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Quantification of the Electrophilic Reactivities of Nitroalkenes

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Erklärung

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Eidesstattliche Versicherung

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Ivo Zenz

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Publikationen

Electrophilicities of *trans-β*-Nitrostyrenes

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***trans*-2-(2-Nitro-1-phenylethyl)cyclohexane**

Zenz, I.; Mayr, H.; Mayer, P. *Acta Crystallogr., Sect. E: Struct. Rep. Online* **2010**, *66*, o3136.

Konferenzbeiträge

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List of Abbreviations

Anal.	elementary analysis
aq	aqueous
ATR	attenuated total reflectance
Ar	aryl
bp	boiling point
calcd	calculated
$CDCl_3$	deuterated chloroform
d	doublet
dd	doublet of doublets
ddd	doublet of doublets of doublets
dr	diastereomeric ratio
E	electrophilicity parameter
e.g.	exempli gratia
equiv.	equivalents
eq	equation
EI	electron ionization
ESI	electrospray ionization
exp	experimental
FTIR	fourier transform infrared
h	hour(s)
HPLC	high performance liquid chromatography
HRMS	high resolution mass spectrometry
Hz	hertz
i.e.	id est
k	rate constant
K	equilibrium constant
LDA	lithium diisopropylamide
M	mol/L
m	multiplet
min	minute(s)
mp	melting point

N	nucleophilicity parameter
NMR	nuclear magnetic resonance
Ph	phenyl
ppm	parts per million
Pr	propyl
q	quartet
s_N	nucleophile-specific slope parameter
s	singlet
t	triplet
TPCD	tetrapyridinecobalt(II) dichromate
UV	ultraviolet
vis	visible
vs.	versus

Chapter 0: Summary

0.1 Introduction

Reactions in organic chemistry can in many cases be described as combinations between nucleophiles and electrophiles, and the rates of these reactions can be determined by eq 0.1, where N and s_N are nucleophile-specific parameters, E is an electrophilicity parameter, and k_2 is the second-order rate constant.

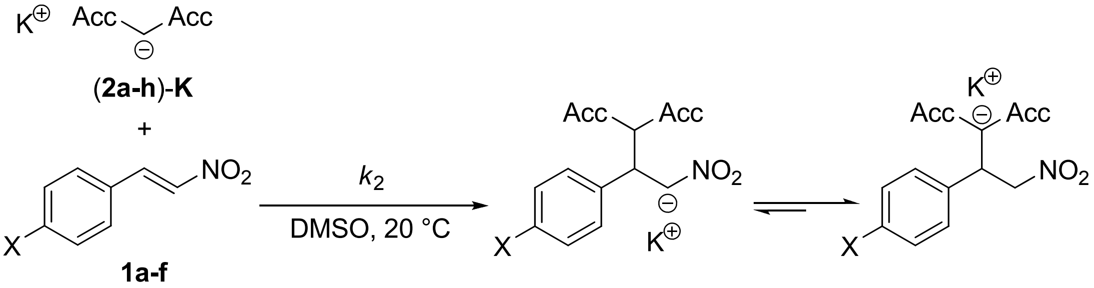
$$\log k_2(20\ °\mathrm{C}) = s_N(N + E) \tag{0.1}$$

This equation has been employed to characterize to date over 700 nucleophiles as well as over 200 electrophiles. However, for the synthetically important class of aliphatic and aromatic nitroalkenes, the E parameters have not been reported so far.

0.2 Electrophilicities of *trans*-*β*-Nitrostyrenes

The kinetics of the reactions of the *trans*-*β*-nitrostyrenes **1a–f** with the acceptor-substituted carbanions **2a–h** have been determined in dimethyl sulfoxide solution at 20 °C (Scheme 0.1). The resulting second-order rate constants were employed to determine the electrophile-specific reactivity parameters E of the *trans*-*β*-nitrostyrenes according to the correlation equation 0.1. The E parameters range from –12 to –15 on our empirical electrophilicity scale (www.cup.lmu.de/oc/mayr/DBintro.html). The second-order rate constants for the reactions of *trans*-*β*-nitrostyrenes with some enamines were measured and found to agree with those calculated from the electrophilicity parameters E determined in this work and the previously published N and s_N parameters for enamines.

SCHEME 0.1. Reactions of the *trans*-*β*-Nitrostyrenes 1a–f with the Carbanions (2a–h)-K.



The correlations in Figure 0.1 show that the rate constants for the reactions of **1a–f** with the carbanions **2b–f** are fairly reproduced by eq 0.1, i.e., the experimental points are close to the calculated correlation lines. Some systematic deviations are obvious, however. Thus, the anion of Meldrum´s acid **2a** reacts faster with all nitrostyrenes, particularly with the less reactive nitrostyrenes **1a–d**. Furthermore, the malonate anion **2g** reacts more slowly, and the nitromethyl anion **2h** reacts faster with the nitrostyrenes **1b–d** than expected from the benzhydrylium-derived reactivity parameters N and s_N of these nucleophiles. While the origin of these deviations is not known, it should be noted, that analogous deviations have also been observed for the reactions of these carbanions with benzylidene Meldrum's acids and benzylidene dimethylbarbituric- and thiobarbituric acids. The value of log (k_2^{exp}/k_2^{calcd}) is always smaller than 0.76, corresponding to a maximum deviation between calculated and experimental rate constants of a factor of 6, which we consider tolerable for a reactivity model covering a range of almost 40 orders of magnitude with only 3 parameters.

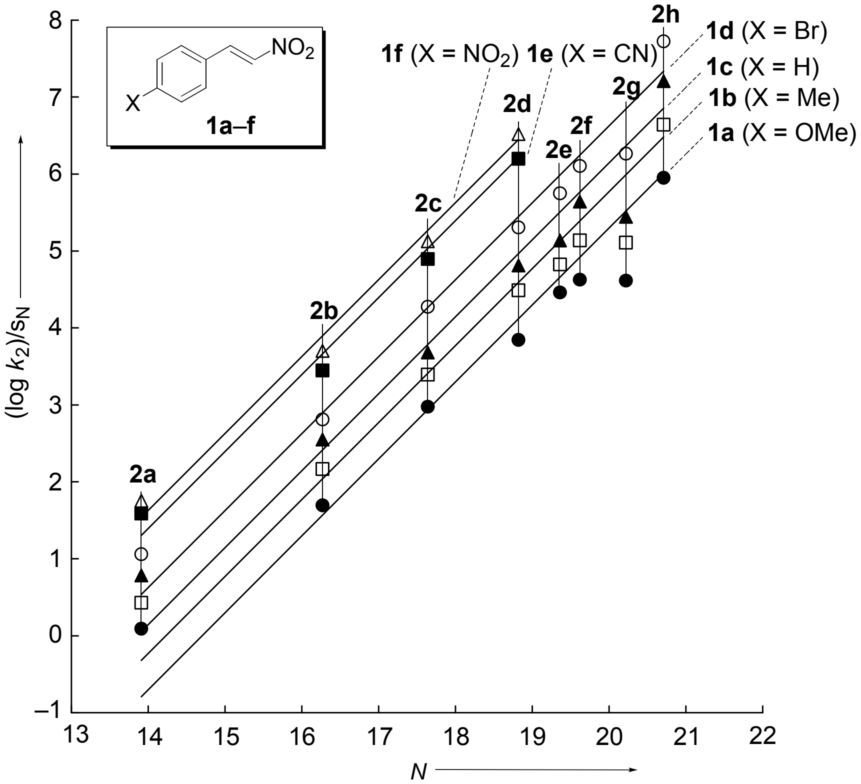


FIGURE 0.1. Correlation of (log k_2)/s_N versus the Nucleophilicity Parameters N of the Carbanions 2a–h for their Reactions with the *trans*-*β*-Nitrostyrenes 1a–f in DMSO at 20 °C. Correlation Lines are Fixed at a Slope of 1.0, as Required by Eq 0.1.

As illustrated in Figure 0.2, the *β*-nitrostyrenes **1** are considerably more electrophilic than benzylidenemalonates and less electrophilic than analogously substituted benzylidenemalononitriles.

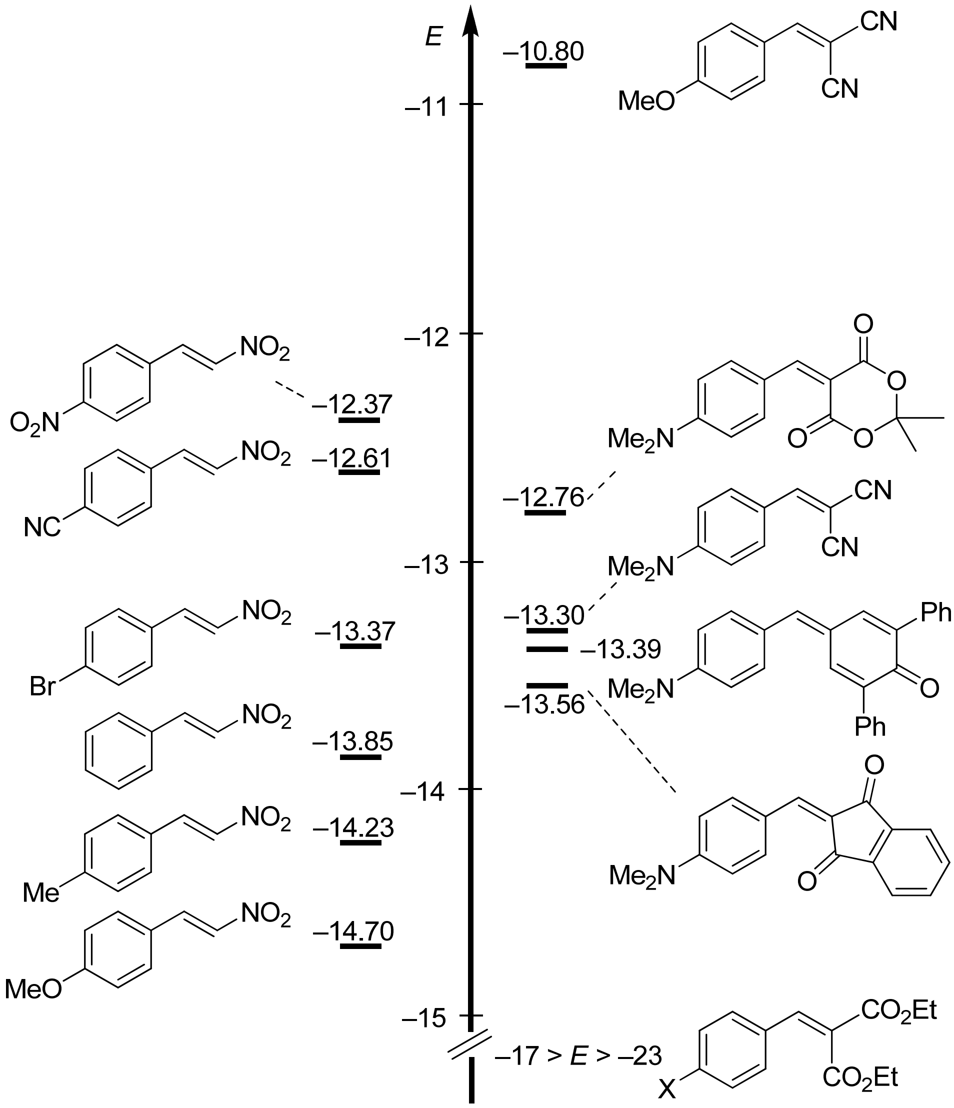
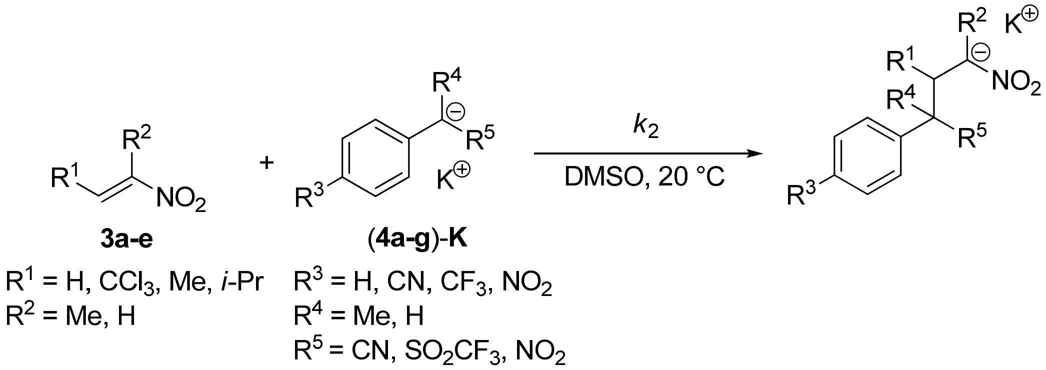


FIGURE 0.2. Comparison of *E* Values for Differently Substituted Michael Acceptors and Quinone Methides.

0.3 Electrophilicities of Aliphatic Nitroolefins

The kinetics of the reactions of the nitroolefins **3a–e** with the acceptor-substituted carbanions **4a–g** have been determined in dimethyl sulfoxide solution at 20 °C (Scheme 0.2). The resulting second-order rate constants were employed to determine the electrophile-specific reactivity parameters *E* of the nitroolefins according to the correlation equation 0.1. The *E* parameters range from –12 to –16 on our empirical electrophilicity scale.

SCHEME 0.2. Reactions of the Nitroolefins 3a–e with the Carbanions (4a–g)-K.



The correlations in Figure 0.3 illustrate, that the rate constants for the reactions of **3a–e** with the carbanions **4a–g** are satisfactorily reproduced by eq 0.1, i.e., the experimental points are close to the calculated correlation lines, the slopes of which are fixed at 1.0. Some systematic deviations are obvious, however. Thus, the anion of 2-(4-nitrophenyl)propanenitrile (**4f**) reacts more slowly with all nitroolefins than expected from its *N* value. Either the tertiary carbanion **4f** behaves differently toward nitroolefins and the reference electrophiles or the published *N* value of **4f** requires revision. The calculated and experimental rate constants always agree within a factor of 2, which we consider tolerable in view of the fact that the reactivity parameters *N* and s_N for **4a–g** have been derived from reactions with benzhydrylium ions, quinone methides, benzylidene-1,3-indandiones, benzylidenebarbituric acids, and diethyl benzylidenemalonates and were not adjusted to the reactions with the electrophiles studied in this work.

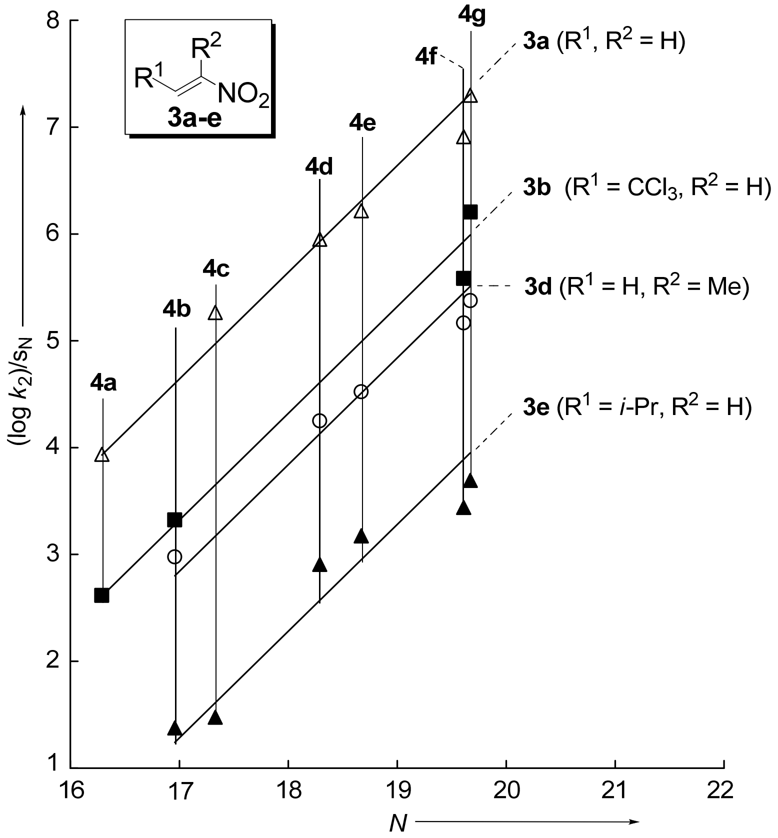


FIGURE 0.3. Correlation of (log k_2)/s_N versus the Nucleophilicity Parameters N of the Carbanions 4a–g for their Reactions with the Nitroolefins 3a, 3b, 3d and 3e in DMSO at 20 °C. The Correlation Lines are Fixed at a Slope of 1.0, as Required by Eq 0.1.

As illustrated in Figure 0.4, **3b** is about one order of magnitude less reactive than **3a**, which must be explained by the steric effect of the trichloromethyl group, because its electronic effect should increase the electrophilicity of the π-system. Steric shielding by the bulkier *iso*-propyl group also explains the significant reactivity difference between **3c** and **3e**. Surprisingly, (E)-1-nitro-1-propene (**3c**) and 2-nitroprop-1-ene (**3d**) have almost identical reactivities. Obviously the stronger electronic retardation by the methyl group in **3d** is compensated by the stronger steric retardation of the methyl group in **3c**.

Figure 0.4 furthermore shows that (*E*)-1-nitro-1-propene (**3c**) has a similar electrophilicity as the phenylogous nitrostyrene (4-methyl-*β*-nitrostyrene, **1b**), and the similar reactivities of nitroethylene and 4,*β*-dinitrostyrene show that the electronic activation by the 4-nitrophenyl group is fully compensated by its steric retarding effect.

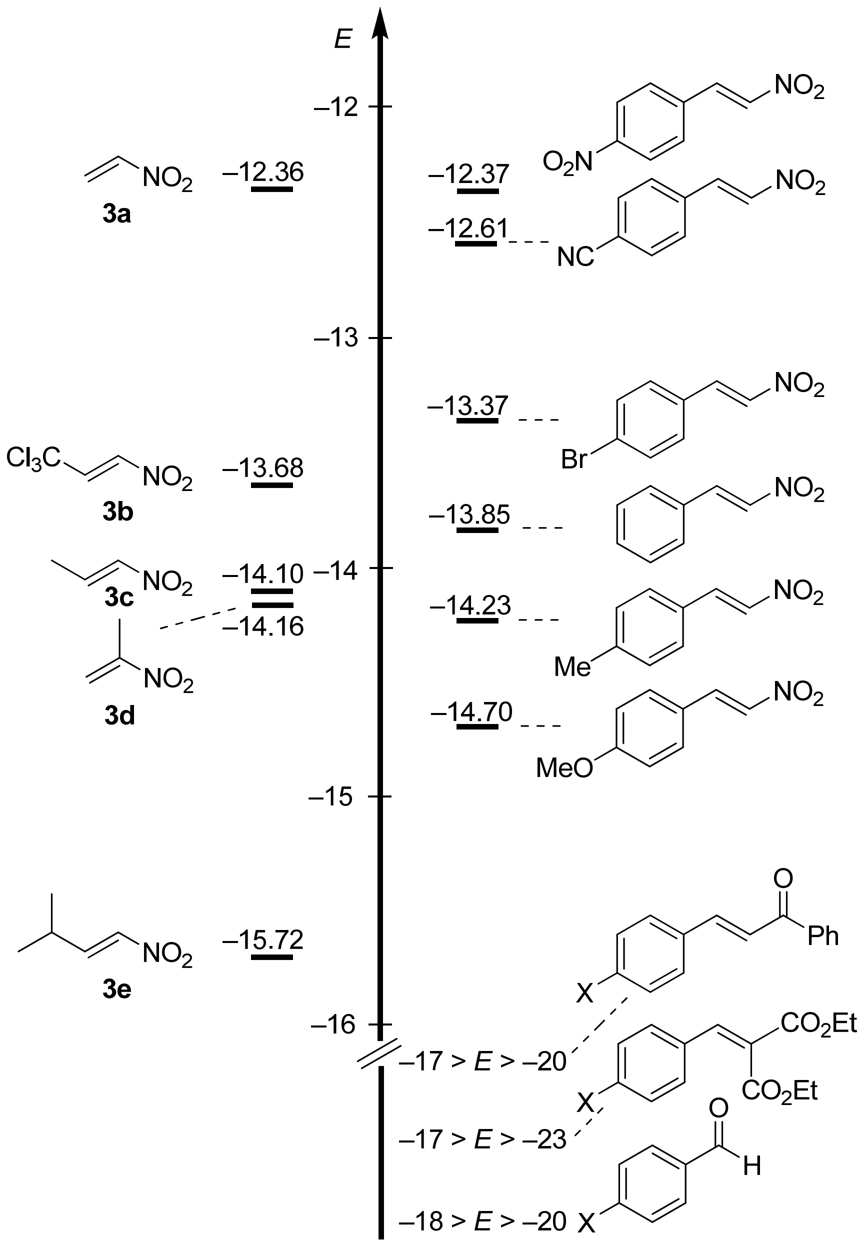


FIGURE 0.4. Comparison of *E* Values for Differently Substituted Michael Acceptors.

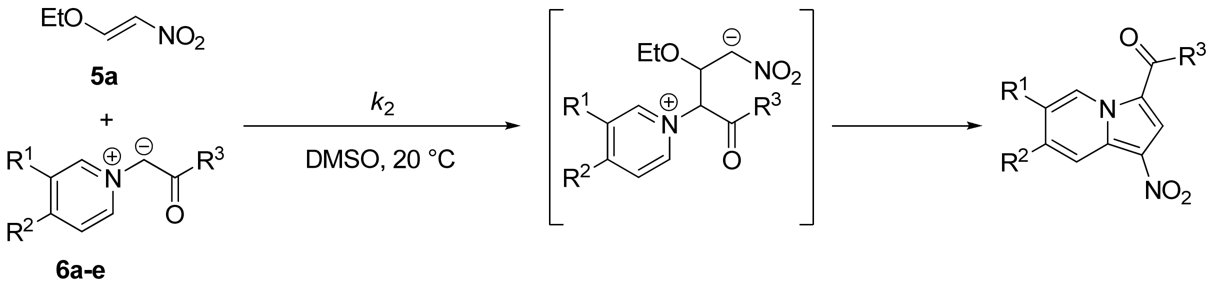
As all nitroolefins investigated so far have E parameters between –16 and –12, one can generalize, that they are more electrophilic than chalcones, aldehydes and benzylidenemalonates, which explains their frequent use in organocatalytic reactions (enamine activation).

The E parameters of the nitroolefins **3** can now be combined with the numerous published N and s_N parameters of nucleophiles to predict scope and limitations of nucleophilic additions to them on the basis of eq 0.1.

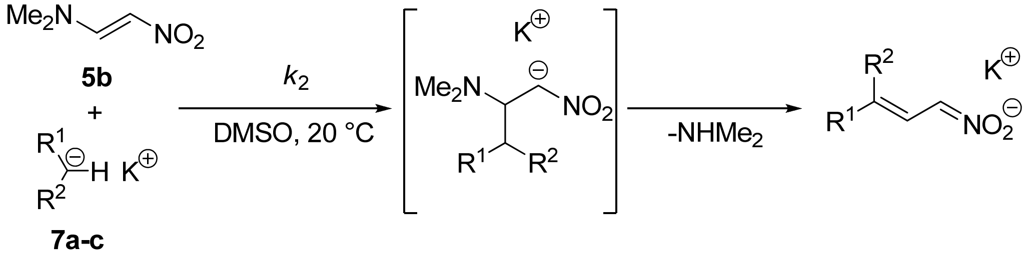
0.4 Electrophilicities of (*E*)-1-Ethoxy-2-nitroethene and (*E*)-*N*,*N*-Dimethyl-2-nitroethenamine

The kinetics of the reactions of (*E*)-1-ethoxy-2-nitroethene (**5a**) with the pyridinium ylides **6a–e** (Scheme 0.3), and of the reactions of (*E*)-*N*,*N*-dimethyl-2-nitroethenamine (**5b**) with the carbanions **7a–c** (Scheme 0.4) have been determined in dimethyl sulfoxide solution at 20 °C. However, only for the nitroolefin **5a**, the resulting second-order rate constants could be employed to determine the electrophile-specific reactivity parameter *E* according to the correlation equation 0.1.

SCHEME 0.3. Reactions of the Nitroolefin 5a with the Pyridinium Ylides 6a–e.



SCHEME 0.4. **Reactions of the Nitroolefin 5b with the Carbanions 7a–c**.



The correlation in Figure 0.5 illustrates, that the rate constants for the reactions of **5a** with the pyridinium ylides **6a–e** are well reproduced by eq 0.1; i.e., the experimental points are close to the calculated correlation lines, the slopes of which are fixed at 1.0. The deviations between calculated and experimental rate constants are always less than a factor of 1.3, which we consider tolerable in view of the fact that the reactivity parameters *N* and s_N for **6a–e** have been derived from reactions with benzhydrylium ions and quinone methides, and were not adjusted to the reactions with the electrophiles studied in this work. Performing kinetics of the reactions of **5a** with the carbanions **7a**–**c** is not possible due to an overlap of the UV-bands. The reactions of the nitroolefin **5b** with the carbanions **7a**–**c** are satisfactorily reproduced by eq 0.1. However, we observed that **5b** does not react (no change of the absorbance of **5b** after the addition of the carbanion) with the carbanions of nitroethane, diethyl malonate, 4-nitrophenylacetonitrile and 4-cyanophenylacetonitrile, carbanions similar to **7a**–**c**, which we currently can not explain. There is also no reaction of **5b** with the pyridinium ylides **6a**–**e**. Therefore we can not assign an electrophilicity value to (*E*)-*N*,*N*-dimethyl-2-nitroethenamine (**5b**) of general validity.

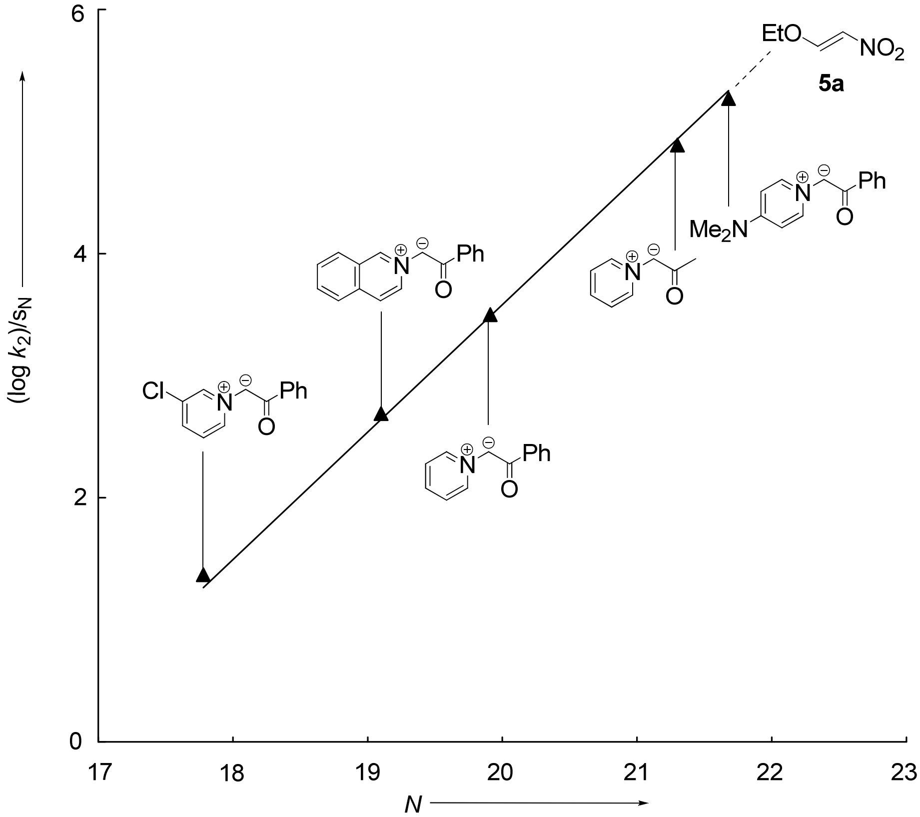


FIGURE 0.5. Correlation of (log k_2)/s_N versus the Nucleophilicity Parameters *N* of the Pyridinium Ylides 6a–e for their Reactions with (*E*)-1-Ethoxy-2-nitroethene (5a) in DMSO at 20 °C. The Correlation Lines are Fixed at a Slope of 1.0, as Required by Eq 0.1.

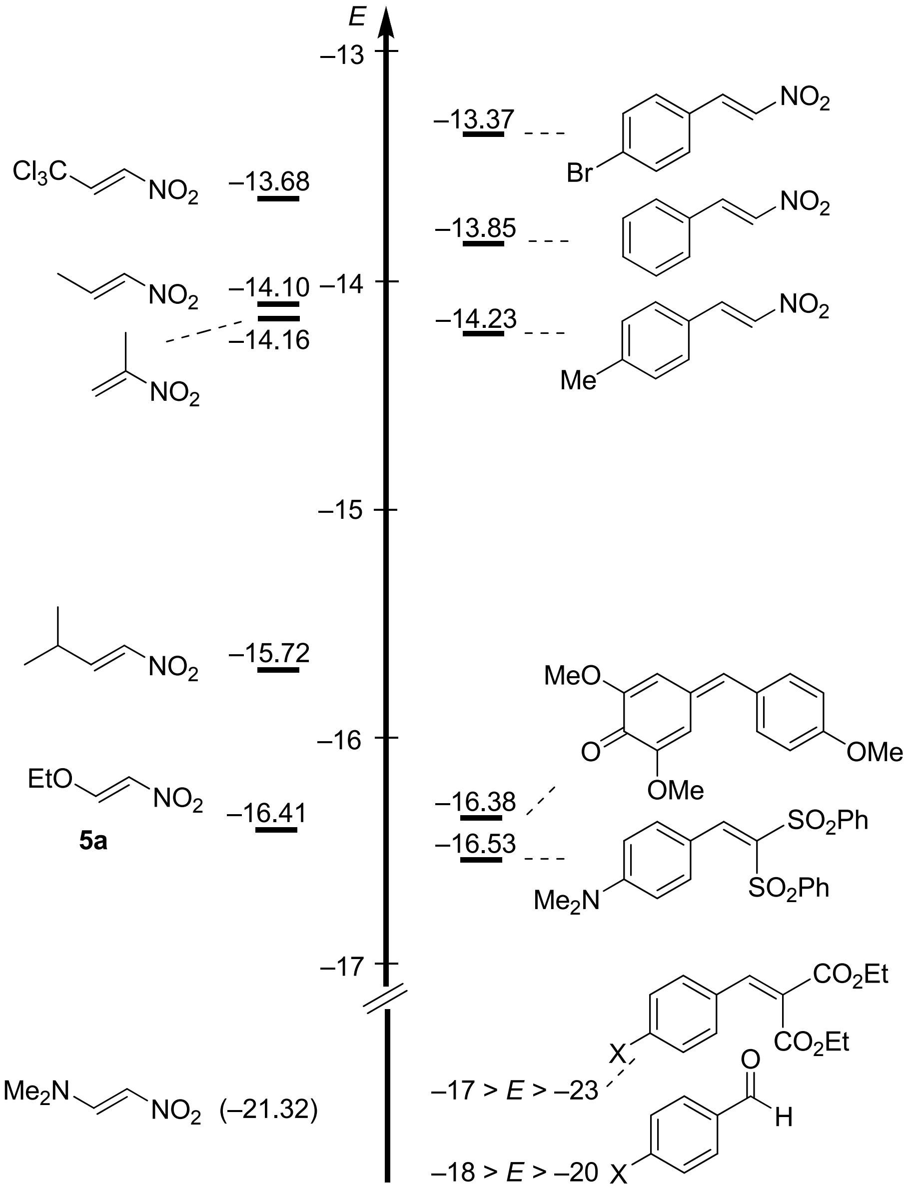


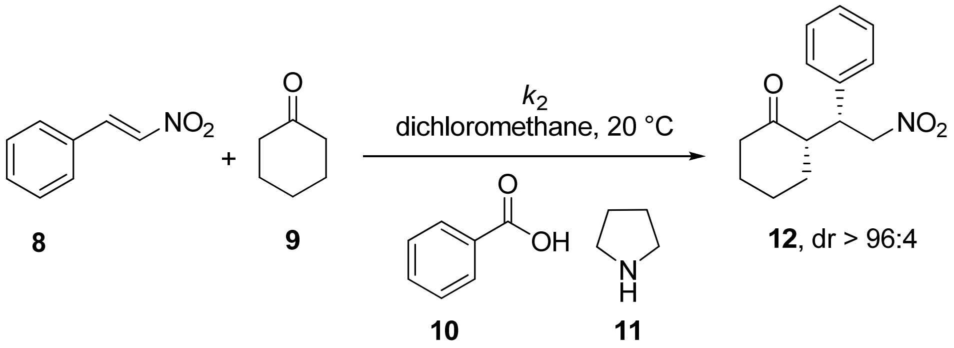
FIGURE 0.6. Comparison of *E* Values for Differently Substituted Michael Acceptors.

As illustrated in Figure 0.6, **5a** is about one order of magnitude less reactive than (*E*)-3-methyl-1-nitrobut-1-ene (E = –15.72, see Chapter 3), which shows that the electronic retardation of the ethoxy group is stronger than the steric retardation by the bulky *iso*-propyl group. **5a** is slightly less reactive than the methoxy-substituted quinone methide, but slightly more reactive than the dimethylamino-substituted bissulfonyl ethylene. **5b** exhibits similar reactivity as benzaldehydes and diethyl benzylidene malonates, though we were not able to assign a generally applicable E value as discussed above.

0.5 *In Situ* IR Investigations of Organocatalytic Michael Additions to *trans-β*-Nitrostyrenes

The kinetics of the reaction of cyclohexanone (**9**) with *trans*-*β*-nitrostyrene (**8**) catalyzed by benzoic acid (**10**) and pyrrolidine (**11**) have been determined in dichloromethane solution at 20 °C via ATR-FTIR spectroscopy (Scheme 0.5). The reaction progress was monitored via following the symmetric N-O stretching vibration of **8** at $\tilde{\nu} = 1343\ \text{cm}^{-1}$.

SCHEME 0.5. Reaction of *trans*-*β*-Nitrostyrene with Cyclohexanone Catalyzed by Pyrrolidine and Benzoic Acid.



In order to obtain the initial rate constants k_{initial}, the slope of a given concentration *vs*. time plot was evaluated considering the first 17 min of the reaction. The plot of log k_{initial} *vs*. log [**8**–**11**]$_0$ provided the reaction orders *a*–*d* for the compounds **8**–**11**. The rate orders reveal that the rate of the reaction mostly depends on the concentrations of cyclohexanone (**9**) and pyrrolidine (**11**), with rate orders of $^b = 0.8$ and $^d = 0.7$, and to a lesser extent, on the concentrations of *trans*-*β*-nitrostyrene (**8**) and benzoic acid (**10**), with rate orders of $^a = 0.5$ and $^c = 0.4$.

$$-\mathrm{d}[\mathbf{8}]/\mathrm{d}t = k\,[\mathbf{8}]^{a}\,[\mathbf{9}]^{b}\,[\mathbf{10}]^{c}\,[\mathbf{11}]^{d} \tag{0.2}$$

The formation of product **12** can be detected at $\tilde{\nu} = 1556\ \mathrm{cm}^{-1}$. However, through partial overlap with the asymmetric N-O stretching vibration of **8** at $\tilde{\nu} = 1525\ \mathrm{cm}^{-1}$, the increase of absorbance caused by the formation of product **12** could not be evaluated (Figure 0.7).

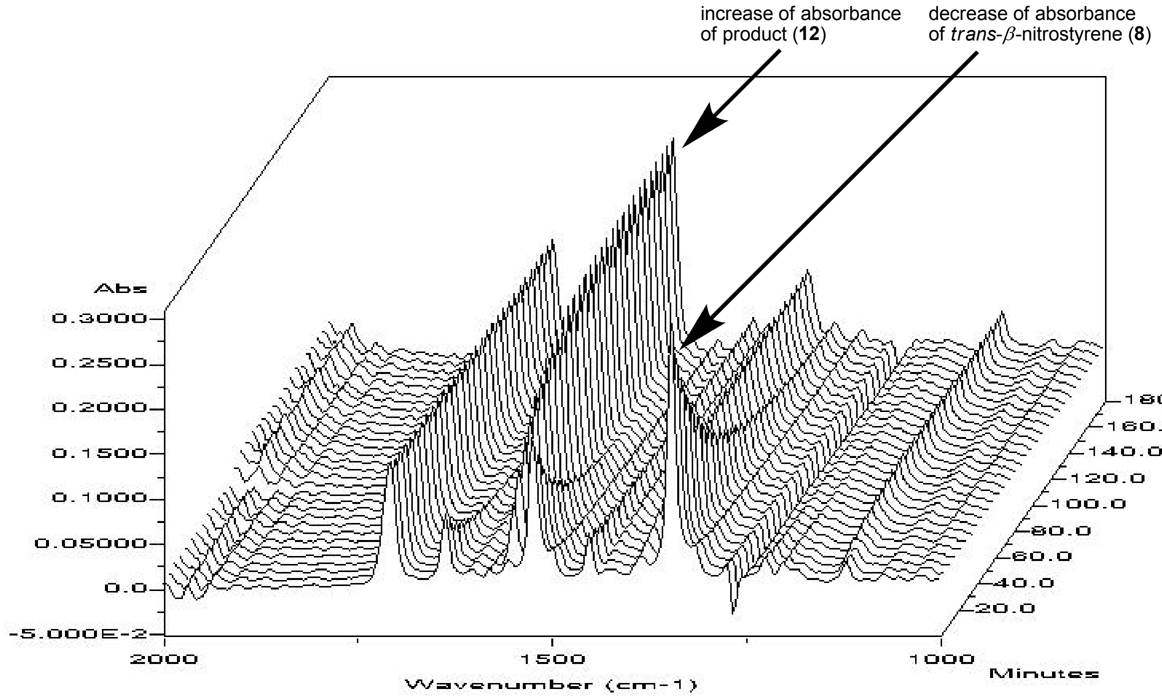
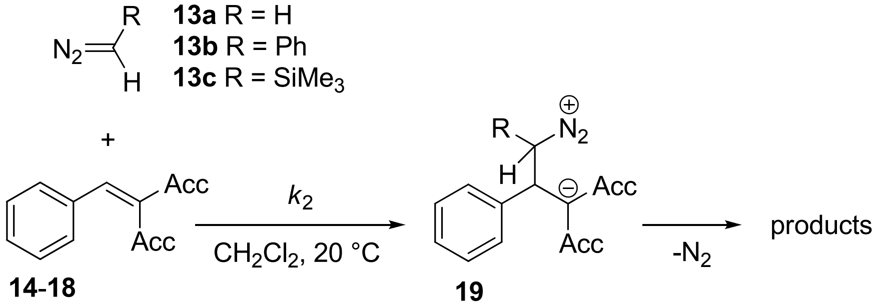


FIGURE 0.7. ATR-FTIR Spectrum Showing the Decrease of Absorbance (A at $\tilde{\nu} = 1343\ \mathrm{cm}^{-1}$, *trans*-β-Nitrostyrene (8)) and the Increase of Absorbance (A at $\tilde{\nu} = 1556\ \mathrm{cm}^{-1}$, 2-(2-Nitro-1-phenylethyl)cyclohexanone (12)). Reaction Conditions: 8 (c = 4.02 × 10^{-1} M), 9 (c = 4.01 × 10^{-1} M), 10 (c = 4.08 × 10^{-2} M), 11 (c = 6.03 × 10^{-2} M), Measured in Dichloromethane at 20 °C.

0.6 Reactions of Diazomethanes with Michael Acceptors

Kinetics of the reactions of the diazomethanes **13a–c** (Scheme 0.6) with benzylidene-1,3-indandiones **14a,b**, benzylidene Meldrum´s acids **15a,b**, benzylidenemalononitriles **16a,b**, 4-nitro-*trans*-*β*-nitrostyrene (**17a**), and (*E*)-3-(4-nitrophenyl)-1-phenylprop-2-en-1-one (**18a**) have been determined.

SCHEME 0.6. Reactions of the Diazomethanes 13a–c with the Michael Acceptors 14–18.



The majority of the products are formed via zwitterionic intermediates **19**, which subsequently undergo cyclizations or 1,2-rearrangements. Accordingly, the observed rate constants agree within a factor of 260 with those calculated for the formation of these zwitterions by eq 0.1. In contrast, the previously reported rate constants for the concerted 1,3-dipolar cycloadditions of diazomethane with ethyl acrylate and diethyl fumarate are 10^4-10^6 times higher than calculated by eq 0.1 for a stepwise process with zwitterionic intermediates.

Chapter 1: Introduction and Objectives

1.1 Introduction

The prediction of organic reactivity is challenging because of the large diversity of different reactions and their ever increasing number. In the 1930s, Ingold introduced the terms “nucleophile” for species with electron surplus and “electrophile” for species with the lack of electrons.[1] The first systematic approach to polar organic reactivity was presented by Swain and Scott (eq 1.1), where the nucleophile is characterized by n, the electrophile by s and k_0.[2]

$$\log (k/k_0) = sn \tag{1.1}$$

Equation (1.1) compares the rate constant k for a nucleophile-electrophile combination with the rate constant for the corresponding reaction with water k_0. The s parameter for methyl bromide was defined as 1.00, and the n parameter of water was set to 0.00.

An important approach to quantify polar organic reactivity was reported by Ritchie (eq 1.2), who reported a “constant selectivity relationship” for the reactions of carbocations and diazonium ions with nucleophiles.[3]

$$\log (k/k_0) = N_+ \tag{1.2}$$

The reactivity scale covers over 13 orders of magnitude and allows one to predict the rate of a reaction with one parameter for the nucleophile (N_+) and one parameter for the electrophile ($\log k_0$). Later it was shown that eq 1.2 is limited in its applicability, and the correlations are improved when different classes of electrophiles are treated separately.[4]

In 1994, Mayr and Patz introduced the linear-free energy relationship (eq 1.3), which has been shown to describe a large variety of reactions of electrophiles with nucleophiles, where N and s_N (previously called s) are nucleophile-specific parameters, E is an electrophilicity parameter, and k_2 is the second-order rate constant.[5]

$$\log k_2(20\ °\mathrm{C}) = s_N(N + E) \tag{1.3}$$

Diarylcarbenium ions have been employed as reference electrophiles for the determination of N and s_N parameters of neutral and anionic nucleophiles.[6] Eq 1.3 equation provides the most comprehensive approach to polar organic reactivity known today, and over 700 nucleophiles and 200 electrophiles have been characterized so far.

1.2 Objectives

While a large variety of nucleophiles (N and s_N) have been characterized according to eq 1.3, the number of E parameters for electrophiles, and specifically for different classes of Michael acceptors remains relatively small. A goal of this work was to include the synthetically important *trans*-β-nitrostyrenes (Chapter 2) and aliphatic nitroolefins (Chapter 3) into our reactivity scale, by measuring the rates of their reactions with stabilized carbanions.

The reactions of (*E*)-1-ethoxy-2-nitroethene with pyridinium ylides, and of (*E*)-*N*,*N*-dimethyl-2-nitroethenamine with stabilized carbanions will be discussed in Chapter 4.

Considerable effort has been spent on the development of organocatalytic asymmetric Michael additions. The reactions of nitrostyrenes with ketones or aldehydes have been used as model reactions for probing the efficiency and selectivity of new organocatalysts. The kinetic of the reaction of *trans*-β-nitrostyrene with cyclohexanone catalyzed by pyrrolidine and benzoic acid has been investigated, and the individual rate orders have been determined in order to provide insight into the catalytic cycle (Chapter 5).

Diazo compounds are common and versatile reagents in organic synthesis despite their hazardous nature. Therefore, the rates of reactions of diazo compounds with Michael acceptors (Chapter 6) have been studied in order to elucidate the degree of concertedness of these 1,3-dipolar cycloadditions, and to investigate if they can be described by eq 1.3.

1.3 References

[1] Ingold, C. K. *Chem. Rev.* **1934**, *15*, 225–274.

[2] Swain, C. G.; Scott, C. B. *J. Am. Chem. Soc.* **1953**, *75*, 141–147.

[3] Ritchie, C. D. *Acc. Chem. Res.* **1972**, *5*, 348–354.

[4] Ritchie; C. *Can. J. Chem.* **1986,** *64*, 2239–2250.

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[6] Mayr, H.; Bug, T.; Gotta, M. F.; Hering, N.; Irrgang, B.; Janker, B.; Loos, R.; Ofial, A. R.; Remennikov, G.; Schimmel, H. *J. Am. Chem. Soc.* **2001**, *123*, 9500–9512.

Chapter 2: Electrophilicities of *trans*-*β*-Nitrostyrenes

Ivo Zenz and Herbert Mayr

J. Org. Chem. **2011**, *76*, 9370–9378.

2.1 Introduction

Nitroalkenes **1** are important reagents in organic chemistry. They are readily accessible via Henry reaction of aldehydes or ketones with nitroalkanes, and the nitro group can easily be converted into a large variety of functional groups like the carbonyl, the amino, the hydroxylamino, or the azo group.[1,2] As the nitro group is one of the strongest electron-withdrawing substituents known, nitroalkenes are highly reactive Michael acceptors, and their use as electrophiles in organocatalytic reactions has led to a renaissance of nitroalkene chemistry.[3,4] Recent examples of organocatalytic reactions include highly enantioselective thiourea-catalyzed additions[5,6,7] to indoles[8,9] and *β*-diketones.[10,11] Enamine activation[12,13] in reactions of nitroalkenes with ketones[14,15,16,17] and aldehydes[18,19,20,21,22,23] has also been reported. Highly diastereo- and enantioselective additions of aldehydes to nitrostyrenes have been achieved with as little as 0.1% of a tripeptide catalyst.[23] Furthermore guanidine derivatives and cinchona alkaloids have been employed as catalysts for additions of malonates[24] and *β*-ketoesters[25] to nitroalkenes. Additions of oxindols to nitroalkenes have been performed under conditions of phase transfer catalysis,[26] and tandem cycloadditions of nitroalkenes[27,28] have been applied to the synthesis of natural products.[29]

Kinetics of the reactions of nitroalkenes with benzylamines,[30] sodium alkoxides,[31] and hydroxide anions[32] have been investigated in order to elucidate the mechanism of nucleophilic additions to the electron-deficient double bond of nitroalkenes.[33]

In previous work, we have shown that a large variety of reactions of electrophiles with nucleophiles can be described by eq 2.1, where N and s_N (previously called s) are nucleophile-specific parameters, E is an electrophilicity parameter, and k_2 is the second-order rate constant.[34]

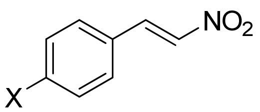
$$\log k_2(20\ °\mathrm{C}) = s_N(N + E) \qquad (2.1)$$

Diarylcarbenium ions have been employed as reference electrophiles for the determination of the nucleophile-specific parameters N and s_N of neutral and anionic nucleophiles.[35]

Furthermore, the kinetics of the reactions of carbanions with Michael acceptors such as quinone methides,[36,37,38] benzylidenemalononitriles,[39] benzylidene-1,3-indandiones,[40] benzylidenebarbituric- and thiobarbituric acids,[41] benzylidene Meldrum´s acids[42] and iminium ions[43] have been employed to determine the E parameters of these electrophiles according to eq 2.1.

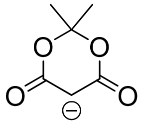
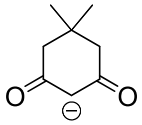
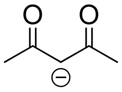
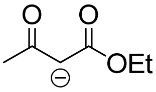
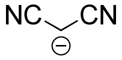
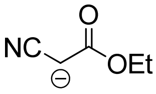
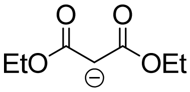
We will now report on the kinetics of the reactions of the *trans*-β-nitrostyrenes **1a**–**f** (Scheme 2.1) with the stabilized carbanions **2a**–**h** (Table 2.1) in DMSO and demonstrate that the second-order rate constants k_2 of these reactions follow eq 2.1. These rate constants will then be used for the determination of the E parameters for *trans*-β-nitrostyrenes **1a**–**f** as part of our program of developing comprehensive nucleophilicity and electrophilicity scales.[44,45,46,47]

SCHEME 2.1. Structures of the *trans*-β-Nitrostyrenes 1a–f.



1a (X = OMe)
1b (X = Me)
1c (X = H)
1d (X = Br)
1e (X = CN)
1f (X = NO_2)

TABLE 2.1. Reactivity Parameters N and s_N of the Carbanions 2a–h in DMSO.

	Nucleophile	N, s_N[a]	pK_{aH} (in DMSO)
2a		13.91, 0.86	7.3[c]
2b		16.27, 0.77	11.2[d]
2c		17.64, 0.73	13.3[d]
2d		18.82, 0.69	14.2[e]
2e		19.36, 0.67	11.1[f]
2f		19.62, 0.67	13.1[g]
2g		20.22, 0.65	16.4[d]
2h	$H_2C{=}NO_2^{\ominus}$	20.71, 0.60[b]	17.2[f]

[a] Ref 38. [b] Ref 36. [c] Ref 48. [d] Ref 49. [e] Ref 50. [f] Ref 51. [g] Ref 52.

2.2 Results

Combination of the *trans*-*β*-nitrostyrenes **1a–f** with equimolar amounts of the potassium salts **2a–K** and **2b–K** in DMSO gave the adducts (**4aa–4fa**)-**K** and (**4ab–4fb**)-**K**, respectively (Scheme 2.2), which were identified by ^{1}H and ^{13}C NMR spectroscopy (Table 2.2). The origin of the adducts can be derived from the formula abbreviations **4xy**: The first letter identifies the electrophile, while the second letter identifies the nucleophile. Thus, compound **4fa** is an adduct from **1f** and **2a**. The higher acidity of Meldrum´s acid (**2a-H**, pK_a^{DMSO} = 7.3)[48] and dimedone (**2b-H**, pK_a^{DMSO} = 11.2)[49] compared with nitromethane (**2h-H**, pK_a^{DMSO} = 17.2)[51] rationalizes, why the initially formed adducts **3** obtained from the nitrostyrenes **1** and **2a-K** or **2b-K**, immediately tautomerize with formation of the carbanions **4**.

SCHEME 2.2. Reactions of the *trans*-*β*-Nitrostyrenes 1a–f with the Carbanions 2a–h.

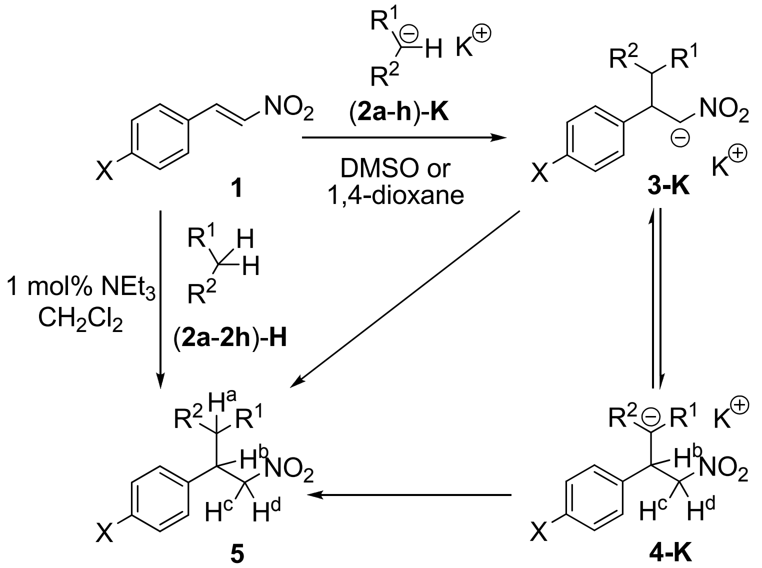


TABLE 2.2. Characteristic ^{1}H and ^{13}C NMR Chemical Shifts of the Michael Adducts 4-K and 5.

Electrophile	Nucleophile	Product	Yield (%)	$\delta(\mathrm{H^a})^f$	$\delta(\mathrm{H^b})^f$	$\delta(\mathrm{H^c}), \delta(\mathrm{H^d})^f$	$\delta(C\text{-}\mathrm{H^b})$
1a	**2a-K**	**4aa-K**	[a]	-	4.53	5.09, 5.08	40.0
1b	**2a-K**	**4ba-K**	[a]	-	4.55	5.10, 5.10	39.8
1c	**2a-K**	**4ca-K**	[a]	-	4.59	5.15, 5.13	40.1
1d	**2a-K**	**4da-K**	[a]	-	4.56	5.15, 5.11	39.6
1e	**2a-K**	**4ea-K**	[a]	-	4.66	5.23, 5.14	40.1
1f	**2a-K**	**4fa-K**	[a]	-	4.72	5.28, 5.17	39.9
1a	**2b-K**	**4ab-K**	[a]	-	4.87	5.38, 4.88	38.6
1b	**2b-K**	**4bb-K**	[a]	-	4.90	5.40, 4.88	38.8
1c	**2b-K**	**4cb-K**	[a]	-	4.95	5.42, 4.93	39.2
1d	**2b-K**	**4db-K**	[a]	-	4.92	5.46, 4.88	38.6
1e	**2b-K**	**4eb-K**	[a]	-	5.04	5.51, 4.94	38.8
1f	**2b-K**	**4fb-K**	[a]	-	5.10	5.59, 4.92	38.8
1a	**2c-H**	**5ac**	79	4.33	4.19	4.59, 4.58	42.2
1b	**2c-H**	**5bc**	71	4.35	4.20	4.60, 4.59	42.6
1c	**2c-H**	**5cc**	71	4.34	4.21	4.61, 4.59	42.9
1d	**2c-H**	**5dc**	63	4.32	4.21	4.61, 4.60	42.3
1e	**2c-H**	**5ec**	38	4.36	4.31	4.66, 4.64	42.7
1f	**2c-H**	**5fc**	50	4.39	4.38	4.69, 4.66	42.4
1c	**2d-H**	**5cd**	55[d]	4.09	4.17	4.72, 4.72	42.4
1c	**2e-K**	**4ce-K**	[a]	-	3.70	4.70, 4.67	43.0
1c	**2f-H**	**5cf**	67[e]	3.93	4.22	5.01, 4.92	42.8
1c	**2g-K**	**5cg**[b]	42	3.79	4.20	4.89, 4.83	43.1
1c	**2h-H**	**5ch**[c]	50	-	4.31	4.78, 4.75	41.8

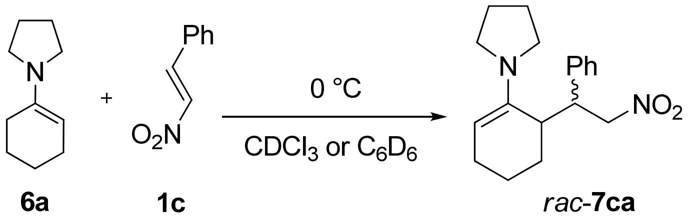
[a] The potassium salts **4-K** were generated in DMSO-d_6 solution and identified *in situ* by ^{1}H and ^{13}C NMR spectroscopy. [b] From **1c** and **2g-K** in 1,4-dioxane and subsequent protonation with aqueous acetic acid (2 mol/L), as reported in ref 54. [c] From **1c** (1.15 mmol) in nitromethane **2h-H** (10 mL) in the presence of NEt_3 (1 mol%), as reported in ref 55. [d] Yield of mixture of diasteromers (dr ~ 8:1). [e] Yield of mixture of diasteromers (dr ~ 1.4:1). [f] Chemical shifts (in ppm) extracted by using DAVINX software (ref 56). Chemical shifts for diastereomeric mixtures refer to the major isomer.

Analogously, **4ce-K** was obtained from *trans*-*β*-nitrostyrene **1c** and **2e-K**, due to the higher acidity of malononitrile (**2e-H**, $pK_a^{DMSO} = 11.1$)[51] relative to nitromethane. The anions **4** show ^{1}H NMR spectra with resonances in the range of δ = 4.7 to 5.6 ppm for the diastereotopic protons H^c and H^d (Table 2.2). Protons H^c and H^d of the products **4aa-K** to **4fa-K** are nearly isochronous (δ = 5.1 to 5.3 ppm) and show similar vicinal coupling constants of J_{bc} = 8.2–9.0 Hz and J_{bd} = 7.5–8.1 Hz. In contrast, the chemical shifts of the protons H^c and H^d of **4ab-K** to **4fb-K** differ by about 0.5 ppm [H^c (δ = 5.4 to 5.6 ppm), H^d ($\delta \approx$ 4.9 ppm)] and the vicinal coupling constants differ by about 3 Hz (J_{bc} = 9.1–9.5 Hz, J_{bd} = 5.9–6.3 Hz).

The Michael adducts **5ac–5fc**, which were obtained in 38–79% isolated yields from **1a–f** and two equivalents of pentane-2,4-dione **2c-H** in CH_2Cl_2 in the presence of NEt_3 (1 mol%) following a report by Brunner and Kimel[53] (Table 2.2), showed ^{1}H NMR spectra with resonances in the range of δ = 4.3 to 4.4 ppm for H^a, δ = 4.2 to 4.4 ppm for H^b, and δ = 4.6 to 4.7 ppm for H^c and H^d.

The reaction of *trans*-*β*-nitrostyrene (**1c**) with enamine **6a** in $CDCl_3$ and C_6D_6 solution gave *rac*-**7ca** with a vinylic proton at δ = 4.54 (t, J = 3.9 Hz). Though unidentified impurities were detected in the NMR spectra, the ^{1}H NMR signals from δ = 3.6–5.1 ppm indicated the formation of a single diastereomer. The intermediate formation of cyclobutanes[57,58,59] could not be observed.

SCHEME 2.3. Reaction of *trans*-*β*-Nitrostyrene (1c) with 1-Pyrrolidinocyclohexene (6a).



The kinetic investigations were performed at 20 °C in DMSO as the solvent. The carbanions **2a**–**h** were either used as preformed potassium salts (CAUTION: **2h**-**K** must not be isolated as it is known to be explosive) or generated in the solutions used for the kinetic investigations by treatment of the corresponding CH-acids with 1.05 equiv. of potassium *tert*-butoxide, which is sufficient for the complete deprotonation of the CH-acids.[42] The rates of the consumptions of the *trans*-*β*-nitrostyrenes **1a**–**d** (λ_{max} = 310–363 nm) were generally followed photometrically at their absorption maxima. Due to an overlap of the absorption bands, the rates of the reactions with the carbanions **2f** and **2h** were followed at the shoulders of the absorption bands of the electrophiles **1a**–**f**. Measurements at the shoulders of the absorption bands of the *trans*-*β*-nitrostyrenes **1e** and **1f** were also performed to determine the kinetics of their reactions with the carbanions **2a**–**d**. In these cases, the absorbances at the monitored wavelengths did not reach zero at the end of the reactions. Only partial conversion was observed for the reactions of **1a**–**d** with the carbanion **2e**; the corresponding equilibrium constants could not be determined, however, because of unknown subsequent reactions.

Only the reactions of **1a**–**d** with the carbanion **2a** were slow enough to be studied by conventional UV-vis spectroscopy ($\tau_{1/2}$ > 30 s); in all other cases the stopped-flow technique was employed. By using a high excess of the carbanions **2** (10–50 equiv.), pseudo-first-order conditions were achieved (eq 2.2). In all cases, we observed monoexponential decays of the absorbances of the nitrostyrenes **1a**–**f**.

$$-d[\mathbf{1}]/dt = k_{obs}[\mathbf{1}] \tag{2.2}$$

The first-order rate constants k_{obs} were obtained by least-squares fitting of the time-dependent absorbances A_t of the electrophiles to the exponential function $A_t = A_0\ e^{-k_{obs}t} + C$. As shown in Figure 2.1 for the reaction of **1a** with **2a**, plots of k_{obs} versus the concentrations of the carbanions [**2**] were linear with almost zero intercepts. According to the relation $k_2 = k_{obs}/[\mathbf{2}]$, the slopes of these correlations gave the second-order rate constants k_2 listed in Table 2.3.

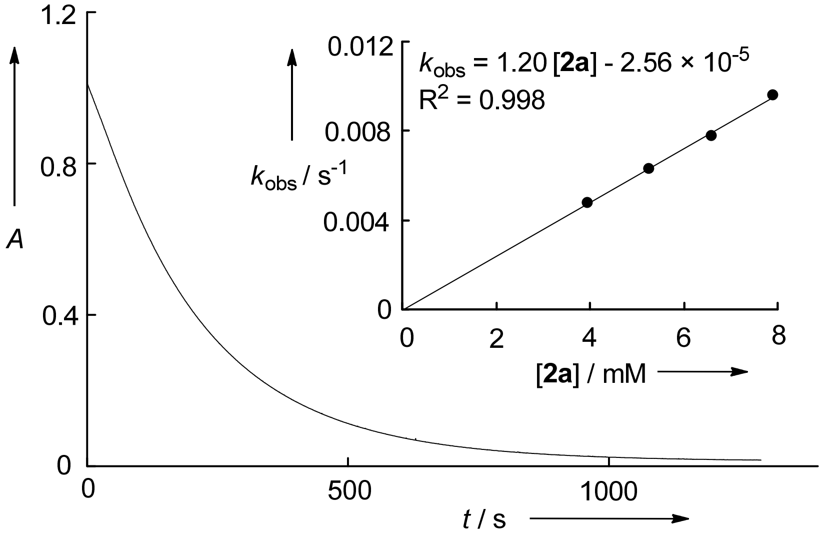


FIGURE 2.1. Exponential Decay of Absorbance (*A* at *λ* = 363 nm) for the Reaction of 1a ($c = 1.06 \times 10^{-4}$ M) with 2a ($c = 3.95 \times 10^{-3}$ M) in DMSO at 20 °C. Insert: Correlation of the pseudo-first-order Rate Constants k_{obs} *vs.* [2a]

TABLE 2.3. Second-Order Rate Constants k_2 for the Reactions of Carbanions 2a–h with *trans*-*β*-Nitrostyrenes 1a–f in DMSO at 20 °C.

1	E^a	2	k_2^{exp} (M^{-1} s^{-1})	k_2^{calcd} (M^{-1} s^{-1})	log (k_2^{exp}/k_2^{calcd})
1a	–14.70	**2a**	1.20 ± 0.04	2.09×10^{-1}	0.76
1a		**2b**	$(2.02 \pm 0.04) \times 10^{1}$	1.61×10^{1}	0.10
1a		**2c**	$(1.49 \pm 0.05) \times 10^{2}$	1.40×10^{2}	0.03
1a		**2d**	$(4.5 \pm 0.1) \times 10^{2}$	7.0×10^{2}	–0.20
1a		**2e**	$(9.8 \pm 0.4) \times 10^{2}$	1.3×10^{3}	–0.13
1a		**2f**	$(1.26 \pm 0.01) \times 10^{3}$	1.98×10^{3}	–0.19
1a		**2g**	$(1.00 \pm 0.02) \times 10^{3}$	3.87×10^{3}	–0.59
1a		**2h**	$(3.7 \pm 0.2) \times 10^{3}$	4.0×10^{3}	–0.03

TABLE 2.3. (Continued).

1b	–14.23	**2a**	2.35 ± 0.04	5.32×10^{-1}	0.65
1b		**2b**	$(4.7 \pm 0.1) \times 10^{1}$	3.7×10^{1}	0.10
1b		**2c**	$(3.01 \pm 0.02) \times 10^{2}$	3.09×10^{2}	–0.01
1b		**2d**	$(1.25 \pm 0.04) \times 10^{3}$	1.47×10^{3}	–0.07
1b		**2e**	$(1.71 \pm 0.09) \times 10^{3}$	2.74×10^{3}	–0.20
1b		**2f**	$(2.77 \pm 0.04) \times 10^{3}$	4.09×10^{3}	–0.17
1b		**2g**	$(2.09 \pm 0.06) \times 10^{3}$	7.84×10^{3}	–0.57
1b		**2h**	$(9.6 \pm 0.3) \times 10^{3}$	7.7×10^{3}	0.09
1c	–13.85	**2a**	4.7 ± 0.2	1.1	0.62
1c		**2b**	$(9.2 \pm 0.4) \times 10^{1}$	7.3×10^{1}	0.10
1c		**2c**	$(4.87 \pm 0.05) \times 10^{2}$	5.80×10^{2}	–0.08
1c		**2d**	$(2.09 \pm 0.08) \times 10^{3}$	2.67×10^{3}	–0.11
1c		**2e**	$(2.76 \pm 0.02) \times 10^{3}$	4.89×10^{3}	–0.25
1c		**2f**	$(6.02 \pm 0.05) \times 10^{3}$	7.30×10^{3}	–0.08
1c		**2g**	$(3.4 \pm 0.2) \times 10^{3}$	1.4×10^{4}	–0.61
1c		**2h**	$(2.11 \pm 0.07) \times 10^{4}$	1.30×10^{4}	0.21
1d	–13.37	**2a**	8.2 ± 0.3	2.9	0.45
1d		**2b**	$(1.46 \pm 0.01) \times 10^{2}$	1.70×10^{2}	–0.07
1d		**2c**	$(1.32 \pm 0.009) \times 10^{3}$	1.30×10^{3}	0.01
1d		**2d**	$(4.58 \pm 0.08) \times 10^{3}$	5.72×10^{3}	–0.10
1d		**2e**	$(7.1 \pm 0.5) \times 10^{3}$	1.0×10^{4}	–0.16
1d		**2f**	$(1.23 \pm 0.02) \times 10^{4}$	1.53×10^{4}	–0.09
1d		**2g**	$(1.18 \pm 0.06) \times 10^{4}$	2.82×10^{4}	–0.38
1d		**2h**	$(4.3 \pm 0.3) \times 10^{4}$	2.5×10^{4}	0.23
1e	–12.61	**2a**	$(2.32 \pm 0.04) \times 10^{1}$	1.32×10^{1}	0.24
1e		**2b**	$(4.5 \pm 0.2) \times 10^{2}$	6.6×10^{2}	–0.17
1e		**2c**	$(3.74 \pm 0.08) \times 10^{3}$	4.73×10^{3}	–0.10
1e		**2d**	$(1.9 \pm 0.1) \times 10^{4}$	1.9×10^{4}	–0.01
1f	–12.37	**2a**	$(3.23 \pm 0.04) \times 10^{1}$	2.10×10^{1}	0.19
1f		**2b**	$(7.1 \pm 0.3) \times 10^{2}$	1.0×10^{3}	–0.15
1f		**2c**	$(5.5 \pm 0.2) \times 10^{3}$	7.0×10^{3}	–0.11
1f		**2d**	$(3.1 \pm 0.1) \times 10^{4}$	2.8×10^{4}	0.04

[a] The E parameters for **1a–f** result from a least-squares minimization of the sum of Δ^2, with $\Delta = \log k_2^{\mathrm{exp}} - s_{\mathrm{N}}(N + E)$; k_2^{exp} taken from this table, N and s_{N} of the carbanions **2a–h** from Table 2.1.

2.3 Discussion

The rate constants k_2 listed in Table 2.3 reveal that the reactivity order of the carbanions **2a–h** toward nitrostyrenes is generally the same as toward benzhydrylium ions and quinone methides, the reference electrophiles of our scales. Slight deviations from this order will be discussed below.

Substitution of the rate constants k_2 (Table 2.3) and the previously published N and s_N parameters of the carbanions (Table 2.1) into eq 2.1 allows one to calculate the electrophilicity parameters E for the *trans*-*β*-nitrostyrenes **1a–f**. The values of E, which are listed in Table 2.3, were obtained by minimizing the sum of Δ^2, i.e., the squares of the deviations between experimental and calculated rate constants, $\Delta = (\log k_2^{\text{exp}}) - s_N(N + E)$.

The correlations in Figure 2.2 show that the rate constants for the reactions of **1a–f** with the carbanions **2b–f** are fairly reproduced by eq 2.1, i.e., the experimental points are close to the calculated correlation lines. Some systematic deviations are obvious, however. Thus, the anion of Meldrum´s acid **2a** reacts faster than predicted by eq 2.1 with all nitrostyrenes, particularly with the less reactive nitrostyrenes **1a–d**. Furthermore, the malonate anion **2g** reacts more slowly, and the nitromethyl anion **2h** reacts faster with the nitrostyrenes **1b–d** than expected from the benzhydrylium-derived reactivity parameters N and s_N of these nucleophiles. While the origin of these deviations is not known, it should be noted, that analogous deviations have also been observed for the reactions of these carbanions with benzylidene Meldrum´s acids[42] and benzylidene dimethylbarbituric- and thiobarbituric acids.[41] The last column of Table 2.3 quantifies these deviations and shows that the absolute value of log $(k_2^{\text{exp}}/k_2^{\text{calcd}})$ is always smaller than 0.76, corresponding to a maximum deviation between calculated and experimental rate constants of a factor of 6, which we consider tolerable for a model covering a reactivity range of almost 40 orders of magnitude with only 3 parameters.

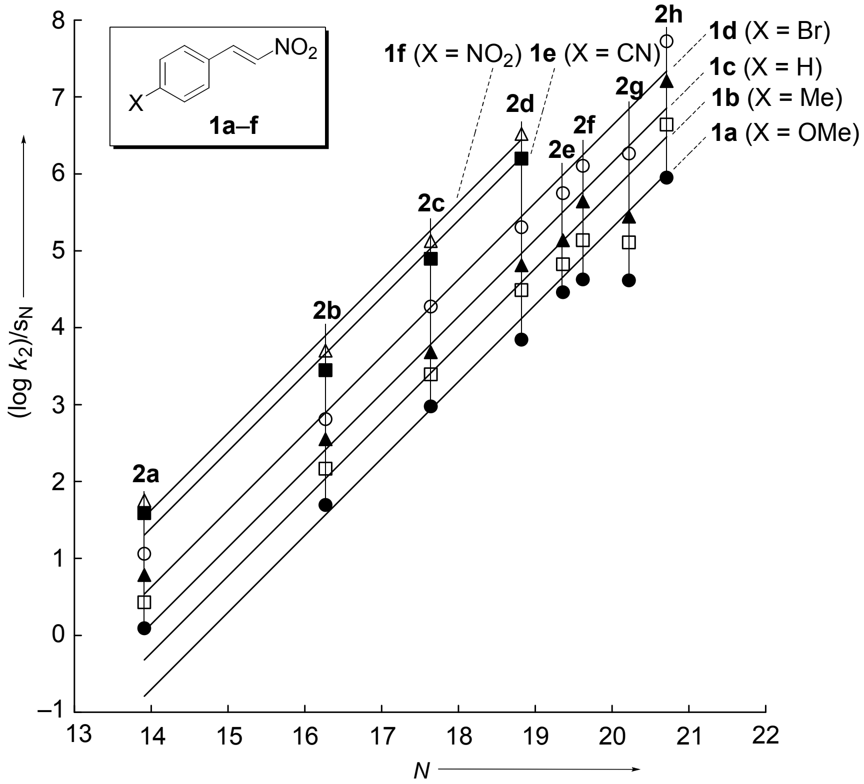


FIGURE 2.2. Correlation of (log k_2)/s_N versus the Nucleophilicity Parameters *N* of the Carbanions 2a–h for their Reactions with the *trans*-*β*-Nitrostyrenes 1a–f in DMSO at 20 °C. Correlation Lines are Fixed at a Slope of 1.0, as Required by Eq 2.1.

The nucleophilic reactivities of most carbanions are reduced in protic solvents, and the reactivity parameters of stabilized carbanions have been determined in several solvents.[60,61,62] Table 2.4 shows that also the rate constants for the reactions of **1b** with **2e** and **2f** in methanol are almost perfectly (within a factor of 2.1) reproduced by eq 2.1.

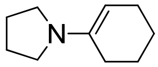
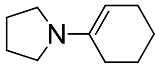
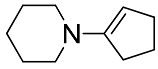
TABLE 2.4. Comparison of Measured and Calculated Second-Order Rate Constants k_2 for the Reactions of the Carbanions 2e and 2f with *trans*-4-Methyl-*β*-nitrostyrene (1b) in Methanol at 20 °C.

Nucleophile	N, s_N[a]	k_2^{exp} (M^{-1} s^{-1})	k_2^{calcd} (M^{-1} s^{-1})
2e (Malononitrile-Na)	18.21, 0.69	384 ± 15	557
2f (Ethyl cyanoacetate-Na)	18.59, 0.65	322 ± 8	682

[a] Reactivity parameters N and s_N for carbanions in methanol from ref 60.

In order to check the applicability of the electrophilicity parameters E of the *trans*-*β*-nitrostyrenes **1** for the prediction of the rates of their reactions with other types of nucleophiles, we measured the rates of the reactions of the *trans*-*β*-nitrostyrenes **1b** and **1c** with the enamines **6a** and **6b** in dichloromethane. We then compared these measured rate constants with those calculated by eq 2.1, from the previously published parameters N and s_N for these enamines[63] and the E parameters of the *trans*-*β*-nitrostyrenes **1** listed in Table 2.3. Table 2.5 shows that also in these cases the deviations between calculated and experimental rate constants are around a factor of 2 or less, despite the fact that the E values for **1b** and **1c** were determined in DMSO.

TABLE 2.5. Comparison of Measured and Calculated Second-Order Rate Constants k_2 for the Reactions of the Enamines 6a and 6b with Electrophiles 1b and 1c in Dichloromethane at 20 °C.

	Enamine	N, s_N[a]	*β*-Nitrostyrene	k_2^{exp} (M^{-1} s^{-1})	k_2^{calcd} (M^{-1} s^{-1})
6a		14.91, 0.86	**1b**	3.1 ± 0.1	3.8
6a		14.91, 0.86	**1c**	7.1 ± 0.3	8.2
6b		15.06, 0.82	**1c**	21.1 ± 0.7	9.82

[a] Reactivity parameters N and s_N from ref 63.

Table 2.6 shows that also the rate constants for the reactions of piperidine and morpholine with β-nitrostyrenes calculated by eq 2.1 agree within a factor of 3 to 20 with those previously measured by Bernasconi in aqueous solution of ion strength $\mu = 0.5$ M.[64] As the electrophilicity parameters of the nitrostyrenes determined in DMSO were used for these calculations, the fair agreement between experimental and calculated numbers again confirms that the use of solvent-independent electrophilicity parameters is justified in many cases, because solvent effects are considered in the nucleophile-specific parameters N and s_N.[65]

TABLE 2.6. Comparison of Measured[a] and Calculated Rate Constants k_2 for the Reactions of β-Nitrostyrenes 1a,c–f with Secondary Amines in Water at 20 °C.

Amine (N, s_N)[b]	β-Nitrostyrene	k_2^{exp} (M^{-1} s^{-1})	k_2^{calcd} (M^{-1} s^{-1})
Piperidine (18.13, 0.44)	**1a**	622	32.3
	1c	661	76.4
	1d	796	124
	1e	989	268
	1f	1100	342
Morpholine (15.62, 0.54)	**1c**	137	9.03

[a] Experimental second-order rate constants k_2^{exp} from ref 64. [b] Reactivity parameters N and s_N from ref 66.

The Hammett plot in Figure 2.3 shows a good correlation between the electrophilicity parameters E of the *trans*-β-nitrostyrenes **1** and the Hammett σ_p values for the para-substituents.[67] One can see that the reactivities of the *trans*-β-nitrostyrenes **1** are affected more by the variation of the *para*-substituents than the reactivities of the aryl-substituted quinone methides **8**, but less than the reactivities of the arylidenemalonates **9**. Multiplication of the slopes of these correlations (1.79 to 3.45, Figure 2.3) with the s_N values of the nucleophilic reaction partners yield the Hammett reaction constants ρ.

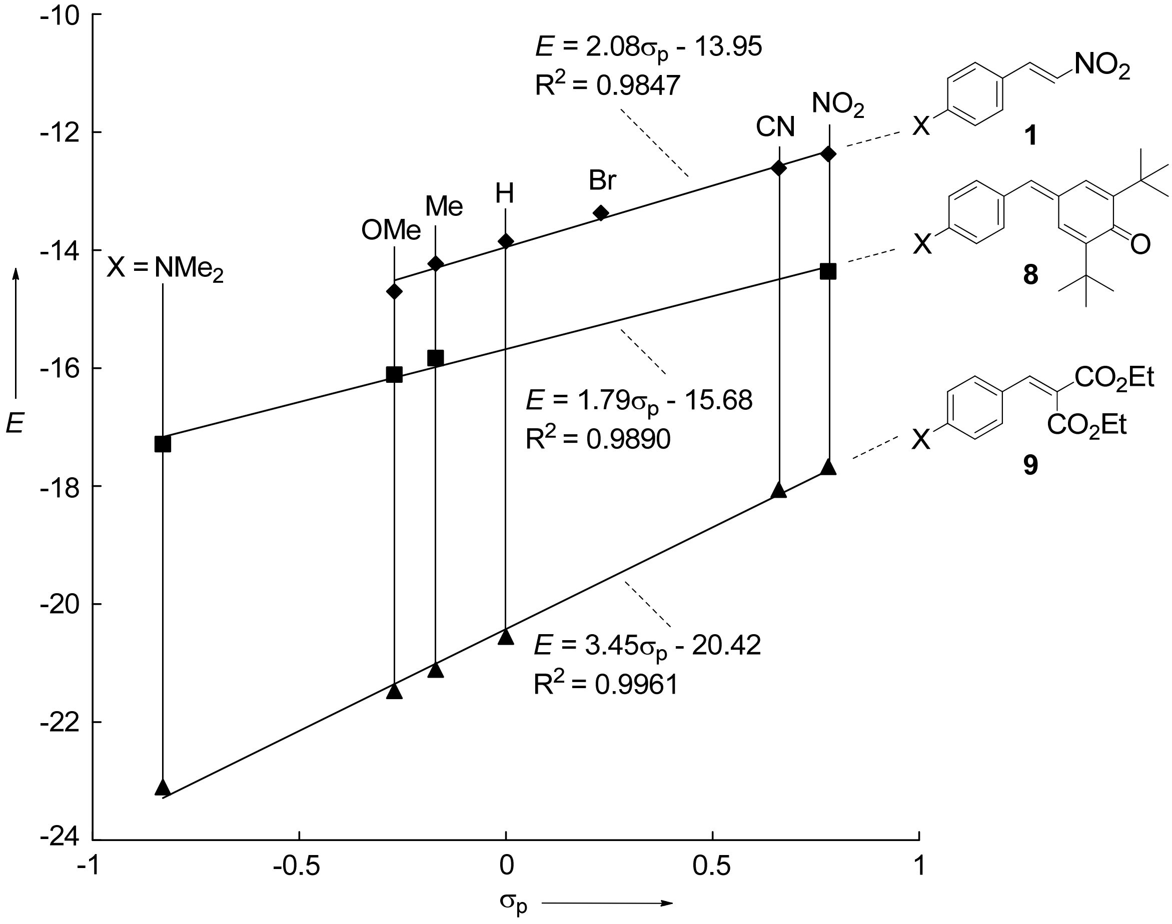


FIGURE 2.3. Correlations of the Electrophilicity Parameters *E* of 1, 8 (from ref 37) and 9 (from ref 68) with Hammett´s σ_p Values (from ref 67).

2.4 Conclusion

The reactivities of the *trans*-β-nitrostyrenes **1** toward nucleophiles can be described by eq 2.1; the experimental rate constants of the reactions of **1** with carbanions in DMSO and in methanol as well as with enamines in dichloromethane and with secondary amines in water agree within one order of magnitude with the rate constants calculated by eq 2.1. As illustrated in Figure 2.4, the β-nitrostyrenes **1** are considerably more electrophilic than substituted benzylidenemalonates and less electrophilic than analogously substituted benzylidenemalononitriles. The fairly good correlation between E and Hammett´s σ_p values (Figure 2.3) allows one to estimate the electrophilicity parameter E for almost any *trans*-β-nitrostyrene, which can be combined with the numerous published N and s_N parameters of nucleophiles[69] to predict scope and limitations of nucleophilic additions to *trans*-β-nitrostyrenes on the basis of eq 2.1.

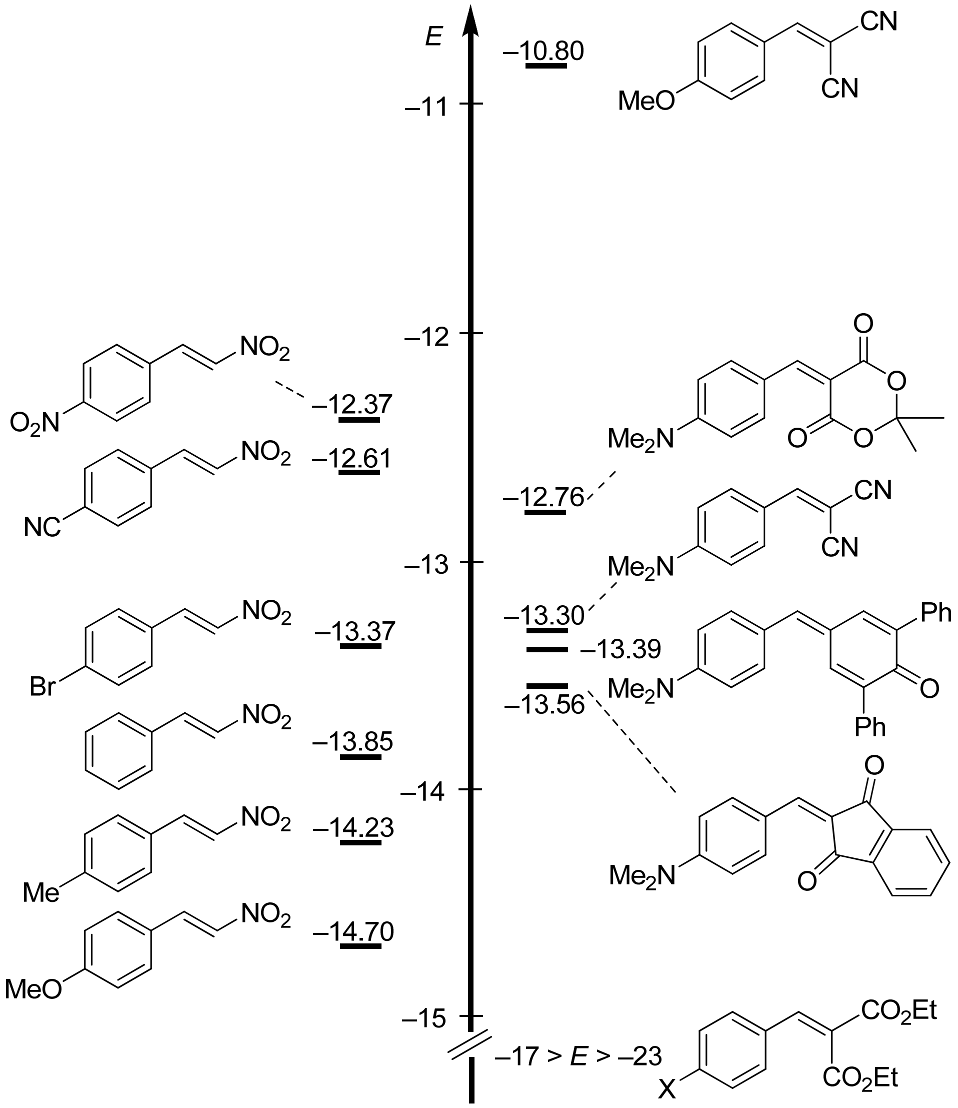


FIGURE 2.4. Comparison of *E* Values for Differently Substituted Michael Acceptors and Quinone Methides.[69]

2.5 Experimental Section

2.5.1 Products

Commercially available DMSO (with < 50 ppm H_2O content), MeOH (HPLC grade), EtOH (> 99.5%, anhydrous) and triethylamine (pure, < 0.5% H_2O content) were used without further purification. Dichloromethane was freshly distilled over CaH_2. *n*-Pentane was freshly distilled over sodium. All reactions were performed under an atmosphere of dry nitrogen. Compounds **1a–d** were purchased and purified by recrystallization from ethanol. The cyano- and nitro-substituted *β*-nitrostyrenes **1e** and **1f** were synthesized by Henry reactions.[2] The ^1H and ^{13}C NMR chemical shifts are given in ppm and refer to DMSO-d_6 (δ_H = 2.50 ppm, δ_C = 39.52 ppm) or to $CDCl_3$ (δ_H = 7.26 ppm, δ_C = 77.16 ppm) as internal standards.[70] The chemical shifts given in brackets are extracted from product spectra using DAVINX software.[56] NMR signal assignments in Table 2.2 are based on additional 2D-NMR experiments (COSY, HSQC). Diastereomeric ratios were determined by ^1H NMR spectroscopy.

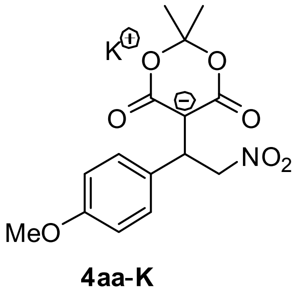
Preparation of potassium salts **2-K**:

The potassium salts (**2a–g**)-**K** were generated by mixing solutions of KOEt in dry EtOH with a solution of the corresponding CH-acids (**2a–g**)-**H** in dry EtOH under nitrogen atmosphere. To precipitate the product, dry *n*-pentane was added. The precipitates were filtered and dried in vacuo (40 °C/5×10^{-3} mbar) to obtain (**2a–g**)-**K** as colorless solids. (CAUTION: Neat **2h-K** must not be isolated as it is known to be explosive).

General procedure A: The nitrostyrenes **1** (0.090 mmol) and the potassium salts of carbanions **2** (0.090 mmol) were dissolved in dry DMSO-d_6 (0.7 mL) in a NMR tube and shaken vigorously. The resulting solutions of the addition products were directly characterized by ^{1}H and ^{13}C NMR spectroscopy.

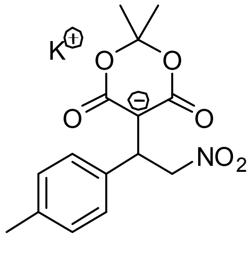
General procedure B: The nitrostyrenes **1** and the CH-acids **2-H** (2 equiv.) were dissolved in dry dichloromethane (5 mL) under nitrogen atmosphere. After addition of triethylamine (1 mol%), the mixture was stirred for 24 h at ambient temperature. Then the solvent was removed under reduced pressure. The crude products were recrystallized from ethanol.

2.5.1.1 Reactions of Potassium 2,2-dimethyl-4,6-dioxo-1,3-dioxan-5-ide (2a-K) with the *trans-β*-Nitrostyrenes 1



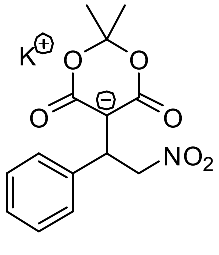
4aa-K

Potassium 5-(1-(4-methoxyphenyl)-2-nitroethyl)-2,2-dimethyl-4,6-dioxo-1,3-dioxan-5-ide (**4aa-K**). From **1a** and **2a-K** by following general procedure A. ^{1}H NMR (400 MHz, DMSO-d_6): δ (ppm) = 1.39 (s, 6 H), 3.69 (s, 3 H), [ABC-system at δ = 4.53 (J = 7.5, 9.0 Hz), 5.08 (J = –11.3, 7.5 Hz), 5.09 (J = –11.3, 9.0 Hz)], 6.73–6.77 (m, 2 H), 7.25–7.29 (m, 2 H). ^{13}C NMR (100 MHz, DMSO-d_6): δ (ppm) = 25.8, 40.0, 54.9, 72.9, 79.0, 99.2, 113.0, 128.6, 135.8, 157.3, 164.7.



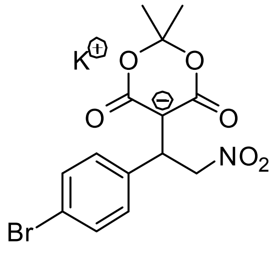
4ba-K

Potassium 2,2-dimethyl-5-(2-nitro-1-p-tolylethyl)-4,6-dioxo-1,3-dioxan-5-ide (**4ba-K**). From **1b** and **2a-K** by following general procedure A. ^{1}H NMR (400 MHz, DMSO-d_6): δ (ppm) = 1.38 (s, 6 H), 2.22 (s, 3 H), [ABC-system at δ = 4.55 (J = 8.0, 8.4 Hz), 5.10 (J = –13.0, 8.4 Hz), 5.10 (J = –13.0, 8.0 Hz)], 6.98–7.00 (m, 2 H), 7.22–7.24 (m, 2 H). ^{13}C NMR (100 MHz, DMSO-d_6): δ (ppm) = 20.6, 25.8, 39.8, 72.8, 78.8, 99.2, 127.5, 128.1, 134.3, 140.7, 164.7.



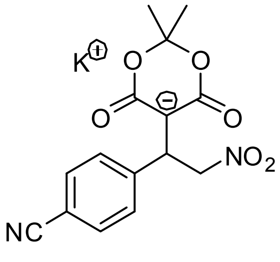
4ca-K

Potassium 2,2-dimethyl-5-(2-nitro-1-phenylethyl)-4,6-dioxo-1,3-dioxan-5-ide (**4ca-K**). From **1c** and **2a-K** by following general procedure A. ^{1}H NMR (400 MHz, DMSO-d_6): δ (ppm) = 1.39 (s, 6 H), [ABC-system at δ = 4.59 (J = 8.1, 8.2 Hz), 5.13 (J = –12.4, 8.1 Hz), 5.15 (J = –12.4, 8.2 Hz)], 7.08–7.11 (m, 1 H), 7.17–7.21 (m, 2 H), 7.34–7.36 (m, 2 H). ^{13}C NMR (100 MHz, DMSO-d_6): δ (ppm) = 25.8, 40.1, 72.7, 78.6, 99.2, 125.5, 127.57, 127.59, 143.7, 164.7.



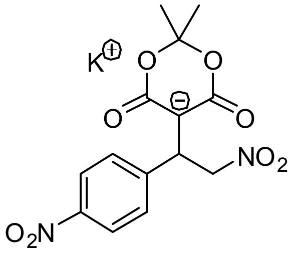
4da-K

Potassium 5-(1-(4-bromophenyl)-2-nitroethyl)-2,2-dimethyl-4,6-dioxo-1,3-dioxan-5-ide (**4da-K**). From **1d** and **2a-K** by following general procedure A. ^{1}H NMR (400 MHz, DMSO-d_6): δ (ppm) = 1.39 (s, 6 H), [ABC-system at δ = 4.56 (J = 7.9, 8.4 Hz), 5.11 (J = –12.1, 7.9 Hz), 5.15 (J = –12.1, 8.4 Hz)], 7.30–7.32 (m, 2 H), 7.37–7.39 (m, 2 H). ^{13}C NMR (100 MHz, DMSO-d_6): δ (ppm) = 25.7, 39.6, 72.5, 78.2, 99.4, 118.5, 129.8, 130.4, 143.1, 164.6.



4ea-K

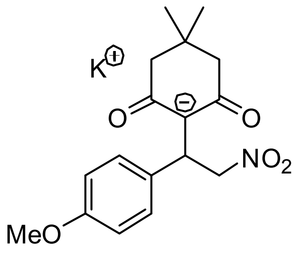
Potassium 5-(1-(4-cyanophenyl)-2-nitroethyl)-2,2-dimethyl-4,6-dioxo-1,3-dioxan-5-ide (**4ea-K**). From **1e** and **2a-K** by following general procedure A. ^{1}H NMR (400 MHz, DMSO-d_6): δ (ppm) = 1.38 (s, 6 H), [ABC-system at δ = 4.66 (J = 7.8, 8.4 Hz), 5.14 (J = –12.4, 7.8, Hz), 5.23 (J = –12.4, 8.4 Hz)], 7.52–7.54 (m, 2 H), 7.66–7.68 (m, 2 H). ^{13}C NMR (100 MHz, DMSO-d_6): δ (ppm) = 25.7, 40.1, 72.3, 77.6, 100.0, 108.3, 119.1, 128.4, 131.6, 149.5, 164.5.



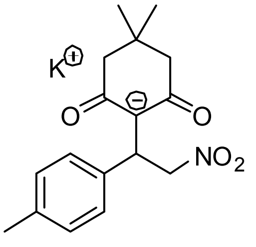
4fa-K

Potassium 2,2-dimethyl-5-(2-nitro-1-(4-nitrophenyl)ethyl)-4,6-dioxo-1,3-dioxan-5-ide (**4fa-K**). From **1f** and **2a-K** by following general procedure A. ^{1}H NMR (400 MHz, DMSO-d_6): δ (ppm) = 1.39 (s, 6 H), [ABC-system at δ = 4.72 (J = 7.7, 8.5 Hz), 5.17 (J = –12.6, 7.7 Hz), 5.28 (J = –12.6, 8.5 Hz)], 7.59–7.62 (m, 2 H), 8.08–8.10 (m, 2 H). ^{13}C NMR (100 MHz, DMSO-d_6): δ (ppm) = 25.7, 39.9, 72.3, 77.5, 99.5, 122.9, 128.5, 145.5, 151.7, 164.5.

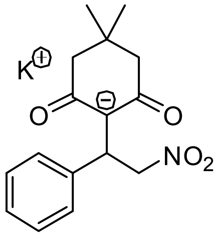
2.5.1.2 Reactions of Potassium 4,4-dimethyl-2,6-dioxocyclohexan-1-ide (2b-K) with the ***trans*-*β***-Nitrostyrenes 1


4ab-K

Potassium 1-(1-(4-methoxyphenyl)-2-nitroethyl)-4,4-dimethyl-2,6-dioxocyclohexan-1-ide (**4ab-K**). From **1a** and **2b-K** by following general procedure A. ^{1}H NMR (400 MHz, DMSO-d_6): δ (ppm) = 0.86 (s, 6 H), 1.85 (s, 4 H), 3.66 (s, 3 H), [ABC-system at δ = 4.87 (J = 6.3, 9.4 Hz), 4.88 (J = –12.0, 6.3 Hz), 5.38 (J = –12.0, 9.4 Hz)], 6.66–6.69 (m, 2 H), 7.24–7.27 (m, 2 H). ^{13}C NMR (100 MHz, DMSO-d_6): δ (ppm) = 28.9, 31.2, 38.6, 51.0, 80.2, 107.5, 112.6, 128.9, 137.0, 156.8, 187.3.

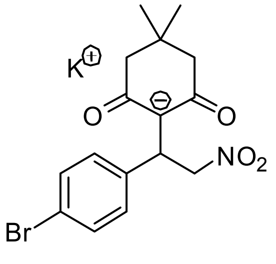

4bb-K

Potassium 4,4-dimethyl-1-(2-nitro-1-p-tolylethyl)-2,6-dioxocyclohexan-1-ide (**4bb-K**). From **1b** and **2b-K** by following general procedure A. ^{1}H NMR (400 MHz, DMSO-d_6): δ (ppm) = 0.86 (s, 6 H), 1.85 (s, 4 H), 2.19 (s, 3 H), [ABC-system at δ = 4.88 (J = –12.0, 6.3 Hz), 4.90 (J = 6.3, 9.3 Hz), 5.40 (J = –12.0, 9.3 Hz)], 6.90–6.92 (m, 2 H), 7.20–7.22 (m, 2 H). ^{13}C NMR (100 MHz, DMSO-d_6): δ (ppm) = 20.6, 28.9, 31.2, 38.8, 51.0, 79.9, 107.5, 127.79, 127.84, 133.5, 141.8, 187.3.


4cb-K

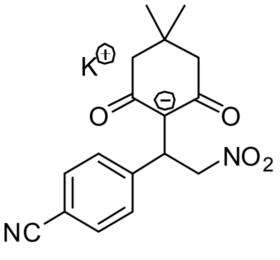
Potassium 4,4-dimethyl-1-(2-nitro-1-phenylethyl)-2,6-dioxocyclohexan-1-ide (**4cb-K**). From **1c** and **2b-K** by following general procedure A. ^{1}H NMR (400 MHz, DMSO-d_6): δ (ppm) = 0.86 (s, 6 H), 1.86 (s, 4 H), [ABC-system at δ = 4.93 (J = –12.1, 6.3 Hz), 4.95 (J = 6.3, 9.1 Hz), 5.42

(J = –12.1, 9.1 Hz)], 7.00–7.04 (m, 1 H), 7.09–7.13 (m, 2 H), 7.33–7.35 (m, 2 H). ^{13}C NMR (100 MHz, DMSO-d_6): δ (ppm) = 28.9, 31.2, 39.2, 51.0, 79.7, 107.3, 124.9, 127.2, 127.9, 144.9, 187.4.



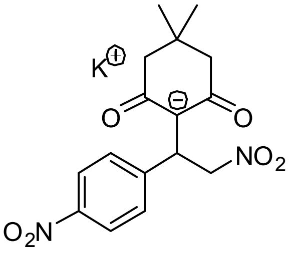
4db-K

Potassium 1-(1-(4-bromophenyl)-2-nitroethyl)-4,4-dimethyl-2,6-dioxocyclohexan-1-ide (**4db-K**). From **1d** and **2b-K** by following general procedure A. ^{1}H NMR (400 MHz, DMSO-d_6): δ (ppm) = 0.85 (s, 6 H), 1.86 (s, 4 H), [ABC-system at δ = 4.88 (J = –12.4, 6.1 Hz), 4.92 (J = 6.1, 9.5 Hz), 5.46 (J = –12.4, 9.5 Hz)], 7.30 (s, 4 H). ^{13}C NMR (100 MHz, DMSO-d_6): δ (ppm) = 28.8, 31.2, 38.6, 50.8, 79.2, 107.0, 117.8, 130.0, 130.1, 144.3, 187.3.



4eb-K

Potassium 1-(1-(4-cyanophenyl)-2-nitroethyl)-4,4-dimethyl-2,6-dioxocyclohexan-1-ide (**4eb-K**). From **1e** and **2b-K** by following general procedure A. ^{1}H NMR (400 MHz, DMSO-d_6): δ (ppm) = 0.85 (s, 6 H), 1.89 (s, 4 H), [ABC-system at δ = 4.94 (J = –12.7, 6.3 Hz), 5.04 (J = 6.3, 9.3 Hz), 5.51 (J = –12.7, 9.3 Hz)], 7.49–7.51 (m, 2 H), 7.59–7.61 (m, 2 H). ^{13}C NMR (100 MHz, DMSO-d_6): δ (ppm) = 28.6, 31.3, 38.8, 50.2, 78.2, 107.1, 107.7, 119.2, 128.5, 131.4, 150.3, 187.2.

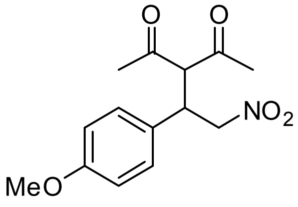


4fb-K

Potassium 4,4-dimethyl-1-(2-nitro-1-(4-nitrophenyl)ethyl)-2,6-dioxocyclohexan-1-ide (**4fb-K**). From **1f** and **2b-K** by following general procedure A. ^{1}H NMR (400 MHz, DMSO-d_6): δ (ppm) = 0.84 (s, 6 H), 1.87 (s, 4 H), [ABC-system at δ = 4.92 (J = –12.8, 5.9

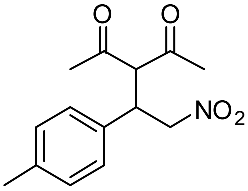
Hz), 5.10 (J = 5.9, 9.5 Hz), 5.59 (J = –12.8, 9.5 Hz)], 7.57–7.59 (m, 2 H), 8.01–8.04 (m, 2 H). ^{13}C NMR (100 MHz, DMSO-d_6): δ (ppm) = 28.7, 31.2, 38.8, 50.5, 78.2, 106.7, 122.6, 128.5, 145.0, 153.0, 187.4.

2.5.1.3 Reactions of Pentane-2,4-dione (2c-H) with the *trans*-*β*-Nitrostyrenes 1



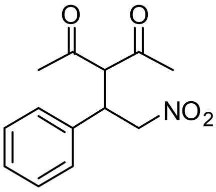
5ac

3-(1-(4-Methoxyphenyl)-2-nitroethyl)pentane-2,4-dione (**5ac**). Obtained from **1a** (129 mg, 0.720 mmol) and **2c-H** following general procedure B: 158 mg (0.566 mmol, 79%), yellow solid, mp 115–117 °C. ^{1}H NMR (300 MHz, CDCl$_3$): δ (ppm) = 1.94 (s, 3 H), 2.28 (s, 3 H), 3.77 (s, 3 H), [ABCD-system at δ = 4.19 (J = 4.5, 8.3, 11.0 Hz), 4.33 (J = 11.0 Hz), 4.58 (J = –12.4, 4.5 Hz), 4.59 (J = –12.4, 8.3 Hz)], 6.81–6.86 (m, 2 H), 7.07–7.12 (m, 2 H). ^{13}C NMR (75.5 MHz, CDCl$_3$): δ (ppm) = 29.6, 30.5, 42.2, 55.4, 71.0, 78.6, 114.8, 127.7, 129.2, 159.6, 201.3, 202.0. Anal.: calcd. for $C_{14}H_{17}NO_5$: C, 60.21; H, 6.14; N, 5.02. Found C, 60.07; H, 6.17; N, 4.99.



5bc

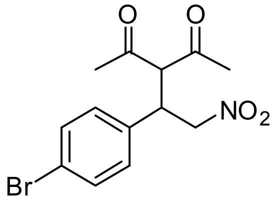
3-(2-Nitro-1-p-tolylethyl)pentane-2,4-dione (**5bc**). Obtained from **1b** (124 mg, 0.760 mmol) and **2c-H** following general procedure B: 142 mg (0.539 mmol, 71%), colorless solid, mp 104 °C. ^{1}H NMR (400 MHz, CDCl$_3$): δ (ppm) = 1.93 (s, 3 H), 2.28 (s, 3 H), 2.30 (s, 3 H), [ABCD-system at δ = 4.20 (J = 4.4, 8.5, 10.9 Hz), 4.35 (J = 10.9 Hz), 4.59 (J = –12.3, 4.4 Hz), 4.60 (J = –12.3, 8.5 Hz)], 7.04–7.07 (m, 2 H), 7.11–7.13 (m, 2 H). ^{13}C NMR (100 MHz, CDCl$_3$): δ (ppm) = 21.2, 29.6, 30.6, 42.6, 70.9, 78.5, 127.9, 130.1, 132.9, 138.5, 201.3, 202.0. Anal.: calcd. for $C_{14}H_{17}NO_4$: C, 63.87; H, 6.51; N, 5.32. Found C, 63.83; H, 6.53; N, 5.31.



5cc

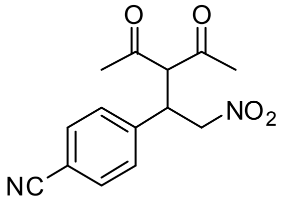
3-(2-Nitro-1-phenylethyl)pentane-2,4-dione (**5cc**). Obtained from **1c** (179 mg, 1.20 mmol) and **2c-H** following general procedure B: 212 mg (0.851 mmol, 71%), pale yellow solid, mp 111–112 °C. ^{1}H NMR (300 MHz, CDCl$_3$): δ (ppm) = 1.93 (s, 3 H), 2.28 (s, 3 H), [ABCD-system at δ = 4.21

(*J* = 4.3, 8.5, 10.8 Hz), 4.34 (*J* = 10.8 Hz), 4.59 (*J* = –12.4, 4.3 Hz), 4.61 (*J* = –12.4, 8.5 Hz)], 7.16–7.20 (m, 2 H), 7.28–7.36 (m, 3 H). ^{13}C NMR (75.5 MHz, CDCl$_3$): *δ* (ppm) = 29.7, 30.6, 42.9, 70.8, 78.3, 128.1, 128.7, 129.5, 136.1, 201.1, 201.9. Anal.: calcd. for $C_{13}H_{15}NO_4$: C, 62.64; H, 6.07; N, 5.62. Found C, 62.51; H, 6.04; N, 5.60.



5dc

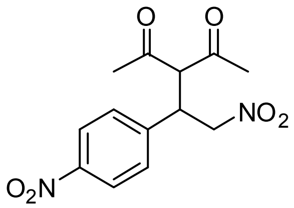
3-(1-(4-Bromophenyl)-2-nitroethyl)pentane-2,4-dione (**5dc**). Obtained from **1d** (141 mg, 0.618 mmol) and **2c-H** following general procedure B: 127 mg (0.387 mmol, 63%), colorless solid, mp 135–137 °C. ^{1}H NMR (300 MHz, CDCl$_3$): *δ* (ppm) = 1.97 (s, 3 H), 2.29 (s, 3 H), [ABCD-system at *δ* = 4.21 (*J* = 3.8, 8.9, 10.8 Hz), 4.32 (*J* = 10.8 Hz), 4.60 (*J* = –12.6, 3.8 Hz), 4.61 (*J* = –12.6, 8.9 Hz)], 7.05–7.09 (m, 2 H), 7.44–7.48 (m, 2 H). ^{13}C NMR (75.5 MHz, CDCl$_3$): *δ* (ppm) = 29.8, 30.6, 42.3, 70.6, 78.0, 122.8, 129.8, 132.6, 135.2, 200.7, 201.5. Anal.: calcd. for $C_{13}H_{14}BrNO_4$: C, 47.58; H, 4.30; N, 4.27. Found C, 47.56; H, 4.40; N, 4.22.



5ec

4-(3-Acetyl-1-nitro-4-oxopent-2-yl)benzonitrile (**5ec**). Obtained as from **1e** (127 mg, 0.729 mmol) and **2c-H** following general procedure B. The crude product was purified by column chromatography (silica gel 70–230 mesh, gradient eluent: *n*-pentane/ethyl acetate = 12/1 to 3/1) and then recrystallized from ethanol: 76 mg (0.28 mmol, 38%), colorless solid, mp 127–128 °C. ^{1}H NMR (300 MHz, CDCl$_3$): *δ* (ppm) = 2.00 (s, 3 H), 2.31 (s, 3 H), [ABCD-system at *δ* = 4.31 (*J* = 4.1, 8.7, 10.6 Hz), 4.36 (*J* = 10.6 Hz), 4.64 (*J* = –13.0, 4.1 Hz), 4.66 (*J* = –13.0, 8.7 Hz)], 7.31–7.35 (m, 2 H), 7.62–7.66 (m, 2 H). ^{13}C NMR (75.5 MHz, DMSO-*d*$_6$): *δ* (ppm) = 30.1, 30.7, 42.7, 70.1, 77.5, 112.8, 118.1, 129.0, 133.1, 141.7, 200.1, 201.0. Anal.: calcd. for $C_{14}H_{14}N_2O_4$: C, 61.31; H, 5.14; N, 10.21. Found C, 61.14; H, 5.30; N, 10.19. IR

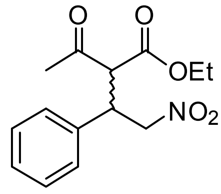
(ATR) $\tilde{\nu}$ (cm^{-1}) = 726, 833, 860, 956, 1075, 1119, 1144, 1176, 1211, 1242, 1268, 1361, 1419, 1439, 1508, 1555, 1609, 1701, 1732.



5fc

3-(2-Nitro-1-(4-nitrophenyl)ethyl)pentane-2,4-dione (**5fc**). Obtained from **1f** (132 mg, 0.680 mmol) and **2c-H** following general procedure B. The crude product was purified by column chromatography (silica gel 70–230 mesh, gradient eluent: *n*-pentane/ethyl acetate = 11/1 to 4/1) and then recrystallized from ethanol: 100 mg (0.340 mmol, 50%), yellowish solid, mp 127–130 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ (ppm) = 2.03 (s, 3 H), 2.32 (s, 3 H), [ABCD-system at δ = 4.38 (J = 4.0, 8.9, 10.1 Hz), 4.39 (J = 10.1 Hz), 4.66 (J = –13.0, 4.0 Hz), 4.69 (J = –13.0, 8.9 Hz)], 7.38–7.43 (m, 2 H), 8.18–8.21 (m, 2 H). ^{13}C NMR (75.5 MHz, $CDCl_3$): δ (ppm) = 30.1, 30.7, 42.4, 70.2, 77.5, 124.6, 129.3, 143.7, 148.0, 200.0, 200.9. Anal.: calcd. for $C_{13}H_{14}N_2O_6$: C, 53.06; H, 4.80; N, 9.52. Found C, 53.07; H, 4.89; N, 9.52.

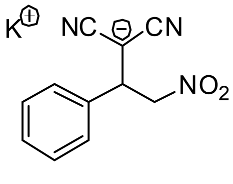
2.5.1.4 Reaction of Ethyl 3-oxobutanoate (2d-H) with *trans*-*β*-Nitrostyrene (1c)



5cd

Ethyl 2-acetyl-4-nitro-3-phenylbutanoate (**5cd**). Obtained from **1c** (160 mg, 1.07 mmol) and **2d-H** following general procedure B: 165 mg (0.591 mmol, 55%, dr ~ 1:8, from ^{1}H NMR integrals of the CH_3 signals of CH_3CO and OCH_2CH_3), colorless solid, mp 73–75 °C. ^{1}H NMR (300 MHz, $CDCl_3$, major diastereomer): δ (ppm) = 1.00 (t, J = 7.1 Hz, 3 H), 2.30 (s, 3 H), 3.96 (q, J = 7.1 Hz, 2 H), [ABCD-system at δ = 4.09 (J = 10.0 Hz), 4.17 (J = 4.6, 8.3, 10.0 Hz), 4.72 (J = –13.1, 8.3 Hz), 4.72 (J = –13.1, 4.6 Hz)], 7.18–7.21 (m, 2 H), 7.26–7.34 (m, 3 H); additional signals for the minor diastereomer: δ (ppm) = 1.27 (t, J = 7.1 Hz, 0.4 H), 2.05 (s, 0.4 H). ^{13}C NMR (75.5 MHz, $CDCl_3$, major diastereomer): δ (ppm) = 13.8, 30.2, 42.4, 62.1, 78.0, 128.1, 128.4, 129.1, 136.5, 167.0, 201.3. HRMS (ESI): calcd. for $C_{14}H_{16}NO_5^-$ [M-H]$^-$ 278.1034. Found 278.1038. Anal.: calcd. for $C_{14}H_{17}NO_5$: C, 60.21; H, 6.14; N, 5.02. Found C, 60.14; H, 6.28; N, 4.98.

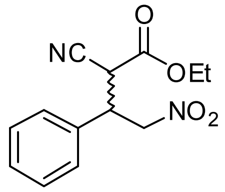
2.5.1.5 Reaction of Potassium dicyanomethanide (2e-K) with *trans*-*β*-Nitrostyrene (1c)



4ce-K

Potassium 1,1-dicyano-3-nitro-2-phenylpropan-1-ide (**4ce-K**). From **1c** and **2e-K** by following general procedure A. ^{1}H NMR (400 MHz, DMSO-d_6): δ(ppm) = [ABC-system at δ = 3.70 (J = 8.2, 8.4 Hz), 4.67 (J = –12.3, 8.4 Hz), 4.70 (J = –12.3, 8.2 Hz)], 7.18–7.31 (m, 5 H). ^{13}C NMR (100 MHz, DMSO-d_6): δ(ppm) = 40.0, 43.0, 79.8, 126.6, 127.0, 128.3, 129.9, 142.5.

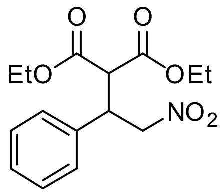
2.5.1.6 Reaction of Ethyl 2-cyanoacetate (2f-H) with ***trans*-*β***-Nitrostyrene (1c)



5cf

Ethyl 2-cyano-4-nitro-3-phenylbutanoate (**5cf**). Obtained from *trans*-*β*-nitrostyrene (**1c**) (298 mg, 2.00 mmol) and **2f-H** following general procedure B: 349 mg (1.33 mmol, 67%, dr ~ 1.4:1, from ^{1}H NMR integrals of the CH_3 signals), colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$, major diastereomer): δ (ppm) = 1.13 (t, J = 7.2 Hz, 1.6 H), [ABCD-system at δ = 3.93 (J = 5.7 Hz), 4.22 (J = 5.7, 6.2, 8.7 Hz), 4.92 (J = –13.6, 8.7 Hz), 5.01 (J = –13.6, 6.2 Hz)], 7.21–7.39 (m, 5 H); additional signals for the minor diastereomer: δ (ppm) = 1.22 (t, J = 7.2 Hz, 1.2 H), 4.09–4.15 (m, 1.6 H), 4.75–4.85 (m, 0.9 H). ^{13}C NMR (100 MHz, $CDCl_3$, major diastereomer): δ (ppm) = 13.8, 41.7, 42.8, 63.4, 76.1, 76.4, 114.4, 127.6, 128.0, 129.4, 129.5, 163.9.

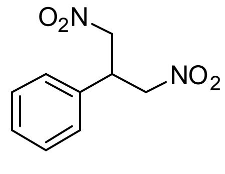
2.5.1.7 Reaction of Potassium 1,3-diethoxy-1,3-dioxopropan-2-ide (2g-K) with *trans-β*-Nitrostyrene (1c)



5cg

Diethyl 2-(2-nitro-1-phenylethyl)malonate (**5cg**). *trans*-*β*-Nitrostyrene (**1c**) (97 mg, 0.65 mmol) and **2g-K** (129 mg, 0.651 mmol) were dissolved in dry 1,4-dioxane (15 mL) and stirred for 10 min under nitrogen atmosphere. Subsequent addition of 2 M aqueous acetic acid (1 mL) furnished a precipitate, which was filtered. The crude product was purified by column chromatography (silica gel 70–230 mesh, gradient eluent: *n*-pentane/ethyl acetate = 10/1 to 3/1) and the recrystallized from ethanol: 82 mg (0.27 mmol, 42%), yellow solid, mp 63–64 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ (ppm) = 1.04 (t, J = 7.1 Hz, 3 H), 1.26 (t, J = 7.1 Hz, 3 H), 4.00 (q, J = 7.1 Hz, 2 H) 4.21–4.27 (m, 2 H), [ABCD-system at δ = 3.79 (J = 9.4 Hz), 4.20 (J = 4.6, 9.4, 9.4 Hz), 4.83 (J = –13.1, 9.4 Hz), 4.89 (J = –13.1, 4.6 Hz)], 7.22–7.32 (m, 5 H). ^{13}C NMR (75.5 MHz, $CDCl_3$): δ (ppm) = 13.9, 14.1, 43.1, 55.1, 62.0, 62.3, 77.8, 128.1, 128.5, 129.0, 136.3, 166.9, 167.6.

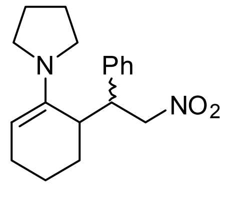
2.5.1.8 Reaction of Nitromethane (2h-H) with *trans*-*β*-Nitrostyrene (1c)



5ch

(1,3-Dinitroprop-2-yl)benzene (**5ch**). *trans*-*β*-Nitrostyrene (**1c**) (171 mg, 1.15 mmol) was dissolved in nitromethane (**2h**-**H**) (10 mL) under nitrogen atmosphere, then triethylamine (1 mol%) was added. The mixture was stirred at ambient temperature for 24 h. The solvent was removed in vacuo, and then the crude product was purified by column chromatography (silica gel 70–230 mesh, gradient eluent: *n*-pentane/ethyl acetate = 10/1 to 3/1), (121 mg, 0.576 mmol, 50%): colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = [AA´BB´C-system at δ = 4.31 (J = 7.0, 7.4 Hz), 4.75 (J = –13.4, 7.4 Hz), 4.78 (J = –13.4, 7.0 Hz)], 7.21–7.24 (m, 2 H), 7.36–7.41 (m, 3 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) = 41.8, 76.8, 127.5, 129.2, 129.7, 134.3.

2.5.1.9 Reaction of 1-Cyclohex-1-enylpyrrolidine (6a) with *trans*-*β*-Nitrostyrene (1c)



rac-**7ca**

1-(6-(2-Nitro-1-phenylethyl)cyclohex-1-enyl)pyrrolidine (*rac*-**7ca**). *trans*-*β*-Nitrostyrene (**1c**) (298 mg, 2.00 mmol) and 1-cyclohex-1-enylpyrrolidine (**6a**) (303 mg, 2.00 mmol) were dissolved in $CDCl_3$ (10 mL) at 0° C. After 5 min, a sample was taken for NMR spectroscopy. Purification by column chromatography resulted in decomposition of the product. ^{1}H NMR (600 MHz, $CDCl_3$): δ (ppm) = 1.32–1.44 (m, 3 H), 1.47–1.55 (m, 1 H), 1.74–1.86 (m, 4 H), 1.95–2.01 (m, 1 H), 2.04–2.09 (m, 1 H), 2.55–2.57 (m, 1 H), 2.69–2.72 (m, 2 H), 2.98–3.02 (m, 2 H), 3.63–3.68 (m, 1 H), 4.54 (t, J = 3.9 Hz, 1 H), 4.66 (dd, J = 10.6, 12.8 Hz, 1 H), 5.04 (dd, J = 5.5, 12.8 Hz, 1 H), 7.08–7.13 (m, 2 H), 7.15–7.18 (m, 1 H), 7.22–7.24 (m, 2 H). ^{13}C NMR (150 MHz, $CDCl_3$): δ (ppm) = 17.2, 23.8, 24.3, 25.2, 38.2, 47.9, 48.8, 79.6, 101.1, 127.4, 128.1, 128.8, 139.7, 144.6.

2.5.2 Kinetics

For the investigation of fast kinetics ($\tau_{1/2}$ < 30 s) stopped-flow spectrophotometer systems were used. Slow kinetics ($\tau_{1/2}$ > 30 s) were followed by using a conventional UV-vis diode array spectrophotometer system that was connected to a quartz immersion probe via fiber optic cables. Due to an overlap of the absorption bands, the rates of the reactions with the carbanions **2f** and **2h** were determined following the decay of absorbance at the shoulders of the absorption bands of the electrophiles **1a**–**f**. Measurements at the shoulders of the absorption bands of the *trans*-β-nitrostyrenes **1e** and **1f** were also performed to determine the kinetics of their reactions with the carbanions **2a**–**d**. All measurements were carried out under first-order conditions (in general $[\mathbf{2}]_0/[\mathbf{1}]_0 > 10$). The first-order rate constants k_{obs} were obtained by least-squares fitting of the time-dependent absorbances A_t of the electrophiles to the exponential function $A_t = A_0\, e^{-k_{\text{obs}}t} + C$. Second-order rate constans k_2^{exp} were then derived from linear correlations of k_{obs} vs. [**2**].

Evaluating the kinetics of the reactions of the carbanions **2e** and **2f** with *trans*-4-methyl-β-Nitrostyrene (**1b**) in methanol required to consider the competing reactions of methoxide anions and methanol (eq 2.3).[71]

$$k_{\text{obs}} = k_2^{\text{exp}}[\mathbf{2}] + k_{2,\text{MeO}}[\text{MeO}^-] + k_{1,\text{MeOH}} \tag{2.3}$$

Since the rate constant $k_{2,\text{MeO}}$ for the reaction between the methoxide anion (N = 15.78 and s_{N} = 0.56 for MeO^- in MeOH)[71a] and **1b** (E = –14.23) was calculated by using eq 2.1, and $[\text{MeO}^-]$ was calculated based on the known K_{CH} values of the CH acids **2e-H** and **2f-H** in methanol,[71b] the terms for the reactions of **1b** with the carbanions and with methanol (eq 2.4, right) can be derived by rearranging eq 2.3 to eq 2.4.

$$k_{1\psi} = k_{\text{obs}} - k_{2,\text{MeO}}[\text{MeO}^-] = k_2^{\text{exp}}[\mathbf{2}] + k_{1,\text{MeOH}} \tag{2.4}$$

Second-order rate constants k_2^{exp} for the reactions of **2e** and **2f** with **1b** in methanol were obtained from the slopes of the linear plots of $k_{1\psi}$ against the concentrations of the carbanions **2e** and **2f**, in analogy to the procedure described in reference 71b.

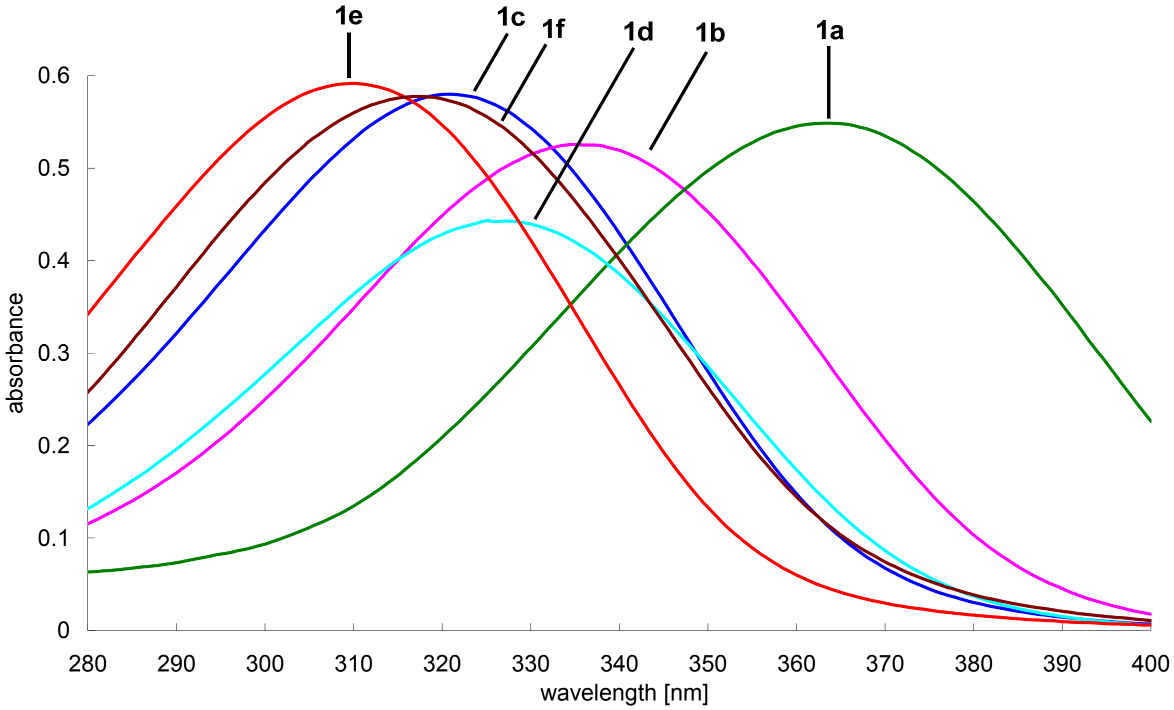


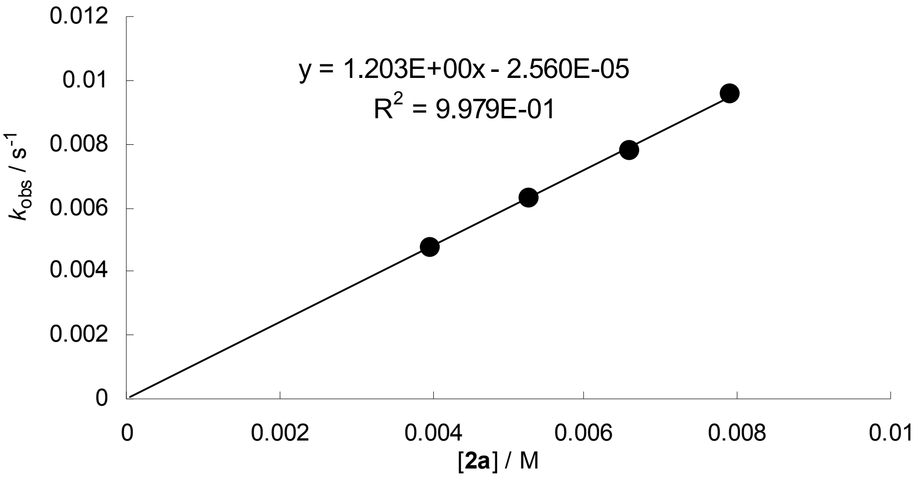
Figure 2.5. UV-Spectra of the *trans*-*β*-Nitrostyrenes 1a–f in DMSO. [1a] /M= 5.47 × 10^{-5}, [1b] /M = 6.01 × 10^{-5}, [1c] /M = 6.64 × 10^{-5}, [1d] /M = 4.52 × 10^{-5}, [1e] /M = 6.03 × 10^{-5}, [1f] /M = 6.04 × 10^{-5}.

2.5.2.1 Kinetics of the Reactions of *trans*-4-Methoxy-*β*-nitrostyrene (1a) with the Carbanions 2 in DMSO

Reaction of **1a** with **2a** (DMSO, 20 °C, conventional, 363 nm)

$k_2 = 1.20$ M^{-1} s^{-1}

[**1a**] /M	[**2a**] /M	k_{obs} / s^{-1}
1.06×10^{-4}	3.95×10^{-3}	4.78×10^{-3}
1.06×10^{-4}	5.27×10^{-3}	6.30×10^{-3}
1.06×10^{-4}	6.59×10^{-3}	7.78×10^{-3}
1.06×10^{-4}	7.90×10^{-3}	9.57×10^{-3}

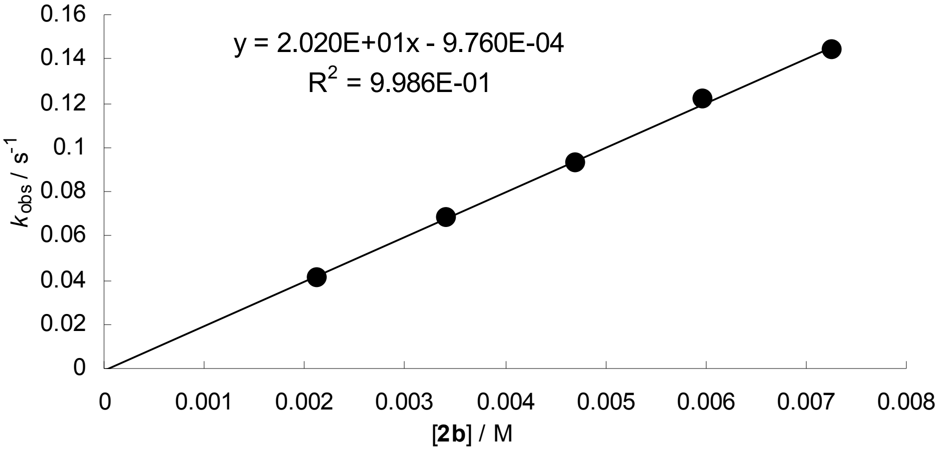


Reaction of **1a** with **2b** (DMSO, 20 °C, stopped-flow, 363 nm)

$k_2 = 2.02 \times 10^{1}$ M^{-1} s^{-1}

[**1a**] /M	[**2b**] /M	k_{obs} / s^{-1}
1.30×10^{-4}	2.13×10^{-3}	4.16×10^{-2}
1.30×10^{-4}	3.41×10^{-3}	6.83×10^{-2}
1.30×10^{-4}	4.69×10^{-3}	9.28×10^{-2}
1.30×10^{-4}	5.97×10^{-3}	1.22×10^{-1}

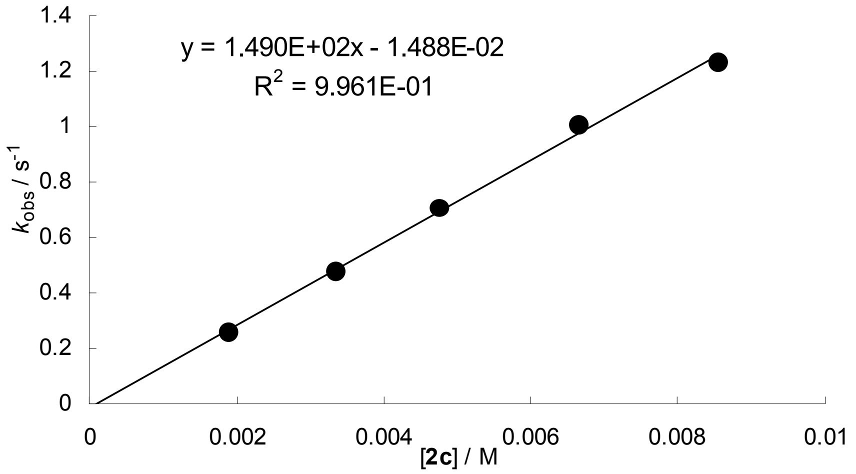
1.30×10^{-4}	7.25×10^{-3}	1.44×10^{-1}



Reaction of **1a** with **2c** (DMSO, 20 °C, stopped-flow, 340 nm)

$k_2 = 1.49 \times 10^2$ M^{-1} s^{-1}

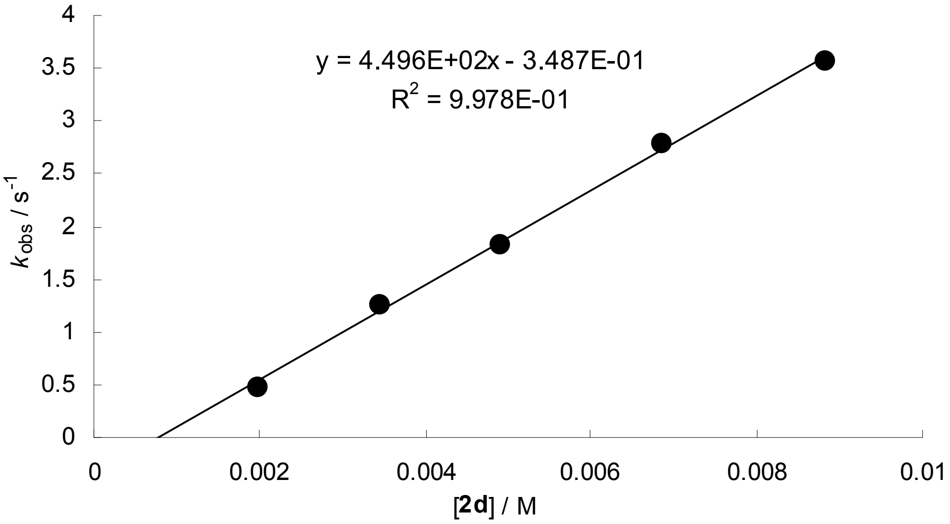
[**1a**] /M	[**2c**] /M	k_{obs} / s^{-1}
1.68×10^{-4}	1.90×10^{-3}	2.55×10^{-1}
1.68×10^{-4}	3.33×10^{-3}	4.75×10^{-1}
1.68×10^{-4}	4.75×10^{-3}	7.08×10^{-1}
1.68×10^{-4}	6.65×10^{-3}	1.01
1.68×10^{-4}	8.55×10^{-3}	1.23



Reaction of **1a** with **2d** (DMSO, 20 °C, stopped-flow, 330 nm)

$k_2 = 4.50 \times 10^2$ M^{-1} s^{-1}

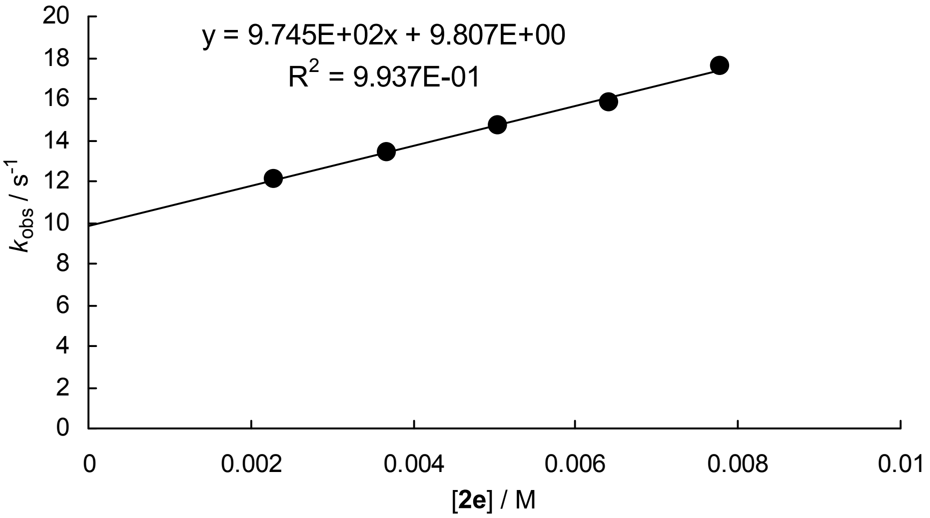
[**1a**] /M	[**2d**] /M	k_{obs} / s^{-1}
1.74×10^{-4}	1.96×10^{-3}	4.73×10^{-1}
1.74×10^{-4}	3.43×10^{-3}	1.26
1.74×10^{-4}	4.90×10^{-3}	1.84
1.74×10^{-4}	6.86×10^{-3}	2.79
1.74×10^{-4}	8.82×10^{-3}	3.57



Reaction of **1a** with **2e** (DMSO, 20 °C, stopped-flow, 363 nm)

$k_2 = 9.75 \times 10^{2}$ M^{-1} s^{-1}

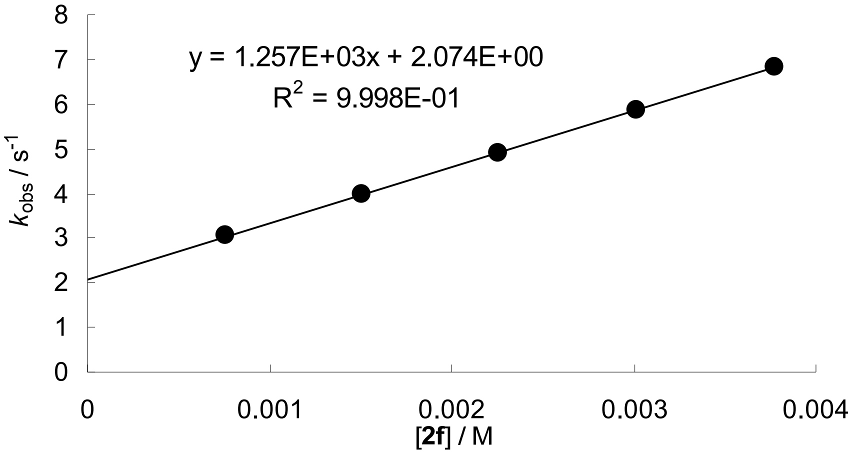
[**1a**] /M	[**2e**] /M	k_{obs} / s^{-1}
1.30×10^{-4}	2.29×10^{-3}	1.21×10^{1}
1.30×10^{-4}	3.67×10^{-3}	1.34×10^{1}
1.30×10^{-4}	5.04×10^{-3}	1.47×10^{1}
1.30×10^{-4}	6.42×10^{-3}	1.58×10^{1}
1.30×10^{-4}	7.79×10^{-3}	1.76×10^{1}



Reaction of **1a** with **2f** (DMSO, 20 °C, stopped-flow, 350 nm)

$k_2 = 1.26 \times 10^{3}$ M^{-1} s^{-1}

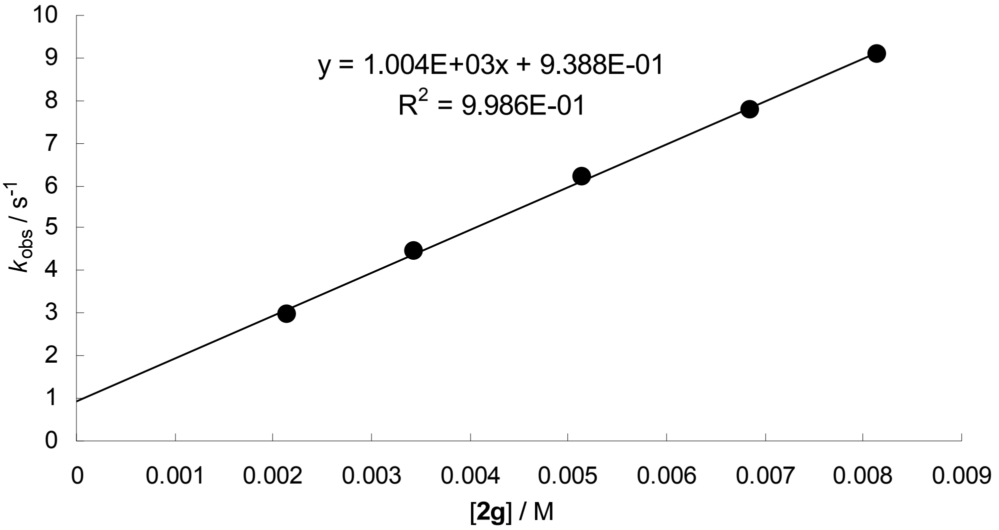
[**1a**] /M	[**2f**] /M	k_{obs} / s^{-1}
6.00×10^{-5}	7.54×10^{-4}	3.04
6.00×10^{-5}	1.51×10^{-3}	3.97
6.00×10^{-5}	2.26×10^{-3}	4.89
6.00×10^{-5}	3.02×10^{-3}	5.85
6.00×10^{-5}	3.77×10^{-3}	6.84



Reaction of **1a** with **2g** (DMSO, 20 °C, stopped-flow, 340 nm)

$k_2 = 1.00 \times 10^3$ M^{-1} s^{-1}

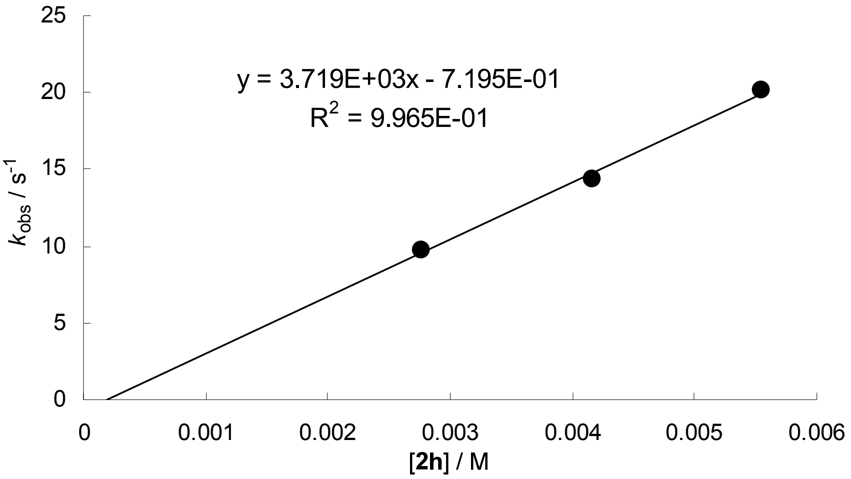
[**1a**] /M	[**2g**] /M	k_{obs} / s^{-1}
1.61×10^{-4}	2.15×10^{-3}	2.99
1.61×10^{-4}	3.43×10^{-3}	4.46
1.61×10^{-4}	5.15×10^{-3}	6.22
1.61×10^{-4}	6.86×10^{-3}	7.79
1.61×10^{-4}	8.15×10^{-3}	9.08



Reaction of **1a** with **2h** (DMSO, 20 °C, stopped-flow, 363 nm)

$k_2 = 3.72 \times 10^3$ M^{-1} s^{-1}

[**1a**] /M	[**2h**] /M	k_{obs} / s^{-1}
1.74×10^{-4}	2.77×10^{-3}	9.76
1.74×10^{-4}	4.16×10^{-3}	1.44×10^{1}
1.74×10^{-4}	5.55×10^{-3}	2.01×10^{1}

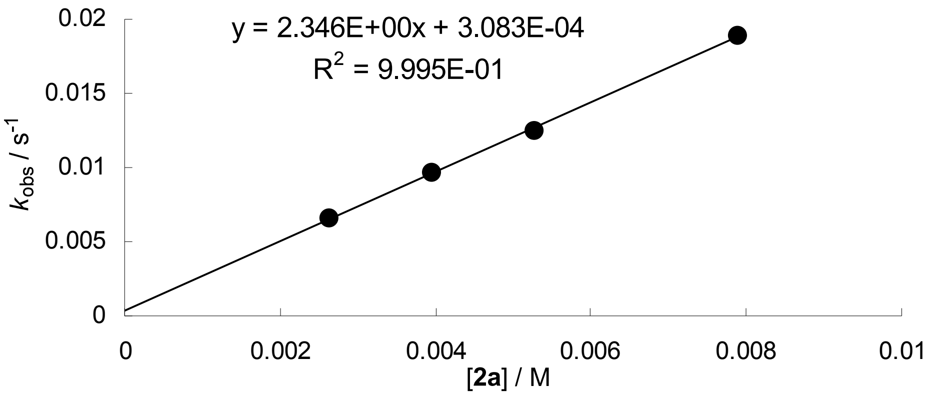


2.5.2.2 Kinetics of the Reactions of *trans*-4-Methyl-β-nitrostyrene (1b) with the Carbanions 2 in DMSO or Methanol

Reaction of **1b** with **2a** (DMSO, 20 °C, conventional, 335 nm)

$k_2 = 2.35\ \mathrm{M^{-1}\ s^{-1}}$

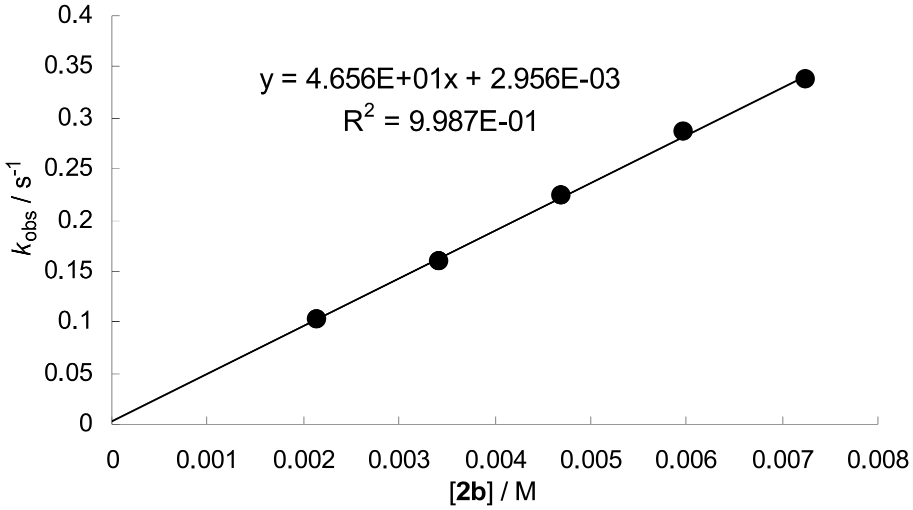
[**1b**] /M	[**2a**] /M	k_{obs} / s^{-1}
1.03×10^{-4}	2.63×10^{-3}	6.49×10^{-3}
1.03×10^{-4}	3.95×10^{-3}	9.67×10^{-3}
1.03×10^{-4}	5.27×10^{-3}	1.25×10^{-2}
1.03×10^{-4}	7.90×10^{-3}	1.89×10^{-2}



Reaction of **1b** with **2b** (DMSO, 20 °C, stopped-flow, 335 nm)

$k_2 = 4.66 \times 10^{1}\ \mathrm{M^{-1}\ s^{-1}}$

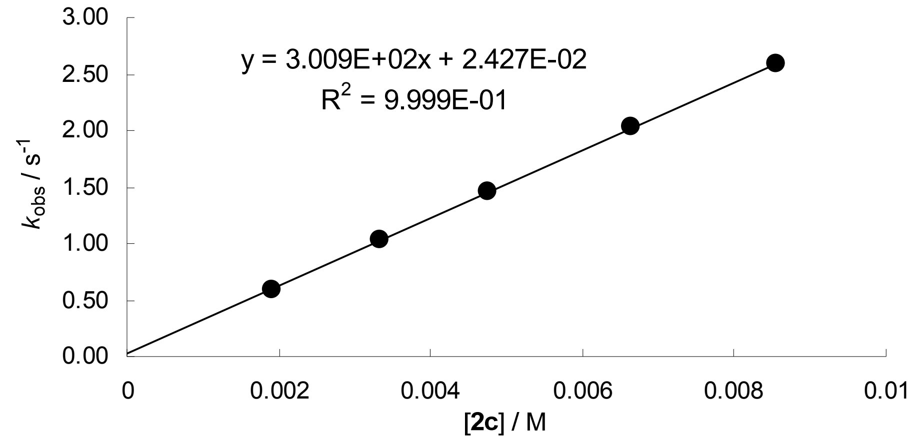
[**1b**] /M	[**2b**] /M	k_{obs} / s^{-1}
1.30×10^{-4}	2.14×10^{-3}	1.02×10^{-1}
1.30×10^{-4}	3.42×10^{-3}	1.60×10^{-1}
1.30×10^{-4}	4.70×10^{-3}	2.24×10^{-1}
1.30×10^{-4}	5.98×10^{-3}	2.86×10^{-1}
1.30×10^{-4}	7.26×10^{-3}	3.37×10^{-1}



Reaction of **1b** with **2c** (DMSO, 20 °C, stopped-flow, 340 nm)

$k_2 = 3.01 \times 10^2$ M^{-1} s^{-1}

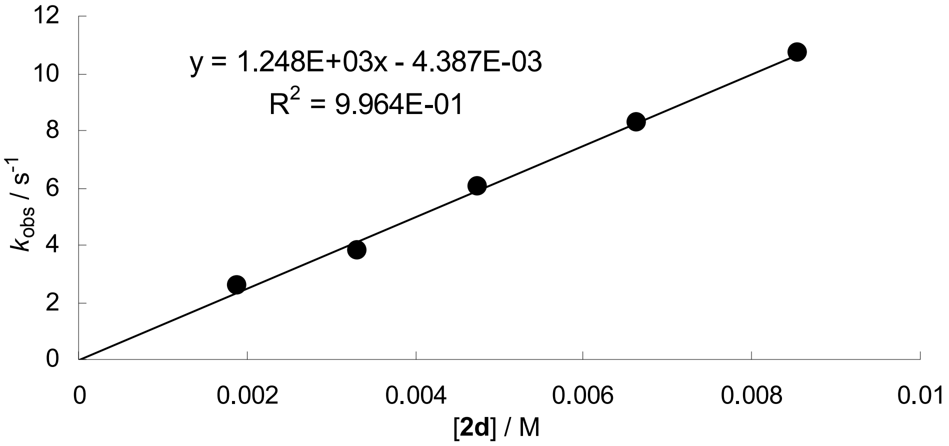
[**1b**] /M	[**2c**] /M	k_{obs} / s^{-1}
1.72×10^{-4}	1.90×10^{-3}	5.88×10^{-1}
1.72×10^{-4}	3.33×10^{-3}	1.03
1.72×10^{-4}	4.75×10^{-3}	1.46
1.72×10^{-4}	6.65×10^{-3}	2.03
1.72×10^{-4}	8.55×10^{-3}	2.59



Reaction of **1b** with **2d** (DMSO, 20 °C, stopped-flow, 330 nm)

$k_2 = 1.25 \times 10^3$ M^{-1} s^{-1}

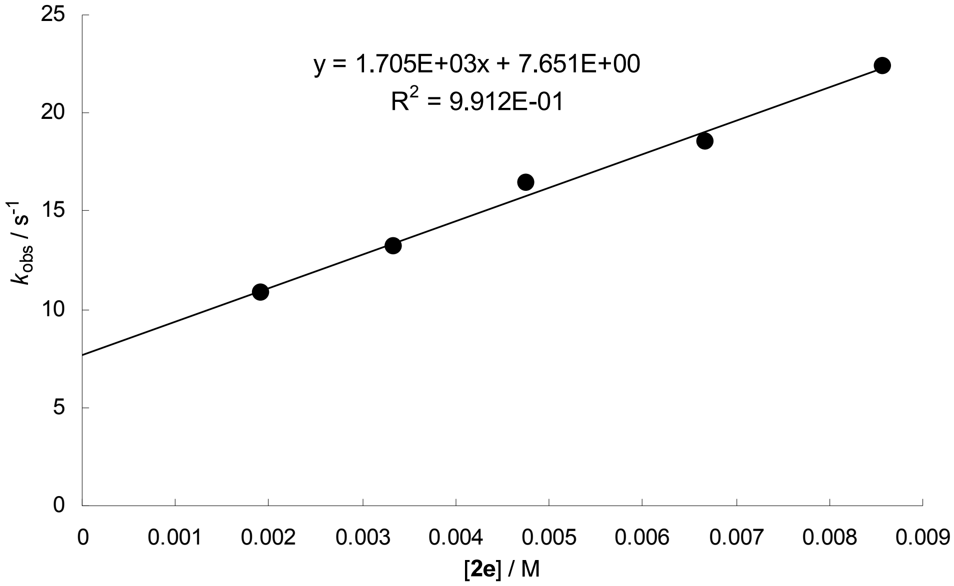
[**1b**] /M	[**2d**] /M	k_{obs} / s^{-1}
1.74×10^{-4}	1.90×10^{-3}	2.57
1.74×10^{-4}	3.32×10^{-3}	3.82
1.74×10^{-4}	4.74×10^{-3}	6.01
1.74×10^{-4}	6.64×10^{-3}	8.26
1.74×10^{-4}	8.54×10^{-3}	1.07×10^1



Reaction of **1b** with **2e** (DMSO, 20 °C, stopped-flow, 340 nm)

$k_2 = 1.71 \times 10^3$ M^{-1} s^{-1}

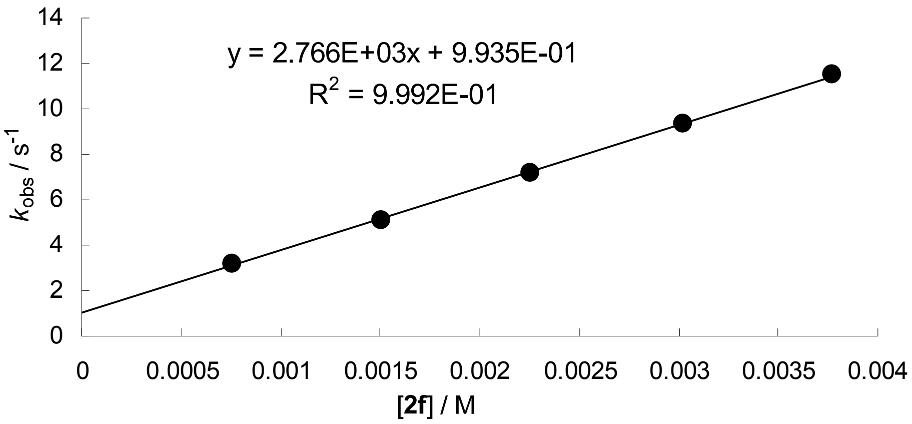
[**1b**] /M	[**2e**] /M	k_{obs} / s^{-1}
1.74×10^{-4}	1.91×10^{-3}	1.08×10^{1}
1.74×10^{-4}	3.33×10^{-3}	1.32×10^{1}
1.74×10^{-4}	4.76×10^{-3}	1.64×10^{1}
1.74×10^{-4}	6.67×10^{-3}	1.85×10^{1}
1.74×10^{-4}	8.57×10^{-3}	2.24×10^{1}



Reaction of **1b** with **2f** (DMSO, 20 °C, stopped-flow, 340 nm)

$k_2 = 2.77 \times 10^3$ M^{-1} s^{-1}

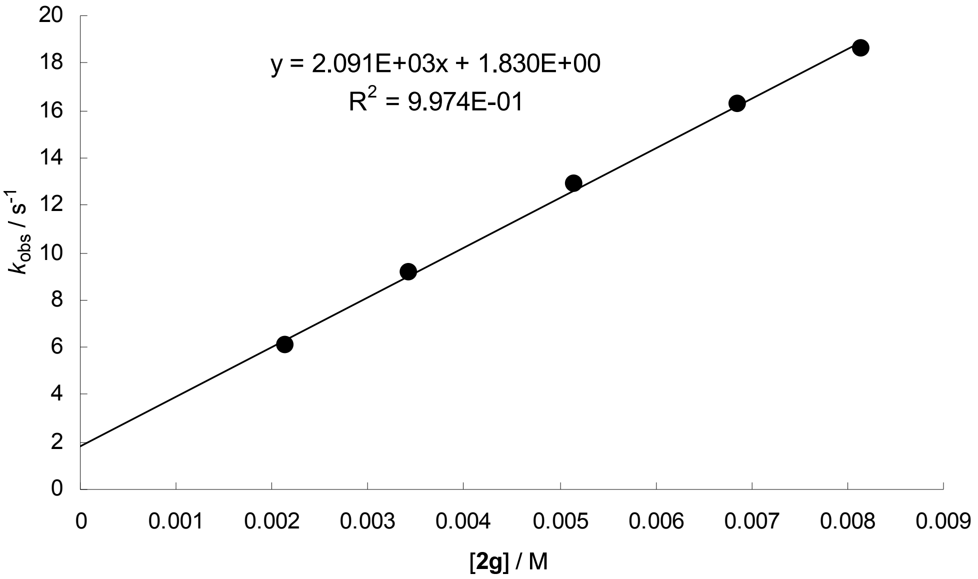
[**1b**] /M	[**2f**] /M	k_{obs} / s^{-1}
6.00×10^{-5}	7.54×10^{-4}	3.19
6.00×10^{-5}	1.51×10^{-3}	5.09
6.00×10^{-5}	2.26×10^{-3}	7.15
6.00×10^{-5}	3.02×10^{-3}	9.33
6.00×10^{-5}	3.77×10^{-3}	1.15×10^{1}



Reaction of **1b** with **2g** (DMSO, 20 °C, stopped-flow, 330 nm)

$k_2 = 2.09 \times 10^3$ M^{-1} s^{-1}

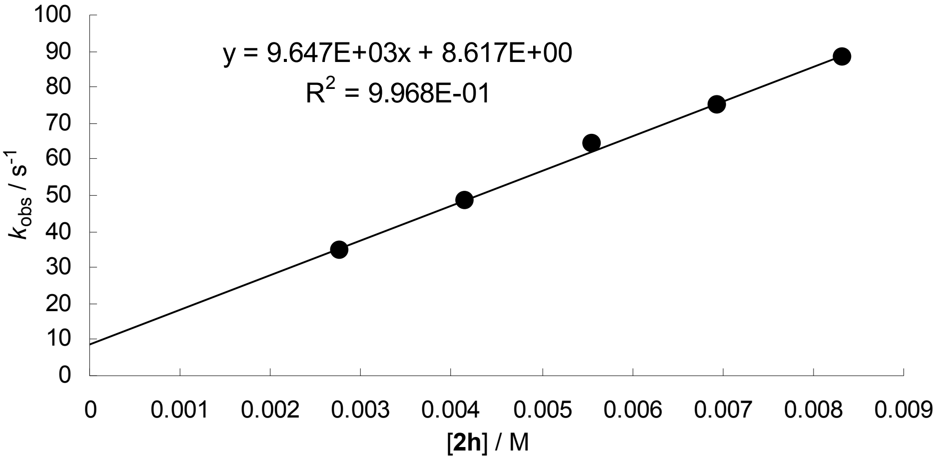
[**1b**] /M	[**2g**] /M	k_{obs} / s^{-1}
1.61×10^{-4}	2.15×10^{-3}	6.05
1.61×10^{-4}	3.43×10^{-3}	9.13
1.61×10^{-4}	5.15×10^{-3}	1.29×10^{1}
1.61×10^{-4}	6.86×10^{-3}	1.63×10^{1}
1.61×10^{-4}	8.15×10^{-3}	1.86×10^{1}



Reaction of **1b** with **2h** (DMSO, 20 °C, stopped-flow, 335 nm)

$k_2 = 9.65 \times 10^3$ M^{-1} s^{-1}

[**1b**] /M	[**2h**] /M	k_{obs} / s^{-1}
1.74×10^{-4}	2.77×10^{-3}	3.48×10^{1}
1.74×10^{-4}	4.16×10^{-3}	4.83×10^{1}
1.74×10^{-4}	5.55×10^{-3}	6.43×10^{1}
1.74×10^{-4}	6.94×10^{-3}	7.48×10^{1}
1.74×10^{-4}	8.32×10^{-3}	8.85×10^{1}

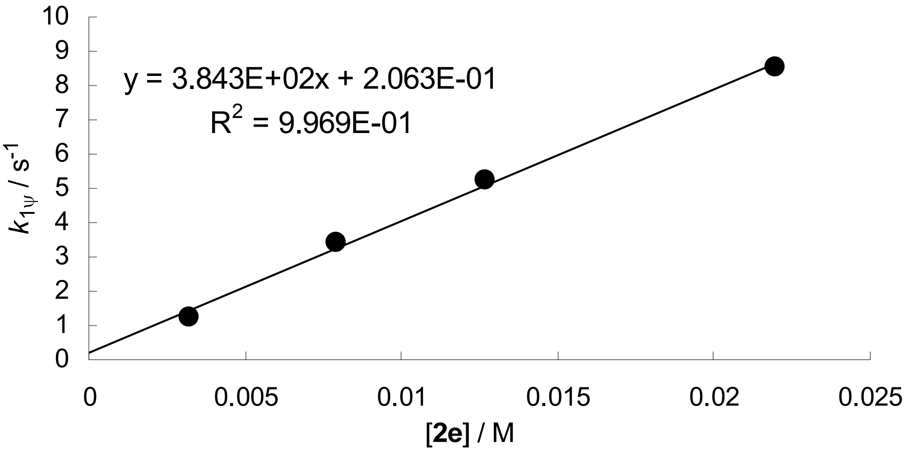


Reaction of **1b** with **2e** (methanol, 20 °C, stopped-flow, 335 nm)

$k_2 = 3.84 \times 10^2$ M^{-1} s^{-1}

[**1b**] /M	[**2e-H**]$_0$ /M	[$^-$OMe]$_0$ /M	[**2e**]$_{eff}$[a]	[$^-$OMe]$_{eff}$[a]	k_{obs} / s^{-1}	$k_{1\psi}$ / s^{-1}
1.50×10^{-4}	4.54×10^{-2}	3.25×10^{-3}	3.19×10^{-3}	6.29×10^{-5}	1.26	1.25
1.50×10^{-4}	4.54×10^{-2}	8.12×10^{-3}	7.95×10^{-3}	1.77×10^{-4}	3.42	3.41
1.50×10^{-4}	4.54×10^{-2}	1.30×10^{-2}	1.27×10^{-2}	3.23×10^{-4}	5.25	5.23
1.50×10^{-4}	4.54×10^{-2}	2.27×10^{-2}	2.20×10^{-2}	7.80×10^{-4}	8.58	8.55

[a] Concentration of [**2e**]$_{eff}$ calculated with K_{CH} = 600 M^{-1} [I]



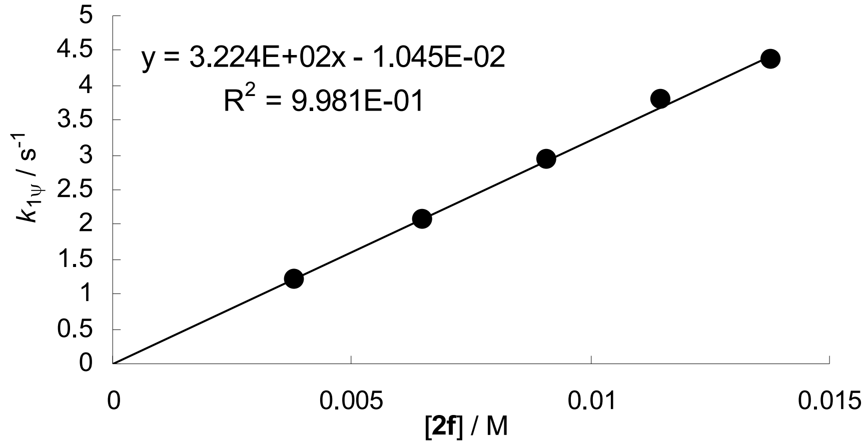
[I] Crampton, M. R.; Kee, T. P.; Wilcock, J. R. *Can. J. Chem.* **1986**, *64*, 1714–1720.

Reaction of **1b** with **2f** (methanol, 20 °C, stopped-flow, 335 nm)

$k_2 = 3.22 \times 10^2$ M^{-1} s^{-1}

[**1b**] /M	[**2f-H**]$_0$ /M	[$^-$OMe]$_0$ /M	[**2f**]$_{eff}$^{a} /M	[$^-$OMe]$_{eff}$ /M	k_{obs} / s^{-1}	$k_{1\psi}$ / s^{-1}
1.48×10^{-4}	4.69×10^{-2}	5.64×10^{-3}	3.80×10^{-3}	1.83×10^{-3}	1.21	1.20
1.48×10^{-4}	4.69×10^{-2}	9.86×10^{-3}	6.51×10^{-3}	3.35×10^{-3}	2.08	2.07
1.48×10^{-4}	4.69×10^{-2}	1.41×10^{-2}	9.09×10^{-3}	5.00×10^{-3}	2.95	2.94
1.48×10^{-4}	4.69×10^{-2}	1.83×10^{-2}	1.15×10^{-2}	6.78×10^{-3}	3.80	3.78
1.48×10^{-4}	4.69×10^{-2}	2.25×10^{-2}	1.38×10^{-2}	8.70×10^{-3}	4.39	4.37

^{a}Concentration of [**2f**]$_{eff}$ calculated with K_{CH} = 24 M^{-1} [II]



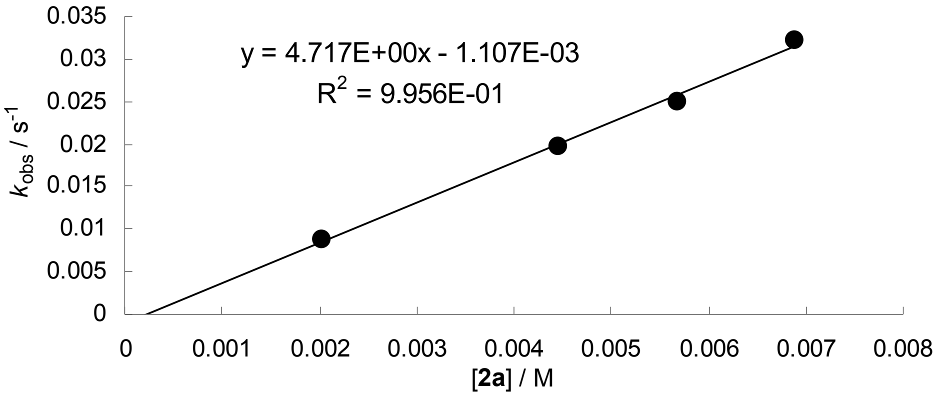
[II] Crampton, M. R.; Stevens, J. A. *J. Chem. Soc, Perkin Trans. 2* **1991**, 1715–1720.

2.5.2.3 Kinetics of the Reactions of *trans*-β-Nitrostyrene (1c) with the Carbanions 2 in DMSO

Reaction of **1c** with **2a** (DMSO, 20 °C, conventional, 321 nm)

$k_2 = 4.72\ M^{-1}\ s^{-1}$

[**1c**] /M	[**2a**] /M	k_{obs} / s^{-1}
1.30×10^{-4}	2.03×10^{-3}	8.78×10^{-3}
1.30×10^{-4}	4.46×10^{-3}	1.97×10^{-2}
1.30×10^{-4}	5.68×10^{-3}	2.49×10^{-2}
1.30×10^{-4}	6.89×10^{-3}	3.21×10^{-2}

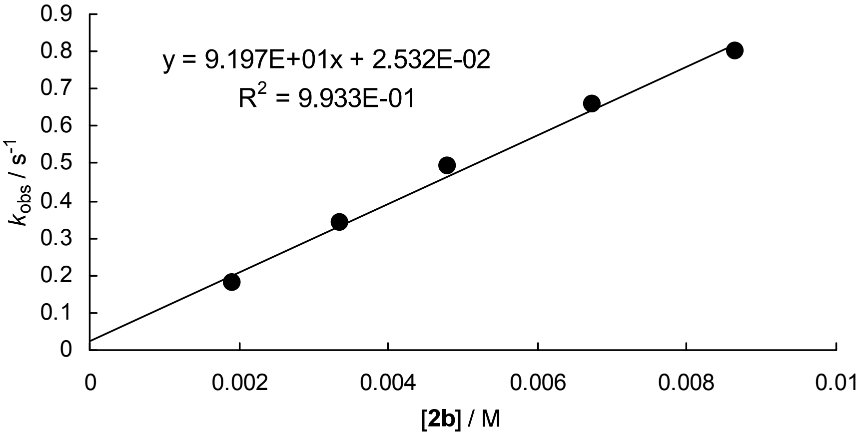


Reaction of **1c** with **2b** (DMSO, 20 °C, stopped-flow, 330 nm)

$k_2 = 9.20 \times 10^{1}\ M^{-1}\ s^{-1}$

[**1c**] /M	[**2b**] /M	k_{obs} / s^{-1}
1.74×10^{-4}	1.92×10^{-3}	1.81×10^{-1}
1.74×10^{-4}	3.36×10^{-3}	3.39×10^{-1}
1.74×10^{-4}	4.81×10^{-3}	4.91×10^{-1}
1.74×10^{-4}	6.73×10^{-3}	6.58×10^{-1}

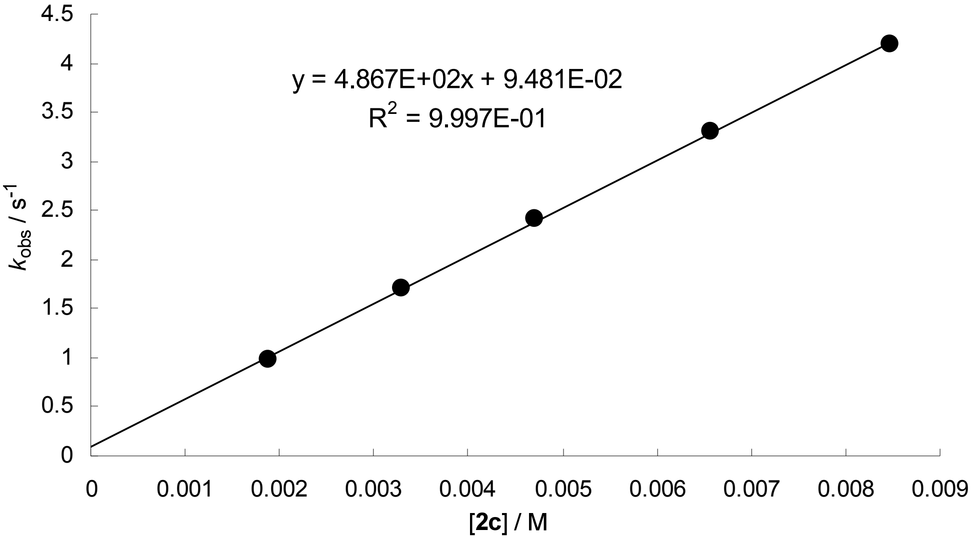
1.74×10^{-4}	8.65×10^{-3}	8.00×10^{-1}



Reaction of **1c** with **2c** (DMSO, 20 °C, stopped-flow, 335 nm)

$k_2 = 4.87 \times 10^2$ M^{-1} s^{-1}

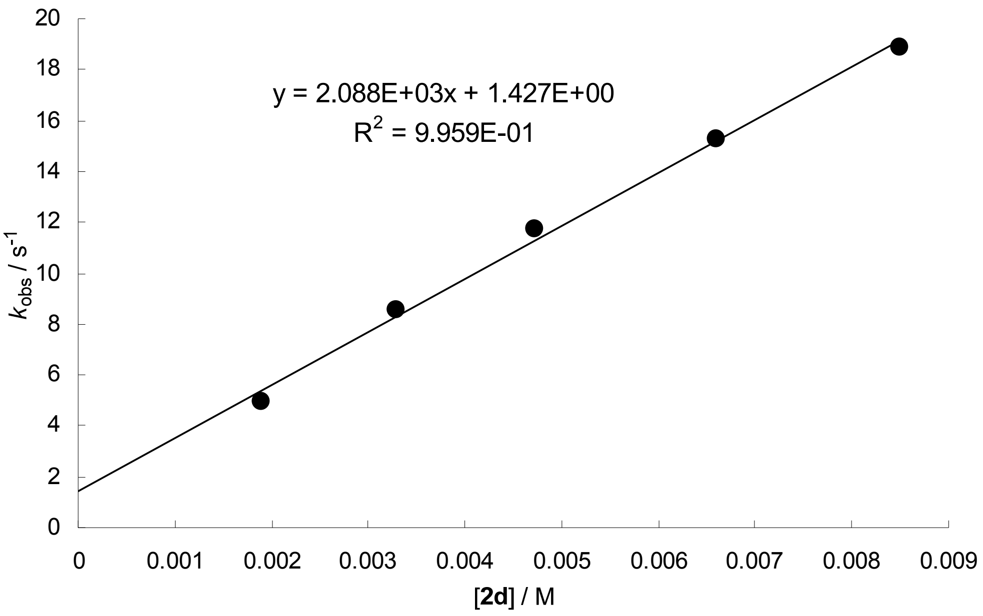
[**1c**] /M	[**2c**] /M	k_{obs} / s^{-1}
1.74×10^{-4}	1.88×10^{-3}	9.82×10^{-1}
1.74×10^{-4}	3.29×10^{-3}	1.71
1.74×10^{-4}	4.70×10^{-3}	2.41
1.74×10^{-4}	6.58×10^{-3}	3.30
1.74×10^{-4}	8.47×10^{-3}	4.20



Reaction of **1c** with **2d** (DMSO, 20 °C, stopped-flow, 330 nm)

$k_2 = 2.09 \times 10^3$ M^{-1} s^{-1}

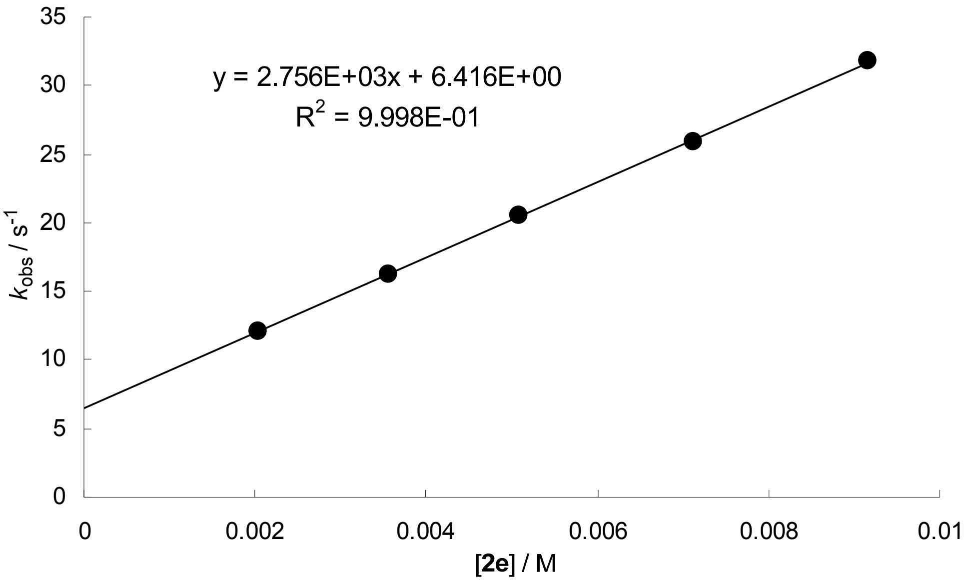
[**1c**] /M	[**2d**] /M	k_{obs} / s^{-1}
1.74×10^{-4}	1.89×10^{-3}	4.94
1.74×10^{-4}	3.30×10^{-3}	8.54
1.74×10^{-4}	4.72×10^{-3}	1.17×10^{1}
1.74×10^{-4}	6.61×10^{-3}	1.53×10^{1}
1.74×10^{-4}	8.50×10^{-3}	1.89×10^{1}



Reaction of **1c** with **2e** (DMSO, 20 °C, stopped-flow, 330 nm)

$k_2 = 2.76 \times 10^3$ M^{-1} s^{-1}

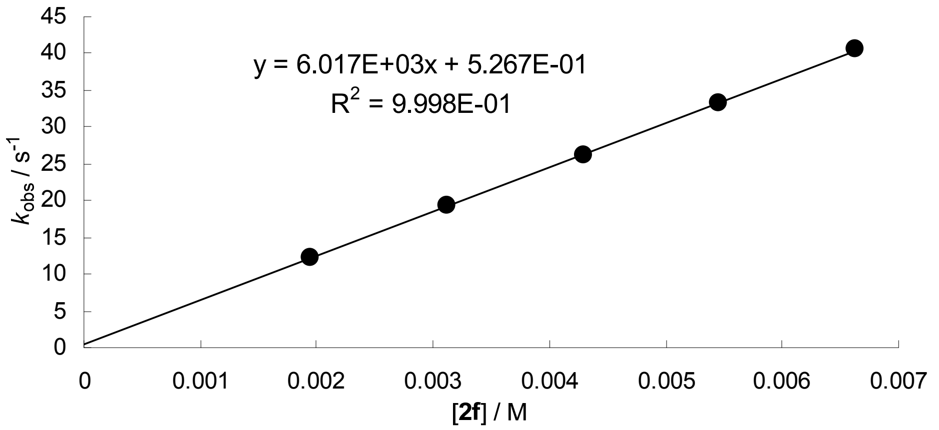
[**1c**] /M	[**2e**] /M	k_{obs} / s^{-1}
1.74×10^{-4}	2.04×10^{-3}	1.21×10^{1}
1.74×10^{-4}	3.57×10^{-3}	1.62×10^{1}
1.74×10^{-4}	5.09×10^{-3}	2.05×10^{1}
1.74×10^{-4}	7.13×10^{-3}	2.59×10^{1}
1.74×10^{-4}	9.17×10^{-3}	3.18×10^{1}



Reaction of **1c** with **2f** (DMSO, 20 °C, stopped-flow, 321 nm)

$k_2 = 6.02 \times 10^3$ M^{-1} s^{-1}

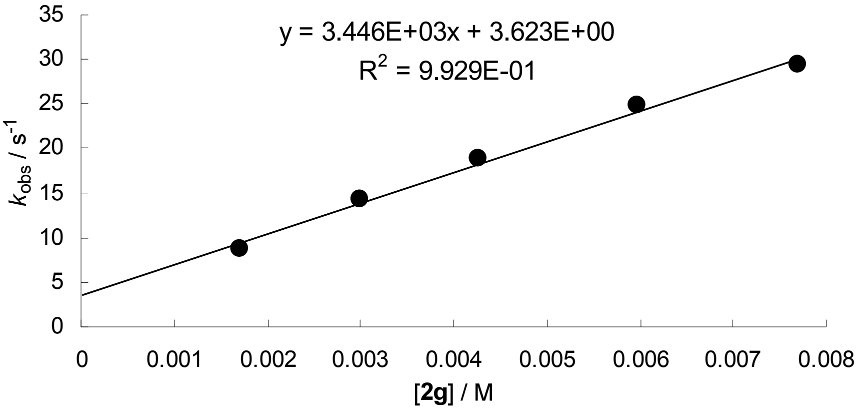
[**1c**] /M	[**2f**] /M	k_{obs} / s^{-1}
1.30×10^{-4}	1.95×10^{-3}	1.23×10^{1}
1.30×10^{-4}	3.12×10^{-3}	1.94×10^{1}
1.30×10^{-4}	4.29×10^{-3}	2.62×10^{1}
1.30×10^{-4}	5.46×10^{-3}	3.32×10^{1}
1.30×10^{-4}	6.63×10^{-3}	4.06×10^{1}



Reaction of **1c** with **2g** (DMSO, 20 °C, stopped-flow, 340 nm)

$k_2 = 3.45 \times 10^3$ M^{-1} s^{-1}

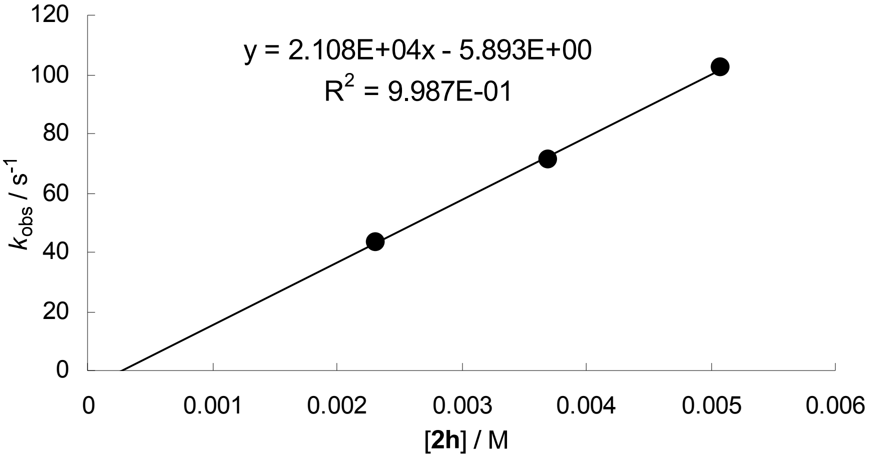
[**1c**] /M	[**2g**] /M	k_{obs} / s^{-1}
1.61×10^{-4}	1.71×10^{-3}	8.74
1.61×10^{-4}	2.99×10^{-3}	1.43×10^{1}
1.61×10^{-4}	4.27×10^{-3}	1.89×10^{1}
1.61×10^{-4}	5.98×10^{-3}	2.48×10^{1}
1.61×10^{-4}	7.69×10^{-3}	2.94×10^{1}



Reaction of **1c** with **2h** (DMSO, 20 °C, stopped-flow, 321 nm)

$k_2 = 2.11 \times 10^4$ M^{-1} s^{-1}

[**1c**] /M	[**2h**] /M	k_{obs} / s^{-1}
1.30×10^{-4}	2.31×10^{-3}	4.34×10^{1}
1.30×10^{-4}	3.70×10^{-3}	7.09×10^{1}
1.30×10^{-4}	5.09×10^{-3}	1.02×10^{2}

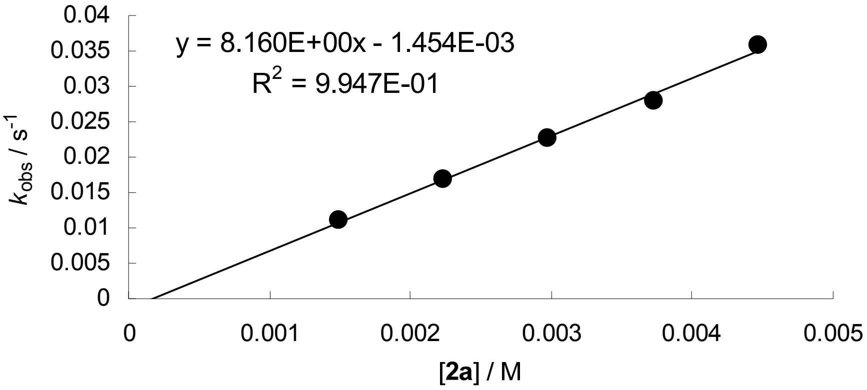

y = 2.108E+04x - 5.893E+00
R2 = 9.987E-01
kobs / s-1
120
100
80
60
40
20
0
0
0.001
0.002
0.003
0.004
0.005
0.006
[2h] / M

2.5.2.4 Kinetics of the Reactions of *trans*-4-Bromo-β-nitrostyrene (1d) with the Carbanions 2 in DMSO

Reaction of **1d** with **2a** (DMSO, 20 °C, conventional, 325 nm)

$k_2 = 8.16\ \mathrm{M^{-1}\ s^{-1}}$

[**1d**] /M	[**2a**] /M	k_{obs} / $\mathrm{s^{-1}}$
9.12×10^{-5}	1.49×10^{-3}	1.11×10^{-2}
9.12×10^{-5}	2.24×10^{-3}	1.68×10^{-2}
9.12×10^{-5}	2.98×10^{-3}	2.26×10^{-2}
9.12×10^{-5}	3.73×10^{-3}	2.80×10^{-2}
9.12×10^{-5}	4.47×10^{-3}	3.59×10^{-2}

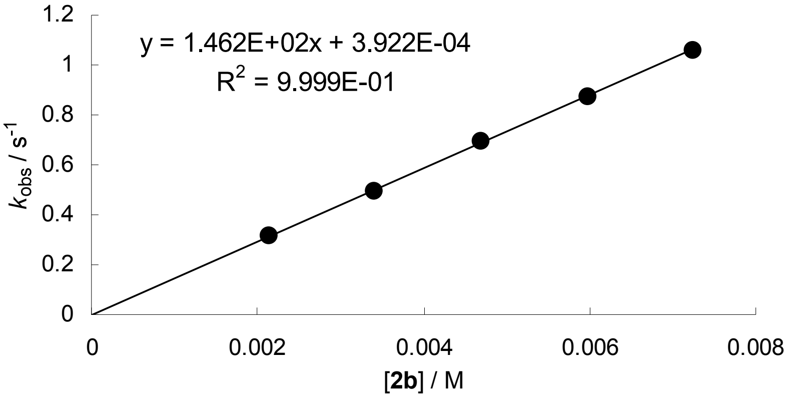


Reaction of **1d** with **2b** (DMSO, 20 °C, stopped-flow, 325 nm)

$k_2 = 1.46 \times 10^{2}\ \mathrm{M^{-1}\ s^{-1}}$

[**1d**] /M	[**2b**] /M	k_{obs} / $\mathrm{s^{-1}}$
1.30×10^{-4}	2.14×10^{-3}	3.14×10^{-1}
1.30×10^{-4}	3.42×10^{-3}	4.96×10^{-1}
1.30×10^{-4}	4.70×10^{-3}	6.92×10^{-1}
1.30×10^{-4}	5.98×10^{-3}	8.75×10^{-1}

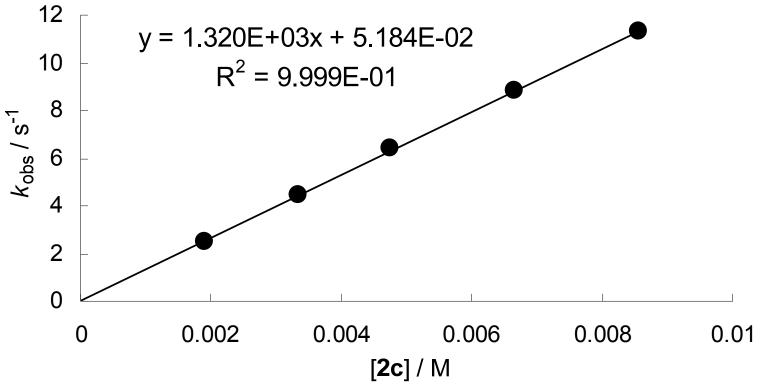
1.30×10^{-4}	7.26×10^{-3}	1.06



Reaction of **1d** with **2c** (DMSO, 20 °C, stopped-flow, 340 nm)

$k_2 = 1.32 \times 10^3$ M^{-1} s^{-1}

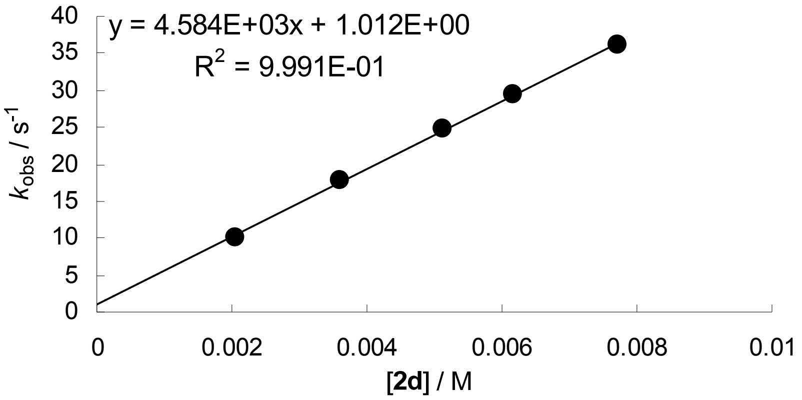
[**1d**] /M	[**2c**] /M	k_{obs} / s^{-1}
1.75×10^{-4}	1.90×10^{-3}	2.52
1.75×10^{-4}	3.33×10^{-3}	4.45
1.75×10^{-4}	4.75×10^{-3}	6.38
1.75×10^{-4}	6.65×10^{-3}	8.85
1.75×10^{-4}	8.55×10^{-3}	1.13×10^1



Reaction of **1d** with **2d** (DMSO, 20 °C, stopped-flow, 330 nm)

$k_2 = 4.58 \times 10^3\ \mathrm{M^{-1}\ s^{-1}}$

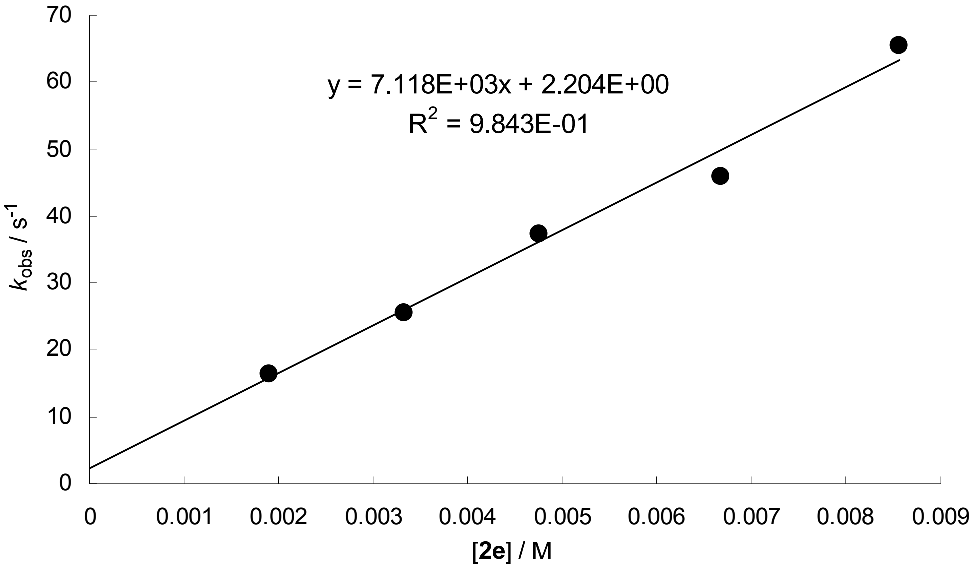
[**1d**] /M	[**2d**] /M	k_{obs} / $\mathrm{s^{-1}}$
1.74×10^{-4}	2.06×10^{-3}	1.01×10^{1}
1.74×10^{-4}	3.60×10^{-3}	1.78×10^{1}
1.74×10^{-4}	5.14×10^{-3}	2.49×10^{1}
1.74×10^{-4}	6.17×10^{-3}	2.93×10^{1}
1.74×10^{-4}	7.71×10^{-3}	3.61×10^{1}



Reaction of **1d** with **2e** (DMSO, 20 °C, stopped-flow, 340 nm)

$k_2 = 7.12 \times 10^3\ \mathrm{M^{-1}\ s^{-1}}$

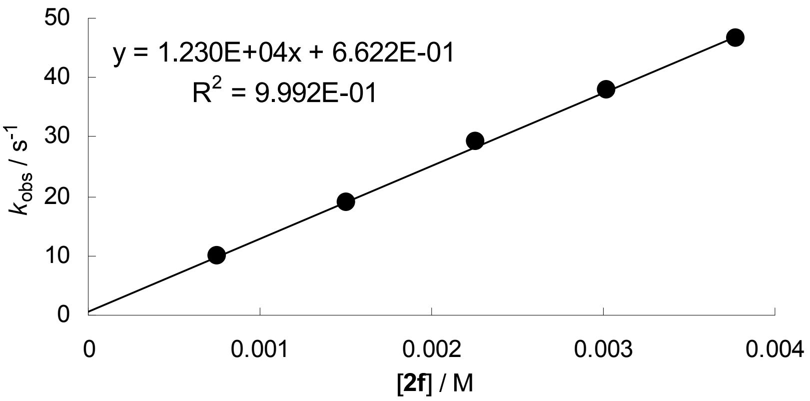
[**1d**] /M	[**2e**] /M	k_{obs} / $\mathrm{s^{-1}}$
1.74×10^{-4}	1.90×10^{-3}	1.64×10^{1}
1.74×10^{-4}	3.33×10^{-3}	2.55×10^{1}
1.74×10^{-4}	4.76×10^{-3}	3.74×10^{1}
1.74×10^{-4}	6.67×10^{-3}	4.58×10^{1}
1.74×10^{-4}	8.57×10^{-3}	6.55×10^{1}



Reaction of **1d** with **2f** (DMSO, 20 °C, stopped-flow, 325 nm)

$k_2 = 1.23 \times 10^4$ M^{-1} s^{-1}

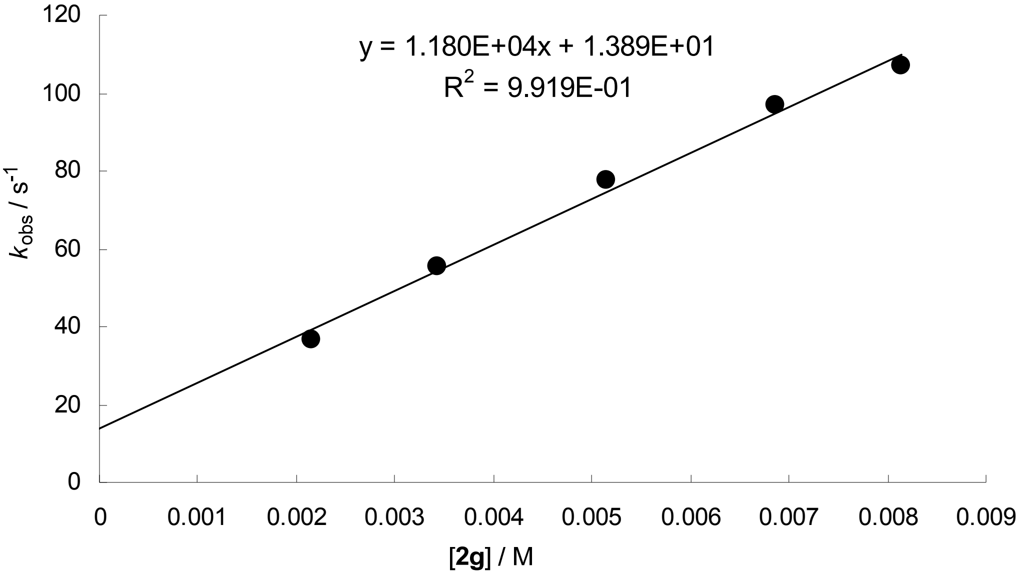
[**1d**] /M	[**2f**] /M	k_{obs} / s^{-1}
6.00×10^{-5}	7.54×10^{-4}	9.83
6.00×10^{-5}	1.51×10^{-3}	1.89×10^{1}
6.00×10^{-5}	2.26×10^{-3}	2.91×10^{1}
6.00×10^{-5}	3.02×10^{-3}	3.79×10^{1}
6.00×10^{-5}	3.77×10^{-3}	4.67×10^{1}



Reaction of **1d** with **2g** (DMSO, 20 °C, stopped-flow, 325 nm)

$k_2 = 1.18 \times 10^4$ M^{-1} s^{-1}

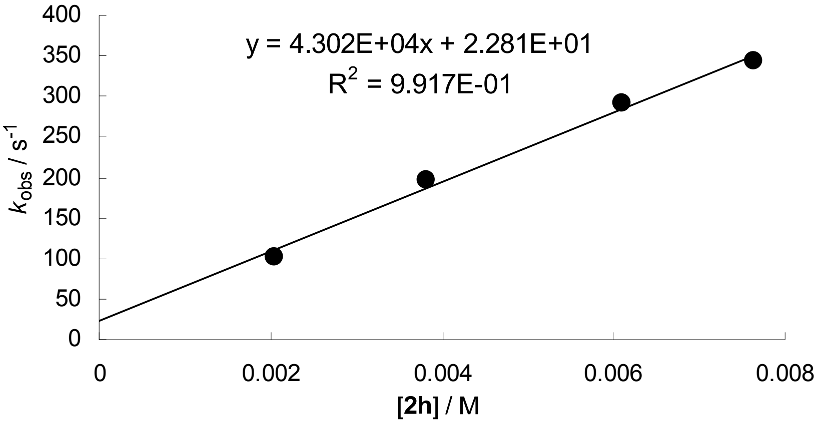
[**1d**] /M	[**2g**] /M	k_{obs} / s^{-1}
1.61×10^{-4}	2.15×10^{-3}	3.68×10^{1}
1.61×10^{-4}	3.43×10^{-3}	5.52×10^{1}
1.61×10^{-4}	5.15×10^{-3}	7.74×10^{1}
1.61×10^{-4}	6.86×10^{-3}	9.67×10^{1}
1.61×10^{-4}	8.15×10^{-3}	1.07×10^{2}



Reaction of **1d** with **2h** (DMSO, 20 °C, stopped-flow, 325 nm)

$k_2 = 4.30 \times 10^4$ M^{-1} s^{-1}

[**1d**] /M	[**2h**] /M	k_{obs} / s^{-1}
1.74×10^{-4}	2.04×10^{-3}	1.02×10^{2}
1.74×10^{-4}	3.82×10^{-3}	1.97×10^{2}
1.74×10^{-4}	6.10×10^{-3}	2.92×10^{2}
1.74×10^{-4}	7.63×10^{-3}	3.43×10^{2}

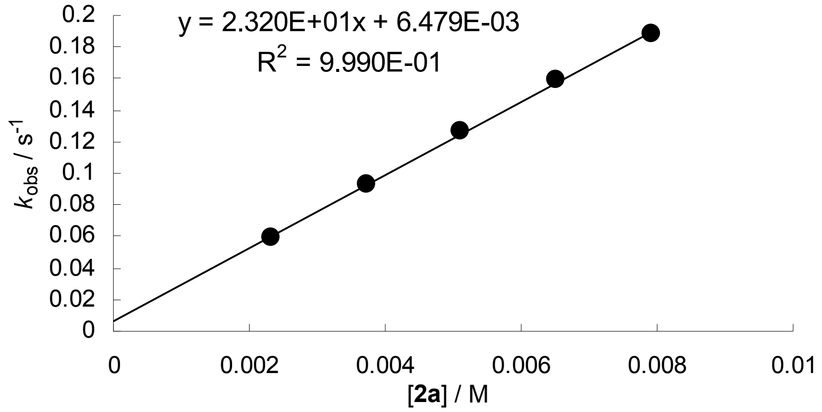

y = 4.302E+04x + 2.281E+01
R2 = 9.917E-01
k_{obs} / s-1
0
50
100
150
200
250
300
350
400
0
0.002
0.004
0.006
0.008
[**2h**] / M

2.5.2.5 Kinetics of the Reactions of *trans*-4-Cyano-β-nitrostyrene (1e) with the Carbanions 2 in DMSO

Reaction of **1e** with **2a** (DMSO, 20 °C, stopped-flow, 310 nm)

$k_2 = 2.32 \times 10^{1}$ M^{-1} s^{-1}

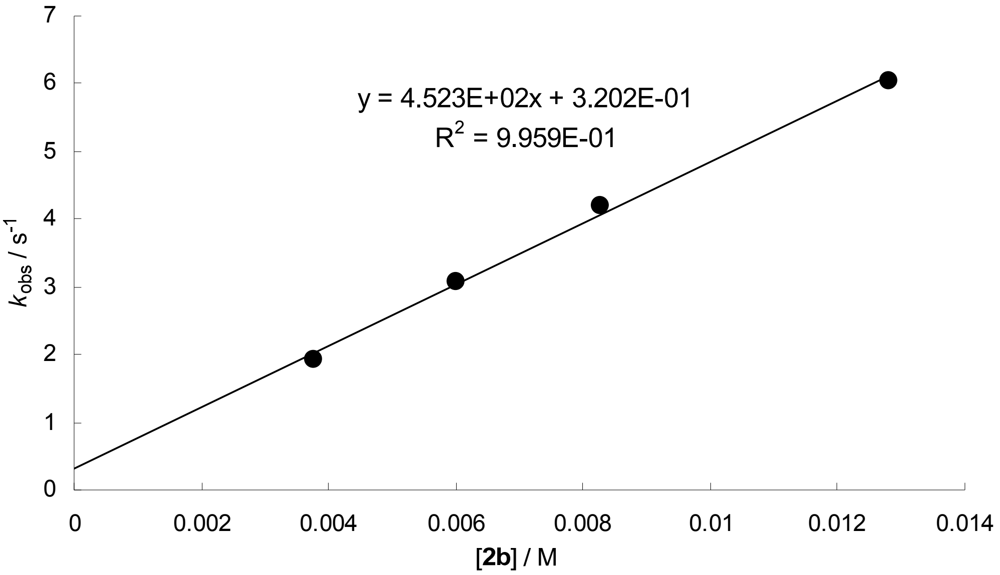
[**1e**] /M	[**2a**] /M	k_{obs} / s^{-1}
1.51×10^{-4}	2.33×10^{-3}	5.94×10^{-2}
1.51×10^{-4}	3.72×10^{-3}	9.26×10^{-2}
1.51×10^{-4}	5.12×10^{-3}	1.27×10^{-1}
1.51×10^{-4}	6.51×10^{-3}	1.59×10^{-1}
1.51×10^{-4}	7.91×10^{-3}	1.88×10^{-1}



Reaction of **1e** with **2b** (DMSO, 20 °C, stopped-flow, 340 nm)

$k_2 = 4.52 \times 10^{2}$ M^{-1} s^{-1}

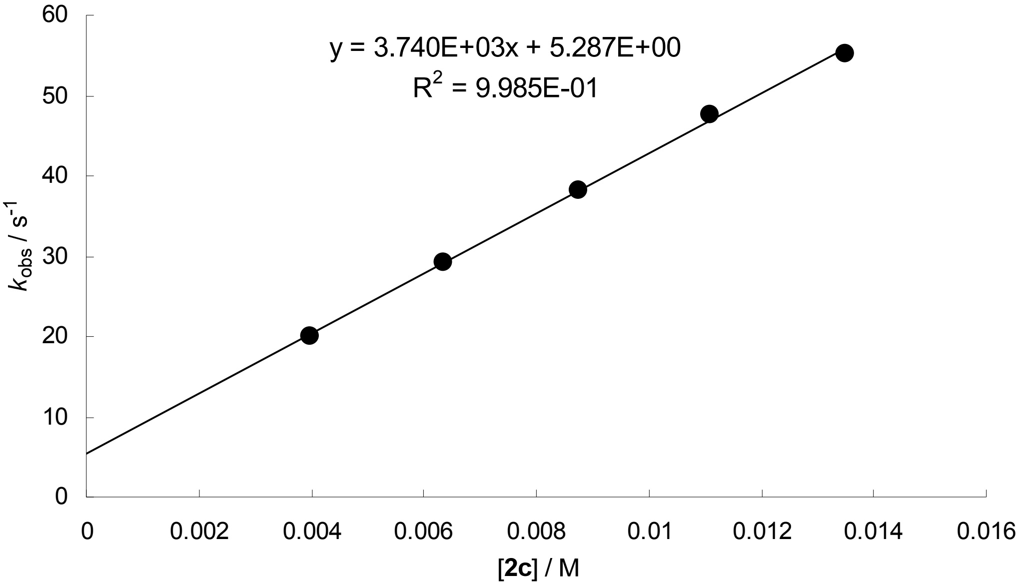
[**1e**] /M	[**2b**] /M	k_{obs} / s^{-1}
3.00×10^{-4}	3.76×10^{-3}	1.92
3.00×10^{-4}	6.01×10^{-3}	3.09
3.00×10^{-4}	8.27×10^{-3}	4.20
3.00×10^{-4}	1.28×10^{-2}	6.04



Reaction of **1e** with **2c** (DMSO, 20 °C, stopped-flow, 340 nm)

$k_2 = 3.74 \times 10^3$ M^{-1} s^{-1}

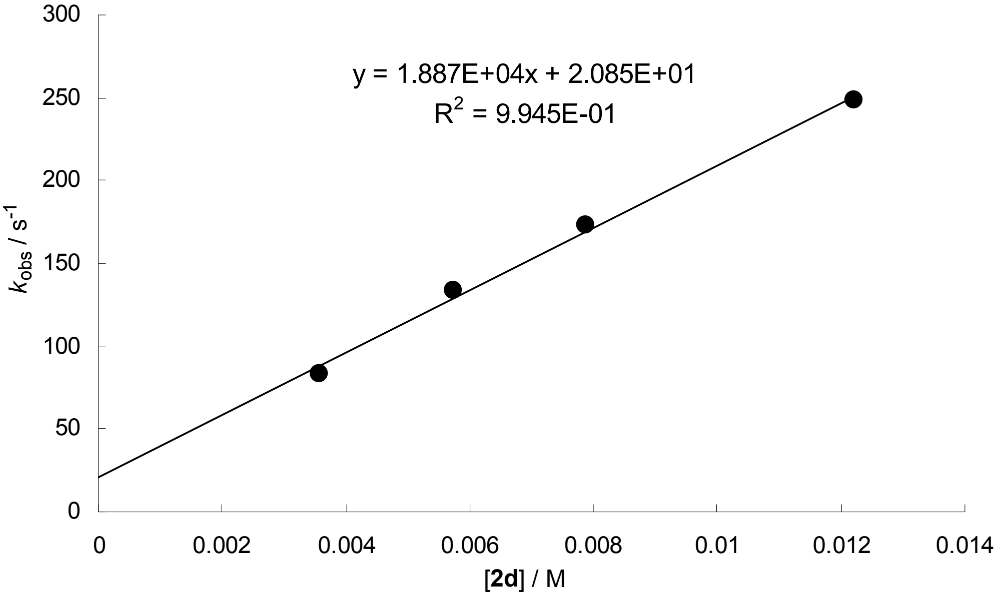
[**1e**] /M	[**2c**] /M	k_{obs} / s^{-1}
3.00×10^{-4}	3.98×10^{-3}	1.99×10^{1}
3.00×10^{-4}	6.37×10^{-3}	2.91×10^{1}
3.00×10^{-4}	8.76×10^{-3}	3.82×10^{1}
3.00×10^{-4}	1.11×10^{-2}	4.76×10^{1}
3.00×10^{-4}	1.35×10^{-2}	5.52×10^{1}



Reaction of **1e** with **2d** (DMSO, 20 °C, stopped-flow, 340 nm)

$k_2 = 1.89 \times 10^4$ M^{-1} s^{-1}

[**1e**] /M	[**2d**] /M	k_{obs} / s^{-1}
3.00×10^{-4}	3.58×10^{-3}	8.28×10^{1}
3.00×10^{-4}	5.73×10^{-3}	1.34×10^{2}
3.00×10^{-4}	7.87×10^{-3}	1.73×10^{2}
3.00×10^{-4}	1.22×10^{-2}	2.48×10^{2}

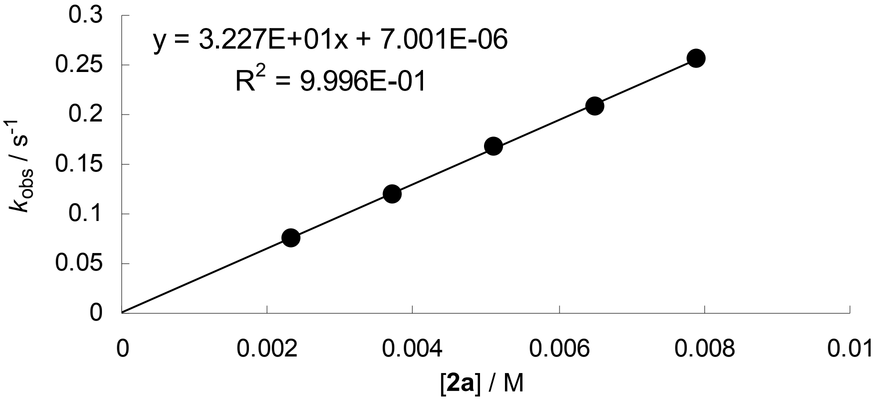


2.5.2.6 Kinetics of the Reactions of *trans*-4-Nitro-*β*-nitrostyrene (1f) with the Carbanions 2 in DMSO

Reaction of **1f** with **2a** (DMSO, 20 °C, stopped-flow, 317 nm)

$k_2 = 3.23 \times 10^1$ M^{-1} s^{-1}

[**1f**] /M	[**2a**] /M	k_{obs} / s^{-1}
1.51×10^{-4}	2.33×10^{-3}	7.49×10^{-2}
1.51×10^{-4}	3.72×10^{-3}	1.20×10^{-1}
1.51×10^{-4}	5.12×10^{-3}	1.67×10^{-1}
1.51×10^{-4}	6.51×10^{-3}	2.08×10^{-1}
1.51×10^{-4}	7.91×10^{-3}	2.56×10^{-1}

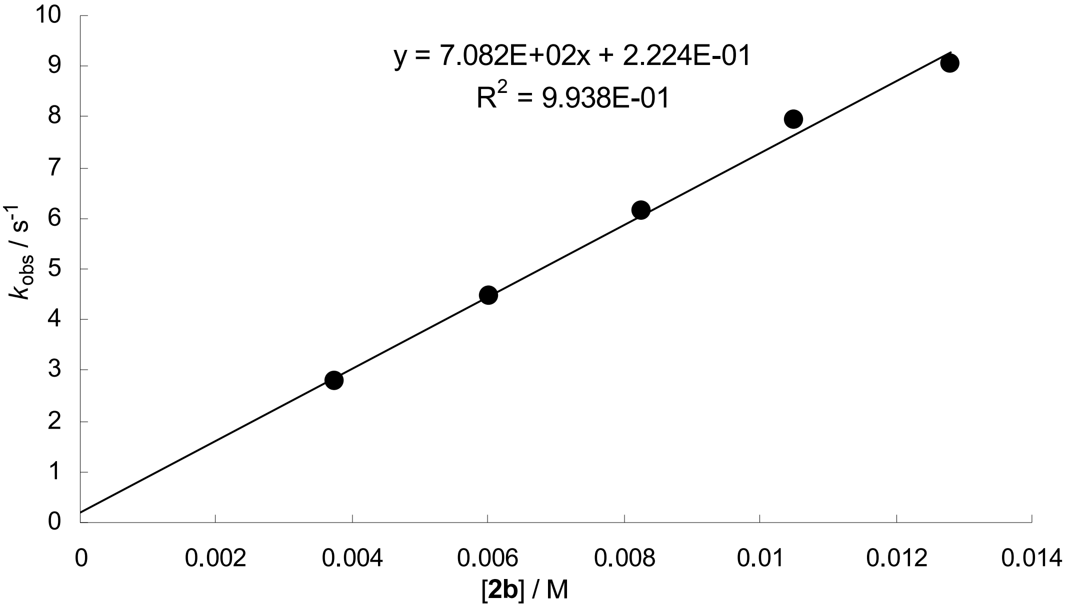


Reaction of **1f** with **2b** (DMSO, 20 °C, stopped-flow, 340 nm)

$k_2 = 7.08 \times 10^2$ M^{-1} s^{-1}

[**1f**] /M	[**2b**] /M	k_{obs} / s^{-1}
2.50×10^{-4}	3.76×10^{-3}	2.79
2.50×10^{-4}	6.01×10^{-3}	4.46
2.50×10^{-4}	8.27×10^{-3}	6.15

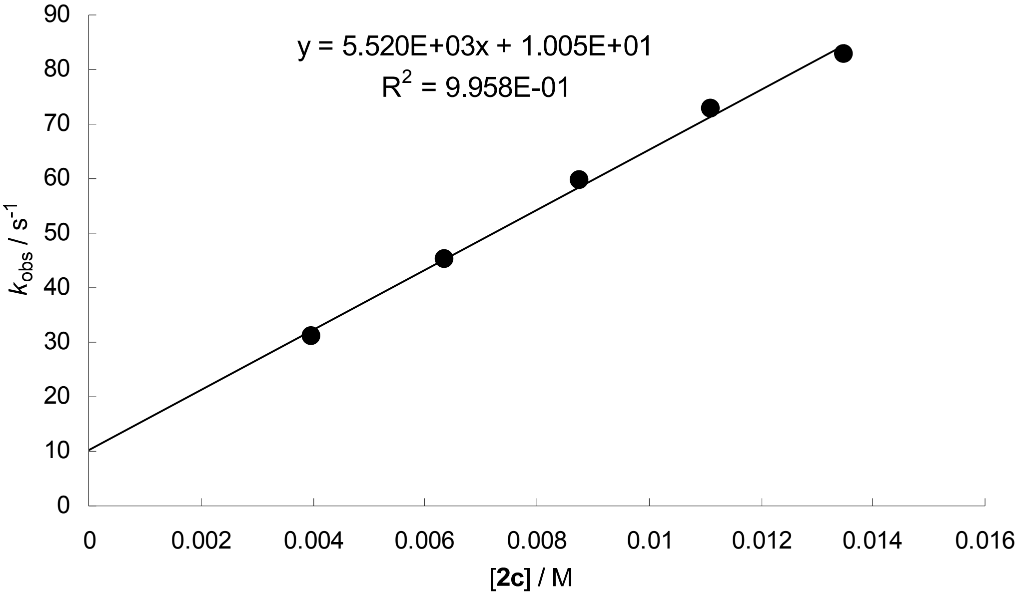
2.50×10^{-4}	1.05×10^{-2}	7.95
2.50×10^{-4}	1.28×10^{-2}	9.05



Reaction of **1f** with **2c** (DMSO, 20 °C, stopped-flow, 340 nm)

$k_2 = 5.52 \times 10^3$ M^{-1} s^{-1}

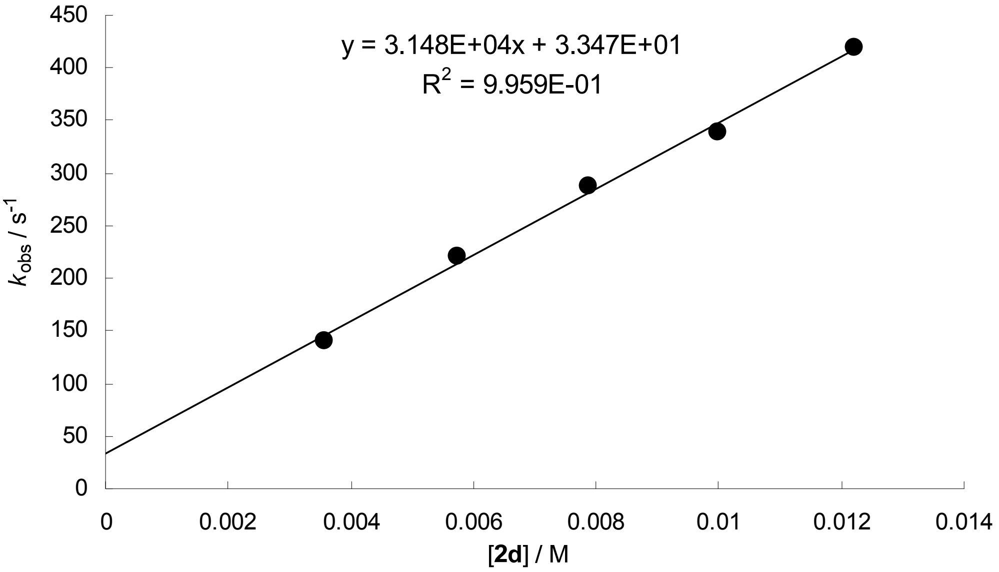
[**1f**] /M	[**2c**] /M	k_{obs} / s^{-1}
2.50×10^{-4}	3.98×10^{-3}	3.11×10^{1}
2.50×10^{-4}	6.37×10^{-3}	4.51×10^{1}
2.50×10^{-4}	8.76×10^{-3}	5.97×10^{1}
2.50×10^{-4}	1.11×10^{-2}	7.27×10^{1}
2.50×10^{-4}	1.35×10^{-2}	8.29×10^{1}



<u>Reaction of **1f** with **2d** (DMSO, 20 °C, stopped-flow, 330 nm)</u>

$k_2 = 3.15 \times 10^4$ M^{-1} s^{-1}

[**1f**] /M	[**2d**] /M	k_{obs} / s^{-1}
2.50×10^{-4}	3.58×10^{-3}	1.41×10^{2}
2.50×10^{-4}	5.73×10^{-3}	2.20×10^{2}
2.50×10^{-4}	7.87×10^{-3}	2.87×10^{2}
2.50×10^{-4}	1.00×10^{-2}	3.39×10^{2}
2.50×10^{-4}	1.22×10^{-2}	4.20×10^{2}

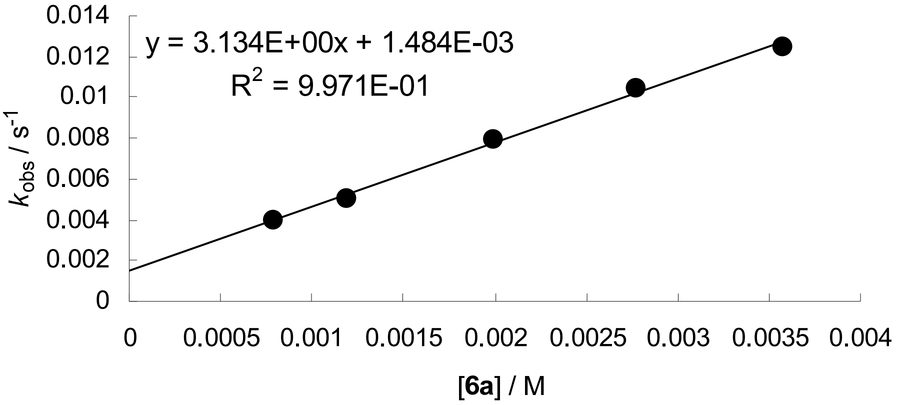


2.5.2.7 Kinetics of the Reactions of the *trans*-*β*-Nitrostyrenes 1b,c with 1-Pyrrolidinocyclohexene (6a) and 1-Piperidinocyclopentene (6b) in Dichloromethane

Reaction of **1b** with **6a** (dichloromethane, 20 °C, conventional, 335 nm)

$k_2 = 3.13\ \mathrm{M^{-1}\ s^{-1}}$

[**1b**] /M	[**6a**] /M	k_{obs} / s^{-1}
5.69×10^{-5}	7.96×10^{-4}	3.96×10^{-3}
5.69×10^{-5}	1.19×10^{-3}	5.04×10^{-3}
5.69×10^{-5}	1.99×10^{-3}	7.91×10^{-3}
5.69×10^{-5}	2.78×10^{-3}	1.04×10^{-2}
5.69×10^{-5}	3.58×10^{-3}	1.25×10^{-2}

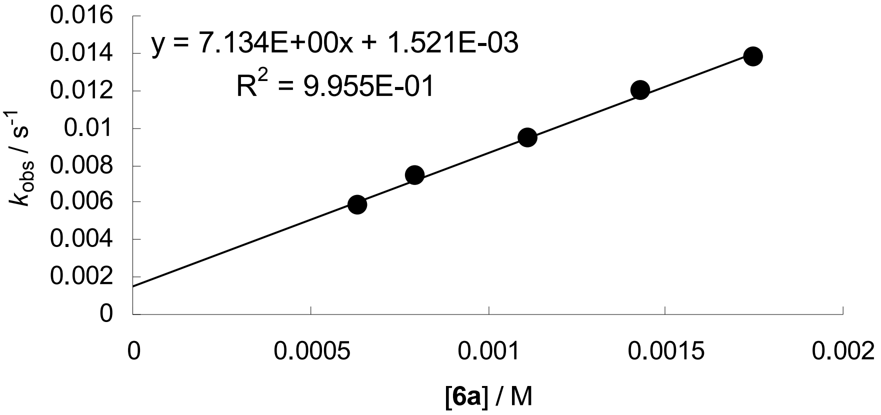


Reaction of **1c** with **6a** (dichloromethane, 20 °C, conventional, 321 nm)

$k_2 = 7.13\ \mathrm{M^{-1}\ s^{-1}}$

[**1c**] /M	[**6a**] /M	k_{obs} / s^{-1}
5.36×10^{-5}	6.36×10^{-4}	5.84×10^{-3}
5.36×10^{-5}	7.96×10^{-4}	7.38×10^{-3}
5.36×10^{-5}	1.11×10^{-3}	9.45×10^{-3}
5.36×10^{-5}	1.43×10^{-3}	1.20×10^{-2}

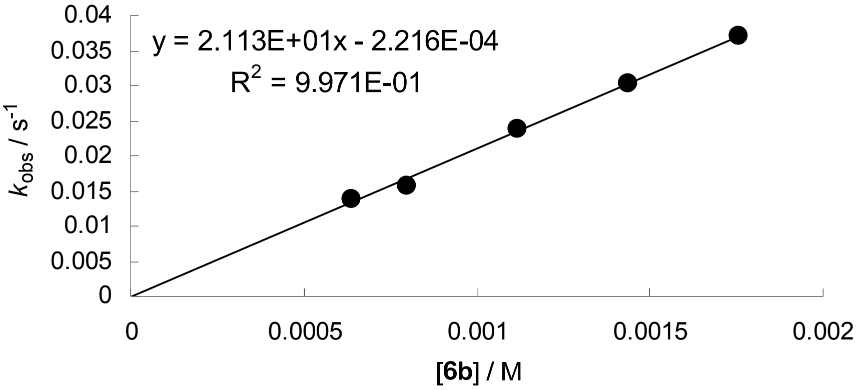
5.36×10^{-5}	1.75×10^{-3}	1.38×10^{-2}



Reaction of **1c** with **6b** (dichloromethane, 20 °C, conventional, 321 nm)

$k_2 = 2.11 \times 10^1\ \mathrm{M}^{-1}\ \mathrm{s}^{-1}$

[**1c**] /M	[**6b**] /M	k_{obs} / s^{-1}
5.36×10^{-5}	6.38×10^{-4}	1.38×10^{-2}
5.36×10^{-5}	7.98×10^{-4}	1.58×10^{-2}
5.36×10^{-5}	1.12×10^{-3}	2.37×10^{-2}
5.36×10^{-5}	1.44×10^{-3}	3.03×10^{-2}
5.36×10^{-5}	1.76×10^{-3}	3.69×10^{-2}



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Chapter 3: Electrophilicities of Aliphatic Nitroolefins

3.1 Introduction

The chemistry of aliphatic nitroolefins **1** is dominated by the powerful electron-withdrawing nitro group, which makes them highly reactive Michael acceptors.[1,2] Often described as a "synthetic chameleon",[3,4,5] the nitro group can be further transformed after the initial addition, e. g., by the Nef reaction,[6,7] Meyer reaction,[8,9] nucleophilic displacement,[10] conversion into a nitrile,[11] amino group[12] or the formation of a cyclic nitronate.[13]

Highly enantioselective thiourea-catalyzed Michael additions of aldehydes,[14] ketones,[15] diphenyl phosphonates,[16] and oxindoles[17] to nitroolefins have recently been reported. Enamine activation in reactions of nitroolefins with aldehydes has attracted great interest.[18,19,20,21] Tripeptides[22] have been employed as catalysts in highly diastereo- and enantioselective reactions of aldehydes with nitroethylene[23] and other nitroalkenes[24,25] using as little as 0.1% catalyst loading.[26] Furthermore, thiophosphoramides[27] and bimorpholines,[28] have been used as catalysts for the addition of aliphatic aldehydes to nitroolefins.

Additions of *β*-ketoesters to nitroethylene have been performed with dinuclear Ni_2-Schiff base complexes[29] and Pd-N-heterocyclic carbene complexes[30] as catalysts. Tetrahydropyrans have been synthesized through tandem oxa-Michael Tsuji-Trost reactions employing a variety of nitroolefins.[31] *γ*-Amino acids as building blocks for peptide synthesis were obtained by reactions of acyloxazolidinones with nitroolefins.[32] In addition, [4+2]-cycloadditions[33,34] and tandem [4+2]/[3+2] cycloadditions[35] with nitroethylene, as well as tandem double-intramolecular [4+2]/[3+2] cycloadditions[36] of nitroalkenes have been reported. Kinetics of the reactions of furyl-substituted nitroethylenes with amines have been investigated.[37]

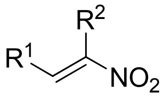
In previous work, we have shown that a large variety of reactions of electrophiles with nucleophiles can be described by eq 3.1, where N and s_N (previously called s) are nucleophile-specific parameters, E is an electrophilicity parameter, and k_2 is the second-order rate constant.[38]

$$\log k_2(20\ °\mathrm{C}) = s_N(N + E) \qquad (3.1)$$

Diarylcarbenium ions and structurally related Michael acceptors have been employed as reference electrophiles for the determination of the nucleophile-specific parameters N and s_N of neutral and anionic nucleophiles.[39,40]

On the other hand, the kinetics of the reactions of carbanions with Michael acceptors such as quinone methides,[41,42,43] benzylidenemalononitriles,[44] benzylidene-1,3-indandiones,[45] benzylidenebarbituric- and thiobarbituric acids,[46] benzylidene Meldrum´s acids,[47] *trans-β*-nitrostyrenes,[48] bissulfonylethylenes,[49] unsaturated acylazolium ions[50] and iminium ions[51,52] have been employed to determine the E parameters of these electrophiles according to eq 3.1. We will now report on the kinetics of the reactions of the nitroolefins **1a**–**e** (Scheme 3.1) with the stabilized carbanions **2a**–**g** (Table 3.1) in DMSO and demonstrate that the second-order rate constants k_2 of these reactions follow eq 3.1. These rate constants will then be used for the determination of the E parameters for the nitroolefins **1a**–**e** as part of our program of developing comprehensive nucleophilicity and electrophilicity scales.[53,54,55,56]

SCHEME 3.1. Structures of the Nitroolefins 1a–e.



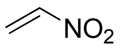
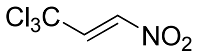
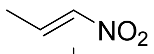
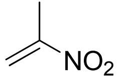
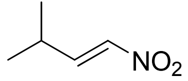
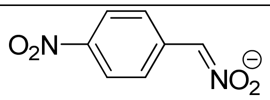
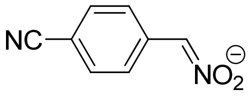
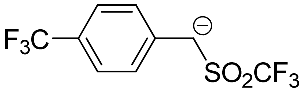
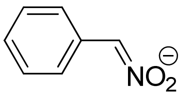
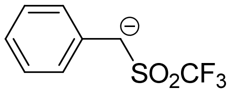
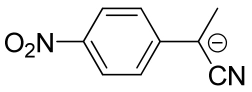
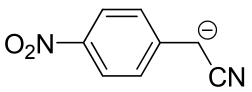
R^1	R^2		
H	H		**1a**
CCl_3	H		**1b**
Me	H		**1c**
H	Me		**1d**
i-Pr	H		**1e**

TABLE 3.1. Reactivity Parameters *N* and s_N and λ_{max} of the Carbanions 2a–g in DMSO.

	Nucleophile	N, s_N	λ_{max} [nm]
2a		16.29, 0.75[a]	512
2b		16.96, 0.73[a]	401
2c		17.33, 0.74[b]	316
2d		18.29, 0.71[a]	344
2e		18.67, 0.68[b]	290
2f		19.61, 0.60[c]	550
2g		19.67, 0.68[c]	539

[a] Ref 41. [b] Ref 60. [c] Ref 61.

3.2 Results

As additions of carbanions to nitroolefins have extensively been studied earlier, product studies have only been performed for representative combinations of **1a–e** with **2a–g**. The numbering of the adducts described in this chapter can be derived from the formula abbreviations **4xy**: The first letter identifies the electrophile and the second letter identifies the nucleophile (Table 3.2). Thus, compound **4af** is an adduct from the nitroolefin **1a** and the carbanion **2f**. The adducts **4ac–ag** and **4cf–eg** were obtained in 48-82% yield by combining the nitroolefins **1** with 1 equiv. of **2-Li** or **2-K** in THF at –90 °C yield followed by acidic workup, according to a procedure described by Seebach[3,57] (Scheme 3.2). **4bf** and **4bg** were generated from **1b** with equimolar amounts of **2-H** and NaOMe in MeOH at 0 °C and isolated in 63 and 71% yield after acidic workup.[58] **4cd** was synthesized from **1c** and 1.25 equivalents of **2d-H** in CH_2Cl_2 in the presence of NEt_3 (1 mol%) following a report by Brunner and Kimel.[59]

SCHEME 3.2. Reactions of the Nitroolefins 1a–e with the Carbanions 2a–g.

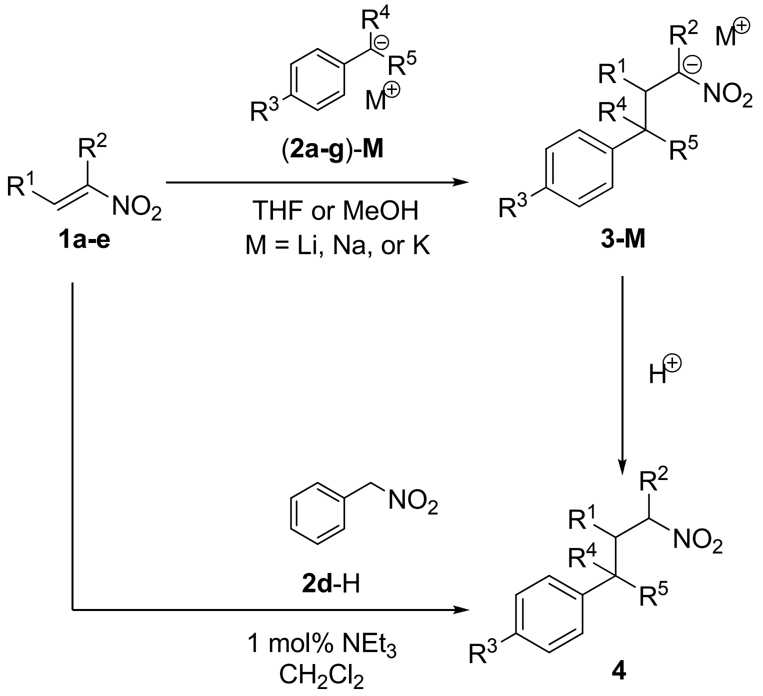
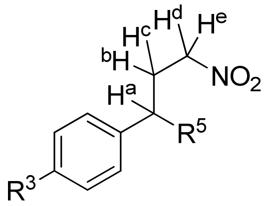


TABLE 3.2. Characteristic ^{1}H NMR Chemical Shifts[a] of the Michael Adducts 4.

Electrophile	Nucleophile	Product	Yield (%)	δ(H^a)	δ(H^b)	δ(H^c)	δ(H^d)	δ(H^e)
1a	**2c**	**4ac**	62	4.76	3.19	2.75	4.55	4.21
1a	**2e**	**4ae**	48	4.67	3.15	2.75	4.49	4.21
1a	**2f**	**4af**	82		2.73	2.78	4.56	4.28
1a	**2g**	**4ag**	72	4.22	2.64	2.58	4.66	4.52
1b	**2f**	**4bf**	71[b]		4.43		5.03	4.37
1b	**2g**	**4bg**	63[c]	5.06	4.05		5.13	4.81
1c	**2d**	**4cd**[d]	54[e]	5.52	3.38		4.07	4.23
1c	**2f**	**4cf**	55[f]		2.96		4.23	4.08
1d	**2g**	**4dg**	61[g]	4.03	2.59	2.22	4.93	
1e	**2g**	**4eg**	63[h]	4.31	2.72		4.55	4.41

[a] Chemical shifts (in ppm) extracted by using DAVINX software (ref 78). Chemical shifts for diastereomeric mixtures refer to the major isomer. [b] Yield of mixture of diastereomers (dr ~ 3:1). [c] Yield of mixture of diastereomers (dr ~ 3:1). [d] From **1c** and nitromethane **2d–H** (1.25 equiv.) in the presence of NEt_3 (1 mol%), as reported in ref 59. [e] Yield of mixture of diastereomers (dr ~ 7:3). [f] Yield of mixture of diastereomers (dr ~ 6:4). [g] Yield of mixture of diastereomers (dr ~ 9:1). [h] Yield of mixture of diastereomers (dr ~ 54:46).

SCHEME 3.3. Positions of the Protons for the Products 4ac–eg (Example shown with R^1, R^2 and R^4 = H).



The Michael adducts show ^{1}H NMR spectra with resonances in the range of $\delta = 4.0$ to 5.5 ppm for H^a, $\delta = 2.2$ to 4.4 ppm for H^b and H^c, and $\delta = 4.1$ to 5.1 ppm for H^d and H^e (Scheme 3.3).

The kinetic investigations were performed at 20 °C in DMSO as the solvent. The carbanions **2a–g** were generated by treatment of the corresponding CH-acids with 1.05 equivalents of potassium *tert*-butoxide, which had been demonstrated to be sufficient for the complete deprotonation of the CH-acids **2a-H** to **2g-H**.[60,61] The solutions thus obtained were directly used for the kinetic investigations at 20 °C, where the rates of the consumption of the carbanions **2a–g** (λ_{max} = 290–550 nm) were followed photometrically at their absorption maxima.

Due to an overlap of the absorption bands with the nitroethylenes or anionic products or partial consumption of the carbanions, the absorbances did not reach zero in all reactions investigated. For the reactions of **1a** and **1c** with **2f**, the equilibrium constants have been measured by UV-vis spectroscopy. Assuming proportionality between the absorbances and the concentrations of the carbanion (as for the evaluation of the kinetic experiments), the equilibrium constants for the reactions (eq 3.2) can be determined from the initial absorbances (A_0) of the carbanion **2f** and the absorbances at equilibrium (A) according to eq 3.3, and the results are listed in Table 3.3.

$$\mathrm{R_2\overset{\ominus}{C}H} + \mathrm{E} \underset{\text{DMSO}}{\overset{K}{\rightleftharpoons}} \mathrm{R_2CH{-}\overset{\ominus}{E}} \qquad (3.2)$$

$$K = \frac{[\mathrm{R_2CH{-}\overset{\ominus}{E}}]}{[\mathrm{R_2\overset{\ominus}{C}H}]\,[\mathrm{E}]} = \frac{A_0 - A}{A\,[E]} \qquad (3.3)$$

The reaction of **2f** with **1c** is slightly more reversible than the reaction of **2f** with **1a**, because **4cf** is a less stabilized carbanion compared to **4af**. For the reaction of **1e** with **2f**, the corresponding equilibrium constant could not be determined, however, because of unknown subsequent reactions.

TABLE 3.3. Equilibrium Constants K and the Reverse Rate Constants ($k_{\leftarrow}$) for the Reactions of the Nitroolefins 1a,c with the Carbanion 2f in DMSO at 20 °C.

Electrophile	Nucleophile	K [M^{-1}]	$k_{\leftarrow}{}^{a}$ [s^{-1}]
1a	**2f**	5.14×10^{3}	2.72
1c	**2f**	4.34×10^{3}	3.39×10^{-1}

[a] $k_{\leftarrow} = k/K$.

While the reaction of **1e** with the carbanion **2c** was studied by conventional UV-vis spectroscopy ($\tau_{1/2}$ > 30 s), the stopped-flow technique was employed in all other cases. By using a high excess of the nitroolefins **1** (10–100 equiv.), pseudo-first-order conditions were achieved (eq 3.4). In all cases, we observed monoexponential decays of the absorbances of the carbanions **2a–g**.

$$-\mathrm{d}[\mathbf{1}]/\mathrm{d}t = k_{\mathrm{obs}}[\mathbf{1}] \tag{3.4}$$

The first-order rate constants k_{obs} were obtained by least-squares fitting of the time-dependent absorbances A_t of the nucleophiles to the exponential function $A_t = A_0\, \mathrm{e}^{-k_{\mathrm{obs}}t} + C$. As shown in Figure 3.1 for the reaction of **1d** with **2f**, plots of k_{obs} versus the concentrations of the nitroolefins [**1**] were linear, and the slopes of these correlations gave the second-order rate constants k_2 listed in Table 3.4.

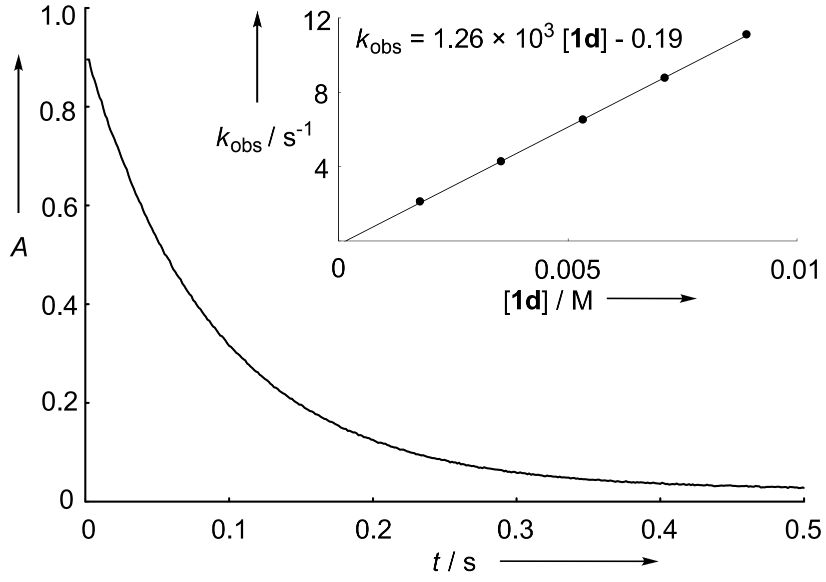


FIGURE 3.1. Exponential Decay of the Absorbance (*A* at λ = 550 nm) for the Reaction of 2f ($c = 9.08 \times 10^{-5}$ M) with 1d ($c = 8.90 \times 10^{-3}$ M) in DMSO at 20 °C. Insert: Linear Correlation of the pseudo-first-order Rate Constants k_{obs} *vs.* [1d].

TABLE 3.4. Second-Order Rate Constants k_2 for the Reactions of the Carbanions 2a–g with the Nitroolefins 1a–e in DMSO at 20 °C.

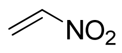
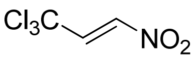
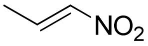
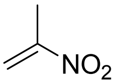
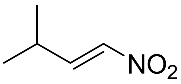
1	E^a	**2**	k_2^{exp} (M^{-1} s^{-1})	k_2^{calcd} (M^{-1} s^{-1})	k_2^{exp}/k_2^{calcd}
1a	–12.36	**2a**	8.98×10^2	8.86×10^2	1.01
		**2c**	7.88×10^3	4.76×10^3	1.65
		2d	1.68×10^4	1.62×10^4	1.04
		2e	1.69×10^4	1.95×10^4	0.87
		2f	1.40×10^4	2.24×10^4	0.63
		2g	9.19×10^4	9.35×10^4	0.99
1b	–13.68	**2a**	9.18×10^1	9.07×10^1	1.01
		**2b**	2.67×10^2	2.48×10^2	1.08
		2f	2.24×10^3	3.61×10^3	0.62
		2g	1.66×10^4	1.18×10^4	1.40

TABLE 3.4. (Continued).

1c	–14.10	**2a**	4.22×10^1	4.39×10^1	0.96
		**2d**	1.16×10^3	9.44×10^2	1.23
		2e	1.32×10^3	1.28×10^3	1.03
		2f	1.47×10^3	2.02×10^3	0.73
		2g	6.40×10^3	6.13×10^3	1.04
1d	–14.16	**2b**	1.49×10^2	1.11×10^2	1.35
		**2d**	1.04×10^3	8.56×10^2	1.22
		2e	1.19×10^3	1.17×10^3	1.02
		2f	1.26×10^3	1.86×10^3	0.68
		2g	4.53×10^3	5.58×10^3	0.81
1e	–15.72	**2b**	1.01×10^1	8.04	1.26
		**2c**	1.24×10^1	1.55×10^1	0.80
		2d	1.16×10^2	6.68×10^1	1.74
		2e	1.44×10^2	1.01×10^2	1.42
		2f	1.16×10^2	2.16×10^2	0.54
		2g	3.25×10^2	4.85×10^2	0.67

[a] The E parameters for **1a–e** result from a least-squares minimization of the sum of Δ^2, with $\Delta = \log k_2^{\mathrm{exp}} - s_{\mathrm{N}}(N + E)$; k_2^{exp} taken from this table, N and s_{N} of the carbanions **2a–g** from Table 3.1.

3.3 Discussion

The rate constants k_2 listed in Table 3.4 reveal, that the reactivity order of the carbanions **2a**–**g** toward nitroolefins is generally the same as toward benzhydrylium ions and quinone methides, the reference electrophiles of our scales. Slight deviations from this order will be discussed below.

Substitution of the rate constants k_2 (Table 3.4) and of the previously published parameters N and s_N of the carbanions (Table 3.1) into eq 3.1 allows one to calculate the electrophilicity parameters E for the nitroolefins **1a**–**e**. The values of E, which are listed in Table 3.4, were obtained by minimizing the sum of Δ^2, i.e., the squares of the deviations between experimental and calculated rate constants, $\Delta = (\log k_2^{\text{exp}}) - s_N(N + E)$.

The correlations in Figure 3.2 illustrate that the rate constants for the reactions of **1a**–**e** with the carbanions **2a**–**g** are satisfactorily reproduced by eq 3.1, i.e., the experimental points are close to the calculated correlation lines, the slopes of which are fixed at 1.0. Some systematic deviations are obvious, however. Thus, the anion of 2-(4-nitrophenyl)propanenitrile (**2f**) reacts more slowly with all nitroolefins than expected from its N value. Either the tertiary carbanion **2f** behaves differently toward nitroolefins and the reference electrophiles or the published N value of **2f** requires revision. The last column of Table 3.4 quantifies these deviations and shows that calculated and experimental rate constants always agree within a factor of 2, which we consider tolerable in view of the fact that the reactivity parameters N and s_N for **2a**–**g** have been derived from reactions with benzhydrylium ions, quinone methides,[62,63,64] benzylidene-1,3-indandiones,[65] benzylidenebarbituric acids,[66] and diethyl benzylidenemalonates[67] and were not adjusted to the reactions with the electrophiles studied in this work.

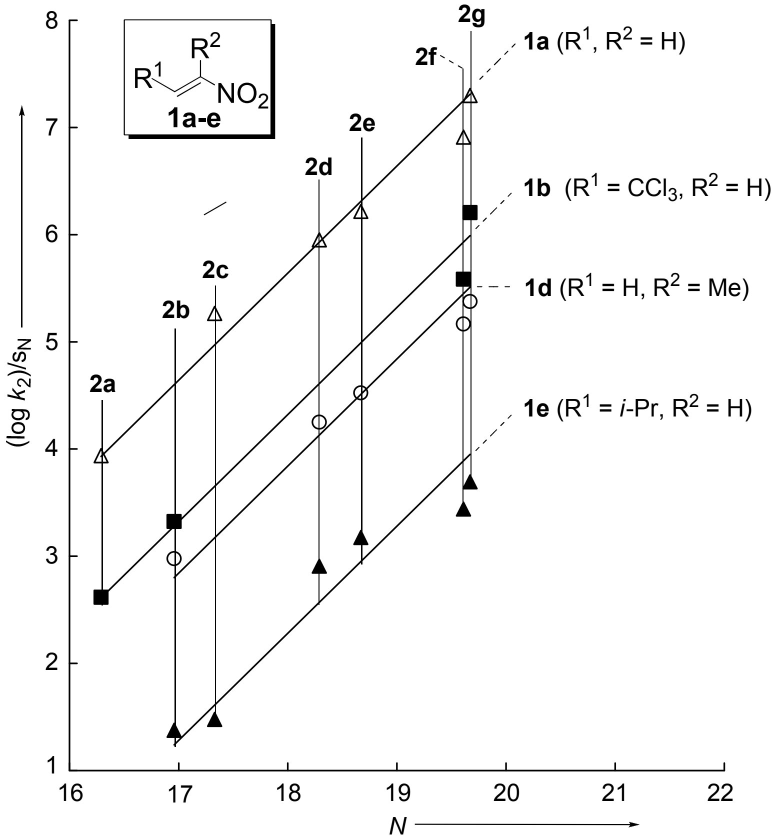


FIGURE 3.2. Correlation of (log k_2)/s_N versus the Nucleophilicity Parameters N of the Carbanions 2a–g for their Reactions with the Nitroolefins 1a, 1b, 1d and 1e in DMSO at 20 °C. The Correlation Lines are Fixed at a Slope of 1.0, as Required by Eq 3.1.

The nucleophilic reactivities of most carbanions (but not of all; for **2c** and **2e** see ref 60) are smaller in protic solvents, and the nucleophilicity parameters of the arylnitronates **2a** and **2b** have been reported to be two to three logarithmic units smaller in methanol than in DMSO.[68] Since Table 3.5 shows an agreement of calculated and experimental rate constants for the reactions of **1c** with **2a** and of **1d** with **2b** in methanol within a factor of 5, we can conclude that the electrophilicity parameters E for the nitroolefins determined in this work can also be treated as solvent-independent. As discussed in detail recently,[69] this does not mean that we are claiming identical solvation of electrophiles in different solvents, but that in a first approximation solvation effects on such reactions can entirely be shifted into the nucleophile-specific parameters N and s_N.

TABLE 3.5. Comparison of Experimental and Calculated Second-Order Rate Constants k_2 for the Reaction of the Carbanions 2a and 2b with Nitroolefins 1c and 1d in MeOH at 20 °C.

Nucleophile	Electrophile	N, s_N[a]	k_2^{exp} (M^{-1} s^{-1})	k_2^{calcd} (M^{-1} s^{-1})
2a (4-Nitrophenylnitromethide-K)	**1c**	14.05, 0.72	1.87×10^{-1}	9.20×10^{-1}
2b (4-Cyanophenylnitromethide-K)	**1d**	13.92, 0.74	2.14×10^{-1}	6.10×10^{-1}

[a] Reactivity parameters N and s_N for carbanions in methanol taken from ref 68.

3.4 Conclusion

Eq 3.1 was found also to be applicable to the reactions of the nitroolefins **1a**–**e** with nucleophiles. Thus, the experimental rate constants of the reactions of **1** with carbanions **2** in DMSO agree within a factor of 2 with the rate constants calculated by eq 3.1, and the two rate constants measured in methanol deviate by less than a factor of 5 from the analogously calculated rate constants. As illustrated in Figure 3.3, **1b** is about one order of magnitude less reactive than **1a**, which must be explained by the steric effect of the trichloromethyl group, because its electronic effects should increase the electrophilicity of the π-system. Steric shielding by the bulkier *iso*-propyl group also explains the significant reactivity difference between **1c** and **1e**. Surprisingly, (*E*)-1-nitro-1-propene (**1c**) and 2-nitroprop-1-ene (**1d**) have almost identical reactivities. Obviously the stronger electronic retardation by the methyl group in **1d** is compensated by the stronger steric retardation of the methyl group in **1c**. Figure 3.3 furthermore shows that (*E*)-1-nitro-1-propene (**1c**) has a similar electrophilicity as the phenylogous nitrostyrene (4-methyl-β-nitrostyrene), and the similar reactivities of nitroethylene and 4,β-dinitrostyrene show that the electronic activation by the 4-nitrophenyl group is fully compensated by its steric retarding effect. As all nitroolefins investigated so far have E parameters between –16 and –12, one can generalize that they are more electrophilic than chalcones, aldehydes and benzylidenemalonates, which explains their frequent use in organocatalytic reactions (enamine activation).[14-28]

The E parameters of the nitroolefins **1** can now be combined with the numerous published N and s_N parameters of nucleophiles[70] to predict scope and limitations of nucleophilic additions to them on the basis of eq 3.1.

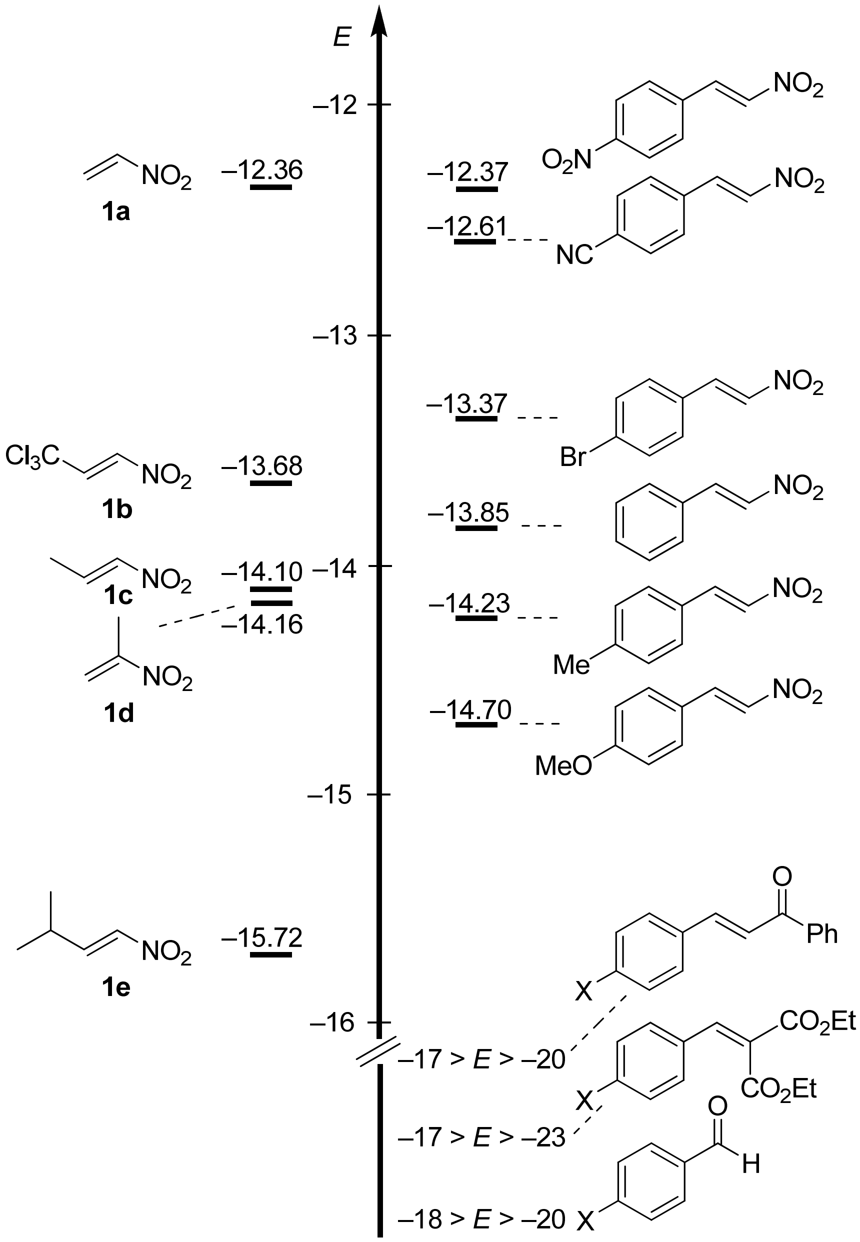


FIGURE 3.3. Comparison of *E* Values for Differently Substituted Michael Acceptors.[70]

3.5 Experimental Section

3.5.1 Products

Commercially available DMSO (with < 50 ppm H_2O content), MeOH (HPLC grade) and triethylamine (pure, < 0.5% H_2O content) were used without further purification. All reactions were performed under an atmosphere of dry nitrogen. The dehydration of 2-nitroethanol[71] provided **1a** as a pale yellow oil.[72] Compound **1b** was obtained as a yellow oil by dehydration of 1,1,1-trichloro-3-nitropropan-2-ol.[73] **1c** and **1d** were prepared by dehydration of 1-nitropropan-2-ol[74] and 2-nitropropan-1-ol[75] as pale yellow oils. **1e** was synthesized by the reaction of isobutyraldehyde with nitromethane, and received as a yellow oil.[76]

The ^1H and ^{13}C NMR chemical shifts are given in ppm and refer to $CDCl_3$ (δ_H = 7.26 ppm, δ_C = 77.16 ppm) as internal standards.[77] The chemical shifts given in parentheses are calculated using DAVINX software.[78] The coupling constants are given in Hz. NMR signal assignments in Table 3.2 are based on additional 2D-NMR experiments (COSY, HSQC). Diastereomeric ratios were determined by ^1H NMR spectroscopy.

General procedure A:

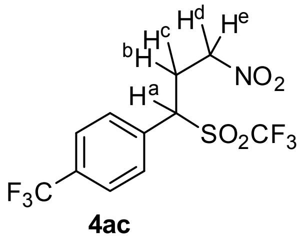
Reactions of the nitroethylenes **1a–e** with the carbanions **2a–g** were carried out by dissolving the CH-acid **2-H** in dry THF, cooling down the solution to –78 °C and adding lithium diisopropylamide (2 M solution in THF/*n*-heptane) or KO^{t}Bu in dry THF. After 1 h, the solution was cooled to –90 °C, and a solution of the nitroethylene **1** in dry THF was added dropwise, and stirring was continued at –78 °C overnight. The solution was treated with 1.5 equiv. of neat acetic acid and allowed to warm to room temperature. After evaporation of the

THF under reduced pressure, the residue was dissolved in dichloromethane (30-50 mL), washed with water and brine, dried over MgSO4 and again evaporated under reduced pressure. The crude products were purified by column chromatography on silica gel (*n*-pentane/Et_2O).

General procedure B:

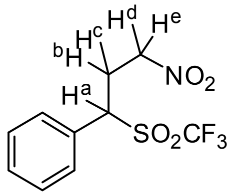
Reactions of the nitroethylenes **1a–e** with carbanions **2a–2g** were carried out by dissolving the CH-acid **2-H** in dry methanol, cooling down the solution to 0 °C, and adding sodium methoxide in dry methanol. After 15 min, a solution of nitroethylene **1** in dry methanol was added dropwise, and the solution was stirred at RT for 6 h. The solution was treated with 1.5 equiv. of concentrated acetic acid. After evaporation of the methanol under reduced pressure, the residue was dissolved in dichloromethane (30-50 mL), washed with water and brine, dried over MgSO4 and again evaporated under reduced pressure. The crude products were purified by column chromatography on silica gel (*n*-pentane/Et_2O).

3.5.1.1 Reactions of Nitroethene (1a) with the Carbanions 2



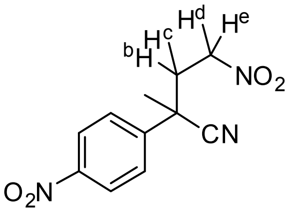
4ac

1-(3-Nitro-1-(trifluoromethylsulfonyl)propyl)-4-(trifluoromethyl) benzene (**4ac**). Obtained from **2c-H** (254 mg, 0.869 mmol), lithium diisopropylamide (0.52 mL 2 M solution, 1.04 mmol) and nitroethylene (**1a**) (64 mg, 0.87 mmol) as a crude product following general procedure A. Column chromatography furnished the product as a white solid (197 mg, 0.539 mmol) in 62% yield, mp 72 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ(ppm) = [ABCDE-system at $\delta = 2.75$ ($J = –14.8, 4.8, 5.7, 9.7$ Hz, 1 H^c), 3.19 ($J = –14.8, 4.6, 5.2, 10.5$ Hz, 1 H^b), 4.21 ($J = –14.6, –0.1, 4.6, 9.7$ Hz, 1 H^e), 4.55 ($J = –14.6, –0.5, 5.2, 5.7$ Hz, 1 H^d), 4.76 ($J = –0.1, 0.5, 4.8, 10.5$ Hz, 1 H^a)], 7.57 (d, $J = 8.3$ Hz, 2 H), 7.76 (d, $J = 8.3$ Hz, 2 H). ^{13}C NMR (75 MHz, $CDCl_3$): δ(ppm) = 26.2, 63.4, 70.9, 119.6 ($J_{CF} = 330$ Hz, SO_2CF_3), 123.6 ($J_{CF} = 274$ Hz, CF_3), 126.9, 130.5, 131.6, 133.0. Anal.: calcd. for $C_{11}H_9F_6NO_4S$: C, 36.17; H, 2.48; N, 3.83. Found C, 36.01; H, 2,52; N, 3.73.



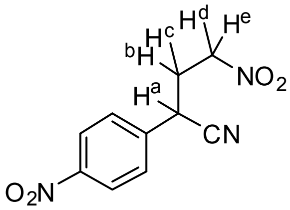
4ae

(3-Nitro-1-(trifluoromethylsulfonyl)propyl)benzene (**4ae**). Obtained from **2e-H** (269 mg, 1.20 mmol), lithium diisopropylamide (0.72 mL 2 M solution in THF/*n*-heptane, 1.44 mmol) and nitroethylene (**1a**) (88 mg, 1.20 mmol) as a crude product following general procedure A. Column chromatography and recrystallization from *n*-pentane/Et_2O furnished the product as a white solid (171 mg, 0.575 mmol) in 48% yield; mp 54 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ(ppm) = [ABCDE-system at $\delta = 2.75$ ($J = –15.3, 4.6, 5.5, 9.5$ Hz, 1 H^c), 3.15 ($J = –15.3, 4.9, 5.5, 11.0$ Hz, 1 H^b), 4.21 ($J = –14.6, 0.2, 4.9, 9.5$ Hz, 1 H^e), 4.49 ($J = –14.6, 0.3, 5.5, 5.5$ Hz, 1 H^d), 4.67 ($J = 0.2, 0.3, 4.6, 11.0$ Hz, 1 H^a)] , 7.39-7.53 (m, 5 H). ^{13}C NMR (75 MHz, $CDCl_3$): δ(ppm) = 26.0, 64.1, 71.0, 119.9 ($J_{CF} = 330$ Hz, SO_2CF_3), 127.2, 129.9, 131.0.



4af

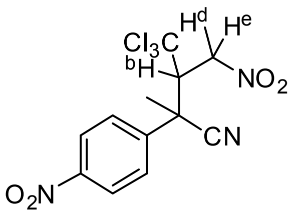
2-Methyl-4-nitro-2-(4-nitrophenyl)butanenitrile (**4af**). Obtained from **2f-H** (141 mg, 0.80 mmol), KO^{t}Bu (108 mg, 0.96 mmol) and nitroethylene (**1a**) (58 mg, 0.80 mmol) as a crude product following general procedure A. Column chromatography furnished the product as a white solid (164 mg, 0.658 mmol) in 82% yield, mp 86 °C. ^{1}H NMR (300 MHz, CDCl$_3$): δ(ppm) = 1.85, s, 3 H, [BCDE-system at δ = 2.73 (J = –14.3, 5.7, 9.6 Hz, 1 H^b), 2.78 (J = –14.3, 5.9, 9.6 Hz, 1 H^c), 4.28 (J = –13.9, 5.7, 9.6 Hz, 1 H^e), 4.56 (J = –13.9, 5.9, 9.6 Hz, 1 H^d)], 7.65-7.70 (m, 2 H), 8.28-8.33 (m, 2 H). ^{13}C NMR (75 MHz, CDCl$_3$): δ(ppm) = 27.8, 38.0, 40.9, 71.5, 120.6, 124.8, 126.7, 144.7, 148.2.



4ag

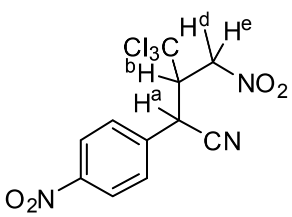
4-Nitro-2-(4-nitrophenyl)butanenitrile (**4ag**). Obtained from 2-(4-nitrophenyl)ethanenitrile (**2g-H**) (141 mg, 0.80 mmol), KO^{t}Bu (108 mg, 0.96 mmol) and nitroethylene (**1a**) (58 mg, 0.80 mmol) following general procedure A as a crude product. Column chromatography furnished the product as a white solid (135 mg, 0.574 mmol) in 72% yield, mp 63 °C. ^{1}H NMR (300 MHz, CDCl$_3$): δ(ppm) = [ABCDE-system at δ = 2.58 (J = –14.8, 5.1, 9.4 Hz, 1 H^c), 2.64 (J = –14.8, 5.4, 6.0, 8.6 Hz, 1 H^b), 4.22 (J = 0.2, 0.5, 6.0, 9.4 Hz, 1 H^a), 4.52 (J = –14.6, 0.5, 5.4, 6.3 Hz, 1 H^e), 4.66 (J = –14.6, 0.2, 5.1, 8.6 Hz, 1 H^d)], 7.56-7.63 (m, 2 H), 8.27-8.34 (m, 2 H). ^{13}C NMR (75 MHz, CDCl$_3$): δ(ppm) = 32.6, 34.5, 71.6, 118.1, 124.9, 128.6, 140.6, 148.4.

3.5.1.2 Reactions of (*E*)-3,3,3-Trichloro-1-nitroprop-1-ene (1b) with the Carbanions 2



4bf

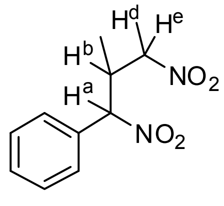
4,4,4-Trichloro-2-methyl-3-(nitromethyl)-2-(4-nitrophenyl) butane nitrile (**4bf**). Obtained from **2f-H** (162 mg, 1.00 mmol), NaOMe (54 mg, 1.00 mmol) and (*E*)-3,3,3-trichloro-1-nitroprop-1-ene (**1b**) (190 mg, 1.00 mmol) following general procedure B as a crude product. Column chromatography furnished the product as a white solid (260 mg, 0.709 mmol) in 71% yield (dr ~ 3:1). ^{1}H NMR (400 MHz, CDCl$_3$): δ(ppm) = 1.70 (d, J = 7.3 Hz, 3 H), 4.04-4.06 (m, 1 H), [BDE-system at δ = 4.37 (J = 2.3 Hz, 0.2 H^e), 4.43 (J = 2.3, 6.0 Hz, 0.2 H^b), 4.45 (J = 2.7, 5.3 Hz, 0.1 H^b)*, 4.90 (J = 5.3 Hz, 0.1 H^e)*, 5.03 (J = 6.0 Hz, 0.2 H^d), 5.15 (J = 2.7 Hz, 0.1 H^d)*], 7.56-7.58 (m, 2 H), 7.81-7.89 (m, 0.7 H)*, 8.26-8.28 (m, 2 H), 8.34-8.36 (m, 0.7 H)*. Signals assigned to the major diastereomer, *additional signals found for the minor diastereomer. ^{13}C NMR (100 MHz, CDCl$_3$): δ(ppm) = 21.4, 27.5, 47.3, 61.5, 75.4, 119.4, 120.3, 124.6, 128.0, 144.1.



4bg

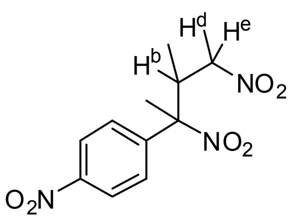
4,4,4-Trichloro-3-(nitromethyl)-2-(4-nitrophenyl)butanenitrile (**4bg**). Obtained from 2-(4-nitrophenyl)ethanenitrile (**2g-H**) (162 mg, 1.00 mmol), NaOMe (54 mg, 1.00 mmol) and (*E*)-3,3,3-trichloro-1-nitroprop-1-ene (**1b**) (190 mg, 1.00 mmol) as a crude product. Column chromatography furnished the product as a white solid (221 mg, 0.627 mmol) in 63% yield (dr ~ 3:1). ^{1}H NMR (400 MHz, CDCl$_3$): δ(ppm) = [ABDE-system at δ = 4.05 (J = 1.9, 4.8, 4.9 Hz, 1 H^b), 4.81 (J = -15.6, 0.3, 4.8 Hz, 1 H^e), 5.06 (J = 0.3, 0.8, 1.9 Hz, 1 H^a), 5.13 (J = -15.6, 0.8, 4.9 Hz, 1 H^d)], 7.70-7.72 (m, 2 H), 8.33-8.35 (m, 2 H). ^{13}C NMR (75 MHz, CDCl$_3$): δ(ppm) = 38.4, 60.8, 73.0, 98.5, 115.7, 125.1, 128.7, 138.3, 148.7.

3.5.1.3 Reactions of (*E*)-1-Nitro-1-propene (1c) with the Carbanions 2 or the CH-Acids 2-H



4cd

(2-Methyl-1,3-dinitropropyl)benzene (**4cd**). (Nitromethyl)benzene (**2d-H**) (257 mg, 1.87 mmol) was dissolved in 4 mL of dry dichloromethane, then 1-nitro-1-propene (**1c**) (131 mg, 1.50 mmol) and triethylamine (2 μL, 15 μmol) was added, and the resulting mixture was stirred for 16 h. After evaporation of the solvent under reduced pressure, the residue was purified by column chromatography (*n*-pentane/Et_2O, 5:1), and the product was obtained as a colorless oil (182 mg, 0.812 mmol) in 54% yield (dr ~ 7:3). ^{1}H NMR (300 MHz, $CDCl_3$): δ(ppm) = 0.95 (d, J = 7.0 Hz, 2 H), 1.28 (d, J = 7.0 Hz, 2 H), [ABDE-system at δ = 3.38 (J = 4.3, 6.6, 11.1 Hz, 1 H^b), 4.07 (J = –13.0, 6.6 Hz, 0.7 H^d), 4.23 (J = –13.0, 4.3 Hz, 0.7 H^e), 4.48 (J = –12.7, 3.9 Hz, 0.35 H^e)*, 4.52, (J = –12.7, 7.1 Hz, 0.35 H^d)*, 5.52 (J = 11.1 Hz, 1 H^a)], 7.42-7.55 (m, 5 H). ^{13}C NMR (75 MHz, $CDCl_3$): δ(ppm) = 14.9, 36.5, 77.9, 94.0, 128.2, 129.7, 130.9, 132.0. Signals assigned to the major diastereomer, *additional signals found for the minor diastereomer.

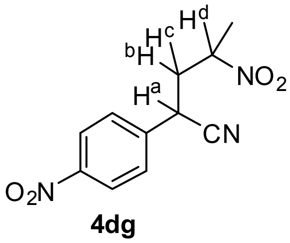


4cf

1-(1,2-dimethyl-1,3-dinitropropyl)-4-nitrobenzene (**4cf**). Obtained from 2-(4-nitrophenyl)propanenitrile (**2f-H**) (141 mg, 1.20 mmol), lithium diisopropylamide (0.72 mL 2 M solution in THF/*n*-heptane, 1.44 mmol) and 1-nitro-1-propene (**1c**) (104 mg, 1.20 mmol) as a crude product following general procedure A. Column chromatography and recrystallization from *n*-pentane/Et_2O furnished the product as a white solid (174 mg, 0.614 mmol) in 55% yield (dr ~ 6:4). ^{1}H NMR (300 MHz, $CDCl_3$): δ(ppm) = 0.97 (d, J = 6.8 Hz, 1.4 H)*, 1.37 (d, J = 6.8 Hz, 1.7 H), 1.81 (d, J = 6.5 Hz, 3 H), [BDE-system at δ = 2.96 (J = 3.5, 10.4 Hz, 1

H^b), 4.08 (J = –12.6, 3.5 Hz, 0.5 H^e), 4.23 (J = –12.6, 10.4 Hz, 0.5 H^d), 4.39 (J = –12.8, 9.0 Hz, 0.5 H^e)*, 4.75 (J = –12.9, 4.7 Hz, 0.5 H^d)*], 7.65-7.69 (m, 2 H), 8.29-8.33 (m, 2 H). ^{13}C NMR (75 MHz, $CDCl_3$): δ (ppm) = 14.1, 26.0, 41.7, 45.8, 78.2, 119.6, 124.9, 127.0, 145.1, 148.0. Signals assigned to the major diastereomer, *additional signals found for the minor diastereomer.

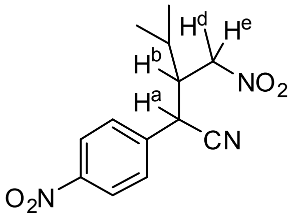
3.5.1.4 Reaction of 2-Nitro-1-propene (1d) with Lithium (4-(trifluoromethyl)phenyl) (trifluoromethylsulfonyl)methanide (2g-Li)



4dg

4-Nitro-2-(4-nitrophenyl)pentanenitrile (**4dg**). Obtained from 2-(4-nitrophenyl)ethanenitrile (**2g-H**) (195 mg, 1.20 mmol), lithium diisopropylamide (0.72 mL 2 M solution, 1.44 mmol) and 2-nitro-1-propene (**1d**) (104 mg, 1.20 mmol) following general procedure A as a crude product. Column chromatography and recrystallization from *n*-pentane/Et_2O furnished the product as a white solid (182 mg, 0.730 mmol) in 61% yield (dr ~ 9:1). ^1H NMR (600 MHz, $CDCl_3$): δ(ppm) = 1.62 (d, J = 6.8 Hz, 0.3 H)*, 1.68 (d, J = 6.8 Hz, 2.7 H), 2.25-2.30 (m, 0.1 H)*, 2.82-2.87 (m, 0.1 H)*, 3.98-4.00 (m, 0.1 H)*, 4.42-4.48 (m, 0.1 H)*, [ABCD-system at δ = 2.22 (J = –14.9, 2.6, 11.8 Hz, 0.9 H^c), 2.59 (J = –14.9, 4.3, 11.8 Hz, 0.9 H^b), 4.03 (J = 0.1, 4.3, 11.8 Hz, 0.9 H^a), 4.93 (J = 0.1, 2.6, 10.9 Hz, 0.9 H^d)], 7.57-7.59 (m, 2 H), 8.28-8.31 (m, 2 H). ^{13}C NMR (150 MHz, $CDCl_3$): δ(ppm) = 20.1, 34.9, 40.6, 80.8, 118.2, 124.9, 128.4, 141.1, 148.3. Signals assigned to the major diastereomer, *additional signals found for the minor diastereomer.

3.5.1.5 Reaction of (*E*)-3-Methyl-1-nitrobut-1-ene (1e) with Lithium (4-(trifluoromethyl) phenyl)(trifluoromethylsulfonyl)methanide (2g-Li)



4eg

4-Methyl-3-(nitromethyl)-2-(4-nitrophenyl)pentanenitrile (**4eg**). Obtained from 2-(4-nitrophenyl)ethanenitrile **2g-H** (162 mg, 1.00 mmol), lithium diisopropylamide (0.60 mL 2 M solution in THF/*n*-heptane, 1.2 mmol) and (*E*)-3-methyl-1-nitrobut-1-ene (**1e**) (115 mg, 1.00 mmol) following general procedure A as a crude product. Column chromatography and recrystallization from *n*-pentane/Et_2O furnished the product as a white solid (175 mg, 0.631 mmol) in 63% yield (dr ~ 54:46). ^{1}H NMR (300 MHz, $CDCl_3$): δ(ppm) = 0.99-1.99 (m, 6 H), 1.93-2.13 (m, 1 H), [ABDE-system at δ = 2.72 (J = 4.7, 5.3, 6.5 Hz, 1 H^b), 4.31 (J = 4.7 Hz, 1 H^a), 4.41 (J = –14.0, 5.3 Hz, 1 H^e), 4.55 (J = –14.0, 6.5 Hz, 1 H^d)], 7.57-7.64 (m, 2 H), 8.27-8.31 (m, 2 H). ^{13}C NMR (75 MHz, $CDCl_3$): δ(ppm) = 17.1*, 19.5, 20.0, 21.9*, 27.8*, 29.8, 37.7, 38.9*, 46.9*, 48.0, 73.7*, 74.2, 117.3, 117.8*, 124.7, 128.9, 129.2*, 140.1, 148.3. Signals assigned to major diastereomer, *additional signals found for minor diastereomer.

3.5.2 Kinetics

For the investigation of fast kinetics ($\tau_{1/2}$ < 30 s) stopped-flow spectrophotometer systems were used. Slow kinetics ($\tau_{1/2}$ > 30 s) were followed by using a conventional UV-vis diode array spectrophotometer system that was connected to a quartz immersion probe via fiber optic cables.

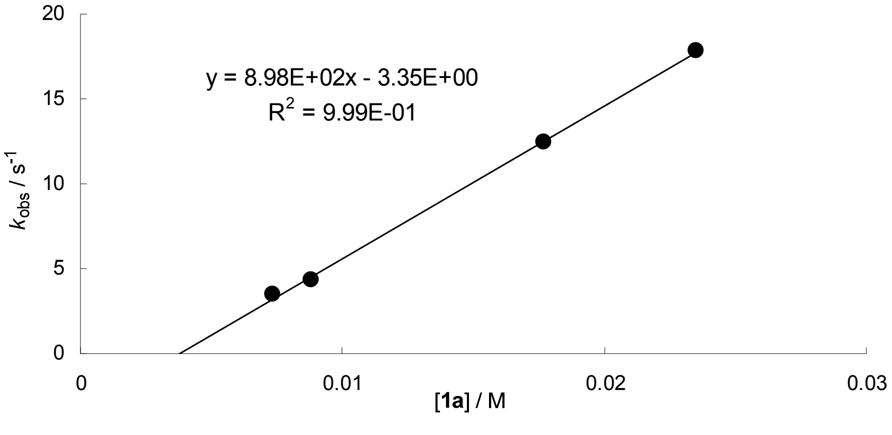
All measurements were carried out under first-order conditions (in general $[\mathbf{1}]_0/[\mathbf{2}]_0 > 10$). The first-order rate constants k_{obs} were obtained by least-squares fitting of the time-dependent absorbances A_t of the electrophiles to the exponential function $A_t = A_0\ e^{-k_{obs}t} + C$. Second-order rate constans k_2^{exp} were then derived from linear correlations of k_{obs} vs. [**1**]. The temperature of the solutions during all equilibrium studies was kept constant at (20.0 ± 0.1) °C using a circulating bath thermostat.

3.5.2.1 Kinetics of the Reactions of Nitroethene (1a) with the Carbanions 2 in DMSO

Reaction of **1a** with **2a** (DMSO, 20 °C, stopped-flow, 512 nm)

$k_2 = 8.98 \times 10^2$ M^{-1} s^{-1}

[**1a**] /M	[**2a**] /M	k_{obs} / s^{-1}
7.36×10^{-3}	2.09×10^{-4}	3.47
8.83×10^{-3}	2.09×10^{-4}	4.36
1.77×10^{-2}	2.09×10^{-4}	1.25×10^{1}
2.35×10^{-2}	2.09×10^{-4}	1.78×10^{1}

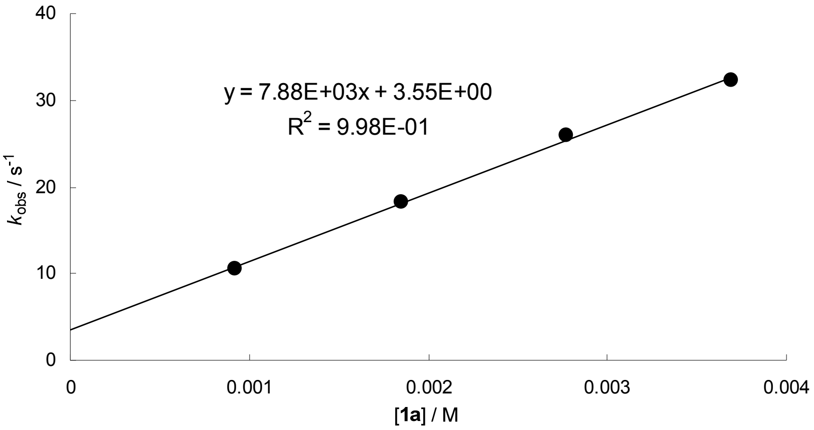


Reaction of **1a** with **2c** (DMSO, 20 °C, stopped-flow, 316 nm)

$k_2 = 7.88 \times 10^3$ M^{-1} s^{-1}

[**1a**] /M	[**2c**] /M	k_{obs} / s^{-1}
9.24×10^{-4}	6.57×10^{-5}	1.06×10^{1}
1.85×10^{-3}	6.57×10^{-5}	1.82×10^{1}

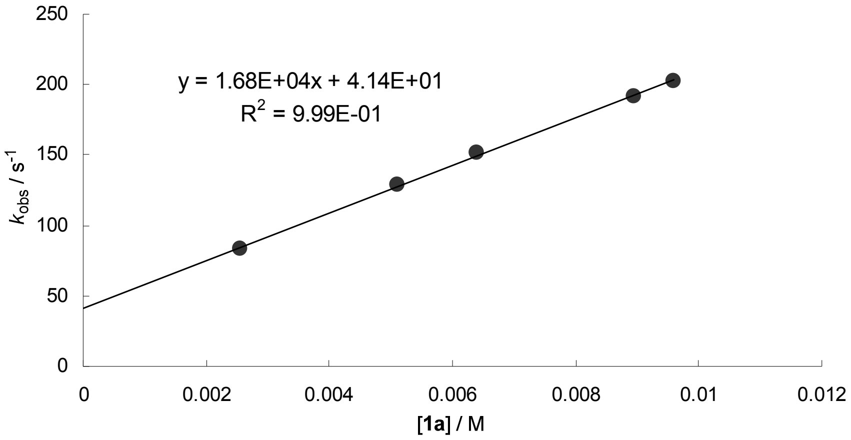
2.77×10^{-3}	6.57×10^{-5}	2.59×10^{1}
3.70×10^{-3}	6.57×10^{-5}	3.23×10^{1}



Reaction of **1a** with **2d** (DMSO, 20 °C, stopped-flow, 344 nm)

$k_2 = 1.68 \times 10^{4}$ M^{-1} s^{-1}

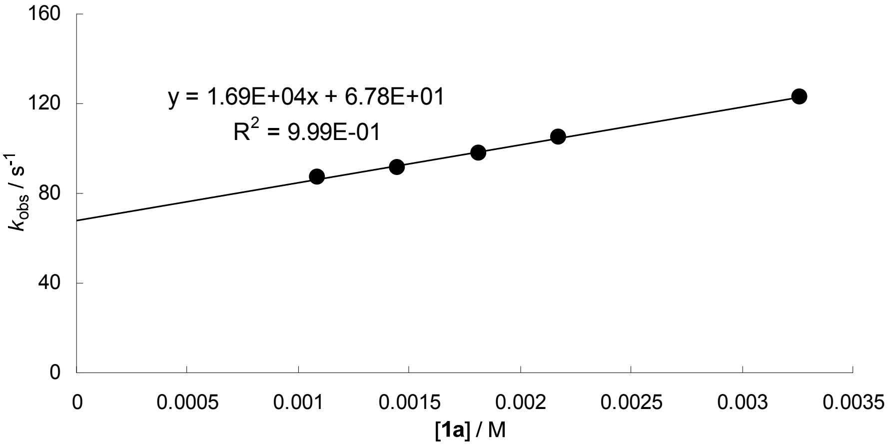
[**1a**] /M	[**2d**] /M	k_{obs} / s^{-1}
2.56×10^{-3}	2.85×10^{-4}	8.29×10^{1}
5.12×10^{-3}	2.85×10^{-4}	1.29×10^{2}
6.40×10^{-3}	2.85×10^{-4}	1.51×10^{2}
8.96×10^{-3}	2.85×10^{-4}	1.92×10^{2}
9.60×10^{-3}	2.85×10^{-4}	2.02×10^{2}



Reaction of **1a** with **2e** (DMSO, 20 °C, stopped-flow, 290 nm)

$k_2 = 1.69 \times 10^4$ M^{-1} s^{-1}

[**1a**] /M	[**2e**] /M	k_{obs} / s^{-1}
1.09×10^{-3}	6.24×10^{-5}	8.68×10^{1}
1.45×10^{-3}	6.24×10^{-5}	9.16×10^{1}
1.81×10^{-3}	6.24×10^{-5}	9.81×10^{1}
2.18×10^{-3}	6.24×10^{-5}	1.05×10^{2}
3.27×10^{-3}	6.24×10^{-5}	1.23×10^{2}

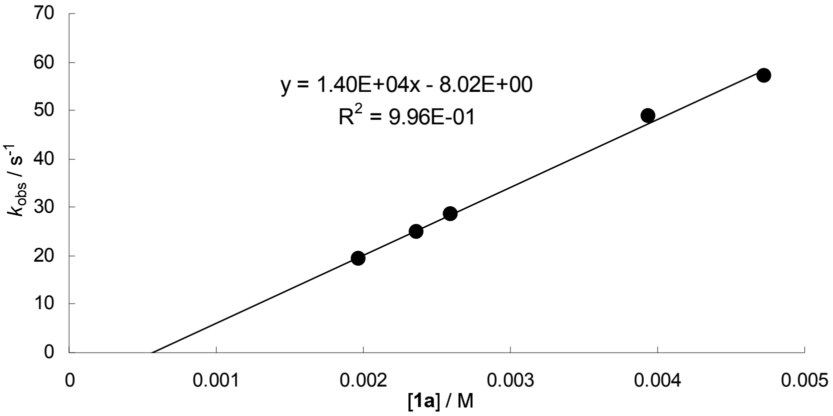


Reaction of **1a** with **2f** (DMSO, 20 °C, stopped-flow, 550 nm)

$k_2 = 1.40 \times 10^4$ M^{-1} s^{-1}

[**1a**] /M	[**2f**] /M	k_{obs} / s^{-1}

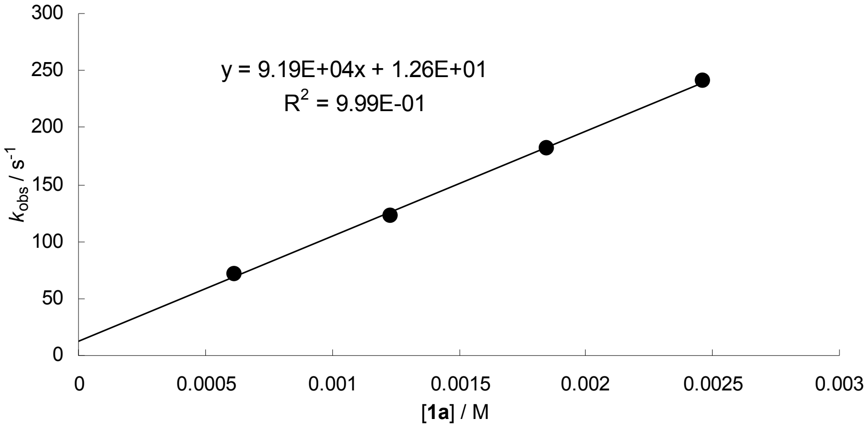
1.97×10^{-3}	5.22×10^{-5}	1.94×10^{1}
2.36×10^{-3}	5.22×10^{-5}	2.48×10^{1}
2.60×10^{-3}	5.22×10^{-5}	2.85×10^{1}
3.94×10^{-3}	5.22×10^{-5}	4.88×10^{1}
4.72×10^{-3}	5.22×10^{-5}	5.72×10^{1}



Reaction of **1a** with **2g** (DMSO, 20 °C, stopped-flow, 539 nm)

$k_2 = 9.19 \times 10^4$ M^{-1} s^{-1}

[**1a**] /M	[**2g**] /M	k_{obs} / s^{-1}
6.16×10^{-4}	7.04×10^{-5}	7.16×10^{1}
1.23×10^{-3}	7.04×10^{-5}	1.23×10^{2}
1.85×10^{-3}	7.04×10^{-5}	1.81×10^{2}
2.46×10^{-3}	7.04×10^{-5}	2.41×10^{2}

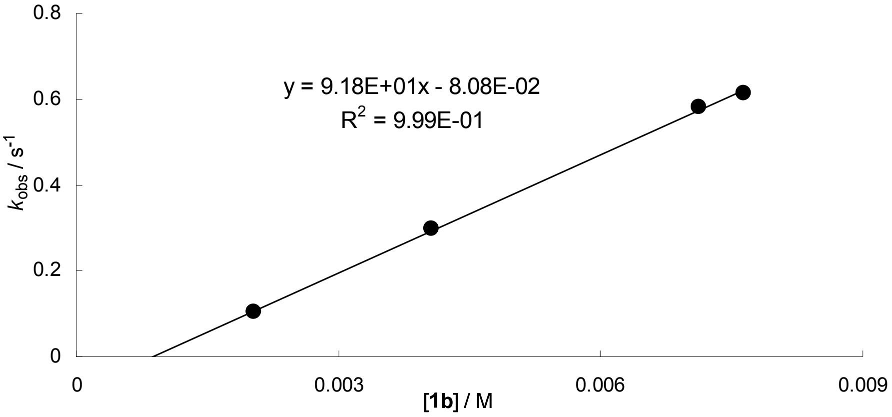

y = 9.19E+04x + 1.26E+01
R^2 = 9.99E-01
k_{obs} / s^{-1}
300
250
200
150
100
50
0
0
0.0005
0.001
0.0015
0.002
0.0025
0.003
[**1a**] / M

3.5.2.2 Kinetics of the Reactions of (*E*)-3,3,3-Trichloro-1-nitroprop-1-ene (1b) with the Carbanions 2 in DMSO

Reaction of **1b** with **2a** (DMSO, 20 °C, stopped-flow, 512 nm)

$k_2 = 9.18 \times 10^1\ \mathrm{M^{-1}\ s^{-1}}$

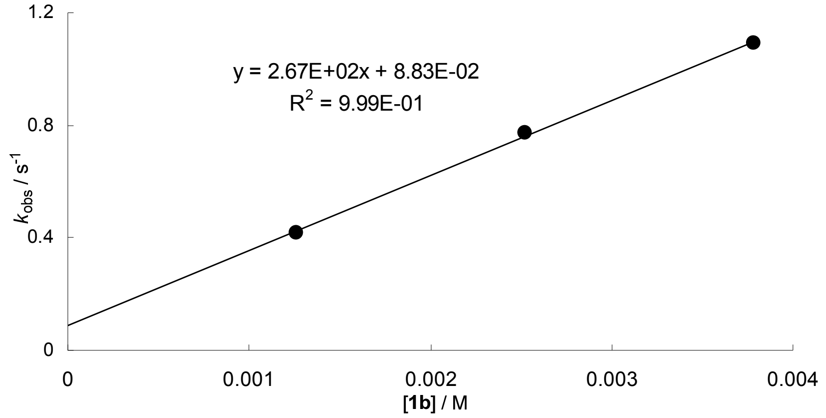
[**1b**] /M	[**2a**] /M	k_{obs} / $\mathrm{s^{-1}}$
2.04×10^{-3}	2.09×10^{-4}	1.04×10^{-1}
4.08×10^{-3}	2.09×10^{-4}	2.96×10^{-1}
7.13×10^{-3}	2.09×10^{-4}	5.82×10^{-1}
7.64×10^{-3}	2.09×10^{-4}	6.13×10^{-1}



Reaction of **1b** with **2b** (DMSO, 20 °C, stopped-flow, 401 nm)

$k_2 = 2.67 \times 10^2\ \mathrm{M^{-1}\ s^{-1}}$

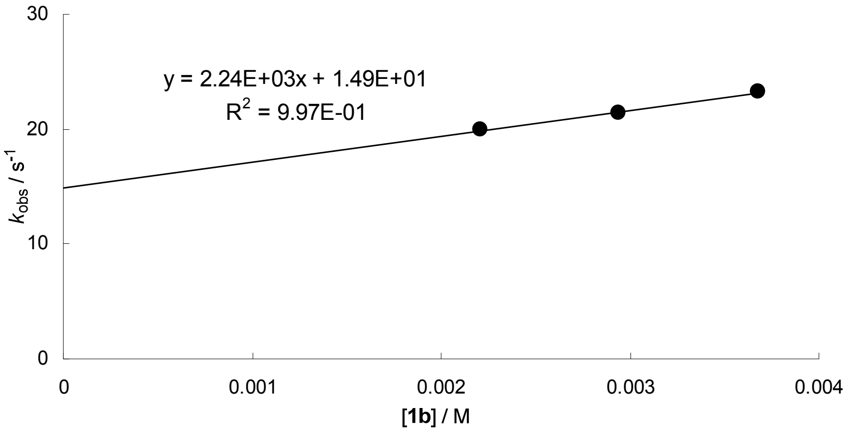
[**1b**] /M	[**2b**] /M	k_{obs} / $\mathrm{s^{-1}}$
1.26×10^{-3}	1.15×10^{-4}	4.18×10^{-1}
2.52×10^{-3}	1.15×10^{-4}	7.73×10^{-1}
3.78×10^{-3}	1.15×10^{-4}	1.09



Reaction of **1b** with **2f** (DMSO, 20 °C, stopped-flow, 550 nm)

$k_2 = 2.24 \times 10^3$ M^{-1} s^{-1}

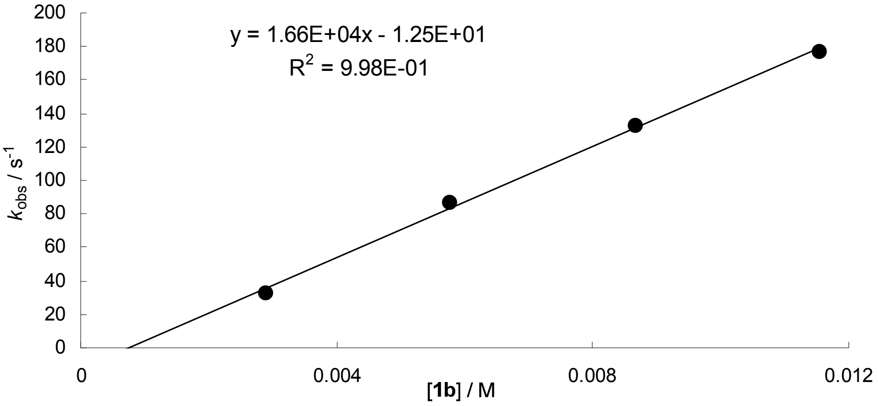
[**1b**] /M	[**2f**] /M	k_{obs} / s^{-1}
2.21×10^{-3}	9.22×10^{-5}	1.99×10^{1}
2.94×10^{-3}	9.22×10^{-5}	2.14×10^{1}
3.68×10^{-3}	9.22×10^{-5}	2.32×10^{1}



Reaction of **1b** with **2g** (DMSO, 20 °C, stopped-flow, 539 nm)

$k_2 = 1.66 \times 10^4$ M^{-1} s^{-1}

[**1b**] /M	[**2g**] /M	k_{obs} / s^{-1}
2.89×10^{-3}	9.87×10^{-5}	3.26×10^{1}
5.78×10^{-3}	9.87×10^{-5}	8.69×10^{1}
8.67×10^{-3}	9.87×10^{-5}	1.32×10^{2}
1.16×10^{-2}	9.87×10^{-5}	1.77×10^{2}

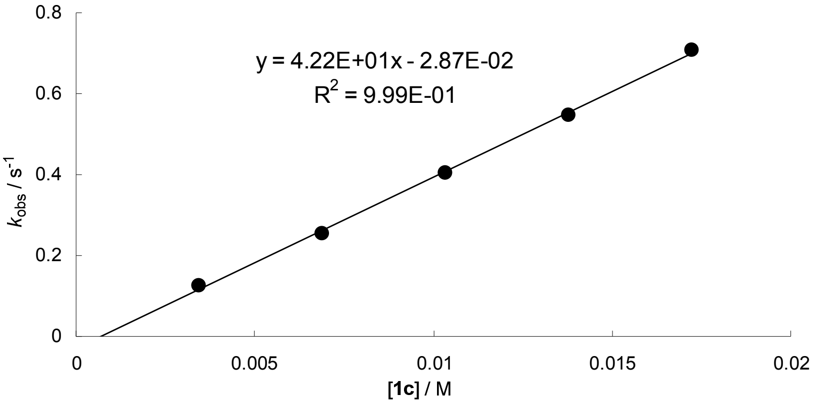


3.5.2.3 Kinetics of the Reactions of (*E*)-1-Nitro-1-propene (1c) with the Carbanions 2 in DMSO or Methanol

Reaction of **1c** with **2a** (DMSO, 20 °C, stopped-flow, 512 nm)

$k_2 = 4.22 \times 10^{1}$ M^{-1} s^{-1}

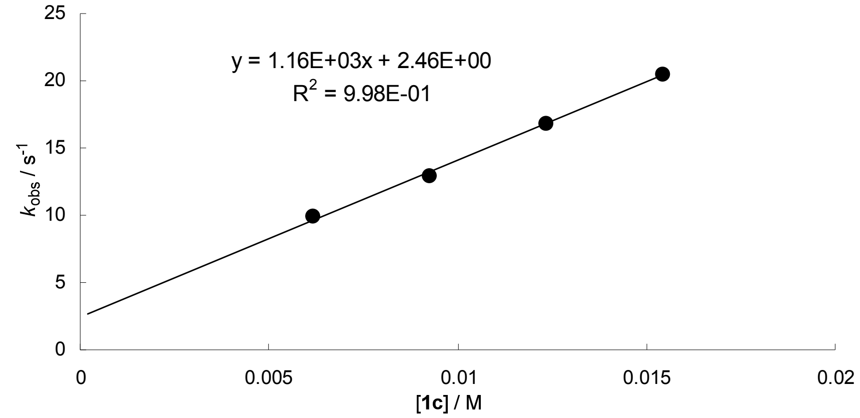
[**1c**] /M	[**2a**] /M	k_{obs} / s^{-1}
3.45×10^{-3}	2.09×10^{-4}	1.26×10^{-1}
6.89×10^{-3}	2.09×10^{-4}	2.55×10^{-1}
1.03×10^{-2}	2.09×10^{-4}	4.03×10^{-1}
1.38×10^{-2}	2.09×10^{-4}	5.48×10^{-1}
1.72×10^{-2}	2.09×10^{-4}	7.07×10^{-1}



Reaction of **1c** with **2d** (DMSO, 20 °C, stopped-flow, 344 nm)

$k_2 = 1.16 \times 10^{3}$ M^{-1} s^{-1}

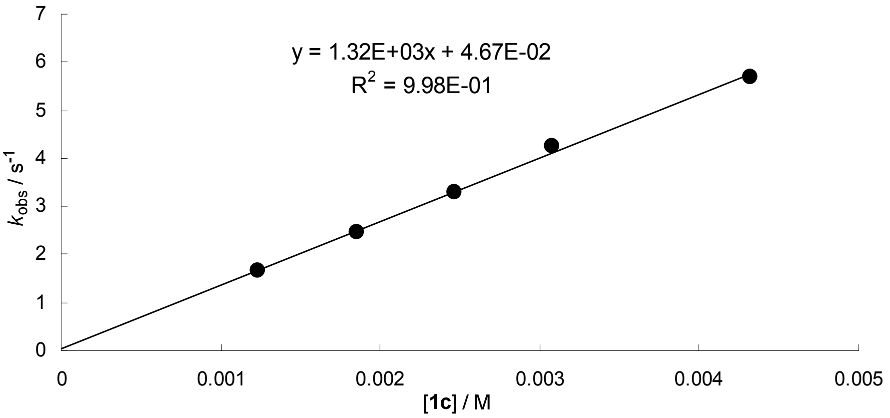
[**1c**] /M	[**2d**] /M	k_{obs} / s^{-1}
6.18×10^{-3}	2.67×10^{-4}	9.85
9.27×10^{-3}	2.67×10^{-4}	1.29×10^{1}
1.24×10^{-2}	2.67×10^{-4}	1.68×10^{1}
1.54×10^{-2}	2.67×10^{-4}	2.05×10^{1}



Reaction of **1c** with **2e** (DMSO, 20 °C, stopped-flow, 290 nm)

$k_2 = 1.32 \times 10^3$ M^{-1} s^{-1}

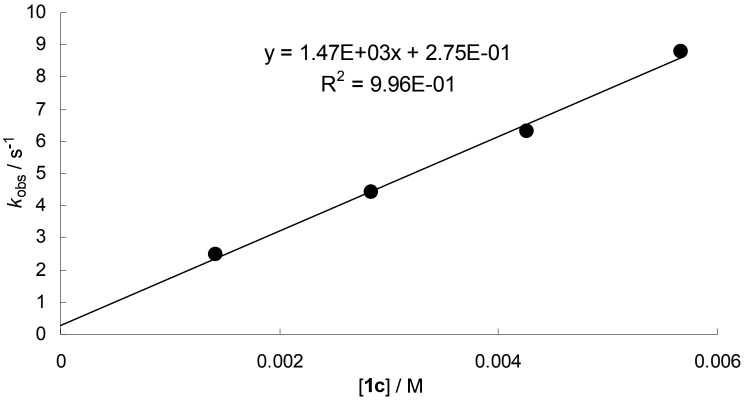
[**1c**] /M	[**2e**] /M	k_{obs} / s^{-1}
1.23×10^{-3}	5.00×10^{-5}	1.66
1.85×10^{-3}	5.00×10^{-5}	2.46
2.47×10^{-3}	5.00×10^{-5}	3.30
3.08×10^{-3}	5.00×10^{-5}	4.25
4.32×10^{-3}	5.00×10^{-5}	5.70



Reaction of **1c** with **2f** (DMSO, 20 °C, stopped-flow, 550 nm)

$k_2 = 1.47 \times 10^3$ M^{-1} s^{-1}

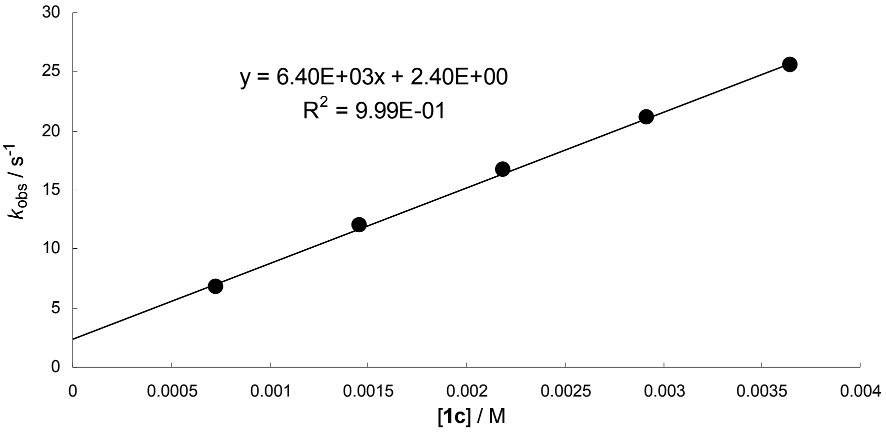
[**1c**] /M	[**2f**] /M	k_{obs} / s^{-1}
1.42×10^{-3}	5.96×10^{-5}	2.46
2.84×10^{-3}	5.96×10^{-5}	4.40
4.26×10^{-3}	5.96×10^{-5}	6.32
5.67×10^{-3}	5.96×10^{-5}	8.77



Reaction of **1c** with **2g** (DMSO, 20 °C, stopped-flow, 539 nm)

$k_2 = 6.40 \times 10^3$ M^{-1} s^{-1}

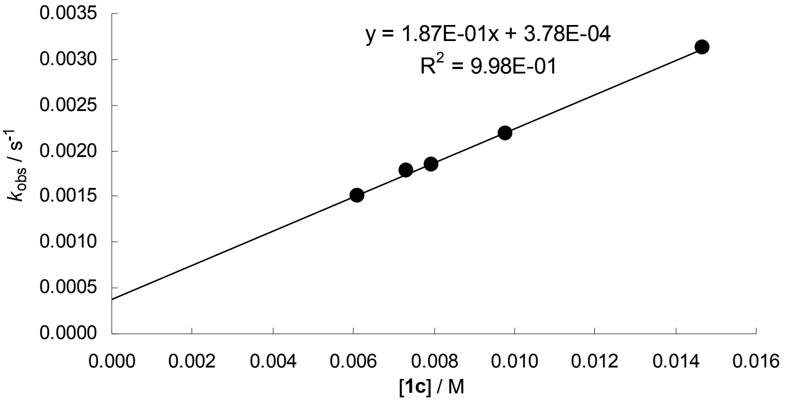
[**1c**] /M	[**2g**] /M	k_{obs} / s^{-1}
7.30×10^{-4}	8.63×10^{-5}	6.78
1.46×10^{-3}	8.63×10^{-5}	1.19×10^{1}
2.19×10^{-3}	8.63×10^{-5}	1.67×10^{1}
2.92×10^{-3}	8.63×10^{-5}	2.11×10^{1}
3.65×10^{-3}	8.63×10^{-5}	2.56×10^{1}



Reaction of **1c** with **2a** (methanol, 20 °C, conventional, 395 nm)

$k_2 = 1.87 \times 10^{-1}$ M^{-1} s^{-1}

[**1c**] /M	[**2a**] /M	k_{obs} / s^{-1}
6.11×10^{-3}	1.15×10^{-4}	1.50×10^{-3}
7.33×10^{-3}	1.15×10^{-4}	1.79×10^{-3}
7.94×10^{-3}	1.15×10^{-4}	1.85×10^{-3}
9.77×10^{-3}	1.15×10^{-4}	2.19×10^{-3}
1.47×10^{-2}	1.15×10^{-4}	3.12×10^{-3}

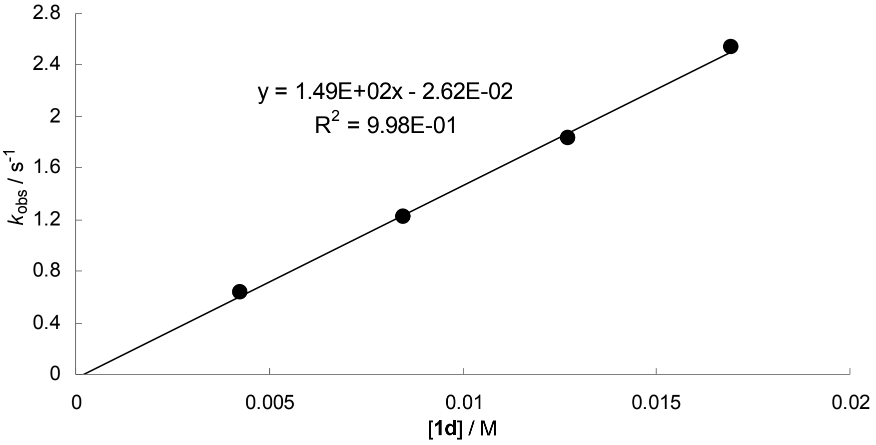


3.5.2.4 Kinetics of the Reactions of 2-Nitroprop-1-ene (1d) with the Carbanions 2 in DMSO or Methanol

Reaction of **1d** with **2b** (DMSO, 20 °C, stopped-flow, 401 nm)

$k_2 = 1.49 \times 10^2$ M^{-1} s^{-1}

[**1d**] /M	[**2b**] /M	k_{obs} / s^{-1}
4.24×10^{-3}	1.14×10^{-4}	6.30×10^{-1}
8.48×10^{-3}	1.14×10^{-4}	1.23
1.27×10^{-2}	1.14×10^{-4}	1.83
1.70×10^{-2}	1.14×10^{-4}	2.54

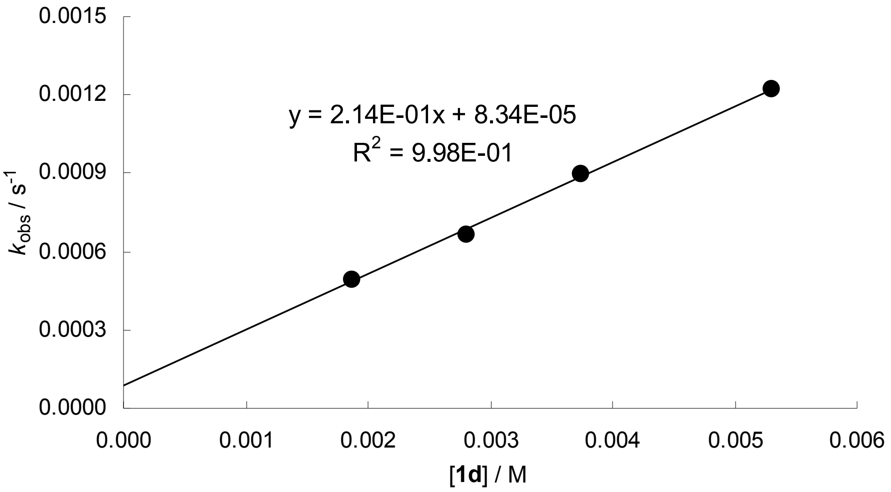


Reaction of **1d** with **2b** (methanol, 20 °C, conventional, 340 nm)

$k_2 = 2.14 \times 10^{-1}$ M^{-1} s^{-1}

[**1d**] /M	[**2b**] /M	k_{obs} / s^{-1}
1.87×10^{-3}	5.33×10^{-5}	4.94×10^{-4}
2.81×10^{-3}	5.33×10^{-5}	6.66×10^{-4}

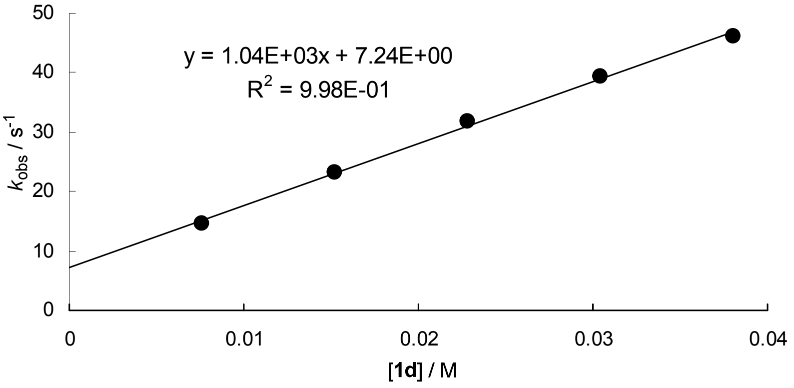
3.75×10^{-3}	5.33×10^{-5}	8.97×10^{-4}
5.31×10^{-3}	5.33×10^{-5}	1.22×10^{-3}



Reaction of **1d** with **2d** (DMSO, 20 °C, stopped-flow, 344 nm)

$k_2 = 1.04 \times 10^{3}\ \mathrm{M}^{-1}\ \mathrm{s}^{-1}$

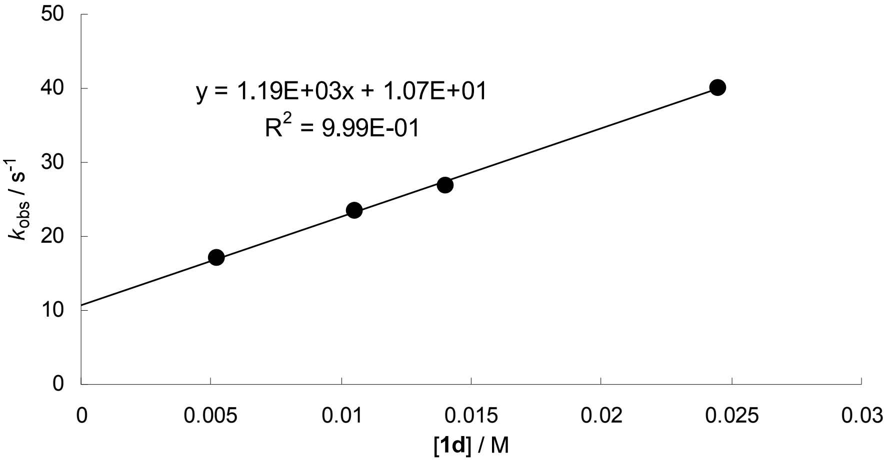
[**1d**] /M	[**2d**] /M	k_{obs} / s^{-1}
7.60×10^{-3}	2.55×10^{-4}	1.46×10^{1}
1.52×10^{-2}	2.55×10^{-4}	2.32×10^{1}
2.28×10^{-2}	2.55×10^{-4}	3.18×10^{1}
3.04×10^{-2}	2.55×10^{-4}	3.92×10^{1}
3.80×10^{-2}	2.55×10^{-4}	4.62×10^{1}



Reaction of **1d** with **2e** (DMSO, 20 °C, stopped-flow, 290 nm)

$k_2 = 1.19 \times 10^3$ M^{-1} s^{-1}

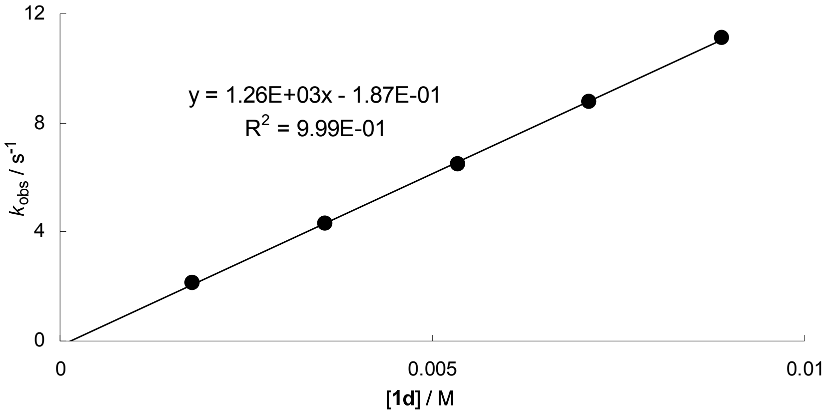
[**1d**] /M	[**2e**] /M	k_{obs} / s^{-1}
5.25×10^{-3}	2.19×10^{-4}	1.71×10^{1}
1.05×10^{-2}	2.19×10^{-4}	2.35×10^{1}
1.40×10^{-2}	2.19×10^{-4}	2.69×10^{1}
2.45×10^{-2}	2.19×10^{-4}	4.01×10^{1}



Reaction of **1d** with **2f** (DMSO, 20 °C, stopped-flow, 550 nm)

$k_2 = 1.26 \times 10^3$ M^{-1} s^{-1}

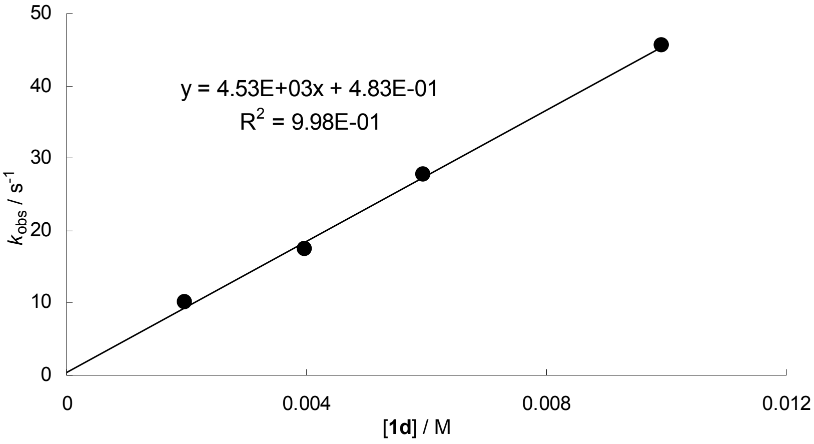
[**1d**] /M	[**2f**] /M	k_{obs} / s^{-1}
1.78×10^{-3}	9.08×10^{-5}	2.12
3.56×10^{-3}	9.08×10^{-5}	4.27
5.34×10^{-3}	9.08×10^{-5}	6.50
7.12×10^{-3}	9.08×10^{-5}	8.78
8.90×10^{-3}	9.08×10^{-5}	1.11×10^{1}



Reaction of **1d** with **2g** (DMSO, 20 °C, stopped-flow, 539 nm)

$k_2 = 4.53 \times 10^3$ M^{-1} s^{-1}

[**1d**] /M	[**2g**] /M	k_{obs} / s^{-1}
1.99×10^{-3}	9.13×10^{-5}	1.01×10^{1}
3.97×10^{-3}	9.13×10^{-5}	1.75×10^{1}
5.96×10^{-3}	9.13×10^{-5}	2.77×10^{1}
9.93×10^{-3}	9.13×10^{-5}	4.56×10^{1}

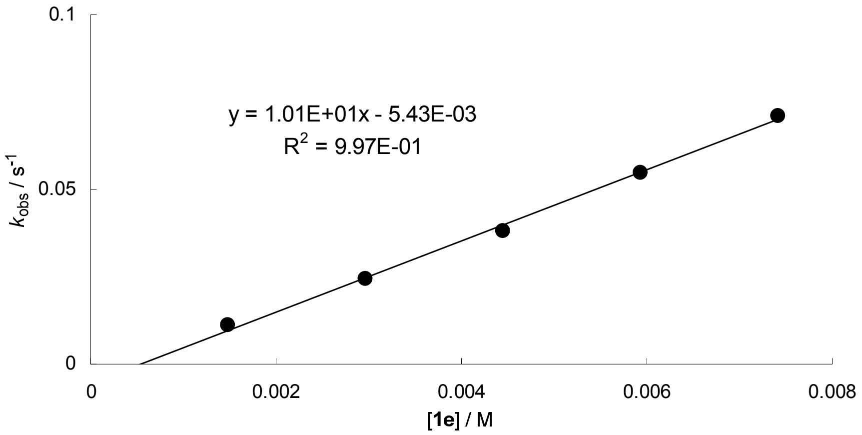

y = 4.53E+03x + 4.83E-01
R^2 = 9.98E-01
k_{obs} / s^{-1}
50
40
30
20
10
0
0
0.004
0.008
0.012
[**1d**] / M

3.5.2.5 Kinetics of the Reactions of (*E*)-3-Methyl-1-nitrobut-1-ene (1e) with the Carbanions 2 in DMSO

Reaction of **1e** with **2b** (DMSO, 20 °C, stopped-flow, 401 nm)

$k_2 = 1.01 \times 10^{1}$ M^{-1} s^{-1}

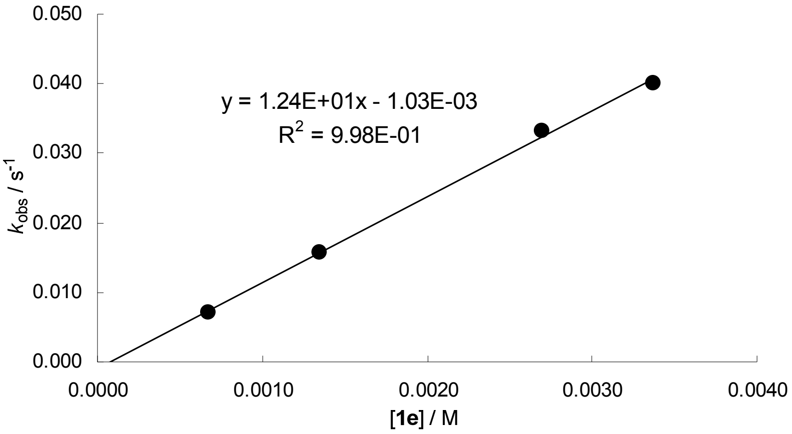
[**1e**] /M	[**2b**] /M	k_{obs} / s^{-1}
1.49×10^{-3}	9.62×10^{-5}	1.09×10^{-2}
2.97×10^{-3}	9.62×10^{-5}	2.43×10^{-2}
4.46×10^{-3}	9.62×10^{-5}	3.79×10^{-2}
5.94×10^{-3}	9.62×10^{-5}	5.48×10^{-2}
7.43×10^{-3}	9.62×10^{-5}	7.10×10^{-2}



Reaction of **1e** with **2c** (DMSO, 20 °C, conventional, 316 nm)

$k_2 = 1.24 \times 10^{1}$ M^{-1} s^{-1}

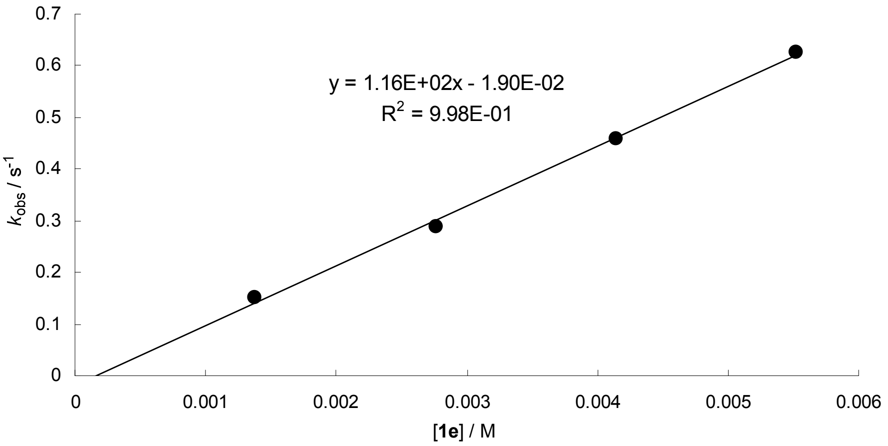
[**1e**] /M	[**2c**] /M	k_{obs} / s^{-1}
6.74×10^{-4}	3.83×10^{-5}	6.99×10^{-3}
1.35×10^{-3}	3.83×10^{-5}	1.58×10^{-2}
2.70×10^{-3}	3.83×10^{-5}	3.32×10^{-2}
3.37×10^{-3}	3.83×10^{-5}	4.00×10^{-2}



Reaction of **1e** with **2d** (DMSO, 20 °C, stopped-flow, 344 nm)

$k_2 = 1.16 \times 10^2$ M^{-1} s^{-1}

[**1e**] /M	[**2d**] /M	k_{obs} / s^{-1}
1.38×10^{-3}	1.31×10^{-4}	1.50×10^{-1}
2.76×10^{-3}	1.31×10^{-4}	2.88×10^{-1}
4.14×10^{-3}	1.31×10^{-4}	4.58×10^{-1}
5.52×10^{-3}	1.31×10^{-4}	6.26×10^{-1}

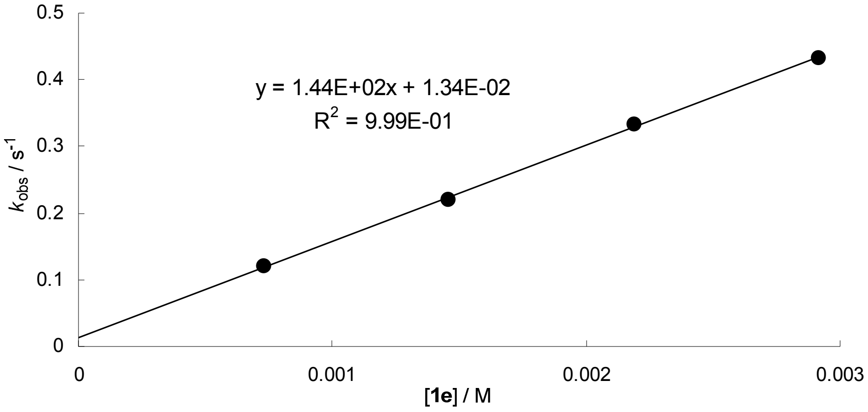


Reaction of **1e** with **2e** (DMSO, 20 °C, stopped-flow, 290 nm)

$k_2 = 1.44 \times 10^2$ M^{-1} s^{-1}

[**1e**] /M	[**2e**] /M	k_{obs} / s^{-1}
7.30×10^{-4}	5.14×10^{-5}	1.19×10^{-1}

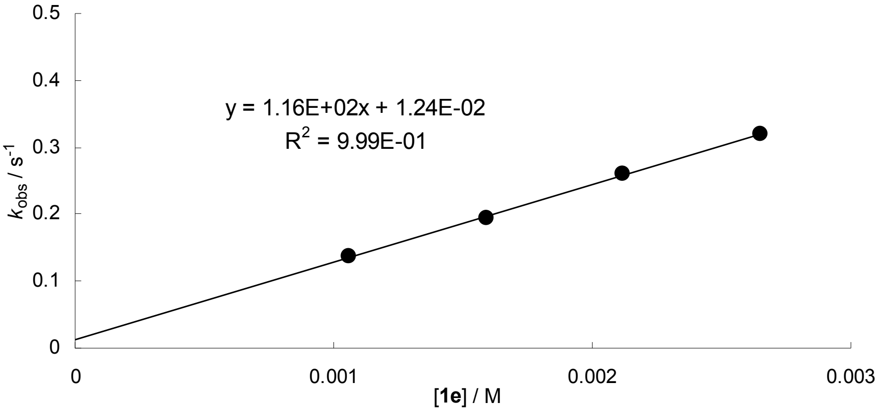
1.46×10^{-3}	5.14×10^{-5}	2.20×10^{-1}
2.19×10^{-3}	5.14×10^{-5}	3.33×10^{-1}
2.92×10^{-3}	5.14×10^{-5}	4.32×10^{-1}



Reaction of **1e** with **2f** (DMSO, 20 °C, stopped-flow, 550 nm)

$k_2 = 1.16 \times 10^2$ M^{-1} s^{-1}

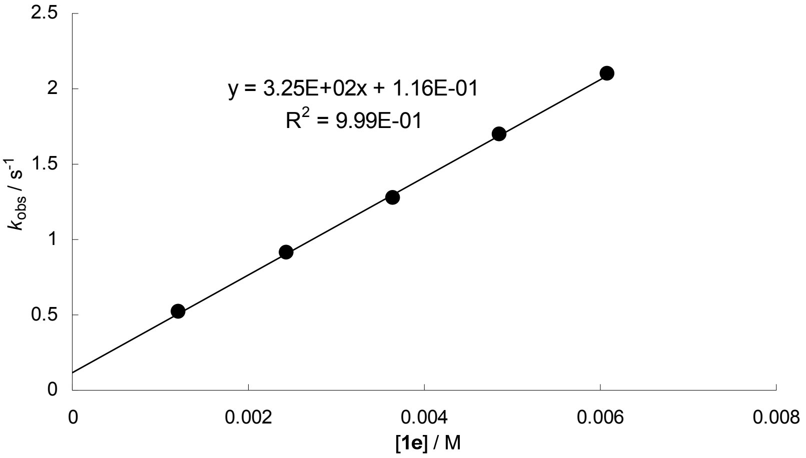
[**1e**] /M	[**2f**] /M	k_{obs} / s^{-1}
1.06×10^{-3}	6.81×10^{-5}	1.37×10^{-1}
1.59×10^{-3}	6.81×10^{-5}	1.94×10^{-1}
2.12×10^{-3}	6.81×10^{-5}	2.61×10^{-1}
2.65×10^{-3}	6.81×10^{-5}	3.20×10^{-1}



reaction of **1e** with **2g** (DMSO, 20 °C, stopped-flow, 539 nm)

$k_2 = 3.25 \times 10^2$ M^{-1} s^{-1}

[**1e**] /M	[**2g**] /M	k_{obs} / s^{-1}
1.22×10^{-3}	8.88×10^{-5}	5.21×10^{-1}
2.43×10^{-3}	8.88×10^{-5}	9.11×10^{-1}
3.65×10^{-3}	8.88×10^{-5}	1.27
4.86×10^{-3}	8.88×10^{-5}	1.70
6.08×10^{-3}	8.88×10^{-5}	2.10



3.5.2.6 Equilibrium Constants *K* for the Reactions of the Nitroolefins 1a,c with 2f in DMSO

Equilibrium constants were measured by UV-vis spectroscopy in DMSO as follows: To a solution of the carbanion salt **2f** in DMSO, small volumes of stock solutions of nitroolefins **1a,c** were added and the resulting absorptions of **2f** were monitored. When the absorbance was constant, another portion of the stock solution was added. This procedure was repeated two times. The end absorbances were obtained by least–squares fitting of the exponential absorbance decay to the mono–exponential function $A_t = A_0\ e^{-k_{\mathrm{obs}}t} + C$. Assuming a proportionality between the absorbances and the concentrations of **2f**, the equilibrium constants (K) can be expressed by the absorbances of the **2f** before (A_0) and after (A) the addition of nitroolefins **1a,c** using the equations 3.2 and 3.3. The temperature of the solutions during all equilibrium studies was kept constant at (20.0 ± 0.1) °C using a circulating bath thermostat.

Determination of the equilibrium constant for the reaction of **1a** with **2f** (DMSO, 20 °C, conventional, 539 nm)

ε [**2f** at 539nm] = 2.73×10^4 M^{-1} cm^{-1} and d = 0.5 cm

Entry	[**1a**]$_0$ /M	A	[**2f**]$_{eq}$ /M	[**4af**]	[**1a**]	K /M^{-1}
0	0	1.421	1.042×10^{-4}	-	-	-
1	1.095×10^{-4}	1.006	7.377×10^{-5}	3.043×10^{-5}	7.907×10^{-5}	5.22×10^3
2	2.190×10^{-4}	0.756	5.544×10^{-5}	4.876×10^{-5}	1.702×10^{-4}	5.17×10^3
3	3.285×10^{-4}	0.595	4.363×10^{-5}	6.057×10^{-5}	2.679×10^{-4}	5.18×10^3
4	4.381×10^{-4}	0.489	3.586×10^{-5}	6.834×10^{-5}	3.698×10^{-4}	5.15×10^3
5	5.476×10^{-4}	0.410	3.006×10^{-5}	7.414×10^{-5}	4.735×10^{-4}	5.21×10^3
0	0	1.396	1.022×10^{-4}	-	-	-
1	1.095×10^{-4}	0.995	7.284×10^{-5}	2.936×10^{-5}	8.014×10^{-5}	5.03×10^3
2	2.190×10^{-4}	0.744	5.447×10^{-5}	4.773×10^{-5}	1.713×10^{-4}	5.12×10^3
3	3.285×10^{-4}	0.589	4.312×10^{-5}	5.908×10^{-5}	2.694×10^{-4}	5.09×10^3
4	4.381×10^{-4}	0.482	3.529×10^{-5}	6.691×10^{-5}	3.712×10^{-4}	5.11×10^3
5	5.476×10^{-4}	0.405	2.965×10^{-5}	7.255×10^{-5}	4.750×10^{-4}	5.15×10^3

K_{av}(20 °C) = 5.14×10^3 M^{-1}

Determination of the equilibrium constant for the reaction of **1c** with **2f** (DMSO, 20 °C, conventional, 539 nm)

ε [**2f** at 539nm] = 2.73×10^4 M^{-1} cm^{-1} and d = 0.5 cm

Entry	[**1c**]$_0$ /M	A	[**2f**]$_{eq}$ /M	[**4cf**]	[**1c**]	K /M^{-1}
0	0	1.395	1.022×10^{-4}	-	-	-
1	1.102×10^{-4}	1.024	7.502×10^{-5}	2.718×10^{-5}	8.302×10^{-5}	4.36×10^{3}
2	2.205×10^{-4}	0.788	5.773×10^{-5}	4.447×10^{-5}	1.760×10^{-4}	4.38×10^{3}
3	3.307×10^{-4}	0.638	4.674×10^{-5}	5.546×10^{-5}	2.752×10^{-4}	4.31×10^{3}
4	4.410×10^{-4}	0.525	3.846×10^{-5}	6.374×10^{-5}	3.773×10^{-4}	4.39×10^{3}
5	5.512×10^{-4}	0.450	3.297×10^{-5}	6.923×10^{-5}	4.820×10^{-4}	4.36×10^{3}
0	0	1.338	9.809×10^{-5}	-	-	-
1	1.194×10^{-4}	0.959	7.031×10^{-5}	2.778×10^{-5}	9.162×10^{-5}	4.31×10^{3}
2	2.389×10^{-4}	0.730	5.352×10^{-5}	4.457×10^{-5}	1.943×10^{-4}	4.29×10^{3}
3	3.583×10^{-4}	0.575	4.215×10^{-5}	5.594×10^{-5}	3.024×10^{-4}	4.39×10^{3}
4	4.777×10^{-4}	0.478	3.504×10^{-5}	6.305×10^{-5}	4.147×10^{-4}	4.34×10^{3}
5	5.972×10^{-4}	0.404	2.962×10^{-5}	6.847×10^{-5}	5.287×10^{-4}	4.37×10^{3}
6	7.306×10^{-4}	0.354	2.595×10^{-5}	7.214×10^{-5}	6.584×10^{-4}	4.22×10^{3}

K_{av}(20 °C) = 4.34×10^3 M^{-1}

3.6 References

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Chapter 4: Electrophilicities of (*E*)-1-Ethoxy-2-nitroethene and (*E*)-*N*,*N*-Dimethyl-2-nitroethenamine

4.1 Introduction

The push-pull-substituted (*E*)-1-ethoxy-2-nitroethene (**1a**) has been employed in a domino nitro-Michael/Henry reaction to form 2-nitropyranosides.[1] Tandem cycloadditions of **1a** with unsaturated alcohols under conditions of Lewis acid catalysis have provided stereoselective routes to bicyclic nitronates.[2] The Reformatsky reagent provides a convenient access to 4-nitrobutanoates via a 1,4-addition to **1a**.[3] Reactions of α-aminoketones with **1a** afforded 3-nitropyrroles, which are supposedly formed via nitroenamine intermediates.[4] *l*-Menthyl 2-nitrovinylethers are easily prepared from **1a** and *l*-menthol.[5] The first use of (*E*)-*N*,*N*-dimethyl-2-nitroethenamine (**1b**) as a compound for nitrovinylation of aldehydes and ketones has been reported by Severin and coworkers.[6,7] Since then, **1b** has been employed mainly in the nitrovinylations of indoles[8,9] and alkylidenetriphenylphosphoranes.[10]

(*E*)-1-Ethoxy-2-nitroethene (**1a**) and (*E*)-*N*,*N*-dimethyl-2-nitroethenamine (**1b**) belong to the group of aliphatic nitroolefins, the electrophilic reactivities of which have been discussed in Chapter 3.

In previous work, we have shown that a large variety of reactions of electrophiles with nucleophiles can be described by eq 4.1, where N and s_N (previously called s) are nucleophile-specific parameters, E is an electrophilicity parameter, and k_2 is the second-order rate constant.[11]

$$\log k_2(20\ ^\circ\mathrm{C}) = s_N(N + E) \tag{4.1}$$

Diarylcarbenium ions and structurally related Michael acceptors have been employed as reference electrophiles for the determination of the nucleophile-specific parameters N and s_{N} of neutral and anionic nucleophiles.[12]

On the other hand, the kinetics of the reactions of carbanions with Michael acceptors such as quinone methides,[13,14,15] benzylidenemalononitriles,[16] benzylidene-1,3-indandiones,[17] benzylidenebarbituric- and thiobarbituric acids,[18] benzylidene Meldrum´s acids,[19] *trans-β*-nitrostyrenes[20] and iminium ions[21,22] have been employed to determine the E parameters of these electrophiles according to eq 4.1.

In this part, we will report on the kinetics of (*E*)-1-ethoxy-2-nitroethene (**1a**) with the pyridinium ylides **2a–e** (Table 4.1) in DMSO, and on the kinetics of (*E*)-*N*,*N*-dimethyl-2-nitroethenamine (**1b**) with the carbanions **3a–c** (Table 4.2) in DMSO, and demonstrate that the second-order rate constants k_2 of these reactions follow eq 4.1. These rate constants will then be used for the determination of the E parameters for (*E*)-1-ethoxy-2-nitroethene (**1a**), and be used, to derive the "restricted" E parameters for (*E*)-*N*,*N*-dimethyl-2-nitroethenamine (**1b**).

TABLE 4.1. Reactivity Parameters N and s_{N} of the Pyridinium Ylides 2a–g in DMSO.

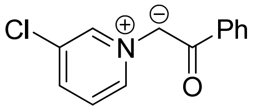
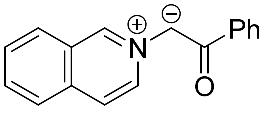
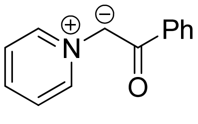
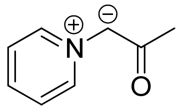
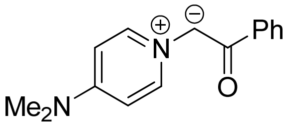
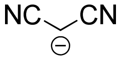
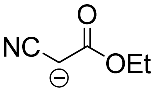
	Nucleophile	N, s_{N}[a]
2a		17.78, 0.63
2b		19.10, 0.51
2c		19.91, 0.57

TABLE 4.1. (Continued).

2d		21.30, 0.50
2e		21.68, 0.56

[a] *N* and s_N D. Allgäuer, manuscript in preparation.

TABLE 4.2. Reactivity Parameters *N* and s_N of the Carbanions 3a–c in DMSO.

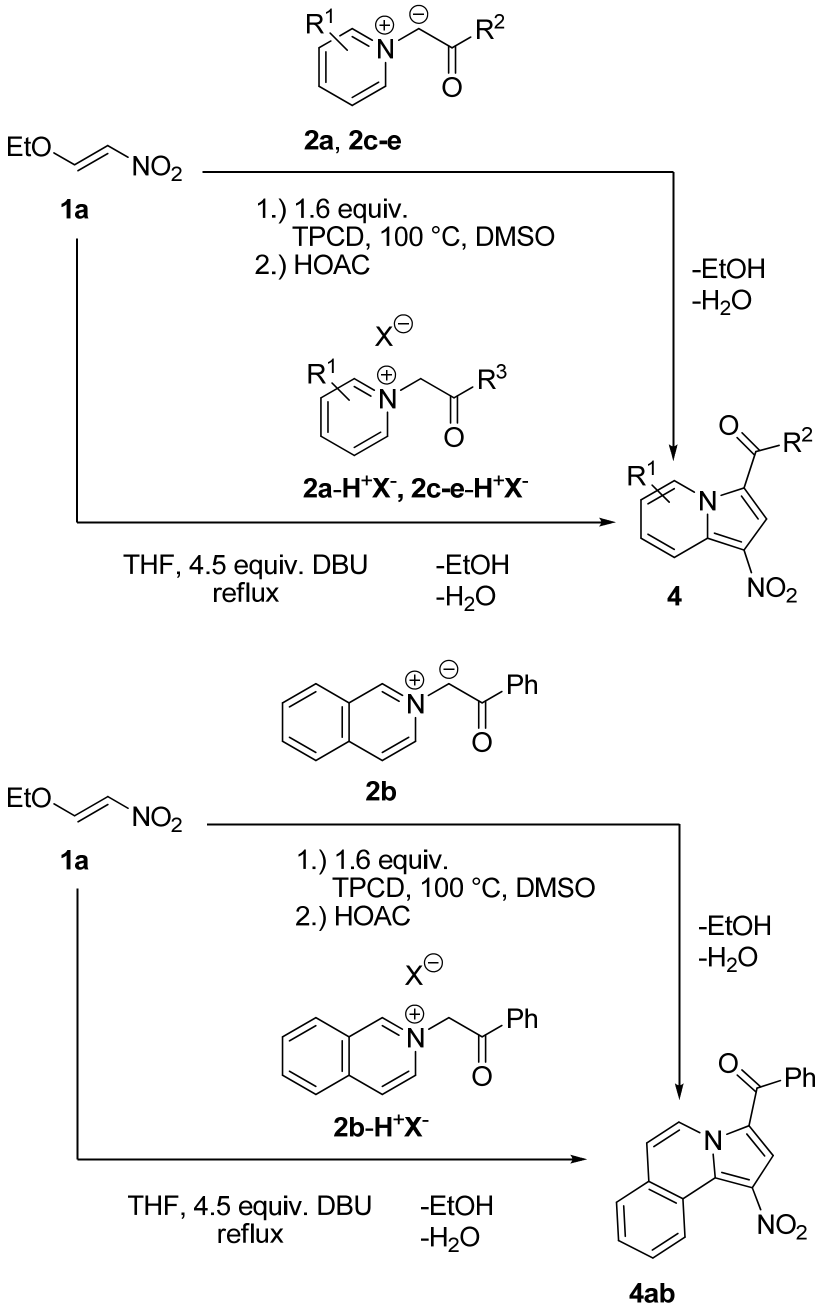
	Nucleophile	N, s_N
3a		19.36, 0.67[a]
3b		19.62, 0.67[a]
3c	$H_2C{=}NO_2^{\ominus}$	20.71, 0.60[b]

[a] Ref 23. [b] Ref 24.

4.2 Results

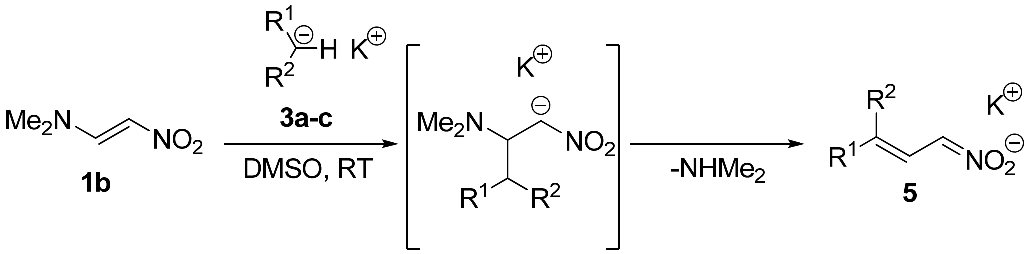
The origin of the adducts described in the following can be derived from the formula abbreviations **4xy**: The first letter identifies the electrophile, while the second letter identifies the nucleophile (Table 4.3). Thus, compound **4ab** is an adduct from **1a** and **2b**.

SCHEME 4.1. Reactions of the Nitroolefin 1a with the Pyridinium Ylides 2a–e.



The products **4ab–ad** were obtained in 55-75% yield by refluxing the nitroolefin **1a** with 2 equiv. of the pyridinium salts **2-H** and 4.5 equiv. DBU in THF.[25] Much lower yields (10-15%) were obtained by heating equimolar amounts of **1a**, pyridinium ylides **2** and 1.6 equiv. of TPCD in DMSO to 100 °C.[26] The reactions were performed under an air atmosphere. After the initial attack and cyclization, these reactions proceed via an dehydrogenative aromatization of the dihydroindolizine moeity, presumably eliminating EtOH and H_2O.[27,28]

SCHEME 4.2. Reactions of the Nitroolefin 1b with the Carbanions 3a–c.



5ba-K and **5bb-K** were isolated as stable potassium salts from **1b** and 1.25 equiv. of **3a**,**b** in DMSO in 71 and 64% yield.

TABLE 4.3. Yields of Products 4 and 5.

Electrophile	Nucleophile	Product	Yield (%)
1a	**2b**	**4ab**	55[a]
1a	**2c**	**4ac**	75[a]
1a	**2d**	**4ad**	71[a]
1a	**2b**	**4ab**	10[b]
1a	**2c**	**4ac**	15[b]
1b	**3a**	**5ba-K**	71[c]
1b	**3b**	**5bb-K**	64[c]

[a] From 2 equiv. of **1a**, 1 equiv. of **2-H** and 4.5 equiv. DBU in THF. [b] From equimolar amounts of **1a**, **2** and 1.6 equiv. of TPCD in DMSO. [c] From 1 equiv. of **1b**, and 1.25 equiv. of **3-H** and KO*t*Bu in DMSO.

The kinetic investigations were performed at 20 °C in DMSO as the solvent. The pyridinium ylides **2a**–**e** and carbanions **3a**–**c** were generated by treatment of the corresponding CH-acids with 1.05 equivalents of potassium *tert*-butoxide, and the solutions thus obtained were directly used for the kinetic investigations. The rates of the consumption of the pyridinium ylides **2a**–**e** ($\lambda_{\max}$ = 425–530 nm) were followed at their absorption maxima by employing the stopped-flow technique ($\tau_{1/2}$ < 30 s). Measurements by conventional UV-vis spectroscopy ($\tau_{1/2}$ > 30 s) were performed at the absorption maximum of **1b** ($\lambda_{\max}$ = 357 nm) in its reactions with the carbanions **3a**–**c**.

By using a high excess of the nitroolefin **1a** (10–100 equiv.) relative to the pyridinium ylides **2a**–**e**, and of the carbanions **3a**–**c** (10–100 equiv.) relative to **1b**, pseudo-first-order conditions were achieved (eq 4.2 and 4.3). In all cases, we observed monoexponential decays of the absorbances of the minor compounds **2a**–**e** and **1b**.

$$-\mathrm{d}[\mathbf{1b}]/\mathrm{d}t = k_{\mathrm{obs}}[\mathbf{1b}] \tag{4.2}$$

$$-\mathrm{d}[\mathbf{2a\text{–}e}]/\mathrm{d}t = k_{\mathrm{obs}}[\mathbf{2a\text{–}e}] \tag{4.3}$$

The first-order rate constants k_{obs} were obtained by least-squares fitting of the time-dependent absorbances A_t of the minor compounds to the exponential function $A_t = A_0\,\mathrm{e}^{-k_{\mathrm{obs}}t} + C$.

As shown in Figure 4.1 for the reaction of **1a** with **2d**, plots of k_{obs} versus the concentrations of the nitroolefin **1a** were linear, and the slopes of these correlations gave the second-order rate constants k_2 listed in Table 4.4.

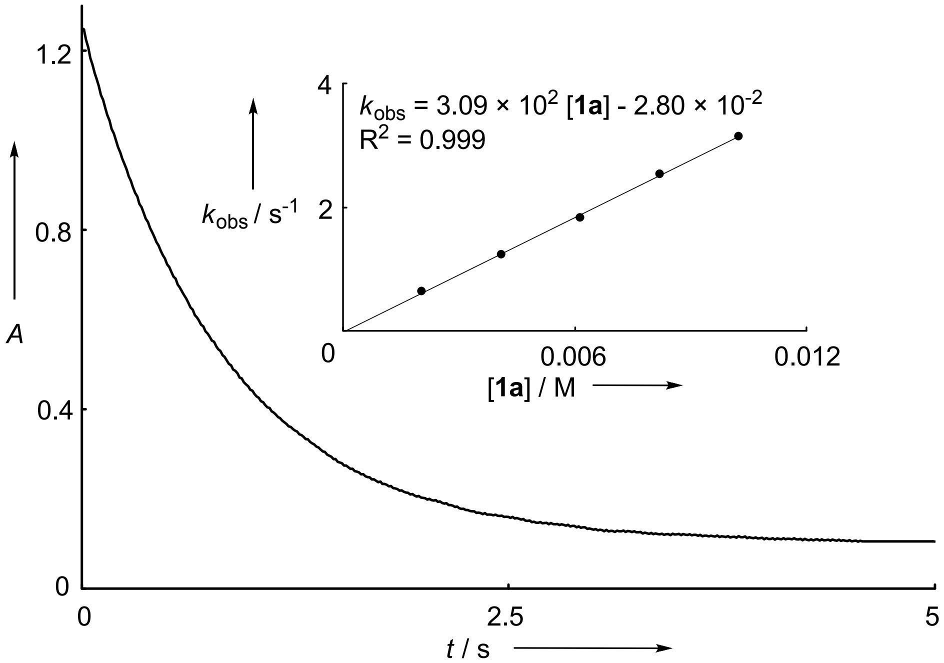
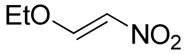
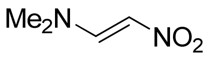


FIGURE 4.1. Exponential Decay of the Absorbance (*A* at λ = 425 nm) for the Reaction of 2d ($c = 2.33 \times 10^{-4}$ M) with 1a ($c = 4.10 \times 10^{-3}$) in DMSO at 20 °C. Insert: Correlation of the pseudo-first order Rate Constants k_{obs} *vs.* [1a].

TABLE 4.4. Second-order Rate Constants k_2 for the Reactions of the Nitroolefins 1a,b with the Pyridinium Ylides 2 and the Carbanions 3 in DMSO at 20 °C.

Electrophile	E^a	**Nucleophile**	k_2^{exp} (M^{-1} s^{-1})	k_2^{calcd} (M^{-1} s^{-1})	k_2^{exp}/k_2^{calcd}
1a	–16.41	**2a**	8.42	7.30	1.15
		**2b**	1.76×10^1	2.35×10^1	0.75
		2c	7.77×10^1	9.89×10^1	0.79
		2d	3.09×10^2	2.79×10^2	1.11
		2e	1.14×10^3	8.94×10^2	1.28
1b	(–21.32)	**3a**	5.73×10^{-2}	4.86×10^{-2}	1.18
		**3b**	4.90×10^{-2}	7.26×10^{-2}	0.67
		3c	5.57×10^{-1}	4.31×10^{-1}	1.29

[a] The E parameters for **1a**,**b** result from a least-squares minimization of the sum of Δ^2, with $\Delta = \log k_2^{exp} - s_N(N + E)$; k_2^{exp} taken from this table, N and s_N of the pyridinium ylides **2a–e** from Table 4.1, N and s_N of the carbanions **3a–c** from Table 4.2.

4.3 Discussion

The rate constants k_2 listed in Table 4.4 reveal, that the reactivity order of the pyridinium ylides **2a–e** toward **1a**, and of the carbanions **3a–c** toward **1b** are generally the same as toward benzhydrylium ions and quinone methides, the reference electrophiles of our scales. Deviations from this order will be discussed below.

Substitution of the rate constants k_2 (Table 4.4) and of the previously shown parameters N and s_N of the pyridinium ylides (Table 4.1) and carbanions (Table 4.2) into eq 4.1 allows one to calculate the electrophilicity parameters E for the nitroolefins **1a** and **1b**. The values of E, which are listed in Table 4.4, were obtained by minimizing the sum of Δ^2, i.e., the squares of the deviations between experimental and calculated rate constants, $\Delta = (\log k_2^{exp}) - s_N(N + E)$. The correlation in Figure 4.2 illustrates, that the rate constants for the reactions of **1a** with the pyridinium ylides **2a–e** are well reproduced by eq 4.1; i.e., the experimental data points are close to the calculated correlation lines, the slopes of which are fixed at 1.0. The last column of Table 4.4 shows that the deviations between calculated and experimental rate constants are always less than a factor of 1.3, which we consider tolerable in view of the fact that the reactivity parameters N and s_N for **2a–e** have been derived from reactions with benzhydrylium ions and quinone methides,[29,30,31] and were not adjusted to the reactions with the electrophiles studied in this work. Performing kinetics of the reactions of **1a** with the carbanions **3a–c** is not possible due to an overlap of the UV-bands.

The reactions of the nitroolefin **1b** with the carbanions **3a–c** are satisfactorily reproduced by eq 4.1. However, we observed that **1b** does not react (no change of the absorbance of **1b** after the addition of the carbanion) with the carbanions of nitroethane, diethyl malonate, 4-nitrophenylacetonitrile and 4-cyanophenylacetonitrile, carbanions similar to **3a–c**, which we currently can not explain. There is also no reaction of **1b** with the pyridinium ylides **2a–e**.

Therefore we can not assign an electrophilicity value to (*E*)-*N*,*N*-dimethyl-2-nitroethenamine (**1b**) of general validity.

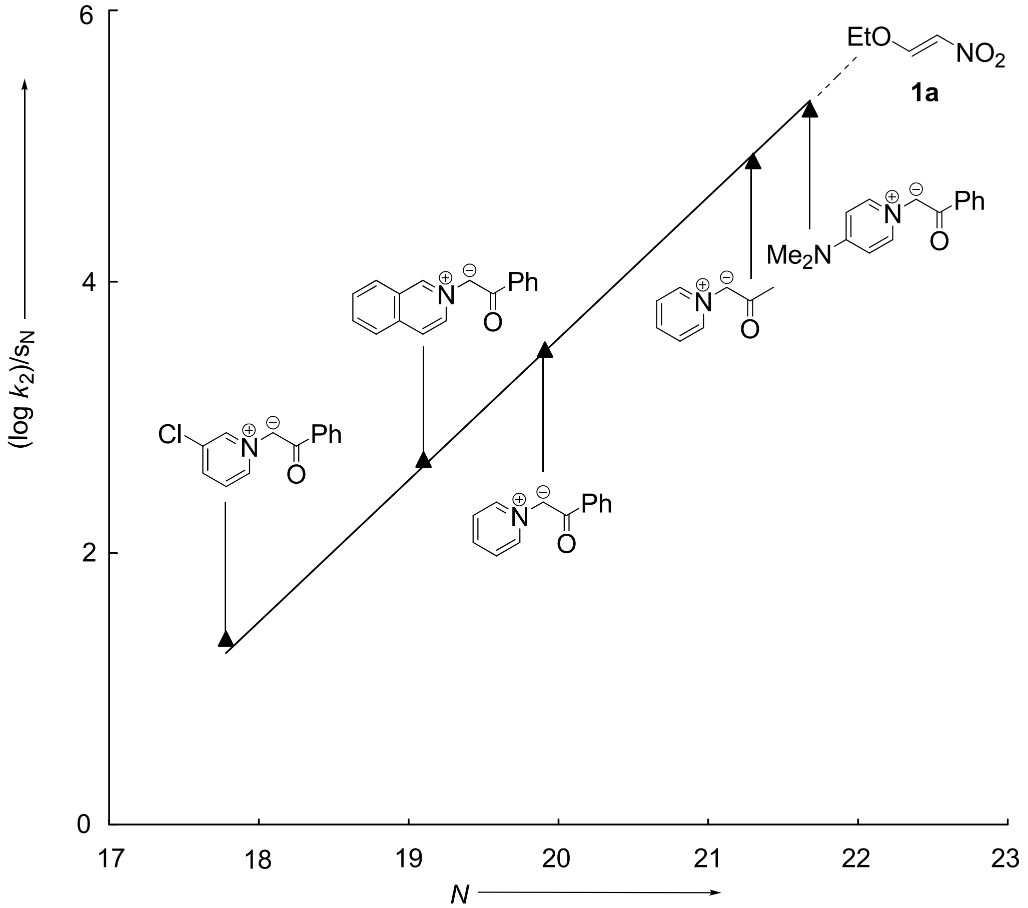


FIGURE 4.2. Correlation of (log k_2)/s_N versus the Nucleophilicity Parameters *N* of the Pyridinium Ylides 2a–e for their Reactions with (*E*)-1-Ethoxy-2-nitroethene (1a) in DMSO at 20 °C. The Correlation Lines are Fixed at a Slope of 1.0, as Required by Eq 4.1.

4.4 Conclusion

Eq 4.1 was found also to be applicable to reactions of the aliphatic nitroolefin **1a** with pyridinium ylides. Thus, the experimental rate constants of the reactions of **1a** with the pyridinium ylides **2a–e** in DMSO agree within a factor of 1.3 with the rate constants calculated by eq 4.1. As illustrated in Figure 4.3, **1a** is about one order of magnitude less reactive than (*E*)-3-methyl-1-nitrobut-1-ene (E = –15.72, see Chapter 3), which shows that the electronic retardation of the ethoxy group is stronger than the steric retardation by the bulky *iso*-propyl group. **1a** is slightly less reactive than the methoxy-substituted quinone methide, but slightly more reactive than the dimethylamino-substituted bissulfonyl ethylene shown in Figure 4.3. **1b** exhibits similar reactivity compared to benzaldehydes and diethyl benzylidene malonates, though we were not able to assign an E value as discussed above.

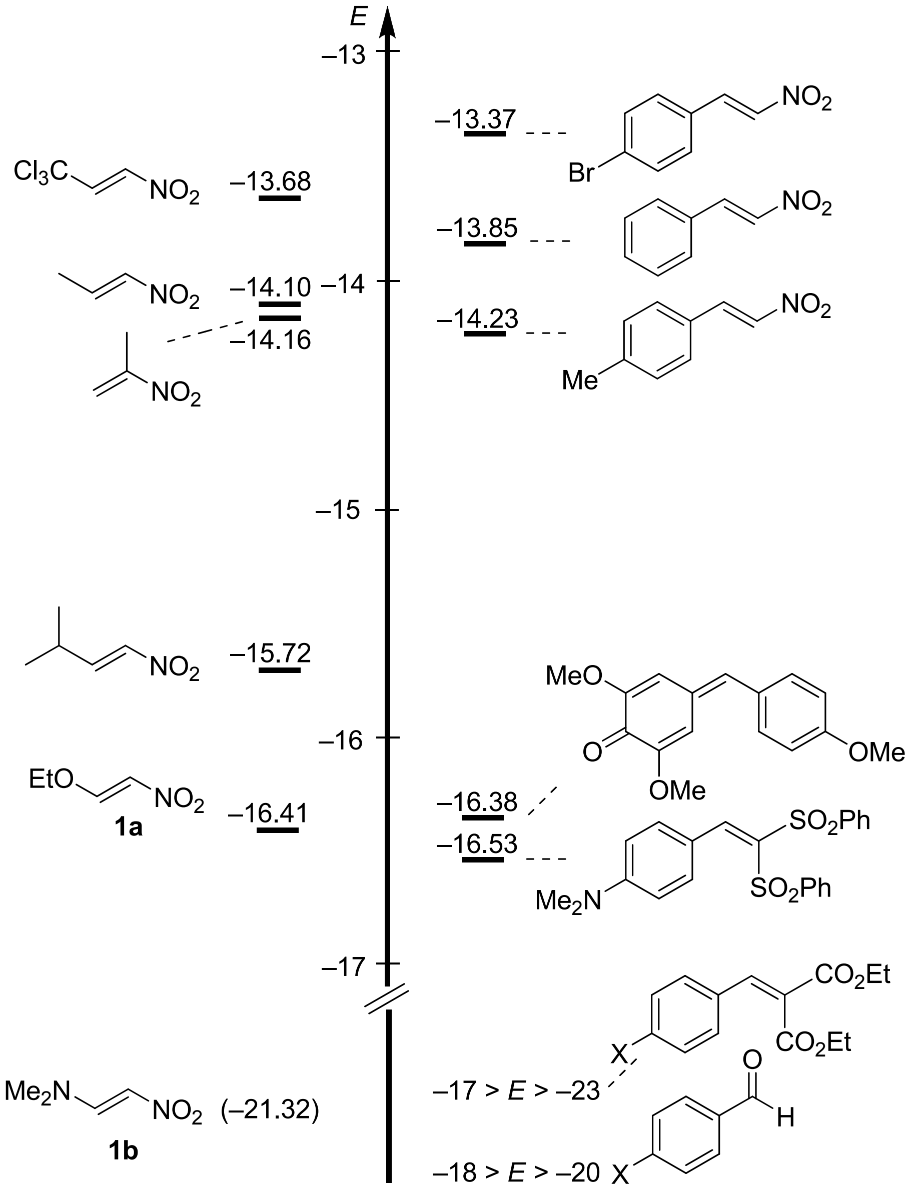


FIGURE 4.3. Comparison of *E* Values for Differently Substituted Michael Acceptors.[32]

4.5 Experimental Section

4.5.1 Products

Commercially available DMSO (with < 50 ppm H_2O content) was used without further purification. CH-acids **3b,c** were purchased and purified by distillation. All kinetic measurements were performed under an atmosphere of dry nitrogen.

(*E*)-1-Ethoxy-2-nitroethene (**1a**) was received by direct nitration of ethoxyethene with acetyl nitrate and following an elimination reaction as yellow oil.[5] (*E*)-*N*,*N*-Dimethyl-2-nitroethenamine (**1b**) was synthesized from dimethylformamide dimethylacetal and nitromethane as a yellow solid.[33]

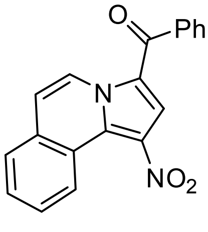
The pyridinium ylides **2a–e** were obtained from a reaction of pyridine, *p*-dimethylaminopyridine or quinoline and the corresponding α-halo ketones in THF. The ^1H and ^{13}C NMR chemical shifts are given in ppm and refer to $CDCl_3$ (δ_H = 7.26 ppm, δ_C = 77.16 ppm) or DMSO-d_6 (δ_H = 2.50 ppm, δ_C = 39.52 ppm) as internal standards.[34] The coupling constants are given in Hz.

General procedure A: Pyridinium ylide **2** (1 mmol) was dissolved in 40 mL of dry tetrahydrofuran, then (*E*)-1-ethoxy-2-nitroethene (**1a**) (2 mmol) and DBU (4.5 mmol) were added. The solution was refluxed for 18 h, after which the solvent was removed in vacuo and the crude products were purified by column chromatography (eluent *n*-pentane/ethyl acetate).

General procedure B: Pyridinium ylide **2** (0.8 mmol) was dissolved in 40 mL of dry tetrahydrofuran, then (*E*)-1-ethoxy-2-nitroethene (**1a**) (0.8 mmol), potassium *tert*-butoxide (0.8 mmol) and TPCD (1.64 mmol) were added. After the solution was heated to 100 °C for 8 h, the resulting mixture was poured on 30 mL water, and the aqueous phase was washed three times with ethyl acetate (30 mL). The solvent was removed in vacuo and the crude products were purified by column chromatography (eluent *n*-pentane/ethyl acetate).

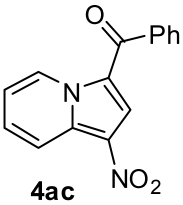
General procedure C: (*E*)-*N*,*N*-Dimethyl-2-nitroethenamine (**1b**) (1.72 mmol) was dissolved in 1 mL DMSO, then potassium *tert*-butoxide (2.15 mmol) and CH-acid **3**-**H** were added. After the solution was stirred for 2 h, ethanol and subsequently *n*-pentane were added to afford precipitation. The crude products were purified by recrystallization from ethanol.

4.5.1.1 Reactions of (*E*)-1-Ethoxy-2-nitroethene (1a) with the Pyridinium Ylides 2



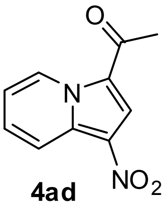
4ab

(1-Nitropyrrolo[2,1-a]isoquinolin-3-yl)(phenyl)methanone (**4ab**). From **1a** (234 mg, 2.00 mmol) and **2b** (327 mg, 1.00 mmol) following general procedure A: 174 mg (0.550 mmol, 55%), red solid, mp 189 °C. This product was also obtained following general procedure B in 10% yield. ^{1}H NMR (400 MHz, CDCl$_3$): δ(ppm) = 7.47-7.67 (m, 5 H), 7.71 (s, 1 H), 7.82 (dd, J = 5.7, 13.4 Hz, 2 H), 7.92-7.96 (m, 1 H), 8.01-8.05 (m, 2 H), 8.42 (d, J = 9.5 Hz, 1 H). ^{13}C NMR (75 MHz, CDCl$_3$): δ(ppm) = 116.5, 120.4, 122.8, 125.4, 126.6, 127.1, 129.0, 129.4, 130.1, 130.4, 132.4, 132.7, 133.9, 135.1, 137.3, 185.2.



4ac

(1-Nitroindolizin-3-yl)(phenyl)methanone (**4ac**). From **1a** (234 mg, 2.00 mmol) and **2c** (278 mg, 1.00 mmol) following general procedure A: 200 mg (0.751 mmol, 75%), yellow solid, mp 171 °C. This product was also obtained following general procedure B in 15% yield. ^{1}H NMR (400 MHz, CDCl$_3$): δ(ppm) = 7.19 (dt, J = 1.4, 7.0, 7.2 Hz, 1 H), 7.45-7.49 (m, 2 H), 7.54-7.58 (m, 1 H), 7.63 (ddd, J = 1.1, 7.0, 8.9 Hz, 1 H), 7.74-7.77 (m, 2 H), 7.92 (s, 1 H), 8.53 (dt, J = 1.2, 1.2, 8.9 Hz, 1 H), 9.93 (dt, J = 1.0, 1.1, 7.0 Hz, 1 H). ^{13}C NMR (100 MHz, CDCl$_3$): δ(ppm) = 117.0, 119.1, 121.5, 123.1, 126.1, 128.8, 129.1, 129.7, 131.1, 132.5, 134.9, 138.9, 186.2. HRMS (EI): calcd. for $C_{15}H_{10}N_2O_3^+$, 266.0686. Found 266.0687.

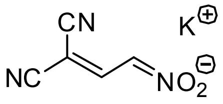


4ad

1-(1-Nitroindolizin-3-yl)ethanone (**4ad**). From **1a** (234 mg, 2.00 mmol) and **2d** (172 mg, 1.00 mmol) following general procedure A: 145mg (0.710 mmol, 71%), yellow solid, mp 210 °C. ^{1}H NMR (300 MHz, CDCl$_3$): δ(ppm) = 2.56 (s, 3 H), 7.13 (dt, J = 1.3, 7.0, 7.0 Hz, 1 H), 7.58 (ddd, J = 1.1, 7.0, 8.9 Hz, 1

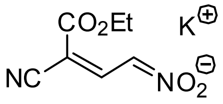
H), 8.10 (s, 1 H), 8.47-8.50 (m, 1 H), 9.89-9.91 (m, 1 H). ^{13}C NMR (75 MHz, $CDCl_3$): δ (ppm) = 27.5, 117.0, 119.0, 120.5, 121.7, 125.8, 130.0, 130.8, 134.4, 188.5. HRMS (EI): calcd. for $C_{10}H_8N_2O_3^+$ 204.0529, found 204.0532.

4.5.1.2 Reactions of (*E*)-*N*,*N*-Dimethyl-2-nitroethenamine (1b) with the Carbanions 3



5ba-K

Potassium (E)-1,1-dicyano-3-nitroprop-2-en-1-ide (**5ba-K**). From **1b** (200 mg, 1.72 mmol) and **3a** (142 mg, 2.15 mmol) following general procedure C: 214 mg (1.22 mmol, 71%), yellow solid. ^{1}H NMR (400 MHz, CDCl$_3$): δ (ppm) = 6.73 (d, *J* = 11.6, 1 H), 7.78 (d, *J* = 11.6 Hz, 1 H). ^{13}C NMR (75 MHz, CDCl$_3$): δ (ppm) = 117.0, 117.5, 119.8, 146.0. Anal.: calcd. for $C_5H_2N_3O_2K$: C, 34.28; H, 1.15; N, 23.99. Found: C, 34.07; H, 1.21; N, 23.77.



5bb-K

Potassium (E)-2-cyano-1-ethoxy-4-nitro-1-oxobut-3-en-2-ide (**5bb-K**). From **1b** (200 mg, 1.72 mmol) and **3b** (243 mg, 2.15 mmol) following general procedure C: 244 mg (1.10 mmol, 64%), yellow solid. ^{1}H NMR (400 MHz, CDCl$_3$): δ (ppm) = 1.18 (t, *J* = 7.1 Hz, 3 H), 4.06 (q, *J* = 7.1 Hz, 2 H), 6.69 (d, *J* = 11.8 Hz, 1 H), 8.24 (d, *J* = 11.8 Hz, 1 H). ^{13}C NMR (75 MHz, CDCl$_3$): δ (ppm) = 14.6, 59.2, 116.2, 118.1, 119.2, 144.3, 165.8. Anal.: calcd. for $C_7H_7N_2O_4K$: C, 37.83; H, 3.17; N, 12.61. Found: C, 37.81; H, 3.20; N, 12.63.

4.5.2 Kinetics

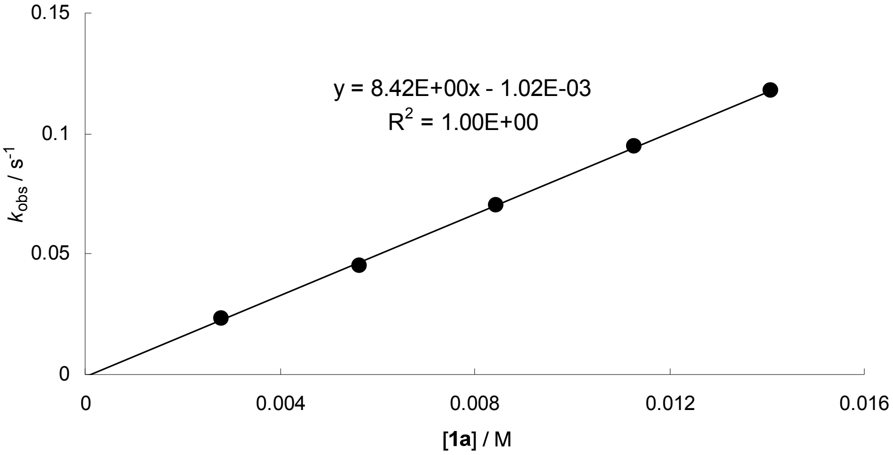
For the investigation of fast kinetics ($\tau_{1/2}$ < 30 s) stopped-flow spectrophotometer systems were used. Slow kinetics ($\tau_{1/2}$ > 30 s) were followed by using a conventional UV-vis diode array spectrophotometer system that was connected to a quartz immersion probe via fiber optic cables. All measurements were carried out under first-order conditions (in general [**1a**]$_0$/[**2**]$_0$ > 10; [**3**]$_0$/[**1b**]$_0$ > 10). The first-order rate constants k_{obs} were obtained by least-squares fitting of the time-dependent absorbances A_t of the electrophiles to the exponential function $A_t = A_0\ e^{-k_{\text{obs}}t} + C$. Second-order rate constans k_2^{exp} were then derived from linear correlations of k_{obs} vs. [**1a**] or [**3a–c**].

4.5.2.1 Kinetics of (*E*)-1-Ethoxy-2-nitroethene (1a) with the Pyridinium Ylides 2

Reaction of **1a** with **2a** (DMSO, 20 °C, stopped-flow, 476 nm)

$k_2 = 8.42\ \mathrm{M^{-1}\ s^{-1}}$

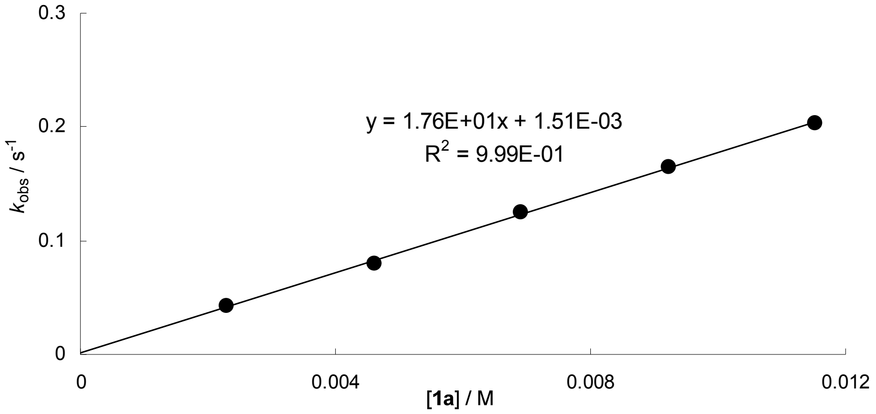
[**1a**] /M	[**2a**] /M	k_{obs} / s^{-1}
2.82×10^{-3}	1.62×10^{-4}	2.35×10^{-2}
5.64×10^{-3}	1.62×10^{-4}	4.52×10^{-2}
8.45×10^{-3}	1.62×10^{-4}	7.04×10^{-2}
1.13×10^{-2}	1.62×10^{-4}	9.45×10^{-2}
1.41×10^{-2}	1.62×10^{-4}	1.18×10^{-1}



Reaction of **1a** with **2b** (DMSO, 20 °C, stopped-flow, 530 nm)

$k_2 = 1.76 \times 10^{1}\ \mathrm{M^{-1}\ s^{-1}}$

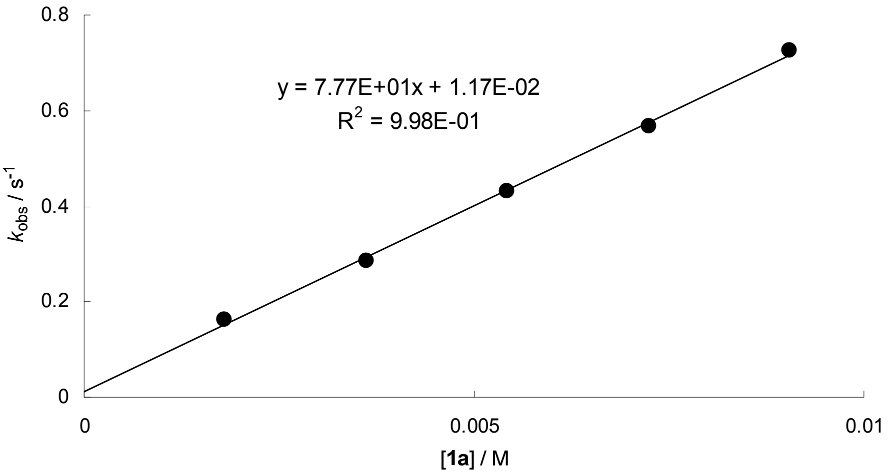
[**1a**] /M	[**2b**] /M	k_{obs} / s^{-1}
2.31×10^{-3}	3.18×10^{-4}	4.26×10^{-2}
4.61×10^{-3}	3.18×10^{-4}	7.99×10^{-2}
6.92×10^{-3}	3.18×10^{-4}	1.25×10^{-1}
9.22×10^{-3}	3.18×10^{-4}	1.65×10^{-1}
1.15×10^{-2}	3.18×10^{-4}	2.03×10^{-1}



Reaction of **1a** with **2c** (DMSO, 20 °C, stopped-flow, 445 nm)

$k_2 = 7.77 \times 10^1$ M^{-1} s^{-1}

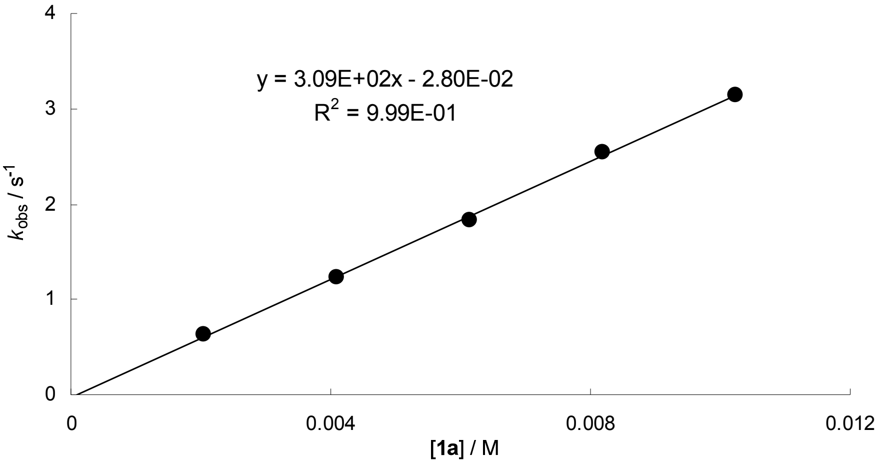
[**1a**] /M	[**2c**] /M	k_{obs} / s^{-1}
1.81×10^{-3}	2.05×10^{-4}	1.62×10^{-1}
3.62×10^{-3}	2.05×10^{-4}	2.85×10^{-1}
5.43×10^{-3}	2.05×10^{-4}	4.31×10^{-1}
7.24×10^{-3}	2.05×10^{-4}	5.66×10^{-1}
9.05×10^{-2}	2.05×10^{-4}	7.25×10^{-1}



Reaction of **1a** with **2d** (DMSO, 20 °C, stopped-flow, 425 nm)

$k_2 = 3.09 \times 10^2$ M^{-1} s^{-1}

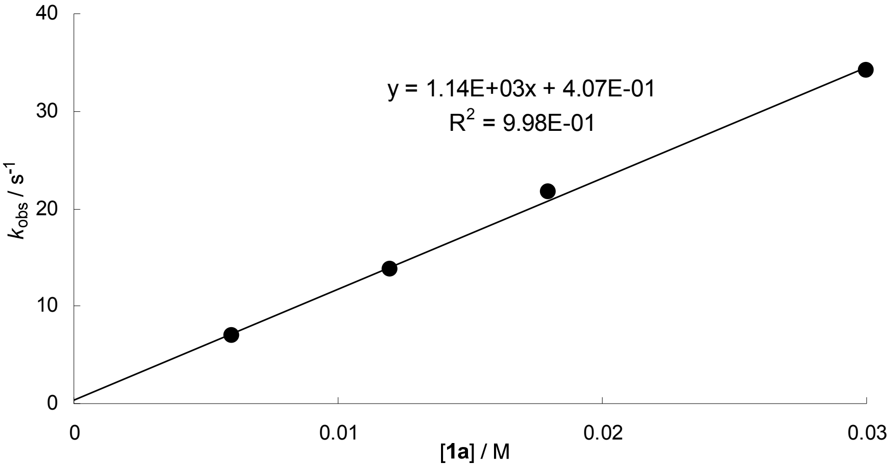
[**1a**] /M	[**2d**] /M	k_{obs} / s^{-1}
2.05×10^{-3}	2.33×10^{-4}	6.30×10^{-1}
4.10×10^{-3}	2.33×10^{-4}	1.22
6.15×10^{-3}	2.33×10^{-4}	1.83
8.20×10^{-3}	2.33×10^{-4}	2.54
1.02×10^{-2}	2.33×10^{-4}	3.14



Reaction of **1a** with **2e** (DMSO, 20 °C, stopped-flow, 425 nm)

$k_2 = 1.14 \times 10^3$ M^{-1} s^{-1}

[**1a**] /M	[**2e**] /M	k_{obs} / s^{-1}
6.00×10^{-3}	2.34×10^{-4}	7.01
1.20×10^{-2}	2.34×10^{-4}	1.38×10^{-1}
1.80×10^{-2}	2.34×10^{-4}	2.18×10^{-1}
3.00×10^{-2}	2.34×10^{-4}	3.42×10^{-1}

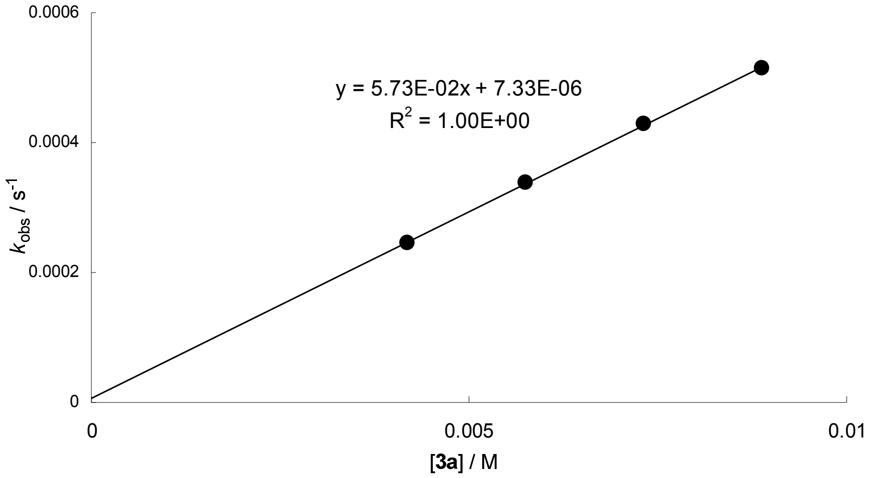

y = 1.14E+03x + 4.07E-01
R^2 = 9.98E-01
k_{obs} / s^{-1}
40
30
20
10
0
0
0.01
0.02
0.03
[**1a**] / M

4.5.2.2 Kinetics of (*E*)-*N*,*N*-Dimethyl-2-nitroethenamine (1b) with the Carbanions 3

Reaction of **1b** with **3a** (DMSO, 20 °C, conventional, 357 nm)

$k_2 = 5.73 \times 10^{-2}$ M^{-1} s^{-1}

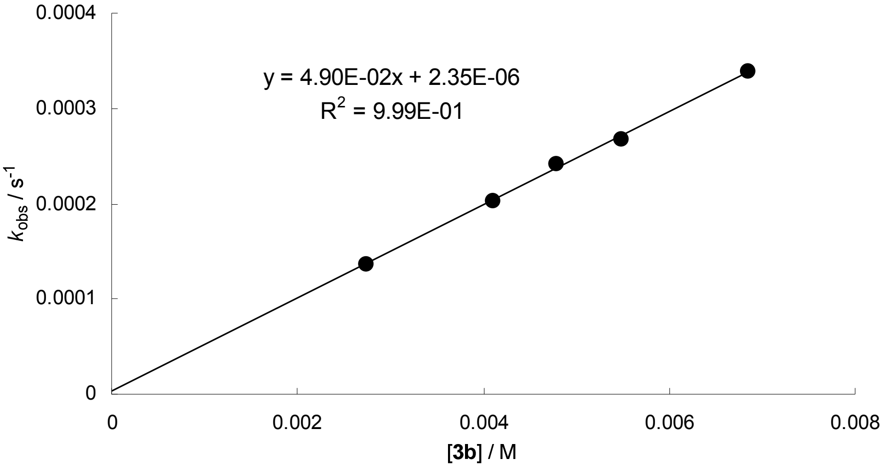
[**1b**] /M	[**3a**] /M	k_{obs} / s^{-1}
6.89×10^{-5}	4.18×10^{-3}	2.45×10^{-4}
6.89×10^{-5}	5.75×10^{-3}	3.38×10^{-4}
6.89×10^{-5}	7.31×10^{-3}	4.29×10^{-4}
6.89×10^{-5}	8.88×10^{-3}	5.14×10^{-4}



Reaction of **1b** with **3b** (DMSO, 20 °C, conventional, 357 nm)

$k_2 = 4.90 \times 10^{-2}$ M^{-1} s^{-1}

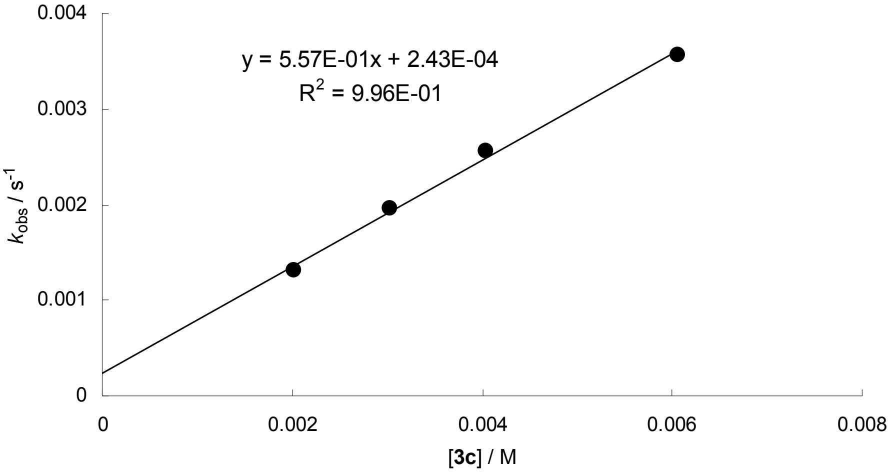
[**1b**] /M	[**3b**] /M	k_{obs} / s^{-1}
6.89×10^{-5}	2.74×10^{-3}	1.36×10^{-4}
6.89×10^{-5}	4.11×10^{-3}	2.03×10^{-4}
6.89×10^{-5}	4.80×10^{-3}	2.41×10^{-4}
6.89×10^{-5}	5.48×10^{-3}	2.68×10^{-4}
6.89×10^{-5}	6.85×10^{-3}	3.38×10^{-4}



Reaction of **1b** with **3c** (DMSO, 20 °C, conventional, 357 nm)

$k_2 = 5.57 \times 10^{-1}$ M^{-1} s^{-1}

[**1b**] /M	[**3c**] /M	k_{obs} / s^{-1}
7.92×10^{-5}	2.02×10^{-3}	1.31×10^{-3}
7.92×10^{-5}	3.03×10^{-3}	1.96×10^{-3}
7.92×10^{-5}	4.04×10^{-3}	2.56×10^{-3}
7.92×10^{-5}	6.06×10^{-3}	3.57×10^{-3}



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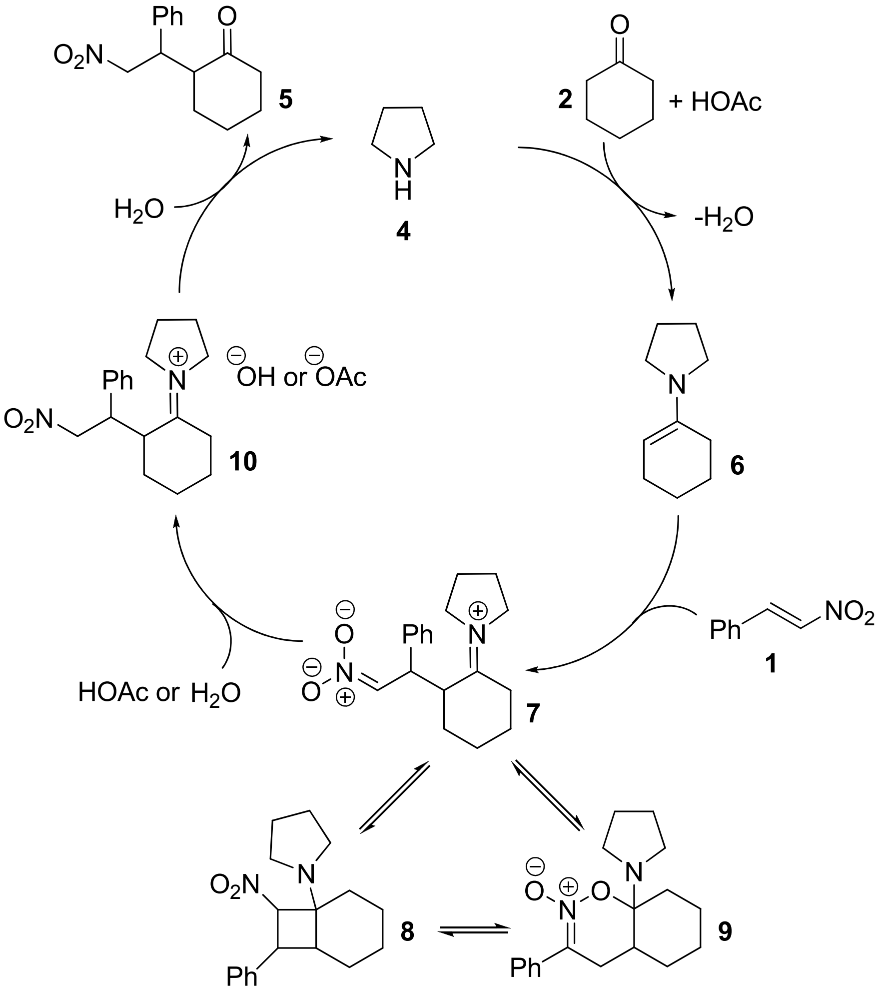
Chapter 5: *In Situ* IR Investigations of Organocatalytic Michael Additions to *trans*-β-Nitrostyrenes

5.1 Introduction

The Michael addition is widely recognized as one of the most important reactions for the formation of CC-bonds. Following the work of List[1] and Barbas,[2] considerable efforts have been focused on the development of asymmetric organocatalytic versions.[3] Nitrostyrenes[4] are known to be highly reactive Michael acceptors, and their organocatalytic transformations with aldehydes and ketones have become a benchmark for probing the efficiency and selectivity of new organocatalysts.[5,6] These transformations are also particularly important, beause they afford synthetically useful γ-nitro carbonyl compounds.[7] Recent examples include highly enantioselective thiourea-catalyzed additions[8,9,10] to aldehydes,[11] ketones,[12] and β-nitroketones.[13] The first examples on the use of diarylprolinol silyl ethers in asymmetric synthesis were independently developed by Jørgensen´s[14,15] and Hayashi´s[16] group in 2005, and, since then, they have enjoyed great success in a large variety of enamine-,[17] dienamine- and iminium-activated organocatalytic transformations. *In situ* ATR-FTIR spectroscopy along with NMR spectroscopy provides a powerful tool for reaction monitoring.[18]

We set out to investigate the kinetics of the reaction of *trans*-β-nitrostyrene with cyclohexanone catalyzed by pyrrolidine and benzoic acid as a model reaction in order to elucidate the rate orders of the individual components via *in situ* ATR-FTIR spectroscopy, and, thus provide insight into the catalytic cycle. The investigated reaction proceeds via enamine activation, and is a cheap but non-stereoselective alternative to the widely applied diaryl prolinol silyl ether system.[19] The mechanism of its catalysis in the reactions of aldehydes with nitrostyrenes has been studied in detail.[20,21]

SCHEME 5.1. Proposed Catalytic Cycle for the Conjugate Addition of Cyclohexanone to *trans-β*-Nitrostyrene Catalyzed by Pyrrolidine and Benzoic Acid.[21]



The generally accepted catalytic cycle starts with the formation of enamine **6** from the condensation of pyrrolidine (**4**) with cyclohexanone (**2**). The enamine **6** adds to the *trans-β*-nitrostyrene (**1**) to give a zwitterion **7**, which is in an equilibrium with cyclobutane **8** and cyclic nitronate **9**.[20] Zwitterion **7** is protonated at the nitronate C-atom to give an iminium ion **10**, which is then hydrolyzed to form the product **5**. Three roles of the benzoic acid (**3**) were proposed: The activation of the keto group of cyclohexanone (**2**) in the addition to the pyrrolidine (**4**) as well as the elimination of H_2O of the pyrrolidinium cyclohexanolate intermediate, and the protonation of zwitterion **7** to form iminium ion **10**, an thus promoting the conversion to product **5**.[7]

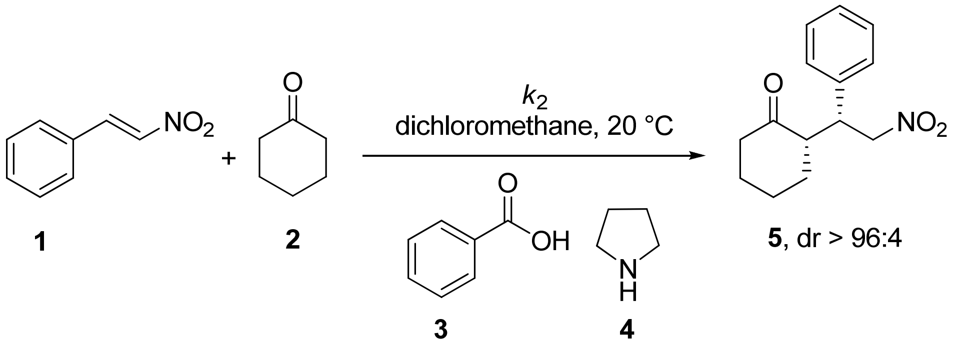
The reaction orders of nitrostyrene, cyclohexanone, pyrrolidine and benzoic acid were determined by performing a series of reactions, where only the concentration of one component was changed.[22] The slope of the linear fit of a log k_{initial} *vs*. log [**1–4**]$_0$ plot provided then the reaction order of the compounds **1–4**.[23,24]

5.2 Results

The conjugate addition of cyclohexanone (**2**) to *trans*-*β*-nitrostyrene (**1**) catalyzed by benzoic acid (**3**) and pyrrolidine (**4**) in dichloromethane at 20 °C, which proceeds in high yield and diastereoselectivity, was used as a model reaction for the kinetic studies (Scheme 5.2).[25]

The reaction progress was monitored via ATR-FTIR spectroscopy following the symmetric N-O stretching vibration of **1** at $\tilde{\nu} = 1343\ \mathrm{cm}^{-1}$. The formation of product **5** can be detected at $\tilde{\nu} = 1556\ \mathrm{cm}^{-1}$. However, through a partial overlap with the asymmetric N-O stretching vibration of **1** at $\tilde{\nu} = 1525\ \mathrm{cm}^{-1}$, the increase of absorbance caused by the formation of product **5** could not be evaluated.

SCHEME 5.2. Reaction of *trans*-*β*-Nitrostyrene with Cyclohexanone Catalyzed by Pyrrolidine and Benzoic Acid.



In order to obtain the initial rate constants k_{initial}, the slope of a given concentration *vs*. time plot was evaluated considering the first 17 min of the reaction.

$$-\mathrm{d}[\mathbf{1}]/\mathrm{d}t = k\,[\mathbf{1}]^a\,[\mathbf{2}]^b\,[\mathbf{3}]^c\,[\mathbf{4}]^d \qquad (5.1)$$

The plot of log k_{initial} *vs*. log $[\mathbf{1}\text{–}\mathbf{4}]_0$ provided the reaction orders *a*–*d* for the compounds **1**–**4**.

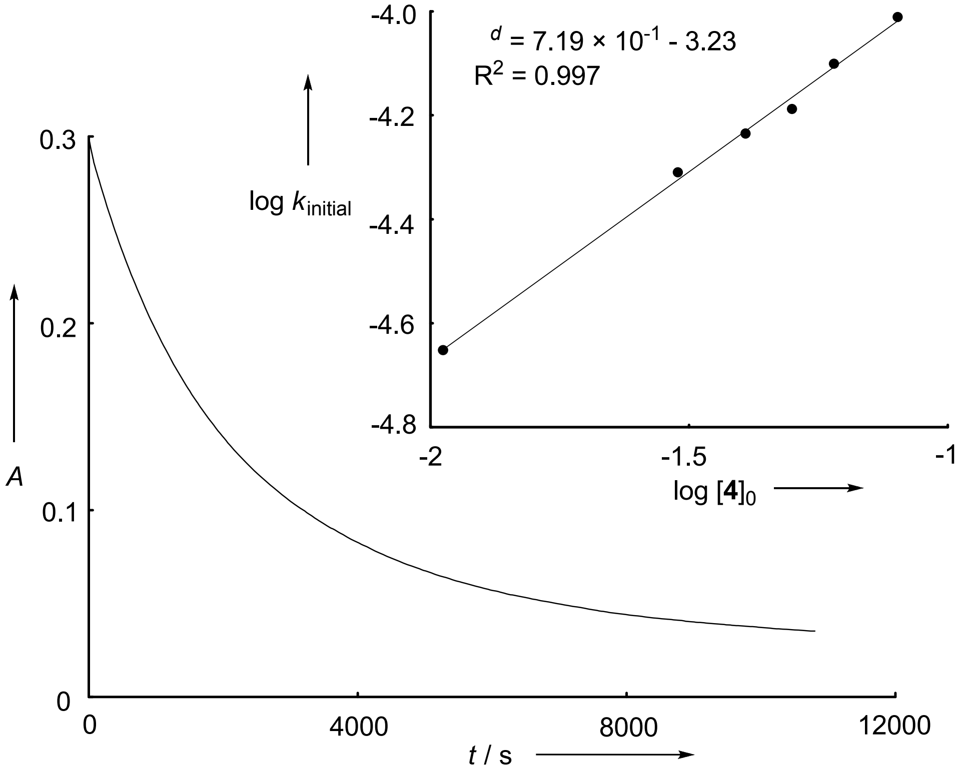


FIGURE 5.1. Decay of Absorbance (*A* at $\tilde{\nu}$ = 1343 cm^{-1}) for the Reaction of 1 (*c* = 4.02 × 10^{-1} M), 2 (*c* = 4.01 × 10^{-1} M), 3 (*c* = 4.08 × 10^{-2} M), and 4 (*c* = 6.03 × 10^{-2} M) in Dichloromethane at 20 °C. Insert: Correlation of log k_{initial} *vs*. log [4]$_0$.

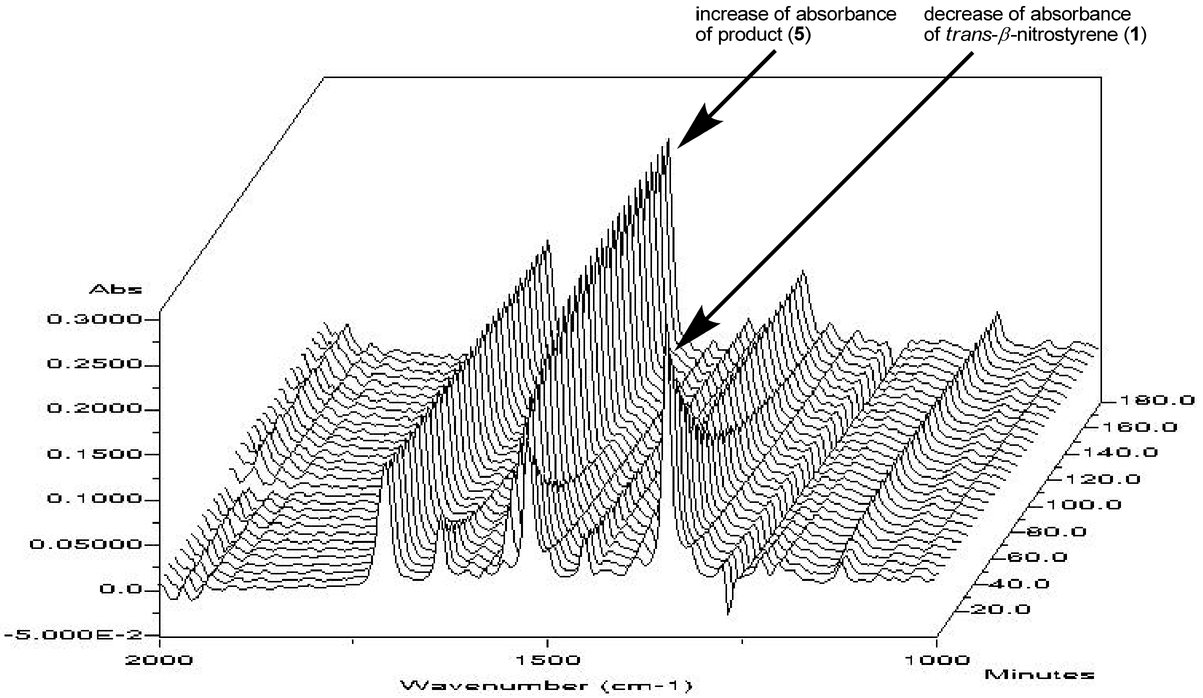
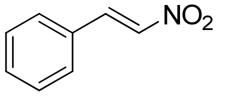


FIGURE 5.2. ATR-FTIR Spectrum Showing the Decrease of Absorbance (*A* at $\tilde{\nu}$ = 1343 cm^{-1}, *trans*-*β*-Nitrostyrene (1)) and the Increase of Absorbance (*A* at $\tilde{\nu}$ = 1556 cm^{-1}, 2-(2-Nitro-1-phenylethyl)cyclohexanone (5)). The Reaction Conditions are Identical to those Reported in Figure 5.1.

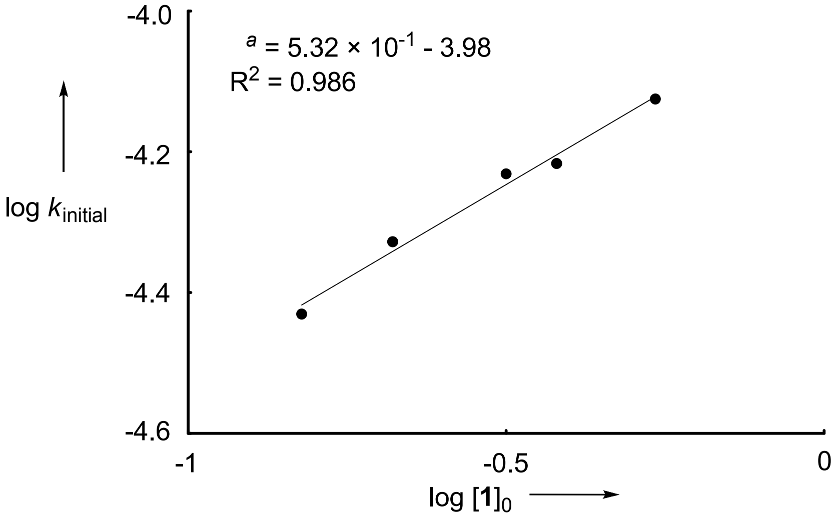
TABLE 5.1. Initial Rates, Initial Concentrations and Rate Orders of 1–4.

Rate order of **1**, ^{a} = 0.5

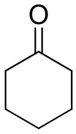


[**1**] /M	[**2**] /M	[**3**] /M	[**4**] /M	log [**1**]$_0$	k_{initial}
1.51×10^{-1}	4.03×10^{-1}	4.07×10^{-2}	4.07×10^{-2}	-0.821	3.71×10^{-5}
2.10×10^{-1}	4.04×10^{-1}	4.08×10^{-2}	4.07×10^{-2}	-0.678	4.70×10^{-5}
3.16×10^{-1}	4.06×10^{-1}	4.10×10^{-2}	4.09×10^{-2}	-0.500	5.87×10^{-5}
3.80×10^{-1}	4.06×10^{-1}	4.10×10^{-2}	4.09×10^{-2}	-0.420	6.07×10^{-5}
5.43×10^{-1}	4.02×10^{-1}	4.06×10^{-2}	4.06×10^{-2}	-0.265	7.50×10^{-5}

TABLE 5.1. (Continued).

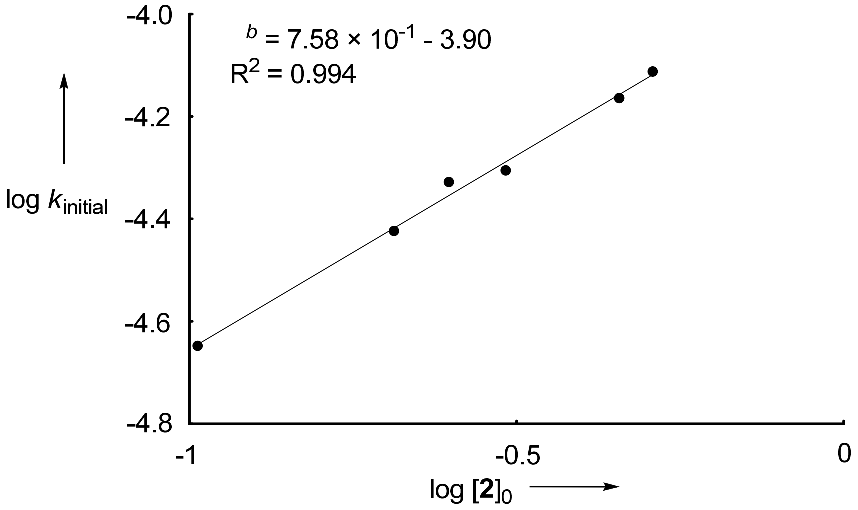


Rate order of **2**, ^{b} = 0.8

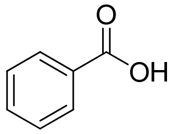


[**1**] /M	[**2**] /M	[**3**] /M	[**4**] /M	log [**2**]$_0$	k_{initial}
4.04×10^{-1}	1.03×10^{-1}	4.01×10^{-2}	4.06×10^{-2}	-0.987	2.25×10^{-5}
4.03×10^{-1}	2.05×10^{-1}	4.00×10^{-2}	4.05×10^{-2}	-0.687	3.77×10^{-5}
4.06×10^{-1}	2.49×10^{-1}	4.03×10^{-2}	4.08×10^{-2}	-0.603	4.70×10^{-5}
4.03×10^{-1}	3.04×10^{-1}	4.00×10^{-2}	4.05×10^{-2}	-0.516	4.95×10^{-5}
4.00×10^{-1}	4.54×10^{-1}	4.00×10^{-2}	4.03×10^{-2}	-0.343	6.85×10^{-5}
4.00×10^{-1}	5.11×10^{-1}	4.00×10^{-2}	4.03×10^{-2}	-0.292	7.72×10^{-5}

TABLE 5.1. (Continued).



Rate order of **3**, ^{c} = 0.4



[**1**] /M	[**2**] /M	[**3**] /M	[**4**] /M	log [**3**]$_0$	k_{initial}
4.10×10^{-1}	4.08×10^{-1}	1.06×10^{-2}	4.07×10^{-2}	-1.98	4.76×10^{-5}
4.02×10^{-1}	4.03×10^{-1}	3.00×10^{-2}	4.09×10^{-2}	-1.52	7.04×10^{-5}
4.03×10^{-1}	4.04×10^{-1}	5.09×10^{-2}	4.10×10^{-2}	-1.29	9.08×10^{-5}
4.02×10^{-1}	4.04×10^{-1}	6.02×10^{-2}	4.09×10^{-2}	-1.22	9.34×10^{-5}

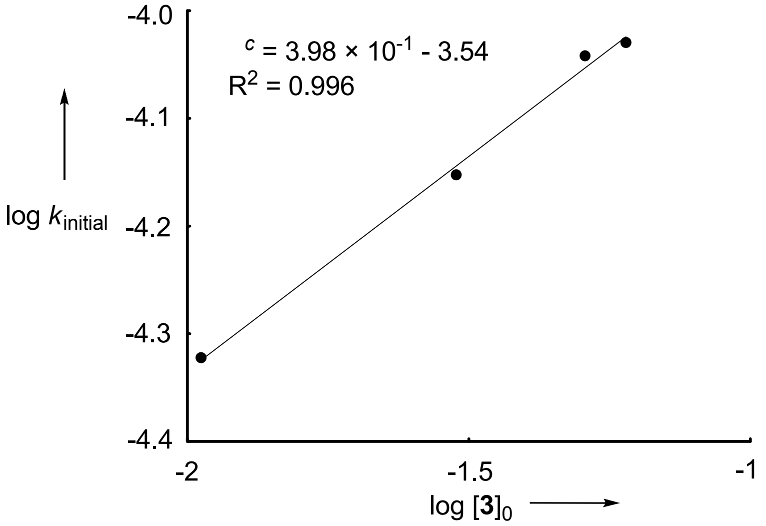
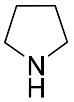
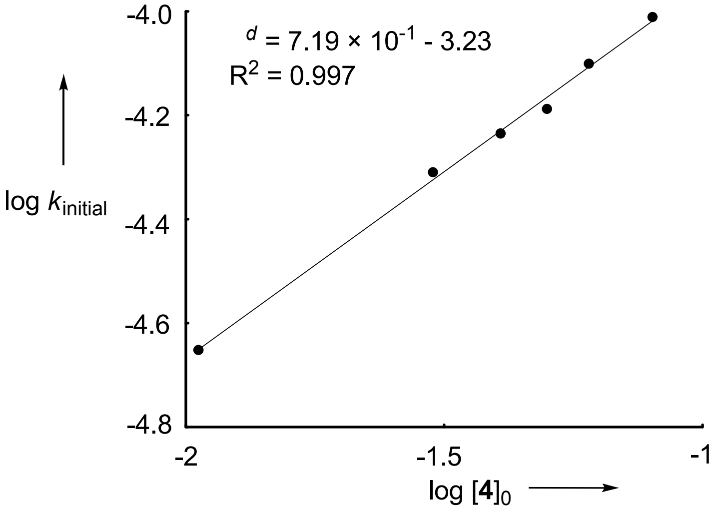


TABLE 5.1. (Continued).

Rate order of **4**, ^{d} = 0.7



[**1**] /M	[**2**] /M	[**3**] /M	[**4**] /M	log [**4**]$_0$	k_{initial}
4.09×10^{-1}	4.09×10^{-1}	4.15×10^{-2}	1.06×10^{-2}	-1.98	2.23×10^{-5}
4.01×10^{-1}	4.01×10^{-1}	4.07×10^{-2}	3.01×10^{-2}	-1.52	4.90×10^{-5}
4.03×10^{-1}	4.03×10^{-1}	4.09×10^{-2}	4.07×10^{-2}	-1.39	5.82×10^{-5}
4.03×10^{-1}	4.02×10^{-1}	4.09×10^{-2}	5.00×10^{-2}	-1.30	6.49×10^{-5}
4.02×10^{-1}	4.01×10^{-1}	4.08×10^{-2}	6.03×10^{-2}	-1.22	7.93×10^{-5}
4.01×10^{-1}	4.00×10^{-1}	4.07×10^{-2}	8.01×10^{-2}	-1.10	9.75×10^{-5}



5.3 Discussion

The rate orders of the compounds shown in Table 5.1 reveal that the rate of the reaction mostly depends on the concentrations of cyclohexanone (**2**) and pyrrolidine (**4**), with rate orders of ^{b} = 0.8 and ^{d} = 0.7, and to a lesser extent, on the concentrations of *trans-β*-nitrostyrene (**1**) and benzoic acid (**3**), with rate orders of ^{a} = 0.5 and ^{c} = 0.4. A report by Wennemers and coworkers also claims a 0.5 order dependence on the nitrostyrene, but they reported the CC-bond formation step to form a zwitterion analogous to **7** and the hydrolysis to form the reaction product both to be rate determining in the reaction of *n*-butanal with nitrostyrene catalyzed by tripeptide H-D-Pro-Pro-Glu-NH_2.[24] In contrast, Blackmond and coworkers found in a reaction of *n*-butanal with nitrostyrene catalyzed by Hayashi´s diarylprolinol ether[16] the protonation of a zwitterion analogous to **7** as the rate-determining and the first irreversible step of the catalytic cycle.[20]

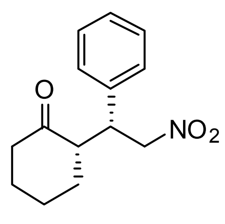
The formation of cyclobutanes from the reactions of enamines with nitroolefins,[26] acrylates,[27] and fumarates[28] has been described in literature. In 2011, Seebach and Blackmond independently investigated reactions of enamines derived from diaryl prolinol ethers with nitroolefins to form cyclobutanes analogous to **8**, and considered them to be involved in the corresponding catalytic cycle.[7,20] Cyclobutanes bearing bulky substituents were stable enough to be isolated. In the presence of H_2O, cyclobutanes are converted to the *γ*-nitroketones analogous to **5**. It is concluded that the cyclobutanes are off-cycle species formed through [2+2]-cycloadditions,[29] and that they are in an equilibrium with zwitterions analogous to **7**. Blackmond described the formed cyclobutanes as catalyst resting states playing a critical role beneficial to stereoselection by preventing the accumulation of iminium ions analogous to **10**.[20] We could not observe the formation of a cyclobutane in the reaction of *trans-β*-nitrostyrene (**1**) with enamine **6** in $CDCl_3$ or C_6D_6.[4] Blackmond and Seebach observed the formation of cyclobutanes from enamines derived from acyclic ketones and nitroalkenes. In contrast, our enamine **6** is derived from cyclohexanone (**2**) and *trans-β*-nitrostyrene (**1**). **6** forms the sterically hindered iminium ion **7**, which is obviously unable to form the strained cyclobutane **8**. Recently, Seebach proposed 1,2-oxazine N-oxides analogous to **9** as catalyst resting states being in an equilibrium with both a cyclobutane analogous to **8** and with a zwitterion analogous to **7**. The 1,2-oxazine N-oxides were isolated from a reaction of an enamine derived from Hayashi´s diarylprolinol ether[16] with isovaleraldehyde with (*E*)-2-nitro-1-phenylprop-1-ene.[30] The mechanism of organocatalytic Michael additions via enamine activation is yet not completely understood.

5.4 Experimental Section

5.4.1 Products

Commercially available dichloromethane was freshly distilled over CaH_2. All reactions were performed under an atmosphere of dry nitrogen. Commercially available pyrrolidine (> 99%) and cyclohexanone (> 99%) were purified by distillation. Benzoic acid (> 99.5%) was used as purchased. *trans-β*-Nitrostyrene (**1**) was synthesized by a Henry reaction[31] and purified by recrystallization from ethanol. The ^{1}H and ^{13}C NMR chemical shifts are given in ppm and refer to $CDCl_3$ (δ_H = 7.26 ppm, δ_C = 77.16 ppm) as internal standards.[32] The coupling constants are given in Hz.

For the investigation of the kinetics, an ATR-FTIR spectrometer with a MCT detector was used. All measurements were carried out under a nitrogen atmosphere at 20 °C. The absorbance was measured in the range of $\tilde{\nu}$ = 4000 to 400 cm^{-1} in intervals of 30 seconds with 38 scans per measuring point. The resolution was set to 8, corresponding to a vertical resolution of the measuring points of 4 cm^{-1}. The reaction progress was monitored following the N-O stretch of **1** at $\tilde{\nu}$ = 1343 cm^{-1}.



rac-**5**

(S)-2-((R*)-2-Nitro-1-phenylethyl)cyclohexanone* (*rac*-**5**). **1** (597 mg, 4.00 mmol), **2** (393 mg, 4.00 mmol), **3** (48.8 mg, 0.40 mmol) and **4** (42.7 mg, 0.60 mmol) were dissolved in 10 mL dichloromethane under nitrogen atmosphere. After the solution was stirred for 24 h, the solvent was removed in vacuo and the crude product was purified by recrystallization from ethanol: 809 mg (3.27 mmol, 82%), dr (*syn*:*anti*) > 96 : 4, determined via the integrals of the *syn* and *anti* C*H*-Ar protons,[25] white solid. ^{1}H NMR (300 MHz, $CDCl_3$): δ (ppm) = 1.10-1.24 (m, 1 H),

1.43-1.75 (m, 4 H), 1.96-2.06 (m, 1 H), 2.26-2.45 (m, 2 H), 2.57-2.66 (m, 1 H), 3.65-3.73 (m, 1 H), 3.90-3.97 (m, 0.04 H)#, 4.52-4.60 (m, 1 H), 4.84-4.89 (m, 1 H), 7.07-7.11 (m, 2 H), 7.16-7.28 (m, 3 H). ^{13}C NMR (75 MHz, $CDCl_3$): δ (ppm) = 25.2, 28.7, 33.3, 42.9, 44.1, 52.7, 79.0, 127.9, 128.3, 129.1, 137.9, 212.0. Anal.: calcd. for $C_{14}H_{17}NO_3$: C, 68.00; H, 6.93; N, 5.66. Found: C, 67.94; H, 6.94; N 5.66. # Additional signal found for the minor *anti* diastereomer.

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Chapter 6: Reactions of Diazomethanes with Michael Acceptors

6.1 Introduction

Diazomethanes are ambiphilic compounds, which are usually attacked at the carbon atom by electrophiles, whereas nucleophiles preferably attack at the nitrogen atom.[1] Despite their hazardous nature, diazomethanes are common and versatile reagents[2,3,4] employed in dipolar cycloadditions,[5,6] esterifications,[7,8,9] epoxidations,[10] aziridinations,[11] cyclopropanations[12,13] and carbonyl homologations.[14,15] The pioneering work of Huisgen has provided a general definition of 1,3-dipolar cycloadditions.[16,17] The mechanism of the 1,3-dipolar cycloadditions of diazomethanes with dipolarophiles has extensively been discussed in favor of a concerted reaction pathway,[18,19,20] and not of a stepwise diradical pathway.[21] MO pertubation treatment allows a classification of 1,3-dipoles into three types according to their frontier orbital energies.[22,23] 1,3-Dipolar cycloadditions of diazomethanes with dipolarophiles are predominantly controlled by the HOMO (diazomethane)-LUMO (dipolarophile) interaction.[24,25]

Kinetics of cycloadditions of diazomethanes with acrylates, crotonates, and several other olefins were reported.[26,27,28] The 1,3-dipolar cycloadditions of diazomethanes with olefins lead to 1-pyrazolines,[29] which are known to be unstable when they bear phenyl, vinyl, or CO_2Me-groups as substituents,[30,31] and therefore, readily tautomerize to 2-pyrazolines or undergo thermal[32,33,34,35] or photochemical[36] decomposition to form cyclopropanes.[37,38]

Metal-catalyzed (Cu, Ru, Rh or Co) cyclopropanations with diazomethanes proceed via metal carbene complexes, which subsequently attack the olefins to give cyclopropanes without any detectable pyrazoline intermediate.[39,40]

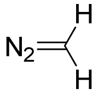
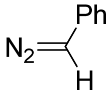
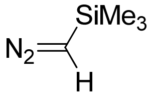
While the stereospecific course of 1,3-dipolar cycloadditions is an indispensable but not conclusive criterion for the concertedness of cycloadditions, a violation of stereospecificity would establish a two-step mechanism.[41] Huisgen reported non-stereoselective 1,3-dipolar cycloadditions of thiocarbonyl ylides with dimethyl 2,3-dicyanofumarate,[42,43,44] and thus described the mechanism as a two-step mechanism.

In previous work, we have shown that a large variety of reactions of electrophiles with nucleophiles can be described by eq 6.1, where N and s_N (previously called s) are nucleophile-specific parameters, E is an electrophilicity parameter, and k_2 is the second-order rate constant.[45]

$$\log k_2(20\ °\mathrm{C}) = s_N(N + E) \tag{6.1}$$

Kinetics of the reactions of diazomethanes **1** with benzhydrylium ions were measured previously, from which the nucleophile-specific parameters N and s_N were determined.[46] We now report on the kinetics of the reactions of diazomethanes **1a–c** (Table 6.1) with Michael acceptors with known electrophilicities such as benzylidene-1,3-indandiones **2a,b**,[47] benzylidene Meldrum´s acids **3a,b**,[48] benzylidenemalononitriles **4a,b**,[49] 4-nitro-*trans*-*β*-nitrostyrene (**5a**),[50] and enone **6b**[51] (Table 6.2). The kinetics of the reactions of **1a** with diethyl fumarate (**6a**) and ethyl acrylate (**6c**),[52] and of **1b** with **6c** have previously been reported.[54,55]

TABLE 6.1. Reactivity Parameters *N* and s_N of the Diazomethanes 1a–c in Dichloromethane.

	Diazomethane	N, s_N[a]
1a		10.48, 0.78
1b		9.35, 0.83
1c		8.97, 0.75

[a] Ref 46.

TABLE 6.2. Reactivity Parameters *E* of the Michael Acceptors 2–6 in DMSO.

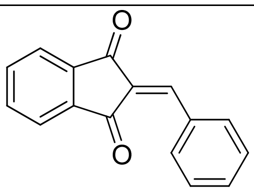
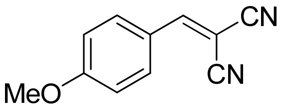
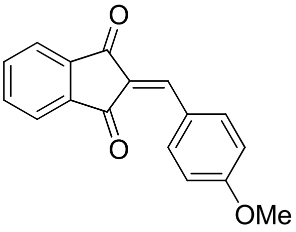
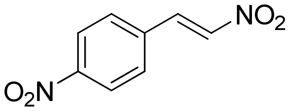
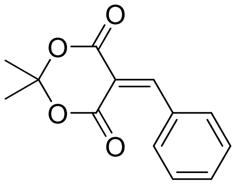
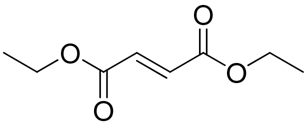
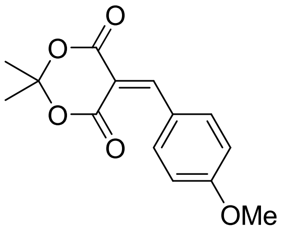
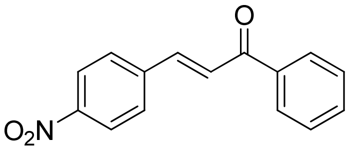
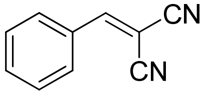
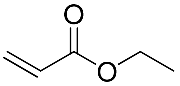
	Michael acceptor	*E*		Michael acceptor	*E*
2a		–10.11[a]	**4b**		–10.80[c]
2b		–11.32[a]	**5a**		–12.37[d]
3a		–9.15[b]	**6a**		–16.99[e]
3b		–10.28[b]	**6b**		–17.33[f]

TABLE 6.2. (Continued).

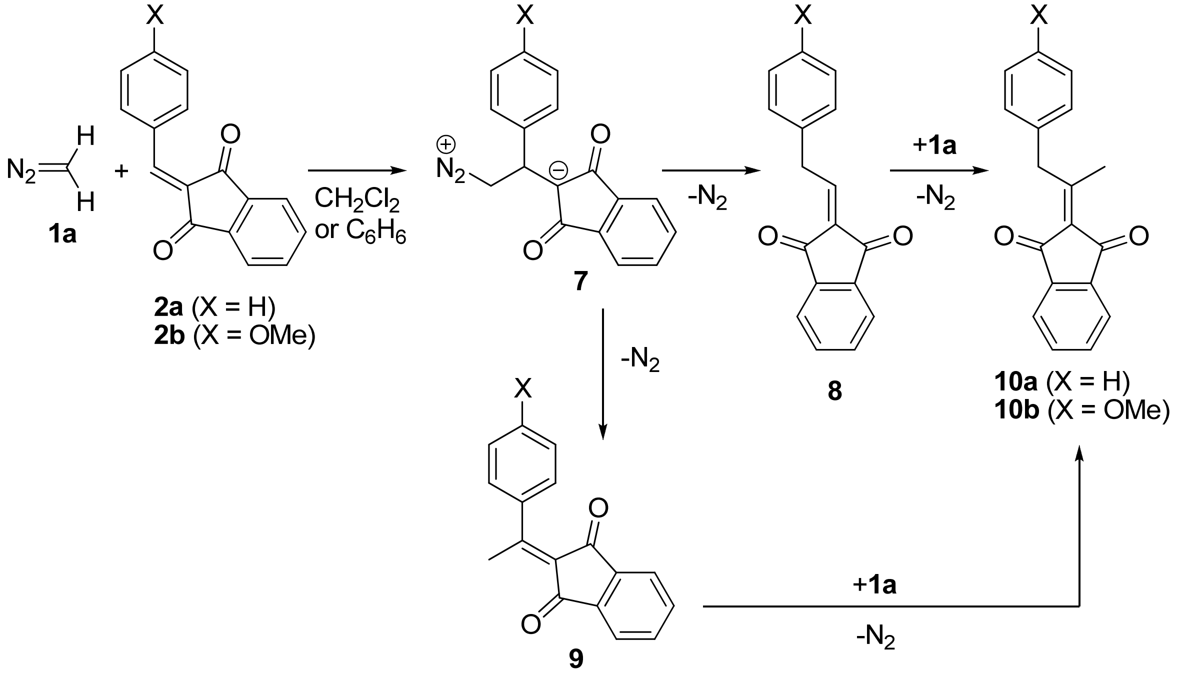
4a		–9.42[c]	**6c**		–18.73[e]

[a] Ref 47.[b] Ref 48.[c] Ref 49.[d] Ref 50.[e] Ref 52.[f] Ref 51.

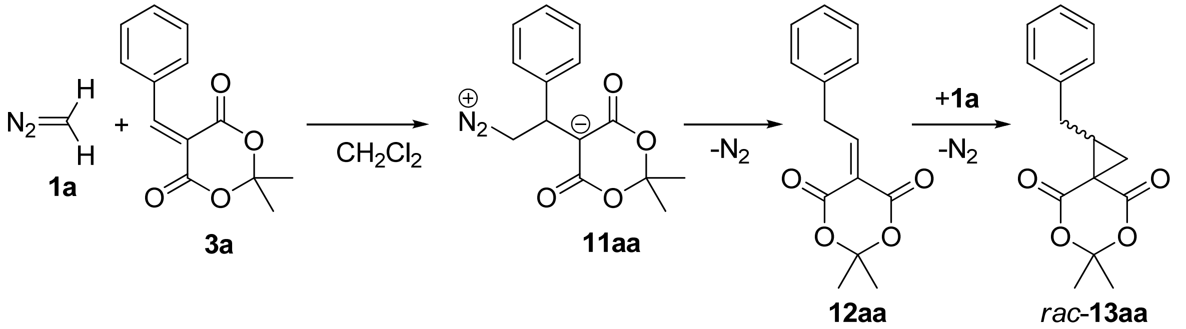
6.2 Results

The reactions of 2 equiv. of diazomethane (**1a**) with **2a** and **2b** form **10a** (72% yield in dichloromethane, 38% yield in benzene) and **10b** (67% yield in dichloromethane). Initially, **1a** and **2a**,**b** can be assumed to give **7** (Scheme 6.1). This either forms **8** through a 1,2-aryl shift, followed by attack of a second diazomethane molecule at the double bond and a 1,2-hydride shift to form **10**. Alternatively, **7** undergoes first a 1,2-hydride shift to form **9**, followed by attack of a second diazomethane molecule at the double bond and a 1,2-aryl shift to form **10**. We have no experimental evidence to decide which pathway prevails.

SCHEME 6.1. Reactions of Diazomethane (1a) with the Benzylidene-1,3-indandiones 2a,b and Benzylidene Meldrum´s acid (3a).

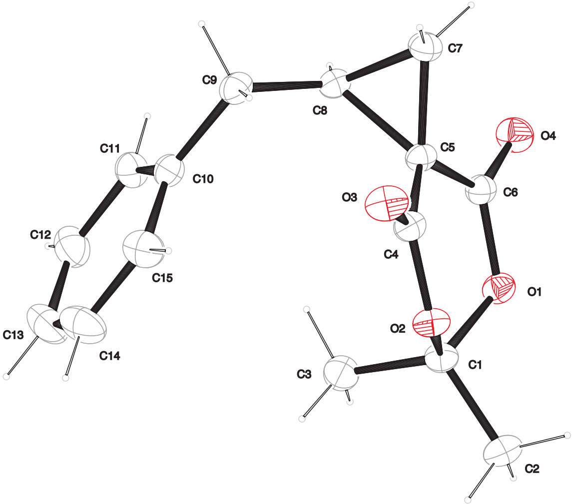


SCHEME 6.1. (Continued).

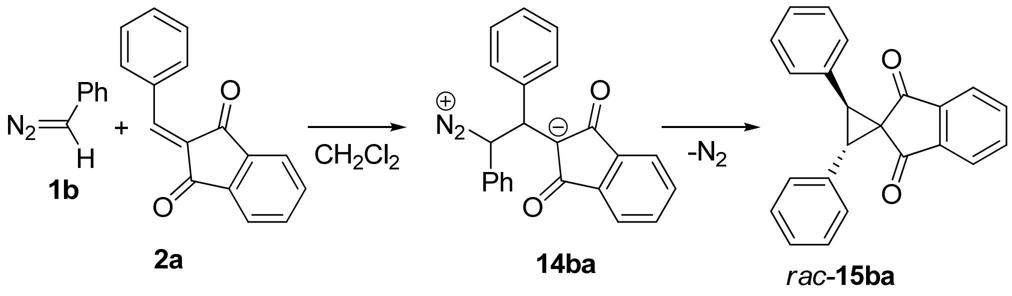


When 2 equiv. of diazomethane (**1a**) are combined with benzylidene Meldrum´s acid (**3a**) in dichloromethane, *rac*-**13aa** is received in 60% yield (Figure 6.1). **12aa** can be assumed to be formed from **11aa** by a 1,2-aryl shift, which is subsequently attacked by a second diazomethane molecule to form *rac*-**13aa** through ring closure. This product has been previously described by bernabe and coworkers.[53] A pathway via a 1,2-hydride shift to form a structure analogously to **9** can be excluded, as this would lead to a product different to *rac*-**13aa**, which has not been observed.

FIGURE 6.1. Crystal Structure of the (*R*)-Enantiomer of *rac*-13aa.

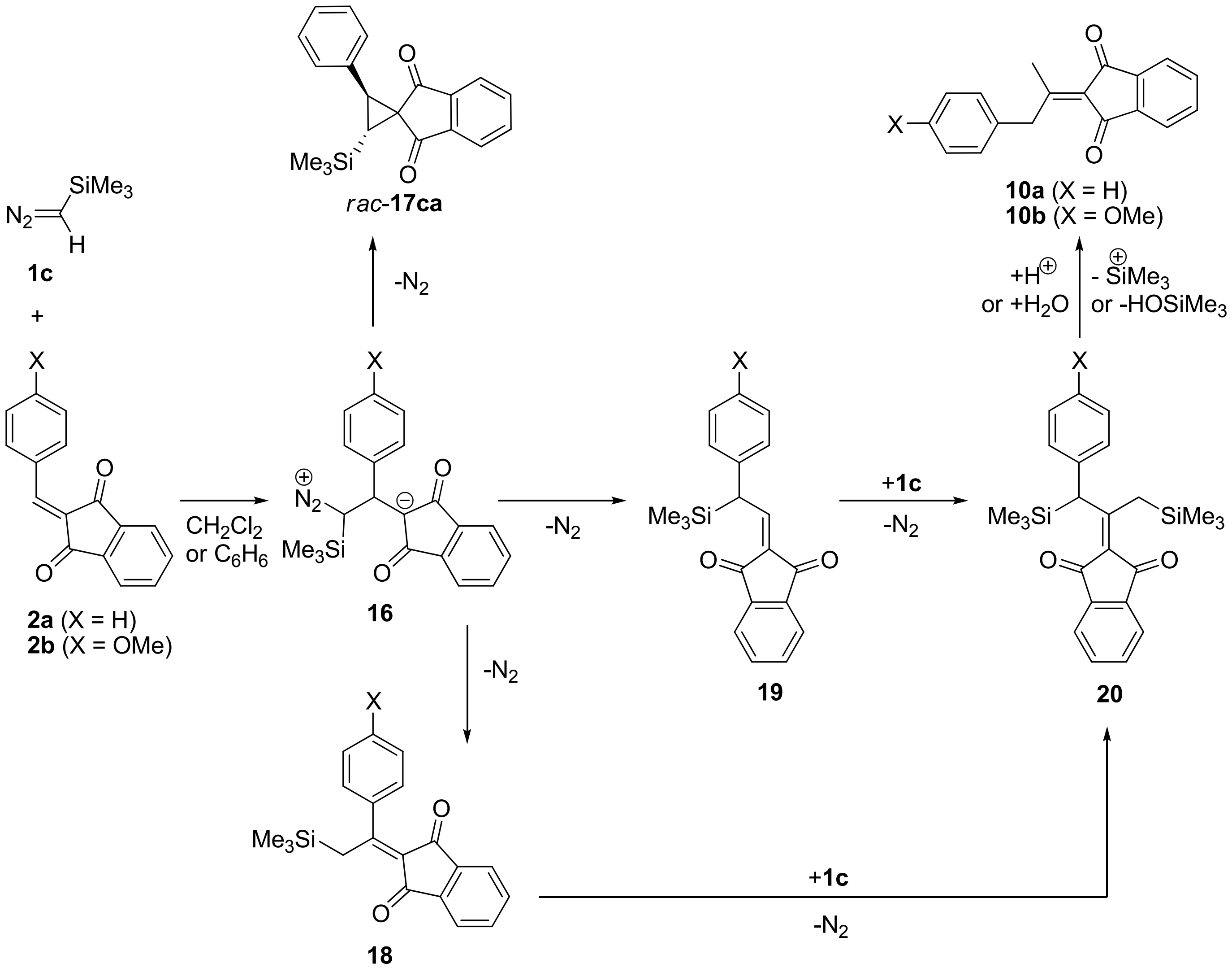


SCHEME 6.2. Reaction of Phenyldiazomethane (1b) with Benzylidene-1,3-indandione (2a).



Phenyldiazomethane (**1b**, 2 equiv.) reacts with **2a** in dichloromethane to form *rac*-**15ba** in 56% yield (Scheme 6.2). The identical ^{13}C NMR shifts of the carbonyl groups, and the four C_{Ar}-H atoms of the indan-1,3-dione moiety to give the NMR signals of an AA´BB´ system indicate, that the molecule has C_2 symmetry and is, hence, *trans* configured.

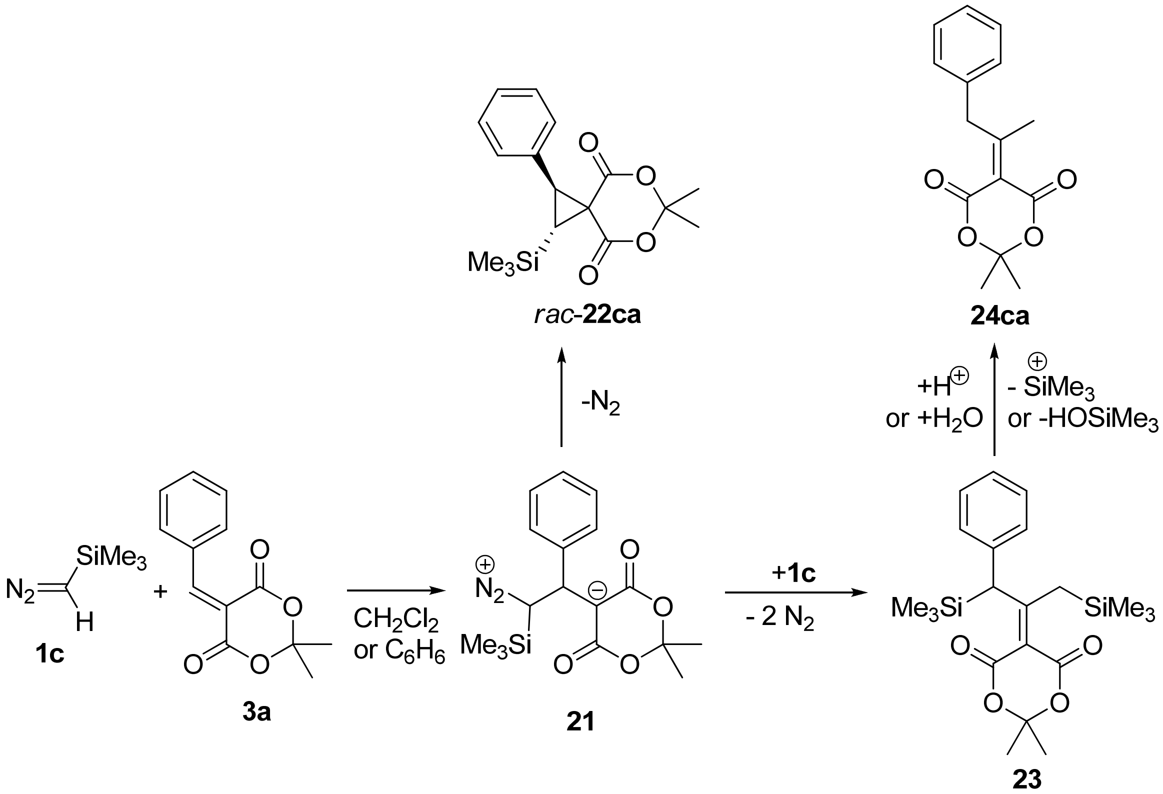
SCHEME 6.3. Reactions of Trimethylsilyldiazomethane (1c) with the Benzylidene-1,3-indandiones 2a,b.



Trimethylsilyldiazomethane (**1c**, 2 equiv.) reacts with **2a** to form a mixture of *rac*-**17ca** and **10a** in 14% and 63% yield (solvent: dichloromethane). The same products were received in 38% and 29% yield in benzene. 2 equiv. of **1c** reacts with **2b** to form **10b** as the only product received in 68% yield (solvent: dichloromethane). The reactions of **1c** with **2a,b** can be assumed to give **16** initially, this either forms *rac*-**17ca** through ring closure, or **19** through a 1,2-aryl shift (Scheme 6.3). Attack of a second diazomethane molecule at the double bond and a 1,2-hydride shift gives **20**, which is desilylated on a silica gel column to form **10**.

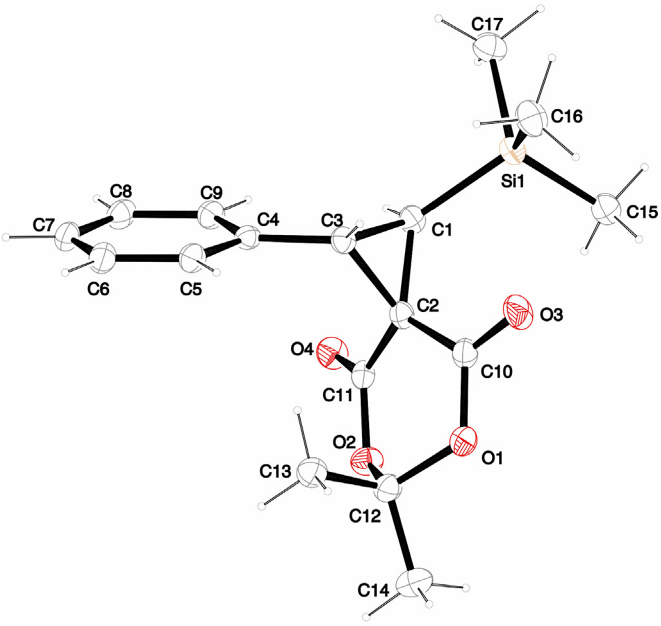
Alternatively, **16** undergoes first a 1,2-hydride shift to form **18**, followed by a second diazomethane attack at the double bond and a 1,2-aryl shift to form **20**, which could not be isolated. Attempted purification by column chromatography on silica gel yielded the desilylated products **10a** and **10b**. *Rac*-**17ca** shows in the 2D NOESY no NOE effect for the two vicinal cyclopropyl protons, but an NOE effect for the *ortho*-protons of the phenyl group with both cyclopropyl protons, indicating *trans* configuration.

SCHEME 6.4. Reactions of Trimethylsilyldiazomethane (1c) with Benzylidene Meldrum´s Acid (3a).



When 2 equiv. of **1c** react with **3a** in dichloromethane, **24ca** is obtained in 56% yield (Scheme 6.4). In contrast, this reaction leads to 63% of *rac*-**22ca** in benzene. The crystal structure of *rac*-**22ca** confirms the *trans* configuration of the molecule. In addition, no NOE effect was observed in the 2D NOESY NMR experiment for the two vicinal cyclopropyl protons, which show a coupling constant of 11.5 Hz in the ^{1}H NMR spectrum.

FIGURE 6.2. Crystal Structure of the (*S*, *R*)-Diastereomer of *rac*-22ca.



The kinetic investigations were performed at 20 °C in dichloromethane solution. The rates of the consumptions of the Michael acceptors **2–6** were always followed at their absorption maxima (λ_{max} = 317–380 nm). While the reactions of **1a** with the benzylidene Meldrum´s acids **3a,b** were studied by the stopped-flow technique ($\tau_{1/2}$ < 30 s), conventional UV-vis spectroscopy ($\tau_{1/2}$ > 30 s) was used in all other cases. By using a high excess of the diazomethanes **1** (10–100 equiv.) relative to the electrophiles, pseudo-first-order conditions were achieved (eq 6.2). In all cases, we observed monoexponential decays of the absorbances of the Michael acceptors **2–6**.

$$-\mathrm{d}[\mathbf{2\text{–}6}]/\mathrm{d}t = k_{\mathrm{obs}}[\mathbf{2\text{–}6}] \qquad (6.2)$$

The first-order rate constants k_{obs} were obtained by least-squares fitting of the time-dependent absorbances A_t of the electrophiles to the exponential function $A_t = A_0\, e^{-k_{\text{obs}}t} + C$. As shown in Figure 6.3 for the reaction of **1a** with **3b**, plots of k_{obs} versus the concentrations of the diazomethanes [**1**] were linear (eq 6.2), the slopes of which gave the second-order rate constants k_2, which are listed in Table 6.3.

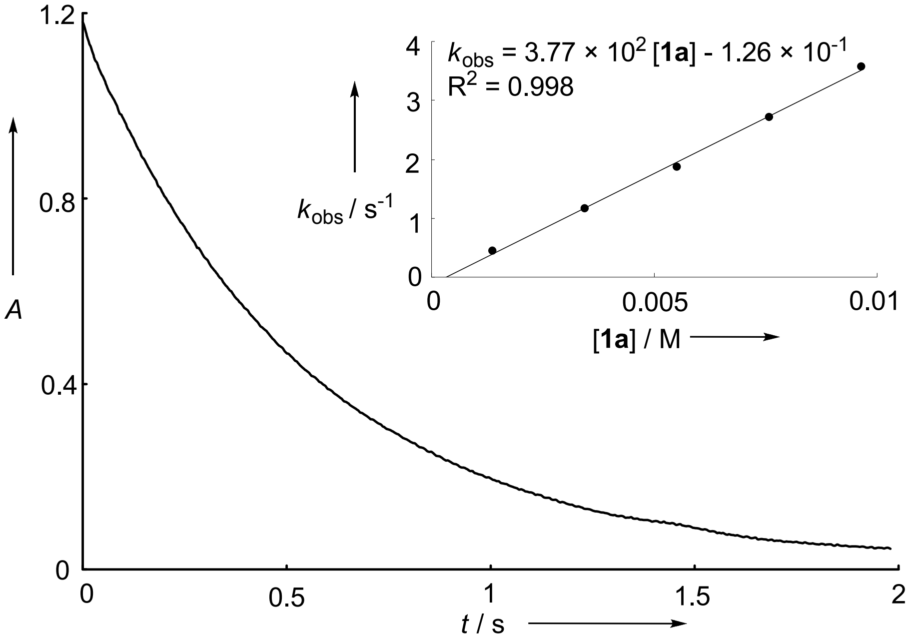
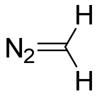
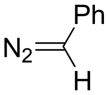
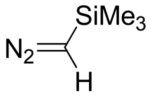


FIGURE 6.3. Exponential Decay of the Absorbance (A at λ = 365 nm) for the Reaction of 3b ($c = 9.15 \times 10^{-5}$ M) with 1a ($c = 5.52 \times 10^{-3}$ M) in Dichloromethane at 20 °C. Insert: Correlation of the pseudo-first order Rate Constants k_{obs} *vs.* [1a].

TABLE 6.3. Second-order Rate Constants for the Reactions of the Michael Acceptors 2–6 with the Diazomethanes 1a–c in Dichloromethane at 20 °C.

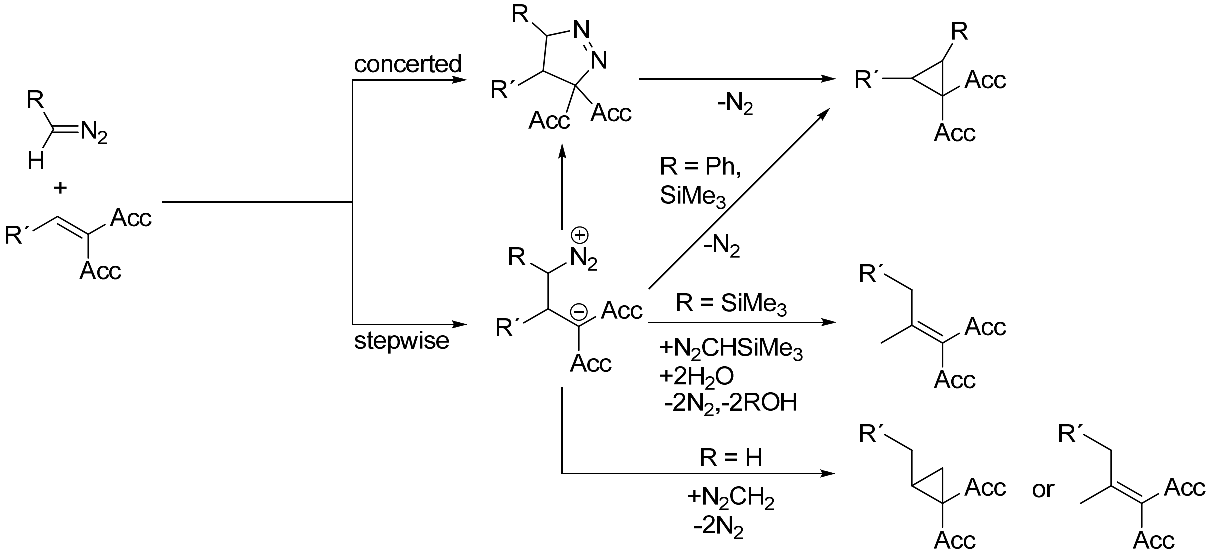
1	N, s_N[a]	Electrophile	E[b]	k_2^{exp} (M^{-1} s^{-1})	k_2^{calc} (M^{-1} s^{-1})[c]	k_2^{exp}/k_2^{calc}
1a	10.48, 0.78	**2a**	–10.11	5.79×10^{1}	1.94	29.8
		**2b**	–11.32	8.52	2.21×10^{-1}	38.5
		3a	–9.15	1.90×10^{3}	1.09×10^{1}	174
		3b	–10.28	3.77×10^{2}	1.43	263
		4a	–9.42	3.42×10^{-1}	6.71	5.10×10^{-3}
		4b	–10.80	2.10×10^{-1}	5.63×10^{-1}	3.73×10^{-1}
		5a	–12.37	6.14×10^{-1}	3.36×10^{-2}	18.3
		6a	–16.99	9.20×10^{-2}[d]	8.36×10^{-6}	1.10×10^{4}
		6c	–18.73	9.40×10^{-1}[e]	3.67×10^{-7}	2.56×10^{6}
1b	9.35, 0.83	**2a**	–10.11	1.44	2.34×10^{-1}	6.15
		**2b**	–11.32	2.37×10^{-1}	2.32×10^{-1}	10.2
		3a	–9.15	4.95×10^{1}	1.47	33.8
		3b	–10.28	7.69	1.69×10^{-1}	45.5
		4a	–9.42	2.37×10^{-2}	8.75×10^{-1}	2.71×10^{-2}
		4b	–10.80	1.50×10^{-2}	6.26×10^{-2}	2.40×10^{-1}
		6c	–18.73	1.20×10^{-1}[e]	1.64×10^{-8}	7.32×10^{6}
1c	8.97, 0.75	**2a**	–10.11	1.06	1.40×10^{-1}	7.59
		**2b**	–11.32	1.36×10^{-1}	1.73×10^{-2}	7.87
		3a	–9.15	4.49×10^{1}	7.33×10^{-1}	61.3
		3b	–10.28	5.62	1.04×10^{-1}	54.0
		4a	–9.42	7.90×10^{-2}	4.60×10^{-1}	1.72×10^{-1}
		4b	–10.80	8.27×10^{-3}	4.24×10^{-2}	1.95×10^{-1}
		5a	–12.37	8.56×10^{-3}	2.82×10^{-3}	3.04
		6b	–17.33	6.67×10^{-3}	5.37×10^{-7}	1.24×10^{4}

[a] The N and s_N parameters are taken from ref 46. [b] The E parameters are taken from refs 47–52. [c] Calculated from eq 6.1. [d] Experimental second-order rate constants (in THF at 25 °C) taken from ref 54. [e] Experimental second-order rate constants in DMF calculated from activation parameters in ref 55.

6.3 Discussion and Conclusion

The formation of cyclopropanes from diazoalkanes can either be formulated via concerted or stepwise 1,3-dipolar cycloadditions with the formation of 1-pyrazolines, which subsequently eliminate N_2 to give cyclopropanes (Scheme 6.5). The stepwise pathway involves the formation of zwitterions (for strong electron-withdrawing acceptor groups, the zwitterionic character of the intermediates is more pronounced than the diradical character), that either cyclize with formation of 1-pyrazolines or eliminate nitrogen and give cyclopropanes directly. Alternatively, the elimination of N_2 is accompanied by 1,2-rearrangements and formation of CC-double bonds, which may react with a second diazoalkane unit.

SCHEME 6.5. Concerted and Stepwise Mechanism for the Reactions of Michael Acceptors with Diazomethanes



The majority of the products described in the results section were supposedly formed via zwitterionic intermediates and subsequent 1,2-rearrangements, i.e., by stepwise processes, as indicated by the small $k_2^{\mathrm{exp}}/k_2^{\mathrm{calc}}$ values. However, the cyclopropanes *rac*-**15ba**, *rac*-**17ca** and *rac*-**22ca** may have been formed by concerted dipolar cycloadditions involving the formation of 1-pyrazolines following the expulsion of nitrogen. If the reactions proceed via 1-pyrazolines, their formation must occur stepwise or concerted with a small energy of concert, as the values of k_2^{exp} and k_2^{calc} are very close to each other, i.e., within the error limit associated with eq 6.1.

In contrast, the reactions of diazomethane (**1a**) with diethyl fumarate (**6a**) and of trimethylsilyldiazomethane (**1c**) with enone **6b** are 4 orders of magnitude faster than calculated for a stepwise mechanism. This observation rules out the stepwise mechanism and shows that the transition state of the pericyclic reaction is 23 kJ mol^{-1} lower in energy than that of the hypothetical stepwise process via a zwitterionic intermediate. The diazomethanes **1a** and **1b** react 10^6 times faster with **6c** than calculated by eq 6.1, indicating a concerted 1,3-dipolar cycloaddition with a transition state, which is 36-39 kJ mol^{-1} lower in energy than the transition state of the hypothetical stepwise process via zwitterions. Table 6.3 shows that the preference of the concerted pathway increases with decreasing electrophilicity of the dipolarophile.

While reactions of the diazomethanes **1** with the highly electrophilic Michael acceptors **2–5** do not profit from a concerted pathway, the large $k_2^{\text{exp}}/k_2^{\text{calc}}$ values for the reactions of **1a–c** with the less electrophilic Michael acceptors **6a–c** are in line with the concerted reaction pathway previously suggested by Huisgen and coworkers.

6.4 Experimental Section

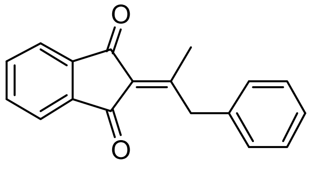
6.4.1 Products

Commercially available benzene (with < 50 ppm H_2O content) and (trimethylsilyl)diazomethane solution (**1c**, 2 M in hexane) were used without further purification. Dichloromethane was freshly distilled over CaH_2. Diethylether was freshly distilled over sodium. All reactions were performed under an atmosphere of dry nitrogen. Compound **1a** was prepared from a reaction of *N*-methyl-*N*-nitroso-*p*-toluenesulfonamide with potassium hydroxide in dichloromethane/2-(2-ethoxyethoxy)ethanol.[56] The concentration of the resulting solution of **1a** in dichloromethane was determined by reacting with an excess of benzoic acid and back titration of the unreacted acid with KOH solution.[57] The determination of the concentration of the solution of **1c** was performed by ^{1}H NMR analysis.[58] **1b** was synthesized by a reaction of benzaldehyde tosylhydrazone with sodium methoxide.[59] The ^{1}H and ^{13}C NMR chemical shifts are given in ppm and refer to DMSO-d_6 (δ_H = 2.50 ppm, δ_C = 39.52 ppm) or to $CDCl_3$ (δ_H = 7.26 ppm, δ_C = 77.16 ppm) as internal standards.[60] The coupling constants are given in Hz.

General procedure A: The Michael acceptors **2,3** (1 mmol) were dissolved in 10 mL of dry dichloromethane at 0 °C under nitrogen atmosphere. Solutions of diazomethanes **1** (2 mmol) in 10 mL of dry dichloromethane were added slowly. The solution was stirred for 16 h, after which the solvent was removed in vacuo and the crude products were purified by column chromatography (eluent *n*-pentane/diethylether).

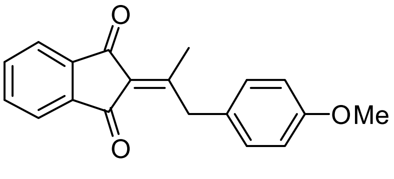
General procedure B: The Michael acceptors **2,3** (1 mmol) were dissolved in 10 mL of dry benzene under nitrogen atmosphere. Diazomethanes **1** (2 mmol) were added slowly in 5 mL of dry benzene. The solution was stirred for 16 h, after which the solvent was removed in vacuo and the crude products were purified by column chromatography (eluent *n*-pentane/diethylether).

6.4.1.1 Reactions of Diazomethane (1a) with the Benzylidene-1,3-indandiones 2a,b and Benzylidene Meldrum´s acid (3a)



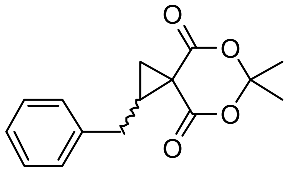
10a

2-(1-Phenylpropan-2-ylidene)-1H-indene-1,3(2H)-dione (**10a**). From **1a** and **2a** (176 mg, 0.751 mmol) following general procedure A: 142 mg (0.541 mmol, 72%), following general procedure B: 75 mg (0.286 mmol, 38%), pale yellow solid, mp 63 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ(ppm) = 2.45 (s, 3 H), 4.38 (s, 2 H), 7.12-7.25 (m, 5 H), 7.67-7.72 (m, 2 H), 7.82-7.92 (m, 2 H). ^{13}C NMR (75 MHz, $CDCl_3$): δ(ppm) = 21.3 (CH_3), 41.0 (CH_2), 123.0 (C_{Ar}-H), 123.3 (C_{Ar}-H), 126.9 (C_{Ar}-H), 127.3, 128.8 (C_{Ar}-H), 129.5 (C_{Ar}-H), 135.0 (C_{Ar}-H), 135.1 (C_{Ar}-H), 137.8, 141.0, 141.1, 170.8, 191.2 (C=O), 191.7 (C=O). HRMS (EI): calcd. for $C_{18}H_{14}O_2^+$, 262.0988; found 262.0982. Anal.: calcd. for $C_{18}H_{14}O_2$: C, 82.42; H, 5.38. Found: C, 82.20; H, 5.48.



10b

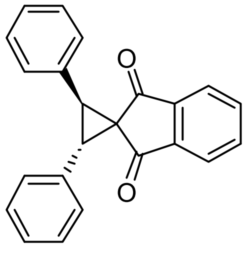
2-(1-(4-Methoxyphenyl)propan-2-ylidene)-1H-indene-1,3(2H)-dione (**10b**). From **1a** and **2b** (198 mg, 0.749 mmol) following general procedure A: 147 mg (0.503 mmol, 67%), white solid, mp 110 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ (ppm) = 2.45 (s, 3 H), 3.71 (s, 3 H), 4.31 (s, 2 H), 6.74-6.77 (m, 2 H), 7.10-7.13 (m, 2 H), 7.67-7.73 (m, 2 H), 7.82-7.92 (m, 2 H). ^{13}C NMR (75 MHz, $CDCl_3$): δ (ppm) = 21.3 (CH_3), 41.0 (CH_2), 55.4 (CH_3), 114.3 (C_{Ar}-H), 123.0 (C_{Ar}-H), 123.2 (C_{Ar}-H), 127.0, 129.8, 130.5 (C_{Ar}-H), 135.0 (C_{Ar}-H), 135.1 (C_{Ar}-H), 141.0, 141.1, 158.7, 171.4, 191.2 (C=O), 191.8 (C=O).



rac-**13aa**

rac-1-Benzyl-6,6-dimethyl-5,7-dioxaspiro[2.5]octane-4,8-dione (*rac*-**13aa**). From **1a** and **3a** (174 mg, 0.749 mmol) following general procedure A: 117 mg (0.450 mmol, 60%), white solid, mp 84 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ (ppm) = 1.11 (s, 3 H), 1.61 (s, 3 H), 2.03-2.07 (m, 1 H), 2.20-2.24 (m, 1 H), 2.48-2.59 (m, 1 H), 2.82-2.90 (m, 1 H), 3.12-3.19 (m, 1 H), 7.11-7.25 (m, 5 H). ^{13}C NMR (75 MHz, $CDCl_3$): δ (ppm) = 26.6 (CH_3), 27.8 (CH_3), 28.4 (CH_2), 29.0, 33.1 (CH_2), 41.8 (CH), 105.2, 127.1 (C_{Ar}-H), 129.0 (C_{Ar}-H), 129.0 (C_{Ar}-H), 138.7, 166.3 (C=O), 168.5 (C=O).

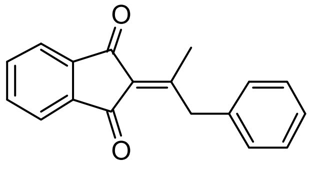
6.4.1.2 Reaction of Phenyldiazomethane (1b) with Benzylidene-1,3-indandione (2a)



rac-**15ba**

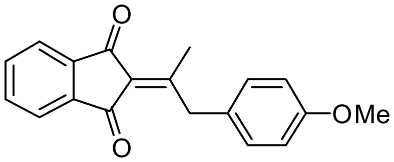
(2S,3S*)-2,3-Diphenylspiro[cyclopropane-1,2'-indene]-1',3'-dione* (*rac*-**15ba**). From **1b** and **2a** (468 mg, 2.00 mmol) following general procedure A: 360 mg (1.11 mmol, 56%), pale yellow solid, single diastereomer. ^{1}H NMR (300 MHz, $CDCl_3$): δ (ppm) = 4.11 (s, 2 H), 7.17-7.33 (m, 10 H), 7.65-7.68 (m, 2 H), 7.75-7.78 (m, 2 H). ^{13}C NMR (75 MHz, $CDCl_3$): δ (ppm) = 43.7 (CH), 48.6, 122.7 (C_{Ar}-H), 128.0 (C_{Ar}-H), 128.5 (C_{Ar}-H), 129.4 (C_{Ar}-H), 134.0, 134.8 (C_{Ar}-H), 142.2, 195.6 (C=O).

6.4.1.3 Reactions of Trimethylsilyldiazomethane (1c) with the Benzylidene-1,3-indandiones 2a,b and Benzylidene Meldrum´s acid (3a)



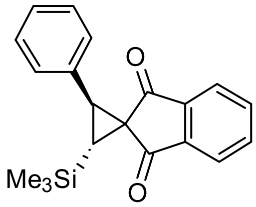
10a

2-(1-Phenylpropan-2-ylidene)-1H-indene-1,3(2H)-dione (**10a**). From **1c** and **2a** (234 mg, 1.00 mmol) following general procedure A: 165 mg (0.630 mmol, 63%) was received as the main product as pale yellow solid. The analytical data of **10a** has previously been described. This reaction following general procedure B yields **10a** in 29% yield as the byproduct.



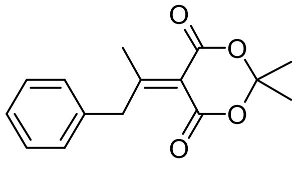
10b

2-(1-(4-Methoxyphenyl)propan-2-ylidene)-1H-indene-1,3 (2H)-dione (**10b**). From **1c** and **2b** (264 mg, 1.00 mmol) following general procedure A: 200 mg (0.680 mmol, 68%), white solid. The analytical data of **10b** has previously been described.



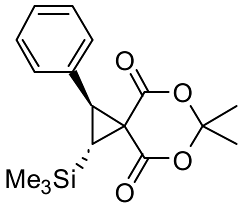
rac-**17ca**

(2S,3R*)-2-Phenyl-3-(trimethylsilyl)spiro[cyclopropane-1,2'-indene]-1',3'-dione* (*rac*-**17ca**). From **1c** and **2a** (234 mg, 1.00 mmol) following general procedure A: 45 mg (0.140 mmol, 14%) was received as the byproduct as pale yellow solid, single diastereomer. ^{1}H NMR (300 MHz, CDCl$_3$): δ (ppm) = 0.15 (s, 9 H), 2.02 (d, J = 10.8 Hz), 3.41 (d, J = 10.8 Hz), 7.17-7.23 (m, 5 H), 7.63-7.73 (m, 3 H), 7.86-7.89 (m, 1 H). ^{13}C NMR (75 MHz, CDCl$_3$): δ (ppm) = –0.66 (Si-(CH$_3$)$_3$), 27.6 (CH), 46.4 (CH), 47.5, 122.3 (C$_{Ar}$-H), 122.6 (C$_{Ar}$-H), 127.8, 128.2 (C$_{Ar}$-H), 129.3 (C$_{Ar}$-H), 134.7 (C$_{Ar}$-H), 134.9 (C$_{Ar}$-H), 135.3 (C$_{Ar}$-H), 141.8, 142.4, 196.3 (C=O), 199.5 (C=O). This reaction following general procedure B yields *rac*-**17ca** in 38% yield as the main product. **10a** and *rac*-**17ca** were separated via column chromatography.



24ca

2,2-Dimethyl-5-(1-phenylpropan-2-ylidene)-1,3-dioxane-4,6-dione (**24ca**). From **1c** and **3a** (232 mg, 1.00 mmol) following general procedure A: 145 mg (0.557 mmol, 56%), white solid. ^{1}H NMR (300 MHz, $CDCl_3$): δ (ppm) = 1.67 (s, 6 H), 2.31 (s, 3 H), 4.15 (s, 2 H), 7.16-7.27 (m, 5 H). ^{13}C NMR (75 MHz, $CDCl_3$): δ (ppm) = 24.3 (CH_3), 27.4 (CH_3), 43.6 (CH_2), 103.9, 117.1, 127.4 (C_{Ar}-H), 129.0 (C_{Ar}-H), 129.3 (C_{Ar}-H), 136.8, 161.3, 176.5 (C=O).



rac-**22ca**

(1S,2R*)-6,6-Dimethyl-1-phenyl-2-(trimethylsilyl)-5,7-dioxaspiro [2.5]octane-4,8-dione* (*rac*-**22ca**). From **1c** and **3a** (348 mg, 1.50 mmol) following general procedure B: 314 mg (0.945 mmol, 63%), white solid. ^{1}H NMR (300 MHz, $CDCl_3$): δ (ppm) = 0.23 (s, 9 H), 1.69 (s, 3 H), 1.72 (s, 3 H), 2.24 (d, J = 11.5 Hz), 3.37 (d, J = 11.5 Hz), 7.29-7.37 (m, 5 H). ^{13}C NMR (75 MHz, $CDCl_3$): δ (ppm) = –0.64 (Si-$(CH_3)_3$), 27.0 (CH), 27.9 (CH_3), 28.1 (CH_3), 37.4, 48.8 (CH), 104.6, 128.5 (C_{Ar}-H), 128.7 (C_{Ar}-H), 129.5 (C_{Ar}-H), 133.0, 164.6 (C=O), 168.1 (C=O).

6.4.2 Kinetics

For the investigation of fast kinetics ($\tau_{1/2} < 30$ s) stopped-flow spectrophotometer systems were used. Slow kinetics ($\tau_{1/2} > 30$ s) were followed by using a conventional UV-vis diode array spectrophotometer system that was connected to a quartz immersion probe via fiber optic cables.

All measurements were carried out under first-order conditions (in general $[\mathbf{1}]_0/[\mathbf{2}\text{-}\mathbf{6}]_0 > 10$). The first-order rate constants k_{obs} were obtained by least-squares fitting of the time-dependent absorbances A_t of the electrophiles to the exponential function $A_t = A_0\ \mathrm{e}^{-k_{\text{obs}}t} + C$.

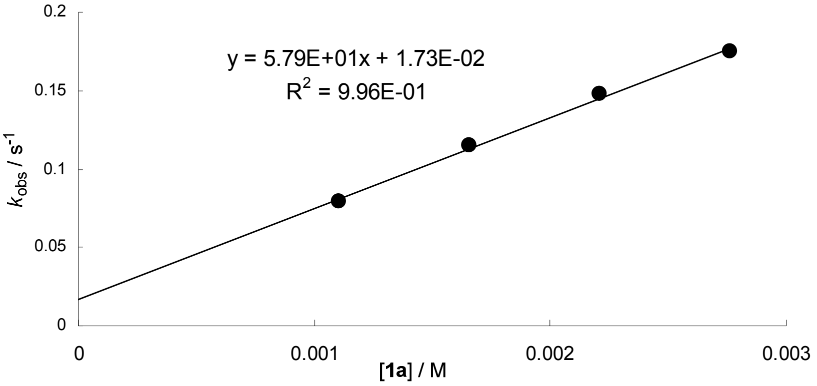
Second-order rate constans k_2^{exp} were then derived from linear correlations of k_{obs} vs. [**1**]. The temperature of the solutions during all kinetic studies was kept constant at (20.0 ± 0.1) °C using a circulating bath thermostat.

6.4.2.1 Kinetics of the Reactions of Diazomethane (1a) with the Michael Acceptors 2-5 in Dichloromethane

Reaction of **1a** with **2a** (dichloromethane, 20 °C, conventional, 343 nm)

$k_2 = 5.79 \times 10^{1}$ M^{-1} s^{-1}

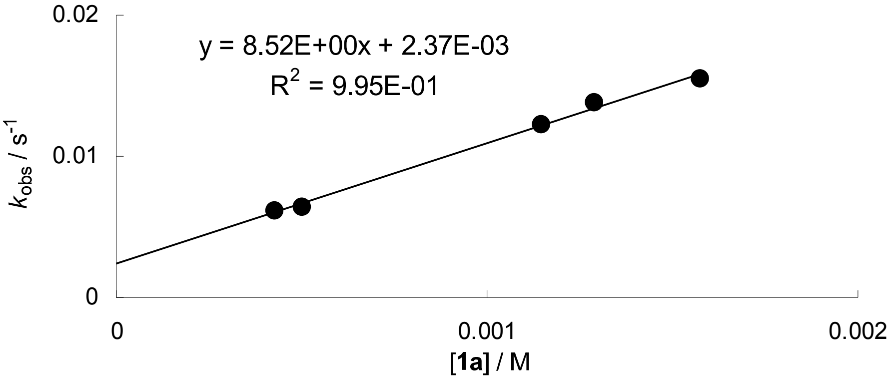
[**1a**] /M	[**2a**] /M	k_{obs} / s^{-1}
1.10×10^{-3}	6.15×10^{-5}	7.93×10^{-2}
1.66×10^{-3}	6.15×10^{-5}	1.15×10^{-1}
2.21×10^{-3}	6.15×10^{-5}	1.48×10^{-1}
2.76×10^{-3}	6.15×10^{-5}	1.75×10^{-1}



Reaction of **1a** with **2b** (dichloromethane, 20 °C, conventional, 380 nm)

$k_2 = 8.52$ M^{-1} s^{-1}

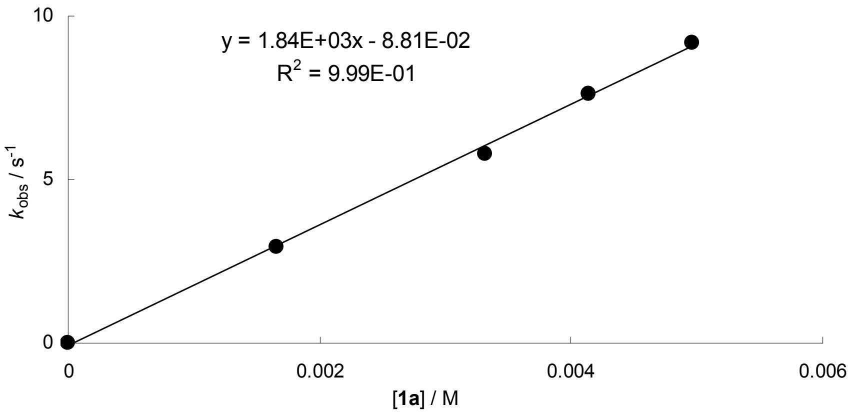
[**1a**] /M	[**2b**] /M	k_{obs} / s^{-1}
4.31×10^{-4}	4.72×10^{-5}	6.12×10^{-3}
5.02×10^{-4}	4.72×10^{-5}	6.42×10^{-3}
1.15×10^{-3}	4.72×10^{-5}	1.23×10^{-2}
1.29×10^{-3}	4.72×10^{-5}	1.38×10^{-2}
1.58×10^{-3}	4.72×10^{-5}	1.55×10^{-2}



Reaction of **1a** with **3a** (dichloromethane, 20 °C, stopped-flow, 340 nm)

$k_2 = 1.84 \times 10^3$ M^{-1} s^{-1}

[**1a**] /M	[**3a**] /M	k_{obs} / s^{-1}
1.66×10^{-3}	1.48×10^{-4}	2.92
3.31×10^{-3}	1.48×10^{-4}	5.80
4.14×10^{-3}	1.48×10^{-4}	7.62
4.97×10^{-3}	1.48×10^{-4}	9.17

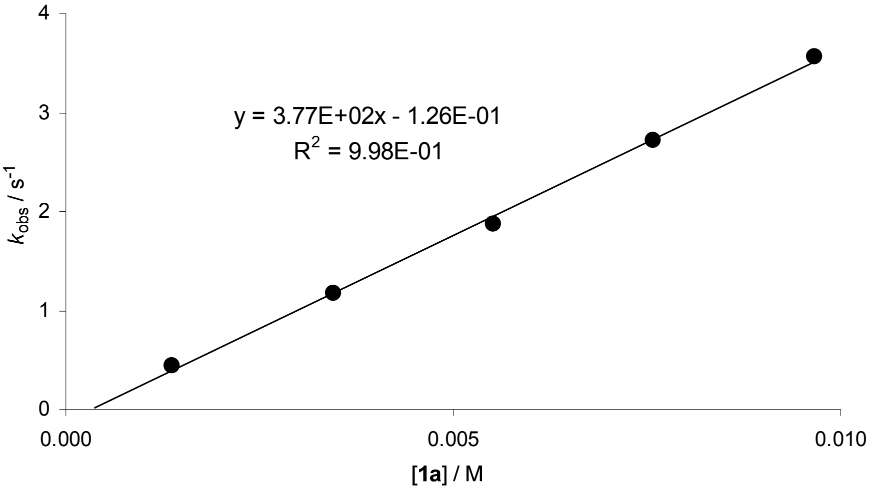


Reaction of **1a** with **3b** (dichloromethane, 20 °C, stopped-flow, 365 nm)

$k_2 = 3.77 \times 10^2$ M^{-1} s^{-1}

[**1a**] /M	[**3b**] /M	k_{obs} / s^{-1}
1.38×10^{-3}	9.15×10^{-5}	4.46×10^{-1}
3.45×10^{-3}	9.15×10^{-5}	1.17

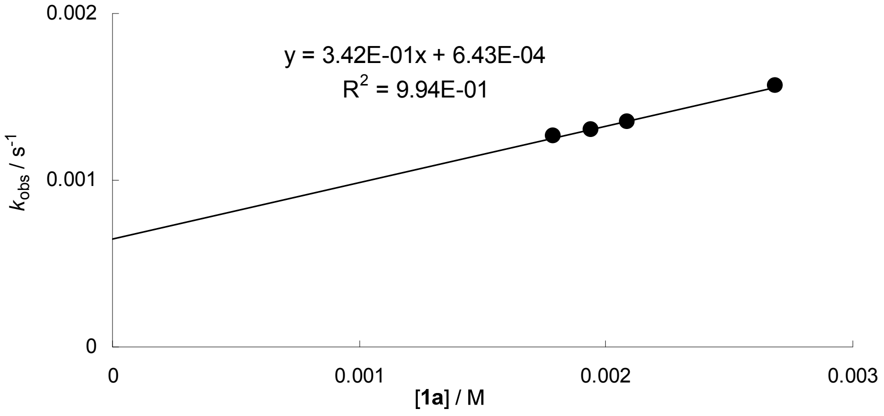
5.52×10^{-3}	9.15×10^{-5}	1.87
7.59×10^{-3}	9.15×10^{-5}	2.72
9.66×10^{-3}	9.15×10^{-5}	3.57



Reaction of **1a** with **4a** (dichloromethane, 20 °C, conventional, 333 nm)

$k_2 = 3.42 \times 10^{-1}$ M^{-1} s^{-1}

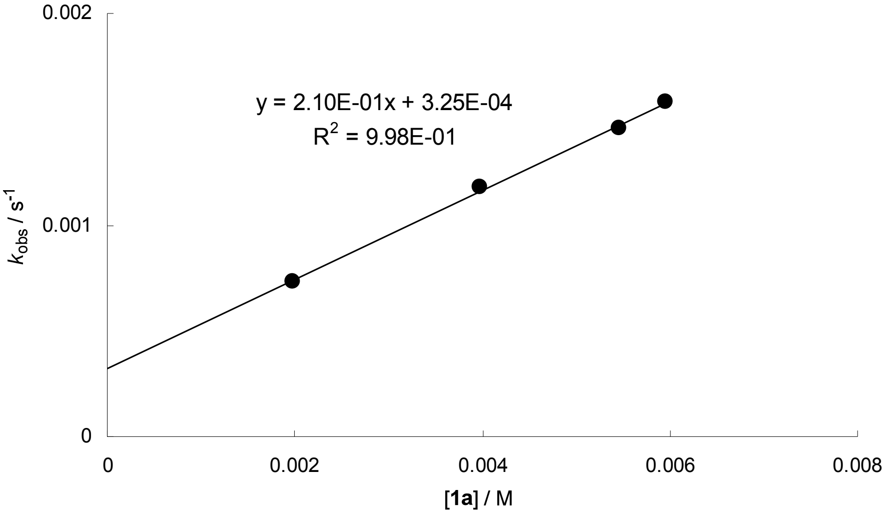
[**1a**] /M	[**4a**] /M	k_{obs} / s^{-1}
1.79×10^{-3}	1.04×10^{-4}	1.27×10^{-3}
1.94×10^{-3}	1.04×10^{-4}	1.30×10^{-3}
2.09×10^{-3}	1.04×10^{-4}	1.35×10^{-3}
2.69×10^{-3}	1.04×10^{-4}	1.57×10^{-3}



Reaction of **1a** with **4b** (dichloromethane, 20 °C, conventional, 340 nm)

$k_2 = 2.10 \times 10^{-1}$ M^{-1} s^{-1}

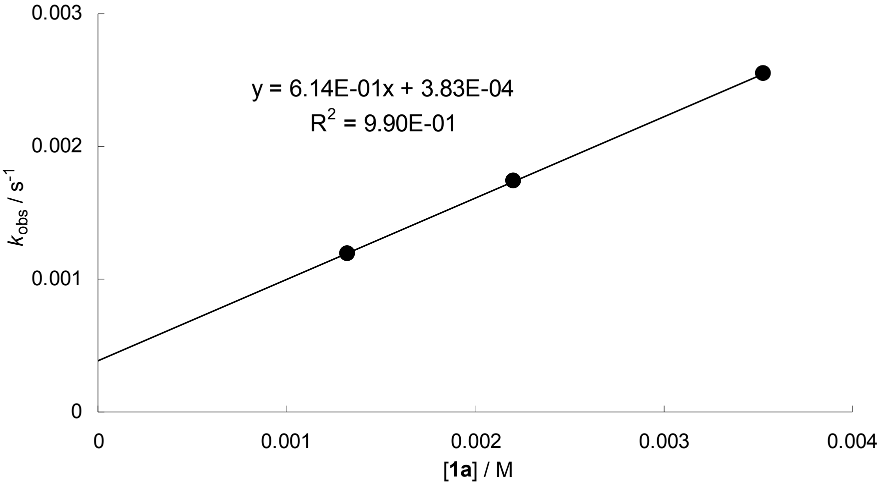
[**1a**] /M	[**4b**] /M	k_{obs} / s^{-1}
1.99×10^{-3}	5.70×10^{-5}	7.35×10^{-4}
3.97×10^{-3}	5.70×10^{-5}	1.18×10^{-3}
5.47×10^{-3}	5.70×10^{-5}	1.46×10^{-3}
5.96×10^{-3}	5.70×10^{-5}	1.58×10^{-3}



Reaction of **1a** with **5a** (dichloromethane, 20 °C, conventional, 317 nm)

$k_2 = 6.14 \times 10^{-1}$ M^{-1} s^{-1}

[**1a**] /M	[**5a**] /M	k_{obs} / s^{-1}
1.33×10^{-3}	1.24×10^{-4}	1.20×10^{-3}
2.21×10^{-3}	1.24×10^{-4}	1.74×10^{-3}
3.53×10^{-3}	1.24×10^{-4}	2.55×10^{-3}

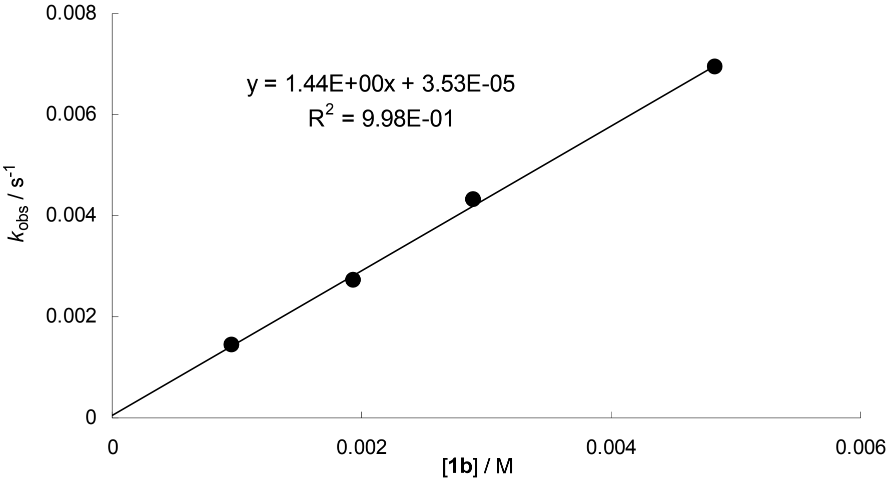

y = 6.14E-01x + 3.83E-04
R^2 = 9.90E-01
k_{obs} / s^{-1}
0.003
0.002
0.001
0
0
0.001
0.002
0.003
0.004
[**1a**] / M

6.4.2.2 Kinetics of the Reactions of Phenyldiazomethane (1b) with the Michael Acceptors 2-4 in Dichloromethane

Reaction of **1b** with **2a** (dichloromethane, 20 °C, conventional, 343 nm)

$k_2 = 1.44\ \mathrm{M^{-1}\ s^{-1}}$

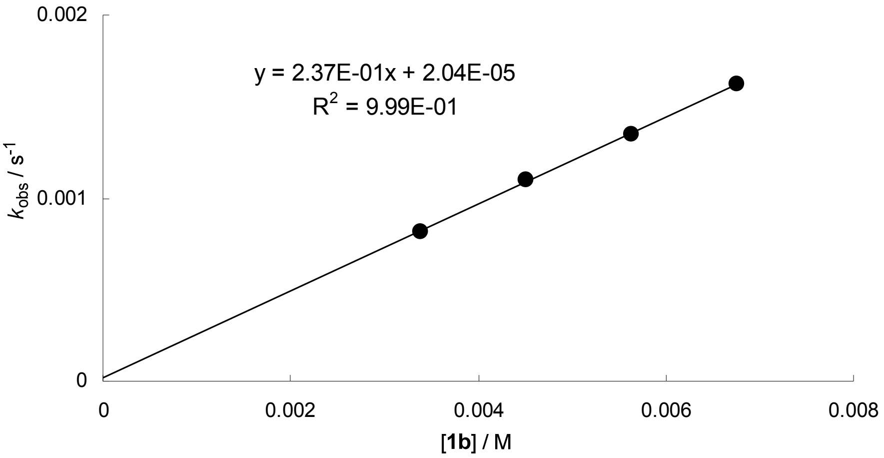
[**1b**] /M	[**2a**] /M	k_{obs} / $\mathrm{s^{-1}}$
9.66×10^{-4}	6.15×10^{-5}	1.43×10^{-3}
1.93×10^{-3}	6.15×10^{-5}	2.72×10^{-3}
2.90×10^{-3}	6.15×10^{-5}	4.33×10^{-3}
4.83×10^{-3}	6.15×10^{-5}	6.94×10^{-3}



Reaction of **1b** with **2b** (dichloromethane, 20 °C, conventional, 380 nm)

$k_2 = 2.37 \times 10^{-1}\ \mathrm{M^{-1}\ s^{-1}}$

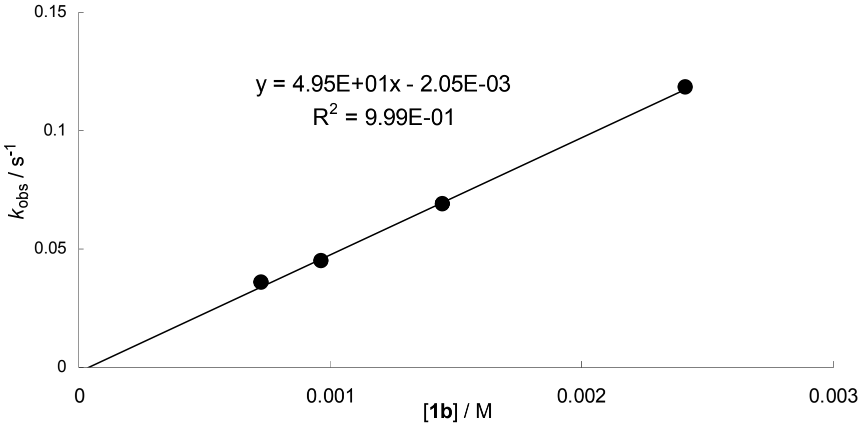
[**1b**] /M	[**2b**] /M	k_{obs} / $\mathrm{s^{-1}}$
3.38×10^{-3}	6.45×10^{-5}	8.17×10^{-4}
4.51×10^{-3}	6.45×10^{-5}	1.10×10^{-3}
5.64×10^{-3}	6.45×10^{-5}	1.35×10^{-3}
6.77×10^{-3}	6.45×10^{-5}	1.63×10^{-3}



Reaction of **1b** with **3a** (dichloromethane, 20 °C, conventional, 340 nm)

$k_2 = 4.95 \times 10^{1}$ M^{-1} s^{-1}

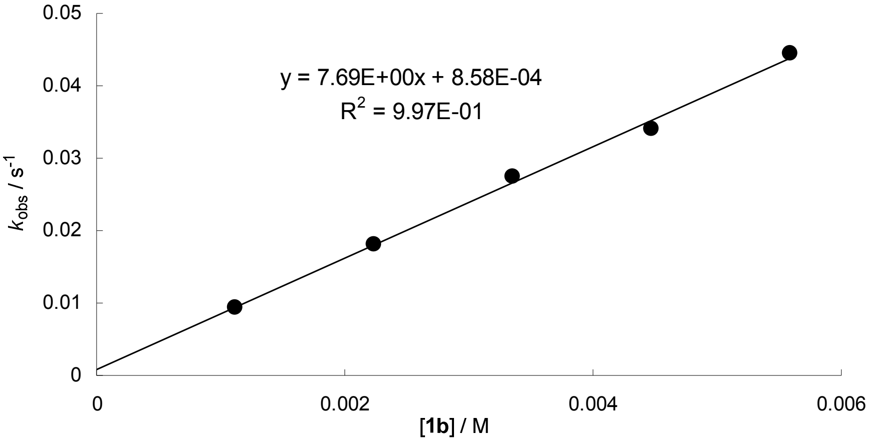
[**1b**] /M	[**3a**] /M	k_{obs} / s^{-1}
7.25×10^{-4}	5.44×10^{-5}	3.55×10^{-2}
9.67×10^{-4}	5.44×10^{-5}	4.45×10^{-2}
1.45×10^{-3}	5.44×10^{-5}	6.86×10^{-2}
2.42×10^{-3}	5.44×10^{-5}	1.18×10^{-1}



Reaction of **1b** with **3b** (dichloromethane, 20 °C, conventional, 365 nm)

$k_2 = 7.69$ M^{-1} s^{-1}

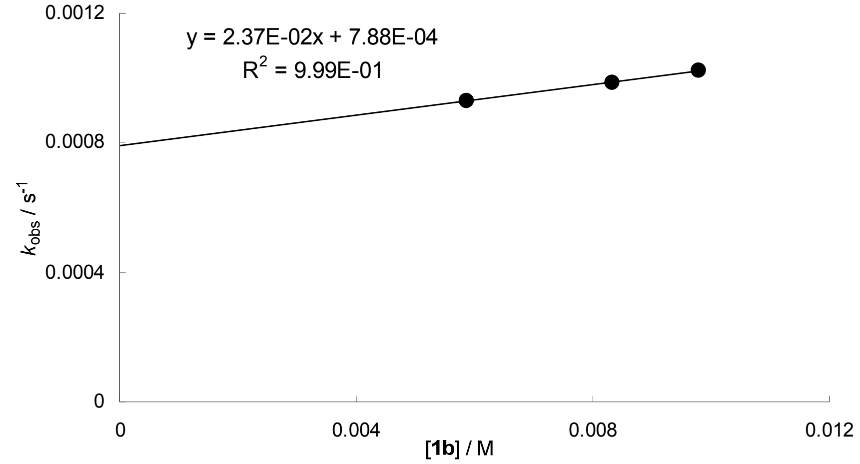
[**1b**] /M	[**3b**] /M	k_{obs} / s^{-1}
1.12×10^{-3}	7.18×10^{-5}	9.38×10^{-3}
2.24×10^{-3}	7.18×10^{-5}	1.81×10^{-2}
3.36×10^{-3}	7.18×10^{-5}	2.74×10^{-2}
4.47×10^{-3}	7.18×10^{-5}	3.41×10^{-2}
5.59×10^{-3}	7.18×10^{-5}	4.44×10^{-2}



Reaction of **1b** with **4a** (dichloromethane, 20 °C, conventional, 333 nm)

$k_2 = 2.37 \times 10^{-2}$ M^{-1} s^{-1}

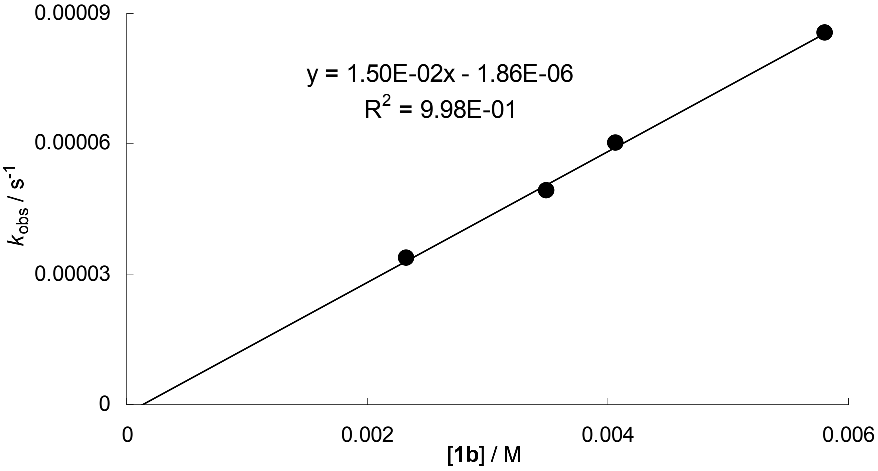
[**1b**] /M	[**4a**] /M	k_{obs} / s^{-1}
5.88×10^{-3}	1.06×10^{-4}	9.28×10^{-4}
8.34×10^{-3}	1.06×10^{-4}	9.84×10^{-4}
9.81×10^{-3}	1.06×10^{-4}	1.02×10^{-3}



Reaction of **1b** with **4b** (dichloromethane, 20 °C, conventional, 340 nm)

$k_2 = 1.50 \times 10^{-2}$ M^{-1} s^{-1}

[**1b**] /M	[**4b**] /M	k_{obs} / s^{-1}
2.33×10^{-3}	7.08×10^{-5}	3.35×10^{-5}
3.49×10^{-3}	7.08×10^{-5}	4.92×10^{-5}
4.07×10^{-3}	7.08×10^{-5}	6.03×10^{-5}
5.81×10^{-3}	7.08×10^{-5}	8.55×10^{-5}

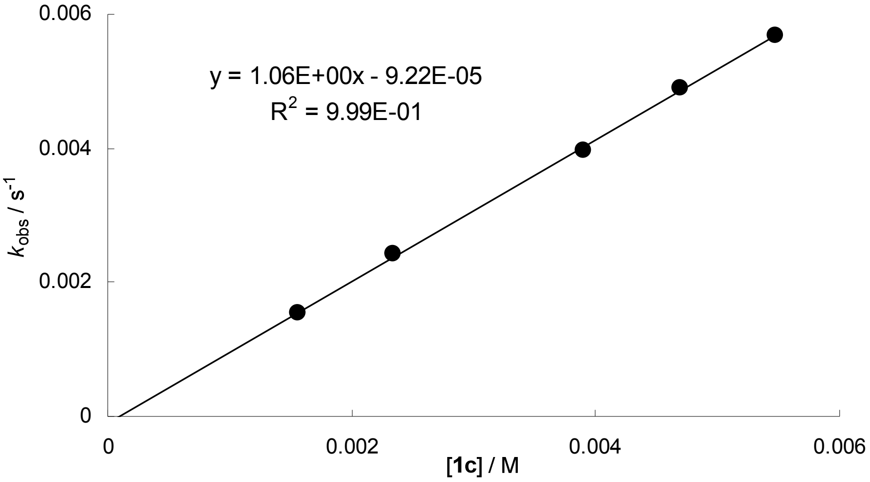


6.4.2.3 Kinetics of the Reactions of Trimethylsilyldiazomethane (1c) with the Michael Acceptors 2-6 in Dichloromethane

Reaction of **1c** with **2a** (dichloromethane, 20 °C, conventional, 343 nm)

$k_2 = 1.06\ \mathrm{M}^{-1}\ \mathrm{s}^{-1}$

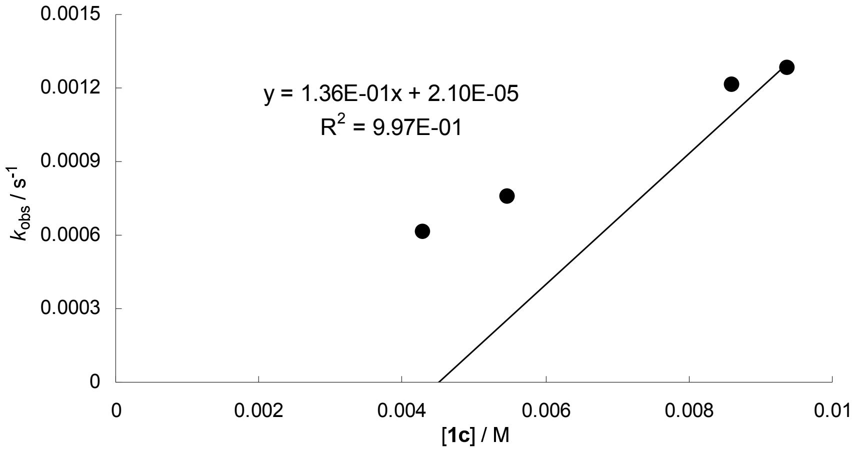
[**1c**] /M	[**2a**] /M	k_{obs} / s^{-1}
1.56×10^{-3}	7.15×10^{-5}	1.54×10^{-3}
2.34×10^{-3}	7.15×10^{-5}	2.43×10^{-3}
3.91×10^{-3}	7.15×10^{-5}	3.97×10^{-3}
4.69×10^{-3}	7.15×10^{-5}	4.91×10^{-3}
5.47×10^{-3}	7.15×10^{-5}	5.68×10^{-3}



Reaction of **1c** with **2b** (dichloromethane, 20 °C, conventional, 380 nm)

$k_2 = 1.36 \times 10^{-1}\ \mathrm{M}^{-1}\ \mathrm{s}^{-1}$

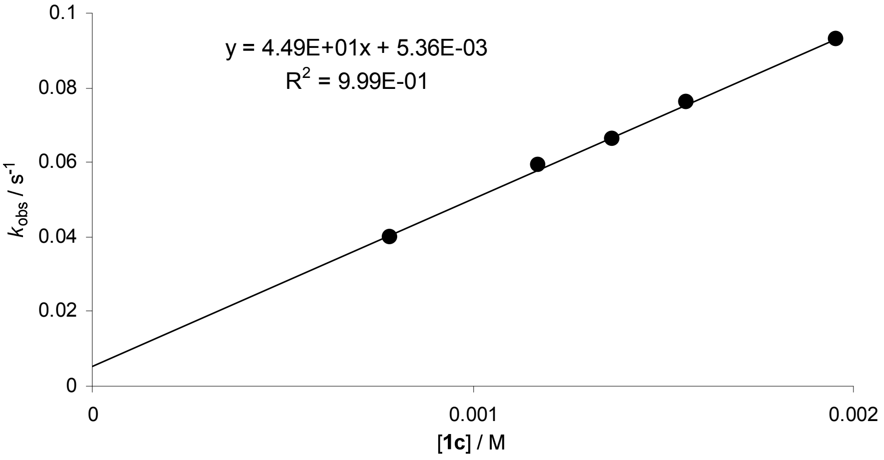
[**1c**] /M	[**2b**] /M	k_{obs} / s^{-1}
4.30×10^{-3}	7.05×10^{-5}	6.10×10^{-4}
5.47×10^{-3}	7.05×10^{-5}	7.56×10^{-4}
8.60×10^{-3}	7.05×10^{-5}	1.21×10^{-3}
9.38×10^{-3}	7.05×10^{-5}	1.28×10^{-3}



Reaction of **1c** with **3a** (dichloromethane, 20 °C, conventional, 340 nm)

$k_2 = 4.49 \times 10^1$ M^{-1} s^{-1}

[**1c**] /M	[**3a**] /M	k_{obs} / s^{-1}
7.81×10^{-4}	7.23×10^{-5}	4.00×10^{-2}
1.17×10^{-3}	7.23×10^{-5}	5.91×10^{-2}
1.37×10^{-3}	7.23×10^{-5}	6.61×10^{-2}
1.56×10^{-3}	7.23×10^{-5}	7.60×10^{-2}
1.95×10^{-3}	7.23×10^{-5}	9.29×10^{-2}

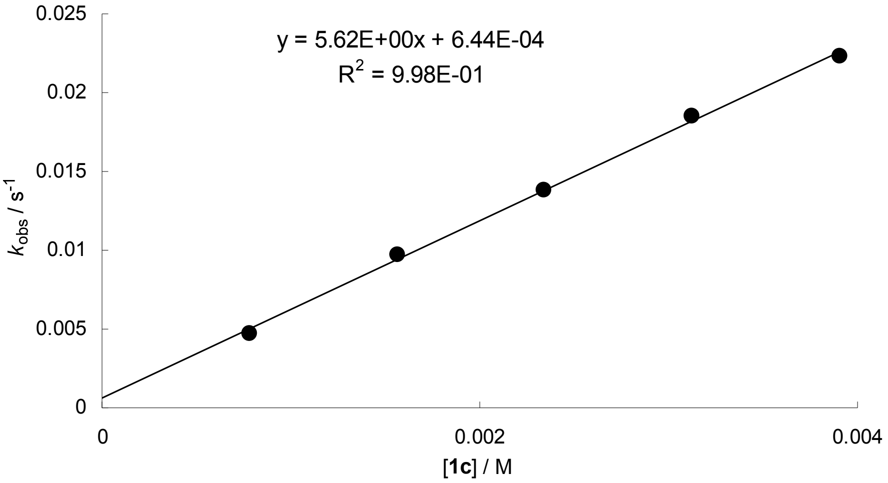


Reaction of **1c** with **3b** (dichloromethane, 20 °C, conventional, 365 nm)

$k_2 = 5.62$ M^{-1} s^{-1}

[**1c**] /M	[**3b**] /M	k_{obs} / s^{-1}

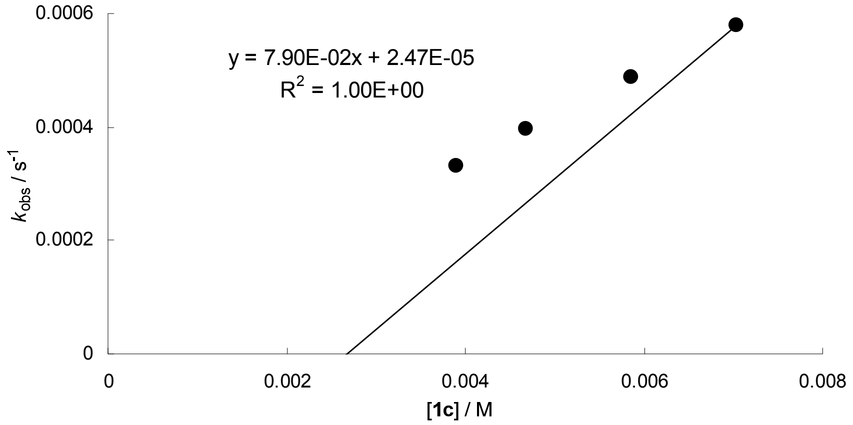
7.81×10^{-4}	6.41×10^{-5}	4.73×10^{-3}
1.56×10^{-3}	6.41×10^{-5}	9.74×10^{-3}
2.34×10^{-3}	6.41×10^{-5}	1.38×10^{-2}
3.13×10^{-3}	6.41×10^{-5}	1.85×10^{-2}
3.91×10^{-3}	6.41×10^{-5}	2.23×10^{-2}



Reaction of **1c** with **4a** (dichloromethane, 20 °C, conventional, 333 nm)

$k_2 = 7.90 \times 10^{-2}$ M^{-1} s^{-1}

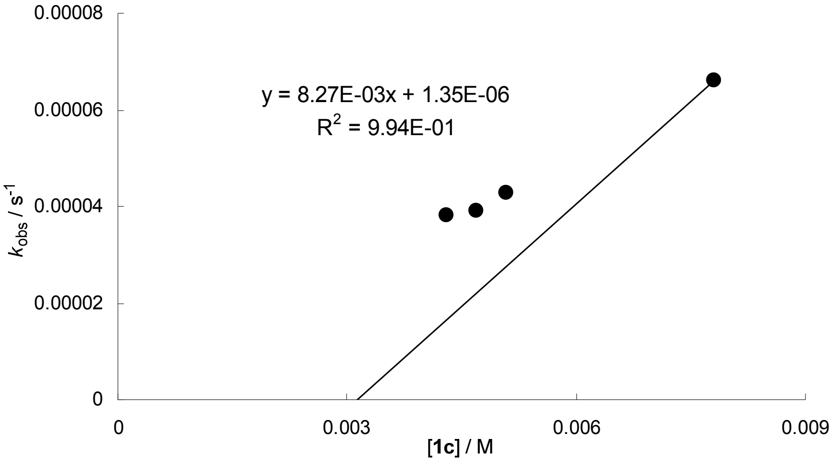
[**1c**] /M	[**4a**] /M	k_{obs} / s^{-1}
3.91×10^{-3}	1.04×10^{-4}	3.32×10^{-4}
4.67×10^{-3}	1.04×10^{-4}	3.96×10^{-4}
5.86×10^{-3}	1.04×10^{-4}	4.89×10^{-4}
7.03×10^{-3}	1.04×10^{-4}	5.79×10^{-4}



Reaction of **1c** with **4b** (dichloromethane, 20 °C, conventional, 340 nm)

$k_2 = 8.27 \times 10^{-3}$ M^{-1} s^{-1}

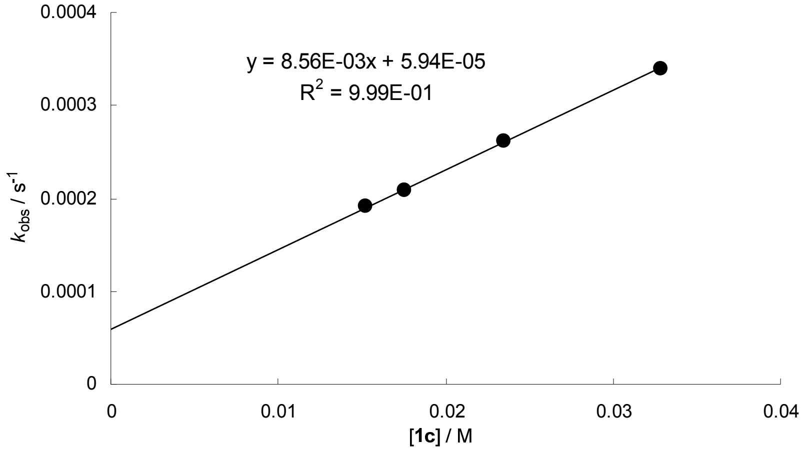
[**1c**] /M	[**4b**] /M	k_{obs} / s^{-1}
4.30×10^{-3}	8.69×10^{-5}	3.82×10^{-5}
4.69×10^{-3}	8.69×10^{-5}	3.92×10^{-5}
5.08×10^{-3}	8.69×10^{-5}	4.27×10^{-5}
7.81×10^{-3}	8.69×10^{-5}	6.62×10^{-5}



Reaction of **1c** with **5a** (dichloromethane, 20 °C, conventional, 317 nm)

$k_2 = 8.56 \times 10^{-3}$ M^{-1} s^{-1}

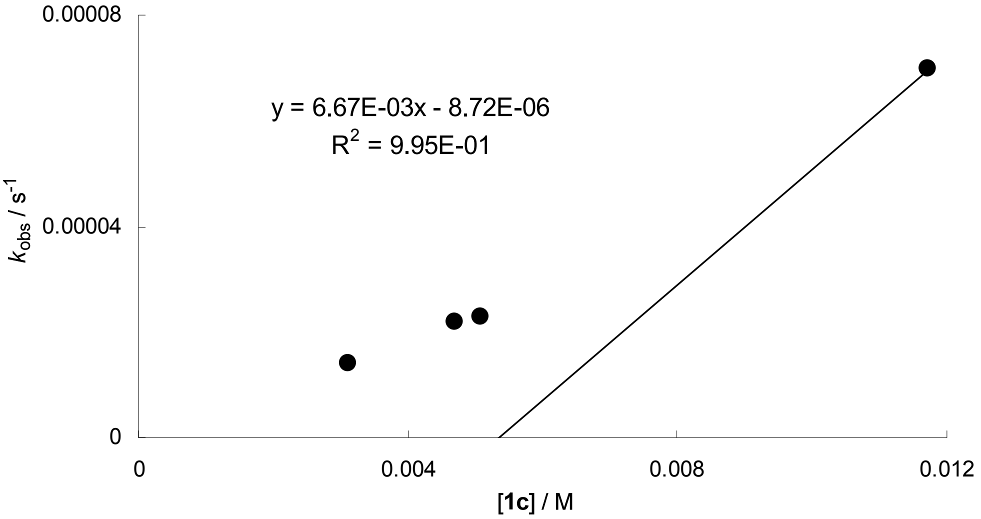
[**1c**] /M	[**5a**] /M	k_{obs} / s^{-1}
1.52×10^{-2}	1.65×10^{-4}	1.91×10^{-4}
1.76×10^{-2}	1.65×10^{-4}	2.08×10^{-4}
2.34×10^{-2}	1.65×10^{-4}	2.62×10^{-4}
3.28×10^{-2}	1.65×10^{-4}	3.40×10^{-4}



Reaction of **1c** with **6b** (dichloromethane, 20 °C, conventional, 317 nm)

$k_2 = 6.67 \times 10^{-3}$ M^{-1} s^{-1}

[**1c**] /M	[**6b**] /M	k_{obs} / s^{-1}
3.13×10^{-3}	6.82×10^{-5}	1.42×10^{-5}
4.69×10^{-3}	6.82×10^{-5}	2.20×10^{-5}
5.08×10^{-3}	6.82×10^{-5}	2.30×10^{-5}
1.17×10^{-2}	6.82×10^{-5}	7.00×10^{-5}



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