Np	Neopenhyl
Nphyl	Neophyl
Nu	nucleophile
o	*ortho*
p	*para*
Pent	pentyl
PG	protecting group
Ph	phenyl
q	quartet
quant.	quantitative
rt	room temperature
s	singlet
s-Bu	*sec*butyl
sec	seconds
t	triplet
t-Bu	*tert*-butyl
TEA	triethylamine
TMEDA	N,N,N',N'-Tetramethylethylendiamine
TFA	trifluoroacetic acid
THF	tetrahydrofuran
TLC	thin layer chromatography
TMS	trimethylsilyl
TMSCl	chlorotrimethylsilane
TP	typical procedure

THEORETICAL PART

1 Overview

The evolution of organometallic chemistry during the second half of the 20th century has transformed chemical science and technology to a degree and in ways that have rarely been matched throughout the history of chemistry.[1] These include the discovery of radically new types of chemical compounds, powerful new synthetic methodologies, novel structures and bonding modes, unprecedented reactivity patterns, new classes of catalysts and catalytic processes of extraordinary versatility and selectivity. The impact of these developments, which still are unfolding, has been truly revolutionary. The importance of organometallic chemistry was recently acknowledged when Dr. Yves Chauvin, Prof. Dr. Robert H. Grubbs and Prof. Dr. Richard R. Schrock were awarded the Nobel Prize for their great work on the development of the metathesis method.[2] Although various organometallics and efficient methods have been developed, the increasing complexity of target molecules and the constant need of highly functionalized building blocks make it necessary to develop new methods for a straightforward and efficient preparation of functionalized organometallic reagents.[3]

Conventional approaches using extensive protecting-group strategies are not satisfactory, because of a mediocre atom economy.[4] Radical reactions are more attractive but are more difficult to tune than polar reactions.[5] On the other hand, polyfunctional organometallic compounds provide a general entry into complex molecules and extensive applications in total synthesis were described.[6] There are two difficulties associated with such oragnometallic reagents: 1) tolerance of functional groups present in their preparation requires mild reaction conditions; 2) their reactivity is in many cases too low so that a transition metal catalyst is required, such as palladium or nickel complexes, to promote the reaction of these nucleophiles.[7] In principle, the reactivity of an organometallic reagent increases with the ionic character of the carbon-metal bond.[8] Through the use of highly reactive organometallic species, such as organolithium reagents, selectivity is often

[1] Halpern, J. *Pure Appl. Chem*. **2001**, *73*, 209.
[2] The Royal Swedish Academy of Science, Press Release: **2005**.
[3] Knochel, P. *Handbook of Functionalized Organometallics*, Wiley-VCH, Weinheim, **2005**.
[4] Trost, B. M. *Angew. Chem*. **1995**, *107*, 259; *Angew. Chem. Int. Ed*. **1995**, *34*, 285.

[5] Motherwell, W. B.; Chrich, D. *Free Radiacl Chain Reaction in Organic Synthesis*, Academic Press, London, **1992**.
[6] Nicolaou, K. C.; Snyder, S. A. *Classics in Total Synthesis II*, Wiley-VCH, Weinheim, **2003**.
[7] de Meijere, A.; Diederich, F. *Metal-Catalyzed Cross-Coupling Reactions*, Wiley-VCH, Weinheim, **2004**.
[8] Boudier, A.; Bromm, L. O.; Lotz, M.; Knochel, P. *Angew. Chem*. **2000**, *112*, 4585; *Angew. Chem. Int. Ed*. **2000**, *39*, 4415.

compromised. Furthermore, reduced tolerance toward sensitive functional groups, such as esters, nitriles, ketones and aldehydes, is always observed. However, the less reactive organometallic species, such as organozinc,[9] organotin[10] and organocopper reagents,[11] display only moderate reactivity towards most organic electrophiles and thus tolerate many functional groups.

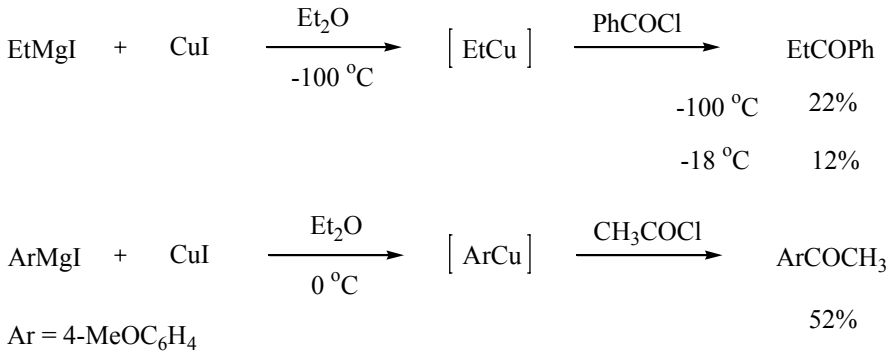
Due to their unique chemoselectivity and reactivity, organocopper reagents, occupy a special place in organic synthesis.[11] Gilman,[12] House[13] and Corey[14] showed in an impressive manner the broad scope of these organometallics in organic synthesis. The special covalent character of the carbon-copper bond confers them a satisfactory thermal stability and moderate reactivity towards polar functional groups, such as ketones or aldehydes. These special properties make it possible to prepare functionalized organocopper reagents. In this work, the attention was focused on the synthesis of functionalized organocopper reagents by a halogen-copper exchange and their reactions with various electrophiles.

1.1 Historical Perspective and Types of Organocopper Reagents

The first attempts to prepare organocopper compounds date back to 1859, when the reaction between diethyl zinc and CuCl was studied. The reaction resulted in the formation of metallic mirrors and, therefore, it was concluded that it was impossible to bind an organic group to copper.[15] More than 60 years later, the isolation of phenylcopper from the reaction between a arylmagnesium reagent and CuI was reported by R. Reich.[16] This can be regarded as the start of organocopper chemistry. The pioneering work from Gilman and coworkers in 1936 marked the beginning of the era of organocopper reagents as synthetic

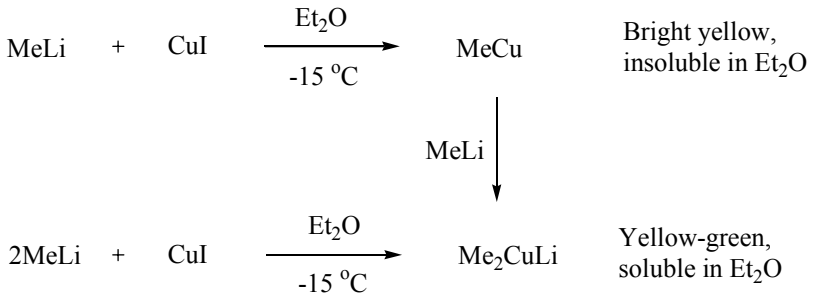
[9] a) Knochel, P.; Jones, P. *Organozinc Reagents: A Pratical Approach*, Oxford Press, **1999**; b) Knochel, P.; Millot, N.; Rodriguez, A. L.; Tucker, C. E. *Org. React*. **2001**, *58*, 417; c) Erdik, E. *Organozinc Reagents in Organic Synthesis*, CRC Press, Boca Raton, **1996**; d) Knochel, P.; Singer, R. D. *Chem. Rev.* **1993**, *93*, 2117.
[10] Davies, A. G. *Organotin Chemistry* Wiley-VCH, Weinheim, **2004**.
[11] a) Krause, N. *Modern Organocopper Chemistry*, Wiley-VCH, Weinheim, **2002**; b) Taylor, R. J. K.; *Organocopper Reagents. A Practical Approach*, Oxford University Press, **1994**; c) Lipshutz, B. H.; Sengupta, S. *Org. React.* **1992**, *41*, 135.
[12] Gilman, H.; Jones, R. G.; Woods, L. A. *J. Org. Chem.* **1952**, *17*, 1630.
[13] House, H. O.; Respess, W. L.; Whitesides, G. M. *J. Org. Chem.* **1966**, *31*, 3128.
[14] Corey, E. J.; Katzenellenbogen, J. A.; Gilman, N. W.; Roman, S. A.; Erickson, B. W. *J. Am. Chem. Soc.* **1968**, *90*, 5618.
[15] Buckton, G. *Ann*. **1859**, *109*, 225.
[16] Reich, R.; Hebd, C. R. *Seances Acad. Sci.* **1923**, *177*, 322.

tools in organic chemistry, describing the preparation of mono-organocopper reagents and their considerable synthetic potential (Scheme 1).[17]



Scheme 1: Pioneering preparation of mono-organocopper reagents.

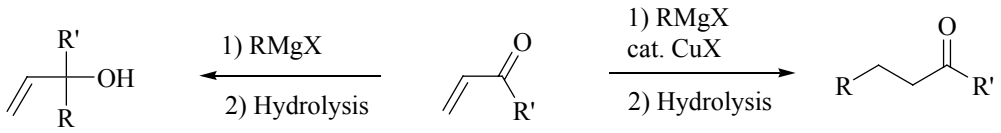
Furthermore, in 1952 Gilman *et al.* described another important observation that the insoluble yellow methylcopper redissolved in Et_2O on the addition of a second equivalent of methyllithium (Scheme 2).[12] This was the first report of what are now known as organocuprate reagents (or Gilman reagents).



Scheme 2: Pioneering preparation of Gilman reagent.

About the same time, the use of copper salts as catalysts in organometallic reactions was becoming popular. The observation that catalytic amounts of copper halides favored 1,4-addition over the usually observed 1,2-addition in the reaction between Grignard reagents and α,β-unsaturated ketones was of crucial importance for the further development of organocopper reagents as synthetic tools in organic chemistry (Scheme 3).[18]

[17] Gilman, H.; Straley, J. M. *Recl. Trav. Chim. Pays-Bas* **1936**, *55*, 821.
[18] Kharasch, M. S.; Tawney, P. O. *J. Am. Chem. Soc.* **1941**, *63*, 2308.



Scheme 3: Copper-catalyzed conjugated addition reaction of organomagnesium reagents.

Following these pioneering studies, an avalanche of publications appeared describing the preparation of new types of organocopper reagents and new synthetic applications. Herein, a summary of the available types of organocopper reagents are given in Table 1.[11b, 19] It should be noted, that only the organocopper reagents used in stoichiometric amounts are mentioned here.

Table 1: Types of organocopper reagents[a]

Type	Composition[b]
Mono-organocopper reagents (Organocopper reagents)	RCu
Homocuprate reagents (C uprate or Gilman reagents)	R_2CuM
Heterocuprate reagents	RCu(Z)M
Higher order heterocuprates, e.g. $R_{m+n}Cu_mLi_n$ (m + n > 2)	R_3Cu_2Li or $R_5Cu_3Li_2$
Higher order heterocuprates, e.g. Higher order cyanocuprates	$R_2Cu(CN)M_2$

a: In order to avoid confusion, the term organocopper reagent will be employed in a generic sense to describe all type of copper-based organometallic system. The specific reagent type with the stoichiometry RCu will be refered as a mono-organocopper reagent.

b: M is usually Li or Mg; X is usually I or Br; Z is usually SPh or O*t*-Bu.

[19] Lipshutz, B. H. *Organocopper Reagents and Procedures* in *Organometallics in Synthesis A manual II*, Schlosser, M., Ed., John Wiely and Sons, Chichester, UK, **1998**.

Mono-organocopper reagents are usually unreactive. However, in the presence of a metal salt, a cuprate, such as $(RCuX)^-$, is the reactive species.[20] Reagents of this type are often insoluble due to their oligomeric or polymeric structures and are not thermally stable.[21] Homocuprate reagents (usually R_2CuLi or R_2CuMgX) are the most widely used organocopper reagents. In general, this type of copper reagents possesses enhanced nucleophilicity and stability compared to their mono-organocopper counterparts. Heterocuprate reagents are also efficient with respect to organic group transfer and, although they are usually less reactive than homocuprate reagents, they often display improved thermal stability.[22] Higher order homocuprates were formed by varying the ratio CuX:RLi.[23] A few synthetic application of these reagents have been developed, for example, R_3Cu_2M (M = Li or MgBr) effects the carbocupration of terminal alkynes.[24] Higher order heterocuprates, particularly the cyanocuprates, proved to be extremely versatile synthetic reagents. They are formed easily[25] and combine the stability of heterocuprates with the reactivity of homocuprates. They also have the advantage that the copper precursor, CuCN, is inexpensive, nonhydroscopic, not sensitive, and prefers the copper (I) oxidation level.

The value of these organocopper reagents in organic synthesis is well measured by the extent of their usage in the synthesis of complex natural products. An excellent example with a focus on applications of organocopper reagents was shown in a total synthesis of brevetoxin B **1**, an active compound of poisonous waters associated with the red tide phenomenon. K. C. Nicolaou and co-workers employed a substitution reaction on a sp^2-hybridized carbon center by a functional organocopper reagent **2** as one of the key steps to carry out the formation of the D ring (Scheme 4).[26]

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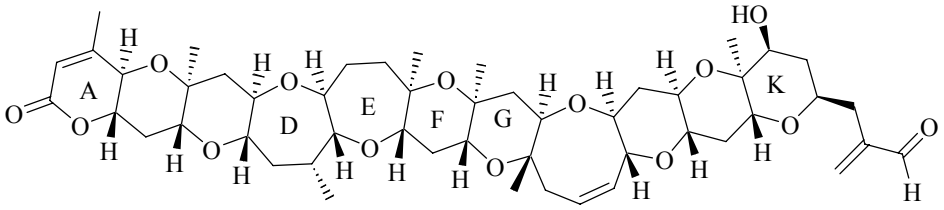
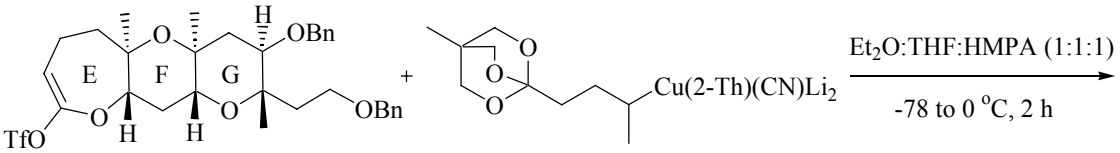
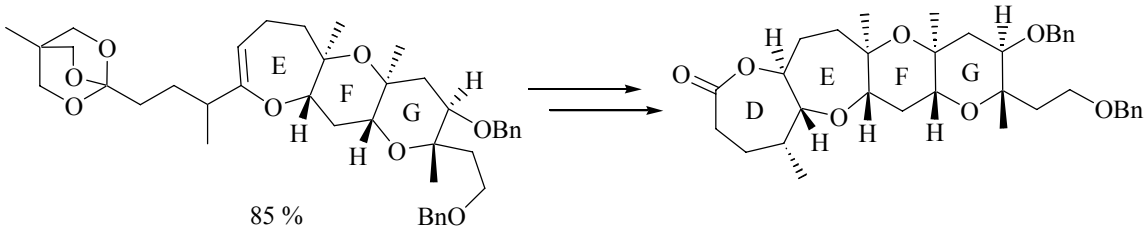
[20] Posner, G. H. *Org. React*. **1975**, *22*, 253.
[21] Bertz, S. H.; Dabbagh, G. *Tetrahedron* **1989**, *45*, 425.
[22] a) Posner, G. H.; Whitten, C. E.; Sterling, J. J. *J. Am Chem. Soc.* **1973**, *95*, 7788; b) Bertz, S. H.; Dabbagh, G. *J. Org. Chem*. **1984**, *49*, 1119; c) Cowley, A. H. *J. Am Chem. Soc.* **1988**, *110*, 7226.
[23] Ashby, E. C.; Lin, J. J. *J. Org. Chem.* **1977**, *42*, 2805.
[24] Westmijze, H.; Kleijn, H.; Meijer, M.; Vermeer, P. *Recl. Trav. Chim. Pays-Bas* **1981**, *100*, 98.
[25] a) Lipshutz, B. H.; Wilhelm. R. S.; Kozlowski, J. A. *Tetrahedron* **1984**, *40*, 5005; b) Lipshutz, B. H.; Wilhelm. R. S.; Floyd, D. M. *J. Am Chem. Soc.* **1981**, *103*, 7672; c) Lipshutz, B. H.; Kozlowski, J. A.; Wilhelm. R. S. *J. Org. Chem.* **1983**, *48*, 546.
[26] Nicolaou, K. C.; Theodorakis, E. A.; Rutjes, F. P. J. T.; Sato, M.; Tiebes, J.; Xiao, X. Y.; Hwang, C. K.; Duggan, M. E.; Yang, Z.; Couladouros, E. A.; Sato, F.; Shin, J.; He, H. M.; Bleckman, T. *J. Am. Chem. Soc.* **1995**, *117*, 10239.



Brevetoxin B **1**



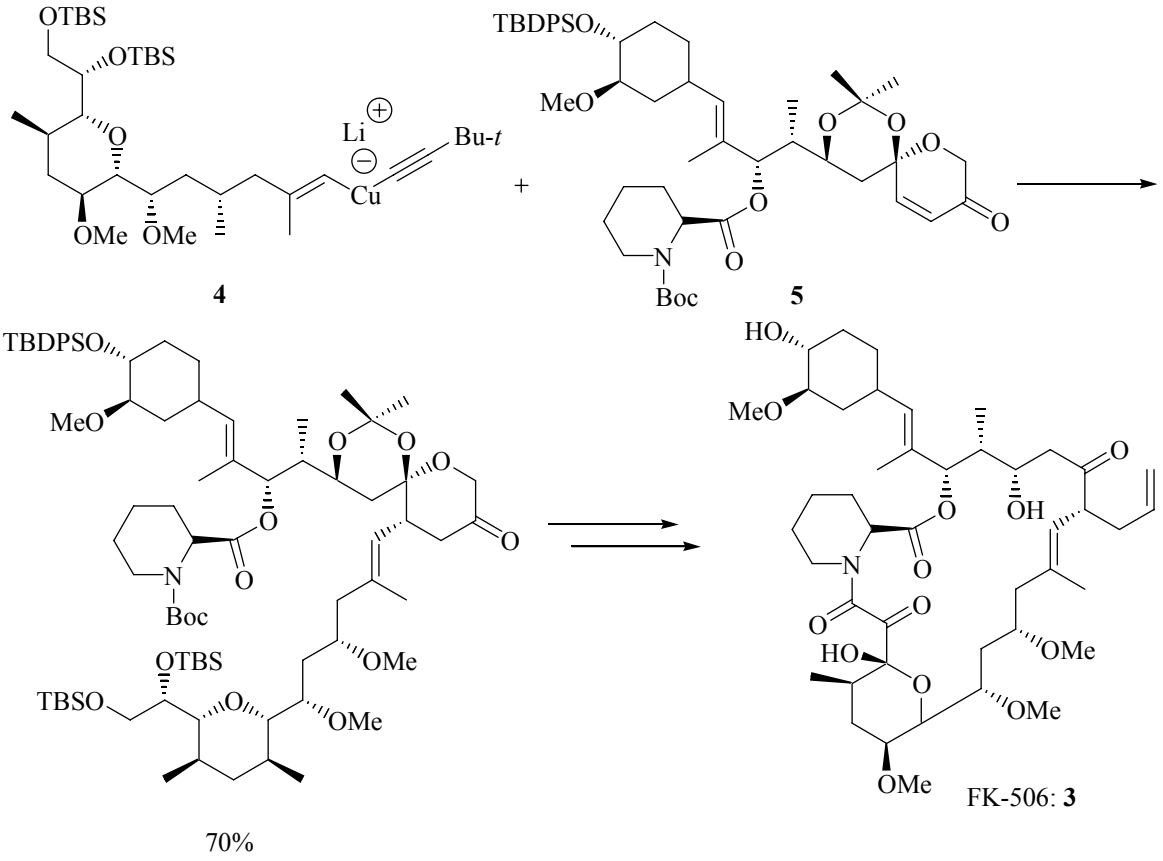
2



Scheme 4: Application of an organocopper reagent in the synthesis of brevetoxin B.

Another impressive use of organocopper reagents in the field of total synthesis was provided by the group of R. E. Ireland,[27] in the synthesis of the immunosuppressant FK-506 **3**. In their strategy the conjugated addition of a vinylic copper reagent **4** to an α,β-unsaturated ketone **5** served as a key step to couple the two huge building blocks (Scheme 5).

[27] a) Ireland, R. E.; Gleason, J. L.; Gegnas, L. D.; Highsmith, T. K. *J. Org. Chem.* **1996**, *61*, 6856; b) Irelan, R. E.; Liu, L.; Roper, T. D. *Tetrohedron* **1997**, *53*, 13221.



Scheme 5: Alkenylcopper reagent in the synthesis of immunosuppressant FK-506.

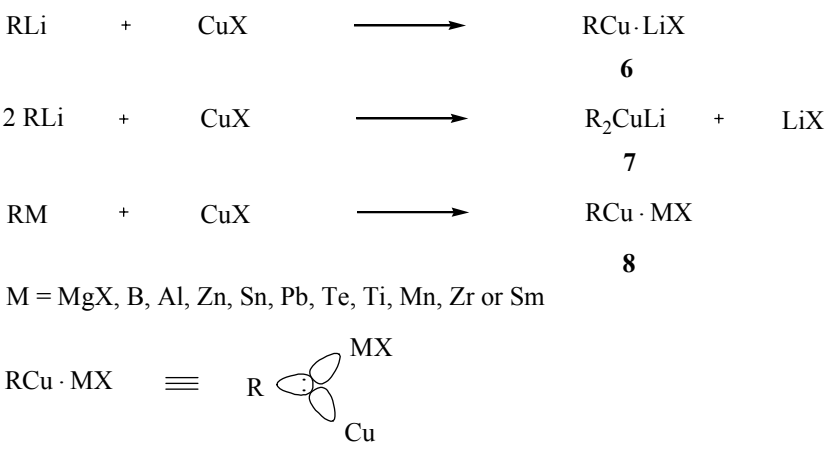
1.2 Preparation of Organocopper Reagents

1.2.1 Conventional Preparation Methods

Up to now, the vast majority of protocols for the preparation of organocopper reagents involve the transmetalation process from other organometallic species such as organolithium or organomagnesium. Most reports use organocopper reagents of type **6** or **7**, which are prepared from organolithiums (Scheme 6). In principle all organometallics, in which the metal M is less electronegative than copper, and all organometallic species of similar electronegativity but with weaker carbon-metal bond, are potential candidates for the transmetalation reactions.[28] Thus, reaction conditions allowing the transmetalation of organoboron, -aluminium, -zinc, -tin, -lead, -tellurium, -titanium, -manganese, -zirconium and -samarium compounds have all been developed, resulting in a variety of new organocopper reagents of type **8**. Their reactivity is dependent on the nature of the original

[28] Negishi, E. *Organometallics in organic Synthesis*, Wiley, New York, **1980**.

metal M, which in many cases is still intimately associated with the resulting organocopper reagents (Scheme 6).[29]



Scheme 6: Transmetalations producing organocopper reagents.

Unfortunately, in many cases this transmetalation approach precludes the presence of most functional groups in these copper reagents, since they would not be tolerated in the starting organometallic species. Recently, P. Knochel and co-workers developed two new methods to prepare functionalized organozinc and organomagnesium reagents.[30] These organometallic reagents react easily with copper salts to generate the corresponding organocopper compounds. In this way, these methodologies to some extent solved the problems of functional group tolerance. However, to more sensitive groups, such as ketones or aldehydes, these methods still have some limitations.

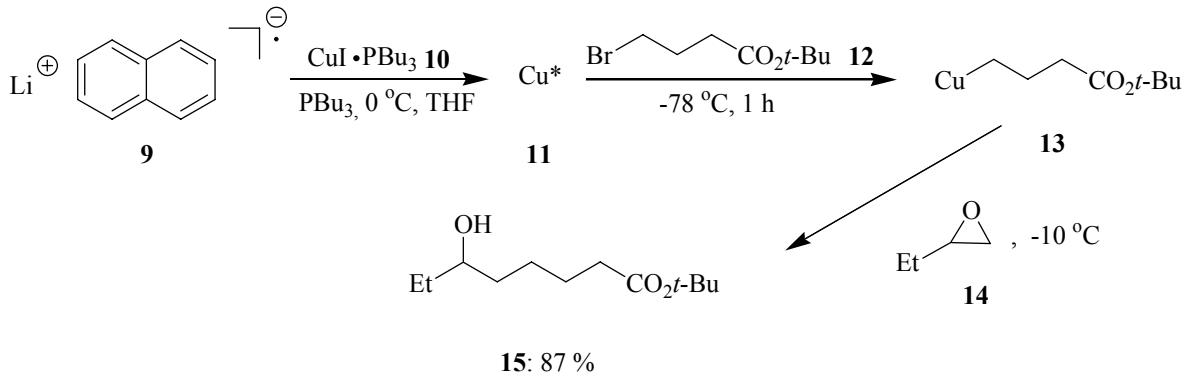
Direct insertion of activated copper metal into the halide-carbon bond is another common method for the preparation of organocopper reagents. Major improvements have been achieved in this area. Most notably, R. D. Rieke and coworkers have developed several reactive forms of zerovalent copper in combination with additives that allow the preparation of organocopper reagents.[31] Thus, the treatment of lithium naphthalenide **9** with $CuCN{\cdot}PBu_3$ **10** at −78 °C led to the activated copper (0) **11**, which was reacted with *t*-butyl

[29] a) Krause, N. *Angew. Chem.* **1999**, *111*, 83; *Angew. Chem. Int. Ed.* **1999**, *38*, 79; b) Boche, G.; Bosold, M.; Harms, K. *Angew. Chem.* **1998**, *110*, 1779; *Angew. Chem. Int. Ed.* **1998**, *37*, 1684.

[30] a) Knochel, P.; Yeh, M. C.; Berk, S. C.; Talbert, J. *J. Org. Chem.* **1988**, *53*, 2390; b) Boymond, L.; Rottländer, M.; Cahiez, G.; Knochel, P. *Angew. Chem.* **1998**, *110*, 1801; *Angew. Chem. Int. Ed.* **1999**, *37*, 1701; c) Varchi, G.; Jensen, A. E.; Dohle, W.; Ricci, A.; Knochel, P. *Synlett*, **2001**, 477.

[31] a) Ebert, G. W.; Rieke, R. D. *J. Org. Chem.* **1984**, *49*, 5280; b) Wehmeyer, R. M.; Rieke, R. D. *J. Org. Chem.* **1987**, *52*, 5056; c) Ebert, G. W.; Rieke, R. D. *J. Org. Chem.* **1988**, *53*, 4482; d) Rieke, R. D.; Klein, W. R. in *Organocopper Reagents. A Practical Approach*, Ed. Taylor, R. J. K. Oxford University Press, **1994**.

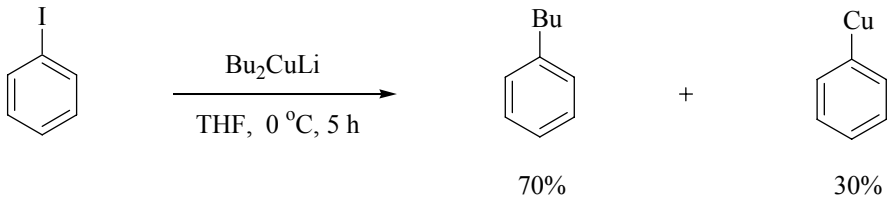
4-bromobutyrate **12**, providing the corresponding copper derivative **13**. The presence of phosphine ligands was crucial for this reaction, because it enhances the reactivity of highly active copper due to its electron-donating nature and reduces the amount of homocoupled side products. The resulting monocopper reagent readily reacted with epoxide **14**, furnishing the corresponding alcohol **15** in 87% yield (Scheme 7). But again, this method is neither general nor applicable in the presence of a number of sensitive functional groups.



Scheme 7: Preparation of organocopper reagent by direct insertion of activated copper.

1.2.2 Halogen-Copper Exchange Reaction for The Preparation of Organocopper Reagents

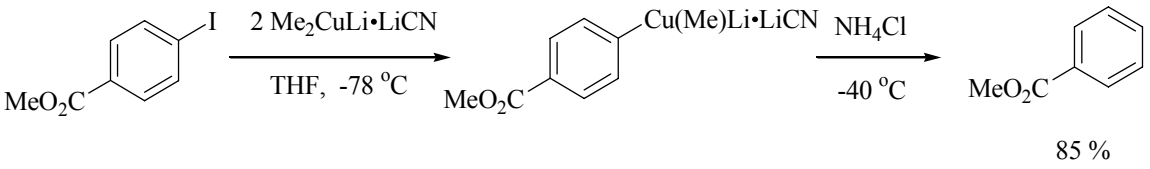
Quite surprisingly, the formation of functionalized organocopper reagents *via* halogen-copper exchange was not yet extensively studied. The first iodine-copper exchange reaction was reported by E. J. Corey and G. H. Posner.[32] They observed that lithium dialkylcuprates reacted with aryl iodides leading to the expected cross-coupling product and a competitive halogen-metal exchange reaction (Scheme 8).



Scheme 8: Cross-coupling and exchange reaction of dibutylcuprate with iodobenzene.

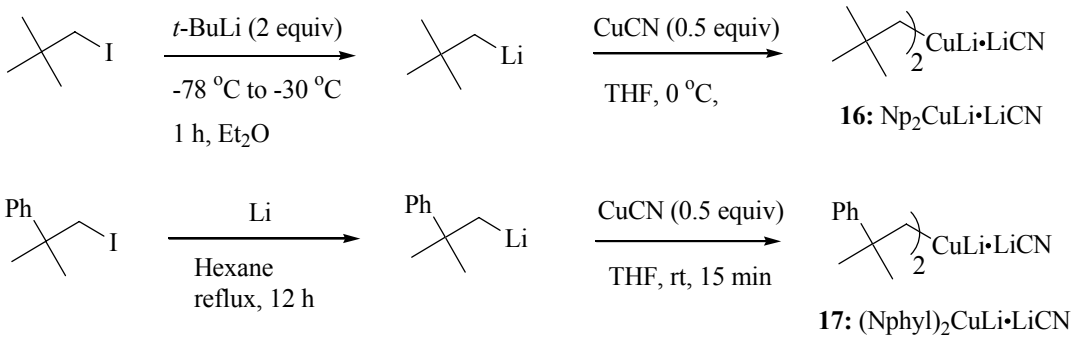
[32] a) Corey, E. J.; Posner, G. H. *J. Am. Chem. Soc.* **1967**, *89*, 3911; b) Corey, E. J.; Posner, G. H. *J. Am. Chem. Soc.* **1968**, *90*, 5615.

Kondo and Sakamoto described that the use of lithium dimethylcuprate allowed the performance of an I/Cu-exchange on a functionalized aryl iodide bearing an ester group.[33] However, an excess of the cuprate is required due to the reaction with methyl iodide formed during the exchange reaction (Scheme 9).



Scheme 9: I/Cu-exchange reaction for preparation of functionalized cuprate reagents.

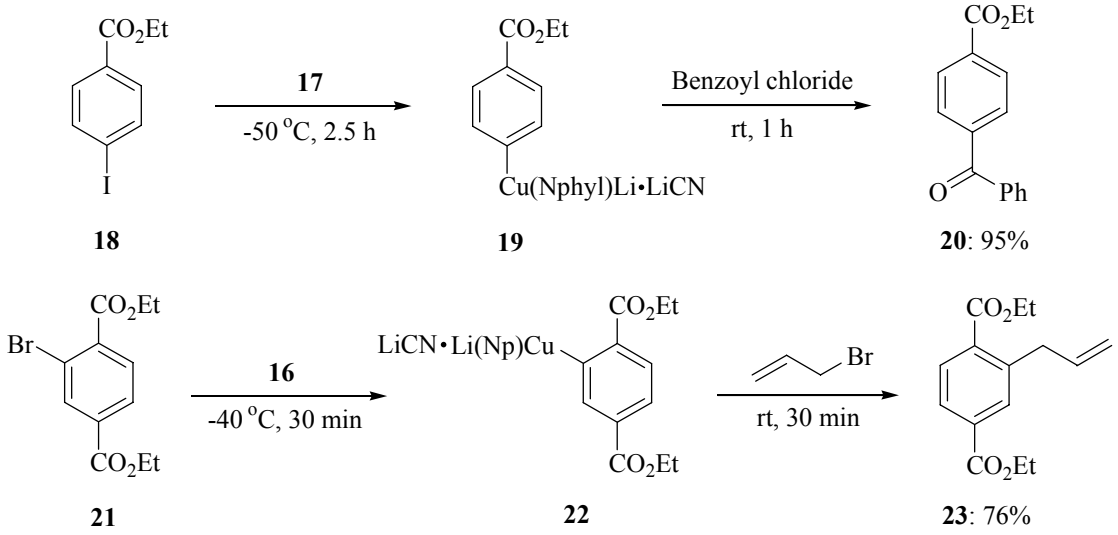
More recently, P. Knochel and C. Piazza reported for the first time that sterically hindered lithium dialkylcuprates, such as lithium dineopentylcuprate ($(Me_3CCH_2)_2CuLi{\cdot}LiCl$; **16**) and lithium dineophylcuprate ($(Me_2PhCCH_2)_2CuLi{\cdot}LiCl$; **17**) rapidly reacted with various functionalized aryl halides to generate the corresponding functionalized organocopper reagents.[34] Cuprates **16** and **17** are easily prepared from the corresponding lithium reagents and CuCN (Scheme 10).[35] The steric hindrance of the neopentyl and neophyl groups in **16** and **17** are essential for the selectivity of the halogen-copper exchange.[36] On the other hand, these two groups are also non-transferable. Several other groups and copper salts were also tested for this exchange reaction, but gave inferior results.



Scheme 10: Preparation and structure of cuprates **16** and **17**.

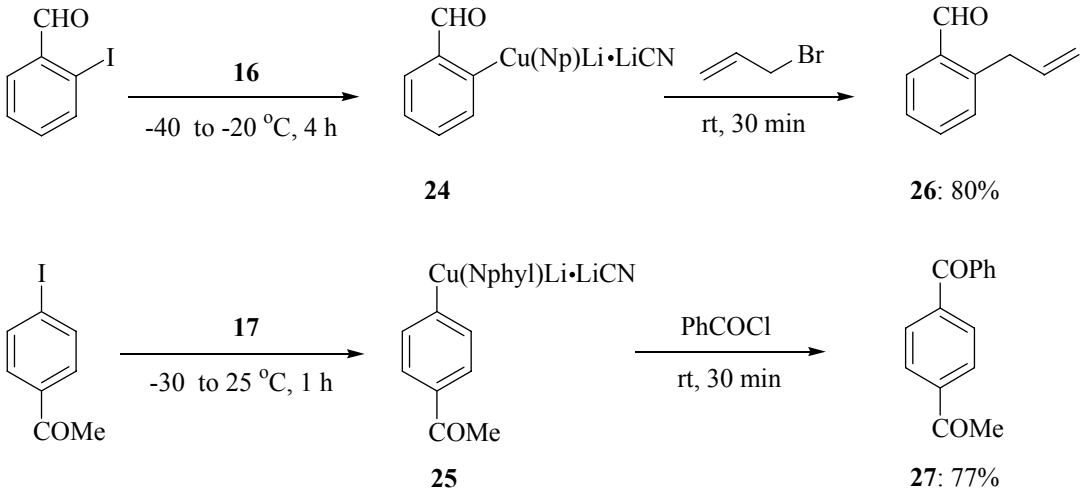
[33] Kondo, Y.; Matsudaira, T.; Sato, J.; Muraka, N.; Sakamoto, T. *Angew. Chem*. **1996**, *108*, 818; *Angew. Chem. Int. Ed.* **1996**, *35*, 736.
[34] Piazza, C.; Knochel, P. *Angew. Chem. Int. Ed.* **2002**, *41*, 3263.
[35] a) Negishi, E.; Swanson, D. R.; Rousset, C. J. *J. Org. Chem.* **1990**, *55*, 5406; b) Cano, A.; Cuenca, T.; Galakov, M.; Rodriguez, G. M.; Royo, P.; Cardin, C. J.; Convery, M. A. *J. Organomet. Chem.* **1995**, *17*, 493.
[36] Kondo, Y.; Asai, M.; Uchiyama, T.; Sakamoto, T.; *Org. Lett.* **2001**, *3*, 13.

(Nphyl)$_2$CuLi·LiCl (**17**) is slightly less reactive than the Np$_2$CuLi·LiCl (**16**) and, therefore, shows better chemoselectivity. Thus, the iodoester **18** reacted with (Nphyl)$_2$CuLi·LiCl (**17**) to generate the corresponding copper derivative **19** within 2.5 h at –50 °C. Its reaction with benzoyl chloride provided the desired product **20** in 95% yield. Interestingly, a Br/Cu-exchange could also be performed with Np$_2$CuLi·LiCl (**16**). Thus, aryl bromide **21** was readily converted by **16** within 30 min at –40 °C to the cuprate **22**, which was allylated with allyl bromide to give the desired product **23** in 76% yield (Scheme 11).



Scheme 11: Preparation of functionalized arylcopper reagents *via* halogen-copper exchange.

Furthermore, the use of the sterically hindered Np$_2$CuLi·LiCl (**16**) and (Nphyl)$_2$CuLi·LiCl (**17**) allowed the preparation of arylcopper derivatives, even when bearing an aldehyde or a ketone function such as the cuprates **24** and **25**. Their reactions with benzoyl chloride or allyl bromide provided the expected products **26** and **27** in 80% and 77% yield, respectively (Scheme 12).[34]

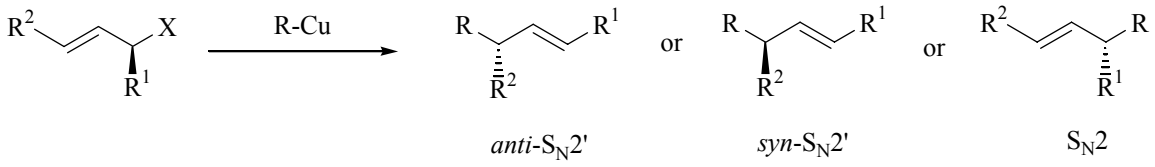


Scheme 12: Preparation of functionalized cuprates **24** and **25**.

These excellent priliminary results showed that the halogen-copper exchange reaction is a promising method for the preparation of functionalized cuprates. A further extension of this method would be described in this work.

1.3 Allylic Substitution Reactions of Organocopper Reagents

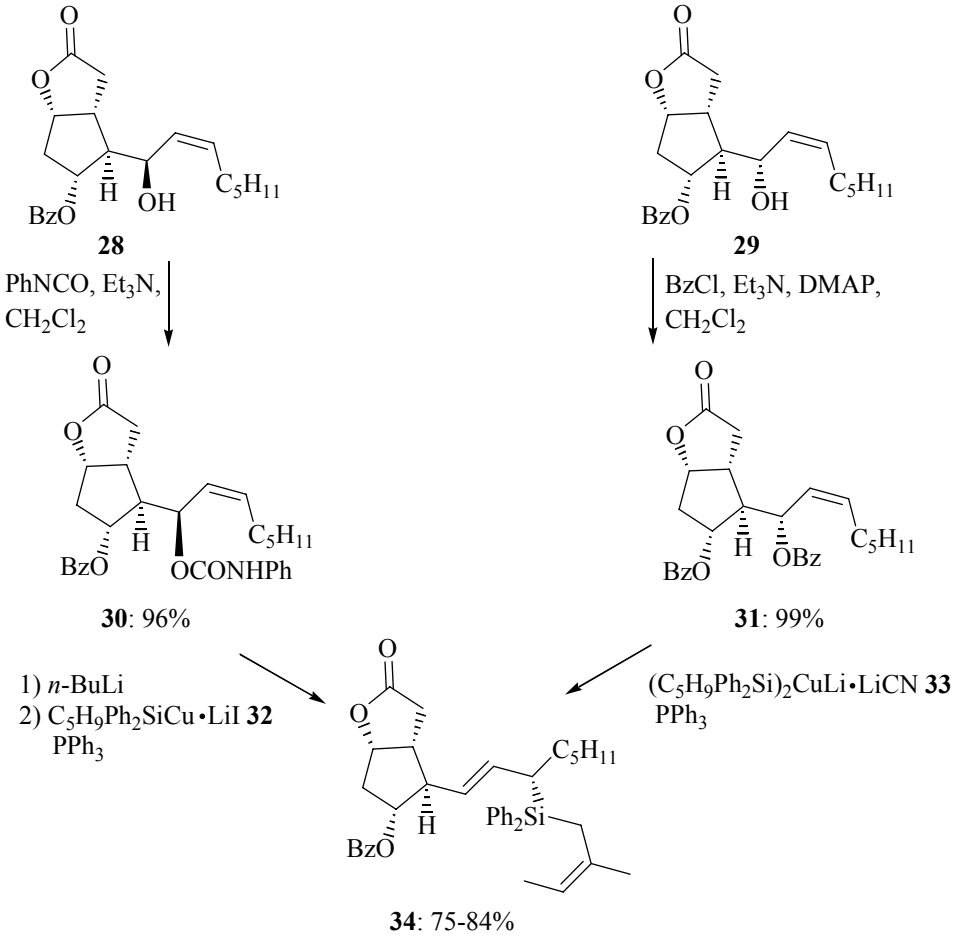
Synthetic methods involving the formation of a new C-C bond with absolute stereocontrol constitute a very valuable tool for the preparation of complex natural products where numerous successive synthesis steps need to be carried out selectively.[37] Allylic substitution reactions of organocopper reagents allow a highly selective formation of new C-C bonds. Thereby, a new stereogenic center can be introduced in the course of the reaction (Scheme 13).[11a, 38]



Scheme 13: Copper-mediated asymmetric allylic substitution reaction.

[37] a) Lin, G.-Q.; Li, Y.-M.; Chan, A. S. C. *Principles and Applications of Asymmetric Synthesis*, Wiley-Interscience, **2001**; b) Gawley, R. E.; Aubé, J. *Principles of Asymmetric Synthesis*, Pergamon, **1996**.
[38] Spino, C.; Beaulieu, C. *J. Am. Chem. Soc.* **1998**, *120*, 11832; b) Belelie, J. L.; Chong, J. M. *J. Org. Chem.* **2001**, *66*, 5552; c) Smitrovich, J. H.; Woerpel, K. A. *J. Org. Chem.* **2000**, *65*, 1601.

An elegant illustration of the power of a diastereoselective cuprate addition to allylic system was reported in the course of a synthesis of prostaglandins (Scheme 14). The starting diastereometric *Z* allylic alcohols **28** and **29** were first transformed either into the carbamate **30** or into the benzoate **31**. Allylic substitution of both substrates with the organocopper reagents **32** and **33** converged to the formation of a single diastereomer **34** in good yields.[39]



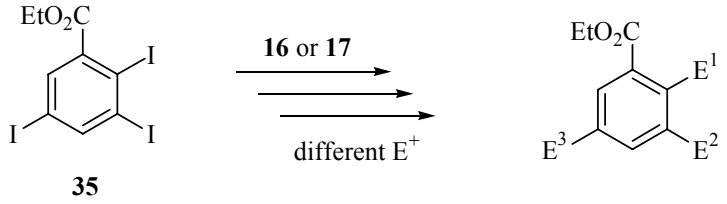
Scheme 14: Allylic substitution with cuprates in the course of a prostaglandin synthesis.

Since the preparation of functionalized cuprates is possible, the application of these cuprates to selective allylic substitution reaction should be a potential research topic for the preparation of chiral compounds.

[39] a) Fleming, I,; Winter, S. B. D. *Tetrahedron Lett.* **1995**, *36*, 1733; b) Fleming, I,; Winter, S. B. D. *J. Chem. Soc., Perkin Trans. I* **1998**, 2687.

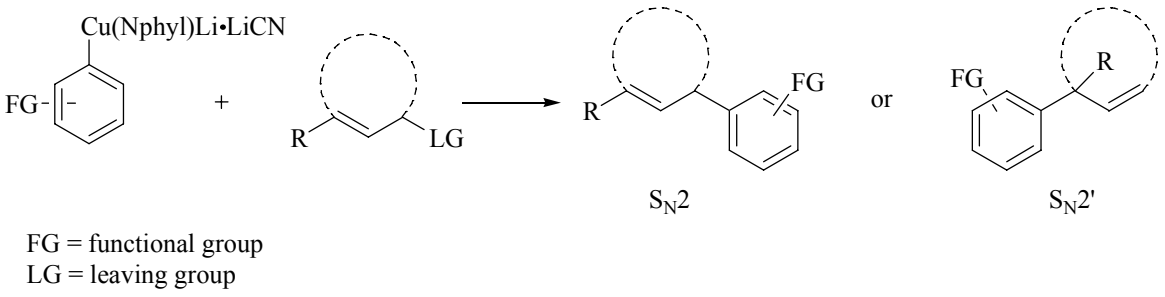
2 Objectives

As mentioned above, numerous applications of organocopper reagents in organic synthesis make it always necessary to further develop new methods for the preparation of functionalized organocopper reagents. Following the initial and successful development of a mild and chemoselective halogen-copper exchange reactions to generate functionalized cuprate reagents in our group,[34] the first objective of this work is to further apply this method to the functionalization of polyhalogenated aromatic compounds **35**, using the regioselective halogen-copper exchange reaction (Scheme 15).



Scheme 15: Successive I/Cu-exchange reaction for selective functionalization of triiodobenzoate **35**.

Since the preparation of functionalized aryl cuprates *via* halogen-copper is possible, the second objective is to investigate the reactivity of these functionalized cuprates with allylic electrophiles (Scheme 16).

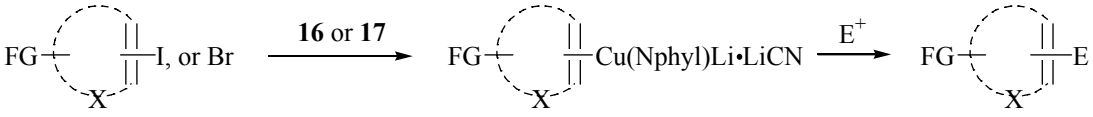


Scheme 16: Application of functionalized copper reagents in allylic substitution reactions.

In order to broaden the scope of the halogen-copper exchange reaction, various functionalized heteroaryl and alkenyl systems were studied to determine its range of

applicability and in particular its functional group compatibility. Thus, following objectives will be included (Scheme 17).

- Preparation of highly functionalized heteroaryl cuprates *via* halogen-copper exchange reaction.
- Preparation of highly functionalized alkenyl cuprates *via* halogen-copper exchange reaction.

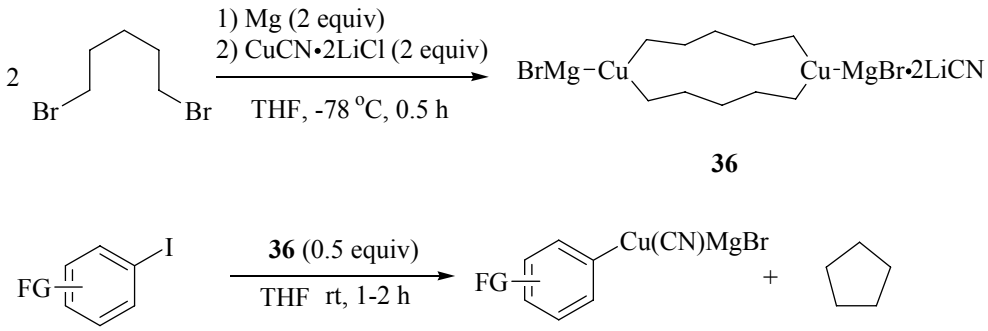


FG =aldehyde, Ketone, ester, CN, Br, I, OMe, OTs

X = N, O, S

Scheme 17: Synthesis of functionalized organocopper reagents.

Finally, a new related I/Cu-exchange reaction will be explored, which allows a clean way to prepare functionalized organocopper reagents by using the new magnesium cuprate reagent **36** (Scheme 18).

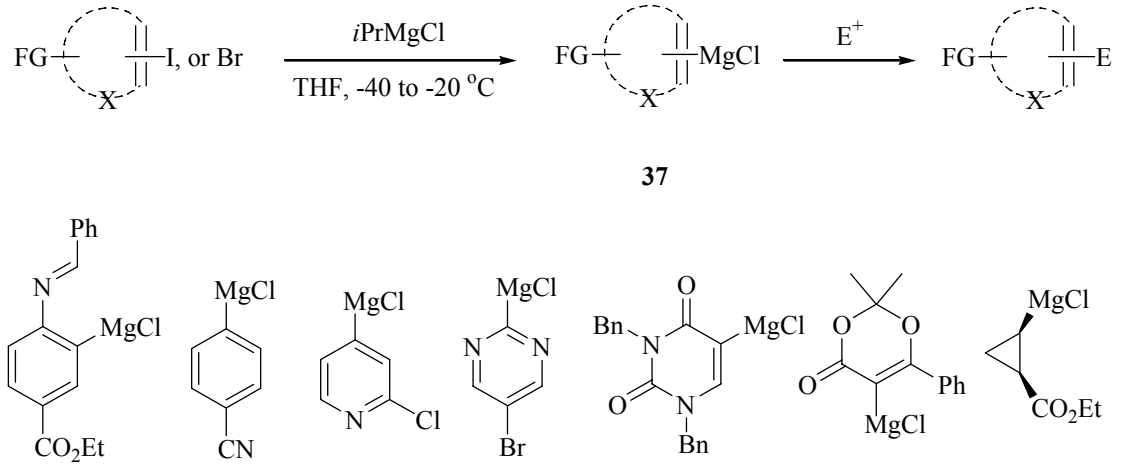


Scheme 18: Preparation of functionalized magnesium cuprates *via* an I/Cu-exchange reaction.

3 Preparation of Functionalized Arylcuprates *via* Halogen-Copper Exchange and Their Application in Allylic Substitution Reactions

3.1 Introduction

Highly functionalized organometallic compounds are key intermediates for the preparation of polyfunctionalized molecules.[40] Halogen-metal exchange reaction is a general and chemoselective method for preparing functionalized organometallics, such as organolithium[41] or organomagnesium.[42] Recently, P. Knochel and co-workers showed for the first time that I/Mg-exchange reaction allows the preparation of various polyfunctionalized arylmagnesium reagents of type **37** at low temperature, which bear different functional groups.[43] Since then, this reaction has been considerably extended to a variety of substrates (Scheme 19).



Scheme 19: Functionalized organomagnesium reagents prepared *via* halogen-magnesium exchange reaction.

[40] a) Knochel, P.; Millot, N.; Rodriguez, A. L.; Tucker, C. E. *Org. React.* **2001**, *58*, 417; b) Jensen, A. E.; Dohle, W.; Sapountzis, I.; Lindsay, D. M.; Vu, V. A.; Knochel, P. *Synthesis* **2002**, 265.
[41] a) Wakefield, B. J. *The Chemistry of Organolithium Compounds* Pergamon Press, Oxford, **1974**. b) Wakefield, B. J. *Organolithium Method* Academic Press, London, **1988**.
[42] Tamborski, C.; Moore, G. J. *J. Organomet. Chem.* **1971**, *26*, 153; b) Paradies, H. H.; Gorbing, M. *Angew. Chem. Int. Ed.* **1969**, *8*, 279.
[43] Knochel, P,; Dohle, W.; Gommermann, N.; Kneisel, F. F.; Kopp, F.; Korn, T.; Sapountzis, I.; Vu, V. A. *Angew. Chem. Int. Ed.* **2003**, *42*, 4302.

However, more sensitive functionalities, such as ketones and aldehydes are usually not compatible with these reagents. To overcome these problems, more recently Dr. Claudia Piazza in our group has developed a halogen-copper exchange reaction, which allowed a practical preparation of functionalized lithium cuprates in the presence of a ketone or even an aldehyde group.[34] As already mentioned in the introduction, these pioneering results showed that such halogen-copper exchange reaction could be a promising method for preparing functionalized organocopper reagents.

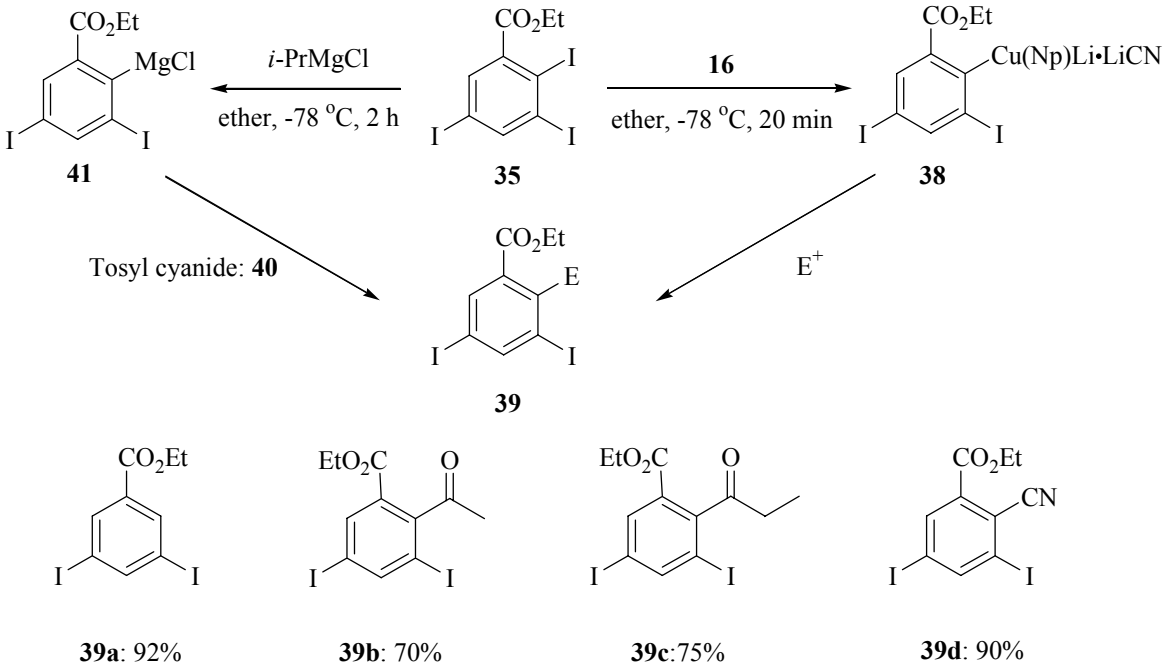
3.2 Successive I/Cu-Exchange Reactions for the Selective Functionalization of Polyhalogenated Aromatics

Our initial attention focused on the functionalization of polyhalogenated aromatic compounds. In general the rate of the halogen-metal exchange reaction greatly depends on the electron-density of the aromatic or heterocyclic ring (electron-rich system react slower), so that an aromatic or heterocyclic dibromide or diiodide undergoes only a mono-exchange.[44] Thus, readily available ethyl 2,3,5-triiodobenzoate (**35**) was treated with lithium $Np_2CuLi{\cdot}LiCl$ (**16**) (1.1 equiv) in diethyl ether at –78 °C. A highly regioselective I/Cu-exchange reaction was observed within 20 min, as indicated by the GC analysis of the reaction mixture, giving rise to the desired cuprate **38** (Scheme 20). The regioselectivity was proved unambiguously by the NMR spectra of a symmetric compound **39a** which was obtained from the hydrolysis of cuprate **38**. The observed selectivity of the I/Cu-exchange of the triiodobenzoate **35** was explained by a precomplexation of $Np_2CuLi{\cdot}LiCl$ (**16**) through the ester function that favors the exchange reaction in the *ortho*-position. The mixed lithium cuprate **38** reacted well with acyl halides.[45] The acylation of cuprate **38** with acetyl chloride and propionyl chloride led to the ketoester **39b** and **39c** in 70% and 75% yields, respectively. The introduction of cyanide group with tosyl cyanide **40** was unsuccessful due to the low reactivity of the cuprate **38**. An alternative route using iodine-magnesium exchange reaction led to the corresponding organomagnesium reagent **41** regioselectively within 2 h at -78 ^{o}C, which reacted readily with tosyl cyanide providing the desired product **39d** in 90% yield (Scheme 20).

---

[44] a) Varchi, G.; Jensen, A. E.; Dohle, W.; Ricci, A.; Cahiez, G.; Knochel, P. *Synlett* **2001**, *4*, 477; b) Abarbri, M.; Dehmel, F.; Knochel, P. *Tetrahedron Lett*. **1999**, *40*, 7449; c) Vu, V. A.; Marek, I.; Polborn, K.; Knochel, P. *Angew. Chem. Int. Ed.* **2002**, *41*, 351; d) Trécourt, F.; Breton, G.; Bonnet, V.; Mongin, F.; Marsais, F.; Quéguiner, G. *Tetrahedron Lett.* **1999**, *40*, 4339.

[45] Lipshutz, B. H.; Sengupta, S. *Org. React.* **1992**, *41*, 135.

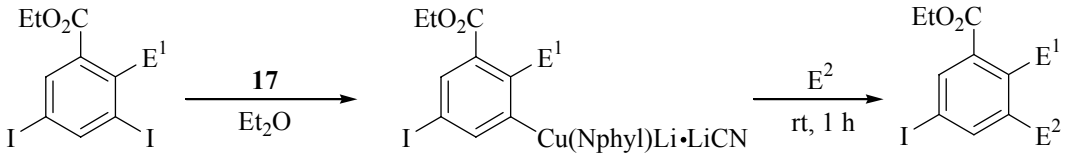


Scheme 20: Regioselectively functionalized polyiodobenzoate **35** *via* iodine-metal exchange reactions.

Products of type **39** were again subjected to an I/Cu-exchange reaction (Scheme 21; Table 2). As already mentioned, $(Nphyl)_2CuLi{\cdot}LiCl$ (**17**) was proved to be slighty less reactive than $(Np)_2CuLi{\cdot}LiCl$ (**16**). However, its low reactivity became advantageous, when very sensitive functional groups, such as ketone groups, are involved in the exchange reaction. Furthermore, its straightforward and inexpensive preparation makes it a very attractive reagent, particularly for industrial applications. Thus, the treatment of iodoaryl ketones **39b** and **39c** with **17** in Et_2O at –78 °C provided selectively within 2 h the corresponding cuprates **42a** and **42b**, respectively. The resulting **42a** was treated with allyl bromide[46] (entry 1 of Table 2) leading to the desired products **43a** in 75% yield. Aromatic and heterocyclic acid chlorides were also treated with **42a** and **42b** furnishing the corresponding ketones **43b-d** in 68-71% yields, respectively (entries 2-4). Similarly, the reaction of the diiodobenzonitrile derivative **39d** with **17** (THF, –78 °C, 2 h) led to the formation of the mixed cuprate **42c** (entry 5). Its reaction with ethyl cyanoformate (–78 °C to 25 °C, 24 h) furnished the symmetrical product **43e** in 70% yield (entry 5). In each case, a selective

[46] Villieras, J.; Rambaud, M. *Synthesis* **1982**, 924.

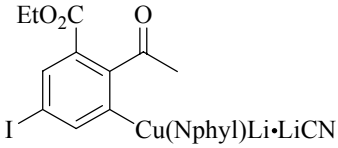
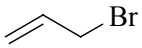
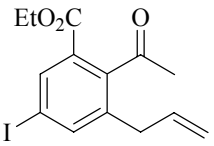
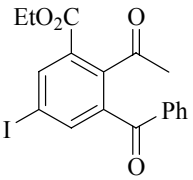
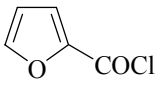
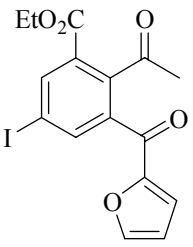
I/Cu-exchange reaction was observed. This selectivity was probably due to the presence of a directing *ortho*-substituent,[47] which by chelating or inductive effect triggered the reaction.



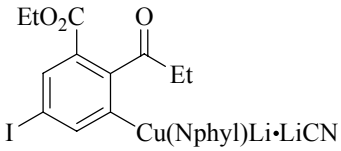
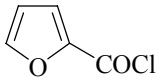
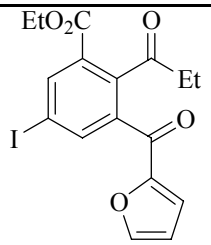
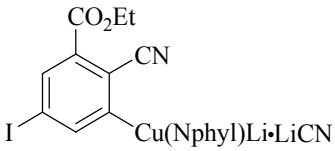
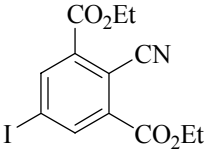
39 **42** **43**

Scheme 21: Selective preparation of cuprates **42** *via* I/Cu-exchange reaction.

Table 2: Selective formation of polyfunctional monoiodoaryl compounds **43** *via* I/Cu-exchange reaction.

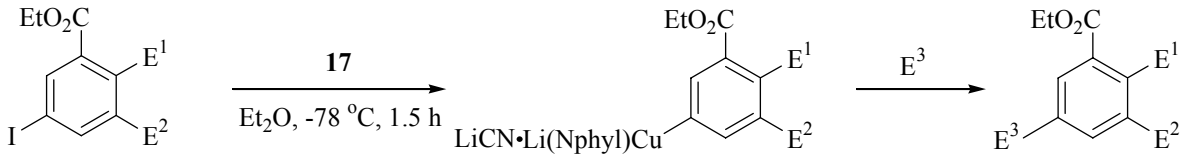
Entry	Cuprate Reagent **42**	Electrophile	Product of Type **43**	Yield (%)[a]
1	 **42a**		 **43a**	75
2	**42a**	PhCOCl	 **43b**	70
3	**42a**		 **43c**	68

[47] This effect has been extensively used to perform *ortho*-directed metalations: Snieckus, V. *Chem. Rev.* **1990**, *90*, 879.

Entry	Cuprate Reagent **42**	Electrophile	Product of Type **43**	Yield (%)[a]
4	 **42b**		 **43d**	71
5	 **42c**	$NC\text{-}CO_2Et$	 **43e**	70

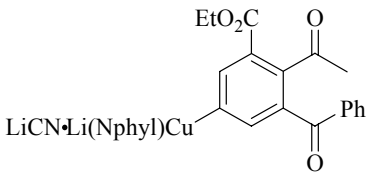
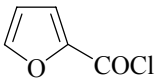
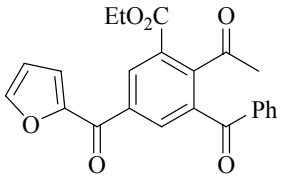
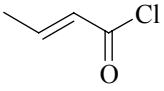
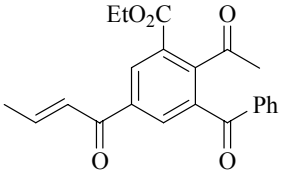
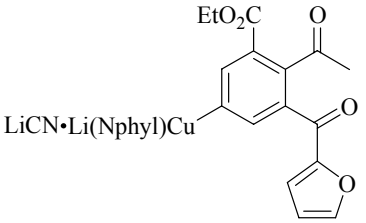
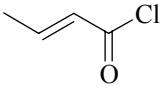
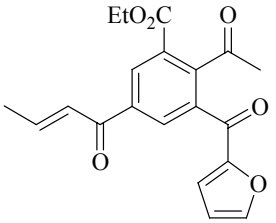
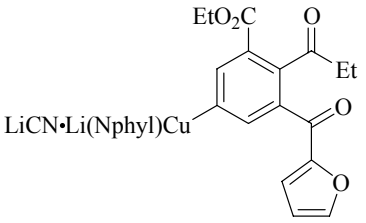
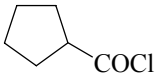
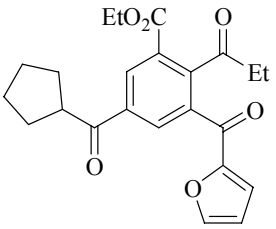
[a] Isolated yield of analytically pure product.

Finally, a third I/Cu-exchange could also be performed on the diketoesters **43b-d**. Their reactions with $Nphyl_2CuLi{\cdot}LiCl$ (**17**) (Et_2O, –78 °C, 1.5 h) produced the corresponding cuprates **44a-c**, which reacted with various aliphatic, heterocyclic or unsaturated acid chlorides leading to the tetrasubstituted benzenes **45a-d** in 60–67% yield (Scheme 22; Table 3). Compounds of type **45** are very difficult to prepare by standard methods. Our synthetic method offers a general approach to this class of functionalized aromatic molecules.



Scheme 22: Preparation polyfunctionalized cuprates **44** *via* I/Cu-exchange reaction.

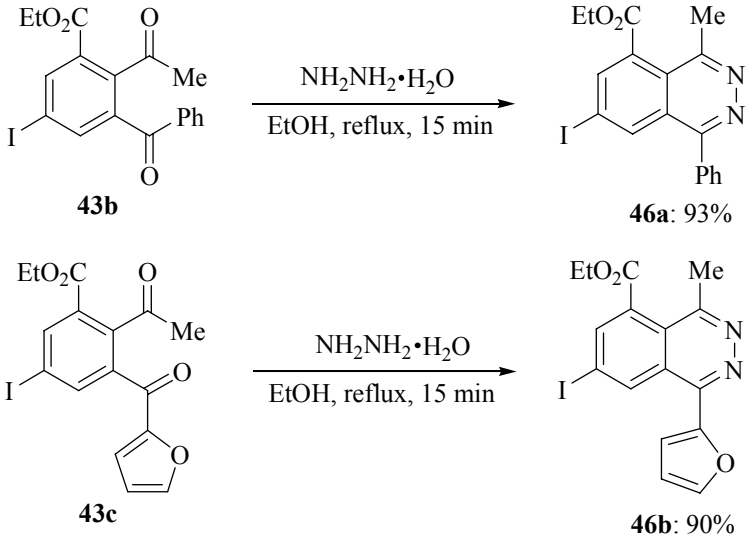
Table 3: Preparation of tetrasubstituteded arenes **45** *via* an I/Cu-exchange reaction.

Entry	Cuprate **44**	Electrophile	Product of Type **45**	Yield (%)[a]
1	 **44a**		 **45a**	65
2	**44a**		 **45b**	67
3	 **44b**		 **45c**	60
4	 **44c**		 **45d**	62

[a] Isolated yield of analytically pure product.

These polyacylated compounds are very useful building blocks for the synthesis of heterocycles. This was demonstrated by treating the iodoarenes **43b** and **43c** with hydrazine monohydrate in ethanol (reflux, 15 min), providing the polyfunctional phthalazines **46a** and **46b** in 90-93% yields (Scheme 23).[48]

[48] Haddadin, M. J.; Agha, B. J.; Tabri, R. F. *J. Org. Chem.* **1979**, *44*, 494.

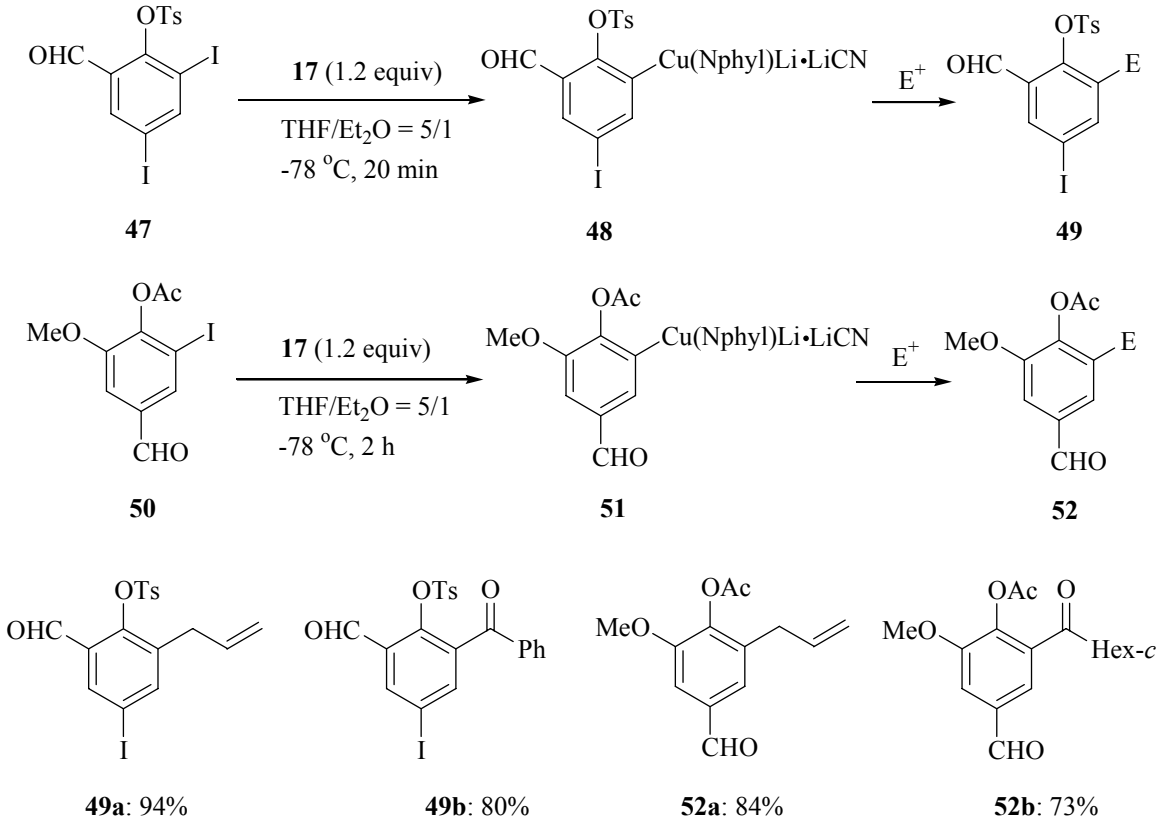


Scheme 23: Synthesis of phthalazine of type **46**.

3.2 Preparation of Highly Functionalized Aryl Cuprates in the Presence of an Aldehyde Group

Remarkably, even aldehydes were found to be compatible with this I/Cu-exchange reaction. Thus, aldehyde **47**[49] underwent a smooth I/Cu-exchange reaction with $(Nphyl)_2CuLi \cdot LiCl$ (**17**) (1.2 equiv, -78 °C, 20 min) to afford the desired mixed cuprate **48**, which reacted with electrophiles, such as allyl bromide or benzoyl chloride, to afford the desired products **49a-b** in 94% and 80% yields, respectively (Scheme 24). Similarly, treatment of aldehyde **50**[50] with **17** provided the corresponding cuprate **51**, which was subsequently allylated with allyl bromide and acylated with cyclohexanecarbonyl chloride providing the products **52a-b** in 84% and 73% yields, respectively (Scheme 24). As mentioned in the previous part, the rate of the halogen-metal exchange greatly depends on the electron-density of the aromatic ring. Therefore, in the reaction of aldehyde **50** with **17**, a much slower I/Cu-exchange reaction was observed due to the presence of the electron-donating methoxy group.

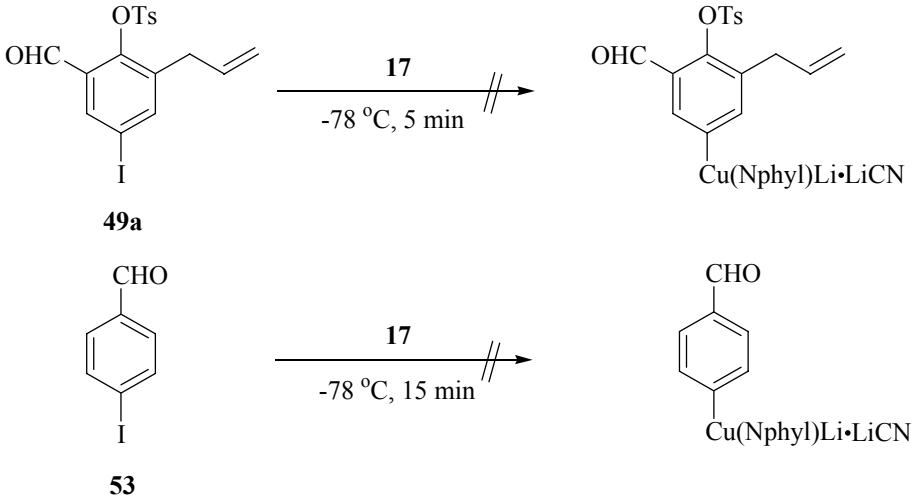
[49] Obtained from the reaction of 2-hydroxy-3,5-diiodo-benzaldehyde with TsCl in the presence of Et_3N.
[50] This aldehyde is commercially available from Lancaster.



Scheme 24: Functionalization of aldehyde compounds *via* I/Cu-exchange reaction.

We also observed that the presence of an adjacent chelating group was essential for the chemoselectivity of the I/Cu-exchange reaction, because the chelation of the *otho*-substituent significantly reduces the reactivity of the formed cuprate. Thus, an intermolecular addition to the aldehyde group can be avoided. However, in the absence of this stabilization, the reaction of the cuprate reagents with the aldehyde group will occur.

As shown in Scheme 25, the treatment of compounds **49a** or **53** with **17** (THF/Et_2O = 3/1, -78 °C, 5-15 min) did not lead to the exchange product, but led instead only to the addition products of **17** to the aldehyde group, resulting in the formation of the alcohols compounds, as indicated by GC-MS analysis of the crude reaction mixtures.



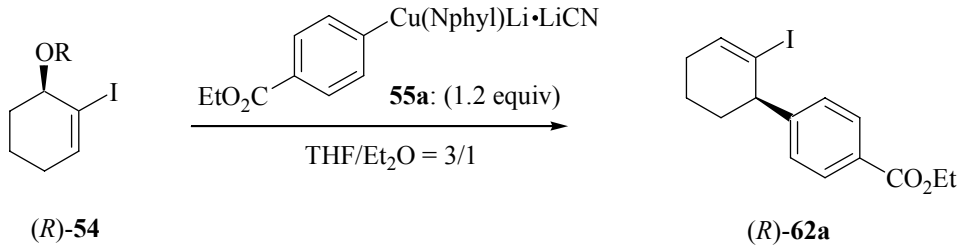
Scheme 25: Unsuccessful experiments.

3.3 Application of the Functionalized Aryl Cuprate in Allylic Substitution Reactions

As discussed in the introduction, allylic substitution reactions of organocopper reagents with chiral allylic electrophiles allow a selective formation of a new C-C bond with an efficient transfer of chirality. Since the I/Cu-exchange provides a new method to prepare the highly functionalized aryl cuprates, it will be very interesting to apply these functionalized cuprates in the allylic substitution reactions.

Our initial attention focused on the use of chiral 2-iodo-1-cyclohexenyl alcohol derivatives **54** as the electrophilic component.[51] After careful screening of the leaving groups, such as AcO, C_6F_5COO and $(EtO)_2P(O)O$, it was found that the acetate group allowed the best transfer of stereochemical information (Scheme 26; Table 4). It is important to note that the low reaction temperature is crucial for the enantioselectivity.

[51] Calaza, M. I.; Hupe, E.; Knochel, P. *Org. Lett*. **2003**, *5*, 1059.



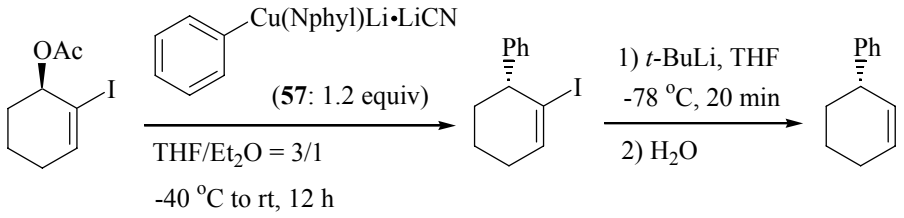
(*R*)-**54** (*R*)-**62a**

Scheme 26: Screening of leaving groups for the allylic substitution reaction.

Table 4: Leaving group and reaction condition for the allylic substitution reaction of Cuprate reagents

R	*ee* (%)	Temperature	Yield (%)	*ee* (%)
54a: R = $COCH_3$	98	-40 to -20 ^oC	77	98
54b: R = COC_6F_5	98	-78 ^oC	74	90
54c: R = $P(O)(OEt)_2$	98	-78 ^oC	83	33

The mechanism of this substitution reaction was established by the preparation of (*S*)-3-phenylcyclohexene **56** by our method (Scheme 27).[52]



(*R*)-**54a**: 94% *ee* (*R*)-**58**: 65%; 87% *ee*, (*S*)-**56**: 32%

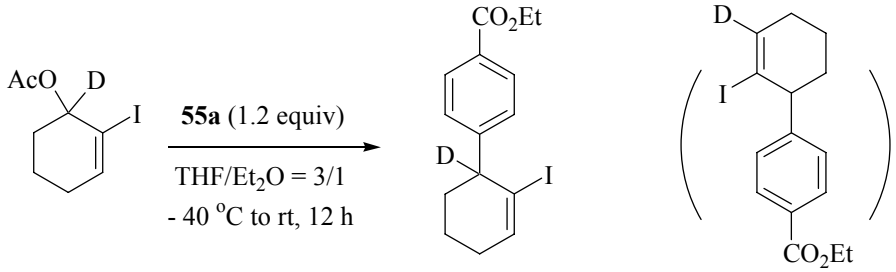
$[a]_D = -147.2^o$ (c 0.795, benzene, 25 ^oC)

Scheme 27: Preparation of (*S*)-**56** *via* allylic substitution of cuprate **57**.

[52] Berti, G.; Macchia, B.; Macchia, F.; Monti, L. *J. Org. Chem*. **1968**, *33*, 4045.

Thus, treatment of (*R*)-**54a** with cuprate **57** afforded (*R*)-**58** in 65% yield and 87% *ee*. I/Li-Exchange and protonation furnished (*S*)-**56** in 32% yield. Comparison of the $[\alpha]_D$ value of (*S*)-**56** ($[\alpha]_D$ = -147.2°, benzene, 25 °C)) and the data reported in literature for (*R*)-3-phenylcyclohexene ($[\alpha_D]$ = +149.7°, benzene, 29 °C) indicated that the sterogenic center in **56** has *S* configuration. That means that (*S*)-**56** should result from an S_N2 or *syn*-S_N2' mechanism.

To distinguish these two mechanisms, we prepared 1-*D*-2-iodo-2-cyclohexenyl acetate (±)-**59**[53] and treated it with the mixed lithium cuprate **55a** under our standard conditions. We have observed only the formation of the product (±)-**60** having the deuterium atom at the allylic position, clearly indicating the occurrence of an S_N2-substitution. On the other hand the *syn*-S_N2' would furnish (±)-**61** having deuterium at the vinylic position. These two compounds could be easily distinguished by ^{1}H-NMR analysis (Scheme 28).

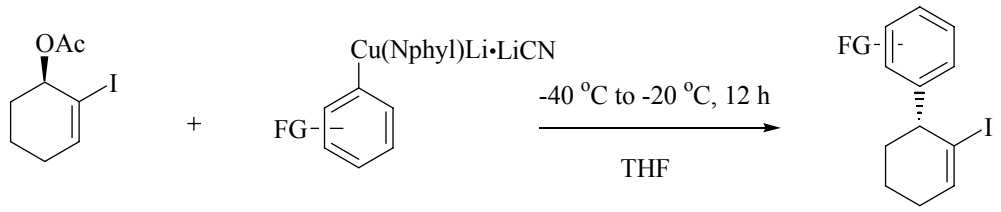


59 **60**: 53% **61**

Scheme 28: Stereoselective S_N2-substitution of 1-*d*-2-iodo-2-cyclohexenyl acetate (±)-**59** with **55a**.

With these initial results in hands, a series of functionalized cuprates **55** were prepared from the corresponding functionalized aryl halides *via* a halogen-copper exchange reaction. The reaction of **55** with (*R*)-**54a** stereoselectively provided the enantiomerically enriched compound (*R*)-**62** in moderate to good yields with excellent enantioselectivities (Scheme 29; Table 5).

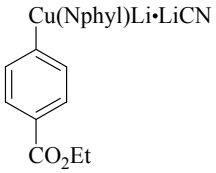
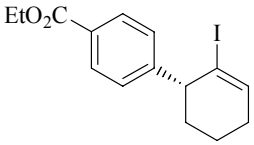
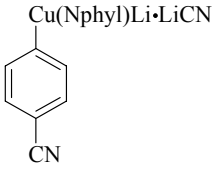
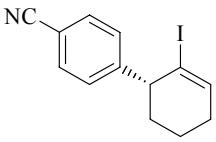
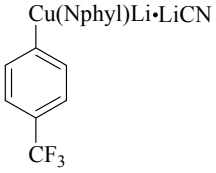
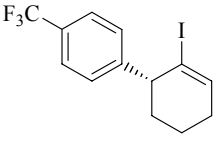
[53] The 1-*d*-2-iodo-2-cyclohexenyl acetate (±)-**59** was prepared in two steps from 2-iodo-2-cyclohexen-1-one (i) reduction with $NaBD_4$ and $CeCl_3 \cdot 7H_2O$ in methanol (25 °C, 3 h; 76%) followed by an acylation with Ac_2O in pyridine (83%).

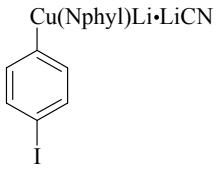
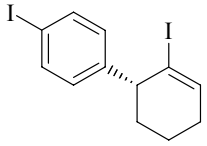
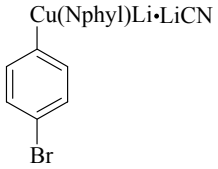
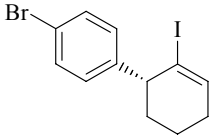
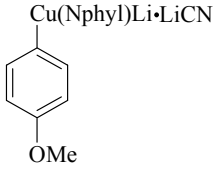
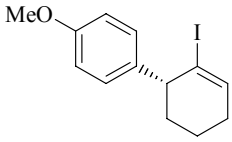
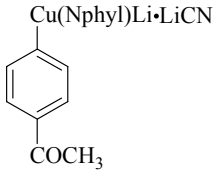
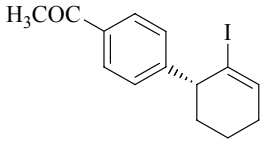
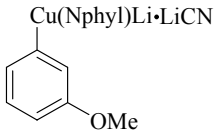
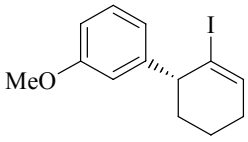


(*R*)-**54a**: 98% *ee* **55** (*R*)-**62**

Scheme 29: Stereoselective S_N2-substitution of 2-iodo-2-cyclohexenyl acetate (*R*)-**54a** with functionalized cuprates **55**.

Table 5: Enantioselective preparation of compounds (*R*)-**62** *via* allylic substitution of cuprates **55**.

Entry	Cuprate **55**	Product of type (*R*)-**62**	Yield (%)[a]	*ee* (%)[b]
1	 **55a**	 (*R*)-**62a**	77	98
2	 **55b**	 (*R*)-**62b**	66	96
3	 **55c**	 (*R*)-**62c**	70	94

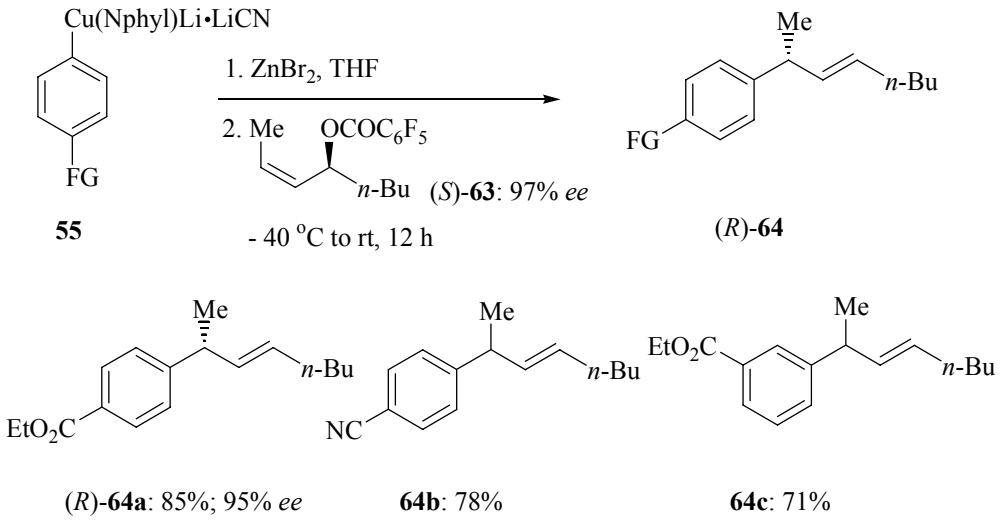
Entry	Cuprate **55**	Product of type (*R*)-**62**	Yield (%)[a]	*ee* (%)[b]
4	 **55d**	 (*R*)-**62d**	82	94
5	 **55e**	 (*R*)-**62e**	89	96
6	 **55f**	 (*R*)-**62f**	85	95
7	 **55g**	 (*R*)-**62g**	67	89
8	 **55h**	 (*R*)-**62h**	86	92

[a] Isolated yield of analytically pure product; [b] The enantiomeric excess was determined by HPLC-analysis and chiral-GC. In each case, the racemic product was prepared for calibration.

As shown in the Table 5, (*R*)-2-iodo-2-cyclohexenyl acetate (*R*)-**54a** reacted with arylcuprates **55**, bearing both electron-withdrawing and electron-donating groups leading to the products (*R*)-**62a-h** in 66-89% yields and excellent enantioselectivities (89-98% *ee*). A

broad range of functional groups were tolerated in the arylcuprate (CO_2Et, CN, CF_3, MeO, $COCH_3$). Remarkably, reactive halogen substituent, such as an iodide (entry 4) or a bromide (entry 5) were compatible with the substitution reaction. The resulting chiral dihalogenated products (*R*)-**62d-e** (94-96% *ee*) are versatile building blocks in which the two halogen-carbon bonds can be differentiated in further transformations. Interestingly, the presence of a ketone group in the cuprate **55g** is viable (entry 7). The desired product (*R*)-**62g** was obtained in 67% yield and 89% *ee,* showing ca. 5% of racemization (enantiomer ratio from 99:1 to 95:5). This is may be due to the competitive enolization of the ketone group by $(Nphyl)_2CuLi{\cdot}LiCl$ (**17**) leading to a new copper species bearing an enolate ligand and displaying a different chemoselectivity. The iodine substituent in compounds of type (*R*)-**62** is very useful for further transformations, which will be discussed in chapter 5.

The nucleophilic substitution of the functionalized arylcuprates **55** with chiral open-chain allylic pentafluorobenzoates (*S*)-**63**[54] was examined in the presence of zinc salts (Scheme 30).



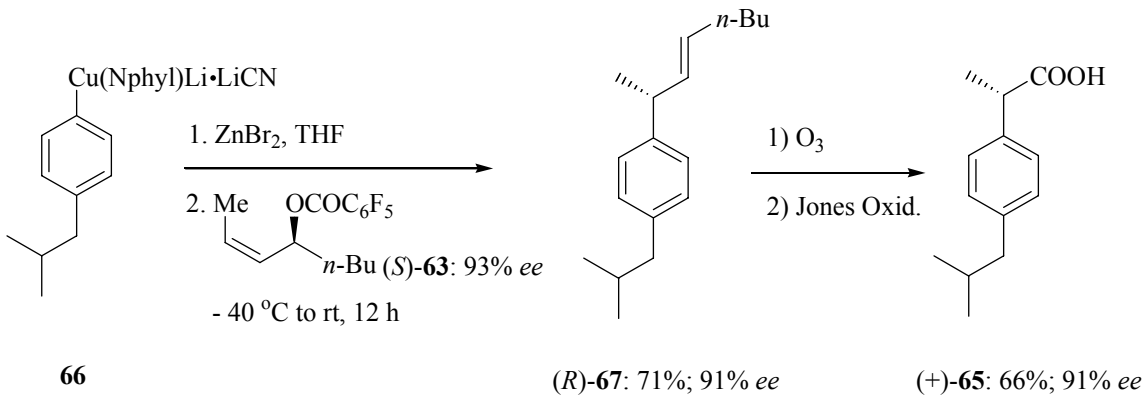
Scheme 30: Stereoselective *anti*-S_N2'-substitution of arylcuprates **55** with chiral open-chain allylic pentafluorobenzoates (*S*)-**63**.

In this system, it was found that the presence of zinc salts strongly favors the S_N2'-substitution reaction. Therefore, in the absence of zinc salts ($ZnBr_2$), the arylcuprate **55** reacted non-regioselectively with the chiral *cis*-allylic pentafluorobenzoate (*S*)-**63**, leading

[54] Harrington-Frost, N.; Leuser, H.; Calaza, M. I.; Knochel, P. *Org. Lett.* **2003**, *5*, 2111.

to a mixture of S_N2 and S_N2' products as indicated by GC-MS analysis of the crude reaction mixture. However, the addition of zinc bromide (1.0 equiv) allows a highly stereoselective *anti*-S_N2'substitution, as it has been observed with zinc-copper reagents prepared from organozinc reagents.[54] Thus, the reaction of cuprate **55a** with a THF solution of $ZnBr_2$ followed by addition of (*S*)-**63** (97% *ee*) in THF:ether (3:1) regioselectively led to S_N2' product (*R*)-**64a** (85%; 95% *ee*). The ^{1}H-NMR of this product clearly indicates that the reaction proceed *via* a S_N2' mechanism. Several other products of type **64b-c** were also prepared in the similar way. Unfortunately, their *ee* values were not possible to be determined by chiral GC and HPLC, even after derivatization.

The *anti*-S_N2'mechanism of this reaction was established by the synthesis of literature known compound (+)-ibuprofen **65** using our method (Scheme 31).[54, 55]



Scheme 31: Stereoselective synthesis of (+)-ibuprofen **65** *via* an *anti*-S_N2' substitution reaction.

Thus, cuprate **66**, prepared by the reaction of 1-iodo-4-isobutylbenzene with $(Nphyl)_2CuLi{\cdot}LiCl$ (**17**), smoothly reacted with (*S*)-**63** leading to the S_N2' product (*R*)-**67** in 71% yield. Compound (*R*)-**67** was readily converted to (+)-**65** *via* a successive ozonolysis and Jones oxidation. Comparing the $[\alpha]_D$ value of (+)-**65** ($[\alpha]_D$ = +84.5°, $CHCl_3$, 25 °C)) with literature known compound (+)-ibuprofen ($[\alpha_D]$ = +149.7°, $CHCl_3$, 25 °C) indicated that the stereogenic center in (+)-**65** has a *S* configuration. That means that (+)-**65** should result from an *anti*-S_N2' mechanism.

[55] a) Corey, E. J.; Helal, C. J. *Angew. Chem. Int. Ed.* **1998**, *37*, 1986; b) Wallbaum, S.; Martens, J. *Tetrahedron: Asymmetry* **1992**, *3*, 1475.

In summary, it was shown that functionalized iodoarenes or polyiodoarenes undergo a selective I/Cu-exchange reaction. The I/Cu-exchange reaction was found to tolerate a variety of sensitive functional groups, such as acyl groups, ester, cyanide and even an aldehyde. A range of new polyacylated benzenes, such as **45a-d**, were available by this method. A further application of this halogen-copper exchange reaction for preparation of functionalized arylcuprates and their enantioselective reactions with chiral cyclic and open-chain allylic electrophiles were also presented. In each case the mechanism was proved by the synthesis of literature known compounds by our method.

4 Preparation of Functionalized Heteroaryl Cuprate Reagents *via* an Iodine-Copper Exchange Reaction

4.1 Introduction

The development of new methodologies for the preparation of polyfunctionalized heterocyclic compounds is an area of fundamental importance in many research fields, such as natural product synthesis,[56] drug design,[57] molecular recognition[58] and preparation of new materials with defined properties.[59] The direct oxidative addition of activated metals to organic halides,[60] carbometalation,[61] hydrometalation,[62] selective deprotonation[63] or halogen-metal exchange reaction[30, 43, 64] have been used successfully to provide very selective methods for the preparation of a wide range of metalated heterocycles. However, the presence of sensitive functional groups makes their preparation more complicated and the conventional methods are often not applicable or not general. As shown previously, the excellent functional group tolerance and mild reaction condition of the halogen-copper exchange reaction makes it a promising candidate for the preparation of functionalized heteroaryl cuprate reagents. The further application of this method to prepare functionalized heterocyclic cuprates should be of importance and interest.

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[56] a) Nicolaou, K. C.; Sorensen, E. J. in *Classics in Total Synthesis*, Wiley-VCH, Weinheim 1996; b) Wipf, W.; Venkatraman, S. *J. Org. Chem.* **1996**, *61*, 6517; c) Wipf, P.; Hayes, G. B. *Tetrahedron* **1998**, *54*, 6987; d) Wipf, P.; Xu, W. *J. Org. Chem*. **1996**, *61*, 6556.

[57] a) Newkome, G. R.; Pandler, W. W. in *Contemporary Heterocyclic Chemistry*, Wiley, New York 1982; b) Gilchrist T. L. in *Heterocyclic Chemistry*, Wiley-VCH, Weinheim 1995; c) Boucher, E.; Simard, M.; Wuest, J. D. *J. Org. Chem.* **1995**, *60*, 1408.

[58] a) Peczuh, M. W.; Hamilton, A. D.; Sanchez-Quesada, J.; de Mendoza, J.; Haack, T.; Giralt, E. *J. Am. Chem. Soc.* **1997**, *119*, 9327; b) Fan, E.; Vincent, C.; Goodman, C. M.; Jubian, V.; Hamilton, A. D. *Tetrahedron Lett.* **1995**, *36*, 2551.

[59] Ziessel, R. *Synthesis* **1999**, 1839.

[60] a) Snieckus, V. *Chem. Rev*. **1990**, *90*, 879; b) Lee, J.; Velarde-Ortiz, R.; Guijarro, A.; Wurst, J. R.; Reike, R. D. *J. Org. Chem*. **2000**, *65*, 5428.

[61] a) Normant, J. F.; Alexakis, A. *Synthesis* **1981**, 841; b) Rao, S. A.; Knochel, P. *J. Am. Chem. Soc*. **1991**, *113*, 5735.

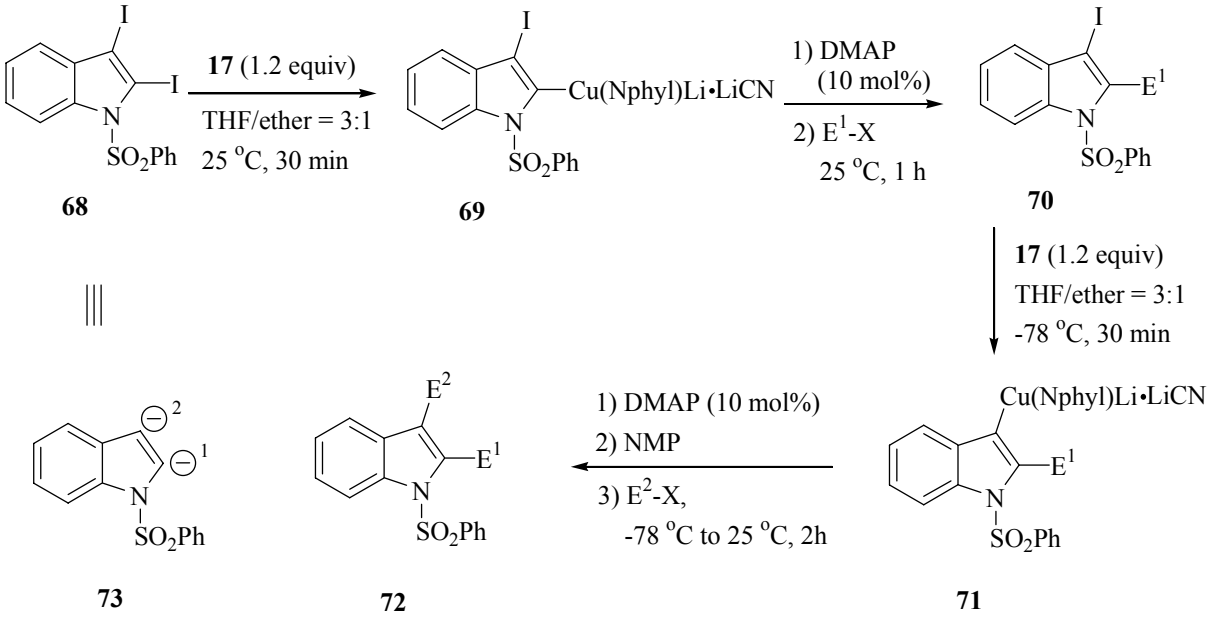
[62] a) Trost, B. M. *Chem. Eur. J*. **1998**, *4*, 2405; b) Mattesonin, D. S. *The Chemistry of the Metal-Carbon Bond, Volume 4,* (Ed.: Hartley, F. R.), Wiley, New York, **1987**, p. 307.

[63] a) Zhang, M.-X.; Eaton, P. E. *Angew. Chem.* **2002**, *114*, 2273; *Angew. Chem. Int. Ed.* **2002**, *41*, 2169; b) Hoppe, D.; Heuse, T. *Angew. Chem.* **1997**, *109*, 2376; *Angew. Chem. Int. Ed.* **1997**, *36*, 2282; c) Metallions, C.; Snieckus, V. *Org. Lett*. **2002**, *4*, 1935.

[64] Lipshutz, B. H.; Hagen, W. *Tetrahedron Lett.* **1992**, *33*, 5865.

4.2 Selective Functionalization of Indole Derivatives *via* an I/Cu- Exchange Reaction

The indole system occurs in numerous natural products as well as in many therapeutic agents.[65] The preparation of polyfunctional indoles is therefore an important research field and numerous methods have been developed.[66] The direct lithiation of indoles in position 2 and 3 was described.[67] However the resulting lithiated indoles was found with only weakly electrophilic functional groups on the indole ring. Herein, we wish to present an application of the I/Cu-exchange reaction for performing a selective metalation of the 2,3-diiodoindole derivative **68** (Scheme 32).[68]



Scheme 32: Regioselective functionalization of indole derivative **68** *via* an I/Cu-exchange reaction.

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[65] Joule, J. A. *Science of Synthesis*, **2001**, *10*, 361.

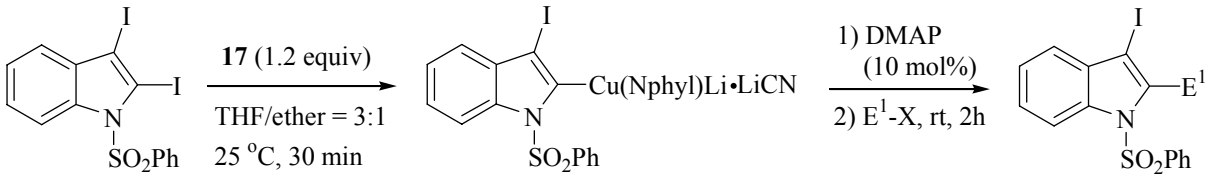
[66] For some recent methods, see: a) Ackermann, L. *Org. Lett*. **2005**, *7*, 439; b) Cacchi, S.; Fabrizi, G. *Chem. Rev.* **2005**, *105*, 2873; c) Perez-Serrano, L.; Dominguez, G.; Perez-castells, J. *J. Org. Chem.* **2004**, *69*, 5413; d) Battistuzzi, G.; Cacchi, S.; Fabrizi, G. *Eur. J. Org. Chem.* **2002**, 2671; e) Battistuzzi, G.; Cacchi, S.; Fabrizi, G. Marinelli, F.; Parisi, L. M. *Org. Lett*. **2002**, *4*, 1355; f) Coleman, R. S.; Chen, W. *Org. Lett*. **2001**, *3*, 1141; g) Watanabe, M.; Yamamoto, T.; Nishiyama, M. *Angew. Chem. Int. Ed.* **2000**, *39*, 2501; h) Takeda, A.; Kamijo, S.; Yamamoto, Y. *J. Am. Chem. Soc*. **2000**, *122*, 5662; i) Koradin, C.; Dohle, W.; Rodriguez, A. L.; Schmid, B.; Knochel, P. *Tetrahedron* **2003**, *59*, 1571; j) Köhling, P.; Schmidt, A. M.; Eilbracht, P. *Org. Lett*. **2003**, *5*, 3213; k) Knepper, K.; Bräse, S. *Org. Lett*. **2003**, *5*, 2829; l) Barluenga, J. *Pure Appl. Chem*. **2002**, *74*, 1317.

[67] a) Matsuzono, M.; Fukuda, T.; Iwao, M.; *Tetrahedron Lett*. **2001**, *42*, 7621; b) Liu, Y.; Gribble, G. W. *Tetrahedron Lett*. **2000**, *41*, 8717.

[68] a)Witulski, B.; Buschmann, N.; Bergsträßer, U. *Tetrahedron* **2000**, *56*, 8473; b) Saulnier, M. G.; Gribble, G. W. *J. Org. Chem*. **1982**, *47*, 757.

Thus, the treatment of **68** with **17** (1.2 equiv) in a mixture of THF and diethyl ether (THF/Et_2O = 3:1) at 25 °C smoothly provided the cuprate **69** within 0.5 h. The assignment of the regioselectivity was deduced from the NMR data analysis of the hydrolysis product of **69** and the authentic one.[68] The treatment of **69** with various electrophiles (E^1) furnished polyfunctional indoles of type **70**. These functionalized 3-iodoindoles **70** reacted again readily with **17** (1.2 equiv) in a 3:1 THF/Et_2O mixture at –78 °C for 30 min, leading to highly functionalized copper species of type **71**. Subsequent reaction of **71** with various electrophiles (E^2) led to the indole derivatives of type **72**. According to this sequence, the diiodoindole **68** is a synthetic equivalent of the 1,2-bianionic synthon **73**.

The allylation of cuprate **69** with allyl bromide led to the 3-iodo-2-allylindole derivative **70a** in 92% yield (Scheme 33; entry 1 of Table 6). The direct acylation of the indolyl cuprate **69** led to the desired product in poor yield. However, it was found that 4-dimethylaminopyridine (DMAP, 10 mol%)[69] catalyzed this acylation process. Under these conditions, aliphatic acid chlorides (entries 2 and 3) as well as aromatic acid chlorides (entries 4, 5 and 6) provided the iodoketones **70b-f** in 78-86% yields. The sensitive acrylic acid chloride reacted as expected, furnishing the unsaturated ketone **70g** in 67% yield. The acylation with ethyl oxalyl chloride led to the iodoketoester **70h** in 75% yield (entry 8). Finally, the reaction with 3-iodo-2-cyclohexen-1-one provided the addition-elimination product **70i** in 66% yield (entry 9). The selectivity for an I/Cu-exchange in position 2 rather than in position 3 is best explained by considering the higher electronegativity of C(2) compared to C(3).

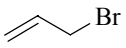
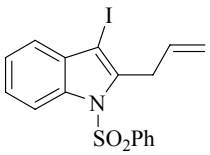
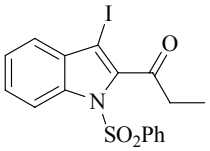
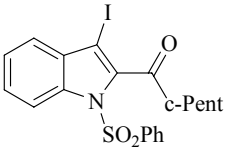
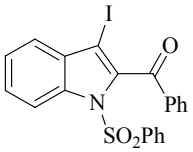
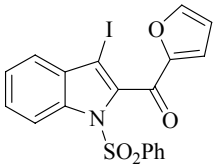
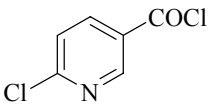
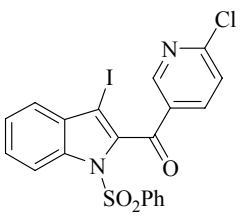


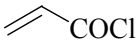
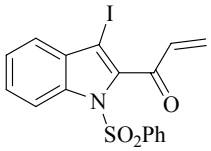
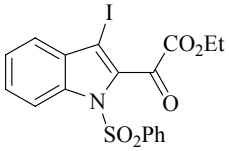
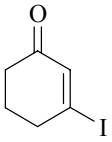
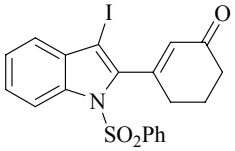
68 **69** **70**

Scheme 33: Selective functionalization of indole derivative **68** at the 2 position *via* an I/Cu-exchange reaction.

[69] a) Heinrich, M. R.; Klisa, H. S.; Mayr, H.; Steglich, W.; Zipse, H. *Angew. Chem. Int. Ed.* **2003**, *42*, 4826; b) Steglich, W.; Höfle, G. *Angew. Chem. Int. Ed.* **1969**, *8*, 981; c) Höfle, G.; Steglich, W.; Vorbrüggen, A. *Angew. Chem. Int. Ed.* **1978**, *17*, 569.

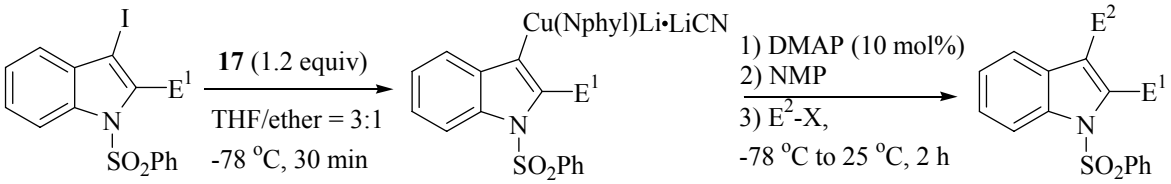
Table 6: Preparation of 3-iodoindoles **70** from the reaction of functionalized cuprates **69** with various electrophiles.

Entry	Cuprate **69**	Electrophile	Product of type **70**	Yield (%)[a]
1	**69**		 **70a**	92[b]
2	**69**	EtCOCl	 **70b**	84
3	**69**	*c*-PentCOCl	 **70c**	86
4	**69**	PhCOCl	 **70d**	84
5	**69**	2-FurCOCl	 **70e**	78
6	**69**		 **70f**	78

Entry	Cuprate **69**	Electrophile	Product of type **70**	Yield (%)[a]
7	**69**		 **70g**	67
8	**69**	$ClCOCO_2Et$	 **70h**	75
9	**69**		 **70i**	66

[a]Isolated yield of analytically pure product. [b]The reaction was performed without DMAP (10 mol%).

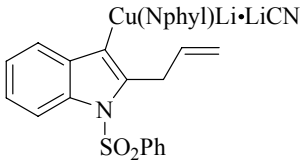
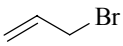
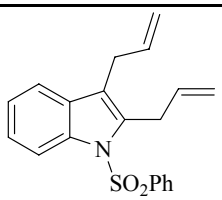
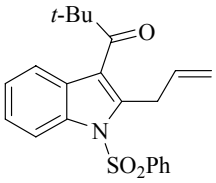
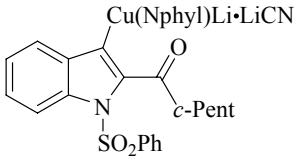
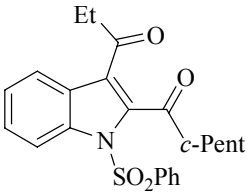
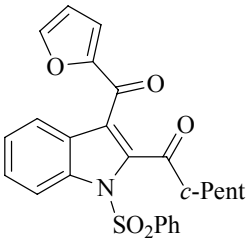
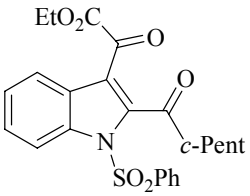
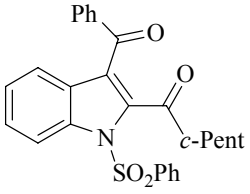
For the second exchange reaction, we treated the 3-iodoindoles **70a**, **c**, **d**, **f, i** with **17** (1.2 equiv) in a 3:1 mixture of THF and Et_2O at – 78 °C, leading to the cuprates **71** within 30 min. Reaction of **71** with various electrophiles provided the disubstituted indoles **72** in 63-88% yields (Scheme 34; Table 7).

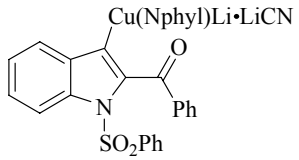
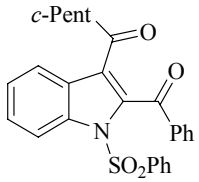
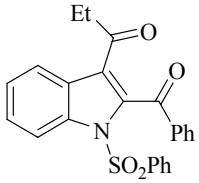
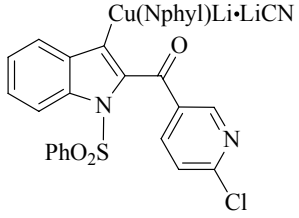
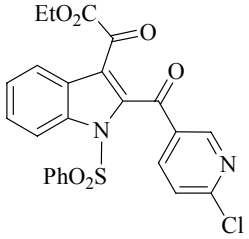
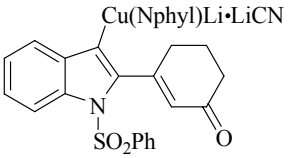
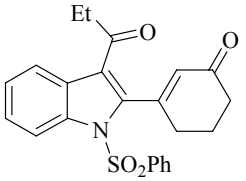
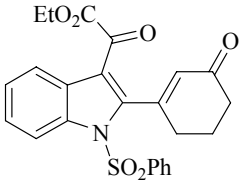


70 **71** **72**

Scheme 34: Functionalization of 3-iodoindole **70** *via* I/Cu-exchange reaction.

Table 7: 2,3-Disubstituted indoles obtained by the reaction of the cuprates **71a**, **b**, **c**, **d, e** with electrophiles.

Entry	Cuprate **71**	Electrophile	Product of type **72**	Yield (%)[a]
1	 **71a**		 **72a**	88[b]
2	**71a**	*t*-BuCOCl	 **72b**	68
3	 **71b**	EtCOCl	 **72c**	68
4	**71b**	2-FurCOCl	 **72d**	63
5	**71b**	$ClCOCO_2Et$	 **72e**	71
6	**71b**	PhCOCl	 **72f**	73

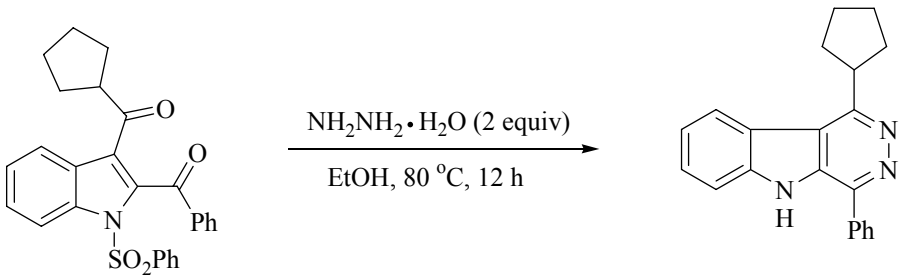
Entry	Cuprate **71**	Electrophile	Product of type **72**	Yield (%)[a]
7	 **71c**	*c*-PentCOCl	 **72g**	65
8	**71c**	EtCOCl	 **72h**	70
9	 **71d**	$ClCOCO_2Et$	 **72i**	71
10	 **71e**	EtCOCl	 **72j**	80
11	**71e**	$ClCOCO_2Et$	 **72k**	72

[a]Isolated yield of analytically pure product. [b]The reaction was performed without NMP as cosolvent and DMAP (10 mol%) as catalyst.

Thus, the copper reagent **71a** was readily allylated with allyl bromide giving the bis-allylated product **72a** in 88% yield (entry 1 of Table 7). For performing the acylation

reactions, it was found that the use of *N*-methylpyrrolidinone (NMP) as cosolvent[70] and DMAP (10 mol%) as catalyst was advantageous.[69] Thus, the reaction of **71a** with pivaloyl chloride furnished the desired indolylketone **72b** in 68% yield (entry 2). The ketone-substituted indolylcuprates **71b**, **c**, **d** were readily prepared by the I/Cu-exchange reaction. Good yields of the corresponding 1,2-diketones **72c-i** can therefore be obtained (entries 3-9). Remarkably, even the *α,β*-unsaturated keto-substituted indolylcuprate **71e** can be readily prepared in this way. After acylation with propionyl chloride and ethyl oxalyl chloride, the desired product **72j** and **72k** were obtained in 80% and 72% yields, respectively (entries 10-11).

This method provided functionalized organocopper intermediates and gave a simple access to diketones, which are otherwise difficult to prepare. These diketones are versatile building blocks for further conversion to more complex heterocycles. Thus, treatment of the diketone **72g** with $NH_2NH_2 \cdot H_2O$ (2 equiv) in refluxing ethanol for 12 h afforded the tricyclic heterocycle **74**.[48] Interestingly, the phenylsulfonyl group was also removed during the heterocycle synthesis (Scheme 35).

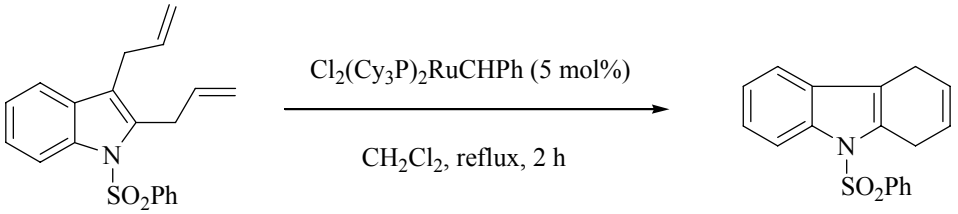


72g **74:** 88%

Scheme 35: Synthesis of indolopyridazine **74**.

[70] NMP often shows great influence on organometallic transformation, See also: a) Kneisel, F. F.; Dochnahl, M.; Knochel, P. *Angew. Chem. Int. Ed.* **2004**, *43*, 1017; b) Kneisel, F. F.; Knochel, P. *Synlett* **2002**, *11*, 1799.

By performing a metathesis reaction of the diallylated product **72a** with Grubbs catalyst (5 mol%) in refluxing CH_2Cl_2, the dihydrocarbazole **75** was obtained in nearly quantitative yield (Scheme 36).[71]



72a **75**: 95%

Scheme 36: Formation of dihydrocarbazole **75** *via* methathesis reaction.

4.3 Functionalization of Indazoles in Position 3 *via* an I/Cu-Exchange Reaction

The indazole ring system is a common structural motif found in numerous biologically active molecules. For instance, it was found to inhibit the platelet aggregation,[72] HIV protease inhibitors[73] or antagonists of integrin $\alpha_v\beta_3$ (Scheme 37).[74] The preparation of functionalized indazoles is therefore a very important synthetic task. Several procedures were developed for the functionalization of indazoles at position 3 using palladium catalysts. [75] However the acylation of indazoles in position 3 is difficult. The direct metalation of 3-bromoindazole is possible, giving tht dilithio-derivative, however the resulting lithiated indazole is compatible with only weakly electrophilic functional groups and the yields of products are variable.[76]

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[71] a) Fürstner, A, *Angew. Chem. Int. Ed*. **2000**, *39*, 3012; b) Clark, J. S.; Hamelin, O. *Angew. Chem. Int. Ed*. **2000**, *39*, 372; c) Grobelny, Z.; Stolarzewicz, A.; Adamus, G.; Buika, G.; Grazulevicius, J. V. *J. Organomet. Chem.* **2000**, *595*, 66.

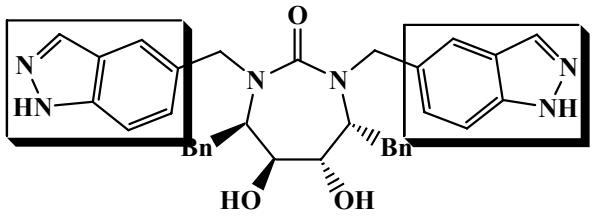
[72] Collot, V.; Dallemagne, P.; Bovy, P. R.; Rault, S. *Tetrahedron* **1999**, *55*, 6917.

[73] Sun, J.-H.; Teleha, C. A.; Yan, J.-S.; Rodgers, J. D.; Nugiel, D. A. *J. Org. Chem.* **1997**, *62*, 5627.

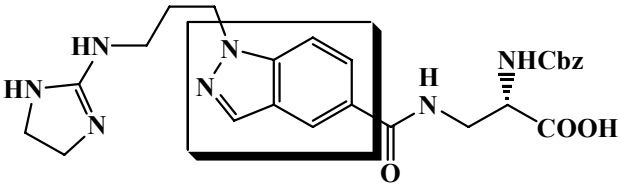
[74] Batt, D. G.; Petraitis, J. J.; Houghton, G. C.; Modi, D. P.; Cain, G. A.; Corjay, M. H.; Mousa, S. A.; Bouchard, P. J.; Forsythe, M. S.; Harlow, P. P.; Barbera, F. A.; Spitz, S. M.; Wexler, R. R.; Jadhav, P. K. *J. Med. Chem*. **2000**, *43*, 41.

[75] a) Kazzouli, S. E.; Bouissane, L.; Khouili, M.; Guillaumet, G. *Tetrahedron Lett.* **2005**, *46*, 6163; b) Arnautu, A.; Collot, V.; Ros, J. C.; Alayrac, C.; Witulski, B.; Rault, S. *Tetrahedron Lett.* **2002**, *43*, 2695; c) Collot, V.; Varlet, D.; Rault, S. *Tetrahedron Lett*. **2000**, *41*, 4363; d) Gordon, D. W. *Synlett* **1998**, 1065; e) Collot, V.; Bovy, P. R.; Rault, S. *Tetrahedron Lett*. **2000**, *41*, 9053.

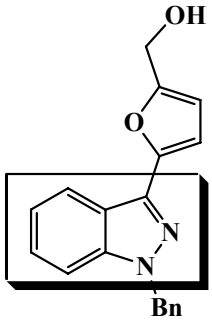
[76] Welch, W. M.; Hanau, C. E.; Whalen, W. M. *Synthesis* **1992**, 937.



SE063: HIV protease inhibition



Potent antagonists of the integrin $\alpha_v\beta_3$



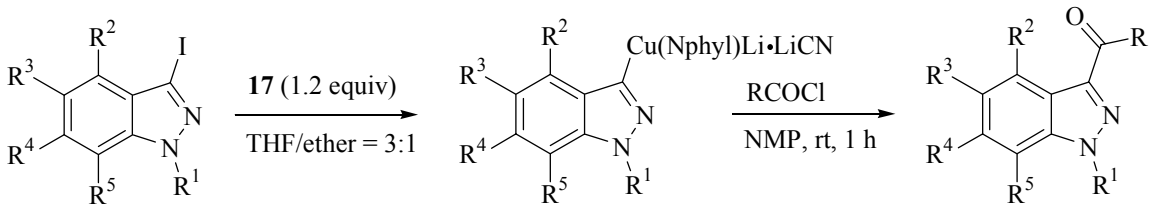
YC-1: a potent inhibitor of platelet aggregation

Scheme 37: Some examples for bioactive indazole derivatives

Since the I/Cu-exchange reaction allowed the preparation of heterocyclic-copper derivatives, bearing a broad range of functionalities, an application of this reaction to the indazole system should be promising and interesting.

A variety of literature known functionalized 3-iodoindazoles of type **76**[75, 77] were subjected to the I/Cu-exchange reaction with $(Nphyl)_2CuLi{\cdot}LiCl$ (**17**), leading to the corresponding cuprates of type **77**, bearing either an ester (**77a**; $R^2 = CO_2Et$), an alkyl group (**77b**, R^5 = Me), a methoxy group (**77c**, R^3 = OMe), a bromine (**77d**, R^5 = Br), an iodine (**77e**, R^3 = I), a nitrile (**77f**, R^4 = CN), or a ketone group (**77g**, R^4 = COEt). The subsequent reaction with various acid chlorides provided the acylation products of type **78** in good yields (Scheme 38, Table 8).

[77] a) Bartsch, R. A.; Yang, II-W. *J. Heterocyclic Chem*. **1984**, *21*, 1063; b) Collot, V.; Dallemagne, P.; Bovy, P. R.; Rault, S. *Tetrahedron*, **1999**, *55*, 6917; c) Benchidmi, M.; Bouchet, P.; Lazaro, R. *J. Heterocyclic Chem*. **1979**, *16*, 1599.



76a: R^1 = Bn; $R^3 = R^4 = R^5$ = H; R^2 = CO_2Et
76b: R^1 = Bn; $R^2 = R^3 = R^4$ = H; R^5 = Me
76c: R^1 = Bn; $R^2 = R^4 = R^5$ = H; R^3 = OMe
76d: R^1 = Bn; $R^2 = R^3 = R^4$ = H; R^5 = Br
76e: R^1 = Bn; $R^2 = R^4 = R^5$ = H; R^3 = I
76f: R^1 = Boc; $R^2 = R^3 = R^5$ = H; R^4 = CN
76g: R^1 = Boc; $R^2 = R^3 = R^5$ = H; R^4 = COEt

77

78: (70-91%)

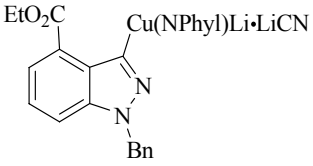
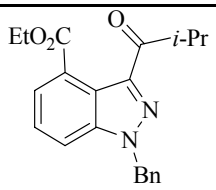
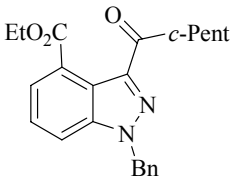
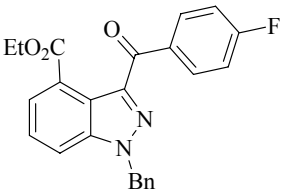
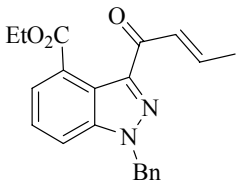
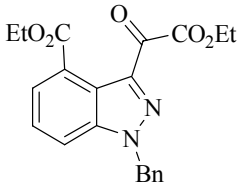
Scheme 38: Functionalization of indazole derivative **76** in position 3 *via* an I/Cu-exchange reaction.

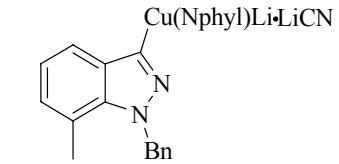
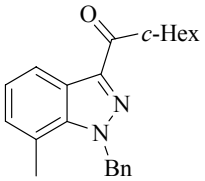
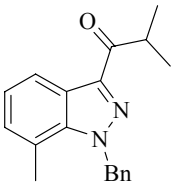
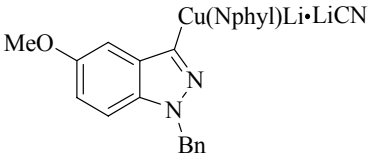
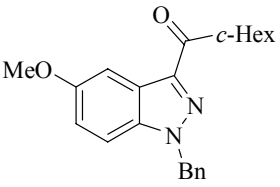
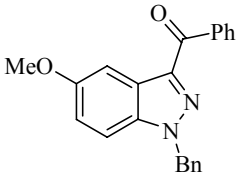
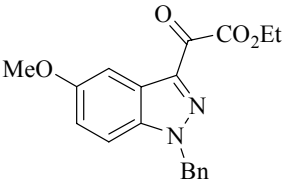
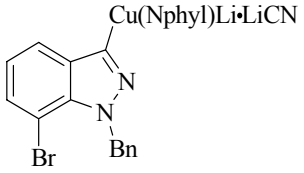
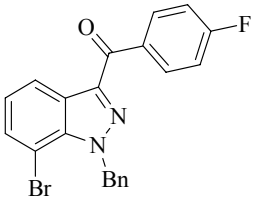
Thus, the 3-iodoindazoles **76a** underwent a smooth exchange reaction with **17** (1.2 equiv) in a 3:1 mixture of THF and Et_2O at 25 °C providing the corresponding cuprate **77a** within 0.5 h. The treament of **77a** with aliphatic acid chlorides (entries 1 and 2 of Table 8) as well as aromatic acid chlorides (entry 3) in the presence of NMP led to the desired products **78a-c** in 85-88% yields.[70, 78] Interestingly, unsaturated acid chlorides (entry 4) as well as ethyl oxalyl chloride reacted well with **77a** affording the corresponding heterocyclic ketones **78d-e** in 78-82% yields (entries 4 and 5). In a similar way, **76b**, **76c** and **76d** were readily converted to the corresponding cuprates **77b-d** at rt (0.5 h), which underwent the acylation reaction smoothly with various acid chlorides, furnishing the compounds **78f-l** in 77-91% yields (entries 6, 7, 8, 9, 10, 11 and 12). It is worth noting that in the case of **76d** no competitive Br/Cu-exchange was observed. In the case of diiodoindazole **76e**, it was found that the reaction temperature was crucial for the regioselectivity. The performance of the exchange at low temperature (–10 °C, 1 h) ensured a perfect selectivity, leading only to the exchange in position 3. The resulting cuprate **77e** reacted with cyclopentane carbonyl chloride, benzoyl chloride or ethyl oxalyl chloride, giving the acylated indazoles **78m-o** in good yields (entries 13, 14 and 15). Remarkably, even in the presence of a *t*-butoxycarbonyl (Boc) protecting group and a cyanide or ketone group, the corresponding indazoles **76f** and **76g** smoothly underwent the I/Cu-exchange with **17** (1.2 equiv) at –78 °C (30 min) leading to the cuprates **77f** and **77g**. The resulting cuprated indazoles **77f** and **77g** were readily

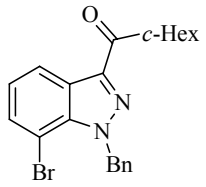
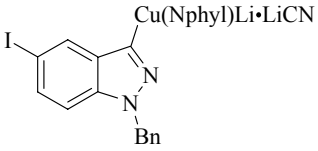
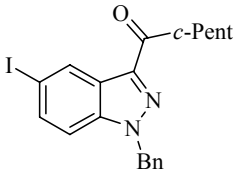
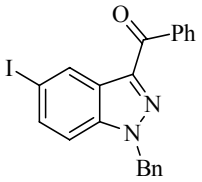
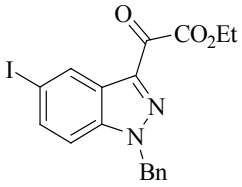
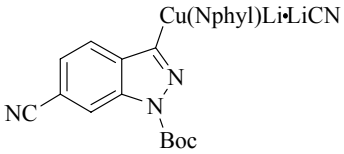
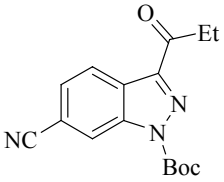
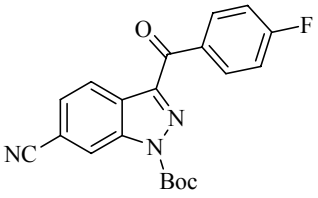
[78] Dieter, R. K. *Tetrahedron* **1999**, *55*, 4177.

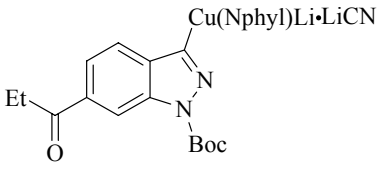
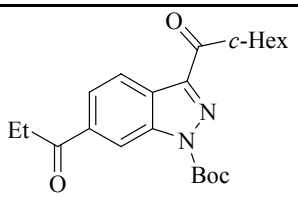
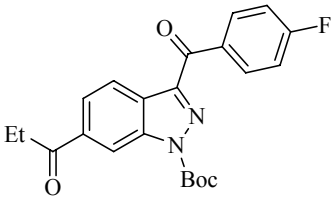
acylated with a wide range of acid chlorides in the presence of NMP leading to the 3-acylindazoles **78p-s** in 70-89% yields (entries 16, 17, 18 and 19).

Table 8: 3-Acylindazoles **78** obtained by the reaction of the cuprated indazoles **77a-g** with various acid chlorides.

Entry	Cuprate **77**	Acid chloride (R)	Product of type **78**	Yield (%)[a]
1	 **77a**	*i*-Pr	 **78a**	86
2	**77a**	*c*-Pent	 **78b**	88
3	**77a**	4-F-C_6H_4	 **78c**	85
4	**77a**	(*E*)-CH=CHCH$_3$	 **78d**	78
5	**77a**	CO_2Et	 **78e**	82

Entry	Cuprate **77**	Acid chloride (R)	Product of type **78**	Yield (%)[a]
6	 **77b**	*c*-Hex	 **78f**	85
7	**77b**	i-Pr	 **78g**	77
8	 **77c**	C_6H_5	 **78h**	82
9	**77c**	C_6H_5	 **78i**	80
10	**77c**	CO_2Et	 **78j**	85
11	 **77d**	4-F-C_6H_4	 **78k**	87

Entry	Cuprate **77**	Acid chloride (R)	Product of type **78**	Yield (%)[a]
12	**77d**	*c*-Hex	 **78l**	91
13	 **77e**	*c*-Pent	 **78m**	79
14	**77e**	C_6H_5	 **78n**	70
15	**77e**	CO_2Et	 **78o**	82
16	 **77f**	COEt	 **78p**	81
17	**77f**	4-F-C_6H_4	 **78q**	89

Entry	Cuprate **77**	Acid chloride (R)	Product of type **78**	Yield (%)[a]
18	 **77g**	*c*-Hex	 **78r**	76
19	**76g**	4-F-C_6H_4	 **78s**	70

[a] Isolated yield of analytically pure products.

In conclusion, we prepared a range of polyfunctional cuprated indazoles of type **77** and showed that they can be readily acylated by various acid chlorides, leading to the new 3-acylindazoles **78**, which are very difficult to prepare by other methods.

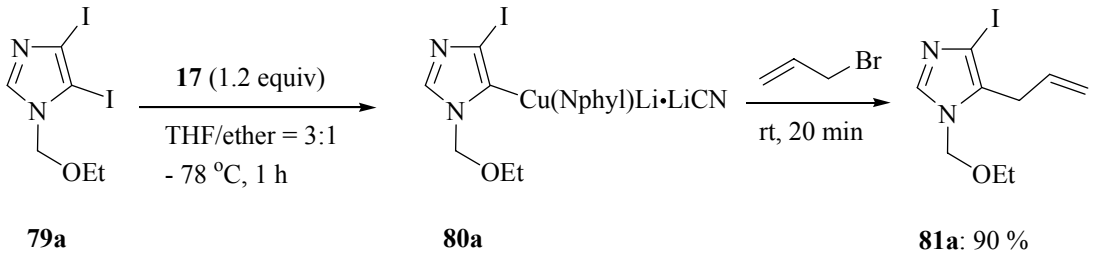
4.4 Functionalization of Imidazoles *via* an I/Cu-exchange Reaction

Imidazole is an important 5-membered ring heteroaromatics. It is present in a wide variety of naturally occurring compounds as well as in many pharmacological and chemotherapeutic agents.[79] The preparation of polyfunctional imidazoles is therefore an important research field. The direct lithiation of imidazoles was described. However, the resulting lithiated imidazoles are compatible with only weakly electrophilic functional groups at the imidazole ring.[80] Another drawback of this procedure is that the carbon in the position 2 has to be protected due to the acidic hydrogen in this position.[81] This precaution is not necessary when magnesium reagents are used, but again the resulting highly polar

[79] a) Jacquot, D. E. N.; Zöllinger, M.; Lindel, T. *Angew. Chem. Int. Ed*. **2005**, *44*, 2295; b) Hoffmann, H.; Lindel, T. *Synthesis*, **2003**, 1753; c) Zhong, J.; Li, Z.; Huang, R. *Nat. Prod. Rep*. **2002**, *19*, 454; d) Baker, D. D.; Alvi, K. A. *Current Opinion in Biotechnology* **2004**, *15*, 576; e) Bastos, M. M.; Barbosa, A. C.; Pinto, A. C.; Kover, W. B.; Taheuchi, Y.; Boechat, N. *J. Braz. Chem. Soc*. **2001**, *12*, 417.
[80] a) Groziak, M. P.; Wei, L. *J. Org. Chem.* **1991**, *56*, 4296; b) Groziak, M. P.; Wei, L. *J. Org. Chem.* **1992**, *57*, 3776.
[81] Eriksen, B. L.; Vedso, P.; Begtrup, M. *J. Org. Chem*. **2001**, *66*, 8344.

magnesium-carbon bond usually does not tolerate numerous functional groups.[82] Herein we wish to present our results about the preparation of functionalized imidazoles by I/Cu-exchange reactions.

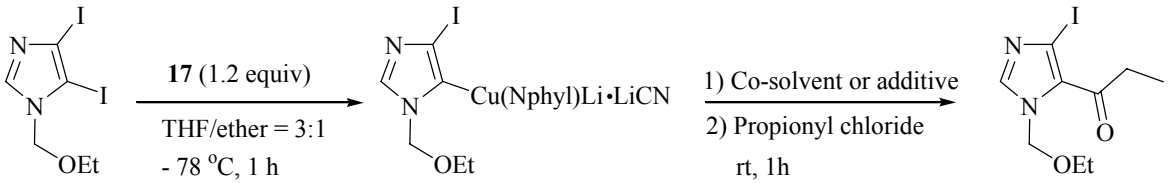
In preliminary experiment, 1-ethoxymethyl-4, 5-diiodoimidazole **79a**[83] was treated with $(Nphyl)_2CuLi{\cdot}LiCl$ (**17**) in a mixture of THF and diethyl ether (Et_2O/THF = 3 : 1) at –78 °C. Within 1 h, a complete I/Cu-exchange was observed with high regioselectivity for position 5, leading to the formation of cuprate **80a**. The regioselectivity was proved by comparing the NMR spectra of the hydrolysis product of **80a** with literature results.[84] The resulting copper reagents **80a** reacted with allyl bromide within 20 min at rt, leading to the allylated imidazole **81a** in 90% isolated yield. The regioselectivity was probably due to the presence of an *ortho*-substituent, which directed the I/Cu-exchange reaction by chelating or inductive effect (Scheme 39).



Scheme 39: Regioselective I/Cu-exchange reaction for the functionalization of imidazole **79a**.

However, further reaction of **80a** with other electrophiles, like acid chlorides, led only to traces of the desired product. After a careful study of the solvent and additive effects, NMP and DMAP were found to favor the reaction.[69, 70] These observations can be the result of the activation of an acid chloride by DMAP and the complexation of copper with NMP, which enhances the nucleophilic nature of the copper reagent (Scheme 40).

[82] Chen, Y.; Dias, H. V. R.; Lovely, C. J. *Tetrahedron Lett*. **2003**, *44*, 1379.
[83] Desforges, G.; Bossert, C.; Montagne, C.; Joseph, B. *Synlett* **2004**, 1306.
[84] Cliff, M. D.; Pyne, S. G. *J. Org. Chem.* **1995**, *60*, 2378.

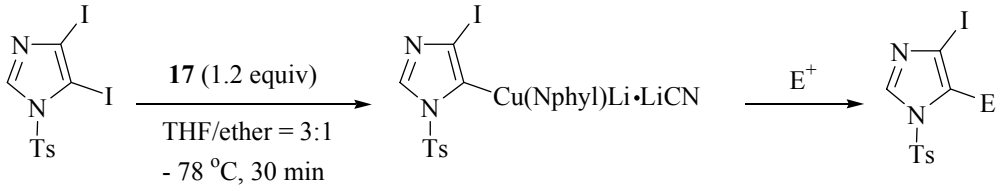


79a **80a** **81b**

co-Solvent or additive	___	NMP (0.5 mL/mmol)	DMAP (10 mmol%)	HMPA (0.5 mL/mmol)
Isolated Yield (%)	Trace	86	84	53

Scheme 40: Optimization of the reaction conditions of **80a** with propionyl chloride.

By changing the protecting group from ethoxymethyl in **79a** to a tosyl group in **79b**, a faster I/Cu-exchange reaction (30 min at –78 °C) was observed, leading to the cuprate **80b**. This effect was explained by the stronger electron-withdrawing nature of the tosyl group, which increased the exchange rate (Scheme 41).

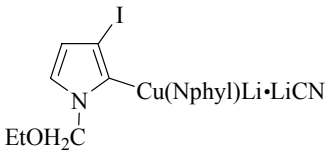
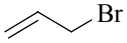
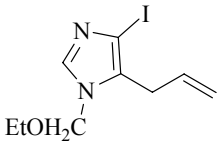
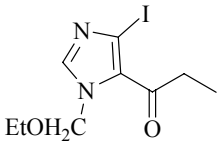
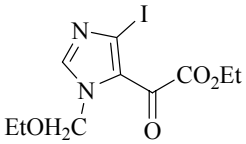
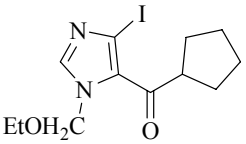
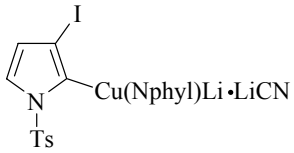
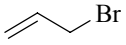
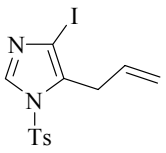
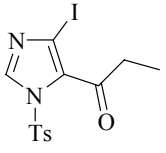


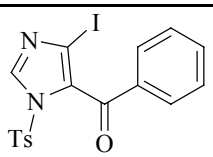
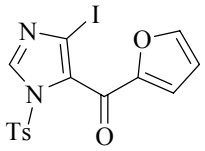
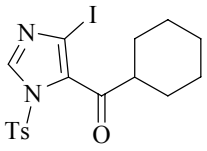
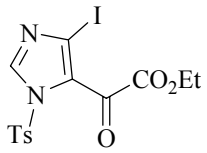
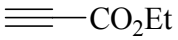
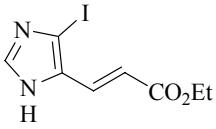
79b **80b** **81**

Scheme 41: Preparation of cuprate **80b** *via* I/Cu-exchange reaction.

Following these observations, a variety of monoiodoimidazoles **81** were prepared regioselectively by the exchange reaction (Table 9).

Table 9: Product **81a-j** obtained by the reaction of cuprate **80** with various electrophiles

Entry	Cuprate **80**	Electrophile	Product of Type **81**	Yield (%)[a]
1	 **80a**		 **81a**	90[b]
2	**80a**	EtCOCl	 **81b**	86
3	**80a**	EtOCOCOCl	 **81c**	74
4	**80a**	*c*-PentCOCl	 **81d**	81
5	 **80b**		 **81e**	93[b]
6	**80b**	EtCOCl	 **81f**	81

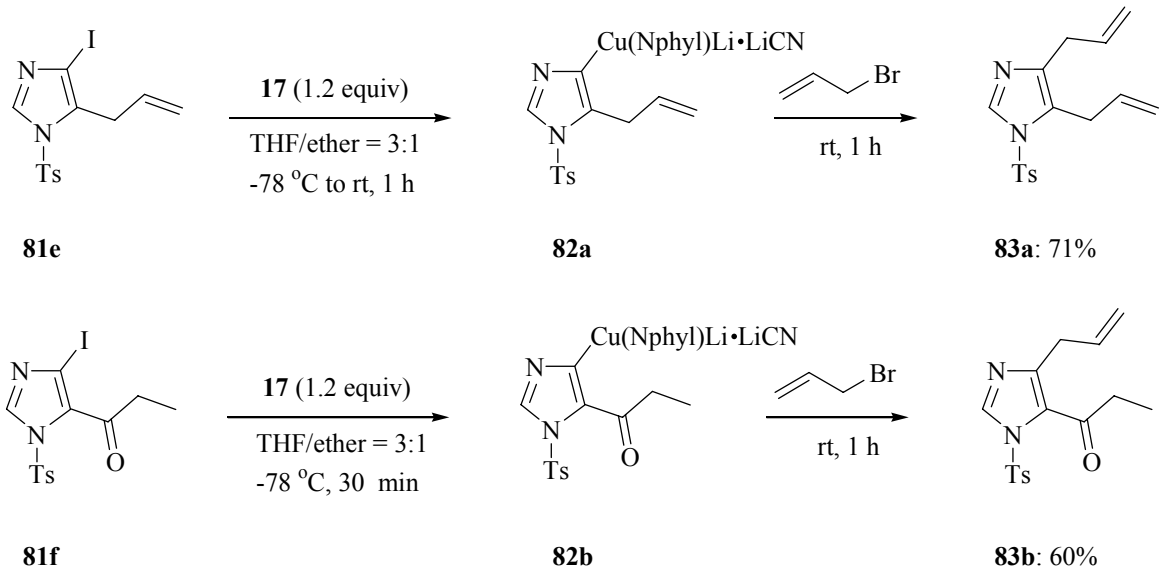
Entry	Cuprate **80**	Electrophile	Product of type **81**	Yield (%)[a]
7	**80b**	PhCOCl	 **81g**	85
8	**80b**	2-FurCOCl	 **81h**	71
9	**80b**	*c*-HexCOCl	 **81i**	84
10	**80b**	EtO_2CCOCl	 **81j**	76
11	**80b**		 **81k**	54

[a]Isolated yield of analytically pure product. [b]The reaction was performed without NMP as cosolvent.

As shown in Table 9, a variety of monoiodoimidazoles were accessible with this method. The reaction of cuprates **80a** and **80b** with allyl bromide furnished the corresponding products **81a** and **81e** in 90% and 93% yields, respectively (entries 1 and 5). Acylation of cuprates **80a** and **80b** with various aliphatic acid chlorides (entries 2, 4, 6, and 9) as well as aromatic acid chlorides (entries 7 and 8) in the presence of co-solvent NMP led to the corresponding 3-acylimidazoles in 71-86% yields. Furthermore, ethyl oxalyl chloride also reacted smoothly with **80a** and **80b** to afford the corresponding functionalized imidazoles **81c** and **81j** in 74% and 76% yields, respectively. Interestingly, the reaction of cuprate **80a**

with ethyl propiolate stereoselectively resulted in the formation of *trans*-alkenyl product **81k** in 54 % yield. The tosyl group was also removed during the reaction.

With the mono-iodoimidazole of type **81** in hands, our attention was turned to the performance of the second I/Cu-exchange reaction. As shown in Scheme 42, compound **81e** was treated with **17** (1.2 equiv) in a mixture of diethyl ether and THF (Et_2O/THF = 5/1) at – 78 °C, leading to the corresponding cuprate **82a** within 1.5 h. Allylation of **82a** with allyl bromide provided the diallyl compound **83a** in 71% yield. In a similar way, monoiodoimidazole **81f** was converted into the compound **83b** in 60% yield (Scheme 42).



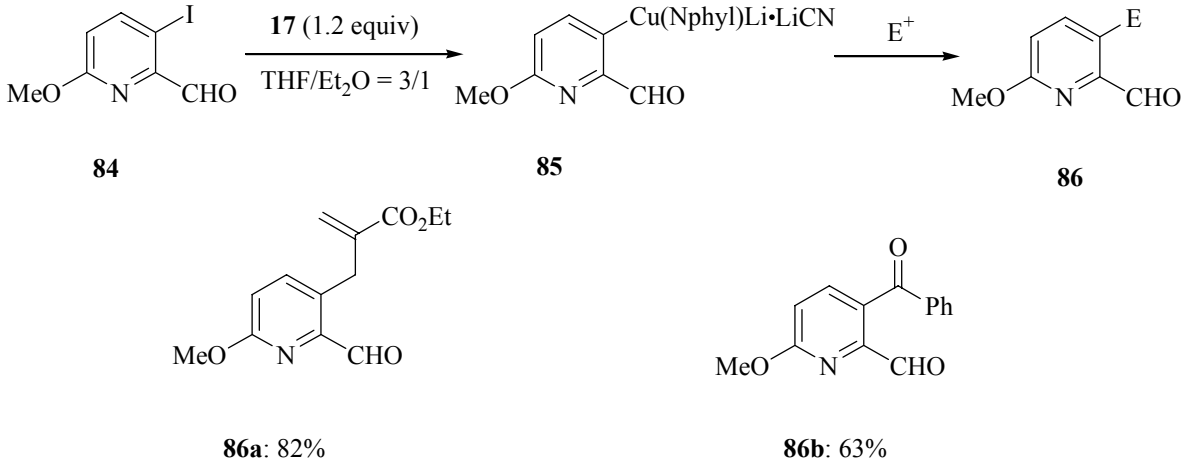
Scheme 42: Synthesis of 4,5-disubstituted imidazole **83a** and **83b**.

However, further reactions with other electrophiles, such as acid chlorides or 3-iodo-2-cyclohexen-1-one were proved less successful. Different solvents and different reaction temperatures were also probed without any improvement.

4.5 Preparation of Highly Functionalized Heteroaryl Cuprates in the Presence of an Aldehyde Group

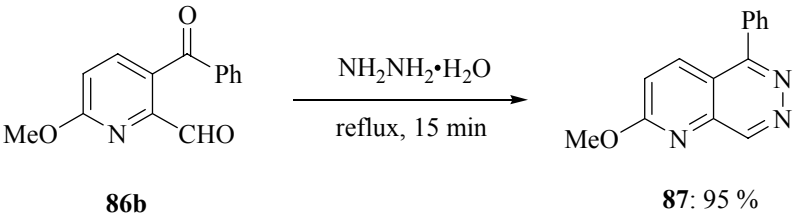
Encouraged by these results obtained, we envisioned to prepare functionalized heteroaryl cuprates bearing an aldehyde group. As discussed in the previous part, the chelation effect is essential for the functional group tolerance during the I/Cu-exchange reaction. Therefore,

functionalized pyridine **84**[85] reacted readily with **17** (1.2 equiv) in a mixture of THF and diethyl ether (THF/Et_2O = 5/1) from -78 °C to –60 °C within 3 h, leading to the corresponding cuprate **85**, which in reactions with ethyl (2-bromomethyl)acrylate or benzoyl chloride and provided the trisubstituted functionalized pyridines **86a** and **86b** in 82% and 63% yields (Scheme 43).



Scheme 43: Functionalization of pyridine **84** *via* I/Cu-exchange reaction.

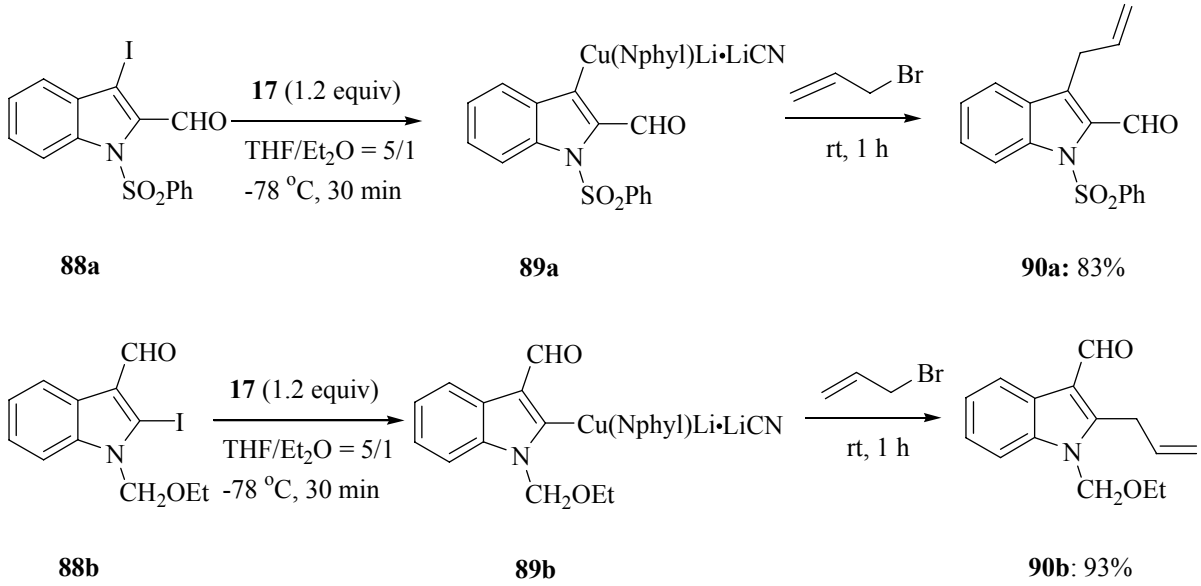
These highly functionalized pyridines are very useful precursor for further transformations. This was demonstrated by treating the dicarbonylated pyridine **86b** with hydrazine monohydrate in ethanol (reflux, 15 min), providing the pyridopyridazine **87** in 95% yield (Scheme 44).[48]



Scheme 44: Synthesis of pyridazine **87**.

Furthermore, we also found that this exchange reaction could be applied to the indole system with an aldehyde group at 2 or 3 position (Scheme 45).

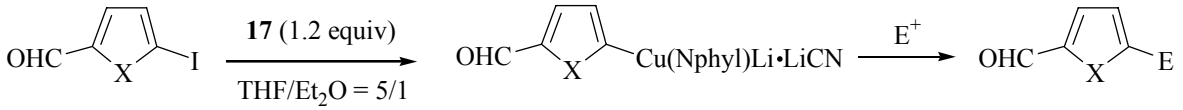
[85] Comins, D. L.; Killpack, M. O. *J. Org. Chem.* **1990**, *55*, 69.



Scheme 45: Functionalization of indole derivatives **89a-b** *via* an I/Cu-exchange reaction.

Thus, protected iodoindole **88a**[86] underwent a smooth I/Cu-exchange reaction with **17** at –78 °C within 30 min, furnishing the corresponding cuprate **89a**. Subsequent treatment of **89a** with allyl bromide furnished 3-allylated indole **90a** in 83% yield. Interestingly, even indole derivative **88b**[87] underwent an I/Cu-exchange reaction. Thus, the reaction of **88b** with **17** at –78 °C within 30 min led to the functionalized cuprate **89b**, which reacted readily with allyl bromide, providing product **90b** in 93% yield.

Finally, this exchange reaction was successfully applied to five-membered ring heterocycles (Scheme 46; Table 10).



91a: X = S
91b: X = O
91c: X = NMe

92a: X = S
92b: X = O
92c: X = NMe

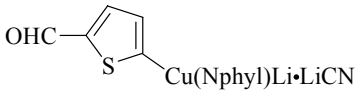
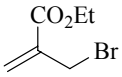
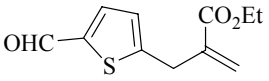
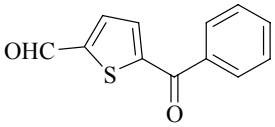
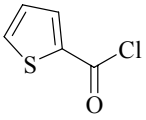
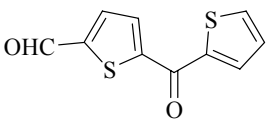
93

Scheme 46: Funtionalization of compounds of type **91** *via* I/Cu-exchange reaction.

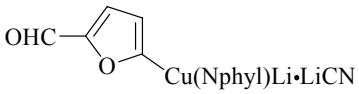
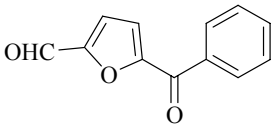
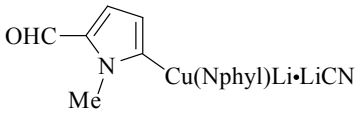
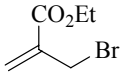
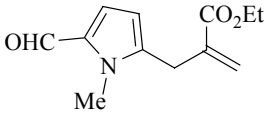
[86] a) Choshi, T.; Sada, T.; Fujimoto, H.; Nagayama, C.; Sugino, E.; Hibino, S. *J. Org. Chem.* **1997**, *62*, 2535; b) Echavarren, A. *J. Org. Chem.* **1990**, *55*, 4255; c) Suzuki, H.; Unemoto, M.; Hagiwara, M.; Ohyama, T.; Yokoyama, Y.; Murakami, Y. *J. Chem. Soc., Perkin Trans. 1,* **1999**, 1717.
[87] Comins, D. L.; Killpack, M. O. *J. Org. Chem.* **1987**, *52*, 104.

Thus, 5-iodo-thiophene-2-carbaldehyde **91a**[88] underwent a smooth I/Cu-exchange reaction with **17** (1.2 equiv, -78 °C, 15 min) leading to the desired mixed cuprate **92a**, which reacted with electrophiles, such as ethyl (2-bromomethyl)acrylate, benzoyl chloride or 2-thiophene carbonyl chloride, affording the desired products **93a-c** in 72-85% yields (entries 1, 2, 3 of Table 10). Similarly, treatment of 5-iodo-furan-2-carbaldehyde **91b**[89] with **17** (1.2 equiv, -78 °C, 15 min) provided cuprate **92b**, which was subsequently acylated with benzoyl chloride to give the product **93d** in 61% (entry 4). Interestingly, the protected iodopyrrole **91c**[88] reacted with **17** (-78 °C, 1 h), furnishing the mixed cuprate **92c**. Reaction of **92c** with (2-bromomethyl)acrylate afforded the 2-allylated pyrrol **93e** in 79% yield (entry 5). Although in each case, there was no chelating substituent on the five-membered ring, the stabilization of the resulting anion by the adjacent heteroatoms reduced the reactivity of the formed cuprates and, therefore, no addition to the aldehyde occured.

Table 10: Functionalized heterocycles of type **93** prepared from the reaction of cuprate **92** with various electrophiles.

Entry	Cuprate **92**	Electrophile	Product of type **92**	Yield (%)[a]
1	 **92a**		 **93a**	85
2	**92a**	PhCOCl	 **93c**	80
3	**92a**		 **93c**	72

[88] De Sousa Jr., P.; Taylor, R. J. K. *Synlett* **1990**, 755.
[89] 5-Iodo-furan-2-carbaldehyde is commercially available from Acros.

Entry	Cuprate **92**	Electrophile	Product of type **92**	Yield (%)[a]
4	 **92b**	PhCOCl	 **93d**	61
5	 **92c**		 **93e**	79

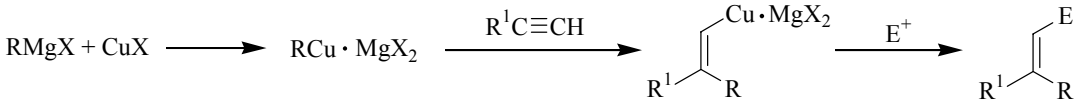
[a]Isolated yield of analytically pure product.

In summary, applications of the I/Cu-exchange reaction for the generation of highly functionalized heterocyclic cuprates were intensively studied. A series of sensitive functional groups, such as aldehyde, ketones, ester, nitrile, iodide, bromide and methoxy, were compatible with this exchange reaction. The subsequent reactions of these heterocyclic cuprates with different electrophiles provided a broad range of polyfunctionalized heterocycles, which are otherwise difficult to prepare.

5 Preparation of Functionalized Alkenyl Cuprate Reagents *via* an Iodine-Copper Exchange Reaction

5.1 Introduction

The preparation of functionalized alkenyl organometallics is an important synthetic task since these reagents are frequently used in organic chemistry. Numerous methods were developed for the preparation of alkenyl organometallics.[28, 90] The addition of organocopper reagents to terminal alkynes and to acetylene represents an efficient way to synthesize vinylic copper reagents with an established geometry.[91] The addition proceeds in a Markownikov way and *syn*-specific fashion. The organic cuprate is normally prepared from a Grignard or a lithium reagent and a copper (I) salt (Scheme 47).

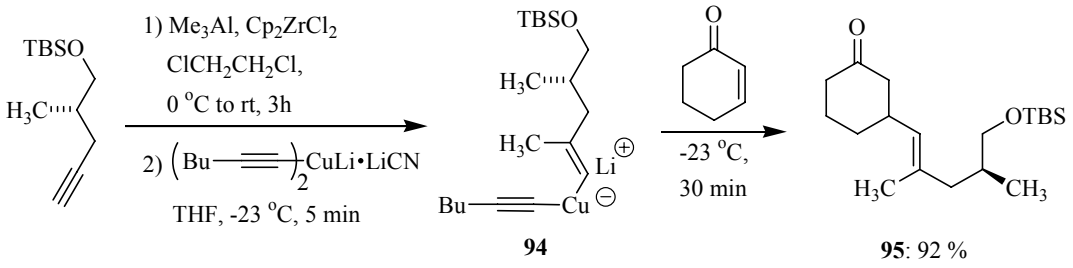


Scheme 47: Formation of alkenylcopper reagents from alkynes.

J. F. Normant and A. Alexakis[92] extensively studied this methodology and its application in the synthesis of conjugated dienes, allylic thioethers and allylic amides. G. Cahiez and P. Knochel prepared polyfunctional and stereochemically pure (*E*) and (*Z*) alkenylcopper reagents by the carbocupration of terminal alkynes and reacted them with alkylidenemalonates.[93] More recently, a variety of metalated vinylcuprate intermediates, resulting from silyl- or stannylcupration of silyl- and tin-containing acetylenes were obtained, affording interesting functionalized polymetalated olefins.[94] A second way of preparing vinylic cuprates involves the carbometalation of an alkyne and a subsequent

[90] Fürstner, A. *Active Metals*, Wiley-VCH, Weinheim, **1996**.
[91] Normant, J. F. *Organocopper Reagents. A Practical Approach* (ed. R. J. K. Taylor), Oxford Unversity Press, **1994**, cp.11, p. 237.
[92] a) Jabri, N.; Alexakis, A.; Normant, J. F. *Tetrahedron Lett.* **1981**, *22*, 3851. b) Alexakis, A.; Normant, J. F. *Tetrahedron Lett.* **1982**, *23*, 5151. c) Germon, C.; Alexakis, A.; Normant, J. F. *Synthesis* **1984**, 40. d) Germon, C.; Alexakis, A.; Normant, J. F. *Synthesis* **1984**, 43.
[93] Cahiez, G.; Venegas, P.; Tucker, C. E.; Majid, T. N.; Knochel, P. *J. Chem. Soc. Chem. Commun.* **1992**, 1406.
[94] Cuadrado, P.; González-Nogal, A.; Sánchez, A. *J. Org. Chem.* **2001**, *66*, 1961.

transmetalation to copper. Thus, vinylic stannanes,[95] tellurides[96] and zirconates[97] readily exchanged their vinylic ligands for alkyl groups on copper. Vinylic alanes, formed *via* a Negishi-type carbometalation with Me_3Al/catalytic Cp_2ZrCl_2[98] were also converted into mixed higher order cyanocuprates, which transfer their vinylic residues in a Michael sense to enones.[99] An excellent example was reported by P. Wipf's group. They published a method for the direct carboalumination of alkynes and *in situ* Zr/Cu-exchange which allowed the conjugate addition of disubstituted or monosubstituted alkenylcopper species such as **94** to α,β-unsaturated ketones, leading to the Michael adduct **95** in 92 % yield (Scheme 48).[100]

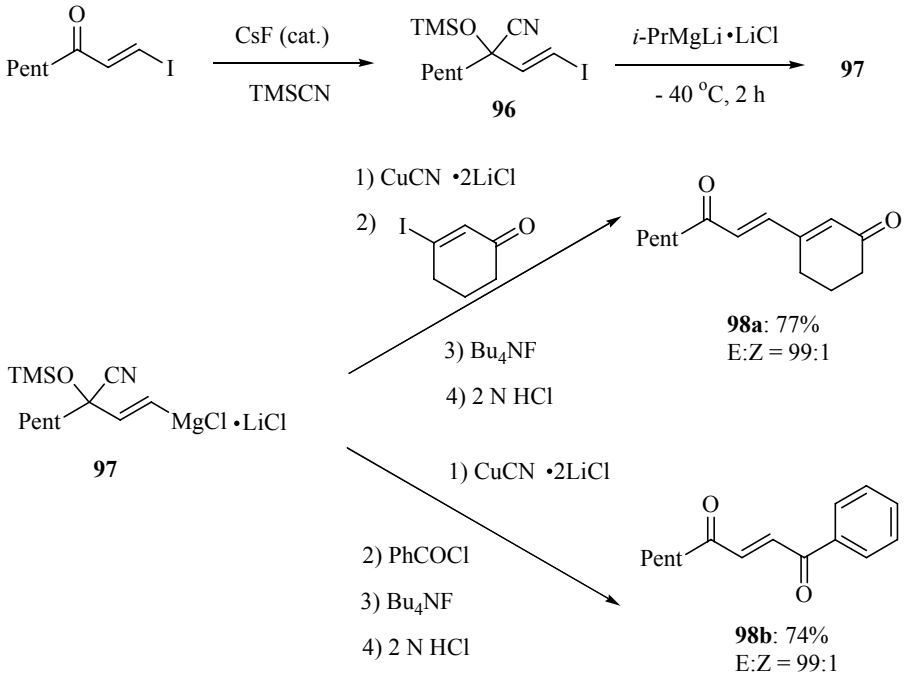


Scheme 48: Carboalumination and transmetallation reactions for the preparation of alkenyl copper reagents.

Very recently, P. Knochel and co-workers have developed an efficient method to generate various cyclic and acyclic alkenyl Grignard reagents *via* an iodine-magnesium exchange reaction.[43, 101] The resulting Grignard reagents reacted readily with CuCN·2LiCl to form the corresponding alkenylcopper reagents. Thus, the β-iodo-α,β-unsaturated ketone underwent a "Transient protection" to give the cyanohydrine **96**, which was readily converted into the corressponding magnesium species **97** and reacted, after transmetallation with CuCN·2LiCl, with 3-iodocyclohexane or benzoyl chloride, leading to the unsaturated diketones **98a** and

[95] Behling, J. R.; Babiak, K. A.; Ng, J. S.; Campbell, A. L.; Moretti, R.; Koerner, M.; Lipshutz, B. H. *J. Am. Chem. Soc.* **1988**, *110*, 2641.
[96] a) Comasseto, J. V.; Berriel, J. N. *Synth. Commun.* **1990**, *20*, 1681. b) Moraes, D. N.; Barrientos-Astigarraga, R.E.; Castelani, P.; Comasseto, J. V *Tetrahedron* **2000**, *56*, 3327.
[97] a) Lipshutz, B. H.; Ellsworth, E. L. *J. Am. Chem. Soc.* **1990**, *112*, 7440. b) Babiak, K. A.; Behling, J. R.; Dygos, J. H.; McLaughlin, K. T.; Ng, J. S.; Kalish, V. J.; Kramer, S. W.; Shone, R. L. *J. Am. Chem. Soc.* **1990**, *112*, 7741. c) Lipshutz, B. H.; Kato, K. *Tetrahedron Lett.* **1991**, *32*, 5647.
[98] Negishi, E. *Pure Appl. Chem.* **1981**, *53*, 2333.
[99] a) Ireland, R. E.; Wipf, P. *J. Org. Chem.* **1990**, *55*, 1425. b) Lipshutz, B. H.; Dimock, S. H. *J. Org. Chem.* **1991**, *56*, 5761.
[100] Wipf, P.; Smitrovich, J. H.; Moon, C.-W. *J. Org. Chem.* **1992**, *57*, 3178.
[101] a) Ren. H.; Krasovskiy, A.; Knochel, P. *Org. Lett.* **2004**, *6*, 4215; b) Ren, H.; Krasovskiy, A.; Knochel, P. *Chem. Commun*. **2005**, 543.

98b in 77% and 74%, after deprotection of the intermediate cyanohydrin derivatives with Bu_4NF and HCl (2M in H_2O) (Scheme 49).



Scheme 49: I/Mg-exchange and transmetallation reactions for the generation of alkenyl cuprates.

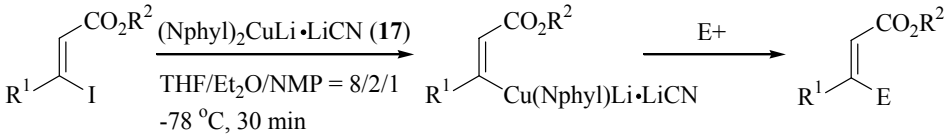
However, the generation of functionalized alkenyl cuprates *via* direct halogen-copper exchange reaction was never reported. Taking into account the successful preparation of aryl and heteroaryl cuprate reagents *via* halogen-copper exchange reaction, it is promising to apply this method to vinylic substrates.

5.2 Functionalization of β-Iodo-α,β-unsaturated Esters *via* an I/Cu-Exchange Reaction

Our initial attempt focussed on the β-iodo-α,β-unsaturated esters **99** which are all literature known.[102] Thus, methyl (2*Z*)-3-iodo-octenoate **99a** was subjected to the exchange reaction with $(Nphyl)_2CuLi{\cdot}LiCl$ (**17)** at –78 °C. Probably due to the chelating effect of the carbonyl group, a smooth I/Cu-exchange was observed within 30 min, stereoselectively leading to the

[102] a) Piers, E.; Wong, T.; Coish, P. D.; Rogers, C. *Can. J. Chem.* **1994**, *72*, 1816; b) Meyer, C.; Marek, I.; Normant, J.-F. *Synlett* **1993**, 386; c) Ma. S.; Lu, X.; Li, Z. *J. Org. Chem.* **1992**, *57*, 709.

corresponding alkenyl cuprate **100a** with retention of the double bond configuration. No competitive 1,4-addition or 1,2-addition products were observed. Hydrolysis of **100a** provided only *trans*-alkene **101a** in 92% yield, which clearly indicated the stereoselectivity of this exchange reaction (entry 1 of Table 11).[103] The subsequent reaction of **100a** with other electrophiles proved to be less successful, probably due to the strong complexation between the ester group and copper, which reduces the reactivity of cuprate **100a**. This problem was efficiently solved by the addition of the strong polar co-solvent NMP,[70] which enhanced the nucleophilic reactivity of cuprate **100a**. The change of β-substitution of compound **99a** to a phenyl or the electron-donating group like trimethylsilyl did not affect the exchange. Thus, **99b** and **99c** reacted smoothly with **17** at –78 °C, leading to the functionalized alkenyl cuprates **100b** and **100c** within 30 min. The resulting cuprate **100** reacted with various electrophiles providing highly functionalized compounds of type **101** in good to excellent yields (Scheme 50, Table 11).



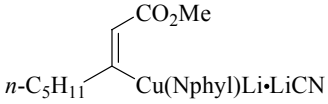
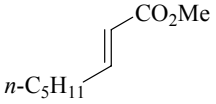
99a: $R^1 = n\text{-}C_5H_{11}$; R^2 = Me
99b: R^1 = Ph; R^2 = Et
99c: R^1 = TMS; R^2 = Et

100a: $R^1 = n\text{-}C_5H_{11}$; R^2 = Me
100b: R^1 = Ph; R^2 = Et
100c: R^1 = TMS; R^2 = Et

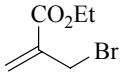
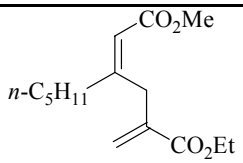
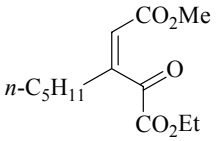
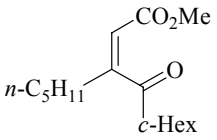
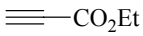
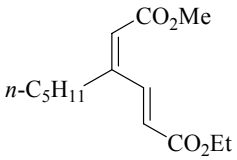
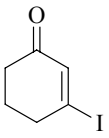
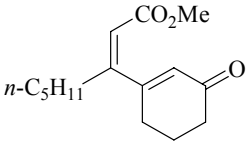
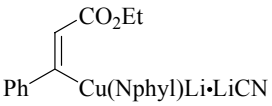
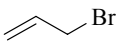
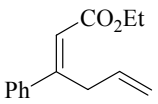
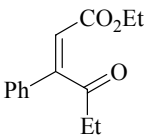
101

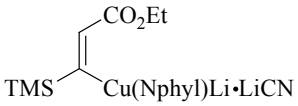
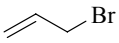
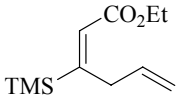
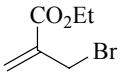
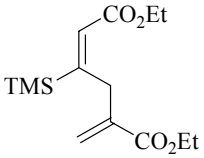
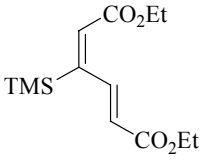
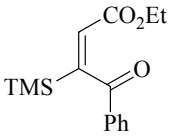
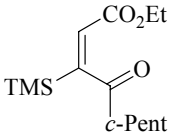
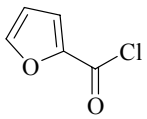
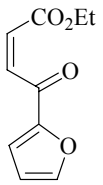
Scheme 50: Generation of functionalized alkenyl cuprates **100** *via* I/Cu-exchange reaction.

Talbe 11: Preparation of highly functionalized compounds **101** from the reaction of alkenyl cuprates **100** with various electrophiles.

Entry	Cuprate **100**	Electrophile	Product of type **101**	Yield (%)[a]
1	 **100a**	H_2O	 **101a**	92[b]

[103] Trost, B. M.; Ball, Z. T.; Jöge, T. *J. Am. Chem. Soc.* **2002**, *124*, 7922.

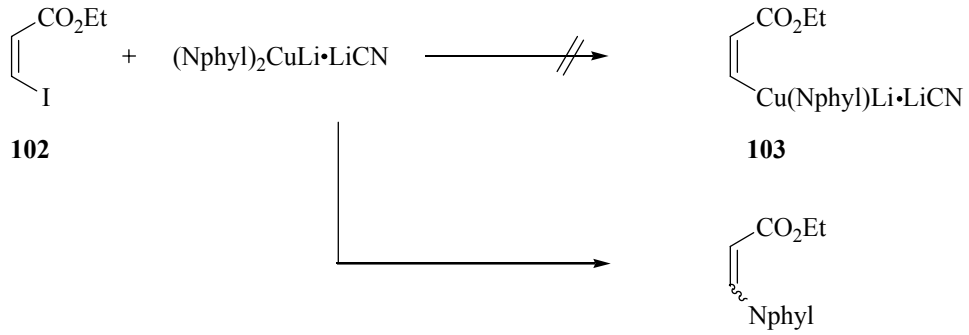
Entry	Cuprate **100**	Electrophile	Product of type **101**	Yield (%)[a]
2	**100a**		 **101b**	89
3	**100a**	EtO_2CCOCl	 **101c**	78
4	**100a**	*c*-HexCOCl	 **101d**	83
5	**100a**		 **101e**	68
6	**100a**		 **101f**	81
7	 **100b**		 **101g**	92
8	**100b**	EtCOCl	 **101h**	86

Entry	Cuprate **100**	Electrophile	Product of type **101**	Yield (%)[a]
9	 **100c**		 **101i**	93
10	**100c**		 **101j**	81
11	**100c**		 **101k**	80
12	**100c**	PhCOCl	 **101l**	85
13	**100c**	*c*-PentCOCl	 **101m**	89
14	**100c**		 **101n**	75

[a] Isolated yield of analytically pure product. [b] The reaction was performed without NMP as cosolvent.

As shown in the Table 11, the allylation of cuprates **100a**, **b** and **c** with allyl bromide (entries 7 and 9 of Table 10) or with more reactive ethyl (2-bromomethyl)acrylate (entries 2 and 10) furnished the corresponding products **101b**, **g**, **i** and **j** in 81% - 93% yields. Similarly, the acylation of cuprate **100a**, **b** and **c** with various acid chlorides provided the highly functionalized ketones **101c**, **d**, **h**, **l** and **m** in 78% - 89% yields (entries 3, 4, 8, 12 and 13). Interestingly, the cleavage of the trimethylsilyl group was observed during the reaction of **100c** with furoyl chloride, leading to the *cis*-alkene **101n** in 75% yield (entry 14). Furthermore, the carbocupration of ethyl propiolate with **100a** and **100c** led stereoselectively to the diene compound **101e** and **101k** in 68% and 80% yields, respectively (entry 5 and 11). Finally, copper derivative **100a** readily participated in an addition-elimination reaction as well, leading to product **101f** upon reaction with 3-iodo-2-cyclohexenone in 81% (entry 6).

The steric effect proved to be essential for the chemoselectivity of this exchange reaction. The reaction of (*Z*)-3-iodo-acrylic acid ethyl ester **102**[102a] with **17** at –78 °C in 5 min led only to the addition-elimination product. No cuprate **103** was formed. Different solvents and temperatures were probed without any improvement of the exchange reaction (Scheme 51).

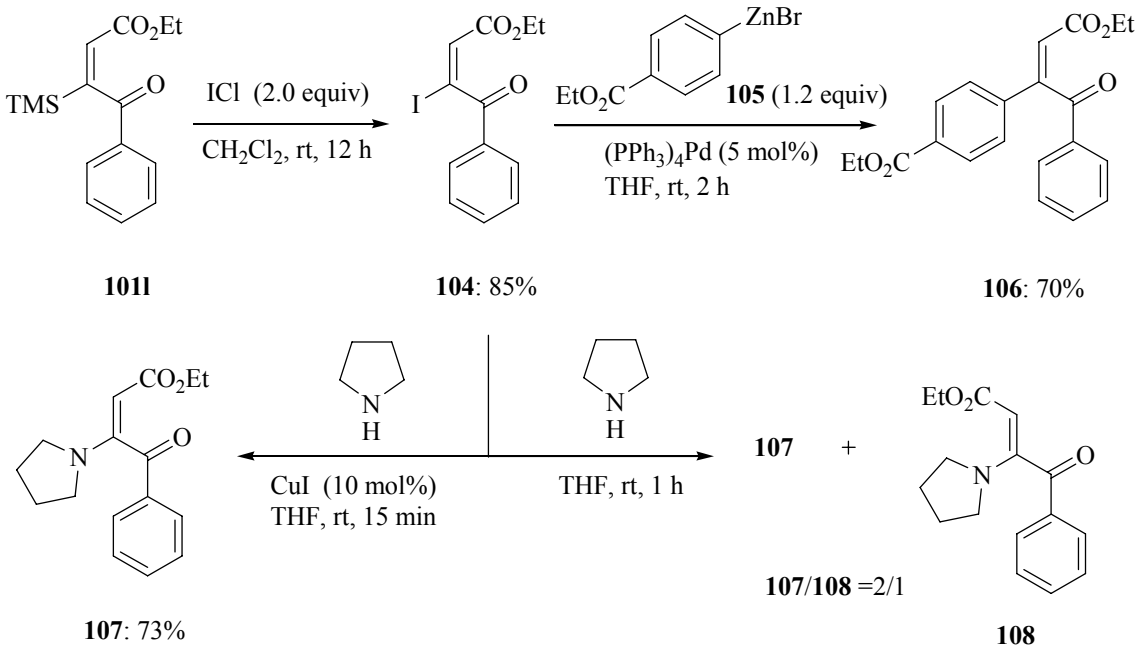


Scheme 51: Attempts to generate cuprate **103**.

The compounds of type **101** are versatile building blocks for further transformations. In the presence of ICl, compound **101l** was readily converted into iodosubstituted product **104** in 85% yield.[104] The resulting compound **104** allowed a palladium-catalyzed Negishi cross-coupling reaction with the functionalized arylzinc reagent **105**, providing the β-disubstituted-α,β-unsaturated ester **106** in 70% yield.[105] Similarly, a copper-catalyzed

[104] Chou, S.-S. P.; Kuo, H.-L.; Wang, C.-J.; Tsai, C.-Y.; Sun, C.-M. *J. Org. Chem.* **1989**, *54*, 868.
[105] a) Negishi; E. *Acc. Chem. Res.* **1982**, *15*, 340; b) Negishi, E.; Matsushita, M.; Kobayashi, M.; Rand, C. L. *Tetrahedron Lett.* **1983**, *24*, 3822; c) Negishi, E.; Owczarczyk, Z. *Tetrahedron Lett.* **1991**, *32*, 6683.

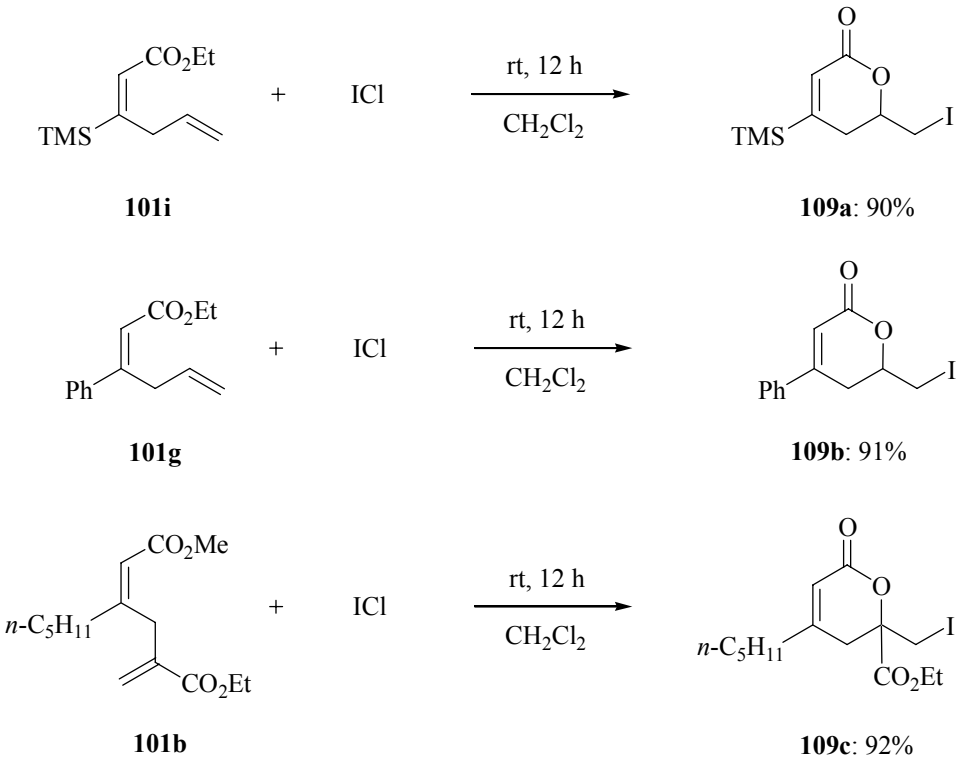
amination reaction was also performed, furnishing smoothly the product **107** in 73% yield with retention of the configuration of the double bond.[106] However, without catalyst CuI, a mixture of the isomer was formed (**107** : **108** = 2 : 1) (Scheme 52).[107]



Scheme 52: Further derivatization of **101k**.

Interestingly, the reaction of **101i** with ICl did not lead to the substitution of the TMS group. Instead, a cyclization product **109a** was isolated in 90% yield (Scheme 53). We envisioned that ICl first activated the allylic double bond and a subsequent intramolecular addition of the ester carbonyl to the double bond finally led to the lactone **109a**.[108] In a similar way, compound **101g** was readily converted into the cyclization product **109b** in 91% yield. In the case of **101b**, a complete regioselective cyclization took place with the formation of single product **109c** in 92% yield. This is probably, because the less sterically hindered double bond favored the intramolecular attack of the ester group (Scheme 53).

[106] a) Qing, F.-L.; Gao, W.-Z. *Tetrahedron Lett.* **2000**, *41*, 7727; b) Marshall, J. A.; Pinney, K. G. *J. Org. Chem*. **1993**, *58*, 7180.
[107] a) Rainka, M. P.; Aye Y.; Buchwald, S. L. *P. N. A. S.* **2004**, *101*, 5821; b) Pan. X.; Cai, Q.; Ma, D. *Org. Lett.* **2004**, *6*, 1809.
[108] a) Yao, T.; Larock, R. C. *J. Org. Chem.* **2005**, *70*, 1432; b) Yue, D.; Ca, D.; Larock, R. C. *Org. Lett.* **2004**, *6*, 1581; c) Yao, T.; Larock, R. C. *Tetrahedron Lett.* **2002**, *43*, 7401; d) Huang, Q.; Hunter, J.; Larock, R. C. *Org. Lett.* **2002**, 3, 2973; e) Hunter, J.; Larock, R. C. *J. Org. Chem*. **2002**, *67*, 3437.



Scheme 53: ICl-mediated cyclization of compounds **101a**, **101h**, and **101f**.

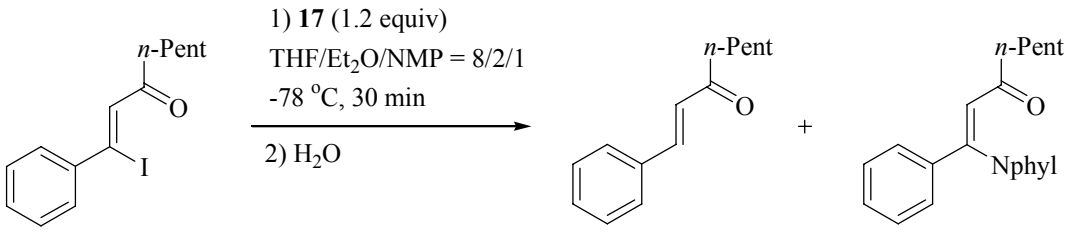
5.3 Functionalization of β-Iodo-α,β-unsaturated Ketones *via* an I/Cu-Exchange Reaction

After the successful application of the I/Cu-exchange reaction on β-iodo-α,β-unsaturated esters, we have applied this methodology on the more sensitive functionalized alkeny compounds, such as β-iodo-α,β-unsaturated ketones. The functionalization of β-iodo-α,β-unsaturated ketones is a challenging task for organic chemists since β-substituted-α,β-unsaturated ketones usually react with organometallics *via* an addition-elimination pathway.[11]

Thus, the literature known (1*Z*)-1-Iodo-1-phenyl-1-octen-3-one[109] **110a** was first reacted with **17** under our standard reaction conditions. The GC-MS analysis of the crude reaction mixture showed clearly that both exchange product **111** and addition–elimination product

[109] A) Taniguchi, M.; Kobayashi, S.; Nakagawa, M.; Hino, T. *Tetrahedron Lett.* **1986**, *27*, 4763; b) Verkruijsse, H. D.; Heus-Kloos, Y. A.; Brandsma, L. *J. Organomet. Chem.* **1988**, *338*, 289.

112 were formed in a ratio of 5:1. To our delight, the carbonyl group was tolerated during the reaction and the exchange reaction occured stereoselectively with retention of the double bond configuration, which was proved by analysing the NMR spetra of *trans*-alkene **111**[110] (Scheme 54).

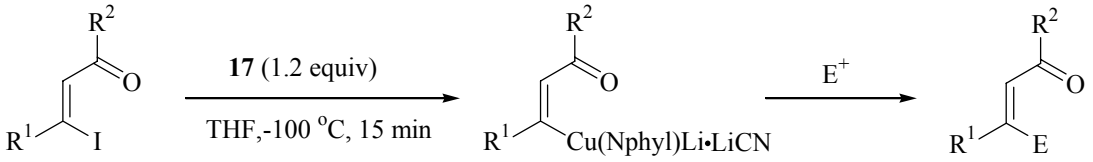


110a **111** **112**

111/**112** = 5/1

Scheme 54: I/Cu-exchange reaction of **110a** with **17**.

After careful tuning of solvent and temperature to avoid the competitive addition-elimination reaction, we found that THF was the best solvent and a low reaction temperature (–100 °C) is necessary for this reaction. Under these optimized reaction conditions, the exchange reaction of different β-iodo-α,β-unsaturated carbonyl compounds of type **110** with **17** was completed within 15 min, furnishing the functionalized alkenyl cuprates **113**. Their reaction with various electrophiles (E^+) provided highly functionalized trisubstituted enones of type **114** in good to excellent yields (Scheme 55; Table 12).



110a: R^1 = Ph, R^2 = *n*-Pent
110b: R^1 = *n*-Bu, R^2 = *n*-Hept
110c: R^1 = TMS, R^2 =Et

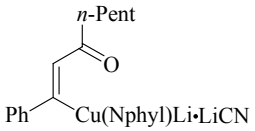
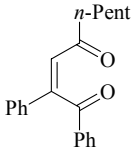
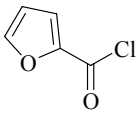
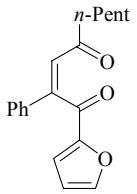
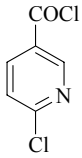
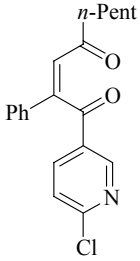
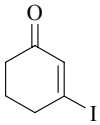
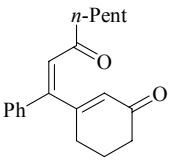
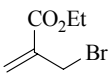
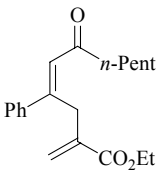
113a: R^1 = Ph, R^2 = *n*-Pent
113b: R^1 = *n*-Bu, R^2 = *n*-Hept
113c: R^1 = TMS, R^2 =Et

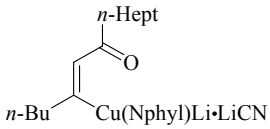
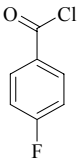
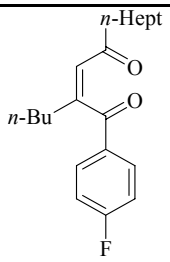
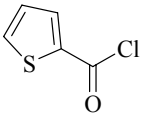
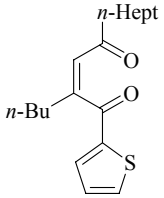
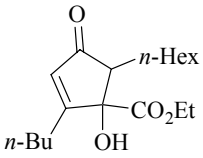
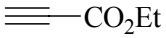
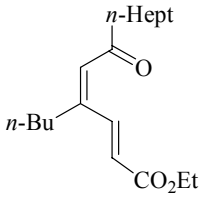
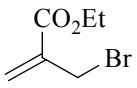
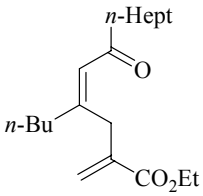
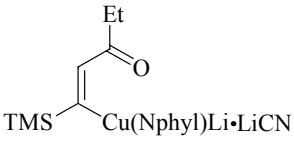
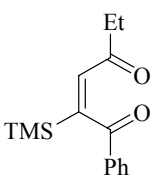
114

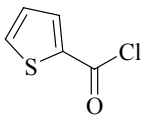
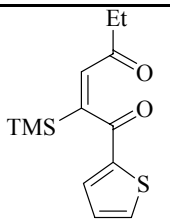
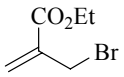
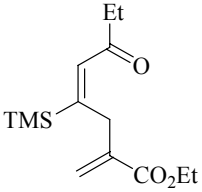
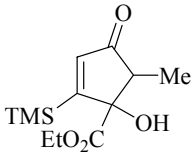
Scheme 55: Functionalization of β-iodo-α,β-unsaturated ketone **110** *via* I/Cu-exchange reaction.

[110] Katritzky, A. R.; Feng, D.; Lang, H. *J. Org. Chem.* **1997**, *62*, 706.

Table 12: Preparation of highly functionalised compounds **114** *via* an I/Cu-exchange reaction.

Entry	Cuprate **113**	Electrophile	Product of type **114**	Yield (%)[a]
1	 **113a**	PhCOCl	 **114a**	83
2	**113a**		 **114b**	78
3	**113a**		 **114c**	81
4	**113b**		 **114d**	71
5	**113b**		 **114e**	82

Entry	Cuprate **113**	Electrophile	Product of type **114**	Yield (%)[a]
6	 **113b**		 **114f**	75
7	**113b**		 **114g**	78
8	**113b**	EtO_2CCOCl	 **114h**	71
9	**113b**		 **114i**	80
10	**113b**		 **114j**	90
11	 **113c**	PhCOCl	 **114k**	84

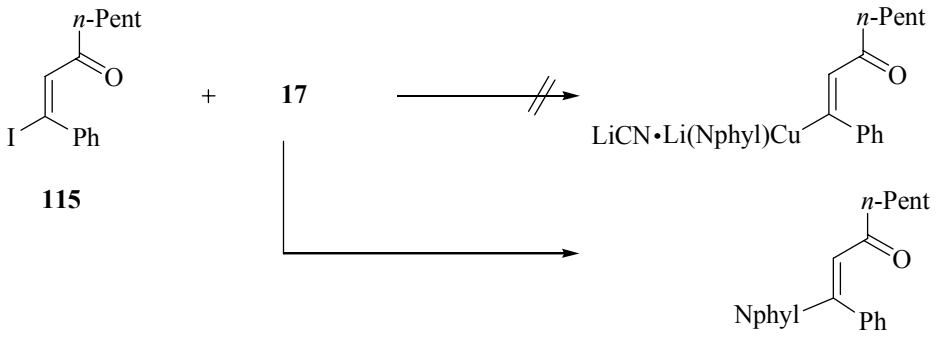
Entry	Cuprate **113**	Electrophile	Product of type **114**	Yield (%)[a]
12	**113c**		 **114l**	76
13	**113c**		 **114m**	89
14	**113c**	EtO_2CCOCl	 **114n**	71

[a] Isolated yield of analytically pure product.

As shown in the Table 12, the phenyl substituted alkenyl cuprate **113a** reacted with various aromatic and heteroaromatic acid chlorides leading to diketones **114a-c** in moderate to good yields (78%-83%, entries 1, 2 and 3 of Table 12). The reaction with 3-iodo-2-cyclohexenone provided addition-elimination product **114d** in 71% yield (entry 4). Furthermore, the treatment of **113a** with ethyl (2-bromomethyl)acrylate, providing **114e** in 82% yield (entry 5). In a similar way, the *bis*-alkyl substituted alkenyl cuprate **113b** was readily acylated with acyl chlorides, giving the diketones **114f-g** in 75-78% yields, respectively (entries 6 and 7). Acylation with ethyl oxalyl chloride led after a ring closure to the 5-membered enone **114h** in 71% yield (entry 8). Carbocupration of ethyl propiolate with **113b** stereoselectively led to the dienone **114i** in 80% yield (entry 9). Finally, allylation of cuprate **113b** was possible with ethyl (2-bromomethyl)acrylate, providing **114j** in 90% yield (entry 10). Even a change of the substituent R^1 in **110** from phenyl in **110a** or alkyl group in **110b** to the electron-donating trimethylsilyl group in **110c** did not affect the exchange reaction. The corresponding cuprate **113c** readily underwent acylation with benzoyl chloride

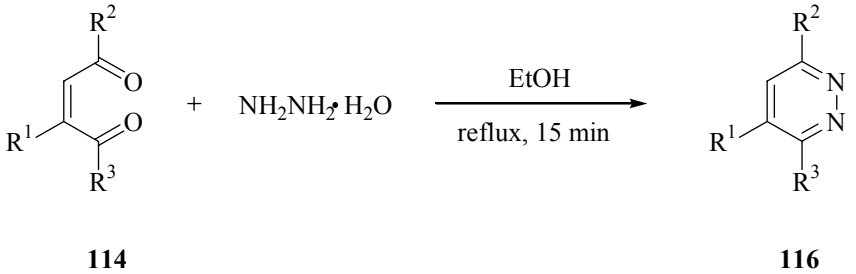
and 2-thiophenecarbonyl chloride, providing the diketones **114k** and **114l** in 84% and 76% yields, respectively (entries 11 and 12). Allylation with ethyl (2-bromomethyl)acrylate furnished ketone **114m** in 89% (entry 13). As with cuprate **113b**, acylation of **113c** with ethyl oxalyl chloride led to the aldol addition product **114n** in 71% yield (entry 14).

The *Z*-configuration of the iodine to the carbonyl group in the starting material **110** was crucial for the success of the exchange reaction. The *E*-isomer **115**[109a] was subjected to the reaction with **17** under standard conditions. Instead of the exchange reaction, only the addition-elimination product was observed. This means that the *Z*-configuration favored the chelation of the carbonyl group to copper and therefore favors the exchange reaction (Scheme 56).



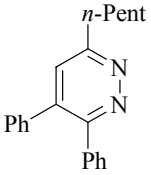
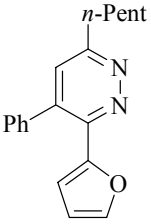
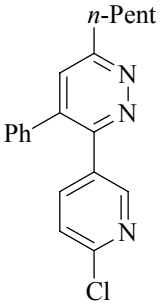
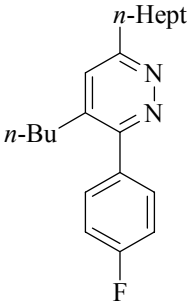
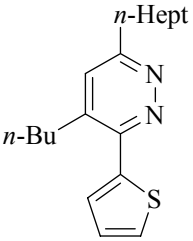
Scheme 56: Influence of the double bond configuration on the exchange reaction.

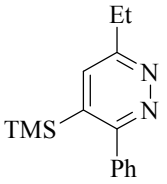
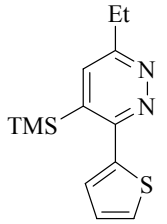
Compounds of type **114** are versatile building blocks for the synthesis of heterocyclic compounds. Thus, diketones **114a**, **b**, **c**, **f**, **g**, **k, l** were treated with hydrazine monohydrate in ethanol (reflux, 15 min), providing the corresponding pyridazines **116a-g** in excellent yields of more than 90% regardless of the substituents on the starting diketones **114** (Scheme 57; Table 13).[48]



Scheme 57: Synthesis of pyridazines of type **116**.

Table 13: Synthesis of pyridazines of type **116**.

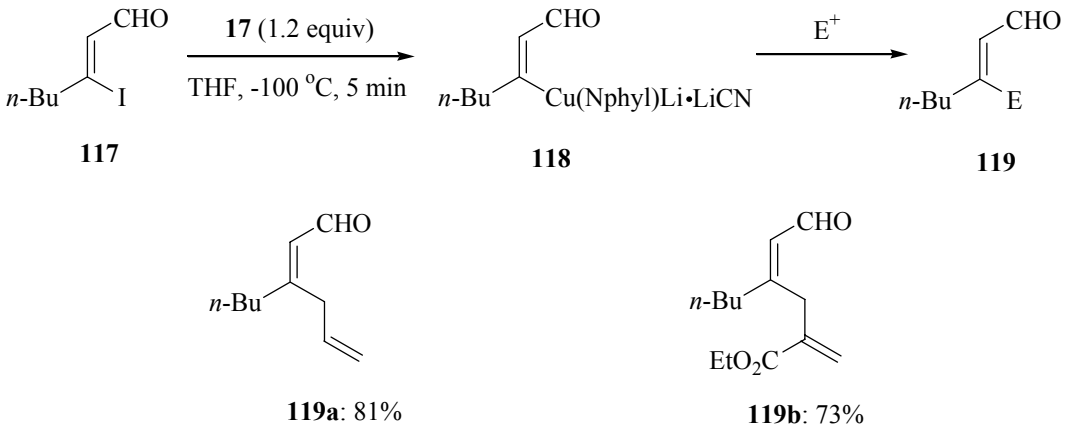
Entry	Diketone **114**	Product of type **116**	Yield (%)[a]
1	**114a**	 **116a**	92
2	**114b**	 **116b**	96
3	**114c**	 **116c**	95
4	**114f**	 **116d**	90
5	**114g**	 **116e**	92

Entry	Diketone **114**	Product of Type **116**	Yield (%)[a]
6	**114k**	 **116f**	92
7	**114l**	 **116g**	90

[a]Isolated yield of analytically pure product.

5.4 Functionalization of β-Iodo-α,β-unsaturated Aldehydes *via* an I/Cu-Exchange Reaction

Surprisingly, we found that β-iodo-α,β-unsaturated aldehydes could also be subjected to the I/Cu-exchange reaction with **17** (Scheme 58).



117 **118** **119**

119a: 81% **119b**: 73%

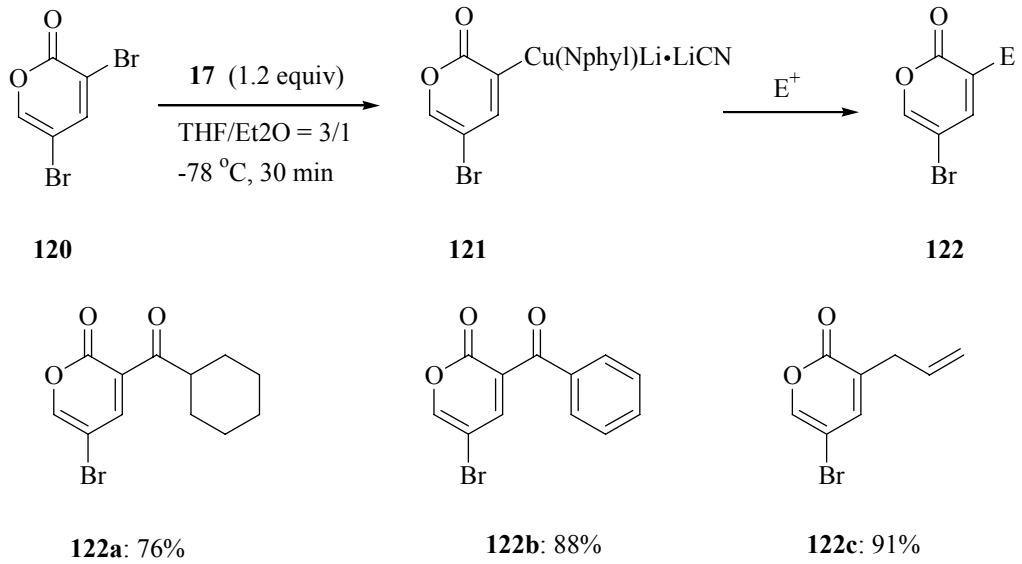
Scheme 58: Preparation of functionalized compounds **119** *via* an I/Cu-exchange reaction.

Thus, (2*Z*)-3-iodo-2-heptenal **117**[111] underwent a smooth I/Cu-exchange reaction with **17** in pure THF within a few minutes at –100 °C, stereoselectively leading to the functionalized alkenyl cuprate **118**. The stereoselectivity was proved by comparing the NMR data of hydrolysis product of **118** with literature results.[112] Subsequent reaction of **118** with allyl bromide or ethyl (2-bromomethyl)acrylate furnished the trisubstituted alkenes **119a** and **119b** in 81% and 73% yields.

However, further reactions with other electrophiles, such as acid chlorides and 3-iodo-2-cyclohexenone, proved unsuccessful. This may be explained by the strong complexation between the aldehyde group and the copper species which reduces the reactivity of cuprate **118**. On the other hand, an increasing of the reaction temperature will result in the decomposition of the cuprate **118** or even the desired product.

5.5 Preparation of Other Alkenyl Cuprates *via* Iodine or Bromine-Copper Exchange Reaction

In addition to the preparation of functionalized alkenyl cuprates *via* I/Cu-exchange reaction, a bromine-copper exchage reaction also allowed the functionalization of α-pyrones (Scheme 59).

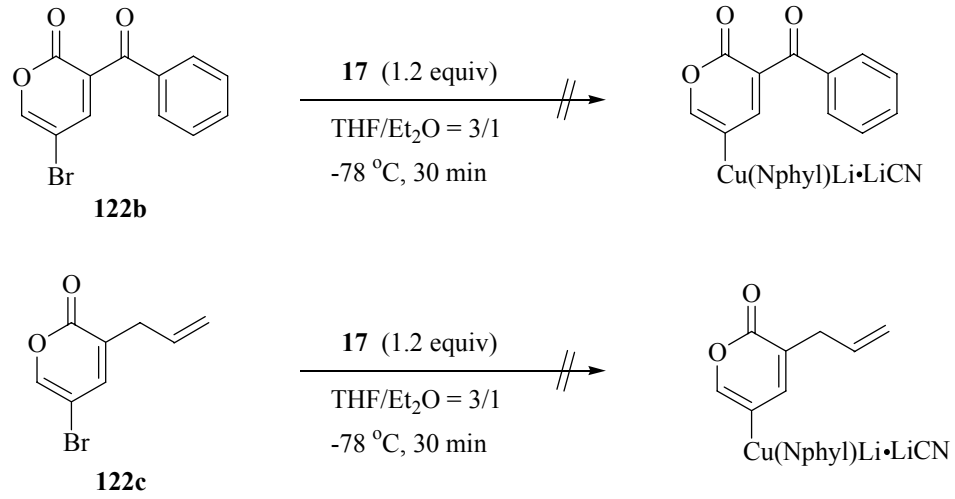


Scheme 59: Selective Br/Cu-exchange for preparation of alkenyl cuprate **121**.

[111] Arnold, L. A.; Naasz, R.; Minnaard, A. J.; Feringa, B. L. *J. Am. Chem. Soc.* **2001**, *123*, 5841.
[112] Baillargeon, V. P.; Stille, J. K. *J. Am. Chem. Soc.* **1986**, *108*, 459.

Thus, the reaction of 3,5-dibromo-2H-pyran-2-one **120**[113] with **17** in a 3:1 mixture of THF and diethyl ether at –78 °C within 30 min led to cuprate derivative **121** *via* a selective Br/Cu-exchange reaction on position 3. The resulting cuprate **121** can be readily acylated with *c*-HexCOCl and PhCOCl providing the ketones **122a-b** in 76% and 88% yield, respectively. Allylation of **121** with allyl bromide was possible and led to the product **122c** in 91% yield.

However, the second Br/Cu-exchange reaction on compound **122** proved unsuccessful. The performance of Br/Cu-exchange reaction of **122b** and **122c** with **17** at -78 °C within 5 min led to a complex reaction mixture instead of the exchange reaction (Scheme 60).

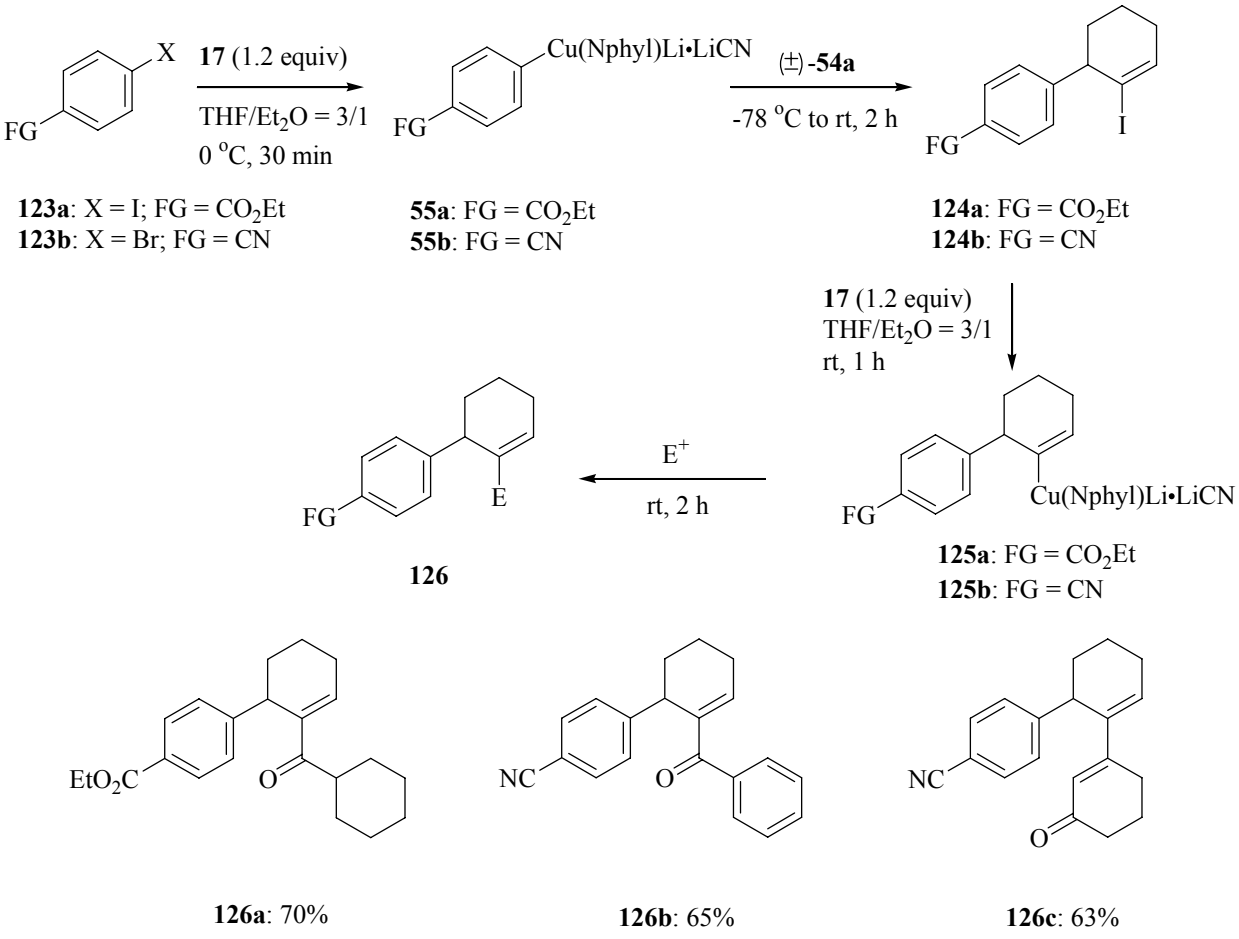


Scheme 60: Attempts to perform the second Br/Cu-exchange on compounds **122**.

Finally, a one-pot procedure was developed for the generation of unactivated alkenyl cuprates *via* successive iodine or bromine-copper exchange reactions. Thus, commercial available ethyl 4-iodobenzoate **123a** underwent a smooth I/Cu-exchange reaction with **17** at 0 °C within 30 min, leading to cuprate **55a**. The S_N2 substitution reaction of **55a** with racemic cyclic 2-iodoallylic acetate (±)-**54a** provided the iodocyclohexene **124a**, as was indicated by the GC-MS analysis of the reaction mixture. As mentioned in chapter 2, the iodine substituent is very useful for further transformations. Without any work-up, **124a** reacted directly with **17** at rt within 0.5 h, leading to the corresponding alkenyl cuprates **125a**. Treatment of **125a** with cyclohexane carbonyl chloride readily provided the α,β-unsaturated ketone **126a** in 70% yield. In a similar way, 4-cyanobromobenzene **123b**

[113] A) Kim, W.-S.; Kim, H.-J.; Cho, C.-G. *J. Am. Chem. Soc.* **2003**, *125*, 14288; b) Cho, C.-G. Kim, Y.-W.; Lim, Y.-K.; Park, J.-S.; Lee, H.; Koo, S. *J. Org. Chem.* **2002**, *67*, 290.

was readily converted into the alkenyl cuprate **125b**, which can be reacted with benzoyl chloride, or 3-iodo-2-cyclohexenone, providing desired products **126b** and **126c** in 65% and 63% yields, respectively (Scheme 61).



Scheme 61: One-pot procedure for the synthesis of compounds **126** *via* alkenyl cuprates **125**.

In conclusion, further applications of I/Cu-exchange reactions for the generation of highly functionalized alkenyl cuprates were intensively investigated. A series of sensitive functional groups, such as aldehyde, ketones, ester and cyanide are compatible with this exchange reaction. The subsequent reactions of these alkenyl cuprates with various electrophiles provided a broad range of polyfunctionalized alkenes.

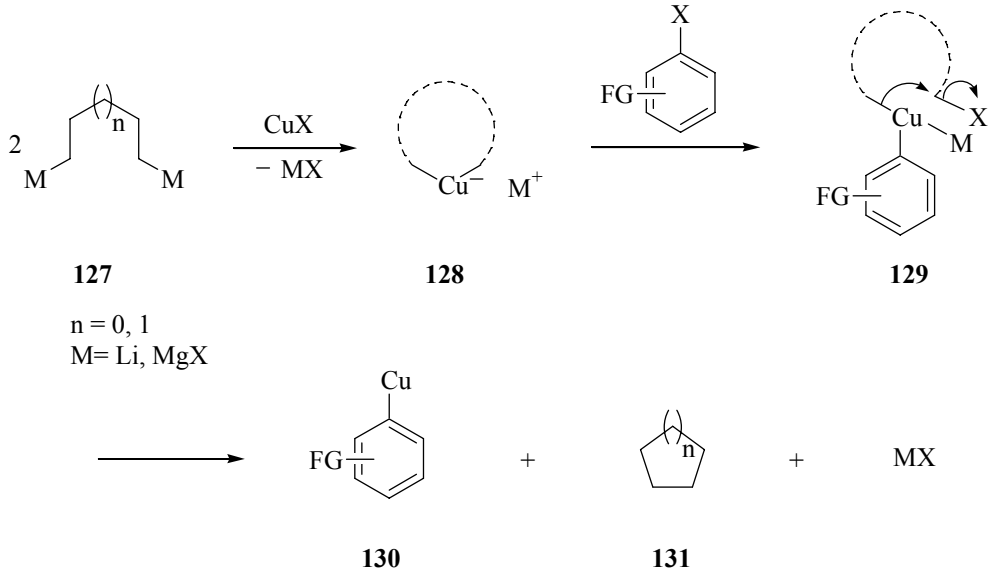
6 Preparation and Reactions of Polyfunctional Magnesium Arylcuprates Obtained by an Iodine-Copper Exchange

6.1 Introduction

As shown in the previous sections, the halogen-copper exchange reaction proved to be a general and mild methodology for the preparation of a variety of new functionalized aryl, heteroaryl and alkenyl cuprate reagents, which has extended extremely the range of functionalized copper reagents available for synthetic purposes. A variety of functional groups such as ester, nitrile, iodide, and bromide as well as sensitive groups, such as ketones and aldehydes can be tolerated in these organocopper reagents. However, during the study we also realized that the purification of the reaction mixture was slightly complicated due to the formation of several side-products like Nphyl-I, Nphyl-Nphyl and Nphyl-E. To overcome such a drawback, it is necessary and interesting to develop a new related method, which allows the performance of reaction in a cleaner way.

6.2 Attempts to Generate Functionalized Magnesium Cuprates *via* I/Cu-Exchange Reaction.

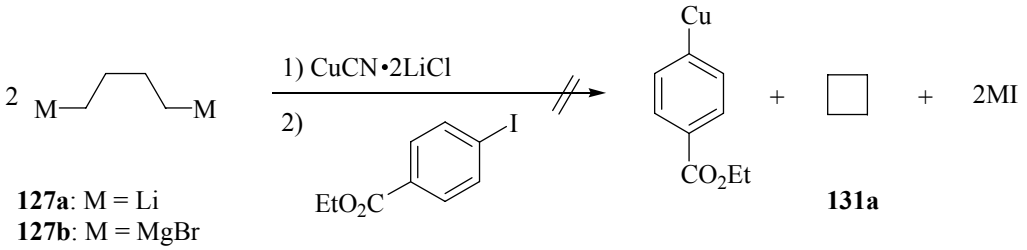
The initial idea is pictured in Scheme 62. The *bis*-metalated alkane **127** was supposed to react with copper salts leading to the formation of cyclic cuprate **128** and one equivalent salt MX. The subsequent treatment of cuprate **128** with functionalized aryl halides compounds was envisioned to provide intermediate **129** *via* a halogen-copper exchange reaction. The resulting cuprate **129** was again proposed to undergo a rapid intramolecular elimination reaction, furnishing the desired copper reagent **130** with the formation of cycloalkane **131** and one equivalent salt MX. If this reaction sequence can be performed as expected, it will provide a very clean method to generate functionalized organocopper reagents **130** with the formation of cycloalkane **131** as the only side-product.



Scheme 62: Hypothesis for preparation of functionalized copper reagents *via* halogen-copper exchange reaction.

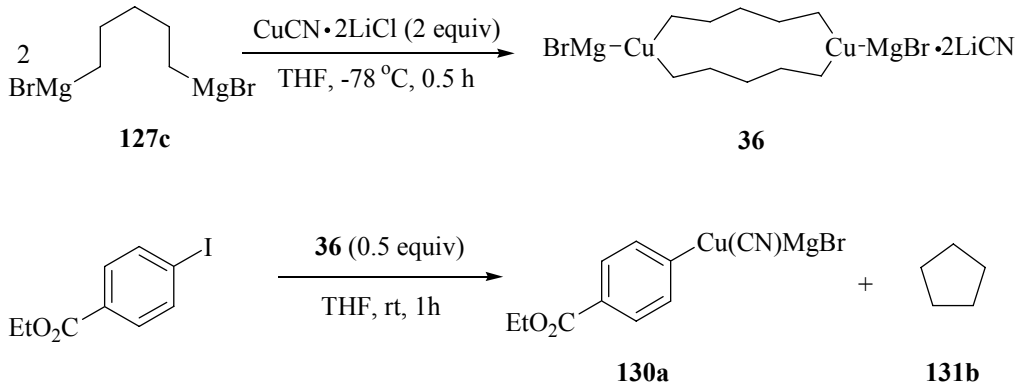
In the initial reaction, 1,4-*bis*-lithio-butane **127a**[114] or 1,4-*bis*-bromomagnesio-butane **127b**[115] was used to perform the exchange reaction with ethyl 4-iodobenzoate using CuCN·2LiCl[116] as a copper source. However, no exchange reaction was observed by GC-MS analysis of the reaction mixture. Several by-products were formed during the reaction. Other copper salts such as CuI, CuCN and CuCl were also tested, but they did not work either. We envisioned that the formation of high energy cyclobutane **131a** hampered the exchange reaction (Scheme 63). On the other hand, we observed that the use of 1,4-*bis*-lithium-butane **127a** usually resulted in a very complex reaction mixture due to the high reactivity of the lithium reagent.

[114] Negishi, E.-I.; Swanson. D. R.; Rousset, C. J. *J. Org. Chem.* **1990**, *55*, 5406.
[115] a) Whitesides, G. M.; Gutowski, F. D. *J. Org. Chem.* **1976**, *41*, 2882; b) Bickelhaupt F. *Pure Appl. Chem.* **1986**, *58*, 537; c) Spek, A. L.; Schat, G.; Holtkamp, H. C.; Blomberg, C.; Bickelhaupt, F. *J. Organomet. Chem.* **1977**, *131*, 331; d) Bickelhaupt F. *Grignard Reagents* **2000**, p. 367-393, John Wiley & Sons Ltd, Chichester, UK.
[116] Knochel, P.; Yeh, M. C. P.; Berk, S. C.; Talbert, J. *J. Org. Chem.* **1988**, *53*, 2390.



Scheme 63: Attempts to generate functionalized copper reagents using 1,4-*bis*(metalated)butane.

Based on the previous results, 1,5-*bis*-bromomagnesio-pentane **127c**, which was readily prepared from 1,5-dibromopentane and magnesium,[115a] was used to perform the exchange reaction (Scheme 64).



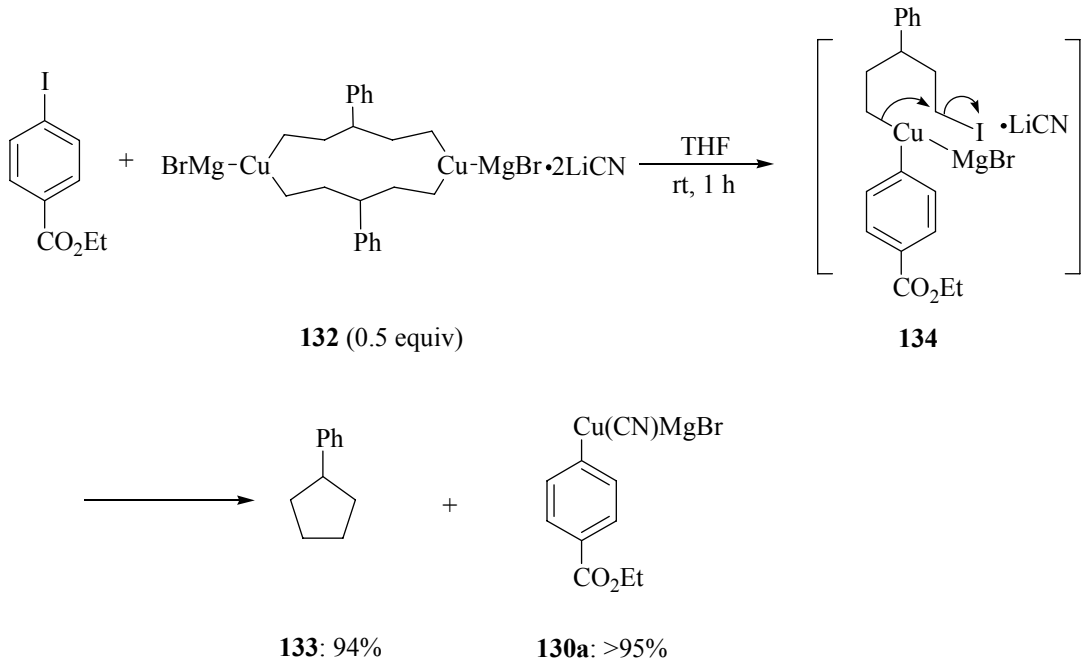
Scheme 64: Preparation of functionalized copper reagent **130a** *via* an I/Cu-exchange reaction.

Treatment of **127c** with the THF-soluble copper salt CuCN·2LiCl provided a magnesium cuprate reagent tentatively drawn as **36**.[11, 117] Reaction of **36** with ethyl iodobenzoate at rt within 1 h in THF provided the functionalized magnesium arylcuprate **130a** with the formation of cyclopentane **131b**. Due to its possible coordination of the cyanide anion, copper reagent **36** is potentially reactive and useful for an iodine-copper exchange.[118]

[117] a) Dieter, R. K. *Tetrahedron* **1999**, *55*, 4177; b) Spek, A. L.; Schat, G.; Holtkamp, H. C.; Blomberg, C.; Bickelhaupt, F. *J. Organomet. Chem.* **1977**, *131*, 331.
[118] a) Jastrzebski, J.; Johann, T. B. H.; van Koten, G. *Modern Organocopper Chemistry* **2002**, p. 1-44, Wiley-VCH Verlag GmbH, Weinheim, Germany; b) Hamon, L.; Levisalles, J. *Journal of Organomet. Chem.* **1983**, *251*, 133; c) Huang, H.; Alvarez, K.; James, P.; Penner-Hahn, J. E. *J. Am. Chem. Soc.* **1996**, *118*, 8808.

Furthermore, the nature of the cation (MgBr instead of the previously used Li) allowed performing the exchange reaction very conveniently at room temperature. Especially interesting is that the reaction proceeded in a very clean way with the only side-product cyclopentane **131b**.

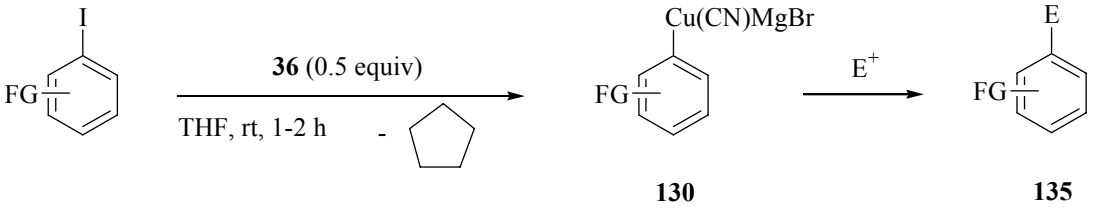
Since the detection of cyclopentane in the crude reaction mixture was difficult, we have prepared cuprate **132** from 3-phenyl substituted 1,5-*bis*-bromomagnesio-pentane[119] and performed the reaction with ethyl 4-iodobenzoate under our standard reaction conditions to prove the formation of a cyclopentane **131b** as reaction product. We observed a rapid exchange and detected the formation of phenylcyclopentane **133** (94%)[120] and of the expected cuprate **130a** as the sole reaction products. Cyclopentane derivative **133** was formed *via* a fast intramolecular substitution of the intermediate **134**, generated during the I/Cu-exchange reaction (Scheme 65).



Scheme 65: Experiment to prove the formation of cyclopentane **131b**.

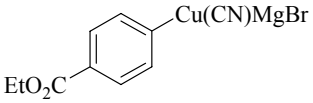
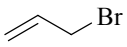
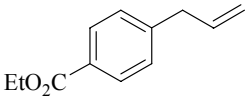
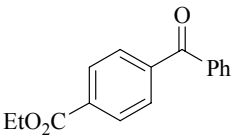
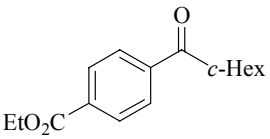
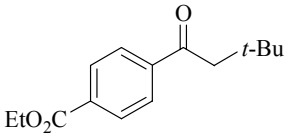
A wide range of aromatic iodides undergo an I/Cu-exchange with reagent **36** (0.5 equiv) within 1-2 h at 25 °C in THF, providing the cyanocuprates of type **130**, which were quenched with various electrophiles, leading to products of type **135** in excellent yields (Scheme 66; Table 14).

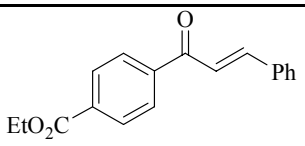
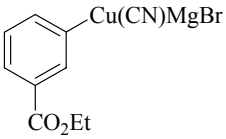
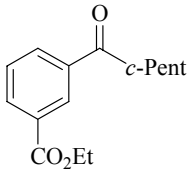
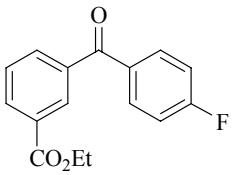
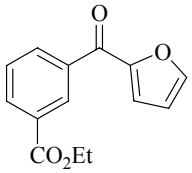
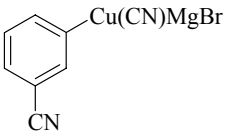
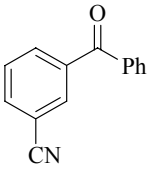
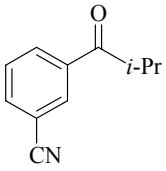
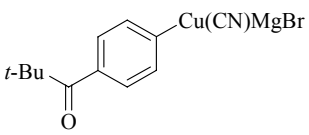
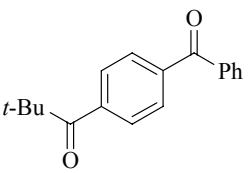
[119] Stapp, P. R.; Drake, C. A. *J. Org. Chem.* **1971**, *36*, 522.
[120] Choudary, B. M.; Rao, B. P. C.; Chowdari, N. S.; Kantam, M. L. *Catalysis Communications* **2002**, *3*, 363.

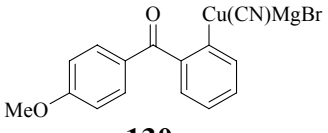
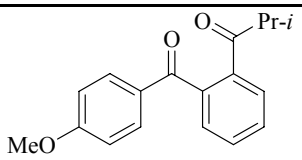
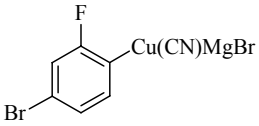
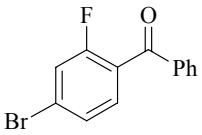
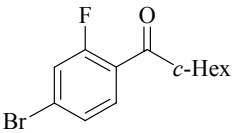


Scheme 66: Functionalization of aryl iodides with magnesium cuprate **36** *via* I/Cu-exchange reaction.

Table 14: Compound **135** obtained from the reaction of copper reagents **130** with various electrophiles.

Entry	Copper reagent **130**	Electrophile	Product of type **135**	Yield (%)[a]
1	 **130a**		 **135a**	91
2	**130a**	PhCOCl	 **135b**	94
3	**130a**	*c*-HexCOCl	 **135c**	93
4	**130a**	*t*-BuCH$_2$COCl	 **135d**	92

Entry	Copper reagent **130**	Electrophile	Product of type **135**	Yield (%)[a]
5	**130a**	(*E*)-PhCHCHCOCl	 **135e**	85
6	 **130b**	*c*-PentCOCl	 **135f**	91
7	**130b**	4-FC_6H_4COCl	 **135g**	84
8	**130b**	2-FurylCOCl	 **135h**	85
9	 **130c**	PhCOCl	 **135i**	90
10	**130c**	i-PrCOCl	 **135j**	92
11	 **130d**	PhCOCl	 **135k**	70

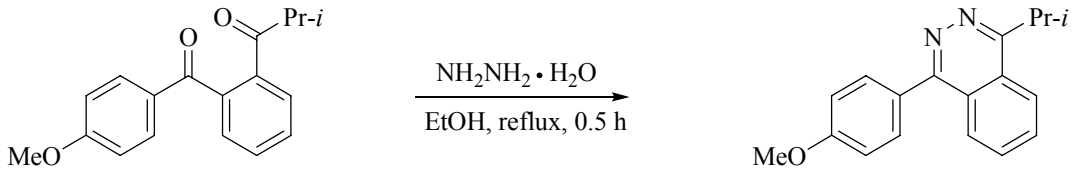
Entry	Copper reagent **130**	Electrophile	Product of type **135**	Yield (%)[a]
12	 **130e**	i-PrCOCl	 **135l**	85
13	 **130f**	PhCOCl	 **135m**	95
14	**130f**	c-HexCOCl	 **135n**	92

[a]Isolated yield of analytically pure product.

Cyanocuprate **130a** was allylated with allyl bromide, affording the desired product **135a** in 91% yield (entry 1 of Table 14). This test reaction indicated that the preparation of the cuprate was complete and the functionalized magnesium cyanocuprates reacted as expected. Then, our attention was focused on the preparation of polyfunctional ketones and performed the acylation reaction of **130a** with a range of acid chlorides[121] (Table 13). We found that the reaction of the magnesium cuprate **130a** with benzoyl chloride was completed within 15 min at rt, leading to ketone **135b** in 94% yield (entry 2). Similarly, aliphatic acid chlorides, such as *c*-HexCOCl and *t*-BuCH_2COCl, provided the corresponding products in 92-93% yields (entries 3 and 4). The acylation of **130a** with an unsaturated acid chloride like cinnamyl chloride led to the (*E*)-ketoester **135e** in 85% yield (entry 5). Ethyl 3-iodobenzoate was treated with cuprate **36** (0.5 equiv, 25 ^{o}C, 2 h) leading to the cyanocuprate **130b** and reacted with typical acid chlorides in 84-91% yields (entries 6-8). A cyano group was also well tolerated in the starting aryl iodide and the I/Cu- exchange was completed within 40 min at 25 ^{o}C, furnishing the magnesium cyanocuprate **130c**. Its reaction with PhCOCl and *i*-PrCOCl gave the cyanoketones **135i** and **135j** in 90-92% yields (entries 9 and 10).

[121] a) Dieter, R. K. *Modern Organocopper Chemistry* **2002**, p. 79-144, Wiley-VCH Verlag GmbH, Weinheim, Germany; b) Rieke, R. D.; Wehmeyer, R. M., Tse, C.; Ebert, G. W. *Tetrahedron* **1989**, *45*, 443.

Aromatic ketones were also successfully subjected to the I/Cu-exchange reaction with **36**. Thus, 1-(4-iodophenyl)-2,2-dimethyl-1-propanone and (2-iodophenyl)-(4-methoxylphenyl) methanone were converted to the corresponding cuprates **130d** and **130e** by the reaction with **36**. In these cases, the iodoketones were added at –78 °C and the reaction mixtures were allowed to warm slowly to rt over 2 h. Quenching with acid chlorides, such as PhCOCl and *i*-PrCOCl, furnished the expected diketones **135k** and **135l** in 70-85% yields. The resulting ketone **135l** can be readily converted into the heterocycle **136** by treatment with hydrazine monohydrate (EtOH, reflux, 30 min, 91% yield; Scheme 67).[48]



135l **136**: 91%

Scheme 67: Synthesis of phthalazine **136**.

Finally, we examined the reaction of polyhalogenated aromatic substrate 1-iodo-2-fluoro-4-bromobenzene with **36**. Only the I/Cu-exchange was observed and no Br/Cu-exchange could be detected. After the reaction with acid chlorides like PhCOCl and *c*-HexCOCl, the expected halogenated ketones **135m** and **135n** were obtained in 92-95% yields (entries 13-14).

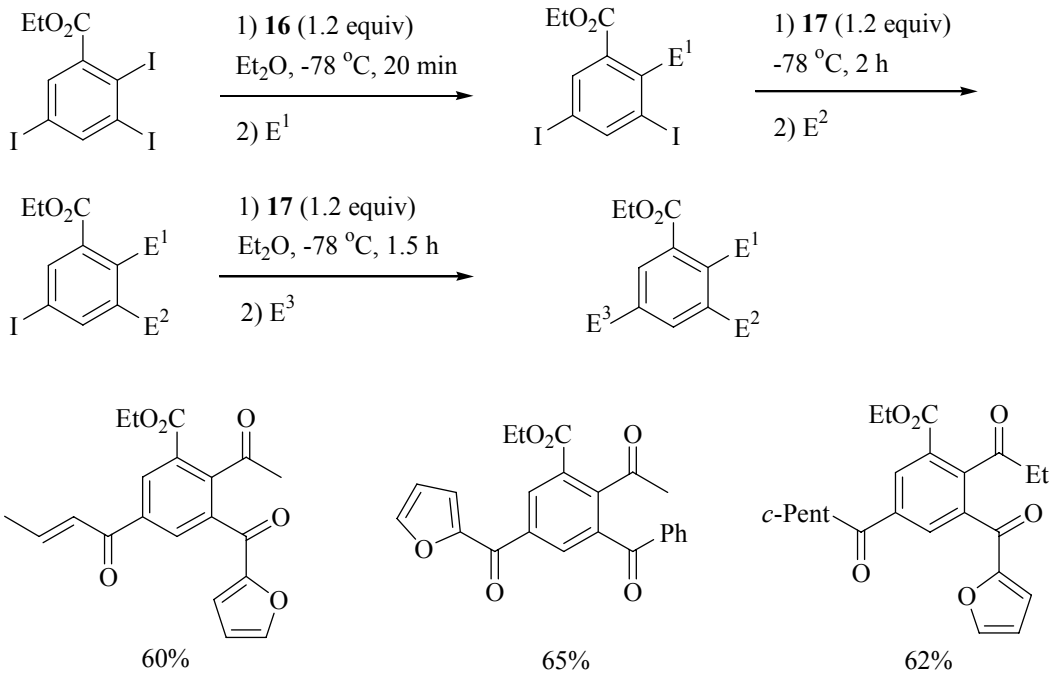
In conclusion, it was shown that the magnesium cuprate **36** is an excellent reagent for performing an I/Cu-exchange reaction, providing for the first time a range of new polyfunctional cyanocuprate **130**, which react with acid chlorides, leading to highly functionalized ketones in high yields.

7 Summary and Outlook

This work has been focused on the preparation of new functionalized cuprate reagents *via* an halogen-copper exchange reaction and their reaction with various electrophiles to generate polyfunctionalized compunds. A novel related I/Cu-exchange reaction was also developed, which can provide functionalized magnesium cuprate reagents in a very clean way.

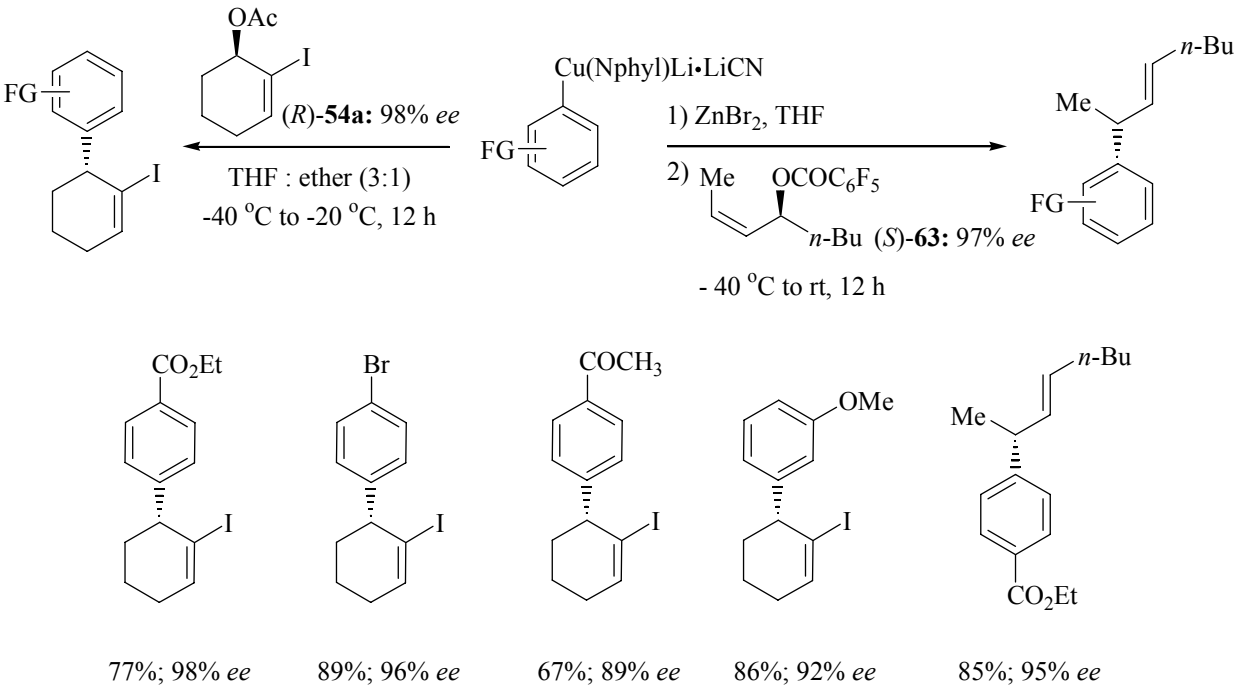
7.1 Preparation of Functionalized Aryl Cuprates and Application in Allylic Substitution Reactions

In the first project, it was shown that functionalized di- or tri-iodoarenes underwent a regioselective I/Cu-exchange reaction with sterically hindered lithium dialkyl cuprate reagents $(Me_3CCH_2)_2CuLi{\cdot}LiCl$ (**16**) and $(Me_2PhCCH_2)_2CuLi{\cdot}LiCl$ (**17**) to generate the corresponding functionalized cuprate reagents. The presence of a chelating group was found to direct the exchange reaction. A range of new polyacylated benzenes were available by this method (Scheme 68).



Scheme 68: Functionalization of polyiodoarene *via* an I/Cu-exchange reaction.

The application of functionalized aryl cuprates obtained *via* I/Cu-exchange reaction in stereoselective allylic substitution reaction was also described. These reagents reacted with excellent stereoselectivity with chiral 2-iodo-cycloalkenyl acetates (*R*)-**54a**, affording the S_N2-substitution products. The addition of zinc bromide dramatically changes such a behavior and provides with an open-chain allylic pentafluorobenzoate (*S*)-**63** only the *anti*-S_N2'-substitution product (Scheme 69).

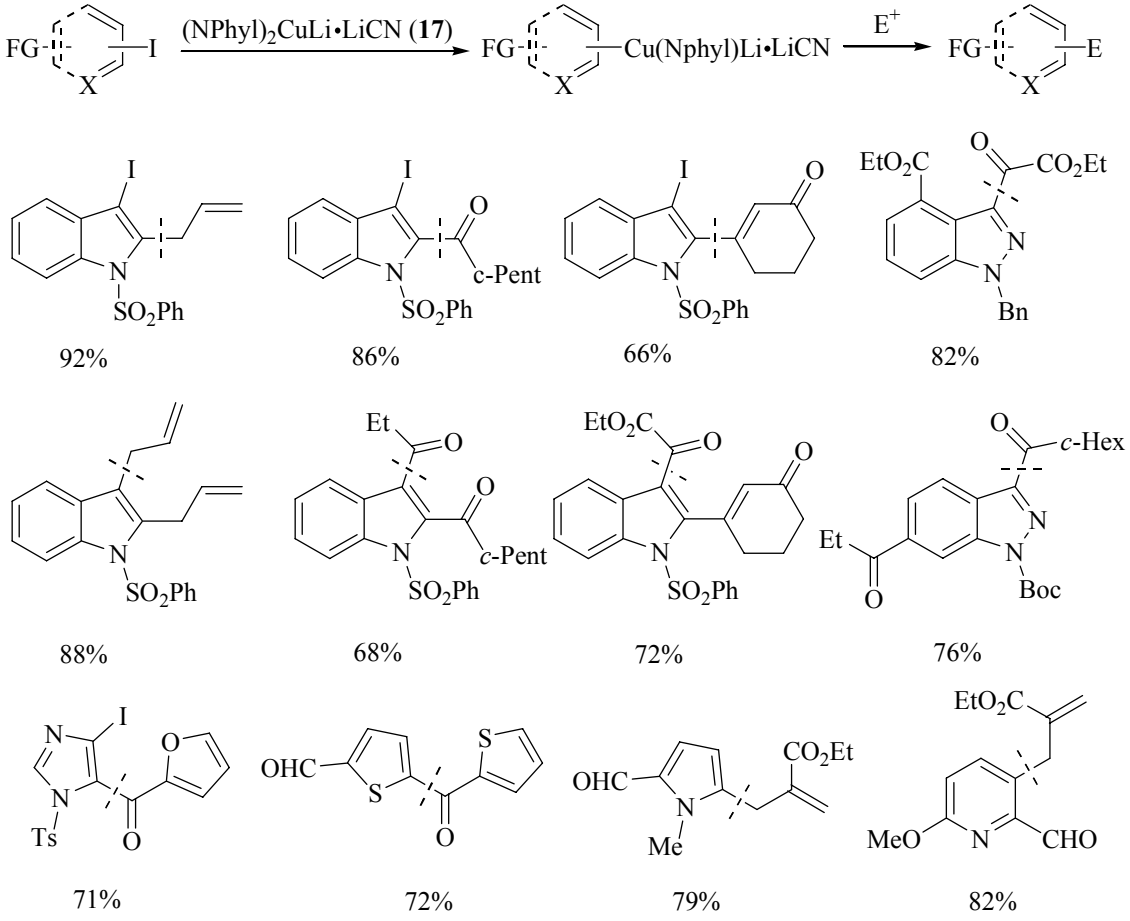


Scheme 69: Stereoselective allylic substitution of functionalized aryl cuprates.

Since these functionalized chiral compounds are versatile building block in organic synthesis, it will be very interesting to further investigate this stereoselective allylic substitution reaction using heteroaryl cuprate or alkenyl cuprate reagents. A particularly stimulating synthetic task will be the application of this methodology in the synthesis of natural product.

7.2 Preparation of Functionalized Heterocyclic Cuprate Reagents

As an extention of the I/Cu-exchange reaction, a series of highly functionalized heteroaryl cuprates were prepared, such as indoles, indazoles, imidazoles, furans, pyrrols, thiophenes and pyridines. Various sensitive functional groups, like aldehyde, ketone, ester, cyanide, iodine, bromide and methoxyl were compatible with this reaction. The subsequent reactions of these heterocyclic mixed cuprates with different electrophiles provided a broad range of highly functionalized heterocycles (Scheme 70).

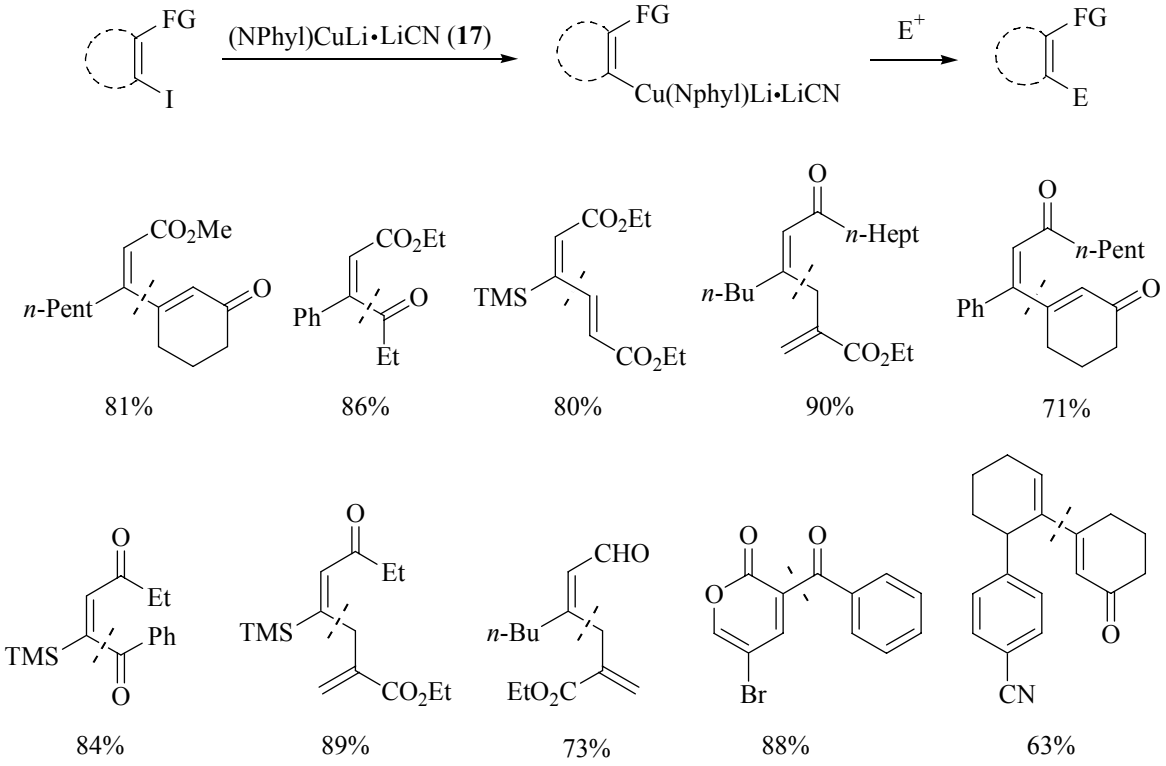


Scheme 70: Preparation of highly functionalized heterocyclic compounds *via* I/Cu-exchange reaction.

The important role of heterocycles in biologically active compounds chemistry makes it very interesting to investigate this method further for some special heterocyclic substrates, such as purine, pyrimidine and pyridazine.

7.3 Preparation of Functionalized Alkenyl Cuprates *via* Iodine or Bromine-Copper Exchange Reaction

Moreover, the iodine- or bromine-copper exchange reaction was also found to be applicable to functionalized alkenyl halides, especially the β-iodo-α,β-unsaturated esters and ketones. A variety of functionalized alkenyl cuprate were thus obtained by this method. The subsequent reactions of these mixed cuprates with different electrophiles provide a broad range of polyfunctionalized alkenes (Scheme 71).

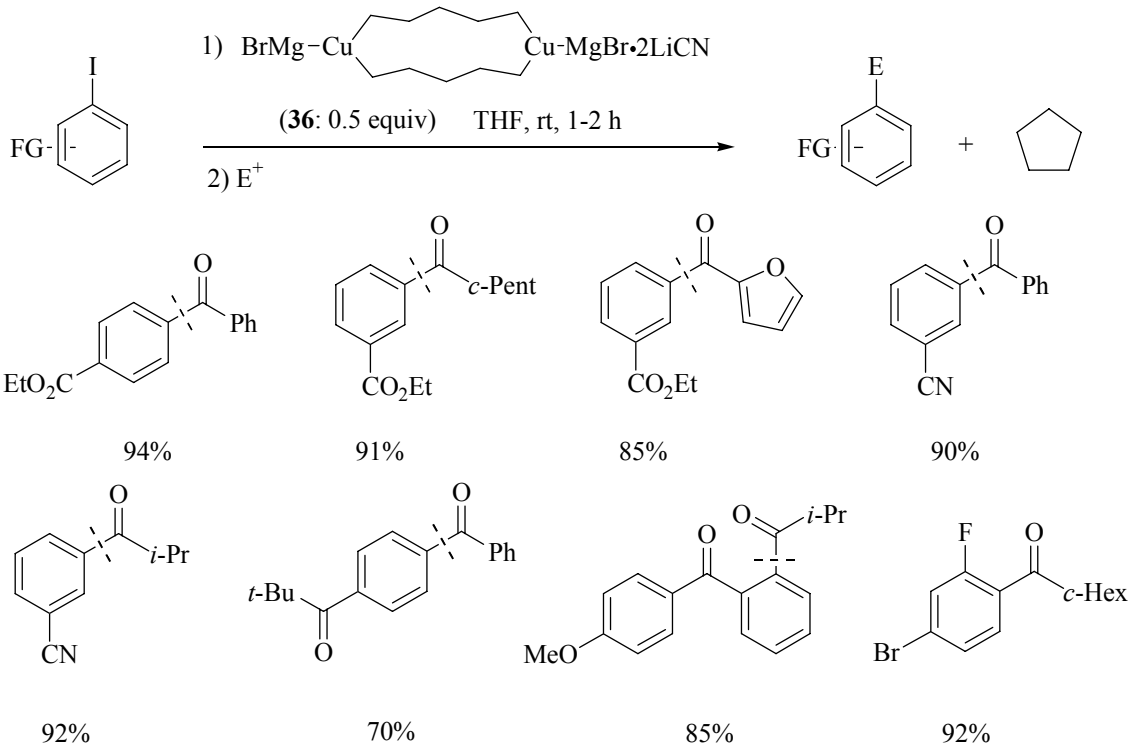


Scheme 71: Alkenyl cuprates obtained *via* halogen-copper exchange reaction.

The successful application of this I/Cu-exchange reaction on β-iodo-α,β-unsaturated esters and ketones makes it to be a quite promising and exciting method to functionalize β-bromo- or β-chloro-α,β-unsaturated systems *via* a bromide-, or chloride-copper exchange reaction.

7.4 Preparation and Reactions of Polyfunctional Magnesium Arylcuprates obtained by an I/Cu-Exchange

Finally, a related new method was developed for the preparation of polyfunctional magnesium arylcuprates obtained by an I/Cu-exchange reaction. Especial interest was that the reaction proceeded in a very clean way with the only side-product cyclopentane. Various functionalized organocopper reagents were obtained (Scheme 72).



Scheme 72: Functionalization of aryl iodides with magnesium cuprate **36** *via* an I/Cu-exchange reaction.

This method provides an alternative procedure giving an access to functionalized organocopper reagents *via* I/Cu-exchange reaction. Extension of this method to functionalize various substrates would be very interesting. Furthermore, applications of the resulting cuprates to synthesize more complex molecules is promising.

EXPERIMENTAL PART

8 General Conditions

All reactions were carried out with magnetic stirring and, if air or moisture sensitive, in flame-dried glassware under argon. Syringes which were used to transfer reagents and solvents were purged with argon prior to use.

Solvents

Solvents were dried according to standard methods by distillation over drying agents as stated below and were stored under argon. CH_2Cl_2, DMF, NMP and pentane (CaH_2), diethyl ether, hexane and THF (Na/benzophenone), pyridine and triethylamine (KOH), toluene (Na).

Reagents

Reagents of >98 % purity were used as obtained.
n-Butyllithium was used as 1.5 M solution in hexane.
t-Butyllithium was used as 1.5 M solution in pentane.

CuCN·2LiCl solution (1 M) was prepared by drying CuCN (896 mg, 10 mmol) and LiCl (848 mg, 20 mmol) in a Schelenk flask under vacuum for 5 h at 140 °C. After cooling to rt, dry THF (10 mL) was added and stirring was continued until the salts was dissolved.

$ZnBr_2$ solution (1 M) was prepared by drying $ZnBr_2$ (3.4 g, 15 mmol) in a Schelenk flask under vacuum for 5 h at 150 °C. After cooling to rt, dry THF (15 mL) was added and stirring was continued until the salts was dissolved.

The following reagents were prepared according to literature procedures: (*R*)-2-iodo-cyclohexen-1-ol,[51] (1*S*, 2*Z*)-1-butyl-2-butenyl 2,3,4,5,6,-pentafluorobenzoate **63**,[54] ethyl bromomethylacrylate, [122] 3-iodo-2-cyclohexen-1-one, [123] 2,3-diiodoindole derivative **68**,[68] 3-iodoindazole derivatives**76**,[75, 77] 1-ethoxymethyl-4,5-diiodoimidazole **79a**,[83] 3-iodo-6-methoxy-2-pyridinecarboaldehyde **84**,[85] indoel derivatives **88a**[86] and **88b**,[87] 5-iodo-thiophene-2-carbaldehyde **91a**,[88] 5-iodo-1-methyl-1*H*-pyrrole-2-carboaldehyde

[122] Byun, H.-S.; Reddy, K. C.; Bittman, R. *Tetrahedron Lett.* **1994**, *35*, 1371.
[123] Piers, E.; Grierson, J. R.; Lau, C. K. ; Nagakura, I. *Can. J. Chem.* **1982**, *60*, 210.

91c,[87] *β*-iodo-*α,β*-unsaturated esters **99**,[102] (*Z*)-3-iodo-acrylic acid ethyl ester **102**,[102a] *β*-iodo-*α,β*-unsaturated Ketone **110**,[109] (1*E*)-1-iodo-1-phenyl-1-octen-3-one **115**,[109a] (2*Z*)-3-iodo-2-heptenal **117**,[111] 3,5-dibromide-2H-pyran-2-one **120**,[113] 1,5-*bis*-bromomagnesium–pentane **36**,[115a] 1,5-dibromo-3-phenylpentane.[119]

Content determination of organometallic reagent

Organolitium and organomagnesium solution were titrated using the method of Paquette.[124] The concentrations of organozinc solutions were determined by back titration of iodine with an aqueous $Na_2S_2O_3$ solution.

Chromatography

Thin layer chromatography (TLC) was performed using aluminium plates covered with SiO_2 (Merck 60, F-254). The chromatograms were viewed under UV light and /or by treatment of the TLC plate with one of the solutions below followed by heating with a heat gun:

$KMnO_4$ (0.3 g), K_2CO_3 (20 g), KOH (0.3 g) in water (300 mL).

Phosphormolybdic acid (5.0 g), $Ce(SO_4)_2$ (2.0 g), conc. H_2SO_4 (12 mL) in water(230 mL).

Flash column chromatography was performed using SiO_2 60 (0.040-0.063 mm; 230-400 mesh ASTM) from Merck and the amount of silicagel were calculated acording to the recommendation of W. C. Still.[125]

Analytical data

Melting points were determined on a Büchi B-540 apparatus and are uncorretted.

NMR spectra were recorded on Brucker ARX 200, AC 300 or WH 400 instruments. Chemical shifts are reported as δ-values in ppm relative to the deuterated solvent peak: $CDCl_3$ (δ_H: 7.27, δ_C: 77.0), DMSO-d_6 (δ_H: 2.50, δ_C: 39.4), Acetone-d_6 (δ_H: 2.04, δ_C: 29.3). For the characterization of the observed signal multiplicities the following abbreviations

[124] Lin, H.-S.; Paquette, L. A. *Synth. Commun.* **1994**, *24*, 2503.
[125] Still, W. C.; Khan, M.; Mitra, A. *J. Org. Chem.* **1978**, *43*, 2923.

were applied: s (singlet), d (doublet), dd (double doublet), dt (double triplet), h (heptet), t (triplet), q (quartet), m (multiplet), as well as br (broad).

Infrared spectra were recorded from 4000-400 cm^{-1} on a Nicolet 510 FT-IR or a Perkin-Elmer 281 IR spectrometer. Samples were measured either as a film between sodium chloride plates or (for solids) as potassium tablets. The absorption bands are reported in wave numbers (cm^{-1}). For the band characterization the following abbreviations were applied: br (broad), vs (very strong), s (strong), m (medium), w (weak).

Optical rotations were measured on the Perkin-Elmer 241 polarimeter.

Gas chromatography (GC) was performed using Hewlett-Packard 6890 or 5890 Series II.

Column A: 5 % phenylmethylpolysiloxane (HP Ultra 2) 12 m x 0.2 mm

Column B: 5 % phenylmethylpolysiloxane (HP %) 5 m x 0.25 mm

The compounds were detected with a flame ionisation detector.

Mass spectroscopy: Mass spectra were recorded on a Finnigan MAT 95Q or Finnigan 90 instrument for electro impact ionisation (EI). High resolution mass spectra (HRMS) were recorded on the same instruments. Fast atom bombardment (FAB) samples were recorded in either a 2-nitrobenzyl alcohol or glycerine-matrix. Additionally, for the combination of gas chromatography with mass spectroscopic detection, a GC/MS from Hewlwtt-Packard HP 6890/MSD 5973 was used.

Column C: 5% phenylmethylpolysiloxane (HP 5) 30m x 250 µm x 0.25 m

Elemental analysis was carried out on a Heraeus CHN-Rapid-Elementanalyzer in the microanalytical laboratories of the Department für Chemie und Pharmazie, Ludwig-Maximilians Universität Munich.

High Performance Liquid Chromatography (HPLC) was performed using Gynkotec-HPLC with a diode-array UV-VIS detector. Chiral column: OD-H (0.46 cm × 25 cm)**,** OD (0.46 cm × 25 cm) and AD (0.46 cm × 25 cm) (Diacel Chemical Industries) with n-heptane/I-propanol as mobile phase. Racemic compounds were used for optimizing the operating conditions for the resolution of the enantiomer peaks.

9 Typical Procedures (TP)

9.1 Typical Procedure for the Synthesis of Lithium Dineopentylcuprate 16 and Lithium Dineophylcuprate 17 (TP 1)

1) A 10 mL round-bottomed flask, flame dried and flushed with argon was charged with neopentyl iodide (0.3 mL, 2.2 mmol) and the compound dissolved in 2 mL of diethyl ether. The solution was cooled to -78 °C and *t*-BuLi (3.1 mL, 4.6 mmol) was added dropwise. The reaction mixture was stirred for 1 h at -78 °C and warmed to rt.[126] After stirring for another hour the mixture was then cannulated into a suspension of CuCN (110 mg, 1.2 mmol) in THF (1 mL) cooled to -78 °C. The reaction mixture was allowed to warm to 0 °C, furnishing the expected cuprate **16** ready to use.

2) A 500 mL round-bottomed flask, flame dried and flushed with argon was charged with lithium metal (3.0 g, 432 mmol) and neophylchloride (14.0 mL, 86.9 mmol) in hexane (75 mL). The reaction mixture was heated under reflux overnight. After cooling to rt, the hexane was removed *in vacuo* and diethyl ether was added to the resulting mixture. The resulting mixture was stirred at rt for few mins and then kept static for another few mins. The solution was cannulated into a flame dried Schlenk tube and was centrifuged (2000 rpm, 30 min). The clear solution of neophyllithium thus obtained was titrated before use with menthol using *o*-phenantroline as indicator and could be stored at -30 °C for several days.

A 25 mL round-bottomed flask, flame dried and flushed with argon was charged with CuCN (110 mg, 1.2 mmol). THF (3 mL) was added and the suspension cooled to -78 °C. The freshly titrated solution of neophyllithium (2.4 mmol) was added and the mixture quickly warmed to rt and stirred for 10 min, till a clear yellow solution of the desired cuprate **17** was obtained.

[126] Negishi, E.; Swanson, D. R.; Rousset, C. J. *J. Org. Chem.* **1990**, *55*, 5406.

9.2 Typical Procedure for the I/Cu-Exchange Reaction on Aryl Substrates (TP 2)

A dry and argon flushed 10 mL flask, equipped with a magnetic stirrer and a septum, was charged with a solution of aryl halide (1.0 mmol) in dry THF (2 mL). The solution was cooled to -78 °C and a solution of the freshly prepared lithium dineopentylcuprate (**16**) (1.2 equiv) or lithium dineophylcuprate (**17**) (1.2 equiv) was cannulated. The mixture was warmed to the required temperature. The halogen-copper exchange was complete within 0.5-2 h (checked by GC-MS analysis of reaction aliquots) and the electrophile (3 mmol) was added to the resulting mixed organocuprate. The resulting mixture was warmed up to rt. After 0.5-1 h of stirring at rt, the reaction mixture was quenched with saturated aqueous NH_4Cl (2 mL) and poured into water (25 mL). The aqueous phase was extracted with diethyl ether (3 × 20 mL). The organic fractions were washed with brine (30 mL), dried with Na_2SO_4 and concentrated *in vacuo*. Purification by flash chromatography yielded the desired product.

9.3 Typical Procedure for Synthesis of Diazines from the Reaction of Diketones with Hydrazine Monohydrate (TP 3)

A 10 mL flask, equipped with a magnetic stirrer, a refluxing condensor and a septum, was charged with a solution of diketone (0.5 mmol) in ethanol (5 mL). The solution was refluxed and a solution of hydrazine monohydrate in ethanol (0.5 M/ethanol, 1.2 mmol, 0.6 mmol) was added. The resulting mixture was refluxed for 15-30 min to complete the cyclization (checked by GC-MS analysis of reaction aliquots). The solution was directly concentrated *in vacuo*. Purification by flash chromatography yielded desired product.

9.4 Typical Procedure for Allylic Substitution Reaction of Aryl Cuprate Reagent with (*R*)-2-Iodo-2-cyclopenten-1-yl Acetate 54a (TP 4)

A dry and argon flushed 25 mL flask, equipped with a magnetic stirrer and a septum, was charged with a solution of lithium dineophylcuprate (**17**) (1.2 mmol). A solution of Aryl

halide (1.2 mmol) in THF (2 mL) was added over the solution of **17**, and the mixture was stirred at 0 °C until I/Cu-exchange was completed. The mixture was cooled at -40 °C and a solution of (*R*)-2-iodo-2-cyclopenten-1-yl acetate (**54a**) (252 mg, 1.0 mmol) in THF (1.5 mL) was added. The resulting reaction mixture was allowed to warm to –20 °C and stirred at this temperature for 12 h. Saturated aqueous NH_4Cl sol. (20 mL) was added followed by 25% aqueous ammonia solution (1 mL). The reaction mixture was stirred at 25 °C until the copper salts had dissolved and was extracted with Et_2O (3 × 20 mL). The combined extracts were washed with brine and dried with Na_2SO_4. Evaporation of the solvents and purification by column chromatography afforded desired product.

9.5 Typical Procedure for Allylic Substitution Reaction of Cuprate Reagent with (1*S*, 2*Z*)-1-Butyl-2-butenyl 2,3,4,5,6-pentafluorobenzoate 63 (TP 5)

A dry and argon flushed 25 mL flask, equipped with a magnetic stirrer and a septum, was charged with a solution of lithium dineophylcuprate (**17**) (1.2 mmol). A solution of aryl halide (1.2 mmol) in THF (2 mL) was added over the solution of **17**, and the mixture was stirred at 0 °C until I/Cu-exchange was completed (30 min). Then the reaction was cooled to –78 °C and the solution of $ZnBr_2$ in THF (1.5 M, 0.8 mL, 1.2 mmol) was added at this temperature. After 10 min, a solution of (1*S*, 2*Z*)-1-butyl-2-butenyl 2,3,4,5,6-pentafluorobenzoate (**63**) (1.0 mmol) in THF (1.5 mL) was added at –40 °C. The resulting reaction mixture was allowed to warm slowly to rt and stirred at this temperature for 12 h. Saturated aqueous NH_4Cl solution (20 mL) was added followed by 25% aqueous ammonia solution (1 mL). The reaction mixture was stirred at 25 °C until the copper salts had dissolved and was extracted with Et_2O (3 × 20 mL). The combined extracts were washed with brine and dried (Na_2SO_4). Evaporation of the solvents and purification by column chromatography afforded desired product.

9.6 Typical Procedure for the Performance of I/Cu-Exchange Reaction on Heteroaryl Halides (TP 6)

A dry and argon flushed 25 mL flask, equipped with a magnetic stirrer and a septum, was charged with a solution of heterocyclicaryl halide (1.0 mmol) in dry THF (4 mL) at –78 °C. A solution of the freshly prepared lithium dineophylcuprate **17** (1.2 mmol) was cannulated. The mixture was warmed to the required temperature. The halogen-copper exchange was complete within the required time (checked by GC-MS analysis of reaction aliquots). Then the co-solvent NMP (0.2 mL) or DMAP (12 mg, 0.1 mmol) was added at the required exchange temperature and the resulting mixture was stirred at this temperature for 10 min. (If no co-solvent or additive is required, please directly perform the next step). Then electrophile (3.0 mmol) was added and the resulting solution was stirred at rt for 1 h. The reaction was quenched with saturated aqueous NH_4Cl solution and poured into water (40 mL). The aqueous phase was extracted with diethyl ether (3 × 30 mL). The combined organic fractions were washed with brine (30 mL), dried over Na_2SO_4 and concentrated *in vacuo*. Purification by flash chromatography yielded the desired product.

9.7 Typical Procedure for the Performance of Halogen-Copper Exchange Reaction on Alkenyl Halides (TP 7)

A dry and argon flushed 25 mL flask, equipped with a magnetic stirrer and a septum, was charged with a solution of alkenyl halide (1.0 mmol) in dry THF (4 mL) at –78 °C. A solution of the freshly prepared lithium dineophylcuprate **17** (1.2 mmol) was cannulated. The mixture was warmed to the required temperature. The halogen-copper exchange was complete within the required time (checked by GC-MS analysis of reaction aliquots). Then the co-solvent NMP (0.2 mL) was added at the required exchange temperature and the resulting mixture was stirred at this temperature for 10 min. (If no co-solvent is required, please directly perform the next step). Then electrophile (3.0 mmol) was added and the resulting solution was stirred at rt for 1 h. The reaction was quenched with saturated aqueous NH_4Cl solution and poured into water (40 mL). The aqueous phase was extracted with diethyl ether (3 × 30 mL). The combined organic fractions were washed with brine (30 mL), dried over Na_2SO_4 and concentrated *in vacuo*. Purification by flash chromatography yielded the desired product.

9.8 Typical Procedure for the Performance of ICl-Mediated Cyclization of β-Allylated-α,β-unsaturated Ester (TP 8)

To a solution of β-allylated-α,β-unsaturated ester (1.0 mmol) in dry CH_2Cl_2 (5 mL) at rt, a solution of ICl (2.0 mmol) in dry CH_2Cl_2 (2 mL) was added and the resulting solution was stirred at rt overnight. The reaction mixture was poured into an aqueous 10% $Na_2S_2O_3$ solution (10 mL) and the organic layer was separated. The aqueous layer was extracted with CH_2Cl_2 (10 mL × 2). The combined layers were washed wth brine (15 mL), dried with Na_2SO_4 and concentrated in vacuum. The residue was purified flash chromatography to give the desired product.

9.9 Typical Procedure for the Performance of I/Cu-Exchange Reaction on β-Iodo-α,β-unsaturated Ketone or Aldehyde (TP 9)

A dry and argon flushed 25 mL flask, equipped with a magnetic stirrer and a septum, was charged with a solution of freshly prepared lithium dineophylcuprate **17** (1.2 mmol) in a mixture of dry THF and diethyl ether (THF/Et_2O = 2/1). The ether solvent in the solution **17** was carefully removed under vacuum and then dry THF (3 mL) was added. The resulting cuprate **17** in pure THF solvent was was cooled to -100 ^oC and cannulated into a solution of β-Iodo-α,β-unsaturated ketone or aldehyde (1.0 mmol) in dry THF at –100 ^oC. The resulting mixture was stirred at –100 ^oC for required time untill the I/Cu-exchange was complete (checked by GC-MS analysis of reaction aliquots). Then electrophile (3.0 mmol) was added and the resulting solution was stirred at rt for 1 h. The reaction was quenched with saturated aqueous NH_4Cl solution and poured into water (40 mL). The aqueous phase was extracted with diethyl ether (3 × 30 mL). The combined organic fractions were washed with brine (30 mL), dried over Na_2SO_4 and concentrated *in vacuo*. Purification by flash chromatography yielded the desired product.

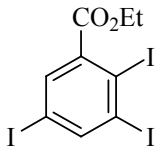
9.10 Typical Procedure for Preparation the Performance of I/Cu-Exchange Reaction on Aryl Iodides with Magnesium Cuprate Reagent 36 (TP 10)

A dry and argon flushed 25 mL flask, equipped with a magnetic stirrer and a septum, was charged with a solution of 1,5-*bis*-bromomagnesium-pentane (2.0 mmol) in THF (8 mL). The solution of CuCN·2LiCl in THF (1.0 M/THF, 2.0 mL, 2.0 mmol) was added dropwise at –78 ^{o}C. The resulting mixture was stirred at –78 ^{o}C for 30 min, furnishing the desired magnesium cuprate **36** ready to use.

To the fresh prepared magnesium cuprate **36** solution (0.5 mmol) at -78 ^{o}C under argon, aryl iodide (1.0 mmol) was added at –78 °C. The resulting mixture was warmed to rt for 1 h and then electrophiles (1.2 mmol) was added. After 30 min, the solution was quenched with saturated aqueous NH_4Cl solution and poured into water (10 mL). The organic layer was separated and the aqueous phase was extracted with diethyl ether (3 × 20 mL). The organic fractions were washed with brine (20 mL), dried over $MgSO_4$ and concentrated *in vacuo*. Purification by chromatography yielded desired product.

10 Preparation of Functionalized Aryl Cuprates *via* I/Cu-Exchange reaction

Synthesis of Ethyl 2,3,5-triiodobenzoate (35)



A 500 mL round-bottomed flask was charged with a solution of 2,3,5-triiodobenzoic acid[127] (10 g, 20 mmol) in ethanol (60 ml). Conc. H_2SO_4 (3 ml) was added slowly and the resulting solution was refluxed overnight. After cooling to rt, the reaction solution was extracted with CH_2Cl_2 (3 × 150 mL). The organic fractions were washed with 10% aqueous $NaHCO_3$ solution (3 × 100 mL) and brine (150 mL), dried over $MgSO_4$ and concentrated *in vacuo*. Purification by flash chromatography (*n*-pentane/diethyl ether = 20/1) yielded ethyl compound **35** as white solid (10.0 g, 95% yield).

mp.: 90-91 °C.

^{1}H-NMR ($CDCl_3$, 300 MHz): δ = 8.23-8.22 (d, *J* = 2.0 Hz, 1H), 7.66-7.65 (d, *J* = 2.0 Hz, 1H), 4.36-4.28 (q, *J* = 7.1 Hz, 2H), 1.35-1.31 (t, *J* = 7.1 Hz, 3H).

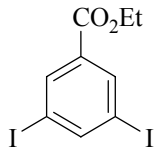
^{13}C-NMR ($CDCl_3$, 75 MHz): δ = 166.5, 149.0, 142.2, 137.2, 113.7, 106.9, 94.1, 62.9, 14.5.

MS (EI, 70 ev), *m/z* (%): 528 (100) [M^+], 500 (23), 483 (54), 455 (18), 373 (10), 328 (10), 218 (10), 201 (32), 74 (20).

IR (KBr, cm^{-1}): $\tilde{\nu}$ = 3440 (w), 2978 (w), 1736 (vs), 1270 (vs), 1184 (vs), 773 (w).

$C_9H_7I_3O_2$	HRMS (EI)	Calcd.	527.7580
		Found	527.7579

Synthesis of ethyl 2-acetyl-3,5-diiodobenzoate (39a)



[127] 2,3,5-Triiodobenzoic acid is commercially available from Aldrich.

Prepared according to TP 2 from ethyl 2,3,5-triiodobenzoate (**35**) (528 mg, 1.0 mmol), lithium dineopentylcuprate **16** (1.2 mmol) and water. Reaction time: 20 min at –78 °C. Purification by flash chromatography (*n*-pentane/diethyl ether = 10/1) yielded compound **39a** as white solid (370 mg, 92%).

mp.: 84-85 °C.

^{1}H-NMR ($CDCl_3$, 300 Hz): δ =8.24-8.23 (d, *J* = 2.0 Hz, 2H), 8.15-8.14 (d, *J* = 2.0 Hz, 1H), 4.34-4.27 (q, *J* = 7.1, 2H), 1.34-1.30 (t, *J* = 7.1, 3H).

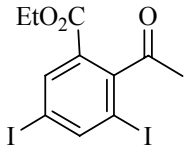
^{13}C-NMR ($CDCl_3$, 75 Hz): δ = 164.1, 149.5, 147.1, 138.1, 134.0, 94.7, 62.2, 14.7.

IR (KBr, cm^{-1}): $\tilde{\nu}$ = 3413 (w), 2978 (w), 1724 (vs), 1544 (s), 1415 (m), 1265(vs), 1021(m), 873 (w), 762 (m), 707(w).

MS (EI, 70 ev), *m/z* (%): 402 (100) [M^+], 374 (65), 357 (92), 329 (21), 247 (17), 202 (19), 75 (85).

$C_9H_8I_2O_2$	HRMS (EI)	Calcd.	401.8614
		Found	401.8617

Synthesis of ethyl 2-acetyl-3,5-diiodobenzoate (39b)



Prepared according to TP 2 from ethyl 2,3,5-triiodobenzoate (**35**) (528 mg, 1.0 mmol), lithium dineopentylcuprate **16** (1.2 mmol) and acetyl bromide (369 mg, 3.0 mmol). Reaction time: 20 min at –78 °C. Purification by flash chromatography (*n*-pentane/diethyl ether = 10/1) yielded compound **39b** as white solid (310 mg, 70%).

mp.: 76-77 °C.

^{1}H-NMR ($CDCl_3$, 300 Hz): δ =8.29-8.28 (d, *J* = 1.8 Hz, 2H), 8.25-8.24 (d, *J* = 1.8 Hz, 2H), 4.31-4.24 (q, *J* = 7.1, 2H), 2.51 (s, 3H), 1.33-1.28 (t, *J* = 7.1, 3H).

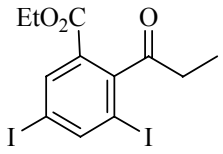
^{13}C-NMR ($CDCl_3$, 75 Hz): δ = 202.5, 162.3, 149.8, 147.1, 137.8, 128.7, 93.2, 90.7, 61.4, 29.5, 13.0.

IR (KBr, cm^{-1}): $\tilde{\nu}$ = 3409 (w), 2982 (w), 1712 (vs), 1711 (vs), 1557 (s), 1533(s), 1470 (w), 1422(m), 1353 (s), 1238(vs), 1205(vs), 1113 (m), 1021(s), 885 (m), 755 (m), 567(m).

MS (EI, 70 ev), *m/z* (%): 444 (18) [M^+], 429 (88), 401 (100), 373 (7), 357 (6), 229 (5), 201 (6), 74 (9).

$C_{11}H_{10}I_2O_3$	HRMS (EI)	Calcd.	443.8719
		Found	443.8742

Synthesis of ethyl 2-propionyl-3,5-diiodobenzoate (39c)



Prepared according to TP 2 from ethyl 2,3,5-triiodobenzoate (**35**) (3.0 g, 5.7 mmol), lithium dineopentylcuprate **16** (6.8 mmol) and propionyl chloride (1.4 g, 15 mmol). Reaction time: 20 min at –78 °C. Purification by flash chromatography (*n*-pentane/diethyl ether = 10/1) yielded compound **39c** as white solid (2.0 g, 75%).

mp.: 74-76 °C.

^{1}H-NMR ($CDCl_3$, 300 Hz): δ =8.37-8.36 (d, *J* = 1.7 Hz, 1H), 8.34-8.33 (d, *J* = 1.7 Hz, 1H), 4.38-4.31 (q, *J* = 7.1, 2H), 2.89-2.82 (q, *J* = 7.1, 2H), 1.39-1.36 (t, *J* = 7.1, 3H), 1.31-1.28 (t, *J* = 7.1, 3H).

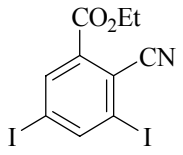
^{13}C-NMR ($CDCl_3$, 75 Hz): δ = 206.7, 163.7, 151.1, 148.5, 139.2, 130.3, 94.5, 92.8, 62.7, 36.6, 14.5, 7.8.

IR (KBr, cm^{-1}): $\tilde{\nu}$ = 3410 (w), 2925 (s), 1721 (vs), 1560 (w), 1535(s), 1461 (w), 1271 (vs), 1204 (m), 1103 (w), 1017 (w), 878 (w), 738 (vs), 704 (m).

MS (EI, 70 ev), *m/z* (%): 458 (5) [M^+], 429 (80), 401 (100), 373 (5), 356 (5), 274 (10), 201 (5), 74 (5).

$C_{12}H_{12}I_2O_3$	HRMS (EI)	Calcd.	457.8876
		Found	457.8851

Synthesis of ethyl 2-cyano-3,5-diiodobenzoate (39d)



A dry and argon flushed 50 mL flask, equipped with a magnetic stirrer and a septum, was charged with a solution of ethyl 2,3,5-triiodobenzoate (**35**) (528 mg, 1.0 mmol) in dry diethyl ether (30 mL). *i*-PrMgCl (1.0 M/diethyl ether, 1.1 mmol) was added slowly at –90 °C and the resulting mixture was warmed up slowly to –78 °C and stirred at this temperature for 2 h to complete the iodine-magnesium exchange (checked by GC-MS analysis of reaction aliquots). Then a solution of *p*-toluenesulfonyl cyanide (218 mg, 1.2 mmol) in dry THF (5 mL) was added. The mixture was warmed up to rt and was quenched after 1 h with saturated aqueous NH_4Cl solution (15 mL) and poured into water (20 mL). The aqueous phase was extracted with diethyl ether (3 × 20 mL). The combined organic fractions were washed with brine (30 mL), dried over $MgSO_4$ and concentrated *in vacuo*. Purification by flash chromatography (*n*-pentane/diethyl ether = 5/1) yielded compound **39d** as white solid (384 mg, 90% yield).

mp.: 113 °C.

^{1}H-NMR ($CDCl_3$, 300 Hz): δ = 8.52-8.51 (d, *J* = 1.5 Hz, 1H), 8.40-8.39 (d, *J* = 1.5 Hz, 1H), 4.47 (q, *J* = 7.1 Hz, 2H),1.46 (t, *J* = 7.1 Hz, 3H).

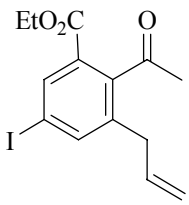
^{13}C-NMR ($CDCl_3$, 75 Hz): δ = 162.3, 151.2, 139.7, 136.2, 120.0, 117.9, 103.0, 100.1, 63.5, 14.4.

IR (KBr, cm^{-1}): $\tilde{\nu}$ = 3426 (s), 2900 (w), 2228 (m), 1723 (vs), 1555 (s), 1475(w), 1422 (w), 1368 (m), 1272(vs), 1256(vs), 1193 (m), 1175(w), 1071 (m), 879 (m), 781 (m), 620(m).

MS (EI, 70 ev), *m/z* (%): 427 (95) [M^+], 412 (5), 399 (88), 382 (94), 355 (60), 272 (10), 227 (40), 201 (10), 127 (15), 100 (100), 74 (20).

$C_{10}H_7I_2NO_2$	HRMS (EI)	Calcd.	426.8566
		Found	426.8553

Synthesis of ethyl 2-acetyl-3-allyl-5-iodobenzoate (43a)



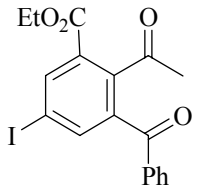
The reaction was carried out according to TP 2 from ethyl 2-acetyl-3,5-diiodobenzoate (**39b**) (222 mg, 0.5 mmol), lithium dineophylcuprate **17** (0.6 mmol) and allyl bromide (181 mg,

1.5 mmol). Reaction time: 2 h at –78 °C. Purification by flash chromatography (SiO_2, *n*-pentane/diethyl ether = 20:1) yielded **43a** as a yellow oil (135 mg, 75%).

^{1}H-NMR ($CDCl_3$, 300 MHz): δ = 8.19-8.18 (d, *J* = 1.8 Hz, 1H), 7.74-7.73 (d, *J* = 1.8 Hz, 1H), 5.92-5.77 (m, 1H), 5.11 (m, 1H), 5.03 (m, 1H), 4.34-4.30 (q, *J* = 7.1 Hz, 2H), 3.25-3.23 (d, *J* = 6.2 Hz, 2H), 2.46 (s, 3H), 1.36-1.32 (t, *J* = 7.1 Hz, 3H).
^{13}C-NMR ($CDCl_3$, 75 MHz): δ = 204.6, 164.4, 143.3, 142.9, 137.6, 136.9, 135.3, 128.4, 117.6, 93.7, 61.9, 36.0, 32.2, 14.0.
IR (film, cm^{-1}): 3079 (vw), 2981 (w), 1720 (vs), 1570 (s), 1446 (m), 1281 (vs), 1175 (s), 919 (m), 791 (m).
MS (EI, 70 ev): 358 (8) [M^+], 343 (51), 315 (38), 297 (100), 185 (25).

$C_{14}H_{15}IO_3$	HRMS (EI)	Calcd.	358.0066
		Found	358.0104

Synthesis of ethyl 2-acetyl-3-benzoyl-5-iodobenzoate (43b)



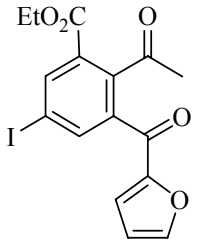
Prepared according to TP 2 from ethyl 2-acetyl-3,5-diiodobenzoate (**39b**) (444 mg, 1.0 mmol), lithium dineophylcuprate **17** (1.2 mmol) and benzoyl chloride (420 mg, 3.0 mmol). Reaction time: 2 h at –78 °C. Purification by flash chromatography (*n*-pentane/diethyl ether = 10/1) yielded **43b** as colorless oil (295 mg, 70%).

^{1}H-NMR ($CDCl_3$, 300 Hz): δ = 8.40-8.39 (d, *J* = 1.8 Hz, 1H), 7.85-7.84 (d, *J* = 1.8 Hz, 1H), 7.70-7.67 (m, 2H), 7.59-7.54 (m, 1H), 7.45-7.42 (m, 2H), 4.33-4.31 (q, *J* = 7.1 Hz, 2H), 2.49 (s, 3H), 1.35-1.30 (t, *J* = 7.1, 3H).
^{13}C-NMR ($CDCl_3$, 75 Hz): δ = 203.7, 195.0, 164.4, 144.9, 141.8, 141.5, 139.5, 136.5, 134.3, 130.7, 130.5, 129.1, 93.2, 62.8, 32.6, 14.4.
IR (film, cm^{-1}): $\tilde{\nu}$ = 3064 (w), 2981 (w), 1716 (vs), 1714 (vs), 1667 (vs), 1596 (s), 1566(s), 1449 (m), 1366(w), 1352 (m), 1283(vs), 1248(vs), 1213 (m), 1179(s), 1115 (m), 1055 (m), 976 (s), 895 (m), 775 (m), 710 (s), 689 (m), 582(m).

MS (EI, 70 ev), *m/z* (%): 422 (10) [M^+], 407 (100), 379 (45), 301 (70), 229 (12), 174 (9), 151 (10), 105 (33), 77 (30).

$C_{18}H_{15}IO_4$	HRMS (EI)	Calcd.	422.0015
		Found	422.0006

Synthesis of ethyl 2-acetyl-3-furoyl-5-iodobenzoate (43c)



Prepared according to TP 1 from ethyl 2-acetyl-3,5-diiodobenzoate (**39b**) (444 mg, 1.0 mmol), lithium dineophylcuprate **17** (1.2 mmol) and furoyl chloride (422 mg, 3.0 mmol). Reaction time: 2 h at –78 °C. Purification by flash chromatography (*n*-pentane/diethyl ether = 2/1) yielded **43c** as white solid (280 mg, 68%).

mp.: 128-129 °C

^{1}H-NMR ($CDCl_3$, 300 Hz): δ = 8.41-8.40 (d, *J* = 1.8 Hz, 1H), 8.14-8.13 (d, *J* = 1.8 Hz, 1H), 7.65-7.64 (dd, *J* = 1.7 Hz, *J* = 0.8 Hz, 1H), 7.12-7.11 (dd, *J* = 3.5 Hz, *J* = 0.8 Hz, 1H), 6.55-6.54 (dd, *J* = 3.5 Hz, *J* = 1.7 Hz, 1H), 4.32 (q, *J* = 7.1 Hz, 2H), 2.52 (s, 3H), 1.32 (t, *J* = 7.1 Hz, 3H).

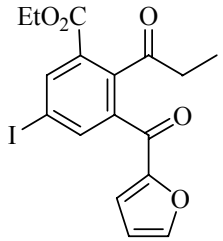
^{13}C-NMR ($CDCl_3$, 75 Hz): δ = 203.6, 180.8, 164.3, 151.9, 148.7, 144.9, 141.8, 141.7, 138.2, 130.5, 122.6, 113.2, 93.3, 62.8, 32.7, 14.4.

IR (KBr, cm^{-1}): $\tilde{\nu}$ = 3421 (m), 2983 (w), 1718 (vs), 1697 (vs), 1649 (vs), 1562 (s), 1463(s), 1385(m), 1284(vs), 1253 (vs), 1178(s), 1149 (m), 1018 (s), 983 (w), 779 (m), 580(w).

MS (EI, 70 ev), *m/z* (%): 412 (20) [M^+], 397 (34), 384 (25), 301 (100), 229 (16), 174 (10), 95 (22), 75 (8).

$C_{16}H_{13}IO_5$	HRMS (EI)	Calcd.	411.9808
		Found	411.9834

Synthesis of ethyl 3-furoyl-2-propionyl-5-iodobenzoate (43d)



Prepared according to TP 2 from ethyl 2-propionyl-3,5-diiodobenzoate (**39c**) (1.5 g, 3.3 mmol), lithium dineophylcuprate **17** (4.0 mmol) and furoyl chloride (1.3 g, 10.0 mmol). Reaction time: 2 h at –78 °C. Purification by flash chromatography (*n*-pentane/diethyl ether = 3/1) yielded **43d** as white solid (1.0 g, 71%).

mp.: 116-118 °C

^{1}H-NMR ($CDCl_3$, 300 Hz): δ = 8.49 (d, *J* = 1.7 Hz, 1H), 8.21 (d, *J* = 1.7 Hz, 1H), 7.73 (dd, *J* = 1.7 Hz, *J* = 0.8 Hz, 1H), 7.19-7.18 (dd, *J* = 3.6 Hz, *J* = 0.8 Hz, 1H), 6.64-6.62 (dd, *J* = 3.6 Hz, *J* = 1.7 Hz, 1H), 4.42-4.36 (q, *J* = 7.1 Hz, 2H), 2.91-2.84 (q, *J* = 7.1 Hz, 2H), 1.42-1.37 (t, *J* = 7.1 Hz, 3H), 1.24-1.19 (t, *J* = 7.1 Hz, 3H).

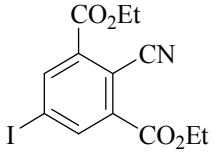
^{13}C-NMR ($CDCl_3$, 75 Hz): δ = 206.4, 180.8, 164.4, 151.9, 148.7, 144.8, 141.8, 141.6, 138.2, 130.8, 122.6, 113.2, 93.2, 62.8, 38.3, 14.5, 8.1.

IR (KBr, cm^{-1}): $\tilde{\nu}$ = 3055 (w), 2926 (s), 1722 (vs), 1656 (s), 1565 (m), 1463 (s), 1264 (vs), 1178 (m), 1017 (w), 738 (vs).

MS (EI, 70 ev), *m/z* (%): 426 (2) [M^+], 397 (80), 381 (5), 301 (100), 229 (20), 174 (15), 95 (20), 75 (8).

$C_{17}H_{15}IO_5$	HRMS (EI)	Calcd.	425.9964
		Found	425.9969

Synthesis of ethyl 2-cyano-3,5-diiodobenzoate (43e)



Prepared according to TP 2 from ethyl 2-cyano-3,5-diiodobenzoate (**39d**) (427 mg, 1.0 mmol), lithium dineophylcuprate **17** (1.2 mmol) and ethyl chloroformate (297 mg, 3.0 mmol) Reaction time: 24 h from–78 °C to rt. Purification by flash chromatography (*n*-pentane/diethyl ether = 5/1) yielded **43d** as white solid (261 mg, 70%).

mp.: 105 °C

^{1}H-NMR ($CDCl_3$, 300 MHz): δ = 8.45 (s, *2*H), 4.45-4.39 (q, *J* = 7.1, 4H), 1.41-1.35 (t, *J* = 7.1, 6H).

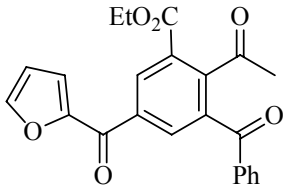
^{13}C-NMR ($CDCl_3$, 75 MHz): δ = 163.2, 143.1 136.6 114.8, 111.7, 99.0, 63.4, 14.4.

IR (KBr, cm^{-1}): $\tilde{\nu}$ = 3441 (w), 2984 (w), 2238 (w), 1737 (vs), 1565 (m), 1470 (w), 1446 (w), 1394 (w), 1286 (vs), 1245 (vs), 1208 (vs), 1022 (s), 792 (m).

MS (EI, 70 ev): 373 (48) [M^+], 345 (17), 328 (73), 316 (21), 300 (100), 273 (62), 255 (8), 229 (22), 100 (37).

$C_{13}H_{12}INO_4$	HRMS (EI)	Calcd.	372.9811
		Found	372.9825

Synthesis of ethyl 2-acetyl-3-benzoyl-5-furoylbenzoate (45a)



Prepared according to TP 2 from ethyl 2-acetyl-3-benzoyl-5-iodobenzoate (**43b**) (211 mg, 0.5 mmol), lithium dineophylcuprate **17** (0.75 mmol) and 2-furoyl chloride (261 mg, 2.0 mmol). Reaction time: 1.5 h at –78 °C. Purification by flash chromatography (*n*-pentane/diethyl ether = 2/1) yielded **45a** as a colorless oil (127 mg, 65%).

^{1}H-NMR ($CDCl_3$, 300Hz): δ =8.70-8.69 (d, *J* = 1.8 Hz, 1H), 8.16-8.15 (d, *J* = 1.8 Hz, 1H), 7.71-7.74 (m, 2H), 7.64-7.63 (dd, *J* = 1.7 Hz, *J* = 0.8 Hz, 1H), 7.58-7.53 (m, 1H), 7.44-7.39 (m, 2H), 7.26-7.25 (d, *J* = 3.5 Hz, 1H), 6.57-6.55 (dd, *J* = 3,5 Hz, *J* = 1.7 Hz, 1H), 4.37-4.35 (q, *J* = 7.1 Hz, 2H), 2.58 (s, 3H), 1.37-1.32 (t, *J* = 7.1 Hz, 3H).

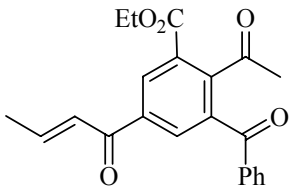
^{13}C-NMR ($CDCl_3$, 75 Hz): δ =203.9, 195.7, 180.0, 165.0, 152.3, 148.8, 148.1, 138.2, 137.0, 136.6, 134.3, 134.0, 133.7, 130.8, 129.5, 129.1, 121.6, 113.2, 62.8, 32.5, 14.4.

IR (film, cm^{-1}): $\tilde{\nu}$ = 3432 (vs), 2929 (w), 1721 (vs), 1654 (vs), 1596 (w), 1563(w), 1463 (m), 1449 (w), 1391(w), 1352 (w), 1275 (m), 1248(vs), 1189(w), 1013 (m), 707 (w).

MS (EI, 70 ev), *m/z* (%): 390 (8) [M^+], 375 (100), 347 (40), 329 (10), 300 (7), 269 (75), 197 (18), 169 (15), 99 (45), 105 (50), 77 (45).

$C_{23}H_{18}O_6$	HRMS (EI)	Calcd.	390.1103
		Found	390.1117

Syntheisi of ethyl 2-acetyl-3-benzoyl-5-crotonylbenzoate (45b)



Prepared according to TP 2 from ethyl 2-acetyl-3-benzoyl-5-iodobenzoate (**43b**) (211 mg, 0.5 mmol), lithium dineophylcuprate **17** (0.75 mmol) and *trans*-crotonyl chloride (209 mg, 2.0 mmol). Reaction time: 1.5 h at –78 °C. Purification by flash chromatography (*n*-pentane/diethyl ether = 2/1) yielded **45b** as a colorless oil (122 mg, 67%).

^{1}H-NMR ($CDCl_3$, 300Hz): δ =8.58-8.57 (d, *J* = 1.7 Hz, 1H) , 8.07-8.06 (d, *J* = 1.7 Hz, 1H), 7.71-7.68 (m, 2H), 7.59-7.53 (m, 1H), 7.44-7.39 (m, 2H), 7.14-7.02 (qd, *J* = 15 Hz, *J* = 6.8 Hz, 1H), 6.83-6.76 (dq, *J* = 15 Hz, *J* = 1.7 Hz, 1H), 4.37-4.35 (q, *J* = 7.1 Hz, 2H), 2.55 (s, 3H), 1.96-1.93 (dd, *J* = 6.8 Hz, *J* = 1.7 Hz, 3H), 1.37-1.32 (t, *J* = 7.1 Hz, 3H).

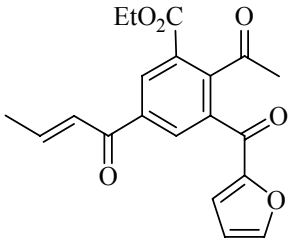
^{13}C-NMR ($CDCl_3$, 75 Hz): δ =203.9, 195.8, 188.6, 165.1, 148.8, 147.9, 138.5, 137.7, 136.7, 134.3, 133.1, 132.7, 130.8, 129.6, 129.1, 127.0, 62.8, 32.5, 19.1 14.5.

IR (film, cm^{-1}): = 3402 (w), 2980 (m), 1723 (vs), 1667 (vs), 1622 (vs), 1597 (m), 1579(m), 1448 (m), 1288 (s), 1245(vs), 1142(w), 1013 (m), 967 (w), 791 (w), 659 (w).

MS (EI, 70 ev), *m/z* (%): 364 (5) [M^+], 349 (100), 321 (40), 303 (10), 243 (70), 171 (15), 105 (30), 77 (45).

$C_{22}H_{20}O_5$	HRMS (EI)	Calcd.	364.1311
		Found	364.1304

Synthesis of ethyl 2-acetyl-3-furoyl-5-crotonylbenzoate (45c)

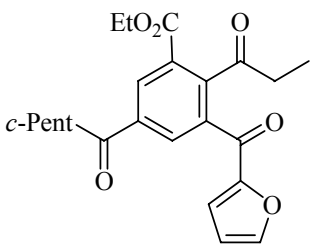


Prepared according to TP 2 from ethyl 2-acetyl-3-furoyl-5-iodobenzoate (**43c**) (206 mg, 0.5 mmol), lithium dineophylcuprate **17** (0.75 mmol) and *trans*-crotonyl chloride (209 mg, 2.0 mmol). Reaction time: 1.5 h at –78 °C. Purification by flash chromatography (SiO_2, *n*-pentane/diethyl ether = 2/1) yielded **45c** as a colorless oil (106 mg, 60%).

^{1}H-NMR ($CDCl_3$, 300 Hz): δ = 8.58-8.57 (d, *J* = 1.8 Hz, 1H), 8.38-8.37 (d, *J* = 1.8 Hz, 1H), 7.65-7.64 (dd, *J* = 1.7 Hz, *J* = 0.8 Hz, 1H), 7.14-7.12 (dd, *J* = 3.5 Hz, *J* = 0.8 Hz, 1H), 7.17-7.05 (qd, *J* = 15.0 Hz, *J* = 7.0 Hz, 1H), 6.85 (dq, *J* = 15.0 Hz, *J* = 1.3 Hz, 1H), 6.56-6.54 (dd, *J* = 3.5 Hz, *J* = 1.7 Hz, 1H), 4.36-4.34 (q, *J* = 7.1 Hz, 2H), 2.58 (s, 3H), 2.00-1.97 (dd, *J*=7.0 Hz, *J* = 1.3 Hz, 3H), 1.37-1.32 (t, *J* = 7.1 Hz, 3H).
^{13}C-NMR ($CDCl_3$, 75 Hz): δ = 203.8, 188.6, 181.6, 165.0, 152.0, 148.8, 148.7, 147.9, 137.9, 137.3, 130.1, 133.0, 129.5, 127.0, 122.6, 113.3, 62.8, 32.6, 19.2, 14.4.
IR (film, cm^{-1}): $\tilde{\nu}$ = 3403 (m), 2982 (w), 1723 (vs), 1715 (vs), 1673 (vs), 1658 (vs), 1651 (vs), 1622 (vs), 1566 (s), 1464(s), 1391(m), 1299(vs), 1212 (vs), 1016 (s), 966 (w), 797(m).
MS (EI, 70 ev), *m/z* (%): 354 (16) [M$^+$], 339 (40), 326 (18), 309 (15), 243 (100), 217 (10), 207 (30), 105 (15), 91 (20), 75 (10).

$C_{20}H_{18}O_6$	HRMS (EI)	Calcd.	354.1103
		Found	354.1118

Synthesis of ethyl 5-cyclopentanecarbonyl-3-furoyl-2-propionylbenzoate (45d)

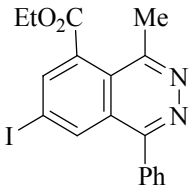


Prepared according to TP 2 from ethyl 2-propionyl-3-furoyl-5-iodobenzoate (**43d**) (1.0 g, 2.3 mmol), lithium dineophylcuprate **17** (3.5 mmol) and cyclopentanecarbonyl chloride (1.1 g, 8.0 mmol). Reaction time: 1.5 h at –78 °C. Standard workup and purification by flash chromatography (SiO_2, *n*-pentane/diethyl ether = 2/1) yielded ethyl **45d** as a colorless oil (565 mg, 62%).

^{1}H-NMR ($CDCl_3$, 300 Hz): δ = 8.63-8.62 (d, *J* = 1.7 Hz, 1H) , 8.42-8.41 (d, *J* = 1.7 Hz, 1H), 7.64-7.63 (dd, *J* = 1.7 Hz, *J* = 0.8 Hz, 1H), 7.11-7.10 (dd, *J* = 3.5 Hz, *J* = 0.8 Hz, 1H), 6.55-6.54 (dd, *J* = 3.5 Hz, *J* = 1.7 Hz, 1H), 4.35-4.31 (q, *J* = 7.1 Hz, 2H), 3.68-3.63 (quint, *J* = 8.3 Hz, 1H), 2.86-2.82 (q, *J* = 7.1 Hz, 2H), 1.92-1.85 (m, 4H), 1.68-1.60 (m, 4H), 1.34-1.31 (t, *J*=7.0 Hz, *J* = 1.3 Hz, 3H), 1.17-1.15 (t, *J*=7.0 Hz, *J* = 1.3 Hz, 3H).
^{13}C-NMR ($CDCl_3$, 75 Hz): δ = 205.6, 199.8, 180.7, 164.1, 151.1, 147.8, 147.6, 136.2, 135.7, 132.1, 131.9, 128.9, 121.5, 112.2, 61.7, 46.0, 37.1, 29.1, 25.7, 13.4, 7.0.
IR (film, cm^{-1}): $\tilde{\nu}$ = 3405 (w), 2942 (s), 1723 (vs), 1690 (vs), 1657 (vs), 1566 (s), 1463 (s), 1391 (m), 1299 (s), 1222 (s), 1018 (m), 950 (w), 795 (w), 769 (m), 593(w).
MS (EI, 70 ev), *m/z* (%): 396 (5) [M^+], 367 (70), 350 (10), 271 (100), 253 (10), 199 (35), 171 (15), 95 (20), 69 (15).

$C_{23}H_{24}O_6$	HRMS (EI)	Calcd.	396.1573
		Found	396.1588

Synthesis of 7-Iodo-4-methyl-1-phenyl-phthalazine-5-carboxylic acid ethyl ester (46a)



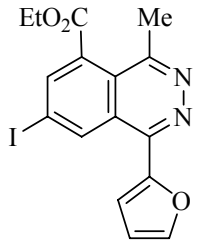
Prepared according to TP 3 from ethyl 2-acetyl-3-benzoyl-5-iodobenzoate (**43b**) (84 mg, 0.2 mmol), hydrazine monohydrate (0.5 M/ethanol, 0.24 mmol). Reaction time: 15 min at 78 °C. Standard workup and purification by flash chromatography (SiO_2, *n*-pentane/diethyl ether = 1/3) yielded ethyl **46a** as a white solid (78 mg, 93%).

mp.: 204 °C.

^{1}H-NMR ($CDCl_3$, 300 Hz): δ = 8.40-8.39 (d, *J* = 1.8 Hz, 1H), 8.11-8.10 (d, *J* = 1.8 Hz, 1H), 7.59-7.49 (m, 5H), 4.48-4.41 (q, *J* = 7.1 Hz, 2H), 2.89 (s, 3H), 1.42-1.37 (t, *J* = 7.1 Hz, 3H).
^{13}C-NMR ($CDCl_3$, 75Hz): δ = 168.1, 157.8, 155.3, 140.9, 138.2, 136.0, 133.0, 130.5, 130.0, 129.2, 127.3, 122.6, 97.3, 63.4, 23.0, 14.4.
IR (KBr, cm^{-1}): $\tilde{\nu}$ = 3426 (m), 2981 (w), 1726 (vs), 1576 (s), 1445 (m), 1388(m), 1361 (m), 1281 (vs), 1180 (vs), 1014 (m), 891 (w), 834 (w), 766 (m), 703 (s), 587 (w).
MS (EI, 70 ev), *m/z* (%): 418 (100) [M^+], 389 (40), 373 (25), 344 (5), 331 (5), 317 (5), 291 (30), 263 (80), 189 (60), 163 (20), 94 (13), 77 (10).

$C_{18}H_{15}IN_2O_2$	HRMS (EI)	Calcd.	418.0178
		Found	418.0152

Synthesis of 1-Furan-2-yl-7-iodo-4-methyl-phthalazine-5-carboxylic acid ethyl ester (46b)



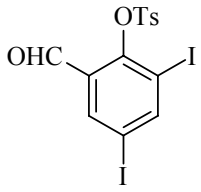
Prepared according to TP 3 from ethyl 2-acetyl-3-furoyl-5-iodobenzoate (**43c**) (206 mg, 0.5 mmol), hydrazine monohydrate (0.5 M/ethanol, 0.6 mmol). Reaction time: 15 min at 78 °C. Standard workup and purification by flash chromatography (SiO_2, *n*-pentane/diethyl ether = 1/3) yielded ethyl **46b** as a white solid (184 mg, 90%).

mp.: 152 °C.
^{1}H-NMR ($CDCl_3$, 300 Hz): δ = 9.19-9.18 (d, *J* = 1.8 Hz, 1H), 8.12-8.11 (d, *J* = 1.8 Hz, 1H), 7.71-7.70 (dd, *J* = 1.7 Hz, *J* = 0.8 Hz, 1H), 7.35-7.33 (dd, *J* = 3.5 Hz, *J* = 0.8 Hz, 1H), 6.61-6.59 (dd, *J* = 3.5 HZ, *J* = 1.7 Hz, 1H), 4.47-4.40 (q, *J* = 7.1 Hz, 2H), 2.86 (s, 3H), 1.41-1.36 (t, *J* = 7.1 Hz, 3H).
^{13}C-NMR ($CDCl_3$, 75 Hz): δ = 168.1, 155.0, 151.8, 147.3, 145.5, 141.0, 137.9, 132.9, 125.7, 122.7, 114.4, 112.7, 97.6, 63.3, 23.1, 14.4.
IR (KBr, cm^{-1}): $\tilde{\nu}$ = 3434 (m), 2978 (w), 1727 (vs), 1573 (m), 1444 (w), 1392 (m), 1353 (m), 1270 (vs), 1194 (vs), 1096 (m), 1014 (m), 886 (w), 830 (w), 758 (m), 595 (w).

MS (EI, 70 ev), *m/z* (%): 408 (100) [M^+], 380 (7), 363 (24), 351 (92), 333 (9), 321 (5), 295 (8), 168 (27), 152 (62), 139 (51), 126 (30), 77 (17).

$C_{16}H_{13}IN_2O_3$	HRMS (EI)	Calcd.	407.9971
		Found	407.9963

Synthesis of 2-formyl-4,6-diiodophenyl-4-methylbenzenesulfonate (47)



To a solution of 2-hydroxy-3,5-diiodobenzaldehyde (5.6 g, 15.0 mmol) and TsCl (3.0 g, 15.7 mmol) in CH_2Cl_2 (50 mL) at rt, Et_3N (5 mL) was added and the resulting mixture was stirred at rt for 12 h. The solid was filtered off and the resulting clear solution was concentrated in vacuum. The residue was purified by flash chromatography (SiO_2, *n*-pentane/diethyl ether = 10/1) yielded ethyl **47** as a white solid (7.1 g, 90%).

mp.: 137 °C

^{1}H-NMR ($CDCl_3$, 300 MHz): δ = 9.93 (s, 1 H), 8.36-8.35 (d, *J* = 2.21 Hz, 1 H), 8.22-8.21 (d, *J* = 2.21 Hz, 1 H), 7.85-7.82 (d, *J* = 8.40 Hz, 2 H), 7.43-7.40 (d, *J* = 8.40 Hz, 2 H), 2.52 (s, 3 H).

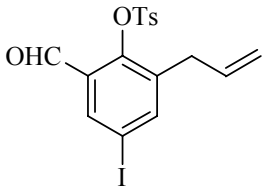
^{13}C-NMR ($CDCl_3$, 75 MHz): δ = 186.1, 153.1, 151.8, 147.3, 138.2, 133.0, 132.4, 130.7, 129.5, 94.3, 93.4, 22.3.

IR (film, cm^{-1}): $\tilde{\nu}$ = 3045 (w), 1681 (vs), 1558 (w), 1386 (vs), 1223 (m), 1174 (vs), 1126 (s), 1085 (s), 833 (m).

MS (EI, 70 eV): 528 (M^+, 32), 372 (32), 218 (15), 155 (100), 91 (80), 65 (17).

$C_{14}H_{10}I_2O_4S$	HRMS (EI)	Calcd.	527.8389
		Found	527.8393

Synthesis of 2-allyl-6-formyl-4-iodophenyl-4-methylbenzenesulfonate (49a)

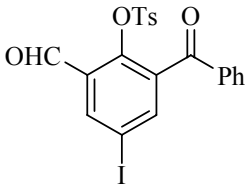


Prepared according to TP 2 from 2-formyl-4,6-diiodophenyl-4-methylbenzenesulfonate (**47**) (527 mg, 1.0 mmol), lithium dineophylcuprate **17** (1.2 mmol) and allyl bromide (360 mg, 3.0 mmol). Reaction time: 20 min at –78 °C. Purification by flash chromatography (SiO_2, *n*-pentane/diethyl ether = 3/1) yielded ethyl **49a** as a light yellow thick oil (415 mg, 94%).

^{1}H-NMR ($CDCl_3$, 300 MHz): δ = 9.78 (s, 1 H), 8.08-8.07 (dt, *J* = 2.32 Hz, *J* = 0.44 Hz, 2 H), 7.82-7.81 (dt, *J* = 2.32 Hz, *J* = 0.55 Hz, 1 H), 7.80-7.77 (d, *J* = 8.40 Hz, 2 H), 7.43-7.40 (d, *J* = 8.40 Hz, 2 H), 5.85-5.72 (m, 1 H), 5.18-5.08 (m, 2 H), 3.32-3.30 (d, *J* = 6.75 Hz, 2 H), 2.51 (s, 3 H).
^{13}C-NMR ($CDCl_3$, 75 MHz): δ = 186.4, 149.1, 147.1, 145.3, 138.6, 136.2, 134.6, 132.1, 131.8, 130.8, 128.9, 118.6, 92.9, 33.9, 22.2.
IR (film, cm^{-1}): $\tilde{\nu}$ = 2874 (w), 1694 (s), 1494 (m), 1385 (vs), 1234 (m), 1195 (s), 1180 (s), 1153 (s), 1088 (s), 866 (m), 816 (s), 721 (vs), 579 (m).
MS (EI, 70 eV): 442 (M^+, 1), 287 (80), 155 (78), 131 (20), 115 (5), 103 (15), 91 (100), 77 (12), 65 (13).

$C_{17}H_{15}IO_4S$	HRMS (EI)	Calcd.	441.9736
		Found	441.9719

Synthesis of 2-benzoyl-6-formyl-4-iodophenyl-4-methylbenzenesulfonate (49b)



Prepared according to TP 2 from 2-formyl-4,6-diiodophenyl-4-methylbenzenesulfonate (**47**) (527 mg, 1.0 mmol), lithium dineophylcuprate **17** (1.2 mmol) and benzoyl chloride (420 mg,

3.0 mmol). Reaction time: 20 min at –78 °C. Purification by flash chromatography (SiO_2, *n*-pentane/diethyl ether = 2/1) yielded ethyl **49b** as a light yellow solid (404 mg, 80%).

mp.: 106 °C

^{1}H-NMR ($CDCl_3$, 300 MHz): δ = 10.07 (s, 1 H), 8.43-8.42 (d, *J* = 2.32 Hz, 1 H), 8.05-8.04 (d, *J* = 2.32 Hz, 1 H), 7.73-7.70 (d, *J* = 7.62 Hz, 2 H), 7.67-7.62 (m, 1 H), 7.51-7.46 (m, 4H), 7.25-7.22 (d, *J* = 7.62 Hz, 2 H), 2.42 (s, 3 H).

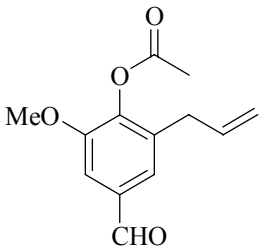
^{13}C-NMR ($CDCl_3$, 75 MHz): δ = 191.0, 147.9, 147.1, 144.7, 140.3, 137.1, 136.2, 134.2, 132.8, 130.9, 130.6, 130.5, 129.4, 129.0, 128.9, 92.4, 22.2.

IR (KBr, cm^{-1}): $\tilde{\nu}$ = 3436 (vs), 1696 (vs), 1670 (vs), 1596 (m), 1448 (w), 1386 (vs), 1286 (m), 1178 (s), 1157 (s), 1087 (s), 841 (w), 707 (vs), 563 (m).

MS (EI, 70 eV): 506 (M^+, 1), 351 (88), 273 (9), 223 (6), 155 (75), 139 (18), 105 (20), 91 (100), 77 (43), 51 (6).

$C_{21}H_{15}IO_5S$	HRMS (EI)	Calcd.	505.9685
		Found	505.9689

Synthesis of 2-allyl-4-formyl-6-methoxyphenyl acetate (52a)



Prepared according to TP 2 from 2-iodo-4-formyl-6-methoxyphenyl acetate (**50**) (320 mg, 1.0 mmol), lithium dineophylcuprate **17** (1.2 mmol) and allyl bromide (360 mg, 3.0 mmol). Reaction time: 2 h at –78 °C. Purification by flash chromatography (SiO_2, *n*-pentane/diethyl ether = 3/1) yielded ethyl **52a** as a colorless oil (197 mg, 84%).

^{1}H-NMR ($CDCl_3$, 300 MHz): δ = 9.98 (s, 1 H), 7.44 (s, 1 H), 6.03-5.90 (m, 1 H), 5.22-5.15 (m, 2 H), 3.96 (s, 3 H), 3.45-3.42 (dt, *J* = 6.63 Hz, *J* = 1.44 Hz, 2 H), 2.41 (s, 3 H).

^{13}C-NMR ($CDCl_3$, 75 MHz): δ = 191.6, 168.4, 152.5, 143.8, 135.3, 135.0, 134.7, 126.1, 117.5, 109.2, 56.6, 34.8, 20.8.

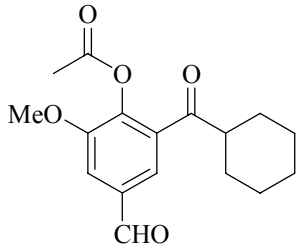
IR (film, cm^{-1}): $\tilde{\nu}$ 2977 (w), 1767 (vs), 1697 (vs), 1591 (m), 1464 (m), 1301 (m), 1188

(vs), 1135 (vs), 899 (w), 730 (w).

MS (EI, 70 eV): 234 (M^+, 5), 192 (100), 177 (4), 163 (6), 149 (5), 131 (20), 121 (7), 103 (18), 91 (15), 77 (12), 51 (3).

$C_{13}H_{14}O_4$	HRMS (EI)	Calcd.	234.0892
		Found	234.0883

Synthesis of 2-(cyclohexylcarbonyl)-4-formyl-6-methoxyphenyl acetate (52b)



Prepared according to TP 2 from 2-iodo-4-formyl-6-methoxyphenyl acetate (**50**) (320 mg, 1.0 mmol), lithium dineophylcuprate **17** (1.2 mmol) and cyclohexylcarbonyl chloride (438 mg, 3.0 mmol). Reaction time: 2 h at –78 °C. Purification by flash chromatography (SiO_2, *n*-pentane/diethyl ether = 3/2) yielded ethyl **52b** as a white solid (222 mg, 73%).

mp.: 94 °C

^{1}H-NMR ($CDCl_3$, 300 MHz): δ = 9.99 (s, 1 H), 7.71-7.70 (d, *J* = 1.77 Hz, 1 H), 7.60-7.59 (d, *J* = 1.77 Hz, 1 H), 3.94 (s, 3 H), 3.07-2.97 (m, 1 H), 2.36 (s, 3 H), 1.91-1.21 (m, 10 H).

^{13}C-NMR ($CDCl_3$, 75 MHz): δ = 203.6, 190.8, 168.3, 153.2, 143.5, 134.8, 133.9, 124.1, 113.2, 56.9, 49.6, 29.1, 26.2, 26.1, 20.9.

IR (KBr, cm^{-1}): $\tilde{\nu}$ 3436 (vs), 2932 (s), 1761 (vs), 1706 (vs), 1690 (vs), 1589 (m), 1469 (w), 1386 (m), 1289 (s), 1187 (vs), 1136 (vs), 1004 (m), 893 (w), 674 (w).

MS (EI, 70 eV): 304 (M^+, 3), 262 (32), 233 (11), 215 (4), 194 (5), 179 (100), 164 (2), 136 (3), 55 (3).

$C_{17}H_{20}O_5$	HRMS (EI)	Calcd.	304.1311
		Found	304.1286

11 Preparations of Functionalized Chiral Compounds *via* Allyl substitution reaction of Aryl Cuprates

General considerations for measuring the *ee* value

Enantiomeric purity was determined by chiral HPLC or capillary GC analysis. In all cases, the analysis was calibrated with a sample of the racemate.

Chiral HPLC:

column A: Chiralcel OD-H, 0.46 cm × 25 cm

column B: Chiralcel OD, 0.46 cm × 25 cm

column C: Chiralcel AD, 0.46 cm × 25 cm

Chiral GC:

column A: TFA gamma-cyclodextrin, 30.0 m × 0.25 mm

column B: Chiraldex B-PH, 30.0 m × 0.25 mm

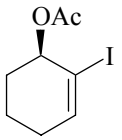
method A: 40 °C (2 min), ramp of 20 °C/min to 150 °C (45 min)

method B: 130 °C (100 min).

method C: 150 °C (150 min).

method D: 160 °C (150 min).

Synthesis (*R*)-2-Iodo-2-cyclohexen-1-yl acetate ((*R*)-54a)



To a solution of (1*R*)-2-iodo-2-cyclohexen-1-ol (3.7 g, 16.5 mmol) in 20 mL pyridine, acetic anhydride (8.5 g, 82.6 mmol) was added at rt. The resulting mixture was stirred at rt for 12 h and then diluted with 100 mL diethyl ether. The solution was washed with 2M HCL (100 mL) and brine (100 mL × 2). The organic phase was dried ($NaSO_4$) and concentrated in vacuum. The residue was purified by column chromatography (SiO_2, pentane/diethyl ether = 10/1) to give **54a** as a colorless oil (4.2 g, 95%).

GC (column A, method A): t_R/min = 10.24 (major), 11.04 (minor); 98 % *ee*.

$[\alpha]_D^{20}$ = + 21.6 (c 1.08, $CHCl_3$)

^{1}H-NMR ($CDCl_3$, 300 MH_Z): δ = 6.65-6.64 (m 1H), 5.40-5.39 (m, 1H), 2.11 (s. 3H), 2.11-1.70 (m, 6H).

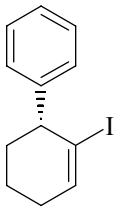
^{13}C-NMR ($CDCl_3$, 75 MH_Z): δ = 170.5, 143.9, 95.8, 73.8, 30.3, 29.5, 21.6, 17.8.

IR (film): 2944 (w), 1735 (vs), 1427 (w), 1371 (m), 1233 (vs), 977 (m), 917 (w), 730 (w).

MS (EI, 70 ev), *m/z* (%): 206 (4) $[M\text{-}AcO\text{-}H]^+$, 139 (85), 126 (15), 97 (100), 79 (47), 55 (4).

$C_8H_{11}IO_2$	Calcd.	C, 36.11	H, 4.17
	Found	C, 33.38	H, 4.06.

Synthesis (1*S*)-2-iodo-2-cyclohexen-1-yl benzene ((*R*)-58)



Prepared according to TP 4 from (*R*)-2-Iodo-2-cyclohexen-1-yl acetate ((*R*)-**54a**) (266 mg, 1.0 mmol, 94% *ee*), lithium dineophylcuprate **17** (1.2 mmol) and iodobenzene (245 mg, 1.2 mmol). Reaction Purification by flash chromatography (SiO_2, *n*-pentane/diethyl ether = 99/1) yielded ethyl (*R*)-**58** as a corloress oil (185 mg, 65%).

GC (column b, method A): t_R/min = 31.9 (minor), 32.6 (major); 87 % *ee*.

^{1}H-NMR ($CDCl_3$, 300 MH_Z): δ = 7.30-7.03 (m, 5H), 6.59 (dt, J = 3.98 Hz, J = 1.31 Hz, 1H), 3.62, (m, 1 H), 2.17-1.99 (m, 3 H), 1.77-1.47 (m, 3H).

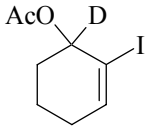
^{13}C-NMR ($CDCl_3$, 75 MH_Z): δ = 144.1, 140.2, 128.3, 126.6, 101.3, 52.6, 33.6, 29.3, 17.8.

IR (film): 2935 (vs), 2863 (s), 1680 (m), 1492 (s), 1451 (s), 1329 (w), 985 (m), 700 (vs), 555 (w), 535 (w).

MS (EI, 70 ev), *m/z* (%): 284 (73) $[M]^+$, 206 (83), 157 (75), 42 (22), 129 (100), 115 (53) 102 (10).

$C_{12}H_{13}I$	HRMS (EI)	Calcd.	284.0062
		Found	284.0066

Synthesis of 1-d-2-iodo-2-cyclohexen-1-yl acetate ((±)-59)



To a solution of 2-iodo-2-cyclohex-1-one (1.11 g, 5 mmol) and $CeCl_3 \cdot 7H_2O$ (1.86 g, 5 mmol) in MeOH (8 mL) cooled at 0 ^oC, $NaBD_4$ was added in small portions. The resulting mixture was stirred at 25 ^oC for 3 h. The reaction mixture was poured into cold water and extracted with Et_2O (3 × 20 mL). The combined organic phase was washed with brine and dried (Na_2SO_4). The solvent was removed and the crude product was purified by column chromatography (SiO_2, pentane/diethyl ether = 5/1) to give 1-d-2-iodo-2-cyclohexenol as a colorless oil (856 mg, 76%).

To a solution of 1-d-2-iodo-2-cyclohexenol (788 mg, 3.51 mmol) in pyridine (3.1 mL), Ac_2O (1.9 mL) was added. The resulting mixture was stirred at 25 ^oC for 2 h. The reaction mixture was quenched with 2 M HCl (5 mL) and extracted with Et_2O (3 × 20 mL). The combined organic phase was washed with H_2O, saturated aqueous $NaHCO_3$ solution, brine, and dried (Na_2SO_4). The solvent was removed and the crude product was purified by column chromatography (SiO_2 , pentane/diethyl ether = 10:1) to give (±)-**59** as a colorless oil (775 mg, 83%).

^{1}H-NMR ($CDCl_3$, 300 MHz): δ = 6.65-6.50 (m, 1H), 2.08-1.64 (m, 9H).

^{13}C-NMR ($CDCl_3$, 75 MHz): δ = 169.6, 144.0, 95.8, 72.0, 30.3, 29.5, 21.6, 17.7.

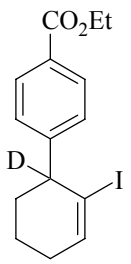
IR (film): 2944 (m), 1738 (s), 1369 (m), 1264 (m), 1240 (s), 1013 (m), 922 (m).

MS (EI, 70 ev), *m/z* (%): 208 (3), 207 (5), 140 (79), 127 (10), 98 (100), 80 (33).

C_6H_7DI [M^+-OAc] HRMS (EI) Calcd. 207.9732

Found 207.9733

Synthesis of ethyl 4-(1-d-2-iodo-2-cyclohexen-1-yl)benzoate (60)

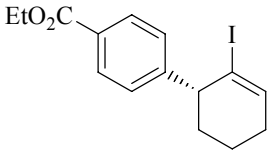


The reaction was carried out according to TP 4 with 1-d-2-iodo-2-cyclohexen-1-yl acetate ((±)-**59**) (267 mg, 1.0 mmol), lithium dineophylcuprate **17** (1.2 mmol), ethyl 4-iodobenzoate (331 mg, 1.2 mmol). Purification by flash chromatography (SiO_2, *n*-pentane/diethyl ether = 10/1) yielded **60** as a colorless oil (189 mg, 53%).

^{1}H-NMR ($CDCl_3$, 300 MHz): δ = 7.97-7.96 (m, 2H), 7.23-7.17 (m, 2H), 6.65-6.60 (m, 1H), 4.30 (q, *J* = 7.1 Hz, 2H), 2.18-2.04 (m, 3H), 1.76-1.64 (m, 1H), 1.62-1.50 (m, 2H), 1.31 (t, *J* = 7.1 Hz, 3H).
^{13}C-NMR ($CDCl_3$, 75 MHz): δ = 167.0, 149.7, 141.2, 130.1, 129.4, 128.7, 100.2, 61.2, 52.6, 33.9, 29.7, 18.1, 14.8.
IR (film): 2935 (m), 1716 (s), 1610 (m), 1276 (s), 1178 (m), 1104 (s), 1022 (m), 771 (m), 707 (m).
MS (EI, 70 ev), *m/z* (%): 357 [M^+], (100), 312 (37), 230 (23), 207 (31), 156 (28), 142 (15), 129 (48), 116 (14).

$C_{15}H_{16}DIO_2$	HRMS (EI)	Calcd.	357.0335
		Found	357.0334

Synthesis of ethyl 4-[(1*S*)-2-iodocyclohex-2-en-1-yl]beozoate ((*R*)-62a)



The reaction was carried out according to TP4 with (*R*)-2-iodo-2-cyclohexen-1-yl acetate ((*R*)-**54a**) (266 mg, 1.0 mmol, 98% *ee*), lithium dineophylcuprate **17** (1.2 mmol) and ethyl 4-iodobenzoate (331 mg, 1.2 mmol). Purification by column chromatography (SiO_2, *n*-pentane/diethyl ether = 10/1) yielded (*R*)-**62a** as a colorless oil (274 mg, 77%).

Chiral HPLC (column C, heptane : *i*PrOH = 99:1, 0.5 ml/min): t_R/min = 18.3 (minor), 19.8 (major): 98% *ee*.
$[\alpha]_D^{20}$ = + 12.1 (c 0.99, $CHCl_3$)

^{1}H-NMR ($CDCl_3$, 300 MH_Z): δ = 7.96-7.92 (d, *J* = 8.4 Hz, 2H), 7.22-7.19 (d, *J* = 8.4 Hz, 2H), 6.62 (m, 1H), 4.33-4.26 (q, *J* = 7.1 Hz, 2H), 3.68 (m, 1H), 2.09 - 1.53 (m, 6H), 1.34-1.31 (t, *J* = 7.1 Hz, 3H).

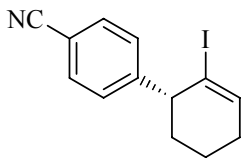
^{13}C-NMR ($CDCl_3$, 75 MH_Z): δ =167.0, 149.8, 141.2, 130.1, 129.4, 128.7, 100.2, 61.2, 53.0, 33.9, 29.7, 18.1, 14.8.

IR (film, cm^{-1}): 3415 (w), 2937 (s), 1715 (vs), 1609 (m), 1444 (m), 1417 (m), 1366 (m), 1276 (vs), 1178 (s), 1102 (vs), 1021 (m), 769 (m), 707 (m).

MS (EI, 70 ev), *m/z* (%): 356 (100) [M^+], 311 (32), 229 (27), 206 (19), 183 (7), 155 (20), 129 (25), 115 (13), 91 (7).

$C_{15}H_{17}IO_2$	HRMS (EI)	Calcd.	356.0273
		Found	356.0280

Synthesis of 4-[(1*R*)-2-iodocyclohex-2-en-1-yl]benzonitrile ((*R*)-62b)



The reaction was carried out according to TP4 with (*R*)-2-iodo-2-cyclohexen-1-yl acetate ((*R*)-**54a**) (266 mg, 1.0 mmol, 98% *ee*), lithium dineophylcuprate **17** (1.2 mmol) and 4-bromobenzonitrile (218 mg, 1.2 mmol, 1.2 equiv). The temperature for the Br/Cu-exchange: 30 min at rt. Purification by column chromatography (SiO_2, *n*-pentane/diethyl ether = 15/1) yielded (*R*)-**62b** as a colorless oil (204 mg, 66%).

Chiral GC (column A, method B): t_R/min = 33.73 (minor), 34.98 (major): 96% *ee*.

$[\alpha]_D^{20}$ = + 18.5 (c 1.26, $CHCl_3$).

^{1}H-NMR ($CDCl_3$, 300 MH_Z): δ = 7.58-7.54 (d, *J* = 8.4 Hz, 2H), 7.26-7.22 (d, *J* = 8.4 Hz, 2H), 6.66-6.63 (m, 1H), 3.69 (m, 1H), 2.09-1.53 (m, 6H).

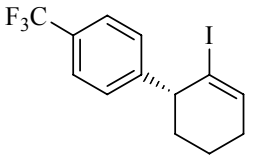
^{13}C-NMR ($CDCl_3$, 75 MH_Z): δ = 148.7, 140.4, 131.2, 128.1, 118.0, 109.6, 97.6, 51.6, 32.4, 28.2, 16.6.

IR (film, cm^{-1}): 4306 (w), 2907 (m), 2229 (vs), 1604 (s), 1503 (s), 1411 (s), 975(s), 833 (vs), 690 (s), 563 (vs), 483 (w).

MS (EI, 70 ev), *m/z* (%): 309 (100) [M^+], 182 (41), 154 (63), 140 (26), 127 (19), 116 (57).

$C_{13}H_{12}IN$	HRMS (EI)	Calcd.	309.0014
		Found	309.0008

Synthesis of 1-[(1*R*)-2-iodocyclohex-2-en-1-yl]-4-(trifluoromethyl)benzene ((*R*)-62c)

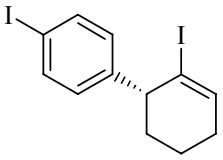


The reaction was carried out according to TP4 with (*R*)-2-Iodo-2-cyclohexen-1-yl acetate ((*R*)-**54a**) (266 mg, 1.0 mmol, 98% *ee*), lithium dineophylcuprate **17** (1.2 mmol) and 1-iodo-4-trifluoromethylbenzene (326 mg, 1.2 mmol). Purification by column chromatography (SiO_2, *n*-pentane/diethyl ether = 15/1) yielded (*R*)-**62c** as a colorless oil (250 mg, 70%).

Chiral GC (column A, method B): t_R/min = 24.56 (minor), 25.91 (major); 94%.
$[\alpha]_D^{20}$ = + 11.7 (c 1.36, $CHCl_3$).
^{1}H-NMR ($CDCl_3$, 300 MH_Z): δ = 7.53-7.51 (d, *J* = 8.0 Hz, 2H), 7.24-7.18 (d, *J* = 8.0 Hz, 2H), 6.65-6.62 (m, 1H), 3.68 (m, 1H), 1.53-2.12 (m, 6H).
^{13}C-NMR ($CDCl_3$, 75 MH_Z): δ = 148.5, 141.4, 129.0, 125.7 (q, *J* = 3.8 H_Z), 124 (q, *J* = 272 H_Z), 99.8, 52.8, 33.9, 29.6 17.9.
IR (film, cm^{-1}): 2938 (s), 1618 (s), 1445 (m), 1418 (m), 1325 (vs), 1163 (vs), 1124 (vs), 1110 (vs), 985 (m), 834 (m), 606 (w).
MS (EI, 70 ev), *m/z* (%): 352 (100) [M^+], 333 (15), 225 (41), 197 (25), 177 (23), 159 (42), 128 (8).

$C_{13}H_{12}F_3I$	HRMS (EI)	Calcd.	351.9936
		Found	351.9916

Synthesis of 1-iodo-4-[(1*R*)-2-iodocyclohex-2-en-1-yl]benzene ((*R*)-62d)

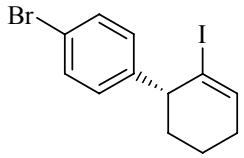


The reaction was carried out according to TP4 with (*R*)-2-Iodo-2-cyclohexen-1-yl acetate ((*R*)-**54a**) (266 mg, 1.0 mmol, 98% *ee*), lithium dineophylcuprate **17** (1.2 mmol) and 1,4-diiodobenzene (394 mg, 1.2 mmol). Purification by column chromatography (SiO_2, *n*-pentane/diethyl ether = 15/1) yielded (*R*)-**62d** as a colorless oil (336 mg, 82%).

Chiral GC (column A, method C): t_R/min = 78.77 (minor), 82.21 (major); 94% *ee*.
[α]$_D^{20}$ = + 25.2 (c 1.58, $CHCl_3$).
^{1}H-NMR ($CDCl_3$, 300 MH_Z): δ = 7.60-7.56 (d, *J* = 8.4 Hz, 2H), 6.90-6.86 (d, *J* = 8.4 Hz, 2H), 6.60-6.58 (m, 1H), 3.57 (m, 1H), 2.14-1.46 (m, 6H).
^{13}C-NMR ($CDCl_3$, 75 MH_Z): δ =142.5, 139.4, 136.1, 129.1, 98.8, 90.7, 50.9, 32.2, 28.0, 16.3.
IR (film, cm^{-1}): 2934 (s), 1627 (w), 1479 (s), 1400 (m), 1141 (w), 1060 (m), 1006 (s), 981 (m), 818 (s), 551 (w).
MS (EI, 70 ev), *m/z* (%): 410 (100) [M^+], 283 (23), 217 (26), 156 (36), 141 (19), 128 (37), 115 (17).

$C_{12}H_{12}I_2$	HRMS (EI)	Calcd.	409.9028
		Found	409.9017

Synthesis of 1-bromo-4-[(1*R*)-2-iodocyclohex-2-en-1-yl]benzene ((*R*)-62e)



The reaction was carried out according to TP4 with (*R*)-2-Iodo-2-cyclohexen-1-yl acetate ((*R*)-**54a**) (266 mg, 1.0 mmol, 98% *ee*), lithium dineophylcuprate **17** (1.2 mmol) and 4-bromo-iodobenzene (339 mg, 1.2 mmol). Purification by column chromatography (SiO_2, *n*-pentane) yielded (*R*)-**62e** as a colorless oil (323 mg, 89%).

Chiral GC (column A, method B): t_R/min = 117.46 (minor), 132.05 (major); 96% *ee*
[α]$_D^{20}$ = + 14.8 (c 1.43, $CHCl_3$).
^{1}H-NMR ($CDCl_3$, 300 MH_Z): δ = 7.40-7.36 (d, *J* = 8.4 Hz, 2H), 7.03-6.99 (d, *J* = 8.4 Hz, 2H), 6.60-6.57 (m, 1H), 3.61 (m, 1H), 1.50-2.14 (m, 6H).

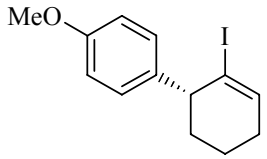
^{13}C-NMR ($CDCl_3$, 75 MH_Z): δ = 143.6, 141.1, 131.9, 130.5, 120.9, 100.6, 52.5, 33.9, 29.7, 18.0.

IR (film, cm^{-1}): 2934 (vs), 1898 (w), 1628 (m), 1483 (vs), 1442 (s), 1404 (s9, 1073 (s), 1010 (vs), 984 (s), 895 (m), 820 (s),701 (m9, 552 (w).

MS (EI, 70 ev), *m/z* (%): 362 (45) [M^+], 235 (35), 206 (31), 169 (40), 156 (100), 141 (34), 128 (77), 115 (29), 77 (15).

$C_{12}H_{12}BrI$	HRMS (EI)	Calcd.	361.9167
		Found	361.9153

1-[(1*R*)-2-Iodocyclohex-2-en-1-yl]-4-methoxybenzene ((*R*)-62f)



The reaction was carried out according to TP4 with (*R*)-2-Iodo-2-cyclohexen-1-yl acetate ((*R*)-**54a**) (266 mg, 1.0 mmol, 98% *ee*), lithium dineophylcuprate **17** (1.2 mmol) and 4-iodoanisole (291 mg, 1.2 mmol). Purification by column chromatography (SiO_2, *n*-pentane/Et_2O = 150/1) yielded (*R*)-**62f** as a colorless oil (267 mg, 85%).

Chiral GC (column A, method B): t_R/min = 96.5 (minor), 102.2 (major); 95% *ee*.

$[\alpha]_D^{20}$ = + 15.2 (c 1.04, $CHCl_3$).

^{1}H-NMR ($CDCl_3$, 300 MH_Z): δ = 7.05-7.03 (d, *J* = 8.4 Hz, 2H), 6.81-6.79 (d, *J* = 8.4 Hz, 2H), 6.56 (m, 1H), 3.73 (s, 3H), 3.57 (m, 1H), 2.12-1.54 (m, 6H).

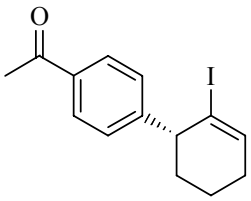
^{13}C-NMR ($CDCl_3$, 75 MH_Z): δ = 158.7, 140.4, 136.7, 129.7, 114.1, 102.5, 55.6, 52.2, 34.1, 29.7, 18.2.

IR (film, cm^{-1}): 2933 (vs), 2832 (s), 1610 (s), 1510 (vs), 1463 (s), 1302 (m), 1249 (vs), 1176 (s), 1036 (s), 828 (m), 602 (w).

MS (EI, 70 ev), *m/z* (%): 314 (100) [M^+], 286 (4), 208 (18), 187 (31), 171(10), 159 (24), 144 (22), 121 (43), 108 (23), 77 (11).

$C_{13}H_{15}IO$	HRMS (EI)	Calcd.	314.0168
		Found	314.0150

Synthesis of 1-{4-[(1*R*)-2-Iodocyclohex-2-en-1-yl]phenyl}ethanone ((*R*)-62g)



The reaction was carried out according to TP4 with (*R*)-2-Iodo-2-cyclohexen-1-yl acetate ((*R*)-**54a**) (266 mg, 1.0 mmol, 98% *ee*), lithium dineophylcuprate **17** (1.2 mmol) and 4-iodo-acetobenzene (295 mg, 1.2 mmol). Purification by column chromatography (SiO_2, *n*-pentane/diethyl ether = 10/1) yielded (*R*)-**62g** as a colorless oil (218 mg, 67%).

Chiral HPLC (column C, heptane : *i*PrOH = 99 : 1, 0.4 ml/min): t_R/min = 47.19 (minor), 51.78 (major); 89% *ee*.

$[\alpha]_D^{20}$ = + 24.7 (c 1.43, $CHCl_3$).

^{1}H-NMR ($CDCl_3$, 300 MH_Z): δ = 7.88-7.85 (d, *J* = 8.4 Hz, 2H), 7.24-7.22 (d, *J* = 8.4 Hz, 2H), 6.63 (m, 1H), 3.69 (m, 1H), 2.53 (s, 3H), 2.12-1.57 (m, 6H).

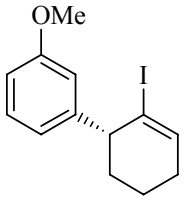
^{13}C-NMR ($CDCl_3$, 75 MH_Z): δ =198.1, 150.1, 141.3, 136.1, 129.0, 100.0, 53.0, 33.9, 29.7, 27.0, 18.1.

IR (film, cm^{-1}): 2935 (s), 1681 (vs), 1605 (s), 1412 (m), 1357 (s), 1268 (s), 938 (m), 830 (m), 589 (m), 553 (w).

MS (EI, 70 ev), *m/z* (%): 326 (100) [M^+], 311 (48), 206 (13), 199 (18), 154 (20), 128 (20), 115 (14), 77 (7).

$C_{14}H_{15}IO$	HRMS (EI)	Calcd.	326.0168
		Found	326.0162

Synthesis of 1-[(1*R*)-2-iodocyclohex-2-en-1-yl]-3-methoxybenzene ((*R*)-62h)



The reaction was carried out according to TP4 with (*R*)-2-Iodo-2-cyclohexen-1-yl acetate ((*R*)-**54a**) (266 mg, 1.0 mmol, 98% *ee*), lithium dineophylcuprate **17** (1.2 mmol) and

3-iodoanisole (281 mg, 1.2 mmol). Purification by column chromatography (SiO_2, *n*-pentane/diethyl ether = 100/1) yielded (*R*)-**62h** as a colorless oil (270 mg, 86%).

HPLC (column A, heptane : *i*PrOH = 99 : 1, 0.2 ml/min): t_R/min = 31.52 (minor), 38.05 (major); 92% *ee*.

$[\alpha]_D^{20}$ = + 27.6 (c 1.27, $CHCl_3$).

^{1}H-NMR ($CDCl_3$, 300 MH_Z): δ = 7.28 (t, *J* = 8.4 Hz, 1H), 6.84-6.78 (m, 3H), 6.68 (m, 1H), 3.84 (s, 3H), 3.70 (m, 1H), 2.17-1.63 (m, 6H).

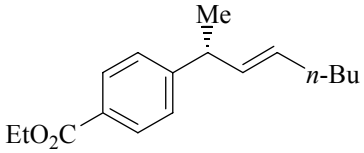
^{13}C-NMR ($CDCl_3$, 75 MH_Z): δ = 160.0, 146.2, 140.7, 129.7, 121.2, 114.8, 112.0, 101.4, 55.6, 53.0, 34.0, 29.1, 18.2.

IR (film, cm^{-1}): 2935 (vs), 2832 (w), 1660 (vs), 1583 (vs), 1464 (vs), 1485 (s), 1435 (s), 1347 (m), 1252 (vs), 1154 (s), 1052 (s), 985 (m), 779 (m), 700 (s), 568 (w).

MS (EI, 70 ev), *m/z* (%): 314 (100) [M^+], 187 (46), 172 (9), 159 (14), 144 (12), 121 (37), 115 (30), 79 (15).

$C_{13}H_{15}IO$	HRMS (EI)	Calcd.	314.0168
		Found	314.0157

Synthesis of ethyl 4-[(1*R*,2*E*)-1-methylhept-2-en-1-yl]benzoate ((*R*)-64a)



The reaction was carried out according to TP5 with ethyl 4-iodobenzoate (331 mg, 1.2 mmol), (1*S*, 2*Z*)-1-butyl-2-butenyl 2,3,4,5,6-pentafluorobenzoate ((*S*)-**63**) (1.0 mmol, 97% *ee*), and lithium dineophylcuprate **17** (1.2 mmol). Purification by flash chromatography (SiO_2, *n*-pentane/diethyl ether = 80/1) yielded (*R*)-**64a** as a colorless oil (220 mg, 85%).

Chiral HPLC (column B, heptane/*i*PrOH = 99/1, 0.2 ml/min): t_R/min = 21.87 (major), 23.86 (minor); 95% *ee*.

$[\alpha]_D^{20}$ = –35.4 (c 1.01, $CHCl_3$).

^{1}H-NMR ($CDCl_3$, 300 MH_Z): δ = 7.86-7.85 (d, *J* = 8.4 Hz, 2H), 7.20-7.18 (d, *J* = 8.4 Hz, 2H), 5.48-5.41 (m, 2H), 4.32-4.25 (q, *J* = 7.07 Hz, 2H), 3.40 (m, 1H), 1.94 (m, 2H), 1.33-1.22 (m 10H), 0.83-0.79 (t, *J* = 7.07, 3H).

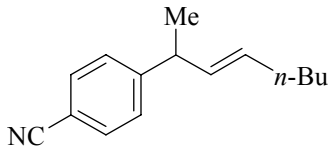
^{13}C-NMR ($CDCl_3$, 75 MH_Z): δ =167.1, 152.3, 134.4, 130.5, 130.1, 128.6, 127.5, 61.1, 42.7, 32.6, 32.0, 22.6, 21.7, 14.7, 14.1.

IR (film, cm^{-1}): 3409 (s), 2959 (s), 2932 (s), 1718 (vs), 1608 (w), 1465 (w), 1408 (w), 1367 (m), 1276 (vs), 1181 (m), 1107 (vs), 1019 (m), 856 (w), 771 (m), 707 (w).

MS (EI, 70 ev), *m/z* (%): 260 (66) [M^+], 245 (9), 231 (12), 215 (50), 190 (91), 175 (20), 162 (41), 145 (66), 131 (100), 117 (41), 105 (12), 91 (15), 77 (7).

$C_{17}H_{24}O_2$	HRMS (EI)	Calcd.	260.1776
		Found	260.1763

Synthesis of 4-[(2*E*)-1-methylhept-2-en-1-yl]benzonitrile (64b)



The reaction was carried out according to TP5 with 4-iodobenzonitrile (275 mg, 1.2 mmol), (1*S*, 2*Z*)-1-butyl-2-butenyl 2,3,4,5,6-pentafluorobenzoate ((±)-**63**) (1.0 mmol, 97% *ee*), and lithium dineophylcuprate **17** (1.2 mmol). Purification by flash chromatography (SiO_2, *n*-pentane/diethyl ether = 90/1) yielded **64b** as a colorless oil (166 mg, 78%).

^{1}H-NMR ($CDCl_3$, 300 MH_Z): δ = 7.51-7.49 (d, *J* = 8.5 Hz, 2H), 7.24-7.22 (d, *J* = 8.5 Hz, 2H), 5.45-5.40 (m, 2H), 3.40 (m, 1H), 1.94 (m, 2H), 1.33-1.22 (m 7H), 0.83-0.79 (t, *J* = 7.07, 3H).

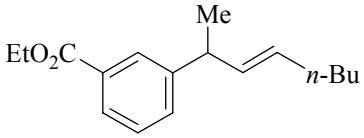
^{13}C-NMR ($CDCl_3$, 75 MH_Z): δ =151.1, 132.3, 131.2, 129.7, 127.0, 118.1, 108.7, 41.4, 31.1, 30.5, 21.2, 20.2, 12.9.

IR (film, cm^{-1}): 4306 (w), 2907 (m), 2229 (vs), 1604 (s), 1503 (s), 1411 (s), 975(s), 833 (vs), 690 (s), 563 (vs), 483 (w).

MS (EI, 70 ev), *m/z* (%): 213 (17) [M^+], 156 (46), 143 (100), 130 (17), 116 (23), 103 (7), 89 (4), 77 (4).

$C_{15}H_{19}N$	HRMS (EI)	Calcd.	213.1517
		Found	213.1499

Synthesis of ethyl 3-[(2*E*)-1-methylhept-2-en-1-yl]benzoate (64c)



The reaction was carried out according to TP5 with ethyl 3-iodobenzoate (331 mg, 1.2 mmol), (1*S*, 2*Z*)-1-butyl-2-butenyl 2,3,4,5,6-pentafluorobenzoate ((±)-**63**) (1.0 mmol, 97% *ee*), and lithium dineophylcuprate **17** (1.2 mmol). Purification by flash chromatography (SiO_2, *n*-pentane/diethyl ether = 80/1) yielded **64c** as a colorless oil (182 mg, 71%).

^{1}H-NMR ($CDCl_3$, 300 MH_Z): δ = 7.82-7.78 (m, 2H), 7.31-7.27 (m, 2H), 5.55-5.33 (m, 2H), 4.33-4.27 (q, *J* = 7.07 Hz, 2H), 3.40 (m, 1H), 1.92 (m, 2H), 1.36-1.19 (m 10H), 0.83-0.79 (t, *J* = 7.07, 3H).

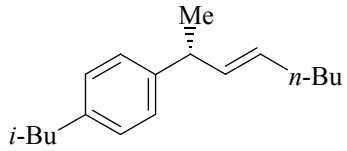
^{13}C-NMR ($CDCl_3$, 75 MH_Z): δ =165.8, 145.9, 134.3, 130.8, 129.5, 128.9, 127.3, 126.2, 59.9, 41.1, 31.2, 30.6, 21.2, 20.5, 113.3, 12.9.

IR (film, cm^{-1}): 3425 (w), 2961 (s), 2929 (s), 1721 (vs), 1604 (w), 1452 (w), 1367 (w), 1277 (vs), 1188 (m), 1107 (s), 1027 (w), 755 (w).

MS (EI, 70 ev), *m/z* (%): 260 (54) [M^+], 245 (8), 231 (14), 215 (7), 190 (100), 162 (28), 145 (44), 131 (75), 117 (32), 105 (8), 91 (12), 77 (5).

$C_{17}H_{24}O_2$	HRMS (EI)	Calcd.	260.1776
		Found	260.1776

Synthesis of 1-isobutyl-4-[(1*R*, 2*E*)-1-methylhept-2-en-1-yl]benzene ((*R*)-67)



The reaction was carried out according to TP4 with ethyl 1-iodo-4-isobutylbenzene (312 mg, 1.2 mmol), (1*S*, 2*Z*)-1-butyl-2-butenyl 2,3,4,5,6-pentafluorobenzoate ((*S*)-**63**) (1.0 mmol, 93% *ee*), and lithium dineophylcuprate **17** (1.2 mmol). Purification by flash chromatography (SiO_2, *n*-pentane/diethyl ether = 80/1) yielded (*R*)-**67** as a colorless oil (182 mg, 71%).

Chiral GC (column B, method C): t_R/min = 53.8 (major), 54.8 (minor); 91% *ee*.

$[\alpha]_D^{20}$ = –15.2 (c 1.56, $CHCl_3$).

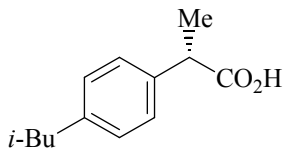
^{1}H-NMR ($CDCl_3$, 300 MH_Z): δ = 7.05-7.14 (m, 4H), 5.61-5.57 (m, 2H), 2.47-2.43 (d, *J* = 6.78 Hz, 2H), 2.06-1.98 (m, 2H), 1.85-0.91 (m, 14H), 0.92-0.87 (t, *J* = 7.07, 3H).

^{13}C-NMR ($CDCl_3$, 75 MH_Z): δ =143.8, 139.1, 135.1, 129.0, 126.8, 45.1, 41.9, 32.2, 31.8, 30.2, 22.4, 22.2, 21.6, 13.9.

MS (EI, 70 ev), *m/z* (%): 244 (31) [M^+], 229 (18), 201 (24), 187 (89), 174 (32), 145 (28), 131 (100), 117 (33), 105 (8), 91 (12), 57 (11).

$C_{18}H_{28}$	HRMS (EI)	Calcd.	244.2200
		Found	244.2191

Synthesis of (*S*)-(+)-ibuprofen ((*S*)-65)



Ozone was dubbled through a solution of (*R*)-**67** (100 mg, 0.41 mmol) in acetone (10 ml) at -78 ^oC until the solution turned blue, then nitrogen was bubbled through the reaction mixture until it became colorless again. The cooling bath was replaced with a ice bath and Jones reagent (2.67 M in Cr(VI); 26.7 g CrO_3, 23 mL conc. H_2SO_4, diluted with water to 100 mL) was added dropwise until the organge coloue persisted. The mixture was stirred at 0 ^oC for 15 min and *i*-PrOH was added until the mixture turned green. The reaction was stirred at 0 ^oC for 15 min and then rt for 1 h. The precipitate was filtered off. The solvent was evaporated and the residue was dissolved in Et_2O and washed with water, then brine, and dried (Na_2SO_4). The solvent was evaporated *in vacuo*. Evaporation of the pentanoic acid by-product *in vacuo* (oil pump) provide (*S*)-**65** as a colorless oil (56 mg, 66%).

Chiral GC (column B, method D): t_R/min = 97.2 (major), 104.4 (minor); 91% *ee*.

$[\alpha]_D^{20}$ = +84.5 (c 1.22, $CHCl_3$).

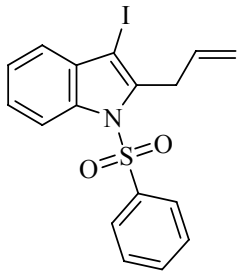
^{1}H-NMR ($CDCl_3$, 300 MH_Z): δ = 7.26-7.06 (m, 4H), 3.71 (q, *J* = 6.78, 1H), 2.47-2.43 (d, *J* = 6.78 Hz, 2H), 1.79-1.75 (m, 1H), 1.52-1.49 (d, *J* = 7.07, 3H), 0.91-0.88 (d, *J* = 7.07, 6H).

^{13}C-NMR ($CDCl_3$, 75 MH_Z): δ =180.6, 140.9, 137.0, 129.4, 127.3, 45.1, 45.0, 30.2, 22.4, 18.1.

IR (KBr, cm^{-1}): $\tilde{\nu}$ = 3600-2300 (br), 1720 (s), 1510 (m), 1342 (w), 729 (w).

12 Preparation of Polyunctionalized Heteroaryl Compounds *via* I/Cu-Exchange Reaction

Synthesis of 2-allyl-1-benzenesulfonyl-3-iodo-1H-indole (70a)



Prepared according to TP 6 from 2,3-diiodo-1-(phenylsulfonyl)-1*H*-indole (**68**) (1.02 g, 2.0 mmol), lithium dineophylcuprate **17** (2.4 mmol, 1.2 equiv) and allyl bromide (726 mg, 6.0 mmol). Reaction time: 30 min at rt. Purification by flash chromatography (*n*-pentane/diethyl ether = 4/1) yielded **70a** as a colorless oil (778 mg, 92%).

^{1}H-NMR ($CDCl_3$, 300 MHz): δ = 8.06-8.03 (m, 1H), 7.69-7.66 (m, 2H), 7.45-7.40 (m, 1H), 7.33-7.16 (m, 5H), 5.95-5.82 (m, 1H), 5.07-4.98, (m, 2H), 3.86 (dt, *J* = 5.9 Hz, *J* = 1.5 Hz, 2H).

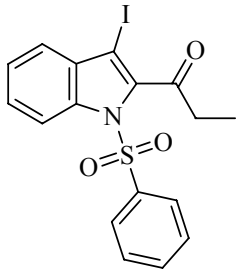
^{13}C-NMR ($CDCl_3$, 75 MHz): δ = 139.2, 139.0, 136.9, 134.3, 133.9, 132.1, 129.6, 126.9, 125.9, 124.6, 12.0, 117.5, 115.4, 75.0, 33.6.

IR (film, cm^{-1}): $\tilde{\nu}$ = 3068 (w), 1638 (w), 1552 (w), 1447 (vs), 1372 (vs), 1189 (vs), 1150 (vs), 1120 (s), 729 (vs), 753 (vs), 571 (vs).

MS (EI, 70 ev): 423 (80) [M^+], 282 (23), 154 (100), 127 (20), 77 (21).

$C_{17}H_{14}INO_2S$	HRMS (EI)	Calcd.	422.9790
		Found	422.9786

Synthesis of 1-(1-benzenesulfonyl-3-iodo-1H-indol-2-yl)-propan-1-one (70b)



Prepared according to TP 6 from 2,3-diiodo-1-(phenylsulfonyl)-1*H*-indole (**68**) (509 mg, 1.0 mmol), lithium dineophylcuprate **17** (1.2 mmol, 1.2 equiv), DMAP (12 mg. 0.1 mmol) and propionyl chloride (278 mg, 3.0 mmol, 3.0 equiv). Reaction time: 30 min at rt. Purification by flash chromatography (*n*-pentane/diethyl ether = 4/1) yielded **70b** as a white solid (369 mg, 84%).

mp.: 95 °C

^{1}H-NMR ($CDCl_3$, 300 MHz): δ = 8.06-8.04 (d, *J* = 8.3 Hz, 1H), 7.89-7.86 (m, 2H), 7.59-7.35 (m, 6H), 3.16-3.08 (q, *J* = 7.3 Hz, 2H), 1.40-1.35 (t, *J* = 7.3 Hz, 3H).

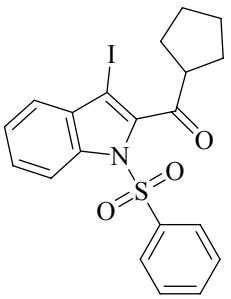
^{13}C-NMR ($CDCl_3$, 75 MHz): δ = 199.4, 140.3, 136.5, 136.0, 134.7, 132.5, 129.6, 127.8, 127.7, 125.5, 123.5, 115.3, 72.4, 38.7, 8.5.

IR (KBr, cm^{-1}): $\tilde{\nu}$ = 3435 (w), 2906 (w), 1773 (s), 1704 (vs), 1445 (s), 1374 (vs), 1247 (s), 1178 (vs), 1124 (s), 1090 (s), 963 (w), 731 (s), 585 (s), 569 (w).

MS (EI, 70 ev): 439 (95) [M^+], 410 (50), 298 (40), 270 (100), 242 (18), 143 (16), 114 (47), 77 (20).

$C_{17}H_{14}INO_3S$	HRMS (EI)	Calcd	438.9739
		Found	438.9735

Synthesis (1-benzenesulfonyl-3-iodo-1H-indol-2-yl)-cyclopentyl-methanone (70c)



Prepared according to TP 6 from 2,3-diiodo-1-(phenylsulfonyl)-1*H*-indole (**68**) (1.53 g, 3.0 mmol), lithium dineophylcuprate **17** (3.6 mmol, 1.2 equiv), DMAP (36 mg. 0.3 mmol) and cyclopentane carbonyl chloride (1.26 g, 9.0 mmol). Reaction time: 30 min at rt. Purification by flash chromatography (*n*-pentane/diethyl ether = 10/1) yielded **70c** as a white solid (1.2 g, 86%).

mp.: 153 °C

^{1}H-NMR ($CDCl_3$, 300 MHz): δ = 7.95-7.92 (d, *J* = 8.3 Hz, 1H), 7.64-7.60 (m, 2H), 7.38-7.20 (m, 6H), 3.73-3.68 (quint, *J* = 8.07 Hz , 1H), 1.92-1.56, (m, 8H).

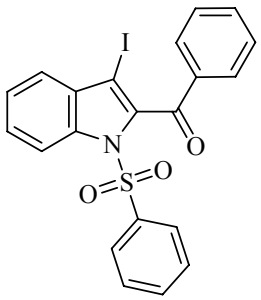
^{13}C-NMR ($CDCl_3$, 75 MHz): δ = 200.9, 141.0, 136.4, 136.2, 134.6, 132.9, 129.4, 128.0, 127.6, 125.7, 123.8, 115.7, 74.8, 54.0, 30.0, 26.5.

IR (KBr, cm^{-1}): $\tilde{\nu}$ = 3436 (s), 1683 (s), 1521 (w), 1448 (s), 1373 (vs), 1183 (vs), 1176 (vs), 1089 (s), 756 (s), 728 (w), 596 (s), 571 (s).

MS (EI, 70 ev): 479 (40) [M^+], 410 (100), 383 (15), 270 (50), 143 (10), 114 (12), 77 (8).

$C_{20}H_{18}INO_3S$	HRMS (EI)	Calcd.	479.0052
		Found	479.0062

Synthesis (1-benzenesulfonyl-3-iodo-1H-indol-2-yl)-phenyl-methanone (70d)



Prepared according to TP 6 from 2,3-diiodo-1-(phenylsulfonyl)-1*H*-indole (**68**) (1.02 g, 2.0 mmol), lithium dineophylcuprate **17** (2.4 mmol), DMAP (24 mg. 0.3 mmol) and benzoyl chloride (840 mg, 6.0 mmol). Reaction time: 30 min at rt. Purification by flash chromatography (*n*-pentane/diethyl ether = 10/1) yielded **70d** as a colorless solid (818 mg, 84%).

mp.: 158 °C

^{1}H-NMR ($CDCl_3$, 300 MHz): δ = 7.97-7.90 (d, *J* = 8.3 Hz 1H), 7.89-7.83 (m, 4H), 7.58-7.27 (m, 9H).

^{13}C-NMR ($CDCl_3$, 75 MHz): δ = 189.5, 137.9, 137.1, 135.7, 134.7, 134.5, 132.2, 130.4, 129.6, 129.2, 127.9, 127.6, 125.3, 123.3, 114.9, 89.2, 73.0.

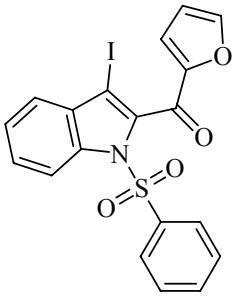
IR (KBr, cm^{-1}): $\tilde{\nu}$ = 3435 (w), 1665 (w), 1596 (w), 1581 (w), 1447 (s), 1372 (vs), 1319 (s), 1253 (s), 1178 (vs), 1089 (s), 953 (w), 135 (s) 686 (vs), 604 (s), 596 (s).

MS (EI, 70 ev): 487 (80) [M^+], 346 (65), 219 (100), 190 (55), 77 (60).

$C_{21}H_{14}INO_3S$ HRMS (EI) Calcd. 486.9739

Found: 486.9703

Synthesis (1-benzenesulfonyl-3-iodo-1H-indol-2-yl)-furan-2-yl-methanone (70e)



Prepared according to TP 6 from 2,3-diiodo-1-(phenylsulfonyl)-1*H*-indole (**68**) (255 mg, 0.5 mmol), lithium dineophylcuprate **17** (0.6 mmol), DMAP (6 mg. 0.05 mmol) and furoyl chloride (195 mg, 1.5 mmol). Reaction time: 30 min at rt. Purification by flash chromatography (*n*-pentane/diethyl ether = 4/1) yielded **70e** as a white solid (148 mg, 78%).

mp.: 155 °C

^{1}H-NMR ($CDCl_3$, 300 MHz): δ = 8.00-7.97 (d, *J* = 8.3 Hz, 1H), 7.86-7.85 (m, 2H), 7.63 (d, *J* = 1.7, 1H), 7.46-7.26 (m, 6H), 7.16-7.14 (d, *J* = 3.4, 1H), 6.54-6.53 (dd, *J* = 3.4, *J* = 1.7, 1H).

^{13}C-NMR ($CDCl_3$, 75 MHz): δ = 175.8, 152.8, 148.5, 137.1, 137.0, 136.0, 134.8, 132.2, 129.6, 127.9, 125.4, 123.6, 122.1, 115.1, 113.4, 74.3.

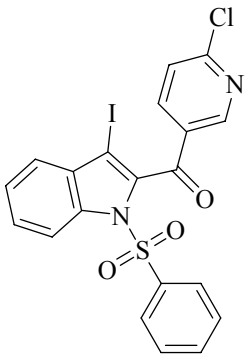
IR (KBr, cm^{-1}): $\tilde{\nu}$ = 3435 (vs), 2924 (w), 1650 (vs), 1565 (s), 1447 (s), 1460 (w), 1373 (vs), 1176 (vs), 1089 (s), 1017 (w), 757 (w), 590 (s), 571 (w).

MS (EI, 70 ev): 477 (100) [M^+], 336 (80), 269 (20), 209 (30), 153 (23), 114 (7), 77 (10).

$C_{19}H_{12}INO_4S$ HRMS (EI) Calcd. 476.9532

Found 476.9568

Synthesis of (1-benzenesulfonyl-3-iodo-1H-indol-2-yl)-(6-chloro-pyridin-3-yl)-methanone (70f)



Prepared according to TP 6 from 2,3-diiodo-1-(phenylsulfonyl)-1*H*-indole (**68**) (2.55 g, 5 mmol), lithium dineophylcuprate **17** (6 mmol), DMAP (60 mg. 0.5 mmol) and 6-chloronicotinoyl chloride (2.6 g, 15 mmol). Reaction time: 30 min at rt. Purification by flash chromatography (*n*-pentane/diethyl ether = 5/1) yielded **70f** as a light yellow solid (2.04 g, 78%).

mp.: 61-62 °C

^{1}H-NMR ($CDCl_3$, 300 MHz): δ = 8.78-8.77 (d, *J* = 2.3 Hz, 1H), 8.12-8.08 (dd, *J* = 8.4 Hz, *J* = 2.3 Hz, 1H), 7.99-7.96 (d, *J* = 8.3 Hz, 1H), 7.83-7.80 (m, 2H), 7.52-7.29 (m, 7H).

^{13}C-NMR ($CDCl_3$, 75 MHz): δ = 186.9, 156.5, 151.8, 139.7, 136.8, 136.6, 136.1, 135.0, 132.2, 131.9, 129.7, 127.8, 125.7, 125.1, 123.7, 115.2, 75.0.

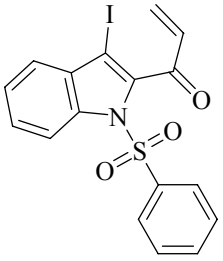
IR (KBr, cm^{-1}): $\tilde{\nu}$ = 3435 (vs), 2926 (w), 1673 (vs), 1581 (vs), 1447 (s), 1375 (s), 1364 (s), 1254 (m), 1176 (vs), 1089 (s), 1020 (w), 952 (m), 757 (m), 570 (m).

MS (EI, 70 ev): 522 (20) [M^+], 380 (41), 254 (55), 226 (17), 191 (23), 164 (20), 141 (32), 114 (30), 77 (100).

$C_{20}H_{12}ClIN_2O_3S$ HRMS (EI) Calcd. 521.9302

Found 521.9277

Synthesis of 1-(1-benzenesulfonyl-3-iodo-1H-indol-2-yl)-propenone (70g)

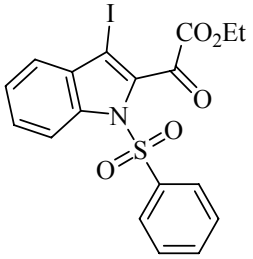


Prepared according to TP 6 from 2,3-diiodo-1-(phenylsulfonyl)-1*H*-indole (**68**) (255 mg, 0.5 mmol), lithium dineophylcuprate **17** (0.6 mmol, 1.2 equiv), DMAP (6 mg. 0.05 mmol) and acryloyl chloride (136 mg, 1.5 mmol). Reaction time: 30 min at rt. Purification by flash chromatography (*n*-pentane/diethyl ether = 3/1) yielded **70g** as a colorless oil (146 mg, 67%).

^{1}H-NMR ($CDCl_3$, 300 MHz): δ = 7.96-7.94 (d, *J* = 8.3 Hz, 1H), 7.76-7.79 (m, 2H), 7.46-7.23 (m, 6H), 6.76 (dd, *J* = 17.4, *J* = 10.4, 1H), 6.15-6.06 (m, 2H).
^{13}C-NMR ($CDCl_3$, 75 MHz): δ = 188.8, 137.9, 137.3, 136.8, 136.1, 134.7, 132.6, 129.6, 127.9, 127.8, 125.45, 123.6, 115.2, 74.4.
IR (film, cm^{-1}): $\tilde{\nu}$ = 3072 (w), 2964 (w), 1728 (w), 1698 (w), 1660 (vs), 1519 (w), 1403 (s), 1378 (vs), 1177 (vs), 1089 (s), 1020 (s), 968 (s), 750 (s), 590 (s), 571 (s).
MS (EI, 70 ev): 437 (20) [M^+], 296 (100), 270 (10), 141 (13), 114 (12), 77 (5).

$C_{17}H_{12}INO_3S$	HRMS (EI)	Calcd.	436.9583
		Found	436.9573

Synthesis of (1-benzenesulfonyl-3-iodo-1H-indol-2-yl)-oxo-acetic acid ethyl ester (70h)



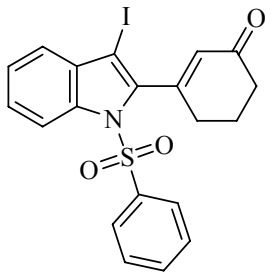
Prepared according to TP 6 from 2,3-diiodo-1-(phenylsulfonyl)-1*H*-indole (**68**) (255 mg, 0.5 mmol), lithium dineophylcuprate **17** (0.6 mmol), DMAP (6 mg. 0.05 mmol) and ethyl oxayl chloride (205 mg, 1.5 mmol). Reaction time: 30 min at rt. Purification by flash

chromatography (*n*-pentane/diethyl ether = 4/1) yielded **70h** as a colorless oil (181 mg, 75%).

^{1}H-NMR ($CDCl_3$, 300 MHz): δ = 7.88-7.86 (d, *J* = 8.3 Hz, 1H), 7.61-7.59 (m, 2H), 7.46-7.24 (m, 6H), 4.43-4.35 (q, *J* = 7.3 Hz, 2H), 1.39-1.36 (t, *J* = 7.3 Hz, 3H).
^{13}C-NMR ($CDCl_3$, 75 MHz): δ = 179.0, 160.2, 136.7, 136.0, 134.9, 133.0, 129.7, 129.4, 127.6, 127.5, 125.9, 124.7, 115.3, 81.2, 63.5, 14.3.
IR (film, cm^{-1}): $\tilde{\nu}$ = 3435 (s), 2983 (w), 1761 (s), 1737 (s), 1698 (s), 1447 (s), 1366 (vs), 1232 (s), 1174 (vs), 1152 (s), 1087 (vs), 1017 (s), 990 (s), 727 (w), 600 (s).
MS (EI, 70 ev): 483 (21) [M^+], 410 (100), 269 (40), 114 (17), 77 (5).

$C_{18}H_{14}INO_5S$	HRMS (EI)	Calcd.	482.9637
		Found:	482.9648

Synthesis of 3-(1-benzenesulfonyl-3-iodo-1H-indol-2-yl)-cyclohex-2-enone (70i)



Prepared according to TP 6 from 2,3-diiodo-1-(phenylsulfonyl)-1*H*-indole (**68**) (255 mg, 0.5 mmol), lithium dineophylcuprate **17** (0.6 mmol), DMAP (6 mg. 0.05 mmol) and 3-iodo-cyclohex-2-enone (333 mg, 1.5 mmol). Reaction time: 30 min at rt. Purification by flash chromatography (*n*-pentane/diethyl ether = 5/1) yielded **70i** as a white solid (157 mg, 66%).

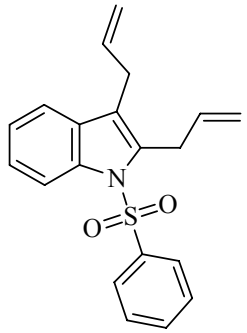
mp.: 152 °C
^{1}H-NMR ($CDCl_3$, 300 MHz): δ = 8.10-8.07 (d, *J* = 8.3 Hz, 1H), 7.57-7.54 (m, 2H), 7.46-7.26 (m, 6H), 6.00 (s, 1H), 2.98-2.17 (m, 6H).
^{13}C-NMR ($CDCl_3$, 75 MHz): δ = 199.6, 154.9, 140.2, 137.4, 137.1, 134.7, 133.0, 132.0, 131.9, 129.6, 127.4, 127.1, 125.6, 123.5, 116.0, 38.2, 32.0, 23.2.

IR (KBr, cm^{-1}): $\tilde{\nu}$ = 3436 (vs), 2941 (w), 1657 (vs), 1582 (w), 1445 (s), 1375 (vs), 1184 (vs), 1090 (w), 757 (s), 598 (s), 571 (s), 556 (s).

MS (EI, 70 ev): 477 (100) [M^+], 336 (70), 209 (50), 180 (67), 153 (15), 77 (18).

$C_{20}H_{16}INO_3S$	HRMS (EI)	Calcd.	476.9896
		Found	476.9890

Synthesis of 2,3-diallyl-1-benzenesulfonyl-1H-indole (72a)



Prepared according to TP 6 from 2-allyl-1-benzenesulfonyl-3-iodo-1H-indole (**70a**) (133 mg, 0.3 mmol), lithium dineophylcuprate **17** (0.36 mmol), and allyl bromide (109 mg, 0.9 mmol). Reaction time: 30 min at -78 °C. Purification by flash chromatography (*n*-pentane/diethyl ether = 4/1) yielded **72a** as a colorless oil (89 mg, 88%).

^{1}H-NMR ($CDCl_3$, 300 MHz): δ = 8.11-8.09 (d, *J* = 8.5 Hz, 1H), 7.63-7.62 (d, *J* = 7.6 Hz, 2H), 7.44-7.12 (m, 7H), 5.97-5.71 (m, 2H), 4.96-4.79, (m, 4H), 3.73-3.69 (d, *J* = 5.8 Hz, 2H), 3.30-3.28 (d, *J* = 5.8 Hz, 2H).

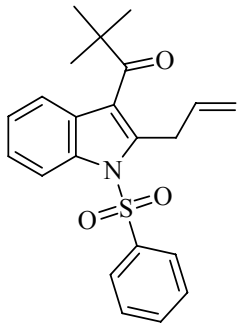
^{13}C-NMR ($CDCl_3$, 75 MHz): δ = 139.4, 137.1, 135.6, 135.5, 135.4, 133.9, 130.9, 129.4, 126.7, 124.7, 123.9, 120.0, 119.3, 116.6, 116.1, 115.6, 30.5, 28.7.

IR (film, cm^{-1}): $\tilde{\nu}$ = 3076 (w), 1638 (w), 1583 (w), 1475 (w), 1448 (vs), 1365 (vs), 1172 (vs), 1189 (s), 1121(s), 988(s), 914 (s), 748 (vs), 728 (vs) 589 (vs), 574 (vs).

MS (EI, 70 ev): 337 (70) [M^+], 295 (3), 196 (100), 180 (49), 168 (42), 154 (71), 142 (17), 130 (25), 77 (27).

$C_{20}H_{19}INO_2S$	HRMS (EI)	Calcd.	337.1136
		Found	337.1157

Synthesis of 1-(2-allyl-1-benzenesulfonyl-1H-indol-3-yl)-2,2-dimethyl-propan-1-one (72b)



Prepared according to TP 6 from 2-allyl-1-benzenesulfonyl-3-iodo-1H-indole (**70a**) (212 mg, 0.5 mmol), lithium dineophylcuprate **17** (0.6 mmol), NMP (0.2 mL), DMAP (6 mg, 0.05 mmol) and pivaloyl chloride (180 mg, 1.5 mmol). Reaction time: 30 min at -78 °C. Purification by flash chromatography (*n*-pentane/diethyl ether = 4/1) yielded **72b** as a colorless oil (130 mg, 68%).

^{1}H-NMR ($CDCl_3$, 300 MHz): δ = 8.07-8.06 (d, *J* = 8.1 Hz, 1H), 7.65-7.64 (d, *J* = 7.1 Hz, 2H), 7.47-7.42 (m, 1H), 7.35-7.12 (m, 5H), 5.95-5.84 (m, 2H), 5.04-4.97, (m, 4H), 3.64-3.62 (d, *J* = 5.9 Hz, 2H), 1.11 (s, 9H).

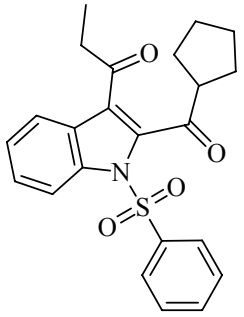
^{13}C-NMR ($CDCl_3$, 75 MHz): δ = 211.7, 139.0, 136.7, 136.5, 135.2, 134.3, 129.7, 128.4, 126.8, 125.3, 125.1, 124.5, 120.7, 117.7, 115.7, 45.6, 32.1, 27.6.

IR (film, cm^{-1}): $\tilde{\nu}$ = 3071 (w), 2969 (s), 1684 (vs), 1584 (w), 1568 (w), 1477 (w), 1449 (vs), 1374 (vs), 1197 (vs), 1174 (s), 1089(s), 991(s), 923 (s), 750 (vs), 729 (vs) 599 (vs), 576 (vs).

MS (EI, 70 ev): 381 (11) [M^+], 366 (6), 324 (100), 240 (5), 183 (45), 154 (27), 77 (8).

$C_{20}H_{19}INO_2S$	HRMS (EI)	Calcd.	381.1399
		Found	381.1405

Synthesis of 1-(1-benzenesulfonyl-2-cyclopentanecarbonyl-1H-indol-3-yl)-propan -1-one (72c)

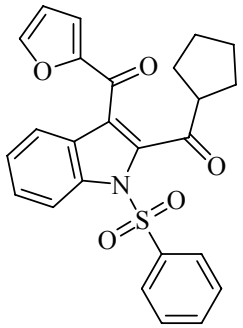


Prepared according to TP 6 from (1-benzenesulfonyl-3-iodo-1H-indol-2-yl)-cyclopenty -methanone (**70c**) (239 mg, 0.5 mmol), lithium dineophylcuprate **17** (0.6 mmol), DMAP (6.0 mg, 0.05 mmol), NMP (0.2 ml) and propionyl chloride (139 mg, 1.5 mmol). Reaction time: 30 min at -78 °C. Purification by flash chromatography (*n*-pentane/diethyl ether = 4/1) yielded **72c** as a colorless oil (139 mg, 68%).

^{1}H-NMR ($CDCl_3$, 300 MHz): δ = 8.03-8.01 (d, *J* = 8.4 Hz, 1H), 7.88-7.87 (d, *J* = 8.0 Hz, 2H), 7.79-7.78 (d, *J* = 8.2 Hz, 1H), 7.48-7.26 (m, 5H), 3.50 (quint, *J* = 8.4 Hz , 1H), 2.85-2.81 (q, *J* = 7.3 Hz, 2H), 2.00-1.51, (m, 8H), 1.13-1.09 (t, *J* = 7.3 Hz, 3H).
^{13}C-NMR ($CDCl_3$, 75 MHz): δ = 201.9, 196.2, 140.7, 135.6, 134.1, 133.5, 128.3, 126.7, 125.1, 124.1, 121.0, 120.7, 113.7, 52.9, 35.5, 28.5, 24.9, 6.7.
IR (film, cm^{-1}): $\tilde{\nu}$ = 3329 (w), 2958 (vs), 1698 (vs), 1674 (vs), 1519 (s), 1448 (s), 1382 (vs), 1177 (vs), 1089 (s), 974 (s), 749 (s), 725 (s), 685 (w), 587 (s), 571 (s).
MS (EI, 70 ev): 409 (5) [M^+], 340 (100), 284 (20), 268 (65), 240 (18), 200 (60), 170 (24), 141 (16), 77 (40).

$C_{23}H_{23}NO_4S$	HRMS (EI)	Calcd.	409.1348
		Found	409.1373

Synthesis of (1-benzenesulfonyl-2-cyclopentanecarbonyl-1H-indol-3-yl)-furan-2-yl-methanone (72d)



Prepared according to TP 6 from (1-benzenesulfonyl-3-iodo-1H-indol-2-yl)-cyclopentyl-methanone (**70c**) (239 mg, 0.5 mmol), lithium dineophylcuprate **17** (0.6 mmol), DMAP (6.0 mg, 0.05 mmol), NMP (0.2 ml) and 2-furoyl chloride (195 mg, 1.5 mmol). Reaction time: 30 min at -78 °C. Purification by flash chromatography (*n*-pentane/diethyl ether = 4/1) yielded **72d** as a colorless oil (141 mg, 63%).

^{1}H-NMR ($CDCl_3$, 300 MHz): δ = 8.02 (d, *J* = 8.5 Hz, 1H), 8.00-7.95 (m, 2H), 7.57 (m, 1 H), 7.53-7.18 (m, 6H), 6.96 (d, *J* = 3.4 Hz, 1H), 6.48 (dd, *J* = 3.4 Hz, *J* = 1.5 Hz, 1H), 3.34 (quint, *J* = 8.2 Hz , 1H), 2.91-1.50 (m, 8H).

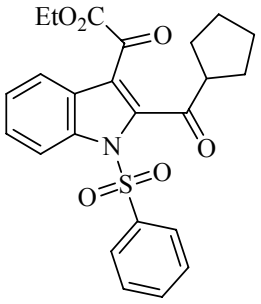
^{13}C-NMR ($CDCl_3$, 75 MHz): δ = 201.2, 177.6, 152.9, 148.2, 141.0, 137.5, 136.0, 134.8, 129.6, 128.1, 128.0, 127.2, 125.2, 123.0, 122.2, 121.8, 115.4, 113.0, 54.4, 30.1, 26.4.

IR (film, cm^{-1}): $\tilde{\nu}$ = 3435 (vs), 2954 (s), 1696 (s), 1638 (vs), 1565 (w), 1462 (s), 1447 (s), 1378 (s), 1246 (w), 1186 (vs), 1086 (w), 752 (s), 726 (w), 685 (w), 583 (s), 568 (s).

MS (EI, 70 ev): 447 (5) [M^+], 378 (100), 306 (90), 238 (68), 209 (44), 170 (15), 141 (36), 95 (20), 77 (60).

$C_{25}H_{21}NO_5S$	HRMS (EI)	Calcd.	447.1140
		Found	447.1130

Synthesis of (1-benzenesulfonyl-2-cyclopentanecarbonyl-1H-indol-3-yl)-oxo-acetic acid ethyl ester (72e)



Prepared according to TP 6 from (1-benzenesulfonyl-3-iodo-1H-indol-2-yl)-cyclopentyl-methanone (**70c**) (239 mg, 0.5 mmol), lithium dineophylcuprate **17** (0.6 mmol), DMAP (6.0 mg, 0.05 mmol), NMP (0.2 ml) and oxalyl chloride (195 mg, 1.5 mmol). Reaction time: 30 min at -78 ^{o}C. Purification by flash chromatography (*n*-pentane/diethyl ether = 4/1) yielded **72e** as a colorless oil (161 mg, 71%).

^{1}H-NMR ($CDCl_3$, 300 MHz): δ = 8.29-8.28 (d, *J* = 8.5 Hz, 1H), 8.13-8.09 (m, 2H), 8.05-8.02 (m, 1 H), 7.80-7.52 (m, 5H), 4.63 (q, *J* = 7.2 Hz, 2H), 3.85 (quint, *J* = 8.4 Hz , 1H), 2.29-1.64, (m, 8H), 1.64 (t, *J* = 7.2 Hz, 3H).

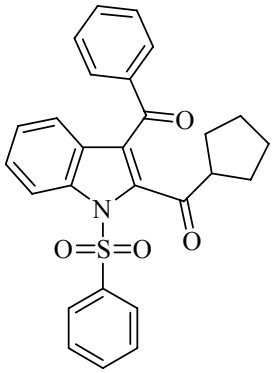
^{13}C-NMR ($CDCl_3$, 75 MHz): δ = 201.6, 182.4, 163.6, 145.1, 136.5, 135.8, 135.3, 129.8, 128.0, 127.5, 127.4, 126.9, 126.1, 122.3, 115.2, 63.1, 54.3, 29.8, 26.3, 14.4.

IR (film, cm^{-1}): $\tilde{\nu}$ = 3325 (s), 2960 (s), 1738 (vs), 1704 (vs), 1681 (s), 1668 (vs), 1582 (w), 1516 (w), 1448 (s), 1380 (vs), 1229 (s), 1177 (vs), 1086 (s), 991 (w), 754 (s), 726 (s), 685 (w), 593 (s), 569 (s).

MS (EI, 70 ev): 453 (8) [M^{+}], 380 (100), 362 (9), 312 (18), 284 (14), 240 (15), 170 (24), 141 (56), 77 (60).

$C_{24}H_{23}NO_6S$	HRMS (EI)	Calcd.	453.1246
		Found	453.1211

Synthesis of (1-benzenesulfonyl-3-benzoyl-1H-indol-2-yl)-cyclopentyl-methanone (72f)



Prepared according to TP 6 from (1-benzenesulfonyl-3-iodo-1H-indol-2-yl)-cyclopentyl -methanone (**70c**) (239 mg, 0.5 mmol), lithium dineophylcuprate **17** solution (0.6 mmol), DMAP (6.0 mg, 0.05 mmol), NMP (0.2 ml) and benzoyl chloride (420 mg, 1.5 mmol). Reaction time: 30 min at -78 °C. Purification by flash chromatography (*n*-pentane/diethyl ether = 4/1) yielded **72f** as a white solid (167 mg, 73%).

mp.: 122 °C

^{1}H-NMR ($CDCl_3$, 300 MHz): δ = 8.15 (d, *J* = 8.5 Hz, 1H), 8.08-8.05 (m, 2H), 7.75-7.72 (m, 2H), 7.68-7.62 (m, 2H), 7.57-7.43 (m, 5H), 7.26-7.17 (m, 2H), 3.55 (quint, *J* = 8.5 Hz , 1H), 2.11-1.55, (m, 8H).

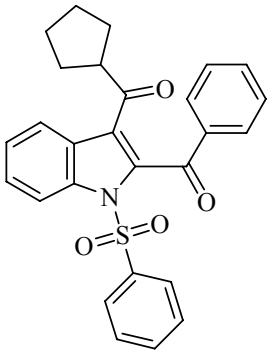
^{13}C-NMR ($CDCl_3$, 75 MHz): δ = 201.2, 191.4, 141.5, 138.1, 137.1, 136.1, 134.8, 134.1, 130.1, 129.6, 129.0, 128.4, 128.1, 127.1, 125.3, 124.7, 122.4, 115.6, 53.9, 30.1, 26.4.

IR (KBr, cm^{-1}): $\tilde{\nu}$ = 3436 (s), 2598 (s), 1693 (vs), 1663 (vs), 1596 (w), 1549 (w), 1448 (s), 1375 (vs), 1241 (s), 1177 (vs), 1089 (w), 974 (w), 756 (s), 685 (w), 584 (s), 569 (s).

MS (EI, 70 ev): 457 (18) [M^+], 388 (80), 316 (91), 248 (100), 220 (27), 190 (14), 165 (12), 141 (26), 105 (65), 77 (76).

$C_{27}H_{23}NO_4S$	HRMS (EI)	Calcd.	457.1348
		Found	457.1357

Synthesis of (1-benzenesulfonyl-2-benzoyl-1H-indol-3-yl)-cyclopentyl-methanone (72g)



Prepared according to TP 6 from (1-benzenesulfonyl-3-iodo-1H-indol-2-yl)-phenyl-methanone (**70d**) (162 mg, 0.3 mmol), lithium dineophylcuprate **17** (0.36 mmol), DMAP (4.8 mg, 0.03 mmol), NMP (0.1 ml) and cyclopentane carbonyl chloride (133 mg, 1.0 mmol). Reaction time: 30 min at -78 ^{o}C. Purification by flash chromatography (*n*-pentane/diethyl ether = 4/1) yielded **72g** as a white solid (89 mg, 65%).

mp.: 191 ^{o}C

^{1}H-NMR ($CDCl_3$, 300 MHz): δ = 8.06-7.94 (m, 4H), 7.87-7.83 (m, 2H), 7.55 – 7.29 (m, 8H), 3.33-3.23 (m, 1H), 1.36-1.76, (m, 8H).

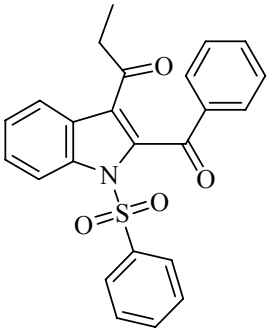
^{13}C-NMR ($CDCl_3$, 75 MHz): δ = 199.6, 190.1, 140.2, 137.7, 137.4, 135.5, 135.0, 134.3, 129.8, 129.7, 129.6, 129.5, 129.2, 128.4, 128.0, 126.8, 122.7, 114.5, 50.5, 29.8, 26.4.

IR (KBr, cm^{-1}): $\tilde{\nu}$ = 3436 (s), 1672 (vs), 1597 (w), 1522 (w), 1447 (s), 1378 (vs), 1190 (vs), 1177 (vs), 1088 (s), 1015 (w), 955 (w), 746 (s), 736 (w), 686 (s), 584 (s), 570 (s).

MS (EI, 70 ev): 457 (20) [M^{+}], 388 (100), 316 (45), 248 (50), 219 (15), 141 (21), 105 (45), 77 (61).

$C_{27}H_{23}NO_4S$	HRMS (EI)	Calcd.	457.1348
		Found	457.1309

Synthesis of 1-(1-benzenesulfonyl-2-benzoyl-1H-indol-3-yl)-propan-1-one (70h)



Prepared according to TP 1 from (1-benzenesulfonyl-3-iodo-1H-indol-2-yl)-phenyl-methanone (**70d**) (244 mg, 0.5 mmol), lithium dineophylcuprate **17** (0.6 mmol), DMAP (6.0 mg, 0.05 mmol), NMP (0.2 ml) and propionyl chloride (139 mg, 1.5 mmol). Reaction time: 30 min at -78 °C. Purification by flash chromatography (*n*-pentane/diethyl ether = 4/1) yielded **72h** as a white solid (146 mg, 70%).

mp.: 159 °C

^{1}H-NMR ($CDCl_3$, 300 MHz): δ = 8.07-7.85 (m, 6H), 7.57-7.30 (m, 8H), 2.69 (q, *J* = 7.0 Hz, 2H), 0.97 (t, *J* = 7.0 Hz, 3 H).

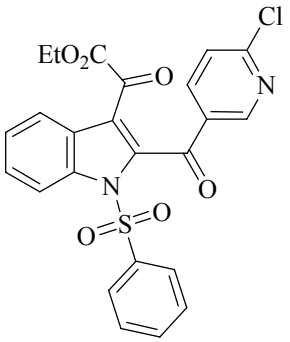
^{13}C-NMR ($CDCl_3$, 75 MHz): δ = 196.8, 190.6, 140.3, 137.7, 137.4, 135.3, 135.1, 134.4, 129.8, 129.6, 129.3, 128.2, 126.9, 126.6, 125.7, 123.0, 122.1, 114.6, 36.5, 8.0.

IR (film, cm^{-1}): $\tilde{\nu}$ = 3435 (w), 1682 (vs), 1657 (vs), 1598 (w), 1583 (w), 1521 (s), 1448 (s), 1368 (s), 1319 (s), 1268 (s), 1188 (vs), 1089 (s), 959 (w), 745 (s) 686 (s), 574 (s), 566 (vs).

MS (EI, 70 ev): 417 (80) [M^+], 388 (71), 276 (74), 248 (75), 105 (90), 77 (100).

$C_{24}H_{19}NO_4S$	HRMS (EI)	Calcd.	417.1035
		Found	417.1026

Synthesis of [1-benzenesulfonyl-2-(6-chloro-pyridine-3-carbonyl)-1H-indol-3-yl] -oxo-acetic acid ethyl ester (70i)



Prepared according to TP 6 from (1-benzenesulfonyl-3-iodo-1H-indol-2-yl)-phenyl-methanone (**70f**) (1.0 g, 1.92 mmol), lithium dineophylcuprate **17** (2.3 mmol), DMAP (24 mg, 0.2 mmol), NMP (0.8 ml) and oxalyl chloride (680 mg, 5 mmol). Reaction time: 30 min at -78 ^{o}C. Purification by flash chromatography (*n*-pentane/diethyl ether = 4/1) yielded **72i** as a white solid (678 mg, 71%).

mp.: 52-54 ^{o}C

^{1}H-NMR ($CDCl_3$, 300 MHz): δ = 8.76 (d, *J* = 2.1 Hz, 1H), 8.04-8.02 (dd, *J* = 8.35 Hz, *J* = 2.1 Hz, 1H), 7.99-7.97 (d, *J* = 8.58 Hz, 1H), 7.95-7.94 (d, *J* = 7.94 Hz, 1H), 7.78-7.76 (d, *J* = 8.58 Hz, 2H), 7.50-7.47 (t, *J* = 7.40 Hz, 1H), 7.40-7.35 (m, 4H), 7.32-7.30 (t, *J* = 7.15 Hz, 1H), 4.12-4.08 (q, *J* = 6.91 Hz, 2H), 1.18-1.15 (t, *J* = 6.91 Hz, 3 H).

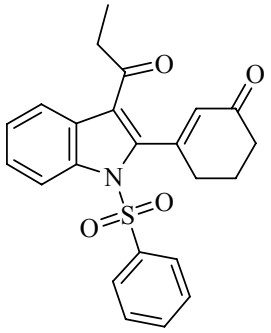
^{13}C-NMR ($CDCl_3$, 75 MHz): δ = 186.6, 181.3, 163.0, 156.4, 151.1, 141.6, 139.1, 136.5, 135.6, 135.6, 132.8, 130.0, 128.0, 126.8, 126.6, 125.0, 123.1, 119.3, 114.8, 63.3, 14.2.

IR (KBr, cm^{-1}): $\tilde{\nu}$ = 3436 (vs), 1735 (s), 1677 (vs), 1582 (m), 1448 (w), 1380 (vs), 1365 (s), 1291 (m), 1152 (s), 1107 (s), 1040 (s), 952 (w) 753 (w), 684 (w), 569 (m).

MS (EI, 70 ev): 356 (8) $[M\text{-}C_6H_3ClNO]^+$, 283 (100), 170 (11), 140 (15), 112 (9), 76 (4).

$C_{24}H_{18}ClN_2O_6S$ $[M+H]^+$	HRMS (FAB)	Calcd.	497.0574
		Found	497.0528

Synthesis of 3-(1-benzenesulfonyl-3-propionyl-1H-indol-2-yl)-cyclohex-2-enone (72j)



Prepared according to TP 6 from 3-(1-benzenesulfonyl-3-iodo-1H-indol-2-yl)-cyclohex-2-enone (**70i**) (477 mg, 1.0 mmol), lithium dineophylcuprate **17** (1.2 mmol, 1.2 equiv), DMAP (12 mg, 0.1 mmol, 0.1 equiv), NMP (0.4 ml) and propionyl chloride (278 mg, 3.0 mmol, 3.0 equiv). Reaction time: 30 min at -78 ^{o}C. Purification by flash chromatography (*n*-pentane/diethyl ether = 4/1) yielded **72j** as a light yellow oil (326 mg, 80%).

^{1}H-NMR ($CDCl_3$, 300 MHz): δ = 8.19 (d, *J* = 8.4 Hz, 1H), 7.62-7.60 (m, 2H), 7.38-7.15 (m, 6H), 5.72 (s, 1H), 3.00-2.17 (m, 6H), 1.07 (t, *J* = 7.3 Hz, 3H).

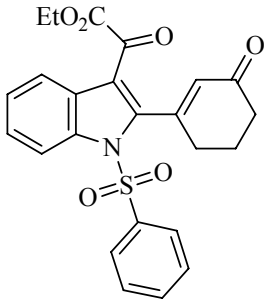
^{13}C-NMR ($CDCl_3$, 75 MHz): δ = 197.3, 153.7, 139.8, 136.6, 135.3, 133.7, 130.2, 128.4, 127.8, 126.3, 125.8, 125.7, 125.2, 124.2, 120.9, 114.0, 36.6, 35.1, 31.0, 21.8, 7.2.

IR (film, cm^{-1}): $\tilde{\nu}$ = 3435 (s), 2935 (w), 1676 (vs), 1666 (vs), 1582 (w), 1448 (s), 1386 (vs), 1186 (vs), 1087 (s), 756 (s), 591 (s), 581 (s), 565 (s).

MS (EI, 70 ev): 407 (6) [M^{+}], 379 (4), 266 (45), 238 (100), 210 (11), 180 (12), 77(14).

$C_{23}H_{21}NO_4S$	HRMS (EI)	Calcd.	407.1191
		Found	407.1179

Synthesis of [1-benzenesulfonyl-2-(3-oxo-cyclohex-1-enyl)-1H-indol-3-yl]-oxo-acetic acid ethyl ester (72k)

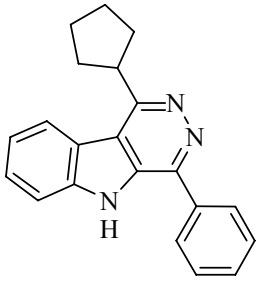


Prepared according to TP 6 from 3-(1-benzenesulfonyl-3-iodo-1H-indol-2-yl)-cyclohex-2-enone (**70i**) (477 mg, 1.0 mmol), lithium dineophylcuprate **17** (1.2 mmol), DMAP (12 mg, 0.1 mmol), NMP (0.4 ml) and oxalyl chloride (409 mg, 3.0 mmol). Reaction time: 30 min at -78 °C. Purification by flash chromatography (*n*-pentane/diethyl ether = 4/1) yielded **72k** as a colorless oil (325 mg, 72%).

^{1}H-NMR ($CDCl_3$, 300 MHz): δ = 8.12 (d, *J* = 8.3 Hz, 1H), 8.06 (d, *J* = 8.0 Hz, 1H), 7.57 (d, *J* = 8.0 Hz, 1H), 7.47 (t, *J* = 7.5 Hz, 1H), 7.37 (t, *J* = 8.2 Hz, 1H), 7.30 (q, *J* = 8.0 Hz, 3H), 5.87(s, 1H), 4.18-3.95 (m, 2H), 3.05-2.16 (m, 6H), 1.21 (t, *J* = 7.3 Hz, 3H).
^{13}C-NMR ($CDCl_3$, 75 MHz): δ = 198.7, 183.3, 164.1, 153.9, 145.9, 137.3, 136.8, 135.4, 132.5, 129.9, 127.9, 127.4, 127.2, 126.4, 123.0, 117.8, 115.4, 62.9, 38.1, 32.7, 23.0, 14.1.
IR (film, cm^{-1}): $\tilde{\nu}$ = 3437 (s), 2952 (w), 1729 (vs), 1680 (vs), 1531 (w), 1449 (s), 1383 (vs), 1279 (s), 1186 (vs), 1071 (vs), 979 (s), 760 (s), 593 (s), 571 (s), 558 (s).
MS (EI, 70 ev): 451 (6) [M^+], 378 (28), 350 (39), 310 (78), 282 (100), 237 (85), 209 (34), 180 (21), 141 (14), 77 (45).

$C_{24}H_{21}NO_6S$	HRMS (EI)	Calcd.	451.1090
		Found	451.1086

Synthesis of 4-cyclopentyl-1-phenyl-9H-2,3,9-triaza-fluorene (74)



To a solution of (1-benzenesulfonyl-2-benzoyl-1H-indol-3-yl)-cyclopentyl-methanone (**72g**) (80 mg, 0.18 mmol) in ethanol (5 ml), hydrazine monohydrate (26 mg, 0.36 mmol) was added and the resulting mixture was refluxed for 12 h. The solvent was removed *in vacuo* and the residue was purified by flash chromatography (*n*-pentane/diethyl ether = 2/3) yielded **74** as a light yellow solid (48 mg, 88%).

mp.: 269 °C

^{1}H-NMR ($CDCl_3$, 300 MHz): δ = 9.86 (br, 1H), 8.20 (d, *J* = 8.3 Hz, 1H), 7.88-7.85 (m, 2H), 7.57–7.25 (m, 6H), 4.10 (quint, *J* = 7.7 Hz, 1H), 2.36-1.70, (m, 8H).

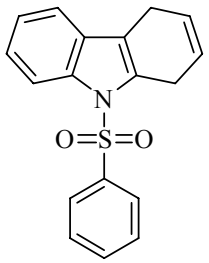
^{13}C-NMR ($CDCl_3$, 75 MHz): δ = 160.0, 146.7, 140.2, 136.1, 134.5, 129.6, 129.4, 128.6, 128.5, 123.9, 122.1, 120.9, 118.7, 112.8, 44.3, 31.8, 26.2.

IR (film, cm^{-1}): $\tilde{\nu}$ = 3432 (s), 2953 (s), 1619 (s), 1543 (w), 1497 (w), 1422(s), 1389 (s), 1325 (vs), 1235 (w), 743 (vs), 698 (s).

MS (EI, 70 ev): 313 (15) [M^+], 284 (10), 272 (100), 136 (6), 77 (4).

$C_{21}H_{19}N_3$	HRMS (EI)	Calcd.	313.1579
		Found	313.1577

Synthesis of 9-Benzenesulfonyl-4,9-dihydro-1H-carbazole (75)



To a solution of 2,3-diallyl-1-benzenesulfonyl-1H-indole (**72a**) (169 mg, 0.5 mmol) in CH_2Cl_2 (10 ml), Grubb's I catalyst (21 mg, 0.025 mmol) was added and the resulting mixture was refluxed for 2 h. The reaction mixture was quenched with H_2O (10 mL) and the organic layer was separated. The aqueous layer was extracted with CH_2Cl_2 (3 × 10 mL). The combined organic layers were washed with brine (20 mL), dried over Na_2SO_4 and concentrated *in vacuo*. Purification by flash chromatography (*n*-pentane/diethyl ether = 5/1) yielded **75** as a white solid (146 mg, 95%).

mp.: 138 °C

^{1}H-NMR ($CDCl_3$, 300 MHz): δ = 8.10 (d, *J* = 8.3 Hz, 1H), 7.70-7.67 (m, 2H), 7.45–7.15 (m, 6H), 5.83 (s, 2H), 3.65-3.59 (m, 2H), 3.24-3.20 (m. 2H).

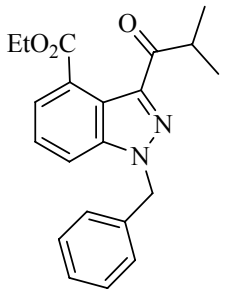
^{13}C-NMR ($CDCl_3$, 75 MHz): δ = 139.6, 136.6, 133.9, 132.7, 130.1, 129.6, 126.7, 124.7, 123.8, 123.6, 118.6, 116.1, 114.7, 26.7, 23.6.

IR (film, cm^{-1}): $\tilde{\nu}$ = 3435 (w), 1449 (s), 1368 (vs), 1174 (vs), 1091 (s), 990 (w), 737 (s), 683 (s), 592 (s), 573 (s), 558 (s).

MS (EI, 70 ev): 309 (11) [M^+], 167 (100), 139 (6), 115 (4), 77 (10).

$C_{18}H_{15}NO_2S$	HRMS (EI)	Calcd.	309.0823
		Found	309.0848

Synthesis of 1-benzyl-3-isobutyryl-1H-indazole-4-carboxylic acid ethyl ester (78a)



Prepared according to TP 6 from 1-benzyl-3-iodo-1H-indazole-4-carboxylic acid ethyl ester (**76a**) (203 mg, 0.5 mmol), lithium dineophylcuprate **17** (0.6 mmol), NMP (0.2 ml) and isobutyryl chloride (160 mg, 1.5 mmol). Reaction time: 30 min at rt. Purification by flash chromatography (*n*-pentane/diethyl ether = 2/1) yielded **78a** as a yellow solid (151 mg, 86%).

mp.: 104 °C

^{1}H-NMR ($CDCl_3$, 300 MHz): δ = 8.03-8.01 (d, *J* = 7.63 Hz, 1H), 7.48-7.44 (t, *J* = 7.63 Hz, 1H), 7.19–7.08 (m, 5H), 6.95-6.93 (d, *J* = 7.63 Hz, 1H), 5.65-5.61 (d, *J* = 14.50 Hz, 1H), 4.44-4.39 (q, *J* = 7.17 Hz, 2H), 4.18-4.14 (d, *J* = 14.50 Hz, 1H), 2.18-2.12 (m. 1H), 1.11-1.10 (d, *J* = 6.57 Hz, 1H), 0.96-0.95 (d, *J* = 6.57 Hz, 1H).

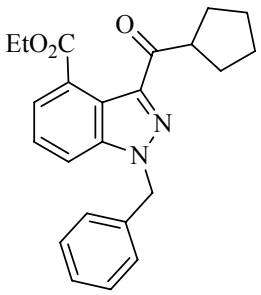
^{13}C-NMR ($CDCl_3$, 75 MHz): δ = 176.4, 163.5, 146.7, 136.5, 135.2, 134.1, 132.8, 130.5, 129.2, 128.6, 128.4, 127.8, 125.9, 114.2, 62.7, 52.3, 32.3, 19.85, 19.53, 14.6.

IR (KBr, cm^{-1}): $\tilde{\nu}$ = 3436 (vs), 2980 (m), 1728 (vs), 1658 (vs), 1586 (w), 1453 (m), 1278 (s), 1211 (m), 700 (w).

MS (EI, 70 ev): 350 (9) [M^+], 280 (27), 251 (68), 233 (3), 205 (4), 91 (100), 71 (5).

$C_{21}H_{22}N_2O_3$	HRMS (EI)	Calcd.	350.1630
		Found	350.1592

Synthesis of benzyl-3-cyclopentanecarbonyl-1H-indazole-4-carboxylic acid ethyl ester (78b)



Prepared according to TP 6 from 1-benzyl-3-iodo-1H-indazole-4-carboxylic acid ethyl ester (**76a**) (203 mg, 0.5 mmol), lithium dineophylcuprate **17** (0.6 mmol), NMP (0.2 ml) and cyclopentanecarbonyl chloride (200 mg, 1.5 mmol). Reaction time: 30 min at rt. Purification by flash chromatography (*n*-pentane/diethyl ether = 2/1) **78b** as a light yellow solid (165 mg, 88%).

mp.: 133 °C

^{1}H-NMR ($CDCl_3$, 300 MHz): δ = 8.02-8.00 (d, *J* = 7.85 Hz, 1H), 7.48-7.42 (t, *J* = 7.85 Hz, 1H), 7.18–6.95 (m, 5H), 6.94-6.92 (d, *J* = 7.85 Hz, 1H), 5.69-5.65 (d, *J* = 14.50 Hz, 1H), 4.45-4.38 (q, *J* = 7.08 Hz, 2H), 4.16-4.11 (d, *J* = 14.50 Hz, 1H), 2.28-2.18 (m, 1H), 1.95-1.46 (m, 4H), 1.41-1.37 (t, *J* = 7.08 Hz, 3H).

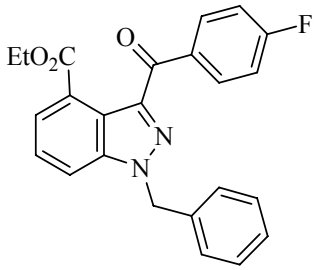
^{13}C-NMR ($CDCl_3$, 75 MHz): δ = 176.3, 163.9, 147.1, 137.0, 135.2 135.1, 133.1, 130.9, 129.6, 128.9, 128.1, 121.8, 114.6, 114.1, 63.1, 52.7, 43.2, 31.8, 31.3, 26.6, 14.4.

IR (KBr, cm^{-1}): $\tilde{\nu}$ = 3434 (m), 2957 (m), 1726 (vs), 1650 (vs), 1585 (w), 1454 (m), 1290 (s), 1277 (vs), 1212 (m), 775 (w).

MS (EI, 70 ev): 376 (10) [M^+], 335(5), 280 (56), 251 (59), 233 (4), 205 (4), 91 (100), 69 (81).

$C_{23}H_{24}N_2O_3$	HRMS (EI)	Calcd.	376.1787
		Found	376.1787

Synthesis of 1-benzyl-3-(4-fluoro-benzoyl)-1H-indazole-4-carboxylic acid ethyl ester (78c)



Prepared according to TP 6 from 1-benzyl-3-iodo-1H-indazole-4-carboxylic acid ethyl ester (**76a**) (203 mg, 0.5 mmol), lithium dineophylcuprate **17** (0.6 mmol), NMP (0.2 ml) and 4-fluorobenzoyl chloride (240 mg, 1.5 mmol). Reaction time: 30 min at rt. Purification by flash chromatography (*n*-pentane/diethyl ether = 2/1) yielded **78c** as a colorless oil (171 mg, 85%).

^{1}H-NMR ($CDCl_3$, 300 MHz): δ = 7.86-7.84 (d, *J* = 7.85 Hz, 1H), 7.42-7.34 (m, 1H), 7.34-7.29 (t, *J* = 7.85 Hz, 1H), 7.22-7.11 (m, 5H), 6.94–6.91 (d, *J* = 7.85 Hz, 1H), 6.85-6.81 (m, 2H), 5.65-5.62 (d, *J* = 14.50 Hz, 1H), 4.62-4.57 (d, *J* = 14.50 Hz, 1H), 4.40-4.33 (q, *J* = 7.18 Hz, 2H), 1.37-1.33 (t, *J* = 7.18 Hz, 3H).

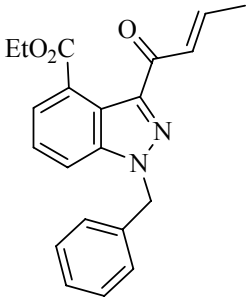
^{13}C-NMR ($CDCl_3$, 75 MHz): δ = 163.9 (d, *J* = 251 Hz, 1H), 163.7, 147.6, 136.2, 134.8, 132.9, 131.7, 131.0, 130.9, 130.2, 129.5, 129.0, 128.5, 115.9, 115.6, 115.0, 113.2, 63.0, 53.8, 14.4.

IR (film, cm^{-1}): $\tilde{\nu}$ = 3032 (w), 2230 (w), 1728 (vs), 1659 (vs), 1652 (vs), 1587 (m), 1453 (m), 1406 (s), 1371 (s), 1281 (vs), 1207 (m), 1157 (m), 846 (m), 760 (m), 736 (w), 701 (w), 604 (w).

MS (EI, 70 ev): 402 (11) [M^+], 374 (7), 357 (4), 279 (23), 267 (5), 233 (5), 123 (100), 91 (33), 65 (5).

$C_{24}H_{19}FN_2O_3$	HRMS (EI)	Calcd.	402.1380
		Cound	402.1384

Synthesis of benzyl-3-but-2-enoyl-1H-indazole-4-carboxylic acid ethyl ester (78d)



Prepared according to TP 6 from 1-benzyl-3-iodo-1H-indazole-4-carboxylic acid ethyl ester (**76a**) (203 mg, 0.5 mmol), lithium dineophylcuprate **17** (0.6 mmol), NMP (0.2 ml) and *trans*-crotonyl chloride (157 mg, 1.5 mmol). Reaction time: 30 min at rt. Purification by flash chromatography (*n*-pentane/diethyl ether = 2/1) yielded **78d** as a colorless oil (136 mg, 78%).

^{1}H-NMR ($CDCl_3$, 300 MHz): δ = 8.03-8.00 (d, *J* = 7.85 Hz, 1H), 7.49-7.44 (t, *J* = 7.85 Hz, 1H), 7.18–6.95 (m, 7H), 5.69-5.65 (d, *J* = 14.50 Hz, 1H), 5.40-5.36 (d, *J* = 15.60 Hz, 1H), 4.45-4.39 (q, *J* = 7.18 Hz, 2H), 4.31-4.26 (d, *J* = 14.50 Hz, 1H), 1.68-1.66 (d, *J* = 6.52 Hz, 3H), 1.40-1.36 (t, *J* = 7.18 Hz, 3H).

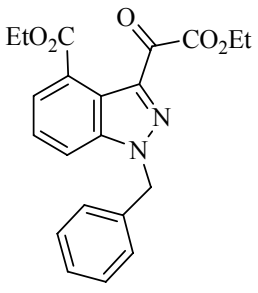
^{13}C-NMR ($CDCl_3$, 75 MHz): δ = 165.6, 163.9, 146.6, 144.4, 136.8, 135.2, 133.1, 130.8, 129.6, 128.9, 128.2, 121.8, 114.5, 113.9, 63.1, 52.5, 18.6, 14.4.

IR (film, cm^{-1}): $\tilde{\nu}$ = 3436 (vs), 2980 (m), 1729 (vs), 1665 (vs), 1630 (vs), 1585 (w), 1453 (m), 1276 (vs), 1210 (m), 700 (w).

MS (EI, 70 ev): 348 (19) [M^+], 333(62), 303 (8), 287 (17), 251 (43), 233 (4), 205 (5), 91 (84), 69 (100).

$C_{21}H_{20}N_2O_3$	HRMS (EI)	Calcd.	348.1474
		Found	348.1474

Synthesis of 1-benzyl-3-ethoxyoxalyl-1H-indazole-4-carboxylic acid ethyl ester (78e)

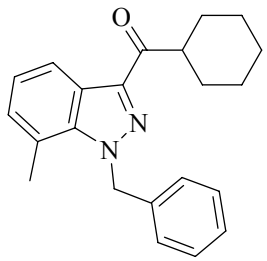


Prepared according to TP 6 from 1-benzyl-3-iodo-1H-indazole-4-carboxylic acid ethyl ester (**76a**) (203 mg, 0.5 mmol), lithium dineophylcuprate **17** (0.6 mmol), NMP (0.2 ml) and ethyl oxalyl chloride (205 mg, 1.5 mmol). Reaction time: 30 min at rt. Purification by flash chromatography (*n*-pentane/diethyl ether = 1/1) yielded **78e** as a colorless oil (156 mg, 82%).

^{1}H-NMR ($CDCl_3$, 300 MHz): δ = 8.03-8.00 (d, *J* = 7.96 Hz, 1H), 7.45-7.40 (t, *J* = 7.96 Hz, 1H), 7.22–7.06 (m, 5H), 6.98-6.94 (d, *J* = 7.96 Hz, 1H), 5.67-5.62 (d, *J* = 14.37 Hz, 1H), 4.45-4.34 (q, *J* = 7.10 Hz, 2H), 4.34-4.33 (d, *J* = 14.37 Hz, 1H), 3.99-3.95 (q, *J* = 7.10 Hz, 2H), 1.41-1.36 (t, *J* = 7.10 Hz, 3H), 1.01-0.96 (t, *J* = 7.10 Hz, 3H).
^{13}C-NMR ($CDCl_3$, 75 MHz): δ = 163.7, 161.3, 160.1, 144.5, 134.6, 132.9, 131.4, 129.8, 129.2, 128.8, 114.3, 113.8, 63.1, 62.7, 52.5, 14.4, 14.0.
IR (film, cm^{-1}): $\tilde{\nu}$ = 2984 (w), 1731 (vs), 1681 (vs), 1588 (m), 1454 (m), 1277 (vs), 1194 (vs), 1016 (m), 765 (w).
MS (EI, 70 ev): 380 (2) [M^+], 351 (10), 307 (17), 279 (18), 251 (13), 171 (6), 91 (100), 65 (8).

$C_{21}H_{20}N_2O_5$	HRMS (EI)	Calcd.	380.1372
		Found	380.1350

Synthesis of (1-benzyl-7-methyl-1H-indazol-3-yl)-cyclohexyl-methanone (7f)



Prepared according to TP 6 from 1-benzyl-3-iodo-7-methyl-1H-indazole (**76b**) (348 mg, 1.0 mmol), lithium dineophylcuprate **17** (1.2 mmol), NMP (0.4 ml) and cyclohexanecarbonyl chloride (440 mg, 3.0 mmol). Reaction time: 30 min at rt. Purification by flash chromatography (*n*-pentane/diethyl ether = 2/1) yielded **78f** as a white solid (282 mg, 85%).

mp.: 143 °C

^{1}H-NMR ($CDCl_3$, 300 MHz): δ = 7.47-7.06 (m, 8H), 5.10-5.05 (d, *J* = 13.78 Hz, 1H), 4.62-4.57 (d, *J* = 13.78 Hz, 1H), 1.76-1.50 (m, 12H).

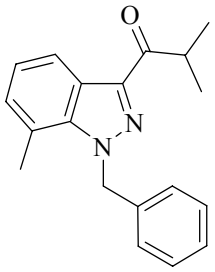
^{13}C-NMR ($CDCl_3$, 75 MHz): δ = 176.1, 143.4, 139.5, 136.4, 136.2, 135.7, 132.3, 131.7, 130.5, 129.4, 129.0, 128.8, 128.3, 116.9, 114.2, 54.4, 52.6, 43.2, 29.7, 26.0, 25.9, 25.8, 18.0.

IR (KBr, cm^{-1}): $\tilde{\nu}$ = 3028 (w), 2938 (s), 2229 (m), 1660 (vs), 1464 (s), 1395 (w), 1266 (s), 1258 (s), 1224 (m), 1195 (m), 1080 (w), 699 (m).

MS (EI, 70 ev): 332 (22) [M^+], 277 (7), 222 (23), 145 (7), 111 (7), 91 (54), 83 (100), 56 (26), 41 (14).

$C_{22}H_{24}N_2O_2$	HRMS (EI)	Calcd.	332.1889
		Found	332.1885

Synthesis of 1-(1-benzyl-7-methyl-1H-indazol-3-yl)-2-methyl-propan-1-one (7g)



Prepared according to TP 6 from 1-benzyl-3-iodo-7-methyl-1H-indazole (**76b**) (348 mg, 1.0 mmol), lithium dineophylcuprate **17** (1.2 mmol), NMP (0.4 ml) and cyclohexanecarbonyl chloride (440 mg, 3.0 mmol). Reaction time: 30 min at rt. Purification by flash chromatography (*n*-pentane/diethyl ether = 2/1) yielded **78g** as a colorless solid (224 mg, 77%).

mp.: 107 °C

^{1}H-NMR ($CDCl_3$, 300 MHz): δ = 7.50-7.06 (m, 8H), 5.11-5.07 (d, *J* = 13.78 Hz, 1H), 4.62-4.57 (d, *J* = 13.78 Hz, 1H), 2.11-1.97 (hep., *J* = 6.74 Hz, 1H), 1.76 (s, 3H), 1.07-1.05 (d, *J* = 6.74 Hz, 3H), 1.00-0.98 (d, *J* = 6.74 Hz, 3H).

^{13}C-NMR ($CDCl_3$, 75 MHz): δ = 177.2, 143.3, 139.5, 136.3, 136.2, 132.3, 130.5, 128.9, 128.8, 128.3, 116.9, 114.2, 52.6, 32.7, 20.5, 19.9, 17.9.

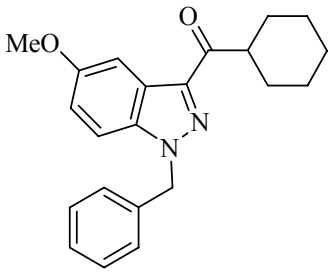
IR (KBr, cm^{-1}): $\tilde{\nu}$ = 2971 (w), 2873 (s), 2229 (m), 1661 (vs), 1468 (m), 1392 (m), 1238 (m), 1199 (w), 1079 (w), 701 (w).

MS (EI, 70 ev): 292 (80) [M^+], 277 (8), 222 (71), 145 (7), 116 (5), 91 (100), 71 (10).

$C_{19}H_{20}N_2O$ HRMS (EI) Calcd. 292.1576

Found 292.1591

Synthesis of (1-benzyl-5-methoxy-1H-indazol-3-yl)-cyclohexyl-methanone (78h)



Prepared according to TP 6 from 1-benzyl-3-iodo-5-methoxy-1H-indazole (**76c**) (364 mg, 1.0 mmol), lithium dineophylcuprate **17** (1.2 mmol), NMP (0.4 ml) and cyclohexanecarbonyl chloride (440 mg, 3.0 mmol). Reaction time: 30 min at rt. Purification by flash chromatography (*n*-pentane/diethyl ether = 2/1) yielded **78h** as a yellow solid (285 mg, 82%).

m.p.: 107 °C

^{1}H-NMR ($CDCl_3$, 300 MHz): δ = 7.28-7.25 (m, 3H), 7.18-7.15 (m, 2H), 7.02-6.98 (dd, *J* = 8.74 Hz, *J* = 2.76 Hz, 1H), 6.80–6.77 (d, *J* = 8.74 Hz, 1H), 5.49-5.44 (d, *J* = 14.37 Hz, 1H), 4.38-4.33 (d, *J* = 14.37 Hz, 1H), 3.86 (s, 3H), 1.96-0.91 (m, 11H).

^{13}C-NMR ($CDCl_3$, 75 MHz): δ = 176.3, 159.2, 137.7, 137.2, 131.9, 129.6, 128.8, 128.0, 120.1, 118.5, 116.2, 114.3, 56.2, 52.8, 42.6, 30.1, 29.5, 25.9, 25.8.

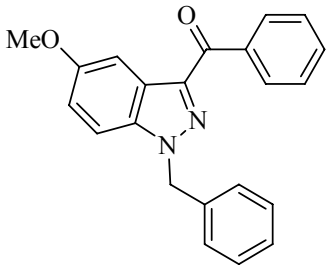
IR (KBr, cm^{-1}): $\tilde{\nu}$ = 3435 (m), 2932 (s), 2229 (w), 1660 (vs), 1603 (w), 1503 (vs), 1451 (m), 1397 (w), 1266 (m), 1198 (m), 1039 (m), 699 (w).

MS (EI, 70 ev): 348 (5) [M^+], 238 (100), 161 (5), 91 (36), 83 (22), 65 (3), 55 (10).

$C_{22}H_{24}N_2O_2$ HRMS (EI) Calcd. 348.1838

Found 348.1840

Synthesis of (1-benzyl-5-methoxy-1H-indazol-3-yl)-phenyl-methanone (78i)



Prepared according to TP 6 from 1-benzyl-3-iodo-5-methoxy-1H-indazole (**76c**) (364 mg, 1.0 mmol), lithium dineophylcuprate **17** (1.2 mmol), NMP (0.4 ml) and benzoyl chloride (420 mg, 3.0 mmol). Reaction time: 30 min at rt. Purification by flash chromatography (*n*-pentane/diethyl ether = 1/1) yielded **78i** as a yellow solid (274 mg, 80%).

m.p.: 101 °C

^{1}H-NMR ($CDCl_3$, 300 MHz): δ = 7.28-6.75 (m, 13H), 5.47-5.42 (d, *J* = 14.26 Hz, 1H), 4.73-4.68 (d, *J* = 14.26 Hz, 1H), 3.61 (s, 3H).

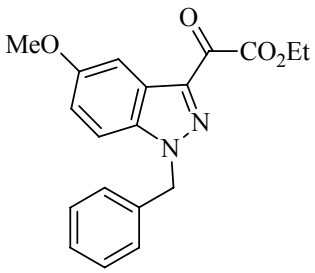
^{13}C-NMR ($CDCl_3$, 75 MHz): δ = 171.0, 158.5, 138.4, 136.7, 136.0, 132.0, 130.3, 129.6, 129.0, 128.7, 128.3, 128.2, 120.0, 118.0, 116.6, 113.9, 56.1, 53.8.

IR (KBr, cm^{-1}): $\tilde{\nu}$ = 2936 (w), 2229 (m), 1651 (vs), 1603 (w), 1503 (vs), 1446 (m), 1419 (w), 1319 (m), 1244 (m), 1159 (w), 1039 (m), 701 (w).

MS (EI, 70 ev): 342 (25) [M^+], 237 (28), 221 (6), 105 (100), 91 (30), 77 (31).

$C_{22}H_{18}N_2O_2$	HRMS (EI)	Calcd.	342.1368
		Found	342.1355

Synthesis of (1-benzyl-5-methoxy-1H-indazol-3-yl)-oxo-acetic acid ethyl ester (78j)



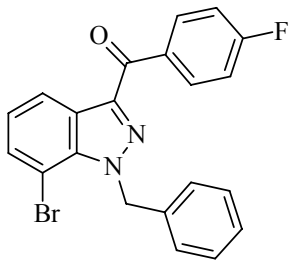
Prepared according to TP 6 from 1-benzyl-3-iodo-5-methoxy-1H-indazole (**76c**) (364 mg, 1.0 mmol), lithium dineophylcuprate **17** (1.2 mmol), NMP (0.4 ml) and oxalyl chloride (410

mg, 3.0 mmol). Reaction time: 30 min at rt. Purification by flash chromatography (*n*-pentane/diethyl ether = 1/1) yielded **78j** as a colorless oil (287 mg, 85%).

^{1}H-NMR ($CDCl_3$, 300 MHz): δ = 7.22-7.10 (m, 5H), 7.09-7.08 (d, *J* = 2.87 Hz, 1H), 6.87-6.83 (dd, *J* = 8.74 Hz, *J* = 2.87 Hz, 1H), 6.75–6.72 (d, *J* = 8.74 Hz, 1H), 5.48-5.43 (d, *J* = 14.26 Hz, 1H), 4.40-4.35 (d, *J* = 14.26 Hz, 1H), 4.01-3.94 (q, *J* = 7.18 Hz, 2H), 3.74 (s, 3H), 1.02-0.98 (t, *J* = 7.18 Hz, 3H).
^{13}C-NMR ($CDCl_3$, 75 MHz): δ = 161.8, 161.4, 159.8, 135.3, 134.5, 132.5, 129.8, 129.1, 128.6, 119.3, 118.8, 115.4, 114.6, 62.3, 56.3, 52.5, 14.1.
IR (film, cm^{-1}): $\tilde{\nu}$ = 2981 (w), 2232 (w), 1742 (vs), 1677 (vs), 1603 (w), 1505 (m), 1421 (w), 1226 (m), 1164 (s), 1011 (m), 701 (m).
MS (EI, 70 ev): 338 (13) [M^+], 265 (7), 237 (18), 221 (2), 159 (6), 91 (100), 65 (5).

$C_{19}H_{18}N_2O_4$	HRMS (EI)	Calcd.	338.1267
		Found	338.1256

Synthesis of (1-benzyl-7-bromo-1H-indazol-3-yl)-(4-fluoro-phenyl)-methanone (78k)



Prepared according to TP 6 from 1-Benzyl-7-bromo-3-iodo-1H-indazole (**76d)** (150 mg, 0.36 mmol), lithium dineophylcuprate **17** (0.44 mmol), NMP (0.2 ml) and 4-fluorobenzoyl chloride (160, 1.0mmol). Reaction time: 1 h at –10 °C. Purification by flash chromatography (*n*-pentane/diethyl ether = 2/1) yielded **78k** as a light yellow solid (128 mg, 87%).

mp.: 117 °C
^{1}H-NMR ($CDCl_3$, 300 MHz): δ = 7.72-7.69 (dd, *J* = 7.74, *J* = 1.47 , 1H), 7.40-7.36 (dd, *J* = 8.85, *J* = 5.31 , 2H), 7.26-7.23 (dd, *J* = 7.74, *J* = 1.47 , 1H), 7.21-7.15 (m, 5H), 7.08-7.03 (t, *J* = 7.74 Hz, 1H), 6.81-8.75 (dd, *J*(H, F) = *J*(H, H) = 8.85, 2H), 5.56-5.08 (d, *J* = 14.26 Hz, 1H), 4.68-4.63 (d, *J* = 14.26 Hz, 1H).

^{13}C-NMR ($CDCl_3$, 75 MHz): δ = 169.4, 165.7-162.4 (d, J = 251.48, 1C), 143.7, 138.7, 134.9, 133.1, 131.9, 130.9, 130.6, 130.5, 129.7, 128.8, 128.7, 125.6, 117.3, 115.7, 115.5, 115.2, 52.3.

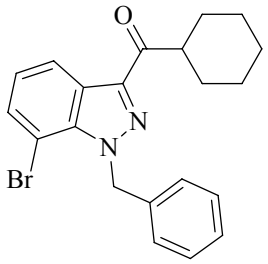
IR (KBr, cm^{-1}): $\tilde{\nu}$ = 3435 (w), 2231 (m), 1659 (vs), 1602 (w), 1507 (w), 1451 (m), 1376 (w), 1229 (w), 1159 (w), 701 (w).

MS (EI, 70 ev): 408 (10) [M^+], 285 (8), 205 (3), 123 (100), 91 (30), 77 (5).

$C_{21}H_{14}BrN_2O$ HRMS (EI) Calcd. 408.0274

Found 408.0290

Synthesis of (1-benzyl-7-bromo-1H-indazol-3-yl)-cyclohexyl-methanone (78l)



Prepared according to TP 6 from 1-Benzyl-2-bromo-3-iodo-1H-indazole (**76d**) (150 mg, 0.36 mmol), lithium dineophylcuprate **17** (0.44 mmol), NMP (0.2 ml) and cyclohexanecarbonyl chloride (146 mg, 1.0 mmol). Reaction time: 0.5 h at rt. Purification by flash chromatography (*n*-pentane/diethyl ether = 2/1) yielded **78l** as a white solid (130 mg, 91%).

mp.: 131 °C

^{1}H-NMR ($CDCl_3$, 300 MHz): δ = 7.82-7.79 (dd, *J* = 8.18, *J* = 1.43 , 1H), 7.51-7.48 (dd, *J* = 7.74, *J* = 1.43 , 2H), 7.24-7.19 (t, *J* = 7.96, 1H), 7.19-7.08 (m, 5H), 5.24-5.19 (d, *J* = 14.04 Hz, 1H), 4.56-4.51 (d, *J* = 14.04 Hz, 1H), 1.82-0.81 (m, 11H).

^{13}C-NMR ($CDCl_3$, 75 MHz): δ = 175.9, 143.6, 138.7, 135.5, 133.2, 130.8, 130.0, 128.7, 128.4, 126.6, 116.9, 115.7, 51.9, 43.9, 30.1, 29.8, 26.0, 25.9, 25.8.

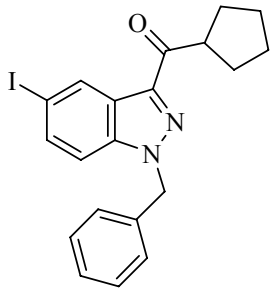
IR (KBr, cm^{-1}): $\tilde{\nu}$ = 3435 (m), 2933 (m), 1667 (vs), 1450 (m), 1390 (w), 1201 (w), 799 (w), 699 (w).

MS (EI, 70 ev): 396 (11) [M^+], 286 (17), 205 (15), 111 (15), 91 (100), 83 (98), 55 (43).

$C_{21}H_{21}BrN_2O$ HRMS (EI) Calcd. 396.0837

Found 396.0870

Synthesis of (1-benzyl-5-iodo-1H-indazol-3-yl)-cyclopentyl-methanone (78m)



Prepared according to TP 6 from 1-benzyl-3,5-diiodo-1H-indazole (**76e**) (184 mg, 0.4 mmol), lithium dineophylcuprate **17** (0.48 mmol), NMP (0.2 ml) and cyclopentanecarbonyl chloride (160 mg, 1.2 mmol). Reaction time: 1 h at –10 °C. Purification by flash chromatography (*n*-pentane/diethyl ether = 3/1) yielded **78m** as a light yellow solid (137 mg, 79%).

mp.: 100 °C

^{1}H-NMR ($CDCl_3$, 300 MHz): δ = 7.94-7.93 (d, *J* = 1.66 Hz, 1H), 7.74-7.70 (dd, *J* = 8.51, *J* = 2.10 , 1H), 7.19-7.07 (m, 5H), 6.56-6.53 (d, *J* = 8.4, 1H), 5.45-5.40 (d, *J* = 14.37 Hz, 1H), 4.31-4.26 (d, *J* = 14.37 Hz, 1H), 2.31-2.21 (m, 1H), 1.94-1.36 (m, 8H).

^{13}C-NMR ($CDCl_3$, 75 MHz): δ = 176.2, 144.9, 143.2, 142.6, 136.7, 132.8, 129.6, 129.0, 128.3, 115.9, 114.8, 93.1, 52.9, 43.1, 31.7, 31.3, 26.7.

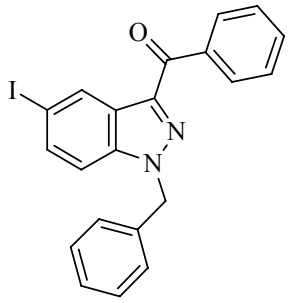
IR (KBr, cm^{-1}): $\tilde{\nu}$ = 3436 (m), 2943 (m), 1663 (vs), 1482 (m), 1394 (m), 1243 (m), 1202 (m), 741 (w), 698 (w).

MS (EI, 70 ev): 430 (7) [M^+], 334 (78), 206 (7), 97 (25), 91 (90), 69 (100), 41 (30).

$C_{20}H_{19}IN_2O$ HRMS (EI) Calcd. 430.0542

Found 430.0512

Synthesis of (1-benzyl-5-iodo-1H-indazol-3-yl)-phenyl-methanone (78n)



Prepared according to TP 6 from 1-benzyl-3,5-diiodo-1H-indazole (**76e**) (460 mg, 1.0 mmol), lithium dineophylcuprate **17** (1.2 mmol), NMP (0.4 ml) and benzoyl chloride (420 mg, 3.0 mmol). Reaction time: 1.0 h at –10 °C. Purification by flash chromatography (*n*-pentane/diethyl ether = 3/1) yielded **78n** as a yellow oil (306 mg, 70%).

^{1}H-NMR ($CDCl_3$, 300 MHz): δ = 7.72-7.71 (d, *J* = 1.4 Hz, 1H), 7.59-7.56 (dd, *J* = 8.50, *J* = 1.80 , 1H), 7.32-7.16 (m, 10H), 6.61-6.58 (d, *J* = 8.5, 1H), 5.46-5.41 (d, *J* = 14.2 Hz, 1H), 4.48-4.43 (d, *J* = 14.2 Hz, 1H).

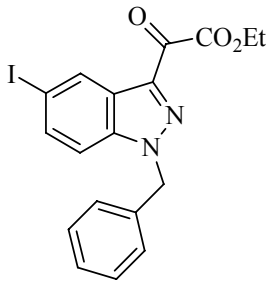
^{13}C-NMR ($CDCl_3$, 75 MHz): δ = 142.8, 142.2, 136.2, 135.3, 132.1, 130.7, 129.4, 129.1, 128.8, 128.6, 128.5, 115.1, 115.0, 92.0, 53.9.

IR (film, cm^{-1}): $\tilde{\nu}$ = 3435 (m), 2229 (w), 1654 (vs), 1600 (w), 1483 (m), 1392 (w), 1289 (w), 1077 (w), 738 (w), 701 (m).

MS (EI, 70 ev): 438 (10) [M^+], 333 (7), 205 (4), 105 (100), 91 (47), 77 (39), 65 (9).

$C_{21}H_{15}IN_2O$	HRMS (EI)	Calcd.	438.0299
		Found	438.0194

Synthesis of (1-benzyl-5-iodo-1H-indazol-3-yl)-oxo-acetic acid ethyl ester (78o)



Prepared according to TP 6 from 1-benzyl-3,5-diiodo-1H-indazole (**76e**) (184 mg, 0.4 mmol), lithium dineophylcuprate **17** (0.48 mmol), NMP (0.2 ml) and oxalyl chloride (153

mg, 1.2 mmol). Reaction time: 1 h at –10 °C. Purification by flash chromatography (*n*-pentane/diethyl ether = 3/1) yielded **78o** as a white solid (142 mg, 82%).

mp.: 104 °C

^{1}H-NMR ($CDCl_3$, 300 MHz): δ = 7.92-7.91 (d, *J* = 1.99 Hz, 1H), 7.71-7.68 (dd, *J* = 8.40, *J* = 2.10 , 1H), 7.21-7.09 (m, 5H), 6.59-6.58 (d, *J* = 8.4, 1H), 5.45-5.40 (d, *J* = 14.2 Hz, 1H), 4.47-4.42 (d, *J* = 14.2 Hz, 1H), 4.04-3.97 (q, *J* = 7.1, 2H), 1.05-1.01 (t, *J* = 7.1, 3H).

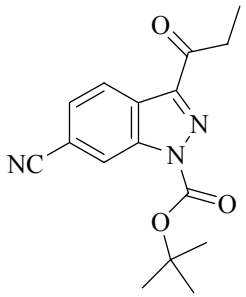
^{13}C-NMR ($CDCl_3$, 75 MHz): δ = 159.8, 159.0, 141.6, 141.1, 140.8, 133.4, 130.1, 128.3, 127.8, 127.4, 113.9, 113.0, 92.6, 61.4, 51.3, 12.7.

IR (KBr, cm^{-1}): $\tilde{\nu}$ = 2982 (w), 2233 (w), 1742 (vs), 1681 (vs), 1485 (m), 1409 (m), 1231 (s), 1101 (m), 739 (w), 701 (w).

MS (EI, 70 ev): 434 (8) [M^+], 361 (10), 333 (22), 206 (7), 91 (100), 65 (10).

$C_{18}H_{15}IN_2O_3$	HRMS (EI)	Calcd.	434.0127
		Found	434.0092

Synthesis of 6-cyano-3-propionyl-indazole-1-carboxylic acid tert-butyl ester (78p)



Prepared according to TP 6 from 6-cyano-3-iodo-indazole-1-carboxylic acid tert-butyl ester (**7f**) (185 mg, 0.5 mmol), lithium dineophylcuprate **17** (0.6 mmol), NMP (0.2 ml) and propionyl chloride (140 mg, 1.5 mmol). Reaction time: 30 min at –78 °C. Purification by flash chromatography (*n*-pentane/diethyl ether = 5/1) yielded **78p** as a yellow solid (121 mg, 81%).

mp.: 83 °C

^{1}H-NMR ($CDCl_3$, 300 MHz): δ = 7.85-7.83 (d, *J* = 7.96 Hz, 1H), 7.77-7.74 (dd, *J* = 7.96, *J* = 1.44 , 1H), 7.57-7.56 (d, *J* = 1.44 Hz, 1H), 3.18-3.10 (q, *J* = 7.30, 2H), 1.44 (s, 9H), 1.27-1.22 (t, *J* = 7.30 Hz, 3H).

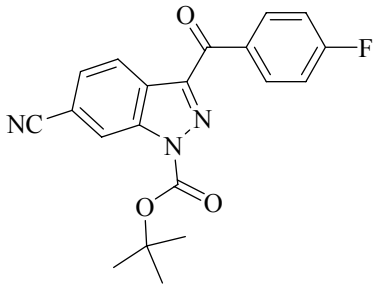
^{13}C-NMR ($CDCl_3$, 75 MHz): δ = 176.8, 150.6, 143.3, 133.9, 133.8, 132.1, 118.1, 117.6, 116.7, 114.8, 85.8, 31.9, 28.1, 9.2.

IR (KBr, cm^{-1}): $\tilde{\nu}$ = 3408 (w), 2984 (m), 2236 (m), 1748 (vs), 1713 (vs), 1609 (w), 1412 (w), 1285 (m), 1258 (s), 1152 (vs), 1088 (m), 949 (m), 848 (w).

MS (EI, 70 ev): 199 (20) $[M\text{-Boc}]^+$, 170 (10), 143 (70), 115 (7), 57 (100).

$C_{16}H_{17}N_3O_3$	HRMS (FAB)	Calcd.	300.1348 $[M + H]^+$
		Found	300.1339

Synthesis of 6-cyano-3-(4-fluoro-benzoyl)-indazole-1-carboxylic acid tert-butyl ester (78q)



Prepared according to TP 6 from 6-cyano-3-iodo-indazole-1-carboxylic acid tert-butyl ester (**7f**) (295 mg, 0.8 mmol), lithium dineophylcuprate **17** (0.96 mmol, 1.2 equiv), NMP (0.4 ml) and 4-fluorobenzoyl chloride (317 mg, 2.0 mmol). Reaction time: 30 min at –78 °C. Purification by flash chromatography (*n*-pentane/diethyl ether = 5/2) yielded **78q** as a white solid (260 mg, 89%).

mp.: 99 °C

^{1}H-NMR ($CDCl_3$, 300 MHz): δ = 7.81-7.77 (m, 3H), 7.72-7.70 (m, 2H), 7.13-7.09 (m, 2H), 1.21 (s, 9H).

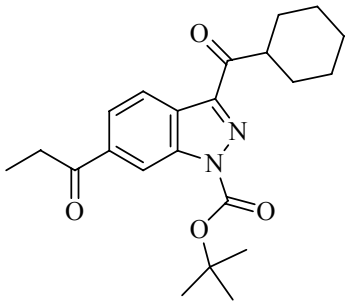
^{13}C-NMR ($CDCl_3$, 75 MHz): δ = 170.7, 166.2 (d, *J* = 254.7 Hz), 151.5, 142.6, 134.3, 134.2, 132.4, 131.8, 131.5, 131.4, 118.2, 117.9, 116.7, 116.1, 116.0, 115.2, 86.4, 27.8.

IR (KBr, cm^{-1}): $\tilde{\nu}$ = 3435 (w), 2935 (w), 2237 (m), 1749 (vs), 1693 (vs), 1603 (m), 1341 (m), 1235 (s), 1162 (m), 1149 (vs), 855 (m), 754 (w), 609 (w).

MS (EI, 70 ev): 265 (20) $[M^+\text{-Boc}]$, 123 (100), 95 (50), 75 (20).

$C_{20}H_{16}FN_3O_3$	HRMS (FAB)	Calcd.	366.1254 $[M + H]^+$
		Found	366.1237

Synthesis of 3-cyclohexanecarbonyl-6-propionyl-indazole-1-carboxylic acid tert-butyl ester (78r)



Prepared according to TP 6 from 3-iodo-6-propionyl-indazole-1-carboxylic acid tert-butyl ester (**76g**) (200 mg, 0.5 mmol), lithium dineophylcuprate **17** (0.6 mmol), NMP (0.2 ml) and cyclohexanecarbonyl chloride (219 mg, 1.5 mmol). Reaction time: 30 min at –78 °C. Purification by flash chromatography (*n*-pentane/diethyl ether = 4/1) yielded **78r** as colorless solid (146 mg, 76 %).

mp.: 90 °C

^{1}H-NMR ($CDCl_3$, 300 MHz): δ = 7.93-7.89 (dd, *J* = 8.07, *J* = 1.66 , 1H), 7.73-7.70 (d, *J* = 8.07 Hz, 1H), 7.69-7.68 (d, *J* = 1.33 Hz, 1H), 3.60-3.51 (m, 1H), 2.97-2.90 (q, *J* = 7.19 Hz, 2H), 1.80-1.20 (m, 10H), 1.34 (s, 9H), 1.19-1.14 (t, *J* = 7.19 Hz, 3H).

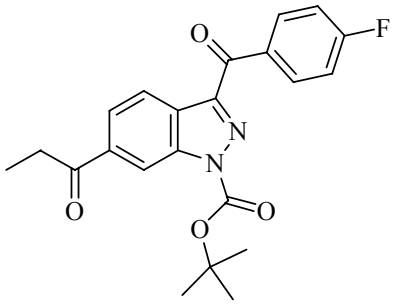
^{13}C-NMR ($CDCl_3$, 75 MHz): δ = 198.9, 179.4, 151.1, 142.3, 141.0, 133.5, 129.4, 127.7, 117.3, 115.7, 85.1, 44.8, 32.6, 29.8, 28.1, 26.2, 26.0, 8.2.

IR (KBr, cm^{-1}): $\tilde{\nu}$ = 3435 (m), 2936 (m), 2234 (w), 1742 (vs), 1704 (s), 1255 (m), 1152 (vs), 1092 (w), 849 (w).

MS (EI, 70 ev): 284 (10) [M^+-Boc], 255 (6), 174 (8), 145 (30), 123 (100), 110 (50), 83 (100), 55 (35).

$C_{22}H_{28}N_2O_4$ $[M + H]^+$	HRMS (FAB)	Calcd.	385.2127
		Found	385.2121

Synthesis of 3-(4-fluoro-benzoyl)-6-propionyl-indazole-1-carboxylic acid tert-butyl ester (78s)



Prepared according to TP 6 from 3-iodo-6-propionyl-indazole-1-carboxylic acid tert-butyl ester (**76g**) (200 mg, 0.5 mmol), lithium dineophylcuprate **17** (0.6 mmol), NMP (0.2 ml) and 4-fluorobenzoyl chloride (237 mg, 1.5 mmol). Reaction time: 30 min at –78 °C. Purification by flash chromatography (*n*-pentane/diethyl ether = 3:1) yielded **78s** as a white solid (138 mg, 70%).

mp.: 114 °C

^{1}H-NMR ($CDCl_3$, 300 MHz): δ = 7.92 (s, 1H), 7.80-7.78 (m, 3H), 7.12-7.05 (m, 3H), 2.98-2.94 (q, *J* = 7.12 Hz, 2H), 1.21 (s, 9H), 1.19-1.17 (t, *J* = 7.12 Hz, 3H).

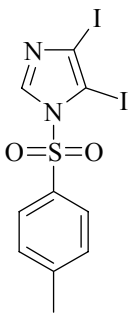
^{13}C-NMR ($CDCl_3$, 75 MHz): δ = 198.7, 171.0, 165.5 (d, *J* = 254.7 Hz), 151.9, 142.3, 141.2, 133.9, 131.4, 131.3, 129.9, 128.2, 117.4, 116.0, 115.9, 85.6, 32.7, 27.9, 8.2.

IR (KBr, cm^{-1}): $\tilde{\nu}$ = 3435 (w), 2980 (w), 2230 (w), 1740 (s), 1728 (s), 1695 (vs), 1603 (m), 1508 (m), 1413 (m), 1342 (m), 1238 (vs), 1160 (m), 1148 (vs), 855 (m), 1049 (w), 853 (m).

MS (EI, 70 ev): 296 (15) [M^+-Boc], 123 (100), 95 (25), 75 (6).

$C_{22}H_{21}FN_2O_4$ $[M + H]^+$	HRMS (FAB)	Calcd.	397.1564
		Found	397.1573

Synthesis of 4,5-diiodo-1-(toluene-4-sulfonyl)-1H-imidazole (79b)



To a mixture of 4,5-diiodo-1H-imidazole (9.6 g, 30 mmol) and 4-methyl-benzenesulfonyl chloride (5.9 g, 31 mmol) in acetone (50 mL) at rt, Et_3N (15 mL) was added and the resulting mixture was stirred at rt for 12 h. The solvent was removed under vacuum and the residue was purified by flash chromatography (*n*-pentane/diethyl ether = 2/1) yielded **79b** as a light yellow solid (13.4g, 94%).

mp.: 156 °C

^{1}H-NMR ($CDCl_3$, 300 MHz): δ = 8.24 (s, 1H), 7.85-7.82 (d, *J* = 8.40 Hz, 2H), 7.33-7.30 (d, *J* = 8.40 Hz, 2H), 2.40 (s, 3H).

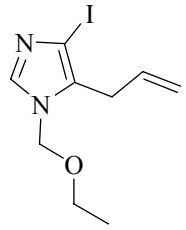
^{13}C-NMR ($CDCl_3$, 75 MHz): δ = 147.5, 142.2, 133.5, 130.7, 129.3, 103.3, 22.2.

IR (KBr, cm^{-1}): $\tilde{\nu}$ = 3435 (w), 3126 (w), 1594 (m), 1467 (m), 1430 (w), 1379 (s), 1192 (s), 1170 (vs), 1150 (s), 1089 (vs), 1030 (m), 923 (w), 812 (w), 673 (vs), 591 (vs), 542 (m).

MS (EI, 70 ev): 474 (82) [M^+], 319 (3), 192 (4), 155 (97), 91 (100), 65 (17).

$C_{10}H_9I_2N_2O_2S$ $[M + H]^+$	HRMS (EI)	Calcd.	474.8474
		Found	474.8497

Synthesis of 5-allyl-1-ethoxymethyl-4-iodo-1H-imidazole (81a)



Prepared according to TP 6 from (4,5-diiodo-1*H*-imidazol-1-yl)methyl ethyl ether (**79a**) (378 mg, 1.0 mmol), lithium dineophylcuprate **17** (1.2 mmol) and allyl bromide (360 mg, 3.0 mmol). Reaction time: 1 h at -78 °C. Purification by flash chromatography (*n*-pentane/diethyl ether = 2/1) yielded **81a** as a colorless oil (263 mg, 90%).

^{1}H-NMR ($CDCl_3$, 300 MHz): δ = 7.51 (s, 1H), 5.90-5.77 (m, 1H), 5.23 (s, 2H), 5.12-4.99 (m, 2H), 3.46-3.43 (m, 2H), 3.46-3.39, (q, *J* = 7.07 Hz, 2H), 1.21-1.16 (t, *J* = 7.07 Hz, 3H).

^{13}C-NMR ($CDCl_3$, 75 MHz): δ = 139.4, 133.9, 132.0, 117.1, 86.2, 64.5, 29.1, 15.0.

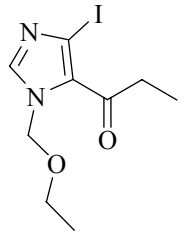
IR (film, cm^{-1}): $\tilde{\nu}$ = 3369 (w), 2978 (m), 1639 (w), 1489 (m), 1425 (w), 1354 (w), 1230 (s), 1177 (s), 1102 (vs), 918 (w), 774 (w), 736 (w).

MS (EI, 70 ev): 292 (100) [M^+], 246 (21), 233 (16), 121 (26), 80 (13), 59 (71).

$C_9H_{13}IN_2O$ HRMS (EI) Calcd. 292.0073

Found 292.0071

Synthesis of 1-(3-ethoxymethyl-5-iodo-3H-imidazol-4-yl)-propan-1-one (81b)



Prepared according to TP 6 from (4,5-diiodo-1*H*-imidazol-1-yl)methyl ethyl ether (**79a**) (378 mg, 1.0 mmol), lithium dineophylcuprate **17** (1.2 mmol), propionyl chloride (278 mg, 3.0 mmol) and NMP (0.5 mL). Reaction time: 1 h at -78 °C. Purification by flash chromatography (*n*-pentane/diethyl ether = 1/2) yielded **81b** as a colorless oil (265 mg, 86%).

^{1}H-NMR ($CDCl_3$, 300 MHz): δ = 7.63 (s, 1H), 5.60 (s, 2H), 3.52-3.45, (q, *J* = 7.07 Hz, 2H), 3.09-3.02, (q, *J* = 7.18 Hz, 2H), 1.16-1.11 (t, *J* = 7.07 Hz, 3H), 1.15-1.10 (t, *J* = 7.18 Hz, 3H).

^{13}C-NMR ($CDCl_3$, 75 MHz): δ = 191.5, 141.7, 131.3, 92.6, 76.9, 64.4, 34.9, 13.9, 7.0.

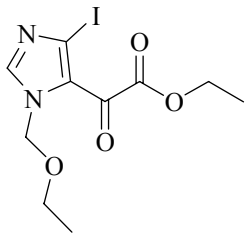
IR (film, cm^{-1}): $\tilde{\nu}$ = 3102 (w), 2977 (m), 1666 (vs), 1495 (s), 1460 (m), 1378 (m), 1235 (s), 1165 (m), 1107 (vs), 908 (w), 756 (m), 658 (w).

MS (EI, 70 ev): 308 (20) [M^+], 279 (100), 261 (6), 249 (4), 221 (15), 59 (16).

$C_9H_{13}IN_2O_2$ HRMS (EI) Calcd. 308.0022

Found 308.0048

Synthesis of (3-ethoxymethyl-5-iodo-3H-imidazol-4-yl)-oxo-acetic acid ethyl ester (81c)



Prepared according to TP 6 from (4,5-diiodo-1*H*-imidazol-1-yl)methyl ethyl ether (**79a**) (189 mg, 0.5 mmol), lithium dineophylcuprate **17** (0.6 mmol), oxalyl chloride (245 mg, 1.5 mmol) and NMP (0.3 mL). Reaction time: 1 h at -78 °C. Purification by flash chromatography (*n*-pentane/diethyl ether = 1/2) yielded **81c** as a colorless oil (130 mg, 74%).

^{1}H-NMR ($CDCl_3$, 300 MHz): δ = 7.75 (s, 1H), 5.61 (s, 2H), 4.43-4.36, (q, *J* = 7.19 Hz, 2H), 3.54-3.47, (q, *J* = 7.07 Hz, 2H), 1.39-1.35 (t, *J* = 7.19 Hz, 3H), 1.17-1.12 (t, *J* = 7.07 Hz, 3H).

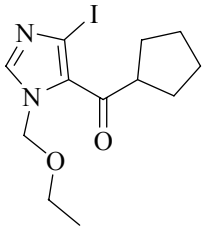
^{13}C-NMR ($CDCl_3$, 75 MHz): δ = 176.9, 161.6, 143.3, 127.3, 97.9, 77.0, 64.6, 62.0, 15.1, 14.2.

IR (film, cm^{-1}): $\tilde{\nu}$ = 3109 (w), 2980 (w), 1735 (vs), 1654 (vs), 1501 (s), 1461 (w), 1441 (w), 1349 (m), 1257 (m), 1206 (vs), 1108 (vs), 1011 (s), 960 (w), 748 (w).

MS (EI, 70 ev): 352 (30) [M^+], 279 (100), 251 (8), 235 (4), 221 (12), 59 (19).

$C_{10}H_{13}IN_2O_4$	HRMS (EI)	Calcd.	351.9920
		Found	351.9928

Synthesis of cyclopentyl-(3-ethoxymethyl-5-iodo-3H-imidazol-4-yl)-methanone (81d)



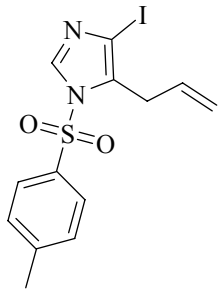
Prepared according to TP 6 from (4,5-diiodo-1*H*-imidazol-1-yl)methyl ethyl ether (**79a**) (189 mg, 0.5 mmol), lithium dineophylcuprate **17** (0.6 mmol), cyclopentanecarbonyl chloride (200 mg, 1.5 mmol) and NMP (0.3 mL). Reaction time: 1 h at -78 °C. Purification

by flash chromatography (*n*-pentane/diethyl ether = 1/2) yielded **81d** as a colorless oil (141 mg, 81%).

^{1}H-NMR ($CDCl_3$, 300 MHz): δ = 7.77 (s, 1H), 5.69 (s, 2H), 4.19-4.08, (m, 1H), 3.61-3.54, (q, *J* = 7.07 Hz, 2H), 2.08-1.70 (m, 8H), 1.27-1.23 (t, *J* = 7.07 Hz, 3H).
^{13}C-NMR ($CDCl_3$, 75 MHz): δ = 195.9, 143.0, 132.3, 114.0, 93.2, 78.1, 65.6, 49.0, 30.1, 26.5, 15.2.
IR (film, cm^{-1}): $\tilde{\nu}$ = 3105 (w), 2955 (vs), 1659 (vs), 1495 (s), 1461 (w), 1384 (m), 1257 (m), 1201 (vs), 1106 (vs), 965 (w), 763 (w).
MS (EI, 70 ev): 348 (91) [M^+], 319 (100), 301 (83), 289 (24), 279 (52), 252 (23) 235 (14), 221 (34), 174 (13), 59 (75)..

$C_{12}H_{17}IN_2O_3$	HRMS (EI)	Calcd.	348.0335
		Found	348.0340

Synthesis of 5-allyl-4-iodo-1-(toluene-4-sulfonyl)-1H-imidazole (81e)



Prepared according to TP 6 from 4,5-diiodo-1-(toluene-4-sulfonyl)-1H-imidazole (**79b**) (474 mg, 1.0 mmol), lithium dineophylcuprate **17** (1.2 mmol), allyl bromide (360 mg, 3.0 mmol) and NMP (0.5 mL). Reaction time: 0.5 h at -78 °C. Purification by flash chromatography (*n*-pentane/diethyl ether = 5/1) yielded **81e** as a colorless oil (360 mg, 93%).

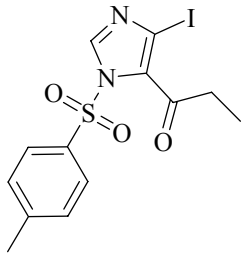
^{1}H-NMR ($CDCl_3$, 300 MHz): δ = 8.01 (s, 1H), 7.69-7.67 (d, *J* = 8.24 Hz, 2H), 7.29-7.27 (d, *J* = 8.24 Hz, 2H), 5.58-5.48 (m, 1H), 4.87-4.77, (m, 2H), 3.40-3.38, (dt, *J* = 5.80 Hz, *J* = 1.83 Hz, 2H), 2.38 (s, 3H).
^{13}C-NMR ($CDCl_3$, 75 MHz): δ = 146.6, 138.8, 134.4, 132.1, 130.6, 130.4, 127.8, 117.0, 89.7, 29.0, 21.7.

IR (film, cm^{-1}): $\tilde{\nu}$ = 3435 (w), 2921 (w), 1639 (w), 1494 (w), 1461 (m), 1383 (s), 1191 (m), 1177 (vs), 1152 (vs), 1111 (vs), 812 (m), 680 (vs), 593 (vs).

MS (EI, 70 ev): 388 (32) [M^+], 233 (23), 155 (42), 91 (100), 65 (7)..

$C_{13}H_{13}IN_2OS$	HRMS (EI)	Calcd.	387.9742
		Found	387.9746

Synthesis of 1-[5-iodo-3-(toluene-4-sulfonyl)-3H-imidazol-4-yl]-propan-1-one (81f)



Prepared according to TP 6 from 4,5-diiodo-1-(toluene-4-sulfonyl)-1H-imidazole (**79b**) (474 mg, 1.0 mmol), lithium dineophylcuprate **17** (1.2 mmol), propionyl chloride (278 mg, 3.0 mmol) and NMP (0.5 mL). Reaction time: 0.5 h at -78 °C. Purification by flash chromatography (*n*-pentane/diethyl ether = 2/1) yielded **81f** as a light yellow solid (327 mg, 81%).

mp.: 102 °C

^{1}H-NMR ($CDCl_3$, 300 MHz): δ = 8.17 (s, 1H), 7.88-7.86 (d, *J* = 8.40 Hz, 2H), 7.33-7.30 (d, *J* = 8.40 Hz, 2H), 2.99-2.91, (q, *J* = 7.19 Hz, 2H), 2.38 (s, 3H), 1.13-1.08 (t, *J* = 7.19 Hz, 3H).

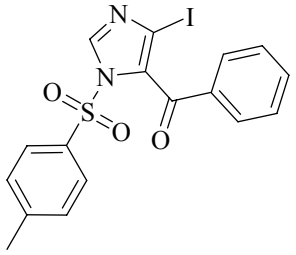
^{13}C-NMR ($CDCl_3$, 75 MHz): δ = 192.7, 146.8, 142.4, 134.6, 134.4, 130.2, 129.4, 129.3, 92.4, 36.9, 22.2, 8.3.

IR (KBr, cm^{-1}): $\tilde{\nu}$ = 3435 (vs), 1685 (vs), 1492 (m), 1375 (s), 1218 (m), 1171 (vs), 1155 (s), 1113 (vs), 813 (m), 671 (vs), 572 (m).

MS (EI, 70 ev): 388 (32) [M^+], 233 (23), 155 (42), 91 (100), 65 (7)..

$C_{13}H_{13}IN_2O_3S$	HRMS (EI)	Calcd.	403.9692
		Found	403.9711

Synthesis of [5-iodo-3-(toluene-4-sulfonyl)-3H-imidazol-4-yl]-phenyl-methanone (81g)



Prepared according to TP 6 from 4,5-diiodo-1-(toluene-4-sulfonyl)-1H-imidazole (**79b**) (474 mg, 1.0 mmol), lithium dineophylcuprate **17** (1.2 mmol), benzoyl chloride (420 mg, 3.0 mmol) and NMP (0.5 mL). Reaction time: 0.5 h at -78 °C. Purification by flash chromatography (*n*-pentane/diethyl ether = 2/1) yielded **81g** as a white solid (384 mg, 85%).

mp.: 96 °C

^{1}H-NMR ($CDCl_3$, 300 MHz): δ = 8.12 (s, 1H), 7.90-7.89 (d, *J* = 8.40 Hz, 2H), 7.76-7.75 (d, *J* = 8.40 Hz, 2H), 7.60-7.57 (m, 1H), 7.44-7.42 (m, 2H), 7.34-7.42 (m, 2H), 2.40 (s, 3H).

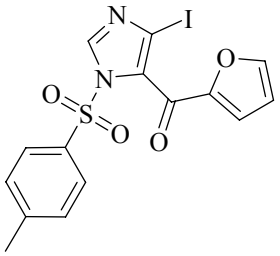
^{13}C-NMR ($CDCl_3$, 75 MHz): δ = 188.2, 147.8, 141.1, 136.6, 134.8, 134.3, 132.4, 130.9, 130.7, 129.6, 129.3, 92.4, 22.3.

IR (KBr, cm^{-1}): $\tilde{\nu}$ = 3435 (w), 1660 (vs), 1596 (m), 1467 (s), 1382 (vs), 1238 (w), 1194 (vs), 1178 (vs), 1133 (vs), 1097 (s), 882 (m), 688 (vs), 586 (vs).

MS (EI, 70 ev): 452 (34) [M^+], 388 (16), 297 (12), 155 (75), 105 (7), 91 (100), 77 (21).

$C_{17}H_{13}IN_2O_3S$	HRMS (EI)	Calcd.	451.9692
		Found	451.9677

Synthesis of furan-2-yl-[5-iodo-3-(toluene-4-sulfonyl)-3H-imidazol-4-yl]-methanone (81h)



Prepared according to TP 6 from 4,5-diiodo-1-(toluene-4-sulfonyl)-1H-imidazole (**79b**) (237 mg, 0.5 mmol), lithium dineophylcuprate **17** (0.6 mmol), 2-furoyl chloride (195 mg,

1.5 mmol) and NMP (0.3 mL). Reaction time: 0.5 h at -78 °C. Purification by flash chromatography (*n*-pentane/diethyl ether = 3/2) yielded **81h** as a white solid (157 mg, 71%).

mp.: 102 °C

^{1}H-NMR ($CDCl_3$, 300 MHz): δ = 8.08 (s, 1H), 7.89-7.87 (d, *J* = 8.16 Hz, 2H), 7.68-7.67 (m, 1H), 7.33-7.32 (d, *J* = 8.16 Hz, 2H), 7.22-7.21 (d, *J* = 3.22 Hz, 1H), 6.58-6.57 (dd, *J* = 3.22 Hz, *J* = 1.50 Hz, 1H), 2.39 (s, 3H).

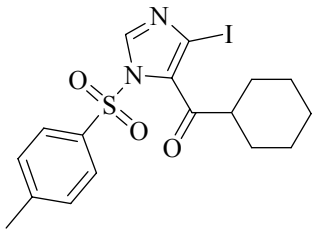
^{13}C-NMR ($CDCl_3$, 75 MHz): δ = 171.3, 150.4, 147.7, 146.0, 139.5, 132.8, 130.2, 129.1, 127.9, 122.2, 112.2, 89.0, 20.8.

IR (KBr, cm^{-1}): $\tilde{\nu}$ = 3436 (w), 1646 (vs), 1563 (w), 1457 (s), 1388 (vs), 1262 (w), 1194 (m), 1178 (vs), 1147 (s), 1104 (s), 849 (m), 671 (vs), 584 (s).

MS (EI, 70 ev): 442 (24) [M^+], 378 (21), 288 (8), 155 (63), 106 (7), 91 (100), 65 (11).

$C_{15}H_{11}IN_2O_4S$	HRMS (EI)	Calcd.	441.9484
		Found	441.9447

Synthesis of cyclohexyl-[5-iodo-3-(toluene-4-sulfonyl)-3H-imidazol-4-yl]-methanone (81i)



Prepared according to TP 6 from 4,5-diiodo-1-(toluene-4-sulfonyl)-1H-imidazole (**79b**) (237 mg, 0.5 mmol), lithium dineophylcuprate **17** (0.6 mmol), 2-furoyl chloride (220 mg, 1.5 mmol) and NMP (0.3 mL). Reaction time: 0.5 h at -78 °C. Purification by flash chromatography (*n*-pentane/diethyl ether = 2/1) yielded **81i** as a white solid (192 mg, 84%).

mp.: 108 °C

^{1}H-NMR ($CDCl_3$, 300 MHz): δ = 8.02 (s, 1H), 7.76-7.75 (d, *J* = 8.16 Hz, 2H), 7.22-7.21 (d, *J* = 8.16 Hz, 2H), 3.21-3.16 (m, 1H), 2.28 (s, 3H), 1.75-1.02 (m, 10H).

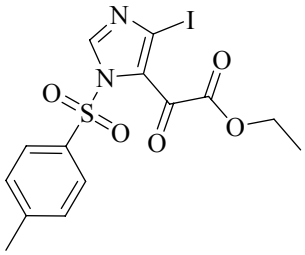
^{13}C-NMR ($CDCl_3$, 75 MHz): δ = 196.1, 146.8, 142.2, 134.7, 133.9, 130.2, 129.3, 91.6, 49.5, 28.8, 26.1, 25.9, 22.2.

IR (KBr, cm^{-1}): $\tilde{\nu}$ = 3436 (w), 2925 (m), 1677 (vs), 1593 (w), 1447 (m), 1374 (vs), 1206 (w), 1175 (vs), 1139 (s), 1099 (vs), 966 (w), 815 (w), 699 (vs), 584 (vs).

MS (EI, 70 ev): 458 (5) [M^+], 375 (51), 303 (75), 221 (22), 155 (96), 91 (100), 65 (11).

$C_{17}H_{19}IN_2O_3S$	HRMS (EI)	Calcd.	458.0161
		Found	458.0163

Synthesis of [5-iodo-3-(toluene-4-sulfonyl)-3H-imidazol-4-yl]-oxo-acetic acid ethyl ester (81j)



Prepared according to TP 6 from 4,5-diiodo-1-(toluene-4-sulfonyl)-1H-imidazole (**79b**) (237 mg, 0.5 mmol), lithium dineophylcuprate **17** (0.6 mmol), ethyl oxayl chloride (205 mg, 1.5 mmol) and NMP (0.3 mL). Reaction time: 0.5 h at -78 °C. Purification by flash chromatography (*n*-pentane/diethyl ether = 2/1) yielded **81j** as a colorless oil (170 mg, 76%).

^{1}H-NMR ($CDCl_3$, 300 MHz): δ = 8.22 (s, 1H), 7.89-7.87 (d, *J* = 8.24 Hz, 2H), 7.33-7.31 (d, *J* = 8.24 Hz, 2H), 4.38-4.33 (q, *J* = 7.32 Hz, 2H), 2.39 (s, 3H), 1.36-1.32 (t, *J* = 7.32 Hz, 3H).

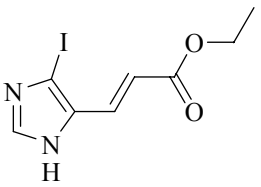
^{13}C-NMR ($CDCl_3$, 75 MHz): δ = 176, 161, 147.1, 143.6, 133.5, 1130.1, 129.8, 129.1, 98.4, 63.4, 21.8, 13.8.

IR (film, cm^{-1}): $\tilde{\nu}$ = 3436 (w), 1741 (vs), 1686 (vs), 1592 (w), 1487 (s), 1386 (vs), 1303 (m), 1247 (m), 1193 (s), 1134 (s), 1081 (vs), 1023 (s), 921 (w), 815 (w), 673 (vs), 591 (vs).

MS (EI, 70 ev): 448 (5) [M^+], 375 (100), 221 (9), 155 (66), 91 (70), 65 (8).

$C_{14}H_{13}IN_2O_5S$	HRMS (EI)	Calcd.	447.9590
		Found	447.9590

Synthesis of 3-(5-iodo-3H-imidazol-4-yl)-acrylic acid ethyl ester (81k)



Prepared according to TP 6 from 4,5-diiodo-1-(toluene-4-sulfonyl)-1H-imidazole (**79b**) (237 mg, 0.5 mmol), lithium dineophylcuprate **17** (0.6 mmol), ethyl propiolate (147 mg, 1.5 mmol) and NMP (0.3 mL). Reaction time: 0.5 h at -78 °C. Purification by flash chromatography (*n*-pentane/diethyl ether = 1/4) yielded **81k** as colorless oil (79 mg, 54%).

^{1}H-NMR ($CDCl_3$, 300 MHz): δ = 7.75-7.73 (d, *J* = 13.97 Hz, 1H), 7.60 (s, 1H), 7.29 (s, 1H), 5.99-5.97 (d, *J* = 13.97 Hz, 1H), 4.22-4.18 (q, *J* = 7.09 Hz, 2H), 1.27-1.25 (t, *J* = 7.09 Hz, 3H).

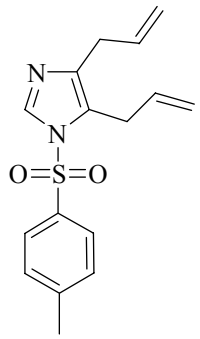
^{13}C-NMR ($CDCl_3$, 75 MHz): δ = 164.5, 138.0, 134.1, 120.8, 107.1, 84.8, 60.1, 13.2.

IR (film, cm^{-1}): $\tilde{\nu}$ = 3436 (w), 1701 (vs), 1652 (vs), 1487 (s), 1372 (w), 1277 (m), 1221 (m), 1204 (vs), 1184 (vs), 1103 (w), 1028 (w), 960 (w), 609 (w).

MS (EI, 70 ev): 292 (100) [M^+], 247 (17), 220 (6), 166 (5), 137 (11), 109 (8), 65 (4).

$C_8H_9IN_2O_2$	HRMS (EI)	Calcd.	291.9709
		Found	291.9728

Synthesis of 4,5-diallyl-1-(toluene-4-sulfonyl)-1H-imidazole (83a)



Prepared according to TP 6 from 5-allyl-4-iodo-1-(toluene-4-sulfonyl)-1H-imidazole (**81e**) (388 mg, 1.0 mmol), lithium dineophylcuprate **17** (1.2 mmol) and allyl bromide (360 mg, 3.0 mmol). Reaction time: 1.5 h at -78 °C. Purification by flash chromatography (*n*-pentane/diethyl ether = 2/1) yielded **83a** as a colorless oil (214 mg, 71%).

^{1}H-NMR ($CDCl_3$, 300 MHz): δ = 7.63-7.60 (d, *J* = 8.51 Hz, 2H), 7.28-7.28 (d, *J* = 8.51 Hz, 2H), 6.58 (s, 1H), 6.06-5.93 (m, 1H), 5.86-5.74 (m, 1H), 5.11-5.01, (m, 4H), 3.70-3.68, (dt, *J* = 6.60 Hz, *J* = 1.30 Hz, 2H), 3.41-3.38, (dt, *J* = 6.74 Hz, *J* = 1.30 Hz, 2H), 2.38 (s, 3H).

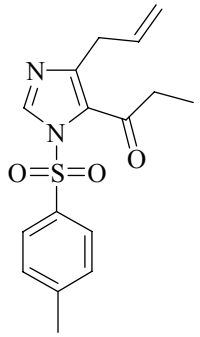
^{13}C-NMR ($CDCl_3$, 75 MHz): δ = 149.7, 146.2, 136.4, 133.8, 133.4, 132.5, 130.6, 127.7, 127.3, 118.3, 118.0, 34.7, 31.0, 22.1.

IR (film, cm^{-1}): $\tilde{\nu}$ = 3080 (w), 1642 (w), 1597 (m), 1374 (vs), 1194 (vs), 1182 (s), 1156 (vs), 1106 (vs), 993 (m), 920 (m), 813 (m), 672 (vs), 598 (vs), 546 (vs).

MS (EI, 70 ev): 302 (97) [M^+], 237 (3), 147 (87), 91 (100), 65 (17).

$C_{16}H_{18}N_2O_2S$	HRMS (EI)	Calcd.	302.1089
		Found	302.1054

Synthesis of 1-[5-allyl-3-(toluene-4-sulfonyl)-3H-imidazol-4-yl]-propan-1-one (83b)



Prepared according to TP 6 from 1-[5-iodo-3-(toluene-4-sulfonyl)-3H-imidazol-4-yl]-propan-1-one (**80f**) (155 mg, 0.38 mmol), lithium dineophylcuprate **17** (0.42 mmol), allyl bromide (137 mg, 1,1 mmol) and NMP (0.2 mL). Reaction time: 0.5 h at -78 °C. Purification by flash chromatography (*n*-pentane/diethyl ether = 2/1) yielded **83b** as a white solid (73 mg, 60%).

mp.: 123 °C

^{1}H-NMR ($CDCl_3$, 300 MHz): δ = 8.24 (s, 1H), 7.86-7.84 (d, *J* = 8.51 Hz, 2H), 7.31-7.28 (d, *J* = 8.51 Hz, 2H), 5.93-5.82 (m 1H), 5.08-4.96 (m, 2H), 3.47-3.45 (m, 2H), 2.74-2.67, (q, *J* = 7.18 Hz, 2H), 2.37 (s, 3H), 1.09-1.04 (t, *J* = 7.19 Hz, 3H).

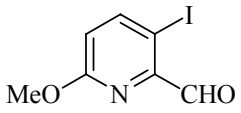
^{13}C-NMR ($CDCl_3$, 75 MHz): δ = 192.4, 147.6, 146.2, 141.5, 135.5, 134.2, 130.0, 129.4, 129.0, 117.6, 35.9, 34.3, 22.2, 8.3.

IR (KBr, cm^{-1}): $\tilde{\nu}$ = 3434 (w), 1676 (vs), 1539 (m), 1464 (m), 1374 (vs), 1224 (s), 1182 (vs), 1177 (vs), 1089 (vs), 989 (m), 924 (m), 815 (m), 667 (vs), 579 (vs), 545 (s).

MS (EI, 70 ev): 318 (47) [M^+], 303 (100), 289 (45), 275 (8), 261 (7), 163 (18), 139 (21), 91 (84), 65 (11).

$C_{16}H_{18}N_2O_3S$	HRMS (EI)	Calcd.	318.1038
		Found	318.1039

Synthesis 3-iodo-6-methoxy-pyridine-2-carbaldehyde (84)



A dry and argon flushed 25 mL flask, equipped with a magnetic stirrer and a septum, was charged with a solution of *N,N,N'*-trimethylethylenediamine (12 mmol) in dry THF (50 mL) at –78 °C. *n*-BuLi (1.68M/*n*-Hex., 6.5 mL, 11 mmol) was added. After 15 min, 6-methoxypyridinecarboxaldehyde (1.37 g, 10 mmol) was added and the resulting mixture was stirred at –78 °C for 15 min. Then *n*-BuLi (1.68M/*n*-Hex., 12 mL, 20 mmol) was added.The resulting mixture was first stirred at –78 °C for 5 h and then at – 42 °C for 5 h. The reaction was recooled to – 78 °C and a solution of iodine (7.6 g, 30 mmol) in dry THF (20 mL) was added. The reaction was stirred at rt for 30 min and poured into a solution of $Na_2S_2O_3$ (10%, 100 mL). The mixture extracted with CH_2Cl_2 (3 × 50 mL). The combined organic fractions were washed with brine (30 mL), dried over Na_2SO_4 and concentrated *in vacuo*. Purification by flash chromatography (*n*-Pentane/Et_2O = 10/1) yielded **84** as a light yellow solid (0.9 g, 35%).

mp.: 61 °C

^{1}H-NMR ($CDCl_3$, 300 MHz): δ = 9.89-9.88 (d, *J* = 0.55 Hz, 1H), 8.29-8.26 (dd, *J* = 8.63 Hz, *J* = 0.55 Hz, 1H), 6.89-6.86 (d, *J* = 8.63 Hz, 1H), 4.00 (s. 3H).

^{13}C-NMR ($CDCl_3$, 75 MHz): δ = 192.8, 165.3, 152.7, 148.7, 118.4, 82.3, 54.6.

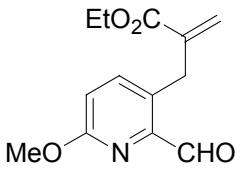
IR (KBr, cm^{-1}): $\tilde{\nu}$ = 3006 (w), 1697 (vs), 1579 (vs), 1467 (vs), 1414 (m), 1322 (s), 1269 (m), 1170 (m), 1032 (s), 1003 (m), 830 (m), 741 (m), 612 (m).

MS (EI, 70 eV): 263 (M^+, 100), 234 (16), 219 (10), 205 (5), 108 (12), 106 (11), 64 (7).

$C_7H_6INO_2$	HRMS (EI)	Calcd.	262.9443

Found 262.9452

Synthesis of 2-(2-formyl-6-methoxy-pyridin-3-ylmethyl)-acrylic acid ethyl ester (86a)



Prepared according to TP 6 from 3-iodo-6-methoxy-pyridine-2-carbaldehyde (**84**) (263 mg, 1.0 mmol), lithium dineophylcuprate **17** (1.2 mmol), and ethyl (2-bromomethyl)acrylate (580 mg, 3.0 mmol). Reaction time: 3 h from –78 °C to –60 °C. Purification by flash chromatography (*n*-pentane/diethyl ether = 10/1) yielded **86a** as colorless oil (204 mg, 82%).

^{1}H-NMR ($CDCl_3$, 300 MHz): δ = 10.03-10.03 (d, *J* = 0.66 Hz, 1H), 7.74-7.71 (dd, *J* = 8.51 Hz, *J* = 0.55 Hz, 1H), 7.03-7.00 (d, *J* = 8.51 Hz, 1H), 6.18-6.17 (q, *J* = 1.11 Hz, 1H), 5.41-5.40 (q, *J* = 1.55 Hz, 1H), 4.21-4.14 (q, *J* = 7.08 Hz, 1H), 4.05 (s. 2H), 1.27-1.23 (t, *J* = 7.08 Hz, 3H).

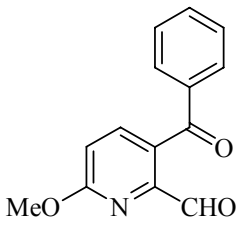
^{13}C-NMR ($CDCl_3$, 75 MHz): δ = 195.1, 167.3, 164.0, 148.0, 144.2, 141.0, 130.5, 126.5, 116.5, 61.7, 54.2, 33.0, 14.8.

IR (film, cm^{-1}): $\tilde{\nu}$ = 3407 (w), 2981 (m), 1713 (vs), 1601 (vs), 1573 (w), 1481 (vs), 1426 (s), 1368 (m), 1337 (s), 1234 (s), 1029 (s), 944 (m), 820 (w), 651 (w).

MS (EI, 70 eV): 249 (M^+, 18), 220 (100), 204 (18), 192 (26), 176 (96), 148 (30), 133 (14), 77 (11).

$C_{13}H_{15}NO_4$ HRMS (EI) Calcd. 249.1001
Found 249.1006

Synthesis of 3-benzoyl-6-methoxy-pyridine-2-carbaldehyde (86b)



Prepared according to TP 6 from 3-iodo-6-methoxy-pyridine-2-carbaldehyde (**84**) (105 mg, 0.4 mmol), lithium dineophylcuprate **17** (0.5 mmol), and benzoyl chloride (168 mg, 1.2 mmol). Reaction time: 3 h at from –78 °C to –60 °C. Purification by flash chromatography (*n*-pentane/diethyl ether = 8/1) yielded **86b** as a light yellow solid (84 mg, 63%).

mp.: 69 °C

^{1}H-NMR (Acetone-d_6, 300 MHz): δ = 10.09-10.08 (d, *J* = 0.55 Hz, 1H), 8.08-8.05 (dd, *J* = 8.40 Hz, *J* = 0.55 Hz, 1H), 7,97-7.93 (m, 2H), 7.85-7.80 (m, 1H), 7.73-7.66 (m, 2H), 7.84-7.38 (d, *J* = 8.51 Hz, 1H), 4.49 (s. 3H).

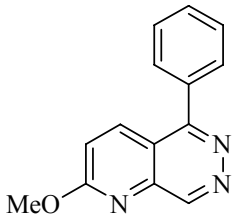
^{13}C-NMR (Acetone-d_6, 75 MHz): δ = 192.9, 165.8, 149.8, 140.6, 138.5, 134.5, 131.3, 130.4, 130.0, 129.9, 116.6, 54.8.

IR (KBr, cm^{-1}): $\tilde{\nu}$ = 3437 (br), 2857 (w), 1705 (s), 1667 (s), 1591 (vs), 1481 (s), 1332 (s), 1268 (vs), 1022 (m), 919 (w), 838 (m), 705 (m).

MS (EI, 70 eV): 241 (M^+, 75), 226 (36), 212 (100), 198 (17), 184 (19), 136 (35), 105 (19), 77 (23).

$C_{14}H_{11}NO_3$	HRMS (EI)	Calcd.	241.0739
		Found	241.0711

Synthesis of 2-methoxy-5-phenyl-pyrido[2,3-d]pyridazine (87)



Prepared according to TP 3 from 3-benzoyl-6-methoxy-pyridine-2-carbaldehyde (**86b**) (80 mg, 0.33 mmol), and hydrazine monohydrate (1M/EtOH, 0.4 mL, 0.4 mmol). Reaction time: 15 min at 78 °C. Purification by flash chromatography (*n*-pentane/diethyl ether = 1/2) yielded **87** as a light yellow solid (74 mg, 95%).

mp.: 158 °C

^{1}H-NMR ($CDCl_3$, 300 MHz): δ = 9.51-9.50 (d, *J* = 0.66 Hz, 1H), 8.15-8.11 (dd, *J* = 9.07 Hz,

J = 0.77 Hz, 1H), 7.66-7.62 (m, 2 H), 7.52-7.49 (m, 3H), 7.15-7.12 (d, *J* = 9.18 Hz, 1H), 4.10 (s. 3H).

^{13}C-NMR ($CDCl_3$, 75 MHz): δ = 167.0, 159.5, 151.4, 142.9, 136.9, 135.7, 130.4, 130.1, 129.1, 119.7, 118.8, 54.9.

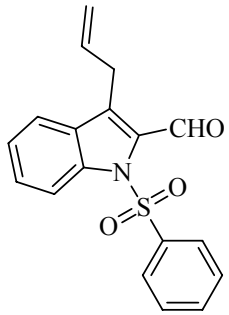
IR (KBr, cm^{-1}): $\tilde{\nu}$ = 3435 (br), 3076 (w), 1606 (vs), 1556 (m), 1473 (s), 1395 (vs), 1372 (s), 1303 (vs), 1253 (w), 1126 (w), 1033 (m), 866 (w) 691 (m).

MS (EI, 70 eV): 237 (M^+, 36), 236 (100), 222 (47), 166 (5), 139 (12), 126 (2), 77 (4).

$C_{14}H_{11}N_3O$ HRMS (EI) Calcd. 237.0902

Found 237.0893

Synthesis of 3-allyl-1-benzenesulfonyl-1H-indole-2-carbaldehyde (90a)



Prepared according to TP 6 from 1-benzenesulfonyl-3-iodo-1H-indole-2-carbaldehyde (**88a**) (206 mg, 0.5 mmol), lithium dineophylcuprate **17** (0.6 mmol), and allyl bromide (180 mg, 1.5 mmol). Reaction time: 30 min at -78 °C. Purification by flash chromatography (*n*-pentane/diethyl ether = 5/1) yielded **90a** as a colorless solid (135 mg, 83%).

mp.: 117 °C

^{1}H-NMR ($CDCl_3$, 300 MHz): δ = 10.65 (s, 1H), 8.30-8.26 (dd, *J* = 8.51 Hz, *J* = 0.89 Hz, 1H), 7.75-7.72 (m, 2H), 7.65-7.53 (m, 2H), 7.44-7.35 (m, 4H), 6.00-5.87 (m, 1H), 5.04-4.88 (m, 2H), 3.83-3.80 (dt, *J* = 5.97 Hz, *J* = 1.66 Hz, 1H).

^{13}C-NMR ($CDCl_3$, 75 MHz): δ = 185.1, 138.1, 137.3, 134.8, 134.5, 133.9, 133.4, 130.4, 129.5, 127.0, 125.2, 122.3, 116.6, 116.4, 29.2.

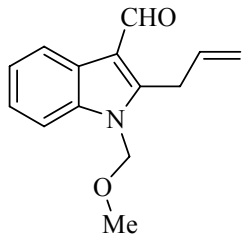
IR (KBr, cm^{-1}): $\tilde{\nu}$ = 2962 (w), 1666 (s), 1540 (s), 1445 (m), 1358 (s), 1223 (m), 1171 (vs), 1145 (vs), 1085 (m), 912 (s), 721 (vs) 697 (vs).

MS (EI, 70 eV): 237 (M^+, 36), 236 (100), 222 (47), 166 (5), 139 (12), 126 (2), 77 (4).

$C_{14}H_{11}N_3O$ HRMS (EI) Calcd. 237.0902

Found 237.0893

Synthesis of 2-allyl-1-methoxymethyl-1H-indole-3-carbaldehyde (90b)



Prepared according to TP 6 from 2-iodo-1-methoxymethyl-1H-indole-3-carbaldehyde (**88b**) (315 mg, 1.0 mmol), lithium dineophylcuprate **17** (1.2 mmol), and allyl bromide (360 mg, 3.0 mmol). Reaction time: 30 min at -78 °C. Purification by flash chromatography (*n*-pentane/diethyl ether = 1/1) yielded **90a** as a light yellow solid (213 mg, 93%).

mp.: 96 °C

^{1}H-NMR ($CDCl_3$, 300 MHz): δ = 9.99 (s, 1H), 8.20-8.18 (d, *J* = 6.75 Hz, 1H), 7.70-7.68 (d, *J* = 7.63 Hz, 1H), 7.35-7.24 (m, 3H), 6.88-6.81 (dq, *J* = 15.81 Hz, *J* = 3.43 Hz, *J* = 1.66 Hz, 1 H), 6.52-6.40 (m. 1H), 5.59 (s, 2H), 3.25 (s, 3H), 2.05-2.02 (dd, *J* = 6.63 Hz, *J* = 1.66 Hz, 2H).

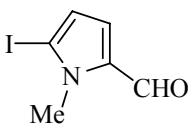
^{13}C-NMR ($CDCl_3$, 75 MHz): δ = 186.1, 149.2, 140.8, 137.0, 125.3, 124.3, 123.2, 121.2, 117.6, 114.9, 111.2, 74.2, 56.1, 19.6.

IR (KBr, cm^{-1}): $\tilde{\nu}$ = 2941 (w), 1637 (vs), 1607 (w), 1521 (m), 1462 (m), 1378 (s), 1191 (w), 1114 (m), 1040 (s), 1048 (m), 968 (w), 756 (m), 633 (w).

MS (EI, 70 eV): 229 (M^+, 38), 214 (100), 198 (10), 184 (12), 170 (13), 154 (15), 128 (10), 77 (5).

$C_{14}H_{15}NO_2$	HRMS (EI)	Calcd.	229.1103
		Found	229.1116

Synthesis of 5-iodo-1-methyl-1H-pyrrole-2-carbaldehyde (91c)



A dry and argon flushed 25 mL flask, equipped with a magnetic stirrer and a septum, was charged with a solution of *N*-methylpiperazine (2.7 mL, 24.2 mmol) in dry benzene (70 mL) at 0 °C. *n*-BuLi (1.68M/*n*-Hex., 13.1 mL, 22 mmol) was added. After 15 min, 1-methyl-2-pyrrolecarboxaldehyde (2.2 g, 20 mmol) was added and the resulting mixture was stirred at 0 °C for 15 min. Then TMEDA (9.1 mL, 60 mmol) and *n*-BuLi (1.68M/*n*-Hex., 36 mL, 60 mmol) were added. The resulting mixture was first stirred at rt for 12 h. Then the reaction was recooled to 0 ^{o}C and dry THF (70 mL) was added. The resulting mixture was further cooled to –42 ^{o}C and a solution of iodine (32 g, 126 mmol) in dry THF (50 mL) was added. The reaction was stirred at rt for 1 h and then poured into a solution of $Na_2S_2O_3$ (10%, 300 mL). The mixture extracted with CH_2Cl_2 (3 × 200 mL). The combined organic fractions were washed with brine (30 mL), dried over Na_2SO_4 and concentrated *in vacuo*. Purification by flash chromatography (Pentane/Et_2O = 10/1) yielded **91c** as a light yellow solid (0.5 g, 11%).

mp.: 100 ^{o}C

^{1}H-NMR ($CDCl_3$, 300 MHz): δ = 9.26 (s, 1H), 7.03-7.02 (d, *J* = 4.20 Hz, 1H), 6.56-6.55 (dd, *J* = 4.20 Hz, 1H), 3.87 (s, 3H).

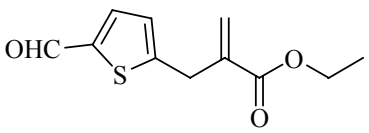
^{13}C-NMR ($CDCl_3$, 75 MHz): δ = 193.5, 135.0, 125.6, 119.8, 92.0, 37.2.

IR (KBr, cm^{-1}): $\tilde{\nu}$ = 3096 (w), 1650 (vs), 1500 (m), 1450 (s), 1355 (m), 1074 (w), 846 (w), 798 (s), 763 (m), 630 (m).

MS (EI, 70 eV): 235 (M^+, 100), 206 (4), 165 (7), 108 (8), 80 (6).

C_6H_6INO	HRMS (EI)	Calcd.	234.9494
		Found	234.9481

Synthesis of 2-(5-formyl-thiophen-2-ylmethyl)-acrylic acid ethyl ester (93a)



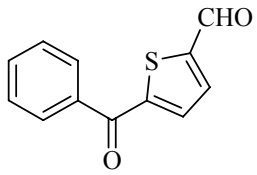
Prepared according to TP 6 from 5-iodo-thiophene-2-carbaldehyde (**91a**) (238 mg, 1.0 mmol), lithium dineophylcuprate **17** (1.2 mmol), and ethyl (2-bromomethyl)acrylate (360 mg, 3.0 mmol). Reaction time: 15 min at -78 ^{o}C. Purification by flash chromatography

(*n*-pentane/diethyl ether = 3/1) yielded **93a** as a light yellow oil (190 mg, 85%).

^{1}H-NMR (DMSO, 300 MHz): δ = 9.81 (s, 1H), 7.86-7.85 (d, *J* = 3.66 Hz, 1H), 7.08-7.07 (d, *J* = 3.66 Hz, 1H), 6.20 (s, 1H), 5.84 (s, 1H), 4.15-4.10 (q, *J* = 7.02 Hz, 2H), 3.88 (s, 2H), 1.20-1.16 (t, *J* = 7.02 Hz, 3H).
^{13}C-NMR (DMSO, 75 MHz): δ = 184.3, 165.9, 153.4, 142.4, 138.8, 138.7, 128.1, 128.1, 61.1, 33.0, 14.4.
IR (film, cm^{-1}): $\tilde{\nu}$ = 2982 (w), 1714 (vs), 1667 (vs), 1633 (m), 1456 (vs), 1226 (s), 1198 (vs), 1155 (s), 1026 (m), 815 (m).
MS (EI, 70 eV): 224 (M^+, 100), 195 (19), 178 (35), 167 (26), 150 (73), 139 (10), 121 (38), 97 (13), 77 (10).

$C_{11}H_{12}O_3S$	HRMS (EI)	Calcd.	224.0507
		Found	224.0483

Synthesis of 5-benzoyl-thiophene-2-carbaldehyde (93b)

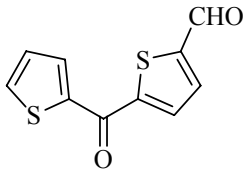


Prepared according to TP 6 from 5-iodo-thiophene-2-carbaldehyde (**91a**) (238 mg, 1.0 mmol), lithium dineophylcuprate **17** (1.2 mmol), and benzoyl chloride (420 mg, 3.0 mmol). Reaction time: 15 min at -78 °C. Purification by flash chromatography (*n*-pentane/diethyl ether = 1/1) yielded **93b** as a white solid (173 mg, 80%).

mp.: 108 °C
^{1}H-NMR ($CDCl_3$, 300 MHz): δ = 10.05 (s, 1H), 8.10-8.09 (d, *J* = 3.97 Hz, 1H), 7.88-7.85 (m, 2H), 7.84-7.83 (d, *J* = 3.97 Hz, 1H), 7.73-7.70 (m, 1H), 7.61-7.57 (m, 2H).
^{13}C-NMR ($CDCl_3$, 75 MHz): δ = 188.2, 186.0, 148.8, 148.5, 137.7, 137.0, 135.8, 133.7, 129.6, 129.3.
IR (KBr, cm^{-1}): $\tilde{\nu}$ = 3436 (vs), 1675 (vs), 1633 (vs), 1577 (m), 1320 (w), 1283 (vs), 1212 (vs), 1125 (w), 705 (m).
MS (EI, 70 eV): 216 (M^+, 100), 187 (25), 273 (10), 139 (58), 105 (75), 177 (40), 51 (8).

$C_{12}H_8O_2S$	HRMS (EI)	Calcd.	216.0245
		Found	216.0232

Synthesis of 5-(thiophene-2-carbonyl)-thiophene-2-carbaldehyde (93c)



Prepared according to TP 6 from 5-iodo-thiophene-2-carbaldehyde (**91a**) (238 mg, 1.0 mmol), lithium dineophylcuprate **17** (1.2 mmol), and 2-thiophenecarbonyl chloride (440 mg, 3.0 mmol). Reaction time: 15 min at -78 °C. Purification by flash chromatography (*n*-pentane/diethyl ether = 1/1) yielded **93b** as a yellow solid (160 mg, 72%).

mp.: 79 °C

^{1}H-NMR ($CDCl_3$, 300 MHz): δ = 10.07 (s, 1H), 8.20-8.11 (m, 4H), 7.37-7.34 (dd, *J* = 4.87 Hz, *J* = 3.87 Hz, 1H).

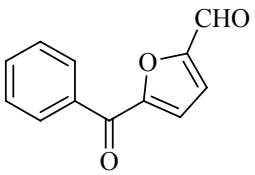
^{13}C-NMR ($CDCl_3$, 75 MHz): δ = 185.8, 178.7, 148.2, 147.8, 141.7, 137.7, 136.9, 135.5, 134.2, 129.6.

IR (KBr, cm^{-1}): $\tilde{\nu}$ = 3101 (w), 1760 (vs), 1713 (s), 1678 (s), 1590 (m), 1515 (w), 1410 (s), 1353 (m), 1202(vs), 1048 (m), 1004 (vs), 859 (w), 727 (s).

MS (EI, 70 eV): 222 (M^+, 59), 139 (16), 273 (10), 111 (100), 183 (12), 57 (13).

$C_{10}H_6O_2S_2$	HRMS (EI)	Calcd.	221.9809
		Found	221.9806

Synthesis of 5-benzoyl-furan-2-carbaldehyde (93d)



Prepared according to TP 6 from 5-iodo-furan-2-carbaldehyde (**91b**) (221 mg, 1.0 mmol), lithium dineophylcuprate **17** (1.2 mmol), and benzoyl chloride (420 mg, 3.0 mmol).

Reaction time: 15 min at -78 °C. Purification by flash chromatography (*n*-pentane/diethyl ether = 1/1) yielded **93d** as a yellow solid (122 mg, 61%).

mp.: 78 °C

^{1}H-NMR ($CDCl_3$, 300 MHz): δ = 9.81 (s, 1H), 7.97-7.95 (m, 2H), 7.73-7.69 (m, 1H), 7.67-7.66 (d, *J* = 3.66 Hz, 1H), 7.61-7.57 (m, 2H), 7.53-7.52 (d, *J* = 3.66 Hz, 1H).

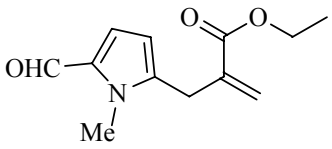
^{13}C-NMR ($CDCl_3$, 75 MHz): δ = 182.8, 180.8, 154.0, 136.5, 133.9, 133.3, 129.7, 129.7, 129.3, 121.5.

IR (KBr, cm^{-1}): $\tilde{\nu}$ = 3436 (s), 1684 (vs), 1646 (vs), 1580 (m), 1294 (s), 1260 (s), 1212 (w), 965 (w), 707 (m).

MS (EI, 70 eV): 200 (M^+, 70), 171 (34), 123 (12), 139 (58), 105 (100), 77 (46), 51 (12).

$C_{12}H_8O_3$	HRMS (EI)	Calcd.	200.0473
		Found	200.0456

Synthesis of 2-(5-formyl-1-methyl-1H-pyrrol-2-ylmethyl)-acrylic acid ethyl ester (93e)



Prepared according to TP 6 from 5-iodo-1-methyl-1H-pyrrole-2-carbaldehyde (**91c**) (235 mg, 1.0 mmol), lithium dineophylcuprate **17** (1.2 mmol), and ethyl (2-bromomethyl)acrylate (360 mg, 3.0 mmol). Reaction time: 1 h at -78 °C. Purification by flash chromatography (*n*-pentane/diethyl ether = 4/1) yielded **93a** as a colorless oil (175 mg, 79%).

^{1}H-NMR ($CDCl_3$, 300 MHz): δ = 9.43 (s, 1H), 6.96-6.94 (d, *J* = 4.09 Hz, 1H), 6.19 (d, *J* = 0.88 Hz, 1H), 6.03-6.02 (d, *J* = 3.98 Hz, 1H), 5.53-5.52 (d, *J* = 1.11 Hz, 1H), 4.19-4.12 (q, *J* = 7.19 Hz, 2H), 3.81 (s, 3H), 3.66 (s, 2H), 1.23-1.19 (t, *J* = 7.19 Hz, 3H).

^{13}C-NMR ($CDCl_3$, 75 MHz): δ = 179.2, 166.0, 141.4, 137.4, 132.1, 127.1, 124.2, 110.0, 61.0, 32.3, 28.4, 14.3.

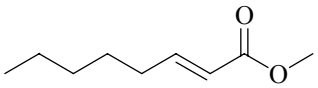
IR (film, cm^{-1}): $\tilde{\nu}$ = 3421 (w), 2982 (s), 1714 (vs), 1658 (vs), 1486 (vs), 1430 (m), 1368 (s), 1146 (s), 1036 (m), 958 (m), 778 (s), 629 (w).

MS (EI, 70 eV): 221 (M^+, 100), 204 (3), 192 (8), 176 (6), 164 (11), 146 (20), 118 (14) 94 (7), 77 (6).

$C_{12}H_{15}NO_3$	HRMS (EI)	Calcd.	221.1052
		Found	221.1030

13 Preparations of Polyfunctionalized Alkenes *via* Halogen-Copper Exchange Reaction

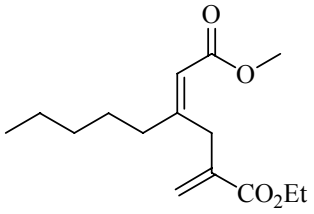
Synthesis of (*E*)-methyl-2-octenoate (101a)



Prepared according to TP 7 from methyl (2*Z*)-3-iodo-2-octenoate (**99a**) (282 mg, 1.0 mmol), lithium dineophylcuprate **17** (1.2 mmol) and water. Reaction time: 0.5 h at –78 °C. Purification by flash chromatography (*n*-pentane/diethyl ether = 50/1) yielded **101a** as colorless oil (144 mg, 92%).

^{1}H-NMR ($CDCl_3$, 300 MHz): δ = 6.71-6.96 (dt, *J* = 15.6 Hz, *J* = 6.8 Hz, 1H), 5.83-5.79 (d, *J* = 15.6 Hz, 1H), 3.73 (s, 3H), 2.22-2.16 (m. 2H), 1.48-1.25 (m, 4H), 0.91-0.87 (t, *J* = 7.1 Hz, 3H)
^{13}C-NMR ($CDCl_3$, 75 MHz): δ = 167.2, 149.8, 120.8, 51.3, 32.2, 31.3, 27.7, 22.4, 13.9.
MS (EI, 70 ev), *m/z* (%): 156 (8) [M^+], 125 (71), 113 (75), 96 (33), 87 (100), 55 (84).

Synthesis of 6-ethyl 1-methyl (2*Z*)-5-methylene-3-pentyl-2-hexenedioate (101b)



Prepared according to TP 7 from methyl (2*Z*)-3-iodo-2-octenoate (**99a**) (282 mg, 1.0 mmol), lithium dineophylcuprate **17** (1.2 mmol) NMP (0.5 mL) and ethyl bromomethylacrylate (576 mg, 3.0 mmol). Reaction time: 0.5 h at –78 °C. Purification by flash chromatography (*n*-pentane/diethyl ether = 15/1) yielded **101b** as colorless oil (238 mg, 89%).

^{1}H-NMR ($CDCl_3$, 300 MHz): δ = 6.24-6.22 (q, *J* = 1.11 Hz, 1H), 5.84 (s, 1H), 5.50-5.49 (d, *J* = 1.11 Hz, 1H), 4.24-4.21 (q, *J* = 7.08 Hz, 2H), 3.71 (s, 2 H), 3.69 (s, 3H), 2.14-2.09 (t, *J* = 7.41 Hz, 2H), 1.51-1.41 (m, 2H), 1.35-1.21 (m, 7H), 0.92-0.87 (m, 3H).

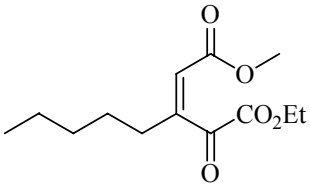
^{13}C-NMR ($CDCl_3$, 75 MHz): δ = 167.4, 167.3, 160.6, 138.0, 125.7, 117.5, 61.2, 51.3, 38.2, 33.6, 31.8, 27.7, 22.8, 14.5, 14.3.

IR (film, cm^{-1}): $\tilde{\nu}$ = 3423 (w), 2955 (m), 2932 (m), 2861 (m), 1720 (vs), 1648 (m), 1434 (m), 1248 (m), 1147 (m), 1029 (m), 873 (w).

MS (EI, 70 ev), *m/z* (%): 268 (3) [M^+], 237 (25), 222 (55), 195 (50), 180 (100), 163 (85), 134 (70), 105 (50), 91 (50), 79 (57), 55 (25).

$C_{15}H_{24}O_4$	HRMS (EI)	Calcd.	268.1675
		Found	268.1676

Synthesis of 6-ethyl 1-methyl (2*Z*)-5-oxo-3-pentyl-2-hexenedioate (101c)



Prepared according to TP 7 from methyl (2*Z*)-3-iodo-2-octenoate (**99a**) (282 mg, 1.0 mmol), lithium dineophylcuprate **17** (1.2 mmol) NMP (0.5 mL) and ethyl oxayl chloride (411 mg, 3.0 mmol). Reaction time: 0.5 h at –78 °C. Purification by flash chromatography (*n*-pentane/diethyl ether = 10/1) yielded **101c** as colorless oil (200 mg, 78%).

^{1}H-NMR ($CDCl_3$, 300 MHz): δ = 6.06-6.05 (t, *J* = 1.55 Hz, 1H), 4.42-4.40 (q, *J* = 7.07 Hz, 2H), 3.77 (s, 3H), 2.49-2.44 (t, *J* = 7.96 Hz, 2H), 1.63-1.52 (m, 2H), 1.46-1.32 (m, 7H), 0.98-0.96 (m, 3H).

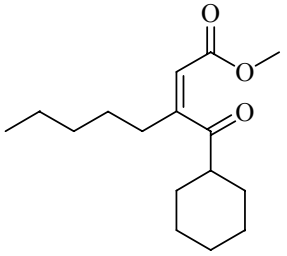
^{13}C-NMR ($CDCl_3$, 75 MHz): δ = 190.2, 166.9, 160.1, 158.5, 120.7, 62.8, 52.5, 34.6, 31.5, 26.9, 22.6, 14.3, 14.2.

IR (film, cm^{-1}): $\tilde{\nu}$ = 3430 (w), 2957 (s), 2933 (s), 2862 (m), 1762 (s), 1714 (vs), 1640 (m), 1438 (m), 1244 (m), 1145 (m), 1041 (m), 726 (w).

MS (EI, 70 ev), *m/z* (%): 256 (2) [M^+], 225 (2), 197 (5), 183 (100), 169 (9), 127 (11), 95 (20), 81 (15).

$C_{13}H_{21}O_5$ $[M+H]^+$	HRMS (EI)	Calcd.	257.1389
		Found	257.1397

Synthesis of methyl (2*Z*)-3-cyclohexyl-2-octenoate (101d)

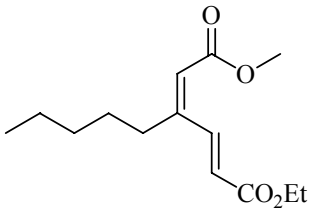


Prepared according to TP 7 from methyl (2*Z*)-3-iodo-2-octenoate (**99a**) (282 mg, 1.0 mmol), lithium dineophylcuprate **17** (1.2 mmol) NMP (0.5 mL) and cyclohexane carbonyl chloride (440 mg, 3.0 mmol). Reaction time: 0.5 h at –78 °C. Purification by flash chromatography (*n*-pentane/diethyl ether = 20/1) yielded **101d** as colorless oil (221 mg, 83%).

^{1}H-NMR ($CDCl_3$, 300 MHz): δ = 5.64-5.63 (t, *J* = 1.60 Hz, 1H), 3.62 (s, 3H), 2.37-2.52 (m, 1H), 2.21-2.15 (m. 2H), 1.74-1.08 (m. 16H), 0.84-0.79 (m. 3H).
^{13}C-NMR ($CDCl_3$, 75 MHz): δ = 211.6, 166.2, 162.5, 116.6, 52.0, 50.2, 35.2, 31.6, 28.7, 27.0, 26.2, 22.7, 14.3.
IR (film, cm^{-1}): $\tilde{\nu}$ = 3427 (w), 2931 (vs), 2855 (vs), 1722 (vs), 1697 (vs), 1637 (m), 1449 (m), 1220 (m), 1146 (s), 1026 (w), 726 (w).
MS (EI, 70 ev), *m/z* (%): 266 (3) [M^+], 235 (5), 207 (5), 183 (100), 169 (15), 127 (8), 95 (15), 55 (15).

$C_{16}H_{27}O_3$ $[M+H]^+$	HRMS (EI)	Calcd.	267.1960
		Found	267.1971

Synthesis of 6-ethyl 1-methyl (2*Z*,4*E*)-3-pentyl-2,4-hexadienedioate (101e)

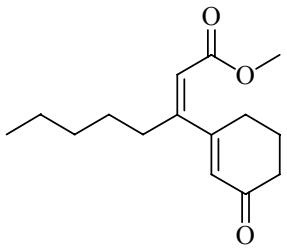


Prepared according to TP 7 from methyl (2*Z*)-3-iodo-2-octenoate (**99a**) (282 mg, 1.0 mmol), lithium dineophylcuprate **17** (1.2 mmol) NMP (0.5 mL) and ethyl propiolate (294 mg, 3.0 mmol). Reaction time: 0.5 h at –78 °C. Purification by flash chromatography (*n*-pentane/diethyl ether = 4/1) yielded **101e** as colorless oil (173 mg, 68%).

^{1}H-NMR ($CDCl_3$, 300 MHz): δ = 8.58-8.52 (dd, *J* = 16.25 Hz, *J* = 0.89 Hz,1H), 6.21-6.16 (dd, *J* = 16.25 Hz, *J* = 0.55 Hz, 1H), 5.92-5.91 (t, *J* = 1.2 Hz, 1H), 4.27-4.25 (q, *J* = 7.18 Hz, 2H), 3.76 (s, 3H), 2.36-2.35 (m, 2H), 1.57-1.47 (m, 2H), 1.37-1.24 (m, 7H), 0.92-0.88 (m, 3H).
^{13}C-NMR ($CDCl_3$, 75 MHz): δ = 167.0, 166.3, 152.4, 140.0, 124.2, 122.4, 61.1, 51.8, 34.3, 31.9, 28.8, 22.8, 14.6, 14.3.
IR (film, cm^{-1}): $\tilde{\nu}$ = 3424 (w), 2956 (m), 2932 (m), 2872 (m), 1723 (vs), 1631 (w), 1600 (m), 1278 (m), 1233 (s), 1154 (vs), 1038 (w), 880 (w).
MS (EI, 70 ev), *m/z* (%): 254 (3) [M^+], 225 (5), 198 (15), 181 (100), 167 (13), 149 (5), 137 (4), 125 (10), 107 (4), 93 (3), 79 (5), 55 (5).

$C_{14}H_{22}O_3$	HRMS (EI)	Calcd.	254.1518
		Found	254.1524

Synthesis of methyl (2*Z*)-3-(3-oxo-1-cyclohexen-1-yl)-2-octenoate (101f)



Prepared according to TP 7 from methyl (2*Z*)-3-iodo-2-octenoate (**99a**) (282 mg, 1.0 mmol), lithium dineophylcuprate **17** (1.2 mmol) NMP (0.5 mL) and 3-iodo-2-cyclohexen-1-one (666 mg, 3.0 mmol). Reaction time: 0.5 h at –78 °C. Purification by flash chromatography (*n*-pentane/diethyl ether = 4/1) yielded **101f** as colorless oil (203 mg, 81%).

^{1}H-NMR ($CDCl_3$, 300 MHz): δ = 5.66-5.65 (t, *J* = 1.22 Hz, 1H), 5.60-5.59 (t, *J* = 1.32 Hz, 1H), 3.60 (s, 3H), 2.39-2.35 (m, 4H), 2.21-2.16 (m, 2H), 2.02-2.10 (m, 2H), 1.44-1.20 (m,

6H), 0.84-0.80 (m, 3H).

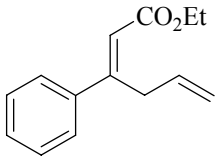
^{13}C-NMR ($CDCl_3$, 75 MHz): δ = 199.4, 166.0, 164.4, 160.0, 125.3, 116.2, 51.7, 38.3, 37.7, 31.6, 29.9, 27.1, 23.4, 22.7, 14.3.

IR (film, cm^{-1}): $\tilde{\nu}$ = 3429 (w), 2952 (s), 2932 (s), 2870 (m), 1722 (vs), 1672 (vs), 1605 (m), 1434 (m), 1217 (s), 1151 (s), 1035 (w), 888 (w).

MS (EI, 70 ev), *m/z* (%): 250 (20) [M^+], 222 (25), 194 (15), 179 (100), 166 (83), 151 (55), 138 (20), 119 (15), 107 (20), 91 (20), 77 (10), 55 (14).

$C_{15}H_{22}O_3$	HRMS (EI)	Calcd.	250.1569
		Found	250.1588

Synthesis of ethyl (2*E*)-3-phenyl-2,5-hexadienoate (101g)



Prepared according to TP 7 from ethyl (2*Z*)-3-iodo-3-phenyl-2-propenoate (**99b**) (302 mg, 1.0 mmol), lithium dineophylcuprate **17** (1.2 mmol) NMP (0.5 mL) and allyl bromide (360 mg, 3.0 mmol). Reaction time: 0.5 h at –78 °C. Purification by flash chromatography (*n*-pentane/diethyl ether = 25/1) yielded **101g** as colorless oil (199 mg, 92%).

^{1}H-NMR ($CDCl_3$, 300 MHz): δ = 7.53-7.48 (m, 2H), 7.40-7.35 (m, 3H), 6.17 (s, 1H), 5.96-5.82 (m, 1H), 5.02-5.16 (m, 2H), 4.28-4.21 (q, *J* = 7.07 Hz, 2H), 3.92-3.89 (m, 2H), 1.31-1.36 (t, *J* = 7.01 Hz, 3H).

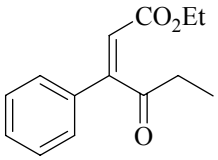
^{13}C-NMR ($CDCl_3$, 75 MHz): δ = 166.7, 157.2, 141.5, 135.7, 129.4, 128.9, 127.2, 118.4, 116.6, 60.3, 35.8, 14.7.

IR (film, cm^{-1}): $\tilde{\nu}$ = 2976 (m), 1733 (vs), 1638 (w), 1445 (m), 1367 (m), 1253 (s), 1157 (s), 1032 (m), 907 (m), 764 (m), 699 (s).

MS (EI, 70 ev), *m/z* (%): 216 (3) [M^+], 187 (1), 170 (11), 141 (79), 128 (100), 115 (18), 102 (3).

$C_{14}H_{16}O_2$	HRMS (EI)	Calcd.	216.1150
		Found	216.1128

Synthesis of ethyl (2*Z*)-4-oxo-3-phenyl-2-hexenoate (101h)



Prepared according to TP 7 from ethyl (2*Z*)-3-iodo-3-phenyl-2-propenoate (**99b**) (302 mg, 1.0 mmol), lithium dineophylcuprate **17** (1.2 mmol) NMP (0.5 mL) and propionyl chloride (280 mg, 3.0 mmol). Reaction time: 0.5 h at –78 °C. Purification by flash chromatography (*n*-pentane/diethyl ether = 7/1) yielded **101h** as colorless oil (200 mg, 86%).

^{1}H-NMR ($CDCl_3$, 300 MHz): δ = 7.45-7.40 (m, 5H), 6.18 (s, 1H), 4.27-4.20 (q, *J* = 7.07 Hz, 2H), 2.73-2.66 (q, *J* = 7.07 Hz, 2H), 1.39-1.34 (t, *J* = 7.01 Hz, 3H), 1.22-1.17 (t, *J* = 7.01 Hz, 3H).

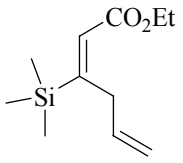
^{13}C-NMR ($CDCl_3$, 75 MHz): δ = 207.6, 165.8, 158.7, 133.7, 130.8, 129.5, 127.1, 116.2, 61.3, 36.4, 14.5, 7.8.

IR (film, cm^{-1}): $\tilde{\nu}$ = 2981 (w), 1713 (vs), 1615 (s), 1576 (w), 1448 (w), 1370 (w), 1331 (w), 1267 (m), 1183 (vs), 1115 (m), 1028 (m), 770 (w).

MS (EI, 70 ev), *m/z* (%): 232 (3) [M^+], 203 (100), 187 (24), 175 (90), 147 (62), 131 (42), 115 (9), 102 (51), 91 (13), 77 (15).

$C_{14}H_{16}O_3$	HRMS (EI)	Calcd.	232.1099
		Found	232.1088

Synthesis of ethyl (2*E*)-3-(trimethylsilyl)-2,5-hexadienoate (101i)



Prepared according to TP 7 from ethyl (2*Z*)-3-iodo-3-(trimethylsilyl)-2-propenoate (**99c**) (298 mg, 1.0 mmol), lithium dineophylcuprate **17** (1.2 mmol) NMP (0.5 mL) and allyl bromide (360 mg, 3.0 mmol). Reaction time: 0.5 h at –78 °C. Purification by flash chromatography (*n*-pentane/diethyl ether = 50/1) yielded **101i** as colorless oil (197 mg,

93%).

^{1}H-NMR ($CDCl_3$, 300 MHz): δ = 5.97-5.96 (t, *J* = 1.00 Hz, 1H), 5.73-5.60 (m, 1H), 4.94-4.82 (m, 2H), 4.07-4.00 (q, *J* = 7.08 Hz, 2H), 3.36-3.32 (m, 2H), 1.18-1.13 (t, *J* = 7.08 Hz, 3 H), 0.00 (s, 9H).

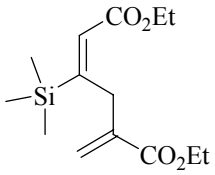
^{13}C-NMR ($CDCl_3$, 75 MHz): δ = 167.0, 164.2, 129.0, 127.5, 117.3, 61.5, 37.0, 15.9, 0.0.

IR (film, cm^{-1}): $\tilde{\nu}$ = 2960 (s), 1718 (vs), 1601 (w), 1250 (m), 1200 (vs), 1177 (vs), 840 (vs), 757 (m).

MS (EI, 70 ev), *m/z* (%): 212 (1) [M^+], 197 (11), 168 (14), 151 (5), 125 (13), 194 (8), 73 (100), 66 (16).

$C_{11}H_{20}O_2Si$	HRMS (EI)	Calcd.	212.1233
		Found	212.1196

Synthesis of diethyl (2*E*)-5-methylene-3-(trimethylsilyl)-2-hexenedioate (101j)



Prepared according to TP 7 from ethyl (2*Z*)-3-iodo-3-(trimethylsilyl)-2-propenoate (**99c**) (150 mg, 0.5 mmol), lithium dineophylcuprate **17** (0.6 mmol) NMP (0.3 mL) and ethyl bromomethylacrylate (188 mg, 1.5 mmol). Reaction time: 0.5 h at –78 °C. Purification by flash chromatography (*n*-pentane/diethyl ether = 50/1) yielded **101j** as colorless oil (115 mg, 81%).

^{1}H-NMR ($CDCl_3$, 300 MHz): δ = 6.16-6.14 (t, *J* = 1.66 Hz, 1H), 6.09-6.07 (dt, *J* = 1.44 Hz, *J* = 1.32 Hz, 1H), 5.25-5.23 (dt, *J* = 1.44 Hz, *J* = 1.32 Hz, 1H), 4.15-4.08 (q, *J* = 7.08 Hz, 2H), 4.07-4.00 (q, *J* = 7.08 Hz, 2H), 3.63-3.62 (m, 2H), 1.22-1.17 (t, *J* = 7.08 Hz, 3H), 1.18-1.13 (t, *J* = 7.08 Hz, 3 H), 0.00 (s, 9H).

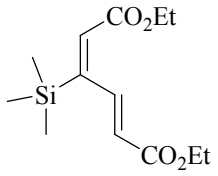
^{13}C-NMR ($CDCl_3$, 75 MHz): δ = 168.7, 166.9, 163.0, 139.7, 131.2, 126.5, 62.6, 61.6, 33.7, 16.0, 0.0.

IR (film, cm^{-1}): $\tilde{\nu}$ = 2981 (s), 2959 (s), 1717 (vs), 1632 (w), 1445 (w), 1367 (w), 1300 (w), 1251 (s), 1178 (vs), 1137 (vs), 841 (vs), 758 (w).

MS (EI, 70 ev), *m/z* (%): 284 (4) [M^+], 269 (25), 239 (25), 223 (55), 199 (30), 195 (33), 167 (40), 151 (60), 93 (31), 73 (100).

$C_{14}H_{24}O_4Si$	HRMS (EI)	Calcd.	284.1444
		Found	284.1427

Synthesis of diethyl (2*E*,4*E*)-3-(trimethylsilyl)-2,4-hexadienedioate (101k)



Prepared according to TP 7 from ethyl (2*Z*)-3-iodo-3-(trimethylsilyl)-2-propenoate (**99c**) (596 mg, 2.0 mmol), lithium dineophylcuprate **17** (2.4 mmol) NMP (0.5 mL) and ethyl propiolate (588 mg, 6 mmol). Reaction time: 0.5 h at –78 °C. Purification by flash chromatography (*n*-pentane/diethyl ether = 10/1) yielded **101k** as colorless oil (432 mg, 80%).

^{1}H-NMR ($CDCl_3$, 300 MHz): δ = 8.08-8.02 (dd, *J* = 16.36 Hz, *J* = 1.55 Hz, 1H), 5.92-5.91 (dd, *J* = 1.55 Hz, *J* = 0.33 Hz, 1H), 5.75-5.69 (dd, *J* = 16.36 Hz, *J* = 0.33 Hz, 1H), 4.03-3.96 (q, *J* = 7.18 Hz, 2H), 4.01-3.93 (q, *J* = 7.18 Hz, 2H), 1.10-1.05 (t, *J* = 7.18 Hz, 3H), 1.09-1.04 (t, *J* = 7.18 Hz, 3H), 0.00 (s, 9H).

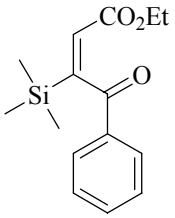
^{13}C-NMR ($CDCl_3$, 75 MHz): δ = 167.4, 166.0, 156.7, 145.2, 132.2, 124.2, 61.6, 15.3, 0.0.

IR (film, cm^{-1}): $\tilde{\nu}$ = 2981 (m), 2961 (m), 1720 (vs), 1622 (m), 1571 (w), 1446 (w), 1367 (w), 1307 (m), 1275 (s), 1188 (vs), 1132 (m), 843 (vs), 761 (w).

MS (EI, 70 ev), *m/z* (%): 270 (1) [M^+], 255 (3), 241 (11), 225 (5), 197 (100), 169 (41), 153 (17), 123 (81), 103 (8), 73 (78).

$C_{13}H_{22}O_4Si$	HRMS (EI)	Calcd.	270.1287
		Found	270.1269

Synthesis of ethyl (2*E*)-3-phenyl-3-(trimethylsilyl)-2-propenoate (101l)

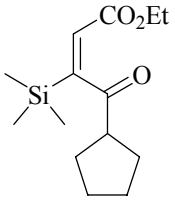


Prepared according to TP 7 from ethyl (2*Z*)-3-iodo-3-(trimethylsilyl)-2-propenoate (**99c**) (298 mg, 1.0 mmol), lithium dineophylcuprate **17** (1.2 mmol) NMP (0.5 mL) and benzoyl chloride (420 mg, 3.0 mmol). Reaction time: 0.5 h at –78 °C. Purification by flash chromatography (*n*-pentane/diethyl ether = 8/1) yielded **101l** as colorless oil (235 mg, 85%).

^{1}H-NMR ($CDCl_3$, 300 MHz): δ = 7.70-7.67 (m, 2H), 7.40-7.34 (m, 1H), 7.29-7.24 (m, 2H), 6.11 (s, 1H), 3.85-3.78 (q, *J* = 7.08 Hz, 2H), 0.88-0.83 (t, *J* = 7.07 Hz, 3H), 0.00 (s, 9H).
^{13}C-NMR ($CDCl_3$, 75 MHz): δ = 201.2, 166.9, 165.9, 138.0, 134.9, 130.6, 130.4, 117.5, 62.8, 15.6, 0.0.
IR (film, cm^{-1}): $\tilde{\nu}$ = 2959 (w), 1721 (vs), 1663 (vs), 1597 (w), 1449 (m), 1367 (w), 1333 (s), 1234 (s), 1192 vs), 1049 (m), 843 (vs), 757 (w).
MS (EI, 70 ev), *m/z* (%): 276 (5) [M^+], 261 (15), 247 (15), 233 (16), 203 (40), 105 (100), 77 (31).

$C_{15}H_{20}O_3Si$	HRMS (EI)	Calcd.	276.1182
		Found	276.1157

Synthesis of ethyl (2*E*)-3-cyclopentyl-3-(trimethylsilyl)-2-propenoate (101m)



Prepared according to TP 7 from ethyl (2*Z*)-3-iodo-3-(trimethylsilyl)-2-propenoate (**99c**) (298 mg, 1.0 mmol), lithium dineophylcuprate **17** (1.2 mmol) NMP (0.5 mL) and cyclopentanecarbonyl chloride (397 mg, 3.0 mmol). Reaction time: 0.5 h at –78 °C. Purification by flash chromatography (*n*-pentane/diethyl ether = 10/1) yielded **101m** as colorless oil (239 mg, 89%).

^{1}H-NMR ($CDCl_3$, 300 MHz): δ = 5.80 (s, 1H), 3.98-3.91 (q, *J* = 7.18 Hz, 2H), 2.79-2.68 (quint, *J* = 8.29 Hz, 1H), 1.67-1.31 (m, 8H), 1.08-1.03 (t, *J* = 7.18 Hz, 3H), 0.00 (s, 9H).

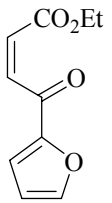
^{13}C-NMR ($CDCl_3$, 75 MHz): δ = 214.4, 169.2, 165.8, 128.4, 62.3, 53.2, 31.0, 27.4, 15.6, 0.0.

IR (film, cm^{-1}): $\tilde{\nu}$ = 2958 (s), 2870 (m), 1720 (vs), 1681 (vs), 1597 (w), 1449 (w), 1367 (w), 1329 (m), 1251 (m), 1200 (vs), 1117 (m), 845 (vs), 761 (w).

MS (EI, 70 ev), *m/z* (%): 268 (1) [M^+], 253 (5), 239 (4), 223 (5), 199 (100), 171 (40), 155 (30), 127 (18), 83 (30), 73 (51).

$C_{14}H_{24}O_3Si$	HRMS (EI)	Calcd.	268.1495
		Found	268.1481

Synthesis of ethyl (2*Z*)-4-(2-furyl)-4-oxo-2-butenoate (101n)



Prepared according to TP 7 from ethyl (2*Z*)-3-iodo-3-(trimethylsilyl)-2-propenoate (**99c**) (298 mg, 1.0 mmol), lithium dineophylcuprate **17** (1.2 mmol) NMP (0.5 mL) and 2-furoyl chloride (393 mg, 3.0 mmol). Reaction time: 0.5 h at –78 °C. Purification by flash chromatography (*n*-pentane/diethyl ether = 10/1) yielded **101n** as colorless oil (146 mg, 75%).

^{1}H-NMR ($CDCl_3$, 300 MHz): δ = 7.71-7.66 (d, *J* = 15.59 Hz, 1H), 7.63-7.62 (dd, *J* = 1.65 Hz, *J* = 0.33 Hz, 2H), 7.31-7.30 (dd, *J* = 3.65 Hz, *J* = 0.33 Hz, 1H), 6.93-6.88 (d, *J* = 15.59 Hz, 1H), 6.56-6.54 (dd, *J* = 3.65 Hz, *J* = 1.65 Hz, 2H), 4.26-4.19 (q, *J* = 7.08 Hz, 2H), 1.30-1.25 (t, *J* = 7.08 Hz, 3H).

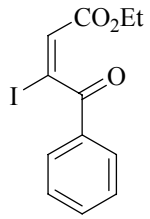
^{13}C-NMR ($CDCl_3$, 75 MHz): δ = 176.9, 165.8, 153.2, 148.2, 135.9, 132.6, 119.9, 113.3, 61.8, 14.5.

IR (film, cm^{-1}): $\tilde{\nu}$ = 3130 (m), 1717vs (m), 1668 (vs), 1626 (vs), 1560 (m), 1467 (vs), 1403 (vs), 1366 (m), 1327 (vs), 1303 (vs), 1259 (m), 1179 (vs), 1012 (m), 783 (s), 768 (m).

MS (EI, 70 ev), *m/z* (%): 194 (45) [M^+], 166 (12), 149 (47), 121 (46), 95 (100), 82 (5).

$C_{10}H_{10}O_4$	HRMS (EI)	Calcd.	194.0579
		Found	194.0568

Synthesis of ethyl (2*E*)-3-iodo-4-oxo-4-phenyl-2-butenoate (104)



To a solution of ethyl (2*E*)-3-phenyl-3-(trimethylsilyl)-2-propenoate (**101l**) (276 mg, 1.0 mmol) in CH_2Cl_2 (5 mL) at 0 °C, a solution of ICl (323 mg, 2.0 mmol) in CH_2Cl_2 (2 mL) was added and the resulting solution was stirred at rt for 12 h. The reaction mixture was poured into a solution of $Na_2S_2O_3$ (10%, 10 mL). The organic layer was separated and the aqueous was extracted with CH_2Cl_2 (10 mL × 3). The combined organic layers were washed with brine, dried over Na_2SO_4 and concentrated in vacuo. The residue was Purified by flash chromatography (*n*-pentane/diethyl ether = 10/1) to give **104** as yellow oil (281 mg, 85%).

^{1}H-NMR ($CDCl_3$, 300 MHz): δ = 7.78-7.76 (m, 2H), 7.45-7.40 (m, 1H), 7.33-7.28 (m, 2H), 6.67 (s, 1H), 3.86-3.79 (q, *J* = 7.08 Hz, 2H), 0.87-0.82 (t, *J* = 7.07 Hz, 3H).

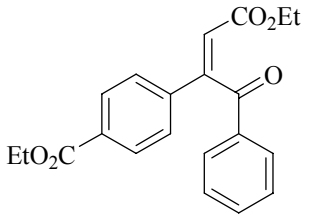
^{13}C-NMR ($CDCl_3$, 75 MHz): δ = 192.0, 163.2, 134.4, 133.8, 132.6, 129.7, 129.3, 114.3, 61.8, 14.0.

IR (film, cm^{-1}): $\tilde{\nu}$ = 3327 (w), 2982 (m), 1715 (vs), 1674 (vs), 1600 (s), 1449 (m), 1367 (w), 1326 (s), 1238 (s), 1192 (vs), 1026 (m), 869 (m), 698 (w).

MS (EI, 70 ev), *m/z* (%): 330 (5) [M^+], 302 (3), 285 (8), 257 (4), 203 (7), 175 (8), 105 (100), 77 (31).

$C_{12}H_{11}IO_3$	HRMS (EI)	Calcd.	329.9753
		Found	329.9754

Synthesis of ethyl 4-[(1*Z*)-1-benzoyl-3-ethoxy-3-oxo-1-propenyl]benzoate (106)



A dry and argon flushed 25 mL flask, equipped with a magnetic stirrer and a septum, was charged with a solution of ethyl 4-iodobenzoate (331 mg, 1.2 mmol) in dry THF (5 mL) at -78 °C. *i*-PrMgCl (1.0 M/THF, 1.2 mL, 1.2 mmol) was added and the resulting mixture was stirred at rt for 30 min. The reaxtion was recooled to -78 °C and a solution of $ZnBr_2$ (1.0 M/THF, 1.2 mL, 1.2 mmol) was added. After stiring at rt for 30 min, the solution was cannulated into a solution of ethyl (2*E*)-3-iodo-4-oxo-4-phenyl-2-butenoate (**104**) (330 mg, 1.0 mmol) in dry THF (3 mL) at -78 °C. The resulting mixture was allowed to be warmed up to rt and then $Pd(PPh_3)_4$ (35 mg, 0.05 mmol) was added. The reaction was stirred at rt for 2 h and then quenched with saturated aqueous NH_4Cl solution (20 mL). The reaction mixture was extracted with CH_2Cl_2 (3 × 20 mL). The combined extracts were washed with brine and dried (Na_2SO_4). Evaporation of the solvents and purification by column chromatography (*n*-pentane/diethyl ether = 5/1) yielded **106** as colorless oil (246 mg, 70%).

^{1}H-NMR ($CDCl_3$, 300 MHz): δ = 7.97-7,94 (d, *J* = 8.51 Hz, 2H), 7.87-7.85 (m, 2H), 7.51-7.45 (m, 1H), 7.50-7,47 (d, *J* = 8.51 Hz, 2H), 7.39-7.28 (m, 2H), 6.48 (s, 1H), 4.33-4.26 (q, *J* = 7.08 Hz, 2H), 4.04-3.97 (q, *J* = 7.08 Hz, 2H), 1.32-1.27 (t, *J* = 7.07 Hz, 3H), 1.07-1.02 (t, *J* = 7.07 Hz, 3H).

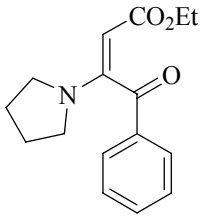
^{13}C-NMR ($CDCl_3$, 75 MHz): δ = 196.2, 166.1, 165.1, 154.8, 138.7, 136.2, 134.1, 132.4, 130.6, 129.3, 129.2, 127.3, 120.1, 110.9, 61.6, 61.5, 14.7, 14.2.

IR (film, cm^{-1}): $\tilde{\nu}$ = 3532 (w), 2981 (m), 1715 (vs), 1677 (vs), 1618 (s), 1449 (m), 1368 (m), 1326 (s), 1243 (s), 1274 (vs), 1186 (vs), 1108 (s), 858 (m), 775 (w).

MS (EI, 70 ev), *m/z* (%): 352 (5) [M^+], 324 (5), 307 (4), 278 (3), 129 (3), 105 (100), 77 (28).

$C_{21}H_{20}O_5$	HRMS (EI)	Calcd.	352.1311
		Found	352.1361

Synthesis of ethyl (2*E*)-4-oxo-4-phenyl-3-(1-pyrrolidinyl)-2-butenoate (107)



To a mixture of ethyl (2*E*)-3-iodo-4-oxo-4-phenyl-2-butenoate (**104**) (330 mg, 1.0 mmol) and CuI (19 mg, 0.1 mmol) in THF (5 mL) at rt, pyrrolidine (1.5 mL) was added and the resulting solution was stirred at rt for 15 min. The reaction mixture was concentrated *in vacuo*. The residue was purified by flash chromatography (*n*-pentane/diethyl ether = 1/1) to give **107** as yellow oil (200 mg, 73%).

^{1}H-NMR ($CDCl_3$, 300 MHz): δ = 8.02-7.99 (m, 2H), 7.61-7.56 (m, 1H), 7.51-7.46 (m, 2H), 4.75 (s, 1H), 3.98-3.91 (q, *J* = 7.18 Hz, 2H), 3.37-3.29 (m, 2H), 2.83-2.71 (m, 2H), 2.02-1.80 (m, 4H), 1.09-1.05 (t, *J* = 7.18 Hz, 3H).

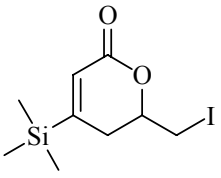
^{13}C-NMR ($CDCl_3$, 75 MHz): δ = 194.2, 168.2, 157.7, 135.6, 134.0, 129.3, 129.1, 85.9, 59.4, 48.5, 24.2, 14.6.

IR (film, cm^{-1}): $\tilde{\nu}$ = 3436 (vs), 2975 (w), 1677 (vs), 1561 (vs), 1439 (w), 1227 (w), 1187 (m), 1151 (s), 962 (w), 692 (w).

MS (EI, 70 ev), *m/z* (%): 273 (35) [M^+], 244 (12), 227 (100), 198 (32), 168 (21), 140 (38), 105 (36), 77 (61).

$C_{16}H_{19}NO_3$	HRMS (EI)	Calcd.	273.1365
		Found	273.1358

Synthesis of 6-(iodomethyl)-4-(trimethylsilyl)-5,6-dihydro-2*H*-pyran-2-one (109a)



Prepared according to TP 8 from ethyl (2*E*)-3-(trimethylsilyl)-2,5-hexadienoate (**101i**) (424 mg, 2.0 mmol) Reaction time: 12 h at rt. Purification by flash chromatography (*n*-pentane/diethyl ether = 1/1) yielded **109a** as colorless oil (560 mg, 90%).

^{1}H-NMR ($CDCl_3$, 300 MHz): δ = 5.99-5.97 (dd, *J* = 2.54 Hz, *J* = 1.00 Hz, 1H), 4.21-4.12 (m, 1H), 3.25-3.20 (dd, *J* = 10.62 Hz, *J* = 5.09 Hz, 1H), 3.21-3.15 (dd, *J* = 10.62 Hz, *J* = 6.52 Hz, 1H), 2.47-2.41 (dd, *J* = 17.91 Hz, *J* = 1.00 Hz, 1H), 2.45-2.39 (dd, *J* = 17.91 Hz, *J* = 1.00 Hz, 1H), 2.29-2.23 (dd, *J* = 17.91 Hz, *J* = 2,54 Hz, 1H), 2.25-2.18 (dd, *J* = 17.91 Hz, *J* = 2,54 Hz, 1H), 0.00 (m, 9H).

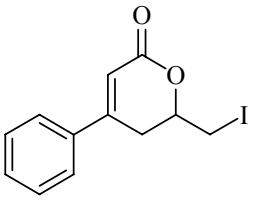
^{13}C-NMR ($CDCl_3$, 75 MHz): δ = 164.8, 164.5, 129.0, 79.0, 34.0, 8.2, 0.0.

IR (film, cm^{-1}): $\tilde{\nu}$ = 2956 (w), 1723 (vs), 1418 (w), 1369 (m), 1251 (vs), 1189 (m), 1014 (s), 842 (vs), 754 (m), 623 (w).

MS (EI, 70 ev), *m/z* (%): 309 (50) [M^+], 295 (76), 185 (46), 169 (74), 140 (28), 73 (100).

$C_9H_{15}IO_2Si$	HRMS (EI)	Calcd.	309.9886
		Found	309.9866

Synthesis of 6-(iodomethyl)-4-phenyl-5,6-dihydro-2*H*-pyran-2-one (109b)



Prepared according to TP 8 from ethyl (2*E*)-3-phenyl-2,5-hexadienoate (**101g**) (216 mg, 1.0 mmol) Reaction time: 12 h at rt. Purification by flash chromatography (*n*-pentane/diethyl ether = 1/1) yielded **109b** as a light yellow solid (286 mg, 91%).

mp.: 75 °C

^{1}H-NMR ($CDCl_3$, 300 MHz): δ = 7.58-7.54 (m, 2H), 7.50-7.45 (m, 3H), 6.37-6.36 (d, *J* = 2.10 Hz, 1H), 4.59-4.50 (m, 1H), 3.56-3.46 (m, 2H), 3.13-3.06 (dd, *J* = 17.47 Hz, *J* = 3.87 Hz, 1H), 2.95-2.85 (dd, *J* = 17.47 Hz, *J* = 2.33 Hz, 1H).

^{13}C-NMR ($CDCl_3$, 75 MHz): δ = 164.7, 154.5, 136.2, 131.3, 129.5, 126.5, 114.8, 76.2, 32.2, 6.1.

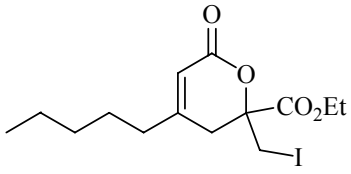
IR (KBr, cm^{-1}): $\tilde{\nu}$ = 2917 (w), 1714 (vs), 1447 (m), 1379 (s), 1261 (vs), 1236 (s), 1188 (s), 1039 (m), 871 (s), 765 (s), 688 (m).

MS (EI, 70 ev), *m/z* (%): 314 (78) [M^+], 187 (10), 173 (100), 145 (36), 115 (92), 102 (11).

$C_{12}H_{21}IO_2$	HRMS (EI)	Calcd.	313.9804

Found 313.9814

Synthesis of ethyl 2-(iodomethyl)-6-oxo-4-pentyl-3,6-dihydro-2*H*-pyran-2-carboxylate (109c)

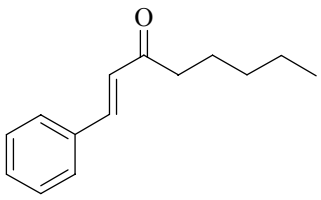


Prepared according to TP 8 from 6-ethyl 1-methyl-(2*Z*)-5-methylene-3-pentyl-2-hexenedioate (**101b**) (268 mg, 1.0 mmol) Reaction time: 12 h at rt. Purification by flash chromatography (*n*-pentane/diethyl ether = 1/1) yielded **109c** as a light yellow oil (350 mg, 92%).

^{1}H-NMR ($CDCl_3$, 300 MHz): δ = 5.80-5.78 (m, 1H), 4.29-4.22 (q, *J* = 7.07 Hz, 2H), 3.65-3.61 (d, *J* = 10.94 Hz, 1H), 3.55-3.51 (d, *J* = 10.94 Hz, 1H), 2.89-2.83 (d, *J* = 17.58 Hz, 1H), 2.78-2.72 (d, *J* = 17.58 Hz, 1H), 2.24-2.19 (t, *J* = 7.07 Hz, 2H), 1.55-1.44 (m, 2H), 1.38-1.25 (m, 4H), 1.32-1.27 (t, *J* = 7.07 Hz, 3H), 0.93-0.89 (t, *J* = 7.07 Hz, 3H).
^{13}C-NMR ($CDCl_3$, 75 MHz): δ = 169.1, 163.1, 158.9, 115.9, 82.1, 63.4, 36.7, 36.3, 31.6, 26.3, 22.7, 14.5, 14.3, 8.1.
IR (film, cm^{-1}): $\tilde{\nu}$ = 2956 (s), 2931 (s), 1732 (vs), 1465 (w), 1368 (m), 1211 (s), 1160 (s), 1038 (m), 867 (w), 753 (w).
MS (EI, 70 ev), *m/z* (%): 380 (2) [M^+], 307 (100), 253 (6), 180 (24), 169 (41), 109 (22) 95 (81), 82 (34), 55 (24).

$C_{14}H_{21}IO_4$	HRMS (EI)	Calcd.	380.0485
		Found	380.0494

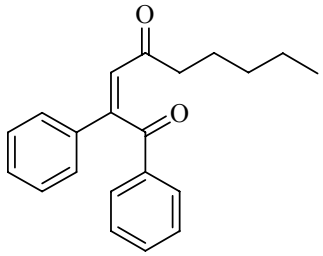
Synthesis of (1*E*)-1-phenyl-1-octen-3-one (111)



Prepared according to TP 9 from (1*Z*)-1-iodo-1-phenyl-1-octen-3-one (**110a**) (328 mg, 1.0 mmol), lithium dineophylcuprate **17** (1.2 mmol) and H_2O. Reaction time: 15 min at –100 °C. Purification by flash chromatography (*n*-pentane/diethyl ether = 50/1) yielded **111** as a yellow oil (188 mg, 93%).

^{1}H-NMR ($CDCl_3$, 300 MHz): δ =7.59-7.50 (m, 3H), 7.40-7.33 (m, 3H), 6.77-6.73 (d, *J* = 16.2 Hz, 1H), 2.66-2.64 (t, *J* = 7.46 Hz, 2 H), 1.74-1.62 (m, 2H), 1.41-1.30 (m, 4H), 0.91-0.89 (t, *J* = 6.86 Hz, 3H).
^{13}C-NMR ($CDCl_3$, 75 MHz): δ = 200.4, 142.1, 134.5, 130.2, 128.8, 128.1, 126.2, 40.8, 31.4, 24.0, 22.4, 13.8.
MS (EI, 70 ev), *m/z* (%): 202 (8) [M^+], 173 (3), 146 (54), 131 (100), 103 (34), 77 (18).

Synthesis of (2*Z*)-1,2-diphenyl-2-nonene-1,4-dione (114a)



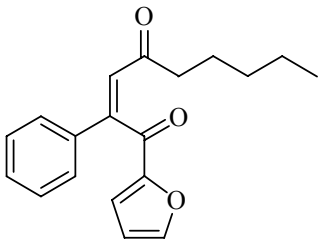
Prepared according to TP 9 from (1*Z*)-1-iodo-1-phenyl-1-octen-3-one (**110a**) (328 mg, 1.0 mmol), lithium dineophylcuprate **17** (1.2 mmol) and benzoyl chloride (420 mg, 3.0 mmol). Reaction time: 15 min at –100 °C. Purification by flash chromatography (*n*-pentane/diethyl ether = 10/1) yielded **114a** as a yellow solid (254 mg, 83%).

mp.: 67 °C
^{1}H-NMR ($CDCl_3$, 300 MHz): δ =7.85-7.82 (m, 2H), 7.47-7,41 (m, 3H), 7.36-7.28 (m, 5H), 6.77 (s, 1H), 2.51-2.46 (t, *J* = 7.30 Hz, 2H), 1.54-1.45 (m, 2H), 1.22-1.13 (m, 4H), 0.80-0.76 (t, *J* = 6.86 Hz, 3H).
^{13}C-NMR ($CDCl_3$, 75 MHz): δ = 199.1, 197.9, 154.3, 136.4, 134.8, 133.6, 130.9, 129.5, 129.1, 127.5, 124.3, 43.8, 31.7, 23.9, 22.8, 14.3.
IR (KBr, cm^{-1}): $\tilde{\nu}$ = 3447 (w), 2933 (m), 1683 (vs), 1671 (vs), 1585 (s), 1573 (s), 1495 (m), 1450 (s), 1347 (m), 1215 (s), 1128 (s), 1079 (s), 947 (m), 689 (m).

MS (EI, 70 ev), *m/z* (%): 306 (18) [M^+], 277 (3), 250 (4), 235 (45), 201 (4), 105 (100), 77 (28).

$C_{21}H_{22}O_2$	HRMS (EI)	Calcd.	306.1620
		Found	306.1598

Synthesis of (2*Z*)-1-(2-furyl)-2-phenyl-2-nonene-1,4-dione (114b)



Prepared according to TP 9 from (1*Z*)-1-iodo-1-phenyl-1-octen-3-one (**110a**) (328 mg, 1.0 mmol), lithium dineophylcuprate **17** (1.2 mmol) and 2-furoyl chloride (393 mg, 3.0 mmol). Reaction time: 15 min at –100 °C. Purification by flash chromatography (*n*-pentane/diethyl ether = 5/1) yielded **114b** as a brown solid (231 mg, 78%).

mp.: 85-86 °C

^{1}H-NMR ($CDCl_3$, 300 MHz): δ =7.46-7.42 (m, 3H), 7.33-7,29 (m, 3H), 7.02-7.01 (dt, *J* = 3.65 Hz, *J* = 0.77 Hz, 1H), 6.70 (s, 1H), 6.42-6.40 (ddd, *J* = 3.54 Hz, *J* = 1.66 Hz, *J* = 0.89 Hz, 1H), 2.53-2.48 (t, *J* = 7.30 Hz, 2H), 1.58-1.48 (m, 2H), 1.26-1.13 (m, 4H), 0.82-0.77 (t, *J* = 7.07 Hz, 3H).

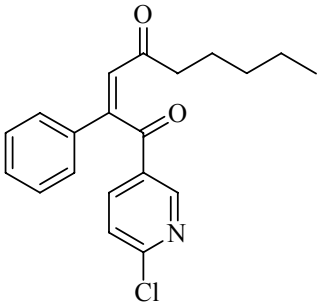
^{13}C-NMR ($CDCl_3$, 75 MHz): δ = 199.2, 185.5, 152.7, 152.3, 147.1, 134.6, 130.9, 129.4, 127.5, 125.2, 118.4, 112.7, 43.9, 31.7, 23.9, 22.8, 14.3.

IR (KBr, cm^{-1}): $\tilde{\nu}$ = 3436 (w), 2929 (w), 1681 (vs), 1654 (vs), 1597 (s), 1574 (w), 1468 (s), 1401 (s), 1371 (m), 1290 (w), 1130 (w), 1081 (s), 1059 (m), 789 (m).

MS (EI, 70 ev), *m/z* (%): 296 (36) [M^+], 267 (100), 239 (4), 225 (14), 211 (4), 197 (5), 141 (4), 115 (4), 95 (93), 77 (2).

$C_{19}H_{20}O_3$	HRMS (EI)	Calcd.	296.1412
		Found	296.1393

Synthesis of (2*Z*)-1-(6-chloro-3-pyridinyl)-2-phenyl-2-nonene-1,4-dione (114c)



Prepared according to TP 9 from (1*Z*)-1-iodo-1-phenyl-1-octen-3-one (**110a**) (328 mg, 1.0 mmol), lithium dineophylcuprate **17** (1.2 mmol) and 6-chloronicotinoyl chloride (528 mg, 3.0 mmol). Reaction time: 15 min at –100 °C. Purification by flash chromatography (*n*-pentane/diethyl ether = 10/1) yielded **114c** as a light yellow solid (277 mg, 81%).

mp.: 67 °C

^{1}H-NMR ($CDCl_3$, 300 MHz): δ =8.66-8.65 (dd, *J* = 2.43 Hz, *J* = 0.66 Hz, 1H), 8.17-8.13 (dd, *J* = 8.30 Hz, *J* = 2.43 Hz, 1H), 7.43-7.28 (m, 6 H), 6.79 (s, 1H), 2.54-2.49 (t, *J* = 7.40 Hz, 2H), 1.56-1.45 (m, 2H), 1.27-1.13 (m, 4H), 0.82-0.77 (t, *J* = 6.80 Hz, 3H).

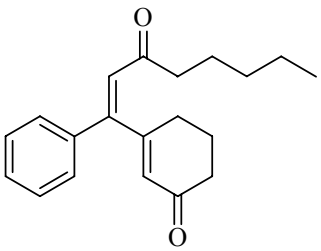
^{13}C-NMR ($CDCl_3$, 75 MHz): δ = 199.4, 195.4, 155.9, 153.0, 150.8, 138.5, 133.6, 131.5, 130.9, 129.8, 127.5, 125.1, 124.8, 43.8, 31.6, 23.8, 22.8, 14.2.

IR (KBr, cm^{-1}): $\tilde{\nu}$ = 3436 (w), 1686 (vs), 1673 (vs), 1585 (vs), 1572 (vs), 1463 (m), 1371 (s), 1299 (m), 1132 (m), 1074 (m), 942 (w), 768 (w), 603 (m).

MS (EI, 70 ev), *m/z* (%): 341 (12) [M^+], 323 (10), 285 (100), 244 (8), 201 (7), 140 (35), 112 (13), 102 (17), 91 (4), 77 (5).

$C_{20}H_{20}ClNO_2$	HRMS (EI)	Calcd.	341.1183
		Found	341.1161

Synthesis of 3-[(1*E*)-3-oxo-1-phenyl-1-octenyl]-2-cyclohexen-1-one (114d)



Prepared according to TP 9 from (1*Z*)-1-iodo-1-phenyl-1-octen-3-one (**110a**) (328 mg, 1.0 mmol), lithium dineophylcuprate **17** (1.2 mmol) and 3-iodo-2-cyclohexen-1-one (666 mg,

3.0 mmol). Reaction time: 15 min at –100 °C. Purification by flash chromatography (*n*-pentane/diethyl ether = 5/1) yielded **114d** as a light yellow oil (210 mg, 71%).

^{1}H-NMR ($CDCl_3$, 300 MHz): δ =7.40-7.25 (m, 5H), 6.45 (s, 1H), 5.77-5.76 (t, *J* = 1.54 Hz, 1H), 2.50-2.36 (m, 6H), 2.16-2.07 (m, 2H), 1.65-1.51 (m, 2H), 1.30-1.19 (m, 5H), 0.85-0.80 (t, *J* = 7.07 Hz, 3H).

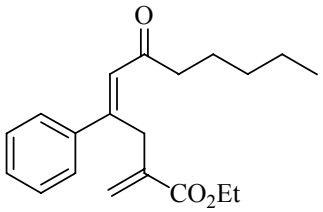
^{13}C-NMR ($CDCl_3$, 75 MHz): δ = 198.8, 198.0, 162.0, 151.9, 135.6, 129.2, 128.0, 126.3, 126.0, 122.1, 43.3, 36.4, 30.4, 28.8, 22.8, 22.0, 21.4, 12.9.

IR (film, cm^{-1}): $\tilde{\nu}$ = 3355 (w), 2954 (s), 2930 (s), 1678 (vs), 1622 (m), 1570 (s), 1447 (m), 1371 (w), 1238 (m), 1132 (m), 1072 (s), 966 (m), 764 (s), 696 (m).

MS (EI, 70 ev), *m/z* (%): 296 (5) [M^+], 268 (21), 240 (100), 225 (14), 211 (7), 197 (65), 141 (15), 115 (11), 91 (5), 77 (2).

$C_{20}H_{24}O_2$	HRMS (EI)	Calcd.	296.1776
		Found	296.1766

Synthesis of ethyl (4*E*)-2-methylene-6-oxo-4-phenyl-4-undecenoate (114e)



Prepared according to TP 9 from (1*Z*)-1-iodo-1-phenyl-1-octen-3-one (**110a**) (1.0 g, 3.0 mmol), lithium dineophylcuprate **17** (3.6 mmol) and ethyl bromomethylacrylate (1.5 g, 8.0 mmol). Reaction time: 15 min at –100 °C. Purification by flash chromatography (*n*-pentane/diethyl ether = 8/1) yielded **114e** as a light yellow oil (770 mg, 82%).

^{1}H-NMR ($CDCl_3$, 300 MHz): δ =7.49-7.46 (m, 2H), 7.38-7.35 (m, 3H), 6.67 (s, 1H), 6.17-6.15 (dd, *J* = 2.65 Hz, *J* = 1.32 Hz, 1H), 5.42-5.40 (dd, *J* = 3.00 Hz, *J* = 1.75 Hz, 1H), 4.24-4.17 (q, *J* = 7.19 Hz, 2H), 4.10-4.09 (t, *J* = 1.55 Hz, 2H), 2.59-2.54 (t, *J* = 7.35 Hz, 2H), 1.71-1.61 (m, 2H), 1.38-1.28 (m, 4H), 1.31-1.27 (t, *J* = 7.08 Hz, 3H), 0.94-0.89 (t, *J* = 6.90 Hz, 3H).

^{13}C-NMR ($CDCl_3$, 75 MHz): δ = 201.1, 167.2, 153.5, 141.1, 138.1, 129.6, 129.0, 127.2,

126.6, 125.4, 61.2, 45.3, 33.0, 31.8, 24.3, 22.9, 14.5, 14.3.

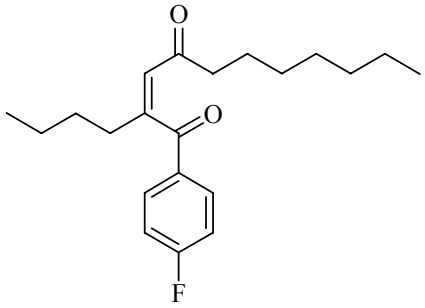
IR (film, cm^{-1}): $\tilde{\nu}$ = 3415 (w), 2957 (s), 2931 (s), 1714 (vs), 1686 (vs), 1601 (m), 1572 (m), 1446 (m), 1367 (m), 1247 (s), 1130 (s), 1075 (m), 951 (w), 761 (w), 697 (m).

MS (EI, 70 ev), *m/z* (%): 314 (13) [M^+], 285 (10), 241 (100), 215 (30), 187 (18), 169 (11), 141 (13), 115 (10), 91 (4), 102 (2).

$C_{20}H_{26}O_3$ HRMS (EI) Calcd. 314.1882

Found 314.1904

Synthesis of (2*Z*)-2-butyl-1-(4-fluorophenyl)-2-undecene-1,4-dione (114f)



Prepared according to TP 9 from (5*Z*)-5-iodo-5-tetradecen-7-one (**110b**) (336 mg, 1.0 mmol), lithium dineophylcuprate **17** (1.2 mmol) and 4-fluoro-benzoyl chloride (477 mg, 3.0 mmol). Reaction time: 15 min at –100 °C. Purification by flash chromatography (*n*-pentane/diethyl ether = 10/1) yielded **114f** as a colorless oil (249 mg, 75%).

^{1}H-NMR ($CDCl_3$, 300 MHz): δ =7.91-7.86 (dd, *J* = 8,74 Hz, *J* = 5.42 Hz, 2H), 7.15-7.09 (t, *J* = 8.56 Hz, 2H), 6.34-6.33 (t, *J* = 1.44 Hz, 1H), 2.49-2.44 (t, *J* = 7.36 Hz, 2H), 2.41-2.35 (dt, *J* = 7.74 Hz, *J* = 1.32 Hz, 2H), 1.62-1.24 (m, 14H), 0.94-0.90 (t, *J* = 7.30 Hz, 3H), 0.90-0.85 (t, *J* = 6.81 Hz, 3H).

^{13}C-NMR ($CDCl_3$, 75 MHz): δ = 199.1, 198.1, 166.2 (d, *J* = 254.7 Hz), 157.9, 132.0, 131.3 (d, *J* = 9.4 Hz), 125.4, 116.2 (d, j = 22.0 Hz), 43.4, 35.2, 32.0, 29.5, 29.4, 29.4, 24.0, 22.9, 22.7, 14.4, 14.1.

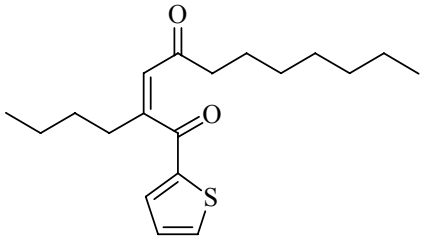
IR (film, cm^{-1}): $\tilde{\nu}$ = 3074 (w), 2957 (vs), 2928 (vs), 2858 (s), 1690 (vs), 1673 (vs), 1598 (vs), 1504 (m), 1466 (w), 1378 (m), 1235 (s), 1150 (m), 956 (w), 849 (m), 772 (w).

MS (EI, 70 ev), *m/z* (%): 332 (6) [M^+], 289 (8), 247 (7), 233 (45), 205 (8), 163 (7), 123 (100), 109 (6), 95 (25), 57 (10).

$C_{21}H_{29}FO_2$ HRMS (EI) Calcd. 332.2152

Found 332.2165

Synthesis of (2*Z*)-2-butyl-1-(2-thienyl)-2-decene-1,4-dione (114g)

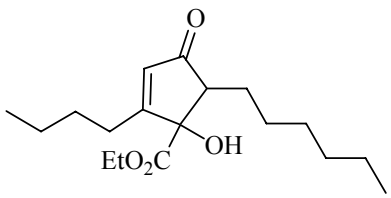


Prepared according to TP 9 from (5*Z*)-5-iodo-5-tetradecen-7-one (**110b**) (336 mg, 1.0 mmol), lithium dineophylcuprate **17** (1.2 mmol) and 2-furoyl chloride (438 mg, 3.0 mmol). Reaction time: 15 min at –100 °C. Purification by flash chromatography (*n*-pentane/diethyl ether = 10/1) yielded **114g** as a colorless oil (250 mg, 78%).

^{1}H-NMR ($CDCl_3$, 300 MHz): δ =7.65-7.63 (d, *J* = 4.87 Hz, 1H), 7.51-7.50 (d, *J* = 4.42 Hz, 1H), 7.10-7.08 (dd, *J* = 4.78 Hz, *J* = 4.42 Hz, 1H), 6.30-6.29 (t, *J* = 1.33 Hz, 1H), 2.49-2.44 (t, *J* = 7.52 Hz, 2H), 2.45-2.40 (dt, *J* = 7.52 Hz, *J* = 1.33 Hz, 2H), 1.59-1.22 (m, 14H), 0.94-0.90 (t, *J* = 7.52 Hz, 3H), 0.90-0.85 (t, *J* = 7.08 Hz, 3H).
^{13}C-NMR ($CDCl_3$, 75 MHz): δ = 198.9, 191.8, 156.9, 143.1, 134.1, 132.8, 128.4, 125.7, 43.5, 35.5, 32.0, 29.6, 29.4, 29.4, 24.1, 22.9, 22.7, 14.4, 14.1.
IR (film, cm^{-1}): $\tilde{\nu}$ = 3103 (w), 2957 (vs), 2929 (vs), 2858 (s), 1692 (s), 1650 (vs), 1614 (vs), 1516 (m), 1413 (s), 1378 (w), 1247 (s), 1051 (m), 721 (m).
MS (EI, 70 ev), *m/z* (%): 320 (6) [M^+], 277 (8), 235 (9), 221 (100), 209 (5), 193 (7), 179 (6), 111 (98), 97 (4), 57 (4).

$C_{19}H_{28}O_2S$	HRMS (EI)	Calcd.	320.1810
		Found	320.1803

Synthesis of 3-butyl-4-butyryl-5-hexyl-4-hydroxy-2-cyclopenten-1-one (114h)

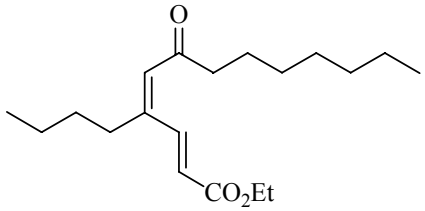


Prepared according to TP 9 from (5*Z*)-5-iodo-5-tetradecen-7-one (**110b**) (336 mg, 1.0 mmol), lithium dineophylcuprate **17** (1.2 mmol) and ethyl oxayl chloride (411 mg, 3.0 mmol). Reaction time: 15 min at –100 °C. Purification by flash chromatography (*n*-pentane/diethyl ether = 10/1) yielded **114h** as a colorless oil (245 mg, 71%).

^{1}H-NMR ($CDCl_3$, 300 MHz): δ = 6.16-6.15 (t, *J* = 1.44 Hz, 1H), 4.35-4.28 (q, *J* = 7.08 Hz, 2H), 2.72-2.67 (dd, *J* = 8.51 Hz, *J* = 5.86 Hz, 1H), 2.54-1-29 (m, 20H), 1.01-0.96 (t, *J* = 7.52 Hz, 3H), 0.96-0.91 (t, *J* = 7.08 Hz, 3H).
^{13}C-NMR ($CDCl_3$, 75 MHz): δ = 204.7, 175.6, 173.8, 131.0, 85.2, 63.5, 59.5, 31.8, 29.7, 29.2, 28.2, 27.8, 25.7, 22.9, 22.7, 14.4, 14.4, 14.1.
IR (film, cm^{-1}): $\tilde{\nu}$ = 3497 (s), 2957 (vs), 2930 (vs), 2860 (s), 1715 (vs), 1627 (w), 1466 (m), 1257 (w), 1215 (m), 1130 (w), 1019 (w), 858 (w).
MS (EI, 70 ev), *m/z* (%): 310 (60) [M^+], 237 (100), 208 (15), 179 (18), 152 (55), 110 (50), 55 (28).

$C_{18}H_{30}O_4$	HRMS (EI)	Calcd.	310.2144
		Found	310.2124

Synthesis of ethyl (2*E*,4*Z*)-4-butyl-6-oxo-2,4-tridecadienoate (114j)



Prepared according to TP 9 from (5*Z*)-5-iodo-5-tetradecen-7-one (**110b**) (336 mg, 1.0 mmol), lithium dineophylcuprate **17** (1.2 mmol) and ethyl propiolate (294 mg, 3.0 mmol). Reaction time: 15 min at –100 °C. Purification by flash chromatography (*n*-pentane/diethyl ether = 10/1) yielded **114i** as a colorless oil (246 mg, 80%).

^{1}H-NMR ($CDCl_3$, 300 MHz): δ = 8.38-8.32 (dd, *J* = 16.25 Hz, *J* = 0.77 Hz, 1H), 6.23 (s, 1H), 6.22-6.16 (d, *J* = 16.70 Hz, 1H), 4.29-4.22 (q, *J* = 7.08 Hz, 2H), 2.53-2.48 (t, *J* = 7.62 Hz, 2H), 2.37-2.32 (dt, *J* = 7.30 Hz, *J* = 0.66 Hz, 2H), 1.65-1.25 (m, 17H), 0.97-0.92 (t, *J* = 7.19 Hz, 3H), 0.92-0.87 (t, *J* = 6.97 Hz, 3H).
^{13}C-NMR ($CDCl_3$, 75 MHz): δ = 201.5, 167.0, 149.7, 140.9, 129.7, 124.6, 61.1, 45.0, 34.2,

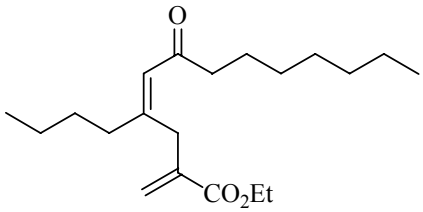
32.0, 31.4, 29.5, 29.5, 24.6, 23.0, 22.9, 14.6, 14.4, 14.2.

IR (film, cm^{-1}): $\tilde{\nu}$ = 3431 (w), 2957 (vs), 2930 (vs), 2858 (s), 1721 (vs), 1686 (s), 1581 (s), 1465 (m), 1274 (s), 1173 (s), 1040 (m), 993 (w), 877 (w).

MS (EI, 70 ev), *m/z* (%): 308 (11) [M^+], 279 (20), 235 (100), 181 (12), 136 (14), 107 (15), 55 (15).

$C_{19}H_{32}O_3$	HRMS (EI)	Calcd.	308.2351
		Found	308.2322

Synthesis of ethyl (4*Z*)-4-butyl-2-methylene-6-oxo-4-tridecenoate (114j)



Prepared according to TP 9 from (5*Z*)-5-iodo-5-tetradecen-7-one (**110b**) (336 mg, 1.0 mmol), lithium dineophylcuprate **17** (1.2 mmol) and ethyl bromomethylacrylate (376 mg, 3.0 mmol). Reaction time: 15 min at –100 °C. Purification by flash chromatography (*n*-pentane/diethyl ether = 10/1) yielded **114j** as a colorless oil (290 mg, 90%).

^{1}H-NMR ($CDCl_3$, 300 MHz): δ = 6.31-6.19 (d, *J* = 34.7 Hz, 1H), 6.19 (s, 1H), 5.58-5.47 (d, *J* = 34.7 Hz, 1H), 4.25-4.18 (q, *J* = 7.08 Hz, 2H), 3.64-3.14 (d, *J* = 149.27 Hz, 2H), 2.57-2.07 (m, 4H), 1.65-1.25 (m, 17H), 0.93-0.86 (m, 6H).

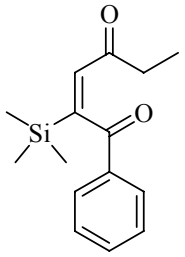
^{13}C-NMR ($CDCl_3$, 75 MHz): δ = 201.2, 167.5, 158.1, 137.9, 127.8, 125.3, 124.5, 61.2, 44.8, 40.7, 38.2, 33.9, 32.1, 31.0, 30.3, 29.5, 24.5, 23.0, 14.5, 14.4.

IR (film, cm^{-1}): $\tilde{\nu}$ = 3433 (w), 2957 (vs), 2929 (vs), 2858 (s), 1719 (vs), 1689 (s), 1618 (s), 1465 (m), 1300 (w), 1138 (s), 1028 (m), 948 (w), 817 (w).

MS (EI, 70 ev), *m/z* (%): 322 (7) [M^+], 293 (20), 235 (11), 249 (100), 195 (10), 177 (8), 150 (9), 121 (6), 57 (9).

$C_{20}H_{34}O_3$	HRMS (EI)	Calcd.	322.2508
		Found	322.2505

Synthesis of (2*E*)-1-phenyl-2-(trimethylsilyl)-2-hexene-1,4-dione (114k)

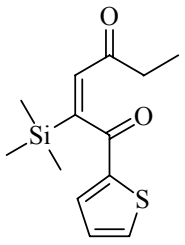


Prepared according to TP 9 from (1*Z*)-1-iodo-1-(trimethylsilyl)-1-penten-3-one (**110c**) (282 mg, 1.0 mmol), lithium dineophylcuprate **17** (1.2 mmol) and benzoyl chloride (420 mg, 3.0 mmol).. Reaction time: 15 min at –100 °C. Purification by flash chromatography (*n*-pentane/diethyl ether = 5/1) yielded **114k** as a colorless oil (218 mg, 84%).

^{1}H-NMR ($CDCl_3$, 300 MHz): δ = 7.67-7.64 (m, 2H), 7.38-7.32 (m, 1H), 7.28-7.23 (m, 2H), 6.43 (s, 1H), 2.40-2.33 (q, *J* = 7.19 Hz, 2H), 0.85-0.80 (t, *J* = 7.19 Hz, 3H), 0.00 (s, 9H).
^{13}C-NMR ($CDCl_3$, 75 MHz): δ = 202.7, 199.8, 165.4, 137.8, 136.2, 134.6, 130.3, 130.0, 37.8, 9.3, 0.0.
IR (film, cm^{-1}): $\tilde{\nu}$ = 2962 (w), 1695 (vs), 1658 (vs), 1581 (m), 1449 (m), 1354 (w), 1250 (m), 1227 (vs), 1122 (s), 10523 (w), 846 (vs), 756 (w), 691 (w).
MS (EI, 70 ev), *m/z* (%): 260 (18) [M^+], 245 (9), 231 (33), 217 (17), 203 (45), 105 (100), 73 (45).

$C_{15}H_{20}O_2Si$	HRMS (EI)	Calcd.	260.1233
		Found	260.1217

Synthesis of (2*E*)-1-(2-thienyl)-2-(trimethylsilyl)-2-hexene-1,4-dione (114l)



Prepared according to TP 9 from (1*Z*)-1-iodo-1-(trimethylsilyl)-1-penten-3-one (**110c**) (282 mg, 1.0 mmol), lithium dineophylcuprate **17** (1.2 mmol) and benzoyl chloride (438 mg, 3.0 mmol).. Reaction time: 15 min at –100 °C. Purification by flash chromatography (*n*-pentane/diethyl ether = 5/1) yielded **114l** as a colorless oil (202 mg, 76%).

^{1}H-NMR ($CDCl_3$, 300 MHz): δ = 7.41-7.39 (dd, *J* = 4.98 Hz, *J* = 1.11 Hz, 1H), 7.24-7.23 (dd, *J* = 3.76 Hz, *J* = 1.22 Hz, 1H), 6.88-6.86 (dd, *J* = 4.98 Hz, *J* = 3.76 Hz, 1H), 6.34 (s, 1H), 2.37-2.30 (q, *J* = 7.29 Hz, 2H), 0.83-0.79 (d, *J* = 7.19 Hz, 3H), 0.00 (s, 9H).

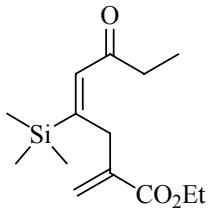
^{13}C-NMR ($CDCl_3$, 75 MHz): δ = 199.9, 194.7, 163.6, 145.4, 136.6, 135.1, 133.9, 129.8, 38.0, 9.4, 0.0.

IR (film, cm^{-1}): $\tilde{\nu}$ = 2961 (w), 1696 (vs), 1634 (vs), 1585 (w), 1412 (vs), 1357 (m), 1236 (vs), 1122 (m), 846 (vs), 723 (m), 632 (w).

MS (EI, 70 ev), *m/z* (%): 266 (25) [M^+], 251 (19), 237 (55), 223 (25), 209 (50), 165 (12), 111 (100), 83 (11), 73 (50).

$C_{13}H_{18}O_2SSi$	HRMS (EI)	Calcd.	266.0797
		Found	266.0788

Synthesis of ethyl (4*E*)-2-methylene-6-oxo-4-(trimethylsilyl)-4-octenoate (114m)



Prepared according to TP 9 from (1*Z*)-1-iodo-1-(trimethylsilyl)-1-penten-3-one (**110c**) (282 mg, 1.0 mmol), lithium dineophylcuprate **17** (1.2 mmol) and ethyl bromomethylacrylate (376 mg, 3.0 mmol). Reaction time: 15 min at –100 °C. Purification by flash chromatography (*n*-pentane/diethyl ether = 10/1) yielded **114m** as a colorless oil (239 mg, 89%).

^{1}H-NMR ($CDCl_3$, 300 MHz): δ = 6.49 (s, 1H), 6.16-6.06 (d, *J* = 32.4 Hz, 1H), 5.31-5.21 (d, *J* = 32.4 Hz, 1H), 4.14-4.07 (q, *J* = 7.07 Hz, 2H), 3.54-3.17 (d, *J* = 113.7 Hz, 1H), 2.43-2.36 (q, *J* = 7.18 Hz, 2H), 1.22-1.17 (t, *J* = 7.19 Hz, 3H), 0.98-0.93 (t, *J* = 7.19 Hz, 3H), 0.00 (s, 9H).

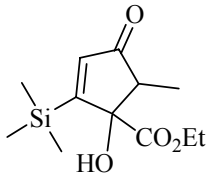
^{13}C-NMR ($CDCl_3$, 75 MHz): δ = 202.5, 168.7, 159.8, 140.5, 137.8, 126.4, 62.4, 41.3, 38.8, 38.1, 33.9, 15.8, 9.5, 0.0.

IR (film, cm^{-1}): $\tilde{\nu}$ = 2979 (m), 1718 (vs), 1692 (s), 1579 (m), 1460 (w), 1302 (w), 1249 (m), 1136 (s), 1028 (m), 84o (vs), 757 (w), 698 (w).

MS (EI, 70 ev), *m/z* (%): 268 (2) [M^+], 239 (12), 211 (10), 195 (100), 183 (14), 121 (12), 93 (11), 73 (35).

$C_{14}H_{24}O_3Si$	HRMS (EI)	Calcd.	268.1495
		Found	268.1466

Synthesis of 1-Hydroxy-5-methyl-4-oxo-2-trimethylsilanyl-cyclopent-2-enecarboxylic acid ethyl ester (114n)



Prepared according to TP 9 from (1*Z*)-1-iodo-1-(trimethylsilyl)-1-penten-3-one (**110c**) (282 mg, 1.0 mmol), lithium dineophylcuprate **17** (1.2 mmol) and ethyl oxayl chloride (411 mg, 3.0 mmol). Reaction time: 15 min at –100 °C. Purification by flash chromatography (*n*-pentane/diethyl ether = 3/1) yielded **114n** as a colorless oil (182 mg, 71%).

^{1}H-NMR ($CDCl_3$, 300 MHz): δ = 6.30 (s, 1H), 4.05-3.98 (q, *J* = 7.19 Hz, 2H), 2.46-2.39 (q, *J* = 7.19 Hz, 2H), 1.07-1.01 (t, *J* = 7.19 Hz, 3H), 0.87-0.85 (d, *J* = 7.29 Hz, 3H), 0.00 (s, 9H).

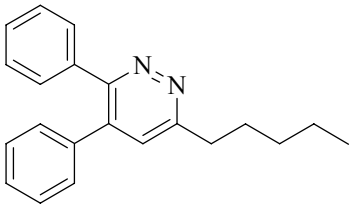
^{13}C-NMR ($CDCl_3$, 75 MHz): δ = 207.1, 178.5, 175.0, 144.6, 88.5, 64.4, 56.4, 15.6, 9.7, 0.0.

IR (film, cm^{-1}): $\tilde{\nu}$ = 3490 (w), 2977 (w), 1719 (vs), 1449 (m), 1216 (m), 1119 (m), 1032 (w), 884 (m), 843 (vs), 760 (m), 60 (w).

MS (EI, 70 ev), *m/z* (%): 256 (5) [M^+], 241 (19), 210 (10), 183 (15), 167 (100), 139 (45), 123 (10), 75 (30), 65 (4).

$C_{12}H_{20}O_4Si$	HRMS (EI)	Calcd.	256.1131
		Found	256.1128

Synthesis of 6-pentyl-3,4-diphenylpyridazine (116a)



Prepared according to TP 3 from (2*Z*)-1,2-diphenyl-2-nonene-1,4-dione (**114a**) (140 mg, 0.45 mmol) Reaction time: 15 min at 78 °C. Purification by flash chromatography (*n*-pentane/diethyl ether = 1/1) yielded **116a** as a yellow oil (125 mg, 92%).

^{1}H-NMR ($CDCl_3$, 300 MHz): δ = 7.37-7.34 (m, 2H), 7.26-7.18 (m, 7 H), 7.13-7.10 (m, 2H), 3.01-2.95 (t, *J* = 7.74 Hz, 2H), 1.84-1.74 (m, 2H), 1.41-1.29 (m, 4H), 0.87-0.82 (d, *J* = 7.19 Hz, 3H).

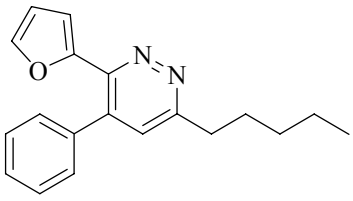
^{13}C-NMR ($CDCl_3$, 75 MHz): δ = 162.8, 158.2, 139.4, 137.6, 137.4, 130.4, 129.5, 129.0, 128.9, 128.9, 128.4, 127.4, 36.3, 31.9, 29.8, 22.8, 14.4.

IR (film, cm^{-1}): $\tilde{\nu}$ = 3058 (w), 2955 (vs), 2927 (vs), 2857 (vs), 1584 (m), 1465 (m), 1447 (m), 1401 (vs), 1112 (w), 765 (vs), 698 (vs), 570 (s).

MS (EI, 70 ev), *m/z* (%): 302 (8) [M$^+$], 273 (9), 259 (28), 246 (100), 215 (5), 178 (4).

$C_{21}H_{22}N_2$	HRMS (EI)	Calcd.	302.1783
		Found	302.1773

Synthesis of 3-(2-furyl)-6-pentyl-4-phenylpyridazine (116b)



Prepared according to TP 3 from (2*Z*)-1-(2-furyl)-2-phenyl-2-nonene-1,4-dione (**114b**) (90 mg, 0.30 mmol) Reaction time: 15 min at 78 °C. Purification by flash chromatography (*n*-pentane/diethyl ether = 1/1) yielded **116c** as a yellow oil (85 mg, 96%).

^{1}H-NMR ($CDCl_3$, 300 MHz): δ = 7.38-7.33 (m, 3H), 7.30-7.29 (dd, *J* = 1.66 Hz, *J* = 0.66 Hz, 1H), 7.22-7.19 (m, 2H), 7.13 (s, 1H), 6.47-6.45 (dd, *J* = 3.43 Hz, *J* = 0.66 Hz, 1H), 6.31-6.30 (dd, *J* = 3.43 Hz, *J* = 1.66 Hz, 1H), 2.98-2.92 (t, *J* = 7.74 Hz, 2H), 1.81-1.71 (m,

2H), 1.38-1.27 (m, 4H), 0.86-0.81 (d, *J* = 7.19 Hz, 3H).

^{13}C-NMR ($CDCl_3$, 75 MHz): δ = 162.4, 150.9, 149.1, 144.1, 138.1, 137.6, 129.1, 129.0, 128.7, 127.6, 113.0, 111.8, 36.2, 31.8, 29.7, 22.8, 14.4.

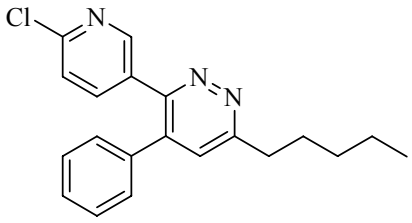
IR (film, cm^{-1}): $\tilde{\nu}$ = 3058 (w), 2955 (vs), 2928 (vs), 2858 (vs), 1573 (m), 1494 (m), 1444 (m), 1403 (s), 1005 (m), 743 (s), 700 (vs), 595 (w).

MS (EI, 70 ev), *m/z* (%): 292 (8) [M^+], 263 (8), 249 (15), 236 (100), 219 (5), 139 (9).

$C_{19}H_{20}N_2O$ HRMS (EI) Calcd. 292.1576

Found 292.3750

Synthesis of 3-(6-chloro-3-pyridinyl)-6-pentyl-4-phenylpyridazine (116c)



Prepared according to TP 3 from (2*Z*)-1-(6-chloro-3-pyridinyl)-2-phenyl-2-nonene-1,4-dione (**114c**) (100 mg, 0.30 mmol) Reaction time: 15 min at 78 °C. Purification by flash chromatography (*n*-pentane/diethyl ether = 1/1) yielded **116c** as a yellow oil (96 mg, 95%).

^{1}H-NMR ($CDCl_3$, 300 MHz): δ = 8.34-8.33 (dd, *J* = 2.43 Hz, *J* = 0.55 Hz, 1H), 7.71-7.68 (dd, *J* = 8.30 Hz, *J* = 2.43 Hz, 1H), 7.34-7.30 (m, 3H), 7.28 (s, 1H), 7.21-7.18 (dd, *J* = 8.30 Hz, *J* = 0.55 Hz, 1H), 7.13-7.10 (m, 2H), 3.02-2.97 (t, *J* = 7.74 Hz, 2H), 1.84-1.74 (m, 2H), 1.37-1.26 (m, 4H), 0.87-0.82 (t, *J* = 7.19 Hz, 3H).

^{13}C-NMR ($CDCl_3$, 75 MHz): δ = 194.1, 163.7, 154.3, 151.8, 150.9, 140.2, 139.7, 136.5, 132.3, 130.0, 129.6, 129.3, 128.8, 127.6, 124.1, 36.3, 31.9, 29.7, 22.8, 14.3.

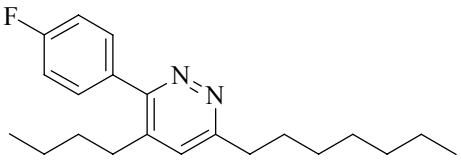
IR (film, cm^{-1}): $\tilde{\nu}$ = 3057 (w), 2955 (vs), 2928 (vs), 2858 (vs), 1586 (s), 1556 (m), 1461 (s), 1401 (s), 1357 (m), 1107 (vs), 1003 (m), 758 (m), 700 (s), 576 (w).

MS (EI, 70 ev), *m/z* (%): 337 (5) [M^+], 308 (8), 294 (18), 281 (100), 216 (3), 151 (3).

$C_{20}H_{20}ClN_3$ HRMS (EI) Calcd. 337.1346

Found 337.1354

Synthesis of 4-butyl-3-(4-fluorophenyl)-6-heptylpyridazine (116d)

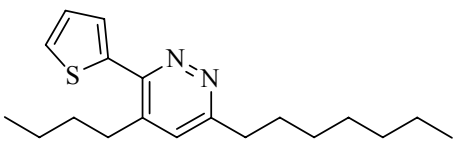


Prepared according to TP 3 from (2*Z*)-2-butyl-1-(4-fluorophenyl)-2-undecene-1,4-dione (**114f**) (166 mg, 0.50 mmol) Reaction time: 15 min at 78 °C. Purification by flash chromatography (*n*-pentane/diethyl ether = 1/1) yielded **116d** as a yellow oil (146 mg, 90%).

^{1}H-NMR ($CDCl_3$, 300 MHz): δ = 7.47-7.42 (m, 2H), 7.13-7.06 (m, 3H), 2.93-2.88 (t, *J* = 7.62 Hz, 2H), 2.56-2.51 (t, *J* = 7.62 Hz, 2H), 1.78-1.68 (m, 2H), 1.46-1.15 (m, 12H), 0.83-0.79 (t, *J* = 6.75 Hz, 3H), 0.79-0.74 (t, *J* = 7.30 Hz, 3H).
^{13}C-NMR ($CDCl_3$, 75 MHz): δ = 163.3 (d, *J* = 248.0 Hz), 162.8, 159.8, 140.5, 133.9 (d, *J* = 3.2 Hz), 131.5 (d, *J* = 8.2 Hz), 126.8, 115.7 (d, *J* = 21.7 Hz), 36.3, 32.1, 32.1, 31.9, 30.1, 29.7, 29.5, 23.0, 22.7, 14.4, 14.0.
IR (film, cm^{-1}): $\tilde{\nu}$ = 3386 (w), 2956 (vs), 2927 (vs), 2857 (vs), 1605 (w), 1508 (m), 1411 (m), 1224 (s), 1157 (w), 841 (m), 817 (w).
MS (EI, 70 ev), *m/z* (%): 328 (6) [M^+], 299 (7), 285 (6), 271 (6), 257 (20), 244 (100), 227 (4) 215 (6), 133 (10).

$C_{21}H_{29}FN_2$	HRMS (EI)	Calcd.	328.2315
		Found	328.2303

Synthesis of 4-butyl-6-heptyl-3-(2-thienyl)pyridazine (116e)



Prepared according to TP 3 from (2*Z*)-2-butyl-1-(2-thienyl)-2-decene-1,4-dione (**114g**) (160 mg, 0.50 mmol) Reaction time: 15 min at 78 °C. Purification by flash chromatography (*n*-pentane/diethyl ether = 1/1) yielded **116e** as a yellow oil (145 mg, 92%).

^{1}H-NMR ($CDCl_3$, 300 MHz): δ = 7.42-7.42 (dd, *J* = 3.78 Hz, *J* = 1.11 Hz, 1H), 7.40-7.38 (dd, *J* = 5.08 Hz, *J* = 1.11 Hz, 1H), 7.09-7.06 (dd, *J* = 5.08 Hz, *J* = 3.78 Hz, 1H), 7.07 (s, 1H), 2.90-2.85 (t, *J* = 7.62 Hz, 2H), 2.80-2.75 (t, *J* = 7.62 Hz, 2H), 1.77-1.67 (m, 2H), 1.63-1.53 (m, 2H), 1.42-1.12 (m, 10H), 0.91-0.87 (t, *J* = 7.30 Hz, 3H), 0.83-0.78 (t, *J* = 6.97 Hz, 3H).

^{13}C-NMR ($CDCl_3$, 75 MHz): δ = 162.1, 154.0, 141.0, 139.3, 128.5, 128.1, 127.8, 127.1, 36.1, 32.8, 32.1, 31.4, 29.9, 29.6, 29.5, 23.0, 22.9, 14.4, 14.2.

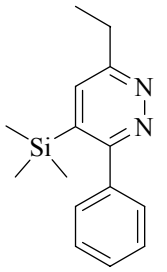
IR (film, cm^{-1}): $\tilde{\nu}$ = 3074 (w), 2956 (vs), 2927 (vs), 2856 (vs), 1583 (w), 1435 (w), 1258 (w), 851 (w), 700 (s), 702 (m).

MS (EI, 70 ev), *m/z* (%): 316 (8) [M^+], 287 (7), 273 (6), 259 (6), 245 (20), 232 (100).

$C_{19}H_{28}N_2S$ HRMS (EI) Calcd. 316.1973

Found 316.1964

Synthesis of 6-ethyl-3-phenyl-4-(trimethylsilyl)pyridazine (116f)



Prepared according to TP 3 from (2*E*)-1-phenyl-2-(trimethylsilyl)-2-hexene-1,4-dione (**114k**) (80 mg, 0.30 mmol) Reaction time: 15 min at 78 °C. Purification by flash chromatography (*n*-pentane/diethyl ether = 1/1) yielded **116f** as a yellow oil (72 mg, 92%).

^{1}H-NMR ($CDCl_3$, 300 MHz): δ = 7.40-7.38 (m, 6H), 3.01-2.94 (q, *J* = 7.63 Hz, 2H), 1.38-1.33 (t, *J* = 7.63 Hz, 3H), 0.00 (s, 9H).

^{13}C-NMR ($CDCl_3$, 75 MHz): δ = 164.8, 162.2, 141.0, 138.8, 132.8, 129.8, 129.1, 128.5, 29.7, 14.3, 0.0.

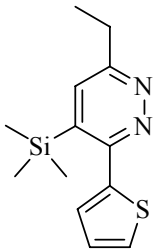
IR (film, cm^{-1}): $\tilde{\nu}$ = 2969 (m), 2935 (w), 2987 (w), 1460 (w), 1395 (vs), 1251 (s), 1121 (w), 1013 (w), 879 (m), 838 (vs), 762 (s), 701 (s), 626 (w).

MS (EI, 70 ev), *m/z* (%): 256 (60) [M^+], 241 (13), 174 (33), 159 (100), 73 (18).

$C_{15}H_{20}N_2Si$ HRMS (EI) Calcd. 256.1396

Found 256.1374

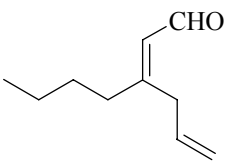
Synthesis of 6-ethyl-3-(2-thienyl)-4-(trimethylsilyl)pyridazine (116g)



Prepared according to TP 3 from (2*E*)-1-(2-thienyl)-2-(trimethylsilyl)-2-hexene-1,4-dione (**114l**) (266 mg, 1.0 mmol) Reaction time: 15 min at 78 °C. Purification by flash chromatography (*n*-pentane/diethyl ether = 1/1) yielded **116g** as a yellow oil (236 mg, 90%).

^{1}H-NMR ($CDCl_3$, 300 MHz): δ = 7.25-7.22 (dd, *J* = 5.08 Hz, *J* = 0.99 Hz, 1H), 7.23 (s, 1H), 7.05-7.04 (dd, *J* = 3.65 Hz, *J* = 1.11 Hz, 1H), 6.91-6.88 (dd, *J* = 5.08 Hz, *J* = 3.65 Hz, 1H), 2.85-2.77 (q, *J* = 7.63 Hz, 2H), 1.22-1.17 (t, *J* = 7.63 Hz, 3H), 0.00 (s, 9H).
^{13}C-NMR ($CDCl_3$, 75 MHz): δ = 162.3, 158.6, 142.6, 138.9, 132.9, 128.8, 128.1, 127.4, 29.66, 14.2, 0.0.
IR (film, cm^{-1}): $\tilde{\nu}$ = 2969 (m), 2898 (w), 1439 (m), 1383 (s), 1251 (s), 1111 (m), 1060 (w), 874 (m), 830 (vs), 758 (w), 702 (s), 626 (w).
MS (EI, 70 ev), *m/z* (%): 262 (55) [M^+], 247 (13), 180 (70), 165 (100), 73 (12).
$C_{13}H_{18}N_2SSi$ HRMS (EI) Calcd. 262.0960
Found 262.0956

Synthesis of (2*Z*)-3-butyl-2,5-hexadienal (119a)



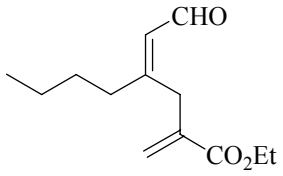
Prepared according to TP 9 from (2*Z*)-3-iodo-2-heptenal (**117**) (238 mg, 1.0 mmol), lithium dineophylcuprate **17** (1.2 mmol) and allyl bromide (360 mg, 3.0 mmol). Reaction time: 5

min at –100 °C. Purification by flash chromatography (*n*-pentane/diethyl ether = 30/1) yielded **119a** as a colorless oil (123 mg, 81%).

^{1}H-NMR (DMSO, 300 MHz): δ = 9.94-9.92 (d, *J* = 7.94, 1
H), 5.90-5.79 (m, 2H), 5.16-5.06 (m, 2H), 3.34-3.33 (d, *J* = 6.41, 2H), 2.21-2.17 (dt, *J* = 7.63 Hz, *J* = 0.92 Hz, 2H), 1.46-1.38 (m, 2H), 1.32-1.24 (m, 2H), 0.88-0.85 (t, *J* = 7.32 Hz, 3H).
^{13}C-NMR (DMSO, 75 MHz): δ = 192.1, 165.6, 135.8, 127.6, 117.5, 37.4, 35.4, 29.3, 22.3, 14.1.
IR (film, cm^{-1}): $\tilde{\nu}$ = 3400 (w), 2958 (s), 2931 (s), 2872 (m), 1673 (vs), 1638 (m), 1466 (w), 1173 (w), 917 (w).
MS (EI, 70 ev), *m/z* (%): 152 (9) [M$^+$], 137 (100), 123 (4), 110 (10), 95 (40), 81 (25), 67 (30).

$C_{10}H_{16}O$	HRMS (EI)	Calcd.	152.1201
		Found	152.1194

Synthesis of ethyl (4*Z*)-4-butyl-2-methylene-6-oxo-4-hexenoate (119b)



Prepared according to TP 9 from (2*Z*)-3-iodo-2-heptenal (**117**) (238 mg, 1.0 mmol), lithium dineophylcuprate **17** (1.2 mmol) and ethyl bromomethylacrylate (376 mg, 3.0 mmol). Reaction time: 5 min at –100 °C. Purification by flash chromatography (*n*-pentane/diethyl ether = 30/1) yielded **119b** as a colorless oil (164 mg, 73%).

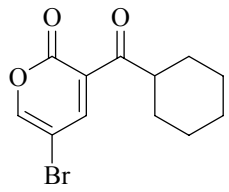
^{1}H-NMR (DMSO, 300 MHz): δ = 10.00-9.99 (d, *J* = 8.11, 1H), 6.23-5.75 (d, *J* = 287.29, 2H), 5.89-5.99 (d, *J* = 8.11, 1H), 4.16-4.13 (q, *J* = 6.91, 2H), 3.63 (s, 2H), 2.17-2.14 (d, *J* = 7.63, 1H), 1.45-1.26 (m, 4H), 1.22-1.20 (t, *J* = 7.15 Hz, 3H), 0.89-0.86 (t, *J* = 7.39 Hz, 3H).
^{13}C-NMR (DMSO, 75 MHz): δ = 190.8, 164.7, 161.9, 136.2, 127.1, 126.3, 50.6, 35.0, 31.7, 27.9, 20.7, 12.9, 12.6.
IR (film, cm^{-1}): $\tilde{\nu}$ = 3422 (w), 2959 (s), 2933 (s), 2872 (m), 1717 (vs), 1675 (vs), 1628 (m),

1466 (w), 1177 (m), 1143 (m), 1027 (m), 915 (w).

MS (EI, 70 ev), *m/z* (%): 224 (5) [M^+], 195 (16), 167 (17), 151 (100), 135 (7), 121 (12), 108 (27), 95 (10), 79 (15).

$C_{13}H_{20}O_3$	HRMS (EI)	Calcd.	224.1412
		Found	224.1382

Synthesis of 5-bromo-3-(cyclohexylcarbonyl)-2*H*-pyran-2-one (122a)



Prepared according to TP 6 from 3,5-dibromo-2*H*-pyran-2-one (**120**) (127 mg, 0.5 mmol), lithium dineophylcuprate **17** (0.6 mmol), cyclohexanecarbonyl chloride (219 mg, 1.5 mmol). Reaction time: 30 min at-78 ^oC. Purification by flash chromatography (*n*-pentane/diethyl ether = 5/1) yielded **122a** as a yellow solid (100 mg, 76%).

mp.: 123 ^oC

^{1}H-NMR ($CDCl_3$, 300 MHz): δ = 8.20-8.19 (d, *J* = 2.21, 1H), 8.15-8.14 (d, *J* = 2.21, 1H), 2.79-2.72 (m, 1H),1.89-1.13 (m, 10H).

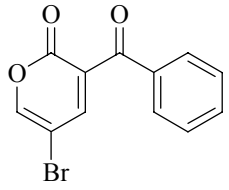
^{13}C-NMR ($CDCl_3$, 75 MHz): δ = 195.9, 155.6, 154.3, 141.2, 117.5, 111.5, 44.8, 28.2, 24.6, 24.5.

IR (KBr, cm^{-1}): $\tilde{\nu}$ = 2931 (vs), 2855 (s), 1747 (vs), 1705 (vs), 1678 (s), 1450 (w), 1255 (s), 980 (m), 869 (w), 758 (w), 754 (w), 676 (w).

MS (EI, 70 ev), *m/z* (%): 284 (45) [M^+], 218 (22), 203 (98), 177 (38), 161 (41), 83 (62), 55(100).

$C_{12}H_{13}BrO_3$	HRMS (EI)	Calcd.	284.0048
		Found	284.0051

Synthesis of 3-benzoyl-5-bromo-2*H*-pyran-2-one (122b)



Prepared according to TP 6 from 3,5-dibromo-2*H*-pyran-2-one (**120**) (127 mg, 0.5 mmol), lithium dineophylcuprate **17** (0.6 mmol), benzoyl chloride (219 mg, 1.5 mmol). Reaction time: 30 min at-78 °C. Purification by flash chromatography (*n*-pentane/diethyl ether = 4/1) yielded **122b** as a yellow solid (123 mg, 88%).

mp.: 93 °C

^{1}H-NMR ($CDCl_3$, 300 MHz): δ = 8.30-8.29 (d, *J* = 2.21, 1H), 8.06-8.05 (d, *J* = 2.21, 1H), 7.77-7.74 (m, 2H), 7.70-7.60 (m, 1H), 7.57-7.47 (m, 2H).

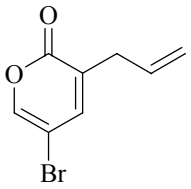
^{13}C-NMR ($CDCl_3$, 75 MHz): δ = 189.6, 155.7, 143.4, 133.8, 130.6, 129.5, 129.4, 128.9, 119.8, 112.9.

IR (KBr, cm^{-1}): $\tilde{\nu}$ = 3453 (w), 3076 (w), 1737 (vs), 1652 (vs), 1578 (w), 1466 (m), 1288 (vs), 1216 (m), 974 (w), 841 (m), 709 (m), 656 (w).

MS (EI, 70 ev), *m/z* (%): 278 (56) [M^+], 251 (10), 199 (50), 171 (24), 115 (15), 105 (100), 77(65).

$C_{12}H_7BrO_3$	HRMS (EI)	Calcd.	277.9579
		Found	277.9580

Synthesis of 3-allyl-5-bromo-2*H*-pyran-2-one (122c)



Prepared according to TP 6 from 3,5-dibromo-2*H*-pyran-2-one (**120**) (254 mg, 1.0 mmol), lithium dineophylcuprate **17** (1.2 mmol), allyl bromide (360 mg, 3.0 mmol). Reaction time: 30 min at-78 °C. Purification by flash chromatography (*n*-pentane/diethyl ether = 10/1) yielded **122c** as a light yellow oil (196 mg, 91%).

^{1}H-NMR ($CDCl_3$, 300 MHz): δ = 7.67-7.66 (d, *J* = 2.21, 1H), 7.37-7.36 (dt, *J* = 2.21, *J* = 1.11, 1H), 5.94-5.81 (m, 1H), 5.28-5.18 (m, 2H), 3.14-3.13 (m, 2H).

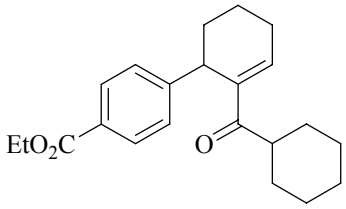
^{13}C-NMR ($CDCl_3$, 75 MHz): δ = 158.6, 147.7, 146.8, 134.3, 118.9, 118.5, 112.8, 33.5.

IR (film, cm^{-1}): $\tilde{\nu}$ = 3084 (w), 1746 (vs), 1729 (vs), 1636 (m), 1528 (m), 1244 (m), 928 (s), 924 (m), 870 (m), 753 (m), 679 (w).

MS (EI, 70 ev), *m/z* (%): 214 (33) [M^+], 186 (10), 135 (50), 107 (52), 77 (100), 51(35).

$C_8H_7BrO_2$	HRMS (EI)	Calcd.	213.9629
		Found	213.9639

Synthesis of ethyl 4-[2-(cyclohexylcarbonyl)-2-cyclohexen-1-yl]benzoate (126a)



A dry and argon flushed 25 mL flask, equipped with a magnetic stirrer and a septum, was charged with a solution of lithium dineophylcuprate (**17**) (1.2 mmol). A solution of ethyl 4-iodobenzoate (276 mg, 1.0 mmol) in THF (2 mL) was added over the solution of **17**, and the mixture was stirred at 0 °C for 30 min. The mixture was cooled to -78 °C and a solution of (±)-2-iodo-2-cyclopenten-1-yl acetate ((±)-**54a**) (532 mg, 2.0 mmol) in THF (3 mL) was added. The resulting reaction mixture was allowed to warm to rt and stirred at this temperature for 12 h. The reaction was cooled to -78 °C and a solution of lithium dineophylcuprate(**17**) (2.4 mmol) was added. The resulting mixture was allowed to be stirred at rt for 30 min. Then cyclohexanecarbonyl chloride (730 mg, 5 mmol) was added and the reaction was stirred at rt for 1 h. Saturated aqueous NH_4Cl sol. (20 mL) was added followed by 25% aqueous ammonia solution (2 mL). The reaction mixture was stirred at 25 °C until the copper salts had dissolved and was extracted with Et_2O (3 × 30 mL). The combined extracts were washed with brine and dried (Na_2SO_4). Evaporation of the solvents and purification by column chromatography (*n*-pentane/diethyl ether = 1/1) afforded **126a** as a light yellow oil (238 mg, 70%).

^{1}H-NMR ($CDCl_3$, 300 MHz): δ = 7.86-7.84 (d, *J* = 8.40, 2H), 7.11-7.08 (d, *J* = 8.40, 2H),

7.10-7.09 (m, 1H), 4.31-4.23 (q, *J* = 7.07, 2H), 3.99-3.98 (t, *J* = 6.91, 1H), 2.93-2.85 (m, 1H), 2.39-2.34 (m, 2H), 1.88-1.02 (m, 14H), 1.32-1.27 (t, *J* = 7.18, 1H).

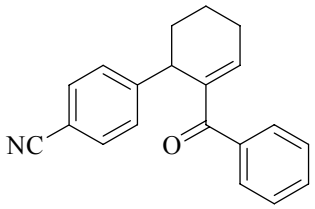
^{13}C-NMR ($CDCl_3$, 75 MHz): δ = 204.3, 167.0, 151.3, 141.0, 139.8, 129.8, 128.5, 128.1, 61.1, 44.8, 39.2, 31,6, 30.5, 29.2, 26.5, 26.4, 26.2, 26.0, 17.7, 14.7.

IR (film, cm^{-1}): $\tilde{\nu}$ = 2932 (vs), 2855 (s), 1715 (vs), 1666 (vs), 1609 (m), 1448 (m), 1276 (vs), 1103 (s), 1020 (m), 938 (w), 769 (m), 707 (m).

MS (EI, 70 ev), *m/z* (%): 340 (28) [M^+], 322 (10), 295 (17), 257 (72), 229 (11), 185(100), 155 (12), 143 (13), 128 (15), 115 (8).

$C_{22}H_{28}O_3$	HRMS (EI)	Calcd.	340.2038
		Found	340.2033

Synthesis of 4-(2-benzoyl-2-cyclohexen-1-yl)benzonitrile (126b)



A dry and argon flushed 25 mL flask, equipped with a magnetic stirrer and a septum, was charged with a solution of lithium dineophylcuprate (**17**) (1.2 mmol). A solution of 4-cyanobromobenzene (182 mg, 1.0 mmol) in THF (2 mL) was added over the solution of **17**, and the mixture was stirred at 0 °C for 30 min. The mixture was cooled to -78 °C and a solution of (±)-2-iodo-2-cyclopenten-1-yl acetate ((±)-**54a**) (532 mg, 2.0 mmol) in THF (2 mL) was added. The resulting reaction mixture was allowed to warm to rt and stirred at this temperature for 2 h. The reaction was cooled to -78 °C and a solution of lithium dineophylcuprate(**17**) (2.4 mmol) was added. The resulting mixture was allowed to be stirred at rt for 30 min. Then beozoyl chloride (700 mg, 5 mmol) was added and the reaction was stirred at rt for 1 h. Saturated aqueous NH_4Cl sol. (20 mL) was added followed by 25% aqueous ammonia solution (1 mL). The reaction mixture was stirred at 25 °C until the copper salts had dissolved and was extracted with Et_2O (3 × 20 mL). The combined extracts were washed with brine and dried (Na_2SO_4). Evaporation of the solvents and purification by column chromatography (*n*-pentane/diethyl ether = 3/1) afforded **126b** as a light yellow oil (187 mg, 65%).

^{1}H-NMR ($CDCl_3$, 300 MHz): δ = 7.58-7.25 (m, 9H), 6.81-6.78 (td, *J* = 3.87, *J* = 1.21, 1H), 4.17-4.13 (m, 1H), 2.43-1.55 (m, 6H).

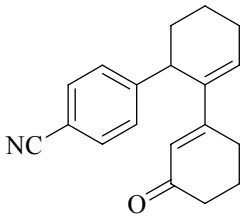
^{13}C-NMR ($CDCl_3$, 75 MHz): δ = 197.0, 151.2, 145.9, 139.9, 138.4, 132.6, 132,2, 129.6, 128.9, 128.6, 119.4, 110.3, 40.5, 31.8, 16.4, 18.6.

IR (film, cm^{-1}): $\tilde{\nu}$ = 2935 (s), 2226 (s), 1722 (m), 1645 (vs), 1605 (m), 1446 (m), 1261 (vs), 1119 (m), 826 (m), 701 (s), 656 (m).

MS (EI, 70 ev), *m/z* (%): 287 (100) [M^+], 258 (11), 158 (17), 145 (9), 105 (82), 77 (75).

$C_{20}H_{17}NO$	HRMS (EI)	Calcd.	287.1310
		Found	287.1292

Synthesis of 4-(3'-Oxo-bicyclohexyl-6,1'-dien-2-yl)-benzonitrile (126c)



A dry and argon flushed 25 mL flask, equipped with a magnetic stirrer and a septum, was charged with a solution of lithium dineophylcuprate (**17**) (1.2 mmol). A solution of 4-cyanobromobenzene (182 mg, 1.0 mmol) in THF (2 mL) was added over the solution of **17**, and the mixture was stirred at 0 °C for 30 min. The mixture was cooled to -78 °C and a solution of (±)-2-iodo-2-cyclopenten-1-yl acetate ((±)-**54a**) (532 mg, 2.0 mmol) in THF (2 mL) was added. The resulting reaction mixture was allowed to warm to rt and stirred at this temperature for 2 h. The reaction was cooled to -78 °C and a solution of lithium dineophylcuprate(**17**) (2.4 mmol) was added. The resulting mixture was allowed to be stirred at rt for 30 min. Then 3-iodocyclohex-2-en-1-one (1.12 g, 5 mmol) was added and the reaction was stirred at rt for 1 h. Saturated aqueous NH_4Cl sol. (20 mL) was added followed by 25% aqueous ammonia solution (1 mL). The reaction mixture was stirred at 25 °C until the copper salts had dissolved and was extracted with Et_2O (3 × 20 mL). The combined extracts were washed with brine and dried (Na_2SO_4). Evaporation of the solvents and purification by column chromatography (*n*-pentane/diethyl ether = 1/2) afforded **126c** as a light yellow oil (176 mg, 63%).

^{1}H-NMR ($CDCl_3$, 300 MHz): δ = 7.50-7.47 (d, *J* = 8.40, 2H), 7.17-7.14 (d, *J* = 8.40, 2H), 6.59-6.56 (t, *J* = 4.20, 1H), 5.64 (s, 1H), 3.80-3.79 (t, *J* = 6.91, 1H), 2.40-1.18 (m, 12H).

^{13}C-NMR ($CDCl_3$, 75 MHz): δ = 200.6, 158.4, 150.7, 136.8, 135.3, 132.9, 132.6, 129.1, 124.8, 110.6, 41.2, 37.7, 32.2, 26.8, 26.7, 22.8, 17.1.

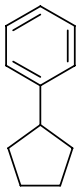
IR (film, cm^{-1}): $\tilde{\nu}$ = 2935 (vs), 2866 (s), 2226 (s), 1667 (vs), 1619 (m), 1413 (w), 1262 (m), 1189 (s), 1135 (m), 886 (w), 833 (m), 581 (w).

MS (EI, 70 ev), *m/z* (%): 277 (100) [M^+], 259 (81), 248 (82), 234 (75), 221 (62), 206 (90), 192 (48), 175 (33), 166 (34), 116 (26), 91 (45).

$C_{19}H_{19}NO$	HRMS (EI)	Calcd.	277.1467
		Found	277.1459

14 Preparation of Functionalized Aryl Compounds *via* an I/Cu-Exchange Reaction of Aryl Iodides with Magnesium Cuprate Reagent 36

Synthesis of Cyclopentylbenzene (133)



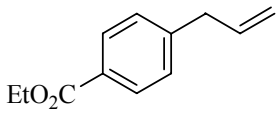
Prepared according to TP 10 from ethyl 4-iodobenzoate (552 mg, 2.0 mmol), 3-phenyl substituted magnesium cuprate reagent **132** (1.0 mmol), and H_2O. Reaction time: 1 h at rt. Purification by flash chromatography (*n*-pentane/diethyl ether = 80/1) yielded **113** as colorless oil (280 mg, 94%).

^{1}H-NMR ($CDCl_3$, 300 MHz): δ = 7.35-7.19 (m, 5H), 3.10-2.99 (m, 1H), 2.18-2.08 (m, 2H), 1.88-1.57 (m, 6H).

^{13}C-NMR ($CDCl_3$, 75 MHz): δ = 146.9, 128.6, 127.5, 126.1, 46.4, 35.0, 26.0.

MS (EI, 70 ev), *m/z* (%): 146 (55) [M^+], 131 (10), 117 (100), 104 (65), 91 (17), 77 (12).

Synthesis of ethyl 4-allylbenzoate (135a)

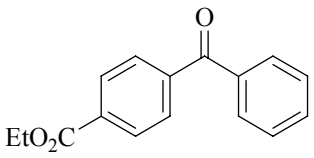


Prepared according to TP 10 from ethyl 4-iodobenzoate (276 mg, 1.0 mmol), magnesium cuprate reagent **36** (0.5 mmol), and allyl bromide (144 mg, 1.2 mmol). Reaction time: 1h at rt. Purification by flash chromatography (*n*-pentane/diethyl ether = 50/1) yielded **135a** as colorless oil (173 mg, 91%).

^{1}H-NMR ($CDCl_3$, 300 MHz): δ = 7.91-7.89 (d, *J* = 8.4 Hz, 2H), 7.20-7.16 (d, *J* = 8.4 Hz, 2H), 5.95-5.82 (m, 1H), 5.05-4.98 (m, 2H), 4.33-4.26 (q, *J* = 7.2 Hz, 2H), 3.37-3.35 (d, *J* = 6.7 Hz, 2H), 1.34-1.29 (t, *J* = 7.2 Hz, 3H).
^{13}C-NMR ($CDCl_3$, 75 MHz): δ = 167.0, 145.7, 136.8, 130.1, 128.9, 128.8, 116.9, 61.2, 40.5, 14.7.
IR (film, cm^{-1}): $\tilde{\nu}$ = 2981 (w), 1718 (vs), 1611 (w), 1417 (w), 1276 (vs), 1177 (m), 1105 (s), 757 (m).
MS (EI, 70 ev), *m/z* (%): 190 (35) [M^+], 175 (2), 162 (19), 145 (100), 117 (62), 115 (60), 91 (17), 77 (4).

$C_{12}H_{14}O_2$	HRMS (EI)	Calcd.	190.0994
		Found	190.1006

Synthesis of ethyl 4-benzoylbenzoate (135b)



Prepared according to TP 10 from ethyl 4-iodobenzoate (276 mg, 1.0 mmol), magnesium cuprate reagent **36** (0.5 mmol), and benzoyl chloride (168 mg, 1.2 mmol). Reaction time: 1h at rt. Purification by flash chromatography (*n*-pentane/diethyl ether = 25/1) yielded **135b** as colorless oil (239 mg, 94%).

^{1}H-NMR ($CDCl_3$, 300 MHz): δ = 8.08-8.05 (d, *J* = 8.6 Hz, 2H), 7.76-7.73 (d, *J* = 8.6 Hz, 2H), 7.75-7.70 (m, 2H), 7.55-7.50 (m, 1H), 7.43-7.38 (m, 2H), 4.37-4.30 (q, *J* = 7.1 Hz, 2H), 1.36-1.21 (t, *J* = 7.1 Hz, 3H).

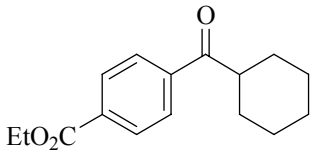
^{13}C-NMR ($CDCl_3$, 75 MHz): δ = 195.0, 164.8, 140.2, 136.0, 132.6, 131.9, 129.1, 128.7, 128.4, 127.4, 60.4, 13.3.

IR (film, cm^{-1}): $\tilde{\nu}$ = 2982 (w), 1720 (vs), 1661 (vs), 1597 (w), 1404 (m), 1273 (vs), 1104 (vs), 1012 (m), 714 (s).

MS (EI, 70 ev), *m/z* (%): 254 (100) [M^+], 226 (20), 209 (73), 177 (78), 149 (28), 105 (92), 77 (30).

$C_{16}H_{14}O_3$	HRMS (EI)	Calcd.	254.0943
		Found	254.0945

Synthesis of ethyl 4-(cyclohexylcarbonyl)benzoate (135c)



Prepared according to TP 10 from ethyl 4-iodobenzoate (276 mg, 1.0 mmol), magnesium cuprate reagent **36** (0.5 mmol), and cyclohexanecarbonyl chloride (175 mg, 1.2 mmol). Reaction time: 1h at rt. Purification by flash chromatography (*n*-pentane/diethyl ether = 25/1) yielded **135c** as colorless oil (242 mg, 93%).

^{1}H-NMR ($CDCl_3$, 300 MHz): δ = 8.05-8.03 (d, *J* = 8.6 Hz, 2H), 7.91-7.88 (d, *J* = 8.6 Hz, 2H), 4.37-4.30 (q, *J* = 7.1 Hz, 2H), 3.23-3.13 (m, 1H), 1.83-1.17 (m, 10H), 1.36-1.31 (t, *J* = 7.1 Hz, 3H).

^{13}C-NMR ($CDCl_3$, 75 MHz): δ = 202.4, 164.8, 138.6, 132.9, 128.8, 127.1, 60.4, 45.0, 28.3, 24.9, 24.7, 13.3.

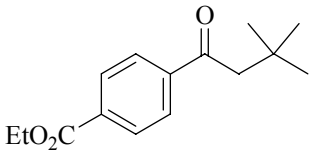
IR (film, cm^{-1}): $\tilde{\nu}$ = 2981 (m), 2932 (vs), 2855 (s), 1722 (vs), 1682 (vs), 1572 (w), 1449 (m), 1406 (m), 1277 (vs), 1105 (vs), 975 (m), 716 (m).

MS (EI, 70 ev), *m/z* (%): 260 (3) [M^+], 231 (9), 215 (11), 205 (8), 187 (39), 177 (100), 149 (25), 121 (6), 104 (10).

$C_{16}H_{20}O_3$	HRMS (EI)	Calcd.	260.1412

Found 260.1417

Synthesis of ethyl 4-(3,3-dimethylbutanoyl)benzoate (135d)

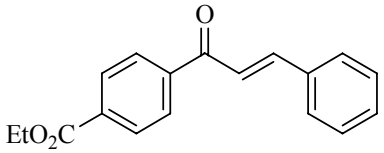


Prepared according to TP 10 from ethyl 4-iodobenzoate (276 mg, 1.0 mmol), magnesium cuprate reagent **36** (0.5 mmol), and 3,3-dimethylbutyryl chloride (162 mg, 1.2 mmol). Reaction time: 1h at rt. Purification by flash chromatography (*n*-pentane/diethyl ether = 25/1) yielded **135d** as colorless oil (228 mg, 92%).

^{1}H-NMR ($CDCl_3$, 300 MHz): δ = 8.05-8.02 (d, *J* = 8.6 Hz, 2H), 7.91-7.88 (d, *J* = 8.6 Hz, 2H), 4.37-4.30 (q, *J* = 7.1 Hz, 2H), 2.81 (s, 2H), 1.36-1.31 (t, *J* = 7.1 Hz, 3H), 0.99 (s, 9H).
^{13}C-NMR ($CDCl_3$, 75 MHz): δ = 199.0, 164.8, 140.7, 132.9, 128.7, 127.0, 60.4, 49.4, 30.5, 29.0, 13.3.
IR (film, cm^{-1}): $\tilde{\nu}$ = 2957 (s), 1722 (vs), 1692 (s), 1681 (s), 1466 (m), 1366 (m), 1276 (vs), 1105 (vs), 1009 (s), 754 (m).
MS (EI, 70 ev), *m/z* (%): 248 (1) [M^+], 219 (5), 203 (17), 192 (92), 177 (100), 164 (21), 149 (36), 121 (8), 104 (12), 76 (7).

$C_{15}H_{21}O_3$[M+H]$^+$	HRMS (EI)	Calcd.	248.1491
		Found	249.1428

Synthesis of 4-(3-Phenyl-acryloyl)-benzoic acid ethyl ester (135e)



Prepared according to TP 10 from ethyl 4-iodobenzoate (276 mg, 1.0 mmol), magnesium cuprate reagent **36** (0.5 mmol), and cinnamoyl chloride (200 mg, 1.2 mmol). Reaction time:

1h at rt. Purification by flash chromatography (*n*-pentane/diethyl ether = 25/1) yielded **135e** as a white solid (238 mg, 85%).

mp.: 95 °C

^{1}H-NMR ($CDCl_3$, 300 MHz): δ = 8.10-8.07 (d, *J* = 8.6 Hz, 2H), 7.98-7.95 (d, *J* = 8.6 Hz, 2H), 7.76-7.71 (d, *J* = 15.7 Hz, 1H), 7.58-7.55 (m, 2H), 7.45-7.40 (d, *J* = 15.7 Hz, 1H), 7.35-7.33 (m, 3H), 4.37-4.30 (q, *J* = 7.1 Hz, 2H), 1.36-1.31 (t, *J* = 7.1 Hz, 3H).

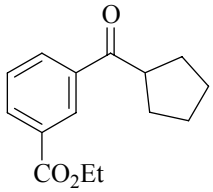
^{13}C-NMR ($CDCl_3$, 75 MHz): δ = 189.1, 164.8, 144.7, 140.5, 133.6, 132.9, 129.8, 128.8, 128.0, 127.5, 127.3, 120.9, 60.4, 13.3.

IR (KBr, cm^{-1}): $\tilde{\nu}$ = 2983 (w), 1709 (vs), 1665 (s), 1602 (vs), 1573 (s), 1448 (m), 1309 (m), 1284 (vs), 1214 (s), 1123 (s), 1107(s), 1026 (s), 1014 (s), 994 (m), 759 (s), 693 (m).

MS (EI, 70 ev), *m/z* (%): 280 (75) [M^+], 251 (44), 235 (19), 207 (56), 178 (39), 149 (10), 131 (29), 121 (6), 103 (28), 77 (15).

$C_{18}H_{16}O_3$	HRMS (EI)	Calcd.	280.1099
		Found	280.1083

Synthesis of ethyl 3-(cyclopentylcarbonyl)benzoate (135f)



Prepared according to TP 10 from ethyl 3-iodobenzoate (276 mg, 1.0 mmol), magnesium cuprate reagent **36** (0.5 mmol), and cyclopentanecarbonyl chloride (159 mg, 1.2 mmol). Reaction time: 1h at rt. Purification by flash chromatography (*n*-pentane/diethyl ether = 10/1) yielded **135f** as a colorless oil (223 mg, 91%).

^{1}H-NMR ($CDCl_3$, 300 MHz): δ = 8.54-8.53 (t, *J* = 1.7 Hz, 1H), 8.16-8.12 (dt, *J* = 7.7 Hz, *J* = 1.6 Hz, 1H), 8.10-8.06 (dt, *J* = 7.7 Hz, *J* = 1.7 Hz, 1H), 7.49-7.44 (t, *J* = 7.7 Hz, 1H), 4.37-4.30 (q, *J* = 7.2 Hz, 2H), 3.73-3.63 (quint, *J* = 7.4 Hz, 1H), 1.92-1.52 (m, 8H), 1.36-1.32 (t, *J* = 7.2 Hz, 3H).

^{13}C-NMR ($CDCl_3$, 75 MHz): δ = 202.4, 166.3, 137.6, 133.8, 132.9, 131.3, 129.9, 129.1, 61.7, 46.8, 30.3, 26.7, 14.7.

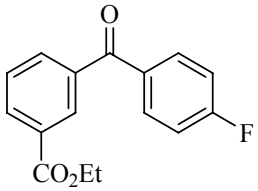
IR (film, cm^{-1}): $\tilde{\nu}$ = 2958 (vs), 2871 (s), 1724 (vs), 1686 (s), 1451 (w), 1367 (w), 1276 (m), 1205 (s), 1117 (m), 1017 (w), 720 (w).

MS (EI, 70 ev), *m/z* (%): 246 (5) [M^+], 205 (15), 177 (100), 149 (46), 121 (12), 76 (8).

$C_{15}H_{18}O_3$ HRMS (EI) Calcd. 246.1256

Found 246.1253

Synthesis of ethyl 3-(4-fluorobenzoyl)benzoate (135g)



Prepared according to TP 10 from ethyl 3-iodobenzoate (276 mg, 1.0 mmol), magnesium cuprate reagent **36** (0.5 mmol), and 4-fluorobenzoyl chloride (190 mg, 1.2 mmol). Reaction time: 1h at rt. Purification by flash chromatography (*n*-pentane/diethyl ether = 10/1) yielded **135g** as a light yellow oil (228 mg, 84%).

^{1}H-NMR ($CDCl_3$, 300 MHz): δ = 8.32-8.30 (dt, *J* = 1.7 Hz, *J* = 0.6 Hz, 1H), 8.18-8.15 (ddd, *J* = 7.7 Hz, *J* = 1.7 Hz, *J* = 0.3 Hz, 1H), 7.87-7.84 (ddd, *J* = 7.6 Hz, *J* = 1.7 Hz, *J* = 0.3 Hz, 1H), 7.77-7.72 (dd, *J* = 8.9 Hz, *J* = 5.4 Hz, 2H), 7.51-7.45 (dt, *J* = 7.7 Hz, *J* = 0.6 Hz, 1H), 7.10-7.05 (t, *J* = 8.9 Hz, 2H), 4.34-4.27 (q, *J* = 7.2 Hz, 2H), 1.32-1.28 (t, *J* = 7.2 Hz, 3H).

^{13}C-NMR ($CDCl_3$, 75 MHz): δ = 193.2, 164.7, 164.5 (d, *J* = 254.9 Hz), 136.8, 132.7, 132.3, (d, *J* = 2.9 Hz), 132.1, 131.7 (d, *J* = 9.4 Hz), 129.8, 129.7, 127.6, 114.7 (d, *J* = 22.0 Hz), 60.4, 13.3.

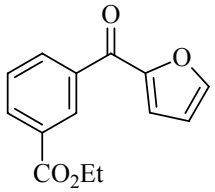
IR (film, cm^{-1}): $\tilde{\nu}$ = 2983 (w), 1721 (vs), 1663 (vs), 1599 (vs), 1505 (m), 1368 (w), 1309 (vs), 1248 (vs), 1156 (s), 1022 (m), 742 (m).

MS (EI, 70 ev), *m/z* (%): 272 (85) [M^+], 244 (15), 227 (53), 199 (14), 177 (23), 149 (11), 123 (100), 95 (28), 77 (8).

$C_{16}H_{13}FO_3$ HRMS (EI) Calcd. 272.0849

Found 272.0846

Synthesis of ethyl 3-(2-furoyl)benzoate (135h)

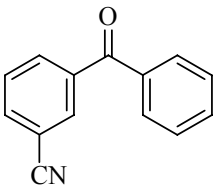


Prepared according to TP 10 from ethyl 3-iodobenzoate (276 mg, 1.0 mmol), magnesium cuprate reagent **36** (0.5 mmol), and 4-furoyl chloride (156 mg, 1.2 mmol). Reaction time: 1h at rt. Purification by flash chromatography (*n*-pentane/diethyl ether = 10/1) yielded **135h** as a light yellow oil (207 mg, 85%).

^{1}H-NMR ($CDCl_3$, 300 MHz): δ = 8.55-8.54 (t, *J* = 1.4 Hz, 1H), 8.18-8.15 (dt, *J* = 7.9 Hz, *J* = 1.4 Hz, 1H), 8.08-8.04 (dt, *J* = 7.7 Hz, *J* = 1.4 Hz, 1H), 7.65-7.64 (d, *J* = 1.7 Hz, 1H), 7.52-7.47 (t, *J* = 7.7 Hz, 1H), 7.19-7.18 (d, *J* = 3.3 Hz, 1H), 6.54-6.52 (dd, *J* = 3.3 Hz, *J* = 1.7 Hz, 1H), 4.36-4.29 (q, *J* = 7.2 Hz, 2H), 1.34-1.30 (t, *J* = 7.2 Hz, 3H).
^{13}C-NMR ($CDCl_3$, 75 MHz): δ = 180.4, 164.7, 151.0, 146.4, 136.4, 132.3, 132.2, 129.8, 129.3, 127.6, 119.8, 111.4, 60.3, 13.3.
IR (film, cm^{-1}): $\tilde{\nu}$ = 2982 (w), 1722 (vs), 1651 (vs), 1604 (m), 1563 (s), 1464 (vs), 1391 (m), 1291 (s), 1184 (s), 1017 (s), 728 (m).
MS (EI, 70 ev), *m/z* (%): 244 (82) [M^+], 216 (23), 199 (100), 171 (16), 149 (8), 115 (11), 95 (9), 77 (43).

$C_{14}H_{12}O_4$	HRMS (EI)	Calcd.	244.0736
		Found	244.0733

Synthesis of 3-benzoylbenzonitrile (135i)



Prepared according to TP 10 from 3-iodobenzonitrile (229 mg, 1.0 mmol), magnesium cuprate reagent **36** (0.5 mmol), and benzoyl chloride (168 mg, 1.2 mmol). Reaction time: 1h at rt. Purification by flash chromatography (*n*-pentane/diethyl ether = 10/1) yielded **135i** as a white solid (186 mg, 90%).

mp.: 92-93 °C

^{1}H-NMR ($CDCl_3$, 300 MHz): δ = 7.98-7.93 (m, 2H), 7.80-7.76 (dt, *J* = 7.6 Hz, *J* = 1.5 Hz, 1H), 7.71-7.67 (m, 2H), 7.59-7.52 (m, 2H), 7.46-7.41 (m, 2H).

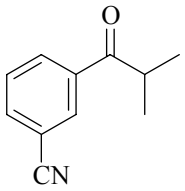
^{13}C-NMR ($CDCl_3$, 75 MHz): δ = 194.8, 139.0, 136.7, 135.7, 134.2, 133.8, 133.7, 130.4, 129.8, 129.1, 118.3, 113.2.

IR (KBr, cm^{-1}): $\tilde{\nu}$ = 3076 (w), 2232 (s), 1663 (vs), 1605 (s), 1596 (m), 1425 (m), 1279 (vs), 1197 (w), 976 (w), 724 (s), 641 (m).

MS (EI, 70 ev), *m/z* (%): 207 (100) [M^+], 130 (11), 105 (48), 77 (10).

$C_{14}H_9NO$	HRMS (EI)	Calcd.	207.0684
		Found	207.0678

Synthesis of 3-isobutyrylbenzonitrile (135j)



Prepared according to TP 10 from 3-iodobenzonitrile (229 mg, 1.0 mmol), magnesium cuprate reagent **36** (0.5 mmol), and isobutyryl chloride (128 mg, 1.2 mmol). Reaction time: 1h at rt. Purification by flash chromatography (*n*-pentane/diethyl ether = 10/1) yielded **135j** as a colorless oil (159 mg, 92%).

^{1}H-NMR ($CDCl_3$, 300 MHz): δ = 8.15 (t, *J* = 1.4 Hz, 1H), 8.11-8.09 (dt, *J* = 7.9 Hz, *J* = 1.4 Hz, 1H), 7.78-7.74 (dt, *J* = 7.9 Hz, *J* = 1.4 Hz, 1H), 7.57-7.52 (t, *J* = 7.9 Hz, 1H), 3.51-3.37 (septett, *J* = 6.9 Hz, 1H), 1.17-1.15 (d, *J* = 6.9 Hz, 6H).

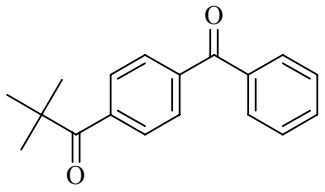
^{13}C-NMR ($CDCl_3$, 75 MHz): δ = 202.6, 137.3, 136.1, 132.7, 132.4, 130.1, 118.4, 113.6, 36.0, 19.3.

IR (film, cm^{-1}): $\tilde{\nu}$ = 3074 (w), 2975 (s), 2232 (s), 1693 (vs), 1598 (w), 1467 (m), 1238 (vs), 1145 (s), 1019 (m), 994 (m), 742 (m), 680 (m).

MS (EI, 70 ev), *m/z* (%): 173 (16) [M^+], 130 (100), 102 (21), 75 (8).

$C_{11}H_{11}NO$	HRMS (EI)	Calcd.	173.0841
		Found	173.0834

Synthesis of 1-(4-benzoylphenyl)-2,2-dimethyl-1-propanone (135k)



Prepared according to TP 10 from 1-(4-iodophenyl)-2,2-dimethyl-1-propanone (288 mg, 1.0 mmol), magnesium cuprate reagent **36** (0.5 mmol), and benzoyl chloride (168 mg, 1.2 mmol). Reaction time: 2h from -78 °C to rt. Purification by flash chromatography (*n*-pentane/diethyl ether = 20/1) yielded **135k** as a light yellow solid (186 mg, 70%).

mp.: 92 °C

^{1}H-NMR ($CDCl_3$, 300 MHz): δ = 7.75-7.71 (m, 4H), 7.65-7.62 (m, 2H), 7.58-7.50 (m, 1H), 7.44-7.40 (m, 2H), 1.28 (s, 9H).

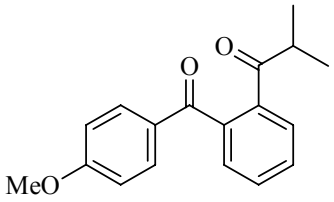
^{13}C-NMR ($CDCl_3$, 75 MHz): δ = 210.3, 196.9, 143.2, 140.1, 138.0, 133.8, 131.0, 130.6, 129.4, 128.3, 45.4, 28.7.

IR (KBr, cm^{-1}): $\tilde{\nu}$ = 2963 (w), 1673 (vs), 1649 (vs), 1596 (w), 1461 (m), 1288 (s), 958 (s), 719 (s), 697 (m).

MS (EI, 70 ev), *m/z* (%): 266 (1) [M^+], 209 (100), 182 (12), 152 (9), 105 (10), 77 (6).

$C_{18}H_{18}O_2$	HRMS (EI)	Calcd.	266.1307
		Found	266.1302

Synthesis of 1-[2-(4-methoxybenzoyl)phenyl]-2-methyl-1-propanone (135l)



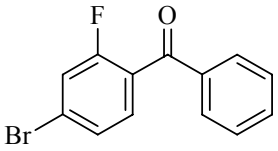
Prepared according to TP 10 from (2-iodophenyl)(4-methoxyphenyl)methanone (338 mg, 1.0 mmol), magnesium cuprate reagent **36** (0.5 mmol), and isobutyryl chloride (128 mg, 1.2

mmol). Reaction time: 2h from -78 °C to rt. Purification by flash chromatography (*n*-pentane/diethyl ether = 20/1) yielded **135l** as a light yellow oil (240 mg, 85%).

^{1}H-NMR ($CDCl_3$, 300 MHz): δ = 7.72-7.67 (m, 1H), 7.68-7.65 (d, *J* = 8.9, 2H), 7.49-7.46 (m, 2H), 7.35-7.32 (m, 1H), 6.84-6.81 (d, *J* = 8.9, 2H), 3.77 (s, 3H), 3.31-3.17 (septett, *J* = 6.9 Hz, 1H), 1.04-1.02 (d, *J* = 6.9 Hz, 6H).
^{13}C-NMR ($CDCl_3$, 75 MHz): δ = 206.3, 196.6, 163.9, 141.4, 138.7, 132.3, 131.6, 130.6, 130.0, 129.0, 128.7, 114.0, 55.9, 37.8, 19.1.
IR (film, cm^{-1}): $\tilde{\nu}$ = 2972 (m), 1682 (vs), 1660 (vs), 1598 (vs), 1463 (m), 1225 (vs), 1150 (m), 1027 (m), 980 (m), 931 (m), 845 (w), 609 (w).
MS (EI, 70 ev), *m/z* (%): 282 (3) [M^+], 267 (4), 239 (100), 224 (2), 210 (2), 196 (2), 181 (2), 168 (2), 152 (2), 135 (2), 107 (1), 92 (1), 77 (2).

$C_{18}H_{18}O_3$	HRMS (EI)	Calcd.	282.1256
		Found	282.1260

Synthesis of (4-bromo-2-fluorophenyl)(phenyl)methanone (135m)



Prepared according to TP 10 from 1-bromo-3-fluoro-4-iodobenzene (301 mg, 1.0 mmol), magnesium cuprate reagent **36** (0.5 mmol), and benzoyl chloride (168 mg, 1.2 mmol). Reaction time: 1h at rt. Purification by flash chromatography (*n*-pentane/diethyl ether = 50/1) yielded **135m** as a colorless solid (266 mg, 95%).

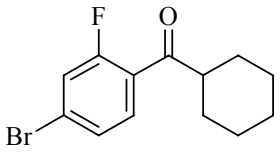
mp.: 56 °C
^{1}H-NMR ($CDCl_3$, 300 MHz): δ = 7.74-7.72 (d, *J* = 8.4 Hz, 2H), 7.56-7.51 (t, *J* = 7.4 Hz, 1H), 7.43-7.35 (m, 4H), 7.31-7.27 (m, 1H).
^{13}C-NMR ($CDCl_3$, 75 MHz): δ = 192.8, 160.3 (d, *J* = 257.3 Hz), 137.5, 134.0, 132.2 (d, *J* = 3.5 Hz), 130.1, 128.9, 128.2 (d, *J* = 3.5 Hz), 126.5 (d, *J* = 9.4 Hz), 126.4 (d, *J* = 14.7 Hz), 120.4 (d, *J* = 25.2 Hz).

IR (KBr, cm^{-1}): $\tilde{\nu}$ = 2924 (w), 1663 (vs), 1598 (vs), 1564 (m), 1448 (w), 1398 (s), 1282 (s), 1214 (m), 1065 (m), 924 (m), 863 (w), 700 (m), 534 (w).

MS (EI, 70 ev), *m/z* (%): 278 (92) [M^+], 250 (3), 201 (70), 173 (15), 105 (100), 77 (43).

$C_{13}H_8BrFO$	HRMS (EI)	Calcd.	277.9743
		Found	277.9749

Synthesis of (4-bromo-2-fluorophenyl)(cyclohexyl)methanone (135n)



Prepared according to TP 10 from 1-bromo-3-fluoro-4-iodobenzene (301 mg, 1.0 mmol), magnesium cuprate reagent **36** (0.5 mmol), and cyclohexanecarbonyl chloride (176 mg, 1.2 mmol). Reaction time: 1h at rt. Purification by flash chromatography (*n*-pentane/diethyl ether = 50/1) yielded **135n** as a white solid (262 mg, 92%).

mp.: 53 °C

^{1}H-NMR ($CDCl_3$, 300 MHz): δ = 7.59-7.54 (t, *J* = 8.0 Hz, 2H), 7.31-7.28 (dd, *J* = 8.4 Hz, *J* = 1.8 Hz, 2H), 7.26-7.22 (dd, *J* = 10.4 Hz, *J* = 1.8 Hz, 1H), 3.03-2.96 (m, 1H), 1.86-1.14 (m, 10H).

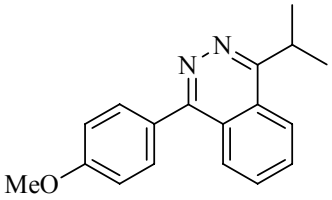
^{13}C-NMR ($CDCl_3$, 75 MHz): δ = 201.9, 161.1 (d, *J* = 257.6 Hz), 132.4 (d, *J* = 3.8 Hz), 128.4 (d, *J* = 3.5 Hz), 127.5 (d, *J* = 9.7 Hz), 125.2 (d, *J* = 13.8 Hz), 120.4 (d, *J* = 27.3 Hz), 50.5, 29.1, 26.3, 26.1.

IR (KBr, cm^{-1}): $\tilde{\nu}$ = 2942 (s), 1677 (vs), 1595 (vs), 1565 (s), 1472 (m), 1396 (vs), 1250 (m), 1196 (s), 1071 (m), 975 (s), 882 (m), 781 (m), 542 (m).

MS (EI, 70 ev), *m/z* (%): 286 (9) [M^+], 229 (16), 201 (100), 175 (25), 150 (10), 94 (33), 55 (23).

$C_{13}H_{14}BrFO$	HRMS (EI)	Calcd.	284.0212
		Found	284.0198

Synthesis of 1-Isopropyl-4-(4-methoxy-phenyl)-phthalazine (xia269)



Prepared according to TP 3 from 1-[2-(4-methoxybenzoyl)-phenyl]-2-methyl-1-propanone (**135l**). Reaction time: 15 min at 78 °C. Purification by flash chromatography (*n*-pentane/diethyl ether = 1/2) yielded **136** as a yellow solid (254 mg, 91%).

mp.: 192 °C

^{1}H-NMR ($CDCl_3$, 300 MHz): δ = 8.15-8.12 (d, *J* = 8.2, 1H), 8.07-8.04 (d, *J* = 8.2, 1H), 7.83-7.78 (m, 1H), 7.74-7.69 (m, 1H), 7.66-7.64 (d, *J* = 8.7, 2H), 7.01-6.98 (d, *J* = 8.7, 2H), 3.92-3.79 (septett, *J* = 6.9 Hz, 1H), 3.82 (s, 3H), 1.51-1.49 (d, *J* = 6.9 Hz, 6H).

^{13}C-NMR ($CDCl_3$, 75 MHz): δ = 163.0, 160.1, 158.6, 132.0, 131.9, 131.7, 129.5, 127.5, 125.8, 125.8, 124.2, 114.3, 55.8, 30.8, 22.4.

IR (KBr, cm^{-1}): $\tilde{\nu}$ = 2966 (m), 1613 (vs), 1519 (s), 1386 (s), 1253 (vs), 1182 (s), 1028 (m), 847 (m), 798 (m), 699 (w).

MS (EI, 70 ev), *m/z* (%): 278 (30) [M^+], 263 (35), 250 (100), 235 (11), 189 (2).

$C_{18}H_{18}N_2O$	HRMS (EI)	Calcd.	278.1419
		Found	278.1431

Curriculum Vitae

Name:	Xiaoyin Yang
Date of birth	29 May 1974
Place of birth	Henan/China
Nationality	Chinese
Marital status	Married

Educational Background

09/02-10/05	Ph. D study at Ludwig-Maximilians-Universität (München) under the supervision of Prof. Dr. Paul Knochel.
09/99–07/02	Diploma study at Shanghai Institute of Materia Medica, Chinese Academy of Sciences under the supervision of Prof. Dr. Yang Ye.
09/94–07/98	Bachelor degree study at the Chemistry Department of Zhenzhou University.

Research and Work Experience

09/02-10/05	Ph. D. under the supervision of Prof. Dr. Paul Knochel Topic: Development of new methods for the synthesis of functionalized organocopper reagents *via* halogen-copper exchange reactions Assistant in the organic chemistry practical course for undergraduate students at Ludwig-Maximilians-Universität, München.
09/99–07/02	Diploma study under the supervision of Prof. Dr. Yang Ye. Topic: (a) Stereoselective synthesis of 3a-hydroxyl-1, 2, 3, 3a, 8, 8a-hexahydropyrrolo [2,3-b]indole-2-carboxylic acid. and derivatization on solid-phase. (b) Derivatization and insecticidal activities test of *stemofoline.* (c) Isolation and structure elucidation of natural products from *Gelidium regidium*, a seaweed collected from Indonesia. (d) Total synthesis of chuangxinmycin's analogs
07/98–09/99	Research Assistant at China Research Institute of Aero–Accessories (CRIAA), Xiangfan, Hubei, China.
01/98–07/98	Research Assistant at Medicine Institute of Zhenzhou University under the supervision of Prof. Dr. Yanchun Guo.

Publications

1 Xiaoyin Yang, Thomas Rotter, Claudia Piazza, Paul Knochel:"Successive Iodine-Magnesium or -Copper Exchange Reactions for the Selective Functionalization of Polyhalogenated Aromatics" *Organic Letters* **2003**, *8*, 1229-1231.

2 Xiaoyin Yang, Christian Haug, Yiping Yang, Zhisheng He, Yang Ye"Stereoselective Synthesis of 3a-Hydroxyl-1,2,3,3a,8,8a-hexahydro pyrrolo [2,3-b] indole-2-carboxylic Acid" *Chinese Chemical Letters* **2003**, *14*, 130-132.

3 Xiaoyin Yang, Paul Knochel: "Preparation and Reactions of Polyfunctional Magnesium Arylcuprates Obtained by an Iodine-Copper Exchange" *Synlett* **2004**, *1*, 81-84.

4 M. Isabel Calaza, Xiaoyin Yang, Darunee Soorukram, Paul Knochel: "Stereoselective S_N2-Substitutions using Polyfunctional Lithium Arylcuprates Prepared by an Iodine-Copper Exchange" *Organic Letters* **2004**, *8*, 1229-1231.

5 Xiaoyin Yang, Andreas Althammer, Paul Knochel: "Selective Functionalized in Position 2 and 3 of Indole via an Iodine-Copper Exchange Reaction" *Organic Letters* **2004**, *6*, 1665-1667.

6 Xiaoyin Yang, Paul Knochel: "Preparation and Acylation of Polyfunctional Copper Derivatives of 3-Iodoindazoles Leading to Polyfunctional 3-Acylindazoles" *Synlett*. **2004**, *13*, 2303-2306.

7 Paul Knochel, Xiaoyin Yang, Nina Gommermann, "Polyfunctional Organocopper Reagents for Organic Synthesis" in P. Knochel (Ed.) *Handbook of Functionalized Organometallics*, Wiley-VCH, Weinheim, **2005**.

Posters and Seminars

1 **"**Synthesis of 3a-Hydroxyl-1,2,3,3a,8,8a-hexahydropyrrolo[2,3-b] indole-2- carboxylic acid and Derivatization on Solid-phase**";** Lecture, Shangahai Institute of Chinese traditional Medicine, Shanghai, China, 7th, June, 2002.

2 **"**Successive Iodine-Magnesium or -Copper Exchange Reactions for the Selective Functionalization of Polyhalogenated Aromatics**";** Poster, Twelfth International Symposium on Organometallic Chemistry directed toward Organic Synthesis (OMCOS-12), Toronto, Canada, 6th-10th, July, 2003.

3 "Novel Applications of Functionalized Arylcuprate and Mixed Zinc-Copper Reagents"; Poster, Industrietag, München, Germany, 17th, October, 2003.

4 "Generation of Highly Functionalized Heterocyclic and Vinylic Cuprate Reagents via Halogen-Copper Exchange Reactions"; Poster, Industrietag, München, Germany, 15th, October, 2004.

Languages

Chinese:	mother tongue
English:	fluent, written and spoken
German:	basic level