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Electrophilicity parameters for 2-benzylidene-indan-1,3-diones—a systematic extension of the benzhydrylium based electrophilicity scale†

Stefan T. A. Berger, Florian H. Seeliger, Florian Hofbauer and Herbert Mayr*

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Kinetics of the reactions of four 2-benzylidene-indan-1,3-diones (**1a–d**) with carbanions (**2a–l**) have been studied photometrically in dimethyl sulfoxide solution at 20 °C, and the electrophilicity parameters E were determined by the linear free energy relationship $\log k_2(20\,^\circ\mathrm{C}) = s(N + E)$ (eqn (1)). The rate-determining step of these reactions is the nucleophilic attack of the carbon nucleophile at the double bond of the Michael acceptor. Comparisons with literature data show that the linear free energy relationship (eqn (1)) allows the semiquantitative prediction of the reactivities of 2-benzylidene-indan-1,3-diones towards various nucleophiles.

Introduction

Numerous kinetic investigations have shown that the rate constants for the reactions of carbocations with nucleophiles can be described by eqn (1).[1–4]

$$\log k_2(20\,^\circ\mathrm{C}) = s(N + E) \qquad (1)$$

Therein, k_2 corresponds to the second-order rate constant in L $\mathrm{mol^{-1}\,s^{-1}}$, 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.

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** (Fig. 1), which are difficult to synthesize, we were looking for more readily accessible alternatives.

Lemek showed that eqn (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 non-linear 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]

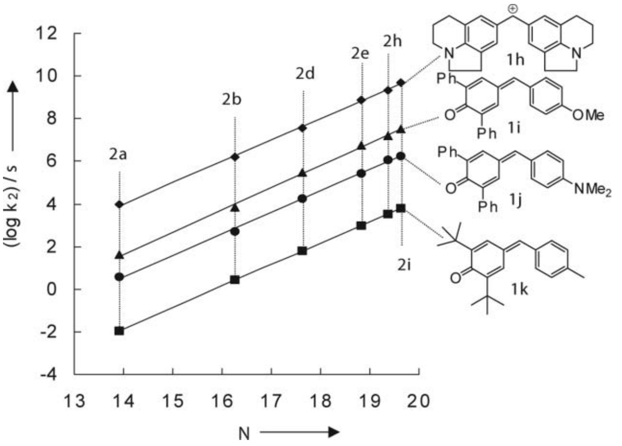


Fig. 1 Correlation of $(\log k_2)/s$ with the nucleophilicity parameter N for the reactions of the benzhydrylium ion **1h** and the quinone methides **1i–k** with carbanions (DMSO, 20 °C, from ref. 5).

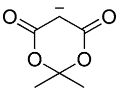
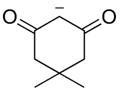
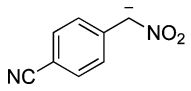
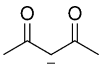
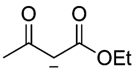
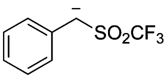
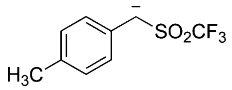
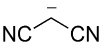
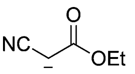
Due to the fact that the double bonds of the 2-benzylidene-indan-1,3-diones are strongly polarized by the mesomeric electron-withdrawing effect of the carbonyl groups, the double bond is highly electrophilic and can be attacked by many nucleophiles. Zalukaevs and Anokhina showed that the reaction of 2-benzylidene-indan-1,3-dione with ethyl acetoacetate gives the corresponding 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] and of phosphonium ylides[14b,14c] 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 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 eqn (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]

Department Chemie und Biochemie, Ludwig-Maximilians-Universität, Butenandtstr. 5-13 (Haus F), 81377 München, Germany. E-mail: herbert.mayr@cup.uni-muenchen.de; Fax: +49-89-2180-77717; Tel: +49-89-2180-77719

† Electronic supplementary information (ESI) available: Preparation and characterization (NMR) of products **3** and details of the kinetic measurements. See DOI: 10.1039/b708025e

Table 1 *N*- and *s*-parameters of the employed nucleophiles in DMSO

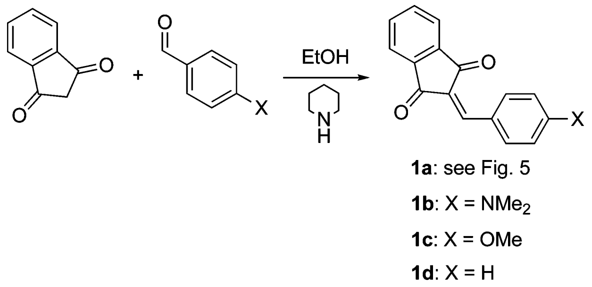
Nucleophile		*N*	*s*
	**2a**	13.91[a]	0.86[a]
	**2b**	16.27[a]	0.77[a]
	**2c**	16.96[b]	0.73[b]
	**2d**	17.64[a]	0.73[a]
	**2e**	18.82[a]	0.69[a]
	**2f**	18.67[c]	0.68[c]
	**2g**	19.35[c]	0.67[c]
	**2h**	19.36[a]	0.67[a]
	**2i**	19.62[a]	0.67[a]
$(CH_3)_2C{=}NO_2^-$	**2j**	20.61[b]	0.69[b]
$H_2C{=}NO_2^-$	**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 1 Preparation of the 2-benzylidene-indan-1,3-diones *via* Knoevenagel condensation.

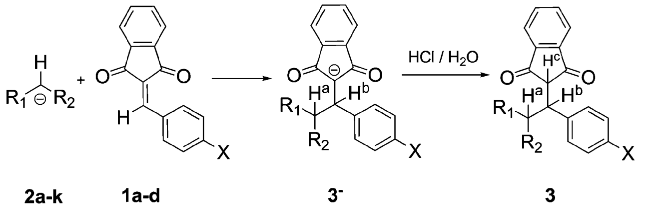
Table 2 Characterized Michael adducts **3**$^-$ or **3** and some characteristic ^{1}H NMR chemical shifts and coupling constants

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 ESI†). [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).

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 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 2).



Scheme 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).

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) 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 (eqn (2)). The first-order rate constants $k_{1\Psi}$ were obtained

Table 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	E^a	C⁻	Base	k_2/L mol⁻¹ s⁻¹
1a^b	−14.68	**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^b	−13.56	**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^b	−11.32	**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^c	−10.11	**2a**	—	1.06×10^3
		2b	—	1.06×10^5
		2d	—	2.72×10^5

[a] Derived from eqn (1). [b] λ_{max}(DMSO) = 523 (**1a**), 493 (**1b**), 388 (**1c**) nm, from this work. [c] λ_{max}(DMSO–H_2O 50 : 50, v/v) = 343 nm, from ref. 20

by least-squares fitting of the time-dependent absorbances of the electrophiles to $A_t = A_0\exp(-k_{1\Psi}t) + C$.

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

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 Fig. 2 and for all other kinetic experiments in the ESI.† In some cases, the $k_{1\Psi}$ *versus* $[\mathbf{2}]_0$ plots do not go through the origin. Because all reactions proceed with quantitative formation of the adducts, we can presently not explain this phenomenon. All second-order rate constants k_2 (L mol⁻¹ s⁻¹) for the Michael additions are listed in Table 3.

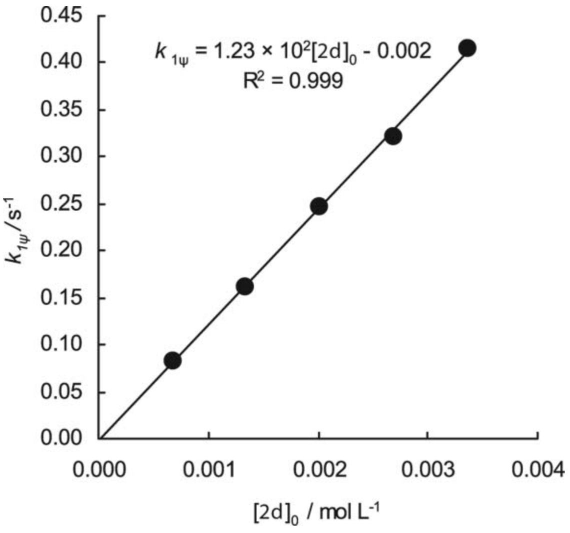


Fig. 2 Determination of the second-order rate constant k_2 = 123 L mol⁻¹ s⁻¹ for the reaction of **1a** with the potassium salt of acetylacetone **2d** in DMSO at 20 °C.

Correlation analysis

If eqn (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. Fig. 3 shows that this is approximately the case.

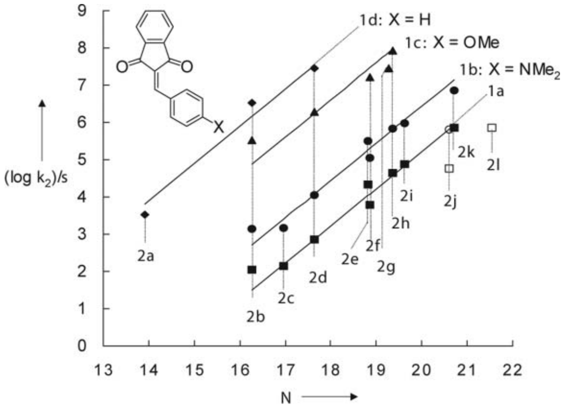


Fig. 3 Correlation of (log k_2)/s with the corresponding nucleophilicity parameters N of the carbanions **2a–l** for the reactions of 2-benzylidene-indan-1,3-diones **1a–d** with carbanions **2a–l** in DMSO at 20 °C. Open symbols were not included for the calculation of the correlation lines.

The correlation lines drawn in Fig. 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 and the N and s parameters of **2a–l** listed in Table 1. Note that this procedure enforces slopes of 1 for plots of (log k_2)/s *vs.* N because eqn (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 eqn (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.

While the correlations in Fig. 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-nitropropyl 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

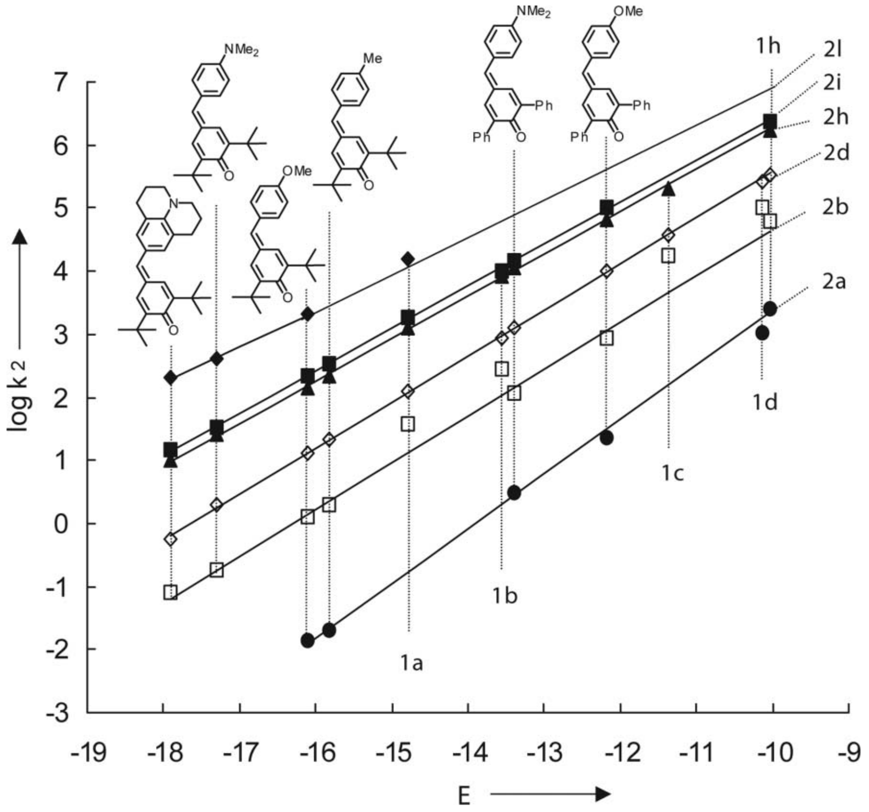


Fig. 4 Rate constants for the reactions of carbanions with the 2-benzylidene-indan-1,3-diones **1a–d** and with reference electrophiles (quinone methides and benzhydrylium ions) in DMSO at 20 °C. The rate constants for the reactions with **1a–d** were not used for the construction of the regression lines.

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 Fig. 4. When the rate constants of the reactions of the carbanions **2** with electrophiles are plotted against the *E* parameters given in ref. 2*e* 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**–**1d** are located above the correlation line for the reference electrophiles, which are depicted in the upper part of Fig. 4.

According to Fig. 5, the electrophilicities of the 2-benzylidene-indan-1,3-diones **1a–d** cover a range of more than four orders of magnitude. This electrophilicity range is located between **1h**, the least reactive representative of our series of reference benzhydrylium ions, and **1k**, the most reactive representative of a series of di-*tert*-butyl substituted quinone methides that have been used as reference electrophiles.[5]

Donor substituents on the phenyl ring lower the electrophilicity, and Fig. 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 the *para* substituents X in a similar way.

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$_2$O, v/v = 90 : 10 to 10 : 90)[23] is much more acidic than malononitrile (pK_a(DMSO) = 11.1, pK_a(H$_2$O) = 11.2).[24,25]

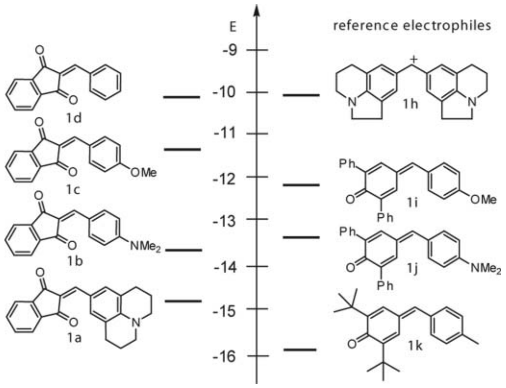


Fig. 5 Comparison of the electrophilicity parameters *E* of 2-benzylidene-indan-1,3-diones **1a–d** with reference electrophiles **1h–k**.

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

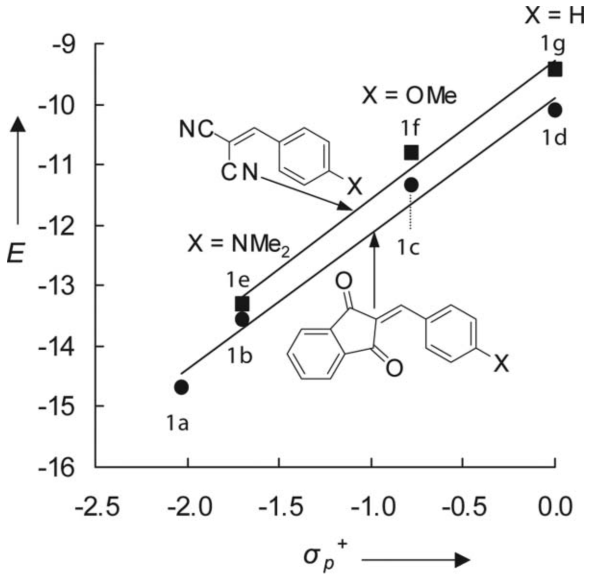


Fig. 6 Correlation between the electrophilicity parameters E in DMSO of the benzylidene-indan-1,3-diones **1a–d** (circles; $E = 2.34\sigma_p^+ - 9.78$) and the benzylidenemalononitriles **1e–g** (squares; $E = 2.30\sigma_p^+ - 9.28$) with the Hammett σ_p^+-values for X. (σ_p^+ Values were taken from ref. 22; σ_p^+ for **1a** was taken from ref. 2*e*).

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 *et al.* 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 4).

Entries 1 and 2 in Table 4 indicate that the experimental second-order rate constants $k_{2,\mathrm{exp}}$ 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 $k_{2,\mathrm{calc}}$ calculated by eqn (1). This agreement is within the previously postulated reliability of eqn (1).

Because the experimental second-order rate constants $k_{2,\mathrm{exp}}$ in DMSO are only about 1.5- to 2-times larger than the corresponding $k_{2,\mathrm{exp}}$ in DMSO–H_2O (50 : 50 v,v, Table 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 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.

Table 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]	$k_{2,\mathrm{calc}}$ (eqn (1))	$k_{2,\mathrm{exp}}$
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 $k_{2,\mathrm{exp}}$ refers to the reaction of **1d** with *n*-butylamine.

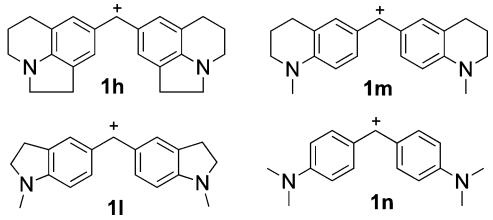
Table 5 Second-order rate constants k_2 for the reactions of piperidine with reference benzhydryliums Ar_2CH^+ in DMSO, DMSO–H_2O (50 : 50 v,v), and water at 20 °C

		k_2/L mol^{-1} s^{-1}		
Ar_2CH^+	E[a]	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 ESI†). [d] From ref. 4a.

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 5).

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) in DMSO than in DMSO–H_2O (50 : 50 v,v) as shown in Table 5.



Scheme 3 Benzhydrylium ions used for the comparison of the nucleophilicities of piperidine in different solvents.

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 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.

Thus, the presence of 50% water in DMSO appears to increase the electrophilicities of the 2-benzylidene-1,3-indandiones **1a**,**b**

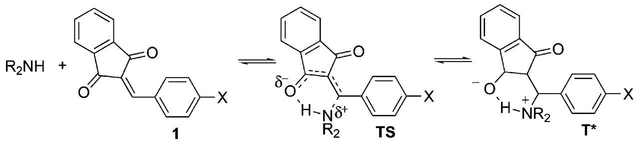
Table 6 Comparison of the second-order rate constants of the reactions of malononitrile anion **2h** with Michael acceptors **1a** and **1b** and the benzhydrylium ion **1h** in different solvents at 20 °C

	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)$_2$CH$^+$	1.76×10^6, [a]	—	1.50×10^5, [b]

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

(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 *et al.*[16,28] and Lee *et al.*[29] have previously suggested that the transition states of the amine additions may also be stabilized by O–H interactions as depicted in Scheme 4. Because the additions of carbanions to **1a–d**, which are described in Table 3, cannot profit from such O–H interactions, the good agreement between calculated and experimental rate constants in Table 4 argues against a large contribution of these interactions.



Scheme 4 Addition of an amine 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 using 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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Notes and references

1 (*a*) H. Mayr and A. R. Ofial, *Pure Appl. Chem.*, 2005, **77**, 1807–1821; (*b*) H. Mayr and A. R. Ofial, in *Carbocation Chemistry*, ed. G. A. Olah and G. K. S. Prakash, Wiley, Hoboken (N.J.), 2004, ch. 13, pp. 331–358; (*c*) A. R. Ofial and H. Mayr, *Macromol. Symp.*, 2004, **215**, 353–367; (*d*) H. Mayr, B. Kempf and A. R. Ofial, *Acc. Chem. Res.*, 2003, **36**, 66–77; (*e*) H. Mayr, O. Kuhn, M. F. Gotta and M. Patz, *J. Phys. Org. Chem.*, 1998, **11**, 642–654; (*f*) H. Mayr, M. Patz, M. F. Gotta and A. R. Ofial, *Pure Appl. Chem.*, 1998, **70**, 1993–2000; (*g*) H. Mayr and M. Patz, *Angew. Chem.*, 1994, **106**, 990–1010, (*Angew. Chem., Int. Ed. Engl.*, 1994, **33**, 938–957).

2 For reactions of carbocations with π-nucleophiles, see: (*a*) S. Lakhdar, M. Westermaier, F. Terrier, R. Goumont, T. Boubaker, A. R. Ofial and H. Mayr, *J. Org. Chem.*, 2006, **71**, 9088–9095; (*b*) A. D. Dilman and H. Mayr, *Eur. J. Org. Chem.*, 2005, **9**, 1760–1764; (*c*) T. Tokuyasu and H. Mayr, *Eur. J. Org. Chem.*, 2004, **13**, 2791–2796; (*d*) B. Kempf, N. Hampel, A. R. Ofial and H. Mayr, *Chem.–Eur. J.*, 2003, **9**, 2209–2218; (*e*) H. Mayr, M. F. Gotta, T. Bug, N. Hering, B. Irrgang, B. Janker, B. Kempf, R. Loos, A. R. Ofial, G. Remennikov and H. Schimmel, *J. Am. Chem. Soc.*, 2001, **123**, 9500–9512.

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

4 For reactions of carbocations with *n*-nucleophiles, see: (*a*) F. Brotzel, Y. C. Chu and H. Mayr, *J. Org. Chem.*, 2007, **72**, 3679–3688; (*b*) F. Brotzel, B. Kempf, T. Singer, H. Zipse and H. Mayr, *Chem.–Eur. J.*, 2007, **13**, 336–345; (*c*) T. B. Phan and H. Mayr, *Eur. J. Org. Chem.*, 2006, 2530–2537; (*d*) B. Kempf and H. Mayr, *Chem.–Eur. J.*, 2005, **11**, 917–927; (*e*) T. B. Phan and H. Mayr, *Can. J. Chem.*, 2005, **83**, 1554–1560; (*f*) S. Minegishi and H. Mayr, *J. Am. Chem. Soc.*, 2003, **125**, 286–295.

5 R. Lucius, R. Loos and H. Mayr, *Angew. Chem.*, 2002, **114**, 97–102, (*Angew. Chem., Int. Ed.*, 2002, **41**, 91–95).

6 T. Lemek and H. Mayr, *J. Org. Chem.*, 2003, **68**, 6880–6886.

7 See references 10–13 cited in: D. B. Ramachary, K. Anebouselvy, N. S. Chowdari and C. F. Barbas III, *J. Org. Chem.*, 2004, **69**, 5838–5849.

8 (*a*) R. Cammi, C. Ghio and J. Tomasi, *Int. J. Quantum Chem.*, 1986, **29**, 527–539; (*b*) E. Liedl and P. Wolschann, *Monatsh. Chem.*, 1982, **113**, 1067–1071; (*c*) H. Goerner, J. Leitich, O. E. Polansky, W. Riemer, U. Ritter-Thomas and B. Schlamann, *Monatsh. Chem.*, 1980, **111**, 309–329; (*d*) P. Margaretha, *Tetrahedron*, 1972, **28**, 83–87; (*e*) P. Margaretha and O. E. Polansky, *Monatsh. Chem.*, 1969, **100**, 576–583.

9 (*a*) J. Bloxham and C. P. Dell, *J. Chem. Soc., Perkin Trans. 1*, 1993, **24**, 3055–3059; (*b*) N. F. Eweiss, *J. Heterocycl. Chem.*, 1982, **19**, 273–277; (*c*) P. P. Righetti, A. Gamba, G. Tacconi and G. Desimoni, *Tetrahedron*, 1981, **37**, 1779–1785; (*d*) J. Bitter, J. Leitich, H. Partale, O. E. Polansky, W. Riemer, U. Ritter-Thomas, B. Schlamann and B. Stilkerieg, *Chem. Ber.*, 1980, **113**, 1020–1032.

10 L. P. Zalukaevs and I. Anokhina, *J. Gen. Chem. USSR*, 1964, **34**, 834–836, (*Zh. Obshch. Khim.*, 1964, **34**, 840–843).

11 T. Zimaity, E.-S. Afsah and M. Hammouda, *Indian J. Chem., Sect. B: Org. Chem. Incl. Med. Chem.*, 1979, **17**, 578–580.

12 L. P. Zalukaevs and D. G. Vnenkovskaya, *Zh. Org. Khim.*, 1966, **2**, 672–674.

13 E. I. Stankevich and G. Y. Yanags, *J. Gen. Chem. USSR*, 1962, **32**, 1123–1126, (*Zh. Obshch. Khim.*, 1962, **32**, 1146–1151).

14 (*a*) B. A. Arbuzov, T. D. Sorokina, N. P. Bogonostseva and V. S. Vinogradova, *Dokl. Akad. Nauk SSSR*, 1966, **171**, 605–608; (*b*) A. Mustafa, M. M. Sidky and F. M. Soliman, *Tetrahedron*, 1967, **23**, 99–105; (*c*) F. M. Soliman, M. M. Said and S. S. Maigali, *Heteroat. Chem.*, 1997, **8**, 157–164.

15 X.-Q. Zhu, H.-Y. Wang, J.-S. Wang and Y.-C. Liu, *J. Org. Chem.*, 2001, **66**, 344–347.

16 C. F. Bernasconi and M. W. Stronach, *J. Am. Chem. Soc.*, 1991, **113**, 2222–2227.

17 T. Bug, T. Lemek and H. Mayr, *J. Org. Chem.*, 2004, **69**, 7565–7576.

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

19 R. K. Behera and A. Nayak, *Indian J. Chem. B*, 1976, **14**, 223–224.

20 (*a*) C. F. Bernasconi, A. Laibelman and J. L. Zitomer, *J. Am. Chem. Soc.*, 1985, **107**, 6563–6570; (*b*) C. F. Bernasconi, A. Laibelman and J. L. Zitomer, *J. Am. Chem. Soc.*, 1985, **107**, 6570–6575.

21 T. B. Phan, M. Breugst and H. Mayr, *Angew. Chem.*, 2006, **118**, 3954–3959, (*Angew. Chem., Int. Ed.*, 2006, **45**, 3869–3874).

22 C. Hansch, A. Leo and R. W. Taft, *Chem. Rev.*, 1991, **91**, 165–195.

23 C. F. Bernasconi and P. Paschalis, *J. Am. Chem. Soc.*, 1986, **108**, 2969–2977.

24 F. G. Bordwell, J. A. Harrelson, Jr. and A. V. Satish, *J. Org. Chem.*, 1989, **54**, 3101–3105.

25 A. Albert and E. P. Serjeant, *The Determination of Ionization Constants: A Laboratory Manual*, Chapman and Hall, London, 3rd edn, 1984, pp. 137–160.

26 C. F. Bernasconi and R. B. Killion, Jr., *J. Org. Chem.*, 1989, **54**, 2878–2885.

27 T. Bug and H. Mayr, *J. Am. Chem. Soc.*, 2003, **125**, 12980–12986.

28 (*a*) C. F. Bernasconi, *Acc. Chem. Res.*, 1987, **20**, 301–308; (*b*) C. F. Bernasconi, *Tetrahedron*, 1989, **45**, 4017–4090.

29 H. K. Oh, J. H. Yang, H. W. Lee and I. Lee, *J. Org. Chem.*, 2000, **65**, 5391–5395.

30 For a database of reactivity parameters *E*, *N*, and *s*, see: http://www.cup.uni-muenchen.de/oc/mayr/DBintro.html.