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Electrophilicity Parameters of 5-Benzylidene-2,2-dimethyl[1,3]dioxane-4,6-diones (Benzylidene Meldrum's Acids)

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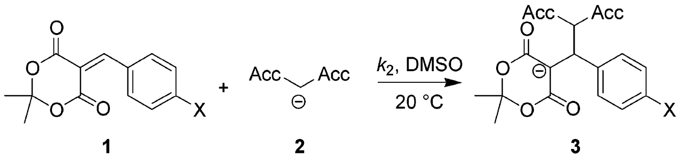

Kinetics of the reactions of four benzylidene Meldrum's acids **1** with acceptor-substituted carbanions **2** were studied photometrically in DMSO at 20 °C. The reactions follow second-order kinetics, and the second-order rate constants were found to follow the correlation $\log k_2$ (20 °C) $= s(N + E)$ (eq 1), which was used to calculate the electrophilicity parameters E for compounds **1**. Hammett correlations are given, which allow one to assign electrophilicity parameters for various β,β-acceptor substituted styrenes and thus to predict a large number of absolute rate constants for a manifold of Michael additions. The reactions of primary and secondary amines are approximately 2 orders of magnitude faster than predicted by the correlation (1), supporting transition states which are stabilized by hydrogen bridges from NH to the carbonyl groups of the benzylidene Meldrum's acids.

Introduction

Numerous kinetic investigations have shown that the rate constants for the reactions of carbocations with carbanions and neutral π-nucleophiles can be described by eq 1, wherein s and N are nucleophile-dependent parameters and E is an electrophile-dependent parameter:[1,2]

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

In order to assign nucleophilicity parameters for strong nucleophiles, such as carbanions,[3−5] amines,[6−8] enamines,[9] silyl enol ethers,[10] and ketene acetals[11] amino-substituted diarylcarbenium ions and structurally related quinone methides have been used as reference electrophiles. It has been shown that eq 1 also holds for the reactions of ordinary Michael acceptors and electron-deficient arenes with carbanions[12−14] and other strong nucleophiles.[15,16]

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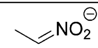
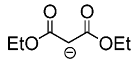
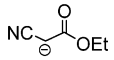
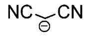
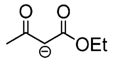
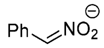
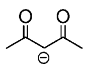
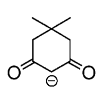
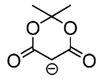
The nucleophilic attack at the electron-deficient double bond of Michael acceptors has long been a field of great interest in physical organic chemistry. Bernasconi studied the kinetics of the reactions of numerous amines, carbanions, and alkoxides toward Michael acceptors, e.g., benzylidene indandiones and benzylidene Meldrum's acids in DMSO/H_2O mixtures.[17−21] Rappoport investigated nucleophilic vinylic substitutions[22] on chloro-substituted benzylidene Meldrum's acids which follow the addition−elimination mechanism.[21,23] In recent years, Oh and Lee[24] reported mechanistic studies and rate constants of the reactions of benzylamines with benzylidene Meldrum's acids and other Michael acceptors in acetonitrile.

Benzylidene Meldrum's acids **1** are usually prepared by condensation of an aldehyde with Meldrum's acid in the presence of catalytic amounts of acid[25] or base in benzene or chloroform solutions,[26] but in some cases subsequent cyclizations occur.[26c] Improved yields have been obtained under solvent-free conditions by grinding the reactants,[27] by DMAP catalysis,[28] or by using water[29] or ionic liquids[30] as solvents. Compounds **1** are useful reactants for the synthesis of pharmacologically active heterocyclic compounds.[31]

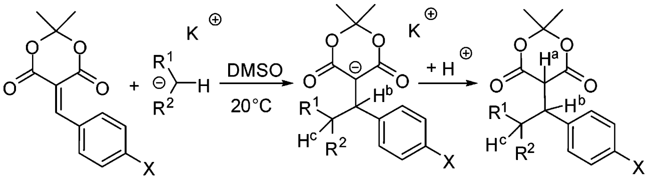
In 1964, benzylidene Meldrum's acids have been termed "electronically neutral Lewis acids" by Swoboda and Wessely.[25] Schuster, Polansky and Wessely reported equilibrium constants for the addition of methoxide to a variety of neutral organic Lewis acids, including benzylidene Meldrum's acids.[32] The formation of zwitterionic addition products from neutral organic Lewis acids and amines or phosphanes was reported by Margaretha.[33]

TABLE 1. ***N* and *s* Parameters of the Carbanions 2a−i in DMSO**

	Nucleophile	*N*	*s*
2a		21.54[a]	0.62[a]
2b		20.22[b]	0.65[b]
2c		19.62[b]	0.67[b]
2d		19.36[b]	0.67[b]
2e		18.82[b]	0.69[b]
2f		18.29[a]	0.71[a]
2g		17.64[b]	0.73[b]
2h		16.27[b]	0.77[b]
2i		13.91[b]	0.86[b]

[a] From ref 5. [b] From ref 4.

SCHEME 1. Reaction of the Carbanions 2 (K$^+$ Salts) with the Benzylidene Meldrum's Acids 1a−d



1a X = H **2a-i** **3** **4**
1b X = OMe
1c X = NMe_2
1d see Scheme 2

Rate and equilibrium constants for the additions of amines to the electrophilic double-bond of these Michael acceptors were determined[34a,b] and the kinetics of their hydrolytic cleavage was investigated in 10% aqueous methanol.[34b] Regio- and stereoselective Cu-catalyzed additions of alkynes[35] and R_2Zn to benzylidene Meldrum's acids have recently been reported by Carreira[36] and Fillion.[37]

The higher electrophilic reactivity of benzylidene Meldrum's acids compared to benzylidene malonic esters, their open-chain analogues, is related to the unusually high acidity of the Meldrum's acid, which was attributed to the fixed bis-anti conformation of the ester groups.[38] Recently, Nakamura em-

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TABLE 2. Characterized Michael Adducts and Some Characteristic ^{1}H NMR Chemical Shifts[a]

electrophile	nucleophile	product (yield/%)	δ (H^a)/ppm	δ (H^b)/ppm	δ (H^c)/ppm	$J_{a,b}$/Hz	$J_{b,c}$/Hz
1a (X = H)	**2h**	**3ah**[b,c]		5.76[c]			
1b (X = OMe)	**2b**	**3bb**[b]		4.38	4.89		12.4
1b	**2b**	**4bb** (41)	4.43−4.47	4.43−4.47	4.78		12.4
1b	**2d**	**4bd** (48)	3.94	4.22	5.10	3.6	12.6
1b	**2e**	**4be** (66)[d]		4.96			
1b	**2g**	**4bg** (85)	4.06	4.44	5.19	4.0	12.0
1b	**2h**	**3bh** (64)[c,e,f]		5.68[c]			
1c (X = NMe$_2$)	**2b**	**3cb**[b]		4.33	4.87		12.6
1c	**2b**	**4cb**	4.33−4.43	4.33−4.43	4.70		12.0
1c	**2d**	**3cd** (66)[e]		4.28	5.75		12.4
1c	**2g**	**3cg**[b]		4.46	5.24		12.4
1c	**2h**	**3ch** (46)[c,e,f]		5.64[c]			
1d (X = jul)	**2a**	**3da**[b,g]		3.94/3.88[g]	5.71/5.85[g]		
1d	**2b**	**3db**[b]		4.20	4.80		12.6
1d	**2b**	**4db**	4.26−4.30	4.26−4.20	4.65		12.0
1d	**2d**	**3dd**[b]		4.12	5.68		12.0
1d	**2d**	**4dd**[e]	4.01	4.18	5.12	3.3	12.5
1d	**2g**	**3dg**[b]		4.33	5.24		12.8

[a] Anionic products **3** were characterized in DMSO-d_6; neutral products **4** were characterized in CDCl$_3$; for numbering, see Scheme 1. [b] Analysis of the crude reaction mixture. [c] Enol form of the dimedone moiety. [d] Diastereomers in a ratio of 58:42. [e] The given yield refers to the reaction in 1,2-dimethoxyethane. [f] Thermally instable, NMR spectra were taken from the crude reaction mixture in DMSO. [g] Diastereomers in a ratio of 52:48.

ployed the "reactive hybrid orbital (RHO) theory" to rationalize the high acidity of Meldrum's acid.[39]

As part of our program of developing comprehensive nucleophilicity and electrophilicity scales, we have now studied the kinetics of the reactions of carbanions **2a**−**i** (Table 1) with the benzylidene Meldrum's acids **1a**−**d** in DMSO (Scheme 1). We will show that eq 1 can be used to describe the rates of these reactions and report on the determination of the electrophilicity parameters E for the Michael acceptors **1a**−**d**. We will furthermore present correlations between the E parameters of these and related electrophiles with Hammett's substituent constants σ_p and thus provide data to predict absolute rate constants for a manifold of Michael additions.

Results and Discussion

Reaction Products. When equimolar amounts of **1** and **2-K**$^+$ were combined in DMSO, the potassium salts **3-K**$^+$ were formed and characterized by ^{1}H and ^{13}C NMR spectroscopy without further workup (Scheme 1, Table 2). Compounds **4** were synthesized from equimolar amounts of **1** and **2-K**$^+$ in DMSO or 1,2-dimethoxyethane solution and subsequent treatment with hydrochloric acid. Since analogous products can be expected for different combinations of the electrophiles **1a**−**d** with the carbanions **2a**−**i**, product studies have not been performed for all combinations which were studied kinetically. In all cases quantitative product formation was indicated by the complete decolorization of the solutions and the fact that the NMR spectra obtained after mixing **1** and **2-K**$^+$ showed the signals of **3-K**$^+$ exclusively. The differences in the isolated yields reported in Table 2 are due to nonoptimized workup procedures.

Generally, the Michael adducts **3** and **4** show ^{1}H NMR spectra with resonances H^a, H^b and H^c in the range of δ = 3.8−5.9 ppm with small coupling constants of 3.3−4.0 Hz between H^a and H^b, and large coupling constants of approximately 12.5 Hz between H^b and H^c. Only the dimedone adducts **3ah**, **3bh**, and **3ch** do not show the absorption of H^c around δ = 5 ppm. Instead, a signal at δ = 13.5 ppm was observed due to the enol form of the dimedone fragment.[40] As a consequence, H^b absorbs as a singlet at δ = 5.7 ppm in the anions **3ah**, **3bh**, and **3ch**.

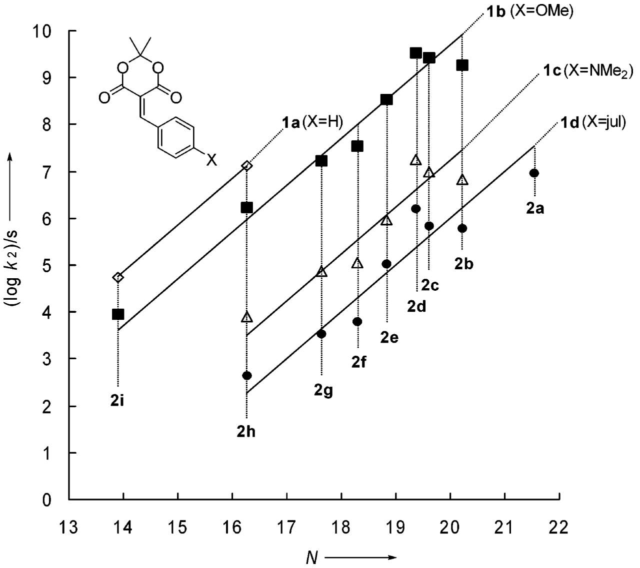

FIGURE 1. Correlation of (log k_2)/s versus the nucleophilicity parameters N of the carbanions **2a**−**i** for the reactions of benzylidene Meldrum's acids **1a**−**d** with carbanions **2a**−**i** in DMSO at 20 °C.

Kinetic Investigations with Carbanions. The kinetic investigations were performed at 20 °C in DMSO as a solvent. Because the benzylidene Meldrum's acids **1a**−**d** show absorption bands at 325, 366, 460, and 484 nm, respectively, and neither the products **3** nor the carbanions **2a**−**i** absorb at these wavelengths, the progress of the reactions can be monitored photometrically at the absorption maxima of these electrophiles. Due to the high rates of these reactions, the stopped-flow technique was generally employed. All reactions described in this paper proceed quantitatively. The carbanions were either

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TABLE 3. Second-Order Rate Constants k_2 for the Reactions of the Carbanions 2a−i (K^+ salts) with Electrophiles 1a−d in DMSO at 20 °C

electrophile	E^a	nucleophile	k_2/M^{-1} s^{-1}
1a (X = H)	-9.15^b	**2h**	2.93×10^5
		2i	1.16×10^4
1b (X = OMe)	-10.28	**2b**	1.15×10^6
		2c	1.96×10^6
		2d	2.51×10^6
		2e	7.42×10^5
		2f	2.23×10^5
		2g	1.89×10^5
		2h	6.00×10^4
		2i	2.39×10^3
1c (X = NMe$_2$)	-12.76	**2b**	2.89×10^4
		2c	4.76×10^4
		2d	7.21×10^4
		2e	1.27×10^4
		2f	3.87×10^3
		2g	3.50×10^3
		2h	9.82×10^2
1d (X = jul)	-13.97	**2a**^{c}	2.12×10^4
		2b	6.08×10^3
		2c	7.98×10^3
		2d	1.48×10^4
		2e	2.83×10^3
		2f	4.93×10^2
		2g	3.84×10^2
		2h	1.08×10^2

[a] The E parameters for **1a−d** result from a least-squares minimization of $\Delta^2 = \Sigma(\log k_2 - s(N + E))^2$ which uses the second-order rate constants k_2 (this table) and the N and s parameters of the carbanions **2a−i** given in Table 1. Details of the calculation of E are discussed below. [b] A value of −9.5 is expected if the same set of reference nucleophiles would be employed as for compounds **1b−d**. [c] The tetra-*n*-butyl ammonium salt of **2a** was used for the kinetic measurements.

used as preformed potassium salts, or the corresponding CH acids were deprotonated with 1.05 equiv of potassium *tert*-butoxide before use. UV−vis spectroscopic monitoring of the titration showed that complete deprotonation of **2f-H** was obtained with 1.05 equiv of KO-*t*-Bu. In order to confirm that the slight excess of KO-*t*-Bu did not affect the observed rate constants, we have also generated the carbanion **2f** by treating **2f-H** with 0.27 equiv of KO-*t*-Bu. In this case, the concentration of the carbanion **2f** is given by the quantity of KO-*t*-Bu, and the second-order rate constant was found to be the same as that obtained with the slight excess of KO-*t*-Bu (Supporting Information, Tables S7a and S7b). In order to obtain pseudo-first-order kinetics, the carbanions were used in large excess (10−100 equiv) over the electrophiles. In all cases reported in Table 3, an exponential decay of the concentration of the electrophiles **1a−d** was observed (eq 2).

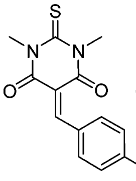
$$-\mathrm{d}[\mathbf{1}]/\mathrm{d}t = k_{1\psi}[\mathbf{1}] \qquad (2)$$

The first-order rate constants $k_{1\psi}$ were obtained by least-squares fitting of the time-dependent absorbances A_t of the electrophiles to the exponential function $A_t = A_0 \exp(-k_{1\psi}t) + C$. Plots of $k_{1\psi}$ versus the carbanion concentration [**2**] resulted in linear correlations with almost zero intercepts, the slopes of which gave the second-order rate constants k_2 (Table 3).

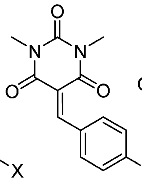
Correlation Analysis. If eq 1 holds for the reactions of the benzylidene Meldrum's acids **1a−d** with carbanions, the plots of (log k_2)/s versus the nucleophilicity parameter N should have slopes of 1.0. Figure 1 shows that this is approximately the case. However, small systematic deviations of some of the nucleophiles are obvious. The dimedone anion (**2h**) and the malononitrile anion (**2d**) react two to four times faster with each of the electrophiles **1b−d** than expected from the correlations, whereas the nitroethyl anion (**2a**), the malonate anion (**2b**), and the phenyl nitronate (**2f**) are about two times less reactive than expected.

Though the correlations are only of moderate quality, one can conclude that the relative electrophilicities of benzylidene Meldrum's acids **1a−d** are almost independent of the nature of the carbanions. Therefore we have calculated the E parameters for **1a-d** by least-squares minimization of $\Delta^2 = \Sigma(\log k - s(N + E))^2$ using the second-order rate constants k_2 given in Table 3 and the N and s parameters of **2a-i** from Table 1. With the E parameters thus determined a different illustration of the reactivities of the carbanions **2a−i** toward the electrophiles **1a−d** and the reference electrophiles **1e−m** becomes possible (Figure 2). The plots of log k_2 against the electrophilicity parameters E show that in general, the reactivities of the carbanions **2a−i** toward **1a−d** correlate well with the electrophilicity parameter E, but the previously mentioned deviations are, again, evident. While, for the sake of clarity, the poorly correlating carbanions **2d** and **2f** are not included in Figure 2, one can see that the reactivities of **1b−d** with the anion of diethyl malonate (**2b**) are below the correlation line defined by the reference electrophiles **1e−m**. On the other hand the dimedone anion (**2h**) generally reacts faster with electrophiles **1b−d** than expected from the rates of its reactions with the reference electrophiles **1e−m**.

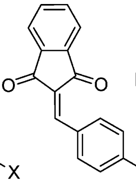
The different behavior of the dimedone anion (**2h**) toward the Michael acceptors **1a−d** and the reference electrophiles **1e−m** reminds of the previously reported behavior of **2h** toward electrophiles **5-X**,[13] **6-X**,[13] and **7-X,**[14] but the reason for these deviations is presently not understood.



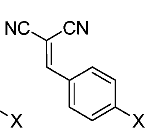
5-X



6-X



7-X



8-X

Figure 3 shows that there are clearly two distinct correlation lines for the different types of electrophiles, one for the reactions of **2h** with the quinone methides **1h−m** and the benzhydrylium ions **1e−g** and another one for the structurally related Michael acceptors **1-X**, **5-X**, **6-X**, and **7-X**. Despite this clear separation, one should note that all deviations from the lower (reference) line are much less than 1 order of magnitude. One can, therefore, conclude that the reactivity order of the carbanions **2a−i** derived from the rates of the reactions with the reference electrophiles **1e−m** also holds roughly for the Michael acceptors **1a−d** and that the E parameters derived in Table 1 can be employed for the general prediction of rate constants for the reactions of **1a−d** with nucleophiles.

The positioning of the combination of dimedone **2h** with **1a** on the "wrong" correlation line of Figure 3 is due to the fact that the electrophilicity parameter of **1a** has been derived from the reactions of **1a** with **2i** and **2h** (Figure 1), i.e., two carbanions which react faster with **1b−c** than expected from their N-parameters. If all carbanions **2a−i** had been used for the determination of E(**1a**), and **1a** followed the same pattern as shown for compounds **1b−d** in Figure 1 one would expect the slightly smaller electrophilicity parameter $E(\mathbf{1a}) \approx -9.5$. An

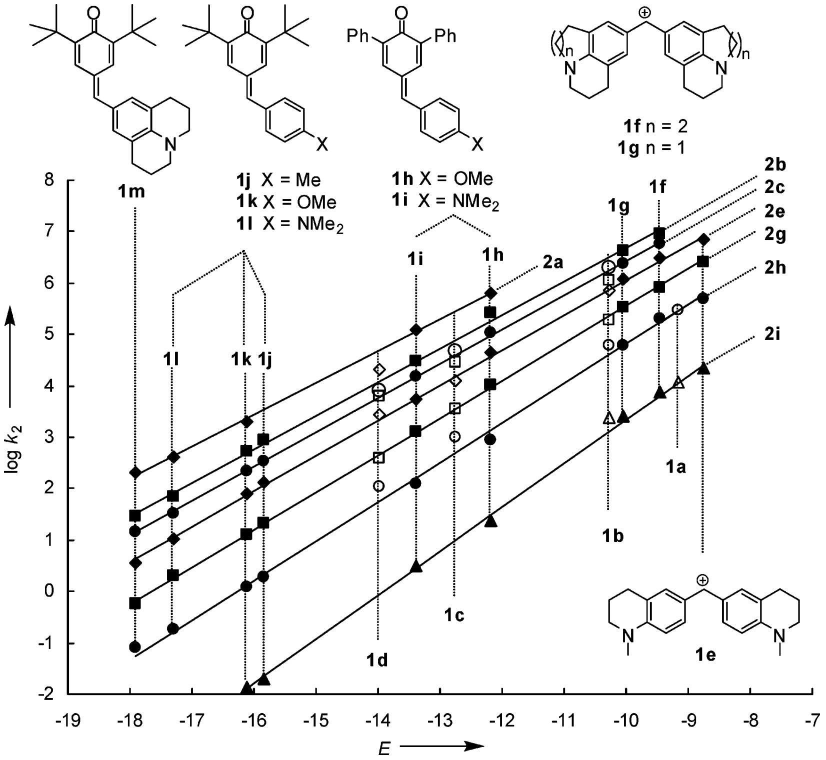


FIGURE 2. Rate constants for the reactions of carbanions **2a**−**i** with electrophiles **1a**−**d** (open symbols) and with reference electrophiles **1e**−**m** (filled symbols) in DMSO (20 °C).

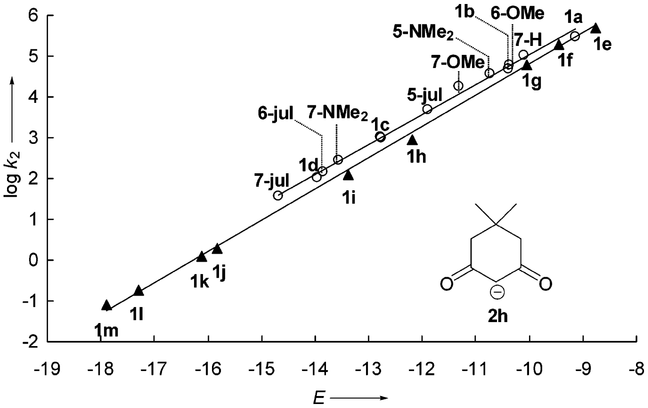


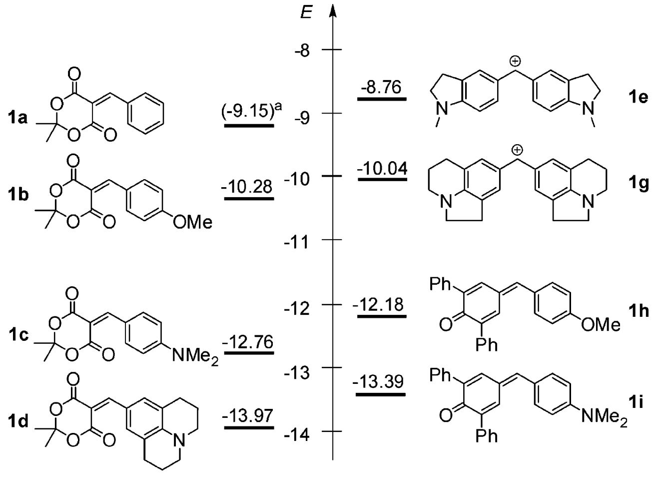
FIGURE 3. Rate constants for the reaction of the dimedone anion (**2h**) with electrophiles **1a**−**d** and **5**−**7** (open symbols, log $k_2 = 0.734E + 12.4$) and reference electrophiles **1e**−**m** (filled symbols, log $k_2 = 0.767E + 12.5$) in DMSO at 20 °C.

experimental test for this hypothesis was not possible because the reactions of **1a** with **2a-g** are too fast to be measured with conventional stopped-flow instruments.

Scheme 2 compares the electrophilicities of the benzylidene Meldrum's acids **1a**−**d** with those of some reference electrophiles and shows that their electrophilic reactivities cover a range of almost 5 orders of magnitude.

According to Figure 4, the electrophilicity parameters E of **1a**−**c**, **6-X**, **7-X**, and **8-X** correlate well with Hammett's σ_p-values for H, OMe, and NMe$_2$. The corresponding plots of E versus σ_p^+ show larger scatter. From the slopes of these correlations (5.20 − 5.74, Table 4), one can derive reaction constants of $\rho \approx 3.8 \pm 0.3$ for reactions with nucleophiles of $s = 0.7$ (Table 1), indicating that in all four reaction series electron-donating substituents in *p*-position exert comparable retarding effects.

SCHEME 2. Comparison of the Electrophilicity Parameters *E* of Benzylidene Meldrum's Acids 1a−d with Those of Some Reference Electrophiles[a]



[a] E (**1a**) has been calculated from the rate constants of the reactions of **1a** with only two nucleophiles (see text). Depending on the choice of other reaction partners, the electrophilicity E may be lower by 0.3−0.4 units.

Substitution of the E parameters for **1d**, **6-jul**, and **7-jul** into the correlation equations listed in Table 4 yields σ_p(jul) = −0.91, −0.86, and −0.92, respectively. When the average of these values, σ_p(jul) = −0.89, is used to locate **5**-jul in Figure 4, a correlation with a similar slope ($\rho = 3.5$) results for the reactions of compounds **5**-X. A considerably more negative value for σ_p^+ (−2.03) of the julolidyl substituent has recently been derived

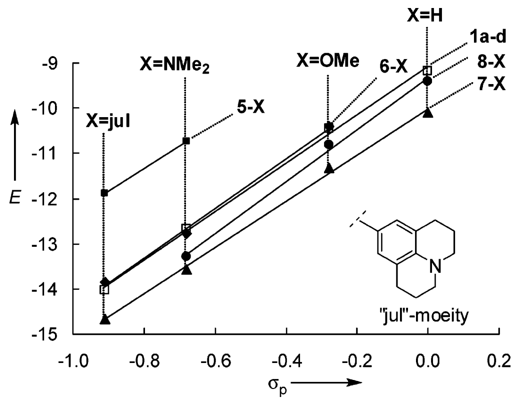


FIGURE 4. Correlation between the electrophilicity parameters E of electrophiles **1a**−**d** (open symbols) and **5**−**8** (closed symbols) in DMSO with Hammett's σ_p-values (from ref 41). σ_p for "jul" calculated as described in the text.

TABLE 4. Correlation between Electrophilicity Parameters *E* for Various Series of Electrophiles and Hammett's Substituent Constants σ_p

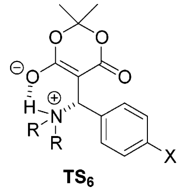
electrophile	correlation, $E =$	R^2
6-X	$5.71\sigma - 8.83$	1.00
1a−**c**	$5.37\sigma - 9.08$	0.99
8-X	$5.74\sigma - 9.34$	0.99
7-X	$5.20\sigma - 10.0$	0.99

from the electrophilicities of benzhydrylium ions.[42] From the similar slopes of the correlation lines for the different series of electrophiles in Figure 4 one can derive the general validity of the electrophilicity order **5-X** > **6-X** ≈ **1-X** > **8-X** > **7-X**.

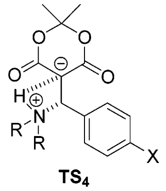
Reactions with Other Nucleophiles. In order to check the applicability of the electrophilicity parameters E of benzylidene Meldrum's acids **1a**−**d** (Scheme 2) for predicting the rates of reactions with other types of nucleophiles, we compared predicted and experimental rate constants for the addition reactions of amines to the electrophilic double bonds of **1a**−**d**.

Kinetics of the reactions of piperidine and morpholine with compounds **1b**−**d** have been determined in DMSO, using the same methodology as described above for the reactions with carbanions. The second-order rate constants for the reactions with piperidine in DMSO (Table 5, entries 8, 13, 18) were found to be 3−6 times greater than those in DMSO/H_2O (50/50) which have previously been determined by Bernasconi (entries 10, 15)[17] and confirmed by us (entries 9, 14). The reactions are roughly 1 order of magnitude faster in neat DMSO than in water (cf entries 8/11 and 13/16). Solvent effects of similar magnitude have been observed for the corresponding additions of morpholine (Table 5, entries 20−32). Though variations of the solvent can be expected to affect nucleophilicities as well as electrophilicities, in the derivation of the parameters for eq 1 solvent effects were exclusively considered in the nucleophile specific parameters N and s.[4] Though this procedure was reported to cause some problems for the reactions with **7**-X,[14] differential solvent effects on the electrophilicities of **1a-d** have not been considered.

Table 5 furthermore shows that the experimental rate constants are generally 20−120 times greater than the calculated values. The reaction of morpholine with **1c** in DMSO is even 580 times faster than calculated (entry 29). Though deviations from experimental values by two orders of magnitude are still within the confidence limit of eq 1,[2,42] the constantly higher experimental rate constants for the additions of secondary amines to **1a**−**d** may be indicative of a change of mechanism. Schuster,[34] Bernasconi,[20,44] and Oh[24] presented evidence that the transition states of amine additions to **1** are stabilized by hydrogen bridging from NH to the carbonyl group (six-membered transition state **TS$_6$**) or from NH to the carbanionic center (four-membered ring **TS$_4$**). Analogous hydrogen bridging may account for the finding that glycinamide and semicarbazide react 200 times faster with **1a** than predicted by eq 1 (Table 5, entries 33, 34).



TS$_6$



TS$_4$

This type of transition state stabilization by hydrogen bridging is not possible in additions of carbanions to **1a**−**d**, the rates of which have been used to derive the E parameters of these electrophiles (Table 3). A related study has recently shown that additions of secondary amines to benzylidene indandiones **7**-X are only three times faster than predicted by eq 1.[14] It has, therefore, been concluded that H-bridging as indicated in **TS$_6$** and **TS$_4$** cannot have a large effect on the transition states of the additions of secondary amines to **7**-X.

Conclusion

Benzylidene Meldrum's acids are another group of electrophiles, the reactivities of which can be described by correlation eq 1. While the reactivities with carbanions can be reproduced with an accuracy of better than a factor of 5, primary and secondary amines react approximately 10^2 times faster than predicted by eq 1. In line with previous work, these deviations are explained by additional stabilizing effect in the transition states (hydrogen bridging).

Accordingly, calculated and experimental rate constants for the reactions of **1** with tertiary amines, which cannot be accelerated by hydrogen bridging, differ by only 1 order of magnitude.[45] It is, therefore, concluded that the E parameters for **1a**−**d** in this work can be used to characterize the electrophilic potential of the title compounds.

Experimental Section

Benzylidene Meldrum's Acids 1a−**c.** Benzylidene Meldrum's acids **1a**−**c** were prepared by following a procedure for the synthesis of structurally related benzylidene barbituric acids:[46] Equimolar amounts of para-substituted benzaldehyde and Meldrum's acid were stirred in EtOH under reflux for 2 h. The product precipitates immediately after cooling the reaction mixture to room temperature.

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TABLE 5. Comparison of Calculated and Experimental Second-Order Rate Constants for the Addition of Amines to Benzylidene Meldrum's Acids 1a−d in Different Solvents (20 °C)

				k_2/L mol^{-1} s^{-1}	
entry	nucleophile	*N*/*s* (solvent)	electrophile	calcd[a]	experimental (solvent)
1	piperidine	17.19/0.71 (DMSO)	**1a**	5.11×10^{5} [b]	2.09×10^{6} (DMSO/H_2O = 90/10)[c]
2					1.40×10^{6} (DMSO/H_2O = 70/30)[c]
3					6.69×10^{5} (DMSO/H_2O = 50/50)[c]
4		18.13/0.44 (H_2O)		8.94×10^{3}	1.70×10^{5} (H_2O)[c]
5					2.70×10^{5} (H_2O, 25 °C)[c]
6					2.30×10^{6} (CH_3CN, 25 °C)[d]
7					1.20×10^{6} ($CHCl_3$, 25 °C)[d]
8		17.19/0.71 (DMSO)	**1b**	8.06×10^{4}	1.93×10^{6} (DMSO)[e]
9					2.89×10^{5} (DMSO/H_2O = 50/50)[e]
10					2.67×10^{5} (DMSO/H_2O = 50/50)[c]
11		18.13/0.44 (H_2O)		2.84×10^{3}	1.70×10^{5} (H_2O, 25 °C)[c]
12					9.50×10^{5} (CH_3CN, 25 °C)[d]
13		17.19/0.71 (DMSO)	**1c**	1.40×10^{3}	1.71×10^{5} (DMSO)[e]
14					3.76×10^{4} (DMSO/H_2O = 50/50)[e]
15					3.96×10^{4} (DMSO/H_2O = 50/50)[c]
16		18.13/0.44 (H_2O)		2.31×10^{2}	2.10×10^{4} (H_2O, 25 °C)[c]
17					1.10×10^{5} (CH_3CN, 25 °C)[d]
18		17.19/0.71 (DMSO)	**1d**	1.93×10^{2}	1.80×10^{4} (DMSO)[e]
19					6.23×10^{3} (DMSO/H_2O = 50/50)[e]
20	morpholine	16.96/0.67 (DMSO)	**1a**	(1.71×10^{5})[b]	8.88×10^{5} (DMSO/H_2O = 90/10)[c]
21					7.33×10^{5} (DMSO/H_2O = 70/30)[c]
22					3.19×10^{5} (DMSO/H_2O = 50/50)[c]
23		15.62/0.54 (H_2O)		3.12×10^{3}	1.47×10^{5} (H_2O)[c]
24					1.75×10^{5} (H_2O, 25 °C)[c]
25					4.0×10^{5} (CH_3CN, 25 °C)[d]
26					1.0×10^{5} ($CHCl_3$, 25 °C)[d]
27		16.96/0.67 (DMSO)	**1b**	(2.99×10^{4})[b]	1.56×10^{5} (DMSO/H_2O = 50/50)[c]
28		15.62/0.54 (H_2O)		6.64×10^{2}	9.90×10^{4} (H_2O, 25 °C)[c]
29		16.96/0.67 (DMSO)	**1c**	6.51×10^{2}	3.78×10^{5} (DMSO)[e,f]
30					1.11×10^{4} (DMSO/H_2O = 50/50)[e]
31					1.46×10^{4} (DMSO/H_2O = 50/50)[c]
32		15.62/0.54 (H_2O)		3.50×10^{1}	1.00×10^{4} (H_2O, 25 °C)[c]
33	glycinamide	12.29/0.58 (H_2O)[g]	**1a**	6.63×10^{1}	1.34×10^{4} (H_2O)[h]
34	semicarbazide	11.05/0.52 (H_2O)[i]	**1a**	9.73	1.64×10^{3} (H_2O)[h]

[a] Calculated according to eq 1 by using the *E* parameters for **1a−d** from Table 3 and the *N* and *s* parameters for amines from refs 7, 8, and 43. [b] For neat DMSO. [c] From ref 17. [d] From ref 34. [e] This work. [f] Fast kinetics, complete decay of the monitored absorbance within 6 ms. [g] From ref 7. [h] From ref 18. [i] From ref 8.

After filtration and recrystallization from EtOH, the electrophiles **1a−c** were obtained as colored crystals. ^{1}H and ^{13}C NMR spectra for **1a−c** agreed with those described in the literature.[26,47] UV−vis spectra of **1a−d** in DMSO are shown in Figure S1 of the Supporting Information.

2,2-Dimethyl-5-(julolidin-9-ylmethylene)-1,3-dioxane-4,6-dione (1d). Meldrum's acid (716 mg, 4.97 mmol) and 9-formyljulolidine (1.00 g, 4.97 mmol) were added to EtOH (25 mL). The solution turned purple immediately. After 10 min under reflux, the solution was allowed to cool to room temperature. The product precipitated from the solution, was filtered and recrystallized from EtOH. The product **1d** (900 mg, 2.75 mmol, 55%) was obtained as purple crystals. Mp: 138.0−138.4 °C. Further attempts to optimize the yield have not been made. ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 1.73$ (s, 6 H, $C(CH_3)_2$), 1.96 (quint, $J = 5.7$ Hz, 4 H, 2 × CH_2), 2.74 (t, $J = 5.7$ Hz, 4 H, 2 × CH_2), 3.36 (t, $J = 5.7$ Hz, 4 H, 2 × CH_2), 7.85 (s, 2 H, ArH), 8.15 (s, 1 H). ^{13}C NMR (75.5 MHz, $CDCl_3$): $\delta = 21.0$ (t, CH_2), 27.2 (q, CH_3), 27.5 (t, CH_2), 50.4 (t, CH_2), 102.6 (s), 103.0 (s), 119.4 (s), 120.5 (s), 136.6 (d, C_{ar}), 149.3 (s), 157.5 (d, $=C-H$), 161.8 (s), 165.6 (s). Signal assignments are based on additional gHSQC experiments. MS (ESI, positive): *m*/*z* (%) = 328 (7) $[M + H]^+$, 270 (100). Anal. Calcd for $C_{19}H_{21}NO_4$ (327.38): N, 4.28; C, 69.71; H, 6.47. Found: N, 4.27; C, 69.45; H, 6.36.

5-[2-Acetyl-1-(4-methoxyphenyl)-3-oxobutyl]-2,2-dimethyl-1,3-dioxane-4,6-dione (4bg). A mixture of **1b** (365 mg, 1.39 mmol) and **2g**-K$^+$ (202 mg, 1.46 mmol) in dry DMSO (2 mL) was stirred until the color of the solution disappeared. Then the reaction mixture was poured on cold water (5 mL) and acidified with 2 M aq HCl. The precipitate was filtered and dissolved in CH_2Cl_2. After removal of the traces of water by filtering the solution over a hot cotton batting, the solvent was evaporated and the residue was dried in vacuum. **4bg** (400 mg, 85%). Colorless solid. Mp: 116.6−116.9 °C. ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 1.27$, 1.62 (2 s, 2 × 3 H, $C(CH_3)_2$), 1.95 (s, 3 H, $COCH_3$), 2.32 (s, $COCH_3$), 3.74 (s, 3 H, OMe), 4.06 (d, $^3J = 4.0$ Hz, 1 H, H^a), 4.44 (dd, $^3J = 4.0$ Hz, 12.0 Hz, 1 H, H^b), 5.19 (d, $^3J = 12$ Hz, 1 H, H^c), 6.79 (d, $^3J = 9.0$ Hz, 2 H, ArH), 7.19 (d, $^3J = 9.0$ Hz, 2 H, ArH). ^{13}C NMR (75.5 MHz, $CDCl_3$): $\delta = 28.3$ (q, $C(\mathit{C}H_3)_2$), 28.5 (q, $C(\mathit{C}H_3)_2$), 29.9 (q, $CO\mathit{C}H_3$), 30.6 (q, $CO\mathit{C}H_3$), 43.2 (d, C^b), 48.2 (d, C^a), 55.4 (q, OCH_3), 71.0 (d, C^c), 105.8 (s, $\mathit{C}(CH_3)_2$), 114.7 (d, Ar), 128.5 (s), 130.8 (d, Ar), 159.7 (s), 165.0 (s, CO_2), 165.9 (s, CO_2), 202.4 (s, $\mathit{C}OCH_3$), 203.5 (s, $\mathit{C}OCH_3$). Signal assignments are based on additional DEPT and gHSQC experiments. ESI-MS (negative): *m*/*z* (%) = 361 (100) $[M - H^+]^-$. HR-MS: calcd 362.1366 ($C_{19}H_{22}O_7$), found 362.1327.

Reaction of 4-Dimethylaminobenzylidene Meldrum's Acid (1c) with Potassium Dicyanomethanide (2d-K$^+$). A mixture of **1c** (71.5 mg, 0.260 mmol) and **2d**-K$^+$ (27.1 mg, 0.260 mol) was stirred in DME (2 mL) at room temperature. After decolorization of the solution, stirring was continued for 5 min. A yellow solid precipitated, and hexane was added to support the precipitation.

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The precipitate was washed with diethyl ether/hexane. **3cd** (65 mg, 66%). Yellow solid. Mp: 129.1−129.5 °C. ^{1}H NMR (400 MHz, DMSO-d_6): $\delta = 1.46$ (s, 6 H, C(CH$_3$)$_2$), 2.85 (s, 6 H, NMe$_2$), 4.28 (d, $^3J = 12.4$ Hz, 1 H, H^b), 5.75 (d, $^3J = 12.0$ Hz, 1 H, H^c), 6.61 (d, $^3J = 8.8$ Hz, 2 H, ArH), 7.29 ppm (d, $^3J = 8.8$ Hz, 2 H, ArH). ^{13}C NMR (100.5 MHz, DMSO-d_6): $\delta = 25.7$ (q, C(*C*H$_3$)$_2$), 26.6 (d, C^c), 40.1 (q, NMe$_2$), 43.2 (d, C^b), 73.2 (s, C^a), 99.7 (s, *C*(CH$_3$)$_2$), 111.8 (d, Ar), 115.1 (s, CN), 128.4 (d, Ar), 129.8 (s), 149.2 (s), 164.6 ppm (s, CO$_2$). Signal assignments are based on additional gHSQC experiments. ESI-MS (negative): m/z (%) = 340 (100) $[M - K^+]^-$, 300 (63), 212 (23).

Kinetics. For the kinetic experiments, standard stopped-flow UV−vis-spectrophotometer systems were used in their single mixing mode. Solutions of the electrophiles **1** in DMSO were mixed with solutions of the carbanions **2** in DMSO (either generated by deprotonation of **2**-H with 1.05 equiv of KO-*t*-Bu in DMSO or by dissolving **2**-K$^+$ in DMSO). In order to obtain pseudo-first-order kinetics, the carbanions were used in large excess (10−100 equiv) over the electrophiles. The temperature of the solutions was kept constant (20 ± 0.1 °C) by using circulating bath thermostats.

Rate constants $k_{1\psi}$ (s^{-1}) were obtained by fitting the single exponential $A_t = A_0 \exp(-k_{1\psi}t) + C$ to the observed time-dependent electrophile absorbance (the monitored wavelenghts are given in the Supporting Information). As depicted in the Supporting Information, the second-order rate constants k_2 (Table 3) were obtained from the slopes of the linear plots of $k_{1\psi}$ versus the carbanion concentrations [**2**].

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Supporting Information Available: Details of the kinetic experiments, synthetic procedures, and NMR spectra of all characterized compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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