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Characterization of Novel Reference Electrophiles and Nucleophiles for the Construction of Comprehensive Reactivity Scales

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Erklärung

Diese Dissertation wurde im Sinne von § 13 Abs. 3 bzw. 4 der Promotionsordnung vom 29. Januar 1998 von Prof. Dr. Herbert Mayr betreut.

Ehrenwörtliche Versicherung

Diese Dissertation wurde selbstständig, ohne erlaubte Hilfe erarbeitet.

München, am …………………. …………..…………………….

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Für meinen Vater

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Teile dieser Dissertation sind publiziert in:

Inverse Solvent Effects in Carbocation Carbanion Combination Reactions: The Unique Behavior of Trifluoromethylsulfonyl Stabilized Carbanions. S. T. A. Berger, A. R. Ofial, H. Mayr, *J. Am. Chem. Soc.* **2007,** *129*, 9753-9761.

Electrophilicity Parameters for 2-Benzylidene-indan-1,3-diones– a systematic extension of the benzhydrylium based electrophilicity scale. S. T. A. Berger, F. H. Seeliger, F. Hofbauer and H. Mayr, *Org. Biomol. Chem.* **2007, DOI:** 10.1039/b708025e.

Electrophilicity of 5-Benzylidene-1,3-dimethyl-barbituric and -thiobarbituric Acids. F. H. Seeliger, S. T. A. Berger, G. Y. Remennikov, K. Polborn, H. Mayr, *J. Org. Chem.* **2007,** in print.

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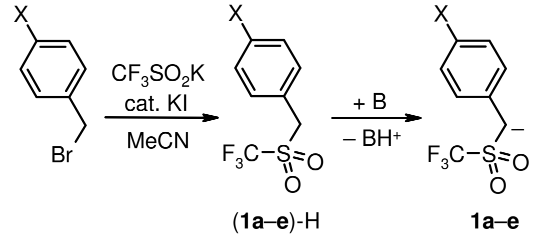
0. Summary

0.1. Nucleophilic reactivities of trifluoromethylsulfonyl substituted benzyl anions

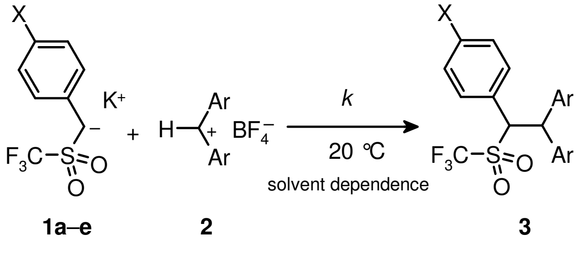
Five para-substituted trifluoromethyl sulfones (**1a**-**e**)-H were synthesized according to Hendrickson`s procedure (Scheme 0.1). Solutions of the corresponding trifluoromethylsulfonyl substituted benzyl anions **1a-e** were obtained by treatment of (**1a**-**e**)-H with 1.05 equivalents of either Schwesinger's P_2-^{t}Bu phosphazene base [$(Me_2N)_3P$=N-$P[NMe_2]_2N$*t*Bu] or KO^{t}Bu in DMSO. Only partial deprotonation was achieved when the sulfones (**1a**-**e**)-H were treated with one equivalent of sodium methoxide in methanol.



1	1a	1b	1c	1d	1e
X	CH_3	H	CF_3	CN	NO_2

Scheme 0.1. Preparation of the 4-X-benzyl trifluoromethyl sulfones (**1a**-**e**)-H according to Hendrickson`s method and generation of the corresponding trifluoromethylsulfonyl substituted benzyl anions **1a**-**e**.

Second-order rate constants for the reactions of the trifluoromethylsulfonyl substituted benzyl anions **1a–e** ($CF_3SO_2CH^-$-C_6H_4-X) with reference electrophiles **2** (benzhydrylium ions and structurally related quinone methides) were determined by UV-vis spectroscopy in DMSO and methanol (Scheme 0.2). Some addition products **3** were characterized by ^{1}H and ^{13}C NMR spectroscopy.



Scheme 0.2. Determination of the kinetics of the reactions of trifluoromethylsulfonyl substituted benzyl anions **1a–e** with reference electrophiles **2** in DMSO and methanol.

The studied reactions proceeded 10-40 times faster in methanol than in DMSO leading to the unique situation that these carbocation carbanion combinations are faster in protic than in dipolar aprotic media. According to the correlation equation 0.1 the nucleophilicity parameters N and s of **1** were derived in DMSO and in methanol (Table 0.1). The pK_a values of some benzyl trifluoromethylsulfones were determined photometrically in methanol (**1c**-H, 17.1; **1d**-H, 16.0; **1e**-H, 15.0) and found to be 5 units larger than the corresponding values in DMSO.

$$\log k_{20°\text{C}} = s(N + E) \qquad (0.1)$$

E = electrophilicity parameter
N = nucleophilicity parameter
s = nucleophile-specific slope parameter

Table 0.1. Nucleophilicity parameters N and s of the trifluoromethylsulfonyl substituted benzyl anions **1a-e** in DMSO and MeOH.

Nucleophile	in DMSO		in MeOH	
	N	s	N	s
1a (X = CH_3)	19.35	0.67	-	-
1b (X = H)	18.67	0.68	-	-
1c (X = CF_3)	17.33	0.74	20.72	0.58
1d (X = CN)	16.28	0.75	19.49	0.63
1e (X = NO_2)	14.49	0.86	18.24	0.66

Rate and equilibrium constants indicate that the trifluoromethylsulfonyl substituted benzyl anions **1a-e** are more effectively solvated by ion-dipole interactions in DMSO than by hydrogen bonding in methanol. Brønsted correlations show that trifluoromethylsulfonyl substituted carbanions **1** are less nucleophilic in DMSO than most other types of carbanions of similar basicity, indicating that the intrinsic barriers for the reactions of the localized carbanions **1** are higher in DMSO than those of delocalized carbanions, including nitroalkyl anions **4** (Figure 0.1).

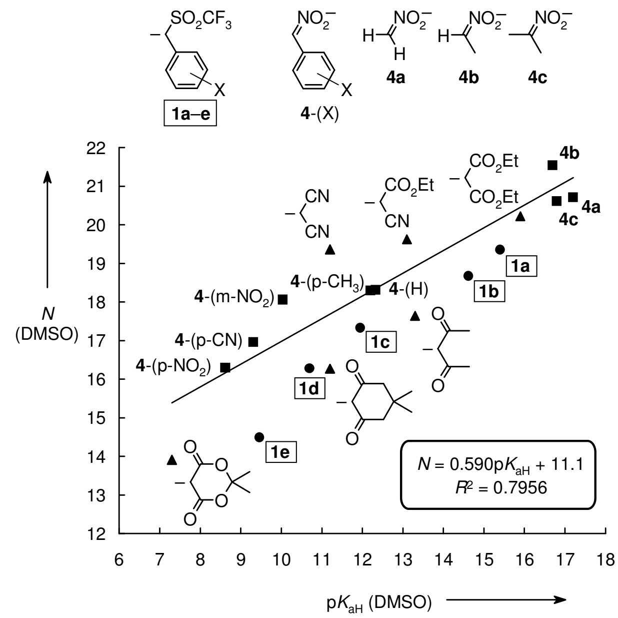


Figure 0.1. Brønsted plot for the reactivities of different carbanions towards benzhydrylium ions and quinone methides in DMSO.

The situation is reversed in methanol, where reactions of the localized triflinate stabilized carbanions **1c-e** possess lower intrinsic barriers than those of resonance stabilized carbanions. This ordering of intrinsic barriers is commonly found for proton transfer processes in protic solvents (Figure 0.2). As a consequence, the relative magnitudes of intrinsic barriers strongly depend on the solvent.

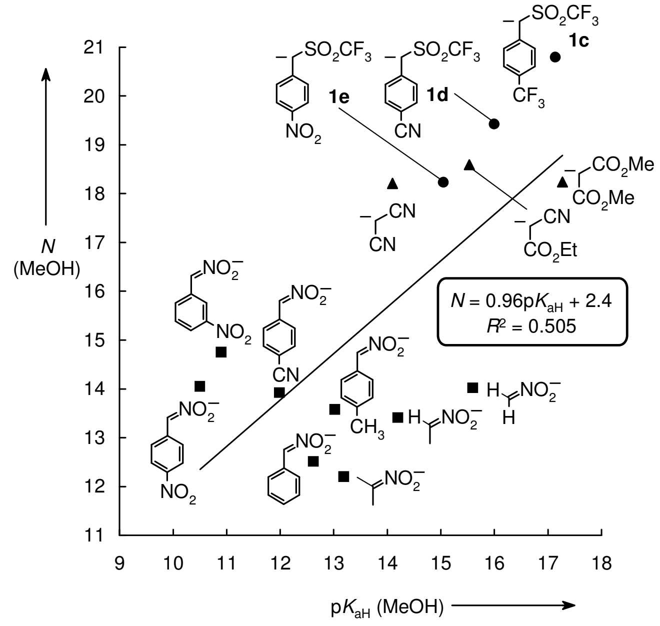
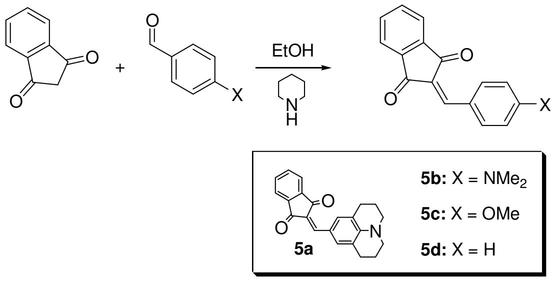


Figure 0.2. Nucleophilicity parameters N (in methanol) for different types of carbanions versus their acidity constants pK_{aH} in methanol.

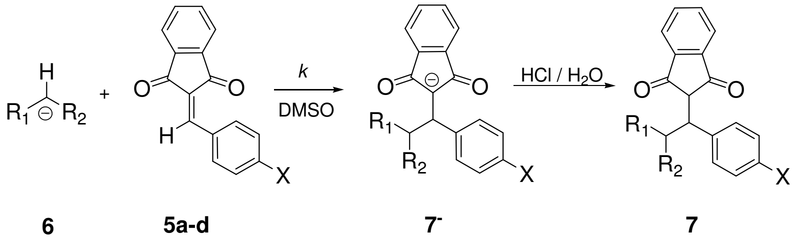
0.2. Electrophilicities of 2-benzylidene-indan-1,3-diones

In collaboration with Florian H. Seeliger four 2-benzylidene-indan-1,3-diones **5a–d** were synthesized via Knoevenagel condensation following the protocol of Behera and Nayak (Scheme 0.3).



Scheme 0.3. Preparation of 2-benzylidene-indan-1,3-diones via Knoevenagel condensation.

The kinetics of the reactions of the 2-benzylidene-indan-1,3-diones **5a-d** with the acceptor-stabilized reference carbanions **6** have been studied photometrically in DMSO at 20 °C. the resulting second-order rate constants have been used to determine the electrophilicity parameters E of **5a-d** according to the linear free energy relationship 0.1. In some cases the anionic reaction products **7⁻** and their conjugate acids **7** have been characterized by ^{1}H and ^{13}C NMR spectroscopy (Scheme 0.4).



Scheme 0.4. Reactions of 2-benzylidene-indan-1,3-diones **5a-d** with reference carbanions **6** in DMSO at 20 °C.

Equation 0.1 was employed to calculate the electrophilicity parameters E of **5a-d** from the rate constants of their reactions with carbanions and the N and s parameters of the corresponding carbanions. The electrophilicity parameters E of the 2-benzylidene-indan-1,3-diones **5a-d** are in the range of $-10 > E > -15$ and are comparable to the most reactive quinone methides in our electrophilicity scale (Figure 0.3).

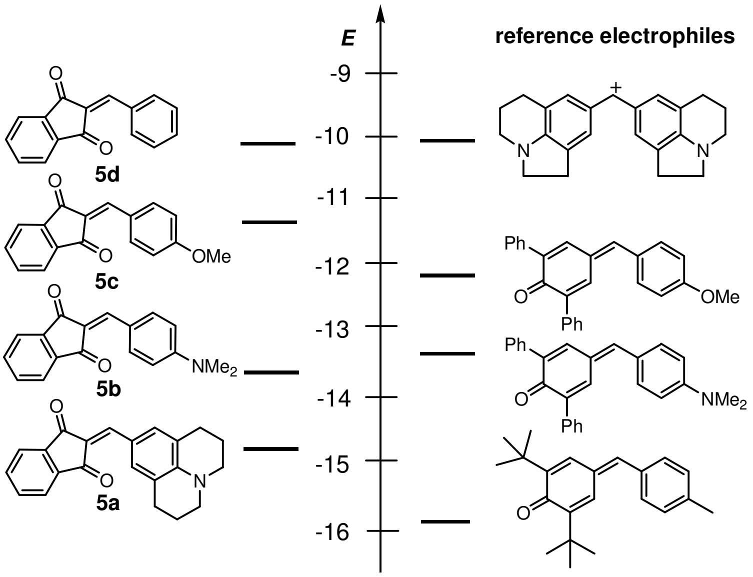
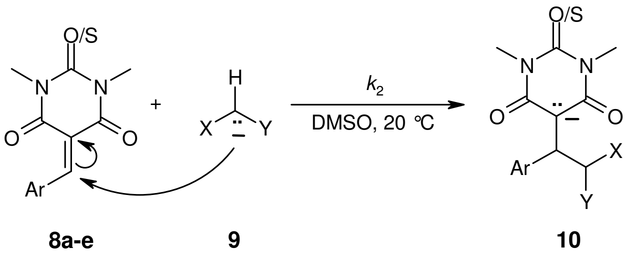


Figure 0.3. Comparison of the electrophilicity parameters of the 2-benzylidene-indan-1,3-diones **5a-d** with reference electrophiles in DMSO.

0.3 Electrophilicities of benzylidenebarbituric and –thiobarbituric acids

In collaboration with Florian H. Seeliger kinetics of the reactions of acceptor-stabilized carbanions **9** with benzylidenebarbituric and –thiobarbituric acids **8a-e** have been determined in dimethyl sulfoxide solution at 20 °C. Product analysis by ^{1}H and ^{13}C NMR spectroscopy indicated that the nucleophilic attack of the carbon nucleophile proceeds at the double bond of the Michael acceptor. (Scheme 0.5).



Scheme 0.5. Reactions of the Michael acceptors **8a-e** with the reference carbanions **9** in DMSO.

The second-order rate constants were employed to determine the electrophilicity parameters *E* of the benzylidenebarbituric and -thiobarbituric acids **8a-e** according to the correlation equation 0.1. With *E* parameters in the range of −10.4 to −13.9 the electrophilicities of **8a-e** are comparable to those of analogously substituted benzylidenemalononitriles and the most reactive quinone methides in our reactivity scale (Figure 0.4).

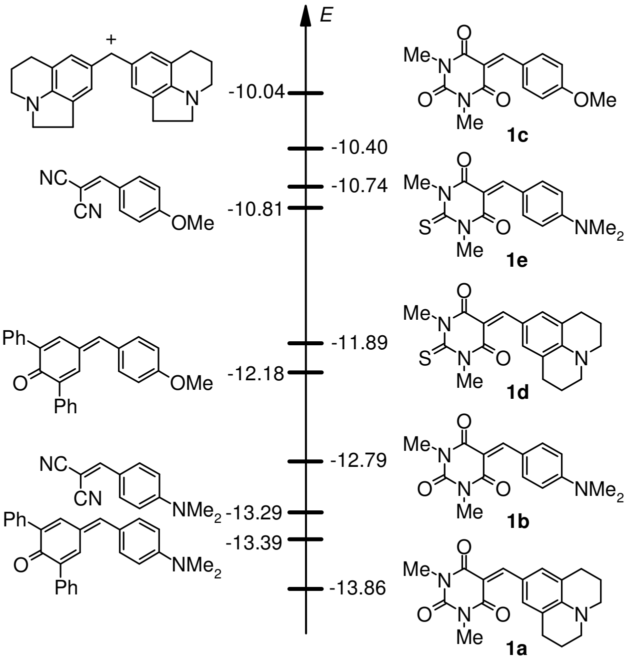


Figure 0.4. Comparison of electrophilicity parameters *E* of the benzylidenebarbituric and –thiobarbituric acids **8a-e** with Michael acceptors, quinone methides and diarylcarbenium ions.

0.4 Nucleophilicity of bis-(4-nitrophenyl)-methyl anion

The nucleophilicity parameters *N* and *s* of the bis-(4-nitrophenyl)-methyl anion **11** (λ_{max} = 783 nm) were derived from the kinetics of its reactions with quinone methides, which were employed as reference electrophiles. With an *N* parameter of 19.87 the nucleophilicity of anion **11** ranks among the most reactive carbanions so far characterized in our nucleophilicity scales (Figure 0.5).

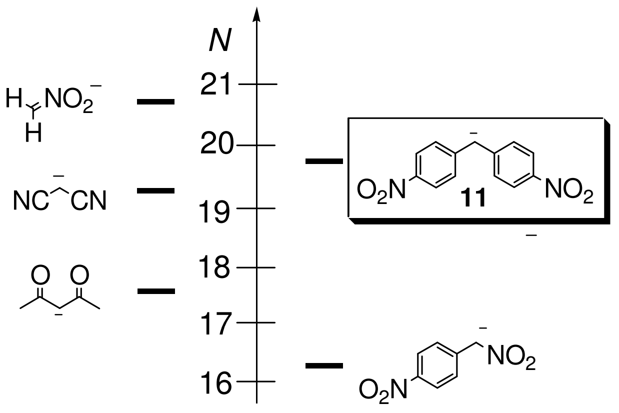


Figure 0.5. Comparison of the nucleophilicity parameters *N* of different acceptor-stabilized carbanions in DMSO.

It was shown that the nucleophilicity parameters *N* and *s* of the bis-(4-nitrophenyl)-methyl anion **11** can be used to estimate the rates of reactions of **11** with other Michael acceptors (open symbols in Figure 0.6).

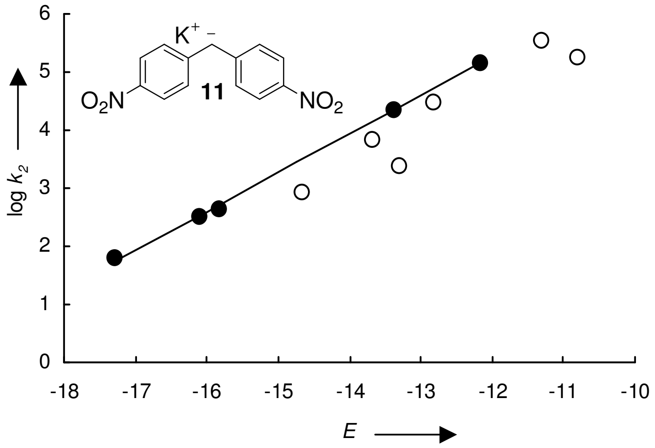


Figure 0.6. Determination of the nucleophilicity parameters *N* and *s* of **11** from its reactions with reference quinone methides. The observed second-order rate constants for the addition reactions of **11** to other Michael acceptors (open symbols) show deviations smaller than 1 order of magnitude and are thus within the previously postulated confidence limit of eq. 0.1.

0.5 Micellaneous experiments

Electrophilicity of the 10-(4-methoxybenzylidene)-9(*10H*)-anthracenone in DMSO (Figure 0.7)

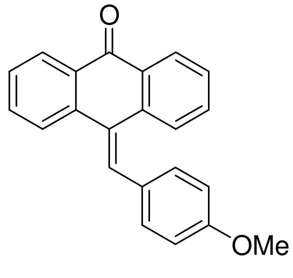


Figure 0.7. Structure of the 10-(4-methoxybenzylidene)-9(*10H*)-anthracenone, simply called p-methoxy-anthrachinonmethide.

The kinetics of the reactions of 10-(4-methoxybenzylidene)-9(*10H*)-anthracenone with carbanions have been investigated in dimethyl sulfoxide solution at 20 °C by following the rate of the reactions at the absorption maximum of the electrophile at 421 nm. Plots of log k_2/s

versus the nucleophilicity parameters *N* of the nucleophiles indicated a poor correlation (Figure 0.8).

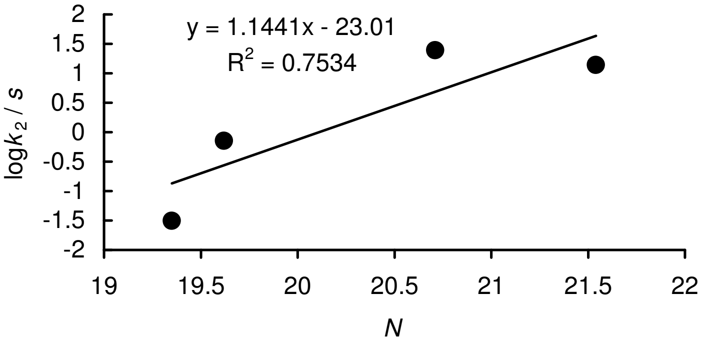


Figure 0.8. Plots of log k_2/s versus the nucleophilicity parameters *N* of the employed nucleophiles.

Because suitable more reactive reference nucleophiles were presently not available the electrophilicity parameter *E* of 10-(4-methoxybenzylidene)-9(*10H*)-anthracenone should be considered preliminary.

Nucleophilicity of of indane-1,3-dione anion in DMSO

The nucleophilicity parameters *N* = 21.83 and *s* = 0.47 of the indane-1,3-dione anion were calculated from the rate constants of its reactions with reference benzhydrylium ions in DMSO (Figure 0.9).

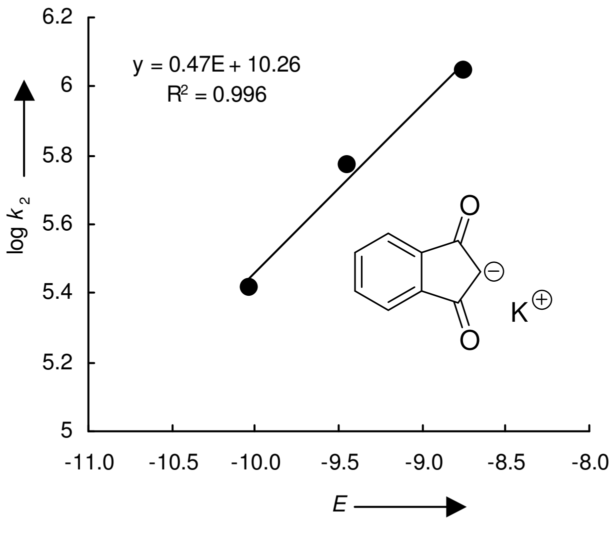
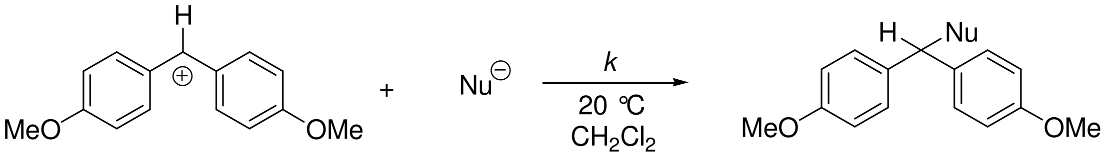


Figure 0.9. Determination of the nucleophilicity parameters *N* and s of the indane-1,3-dione anion in DMSO.

1. Introduction

Kinetic investigations played an important role for the development of the electronic theory of Organic Chemistry.[1] It is now clear that most organic reactions proceed via electrophile nucleophile combinations.[2] Since the 1950s several efforts have been made to quantify the reactivities of nucleophiles[3] and it was realized that it is impossible to construct a general nucleophilicity scale, because relative nucleophilic reactivities depend on the reaction partner as well as on the solvent and on the reaction temperature. In view of these limitations the group of Prof. Mayr attempted to develop a comprehensive nucleophilicity scale with respect to the bis-*p*-methoxybenzhydrylium ion at 20 °C in CH_2Cl_2 (Scheme 1.1).



Scheme 1.1. General equation for the reaction of the red bis-*p*-methoxybenzhydrylium ion with nucleophiles in dichlormethane at 20 °C.

From the second-order rate constants for the reactions of this electrophile with various nucleophiles like alkenes,[4] electron-rich heteroarenes,[5] enol ethers,[6] ketene acetals[6] or water[7] it became possible to compare the relative reactivities of these classes of nucleophiles.

Nevertheless the majority of nucleophiles could not be characterized in this way. While electron poor arenes or alkenes are too weak nucleophiles and do not at all react with the bis-*p*-methoxybenzhydryl cation with measureable rates at 20 °C, enamines or carbanions on the other hand are too reactive that all of them react with similar rates (diffusion control). It is obvious that it is impossible to construct a comprehensive nucleophilicity scale with respect to a single electrophile (Figure 1.1).

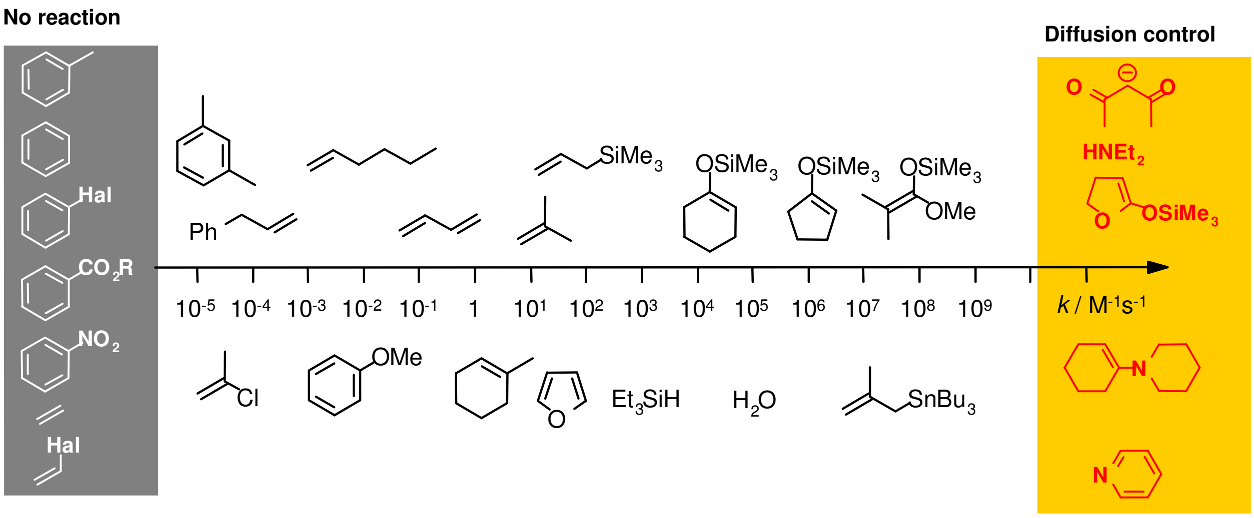


Figure 1.1. Construction of a nucleophilicity scale with respect to the bis-(*p*-methoxybenzhydrylium ion) (20 °C, CH_2Cl_2).

For that reason, a set of 29 para- and meta-substituted benzhydrylium ions and structurally related quinone methides was selected as reference electrophiles which possess all the same steric surroundings at the reaction center and whose reactivities can be modified by the substituents X, Y, Z and R (Figure 1.2).

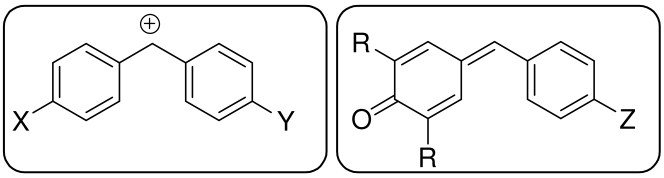


Figure 1.2. Benzhydrylium ions (left) and structurally related quinone methides (right) as reference electrophiles.

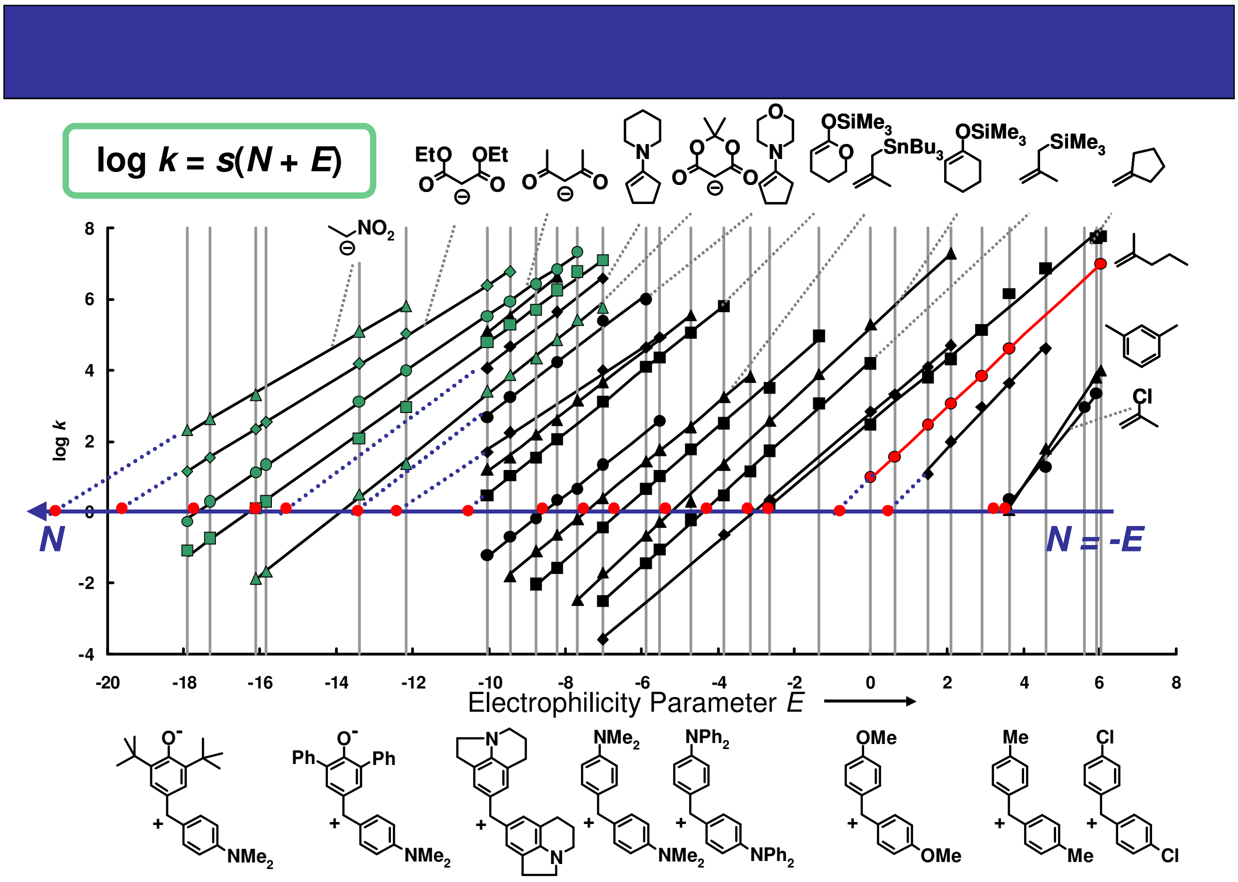
Consecutively, the kinetics of their reactions with a variety of carbon nucleophiles were studied in dichloromethane (carbocations + neutral nucleophiles) or dimethyl sulfoxide (anions + neutral or positively charged electrophiles) by photometric monitoring of the consumption of the electrophiles.[8,9,10] By combining strong electrophiles with weak nucleophiles and weak electrophiles with strong nucleophiles, second-order rate constants between 10^{-5} and 5×10^{7} M^{-1} s^{-1} were measured at 20 °C.

In this way, 29 nucleophilicity scales were obtained, one for each electrophile. Least-squares analysis of the rate constants for the reactions of the 29 reference electrophiles with selected carbon nucleophiles gave the correlation lines shown in Figure 1.3, which can all be described by the correlation equation 1.1. In this equation each electrophile is characterized by one parameter E while each nucleophile is characterized by the two nucleophilicity parameters N and s.

$$\log k_2\ (20°\mathrm{C}) = s(N + E) \qquad (1.1)$$

The bis-*p*-methoxybenzhydryl cation was arbitrarily attributed an electrophilicity parameter E of 0 and the 2-methyl pentene was attributed a nucleophile specific slope parameter s of 1. The nucleophilicity parameter N is given for each nucleophile by the negative intercept of the corresponding line with the abscissa (*i.e.* $\log k = 0$), because there eq.1.1 requires $N = -E$. This definition of nucleophilicity is much more practical than the mathematically equivalent possibility to define nucleophilicity as the intercept of the ordinate (sN), which may be far outside of the experimental range ($sN < -5$ or $sN > 9$). In this case small differences in the slopes may lead to large changes in the intercept on the ordinate.[11]

Equation 1.1 now allows the prediction of second-order rate constants for unknown electrophile nucleophile combinations from known electrophilicity and nucleophilicity parameters E, N, and s when only one single bond is formed in the rate-determining step. In this way it is possible to predict whether a reaction can be expected to take place at 20 °C ($E + N > -5$), or whether a reaction will proceed under diffusion control [$s\ (E + N) > 9$], which is often associated with low selectivity.



J. Am. Chem. Soc. **2001**, *123*, 9500-9512.

Figure 1.3. Second-order rate constants for electrophile-nucleophile-combinations (20 °C).

It was the goal of this work to identify new highly reactive nucleophiles(carbanions) and new Michael acceptors as reference compounds in order to extend the nucleophilicity scale on the high reactivity end and the electrophilicity scale on the low reactivity end. Because of the size of this project, Florian Seeliger, Oliver Kaumanns and I were assigned to the carbanion group, which was supposed to reach this goal in a collaborative effort.

Since the major parts of this thesis have already been published in a series of papers, individual introductions will be given at the beginning of each chapter. In order to identify my contributions to the multiauthor publications the Experimental Sections report exclusively the experiments which were performed by myself. Unpublished investigations are given in chapter 6.

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[11] (a) Mayr, H.; Patz, M. *Angew. Chem* **1994,** *106*, 990-1010; *Angew. Chem. Int., Ed. Engl.* **1994,** *33*, 938-957. (b) Mayr, H.; Patz, M.; Gotta, M. F.; Ofial, A. R. *Pure Appl. Chem.* **1998,** *70*, 1993-2000. (c) For detailed discussions of the advantages of using the intercept on the abscissa ($N = -E$ for $\log k = 0$) as a measure of nucleophilicity, see: Mayr, H.; Ofial, A. R. In *Carbocation Chemistry*, Olah, G. A.; Prakash, G. K. S. (Eds.), Chap. 13, John Wiley, New York (2004).

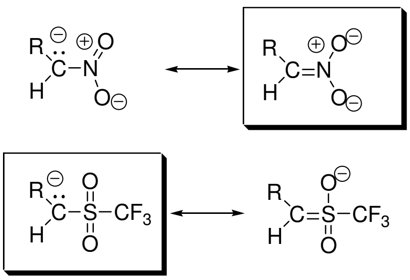
Inverse Solvent Effects in Carbocation Carbanion Combination Reactions: The Unique Behavior of Trifluoromethylsulfonyl Stabilized Carbanions

S. T. A. Berger, A. R. Ofial, H. Mayr, *J. Am. Chem. Soc.* **2007**, *129,* 9753-9761.

Introduction. Relationships between nucleophilicity (i.e., relative rates of reactions of electron-pair donors with a given electrophile) and basicity (i.e., relative affinities for a proton in acid base equilibria) play a central role for our understanding of organic reactivity.[1-5] While it is well-known that good correlations between nucleophilic reactivities and the pK_a values of the conjugate acids can only be obtained when the nature of the reaction center remains unchanged,[6] in some cases anomalous rate equilibrium relationships have been observed, even within families of closely related compounds.[7] The most prominent example for an untypical Brønsted correlation is the so-called "nitroalkane anomaly" which implies that the rates of protonation of nitronate anions decrease with increasing basicity.[8]

Transition state imbalances, due to the extensive π-delocalization of nitro stabilized carbanions, have been claimed to be responsible for the high intrinsic barriers of these reactions.[9] There is ample evidence that nitro-stabilized carbanions are best described by the resonance structure with a CN double bond, as indicated in Scheme 2.1.[9,10]

Scheme 2.1. Nitro- and triflinate stabilized carbanions.



A completely different type of anion stabilization is exerted by the CF_3SO_2 group, which has been known to be one of the strongest electron acceptor groups in organic chemistry since the pioneering investigations by Sheppard[11] and Yagupol'skii.[12] The pK_a values of substituted benzoic acids indicate that the CF_3SO_2 group ($\sigma_p = 0.96$)[12,13] is a stronger electron acceptor than the nitro group ($\sigma_p = 0.81$).[13]

Comparison of the pK_a values of substituted anilinium ions and phenols also showed the greater electron-accepting power of CF_3SO_2 ($\sigma_p^- = 1.63$ or 1.65)[12,13] compared to NO_2 ($\sigma_p^- = 1.24$).[13,14] NMR spectroscopic investigations of triflinate substituted carbanions revealed that the carbanion center is sp^3-hybridized and that resonance stabilization is unimportant, resulting in a high weight of the resonance structure on the left side of Scheme 2.1.[15] In line with this interpretation is the unusual solvent dependence of the pK_a values of the benzyl trifluoromethyl sulfones. In contrast to the behavior of most CH acids, their acidities decrease with increasing water content of DMSO/H_2O mixtures.[8p,15]

In this work we have studied the rates of the reactions of the α-CF_3SO_2-substituted 4-X-benzyl anions **1a–e** (Scheme 2.2) with a set of reference electrophiles (quinone methides **2a–e** and the structurally analogous benzhydrylium ions **2f**-**j**) in order to determine the nucleophilicity parameters N and s (eq. 2.1)[16] of **1a–e** in DMSO and in methanol.

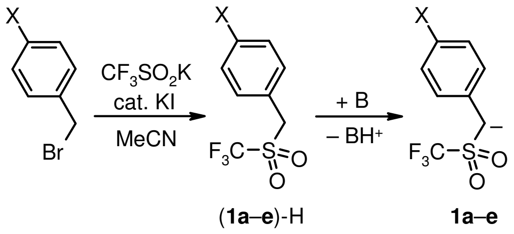
$$\log k_{20^\circ C} = s(N + E) \qquad (2.1)$$

E = electrophilicity parameter
N = nucleophilicity parameter
s = nucleophile-specific slope parameter

We will show that the comparison of the reactivities of nitro- and trifluoromethylsulfonyl substituted carbanions in DMSO and methanol provides significant new insights in the origin of intrinsic barriers.

Preparation and Deprotonation of Benzyl Trifluoromethyl Sulfones. A variety of methods has been developed for the synthesis of the benzyl trifluoromethyl sulfones (**1a**-**e**)-H.[17] We used the procedure described by Hendrickson and coworkers,[18] which combines benzyl bromides with potassium triflinate[19] in boiling acetonitrile in the presence of catalytic amounts of potassium iodide (Scheme 2.2).

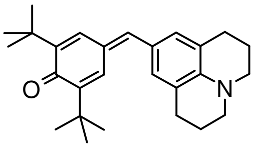
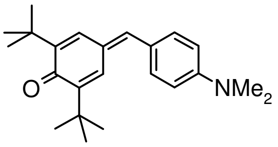
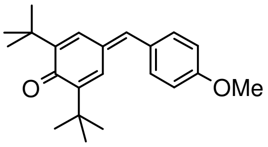
Scheme 2.2. Preparation of the 4-X-benzyl trifluoromethyl sulfones (**1a**-**e**)-H according to the Hendrickson method and generation of the corresponding α-triflinate stabilized carbanions **1a**-**e**.

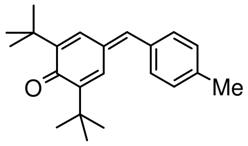
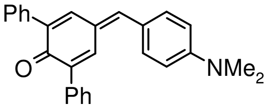
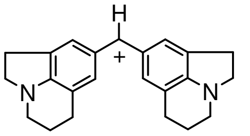
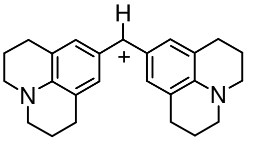
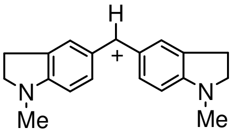
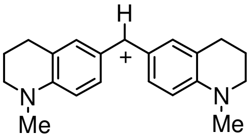
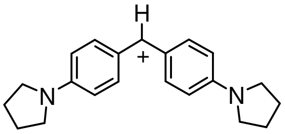


1	1a	1b	1c	1d	1e
X	CH_3	H	CF_3	CN	NO_2

Solutions of **1a-e** were obtained by treatment of the benzyl trifluoromethyl sulfones (**1a**-**e**)-H with 1.05 equivalents of either Schwesinger's P_2-^{t}Bu phosphazene base [$(Me_2N)_3P$=N-P[NMe_2]$_2$N*t*Bu][20,21] or KO*t*Bu in DMSO. The potassium salts (**1d**-**e**)-K precipitated when the benzyl trifluoromethyl sulfones (**1d**-**e**)-H were combined with one equivalent of KO*t*Bu in dichloromethane under a nitrogen atmosphere. Only partial deprotonation was achieved when the sulfones (**1a**-**e**)-H were treated with one equivalent of sodium methoxide in methanol.

Table 2.1. Quinone Methides **2a**-**e** and Benzhydrylium Ions **2f**-**j** Employed in this Work.

	Electrophile	*E*[a]	λ_{max} (nm)[b]
2a		–17.90	521
2b		–17.29	486
2c		–16.11	393

2d		–15.83	371
2e		–13.39	533[c]
2f		–10.04	640
2g		–9.45	643
2h		–8.76	624
2i		–8.22	628
2j		–7.69	621

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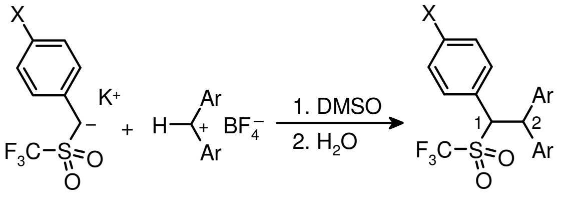
[a] Electrophilicity parameters *E* for **2a–e** from ref. 22a and for **2f–j** from from ref. 16b. [b] In DMSO, from ref. 23. [c] From ref. 24.

Reaction Products. As shown in Scheme 2.3, the triflinate stabilized benzyl anions **1a–e** react with the benzhydrylium ions **2f-j** to give the addition products **3**, several of which have been characterized by ^{1}H and ^{13}C NMR spectroscopy (for details, see Experimental Section).

Scheme 2.3. Reactions of the potassium salts of the trifluoromethylsulfonyl stabilized carbanions **1a**-**e** with the benzhydrylium tetrafluoroborates **2f**-**j** in DMSO.



1a–e **2f–j** **3**

Evidence for the formation of the compounds **3** comes from their ^{1}H NMR spectra, which show doublets (J = 9.3–10.2 Hz) in the range of δ = 5.15–5.28 ppm (1-H) and δ = 4.65–4.81 ppm (2-H) as summarized in Table 2.2.

Table 2.2. ^{1}H NMR Chemical Shifts (in ppm) and Coupling Constants ^3J (in Hz) for 1-H and 2-H of the Products **3**.[a]

Entry	Nucleophile	Ar_2CH^+	Product	δ(1-H)	δ(2-H)	^3J
1	**1a** (X = CH_3)	**2f**	**3af**	5.15	4.74	10.2
2	**1b** (X = H)	**2f**	**3bf**	5.16	4.76	10.2
3	**1b** (X = H)	**2d**	**3bd**	5.17	4.86	9.8
4	**1c** (X = CF_3)	**2g**	**3cg**	5.22	4.68	9.3
5	**1d** (X = CN)	**2f**	**3df**	5.21	4.71	10.1
6	**1d** (X = CN)	**2h**	**3dh**	5.21	4.77	10.2
7	**1d** (X = CN)	**2i**	**3di**	5.18	4.70	9.8
8	**1e** (X = NO_2)	**2f**	**3ef**	5.27	4.74	10.1
9	**1e** (X = NO_2)	**2g**	**3eg**	5.28	4.68	9.6
10	**1e** (X = NO_2)	**2h**	**3eh**	5.27	4.81	10.2

11	**1e** ($X = NO_2$)	**2i**	**3ei**	5.25	4.73	9.9

[a] Assignment not confirmed.

We also studied the reaction of the quinone methide **2d** with the triflinate stabilized carbanion **1b** by ^{1}H NMR spectroscopy (entry 3 in Table 2.2). In contrast to our expectation, only one pair of doublets was observed for 1-H and 2-H indicating the formation of only one diastereoisomer.

Kinetic Investigations in DMSO. The kinetic investigations in DMSO were performed at 20 °C. All reactions proceeded quantitatively, and the rates were determined photometrically by following the decrease of the absorbances of the electrophiles **2** at their absorption maxima (Table 2.1), as shown in Figure 2.1.

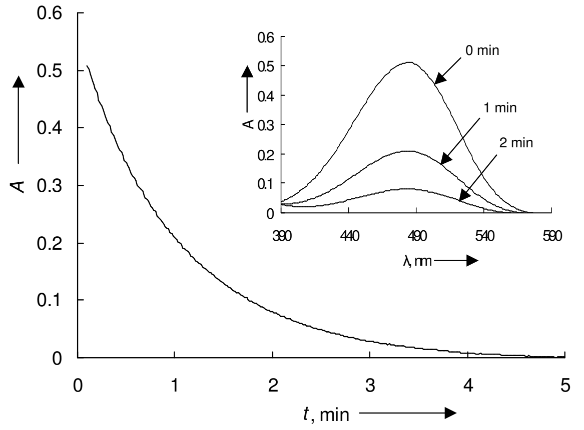


Figure 2.1. UV-vis-spectroscopic monitoring of the reaction of benzyl triflinate (**1b**, 6.29×10^{-4} mol L^{-1}) with the quinone methide **2b** (3.16×10^{-5} mol L^{-1}) at 500 nm in DMSO at 20 °C.

All reactions were studied under pseudo-first-order conditions using 10 to 100 equivalents of the benzyl triflinate ions **1**. The concentrations of **1** (10^{-3}–10^{-4} mol L^{-1}) were thus kept almost constant throughout the kinetic measurements, resulting in an exponential decay of the concentrations of the colored electrophiles (eq. 2.2).

$$-d[\mathbf{2}]/dt = k_{1\Psi}[\mathbf{2}] \qquad (2.2)$$

The pseudo-first-order rate constants $k_{1\Psi}$ (= k_2[**1**]$_0$) were obtained by least-squares fitting of the single-exponential $A_t = A_0\exp(-k_{1\Psi}t) + C$ to the time-dependent absorbance A of the electrophile. Plots of $k_{1\Psi}$ versus the nucleophile concentration [**1**]$_0$ give straight lines with the slope k_2, as shown for one example in Figure 2.2 and for all other experiments in the Supporting Information.

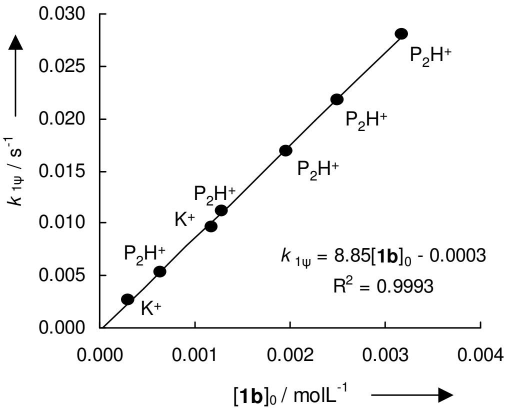
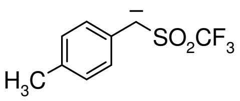
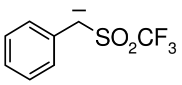
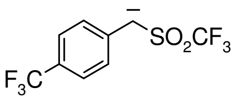
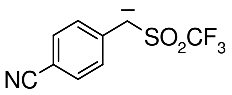
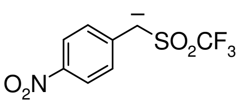


Figure 2.2. Determination of the second-order rate constant k_2 = 8.85 L mol^{-1}s^{-1} for the reaction of benzyl triflinate (**1b**) with the quinone methide **2b** in DMSO at 20 °C from a plot of the first-order rate constants $k_{1\Psi}$ vs. the triflinate concentration. Counter ions were K$^+$ or protonated Schwesinger's phosphazene base *t*Bu-P$_2$H$^+$ (ref. 20).

In several $k_{1\Psi}$ vs. [**1**]$_0$ plots, $k_{1\Psi}$ values obtained with the potassium and the phosphazenium salts of **1** were used side by side. The fact that first-order rate constants obtained with different counter ions are on the same correlation line (see Figure 2.2) demonstrates the independence of the rate constants of the nature of the counter ion. In line with these observations, the same rate constants within experimental error were obtained, when the rate of the reaction of **1d** with **2f** was studied with a solution of the isolated potassium salt **1d**-K or with a solution of the corresponding sulfone **1d**-H and 1.05 equivalents of KO*t*Bu. When solutions of the triflones (**1c**-**e**)-H were combined with KO*t*Bu in DMSO, limiting values of the absorbances of the colored carbanions **1c**-**e** were reached after the addition of 1 equivalent of KO*t*Bu indicating that one equivalent of KO*t*Bu is sufficient for a complete deprotonation of the benzyl trifluoromethyl sulfones.

Table 2.3. Second-Order Rate Constants k_2 for the Reactions of the Quinone Methides **2a**-**e** and Benzhydrylium Ions **2f**-**j** with the α-Triflinate Stabilized Carbanions **1a-e** (DMSO, 20 °C).

Nucleophile		N^a	s^a	Electrophile	Base	k_2 ($M^{-1}s^{-1}$)	Product
1a		19.35	0.67	**2a**	P_2	1.02×10^1	-
				2b	P_2	2.23×10^1	-
				2c	P_2	1.51×10^2	-
				2f	P_2	1.87×10^6	**3af**
1b		18.67	0.68	**2a**	P_2	1.91	-
				2b	P_2 or KO*t*Bu	8.85	-
				2c	P_2 or KO*t*Bu	7.78×10^1	-
				2d	P_2	1.34×10^2	**3bd**[b]
				2e	P_2	4.26×10^3	-
				2f	P_2	6.51×10^5	**3bf**
1c		17.33	0.74	**2e**	P_2	7.97×10^2	-
				2f	P_2	2.35×10^5	
				2g	-	-	**3cg**
1d		16.28	0.75	**2e**	P_2	1.20×10^2	-
				2f	P_2 or KO*t*Bu	6.82×10^4	**3df**
				2f	K^+ salt	6.80×10^4	-
				2g	KO*t*Bu	2.02×10^5	-
				2h	P_2 or KO*t*Bu	3.71×10^5	**3dh**
				2i	KO*t*Bu	7.53×10^5	**3di**
1e		14.49	0.86	**2f**	KO*t*Bu	6.73×10^3	**3ef**
				2g	KO*t*Bu	1.89×10^4	**3eg**
				2h	P_2	8.09×10^4	**3eh**
				2i	-	-	**3ei**
				2j	P_2	6.61×10^5	-

[a] Nucleophilicity parameters *N* and *s* derived by equation 2.1. [b] Characteristic product signals identified by proton NMR in $CDCl_3$.

Kinetic Investigations in Methanol. The evaluation of the kinetic experiments in methanol was more complicated than in DMSO. Because most of the reference electrophiles **2** listed in Table 2.1 react readily with methanol, it was not possible to prepare solutions of these electrophiles in methanol and mix them with methanolic solutions of the triflinates **1a**-**e** in order to determine the rate constants for the reactions of **1a**-**e** with **2** in pure methanol. However, we were able to measure the kinetics of the reactions of the CF_3SO_2-substituted benzyl anions **1c**–**e** with benzhydryl cations **2** in methanol/acetonitrile mixtures (91:9, v/v) in a stopped-flow instrument by mixing 10 volume parts of methanolic solutions of the triflones **1**-H and methoxide with one part of a solution of $Ar_2CH^+ BF_4^-$ (**2**) in acetonitrile.

As previously reported by Terrier,[15] the 4-X-benzyl trifluoromethyl sulfones (**1a-e**)-H are weaker acids in water than in DMSO. In line with this observation, even the acceptor substituted sulfones (**1c**-**e**)-H cannot completely be deprotonated by sodium methoxide in methanol, and the equilibrium (2.4) has to be considered.

$$\mathrm{CH} + \mathrm{MeO}^- \underset{}{\overset{K_{\mathrm{CH}}}{\rightleftharpoons}} \mathrm{C}^- + \mathrm{MeOH}$$

$$K_{\mathrm{CH}} = [\mathrm{C}^-]/([\mathrm{CH}][\mathrm{MeO}^-]) \qquad (2.4)$$

$$\mathrm{p}K_{\mathrm{MeOH}} = -\log\{[\mathrm{MeO}^-][\mathrm{H}^+]\} = 16.92 \text{ (at 20 °C)}^{25} \qquad (2.5)$$

$$\mathrm{p}K_{\mathrm{a}} = -(\log K_{\mathrm{CH}}) + \mathrm{p}K_{\mathrm{MeOH}} \qquad (2.6)$$

For the trifluoromethyl sulfones (**1c**-**e**)-H neither the pK_a nor the K_{CH} values in methanol have been reported. The equilibrium constants K_{CH} (eq. 2.4) were, therefore, determined photometrically at the absorption maxima of the carbanions by titration of (**1c**-**e**)-H with sodium methoxide (Table 2.4). Because quantitative deprotonation of the triflones could not be achieved, the acid dissociation constants K_{CH} (eq. 2.4, Table 2.4) were obtained by least-squares fitting of calculated and experimental concentrations of C^- (= **1c**-**e**) as described in the Experimental Section. The pK_a values were then calculated according to equation 2.6.

Table 2.4. Deprotonation of the Benzyl Trifluoromethyl Sulfones (**1c**-**e**)-H by Sodium Methoxide (20 °C, MeOH).

triflone	λ_{max} (nm)[a]	K_{CH} (M^{-1})	pK_a
1c-H (X = CF_3)	305	0.600	17.1
1d-H (X = CN)	345	8.24	16.0
1e-H (X = NO_2)	476	76.1	15.0

[a] Absorption maxima of the α-triflinate stabilized carbanions (λ_{max} for **1c**, **1d**, and **1e** in DMSO reported in ref. 15b: 316, 347, and 476 nm, respectively).

Phan and Mayr have reported that the ionization constants of *p*-cyanophenylnitromethane in pure methanol and in MeOH/CH_3CN (91:9, v/v) agree within experimental error.[26] The pK_a values for (**1c**-**e**)-H in pure MeOH (Table 4) have, therefore, been used for the calculation of the carbanion concentrations during the kinetic experiments in MeOH/CH_3CN (91:9, v/v). Because of the low acidities of **1a**-H and **1b**-H, we were not able to determine their equilibrium constants K_{CH} in methanol, and therefore we have not performed kinetic investigations with these carbanions in methanol.

As a consequence of the incomplete deprotonation of the triflones (**1c**-**e**)-H in many of the kinetic experiments, it was often not possible to achieve a high excess of the carbanions **1** over the electrophiles **2**. However, even in the case [**1**] ≈ [**2**], pseudo-first-order conditions were warranted when [**1**-H] >> [**2**] because the proton transfer between the carbanions **1c**-**e** and methanol is much faster than the reaction of **1c**-**e** with the electrophiles used in these investigations. Fast proton transfer from **1**-H to methoxide, as expected for the formation of carbanions with little rehybridization, was proven by the observation that treatment of **1c**-H (2.24×10^{-4} mol L^{-1}), **1d**-H (2.36×10^{-4} mol L^{-1}), and **1e**-H (2.21×10^{-4} mol L^{-1}) with sodium methoxide in methanol yielded the equilibrium concentrations of **1c**-**e** in less than 2 ms, the dead time of our stopped-flow instrument.

According to Equation (2.7), the pseudo-first-order rate constants k_{obs} determined in methanol reflect the sum of the reactions of the electrophile with the carbanion ($k_{2,C}[C^-]$), with methoxide ($k_{2,MeO}[MeO^-]$), and with methanol ($k_{1,MeOH}$).

$$k_{\mathrm{obs}} = k_{2,\mathrm{C}}[\mathrm{C}^-] + k_{2,\mathrm{MeO}}[\mathrm{MeO}^-] + k_{1,\mathrm{MeOH}} \tag{2.7}$$

The second-order rate constants $k_{2,\mathrm{MeO}}$ for the reactions of methoxide ion with benzhydrylium ions and the relevant first-order rate constants for the reactions of benzhydrylium ions with methanol, which have previously been reported,[26] are summarized in Table 2.5.

Table 2.5. Second-Order Rate Constants $k_{2,\mathrm{MeO}}$ for the Reactions of Methoxide Anion and First-Order Rate Constants $k_{1,\mathrm{MeOH}}$ for the Reactions of Methanol with Benzhydrylium Ions **2f–k** in MeOH/CH_3CN (91:9, v/v) at 20 °C (from ref. 26)

Electrophile	$k_{2,\mathrm{MeO}}$ (M^{-1} s^{-1})	$k_{1,\mathrm{MeOH}}$ (s^{-1})
2f	1.17×10^3	6.14×10^{-3}
2g	2.48×10^3	3.16×10^{-2} [a]
2h	7.41×10^3	2.13×10^{-1} [a]
2i	1.56×10^4	2.17×10^{-1}
2j	4.80×10^4	9.32×10^{-1}

[a] Calculated according to eq. (2.1)

Rearrangement of Equation 7 gives Equation 2.8,

$$k_{1\Psi} = k_{\mathrm{obs}} - k_{2,\mathrm{MeO}}[\mathrm{MeO}^-] = k_{2,\mathrm{C}}[\mathrm{C}^-] + k_{1,\mathrm{MeOH}} \tag{2.8}$$

which implies that the second-order rate constants $k_{2,\mathrm{C}}$ can be derived from the slopes of plots of $k_{1\Psi}$ vs. [C^-] as shown in Figure 2.3 for the reaction of **2f** with benzyl triflinate **1e**. The intercepts of these correlations correspond to the reactions of the electrophiles **2** with the solvent MeOH. In agreement with the entries in the right column of Table 2.5, these intercepts are small and can be neglected.

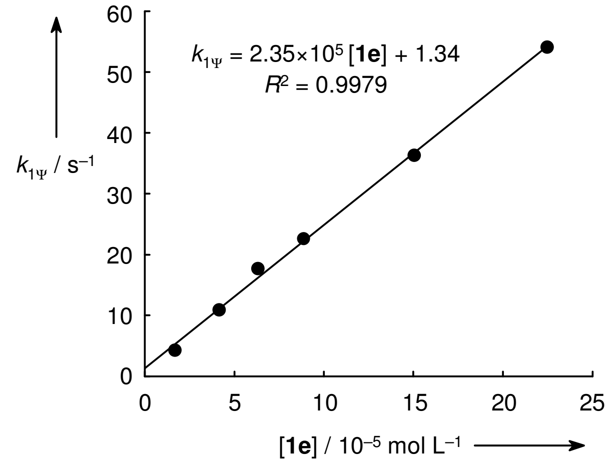


Figure 2.3. Determination of the second-order rate constant $k_{2,\mathrm{C}} = 2.35 \times 10^5$ L mol^{-1} s^{-1} for the reaction of **2f** with benzyl triflinate **1e** in MeOH/CH$_3$CN (91:9, v/v) at 20 °C.

In all kinetic experiments, the term $k_{2,\mathrm{C}}[\mathrm{C}^-]$ was the major contribution to k_{obs}, which excludes major errors in the determination of the carbanion reactivities. For the reaction of **1d** with **2i**, it was furthermore shown that almost the same rate constants $k_{1\Psi}$ were obtained when variable ratios of [**1d**-H]/[MeO$^-$] were employed, as required by the suggested kinetic formalism (Experimental Section).

Table 2.6. Second-Order Rate Constants $k_{2,\mathrm{C}}$ for the Reactions of the α-Triflinate Stabilized Carbanions **1c–e** with the Benzhydrylium Ions **2f–j** in MeOH/CH$_3$CN (91:9, v/v) at 20 °C.

Nucleophile[a]	N[b]	s[b]	Electrophile	$k_{2,\mathrm{C}}$ (M^{-1} s^{-1})
1c (X = CF$_3$)	20.72	0.58	**2f**	1.55×10^6
			2g	4.09×10^6
			2h	9.85×10^6
			2i	2.20×10^7
			2j	3.50×10^7
1d (X = CN)	19.49	0.63	**2f**	8.52×10^5

			2g	1.99×10^6
			2h	5.44×10^6
			2i	1.22×10^7
			2j	2.50×10^7
1e ($X = NO_2$)	18.24	0.66	**2f**	2.35×10^5
			2g	7.98×10^5
			2h	1.31×10^6
			2i	3.85×10^6
			2j	9.83×10^6

---

[a] Generated from the corresponding triflones (**1c**-**e**)-H and NaOMe. [b] Nucleophilicity parameters *N* and *s* derived by equation 2.1.

Discussion

As previously shown for many other nucleophile electrophile combinations,[16,22,26–28] the second-order rate constants given in Tables 2.3 and 2.6 correlate well with the electrophilicity parameters *E* of the benzhydrylium ions **2f–j** and quinone methides **2a–e** (Figures 2.4 and 2.5).

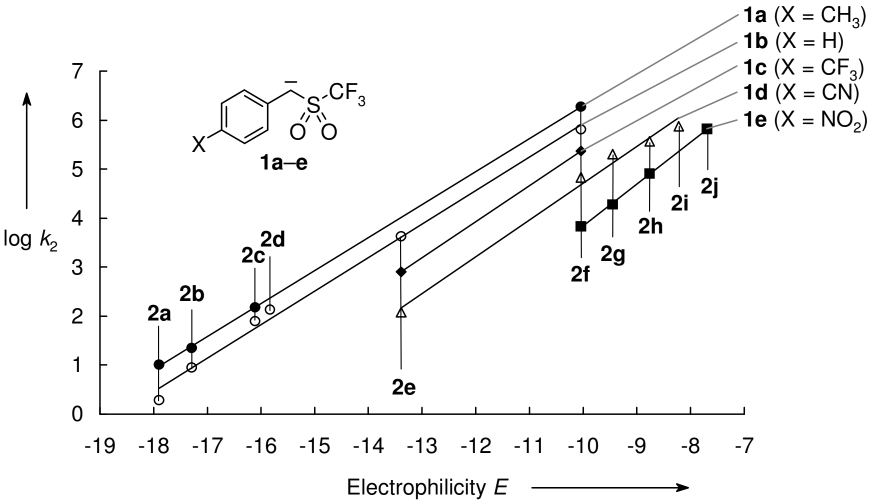


Figure 2.4. Plots of log k_2 for the reaction of the triflinate stabilized anions **1a**-**e** (from Table 2.3) with the quinone methides **2a**-**e** and benzhydryl cations **2f**-**j** in DMSO at 20 °C versus their electrophilicity parameters *E*.

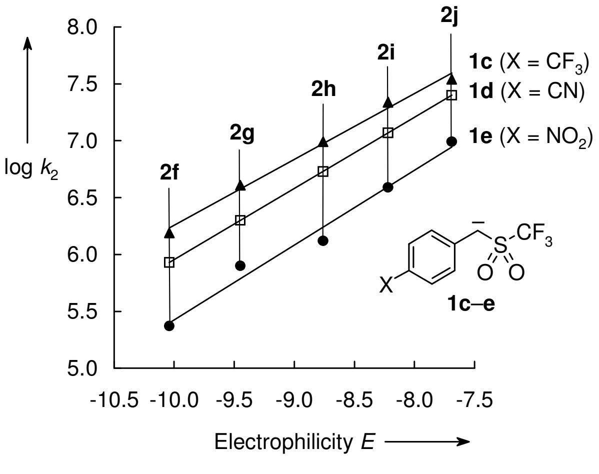


Figure 2.5. Plots of log $k_{2,C}$ for the reactions of the triflinate stabilized anions **1c**-**e** (from Table 2.6) with the benzhydryl cations **2f**-**j** in MeOH at 20 °C versus their electrophilicity parameters *E*.

Figures 2.4 and 2.5 as well as the nucleophilicity parameters *N* in Table 2.7 which were determined by eq. 2.1, show the expected substituent effects on the reactivities of the carbanions. Donors (methyl) increase the nucleophilicities of the triflinate ions **1**, whereas acceptors (trifluoromethyl, cyano, nitro) decrease their reactivity. The similarities of the slopes of the linear correlations in Figures 2.4 and 2.5, which are numerically expressed by the parameters *s* in Table 2.7, imply that the relative nucleophilicities of the triflinate stabilized benzyl anions depend only slightly on the electrophilicity of the reaction partner.

Comparison of the nucleophilicity parameters of α-nitro[28] and α-triflinate substituted benzyl anions (Figure 2.6) shows that both classes of carbanions possess similar nucleophilicities in DMSO, but that variation of the para-substituents has a much larger effect on the triflinate than on the nitro substituted benzyl anions.

Table 2.7. Nucleophilicity Parameters N and s and pK_{aH} Values of the Triflinate Stabilized Carbanions **1a**-**e** in DMSO and MeOH.

Nucleophile	in DMSO			in MeOH		
	pK_{aH}	N	s	pK_{aH}	N	s
1a (X = CH_3)	15.4[a]	19.35	0.67	-	-	-
1b (X = H)	14.62[b]	18.67	0.68	-	-	-
1c (X = CF_3)	11.95[b]	17.33	0.74	17.1	20.72	0.58
1d (X = CN)	10.7[a]	16.28	0.75	16.0	19.49	0.63
1e (X = NO_2)	9.46[b]	14.49	0.86	15.0	18.24	0.66

[a] From ref. 29. [b] From ref. 15b.

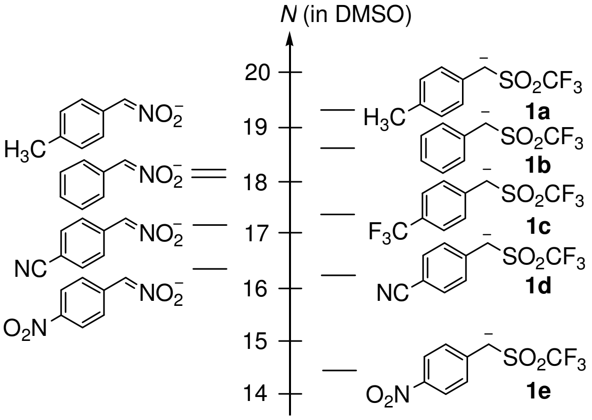


Figure 2.6. Comparison of the nucleophilicities *N* of triflinate stabilized carbanions (**1a–e**) and nitronate anions in DMSO.

This effect, which can be explained by the localization of the negative charge on carbon in the triflinate stabilized carbanions and the charge delocalization in the nitronate anions (with most of the negative charge residing on the oxygen atoms, Scheme 2.1), can also be seen in the different slopes of the Hammett-type correlations in Figure 2.7. In contrast to the good correlation between *N* of the triflinate anions **1a**-**e** with Hammett's σ_p^- the corresponding correlation with σ_p is of considerably lower quality (R^2 = 0.8919).

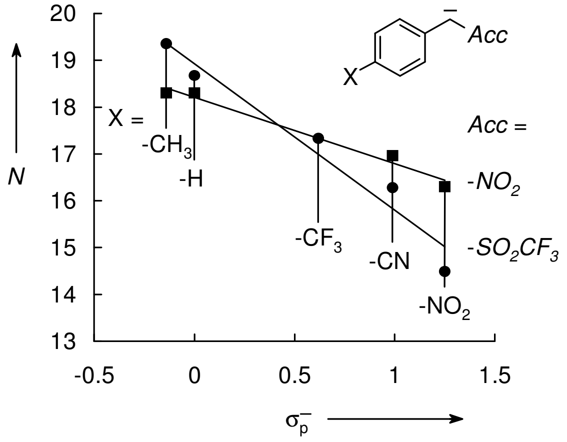


Figure 2.7. Correlations of the nucleophilicity parameters *N* (in DMSO) with the Hammett σ_p^- values for triflinates (circles; $N = -3.12\sigma_p^- + 18.9$, $R^2 = 0.9557$, $n = 5$) and nitronates (squares; $N = -1.42\sigma_p^- + 18.2$, $R^2 = 0.9792$, $n = 4$).

Unusual solvent effects, as previously reported for the basicities of carbanions **1a**-**e**,[15] have now been found for their nucleophilicities. Because the stabilization of most carbanions occurs to a large extent through hydrogen bonding, the basicities as well as the nucleophilicities of carbanions are usually smaller in protic than in aprotic solvents. In line with the observation that the acidities of benzyl triflones are higher in DMSO than in DMSO/water mixtures,[15] Figure 2.8 shows that also the nucleophilic reactivities of the benzyl triflinates **1c**–**e** are higher in methanol than in DMSO. The differences of s for the triflinate anions **1** in methanol and DMSO imply that the relative nucleophilic reactivities in the two solvents depend on the electrophile. The direct comparison of the rate constants in Tables 2.3 and 2.6 shows that the triflinate-stabilized carbanions studied in this work react 10 to 40 times faster (!) with benzhydrylium ions in methanol than in DMSO.

This unusual solvent dependence of the pK_{aH} values has been explained by the electronic structure of the triflinates **1**. Terrier has shown that the negative charge of the triflinates **1** is localized on the benzylic carbon atom and is highly polarizable.[15] For that reason, the carbanions **1** are better solvated in the highly polarizable and dielectric solvent DMSO (ε = 47)[30] than in methanol (ε = 33).[30] The higher acidities of fluorenes in DMSO than in methanol have analogously been rationalized by the high polarizabilities of the resulting carbanions.[31] Because the CC-coupling step of Scheme 2.3 must be preceded by the destruction of the ion-dipole interactions which prevail in DMSO, the kinetic phenomena observed in this work can also be explained by the fact that the highly polarizable triflinate stabilized carbanions **1a**–**e** are better solvated in DMSO.

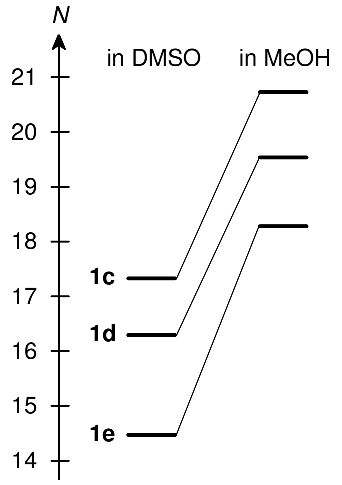


Figure 2.8. Comparison of the nucleophilicity parameters *N* of the benzyl triflinates **1c**-**e** in DMSO and MeOH.

The dominant role of ion-dipole forces for the solvation of the trifluoromethylsulfonyl substituted carbanions **1** is further confirmed by the observation that the reactivity of **1e** (X = NO_2) toward the carbocations **2f–j** (Table 2.8) is considerably higher in the less dipolar solvent acetonitrile ($\varepsilon = 38$)[30] than in DMSO (Figure 2.9).

Table 2.8. Second-Order Rate Constants k_2 for the Reactions of **1e** With the Electrophiles **2f–h** (CH_3CN, 20 °C).[a]

Electrophile	k_2 (M^{-1} s^{-1})
2f	9.41×10^{4} [b]
2g	3.79×10^{5}
2h	6.34×10^{5}
2j	5.04×10^{6}

[a] Carbanion **1e** was generated by mixing **1e**-H with 1.0 equiv. of Verkade's base (2,8,9-triisopropyl-2,5,8,9-tetraaza-1-phosphabicyclo[3.3.3]undecane). [b] A second-order rate constant of $k_2 = 8.28 \times 10^{4}$ M^{-1} s^{-1} was obtained when **1e** was generated from **1e**-H by deprotonation with potassium *tert*-butoxide.

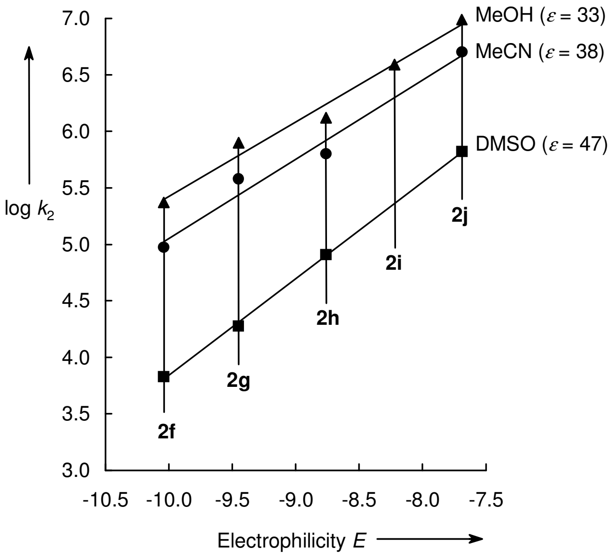


Figure 2.9. Comparison of the rate constants of the reactions of the carbocations **2f–j** with the carbanion **1e** in DMSO, acetonitrile, and methanol (cosolvent: 9 vol-% acetonitrile).

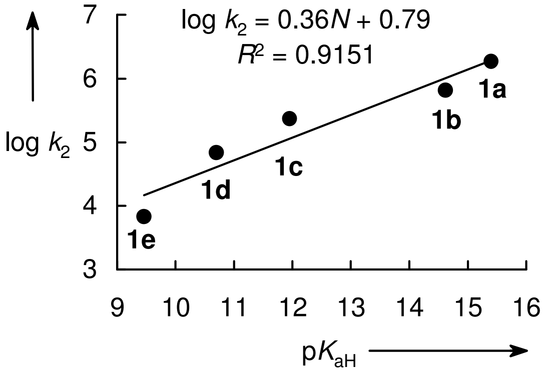


Figure 2.10. Plot of log k_2 for the reactions of the triflinate substituted carbanions **1a–e** with the benzhydrylium ion **2f** in DMSO at 20 °C versus their pK_{aH} values.

Figure 2.10 shows that the Brønsted plot for the reactions of the triflinate stabilized carbanions **1a**-**e** with the benzhydrylium ion **2f** has a slope of 0.36, comparable to that for substituted α-nitrobenzyl anions in DMSO.[28] Because only a small number of carbanions has been studied with respect to a single reference electrophile, more comprehensive nucleophilicity-basicity correlations shall be based on the nucleophilicity parameters *N*.

A correlation of low quality is obtained, when the nucleophilicities of carbanions of variable structure (*N* in DMSO) are plotted against their pK_{aH} values in DMSO (Figure 2.11). The most remarkable feature of this correlation is that the triflinate substituted carbanions **1** are at the lower edge of this "correlation corridor", i.e., that their nucleophilic reactivities are lower than those of most other carbanions of comparable pK_{aH} values, indicating low intrinsic reactivities.[9b,32,33] On the other hand, the resonance-stabilized nitronates are in the center or on the upper edge of this correlation band, indicating high intrinsic reactivities of the anions **4**-(R). These findings were in contrast to our expectation, because we had assumed that in analogy to the behavior of cyano substituted carbanions[34–37] the low reorganization energies of the localized triflinate anions **1**, which had been derived from their fast proton transfer reactions, and the high reorganization energies for the nitronate ions **4**-(R) which had been derived from their slow proton transfer reactions[38] (Table 2.9) should also be reflected in the reactions with carbon electrophiles.[39,40] Why are carbanions **1** and **4** on the "wrong" edges of the "correlation corridor"?

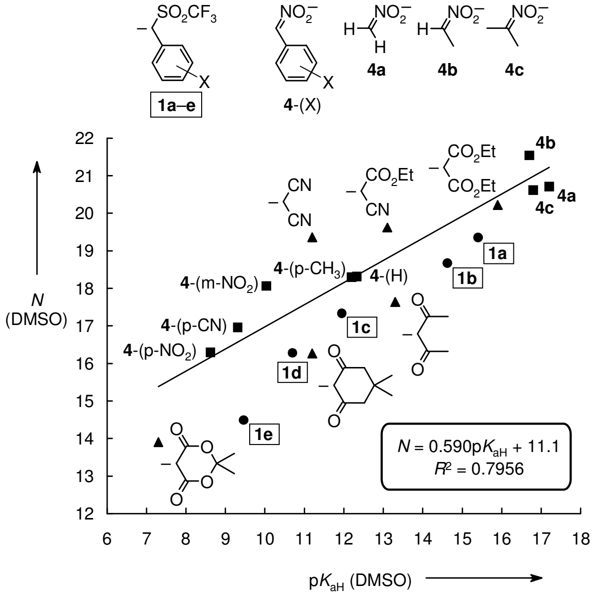


Figure 2.11. Brønsted plot for the reactions of different carbanions with benzhydrylium ions and quinone methides in DMSO (nucleophilicity parameters *N* and pK_{aH} values used for this diagram are compiled in the Experimental Section)

Table 2.9. Intrinsic Rate Constants log k_0 for Deprotonation of some Carbon Acids by primary and secondary Amines in DMSO/water (50:50, v/v) at 25 °C unless indicated otherwise.

Carbon acid	log k_0
$C_6H_5CH_2NO_2$	-0.25^b
CH_3NO_2	0.73^b
acetylacetone	2.75^b
1c-H (X = CF_3)	$\geq 5^a$
1d-H (X = CN)	$\geq 5^a$
1e-H (X = NO_2)	$\geq 5^a$
NC-CH_2-CN	$\sim 7^c$

[a] Reference 15b, [b] At 20 °C, from ref. 41, [c] In water at 20 °C, from ref. 41.

A solution of this paradox came from consideration of the N vs. pK_{aH} correlation in methanol (Figure 2.12). In methanol, the correlation between nucleophilicity[42] and basicity[27l,43] is even worse than in DMSO, but the triflinate substituted carbanions **1** are now found on the upper rim of the correlation corridor, while the nitronate ions are found on the lower edge. In methanol, the intrinsic reactivities of the localized triflinate substituted carbanions **1** are high and those of the delocalized nitronate anions are low as expected from earlier work, where the high reorganization energy of the resonance stabilized nitronate anions was accounted for the high intrinsic barriers of the reactions of nitronate anions.[9]

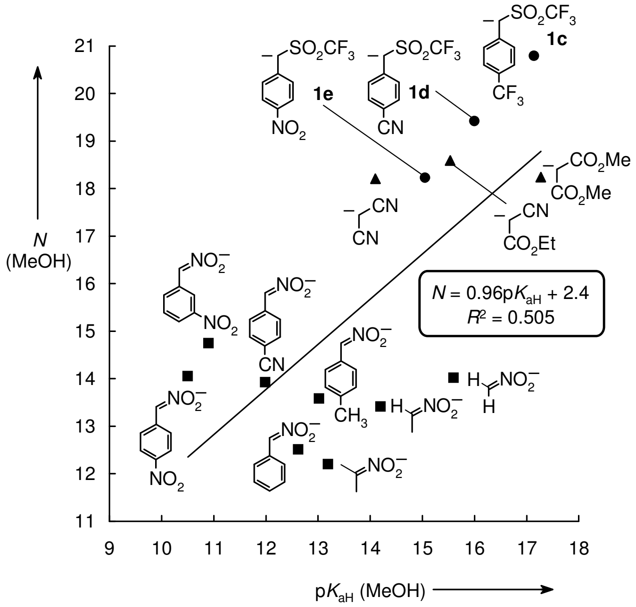


Figure 2.12. Nucleophilicity parameters N (in methanol) for different types of carbanions versus their acidity constants pK_{aH} in methanol (data compilation in the Experimental Section).

Our observation that nitronate anions do not have low intrinsic reactivities in DMSO (Figure 2.11) is in agreement with earlier conclusions that the nitroalkane anomaly[8] only shows up in protic solutions, and not in the gas phase[8g] or DMSO.[8n] While nitronate ions (resonance stabilized carbanions) show low intrinsic reactivities in protic solvents and high or normal intrinsic reactivities in DMSO, we have now found that the opposite holds for the highly polarizable carbanions **1**. Thus, nitro and triflinate substituted carbanions represent two different extremes: While transition state imbalances for reactions of nitronate anions are found in protic solvents, where hydrogen bridging has to be abandoned prior to rehybridization, analogous imbalances for reactions of triflinate substituted carbanions **1** are found in the highly polarizable, dipolar solvent DMSO, where ion-dipole interactions have to be removed prior to bond formation.

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(20) P2-*t*-Bu: 1-(*tert*-butylimino)-1,1,3,3,3-pentakis(dimethylamino)-1λ5, 3λ5-diphosphazene, pK_{BH+} = 21.4 (in DMSO), CAS Registry No. 111324-03-9.

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– Experimental Section –

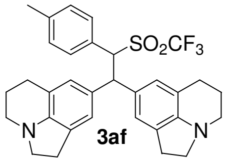
Inverse Solvent Effects in Carbocation Carbanion Combination Reactions: The Unique Behavior of Trifluoromethylsulfonyl Stabilized Carbanions

S. T. A. Berger, A. R. Ofial, H. Mayr, *J. Am. Chem. Soc.* **2007**, *129*, 9753-9761.

Table of Contents

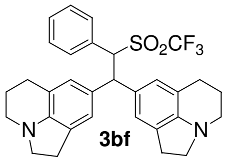
1. Products of the Reactions of Triflinates (1) with Benzhydrylium Ions (2)

Typical Procedure. At room temperature (ca. 20 °C) 1 equiv. of KO*t*Bu (22.7 mg, 0.202 mmol) was added to a solution of the CH acid **1a**-H[S1] (44.3 mg, 0.202 mmol) in DMSO (2 mL) to generate solutions of the corresponding potassium benzyltriflinate (**1**). The C-alkylated product **3af** was obtained by treatment of the benzyltriflinate solution with 1 equiv. of solid benzhydrylium tetrafluoroborate **2f** (82.7 mg, 0.202 mmol). At the end of the reaction (TLC control), addition of water precipitated **3af**, which was purified by recrystallization from MeOH and characterized by NMR spectroscopy.[S2]



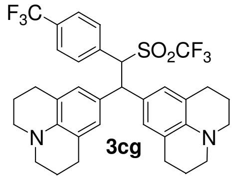
3af

3af: ^{1}H NMR ($CDCl_3$, 600 MHz): δ 1.89–1.93 (m, 2 H), 1.99–2.02 (m, 2 H), 2.20 (s, 3 H), 2.43–2.48 (m, 2 H), 2.59–2.70 (m, 4 H), 2.76–2.85 (m, 4 H), 2.87–2.91 (m, 2 H), 3.06–3.11 (m, 2 H), 3.21 (t, J = 6.9 Hz, 2 H), 4.74 (d, J = 10.2 Hz, 1 H), 5.15 (d, J = 10.2 Hz, 1 H), 6.49 (s, 1 H), 6.60 (s, 1 H), 6.84 (s, 1 H), 6.95–6.97 (m, 3 H), 7.13 (d, J = 7.5 Hz, 2 H); ^{13}C NMR ($CDCl_3$, 150 MHz): δ 21.1 (q), 22.7 (t), 22.8 (t), 23.5 (t), 23.6 (t), 28.4 (t), 28.6 (t), 47.40 (t), 47.42 (t), 51.3 (d), 55.1 (t), 55.2 (t), 72.8 (d), 121.7 (d), 121.9 (d), 125.9 (s), 126.3 (d), 126.5 (d), 129.0 (d), 130.7 (d), 131.0 (d), 139.2 (s).



3bf

3bf (obtained from 0.446 mmol **1b**-H): ^{1}H NMR ($CDCl_3$, 600 MHz): δ 1.87–1.91 (m, 2 H), 1.98–2.02 (m, 2 H), 2.37–2.47 (m, 2 H), 2.59–2.69 (m, 4 H), 2.73–2.80 (m, 2 H), 2.83 (t, J = 7.7 Hz, 2 H), 2.87–2.91 (m, 2 H), 3.02–3.09 (m, 2 H), 3.19 (t, J = 7.7 Hz, 2 H), 4.76 (d, J = 10.2 Hz, 1 H), 5.16 (d, J = 10.2 Hz, 1 H), 6.46 (s, 1 H), 6.59 (s, 1 H), 6.84 (s, 1 H), 6.95 (s, 1 H), 7.16–7.25 (m, 5 H); ^{13}C NMR ($CDCl_3$, 150 MHz): δ 22.9 (t), 23.0 (t), 23.6 (t), 23.8 (t), 28.5 (t), 28.7 (t), 47.36 (t), 47.42 (t), 51.5 (d), 55.1 (t), 55.2 (t), 73.1 (d), 121.7 (d), 122.0 (d), 126.3 (d), 126.6 (d), 128.9 (d), 129.2 (s), 129.3 (s), 129.3 (d), 131.0 (s).

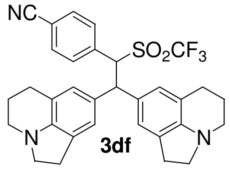


3cg

3cg (obtained from 0.348 mmol **1c**-H): ^{1}H NMR ($CDCl_3$, 400 MHz): δ 1.79–1.85 (m, 4 H), 1.89–1.95 (m, 4 H), 2.50–2.55 (m, 4 H), 2.71 (t, J = 6.5 Hz, 4 H), 2.98 (t, J = 5.7 Hz, 4 H), 3.07 (t, J = 5.7 Hz, 4 H), 4.68 (d, J = 9.3 Hz, 1 H), 5.22 (d, J = 9.3 Hz, 1 H), 6.41 (s, 2 H), 6.78 (s, 2 H), 7.44 (d, J = 8.2 Hz, 2 H), 7.51 (d, J = 8.15 Hz, 2 H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 21.9 (t), 22.0 (t), 27.5 (t), 27.7 (t), 49.8 (t), 49.9 (t), 50.5 (d), 72.2 (d), 121.3 (d), 121.4 (d), 124.97 (s), 125.01 (s), 126.5 (d), 127.0 (d), 131.5 (d), 131.7 (d), 141.6 (s), 142.1 (s).

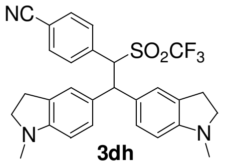
[S1] Triflones (**1a**-**e**)-H were synthesized by Hendrickson's procedure and purified by crystallization from pentane:J. B. Hendrickson, A. Giga, J. Wareing, *J. Am. Chem. Soc.* **1974**, *96*, 2275–2276.

[S2] Chemical shifts (in ppm) refer to Me_4Si (δ_H = 0.00 ppm) or $CDCl_3$ (δ_c = 77.00 ppm).

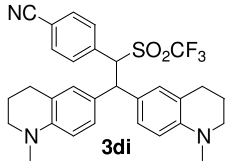

3df

3df: Mixing **1d**-H (72.2 mg, 0.289 mmol), KO*t*Bu (32.5 mg, 0.289 mmol), and **2f** (115 mg, 0.289 mmol) in CDCl$_3$ (700 μL) gave NMR spectra which showed the quantitative conversion to the product **3df**.

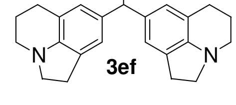
^{1}H NMR (CDCl$_3$, 600 MHz): δ 1.88–1.90 (m, 2 H), 1.97–2.00 (m, 2 H), 2.37–2.45 (m, 2 H), 2.57–2.61 (m, 2 H), 2.63–2.69 (m, 2 H), 2.73–2.83 (m, 4 H), 2.86–2.88 (m, 2 H), 3.02–3.09 (m, 2 H), 3.15–3.18 (m, 2 H), 4.71 (d, *J* = 10.1 Hz, 1 H), 5.21 (d, *J* = 10.1 Hz, 1 H), 6.41 (s, 1 H), 6.54 (s, 1 H), 6.79 (s, 1 H), 6.91 (s, 1 H), 7.38 (d, *J* = 7.9 Hz, 2 H), 7.47 (d, *J* = 8.6 Hz, 2 H); ^{13}C NMR (CDCl$_3$, 150 MHz): δ 22.8 (t), 23.0 (t), 23.7 (t), 23.9 (t), 28.5 (t), 28.7 (t), 47.0 (t), 47.1 (t), 51.7 (d), 54.9 (t), 55.0 (t), 72.4 (d), 113.0 (s), 118.0 (s), 119.0 (s), 119.1 (s), 121.4 (d), 121.7 (d), 126.0 (d), 126.4 (d), 131.87 (d), 131.93 (d), 132.8 (s), 135.2 (s), 148.8 (s), 149.5 (s).


3dh

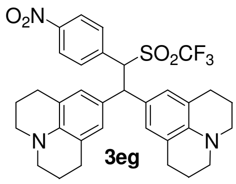
3dh (obtained from 0.231 mmol **1d**-H): ^{1}H NMR (CDCl$_3$, 600 MHz): δ 2.55 (s, 3 H), 2.65 (s, 3 H), 2.67–2.73 (m, 2 H), 2.85 (t, *J* = 8.2 Hz, 2 H), 3.12 (t, *J* = 8.3 Hz, 2 H), 3.22 (t, *J* = 8.1 Hz, 2 H), 4.77 (d, *J* = 10.1 Hz, 1 H), 5.19 (d, *J* = 10.2 Hz, 1 H), 6.09 (d, *J* = 8.6 Hz, 1 H), 6.33 (d, *J* = 8.1 Hz, 1 H), 6.68 (m, 2 H), 7.04–7.07 (m, 2 H), 7.39 (d, *J* = 7.9 Hz, 2 H), 7.47 (d, *J* = 7.9 Hz, 2 H).


3di

3di (obtained from 0.456 mmol **1d**-H): ^{1}H NMR (CDCl$_3$, 600 MHz): δ 1.75–1.78 (m, 2 H), 1.85–1.89 (m, 2 H), 2.46–2.49 (q, *J* = 6.5 Hz, 2 H), 2.64–2.69 (m, 5 H), 2.77 (s, 3 H), 3.03 (t, *J* = 5.6 Hz, 2 H), 3.11 (t, *J* = 5.7 Hz, 2 H), 4.70 (d, *J* = 9.8 Hz, 1 H), 5.18 (d, *J* = 9.8 Hz, 1H), 6.20 (d, *J* = 8.5 Hz, 1 H), 6.44 (d, *J* = 8.4 Hz, 1 H), 6.52 (s, 1 H), 6.66 (d, *J* = 6.4 Hz, 1 H), 6.89 (s, 1 H), 7.03 (d, *J* = 8.5 Hz, 1 H), 7.38 (d, *J* = 7.9 Hz, 2 H), 7.47 (d, *J* = 8.6 Hz, 2 H); ^{13}C NMR (CDCl$_3$, 150 MHz): δ 22.2 (t), 22.3 (t), 27.7 (t), 27.9 (t), 38.8 (q), 38.9 (q), 50.5 (d), 51.0 (t), 51.1 (t), 72.2 (d), 110.7 (d), 110.8 (d), 113.1 (s), 118.1 (s), 122.7 (s), 122.9 (s), 126.3 (d), 126.7 (d), 127.4 (s), 128.9 (d), 129.3 (d), 131.6 (d), 132.0 (s), 135.3 (s), 145.4 (s), 146.0 (s).

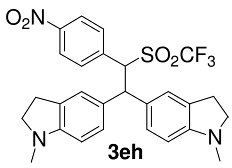

3ef

3ef (obtained from 0.250 mmol **1e**-H): ^{1}H NMR (CDCl$_3$, 600 MHz): δ 1.86–1.90 (m, 2 H), 1.96–2.01 (m, 2 H), 2.35–2.46 (m, 2 H), 2.56–2.69 (m, 4 H), 2.72–2.89 (m, 6 H), 3.02–3.08 (m, 2 H), 3.15–3.18 (m, 2 H), 4.74 (d, *J* = 10.1 Hz, 1 H), 5.27 (d, *J* = 10.1 Hz, 1 H), 6.43 (s, 1 H), 6.56 (s, 1 H), 6.80 (s, 1 H), 6.92 (s, 1 H), 7.44 (d, *J* = 8.2 Hz, 2 H), 8.03 (d, *J* = 8.9 Hz, 2 H); ^{13}C NMR (CDCl$_3$, 150 MHz): δ 22.9 (t), 23.1 (t), 23.7 (t), 23.9 (t), 28.5 (t), 28.7 (t), 47.0 (t), 47.1 (t), 51.8 (d), 54.9 (t), 55.1 (t), 72.2 (d), 119.1 (s), 121.4 (d), 121.7 (d), 123.3 (d), 126.0 (d), 126.4 (d), 129.0 (s), 129.4 (s), 131.9 (s), 132.3 (s), 137.2 (s), 148.1 (s), 148.9 (s), 149.6 (s).uäö



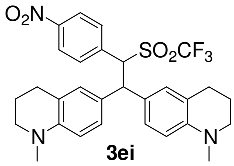
3eg

3eg (obtained from 0.074 mmol **1e**-H): ^{1}H NMR ($CDCl_3$, 600 MHz): δ 1.82 (m, 4 H), 1.94 (dt, *J* = 5.9 Hz, *J* = 11.8 Hz, 4 H), 2.53 (m, 4 H), 2.71 (t, *J* = 6.3 Hz, 4 H), 2.99 (t, *J* = 5.6 Hz, 4 H), 3.09 (m, 4 H), 4.68 (d, *J* = 9.6 Hz, 1H), 5.28 (d, *J* = 9.6 Hz, 1 H), 6.42 (s, 1 H), 6.61 (s, 2H), 6.77 (s, 1 H), 7.50 (d, *J* = 8.2 Hz, 2 H), 8.10 (d, *J* = 8.9 Hz, 2 H).



3eh

3eh (obtained 0.238 mmol **1e**-H): ^{1}H NMR ($CDCl_3$, 300 MHz): δ 2.54 (s, 3 H), 2.65 (s, 3 H), 2.69 (t, *J* = 7.2 Hz, 2 H), 2.86 (t, *J* = 8.1 Hz, 2 H), 3.11 (t, *J* = 8.1 Hz, 2 H), 3.22 (t, *J* = 8.0 Hz, 2 H), 4.81 (d, *J* = 10.2 Hz, 1 H), 5.27 (d, *J* = 10.2 Hz, 1 H), 6.09 (d, *J* = 8.6 Hz, 1 H), 6.33 (d, *J* = 7.9 Hz, 1 H), 6.69–6.71 (m d, *J* = 6.3 Hz, 2 H), 7.06–7.09 (m d, *J* = 8.4 Hz, 2 H), 7.46 (d, *J* = 8.7 Hz, 2 H), 8.03 (d, *J* = 8.9 Hz, 2 H); ^{13}C NMR ($CDCl_3$, 75.5 MHz): δ 28.2 (t), 28.7 (t), 35.4 (q), 35.9 (q), 51.4 (d), 55.8 (t), 56.0 (t), 72.1 (d), 106.6 (d), 106.7 (d), 112.6 (s), 123.5 (d), 123.9 (d), 124.2 (d), 127.1 (d), 127.4 (d), 128.3 (d) 129.1 (s), 130.8 (d), 130.9 (s), 131.8 (s), 137.1 (s), 148.1 (s), 152.3 (s), 152.9 (s).



3ei

3ei (obtained from 0.159 mmol **1e**-H): ^{1}H NMR ($CDCl_3$, 300 MHz): δ 1.75–1.80 (m, 2 H), 1.85–1.91 (m, 2 H), 2.48 (t, *J* = 6.2 Hz, 2 H), 2.64–2.67 (m, 5 H), 2.77 (s, 3 H), 3.00–3.04 (m, 2 H), 3.10–3.13 (m, 2 H), 4.73 (d, *J* = 9.9 Hz, 1 H), 5.25 (d, *J* = 9.9 Hz, 1 H), 6.20 (d, *J* = 8.5 Hz, 1 H), 6.45 (d, *J* = 8.5 Hz, 1 H), 6.54 (s, 1 H), 6.67 (dd, *J* = 8.8 Hz, *J* = 2.2 Hz, 1 H), 6.89 (d, *J* = 2.0 Hz, 1 H), 7.03 (dd, *J* = 2.3 Hz, *J* = 8.4 Hz, 1 H), 7.45 (d, *J* = 8.8 Hz, 2 H), 8.08 (d, *J* = 8.8 Hz, 2 H).

2. Reactivity of Triflinates (1) in DMSO

The temperature of the solutions during all kinetic studies was kept constant (20 ± 0.1°C) by using a circulating bath thermostat. DMSO with a content of H_2O < 50 ppm was used for the kinetic experiments.

The rates of slow reactions ($\tau_{1/2} > 10$ s) were determined by using a J&M TIDAS diode array spectrophotometer controlled by Labcontrol Spectacle software and connected to a Hellma 661.502-QX quartz Suprasil immersion probe (5 mm ligth path) via fiber optic cables and standard SMA connectors. For these experiments three different stock solutions were used: a) solution of the electrophile in DMSO, b) solution of the triflone **1**-H in DMSO and c) a solution of base. The stock solutions of KO*t*Bu in DMSO were prepared under an atmosphere of nitrogen. The stock solutions of the Schwesinger P2-^{t}Bu base[S3] were obtained by mixing the base with THF under an atmosphere of nitrogen.

For the evaluation of fast kinetics ($\tau_{1/2} < 10$ s) the stopped-flow spectrophotometer systems Hi-Tech SF-61DX2 or Applied Photophysics SX.18MV-R stopped-flow reaction analyser were used. Rate constants k_{obs} (s^{-1}) were obtained by fitting the single exponential $A_t = A_0\exp(-k_{\mathrm{obs}}t) + C$ to the observed time-dependent carbocation absorbance (averaged from at least 4 kinetic runs for each nucleophile concentration). For the stopped-flow experiments 2 stock solutions were used: A solution of the electrophile in DMSO and a solution of the carbanion, generated by the deprotonation of the CH acid with 1.05 equivalents of KO*t*Bu or Schwesinger P2-^{t}Bu[S3] base, respectively.

Table S1. Molar Absorption Coefficients of Triflinates **1c**–**e** in DMSO

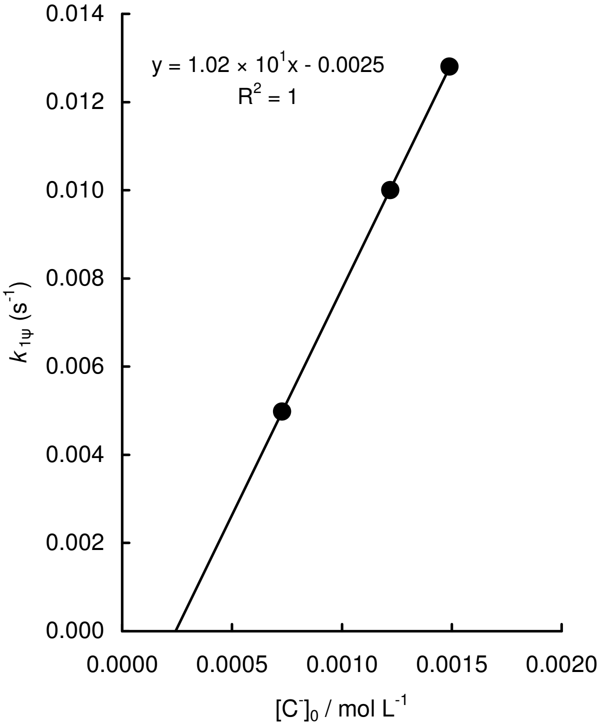
1-H	$[\mathrm{CH}]_0$ / M	$[\mathrm{MeO}^-]_0$ / M	$[\mathrm{MeO}^-]_0/[\mathrm{CH}]_0$	A	$\varepsilon_{\mathrm{DMSO}}$
1c-H	9.55×10^{-5}	1.00×10^{-4}	1.05	0.89 (305 nm)	
	9.55×10^{-5}	1.15×10^{-4}	1.20	0.89 (305 nm)	
	9.55×10^{-5}	1.24×10^{-4}	1.30	0.89 (305 nm)	9.32×10^{3}
1d-H	1.43×10^{-4}	1.50×10^{-4}	1.05	2.10 (346 nm)	
	1.43×10^{-4}	1.71×10^{-4}	1.20	2.10 (346 nm)	
	1.43×10^{-4}	1.86×10^{-4}	1.30	2.10 (346 nm)	1.47×10^{4}
1e-H	2.28×10^{-4}	2.38×10^{-4}	1.05	2.38 (476 nm)	
	2.28×10^{-4}	2.72×10^{-4}	1.20	2.38 (476 nm)	
	2.28×10^{-4}	2.95×10^{-4}	1.30	2.38 (476 nm)	1.04×10^{4}

[S3] Purchased from Fluka (2 M in THF): P2-^{t}Bu = 1-*tert*-Butyl-2,2,4,4,4-pentakis(dimethylamino)-$2\lambda^5,4\lambda^5$-catenadi(phosphazene) $[(\mathrm{Me_2N})_3\mathrm{P{=}N{-}P(NMe_2)_2N}t\mathrm{Bu}]$.

2.1 Kinetics of the Reactions of 4-Methylbenzyltriflinate (**1a**)

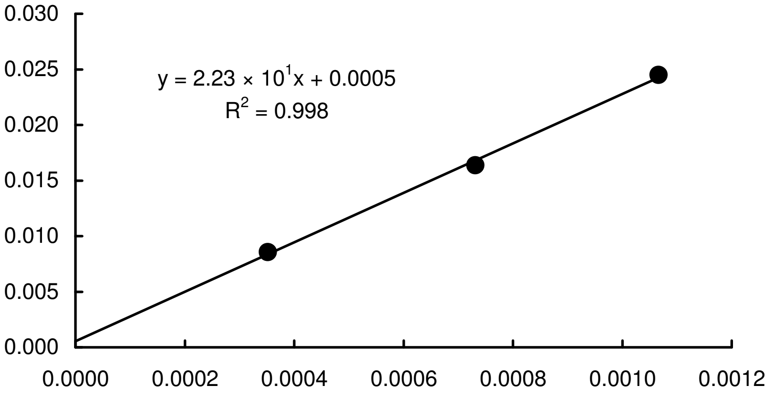
Reaction of **1a** (X = CH_3) with **2a** (J&M, λ = 500 nm, 20 °C, DMSO)

$[E]_0$ (mol L^{-1})	$[C^-]_0$ (mol L^{-1})	Base	$k_{1\psi}$ (s^{-1})
1.91×10^{-5}	7.28×10^{-4}	P_2	4.98×10^{-3}
1.91×10^{-5}	1.22×10^{-3}	P_2	1.00×10^{-2}
1.91×10^{-5}	1.49×10^{-3}	P_2	1.28×10^{-2}



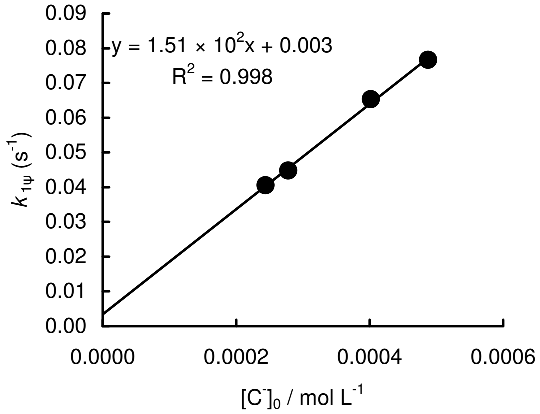
Reaction of **1a** (X = CH_3) with **2b** (J&M, λ = 500 nm, 20 °C, DMSO)

$[E]_0$ (mol L^{-1})	$[C^-]_0$ (mol L^{-1})	Base	$k_{1\psi}$ (s^{-1})
1.61×10^{-5}	3.51×10^{-4}	P_2	8.57×10^{-3}
1.61×10^{-5}	7.31×10^{-4}	P_2	1.64×10^{-2}
1.61×10^{-5}	1.07×10^{-3}	P_2	2.45×10^{-2}



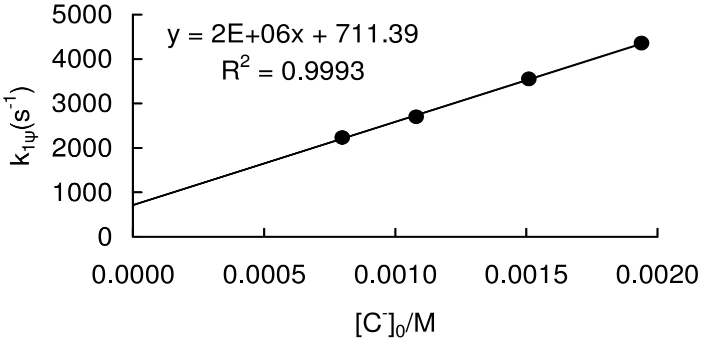
Reaction of **1a** (X = CH_3) with **2c** (J&M, λ = 400 nm, 20 °C, DMSO)

$[E]_0$ (mol L^{-1})	$[C^-]_0$ (mol L^{-1})	Base	$k_{1\psi}$ (s^{-1})
1.60×10^{-5}	2.44×10^{-4}	P_2	4.05×10^{-2}
1.60×10^{-5}	2.78×10^{-4}	P_2	4.49×10^{-2}
1.60×10^{-5}	4.02×10^{-4}	P_2	6.54×10^{-2}
1.60×10^{-5}	4.88×10^{-4}	P_2	7.60×10^{-2}



Reaction of **1a** (X = CH_3) with **2f** (stopped-flow, λ = 639 nm 20 °C, DMSO)

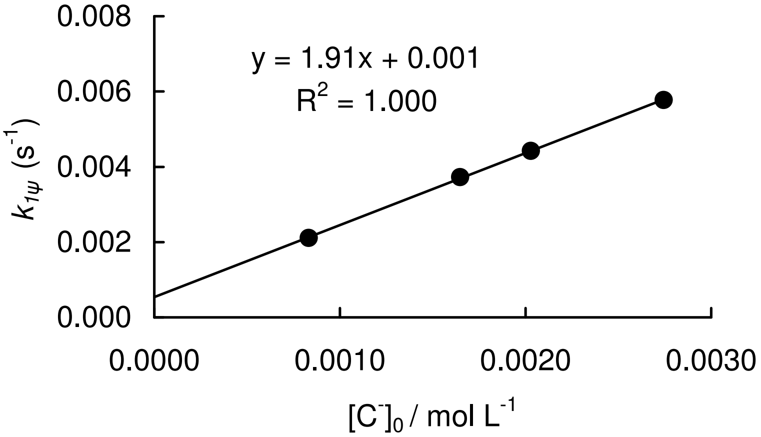
$[E]_0$ (mol L^{-1})	$[C^-]_0$ (mol L^{-1})	Base	$k_{1\psi}$ (s^{-1})
3.64×10^{-5}	7.98×10^{-4}	P_2	2.23×10^{3}
3.64×10^{-5}	1.08×10^{-3}	P_2	2.70×10^{3}
3.64×10^{-5}	1.51×10^{-3}	P_2	3.55×10^{3}
3.64×10^{-5}	1.94×10^{-3}	P_2	4.35×10^{3}



2.2 Kinetics of the Reactions of Benzyltriflinate (**1b**)

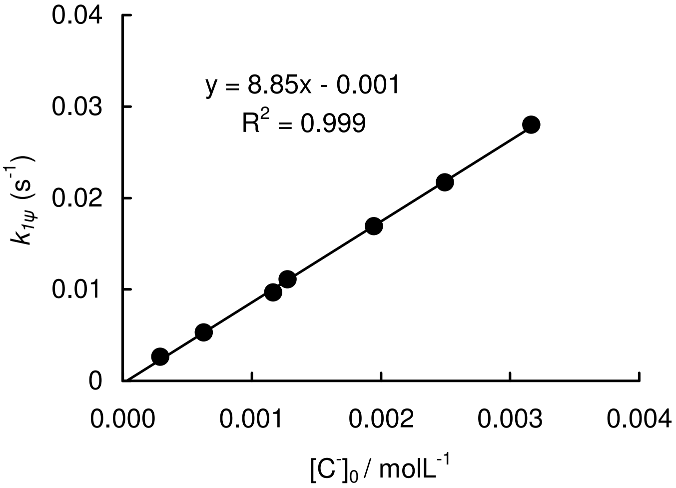
Reaction of **1b** (X = H)with **2a** (J&M, λ = 500 nm, 20 °C, DMSO)

$[E]_0$ (mol L^{-1})	$[C^-]_0$ (mol L^{-1})	Base	$k_{1\psi}$ (s^{-1})
2.75×10^{-5}	8.35×10^{-4}	P_2	2.11×10^{-3}
2.75×10^{-5}	1.65×10^{-3}	P_2	3.72×10^{-3}
2.75×10^{-5}	2.03×10^{-3}	P_2	4.42×10^{-3}
2.75×10^{-5}	2.75×10^{-3}	P_2	5.77×10^{-3}



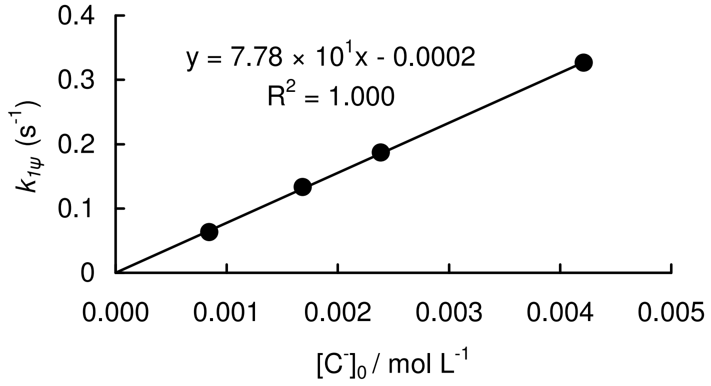
Reaction of **1b** (X = H) with **2b** (J&M, λ = 500 nm, 20 °C, DMSO)

$[E]_0$ (mol L^{-1})	$[C^-]_0$ (mol L^{-1})	Base	$k_{1\psi}$ (s^{-1})
3.16×10^{-5}	2.92×10^{-4}	KO*t*Bu	2.62×10^{-3}
3.16×10^{-5}	6.29×10^{-4}	P_2	5.30×10^{-3}
3.16×10^{-5}	1.16×10^{-3}	KO*t*Bu	9.56×10^{-3}
3.16×10^{-5}	1.28×10^{-3}	P_2	1.11×10^{-2}
3.16×10^{-5}	1.95×10^{-3}	P_2	1.69×10^{-2}
3.16×10^{-5}	2.50×10^{-3}	P_2	2.17×10^{-2}
3.16×10^{-5}	3.16×10^{-3}	P_2	2.80×10^{-2}



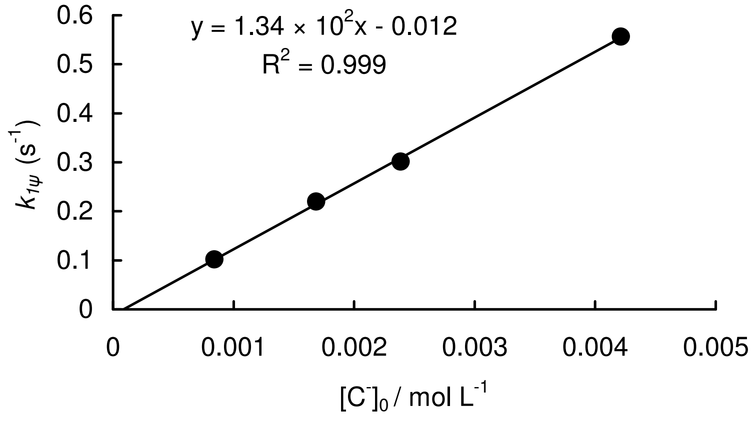
Reaction of **1b** (X = H) with **2c** (stopped-flow, λ = 390 nm, 20 °C, DMSO)

$[E]_0$ (mol L^{-1})	$[C^-]_0$ (mol L^{-1})	Base	$k_{1\psi}$ (s^{-1})
3.97×10^{-5}	8.43×10^{-4}	P_2	6.32×10^{-2}
3.97×10^{-5}	1.69×10^{-3}	P_2	1.33×10^{-1}
3.97×10^{-5}	2.39×10^{-3}	P_2	1.87×10^{-1}
3.97×10^{-5}	4.22×10^{-3}	KO*t*Bu	3.27×10^{-1}



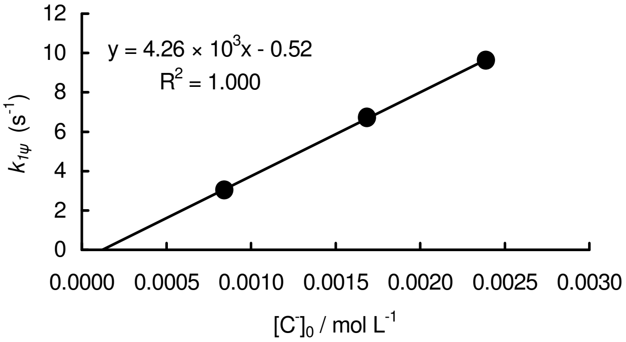
Reaction of **1b** (X = H) with **2d** (stopped-flow, λ = 400 nm, 20 °C, DMSO)

$[E]_0$ (mol L^{-1})	$[C^-]_0$ (mol L^{-1})	Base	$k_{1\psi}$ (s^{-1})
7.94×10^{-5}	8.43×10^{-4}	P_2	1.03×10^{-1}
7.94×10^{-5}	1.68×10^{-3}	P_2	2.20×10^{-1}
7.94×10^{-5}	2.39×10^{-3}	P_2	3.01×10^{-1}
7.94×10^{-5}	4.22×10^{-3}	P_2	5.57×10^{-1}



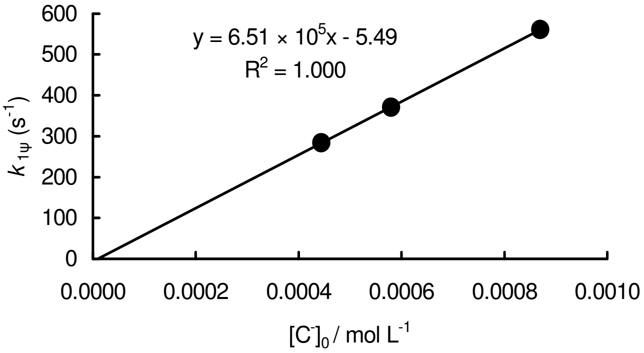
Reaction of **1b** (X = H) with **2e** (stopped-flow, λ = 470 nm, 20 °C, DMSO)

$[E]_0$ (mol L^{-1})	$[C^-]_0$ (mol L^{-1})	Base	$k_{1\psi}$ (s^{-1})
3.69×10^{-5}	8.43×10^{-4}	P_2	3.04
3.69×10^{-5}	1.69×10^{-3}	P_2	6.72
3.69×10^{-5}	2.39×10^{-3}	P_2	9.62



Reaction of **1b** (X = H) with **2f** (stopped-flow, λ = 639 nm, 20 °C, DMSO)

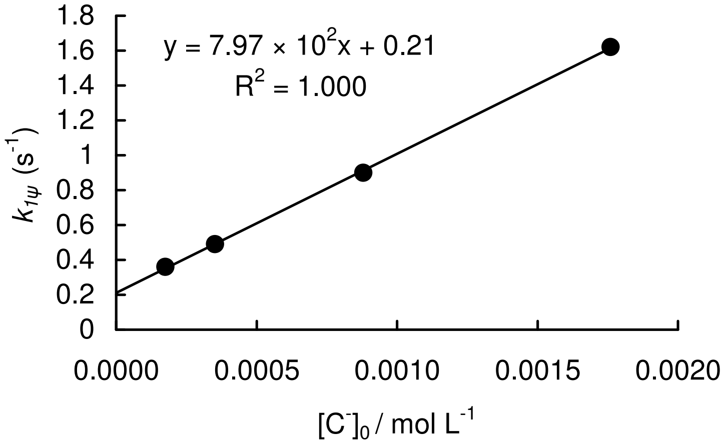
$[E]_0$ (mol L^{-1})	$[C^-]_0$ (mol L^{-1})	Base	$k_{1\psi}$ (s^{-1})
1.81×10^{-5}	4.44×10^{-4}	P_2	2.84×10^{2}
1.81×10^{-5}	5.80×10^{-4}	P_2	3.71×10^{2}
1.81×10^{-5}	8.71×10^{-4}	P_2	5.61×10^{2}



2.3 Kinetics of the Reactions of 4-Trifluoromethylbenzyltriflinate (**1c**)

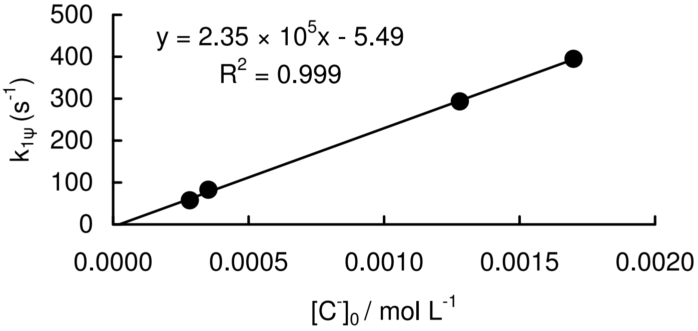
Reaction of **1c** (X = CF_3) with **2e** (stopped-flow, λ = 500 nm, 20 °C, DMSO)

$[E]_0$ (mol L^{-1})	$[C^-]_0$ (mol L^{-1})	Base	$k_{1\psi}$ (s^{-1})
1.70×10^{-5}	1.76×10^{-4}	KO*t*Bu	3.60×10^{-1}
1.70×10^{-5}	3.52×10^{-4}	KO*t*Bu	4.95×10^{-1}
1.70×10^{-5}	8.80×10^{-4}	KO*t*Bu	9.05×10^{-1}
1.70×10^{-5}	1.76×10^{-3}	KO*t*Bu	1.62



Reaction of **1c** (X = CF_3) with **2f** (stopped-flow, λ = 640 nm, 20 °C, DMSO)

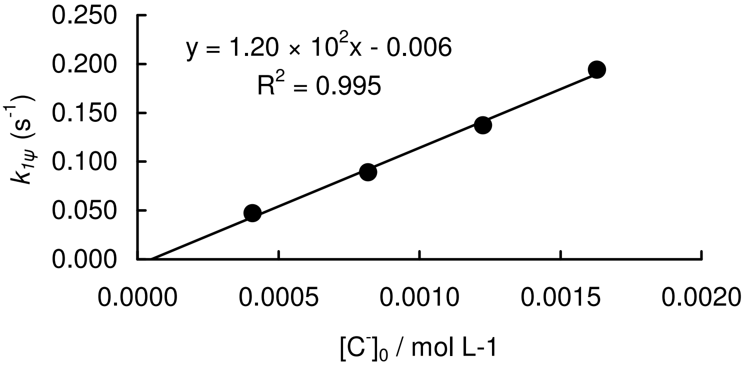
$[E]_0$ (mol L^{-1})	$[C^-]_0$ (mol L^{-1})	Base	$k_{1\psi}$ (s^{-1})
1.50×10^{-5}	2.84×10^{-4}	P_2	5.69×10^{1}
1.50×10^{-5}	3.52×10^{-4}	P_2	8.24×10^{1}
1.50×10^{-5}	1.28×10^{-3}	P_2	2.93×10^{2}
1.50×10^{-5}	1.70×10^{-3}	P_2	3.95×10^{2}



2.4 Kinetics of the Reactions of 4-Cyanobenzyltriflinate (**1d**)

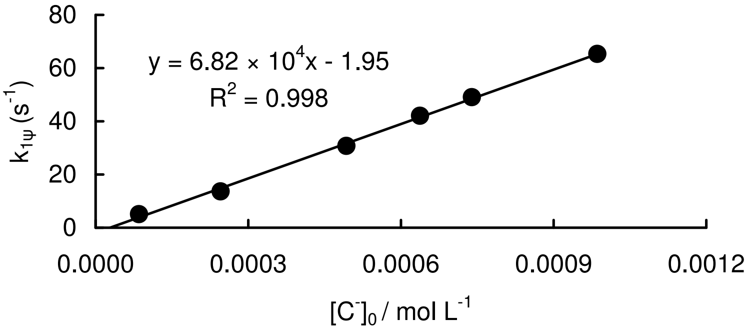
Reaction of **1d** (X = CN) with **2e** (stopped-flow, λ = 540 nm, 20 °C, DMSO)

$[E]_0$ (mol L^{-1})	$[C^-]_0$ (mol L^{-1})	Base	$k_{1\psi}$ (s^{-1})
1.56×10^{-5}	4.09×10^{-4}	P_2	4.74×10^{-2}
1.56×10^{-5}	8.18×10^{-4}	P_2	8.91×10^{-2}
1.56×10^{-5}	1.23×10^{-3}	P_2	1.37×10^{-1}
1.56×10^{-5}	1.63×10^{-3}	P_2	1.94×10^{-1}



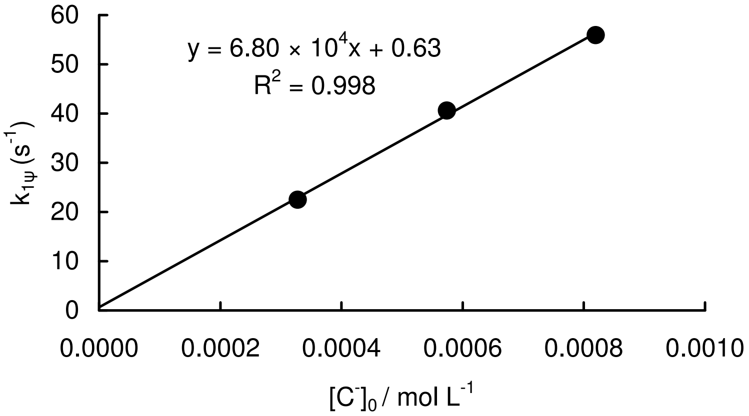
Reaction of **1d** (X = CN) with **2f** (stopped-flow, λ = 640 nm, 20 °C, DMSO)

$[E]_0$ (mol L^{-1})	$[C^-]_0$ (mol L^{-1})	Base	$k_{1\psi}$ (s^{-1})
1.71×10^{-5}	8.53×10^{-5}	KO*t*Bu	5.09
3.26×10^{-5}	2.46×10^{-4}	KO*t*Bu	1.36×10^{1}
3.26×10^{-5}	4.93×10^{-4}	KO*t*Bu	3.07×10^{1}
1.71×10^{-5}	6.38×10^{-4}	P_2	4.24×10^{1}
3.26×10^{-5}	7.40×10^{-4}	KO*t*Bu	4.90×10^{1}
3.26×10^{-5}	9.86×10^{-4}	KO*t*Bu	6.53×10^{1}



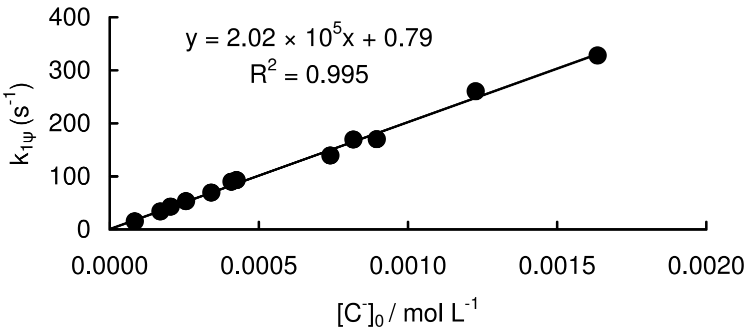
Reaction of the potassium salt of **1d** (X = CN) with **2f** (stopped-flow, λ = 650 nm, 20 °C, DMSO)

$[E]_0$ (mol L^{-1})	$[C^-]_0$ (mol L^{-1})	Base	$k_{1\psi}$ (s^{-1})
1.70×10^{-5}	3.28×10^{-4}	-	2.25×10^{1}
1.70×10^{-5}	5.74×10^{-4}	-	4.06×10^{1}
1.70×10^{-5}	8.20×10^{-4}	-	5.59×10^{1}



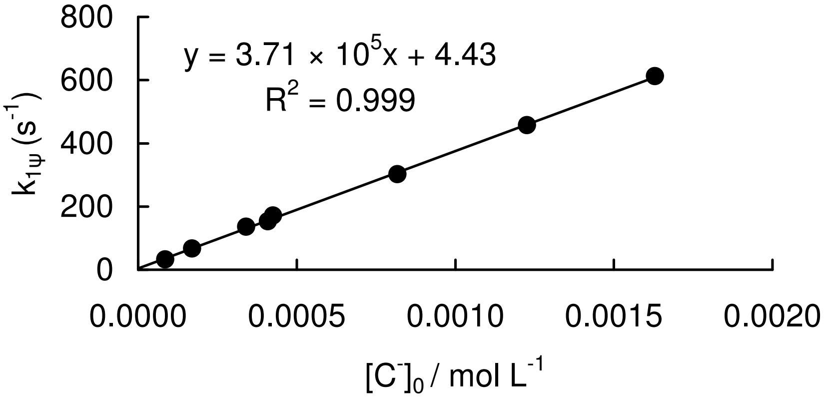
Reaction of **1d** (X = CN) with **2g** (stopped-flow, λ = 640 nm, 20 °C, DMSO)

$[E]_0$ (mol L^{-1})	$[C^-]_0$ (mol L^{-1})	Base	$k_{1\psi}$ (s^{-1})
1.58×10^{-5}	8.53×10^{-5}	KO*t*Bu	1.49×10^{1}
1.58×10^{-5}	1.71×10^{-4}	KO*t*Bu	3.37×10^{1}
3.03×10^{-5}	2.05×10^{-4}	KO*t*Bu	4.30×10^{1}
1.58×10^{-5}	2.56×10^{-4}	KO*t*Bu	5.31×10^{1}
1.58×10^{-5}	3.41×10^{-4}	KO*t*Bu	6.91×10^{1}
3.03×10^{-5}	4.09×10^{-4}	KO*t*Bu	8.95×10^{1}
3.26×10^{-5}	4.26×10^{-4}	KO*t*Bu	9.27×10^{1}
3.26×10^{-5}	7.40×10^{-4}	KO*t*Bu	1.39×10^{2}
3.03×10^{-5}	8.18×10^{-4}	KO*t*Bu	1.69×10^{2}
3.26×10^{-5}	8.96×10^{-4}	KO*t*Bu	1.70×10^{2}
3.03×10^{-5}	1.23×10^{-3}	KO*t*Bu	2.60×10^{2}
3.03×10^{-5}	1.64×10^{-3}	KO*t*Bu	3.28×10^{2}



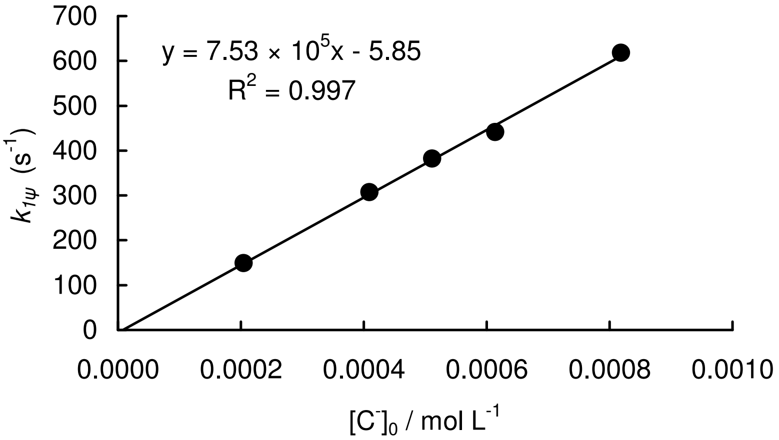
Reaction of **1d** (X = CN) with **2h** (stopped-flow, λ = 625/630 nm, 20 °C, DMSO)

$[E]_0$ (mol L^{-1})	$[C^-]_0$ (mol L^{-1})	Base	$k_{1\psi}$ (s^{-1})
1.05×10^{-5}	8.53×10^{-5}	KO*t*Bu	3.20×10^{1}
1.05×10^{-5}	1.71×10^{-4}	KO*t*Bu	6.70×10^{1}
1.05×10^{-5}	3.41×10^{-4}	KO*t*Bu	1.36×10^{2}
1.56×10^{-5}	4.09×10^{-4}	P_2	1.54×10^{2}
1.05×10^{-5}	4.26×10^{-4}	KO*t*Bu	1.71×10^{2}
1.56×10^{-5}	8.18×10^{-4}	P_2	3.02×10^{2}
1.56×10^{-5}	1.23×10^{-3}	P_2	4.57×10^{2}
1.56×10^{-5}	1.63×10^{-3}	P_2	6.12×10^{2}



Reaction of **1d** (X = CN) with **2i** (stopped-flow, λ = 640 nm, 20 °C, DMSO)

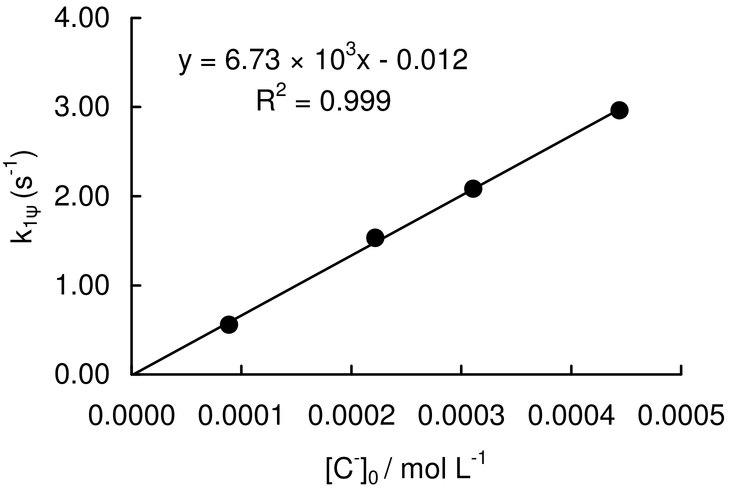
$[E]_0$ (mol L^{-1})	$[C^-]_0$ (mol L^{-1})	Base	$k_{1\psi}$ (s^{-1})
1.05×10^{-5}	2.05×10^{-4}	KO*t*Bu	1.49×10^{2}
1.05×10^{-5}	4.09×10^{-4}	KO*t*Bu	3.07×10^{2}
1.05×10^{-5}	5.12×10^{-4}	KO*t*Bu	3.82×10^{2}
1.56×10^{-5}	6.14×10^{-4}	KO*t*Bu	4.41×10^{2}
1.05×10^{-5}	8.19×10^{-4}	KO*t*Bu	6.18×10^{2}



2.5 Kinetics of the Reactions of 4-Nitrobenzyltriflinate (**1e**)

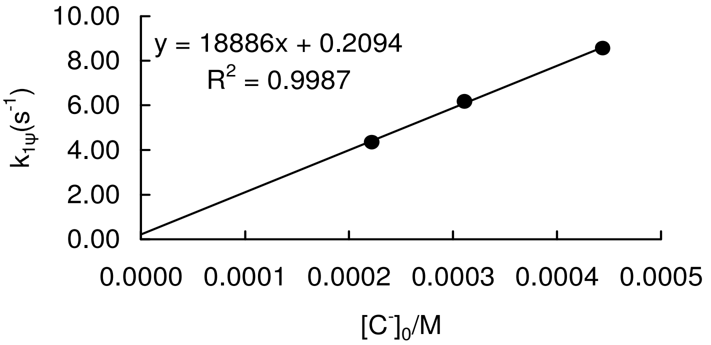
Reaction of **1e** (X = NO_2) with **2f** (stopped-flow, λ = 640 nm 20 °C, DMSO)

$[E]_0$ (mol L^{-1})	$[C^-]_0$ (mol L^{-1})	Base	$k_{1\psi}$ (s^{-1})
1.49×10^{-5}	8.88×10^{-5}	KO*t*Bu	5.58×10^{-1}
1.49×10^{-5}	2.22×10^{-4}	KO*t*Bu	1.53
1.49×10^{-5}	3.11×10^{-4}	KO*t*Bu	2.08
1.49×10^{-5}	4.44×10^{-4}	KO*t*Bu	2.96



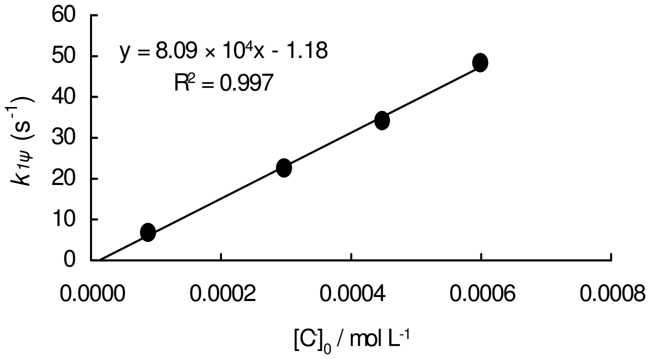
Reaction of **1e** (X = NO_2) with **2g** (stopped-flow, λ = 640 nm, 20 °C, DMSO)

$[E]_0$ (mol L^{-1})	$[C^-]_0$ (mol L^{-1})	Base	$k_{1\psi}$ (s^{-1})
2.56×10^{-5}	2.22×10^{-4}	KO*t*Bu	4.36
2.56×10^{-5}	3.11×10^{-4}	KO*t*Bu	6.17
2.56×10^{-5}	4.44×10^{-4}	KO*t*Bu	8.57



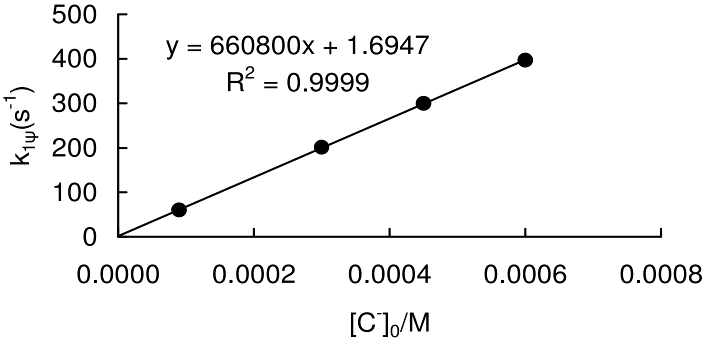
Reaction of **1e** (X = NO_2) with **2h** (stopped-flow, λ = 640 nm, 20 °C, DMSO)

$[E]_0$ (mol L^{-1})	$[C^-]_0$ (mol L^{-1})	Base	$k_{1\psi}$ (s^{-1})
3.21×10^{-5}	9.00×10^{-5}	P_2	6.78
3.21×10^{-5}	3.00×10^{-4}	P_2	2.24×10^{1}
3.21×10^{-5}	4.50×10^{-4}	P_2	3.43×10^{1}
3.21×10^{-5}	6.00×10^{-4}	P_2	4.83×10^{1}



Reaction of **1e** (X = NO_2) with **2j** (stopped-flow, λ = 640 nm, 20 °C, DMSO)

$[E]_0$ (mol L^{-1})	$[C^-]_0$ (mol L^{-1})	Base	$k_{1\psi}$ (s^{-1})
3.05×10^{-5}	9.00×10^{-5}	P_2	6.02×10^{1}
3.05×10^{-5}	3.00×10^{-4}	P_2	2.01×10^{2}
3.05×10^{-5}	4.50×10^{-4}	P_2	2.99×10^{2}
3.05×10^{-5}	6.00×10^{-4}	P_2	3.97×10^{2}

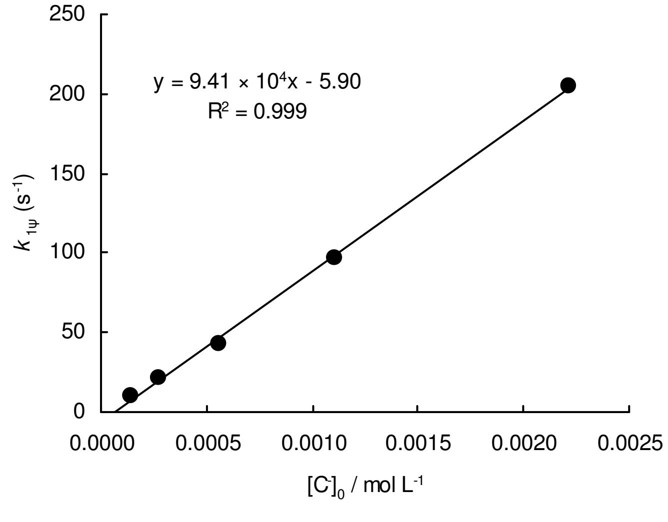


3. Reactivity of Triflinate 1e in CH_3CN

The kinetics were followed with an Applied Photophysics SX.18MV-R stopped-flow reaction analyser. The temperature of the solutions during all kinetic studies was kept constant (20 ± 0.1°C) by using a circulating bath thermostat. Rate constants k_{obs} (s^{-1}) were obtained by fitting the single exponential $A_t = A_0\exp(-k_{obs}t) + C$ to the observed time-dependent carbocation absorbance (averaged from at least 4 kinetic runs for each nucleophile concentration). For the stopped-flow experiments two stock solutions were used: A solution of the electrophile in acetonitrile and a solution of the carbanion, generated by the deprotonation of the corresponding triflone (**1**-H) with 1.00 equivalents of Verkade's base.[S4]

Reaction of **1e** (X = NO_2) with **2f** (λ = 630 nm, 20 °C, CH_3CN)

$[E]_0$ (mol L^{-1})	$[C^-]_0$ (mol L^{-1})	$k_{1\psi}$ (s^{-1})
1.85×10^{-5}	1.39×10^{-4}	1.05×10^{1}
1.85×10^{-5}	2.77×10^{-4}	2.10×10^{1}
1.85×10^{-5}	5.55×10^{-4}	4.26×10^{1}
1.85×10^{-5}	1.11×10^{-3}	9.63×10^{1}
1.85×10^{-5}	2.22×10^{-3}	2.05×10^{2}

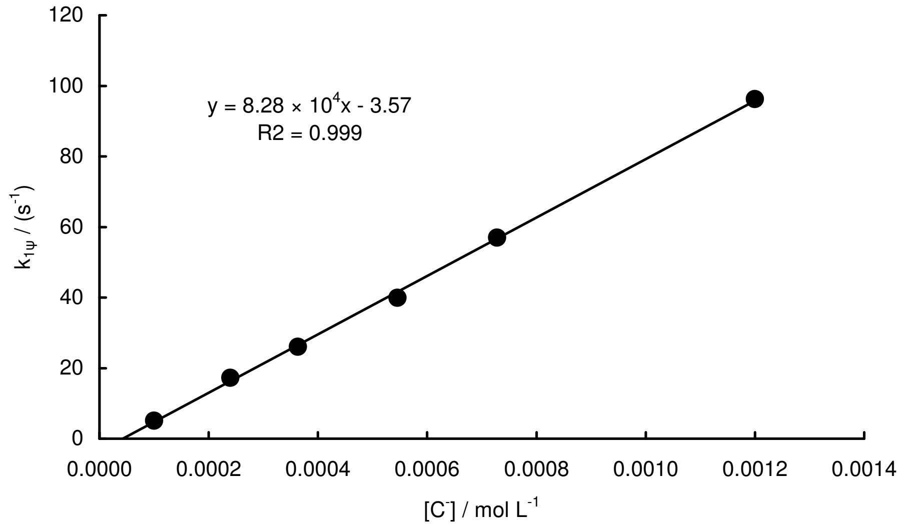


[S4] Verkade's base: 2,8,9-Triisopropyl-2,5,8,9-tetraaza-1-phosphabicyclo[3.3.3]undecane (Fluka).

Reaction of **1e** (X = NO_2) with **2f** (λ = 630 nm, 20 °C, CH_3CN)

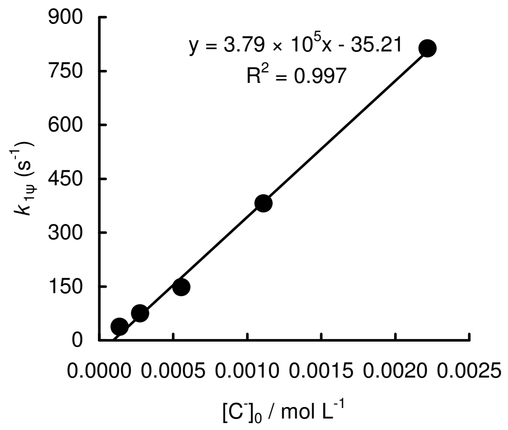
The triflinate **1e** was generated by adding 1.05 equivalents of KO*t*Bu to a solution of the triflone **1e**-H in acetonitrile.

$[E]_0$ (mol L^{-1})	$[C^-]_0$ (mol L^{-1})	$k_{1\Psi}$ (s^{-1})
2.57×10^{-5}	1.00×10^{-4}	5.08
2.57×10^{-5}	2.40×10^{-4}	1.73×10^{1}
3.43×10^{-5}	3.64×10^{-4}	2.61×10^{1}
3.43×10^{-5}	5.64×10^{-4}	3.99×10^{1}
3.43×10^{-5}	7.28×10^{-4}	5.70×10^{1}
2.57×10^{-5}	1.20×10^{-3}	9.63×10^{1}



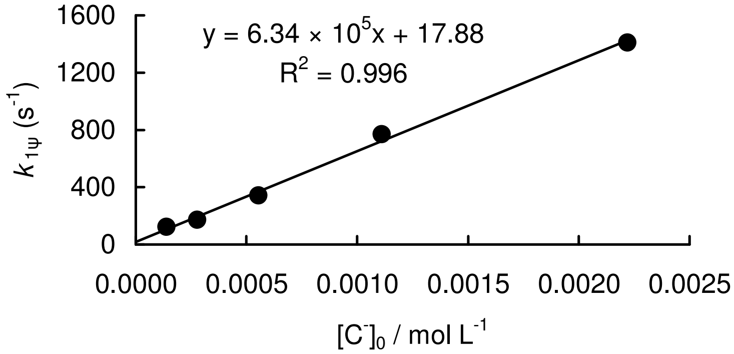
Reaction of **1e** (X = NO_2) with **2g** (λ = 630 nm, 20 °C, CH_3CN)

$[E]_0$ (mol L^{-1})	$[C^-]_0$ (mol L^{-1})	$k_{1\psi}$ (s^{-1})
1.42×10^{-5}	1.39×10^{-4}	3.73×10^{1}
1.42×10^{-5}	2.77×10^{-4}	7.44×10^{1}
1.42×10^{-5}	5.55×10^{-4}	1.47×10^{2}
1.42×10^{-5}	1.11×10^{-3}	3.81×10^{2}
1.42×10^{-5}	2.22×10^{-3}	8.13×10^{2}



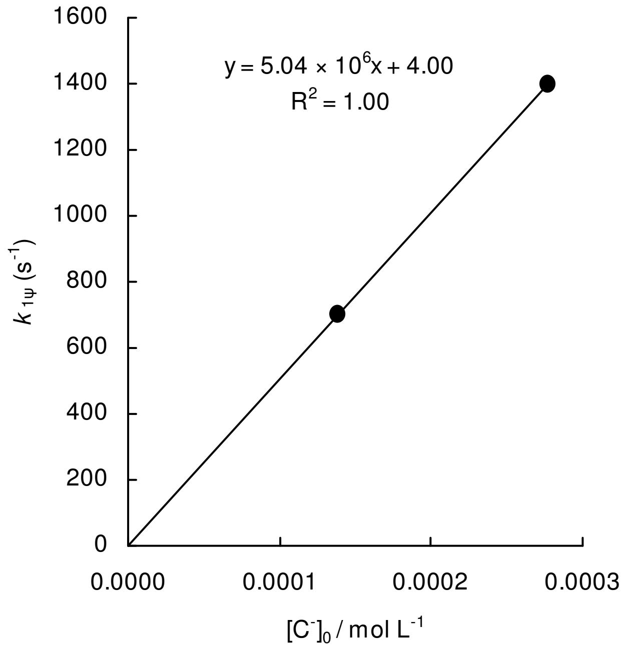
Reaction of **1e** (X = NO_2) with **2h** (λ = 630 nm, 20 °C, CH_3CN)

$[E]_0$ (mol L^{-1})	$[C^-]_0$ (mol L^{-1})	$k_{1\psi}$ (s^{-1})
1.48×10^{-5}	1.39×10^{-4}	1.23×10^{2}
1.48×10^{-5}	2.77×10^{-4}	1.71×10^{2}
1.48×10^{-5}	5.55×10^{-4}	3.42×10^{2}
1.48×10^{-5}	1.11×10^{-3}	7.70×10^{2}
1.48×10^{-5}	2.22×10^{-3}	1.41×10^{3}



Reaction of **1e** (X = NO_2) with **2j** (λ = 630 nm, 20 °C, CH_3CN)

$[E]_0$ (mol L^{-1})	$[C^-]_0$ (mol L^{-1})	$k_{1\psi}$ (s^{-1})
2.96×10^{-5}	1.39×10^{-4}	7.02×10^{2}
2.96×10^{-5}	2.77×10^{-4}	1.40×10^{3}



4. Acidities of Triflones (1c-e)-H in Methanol

The equilibrium concentrations of the carbanions, of the CH acidic compounds and of the methoxide-ions were calculated on the basis of the K_{CH} values of the CH acidic compounds (**1c**-**e**)-H, which were determined photometrically at 20 °C by using the UV-vis absorption of the corresponding carbanion.

$$\mathrm{CH} + \mathrm{MeO^-} \xrightleftharpoons{K_{CH}} \mathrm{C^-} + \mathrm{MeOH}$$

$$K_{CH} = [C^-]_{eq}/([CH]_{eq}[MeO^-]_{eq})$$

When the initial concentrations of the CH acids and methoxide are $[CH]_o$ and $[MeO^-]_o$, their equilibrium concentrations are:

$$[CH]_{eq} = [CH]_0 - [C^-]_{eq} \text{ and } [MeO^-]_{eq} = [MeO^-]_0 - [C^-]_{eq}$$

Due to the fact that in no case a complete deprotonation of the triflone (**1c**-**e**)-H was achieved, the K_{CH} values which are listed in Table 4 have been determined on the basis of the experimental absorbances and known starting concentrations by a least-squares fit of calculated and experimental absorptions minimizing $\Delta^2 = \Sigma(A_{cal} - A_{exp})^2$ (software: *What´s Best!* by Lindo Systems Inc.). The calculated absorptions have been determined by the relation in Equation (S1). Thus the pK_a values were calculated on the basis of the K_{CH} values according to Equation (S2) and (S3).

$$A_{cal} = ([C^-]_{eq}/[CH]_0)\, A_{endcal} \tag{S1}$$

$$[C^-]_{eq} = 0.5([CH]_0 + [MeO^-]_0 + 1/K_{CH} - (([CH]_0 + [MeO^-]_0 + 1/K_{CH})^2 - 4[CH]_0[MeO^-]_0)^{1/2})$$

$$pK_{MeOH} = -\log\{[MeO^-]_{eq}[H^+]_{eq}\} = 16.92 \text{ (at 20°C)}^{a} \tag{S2}$$

$$pK_a = -\log K_{CH} + \log K_{MeOH} \tag{S3}$$

The extinction coefficients in methanol are calculated by: $\varepsilon_{MeOH} = A_{cal}/[C^-]_{eq}$

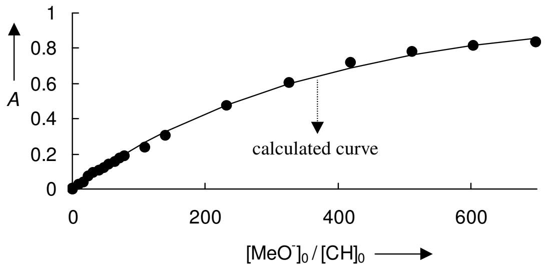
Comparison of the extinction coefficients in methanol and in DMSO shows that the ratio $\varepsilon_{MeOH}/\varepsilon_{DMSO}$ for the carbanions **1c**, **1d** and **1e** is in the range from 1.02 to 1.10.

Acidity of 4-X-benzyl trifluoromethyl sulfone **1c**-H (X = CF_3) in methanol

$[CH]_0$ (M)	$[MeO^-]_0$ (M)	$[MeO^-]_0/[CH]_0$	A_{exp}(305 nm)	A_{cal}	$[C^-]_{eq}$ (M)	$[CH]_{eq}$ (M)	$[MeO^-]_{eq}$ (M)
7.03×10^{-4}	0.00	0.00	0.00	0.00	0.00	0.00	7.03×10^{-4}
7.03×10^{-4}	5.44×10^{-4}	8.00×10^{-1}	6.00×10^{-3}	2.20×10^{-3}	2.30×10^{-7}	5.44×10^{-4}	7.03×10^{-4}
7.00×10^{-4}	5.98×10^{-3}	8.50×10^{0}	3.00×10^{-2}	2.40×10^{-2}	2.51×10^{-6}	5.97×10^{-3}	6.97×10^{-4}
6.97×10^{-4}	1.14×10^{-2}	1.64×10^{1}	3.90×10^{-2}	4.54×10^{-2}	4.75×10^{-6}	1.14×10^{-2}	6.92×10^{-4}
6.94×10^{-4}	1.66×10^{-2}	2.40×10^{1}	7.80×10^{-2}	6.58×10^{-2}	6.88×10^{-6}	1.66×10^{-2}	6.87×10^{-4}
6.91×10^{-4}	2.19×10^{-2}	3.17×10^{1}	9.40×10^{-2}	8.60×10^{-2}	9.00×10^{-6}	2.19×10^{-2}	6.82×10^{-4}
6.88×10^{-4}	2.72×10^{-2}	3.95×10^{1}	1.09×10^{-1}	1.06×10^{-1}	1.11×10^{-5}	2.71×10^{-2}	6.77×10^{-4}
6.86×10^{-4}	3.24×10^{-2}	4.72×10^{1}	1.25×10^{-1}	1.25×10^{-1}	1.31×10^{-5}	3.23×10^{-2}	6.73×10^{-4}
6.85×10^{-4}	3.75×10^{-2}	5.47×10^{1}	1.45×10^{-1}	1.44×10^{-1}	1.51×10^{-5}	3.75×10^{-2}	6.70×10^{-4}
6.80×10^{-4}	4.26×10^{-2}	6.26×10^{1}	1.57×10^{-1}	1.62×10^{-1}	1.70×10^{-5}	4.26×10^{-2}	6.63×10^{-4}
6.77×10^{-4}	4.77×10^{-2}	7.04×10^{1}	1.75×10^{-1}	1.80×10^{-1}	1.89×10^{-5}	4.77×10^{-2}	6.58×10^{-4}
6.74×10^{-4}	5.27×10^{-2}	7.82×10^{1}	1.91×10^{-1}	1.98×10^{-1}	2.07×10^{-5}	5.27×10^{-2}	6.53×10^{-4}
6.64×10^{-4}	7.24×10^{-2}	1.09×10^{2}	2.39×10^{-1}	2.65×10^{-1}	2.77×10^{-5}	7.24×10^{-2}	6.36×10^{-4}
6.53×10^{-4}	1.15×10^{-2}	1.40×10^{2}	3.07×10^{-1}	3.26×10^{-1}	3.41×10^{-5}	9.15×10^{-2}	6.19×10^{-4}
6.24×10^{-4}	1.45×10^{-1}	2.33×10^{2}	4.76×10^{-1}	4.79×10^{-1}	5.02×10^{-5}	1.45×10^{-1}	5.74×10^{-4}
5.97×10^{-4}	1.94×10^{-1}	3.26×10^{2}	6.04×10^{-1}	5.98×10^{-1}	6.26×10^{-5}	1.94×10^{-1}	5.34×10^{-4}
5.72×10^{-4}	2.24×10^{-1}	4.19×10^{2}	7.22×10^{-1}	6.89×10^{-1}	7.21×10^{-5}	2.40×10^{-1}	5.00×10^{-4}
5.50×10^{-4}	2.81×10^{-1}	5.11×10^{2}	7.85×10^{-1}	7.60×10^{-1}	7.96×10^{-5}	2.81×10^{-1}	4.70×10^{-4}
5.29×10^{-4}	3.19×10^{-1}	6.04×10^{2}	8.16×10^{-1}	8.15×10^{-1}	8.53×10^{-5}	3.19×10^{-1}	4.44×10^{-4}
5.09×10^{-4}	3.55×10^{-1}	6.98×10^{2}	8.39×10^{-1}	8.56×10^{-1}	8.96×10^{-5}	3.55×10^{-1}	4.19×10^{-4}
5.09×10^{-4}	3.55×10^{-1}	6.98×10^{2}	8.39×10^{-1}	8.57×10^{-1}	8.97×10^{-5}	3.55×10^{-1}	4.19×10^{-4}

Least squares optimization: $A_{endcal} = 5.25$, $K_{CH} = 6.00 \times 10^{-1}\ M^{-1}$,

$pK_a = 17.14$, $\varepsilon_{MeOH} = 9551$, $\varepsilon_{DMSO} = 9319$

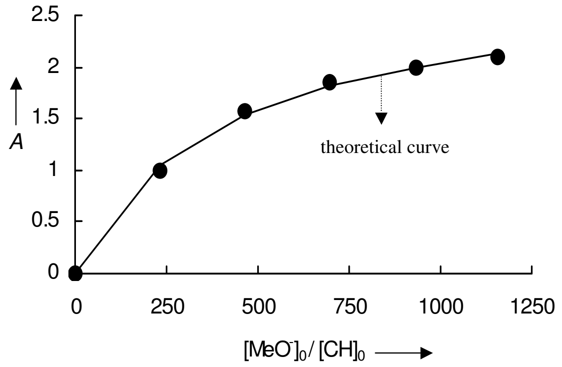


Acidity of 4-X-benzyl trifluoromethyl sulfone **1d**-H (X = CN) in methanol

$[\mathrm{CH}]_0$ (M)	$[\mathrm{MeO}^-]_0$ (M)	$[\mathrm{MeO}^-]_0/[\mathrm{CH}]_0$	A_{exp}(345 nm)	A_{cal}	$[\mathrm{C}^-]_{\mathrm{eq}}$ (M)	$[\mathrm{CH}]_{\mathrm{eq}}$ (M)	$[\mathrm{MeO}^-]_{\mathrm{eq}}$ (M)
2.22×10^{-4}	0.00	0.00	0.00	0.00	0.00	2.22× 10-4	0.00
2.17×10^{-4}	5.06×10^{-2}	2.33×10^{2}	0.999	1.05	6.48×10^{-5}	1.52×10^{-4}	5.05×10^{-2}
2.12×10^{-4}	9.89×10^{-2}	4.66×10^{2}	1.57	1.57	9.65×10^{-5}	1.16×10^{-4}	9.88×10^{-2}
2.08×10^{-4}	1.45×10^{-1}	6.98×10^{2}	1.85	1.86	1.14×10^{-4}	9.36×10^{-5}	1.45×10^{-2}
2.04×10^{-4}	1.89×10^{-1}	9.31×10^{2}	1.99	2.03	1.25×10^{-4}	7.84×10^{-5}	1.89×10^{-1}
1.99×10^{-4}	2.31×10^{-1}	1.16×10^{3}	2.09	2.14	1.31×10^{-4}	6.78×10^{-5}	2.30×10^{-1}

Least squares optimization: $A_{\mathrm{endcal}} = 3.21$, $K_{\mathrm{CH}} = 8.24\ \mathrm{M}^{-1}$,

$\mathrm{p}K_{\mathrm{a}} = 16.00$, $\varepsilon_{\mathrm{MeOH}} = 16240$, $\varepsilon_{\mathrm{DMSO}} = 14685$

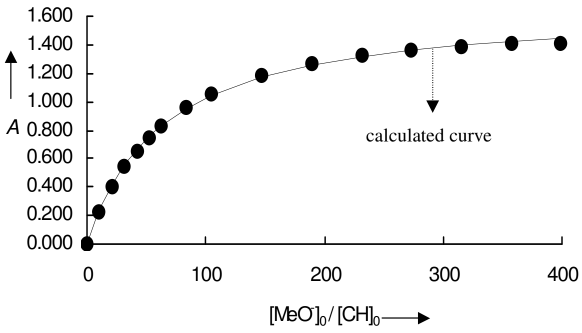


Acidity of 4-X-benzyltrifluoromethyl sulfone **1e**-H (X = NO_2) in methanol

$[CH]_0$ (M)	$[MeO^-]_0$ (M)	$[MeO^-]_0/[CH]_0$	A_{exp}(476 nm)	A_{cal}	$[C^-]_{eq}$ (M)	$[CH]_{eq}$ (M)	$[MeO^-]_{eq}$ (M)
1.74×10^{-4}	0.00	0.00	0.00	0.00	0.00	1.74×10^{-4}	0.00
1.74×10^{-4}	1.83×10^{-3}	1.05×10^{1}	0.23	0.23	2.10×10^{-5}	1.52×10^{-4}	1.81×10^{-3}
1.74×10^{-4}	3.65×10^{-3}	2.10×10^{1}	0.40	0.40	3.74×10^{-5}	1.36×10^{-4}	3.61×10^{-3}
1.73×10^{-4}	5.46×10^{-3}	3.15×10^{1}	0.54	0.54	5.05×10^{-5}	1.23×10^{-4}	5.41×10^{-3}
1.73×10^{-4}	7.26×10^{-3}	4.20×10^{1}	0.66	0.66	6.11×10^{-5}	1.12×10^{-4}	7.20×10^{-3}
1.72×10^{-4}	9.06×10^{-3}	5.25×10^{1}	0.75	0.75	7.00×10^{-5}	1.02×10^{-4}	8.99×10^{-3}
1.72×10^{-4}	1.08×10^{-2}	6.28×10^{1}	0.83	0.83	7.73×10^{-5}	9.47×10^{-5}	1.07×10^{-2}
1.71×10^{-4}	1.43×10^{-2}	8.35×10^{1}	0.96	0.96	8.89×10^{-5}	8.23×10^{-5}	1.42×10^{-2}
1.70×10^{-4}	1.79×10^{-2}	1.05×10^{2}	1.05	1.05	9.80×10^{-5}	7.24×10^{-5}	1.78×10^{-2}
1.69×10^{-4}	2.48×10^{-2}	1.47×10^{2}	1.18	1.18	1.10×10^{-4}	5.87×10^{-5}	2.47×10^{-2}
1.67×10^{-4}	3.17×10^{-2}	1.89×10^{2}	1.27	1.27	1.18×10^{-4}	4.92×10^{-5}	3.15×10^{-2}
1.66×10^{-4}	3.83×10^{-2}	2.31×10^{2}	1.33	1.33	1.23×10^{-4}	4.25×10^{-5}	3.82×10^{-2}
1.64×10^{-4}	4.49×10^{-2}	2.73×10^{2}	1.37	1.37	1.27×10^{-4}	3.73×10^{-5}	4.48×10^{-2}
1.63×10^{-4}	5.13×10^{-2}	3.15×10^{2}	1.39	1.39	1.30×10^{-4}	3.33×10^{-5}	5.12×10^{-2}
1.62×10^{-4}	5.77×10^{-2}	3.57×10^{2}	1.41	1.41	1.32×10^{-4}	3.00×10^{-5}	5.76×10^{-2}
1.59×10^{-4}	6.34×10^{-2}	3.99×10^{2}	1.42	1.42	1.31×10^{-4}	2.73×10^{-5}	6.33×10^{-2}

Least squares optimization: A_{endcal} = 1.706, K_{CH} = 7.60×10^{1} M^{-1}

pK_a = 15.04, ε_{MeOH} = 10747, ε_{DMSO} = 10438



5. Reactivity of Triflinates (1) in 91/9 MeOH/MeCN (v/v)

Reagent grade methanol (99.8%, Acros) was used.

From the stopped-flow experiments (HiTech SF-61DX2), pseudo-first-order rate constants k_{obs} (s^{-1}) were obtained by fitting the single exponential $A_t = A_0\exp(-k_{\mathrm{obs}}t) + C$ to the observed time-dependent carbocation absorbance (averaged from at least 3 kinetic runs for each nucleophile concentration). The term $k_{2,\mathrm{MeO}}[\mathrm{MeO}^-]$ was subtracted from the observed pseudo-first-order rate constants k_{obs} (s^{-1}), then the obtained values $k_{1\Psi}$ (s^{-1}) were plotted against the concentrations of the carbanions giving rise to linear correlations with the slopes corresponding to second-order rate constants of the reactions of the carbanions with the reference electrophiles $k_{2,\mathrm{C}}$ ($\mathrm{M}^{-1}\ \mathrm{s}^{-1}$).

$$k_{\mathrm{obs}} = k_{2,\mathrm{C}}[\mathrm{C}^-] + k_{2,\mathrm{MeO}}[\mathrm{MeO}^-] + k_{1,\mathrm{MeOH}}$$

$$k_{1\Psi} = k_{\mathrm{obs}} - k_{2,\mathrm{MeO}}[\mathrm{MeO}^-] = k_{2,\mathrm{C}}[\mathrm{C}^-] + k_{1,\mathrm{MeOH}}$$

The rate constants for the reactions of methoxide anion with the electrophiles have already been reported. Those which are used in this work are presented in Table S2.

Table S2. Second-order rate constants $k_{2,\mathrm{MeO}}$ ($\mathrm{M}^{-1}\ \mathrm{s}^{-1}$) for the reactions of methoxide anion and first-order rate constants $k_{1,\mathrm{MeOH}}$ for the reactions of methanol with benzhydrylium ions **2f**-**j** in MeOH/CH_3CN (91:9, v/v) at 20 °C.

Electrophile	$k_{2,\mathrm{MeO}}$ ($\mathrm{M}^{-1}\ \mathrm{s}^{-1}$)[a]	$k_{1,\mathrm{MeOH}}$ (s^{-1})[a]
2f $(\mathrm{lil})_2\mathrm{CH}^+$	1.17×10^{3}	6.14×10^{-3}
2g $(\mathrm{jul})_2\mathrm{CH}^+$	2.48×10^{3}	3.16×10^{-2}[b]
2h $(\mathrm{ind})_2\mathrm{CH}^+$	7.41×10^{3}	2.13×10^{-1}[b]
2i $(\mathrm{thq})_2\mathrm{CH}^+$	1.56×10^{4}	2.17×10^{-1}
2j $(\mathrm{pyr})_2\mathrm{CH}^+$	4.80×10^{4}	9.32×10^{-1}

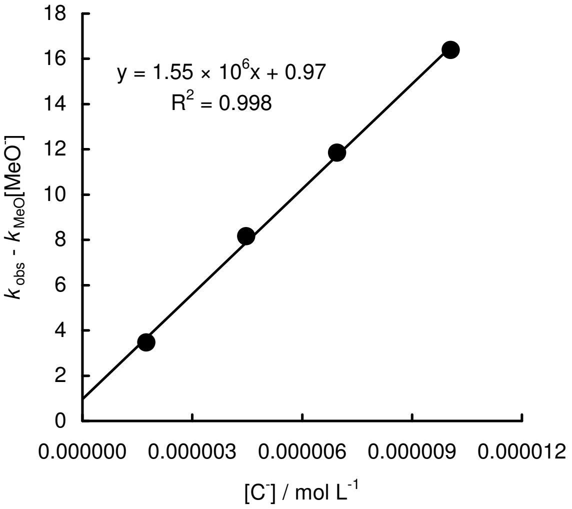
[a] Data from T. B. Phan, H. Mayr, *Can. J. Chem.* **2005**, *83*, 1554-1560. [b] Calculated value.

For the stopped-flow experiments, two types of stock solutions were used: a) A solution of the benzhydrylium ion **2** in CH_3CN and b) a methanolic solution of the triflinate **1**, generated by adding 1 equivalent of methoxide to the corresponding triflone **1**-H. The stopped-flow instrument was set up with a 10/1 mixing ratio (10 volume parts of triflinate solution in methanol were mixed with 1 volume part of benzhydrylium solution in CH_3CN).

5.1 Kinetics of the Reactions of 4-Trifluoromethylbenzyltriflinate (**1c**)

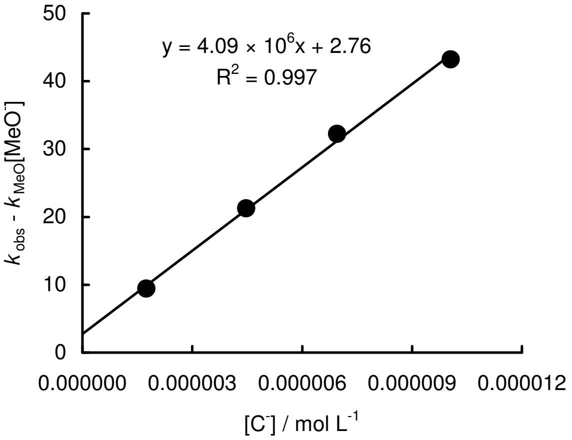
Reaction of **1c** (X = CF$_3$) with (lil)$_2$CH$^+$BF$_4^-$ **2f** (stopped-flow, λ = 620 nm, 20 °C)

$[E]_0$ (mol L^{-1})	$[CH]_0$ (mol L^{-1})	$[MeO^-]_0$ (mol L^{-1})	$[C^-]_{eq}$ (mol L^{-1})	$[MeO^-]_{eq}$ (mol L^{-1})	$k_{\mathrm{MeO}}[MeO^-]$ (L mol^{-1} s^{-1})	k_{obs} (s^{-1})	$k_{1\Psi}$ (s^{-1})
1.09×10^{-5}	1.79×10^{-3}	1.79×10^{-3}	1.92×10^{-6}	1.79×10^{-3}	1.90	5.36	3.46
1.09×10^{-5}	2.87×10^{-3}	2.87×10^{-3}	4.93×10^{-6}	2.87×10^{-3}	3.05	1.12×10^{1}	8.15
1.09×10^{-5}	3.58×10^{-3}	3.58×10^{-3}	7.66×10^{-6}	3.57×10^{-3}	3.80	1.56×10^{1}	1.19×10^{1}
1.09×10^{-5}	4.31×10^{-3}	4.31×10^{-3}	1.11×10^{-5}	4.29×10^{-3}	4.57	2.09×10^{1}	1.64×10^{1}



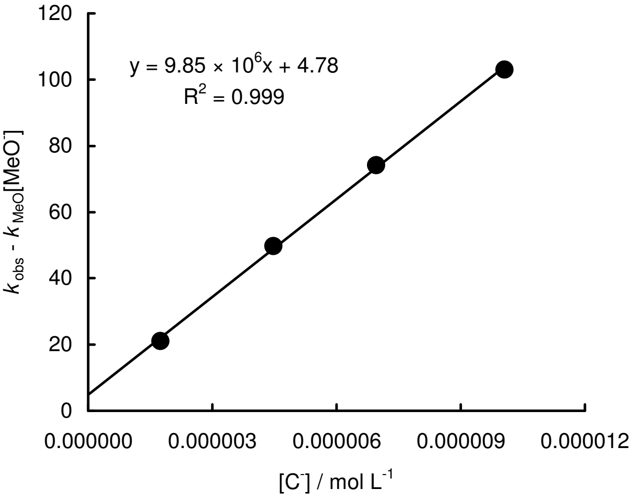
Reaction of **1c** (X = CF$_3$) with (jul)$_2$CH$^+$BF$_4^-$ **2g** (stopped-flow, λ = 620 nm, 20 °C)

$[E]_0$ (mol L^{-1})	$[CH]_0$ (mol L^{-1})	$[MeO^-]_0$ (mol L^{-1})	$[C^-]_{eq}$ (mol L^{-1})	$[MeO^-]_{eq}$ (mol L^{-1})	$k_{\mathrm{MeO}}[MeO^-]$ (L mol^{-1} s^{-1})	k_{obs} (s^{-1})	$k_{1\Psi}$ (s^{-1})
1.08×10^{-5}	1.79×10^{-3}	1.79×10^{-3}	1.92×10^{-6}	1.79×10^{-3}	4.03	1.34×10^{1}	9.41
1.08×10^{-5}	2.87×10^{-3}	2.87×10^{-3}	4.93×10^{-6}	2.87×10^{-3}	6.46	2.77×10^{1}	2.12×10^{1}
1.08×10^{-5}	3.58×10^{-3}	3.58×10^{-3}	7.66×10^{-6}	3.57×10^{-3}	8.05	4.03×10^{1}	3.22×10^{1}
1.08×10^{-5}	4.31×10^{-3}	4.31×10^{-3}	1.11×10^{-5}	4.29×10^{-3}	9.68	5.29×10^{1}	4.32×10^{1}



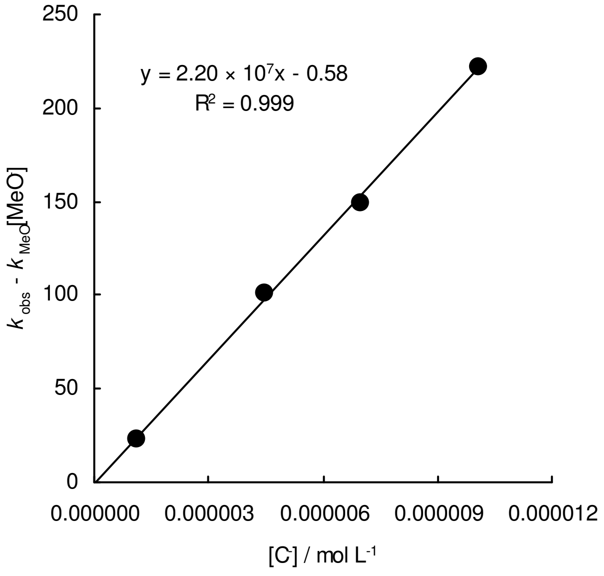
Reaction of **1c** (X = CF_3) with $(ind)_2CH^+BF_4^-$ **2h** (stopped-flow, λ = 620 nm, 20 °C)

$[E]_0$ (mol L^{-1})	$[CH]_0$ (mol L^{-1})	$[MeO^-]_0$ (mol L^{-1})	$[C^-]_{eq}$ (mol L^{-1})	$[MeO^-]_{eq}$ (mol L^{-1})	$k_{MeO}[MeO^-]$ (L mol^{-1} s^{-1})	k_{obs} (s^{-1})	$k_{1\Psi}$ (s^{-1})
1.29×10^{-5}	1.79×10^{-3}	1.79×10^{-3}	1.92×10^{-6}	1.79×10^{-3}	1.20×10^{1}	3.31×10^{1}	2.11×10^{1}
1.29×10^{-5}	2.87×10^{-3}	2.87×10^{-3}	4.93×10^{-6}	2.87×10^{-3}	1.93×10^{1}	6.90×10^{1}	4.97×10^{1}
1.29×10^{-5}	3.58×10^{-3}	3.58×10^{-3}	7.66×10^{-6}	3.57×10^{-3}	2.41×10^{1}	9.83×10^{1}	7.42×10^{1}
1.29×10^{-5}	4.31×10^{-3}	4.31×10^{-3}	1.11×10^{-5}	4.29×10^{-3}	2.89×10^{1}	1.32×10^{2}	1.03×10^{2}



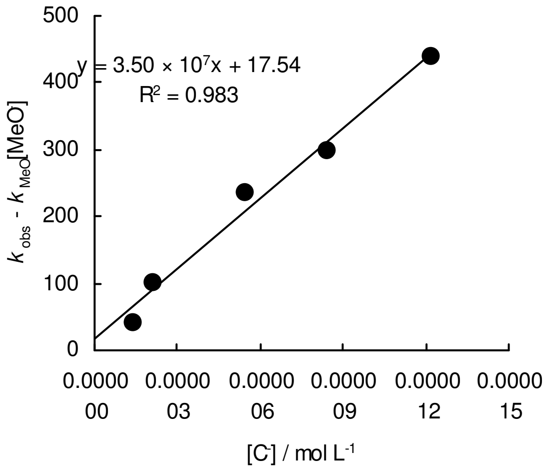
Reaction of **1c** (X = CF_3) with $(thq)_2CH^+BF_4^-$ **2i** (stopped-flow, λ = 620 nm, 20 °C)

$[E]_0$ (mol L^{-1})	$[CH]_0$ (mol L^{-1})	$[MeO^-]_0$ (mol L^{-1})	$[C^-]_{eq}$ (mol L^{-1})	$[MeO^-]_{eq}$ (mol L^{-1})	$k_{MeO}[MeO^-]$ (L mol^{-1} s^{-1})	k_{obs} (s^{-1})	$k_{1\Psi}$ (s^{-1})
1.18×10^{-5}	1.44×10^{-3}	1.44×10^{-3}	1.23×10^{-6}	1.43×10^{-3}	2.03×10^{1}	4.37×10^{1}	2.34×10^{1}
1.18×10^{-5}	2.87×10^{-3}	2.87×10^{-3}	4.93×10^{-6}	2.87×10^{-3}	4.06×10^{1}	1.42×10^{2}	1.01×10^{2}
1.18×10^{-5}	3.58×10^{-3}	3.58×10^{-3}	7.66×10^{-6}	3.57×10^{-3}	5.07×10^{1}	2.01×10^{2}	1.50×10^{2}
1.18×10^{-5}	4.31×10^{-3}	4.31×10^{-3}	1.11×10^{-5}	4.29×10^{-3}	6.09×10^{1}	2.83×10^{2}	2.22×10^{2}



Reaction of **1c** (X = CF_3) with $(pyr)_2CH^+BF_4^-$ **2j** (stopped-flow, λ = 620 nm, 20 °C)

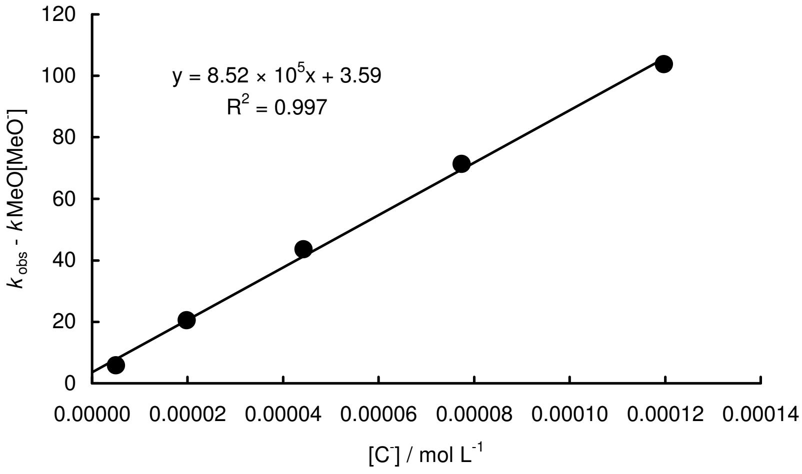
$[E]_0$ (mol L^{-1})	$[CH]_0$ (mol L^{-1})	$[MeO^-]_0$ (mol L^{-1})	$[C^-]_{eq}$ (mol L^{-1})	$[MeO^-]_{eq}$ (mol L^{-1})	$k_{MeO}[MeO^-]$ (L mol^{-1} s^{-1})	k_{obs} (s^{-1})	$k_{1\Psi}$ (s^{-1})
1.22×10^{-5}	1.58×10^{-3}	1.58×10^{-3}	1.49×10^{-6}	1.58×10^{-3}	6.88×10^{1}	1.10×10^{2}	4.07×10^{1}
1.22×10^{-5}	1.97×10^{-3}	1.97×10^{-3}	2.32×10^{-6}	1.97×10^{-3}	8.58×10^{1}	1.89×10^{2}	1.03×10^{2}
1.22×10^{-5}	3.16×10^{-3}	3.16×10^{-3}	5.96×10^{-6}	3.15×10^{-3}	1.38×10^{2}	3.73×10^{2}	2.35×10^{2}
1.22×10^{-5}	3.94×10^{-3}	3.94×10^{-3}	9.26×10^{-6}	3.93×10^{-3}	1.71×10^{2}	4.71×10^{2}	3.00×10^{2}
1.22×10^{-5}	4.74×10^{-3}	4.74×10^{-3}	1.34×10^{-5}	4.72×10^{-3}	2.06×10^{2}	6.46×10^{2}	4.40×10^{2}



5.2 Kinetics of the Reactions of 4-Cyanobenzyltriflinate (**1d**)

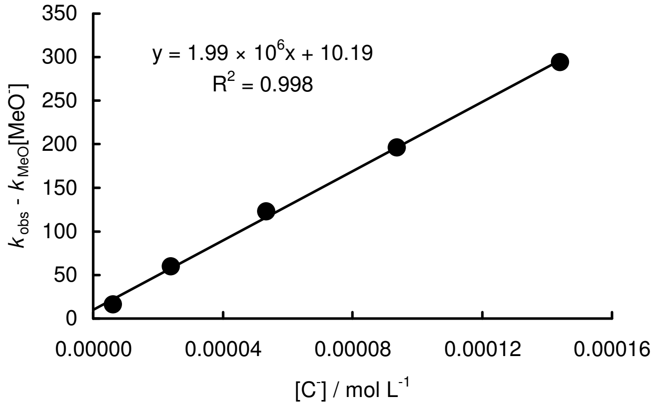
Reaction of **1d** (X = CN) with $(lil)_2CH^+BF_4^-$ **2f** (stopped-flow, λ = 621 nm, 20 °C)

$[E]_0$ (mol L^{-1})	$[CH]_0$ (mol L^{-1})	$[MeO^-]_0$ (mol L^{-1})	$[C^-]_{eq}$ (mol L^{-1})	$[MeO^-]_{eq}$ (mol L^{-1})	$k_{MeO}[MeO^-]$ (L mol^{-1} s^{-1})	k_{obs} (s^{-1})	$k_{1\Psi}$ (s^{-1})
1.15×10^{-5}	8.27×10^{-4}	8.27×10^{-4}	5.56×10^{-6}	8.21×10^{-4}	8.74×10^{-1}	6.66	5.79
1.15×10^{-5}	1.65×10^{-3}	1.65×10^{-3}	2.18×10^{-5}	1.63×10^{-3}	1.73	2.22×10^{1}	2.05×10^{1}
1.15×10^{-5}	2.48×10^{-3}	2.48×10^{-3}	4.87×10^{-5}	2.43×10^{-3}	2.59	4.62×10^{1}	4.36×10^{1}
1.15×10^{-5}	3.31×10^{-3}	3.31×10^{-3}	8.57×10^{-5}	3.22×10^{-3}	3.42	7.47×10^{1}	7.13×10^{1}
1.15×10^{-5}	4.13×10^{-3}	4.13×10^{-3}	1.32×10^{-4}	4.00×10^{-3}	4.25	1.08×10^{2}	1.04×10^{2}



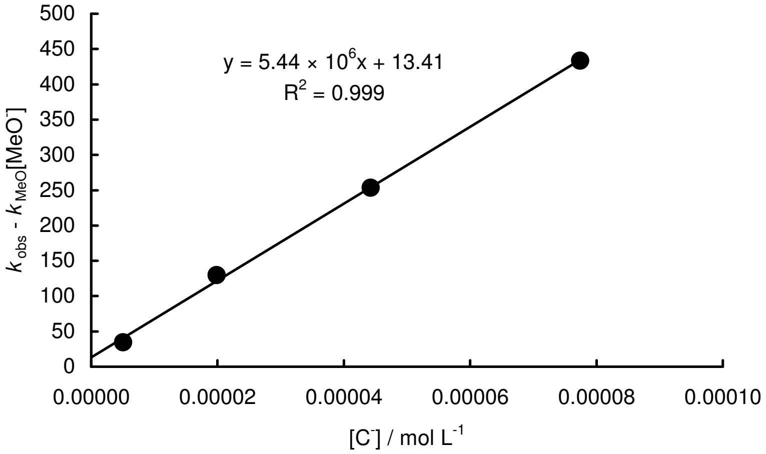
Reaction of **1d** (X = CN) with (jul)$_2$CH$^+$BF$_4^-$ **2g** (stopped-flow, λ = 621 nm, 20 °C)

$[E]_0$ (mol L^{-1})	$[CH]_0$ (mol L^{-1})	$[MeO^-]_0$ (mol L^{-1})	$[C^-]_{eq}$ (mol L^{-1})	$[MeO^-]_{eq}$ (mol L^{-1})	$k_{MeO}[MeO^-]$ (L mol^{-1} s^{-1})	k_{obs} (s^{-1})	$k_{1\Psi}$ (s^{-1})
9.82×10^{-6}	9.10×10^{-4}	9.10×10^{-4}	6.72×10^{-6}	9.03×10^{-4}	2.04	1.83×10^{1}	1.63×10^{1}
9.82×10^{-6}	1.82×10^{-3}	1.82×10^{-3}	2.64×10^{-5}	1.79×10^{-3}	4.03	6.39×10^{1}	5.99×10^{1}
9.82×10^{-6}	2.73×10^{-3}	2.73×10^{-3}	5.87×10^{-5}	2.67×10^{-3}	6.02	1.29×10^{2}	1.23×10^{2}
9.82×10^{-6}	3.64×10^{-3}	3.64×10^{-3}	1.03×10^{-4}	3.54×10^{-3}	7.98	2.05×10^{2}	1.96×10^{2}
9.82×10^{-6}	4.54×10^{-3}	4.54×10^{-3}	1.58×10^{-4}	4.38×10^{-3}	9.89	3.04×10^{2}	2.94×10^{2}



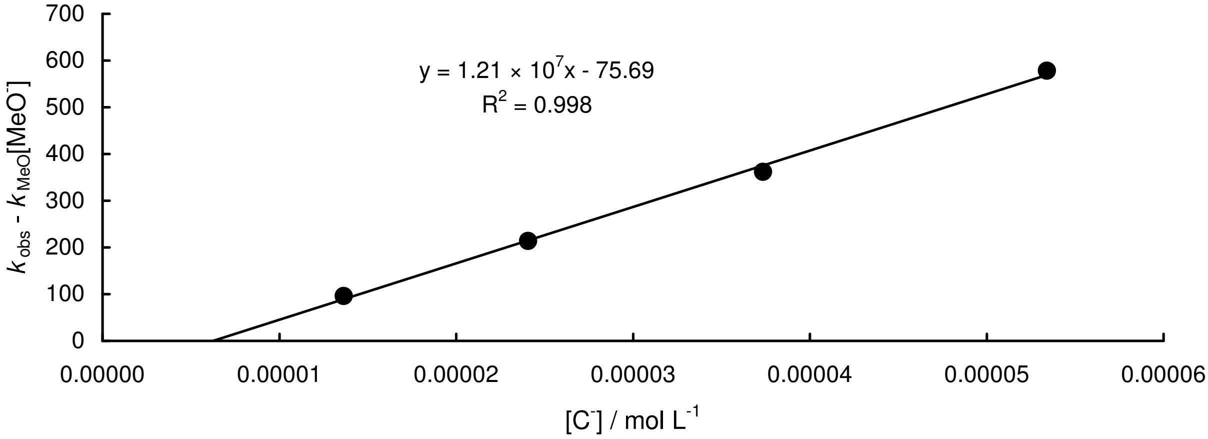
Reaction of **1d** (X = CN) with (ind)$_2$CH$^+$BF$_4^-$ **2h** (stopped-flow, λ = 621 nm, 20 °C)

$[E]_0$ (mol L^{-1})	$[CH]_0$ (mol L^{-1})	$[MeO^-]_0$ (mol L^{-1})	$[C^-]_{eq}$ (mol L^{-1})	$[MeO^-]_{eq}$ (mol L^{-1})	$k_{MeO}[MeO^-]$ (L mol^{-1} s^{-1})	k_{obs} (s^{-1})	$k_{1\Psi}$ (s^{-1})
1.17×10^{-5}	8.27×10^{-4}	8.27×10^{-4}	5.56×10^{-6}	8.21×10^{-4}	5.53	3.99×10^{1}	3.44×10^{1}
1.17×10^{-5}	1.65×10^{-3}	1.65×10^{-3}	2.18×10^{-5}	1.63×10^{-3}	1.10×10^{1}	1.41×10^{2}	1.30×10^{2}
1.17×10^{-5}	2.48×10^{-3}	2.48×10^{-3}	4.87×10^{-5}	2.43×10^{-3}	1.64×10^{1}	2.70×10^{2}	2.55×10^{2}
1.17×10^{-5}	3.31×10^{-3}	3.31×10^{-3}	8.57×10^{-5}	3.22×10^{-3}	2.17×10^{1}	4.55×10^{2}	4.34×10^{2}



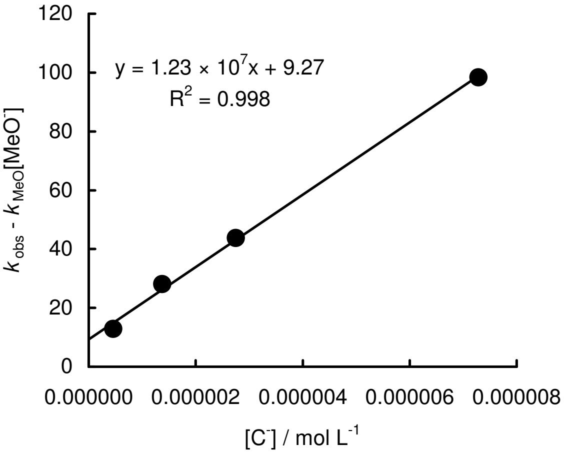
Reaction of **1d** (X = CN) with $(thq)_2CH^+BF_4^-$ **2i** (stopped-flow, λ = 621 nm, 20 °C)

$[E]_0$ (mol L^{-1})	$[CH]_0$ (mol L^{-1})	$[MeO^-]_0$ (mol L^{-1})	$[C^-]_{eq}$ (mol L^{-1})	$[MeO^-]_{eq}$ (mol L^{-1})	$k_{MeO}[MeO^-]$ (L mol^{-1} s^{-1})	k_{obs} (s^{-1})	$k_{1\Psi}$ (s^{-1})
1.27×10^{-5}	1.36×10^{-3}	1.36×10^{-3}	1.50×10^{-5}	1.35×10^{-3}	1.91×10^{1}	1.15×10^{2}	9.59×10^{1}
1.27×10^{-5}	1.82×10^{-3}	1.82×10^{-3}	2.65×10^{-5}	1.79×10^{-3}	2.54×10^{1}	2.39×10^{2}	2.14×10^{2}
1.27×10^{-5}	2.27×10^{-3}	2.27×10^{-3}	4.11×10^{-5}	2.23×10^{-3}	3.17×10^{1}	3.93×10^{2}	3.63×10^{2}
1.27×10^{-5}	2.73×10^{-3}	2.73×10^{-3}	5.88×10^{-5}	2.67×10^{-3}	3.79×10^{1}	6.16×10^{2}	5.78×10^{2}



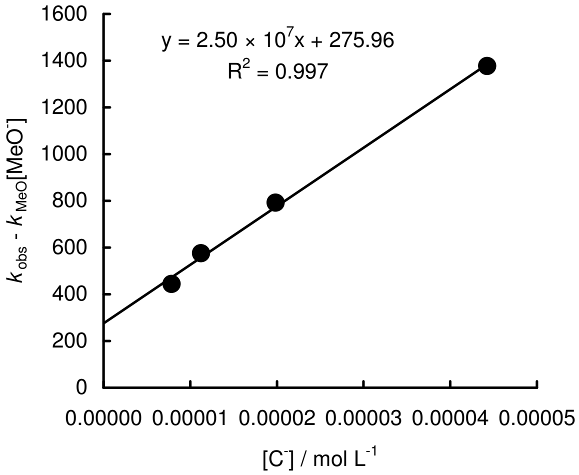
Reaction of **1d** (X = CN) with $(thq)_2CH^+BF_4^-$ **2i** (stopped-flow, λ = 680 nm, 20 °C)

$[E]_0$ (mol L^{-1})	$[CH]_0$ (mol L^{-1})	$[MeO^-]_0$ (mol L^{-1})	$[C^-]_{eq}$ (mol L^{-1})	$[MeO^-]_{eq}$ (mol L^{-1})	$k_{MeO}[MeO^-]$ (L mol^{-1} s^{-1})	k_{obs} (s^{-1})	$k_{1\Psi}$ (s^{-1})
1.00×10^{-5}	2.49×10^{-4}	2.49×10^{-4}	5.07×10^{-7}	2.48×10^{-4}	1.67	1.45×10^{1}	1.28×10^{1}
1.00×10^{-5}	4.97×10^{-4}	3.73×10^{-4}	1.52×10^{-6}	3.71×10^{-4}	2.50	3.06×10^{1}	2.81×10^{1}
1.00×10^{-5}	7.46×10^{-4}	4.97×10^{-4}	3.02×10^{-6}	4.94×10^{-4}	3.33	4.71×10^{1}	4.38×10^{1}
1.00×10^{-5}	9.94×10^{-4}	9.94×10^{-4}	8.02×10^{-6}	9.86×10^{-4}	6.64	1.06×10^{2}	9.84×10^{1}



Reaction of **1d** (X = CN) with (pyr)$_2$CH$^+$BF$_4^-$ **2j** (stopped-flow, λ = 621 nm, 20 °C)

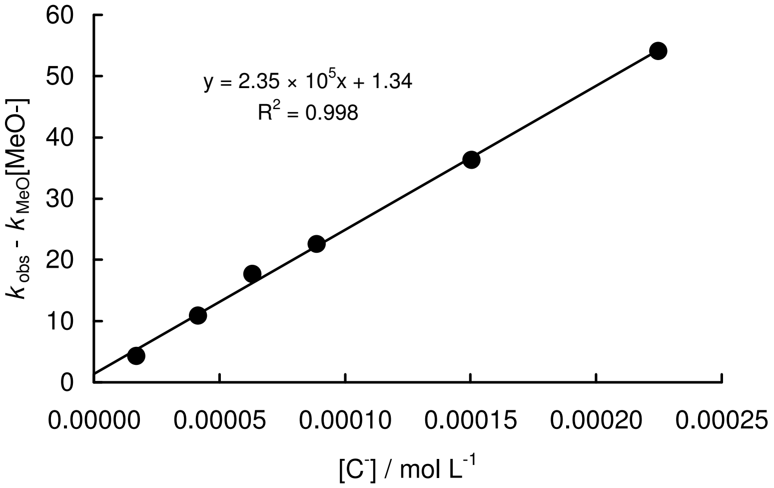
$[E]_0$ (mol L^{-1})	$[CH]_0$ (mol L^{-1})	$[MeO^-]_0$ (mol L^{-1})	$[C^-]_{eq}$ (mol L^{-1})	$[MeO^-]_{eq}$ (mol L^{-1})	$k_{MeO}[MeO^-]$ (L mol^{-1} s^{-1})	k_{obs} / (s^{-1})	$k_{1\Psi}$/ (s^{-1})
1.41×10^{-5}	1.03×10^{-3}	1.03×10^{-3}	8.64×10^{-6}	1.02×10^{-3}	4.47×10^{1}	4.89×10^{2}	4.44×10^{2}
1.41×10^{-5}	1.24×10^{-3}	1.24×10^{-3}	1.24×10^{-5}	1.23×10^{-3}	5.35×10^{1}	6.29×10^{2}	5.75×10^{2}
1.41×10^{-5}	1.65×10^{-3}	1.65×10^{-3}	2.18×10^{-5}	1.63×10^{-3}	7.10×10^{1}	8.62×10^{2}	7.92×10^{2}
1.41×10^{-5}	2.48×10^{-3}	2.48×10^{-3}	4.87×10^{-5}	2.43×10^{-3}	1.06×10^{2}	1.48×10^{3}	1.37×10^{3}



5.3 Kinetics of the Reactions of 4-Nitrobenzyltriflinate (**1e**)

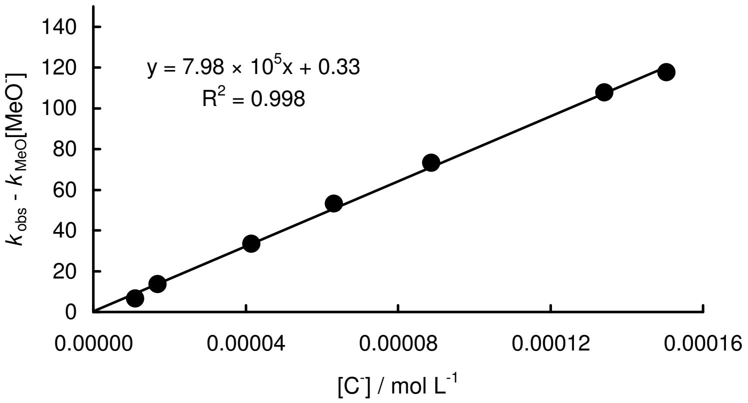
Reaction of **1e** (X = NO$_2$) with (lil)$_2$CH$^+$BF$_4^-$ **2f** (stopped-flow, λ = 620 nm, 20 °C)

$[E]_0$ (mol L^{-1})	$[CH]_0$ (mol L^{-1})	$[MeO^-]_0$ (mol L^{-1})	$[C^-]_{eq}$ (mol L^{-1})	$[MeO^-]_{eq}$ (mol L^{-1})	$k_{MeO}[MeO^-]$ (L mol^{-1} s^{-1})	k_{obs} (s^{-1})	$k_{1\Psi}$ (s^{-1})
1.15×10^{-5}	5.13×10^{-4}	5.13×10^{-4}	1.86×10^{-5}	4.94×10^{-4}	5.25×10^{-1}	4.81	4.28
1.15×10^{-5}	8.20×10^{-4}	8.20×10^{-4}	4.56×10^{-5}	7.74×10^{-4}	8.24×10^{-1}	1.17×10^{1}	1.09×10^{1}
1.15×10^{-5}	1.03×10^{-3}	1.03×10^{-3}	6.95×10^{-5}	9.56×10^{-4}	1.02	1.87×10^{1}	1.77×10^{1}
1.15×10^{-5}	1.23×10^{-3}	1.23×10^{-3}	9.76×10^{-5}	1.13×10^{-3}	1.20	2.38×10^{1}	2.26×10^{1}
1.15×10^{-5}	1.64×10^{-4}	1.64×10^{-4}	1.65×10^{-4}	1.47×10^{-3}	1.57	3.79×10^{1}	3.63×10^{1}
1.15×10^{-5}	2.05×10^{-3}	2.05×10^{-3}	2.47×10^{-4}	1.80×10^{-3}	1.92	5.60×10^{1}	5.41×10^{1}



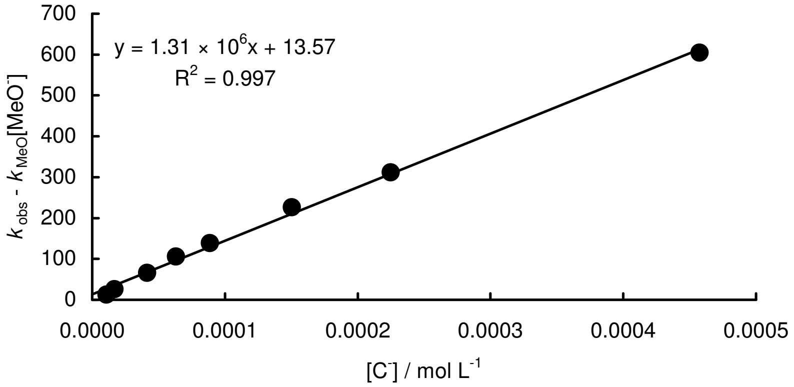
Reaction of **1e** (X = NO_2) with $(jul)_2CH^+BF_4^-$ **2g** (stopped-flow, λ = 620 nm, 20 °C)

$[E]_0$ (mol L^{-1})	$[CH]_0$ (mol L^{-1})	$[MeO^-]_0$ (mol L^{-1})	$[C^-]_{eq}$ (mol L^{-1})	$[MeO^-]_{eq}$ (mol L^{-1})	$k_{MeO}[MeO^-]$ (L mol^{-1} s^{-1})	k_{obs} (s^{-1})	$k_{1\Psi}$ (s^{-1})
9.82×10^{-6}	4.10×10^{-4}	4.10×10^{-4}	1.21×10^{-5}	3.98×10^{-4}	8.97×10^{-1}	7.56	6.66
9.82×10^{-6}	5.13×10^{-4}	5.13×10^{-4}	1.86×10^{-5}	4.94×10^{-4}	1.11	1.47×10^{1}	1.36×10^{1}
9.82×10^{-6}	8.20×10^{-4}	8.20×10^{-4}	4.56×10^{-5}	7.74×10^{-4}	1.75	3.51×10^{1}	3.34×10^{1}
9.82×10^{-6}	1.03×10^{-3}	1.03×10^{-3}	6.95×10^{-5}	9.56×10^{-4}	2.15	5.54×10^{1}	5.32×10^{1}
9.82×10^{-6}	1.23×10^{-3}	1.23×10^{-3}	9.76×10^{-5}	1.13×10^{-3}	2.55	7.58×10^{1}	7.33×10^{1}
9.82×10^{-6}	1.54×10^{-3}	1.54×10^{-3}	1.48×10^{-4}	1.39×10^{-3}	3.14	1.11×10^{2}	1.08×10^{2}
9.82×10^{-6}	1.64×10^{-3}	1.64×10^{-3}	1.65×10^{-4}	1.47×10^{-3}	3.32	1.21×10^{2}	1.18×10^{2}



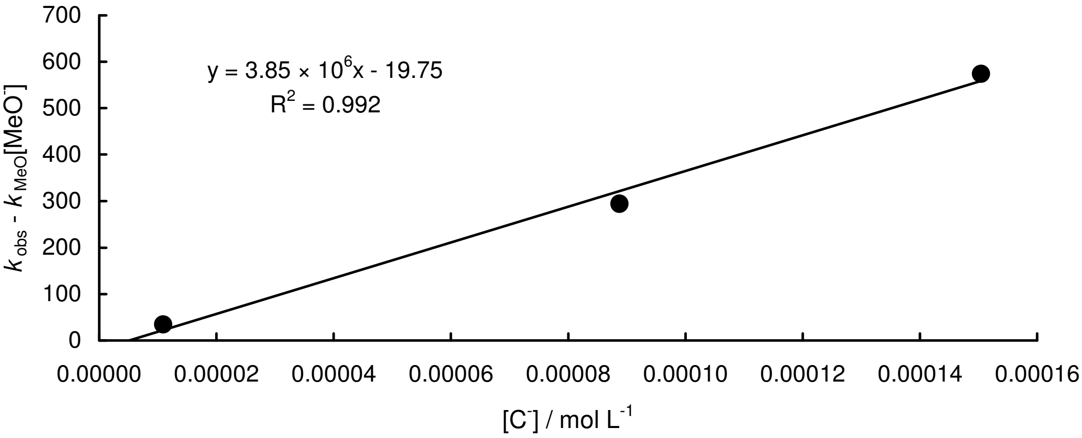
Reaction of **1e** (X = NO_2) with $(ind)_2CH^+BF_4^-$ **2h** (stopped-flow, λ = 620 nm, 20 °C)

$[E]_0$ (mol L^{-1})	$[CH]_0$ (mol L^{-1})	$[MeO^-]_0$ (mol L^{-1})	$[C^-]_{eq}$ (mol L^{-1})	$[MeO^-]_{eq}$ (mol L^{-1})	$k_{MeO}[MeO^-]$ (L mol^{-1} s^{-1})	k_{obs} (s^{-1})	$k_{1\Psi}$ (s^{-1})
1.17×10^{-5}	4.10×10^{-4}	4.10×10^{-4}	1.21×10^{-5}	3.98×10^{-4}	2.68	1.51×10^{1}	1.24×10^{-1}
1.17×10^{-5}	5.13×10^{-4}	5.13×10^{-4}	1.86×10^{-5}	4.94×10^{-4}	3.33	2.92×10^{1}	2.59×10^{1}
1.17×10^{-5}	8.20×10^{-4}	8.20×10^{-4}	4.56×10^{-5}	7.74×10^{-4}	5.22	7.07×10^{1}	6.55×10^{1}
1.17×10^{-5}	1.03×10^{-3}	1.03×10^{-3}	6.95×10^{-5}	9.56×10^{-4}	6.44	1.12×10^{2}	1.06×10^{2}
1.17×10^{-5}	1.23×10^{-3}	1.23×10^{-3}	9.76×10^{-5}	1.13×10^{-3}	7.63	1.46×10^{2}	1.38×10^{2}
1.17×10^{-5}	1.64×10^{-3}	1.64×10^{-3}	1.65×10^{-4}	1.47×10^{-3}	9.93	2.36×10^{2}	2.26×10^{2}
1.17×10^{-5}	2.05×10^{-3}	2.05×10^{-3}	2.47×10^{-4}	1.80×10^{-3}	1.21×10^{1}	3.24×10^{2}	3.12×10^{2}
1.17×10^{-5}	3.08×10^{-3}	3.08×10^{-3}	5.03×10^{-4}	2.57×10^{-3}	1.73×10^{1}	6.22×10^{2}	6.05×10^{2}



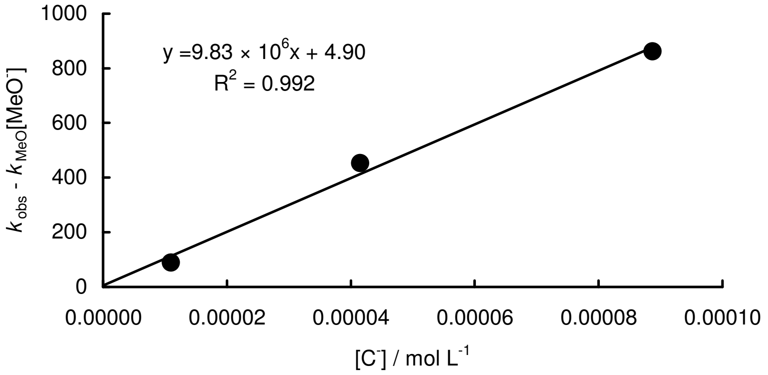
Reaction of **1e** (X = NO$_2$) with (thq)$_2$CH$^+$BF$_4^-$ **2i** (stopped-flow, λ = 620 nm, 20 °C)

$[E]_0$ (mol L^{-1})	$[CH]_0$ (mol L^{-1})	$[MeO^-]_0$ (mol L^{-1})	$[C^-]_{eq}$ (mol L^{-1})	$[MeO^-]_{eq}$ (mol L^{-1})	$k_{MeO}[MeO^-]$ (L mol^{-1} s^{-1})	k_{obs} (s^{-1})	$k_{1\Psi}$ (s^{-1})
1.27×10^{-5}	4.10×10^{-4}	4.10×10^{-4}	1.21×10^{-5}	3.98×10^{-4}	5.64	4.02×10^{1}	3.46×10^{1}
1.27×10^{-5}	1.23×10^{-3}	1.23×10^{-3}	9.76×10^{-5}	1.13×10^{-3}	1.61×10^{1}	3.10×10^{2}	2.94×10^{2}
1.27×10^{-5}	1.64×10^{-3}	1.64×10^{-3}	1.65×10^{-4}	1.47×10^{-3}	2.09×10^{1}	5.95×10^{2}	5.75×10^{2}



Reaction of **1e** (X = NO$_2$) with (pyr)$_2$CH$^+$BF$_4^-$ **2j** (stopped-flow, λ = 620 nm, 20 °C)

$[E]_0$ (mol L^{-1})	$[CH]_0$ (mol L^{-1})	$[MeO^-]_0$ (mol L^{-1})	$[C^-]_{eq}$ (mol L^{-1})	$[MeO^-]_{eq}$ (mol L^{-1})	$k_{MeO}[MeO^-]$ (L mol^{-1} s^{-1})	k_{obs} / (s^{-1})	$k_{1\Psi}$/ (s^{-1})
1.41×10^{-5}	4.10×10^{-4}	4.10×10^{-4}	1.21×10^{-5}	3.98×10^{-4}	1.74×10^{1}	1.06×10^{2}	8.86×10^{1}
1.41×10^{-5}	8.20×10^{-4}	8.20×10^{-4}	4.56×10^{-5}	7.74×10^{-4}	3.38×10^{1}	4.86×10^{2}	4.52×10^{2}
1.41×10^{-5}	1.23×10^{-3}	1.23×10^{-3}	9.76×10^{-5}	1.13×10^{-3}	4.49×10^{1}	9.12×10^{2}	8.62×10^{2}



6. Nucleophilicity and Acidities (pK_{aH}) of Carbanions in DMSO and MeOH

Acidities pK_{aH} (at 25 °C) and nucleophilicity parameters N and s of carbanions in MeOH and DMSO (at 20 °C), respectively.

Carbanion		pK_{aH} in MeOH	N/s in MeOH	pK_{aH} in DMSO	N/s in DMSO
$[4\text{-MeC}_6H_4CHSO_2CF_3]^-$	**1a**	–	–	15.4[Bor88b]	19.28/0.68
$[C_6H_5CHSO_2CF_3]^-$	**1b**	–	–	14.62[Gou03]	18.86/0.66
$[4\text{-CF}_3C_6H_4CHSO_2CF_3]^-$	**1c**	17.14	20.79/0.58	11.95[Gou03]	17.32/0.74
$[4\text{-CNC}_6H_4CHSO_2CF_3]^-$	**1d**	16.00	19.42/0.63	10.70[Bor88b]	16.29/0.75
$[4\text{-NO}_2C_6H_4CHSO_2CF_3]^-$	**1e**	15.05	18.23/0.66	9.46[Gou03]	14.99/0.79
$CH_3CH{=}NO_2^-$	**4a**	14.2[Cox88]	13.41/0.67[Pha06]	16.7[Bor94]	21.54/0.62[Lem03]
$CH_2{=}NO_2^-$	**4b**	15.6[Cox88]	14.02/0.61[Pha06]	17.2[Olm80]	20.71/0.60[Bug04]
$(CH_3)_2C{=}NO_2^-$	**4c**	13.2[Bel69]	12.20/0.71[Pha06]	16.8[Bor94]	20.61/0.69[Bug04]
$C_6H_5CH{=}NO_2^-$	**4d**	12.62[Pha06]	12.51/0.67[Pha06]	12.2[Bor94]	18.29/0.71[Bug04]
$4\text{-MeC}_6H_4CH{=}NO_2^-$	**4e**	13.02[Pha06]	13.58/0.64[Pha06]	12.33[Kee79]	18.31/0.76[Bug04]
$3\text{-NO}_2C_6H_4CH{=}NO_2^-$	**4f**	10.9[Gan97]	14.75/0.71[Pha06]	10.04[Kee79]	18.06/0.71[Bug04]
$4\text{-CNC}_6H_4CH{=}NO_2^-$	**4g**	11.99[Pha06]	13.92/0.73[Pha06]	9.31[Kee79]	16.96/0.73[Bug04]
$4\text{-NO}_2C_6H_4CH{=}NO_2^-$	**4h**	10.5[Gan97]	14.05/0.72[Pha06]	8.62[Kee79]	16.29/0.75[Bug04]
$^-CH(CO_2Me)_2$	**5a**	17.27[Cra91]	18.24/0.64[Pha06]	15.88[Arn84]	—
$^-CH(CO_2Et)_2$	**5a’**	—	—	16.37[Olm80]	20.22/0.65[Luc02]
$^-CH(CN)CO_2Et$	**5b**	15.53[Cra91]	18.59/0.65[Pha06]	13.1[Bor88a]	19.62/0.67[Luc02]
$^-CH(CN)_2$	**5c**	14.1[Cox88]	18.21/0.69[Pha06]	11.1[Bor89]	19.36/0.67[Luc02]
$^-CH(COCH_3)_2$	**5d**	–	–	13.33[Olm80]	17.64/0.73[Luc02]
[dimedone]$^-$	**5e**	–	–	11.16[Olm80]	16.27/0.77[Luc02]
[Meldrum’s acid]$^-$	**5f**	–	–	7.33[Arn87]	13.91/0.86[Luc02]

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[Bor88b] Bordwell, F. G.; Bausch, M. J.; Branca, J. C.; Harrelson, J. A., Jr. *J. Phys. Org. Chem.* **1988**, *1*, 225–241.

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[Bug04] Bug, T.; Lemek, T.; Mayr, H. *J. Org. Chem.* **2004**, *69*, 7565–7576.

[Cox88] Cox, J. P. L.; Crampton, M. R.; Paul, W. *J. Chem. Soc., Perkin. Trans. 2* **1988**, 25–29.

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Electrophilicity Parameters for 2-Benzylidene-indan-1,3-diones – a systematic extension of the benzhydrylium based electrophilicity scale

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Introduction. Numerous kinetic investigations have shown that the rate constants for the reactions of carbocations with nucleophiles can be described by eq. 3.1.[1-4]

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

Therein, k_2 corresponds to the second-order rate constant in L mol^{-1} s^{-1}, s to the nucleophile-specific slope parameter, N to the nucleophilicity parameter, and E to the electrophilicity parameter. By using benzhydrylium ions and quinone methides as reference electrophiles[5] it became possible to compare the reactivities of numerous σ-, n- and π-nucleophiles in a single scale.

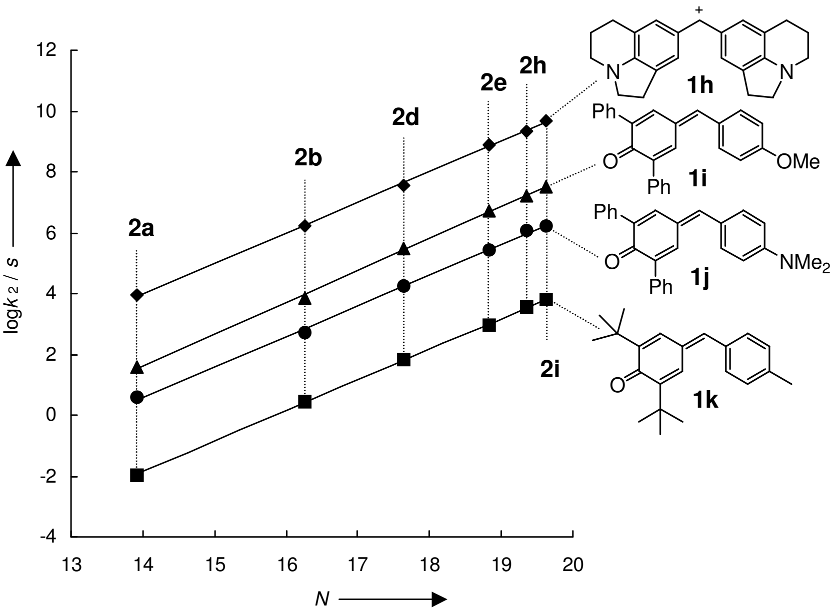


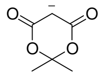
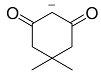
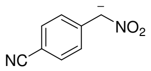
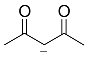
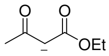
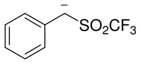
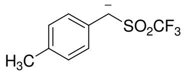
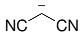
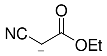
Figure 3.1. Correlation of (log k_2)/s with the nucleophilicity parameter N for the reactions of the benzhydrylium ion **1h** and the quinone methides **1i–k** with carbanions (DMSO, 20 °C, from ref. 5).

For the characterization of many synthetically important nucleophiles, for example stabilized carbanions and amines, reference electrophiles with $-10 > E > -16$ were needed. Because this range is presently only covered by the quinone methides **1i** and **1j** (Figure 3.1), which are difficult to synthesize, we were looking for more readily accessible alternatives.
Lemek showed that eq. 1 is also applicable to reactions of nucleophiles with ordinary Michael acceptors, *e.g.*, benzylidenemalononitriles.[6] We, therefore, expected a similar behavior of the easily producible 2-benzylidene-indan-1,3-diones **1a**–**d**, which have previously been investigated in medical and material chemistry.[7] Some derivatives show antibacterial activities or nonlinear optical properties, some have been used as electroluminescent devices, or as eye lens clarification agents.[7] The 2-benzylidene-indan-1,3-diones can be considered as organic Lewis acids.[8] Because of their low-lying LUMOs they are reactive Michael acceptors and have been used as heterodienes in cycloaddition reactions.[9]

Due to the fact that the double bonds of the 2-benzylidene-indan-1,3-diones are strongly polarized by the mesomeric electron-withdrawing effect of the carbonyl groups, the double bond is highly electrophilic and can be attacked by many nucleophiles. Zalukaevs and Anokhina showed that the reaction of 2-benzylidene-indan-1,3-dione with ethyl acetoacetate gives the correponding Michael adduct.[10] In the reactions of 2-benzylidene-indan-1,3-diones with acetylacetone, ethyl acetoacetate, diethyl malonate, and phenylacetophenone Michael adducts were obtained which undergo consecutive reactions.[11] Additions of arylnitromethanes,[12] dimedone imines,[13] di- and trialkylphosphites[14] of phosphonium ylides[14b,c] have also been described. Recently, hydride transfer from the Hantzsch ester to a benzylidene-indan-1,3-dione derivative has been observed.[15]

We now report on the kinetics of the additions of the stabilized carbanions **2a–l** (Table 3.1) to the 2-benzylidene-indan-1,3-diones **1a**–**d** in DMSO and show that the second-order rate constants k_2 can be described by eq. 3.1. The results will then be compared with Bernasconi's rate constants for the reactions of 2-benzylidene-indan-1,3-dione **1d** with amines in DMSO/H_2O (50/50 v,v).[16]

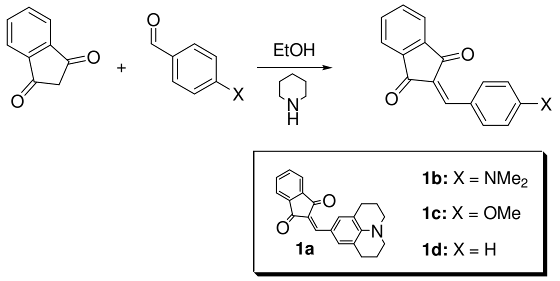
Table 3.1. *N*- and *s*-parameters of the employed nucleophiles in DMSO.

Nucleophile		*N*	*s*
	**2a**	13.91[a]	0.86[a]
	**2b**	16.27[a]	0.77[a]
	**2c**	16.96[b]	0.73[b]
	**2d**	17.64[a]	0.73[a]
	**2e**	18.82[a]	0.69[a]
	**2f**	18.67[c]	0.68[c]
	**2g**	19.35[c]	0.67[c]
	**2h**	19.36[a]	0.67[a]
	**2i**	19.62[a]	0.67[a]
$(CH_3)_2C{=}NO_2^-$	**2j**	20.61[b]	0.69[b]
$H_2C{=}NO_2^-$	**2k**	20.71[b]	0.60[b]
$CH_3CH{=}NO_2^-$	**2l**	21.54[b]	0.62[b]

[a] From ref. 5. [b] From ref. [17]. [c] From ref. [18].

Results and discussion

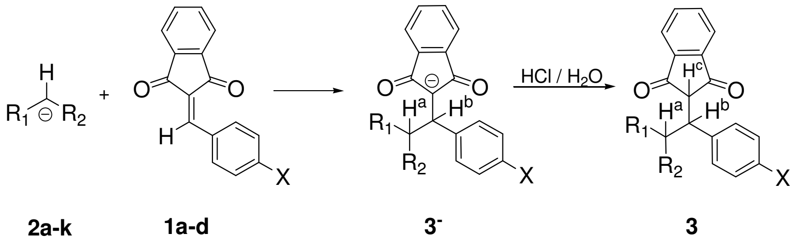
Preparation of the electrophiles 1a-d. The 2-benzylidene-indan-1,3-diones **1a–d** were synthesized by Knoevenagel condensation from indan-1,3-dione and substituted benzaldehydes in the presence of catalytic amounts of piperidine in boiling ethanol (Scheme 1) following the protocol of Behera and Nayak.[19]



Scheme 3.1. Preparation of the 2-benzylidene-indan-1,3-diones via Knoevenagel condensation.

Reaction products. The anionic adducts **3**$^-$ obtained by mixing equimolar amounts of the Michael acceptors **1** and the potassium salts of the carbanions **2** in d_6-DMSO solutions were investigated by NMR spectroscopy. In few cases, the products **3** obtained after protonation of **3**$^-$ were isolated and characterized (Scheme 3.2). Because for other combinations of the electrophiles **1a–d** with the nucleophiles **2a–l** analogous reaction products were expected, products have not been identified for all combinations which were studied kinetically (Table 3.2).

Scheme 3.2. Reactions of the potassium salts of the carbanions **2a-l** with the 2-benzylidene-indan-1,3-diones **1a-d** in DMSO



All Michael adducts **3**$^-$ and **3** show characteristic ^{1}H NMR spectra with H^a and H^b as doublets from δ = 5.03–5.85 ppm for H^a and δ = 3.98–4.40 ppm for H^b. The double set of signals for product **3al** indicates that it exists as a pair of diastereomers (2:1).

Table 3.2. Characterized Michael adducts **3**$^-$ or **3** and some characteristic ^{1}H NMR chemical shifts and coupling constants.

Reactants		adducts	δ(H^a)/ppm	δ(H^b)/ppm	J / Hz
1a	**2d**	**3ad**$^-$	5.23	4.16	12.4
1a	**2h**	**3ah**$^-$	5.76	3.98	11.6
1a	**2l**	**3al**	ds[a]	ds[a]	ds[a]
1b	**2h**	**3bh**$^-$	5.81	4.17	11.3
1b	**2k**	**3bk**	5.03/5.31[b]	4.33[b]	[b]
1c	**2d**	**3cd**$^-$	5.28	4.34	12.3
1c	**2h**	**3ch**$^-$	5.85	4.24	11.4
1d	**2d**	**3dd**$^-$	5.35	4.40	12.3

[a] Diastereomers, double sets of signals in the ratio 2:1 have been found, (see Supporting Information). [b] δ = 4.33 (dt, ^3J = 7.7 Hz, ^3J = 3.9 Hz, 1 H), 5.03 (dd, ^2J = 13.3 Hz, ^3J = 7.4 Hz, 1 H), 5.31 (dd, ^2J = 13.3 Hz, ^3J = 8.5 Hz, 1H).

Kinetic investigations in DMSO. The kinetic investigations were performed at 20 °C in dimethyl sulfoxide by using the stopped-flow technique. All reactions reported in this paper proceeded quantitatively, and the second-order rate constants k_2 (Table 3.3) were determined photometrically by monitoring the decrease of the absorbances of the colored electrophiles **1a–d** at their absorption maxima. The carbanions **2a–l** were either employed as potassium salts or were freshly generated by deprotonation of the corresponding CH acids with 1.05 equivalents of KO*t*Bu. In general, the carbanions were applied in high excess over the electrophiles (10 to 100 equivalents), giving rise to almost constant carbanion concentrations (10^{-3} to 10^{-4} mol L^{-1}) during the kinetic measurements. As a consequence, exponential decays of the concentrations of the colored electrophiles were observed (eq. 3.2). The first-order rate constants $k_{1\Psi}$ were obtained by least-squares fitting of the single-exponentials $A_t = A_0\exp(-k_{1\Psi}t) + C$ to the time-dependent absorbances A of the electrophiles.

$$-\mathrm{d}[1]/\mathrm{d}t = k_{1\Psi}[\mathbf{1}] \qquad (3.2)$$

Plots of $k_{1\Psi}$ versus the nucleophile concentrations $[\mathbf{2}]_0$ give straight lines with the slopes k_2 as shown for one example in Figure 3.2 and for all other kinetic experiments in the Experimental Section. In some cases the $k_{1\Psi}$ versus $[\mathbf{2}]_0$ do not go through the origin. Because all reactions proceed with quantitative formation of the adducts, we cannot presently explain this phenomenon. All second-order rate constants k_2 (L mol^{-1} s^{-1}) for the Michael additions are listed in Table 3.3.

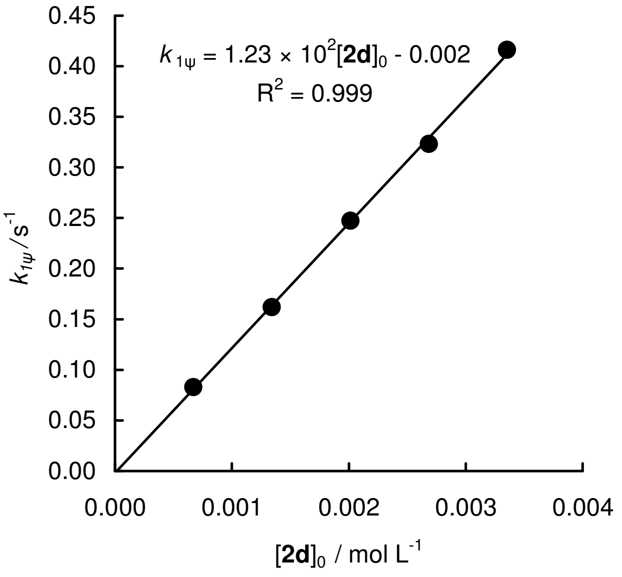
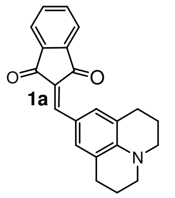
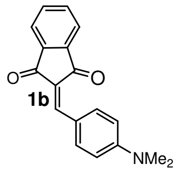
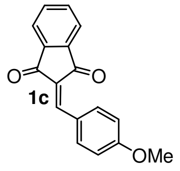
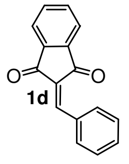


Figure 3.2. Determination of the second-order rate constant k_2 = 123 Lmol^{-1}s^{-1} for the reaction of **1a** with the potassium salt of acetylacetone **2d** in DMSO at 20 °C.

Table 3.3. Second-order rate constants k_2 for the reactions of 2-benzylidene-indan-1,3-diones **1a–d** with stabilized carbanions **2a–l** in DMSO at 20 °C.

Electrophile	C^-	Base	k_2 / $M^{-1}s^{-1}$
 **1a** E = -14.68[a] λ_{max} = 523 nm	**2b**	-	3.78×10^1
	2c	KO*t*Bu	3.73×10^1
	2d	-	1.23×10^2
	2e	-	9.87×10^2
	2f	KO*t*Bu	3.12×10^2
	2h	-	1.27×10^3
	2i	KO*t*Bu	1.86×10^3
	2j	KO*t*Bu	1.94×10^3
	2k	KO*t*Bu	3.31×10^3
	2l	KO*t*Bu	4.32×10^3
 **1b** E = -13.56[a] λ_{max} = 493 nm	**2b**	-	2.79×10^2
	2c	KO*t*Bu	2.08×10^2
	2d	-	8.86×10^2
	2e	-	6.25×10^3
	2f	KO*t*Bu	2.15×10^3
	2h	-	8.17×10^3
	2i	-	1.00×10^4
	2j	KO*t*Bu	6.86×10^3
	2k	KO*t*Bu	1.32×10^4
 **1c** E = -11.32[a] λ_{max} = 388 nm	**2b**	-	1.80×10^4
	2d	-	3.87×10^4
	2f	KO*t*Bu	5.69×10^4
	2g	KO*t*Bu	1.18×10^5
	2h	-	2.07×10^5
 **1d** E = -10.11[a] λ_{max} = 343 nm[b]	**2a**	-	1.06×10^3
	2b	-	1.06×10^5
	2d	-	2.72×10^5

[a] Derived from eq. 1. [b] λ_{max}(DMSO/H_2O 50/50, v/v) = 343 nm, from ref. [20].

Correlation analysis. If eq. 3.1 holds for the reactions of the 2-benzylidene-indan-1,3-diones **1a-d** with the carbanions **2a-l**, plots of (log k_2)/s vs N should be linear with slopes of 1. Figure 3.3 shows that this is approximately the case. The correlation lines drawn in Figure 3.3 result from a least-squares fit of calculated and experimental rate constants (minimization of $\Delta^2 = \Sigma(\log k_2 - s(N + E))^2$ with the nonlinear solver What's Best! by Lindo Systems Inc.) using the second-order rate constants k_2 given in Table 3.3 and the N and s parameters of **2a–l** listed in Table 3.1. Note that this procedure enforces slopes of 1 for plots of (log k_2)/s vs N because eq. 1 does not include an electrophile-specific slope parameter, in contrast to a more general equation which we have recently employed for S_N2 reactions.[21] The nitronate anions **2j** and **2l** deviate strongly from the correlations for the other nucleophiles and have not been included in the minimization process. According to eq. 3.1, the intercepts on the y-axis, which equal the negative intercepts on the x-axis (because of the enforced unity slopes) correspond to the electrophilicity parameters E.

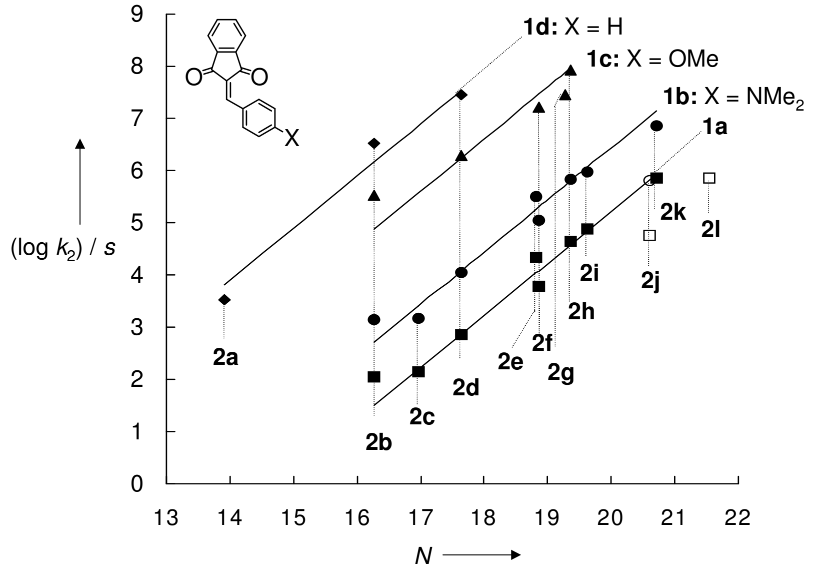


Figure 3.3. Correlation of (log k_2)/s with the corresponding nucleophilicity parameters N of the carbanions **2a-l** for the reactions of 2-benzylidene-indan-1,3-diones **1a-d** with carbanions **2a-l** in DMSO at 20 °C. Open symbols were not included for the calculation of the correlation lines.

While the correlations in Figure 3.3 are only of moderate quality, one can see that the relative electrophilicities of the 2-benzylidene-indan-1,3-diones **1** are almost independent of the nature of the carbanionic reaction partner. However, there seem to be some regularities of the deviations of some of the carbanions. Thus, the 2-nitroisopropyl anion

2j reacts approximately one order of magnitude more slowly with **1a** and **1b** than expected from its nucleophilicity parameters. Because **2j** is the only trisubstituted carbanion studied, this deviation may be a consequence of steric effects due to the fact that the 2-benzylidene-1,3-indandiones **1** are sterically more congested than the reference benzhydrylium ions. On the other hand, the dimedone anion **2b** is generally 2-times more reactive than expected, and it cannot be due to a smaller steric demand of this carbanion, because the analogously shaped anion of Meldrum's acid **2a** deviates slightly in the other direction.

An alternative illustration of this behavior is shown in Figure 3.4. When the rate constants of the reactions of the carbanions **2** with electrophiles are plotted against the *E* parameters given in refs. 2e and 5, all data points for the carbanions **2a**, **2d**, **2h**, **2i**, and **2l** follow good correlations, but in the case of the dimedone anion **2b**, the data points for the reactions with the 2-benzylidene-1,3-indandiones **1a** and **1b** are located above the correlation line for the reference electrophiles, which are depicted in the upper part of Figure 3.4.

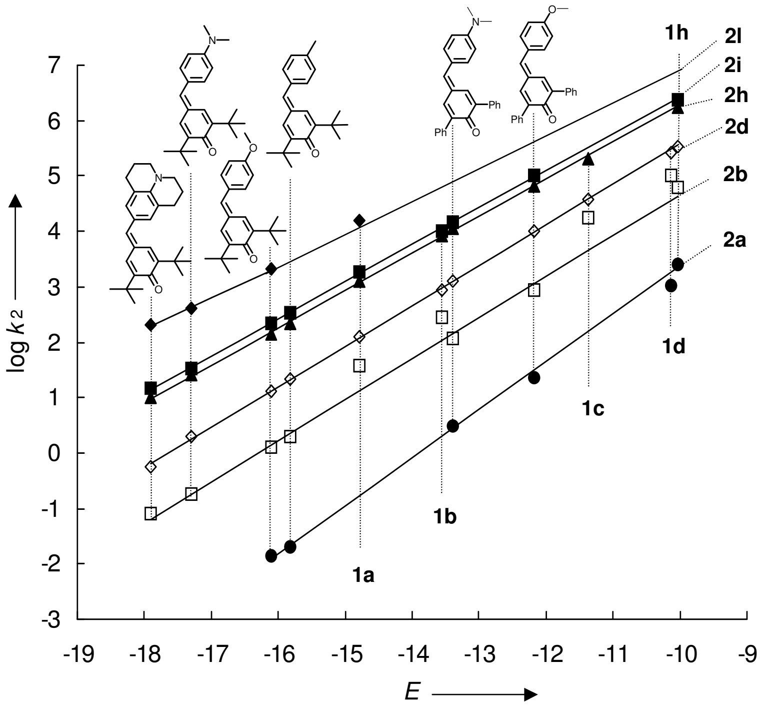


Figure 3.4. Rate constants for the reactions of carbanions with the 2-benzylidene-indan-1,3-diones **1a**-**d** and with reference electrophiles (quinone methides and benzhydrylium ions) in DMSO at 20 °C. The rate constants for the reactions with **1a**-**d** were not used for the construction of the regression lines.

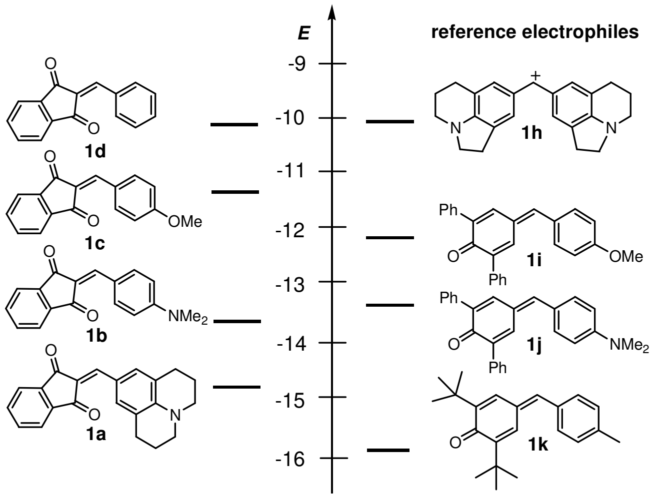


Figure 3.5. Comparison of the electrophilicity parameters *E* of 2-benzylidene-indan-1,3-diones **1a**-**d** with reference electrophiles **1h**-**k**.

According to Figure 3.5, the electrophilicities of the 2-benzylidene-indan-1,3-diones **1a**–**d** cover a range of more than four orders of magnitude and are located between **1h** the least reactive representative of our series of reference benzhydrylium ions and the most reactive representative of the series of di-*tert*-butyl substituted quinone methides (**1k**) that have been used as reference electrophile.[5] Donor substituents on the phenyl ring lower the electrophilicity, and Figure 3.6 shows a linear correlation with Hammett's σ_p^+ constants.[2e,22] For nucleophiles with $s = 0.7$, the slope corresponds to a Hammett reaction constant of $\rho = 1.6$. A comparison with the corresponding values for the structurally related benzylidenemalononitriles **1e**–**g** (**1e**: X = NMe_2; **1f**: X = OMe, **1g**: X = H) indicates that the electrophilicities of these two types of Michael acceptors are affected by para substituents X in a similar way.

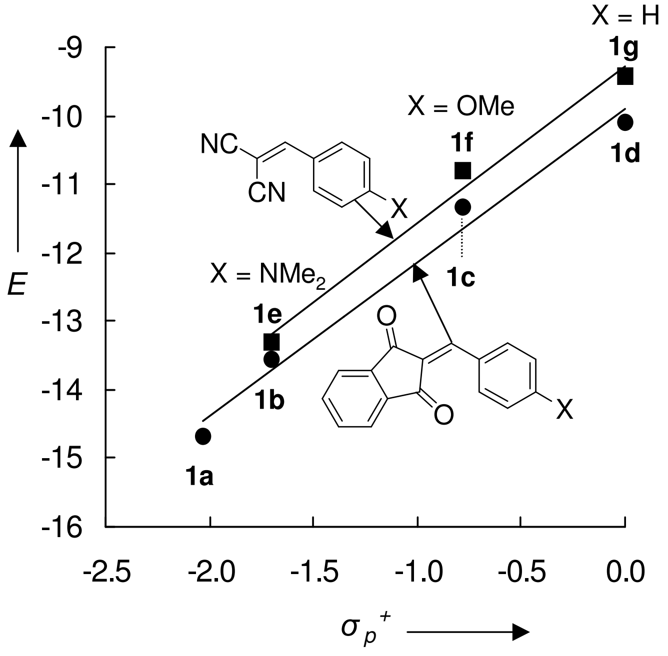


Figure 3.6. Correlation between the electrophilicity parameters E in DMSO of the benzylidene-indan-1,3-diones **1a–d** (circles, $E = 2.34\sigma_p^+ - 9.78$) and the benzylidenemalononitriles **1e–g** (squares, $E = 2.30\sigma_p^+ - 9.28$) with the Hammett σ_p^+-values for X. (σ_p^+ values were taken from ref. 22; σ_p^+ for **1a** was taken from ref. 2e).

However, the benzylidenemalononitriles **1e–g** are about 0.5 orders of magnitude more reactive than the analogously substituted 2-benzylidene-indan-1,3-diones **1b–d**. This reactivity order is surprising because indan-1,3-dione, (pK_a = 6.35–7.82 in DMSO/H_2O, v/v= 90/10 to 10/90)[23] is much more acidic than malononitrile (pK_a(DMSO) = 11.1, pK_a(H_2O) = 11.2).[24,25]

With the assumption that the stabilization of the carbanions obtained by the addition of nucleophiles to 2-benzylidene-1,3-indandiones **1a–d** and benzylidenemalononitriles **1e–g** corresponds to these pK_a values, one would expect that nucleophilic additions to **1a–d** have a higher thermodynamic driving force than the nucleophilic additions to the analogously substituted malononitriles **1e–g**. If ground-state effects are neglected, the higher reactivities of compounds **1e–g** compared to analogously substituted 2-benzylidene-1,3-indandiones **1b–d** must, therefore, be due to lower intrinsic barriers for the additions to **1e–g**. This conclusion has previously been drawn by Bernasconi from a related series of experiments.[20b,26]

In order to examine the applicability of the electrophilicity parameters E of the 2-benzylidene-indan-1,3-diones **1** for their reactions with other types of nucleophiles, we have compared experimental and calculated rate constants for the reactions of **1d** with amines (Table 3.4).

Table 3.4. Comparison of calculated and experimental second-order rate constants (in L mol^{-1} s^{-1}, DMSO, 20 °C) for the additions of amines to 2-benzylidene-indan-1,3-dione (**1d**).

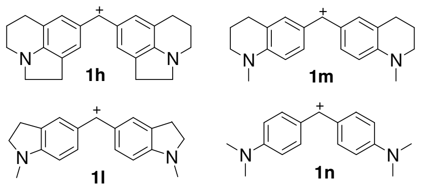
Nucleophile	N/s [a]	$k_{2,\text{calc}}$ (eq. 1)	$k_{2,\text{exp}}$
1 piperidine	17.19/0.71	1.02×10^5	3.01×10^5 [b] 2.10×10^5 [c]
2 morpholine	16.96/0.67	3.77×10^4	1.11×10^5 [b] 6.30×10^4 [c]
3 *n*-propylamine	15.70/0.64	3.63×10^3	9.34×10^3 [c,d]

[a] In DMSO, from ref. 4f, [b] In DMSO, this work, [c] In DMSO/H_2O (50/50 v,v), from ref. 16, [d] The experimental value $k_{2,\text{exp}}$ refers to the reaction of **1d** with *n*-butylamine.

Entries 1 and 2 in Table 3.4 indicate that the experimental second-order rate constants $k_{2,\text{exp}}$ for the addition of piperidine and morpholine to 2-benzylidene-indan-1,3-dione **1d** in DMSO are about three-times larger than the corresponding second-order rate constants $k_{2,\text{calc}}$ calculated by eq. 3.1. This agreement is within the previously postulated reliability of eq. 3.1.

Because the experimental second-order rate constants $k_{2,\text{exp}}$ in DMSO are only about 1.5- to 2-times larger than the corresponding $k_{2,\text{exp}}$ in DMSO/H_2O (50/50 v,v, Table 3.4, right column), we can also compare the calculated second-order rate constants derived from the nucleophilicity parameters N and s of amines in DMSO with Bernasconi's experimental values in DMSO/H_2O (50/50 v,v).[16] Entry 3 in Table 3.4 confirms this conclusion and shows that the calculated rate constant for the addition of *n*-propylamine to **1d** agrees with the experimental rate constant for the addition of *n*-butylamine to **1d** in DMSO/H_2O (50/50 v,v) within a factor of 3.

On the other hand, the close similarity of the rates of the reactions of **1d** with amines in DMSO and DMSO/H_2O (50/50 v,v) is surprising because it is well-known that amine nucleophilicities derived from reactions with benzhydrylium ions are considerably lower in water than in DMSO (Table 3.5).



Scheme 3.3. Benzhydrylium ions used for the comparison of the nucleophilicities of piperidine in different solvents.

In line with previously reported rate constants for reactions of amines with benzhydrylium ions in DMSO[4f] and water,[4a] we have now found that piperidine reacts 32–52 times faster with benzhydrylium ions **1h–n** (Scheme 3.3) in DMSO than in DMSO/H_2O (50/50 v,v) as shown in Table 3.5.

Table 3.5. Second-order rate constants k_2 for the reactions of piperidine with reference benzhydryliums Ar_2CH^+ in DMSO, DMSO/water (50/50 v,v), and water at 20 °C.

Ar_2CH^+	E^a	k_2 / L mol^{-1} s^{-1}		
		in DMSO[b]	in DMSO/H_2O (50/50)[c]	in H_2O[d]
1h	−10.04	1.13×10^5	2.92×10^3	3.05×10^3
1l	−8.76	6.67×10^5	2.06×10^4	9.01×10^3
1m	−8.22	2.51×10^6	4.78×10^4	2.64×10^4
1n	−7.02	-	3.15×10^5	6.09×10^4

[a] From ref. 2e. [b] From ref. 4f. [c] This work (for details see the Experimental Section). [d] From ref. 4a.

Therefore the question arises whether the similar rate of addition of piperidine and morpholine to the Michael acceptor **1d** in DMSO and DMSO/H_2O (50/50 v,v) is caused by an increase of the electrophilicity of **1d** in the presence of water.

In order to examine this question, we have compared the rates of addition of the malononitrile anion **2h** to **1a**, **1b**, and the benzhydrylium ion **1h** in DMSO and in aqueous solvents. The carbanion **2h** has been selected for this purpose because its solvation has been reported to be of similar magnitude in DMSO and water.[5,27] Table 3.6 shows that the reaction of **2h** with **1a** and **1b** is, indeed, 3–5 times faster in DMSO/H_2O (50/50 v,v) than in DMSO, whereas the reaction of this carbanion with the benzhydrylium ion **1h** is 12-times slower in water than in pure DMSO.

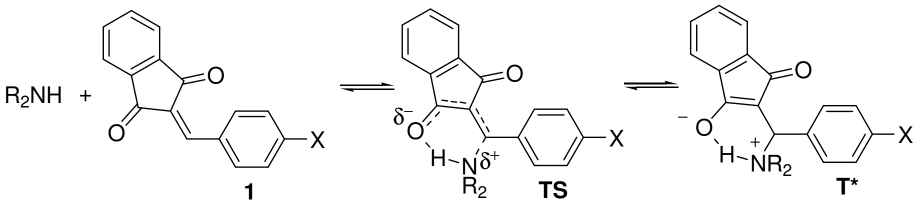
Table 3.6. Comparison of the second-order rate constants of the reactions of malononitrile anion **2h** with Michael acceptors **1a** and **1b** and the benzhydrylium ion **1h** in different solvents at 20°C.

	k_2 / L mol^{-1} s^{-1}		
Electrophile	in DMSO	in DMSO/H_2O (50/50)	in H_2O
1a	1.27×10^3	6.39×10^3	-
1b	8.17×10^3	2.28×10^4	-
$(lil)_2CH^+$	$1.76 \times 10^{6,\,a}$	-	$1.50 \times 10^{5,\,b}$

[a] From ref. 5. [b] From ref. 27.

Thus, the presence of 50% water in DMSO appears to increase the electrophilicities of the 2-benzylidene-1,3-indandiones **1a**,**b** (compared with benzhydrylium ion **1h** as a reference) by approximately one order of magnitude. The observed similar reactivities of amines towards **1** in DMSO and DMSO/H_2O (50/50 v,v) can therefore be explained by a compensation effect, *i.e.*, hydration of amines reduces their nucleophilicities by a similar amount as hydration increases the electrophilicities of the Michael acceptors **1**.

A more quantitative analysis of these data appears problematic, because Bernasconi[16,28] and Lee[29] have previously suggested that the transition states of the amine additions may also be stabilized by O-H interactions as depicted in Scheme 3.4. Because the additions of carbanions to **1a–d**, which are described in Table 3.3, cannot profit from such O-H interactions, we do not have evidence for this type of stabilization.



Scheme 3.4. Addition of an amine nucleophile to 2-benzylidene-1,3-indandione 1 (TS: transition state, T*: zwitterionic intermediate).

Conclusions

The 2-benzylidene-indan-1,3-diones **1a–d** have been shown to have electrophilicity parameters in the range of $-10 > E > -15$. With these data and the previously published nucleophilicity parameters of carbanions and amines,[30] it has become possible to calculate the rates of additions of these nucleophiles to 2-benzylidene-indan-1,3-diones **1a–d** with an accuracy of better than a factor of 3 in dimethyl sulfoxide solution. Because hydration appears to increase the electrophilicities of **1a–d** much more than it affects the electrophilicities of the previously used reference electrophiles (benzhydrylium ions and quinone methides) we recommend to use the E parameters of 2-benzylidene-1-3-indandiones **1a–d** reported in this work only for predictions of rate constants in aprotic solvents.

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– Experimental Section –

Electrophilicity Parameters for 2-Benzylidene-indan-1,3-diones – a systematic extension of the benzhydrylium based electrophilicity scale

S. T. A. Berger, F. H. Seeliger, F. Hofbauer, H. Mayr, *Org. Biomol. Chem.* **2007**, **DOI:** 10.1039/b708025e.

Table of Contents

1. Materials. DMSO (content of $H_2O < 50$ ppm) was used. Stock solutions of KO*t*Bu were prepared by dissolving the corresponding alkoxide salt in DMSO under a nitrogen atmosphere.

The 2-benzylidene-indan-1,3-diones **1a**-**d** were prepared according to a literature procedure:[S1] A solution of indan-1,3-dione (10 mmol) and the corresponding benzaldehyde (10 mmol) in absolute ethanol was treated with a few drops of piperidine and refluxed for 1h, until the product precipitated. It was filtered off and purified by repeated recrystallization from ethanol given rise to the products **1a**-**d** in about 80-90% yield. ^1H and ^{13}C NMR data were found to be in agreement with the literature values.

2. Instruments

^1H and ^{13}C NMR spectra were recorded on a Bruker AMX 400 (400 MHz, 100 MHz) and on a Bruker ARX 300 (300 MHz, 75 MHz) and a Varian Mercury 200 (200 MHz). Chemical shifts are expressed in ppm and refer to d_6-DMSO ($\delta_H = 2.49$ ppm, $\delta_c = 39.7$ ppm) or to $CDCl_3$ ($\delta_H = 7.26$ ppm, $\delta_c = 77.00$ ppm). The coupling constants are in Hz. Abbreviations used are s (singlet), d (doublet), t (triplet), q (quartet), quint (quintet) and m (multiplet).

3. Products of the Reactions of 2-Benzylidene-indan-1,3-dione (1) with Carbanions (2)

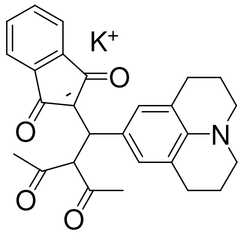
Typical Procedure. If nothing else is quoted, the reactions were performed as NMR-experiments at room temperature (ca. 20 °C). Thus 1 equiv. of the carbanion **2** was added to 1 equiv. of 2-benzylidene-indan-1,3-dione **1** in d_6-DMSO (1 mL). For a better intermixture of the compounds the NMR tube was put into a ultrasound bath.

In all other cases the conditions for the reactions were not optimized for high yields and are described subsequently.

The experiments have been performed by F. H. Seeliger; the evaluations have been done by myself.

[S1] R. K. Behera and A. Nayak, *Indian J. Chem. B,* 1976, **14,** 223-224.

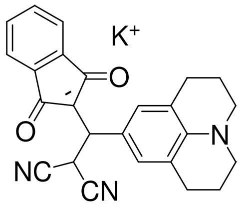
Reaction of 1a with 2d.



3ad$^-$

3ad$^-$: ^{1}H NMR (d$_6$-DMSO, 200 MHz): δ = 1.80 (quint, J = 5.0 Hz, 4 H), 1.91 (s, 3 H), 2.02 (s, 3H), 2.57 (t, J = 6.4 Hz, 4 H), 2.96 (t, J = 5.2 Hz, 4 H), 4.16 (d, J = 12.4 Hz, 1 H), 5.23 (d, J = 12.4 Hz, 1 H), 6.75 (s, 2 H), 6.88 (dd, ^3J = 5.0 Hz, ^4J = 3.0 Hz, 2H), 7.08 (dd, ^3J = 5.0 Hz, ^4J = 3.0 Hz, 2H).

Reaction of 1a with 2h.

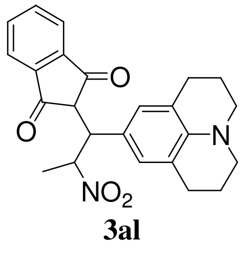


3ah$^-$

3ah$^-$: ^{1}H NMR (d$_6$-DMSO, 200 MHz): δ = 1.82 (quint, J = 5.2 Hz, 4 H), 2.60 (t, J = 6.4 Hz, 4 H), 3.02 (t, J = 5.4 Hz, 4 H), 3.98 (d, J = 11.6 Hz, 1 H), 5.76 (d, J = 11.6 Hz, 1 H), 6.82 (s, 2 H), 7.01 (dd, ^3J = 5.1 Hz, ^4J = 3.0 Hz, 2 H), 7.18 (dd, ^3J = 5.1 Hz, ^4J = 3.0 Hz, 2 H).

Reaction of 1a with 2l.

At room temperature (ca. 20 °C) nitroethane **2l-H** (90 µL, 1.3 mmol) was added to a stirred solution of freshly sublimated KO*t*Bu (137 mg, 1.22 mmol) in DMSO (5 mL). After 2 min of stirring, **1a** was added (304 mg, 0.924 mmol) to give a red clear solution. After 10 min, HCl conc. (1.5 mL) was added, and the mixture was poured into water (50 mL), giving rise to a purple precipitate. The solvent was removed, and the crude product was dried in the vacuum. Recrystallization from ethanol gave **3al** (227 mg, 61%) which was obtained as a mixture of diastereomers in the ratio 2:1.



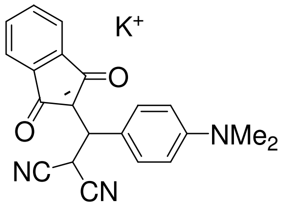
3al

3al: ^{1}H NMR (CDCl$_3$, 300 MHz): major product: δ = 1.72 – 1.86 (m, 7 H), 2.39 – 2.62 (m, 4 H), 2.92 (t, J = 6.0 Hz, 4 H), 3.34 (d, J = 4.1 Hz, 1 H), 3.88 (dd, ^2J = 11.4 Hz, ^3J = 4.1 Hz, 1 H), 5.63 – 5.75 (m, 1 H), 6.43 (s, 2 H), 7.72 – 7.91 (m, 4 H); minor product: δ = 1.39 (d, J = 6.9 Hz, 3 H), 1.72 – 1.86 (m, 4 H), 2.39 – 2.62 (m, 4 H), 3.01 (t, J = 5.7 Hz, 4 H), 3.20 (d, J = 3.6 Hz, 1 H), 3.79 (dd, J = 3.6 Hz, J = 11.4 Hz, 1 H), 5.63 – 5.75 (m, 1 H), 6.49 (s, 2 H), 7.72 – 7.91 (m, 4 H); ^{13}C NMR (CDCl$_3$, 75 MHz): major product:

δ = 19.1 (q), 21.8 (t), 27.4 (t), 48.1 (d), 49.7 (t), 54.7 (d), 85.3 (d), 121.2 (s), 121.5 (s), 122.9 (d), 123.2 (d), 127.1 (d), 135.4 (d), 142.7 (s), 198.1 (s), 199.9

(s). minor product: δ = 19.3 (q), 21.6 (t), 27.5 (t), 47.9 (d), 49.7 (t), 55.6 (d), 84.0 (d), 121.5 (s), 121.6 (s), 122.8 (d), 123.3 (d), 127.6 (d), 135.6 (d), 142.3 (s), 198.0 (s), 199.4.

Reaction of 1b with 2h.

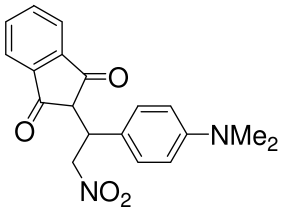


3bh$^-$

3bh: ^{1}H NMR (d_6-DMSO, 400 MHz): δ = 2.85 (s, 6 H, NMe_2), 4.17 (d, J = 11.3 Hz, 1 H), 5.81 (d, J = 11.3 Hz, 1 H), 6.62 (d, J = 8.8 Hz, 2 H), 7.05 (dd, ^{3}J = 5.0 Hz, ^{4}J = 3.0 Hz, 2 H), 7.18 (dd, ^{3}J = 5.1 Hz, ^{4}J = 3.0 Hz, 2 H), 7.35 (d, J = 8.8 Hz, 2 H). ^{13}C NMR (d_6-DMSO, 100 MHz): δ = 26.4, 39.9, 42.2, 101.6, 111.9, 114.6, 116.3, 128.4, 128.5, 129.5, 140.1, 149.2, 187.6.

Reaction of 1b with 2k.

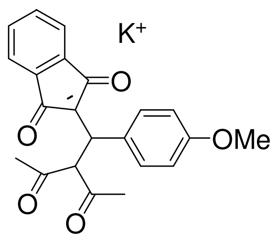
At room temperature (ca. 20 °C) nitromethane **2k-H** (80 µL, 1.5 mmol) was added to a stirred solution of freshly sublimated KO*t*Bu (167 mg ,1.49 mmol) in DMSO (5 mL). After addition of **1b** (336 mg, 1.21 mmol) the mixture was stirred for 10 min giving rise to a clear red solution. The mixture was diluted with conc. HCl (1.5 mL) and water (50 mL). The yellow suspension was extracted with EtOAc (3 × 50 mL), and the organic layer was separated and dried with $MgSO_4$. The solvent was removed, and the crude orange product was dried in the vacuum. Recrystallization from ethanol yielded **3bk** (325 mg, 79%) which was obtained as an enantiomeric mixture.



3bk

3bk: ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 2.81 (s, 6 H), 3.39 (d, J = 3.8 Hz, 1 H), 4.33 (dt, ^{3}J = 7.7 Hz, ^{3}J = 3.9 Hz, 1 H), 5.03 (dd, ^{2}J = 13.3 Hz, ^{3}J = 7.4 Hz, 1 H), 5.31 (dd, ^{2}J = 13.3 Hz, ^{3}J = 8.5 Hz, 1H), 6.46 (d, J = 9.0 Hz, 2 H), 7.00 (d, J = 9.0 Hz, 2 H), 7.71 – 7.91 (m, 4 H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 40.4 (d), 41.7 (q), 55.8 (d), 77.0 (t), 112.6 (d), 122.6 (d), 123.3 (d), 123.5 (d), 129.4 (d), 135.9 (d), 135.9 (d), 142.7 (s), 150.2 (s), 198.1 (s), 199.7 (s).

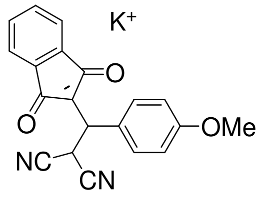
Reaction of 1c with 2d.



3cd$^-$

3cd$^-$: ^{1}H NMR (d_6-DMSO, 200 MHz): δ = 1.87 (s, 3 H), 2.07 (s, 3 H), 3.66 (s, 3 H, OMe), 4.34 (d, J = 12.2 Hz, 1 H), 5.28 (d, J = 12.2 Hz, 1 H), 6.71 (d, J = 8.4 Hz, 2 H), 6.92 (dd, ^3J = 4.8 Hz, ^4J = 3.0 Hz, 2 H), 7.11 (dd, ^3J = 4.8 Hz, ^4J = 3.0 Hz, 2 H), 7.37 (d, J = 8.6 Hz, 2 H).

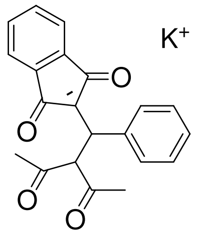
Reaction of 1c with 2h.



3ch$^-$

3ch$^-$: ^{1}H NMR (d_6-DMSO, 400 MHz): δ = 3.72 (s, 3 H, OMe), 4.24 (d, J = 11.6 Hz, 1 H), 5.85 (d, J = 11.2 Hz, 1 H), 6.83 (d, J = 8.8 Hz, 2 H), 7.06 (dd, ^3J = 5.1 Hz, ^4J = 3.0 Hz, 2 H), 7.19 (dd, ^3J = 5.1 Hz, ^4J = 3.0 Hz, 2 H), 7.47 (d, J = 8.8 Hz, 2 H). ^{13}C NMR (d_6-DMSO, 100 MHz): δ = 26.3, 42.1, 54.7, 101.2, 113.3, 114.5, 116.4, 128.6, 128.9, 133.9, 140.0, 157.9, 187.6.

Reaction of 1d with 2d.



3dd$^-$

3dd$^-$: ^{1}H NMR (d_6-DMSO, 200 MHz): δ = 1.88 (s, 3 H), 2.08 (s, 3 H), 4.40 (d, J = 12.3 Hz, 1 H), 5.35 (d, J = 12.3 Hz, 1 H), 6.91 – 7.46 (m, 9 H). ^{13}C NMR (d_6-DMSO, 100 MHz): δ = 28.3, 30.0, 40.8, 70.1, 104.2, 115.7, 124.6, 127.2, 127.8, 128.1, 140.5, 145.1, 187.5, 203.2, 204.1.

4. Reactivities of 2-Benzylidene-indan-1,3-diones in DMSO

4.1 General

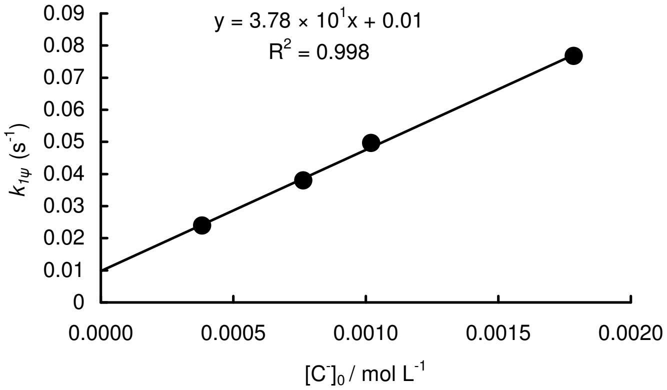
The general method for the kinetic investigations is described in the experimental part of chapter 3. The temperature of the solutions during all kinetic studies was kept constant (20 ± 0.1°C) by using a circulating bath thermostat. DMSO with a content of H_2O < 50 ppm was used for the kinetic experiments.

For the evaluation of the kinetic experiments the stopped-flow spectrophotometer systems Hi-Tech SF-61DX2 or Applied Photophysics SX.18MV-R were used. Rate constants k_{obs} (s^{-1}) were obtained by fitting the single exponential $A_t = A_0\exp(-k_{\text{obs}}t) + C$ to the observed time-dependent carbocation absorbance (averaged from at least 3 kinetic runs for each nucleophile concentration). For the stopped-flow experiments 2 stock solutions were used: A solution of the 2-benzylidene-indan-1,3-dione **1a**-**d** in DMSO and a solution of the carbanion **2**, generated by the deprotonation of the CH acidic compound with 1.05 equivalents of KO*t*Bu in DMSO, respectively, or by adding the corresponding isolated potassium salt into a solution of DMSO.

4.2 Kinetics of the Reactions of Carbanions with 1a

Reaction of **1a** with dimedone **2b** (stopped-flow, 490 nm, 20 °C)

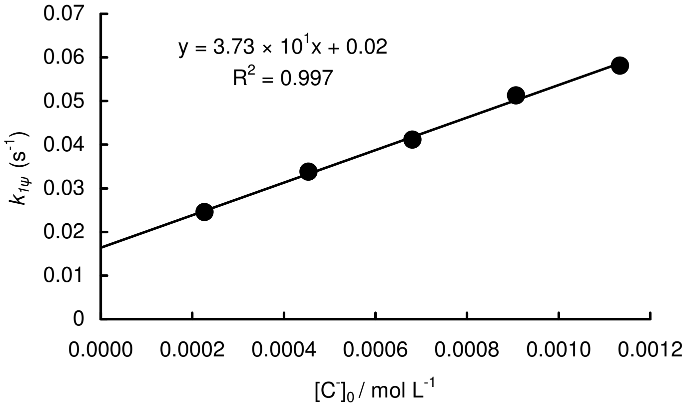
$[E]_0$ / mol L^{-1}	$[C^-]_0$ / mol L^{-1}	$k_{1\psi}$ / s^{-1}
1.74×10^{-5}	3.82×10^{-4}	2.39×10^{-2}
1.74×10^{-5}	7.65×10^{-4}	3.80×10^{-2}
1.74×10^{-5}	1.02×10^{-3}	4.96×10^{-2}
1.74×10^{-5}	1.78×10^{-3}	7.67×10^{-2}



$k_2 = 3.78 \times 10^1$ $Lmol^{-1}s^{-1}$

Reaction of **1a** with 4-cyano-benzylnitronate **2c** (stopped-flow, 520 nm, 20 °C)

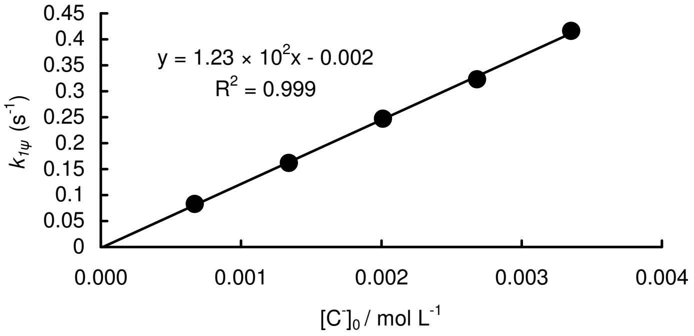
$[E]_0$ / mol L^{-1}	$[C^-]_0$ / mol L^{-1}	$k_{1\psi}$ / s^{-1}
3.64×10^{-5}	2.27×10^{-4}	2.45×10^{-2}
3.64×10^{-5}	4.54×10^{-4}	3.38×10^{-2}
3.64×10^{-5}	6.81×10^{-4}	4.11×10^{-2}
3.64×10^{-5}	9.08×10^{-4}	5.13×10^{-2}
3.64×10^{-5}	1.13×10^{-3}	5.81×10^{-2}



$k_2 = 3.73 \times 10^1$ $Lmol^{-1}s^{-1}$

Reaction of **1a** with the potassium salt of acetylacetone **2d** (stopped-flow, 500 nm, 20 °C)

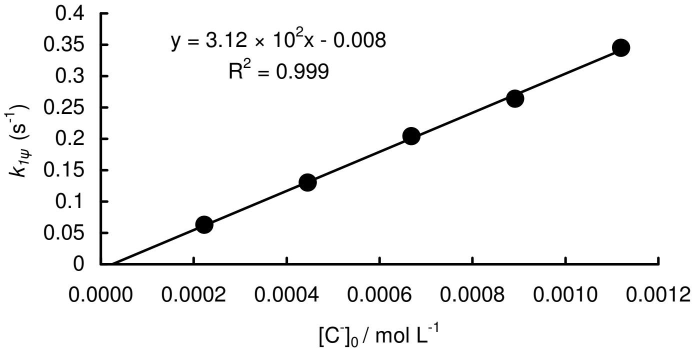
$[E]_0$ / mol L^{-1}	$[C^-]_0$ / mol L^{-1}	$k_{1\psi}$ / s^{-1}
4.14×10^{-5}	6.71×10^{-4}	8.34×10^{-2}
4.14×10^{-5}	1.34×10^{-3}	1.62×10^{-1}
4.14×10^{-5}	2.01×10^{-3}	2.48×10^{-1}
4.14×10^{-5}	2.68×10^{-3}	3.23×10^{-1}
4.14×10^{-5}	3.36×10^{-3}	4.17×10^{-1}



$k_2 = 1.23 \times 10^2$ Lmol^{-1}s^{-1}

Reaction of **1a** with benzyltriflinate **2f** (stopped-flow, 500 nm, 20 °C)

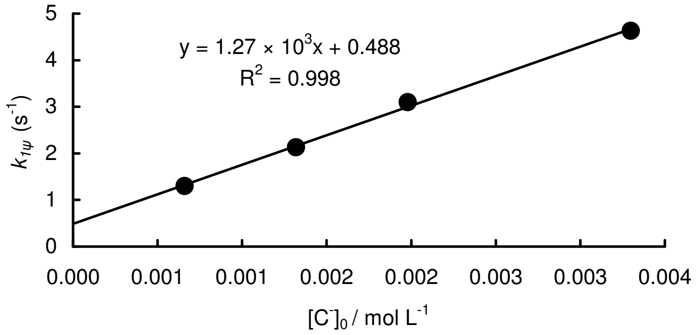
$[E]_0$ / mol L^{-1}	$[C^-]_0$ / mol L^{-1}	$k_{1\psi}$ / s^{-1}
2.74×10^{-5}	2.23×10^{-4}	6.29×10^{-2}
2.74×10^{-5}	4.46×10^{-4}	1.30×10^{-1}
2.74×10^{-5}	6.69×10^{-4}	2.04×10^{-1}
2.74×10^{-5}	8.92×10^{-4}	2.64×10^{-1}
2.74×10^{-5}	1.12×10^{-3}	3.45×10^{-1}



$k_2 = 3.12 \times 10^2$ Lmol^{-1}s^{-1}

Reaction of **1a** with the potassium salt of malononitrile **2h** (stopped-flow, 500 nm, 20 °C)

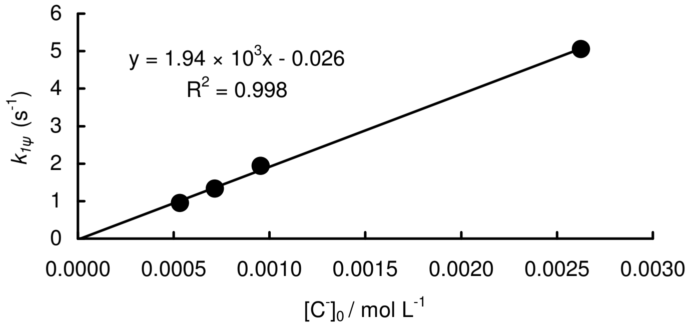
$[E]_0$ / mol L^{-1}	$[C^-]_0$ / mol L^{-1}	$k_{1\psi}$ / s^{-1}
4.14×10^{-5}	1.32×10^{-3}	2.13
4.14×10^{-5}	1.98×10^{-3}	3.10
4.14×10^{-5}	2.64×10^{-3}	4.29
4.14×10^{-5}	3.30×10^{-3}	4.63



$k_2 = 1.27 \times 10^3$ $Lmol^{-1}s^{-1}$

Reaction of **1a** with 2-nitropropane **2j** (stopped-flow, 500 nm, 20 °C)

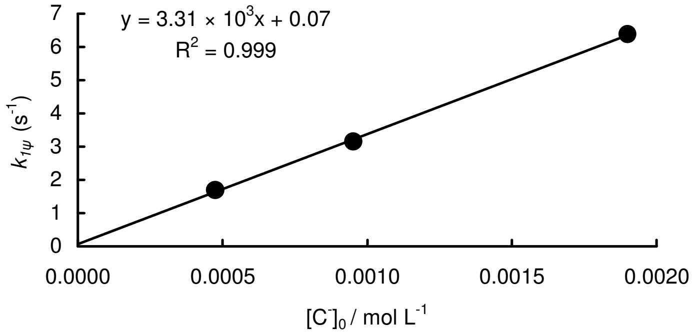
$[E]_0$ / mol L^{-1}	$[C^-]_0$ / mol L^{-1}	$k_{1\psi}$ / s^{-1}
3.03×10^{-5}	5.33×10^{-4}	9.58×10^{-1}
3.03×10^{-5}	7.16×10^{-4}	1.33
3.03×10^{-5}	9.55×10^{-4}	1.94
3.03×10^{-5}	2.63×10^{-3}	5.05



$k_2 = 1.94 \times 10^3$ $Lmol^{-1}s^{-1}$

Reaction of **1a** with nitromethane **2k** (stopped-flow, 500 nm, 20 °C)

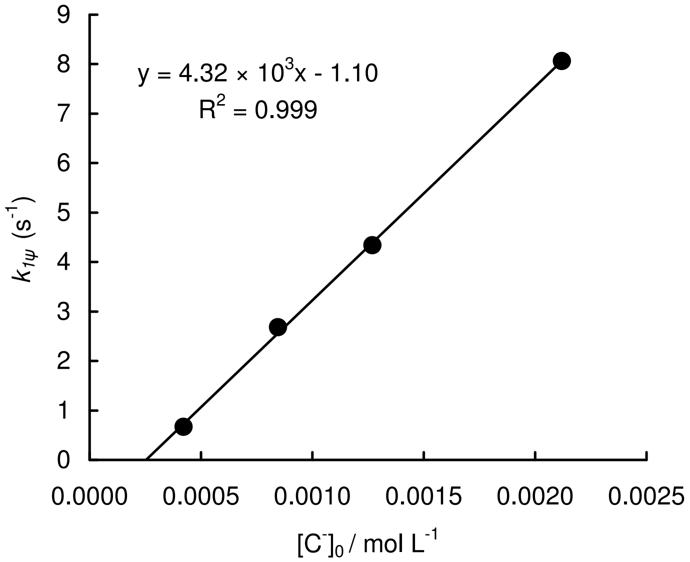
$[E]_0$ / mol L^{-1}	$[C^-]_0$ / mol L^{-1}	$k_{1\psi}$ / s^{-1}
1.75×10^{-5}	4.76×10^{-4}	1.69
1.75×10^{-5}	9.52×10^{-4}	3.15
1.75×10^{-5}	1.90×10^{-3}	6.38



$k_2 = 3.31 \times 10^3$ Lmol^{-1}s^{-1}

Reaction of **1a** with nitroethane **2l** (stopped-flow, 500 nm, 20 °C)

$[E]_0$ / mol L^{-1}	$[C^-]_0$ / mol L^{-1}	$k_{1\psi}$ / s^{-1}
3.64×10^{-5}	4.23×10^{-4}	6.66×10^{-1}
3.64×10^{-5}	8.46×10^{-4}	2.68
3.64×10^{-5}	1.27×10^{-3}	4.34
3.64×10^{-5}	2.12×10^{-3}	8.06

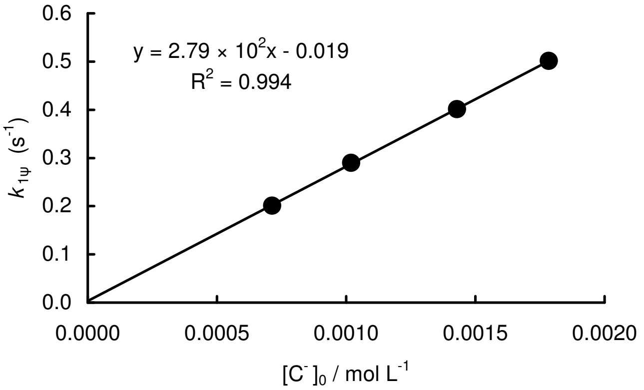


$k_2 = 4.32 \times 10^3$ Lmol^{-1}s^{-1}

4.3 Kinetics of the Reactions of Carbanions with **1b**

Reaction of **1b** with the potassium salt of dimedone **2b** (stopped-flow, 490 nm, 20 °C)

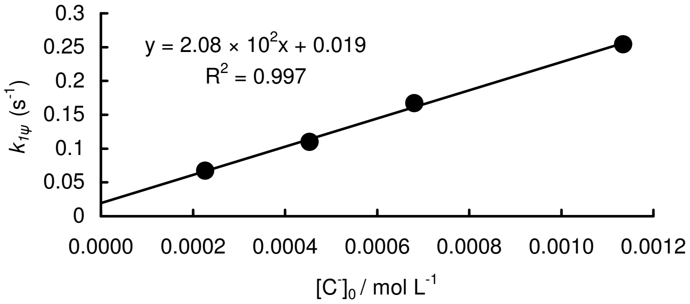
$[E]_0$ / mol L^{-1}	$[C^-]_0$ / mol L^{-1}	$k_{1\psi}$ / s^{-1}
1.80×10^{-5}	7.14×10^{-4}	2.01×10^{-1}
1.80×10^{-5}	1.02×10^{-3}	2.89×10^{-1}
1.80×10^{-5}	1.43×10^{-3}	4.02×10^{-1}
1.80×10^{-5}	1.79×10^{-3}	5.01×10^{-1}



$k_2 = 2.79 \times 10^2$ $Lmol^{-1}s^{-1}$

Reaction of **1b** with 4-cyano-benzylnitronate **2c** (stopped-flow, 520 nm, 20 °C)

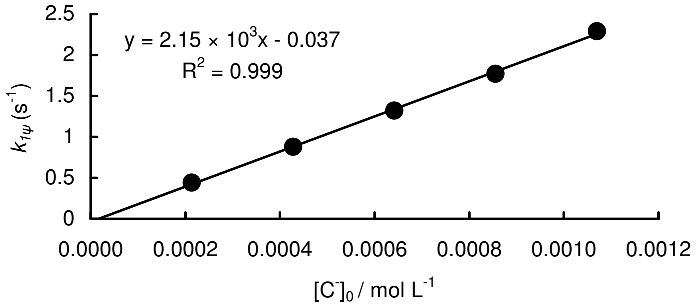
$[E]_0$ / mol L^{-1}	$[C^-]_0$ / mol L^{-1}	$k_{1\psi}$ / s^{-1}
2.89×10^{-5}	2.27×10^{-4}	6.70×10^{-2}
2.89×10^{-5}	4.54×10^{-4}	1.11×10^{-1}
2.89×10^{-5}	6.81×10^{-4}	1.67×10^{-1}
2.89×10^{-5}	1.13×10^{-3}	2.54×10^{-1}



$k_2 = 2.08 \times 10^2$ $Lmol^{-1}s^{-1}$

Reaction of **1b** with benzyltriflinate **2f** (stopped-flow, 500 nm, 20 °C)

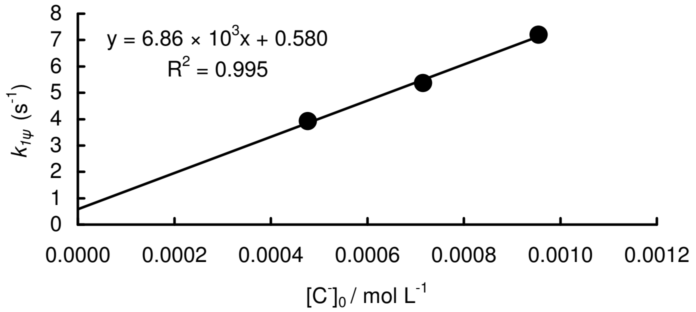
$[E]_0$ / mol L^{-1}	$[C^-]_0$ / mol L^{-1}	$k_{1\psi}$ / s^{-1}
3.64×10^{-5}	2.14×10^{-4}	4.36×10^{-1}
3.64×10^{-5}	4.28×10^{-4}	8.81×10^{-1}
3.64×10^{-5}	6.42×10^{-4}	1.32
3.64×10^{-5}	8.56×10^{-4}	1.77
3.64×10^{-5}	1.07×10^{-3}	2.29



$k_2 = 2.15 \times 10^3$ $Lmol^{-1}s^{-1}$

Reaction of **1b** with 2-nitropropane **2j** (stopped-flow, 500 nm, 20 °C)

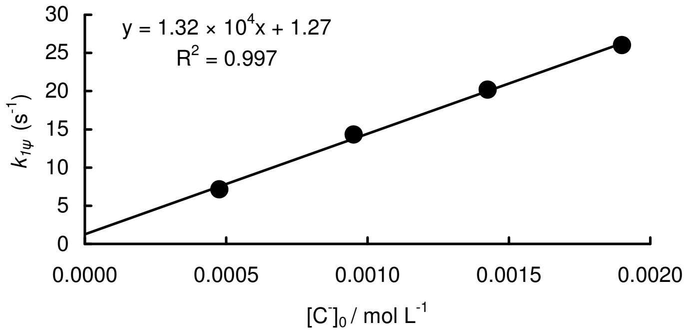
$[E]_0$ / mol L^{-1}	$[C^-]_0$ / mol L^{-1}	$k_{1\psi}$ / s^{-1}
3.69×10^{-5}	4.77×10^{-4}	3.92
3.69×10^{-5}	7.16×10^{-4}	5.36
3.69×10^{-5}	9.55×10^{-4}	7.22



$k_2 = 6.86 \times 10^3$ $Lmol^{-1}s^{-1}$

Reaction of **1b** with nitromethane **2k** (stopped-flow, 500 nm, 20 °C)

$[E]_0$ / mol L^{-1}	$[C^-]_0$ / mol L^{-1}	$k_{1\psi}$ / s^{-1}
1.75×10^{-5}	4.76×10^{-4}	7.14
1.75×10^{-5}	9.52×10^{-4}	1.43×10^{1}
1.75×10^{-5}	1.43×10^{-3}	2.02×10^{1}
1.75×10^{-5}	1.90×10^{-3}	2.60×10^{1}

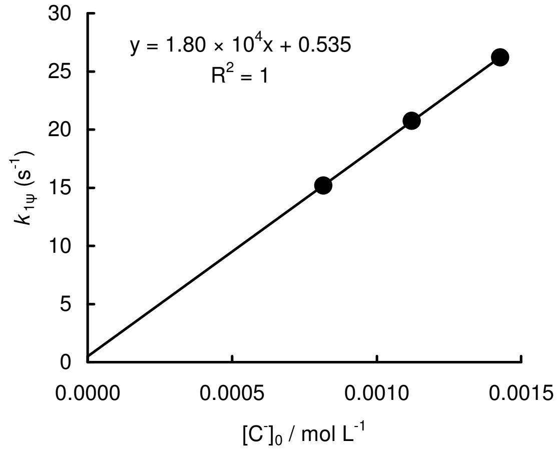


$k_2 = 1.32 \times 10^{4}$ L$mol^{-1}s^{-1}$

4.4 Kinetics of the Reactions of Carbanions with **1c**

Reaction of **1c** with the potassium salt of dimedone **2b** (stopped-flow, 390 nm, 20 °C)

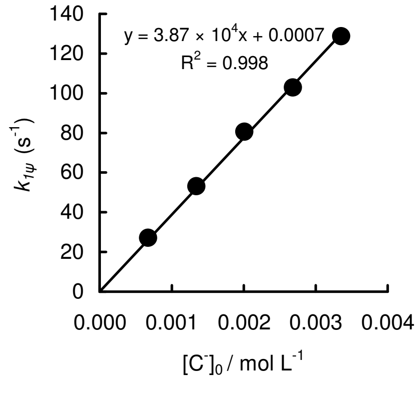
$[E]_0$ / mol L^{-1}	$[C^-]_0$ / mol L^{-1}	$k_{1\psi}$ / s^{-1}
1.79×10^{-5}	8.16×10^{-4}	1.52×10^{1}
1.79×10^{-5}	1.12×10^{-3}	2.08×10^{1}
1.79×10^{-5}	1.43×10^{-3}	2.62×10^{1}



$k_2 = 1.80 \times 10^4$ $Lmol^{-1}s^{-1}$

Reaction of **1c** with the potassium salt of acetylacetone **2d** (stopped-flow, 380 nm, 20 °C)

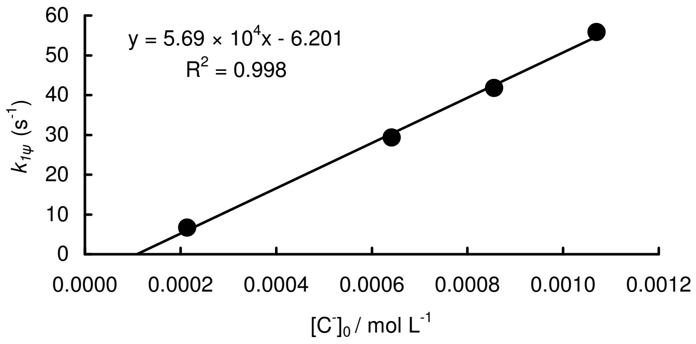
$[E]_0$ / mol L^{-1}	$[C^-]_0$ / mol L^{-1}	$k_{1\psi}$ / s^{-1}
5.16×10^{-5}	6.71×10^{-4}	2.71×10^{1}
5.16×10^{-5}	1.34×10^{-3}	5.31×10^{1}
5.16×10^{-5}	2.01×10^{-3}	8.06×10^{1}
5.16×10^{-5}	2.68×10^{-3}	1.03×10^{2}
5.16×10^{-5}	3.36×10^{-3}	1.29×10^{2}



$k_2 = 3.87 \times 10^4$ $Lmol^{-1}s^{-1}$

Reaction of **1c** with benzyltriflinate **2f** (stopped-flow, 400 nm, 20 °C)

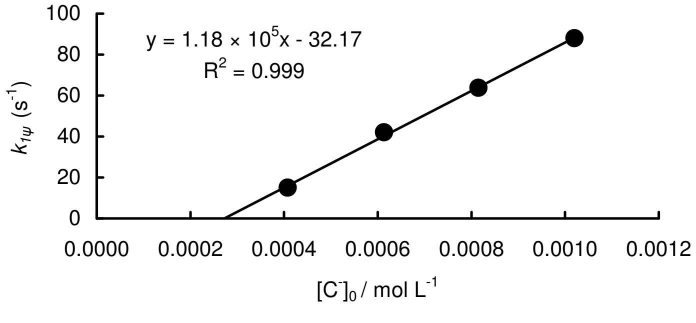
$[E]_0$ / mol L^{-1}	$[C^-]_0$ / mol L^{-1}	$k_{1\psi}$ / s^{-1}
3.78×10^{-5}	2.14×10^{-4}	6.69
3.78×10^{-5}	6.42×10^{-4}	2.93×10^{1}
3.78×10^{-5}	8.56×10^{-4}	4.18×10^{1}
3.78×10^{-5}	1.07×10^{-3}	5.58×10^{1}



$k_2 = 5.69 \times 10^4$ Lmol^{-1}s^{-1}

Reaction of **1c** with 4-methylbenzyltriflinate **2g** (stopped-flow, 400 nm, 20 °C)

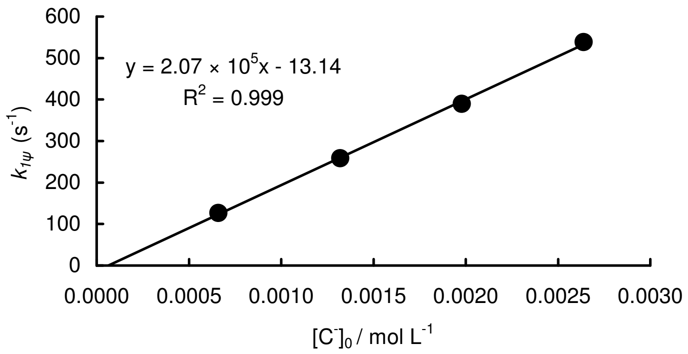
$[E]_0$ / mol L^{-1}	$[C^-]_0$ / mol L^{-1}	$k_{1\psi}$ / s^{-1}
3.78×10^{-5}	4.08×10^{-4}	1.50×10^{1}
3.78×10^{-5}	6.12×10^{-4}	4.20×10^{1}
3.78×10^{-5}	8.16×10^{-4}	6.38×10^{1}
3.78×10^{-5}	1.02×10^{-3}	8.79×10^{1}



$k_2 = 1.18 \times 10^5$ Lmol^{-1}s^{-1}

Reaction of **1c** with the potassium salt of malononitrile **2h** (stopped-flow, 380 nm, 20 °C)

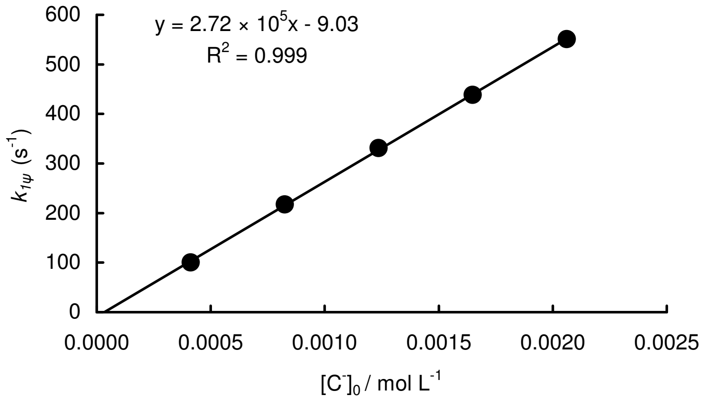
$[E]_0$ / mol L^{-1}	$[C^-]_0$ / mol L^{-1}	$k_{1\psi}$ / s^{-1}
5.16×10^{-5}	6.60×10^{-4}	1.27×10^{2}
5.16×10^{-5}	1.32×10^{-3}	2.59×10^{2}
5.16×10^{-5}	1.98×10^{-3}	3.89×10^{2}
5.16×10^{-5}	2.64×10^{-3}	5.38×10^{2}



$k_2 = 2.07 \times 10^5$ $Lmol^{-1}s^{-1}$

Reaction of **1d** with the potassium salt of acetylacetone **2d** (stopped-flow, 364 nm, 20 °C)

$[E]_0$ / mol L^{-1}	$[C^-]_0$ / mol L^{-1}	$k_{1\psi}$ / s^{-1}
2.13×10^{-5}	4.12×10^{-4}	1.00×10^{2}
2.13×10^{-5}	8.25×10^{-4}	2.17×10^{2}
2.13×10^{-5}	1.24×10^{-3}	3.31×10^{2}
2.13×10^{-5}	1.65×10^{-3}	4.38×10^{2}
2.13×10^{-5}	2.06×10^{-3}	5.51×10^{2}

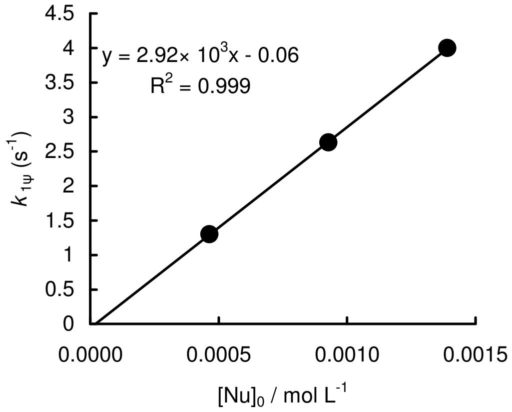


$k_2 = 2.72 \times 10^5$ $Lmol^{-1}s^{-1}$

4.6 Kinetics of the Reactions of Ar_2CH^+ with Piperidine in DMSO/water (50/50 v,v)

Reaction of $(lil)_2CH^+$ (**1h**) with piperidine (stopped-flow, 620 nm, 20 °C)

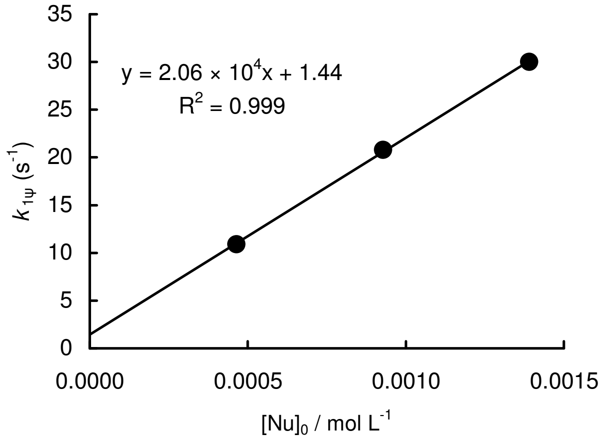
$[E]_0$ / mol L^{-1}	$[Nu]_0$ / mol L^{-1}	$k_{1\psi}$ / s^{-1}
1.03×10^{-5}	4.64×10^{-4}	1.30
1.03×10^{-5}	9.28×10^{-4}	2.63
1.03×10^{-5}	1.39×10^{-3}	4.00



$k_2 = 2.92 \times 10^3$ $Lmol^{-1}s^{-1}$

Reaction of $(ind)_2CH^+$ (**1l**) with piperidine (stopped-flow, 620 nm, 20 °C)

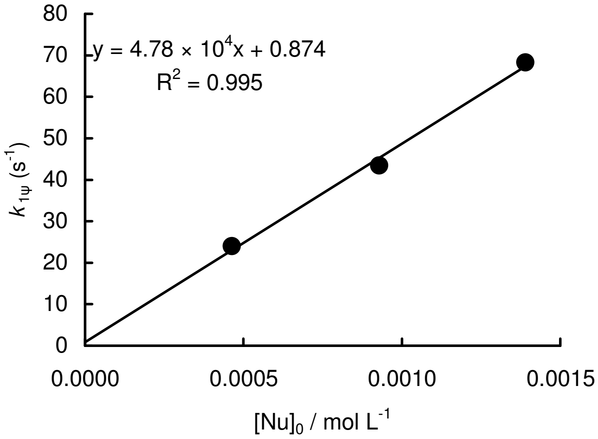
$[E]_0$ / mol L^{-1}	$[Nu]_0$ / mol L^{-1}	$k_{1\psi}$ / s^{-1}
1.27×10^{-5}	4.64×10^{-4}	1.09×10^{1}
1.27×10^{-5}	9.28×10^{-4}	2.08×10^{1}
1.27×10^{-5}	1.39×10^{-3}	3.00×10^{1}



$k_2 = 2.06 \times 10^4$ $Lmol^{-1}s^{-1}$

Reaction of $(thq)_2CH^+$ (**1m**) with piperidine (stopped-flow, 620 nm, 20 °C)

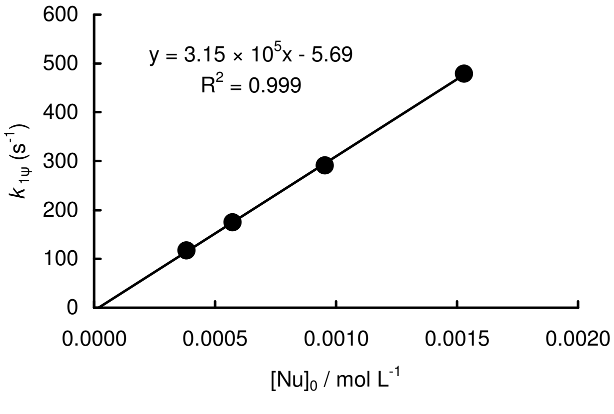
$[E]_0$ / mol L^{-1}	$[Nu]_0$ / mol L^{-1}	$k_{1\psi}$ / s^{-1}
1.33×10^{-5}	4.64×10^{-4}	2.40×10^{1}
1.33×10^{-5}	9.28×10^{-4}	4.34×10^{1}
1.33×10^{-5}	1.39×10^{-3}	6.83×10^{1}



$k_2 = 4.78 \times 10^4$ $Lmol^{-1}s^{-1}$

Reaction of $(dma)_2CH^+$ (**1n**) with piperidine (stopped-flow, 620 nm, 20 °C)

$[E]_0$ / mol L^{-1}	$[Nu]_0$ / mol L^{-1}	$k_{1\psi}$ / s^{-1}
2.30×10^{-6}	3.82×10^{-4}	1.17×10^{2}
2.30×10^{-6}	5.73×10^{-4}	1.75×10^{2}
2.30×10^{-6}	9.55×10^{-4}	2.91×10^{2}
2.30×10^{-6}	1.53×10^{-3}	4.79×10^{2}

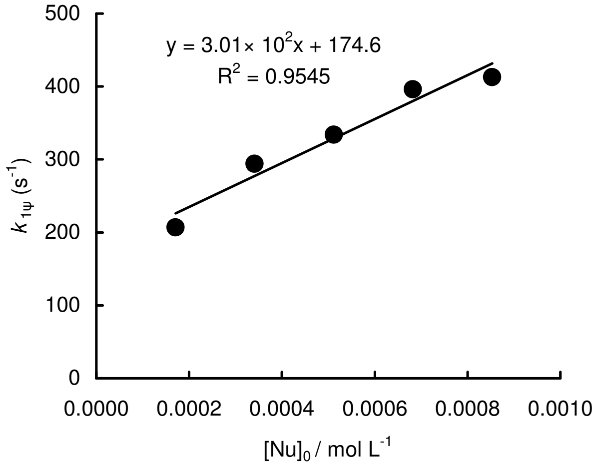


$k_2 = 3.15 \times 10^5$ $Lmol^{-1}s^{-1}$

4.7 Kinetics of the Reactions of Amines with **1d** in DMSO

Reaction of **1d** with piperidine in DMSO (stopped-flow, 341 nm, 20 °C)

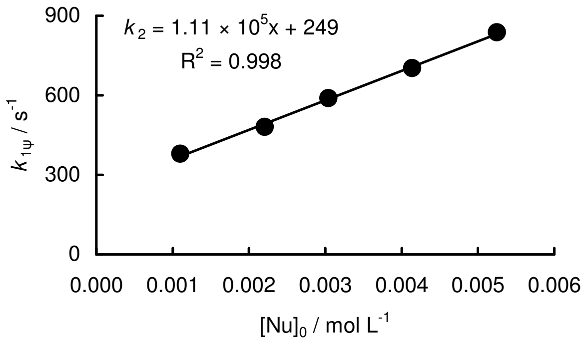
$[E]_0$ / mol L^{-1}	$[Nu]_0$ / mol L^{-1}	$k_{1\psi}$ / s^{-1}
3.37×10^{-5}	1.71×10^{-4}	2.07×10^{2}
3.37×10^{-5}	3.41×10^{-4}	2.94×10^{2}
3.37×10^{-5}	5.12×10^{-4}	3.34×10^{2}
3.37×10^{-5}	6.82×10^{-4}	3.96×10^{2}
3.37×10^{-5}	8.53×10^{-4}	4.13×10^{2}



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

Reaction of **1d** with morpholine in DMSO (stopped-flow, 346 nm, 20 °C)

$[E]_0$ / mol L^{-1}	$[Nu]_0$ / mol L^{-1}	$k_{1\psi}$ / s^{-1}
5.32×10^{-5}	5.25×10^{-3}	837
5.32×10^{-5}	4.14×10^{-3}	703
5.32×10^{-5}	3.04×10^{-3}	589
5.32×10^{-5}	2.21×10^{-3}	481
5.32×10^{-5}	1.10×10^{-3}	379

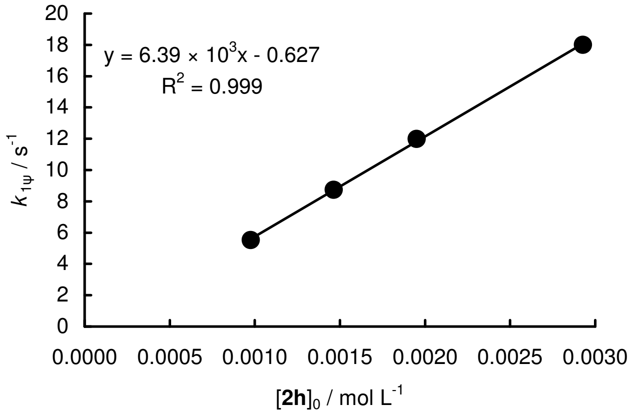


$k_2 = 1.11 \times 10^{5}$ $Lmol^{-1}s^{-1}$

4.8 Kinetics of the Reactions of Malononitrile Anion **2h** with **1a** and **1b** in DMSO/H_2O (50/50 v,v)

Reaction of **1a** with malononitrile anion **2h** (stopped-flow, 529 nm, 20 °C)

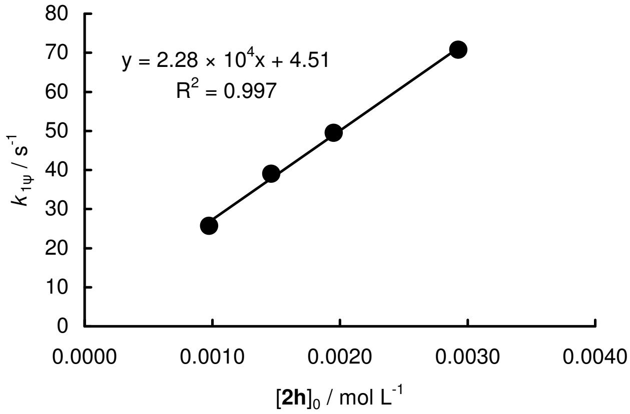
$[E]_0$ / mol L^{-1}	$[C^-]_0$ / mol L^{-1}	$k_{1\psi}$ / s^{-1}
1.06×10^{-4}	9.76×10^{-4}	5.52
1.06×10^{-4}	1.46×10^{-3}	8.73
1.06×10^{-4}	1.95×10^{-3}	1.20×10^{1}
1.06×10^{-4}	2.93×10^{-3}	1.80×10^{1}



$k_2 = 6.39 \times 10^{3}$ $Lmol^{-1}s^{-1}$

Reaction of **1b** with malononitrile anion **2h** (stopped-flow, 491 nm, 20 °C)

$[E]_0$ / mol L^{-1}	$[C^-]_0$ / mol L^{-1}	$k_{1\psi}$ / s^{-1}
2.36×10^{-4}	9.76×10^{-4}	2.57×10^{1}
2.36×10^{-4}	1.46×10^{-3}	3.90×10^{1}
2.36×10^{-4}	1.95×10^{-3}	4.95×10^{1}
2.36×10^{-4}	2.93×10^{-3}	7.07×10^{1}

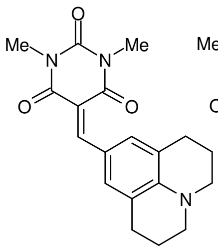


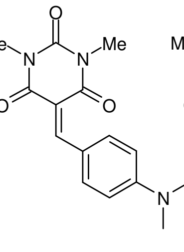
$k_2 = 2.28 \times 10^{4}$ $Lmol^{-1}s^{-1}$

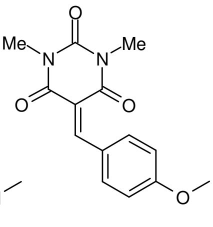
Electrophilicity of 5-Benzylidene-1,3-dimethyl-barbituric and -thiobarbituric Acids

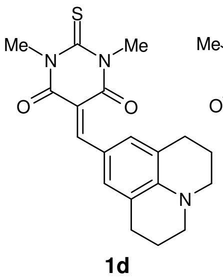
F. H. Seeliger, S. T. A. Berger, G. Y. Remennikov, K. Polborn, H. Mayr, *J. Org. Chem.* **2007,** in print.

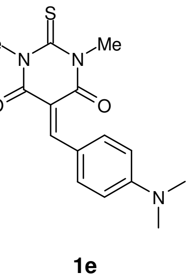
Introduction. Benzylidenebarbituric and –thiobarbituric acids are characterized by their strongly polarized exocyclic double bond with a positive partial charge on the arylidene carbon.[1,2] They have been termed as "electrically neutral organic Lewis acids"[3,4] because they react with typical Lewis bases,[5] such as alkoxides,[3,6] amines,[6-9] thiols,[10] water,[11] and the hydrogensulfite ion.[12] Benzylidenebarbituric and -thiobarbituric acids also react with carbon nucleophiles, *e.g.*, compounds containing an active methylene group,[13,14] isonitriles,[15] phosphacumulene ylids,[16,17] or organo-zinc reagents.[18-20] Due to the fact that the active double bond in benzylidenebarbituric acids can easily be reduced,[21-23] these compounds can be used for the synthesis of unsymmetrical disulfides[24,25] and for the mild oxidation of alcohols.[26,27] Furthermore, benzylidenebarbituric and -thiobarbituric acids are important building blocks in the synthesis of pyrazolo-[3,4-d]pyrimidine derivatives,[28,29] which show broad biological activity.[30-32] Benzylidenethiobarbituric acids also trap radicals and, therefore, can be used as thermal stabilizers in rigid PVC.[33]


1a


1b


1c


1d


1e

Some years ago we showed that the reactions of diarylcarbenium ions with nucleophiles can be described by the linear-free-energy-relationship (4.1) and suggested a set of diarylcarbenium ions and nucleophiles as reference compounds for determining the reactivity of further nucleophiles and electrophiles.[34]

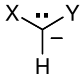
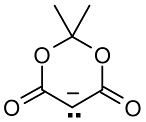
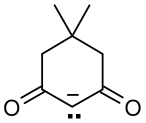
$$\log k_2(20\ ^\circ\mathrm{C}) = s(N + E) \qquad (4.1)$$

E = electrophilicity parameter, N = nucleophilicity parameter, s = nucleophile-specific slope parameter

Equation (4.1) also holds for the reactions of carbanions with quinone methides, which can be considered as uncharged analogs of diarylcarbenium ions,[35,36] and with typical Michael acceptors, like benzylidenemalononitriles[37] or benzylideneindandiones.[38]

Previously, Bernasconi has studied the kinetics of the additions of carbanions, alkoxides, and amines to 2-benzylidene-indan-1,3-diones,[39] benzylidene Meldrum's acids,[40,41] and other electrophiles with polarized double bonds in 50% aqueous DMSO.[42] We have now investigated analogous reactions with benzylidenebarbituric and -thiobarbituric acids in order to examine scope and limitations of equation (1). For this purpose we studied the kinetics of the addition reactions of the potassium salts of different CH-acids (**2a** to **2m**, Table 4.1) to the Michael acceptors **1a-e**.

TABLE 4.1: Reactivity parameters *N* and *s* of the carbanions **2a** to **2m** in DMSO.

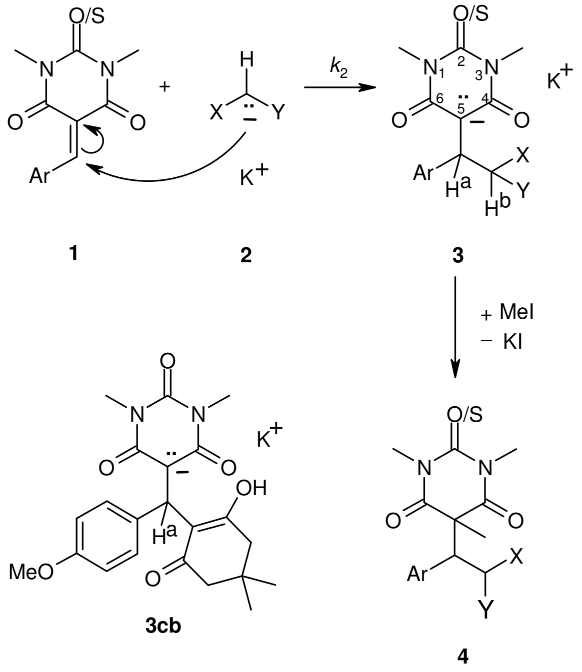
	X	Y	*N* / *s*
2a			13.91 / 0.86[a]
2b			16.27 / 0.77[a]
2c	4-NC-C_6H_4	SO_2CF_3	16.30 / 0.75[b]
2d	4-NC-C_6H_4	NO_2	16.96 / 0.73[c]
2e	COMe	COMe	17.64 / 0.73[a]
2f	C_6H_5	SO_2CF_3	18.72 / 0.69[b]
2g	COMe	CO_2Et	18.82 / 0.69[a]
2h	CN	CN	19.36 / 0.67[a]
2i	CN	CO_2Et	19.62 / 0.67[a]
2k	CO_2Et	CO_2Et	20.22 / 0.65[a]
2l	H	NO_2	20.71 / 0.60[c]
2m	Me	NO_2	21.54 / 0.62[d]

[a]Ref.[36], [b]Ref.[43], [c]Ref.[44], [d]Ref.[37].

Results

Product studies. When equimolar amounts of the benzylidene(thio)barbituric acids **1a-e** and the potassium salts **2** were combined in *d*$_6$-DMSO, quantitative formation of the adducts **3** was observed by ^{1}H and ^{13}C NMR spectroscopy (Scheme 4.1).

SCHEME 4.1: Products of the additions of the carbanions **2** to the active double bond of benzylidene(thio)barbituric acids **1a-e**.



Protons H^a and H^b, which absorb as doublets between δ 4.43–4.81 ppm (H^a) and δ 5.11–6.20 ppm (H^b), are characteristic for the addition products **3**. The high upfield shifts of the ^{1}H NMR signals of the vinylic protons H^a in compounds **1a-e** (δ 8.30–8.47 ppm)[45] to δ 4.43–4.81 ppm in products **3** indicate the nucleophilic attack in β-position of the Michael acceptor.[6] This interpretation is also confirmed by the ^{13}C NMR spectra which show an upfield shift of the benzylidene carbon from δ 159–160 ppm in **1a-e** to δ 31–46 ppm in **3**. The upfield shift of C-5 by an average of 27 ppm from δ 108–115 ppm in **1a-e** to δ 83–86 ppm in **3** reflects the increase of electron density in the pyrimidine rings.

The observation of two signal sets in the ^{1}H NMR spectra of compounds **3cg**, **3ci**, and **3cm** indicates the formation of two diastereomers in these cases (**3cg**, 5:3; **3ci**, 2:1; **3cm**, 9:2).

The enol structure of the dimedone ring of **3cb** (from **1c** and **2b**; Scheme 4.1) is indicated by its ^{13}C NMR spectrum and the OH signal at δ 14.60 ppm. As a consequence, proton H^{a} absorbs as a singlet at δ 6.08 ppm.

TABLE 4.2: ^{1}H and ^{13}C NMR spectroscopic analysis of products **3**.[a]

	δ H^{a} (ppm)	δ H^{b}(ppm)	$^{3}J_{(H^a\text{-}H^b)}$ (Hz)	δ (C-H^{a}) (ppm)	δ (C-5) (ppm)
3ah	4.43	6.02	11.9	43.2	83.7
3bh	4.57	6.08	11.9	43.2	83.6
3cb	6.08	14.60[b]	-	31.0	89.6
3ce	4.81	5.48	12.3	40.5	86.0
3cg[c]	4.78	5.11	12.6	40.5	85.7
3cg[d]	4.76	5.28	12.2	40.4	86.1
3ch	4.61	6.12	12.2	43.2	83.7
3ci[c]	4.59	5.37	12.3	40.3	85.1
3ci[d]	4.65	5.35	12.2	40.3	83.9
3ck	4.70	5.14	12.3	40.5	85.9
3cm[c]	4.45	6.00	11.4	45.8	85.0
3cm[d]	4.43	6.20	11.4	45.7	83.8
3de	4.67	5.41	12.3	34.5	91.5
3dh	4.43	5.96	12.1	43.2	88.9
3ee	4.78	5.47	12.5	40.4	91.4

[a]For assignment of structures see Scheme 4.1 and Table 4.3; **3ah** means product from **1a** and **2h**. [b]See text. [c]Major diastereomer. [d]Minor diastereomer.

Treatment of the potassium salts **3ck** and **3cm** with methyl iodide yields **4ck** and **4cm** by methylation of the 5-position of the pyrimidine ring. After separation of the diastereomers (9:2) of **4cm** by crystallization from ethanol, the structure of the major diastereomer was determined by x-ray crystallography (Figure 4.1).

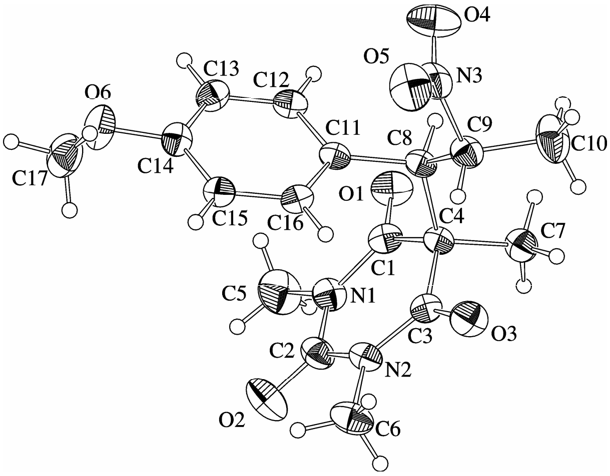
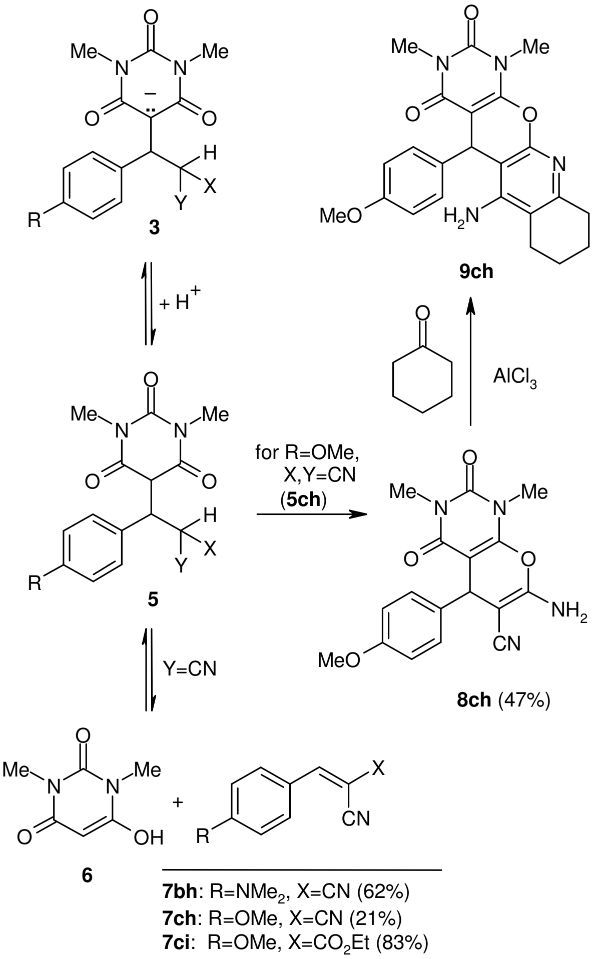


FIGURE 4.1: X-ray crystal structure (ORTEP projection) of the major diastereomer of **4cm**. Atom numbers refer to the x-ray analysis.

The anionic adducts **3** obtained from arylidenebarbituric acids **1b** and **1c** were also treated with aqueous hydrochloric acid. While the adducts **3bm, 3cb**, **3ce**, **3cg**, and **3cm**, derived from dimedone (**2b**), acetylacetone (**2e**), ethyl acetoacetate (**2g**), and nitroethane (**2m**) respectively, yielded the expected protonated species **5** (Scheme 4.2), retro-Michael additions with formation of **7ch** and **7ci** were observed for the adducts **3ch** (from malononitrile) and **3ci** (from ethyl cyanoacetate). Acidification of **3bh** (malononitrile adduct to **1b**) also gave rise to the formation of the corresponding benzylidenemalononitrile **7bh**. Analogous retro-Michael additions were observed by Szántay when methoxy-substituted *β*-nitro styrenes were treated with ethyl cyanoacetate or malononitrile in the presence of a basic catalyst[46] and by us when benzylidenemalononitriles were combined with the carbanion of ethyl cyanoacetate.[37]

SCHEME 4.2: Protonation of the potassium salts **3** leads to compounds **5**. The salts **3bh**, **3ch**, **3ci** undergo a retro Michael addition upon protonation to form cyanoolefins **7bh**, **7ch**, **7ci**. Under these conditions compound **5ch** forms the cyclic dihydropyrano [2,3-d]pyrimidine **8ch**, which reacts with cyclohexanone via Friedländer reaction to pyrano[2,3-b]-quinoline **9ch**.



In addition to the retro-Michael adduct **7ch**, just discussed, acid hydrolysis of **3ch** (from malononitrile anion **2h** and **1c**) yields 47% of the dihydropyrano[2,3-d]pyrimidine **8ch**. Syntheses of analogous pyrano[2,3-d]pyrimidines via reaction of benzylidene-malononitriles with 1,3-dimethylbarbituric acid[47] or via microwave irradiation of barbituric acids, benzaldehyde, and cyanoacetates or malononitriles[48] have been reported. In these reactions the Michael adducts **5** are probably formed as intermediates, which then undergo cyclization by attack of an enolic hydroxy group at one of the cyano functions.

Because of the structural analogy to tacrine,[49,50] which is an inhibitor of acetyl cholinesterase and is a drug that proved to have a beneficial effect on cognition in patients with Alzheimer`s disease,[51,52] dihydropyran **8ch** was used as starting material for the synthesis of a new pyrano[2,3-b]quinoline. In a

Friedländer reaction the acid catalyzed condensation of **8ch** with cyclohexanone gave 69% of the tacrine analogue **9ch**.

Kinetics. Benzylidene(thio)barbituric acids **1a-e** show strong absorption bands in the UV-vis spectra (375–525 nm).[1] By nucleophilic attack at the benzylidene carbon the chromophore is interrupted, and the reaction can be followed by the decrease of the absorbance. All reactions proceeded quantitatively, so that the solutions were completely decolorized. The kinetic experiments were performed under pseudo-first-order conditions using a high excess of the nucleophiles. From the exponential decays of the UV-Vis absorbances of the electrophiles the pseudo-first-order rate constants were obtained (Figure 4.2). In previous work we have demonstrated that the potassium salts of the carbanions studied in this work are not paired under the conditions used for the kinetic experiments.[36,43,44] The second-order rate constants k_2 (Table 4.3), which are obtained as the slopes of $k_{1\Psi}$ versus [**2**] correlations (Figure 4.2, insert), can therefore be considered to reflect the reactivities of free carbanions.

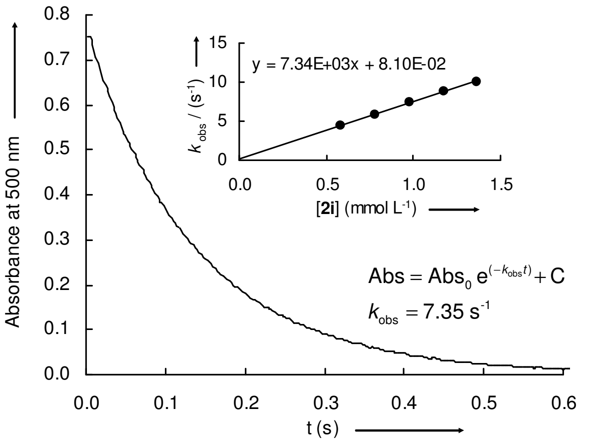


Figure 4.2: Exponential decay of the absorbance at 500 nm during the reaction of **1a** ($c_0 = 2.90 \times 10^{-5}$ mol L^{-1}, λ = 500 nm) with **2i** ($c_0 = 9.78 \times 10^{-4}$ mol L^{-1}) in DMSO at 20 °C.

TABLE 4.3: Second-order rate constants k_2 (DMSO, 20 °C) and characterized products of the reactions of benzylidene(thio)barbituric acids **1a-e** with the potassium salts of different carbanions **2**.

Elec	Nuc	k_2 (L mol^{-1}s^{-1})	Products
1a	**2b**	1.49×10^{2}	-
	2c	5.37×10^{1}	-
	2d	1.88×10^{2}	-
	2e	5.45×10^{2}	-
	2f	1.01×10^{3}	-
	2g	3.78×10^{3}	-
	2h	1.27×10^{4}	**3ah**[a]
	2i	7.34×10^{3}	-
	2k	7.66×10^{3}	-
	2l	1.54×10^{4}	-
	2m	2.98×10^{4}	-
1b	**2b**	1.04×10^{3}	-
	2c	2.18×10^{2}	-
	2e	3.72×10^{3}	-
	2f	5.71×10^{3}	-
	2g	2.03×10^{4}	-
	2h	5.88×10^{4}	**3bh**[a], **7bh**[b]

	2i	4.00×10^4	**-**
	2k	3.49×10^4	**-**
	2m	-	**5bm**[b]
1c	**2a**	1.42×10^3	**-**
	2b	4.83×10^4	**3cb**[a], **5cb**[b]
	2e	1.44×10^5	**3ce**[a], **5ce**[b]
	2f	1.97×10^5	**-**
	2g	1.08×10^6	**3cg**[a], **5cg**[b]
	2h	1.80×10^6	**3ch**[a], **7ch**[b] **8ch**[b]
	2i	1.49×10^6	**3ci**[a], **7ci**[b]
	2k	1.41×10^6	**3ck**[a], **4ck**[b]
	2m	-	**3cm**[a], **4cm**[b] **5cm**[b]
1d	**2b**	4.36×10^3	**-**
	2e	1.17×10^4	**3de**[a]
	2g	7.41×10^4	**-**
	2h	1.64×10^5	**3dh**[a]
	2i	1.06×10^5	**-**

	2k	1.13×10^5	-
1e	**2a**	4.97×10^2	-
	2b	3.72×10^4	-
	2e	1.03×10^5	**3ee**[a]
	2g	4.89×10^5	-
	2i	7.05×10^5	-
	2k	6.71×10^5	-

---

[a] Potassium salts of **3** produced in d_6-DMSO were characterized by ^{1}H and ^{13}C NMR. [b] Characterization of isolated products.

Discussion. Equation 4.1 was used to calculate the *E* parameters of **1a-e** from the rate constants given in Table 4.3 and the previously reported *N* and *s* parameters of the carbanions **2a-m**.[36,37,43,44] A least-squares fit of calculated and experimental rate constants (minimization of $\Delta^2 = \sum(\log k - s(N + E))^2$ with the What's *Best!* nonlinear solver) gave the *E* parameters of the benzylidene(thio)barbituric acids **1a-e**, which are close to the arithmetic means of the *E* values which are calculated from k_2 of the individual electrophile-nucleophile combinations.

However, the reactivities of some carbanions deviate slightly but systematically from the correlation lines. Figure 4.3 shows that the triflinate stabilized carbanion **2f** reacts two to three times slower with each of the electrophiles **1a-c** than expected from its previously published reactivity parameters *N* and *s*.[43] On the other hand, the malononitrile anion **2h** reacts two to four times faster with the electrophiles **1a-c** and **1d** than expected (Figure 4.3 and 4.4).

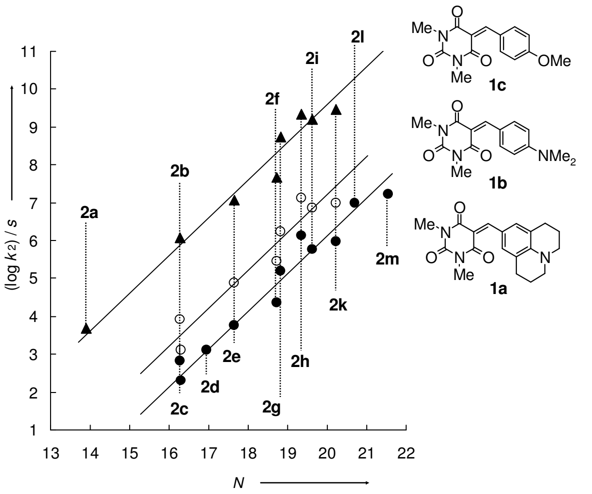


FIGURE 4.3: Plot of (log k_2)/s versus N for the reactions of **1a-c** with selected carbanions **2**. – The correlation lines have a fixed slope of 1.0, as required by eq. 1.

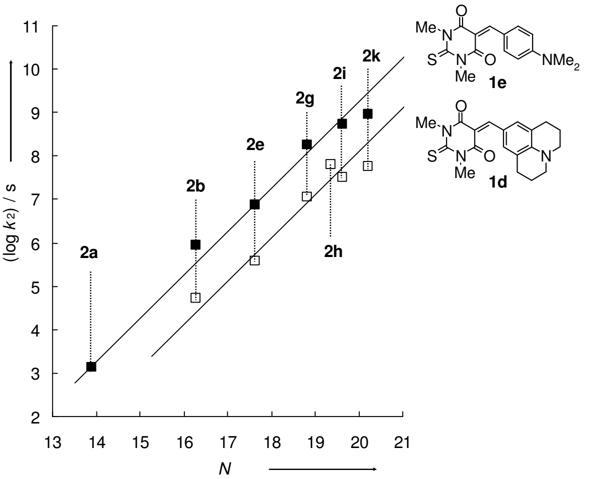


FIGURE 4.4: Plot of (log k_2)/s versus N for the reactions of **1d** and **1e** with different carbanions **2**. – The correlation lines have a fixed slope of 1.0, as required by eq. 1.

A comparison of the electrophilicities of diarylcarbenium ions, quinone methides, and benzylidene(thio)barbituric acids (**1a-e**) is given in Figure 4.5.

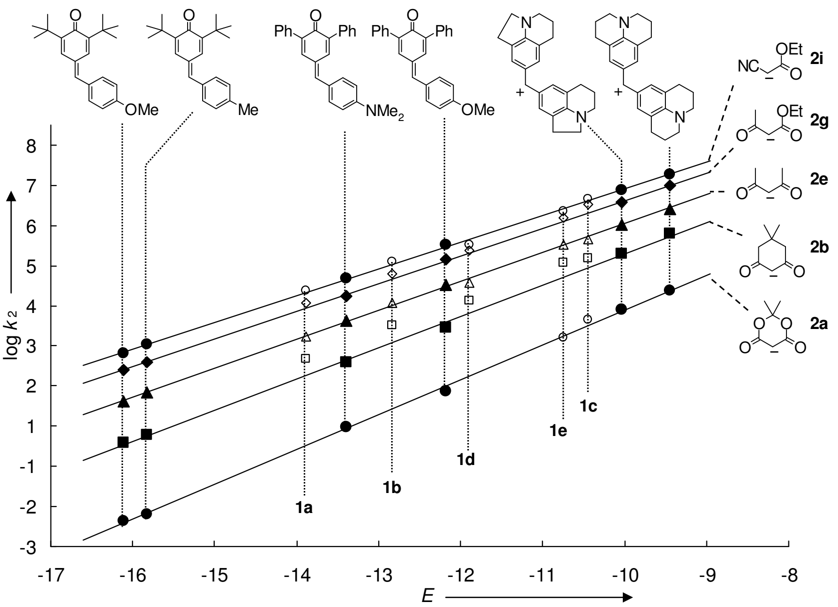


FIGURE 4.5: Rate constants for the reactions of selected carbanions **2** with benzylidene(thio)barbituric acids **1a-e** compared with the reactivities toward reference electrophiles. – The rate constants for the reactions of **1a-e** with **2** were not used for the construction of the correlation lines.

The good fit demonstrates that the nucleophilic reactivity order of carbanions which was derived from the rates of their reactions with diarylcarbenium ions and quinone methides in DMSO also holds for the reactions with typical Michael acceptors. In agreement with the conclusions drawn from Figures 4.3 and 4.4 Figure 4.5 also shows that **2b**, the anion of dimedone, reacts faster with the benzylidene(thio)barbituric acids **1a-e** than expected from the rates of the reactions of **2b** with the reference electrophiles (diarylcarbenium ions and quinone methides).

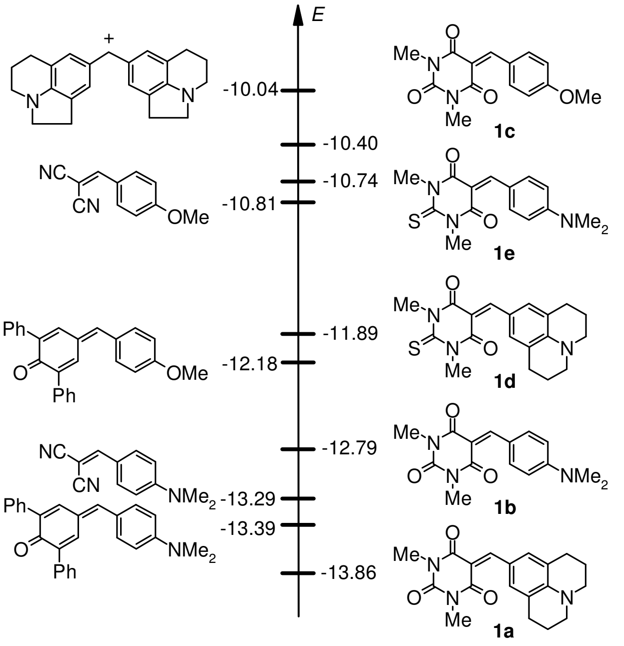
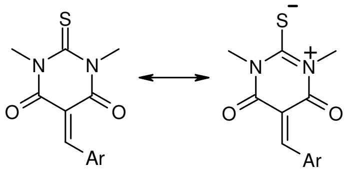


FIGURE 4.6: Comparison of electrophilicity parameters *E* of Michael acceptors, quinone methides and diarylcarbenium ions.

As summarized in Figure 4.6, benzylidene(thio)barbituric acid derivatives have similar electrophilicities as the corresponding benzylidenemalononitriles. It is found that the thiobarbiturates are more reactive than the corresponding oxa analogues. This observation may be surprising because oxygen is more electronegative than sulfur. Obviously different resonance effects in amides and thioamides are responsible for this ranking of reactivity. It has been reported that thiolactams possess greater dipole moments than lactams.[53] The higher rotational barrier for the C–N bond in thioformamides compared with formamides also indicates the high contribution of a resonance structure with C=N double bond.[54] Ab initio MO calculations by Wiberg showed that more electron density is transferred from nitrogen to sulfur in thioformamides than from nitrogen to oxygen in formamides.[55] If one assumes that the thioamide structure with a C=N double bond also has a greater importance in the thiobarbituric acids, one can conclude that the positive polarization of nitrogen in the resonance structures **1d´** and **1e´** (Scheme 4.3) is responsible for the increased electron accepting abilities of the thiobarbituric acids.

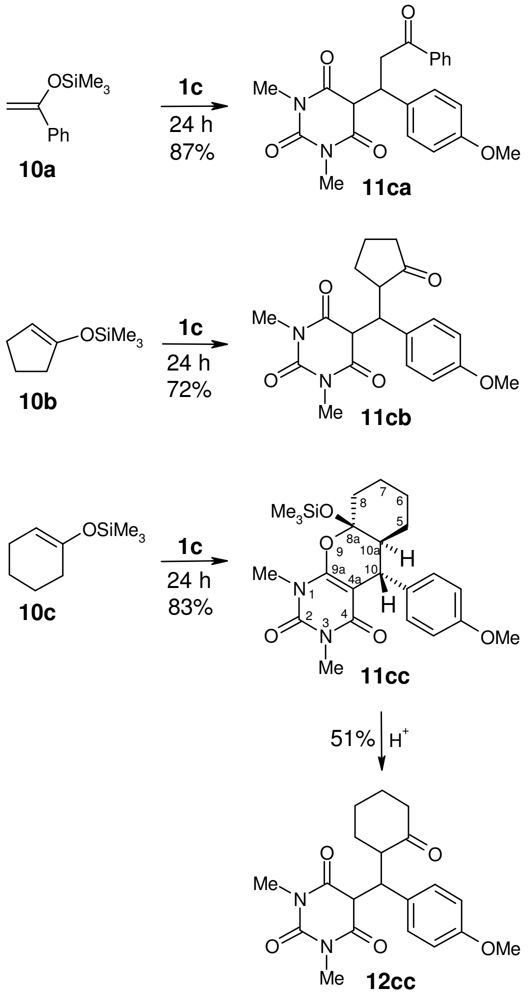
SCHEME 4.3: Resonance effects of benzylidenethiobarbituric acids **1d** and **1e**.



1d, **1e** **1d´**, **1e´**

Reactions with other types of nucleophiles. From the reactivity parameter of **1c** (E = −10.40) one can derive that this electrophile should also be capable of undergoing reactions with electron rich π-systems with $E > 5$, *e.g.*, silyl enol ethers or electron rich arenes. In accord with this conclusion **1c** was found to react with 1-phenyl-1-(trimethylsiloxy)ethene (**10a**, N = 6.22, s = 0.96)[56] and 1-(trimethylsiloxy)cyclopentene (**10b**, N = 6.57, s = 0.93)[56] in DMSO at 20 °C to give **11ca** and **11cb**, respectively, after aqueous workup. Compound **11ca** has previously been synthesized by base catalyzed addition of 1,3-dimethylbarbituric acid to 3-(4-methoxyphenyl)-1-phenylprop-2-en-1-one.[57] Attempts to follow the reaction of **1c** with **10b** kinetically were not successful. At $[\mathbf{1c}]_0 = 9.92 \times 10^{-5}$ mol L^{-1} and $[\mathbf{10b}]_0 = 1.08 \times 10^{-2}$ mol L^{-1}, 50% of **1c** were consumed after 3.5 h, but the decay of **1c** was not monoexponential.

SCHEME 4.4: Reactions of **1c** with silyl enol ethers **10a-c** in DMSO at 20 °C.



The reaction of **1c** with 1-(trimethylsiloxy)cyclohexene (**10c**, *N* = 5.21, *s* = 1.00)[56] did not give the expected cyclohexanone **12cc**. When the solution of the reaction product in DMSO was diluted with water and extracted with ethyl acetate, the hetero Diels-Alder adduct **11cc** was isolated as the only product. X-ray analysis of **11cc** revealed the trans fusion of the cyclohexane and the tetrahydropyran ring with a pseudo equatorial position of the anisole group and a pseudo axial orientation of the trimethylsiloxy group (Figure 4.7).

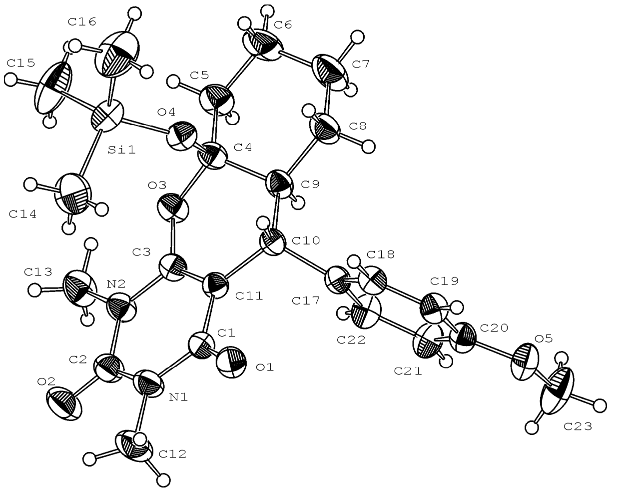
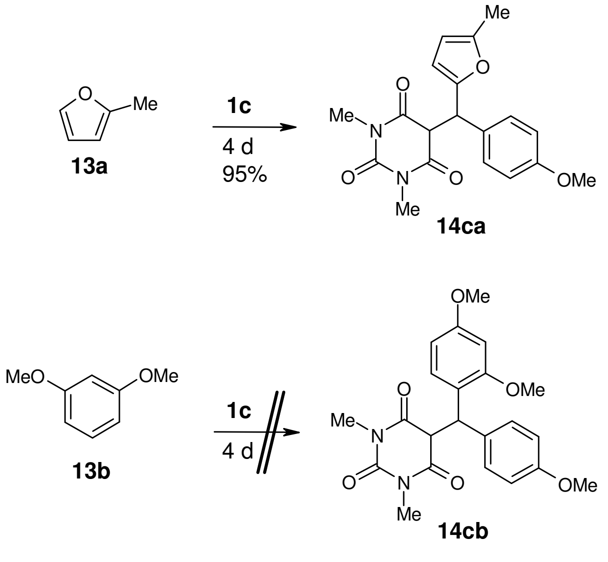


FIGURE 4.7: X-ray crystal structure (ORTEP projection) of **11cc**. Atom numbers refer to the x-ray analysis.

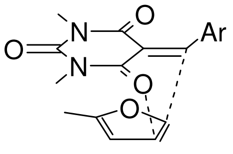
The trans diaxial coupling of the vicinal protons 10-H and 10a-H ($^3J_{10\text{-}10a}$ = 10.8 Hz) is in accord with this structure. The trans fusion of the two rings of the chromene fragment excludes a concerted Diels-Alder reaction.[58] Because the product has not been exposed to acidic conditions, epimerization of the acetal center appears unlikely[59-61] and we assume a stepwise mechanism via a dipolar intermediate.[62]

Treatment of **11cc** with 1 M aqueous HCl cleaves the silylated acetal and yields the initially expected cyclohexanone **12cc** as a 7:1 mixture of two diastereomers.

SCHEME 4.5: Reactions of **1c** with the electron rich arenes **13a** and **13b** in DMSO at 20 °C.



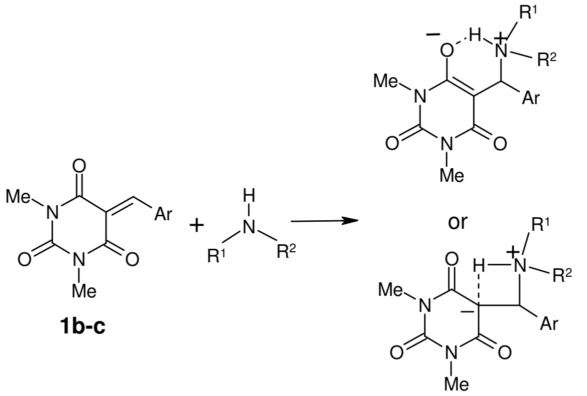
As predicted by equation 4.1, 1,3-dimethoxybenzene (**13b**, $N = 2.48$, $s = 1.09$)[56] does not react with **1c** ($E = -10.40$) in DMSO; after 4 days at room temperature we did not observe any conversion (Scheme 4.5). Analogously, equation 4.1 predicts a very slow reaction ($k_2 = 2.62 \times 10^{-8}$ L mol^{-1} s^{-1}) of **1c** with 2-methylfuran (**13a**, $N = 3.61$, $s = 1.11$).[34] While this rate constant refers to a half reaction time of 12 years for a 0.1 M solution in dichloromethane, the electrophilic substitution product **14ca** was obtained in 95% yield after 4 days in DMSO. The kinetic investigation of this reaction yields a rate constant of $k_2 = 1.24 \times 10^{-4}$ L mol^{-1} s^{-1} (DMSO, 20 °C), *i.e.*, almost four orders of magnitude faster than calculated by equation 4.1. Though reactions of neutral reactants via dipolar intermediates can be expected to show large dependence on solvent polarity,[63] we cannot explain at present why calculated and observed rate constant for the reaction of **1c** with **13a** differ so much. Possibly secondary orbital interactions as indicated in transition state **15** account for the high reactivity of 2-methylfuran (**13a**).



15

In order to check the applicability of the *E* parameters of the benzylidene(thio)barbituric acids listed in Table 4.3 for reactions with other types of nucleophiles, we have also studied the rates of the reactions of **1b** and **1c** with propyl amine and morpholine.

SCHEME 4.6: Reactions of **1b** and **1c** with amines in DMSO at 20 °C.



Because alkyl ammonium ions have higher pK_a values than 5-alkyl substituted barbituric acids,[64] the additions of primary and secondary amines to **1b** and **1c** yield zwitterionic adducts in DMSO as shown in Scheme 4.6. While the additions of propyl amine proceeded quantitatively, the reactions with morpholine were incomplete and the absorbances of the electrophiles **1b** and **1c** did not disappear completely.

TABLE 4.4: Experimental and calculated (eq. 4.1) second-order rate constants k_2 for the reactions of amines with **1b** and **1c** in comparison with literature data.

	Nucleophile	N / s [a, b]	exp. k_2 (L mol^{-1} s^{-1})[b]	calc. k_2 (L mol^{-1} s^{-1})[b]	k_2 (L mol^{-1} s^{-1})[c]
1b	propyl amine	15.70 / 0.64	2.12×10^3	7.28×10^1	-
	morpholine	16.96 / 0.67	2.01×10^4	6.22×10^2	-
	piperidine	17.19 / 0.71	-	1.33×10^3	2.9×10^4
1c	propyl amine	15.70 / 0.64	3.13×10^4	2.47×10^3	-
	morpholine	16.96 / 0.67	2.02×10^5	2.48×10^4	-
	piperidine	17.19 / 0.71	-	6.62×10^4	3.2×10^5

[a] Ref.[65]; [b] DMSO, 20 °C. [c] MeCN, 25 °C, from ref.[7]

Table 4.4 compares calculated and experimental rate constants for the additions of amines and shows that equation 4.1 predicts rate constants for the additions of propyl amine and morpholine to **1c** with an accuracy of one order of magnitude. The corresponding reactions of **1b** proceed 29 and 32 times faster than predicted.

The reported rate constants for the additions of piperidine to **1b** and **1c** in acetonitrile at 25 °C are 22 and 5 times greater than the calculated rate constants for DMSO at 20 °C, again showing qualitative agreement. For the reactions of secondary amines with benzylidene Meldrum's acids in aqueous DMSO Bernasconi postulated an early development of hydrogen bonding on the reaction coordinate which was supposed to be responsible for enhanced intrinsic rate constants k_0.[66,67] Furthermore Oh and Lee proposed that the additions of benzyl amines to dicarbonyl activated olefins in acetonitrile proceed through cyclic transition states with four-membered or six-membered rings, where the amine proton forms a hydrogen bond to C_α of the Michael acceptor or to a carbonyl oxygen.[68-71] As a consequence, it is possible that the constant higher reactivity of amines in reactions with benzylidenebarbituric acids is due to interactions of the N–H bonds with the developing negative charge on C_α or one of the carbonyl oxygens of the Michael acceptor.

However, because the deviation between calculated and experimental rate constants for the reactions of **1a-e** with amines is within the previously suggested confidence limit of equation 4.1 (one to two orders of magnitude)[72,73] these deviations shall not be over interpreted.

Conclusion. The linear-free-energy-relationship $\log k_2(20\ °\mathrm{C}) = s(N + E)$ (equation 4.1) has been found to be suitable for the calculation of the rates of reactions of the benzylidene(thio)barbituric acids **1a**-**e** with carbanions and amines from the *E* parameters of **1a**-**e** determined in this work and the nucleophile-specific parameters *N* and *s* reported earlier.[36,37,43,44] The agreement between calculated and experimental data was within one order of magnitude for carbanions, while the few amines examined react 10-50 times faster than calculated. 2-Methylfuran (**13a**), the only π-nucleophile which was kinetically investigated, reacted 4 orders of magnitude faster than predicted. It is speculated whether stabilizing secondary orbital interactions are responsible for the failure of equation 4.1 to predict this rate constant.

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– Experimental Section –

Electrophilicity of 5-Benzylidene-1,3-dimethylbarbituric and thiobarbituric acids

F. H. Seeliger, S. T. A. Berger, G. Y. Remennikov, K. Polborn, H. Mayr, *J. Org. Chem.* **2007,** in print.

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Kinetic experiments

The temperature of the solutions during all kinetic studies was kept constant (20 ± 0.1°C) by using a circulating bath thermostat. DMSO with a content of H_2O < 50 ppm was used for the kinetic experiments.

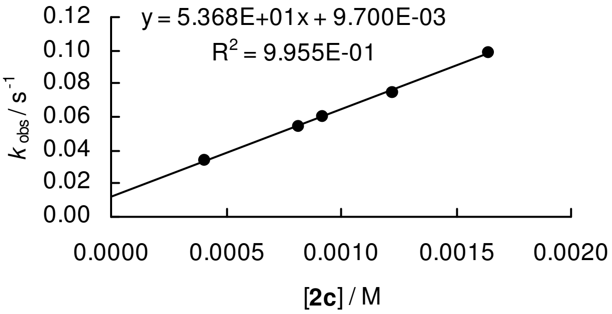
For the evaluation of kinetics the stopped-flow spectrophotometer systems Hi-Tech SF-61DX2 or Applied Photophysics SX.18MV-R stopped-flow reaction analyzer were used. Rate constants k_{obs} (s^{-1}) were obtained by fitting the single exponential $A_t = A_0\exp(-k_{obs}t) + C$ to the observed time-dependent electrophile absorbance (averaged from at least 4 kinetic runs for each nucleophile concentration). For the stopped-flow experiments 2 stock solutions were used: A solution of the electrophile in DMSO and a solution of the carbanion, which was either used as potassium salt or generated by the deprotonation of the CH acid with 1.05 equivalents of KO*t*Bu.

Reactions of electrophile 1a

Reaction of **1a** with **2c**
(DMSO, 20 °C, stopped flow, 480 nm)

[**1a**] / M	[**2c**] / M	k_{obs} / s^{-1}
2.39×10^{-5}	4.09×10^{-4}	3.37×10^{-2}
2.39×10^{-5}	8.18×10^{-4}	5.16×10^{-2}
2.39×10^{-5}	9.20×10^{-4}	5.80×10^{-2}
2.39×10^{-5}	1.23×10^{-3}	7.55×10^{-2}
2.39×10^{-5}	1.64×10^{-3}	9.90×10^{-2}

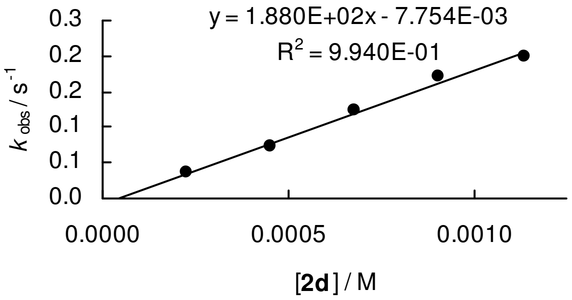
$k_2 = (5.37 \pm 0.21) \times 10^{1}\ M^{-1}s^{-1}$



Reaction of **1a** with **2d**
(DMSO, 20 °C, stopped flow, 520 nm)

[**1a**] / M	[**2d**] / M	k_{obs} / s^{-1}
1.60×10^{-5}	2.27×10^{-4}	3.52×10^{-2}
1.60×10^{-5}	4.54×10^{-4}	7.30×10^{-2}
1.60×10^{-5}	6.81×10^{-4}	1.23×10^{-1}
1.60×10^{-5}	9.08×10^{-4}	1.70×10^{-1}
1.60×10^{-5}	1.13×10^{-3}	2.00×10^{-1}

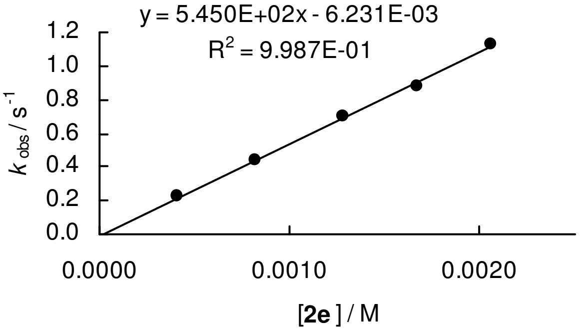
$k_2 = (1.88 \pm 0.08) \times 10^{2}\ M^{-1}s^{-1}$



Reaction of **1a** with **2e**
(DMSO, 20 °C, stopped flow, 487 nm)

[**1a**] / M	[**2e**] / M	k_{obs} / s^{-1}
2.39×10^{-5}	4.11×10^{-4}	2.21×10^{-1}
2.39×10^{-5}	8.22×10^{-4}	4.41×10^{-1}
2.39×10^{-5}	1.28×10^{-3}	6.96×10^{-1}
2.39×10^{-5}	1.67×10^{-3}	8.83×10^{-1}
2.39×10^{-5}	2.06×10^{-3}	1.13

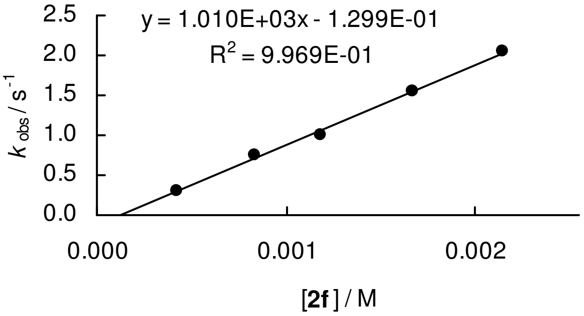
$k_2 = (5.45 \pm 0.11) \times 10^{2}$ M^{-1}s^{-1}



Reaction of **1a** with **2f**
(DMSO, 20 °C, stopped flow, 480 nm)

[**1a**] / M	[**2f**] / M	k_{obs} / s^{-1}
2.08×10^{-5}	4.18×10^{-4}	2.96×10^{-1}
2.08×10^{-5}	8.37×10^{-4}	7.45×10^{-1}
2.08×10^{-5}	1.19×10^{-3}	1.01
2.08×10^{-5}	1.67×10^{-3}	1.59
2.08×10^{-5}	2.15×10^{-3}	2.04

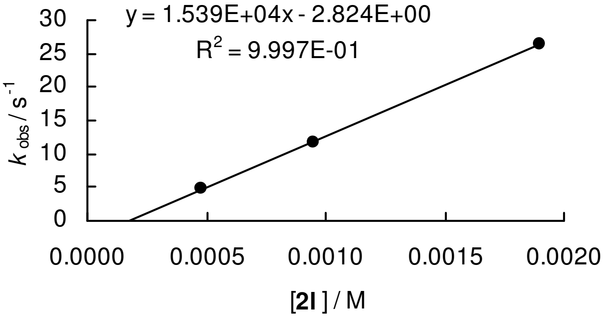
$k_2 = (1.01 \pm 0.03) \times 10^{3}$ M^{-1}s^{-1}



Reaction of **1a** with **2l**
(DMSO, 20 °C, stopped flow, 500 nm)

[**1a**] / M	[**2l**] / M	k_{obs} / s^{-1}
1.75×10^{-5}	4.76×10^{-4}	4.65
1.75×10^{-5}	9.52×10^{-4}	1.16×10^{1}
1.75×10^{-5}	1.90×10^{-3}	2.65×10^{1}

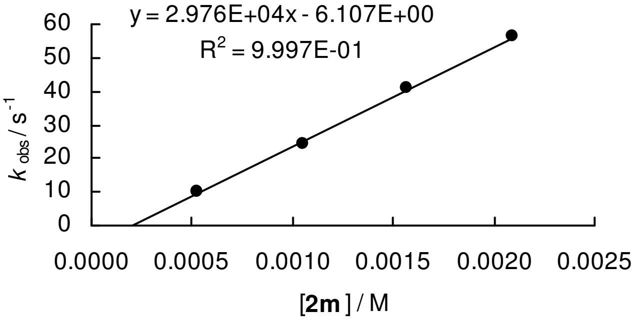
$k_2 = (1.54 \pm 0.03) \times 10^{4}$ M^{-1}s^{-1}



Reaction of **1a** with **2m**
(DMSO, 20 °C, stopped flow, 500 nm)

[**1a**] / M	[**2m**] / M	k_{obs} / s^{-1}
2.98×10^{-5}	5.24×10^{-4}	9.81
2.98×10^{-5}	1.05×10^{-3}	2.46×10^{1}
2.98×10^{-5}	1.57×10^{-3}	4.07×10^{1}
2.98×10^{-5}	2.09×10^{-3}	5.62×10^{1}

$k_2 = (2.98 \pm 0.04) \times 10^{4}$ M^{-1}s^{-1}

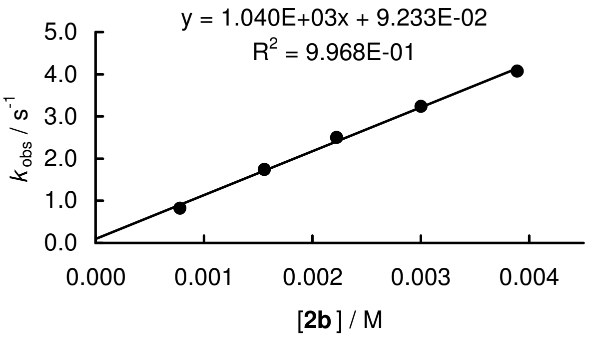


Reactions of electrophile 1b

Reaction of **1b** with **2b**
(DMSO, 20 °C, stopped flow, 487 nm)

[**1b**] / M	[**2b**] / M	k_{obs} / s^{-1}
3.80×10^{-5}	7.78×10^{-4}	8.24×10^{-1}
3.80×10^{-5}	1.56×10^{-3}	1.74
3.80×10^{-5}	2.22×10^{-3}	2.50
3.80×10^{-5}	3.00×10^{-3}	3.23
3.80×10^{-5}	3.89×10^{-3}	4.07

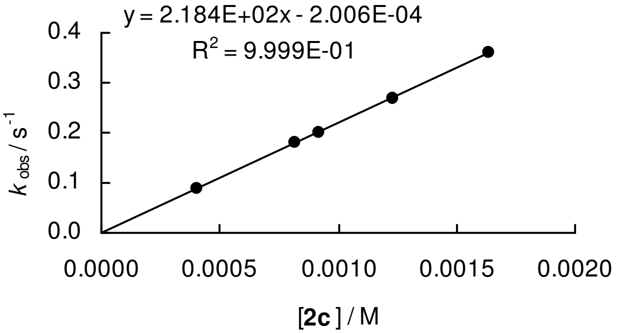
$k_2 = (1.04 \pm 0.03) \times 10^3$ $M^{-1}s^{-1}$



reaction of **1b** with **2c**
(DMSO, 20 °C, stopped flow, 480 nm)

[**1b**] / M	[**2c**] / M	k_{obs} / s^{-1}
2.09×10^{-5}	4.09×10^{-4}	9.14×10^{-2}
2.09×10^{-5}	8.18×10^{-4}	1.82×10^{-1}
2.09×10^{-5}	9.20×10^{-4}	2.03×10^{-1}
2.09×10^{-5}	1.23×10^{-3}	2.74×10^{-1}
2.09×10^{-5}	1.64×10^{-3}	3.70×10^{-1}

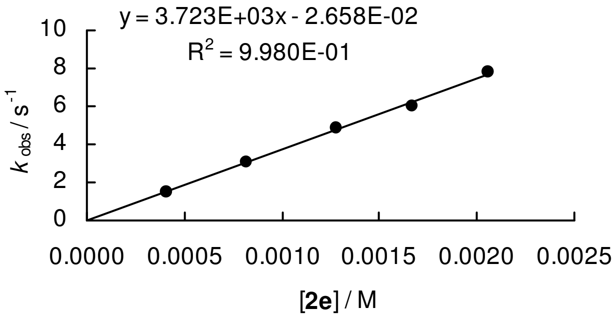
$k_2 = (2.18 \pm 0.01) \times 10^2$ $M^{-1}s^{-1}$



Reaction of **1b** with **2e**
(DMSO, 20 °C, stopped flow, 487 nm)

[**1b**] / M	[**2e**] / M	k_{obs} / s^{-1}
2.09×10^{-5}	4.11×10^{-4}	1.51
2.09×10^{-5}	8.22×10^{-4}	3.05
2.09×10^{-5}	1.28×10^{-3}	4.79
2.09×10^{-5}	1.67×10^{-3}	6.01
2.09×10^{-5}	2.06×10^{-3}	7.75

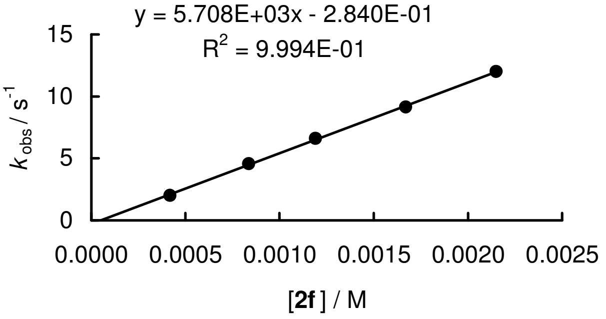
$k_2 = (3.72 \pm 0.10) \times 10^3$ $M^{-1}s^{-1}$



Reaction of **1b** with **2f**
DMSO, 20 °C, stopped flow, 480 nm)

[**1b**] / M	[**2f**] / M	k_{obs} / s^{-1}
2.08×10^{-5}	4.18×10^{-4}	2.01
2.08×10^{-5}	8.37×10^{-4}	4.58
2.08×10^{-5}	1.19×10^{-3}	6.61
2.08×10^{-5}	1.67×10^{-3}	9.14
2.08×10^{-5}	2.15×10^{-3}	1.20×10^{1}

$k_2 = (5.71 \pm 0.08) \times 10^3$ $M^{-1}s^{-1}$

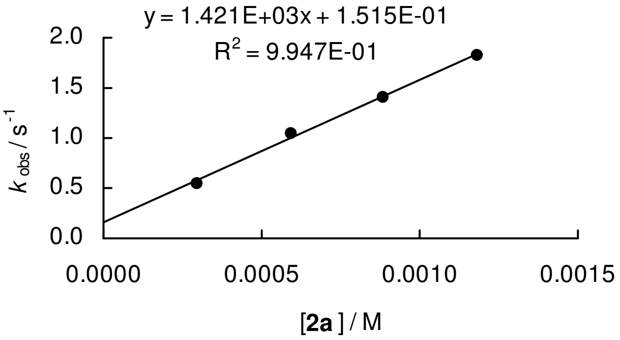


Reactions of electrophile 1c

Reaction of **1c** with **2a**
(DMSO, 20 °C, stopped flow, 364 nm)

[**1c**] / M	[**2a**] / M	k_{obs} / s^{-1}
1.82×10^{-5}	2.96×10^{-4}	5.37×10^{-1}
1.82×10^{-5}	5.93×10^{-4}	1.05
1.82×10^{-5}	8.89×10^{-4}	1.41
1.82×10^{-5}	1.19×10^{-3}	1.82

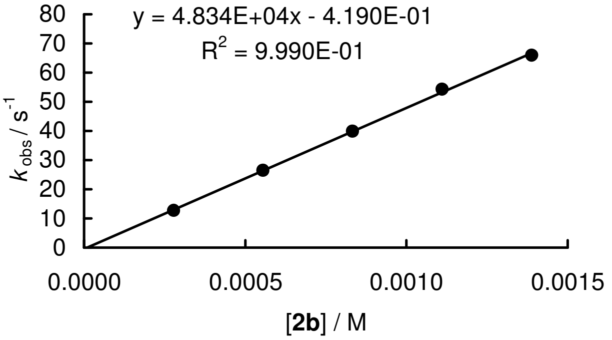
$k_2 = (1.42 \pm 0.07) \times 10^{3}$ $M^{-1}s^{-1}$



Reaction of **1c** with **2b**
(DMSO, 20 °C, stopped flow, 364 nm)

[**1c**] / M	[**2b**] / M	k_{obs} / s^{-1}
1.82×10^{-5}	2.78×10^{-4}	1.27×10^{1}
1.82×10^{-5}	5.55×10^{-4}	2.64×10^{1}
1.82×10^{-5}	8.33×10^{-4}	3.99×10^{1}
1.82×10^{-5}	1.11×10^{-3}	5.43×10^{1}
1.82×10^{-5}	1.39×10^{-3}	6.59×10^{1}

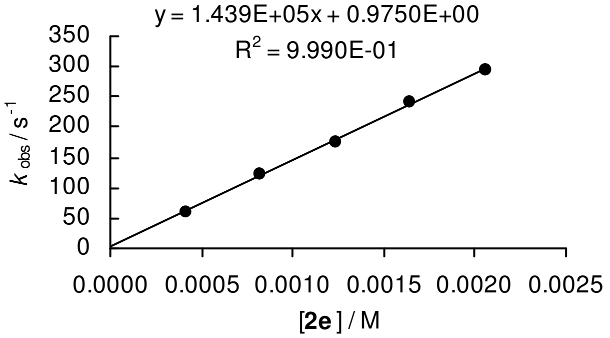
$k_2 = (4.83 \pm 0.09) \times 10^{4}$ $M^{-1}s^{-1}$



Reaction of **1c** with **2e**
(DMSO, 20 °C, stopped flow, 364 nm)

[**1c**] / M	[**2e**] / M	k_{obs} / s^{-1}
1.82×10^{-5}	4.12×10^{-4}	5.95×10^{1}
1.82×10^{-5}	8.25×10^{-4}	1.23×10^{2}
1.82×10^{-5}	1.24×10^{-3}	1.75×10^{2}
1.82×10^{-5}	1.65×10^{-3}	2.40×10^{2}
1.82×10^{-5}	2.05×10^{-3}	2.96×10^{2}

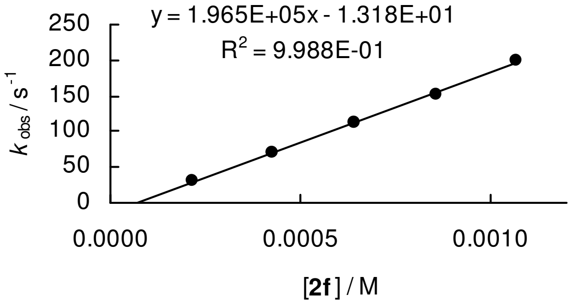
$k_2 = (1.44 \pm 0.02) \times 10^{5}$ $M^{-1}s^{-1}$



Reaction of **1c** with **2f**
(DMSO, 20 °C, stopped flow, 400 nm)

[**1c**] / M	[**2f**] / M	k_{obs} / s^{-1}
3.64×10^{-5}	2.14×10^{-4}	3.04×10^{1}
3.64×10^{-5}	4.28×10^{-4}	7.06×10^{1}
3.64×10^{-5}	6.42×10^{-4}	1.12×10^{2}
3.64×10^{-5}	8.56×10^{-4}	1.52×10^{2}
3.64×10^{-5}	1.07×10^{-3}	2.00×10^{2}

$k_2 = (1.97 \pm 0.04) \times 10^{5}$ $M^{-1}s^{-1}$



Nucleophilicity of the Bis-(4-nitrophenyl)-methyl Anion

Stefan T. A. Berger, Tadeusz Lemek, Herbert Mayr, *ARKIVOC* **2007,** submitted.

Introduction. In previous work, we have demonstrated that the rates of the reactions of carbocations and Michael acceptors with nucleophiles can be calculated by eq. 5.1,

$$\log k_2(20\ °\mathrm{C}) = s(N + E) \qquad (5.1)$$

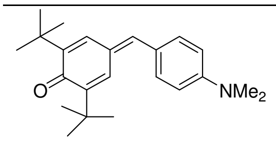
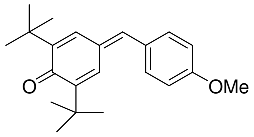
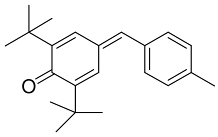
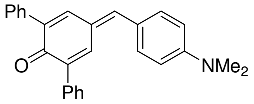
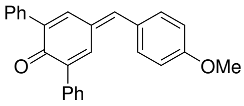
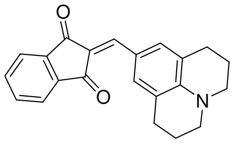
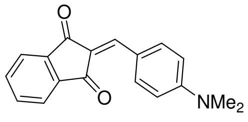
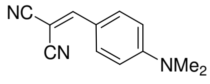
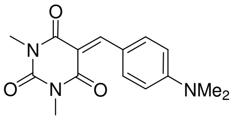
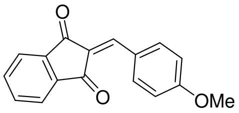
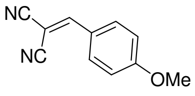
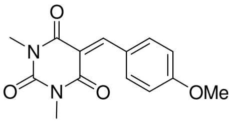
where E represents the reactivity of the electrophile, N represents a nucleophilicity parameter and s is a nucleophile-specific slope parameter.[1, 2, 3, 4]

By using colored benzhydrylium ions and structurally related quinone methides as reference electrophiles, a comprehensive nucleophilicity scale has been developed, which includes a large variety of σ-, n- and π- nucleophiles. This scale allows us to compare the reactivities of different types of nucleophiles on the basis of the nucleophilicity parameters N and s.

The fast characterization of a large number of nucleophiles became possible, because spectrophotometry provides an efficient tool to determine rate constants for the reactions of nucleophiles with the colored reference electrophiles on different time scales. An analogous charaterization of electrophiles, most of which are colorless, requires the availibility of colored reference nucleophiles. In this investigation we have examined whether benzhydryl anions can be employed for this purpose.

The bis-(4-nitrophenyl)-methyl anion **1**, has been reported to show an absorption maximum at 782 nm in a 95/5-mixture of DMSO and methanol (v/v).[5] We now report on the kinetics of the additions of **1** to quinone methides in DMSO and show that the resulting nucleophilicity parameters N and s for **1** can be used to estimate the rates of reactions of **1** with further Michael acceptors.

Table 5.1. Electrophilicity parameters *E* of the electrophiles **2a-l** and second-order rate constants k_2 in Lmol^{-1}s^{-1} for the reactions of **1** with **2a-k** in DMSO at 20 °C.

Electrophile	*E*	k_2 (Lmol^{-1}s^{-1})
 **2a**	-17.29[a]	6.36×10^{1}
 **2b**	-16.11[a]	3.32×10^{2}
 **2c**	-15.83[a]	5.29×10^{2}
 **2d**	-13.39[a]	2.99×10^{4}
 **2e**	-12.18[a]	1.46×10^{5}
 **2f**	-14.68[b]	8.79×10^{2}
 **2g**	-13.56[b]	7.01×10^{3}
 **2h**	-13.30[c]	2.39×10^{3}
 **2i**	-12.80[d]	2.33×10^{4}[e] / 2.24×10^{4}
 **2j**	-11.32[b]	3.54×10^{5}
 **2k**	-10.80[c]	1.81×10^{5}
 **2l**	-10.44[d]	-

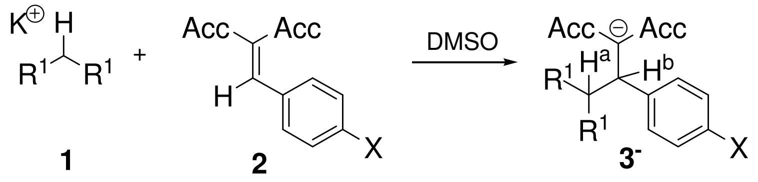
[a]From ref. 6, [b]from ref. 7, [c] from ref. 8 [d]from ref. 9, [e]pseudo-first-order conditions using **1** as the compound in excess.

Reaction products

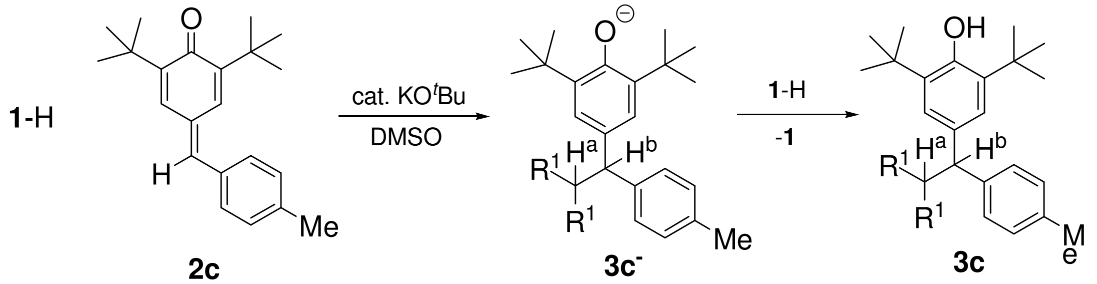
Because the nucleophile **1** can be expected to react analogously with all electrophiles **2** which were studied kinetically (Table 5.1), reaction products have only been identified for some representative substrates as listed in Table 5.2.

The anionic adducts **3**$^-$ obtained by mixing equimolar amounts of the electrophiles **2** and the potassium salt of the carbanion **1** in d_6-DMSO solutions were investigated by ^{1}H NMR spectroscopy (Scheme 5.1). Their neutral analogues which were supposed to develop after protonation of **3**$^-$ with aqueous HCl decomposed to the starting materials.

Scheme 5.1. Reactions of the potassium salts of **1** with the electrophiles **2** in DMSO.



In the case of the reaction of the quinone methide **2c** with **1** we succeeded in isolating the phenol **3c** by using catalytic amounts of KO^{t}Bu for the deprotonation of the CH acid **1**-H. The pK_{aH} value of the addition product **3c**$^-$ can be estimated to be (pK_{aH} > 16)[10] higher than the one of the CH acid **1**-H (pK_a = 15.85, DMSO-EtOH value)[11], so that **3c**$^-$ works as internal base during the reaction (Scheme 5.2).



Scheme 5.2. Reaction of **1**-H with **2c** by using catalytic amounts of KO^{t}Bu.

Evidence for the formation of the reaction products **3**$^-$ and **3c** is given by their ^{1}H NMR spectra which show characteristic doublets for H^a (δ = 4.64–6.05 ppm) and H^b (δ = 3.88–5.10 ppm, Table 5.2).

Table 5.2. Characterized adducts **3**$^-$ or **3** and some characteristic ^{1}H NMR chemical shifts and coupling constants.

Reactants		adducts	δ(H^a)/ppm	δ(H^b)/ppm	J_{ab} / Hz
1	**2c**	**3c**	4.86	4.58	12.2
1	**2h**	**3h**$^-$	4.64	3.88	12.5
1	**2j**	**3j**$^-$	5.82	4.63	12.6
1	**2l**	**3l**$^-$	6.05	5.10	12.6

Kinetic investigations

The kinetic investigations were performed in dimethyl sulfoxide solution at 20 °C by using conventional UV-vis spectroscopy with fiber optics or the stopped-flow technique. All reactions reported in this paper followed second-order kinetics, first-order with respect to the nucleophile concentration and first-order with respect to the electrophile concentration. For the kinetic experiments the bis-(4-nitrophenyl)-methyl anion **1** was either generated freshly by deprotonating the corresponding CH acid **1**-H with 1.05 equivalents of KO^{t}Bu, or the isolated potassium salt of **1** was employed. In general, the reactions of the blue nucleophile **1** with the yellow or orange electrophiles **2a**-**k** were carried out under pseudo-first-order conditions by using an excess of the electrophiles **2a**-**k**. The rates were determined photometrically by following the decrease of the absorbance of the nucleophile **1** at its absorption maximum (Figure 5.1).

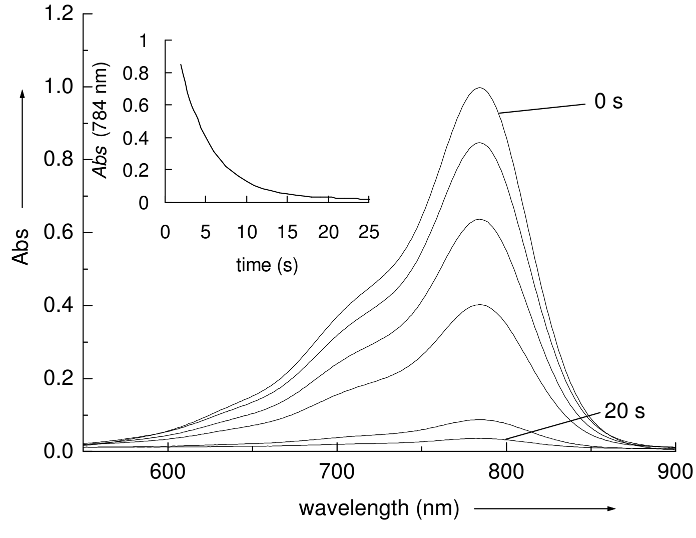


Figure 5.1. UV-vis-spectroscopic monitoring of the reaction of the bis-(4-nitrophenyl)-methyl anion **1** (2.16×10^{-5} mol L^{-1}) with the quinone methide **2c** (4.83×10^{-4} mol L^{-1}) at 784 nm in DMSO at 20 °C.

Because the concentrations of the electrophiles were thus kept almost constant throughout the reactions, an exponential decay of the nucleophile absorbance at 782 nm resulted (eq. 5.2) from which the first-order rate constants k_{obs} were derived by least-squares fitting of the single-exponential $A_t = A_0\exp(-k_{1\Psi}t) + C$.

$$-\mathrm{d}[\mathbf{1}]/\mathrm{d}t = -\mathrm{d}A/\mathrm{d}t = k_{\mathrm{obs}}\,[\mathbf{1}] \qquad (5.2)$$

Plots of k_{obs} versus the concentrations of the electrophile $[\mathbf{2}]_0$ gave straight lines with the slopes k_2 as shown for one example in Figure 5.2 and for all other kinetic experiments in the Experimental Section. All second-order rate constants k_2 (L mol^{-1} s^{-1}) for the reactions of **1** with **2a-k** are listed in Table 5.1.

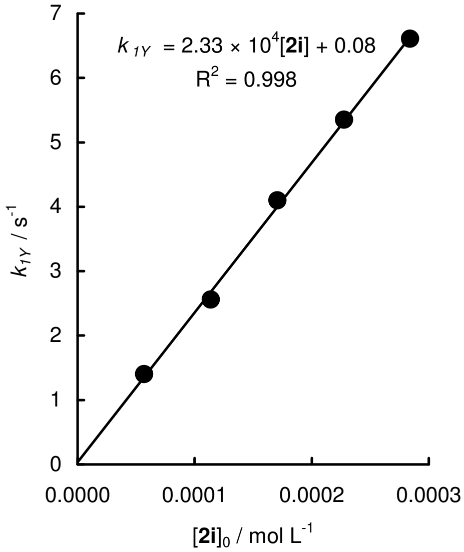


Figure 5.2. Determination of the second-order rate constant $k_2 = 2.33 \times 10^4$ L mol^{-1} s^{-1} for the reaction of **1** with **2i** in DMSO at 20 °C.

The reaction of **1** with **2i** was also studied under pseudo-first order conditions with an excess of the bis-(4-nitrophenyl)-methyl anion **1**; the resulting second-order rate constant differed by 3% from the value obtained with an excess of **2i**. With one exception all reactions proceeded quantitatively. Only the reaction of **1** with benzylidenemalononitrile **2h** was incomplete and the absorbance at the end of the reaction decreased with increasing concentration of **2h** (Figure 5.3).

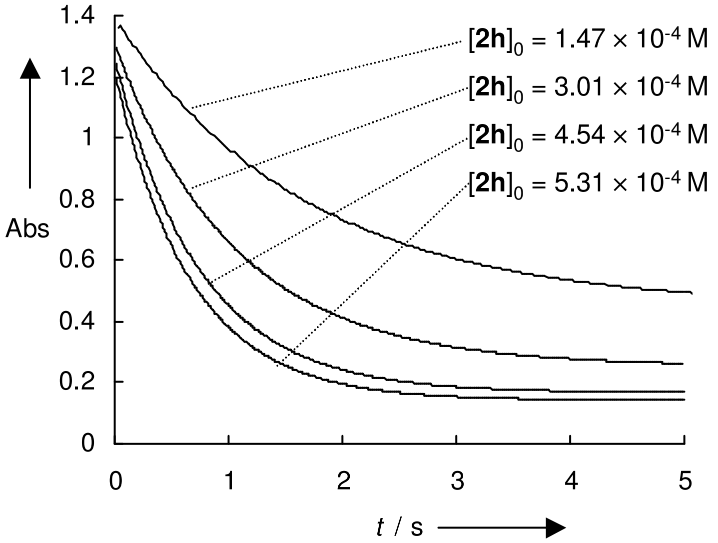


Figure 5.3. Plot of the absorbance (λ = 782 nm) versus t for the reversible reaction of **2h** with **1** (c_0 = 4.86 × 10^{-5} M) at different initial concentrations of **2h** in DMSO (20 °C).

Because the molar absorption coefficient of **1** is known (97000 $\mathrm{Lmol^{-1}cm^{-1}}$)^5 we were able to determine the equilibrium constant K as (61022±2570) $\mathrm{Lmol^{-1}}$corresponding to a reaction free enthalpy of $\Delta_r G_0$ = -26.84 kJ $\mathrm{mol^{-1}}$ (Experimental Section).

Discussion.

When the rate constants (log *k*) for the reactions of **1** with the reference electrophiles **2a**-**e** were plotted against their electrophilicity parameters *E*, a straight line is obtained (Figure 5.4), the slope of which yields the nucleophile-specific parameter *s*, whereas the intercept with the abscissa corresponds to the negative value of the nucleophilicity parameter *N* of **1**. The fact that all data points for the reference electrophiles are exactly on the correlation line indicates the applicability of eq. (5.1).

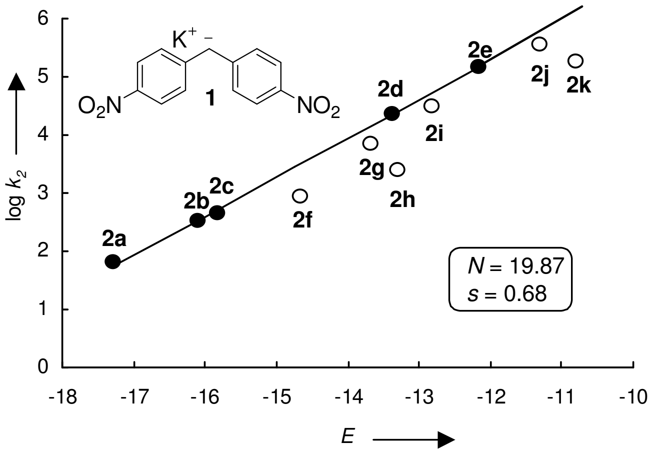


Figure 5.4. Plot of log k_2 for the reaction of the bis-(4-nitrophenyl)-methyl anion **1** (Table 5.1) with the reference electrophiles **2a-e** and the Michael acceptors **2f-k** in DMSO at 20 °C versus the corresponding electrophilicity parameters *E* (Table 5.1). Open symbols were not used for the construction of the correlation line and for the determination of the nucleophilicity parameters of **1**.

It is obvious, however, that the rates of the reactions of the bis-(4-nitrophenyl)-methyl anion **1** with the Michael acceptors **2f-k** are smaller than expected on the basis of their electrophilicity parameters *E*. While we do not yet know why all rate constants for **2f-k** are below the correlation line, it should be emphasized that all deviations are smaller than 1 order of magnitude and thus are within the previously postulated confidence limit of eq. 5.1.[2d]

Possibly the deviations are due to steric effects, because the Michael acceptors **2f-k** are sterically more congested at the reaction center than the quinone methides **2a**-**e** which were used as reference compounds for determining *N* and *s* of **1**. Because of the two phenyl groups at the carbanionic center the bis-(4-nitrophenyl)-methyl anion **1** might be more sensitive towards steric shielding of the electrophiles than the carbanions used for the determination of the *E*-parameters of **2a-k**. However, the particularly strong deviation of the sterically nonshielded benzylidenemalononitriles **2h** and **2k** contradicts this explanation.

The availability of rate and equilibrium constants for the reaction of **1** with **2h** allows us to calculate the intrinsic barrier $\Delta G_0^{\ddagger} = 65.5$ kJ mol^{-1} by substituting $\Delta G^{\ddagger} = 52.8$ kJ mol^{-1} and $\Delta_r G_0 = -26.8$ into the Marcus equation[12] (5.3)

$$\Delta G^{\ddagger} = \Delta G_0^{\ddagger} + 0.5\Delta_r G_0 + [(\Delta_r G_0)^2 / 16\Delta G_0^{\ddagger}] \qquad (5.3)$$

where the work term has been omitted.

As mentioned above, the reaction of **1** with **2h** is the only one of the series listed in Table 5.1 which proceeds incompletely. Despite its unfavorable equilibrium constant, **2h** reacts with similar rate or even faster than several other electrophiles of Table 5.1 which is indicative of a particularly low intrinsic barrier of the reaction of **2h**. This finding is in accord with previous observations of Bernasconi that reactions to arylidene malononitriles have lower intrinsic barriers than olefins activated by alkoxycarbonyl or nitro groups.[13]

The title compound **1** can be considered as a phenylog of *p*-nitrophenylnitronate **4**. Figure 5.5 shows that separation of the nitro group from the carbanionic center by a phenylene group (cf. **4** with **1**) causes an increase of *N* by 3 units . With an *N* parameter of 19.87 the nucleophilicity of anion **1** in DMSO is comparable to those of the methyl nitronate[14] and the malononitrile anion[6] in the same solvent and thus ranks among the most reactive carbanions so far characterized in our nucleophilicity scales.[1]

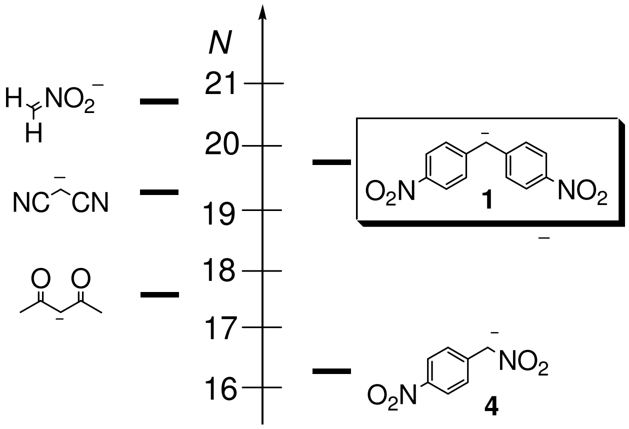


Figure 5.5. Comparison of the nucleophilicities of typical carbanions in DMSO.

Conclusion.

With this investigation we have integrated another colored nucleophile in our comprehensive nucleophilicity scale. The fair correlation depicted in Figure 3 suggests that **1** might be applicable for the determination of the electrophilicities of colorless electrophiles by UV-vis spectroscopy.

Experimental Section

Materials. DMSO (content of H_2O < 50 ppm) was used. Stock solutions of KO^{t}Bu were prepared by adding the potassium salt to DMSO under a nitrogen atmosphere.

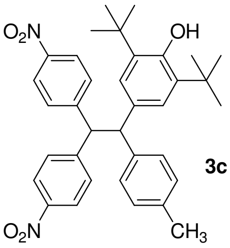
Instruments. ^{1}H NMR spectra were recorded on a Varian Mercury 200 (200 MHz) and on a Bruker AMX 400 (400 MHz). Chemical shifts are expressed in ppm and refer to Me_4Si (δ_H = 0.00 ppm). The coupling constants are given in Hz. The melting point was determined on a Büchi B-540 and is uncorrected. The yield corresponds to a isolated product without optimization of the work up. Abbreviations used are s (singlet), d (doublet). The mass spectrum was measured with a Finnigan MAT 95 Q.

Preparation of the potassium salt of bis-(4-nitrophenyl)-methane 1

A solution of **1**-H (2.58 g, 10.0 mmol) in THF (160 mL) was added dropwise within 15 min to a solution of potassium ethoxide (840 mg, 10.0 mmol) in EtOH/THF (60 mL / 40 mL) at 0 °C. The solution was concentrated by evaporation to 100 mL in vacuum. Then toluene (20 mL) was added and evaporation was continued to give a precipitate of dark-blue crystals. After addition of toluene (20 mL) the mixture was filtered and the crystals were washed with two 10-mL portions of toluene. The product was dried in vacuum at 10^{-5} mbar yielding 2.8 g of **1-K** (94%).

Reaction of 1 with the quinone methide 2c

To a solution of **1**-H (52 mg, 0.20 mmol) and KO^{t}Bu (4.0 mg, 36 µmol) in DMSO (2 mL) a solution of quinone methide **2c** (62 mg, 0.20 mmol) in CH_2Cl_2 (3 mL) was added at ambient temperature.. After stirring for 5 min the mixture was poured into 20 mL of 1% aqueous HCl at 0 °C. The product was extracted with CH_2Cl_2, dried with Na_2SO_4, and purified by column chromatography on silica gel with hexane/ethyl acetate as eluent. Crystallization from hexane yielded **4-[2,2-bis-(4-nitrophenyl)-1-*p*-tolyl-ethyl]-2,6-di-*t*butyl-phenol** (85 mg, 75%); mp. 193-195 °C.


3c

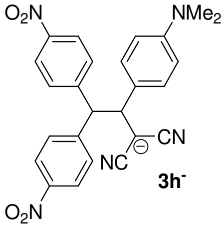
3c: ^{1}H NMR (CDCl$_3$, 200 MHz): δ= 1.24 (s, 18 H), 2.21 (s, 3 H), 4.58 (d, J = 12.2 Hz, 1 H), 4.86 (d, J = 12.2 Hz, 1 H), 4.95 (s, 1 H, OH), 6.75 (s, 2 H), 6.94–6.98 (m, 2 H), 7.05–7.10 (m, 2 H), 7.12–7.18 (m, 2 H), 7.33–7.39 (m, 2 H), 7.93–7.99 (m, 2 H), 7.99–8.05 (m, 2 H). MS (EI, 70eV) m/z (%): 564 (M$^+$ - H$_2$) 309 (100), 293 (91), 265 (39), 251 (66). Anal. Calcd. for C$_{35}$H$_{38}$N$_2$O$_5$: H 6.76 C 74.18 N 4.94. Found: H 6.69 C 74.00 N 4.98.

Reaction of 1 with Michael acceptors

General procedure:

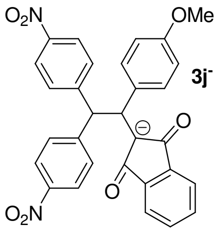
The reactions of **1** with different Michael acceptors were followed by ^{1}H NMR spectroscopy in d$_6$-DMSO. Equimolar amounts of **1** and **2** in d$_6$-DMSO were mixed in an NMR tube and homogenized in an ultrasound bath.

Reaction of 1 with 2h


3h$^-$

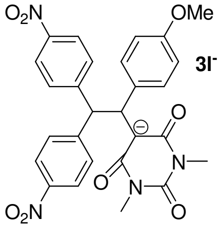
3h$^-$: ^{1}H NMR (d$_6$-DMSO, 200 MHz): δ= 2.76 (s, 6 H), 3.88 (d, J = 12.5 Hz, 1 H), 4.64 (d, J = 12.5 Hz, 1 H), 6.47 (d, J = 8.5 Hz, 2 H), 7.05 (d, J = 8.4 Hz, 2 H), 7.59–7.70 (m, 4 H), 7.81 (d, J = 8.5 Hz, 2 H), 8.14 (d, J = 8.5 Hz, 2 H).

Reaction of 1 with 2j


3j$^-$

3j$^-$: ^{1}H NMR (d$_6$-DMSO, 200 MHz): δ= 3.58 (s, 3 H), 4.63 (d, J = 12.6 Hz, 1 H), 5.82 (d, J = 12.6 Hz, 1 H), 6.59 (d, J = 8.5 Hz, 2 H), 7.12 (d, J = 8.9 Hz, 2 H), 7.36–7.71 (m, 6 H), 7.89–7.95 (m, 6 H).

Reaction of 1 with 2l



3l$^-$

3l$^-$: ^{1}H NMR (d$_6$-DMSO, 400 MHz): δ = 2.89 (s, 3 H), 2.98 (s, 3 H), 3.59 (s, 3 H), 5.10 (d, J = 12.6 Hz, 1 H), 6.05 (d, J = 12.6 Hz, 1 H), 6.57 (d, J = 8.8 Hz, 2 H), 7.42 (d, J = 8.8 Hz, 2 H), 7.53 (d, J = 8.9 Hz, 2 H), 7.65 (d, J = 8.9 Hz, 2 H), 7.95 (d, J = 8.8 Hz, 2 H), 8.00 (d, J = 8.8 Hz, 2 H).

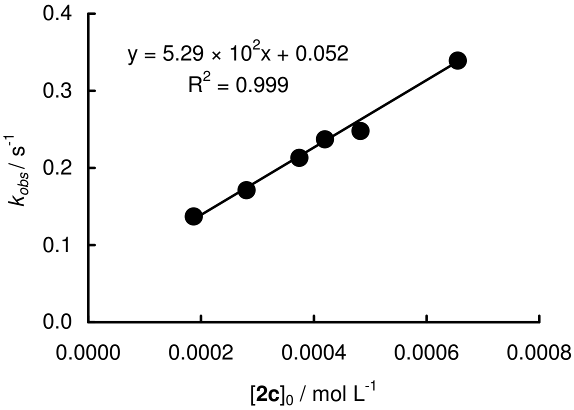
Kinetics in DMSO at 20 °C

The rates of slow reactions ($\tau_{1/2}$ > 10 s) were determined by using a J&M TIDAS diode array spectrophotometer which was controlled by Labcontrol spectacle software and connected to a Hellma 661.502-QX quarz Suprasil immersion probe (5 mm ligth path) via fiber optic cables and standard SMA connectors. The temperature trough the solutions of all kinetic experiments was kept constant (20 ± 0.2 °C) by using a circulating bath thermostat and was monitored with a thermo-coupling probe that was inserted into the reaction mixture. In these experiments three stock solutions were used: A stock solution of the electrophile in DMSO, the CH acid in DMSO and a solution of base. The stock solutions of KO^{t}Bu were prepared as mentioned before. For the evaluation of fast kinetics ($\tau_{1/2}$ < 10 s) the stopped flow spectrophotometer systems Hi-Tech SF-61DX2 or Applied Photophysics SX.18MV-R stopped-flow reaction analyser were used. Rate constants were obtained by fitting the single exponential $A_t = A_0\exp(-k_{obs}t) + C$ to the observed time-dependent carbanion absorbance (averaged from at least 4 kinetic runs for each electrophile concentration). For the stopped flow experiments 2 stock solutions were used: A solution of the electrophile in DMSO and a solution of the carbanion, generated by the deprotonation of the CH acid with 1.05 equiv. of KO^{t}Bu whose preparation was described above.

Reaction of **2c** with **1** (J&M, 783 nm, 20 °C)

[**2c**]$_0$ / mol L^{-1}	[C$^-$]$_0$ / mol L^{-1}	k_{obs} / s^{-1}
1.88×10^{-4}	2.35×10^{-5}	1.37×10^{-1}
2.81×10^{-4}	2.35×10^{-5}	1.71×10^{-1}
3.75×10^{-4}	2.35×10^{-5}	2.13×10^{-1}
4.20×10^{-4}	2.35×10^{-5}	2.37×10^{-1}
4.83×10^{-4}	2.16×10^{-5}	2.48×10^{-1}
6.56×10^{-4}	2.35×10^{-5}	3.39×10^{-1}

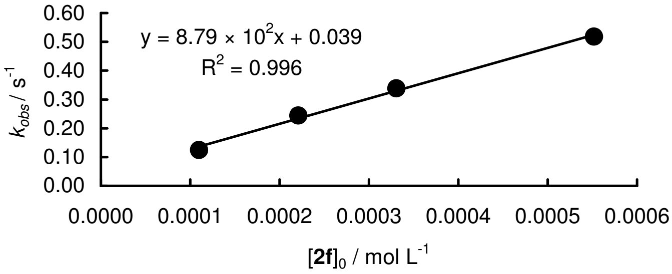
$k_2 = 5.29 \times 10^2$ Lmol^{-1}s^{-1}



Reaction of **2f** with **1** (stopped-flow, 700 nm, 20 °C)

[**2f**]$_0$ / mol L^{-1}	[C$^-$]$_0$ / mol L^{-1}	k_{obs} / s^{-1}
1.10×10^{-4}	1.21×10^{-5}	1.25×10^{-1}
2.21×10^{-4}	1.21×10^{-5}	2.44×10^{-1}
3.31×10^{-4}	1.21×10^{-5}	3.38×10^{-1}
5.52×10^{-4}	1.21×10^{-5}	5.18×10^{-1}

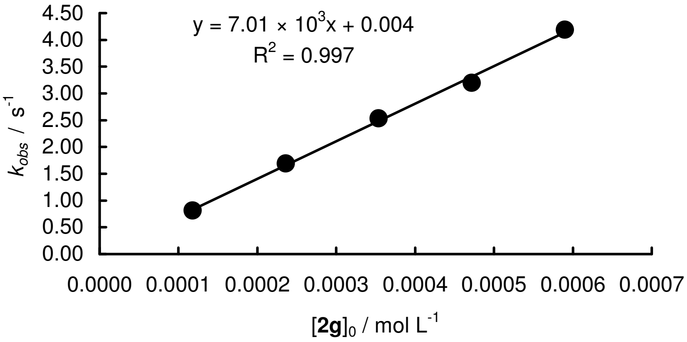
$k_2 = 8.79 \times 10^2$ Lmol^{-1}s^{-1}



Reaction of **2g** with **1** (stopped-flow, 700 nm, 20 °C)

$[\mathbf{2g}]_0$ / mol L^{-1}	$[C^-]_0$ / mol L^{-1}	k_{obs} / s^{-1}
1.18×10^{-4}	1.06×10^{-5}	8.10×10^{-1}
2.36×10^{-4}	1.06×10^{-5}	1.69
3.54×10^{-4}	1.06×10^{-5}	2.54
4.72×10^{-4}	1.06×10^{-5}	3.20
5.90×10^{-4}	1.06×10^{-5}	4.19

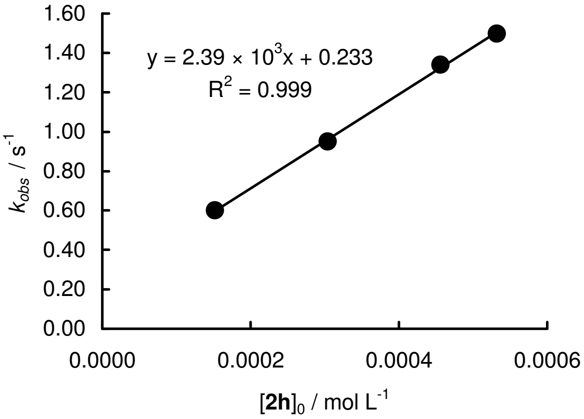
$k_2 = 7.01 \times 10^3$ $Lmol^{-1}s^{-1}$



Reaction of **2h** with **1** (stopped-flow, 783 nm, 20 °C)

$[\mathbf{2h}]_0$ / mol L^{-1}	$[C^-]_0$ / mol L^{-1}	k_{obs} / s^{-1}
1.52×10^{-4}	4.86×10^{-5}	6.00×10^{-1}
3.04×10^{-4}	4.86×10^{-5}	9.52×10^{-1}
4.56×10^{-4}	4.86×10^{-5}	1.34
5.32×10^{-4}	4.86×10^{-5}	1.50

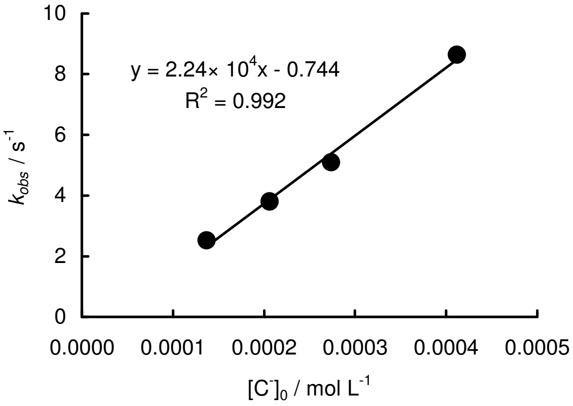
$k_2 = 2.39 \times 10^3$ $Lmol^{-1}s^{-1}$



Reaction of **2i** with **1** (stopped-flow, 470 nm, 20 °C)

$[E]_0$ / mol L^{-1}	$[C^-]_0$ / mol L^{-1}	k_{obs} / s^{-1}
1.22×10^{-5}	1.37×10^{-4}	2.52
1.22×10^{-5}	2.06×10^{-4}	3.80
1.22×10^{-5}	2.74×10^{-4}	5.09
1.22×10^{-5}	4.12×10^{-4}	8.64

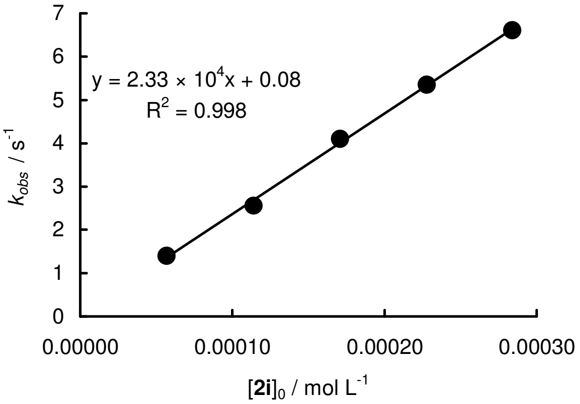
$k_2 = 2.24 \times 10^4$ $Lmol^{-1}s^{-1}$



Reaction of **2i** with **1** (stopped-flow, 700 nm, 20 °C)

[**2i**]$_0$ / mol L^{-1}	[C$^-$]$_0$ / mol L^{-1}	k_{obs} / s^{-1}
5.70×10^{-5}	1.18×10^{-5}	1.46
1.14×10^{-4}	1.18×10^{-5}	2.57
1.71×10^{-4}	1.18×10^{-5}	4.10
2.28×10^{-4}	1.18×10^{-5}	5.38
2.84×10^{-4}	1.18×10^{-5}	6.62

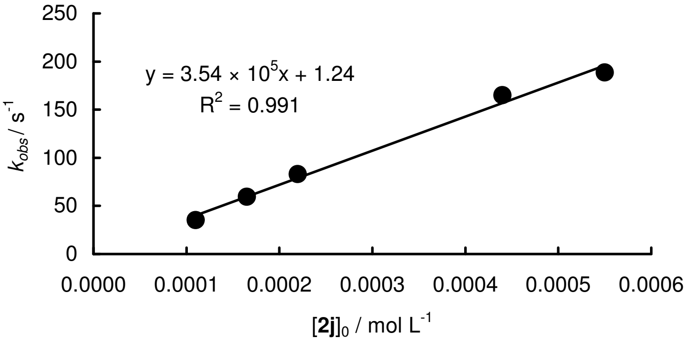
$k_2 = 2.31 \times 10^4$ Lmol^{-1}s^{-1}



Reaction of **2j** with **1** (stopped-flow, 700 nm, 20 °C)

[**2j**]$_0$ / mol L^{-1}	[C$^-$]$_0$ / mol L^{-1}	k_{obs} / s^{-1}
1.10×10^{-4}	1.10×10^{-5}	3.52×10^{1}
1.65×10^{-4}	1.10×10^{-5}	5.95×10^{1}
2.20×10^{-4}	1.10×10^{-5}	8.30×10^{1}
4.40×10^{-4}	1.10×10^{-5}	1.65×10^{2}
5.50×10^{-4}	1.10×10^{-5}	1.89×10^{2}

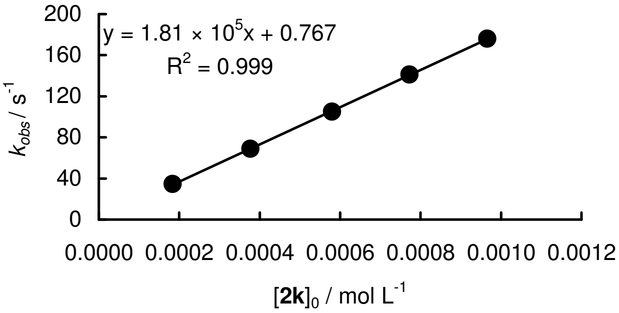
$k_2 = 3.54 \times 10^5$ Lmol^{-1}s^{-1}



Reaction of **2k** with **1** (stopped-flow, 783 nm, 20 °C)

[**2k**]$_0$ / mol L^{-1}	[C$^-$]$_0$ / mol L^{-1}	k_{obs} / s^{-1}
1.84×10^{-4}	1.89×10^{-5}	3.46×10^{1}
3.77×10^{-4}	1.89×10^{-5}	6.88×10^{1}
5.80×10^{-4}	1.89×10^{-5}	1.05×10^{2}
7.73×10^{-4}	1.89×10^{-5}	1.41×10^{2}
9.66×10^{-4}	1.89×10^{-5}	1.76×10^{2}

$k_2 = 1.81 \times 10^5$ Lmol^{-1}s^{-1}



Determination of the equilibrium constant for the reaction of 1 with 2h

While all reactions of the bis-(4-nitrophenyl)-methyl anion **1** with electrophiles **2** investigated in this work proceeded with quantitative formation of the addition products, reversible adduct formation was observed for the combination with the benzylidenemalononitrile **2h**. The equilibrium constant *K* of this reaction was calculated on the basis of the equilibrium concentrations of **1** which were determined photometrically by using the stopped-flow technique (Table 5.3). Therefore different amounts of benzylidenemalononitrile **2h** were added to a constant concentration of **1** and when the equilibrium was reached, the absorbance of the solution was determined photometrically at the absorbance maximum of **1** at 782 nm (Figure 5.3).

$$\mathbf{1} + \mathbf{2h} \xrightleftharpoons{K} \mathbf{3}$$

$$K = [\mathbf{3}]_{eq}/([\mathbf{1}]_{eq}[\mathbf{2h}]_{eq})$$

Assuming the validity of Beer-Lambert's law and that the initial concentrations of **1** and **2h** are $[\mathbf{1}]_o$ and $[\mathbf{2h}]_o$, their equilibrium concentrations are:

$$[\mathbf{1}]_{eq} = \mathrm{Abs} / \varepsilon \text{ and } [\mathbf{2h}]_{eq} = [\mathbf{2h}]_0 - [\mathbf{1}]_{eq}$$

The equilibrium concentration of **3** can be calculated as:

$$[\mathbf{3}]_{eq} = [\mathbf{1}]_0 - [\mathbf{1}]_{eq}$$

Table 5.3. Initial and equilibrium concentrations of **1**, **2h** and **3** for the determination of the equilibrium constant K of the reaction of **1** with **2h**. ε (**1**) = 97000 $\mathrm{Lmol^{-1}cm^{-1}}$, $[\mathbf{1}]_0 = 4.86 \times 10^{-5}$ mol $\mathrm{L^{-1}}$.

$[\mathbf{2h}]_0$ (M)	Abs	$[\mathbf{1}]_{eq}$ (M)	$[\mathbf{2h}]_{eq}$ (M)	$[\mathbf{3}]_{eq}$ (M)	*K* ($\mathrm{Lmol^{-1}}$)
1.52×10^{-4}	0.450	4.64×10^{-6}	1.47×10^{-4}	4.40×10^{-5}	6.43×10^{4}
3.04×10^{-4}	0.254	2.62×10^{-6}	3.01×10^{-4}	4.60×10^{-5}	5.83×10^{4}
4.56×10^{-4}	0.167	1.72×10^{-6}	4.54×10^{-4}	4.69×10^{-5}	5.99×10^{4}
5.32×10^{-4}	0.144	1.44×10^{-6}	5.31×10^{-4}	4.72×10^{-5}	6.16×10^{4}

K = 61022±2570 $\mathrm{Lmol^{-1}}$.

Table 5.3 shows that higher concentrations of **2h** increase the degree of conversion of the bis-(4-nitrophenyl)-methyl anion **1**. The equilibrium constant K calculated as the ratio k_{+}/k_{-} equals 10257 Lmol^{-1}. This value is much smaller than that one derived from the concentrations of reactants and products.

Literature

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[1] (a) H. Mayr, A. R. Ofial, *Pure Appl. Chem.* **2005**, *77*, 1807-1821. (b) H. Mayr, A. R. Ofial in *Carbocation Chemistry* (G. A. Olah, G. K. S. Prakash, Eds.), Wiley, Hoboken (N.J.), **2004**, Chapt. 13, pp 331-358. (c) A. R. Ofial, H. Mayr, *Macromol. Symp.* **2004**, *215*, 353-367. (d) H. Mayr, B. Kempf, A. R. Ofial, *Acc. Chem. Res.* **2003**, *36*, 66-77. (e) H. Mayr, O. Kuhn, M. F. Gotta, M. Patz, *J. Phys. Org. Chem.* **1998**, *11*, 642-654. (f) H. Mayr, M. Patz, M. F. Gotta, A. R. Ofial, *Pure Appl. Chem.* **1998**, *70*, 1993-2000. (g) H. Mayr, M. Patz, *Angew. Chem.* **1994**, *106*, 990-1010; *Angew. Chem., Int. Ed. Engl.* **1994**, *33*, 938-957. (i) For a comprehensive listing of *N*- and *s*-parameters see: www.cup.uni-muenchen.de/oc/mayr/Dbintro.html

[2] For reactions of carbocations with π–nucleophiles, see: (a) S. Lakhdar, M. Westermaier, F. Terrier, R. Goumont, T. Boubaker, A. R. Ofial, H. Mayr, *J. Org. Chem.* **2006**, *71*, 9088-9095. (b) F. Dulich, K.-H. Müller, A. R. Ofial, H. Mayr, *Helv. Chim. Acta* **2005**, *88*, 1754-1768. (c) A. D. Dilman, H. Mayr, *Eur. J. Org. Chem.* **2005**, 1760-1764. (d) T. Tokuyasu, H. Mayr, *Eur. J. Org. Chem.* **2004**, 2791-2796. (e) B. Kempf, N. Hampel, A. R. Ofial, H. Mayr, *Chem. Eur. J.* **2003**, *9*, 2209-2218. (f) H. Mayr, M. F. Gotta, T. Bug, N. Hering, B. Irrgang, B. Janker, B. Kempf, R. Loos, A. R. Ofial, G. Remennikov, H. Schimmel, *J. Am. Chem. Soc.* **2001**, *123*, 9500-9512.

[3] For reactions of carbocations with hydride donors, see: (a) H. Mayr, G. Lang, A. R. Ofial, *J. Am. Chem. Soc.* **2002**, *124*, 4076-4083. (b) M. A. Funke, H. Mayr, *Chem. Eur. J.* **1997**, *3*, 1214-1222.

[4] For reactions of carbocations with *n*-nucleophiles, see: (a) M. Baidya, S. Kobayashi, F. Brotzel, U. Schmidhammer, E. Riedle, H. Mayr, *Angew. Chem.* **2007**, *119*, 6288-6292; *Angew. Chem. Int. Ed* **2007,** *46*, 6176-6179. (b) F. Brotzel, Y. C. Chu, H. Mayr, *J. Org. Chem.* **2007**, *46*,6176-6179. (c) F. Brotzel, B. Kempf, T. Singer, H. Zipse, H. Mayr, *Chem. Eur. J.* **2007**, *13*, 336-345. (d) T. B. Phan, H. Mayr, *J. Phys. Org. Chem.* **2006**, *19*, 706-713.

(e) A. A. Tishkov, U. Schmidhammer, S. Roth, E. Riedle, H. Mayr, *Angew. Chem.* **2005**, *117*, 4699-4703; *Angew. Chem. Int. Ed.* **2005**, *44*, 4623-4626. (f) S. Minegishi, R. Loos, S. Kobayashi, H. Mayr, *J. Am. Chem. Soc.* **2005**, *127*, 2641-2649. (g) B. Kempf, H. Mayr, *Chem. Eur. J.* **2005**, *11*, 917-927. (h) T. B. Phan, H. Mayr, *Can. J. Chem.* **2005**, *83*, 1554-1560. (i) S. Minegishi, H. Mayr, *J. Am. Chem. Soc.* **2003**, *125*, 286-295.

[5] M.-P. Simonnin, H.-Q. Xie, F. Terrier, J. Lelievre, P.G. Farell, *J. Chem. Soc. Perkin Trans 2*, **1989,** 1553-1558.

[6] Lucius, R.; Loos, R.; Mayr, H. *Angew. Chem.* **2002**, *114*, 97–102; *Angew. Chem., Int. Ed.* **2002**, *41*, 91–95.

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[9] F. H. Seeliger, S. T. A. Berger, G. Y. Remennikov, K. Polborn, H. Mayr, *J. Org. Chem.*, accepted.

[10] See http://www.chem.wisc.edu/areas/reich/pkatable/index.htm

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[13] C. F. Bernasconi, F. P. John, S. Fornarini, *J. Am. Chem. Soc.* **1980,** *102*, 2810-2816.

[14] T. Bug, T. Lemek, H. Mayr, *J. Org. Chem.* **2004**, *69*, 7565-7576.

Miscellaneous Experiments

6.1 Electrophilicity of 10-(4-methoxybenzylidene)-9(*10H*)-anthracenone in DMSO at 20 °C (**Figure 6.1**)

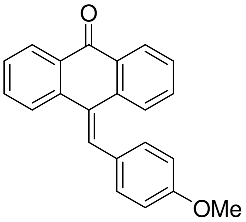


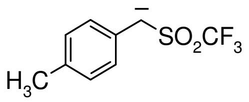
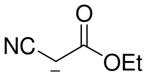
Figure 6.1. Structure of the 10-(4-methoxybenzylidene)-9(*10H*)-anthracenone, simply called *p*-methoxy-anthraquinonemethide.

At the beginning of my work the *p*-julolidene-di-*tert*-butyl substituted quinone methide (E = -17.90) was the weakest reference electrophile in our electrophilicity scale. For the characterization of many synthetically important highly reactive nucleophiles like α-cyanobenzyl anions or the dimsyl anion reference electrophiles with $-19 > E$ were needed. Therefore, one of the goals of the "carbanion group" was to extend the electrophilicity scale toward weaker electrophiles.

The new reference electrophiles should be structurally related to the current reference systems in order to keep the steric hindrance at the reaction center constant. In this case one can expect that the linear free energy relationship $\log k_2(20\ °\text{C}) = s(N + E)$ is fullfilled precisely. This chapter describes the determination of the electrophilicity of the 10-(4-methoxybenzylidene)-9(*10H*)-anthracenone which we simply called *p*-methoxy-anthraquinonemethide.

The kinetics were determined in the same way as described in the previous chapters. Pseudo-first-order reaction conditions were selected with the *p*-methoxy-anthraquinonemethide as the minor compound. All reactions proceeded quantitatively and the course of the reactions was followed at the absorption maximum of the *p*-methoxy-anthraquinonemethide at 421 nm. Table 6.1 summarizes the second-order rate constants of the reactions of the *p*-methoxy-anthraquinonemethide with several carbanions in DMSO which were generated by deprotonation of the corresponding CH-acidic compound with 1.05 equiv. of KO^{t}Bu.

Table 6.1. Second-order rate constants for the reactions *p*-methoxy-anthraquinonemethide with different carbanions in DMSO at 20 °C.

Nucleophile (C^-)	*N*	*s*	k_2 ($Lmol^{-1}s^{-1}$)
	19.35[a]	0.67[a]	9.74×10^{-2}
	19.62[b]	0.67[b]	8.00×10^{-1}
$CH_3CH=NO_2^-$	21.54[c]	0.62[c]	5.12
$H_2C=NO_2^-$	20.71[c]	0.60[c]	6.83

[a]From ref.1, [b]from ref.2, [c]from ref.3.

For all single kinetic experiments in DMSO perfect pseudo-first-order kinetics were obtained but the plot of $k_{1\psi}$ vs the concentration of the employed carbanions on page 166 never showed lines through origin indicating that we are not dealing with simple irreversible second-order kinetics. If the slopes of these correlations are tentatively considered as the second-order rate constants plots of logk_2/*s* versus *N* gave very poor correlations (Figure 6.2). Because of the lack of more reactive reference nucleophiles we have not continued this project to derive the exact electrophilicity parameter *E* for *p*-methoxy-anthraquinonemethide. Oliver Kaumanns is currently working on a class of weak electrophiles which are in the reactivity range needed for the characterization of further colorless highly reactive nucleophiles.

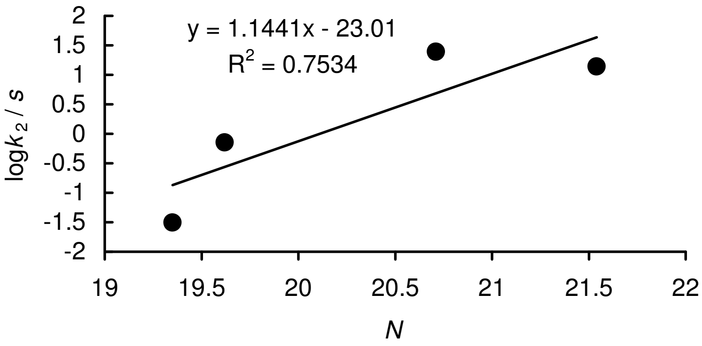
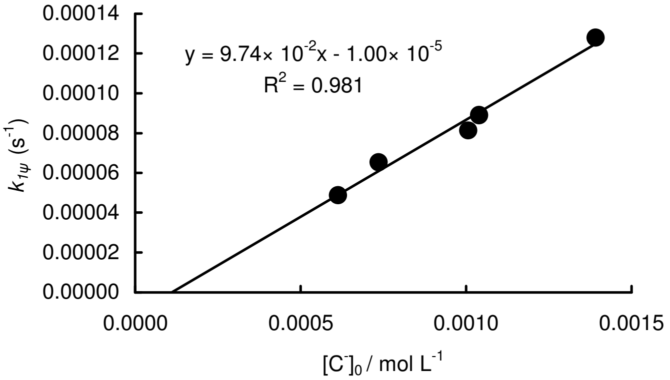


Figure 6.2. Plot of logk_2/*s* for the reactions of *p*-methoxy-anthraquinonemethide with carbanions in DMSO at 20 °C vs the nucleophilicity parameters *N* of the employed carbanions.

Reaction of *p*-methoxy-anthraquinonemethide with *p*-methylbenzyltriflinate (stopped-flow, λ = 421 nm)

$[E]_0$/ mol L^{-1}	$[C^-]_0$/ mol L^{-1}	$k_{1\psi}$ / s^{-1}
3.52×10^{-5}	7.35×10^{-4}	6.50×10^{-5}
3.52×10^{-5}	8.40×10^{-4}	9.10×10^{-5}
3.52×10^{-5}	1.01×10^{-3}	8.10×10^{-5}
3.52×10^{-5}	1.04×10^{-3}	8.90×10^{-5}
3.52×10^{-5}	1.39×10^{-3}	1.28×10^{-4}

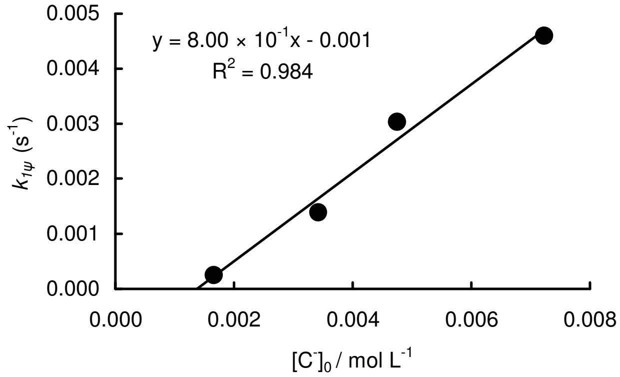
$k_2 = 9.74 \times 10^{-2}$ $Lmol^{-1}s^{-1}$



Reaction of *p*-methoxy-anthraquinonemethide with ethyl cyanoacetate (stopped-flow, λ = 421 nm)

$[E]_0$/ mol L^{-1}	$[C^-]_0$/ mol L^{-1}	$k_{1\psi}$ / s^{-1}
3.52×10^{-5}	1.66×10^{-3}	2.50×10^{-4}
3.52×10^{-5}	3.42×10^{-3}	1.39×10^{-3}
3.52×10^{-5}	4.75×10^{-3}	3.03×10^{-3}
3.52×10^{-5}	7.23×10^{-3}	4.60×10^{-3}

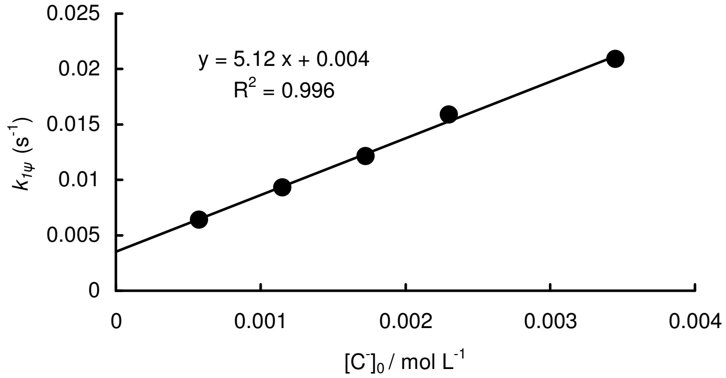
$k_2 = 8.00 \times 10^{-1}$ $Lmol^{-1}s^{-1}$



Reaction of *p*-methoxy-anthraquinonemethide with nitroethyl anion (stopped-flow, λ = 415 nm)

$[E]_0$/ mol L^{-1}	$[C^-]_0$/ mol L^{-1}	$k_{1\psi}$ / s^{-1}
4.48×10^{-5}	5.75×10^{-4}	6.00×10^{-3}
4.48×10^{-5}	1.15×10^{-3}	9.00×10^{-3}
4.48×10^{-5}	1.17×10^{-3}	1.20×10^{-2}
4.48×10^{-5}	2.30×10^{-3}	1.60×10^{-2}
4.48×10^{-5}	3.45×10^{-3}	2.10×10^{-2}

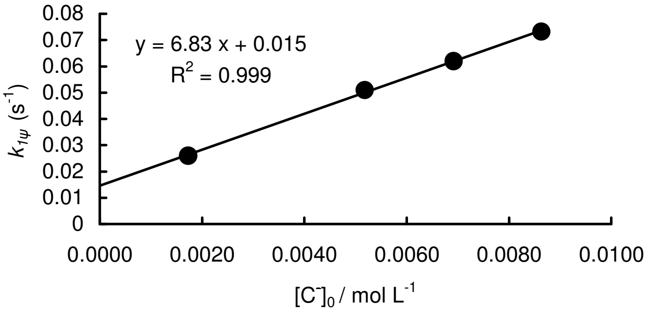
$k_2 = 5.12$ $Lmol^{-1}s^{-1}$



Reaction of *p*-methoxy-anthraquinonemethide with nitromethyl anion (stopped-flow, λ = 421 nm)

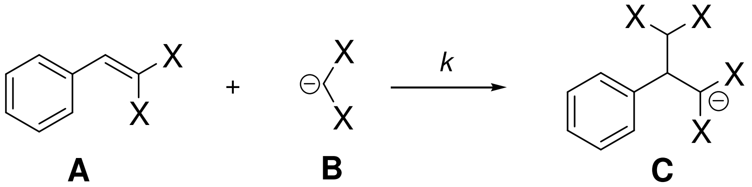
$[E]_0$/ mol L^{-1}	$[C^-]_0$/ mol L^{-1}	$k_{1\psi}$ / s^{-1}
2.23×10^{-5}	1.73×10^{-3}	2.60×10^{-2}
2.23×10^{-5}	5.18×10^{-3}	5.10×10^{-2}
2.23×10^{-5}	6.92×10^{-3}	6.20×10^{-2}
2.23×10^{-5}	8.64×10^{-3}	7.30×10^{-2}

$k_2 = 6.83$ $Lmol^{-1}s^{-1}$



6.2 Determination of the nucleophilicity parameters of the indan-1,3-dione anion in DMSO

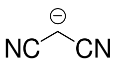
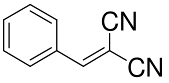
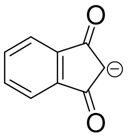
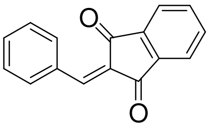
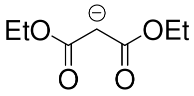
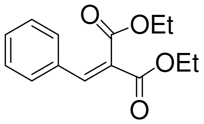
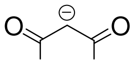
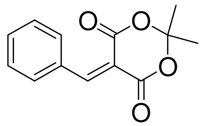
In my work I concentrated on the quantitative determination of nucleophilicities and electrophilicities of different carbanions and Michael acceptors in DMSO. The poor correlation between nucleophilicity and basicity, particularly striking in the case of different families of carbanions (see chapter 2) illustrates the limitation of Brønsted correlations. An explanation for the breakdown of such rate-equilibrium relationships has been given by the principle of non-perfect synchronization of Bernasconi.[4] Reactions which involve high reorganization of charge and solvation cannot be synchronized with bond breaking and making, and therefore give rise to high intrinsic barriers in the Marcus sense. An alternative way for determining differences in intrinsic barriers is to compare the kinetics of the reactions described in Scheme 6.1.



Scheme 6.1. Reaction of the Michael acceptor **A** with the carbanion **B** to give the addition product **C**.

Because the carbanions **B** and **C** are stabilized by analogous substituents, these reactions can be expected to have similar thermodynamic driving forces. Bernasconi had, therefore, compared the rates of several reactions of that type in 50% DMSO-50% water.[4,5] Because we have shown the dependence of the intrinsic barriers on the solvent (chapter 2), we now intended to derive the rates of these reactions in DMSO. As shown in Table 6.2, the nucleophilicity parameters *N* and *s* of the indan-1,3-dione anion are the only quantities missing for a comparison of four systems of that type.

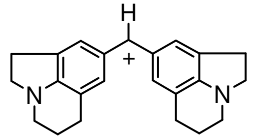
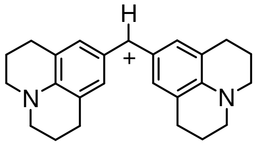
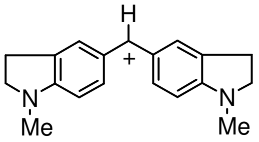
Table 6.2. Nucleophilicity- and electrophilicity parameters of carbanions and Michael acceptors in DMSO.

Nucleophile	*N*	Electrophile	*E*
	19.36[a]		-9.42[b]
	?		-10.13[c]
	20.22[a]		-20.58[d]
	13.91[a]		-9.18[d]

[a]from ref. 2. [b]from ref. 6. [c]from ref.7. [d]unpublished results.[e]derived by the correlation equation $\log k_2 = s(E+N)$.

The nucleophilicity parameters *N* and *s* of the indan-1,3-dione anion were determined by measuring the rates of the reactions of the indan-1,3-dione anion with benzhydrylium ions as reference electrophiles in DMSO at 20 °C (Table 6.3). For that purpose, the carbanion was prepared by deprotonating indan-1,3-dione with 1.05 equiv. of KO^{t}Bu in DMSO and mixed with solutions of the benzhydrylium tetrafluoroborates listed in Table 6.3. The corresponding second-order rate constants k_2 were derived as described in Chapter 2.

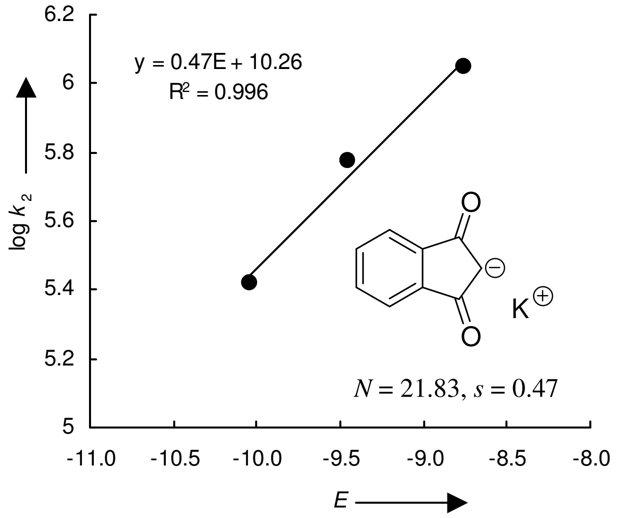
Table 6.3. Second-order rate constants of the reactions of the indan-1,3-dione anion with benzhydrylium ions in DMSO at 20 °C.

Electrophile		E^{a}	k_2 (M^{-1} s^{-1})
	$(lil)_2CH^+$	-10.04	2.63×10^5
	$(jul)_2CH^+$	-9.45	5.93×10^5
	$(ind)_2CH^+$	-8.76	1.12×10^6

[a]From ref. 2.

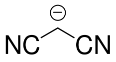
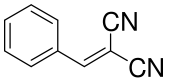
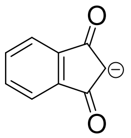
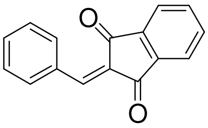
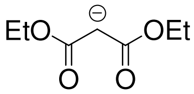
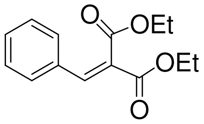
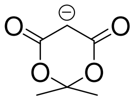
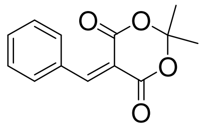
Plots of log k_2 for the reactions of indan-1,3-dione anion with benzhydrylium ions versus their electrophilicity parameters E (Table 6.3) yielded the nucleophilicity parameters N = 21.83 and s = 0.47 of the indan-1,3-dione anion in DMSO (Figure 6.3).

Figure 6.3. Plot of log k_2 for the reactions of indan-1,3-dione anion with benzhydrylium ions versus the electrophilicity parameters E of the benzhydrylium ions.



It is now possible to calculate the rate constants for the general reaction in Scheme 6.1 in DMSO (Table 6.4).

Table 6.4. Calculation of log k_2 for the reaction shown in Scheme 6.1 on the basis of the correalation equation log$k = s(N+E)$.

Nucleophile	N	Electrophile	E	logk_2[e]
	19.36[a]		-9.42[b]	6.65
	21.83		-10.13[c]	5.50
	20.22[a]		-20.58[d]	-0.23
	13.91[a]		-9.18[d]	4.07

[a]from ref. 2. [b]from ref.6. [c]from ref.7. [d]unpublished results.[e]derived by the correlation equation log$k_2 = s(E+N)$.

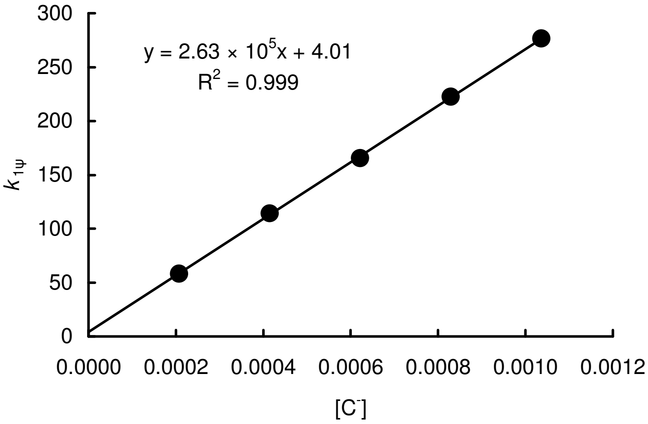
In accord with Bernasconi,[4,5] the malononitrile addition is very fast (low intrinsic barrier) while the addition of diethyl malonate is relatively slow (Table 6.4). Remarkably, the indan-1,3-dione anion is comparable to the malononitrile system (Table 6.4). Low intrinsic barriers imply that the indan-1,3-dione anion is a good nucleophile and at the same time, the 2-benzylidene-indan-1,3-dione is a good electrophile.

We have to admit, however, that the determined nucleophilicity parameters of indan-1,3-dione anion only should be used tentatively because of the untypically low nucleophile-specific slope parameter (slope of the line in Figure 6.3) which may be indicative of a systematic error. Before a detailed discussion of the different magnitudes of the intrinsic barriers it is necessary to confirm the nucleophilicity parameters N and s by studying the rates of the reactions of the indan-1,3-dione anion with weaker reference electrophiles in DMSO.

Reaction of $(\text{lil})_2\text{CH}^+$ with indan-1,3-dione anion (stopped-flow, 641 nm, 20 °C)

$[\text{E}]_0$ / mol L^{-1}	$[\text{C}^-]_0$ / mol L^{-1}	$k_{1\psi}$ / s^{-1}
2.40×10^{-5}	2.07×10^{-4}	5.83×10^{1}
2.40×10^{-5}	4.15×10^{-4}	1.14×10^{2}
2.40×10^{-5}	6.22×10^{-4}	1.66×10^{2}
2.40×10^{-5}	8.29×10^{-4}	2.22×10^{2}
2.40×10^{-5}	1.04×10^{-3}	2.77×10^{2}

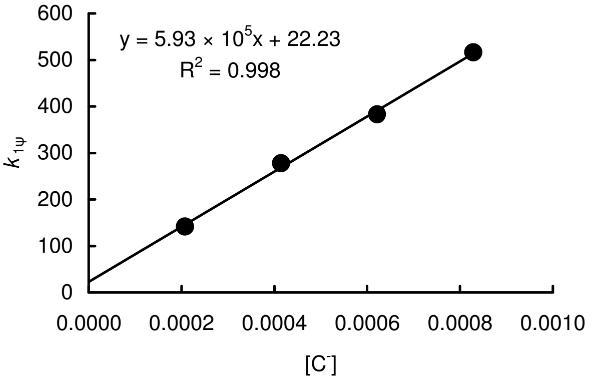
$k_2 = 2.63 \times 10^5$ Lmol^{-1}s^{-1}



Reaction of $(\text{jul})_2\text{CH}^+$ with indan-1,3-dione anion (stopped-flow, 641 nm, 20 °C)

$[\text{E}]_0$ / mol L^{-1}	$[\text{C}^-]_0$ / mol L^{-1}	$k_{1\psi}$ / s^{-1}
1.38×10^{-5}	2.07×10^{-4}	1.41×10^{2}
1.38×10^{-5}	4.15×10^{-4}	2.77×10^{2}
1.38×10^{-5}	6.22×10^{-4}	3.83×10^{2}
1.38×10^{-5}	8.29×10^{-4}	5.16×10^{2}

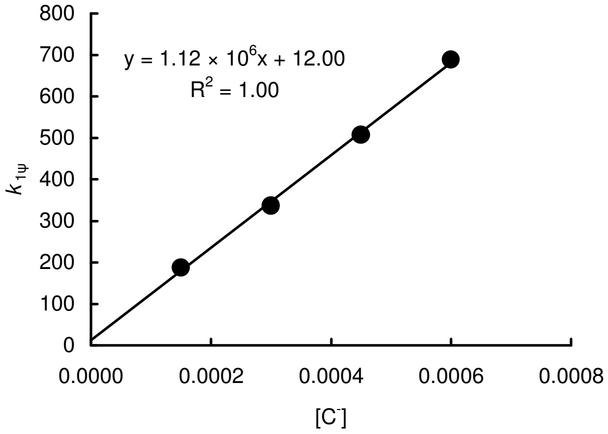
$k_2 = 5.93 \times 10^5$ Lmol^{-1}s^{-1}



Reaction of $(\text{ind})_2\text{CH}^+$ with indan-1,3-dione anion (stopped-flow, 641 nm, 20 °C)

$[\text{E}]_0$ / mol L^{-1}	$[\text{C}^-]_0$ / mol L^{-1}	$k_{1\psi}$ / s^{-1}
1.32×10^{-5}	1.50×10^{-4}	1.88×10^{2}
1.32×10^{-5}	3.00×10^{-4}	3.37×10^{2}
1.32×10^{-5}	4.50×10^{-4}	5.07×10^{2}
1.32×10^{-5}	6.00×10^{-4}	6.89×10^{2}

$k_2 = 1.12 \times 10^6$ Lmol^{-1}s^{-1}



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