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Nucleophilicity Parameters of Arylsulfonyl-Substituted Halomethyl Anions

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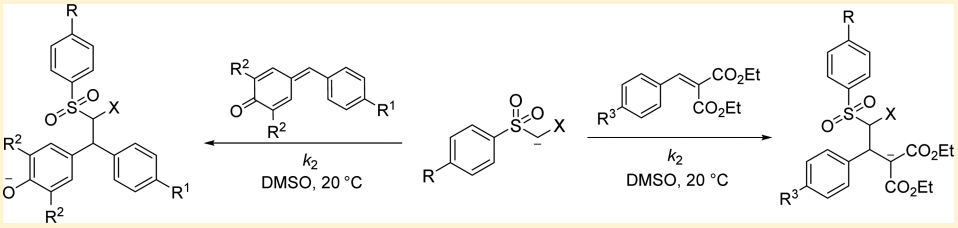
Supporting Information



ABSTRACT: The rates of the reactions of the arylsulfonyl-substituted carbanions carrying α-chloro and α-bromo substituents (**1a−e**) with quinone methides **2a−g** and benzylidenemalonates **2h** and **2i** in DMSO were determined photometrically at 20 °C. The reactions were performed under pseudo-first-order conditions, and the second-order rate constants were obtained as the slopes of the plots of the pseudo-first-order rate constants versus the concentrations of the reactants used in excess. The second-order rate constants correlate linearly with the parameters E of the reference electrophiles according to the linear free energy relationship $\log k_2(20\ °C) = s_N(N + E)$, which allowed us to derive the nucleophile-specific parameters N and s_N of carbanions **1a−e**. The resulting nucleophilicity parameters N ($23 < N < 29$) reveal the title compounds to be among the most reactive nucleophiles so far integrated on our comprehensive nucleophilicity scale.

INTRODUCTION

Carbanions bearing leaving groups at position α are useful reagents in organic synthesis. They are widely used in Darzens condensations,[1] cyclopropanations,[2] and vicarious nucleophilic substitutions.[3] Knowledge of the nucleophilic reactivities of these carbanions would be a valuable tool for designing their use in synthesis. In numerous previous investigations, we had found that the rates of the reactions of nucleophiles with carbocations and acceptor-substituted ethylenes can be predicted by eq 1, which characterizes electrophiles by one parameter, electrophilicity E, and nucleophiles by two solvent-dependent parameters, nucleophilicity parameter N and susceptibility parameter s_N.[4]

$$\log k_2(20\ °C) = s_N(N + E) \quad (1)$$

More than 1000 nucleophiles and 270 electrophiles have so far been characterized on the basis of this linear free energy relationship.[5] We now report on the application of this method to characterize the nucleophilicities of arylsulfonyl-substituted carbanions carrying α-chloro and α-bromo substituents, **1a−e** (Scheme 1). Quinone methides **2a−g** and benzylidenemalonates **2h** and **2i** (Table 1) were used as reference electrophiles for these investigations.

RESULTS AND DISCUSSION

Product Studies. As representative examples of the reactions of carbanions **1** with quinone methides **2a−g**, we have investigated the corresponding reactions with **2c**. Treatment of **1a**-H with 1 equiv of *t*-BuOK in DMF at −50 °C and subsequent addition of 0.5 equiv of **2c** gave a phenolate that was treated with 2% aqueous HCl after 5 min at −50 °C to yield 75% **3a**-H as a mixture of two diastereomers. The reaction of **1d** with **2c** proceeded analogously (Scheme 2).

Scheme 1. Cl-Stabilized Carbanions 1a−d and Br-Stabilized Carbanion 1e

When the reactions of **1a−c** and **1e** with **2c** were performed in DMSO at 20 °C and quenched with 2% aqueous HCl after 10 min, mixtures of **4**-H and **5a**-H were obtained, while **1d** gave a complex mixture of products (Scheme 3). Because of the high melting point of DMSO, low-temperature studies were not possible as in DMF (see above).

The structure of **4a**-H was confirmed by single-crystal X-ray crystallography (Figure 1). Treatment of isolated **4a**-H with *t*-BuOK led to formation of **5a**-H (Scheme 4). To investigate whether the weaker Brønsted base **1a**-K that might be the effective base under the conditions depicted in Scheme 3 can also affect this elimination, **4a**-H was also treated with **1a**-K. As shown in Scheme 4, this reaction proceeded slowly, and after

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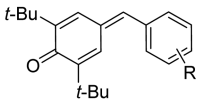
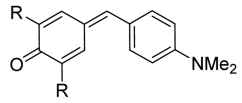
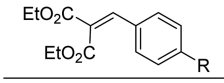
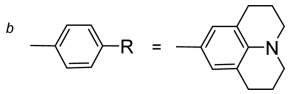
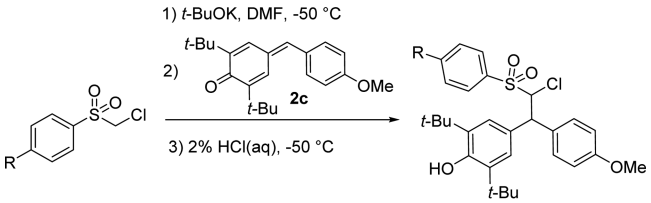
Table 1. Quinone Methides 2a–g and Diethyl Benzylidenemalonates 2h and 2i

Electrophile		R	E^a
	**2a**	3-F	-15.03
	2b	4-Me	-15.83
	2c	4-OMe	-16.11
	2d	4-NMe_2	-17.29
	2e	jul[b]	-17.90
	**2f**	Me	-16.36
	2g	OMe	-17.18
	**2h**	NMe_2	-23.10
	2i	jul[b]	-23.80

[a]Electrophilicity parameters E of **2a**, **2f**, and **2g** were taken from ref 6a, those of **2b–e** from ref 4b, and those of **2h** and **2i** from ref 6b.

[b] 

Scheme 2. Synthesis of Michael Adducts 3-H by the Reactions of Carbanions 1 with Quinone Methide 2c at −50 °C



R=H **1a**-H
R=NO_2 **1d**-H

3a-H (75%, dr ~ 1.3:1)[a]
3d-H (71%, dr ~ 1.1:1)[a]

[a]Diastereomeric ratios (dr) correspond to isolated products.

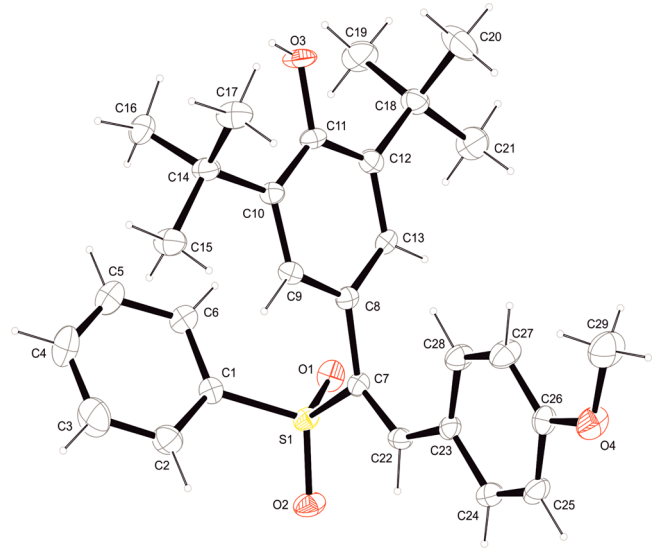
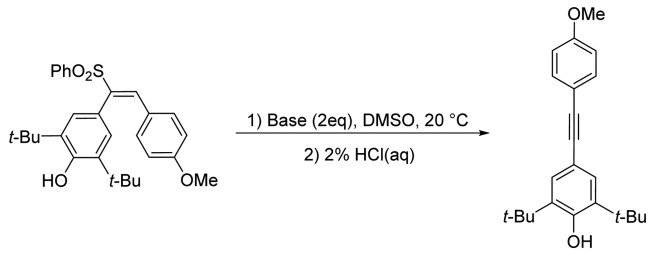


Figure 1. ORTEP drawing of the crystal structure of **4a**-H. The ellipsoid probability level is 50%.

Scheme 4. Transformation of 4a-H into 5a-H



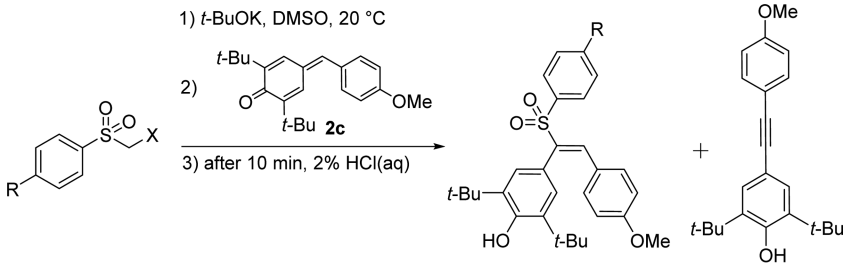
4a-H	Base	**5a**-H[a]	
	t-BuOK	10 min	10%
		30 h	90%
	1a-K	10 min	6%
		60 h	90%

[a]Yield of the isolated product.

10 min, a similar amount of **5a**-H was obtained as in the reaction of **1a** with **2c** described in Scheme 3.

These observations suggest the reaction mechanism described in Scheme 5. Michael addition of the carbanion **1a** to the electrophilic double bond of quinone methide **2c** yields phenolate anion **3a**. This intermediate was trapped by

Scheme 3. Reactions of Carbanions 1a–1e with Quinone Methide 2c at 20 °C



1a-H	R = H	**4a**-H (70%)	**5a**-H (10%)
1b-H	R = Cl	**4b**-H (61%)	**5a**-H (30%)
1c-H	R = CN	**4c**-H (44%)	**5a**-H (45%)
1d-H	R = NO_2	decomposition	none
1e-H	R = H	**4a**-H(70%)	**5a**-H(10%)

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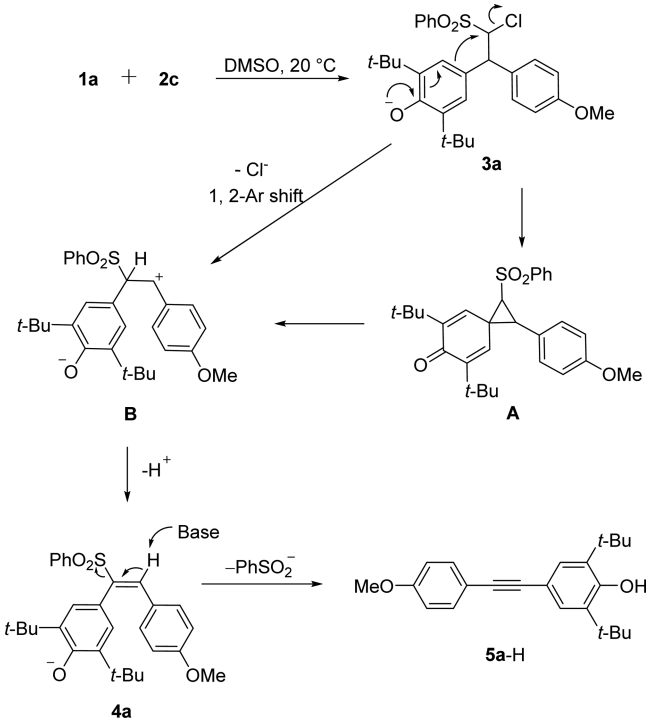
Scheme 5. Plausible Mechanism for the Reaction of 1a with 2c

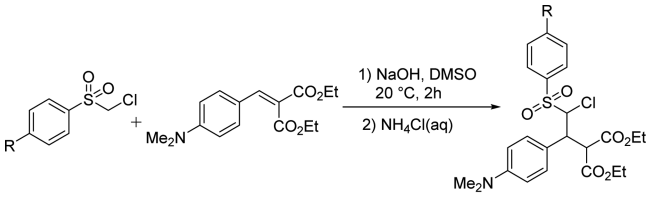


protonation with 2% aqueous HCl, when the reaction was performed in DMF at −50 °C (Scheme 2). At 20 °C, intramolecular cyclization may lead to the formation of spirodienone **A**, which undergoes spontaneous ring opening with formation of mesomerically stabilized zwitterion **B**. As an alternative to this mechanism suggested by Groszek,[7] phenoxide migration with substitution of Cl^- gives **B** directly through a transition state resembling **A**. Deprotonation yields phenolate **4a** [**4a**-H was isolated (Scheme 3 and Figure 1)], which is selectively formed as the *E* diastereomer, probably because of attractive intramolecular $\pi-\pi$ interaction of the two aryl rings in intermediate zwitterion **B**, as previously suggested by Groszek.[7] Slow elimination of $PhSO_2^-$ from **4a** yields alkynyl-substituted phenol **5a**-H. The formation of Michael adducts of type **3**-H and of rearranged elimination products **4**-H from the reaction of tolylsulfonyl chloromethyl anion **1** (R = Me) with quinone methides has previously been reported by Groszek and co-workers.[7]

The NaOH-induced reaction of **1a**-H with benzylidenemalonate **2h** in DMSO gave Michael adduct **6a**-H, as previously reported for the corresponding reaction in DMF.[8] The reaction of **1b**-H with **2h** proceeded analogously (Scheme 6).

Kinetic Investigations. All kinetic investigations were performed in a DMSO solution at 20 °C and monitored photometrically by following the disappearance of the colored quinone methides or benzylidenemalonates. Generally, a large excess of the carbanions over the electrophiles was used to achieve first-order kinetics. As reported previously,[9] carbanions **1a−e** disproportionate slowly at room temperature. For that reason, the double-mixing mode of stopped flow UV−vis spectrometers was used to generate solutions of carbanions **1a−e** by mixing the CH acids (**1a−e**)-H with *t*-BuOK. After a user-defined delay period (1−30 s), the solutions of carbanions were combined with electrophiles **2a−i**.

Scheme 6. Reaction of Benzylidenemalonate 2h with Carbanions 1



R=H	**1a**-H	**2h**	**6a**-H (72%, dr ~ 5:1)[a]
R=Cl	**1b**-H		**6b**-H (70%, dr ~ 2:1)[a]

[a]Diastereomeric ratios (dr) correspond to crude products.

Figure 2 illustrates the decay of the absorption of **2c** (λ_{max} = 393 nm) in DMSO at 20 °C after addition of 20 equiv of **1a**

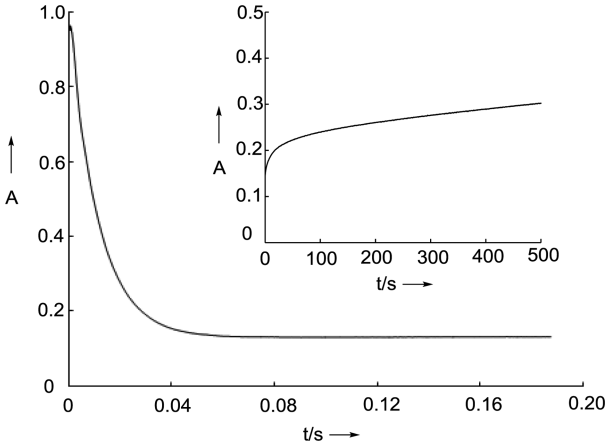


Figure 2. Monoexponential decay of absorbance *A* (at 393 nm) during the first 200 ms of the reaction of **1a** (1.00×10^{-3} mol L^{-1}) with **2c** (5.00×10^{-5} mol L^{-1}) in DMSO at 20 °C. The inset shows the slow increase in the absorbance at 393 nm at 20 °C between 0.05 and 500 s.

(pseudo-first-order conditions). The absorbance decreases to ~15% of its initial value within 50 ms and then shows a very slow increase. Separate UV−vis measurements showed that the residual absorbance after 50 ms is due to the generation of **4a**, which has an absorption maximum at 504 nm. The subsequent slow increase (inset in Figure 2) is due to the formation of **5a** by elimination of $PhSO_2H$ from **4a**. Depending on the excess of base used for these experiments, the alkyne is either formed as anion **5a** or its conjugate acid **5a**-H. While an analogous behavior was observed for all other reactions of **1** with quinone methides **2a−g**, the corresponding reactions with benzylidenemalonates **2h** and **2i** showed only the fast decay of the absorption band of **2h** and **2i**.

The first-order rate constants (k_{obs}) were obtained by least-squares fitting of the exponential function $A = A_0 \exp(-k_{obs}t) + C$ to the observed time-dependent absorbances *A* of quinone methides **2a−g** (in the initial period) and of benzylidenemalonates **2h** and **2i**. According to eqs 2 and 3, the pseudo-first-order rate constant (k_{obs}) should be proportional to the concentration of carbanions **1**. As shown for the reaction of **1a** with **2c** in Figure 3, k_{obs} correlates linearly with the concentrations of carbanions **1**, and the negative intercept may be due to partial decomposition of carbanions **1**. Though the intercept is small and negligible in most of these correlations (Supporting Information), in a few cases even

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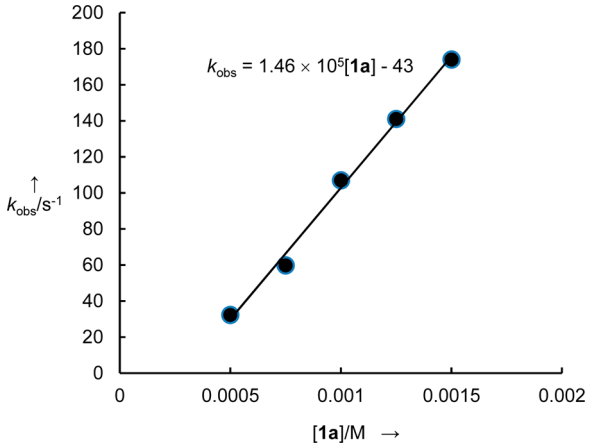

Figure 3. Correlation of k_{obs} for reaction of **1a** with **2c** vs the concentration of **1a**.

small positive intercepts were observed. The second-order rate constants (k_2) listed in Table 2 correspond to the slopes of the

Table 2. Second-Order Rate Constants (k_2) for the Reactions of Carbanions 1a−e with Quinone Methides 2a−g and Benzylidenemalonates 2h and 2i in DMSO at 20 °C

carbanion	electrophile	k_2 (M^{-1} s^{-1})	N, s_N[a]
1a	**2c**	1.46 × 10^5	28.27, 0.42
	2d	3.35 × 10^4	
	2e	2.65 × 10^4	
	2g	3.92 × 10^4	
	2h	1.49 × 10^2	
1b	**2b**	1.08 × 10^5	26.90, 0.45
	2c	8.87 × 10^4	
	2d	2.01 × 10^4	
	2h	4.90 × 10	
	2i	2.85 × 10	
1c	**2d**	1.77 × 10^4	25.59, 0.51
	2e	9.19 × 10^3	
	2f	5.65 × 10^4	
	2g	2.21 × 10^4	
1d	**2a**	6.89 × 10^4	24.88, 0.49
	2b	2.90 × 10^4	
	2c	2.00 × 10^4	
1e	**2a**	2.78 × 10^5	23.90, 0.62
	2c	7.11 × 10^4	
	2d	1.17 × 10^4	
	2e	4.90 × 10^3	

[a]Nucleophile-specific parameters N and s_N were derived from the intercepts (on the abscissa) and the slopes of the correlations between log k_2 (this table) and electrophilicity parameters E from Table 1. For details, see the text and Figure 4.

k_{obs} versus [**1**] correlations. The experimental second-order rate constant (k_2) for the reaction of **1a** with **2h** (149 M^{-1} s^{-1}) is close to that (200 M^{-1} s^{-1}) extrapolated for this reaction in DMF at 20 °C from the measured rate constant at −40 °C.[8]

$$-d[\mathbf{2}]/dt = k_2[\mathbf{1}][\mathbf{2}] \quad (2)$$

$$\text{for } [\mathbf{1}]_0 >> [\mathbf{2}]_0 \Rightarrow k_{obs} = k_2[\mathbf{1}]_0 \quad (3)$$

To determine nucleophile-specific parameters N and s_N of carbanions **1a−e** according to eq 1, the second-order rate constants (log k_2) of their reactions with electrophiles **2** (see Table 2) were plotted versus previously reported electrophilicity parameters E of **2a−i** (Table 1). Figure 4 and Figure

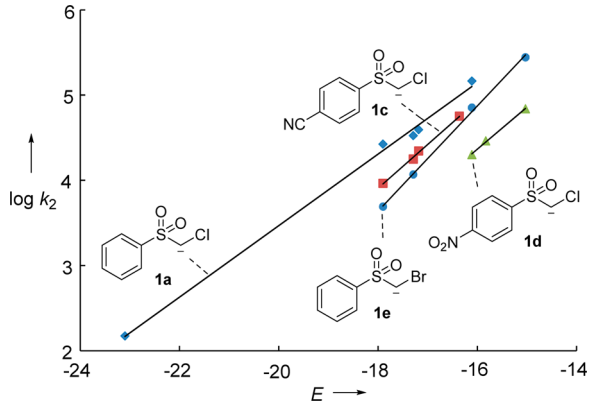

Figure 4. Correlation of log k_2 for the reactions of carbanions **1a** and **1c−e** with quinone methides **2a−g** and benzylidenemalonates **2h** and **2i** vs electrophilicity parameters E of the corresponding electrophiles. For the sake of clarity, the correlation line for **1b** is shown only in the Supporting Information.

S1 show that log k_2 values for these reactions correlate linearly with E as required by eq 1 and thus allow the calculation of nucleophile-specific parameters N and s_N listed in Table 2. The similarities of the slopes of the correlations for carbanions **1b−d** (Figure 4 and Figure S1), which are numerically expressed by the s_N parameters in Table 2, imply that the relative nucleophilicities of carbanions **1b−d** depend only slightly on the electrophilicities of the reaction partners. The Hammett correlation for the reactions of carbanions **1a−d** with benzylidenemalonate **2h** is of moderate quality and gives rise to the Hammett reaction constant ρ = −1.50 (Figure 5). Because the substituted aryl ring is separated from the nucleophilic reaction center by the sulfonyl group, the Hammett reaction constant ρ has a small negative value.

Figure 6 compares the reactivities of **1a−e** with that of the previously characterized phenylsulfonyl-substituted benzyl anion **1f**. As the s_N values for these carbanions differ slightly, their relative nucleophilic reactivities depend somewhat on the electrophilicity of the reaction partner. The reactivities of

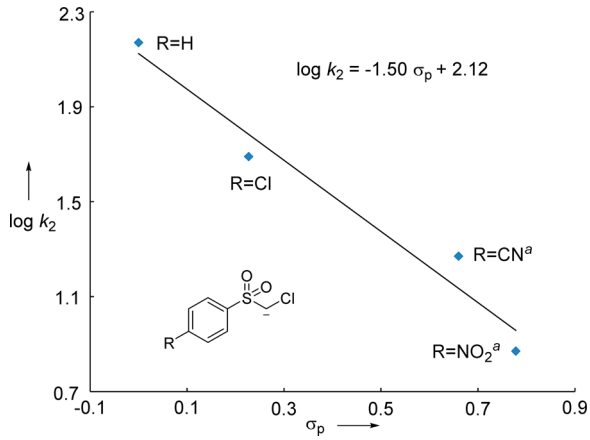

Figure 5. Correlation of log k_2 of the reactions of carbanions **1a−d** with benzylidenemalonate **2h** vs Hammett σ_p values[17] for R. The log k_2 values marked with superscript *a*'s were calculated with eq 1 with E values from Table 1.

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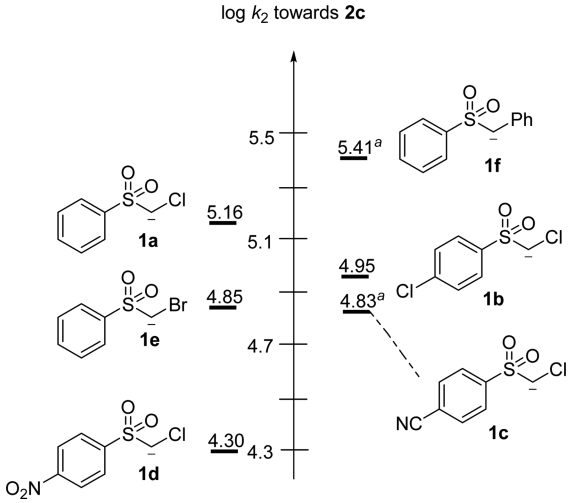

Figure 6. Comparison of log k_2 for the reactions of carbanions **1a–f** with electrophile **2c** in DMSO at 20 °C. The log k_2 (**2c**) values marked with superscript *a*'s were calculated with eq 1 with *E* values from Table 1. *N* and s_N values of **1f** are from ref 12d.

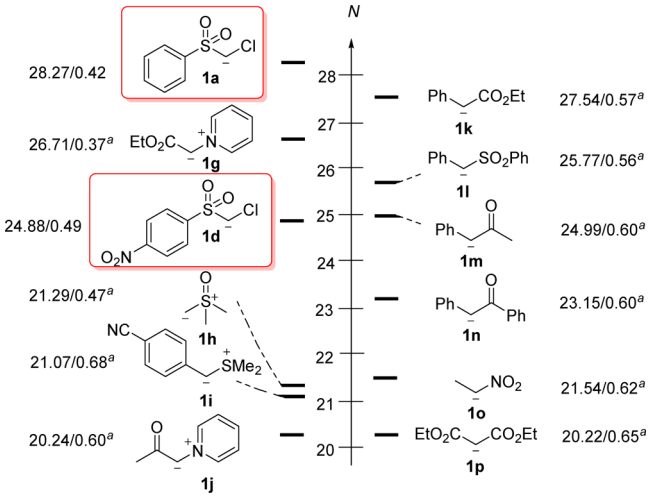

Figure 7. Comparison of nucleophilicity parameters *N* (in DMSO at 20 °C) of **1a** and **1d** with other classes of nucleophiles. As indicated with superscript *a*'s, *N* and s_N values of **1g** and **1j** were taken from ref 12a, those of **1h** and **1i** from ref 12b, those of **1k** from ref 12c, those of **1l–n** from ref 12d, those of **1o** from ref 12e, and those of **1p** from ref 4b.

arylsulfonyl-substituted halomethyl anions **1a–e** toward **2c** differ by a factor of <7. Chloro-substituted carbanion **1a** is 2 times more reactive than corresponding bromo derivative **1e**. The similar nucleophilic reactivities of phenylsulfonyl-substituted carbanions **1a** and **1f** show that α-chloro and α-phenyl substitution has a similar effect on nucleophilic reactivities and on the corresponding basicities in DMSO (for **1a**-H, pK_a = 23.8;[10] for **1f**-H, pK_a = 23.43[11]).

CONCLUSION

The rate constants for the reactions of Cl- and Br-substituted carbanions **1a–e** with the selected reference electrophiles (quinone methides and diethyl benzylidenemalonates) in DMSO follow the linear free energy relationship (eq 1). For that reason, it is possible to include these compounds on our comprehensive nucleophilicity scale and to compare their reactivities with those of other nucleophiles (Figure 7). As they contain halogens in position α, which can be nucleophilically substituted, carbanions **1** show carbenoid character and yield epoxides,[1] aziridines,[1c,13] and cyclopropanes[2] by reaction with carbonyl compounds, imines, and Michael acceptors, respectively. In this respect, they resemble the behavior of sulfur and nitrogen ylides, some representatives of which are also shown on the left side of Figure 7. Though the relative reactivities of these nucleophiles depend somewhat on the electrophilicity of the reaction partner due to the different values of s_N, the ranking based on *N* in Figure 7 gives a rough orientation. Thus, one can see that the arylsulfonyl-substituted chloromethyl anions are stronger nucleophiles than semistabilized sulfur ylides and, therefore, can be used for the synthesis of epoxides from nonactivated ketones. The high nucleophilic reactivities of **1a–e** combined with the high nucleofugality of chloride and bromide also explain their versatile applications in vicarious nucleophilic substitutions.[3]

EXPERIMENTAL SECTION

General. Chloromethyl phenyl sulfone **1a**-H (>97%) and bromomethyl phenyl sulfone **1e**-H (98%) are commercially available compounds. Compounds **1b–d**-H were prepared by chlorination of the corresponding 4-substituted thioanisoles,[14] and subsequent *m*-CPBA oxidation[15] following literature procedures.[14,15] **1b**-H is a known fully characterized compound.[16] For the sake of simplicity, the ^{1}H NMR signals of AA′BB′ spin systems of *p*-disubstituted aromatic rings of all compounds described below were treated as doublets. NMR signal assignments were based on additional two-dimensional NMR experiments (COSY, HSQC, and HMBC).

Chloromethyl 4-Nitrophenyl Sulfone (1d-H) (general procedure 1). 4-Nitrothioanisole (3.50 g, 20.7 mmol) was treated with *N*-chlorosuccinimide (3.18 g, 23.8 mmol) in dry carbon tetrachloride (21 mL) at 35 °C for 24 h. Succinimide precipitated and was removed by filtration. After evaporation of the solvent, the residue was dissolved in 65 mL of DCM and cooled in an ice–water bath while being stirred, and 77% *m*-chloroperoxybenzoic acid (11.0 g, 49.1 mmol) was added in portions within 5 min. The mixture was stirred at 0 °C for 40 min and 5 h at room temperature. After addition of ether, the solution was washed with water, 10% aqueous NaOH, an aqueous solution of $Na_2S_2O_3$, NaI, and NaOH, and a saturated aqueous solution of NaCl. The organic extract was dried over $MgSO_4$, and the solvent was removed using a rotary evaporator. The residue was recrystallized from EtOAc and pentane to give a yellow solid **1d**-H (3.42 g, 14.5 mmol, 70%): mp 138–143 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.50 (d, *J* = 8.8 Hz, 2 H, H-3 and H-5), 8.23 (d, *J* = 8.9 Hz, 2 H, H-2 and H-6), 5.50 (s, 2 H, H-1); ^{13}C NMR (101 MHz, DMSO-d_6) δ 151.1 (C-4), 141.2 (C-7), 130.6 (C-2 and C-6), 124.6 (C-3 and C-5), 57.1 (C-1); HRMS (EI) [$M^{+\bullet}$] calcd for $C_7H_6ClNO_4S$ *m*/*z* 234.9701, found *m*/*z* 234.9702; IR (ATR) $\tilde{\nu}$ 2942, 1607, 1531, 1475, 1401, 1334, 1236, 1209, 1155, 1131, 1083, 1011, 873, 854, 796, 755, 723, 679 cm^{-1}.

Chloromethyl 4-Cyanophenyl Sulfone (1c-H). General procedure 1 was applied to 4-cyanothioanisole (1.49 g, 10.0 mmol), *N*-chlorosuccinimide (1.40 g, 10.5 mmol), and 77% *m*-chloroperoxybenzoic acid (5.31 g, 23.7 mmol). **1c**-H was obtained as a white solid (1.62 g, 7.53 mmol, 75%): mp 133–138 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.21 (d, *J* = 8.7 Hz, 2 H, H-2 and H-7), 8.13 (d, *J* = 8.7 Hz, 2 H, H-3 and H-6), 5.46 (s, 2 H, H-1); ^{13}C NMR (101 MHz, DMSO-d_6) δ 139.9 (C-8), 133.5 (C-2 and C-7), 129.6 (C-3 and C-6), 117.4 (C-5), 117.1 (C-4), 57.0 (C-1); HRMS (EI) [$M^{+\bullet}$] calcd for $C_8H_6ClNO_2S$ *m*/*z* 214.9802, found *m*/*z* 214.9796; IR (ATR) $\tilde{\nu}$ 3019, 2240, 1387, 1327, 1293, 1146, 1081, 1015, 850, 841, 794, 778, 732, 693 cm^{-1}.

Reaction of Carbanion 1a with Quinone Methide 2c in DMF at −50 °C (general procedure 2). To a solution of *t*-BuOK (112 mg, 1.00 mmol) in anhydrous DMF (5 mL) at −50 °C were added a solution of **1a**-H (190 mg, 1.00 mmol) in anhydrous DMF (5 mL) and then a solution of **2c** (162 mg, 0.500 mmol) in anhydrous DMF (5

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mL). After 5 min, 100 mL of 2% aqueous HCl was added and the mixture was extracted with $CHCl_3$. The organic phase was washed with water three times to remove remaining DMF, dried with anhydrous $MgSO_4$, and filtered. The solvent was evaporated under reduced pressure, and the residue was purified by column chromatography to give a pale yellow liquid, 2,6-di-*tert*-butyl-4-[2-chloro-1-(4-methoxyphenyl)-2-(phenylsulfonyl)ethyl]phenol (**3a**-H), an ∼1.3:1 mixture of diastereomers (193 mg, 0.375 mmol, 75%). Diastereomer A: ^{1}H NMR (599 MHz, $CDCl_3$) δ 7.73 (d, J = 7.6 Hz, 2 H, H-15 × 2), 7.57 (t, J = 7.3 Hz, 1 H, H-17), 7.43 (dd, J = 7.2, 7.2 Hz, 2 H, H-16 × 2), 7.33 (d, J = 8.2 Hz, 2 H, H-4 × 2), 7.12 (s, 2 H, H-8 × 2), 6.81 (d, J = 8.0 Hz, 2 H, H-5 × 2), 5.41−5.38 (m, 1 H, H-1, overlap with B), 5.14 (s, 1 H, OH), 5.06 (d, J = 4.7 Hz, 1 H, H-2), 3.78 (s, 3 H, H-7 × 3), 1.39 (s, 18 H, H-11 × 18); ^{13}C NMR (151 MHz, $CDCl_3$) δ 158.8 (C-6), 153.0 (C-12), 137.1 (C-14), 136.0 (C-9 × 2), 134.0 (C-17), 131.0 (C-3), 130.9 (C-13), 130.8 (C-4 × 2), 129.7 (C-15 × 2), 128.8 (C-16 × 2), 125.0 (C-8 × 2), 113.6 (C-5 × 2), 79.4 (C-1), 55.3 (C-7), 50.6 (C-2), 34.4 (C-10 × 2), 30.3 (C-11 × 6). Diastereomer B: ^{1}H NMR (599 MHz, $CDCl_3$) δ 7.67 (d, J = 7.5 Hz, 2 H, H-15 × 2), 7.54 (t, J = 7.1 Hz, 1 H, H-17), 7.38 (dd, J = 7.4, 7.4 Hz, 2 H, H-16 × 2), 7.25 (d, J = 9.3 Hz, 2 H, H-4 × 2), 7.15 (s, 2 H, H-8 × 2), 6.81 (d, J = 8.0 Hz, 2 H, H-5 × 2), 5.41−5.38 (m, 1 H, H-1, overlap with A), 5.12 (s, 1 H, OH), 4.97 (d, J = 5.3 Hz, 1 H, H-2), 3.77 (s, 3 H, H-7 × 3), 1.38 (s, 18 H, H-11 × 18); ^{13}C NMR (151 MHz, $CDCl_3$) δ 158.7 (C-6), 153.1 (C-12), 136.6 (C-14), 135.5 (C-9 × 2), 133.9 (C-17), 132.4 (C-3), 130.0 (C-15 × 2), 129.4 (C-4 × 2), 128.8 (C-13), 128.5 (C-16 × 2), 126.4 (C-8 × 2), 114.1 (C-5 × 2), 79.8 (C-1), 55.3 (C-7), 51.2 (C-2), 34.4 (C-10 × 2), 30.4 (C-11 × 6); HRMS (EI) [$M^{+\bullet}$] calcd for $C_{29}H_{35}ClO_4S$ m/z 514.1939, found m/z 514.1948; IR (ATR, mixture of diastereoisomers) $\tilde{\nu}$ 3634, 2956, 1610, 1511, 1435, 1361, 1322, 1309, 1250, 1212, 1179, 1150, 1135, 1081, 1032, 887, 836, 810, 685, 667 cm^{-1}.

(*E*)-2,6-Di-*tert*-butyl-4-{2-(4-methoxyphenyl)-1-[(4-nitrophenyl)sulfonyl]vinyl}phenol (3d-H). General procedure 2 was applied to **1d**-H (235 mg, 1.00 mmol), **2c** (162 mg, 0.500 mmol), and *t*-BuOK (112 mg, 1.00 mmol). **3d**-H was obtained as a pale yellow liquid and a mixture of diastereomers (199 mg, 0.355 mmol, 71%, dr ∼ 1.1:1). Diastereomer A: ^{1}H NMR (599 MHz, $CDCl_3$) δ 8.20 (d, J = 9.0 Hz, 2 H, H-16 × 2), 7.84 (d, J = 9.0 Hz, 2 H, H-15 × 2), 7.29 (d, J = 8.8 Hz, 2 H, H-4 × 2), 7.08 (s, 2 H, H-8 × 2), 6.78 (d, J = 8.9 Hz, 2 H, H-5 × 2), 5.42 (d, J = 5.5 Hz, 1 H, H-1), 5.16 (s, 1 H, OH), 5.01 (d, J = 5.5 Hz, 1 H, H-2), 3.77 (s, 3 H, H-7 × 3), 1.37 (s, 18 H, H-11 × 18); ^{13}C NMR (151 MHz, $CDCl_3$) δ 159.19 (C-6), 153.35 (C-12), 150.77 (C-17), 142.55 (C-14), 136.28 (C-9 × 2), 131.16 (C-15 × 2), 130.80 (C-4 × 2), 130.42 (C-3), 130.07 (C-13), 125.06 (C-8 × 2), 123.67 (C-16 × 2), 113.83 (C-5 × 2), 79.77 (C-1), 55.38 (C-7), 50.92 (C-2), 34.51 (C-10 × 2), 30.39 (C-11 × 6). Diastereomer B: ^{1}H NMR (599 MHz, $CDCl_3$) δ 8.14 (d, J = 9.1 Hz, 2 H, H-16 × 2), 7.75 (d, J = 9.0 Hz, 2 H, H-15 × 2), 7.20 (d, J = 8.9, 2 H, H-4 × 2), 7.12 (s, 2 H, H-8 × 2), 6.79 (d, J = 8.8 Hz, 2 H, H-5 × 2), 5.45 (d, J = 6.0 Hz, 1 H, H-1), 5.15 (s, 1 H, OH), 4.93 (d, J = 5.9 Hz, 1 H, H-2), 3.75 (s, 3 H, H-7 × 3), 1.34 (s, 18 H, H-11 × 18); ^{13}C NMR (151 MHz, $CDCl_3$) δ 159.06 (C-6), 153.55 (C-12), 150.67 (C-17), 142.15 (C-14), 135.88 (C-9 × 2), 131.53 (C-15 × 2), 131.48 (C-3), 129.45 (C-4 × 2), 128.19 (C-13), 126.45 (C-8 × 2), 123.39 (C-16 × 2), 114.28 (C-5 × 2), 80.29 (C-1), 55.34 (C-7), 51.38 (C-2), 34.41 (C-10 × 2), 30.32 (C-11 × 6); HRMS (EI) [$M^{+\bullet}$] calcd for $C_{29}H_{34}ClNO_6S$ m/z 559.1790, found m/z 559.1795; IR (ATR, mixture of diastereoisomers) $\tilde{\nu}$ 3631, 2956, 1608, 1531, 1511, 1434, 1346, 1309, 1251, 1179, 1150, 1080, 1032, 908, 853, 752, 681 cm^{-1}.

Reaction of Carbanion 1a with Quinone Methide 2c in DMSO at 20 °C (general procedure 3). To a solution of **1a** (190 mg, 1.00 mmol) in anhydrous DMSO (5 mL) was added a solution of *t*-BuOK (112 mg, 1.00 mmol) in anhydrous DMSO (5 mL) at room temperature. After 2 min, a solution of **2c** (162 mg, 0.500 mmol) in anhydrous DMSO (10 mL) was added to the resulting solution. The completion of the reaction was checked by TLC and the reaction quenched with 100 mL of 2% aqueous HCl followed by $CHCl_3$ extraction. The organic extract was washed with water three times to remove remaining DMSO, dried with anhydrous $MgSO_4$, and filtered. The solvent was evaporated under reduced pressure, and the crude product was purified by column chromatography to yield white solid **4a**-H (167 mg, 0.351 mmol, 70%) and byproduct colorless liquid **5a**-H (16.8 mg, 0.0499 mmol, 10%).

(*E*)-2,6-Di-*tert*-butyl-4-[2-(4-methoxyphenyl)-1-(phenylsulfonyl)vinyl]phenol (4a-H). White solid: mp 147−152 °C; ^{1}H NMR (599 MHz, $CDCl_3$) δ 7.84 (s, 1 H, H-1), 7.66−7.57 (m, 2 H, H-15 × 2), 7.50 (t, J = 7.4 Hz, 1 H, H-17), 7.37 (dd, J = 8.5, 7.1 Hz, 2 H, H-16 × 2), 7.05 (d, J = 8.9 Hz, 2 H, H-3 × 2), 6.71 (s, 2 H, H-9 × 2), 6.69 (d, J = 9.0 Hz, 2 H, H-4 × 2), 5.31 (s, 1 H, OH), 3.75 (s, 3 H, H-6 × 3), 1.28 (s, 18 H, H-13 × 18); ^{13}C NMR (151 MHz, $CDCl_3$) δ 161.03 (C-5), 154.60 (C-11), 139.54 (C-14), 139.47 (C-7), 136.62 (C-1), 136.55 (C-10 × 2), 132.83 (C-17), 132.35 (C-3 × 2), 128.83 (C-15 × 2), 128.58 (C-16 × 2), 127.71 (C-9 × 2), 125.96 (C-2), 122.10 (C-8), 113.96 (C-4 × 2), 55.41 (C-6), 34.39 (C-12 × 2), 30.33 (C-13 × 6); HRMS (EI) [$M^{+\bullet}$] calcd for $C_{29}H_{34}O_4S$ m/z 478.2172, found m/z 478.2172; IR (ATR) $\tilde{\nu}$ 3552, 2949, 1606, 1513, 1444, 1419, 1376, 1305, 1282, 1256, 1236, 1177, 1147, 1110, 1036, 1023, 981, 895, 840, 804, 765, 751, 714, 689, 666 cm^{-1}.

2,6-Di-*tert*-butyl-4-[(4-methoxyphenyl)ethynyl]phenol (5a-H). Colorless liquid: ^{1}H NMR (599 MHz, $CDCl_3$) δ 7.46 (d, J = 8.7 Hz, 2 H, H-4 × 2), 7.34 (s, 2 H, H-9 × 2), 6.86 (d, J = 8.7 Hz, 2 H, H-3 × 2), 5.35 (s, 1 H, OH), 3.82 (s, 3 H, H-1 × 3), 1.45 (s, 18 H, H-12 × 18); ^{13}C NMR (151 MHz, $CDCl_3$) δ 159.4 (C-2), 154.3 (C-13), 136.2 (C-10 × 2), 133.0 (C-4 × 2), 128.6 (C-9 × 2), 116.1 (C-5), 114.5 (C-8), 114.1 (C-3 × 2), 89.3 (C-7), 87.0 (C-6), 55.4 (C-1), 34.5 (C-11 × 2), 30.4 (C-12 × 6); HRMS (EI) [$M^{+\bullet}$] calcd for $C_{23}H_{28}O_2$ m/z 336.2084, found m/z 336.2081; IR (ATR) $\tilde{\nu}$ 3625, 2956, 1606, 1509, 1433, 1287, 1174,1152, 1119, 1105, 1031, 885, 830, 806, 774, 757 cm^{-1}.

(*E*)-2,6-Di-*tert*-butyl-4-{1-[(4-chlorophenyl)sulfonyl]-2-(4-methoxyphenyl)vinyl}phenol (4b-H). General procedure 3 was applied to **1b**-H (225 mg, 1.00 mmol), **2c** (162 mg, 0.500 mmol), and *t*-BuOK (112 mg, 1.00 mmol). **4b**-H was obtained as a pale yellow liquid (156 mg, 0.305 mmol, 61%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.82 (s, 1 H, H-1), 7.52 (d, J = 8.6 Hz, 2 H, H-15 × 2), 7.34 (d, J = 8.5 Hz, 2 H, H-16 × 2), 7.06 (d, J = 8.8 Hz, 2 H, H-3 × 2), 6.72 (s, 2 H, H-9 × 2), 6.70 (d, J = 8.8 Hz, 2 H, H-4 × 2), 5.34 (s, 1 H, OH), 3.76 (s, 3 H, H-6 × 3), 1.30 (s, 18 H, H-13 × 18); ^{13}C NMR (101 MHz, $CDCl_3$) δ 161.19 (C-5), 154.72 (C-11), 139.52 (C-17), 139.21 (C-7), 138.03 (C-14), 136.82 (C-1), 136.76 (C-10 × 2), 132.42 (C-3 × 2), 130.29 (C-15 × 2), 128.80 (C-16 × 2), 127.76 (C-9 × 2), 125.78 (C-2), 121.88 (C-8), 114.02 (C-4 × 2), 55.43 (C-6), 34.42 (C-12 × 2), 30.33 (C-13 × 6); HRMS (EI) [$M^{+\bullet}$] calcd for $C_{29}H_{33}ClO_4S$ m/z 512.1783, found m/z 512.1792; IR (ATR) $\tilde{\nu}$ 3628, 2955, 1601, 1510, 1474, 1436, 1375, 1303, 1253, 1176, 1145, 1029, 982, 828, 765, 706, 669 cm^{-1}.

(*E*)-2,6-Di-*tert*-butyl-4-{1-[(4-cyanophenyl)sulfonyl]-2-(4-methoxyphenyl)vinyl}phenol (4c-H). General procedure 3 was applied to **1c**-H (215 mg, 1.00 mmol), **2c** (162 mg, 0.500 mmol), and *t*-BuOK (112 mg, 1.00 mmol). **4c**-H was obtained as a yellow solid (111 mg, 0.220 mmol, 44%): mp 135−140 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.85 (s, 1 H, H-1), 7.71 (d, J = 8.1 Hz, 2 H, H-15 × 2), 7.66 (d, J = 8.2 Hz, 2 H, H-16 × 2), 7.06 (d, J = 8.4 Hz, 2 H, H-3 × 2), 6.74 (s, 2 H, H-9 × 2), 6.71 (d, J = 8.4 Hz, 2 H, H-4 × 2), 5.38 (s, 1 H, OH), 3.77 (s, 3 H, H-6 × 3), 1.30 (s, 18 H, H-13 × 18); ^{13}C NMR (101 MHz, $CDCl_3$) δ 161.5 (C-5), 154.9 (C-11), 144.1 (C-14), 138.2 (C-1 and C-7), 137.0 (C-10 × 2), 132.6 (C-3 × 2), 132.2 (C-16 × 2), 129.4 (C-15 × 2), 127.8 (C-9 × 2), 125.5 (C-2), 121.4 (C-8), 117.4 (C-18), 116.4 (C-17), 114.1 (C-4 × 2), 55.5 (C-6), 34.4 (C-12 × 2), 30.4 (C-13 × 6); HRMS (EI) [$M^{+\bullet}$] calcd for $C_{30}H_{33}NO_4S$ m/z 503.2125, found m/z 503.2124; IR (ATR) $\tilde{\nu}$ 3598, 2956, 2232, 1664, 1603, 1511, 1436, 1422, 1358, 1310, 1174, 1120, 1081, 1033, 978, 892, 826, 755, 670 cm^{-1}.

Reaction of Carbanion 1 with Benzylidenemalonate 2h (general procedure 4). To a solution of **1a** (98.0 mg, 0.516 mmol) and **2h** (100 mg, 0.344 mmol) in anhydrous DMSO (5 mL) was added anhydrous NaOH (20.6 mg, 0.515 mmol). The resulting solution was stirred for 2 h at room temperature and then the reaction quenched with a saturated NH_4Cl solution followed by $CHCl_3$

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extraction. The organic extract was washed with water three times to remove the remaining DMSO, dried with anhydrous $MgSO_4$, and filtered. The solvent was evaporated under reduced pressure, and the residue was purified by column chromatography to yield yellow liquid diethyl 2-{2-chloro-1-[4-(dimethylamino)phenyl]-2-(phenylsulfonyl)-ethyl}malonate (**6a**-H) (119 mg, 0.248 mmol, 72%, dr ∼ 5:1). The major diastereomer could be isolated in pure form, and its full characterization is as same as that reported in the literature.[8]

Diethyl 2-{2-Chloro-2-[(4-chlorophenyl)sulfonyl]-1-[4-(dimethylamino)phenyl]ethyl}malonate (6b-H). General procedure 4 was applied to **1b**-H (117 mg, 0.520 mmol), **2h** (100 mg, 0.344 mmol), and NaOH (20.6 mg, 0.515 mmol). **6b**-H was obtained as a pale yellow liquid (123 mg, 0.238 mmol, 70%, dr ∼ 2:1); the minor diastereomer decomposed during purification. Major diastereomer: ^{1}H NMR (599 MHz, $CDCl_3$) δ 7.60 (d, J = 8.7 Hz, 2 H, H-16 × 2), 7.36 (d, J = 8.6 Hz, 2 H, H-17 × 2), 7.16 (d, J = 8.8 Hz, 2 H, H-11 × 2), 6.49 (d, J = 8.3 Hz, 2 H, H-12 × 2), 5.66 (d, J = 7.3 Hz, 1 H, H-1), 4.44 (d, J = 8.6 Hz, 1 H, H-3), 4.18−4.09 (m, 3 H, H-2 and H-8 × 2), 4.01 (q, J = 7.1 Hz, 2 H, H-5 × 2), 2.91 (s, 6 H, H-14 × 6), 1.21 (t, J = 7.2 Hz, 3 H, H-9 × 3), 1.08 (t, J = 7.1 Hz, 3 H, H-6 × 3); ^{13}C NMR (151 MHz, $CDCl_3$) δ 168.0 (C-7), 167.6 (C-4), 150.4 (C-13), 140.5 (C-18), 136.4 (C-15), 131.1 (C-11 × 2), 130.6 (C-16 × 2), 129.3 (C-17 × 2), 121.5 (C-10), 112.0 (C-12 × 2), 76.5 (C-1), 62.0 (C-8), 61.7 (C-5), 55.4 (C-3), 47.4 (C-2), 40.5 (C-14 × 2), 14.1 (C-9), 13.9 (C-6); HRMS (EI) [$M^{+\bullet}$] calcd for $C_{23}H_{27}Cl_2NO_6S$ m/z 515.0931, found m/z 515.0925; IR (ATR) $\tilde{\nu}$ 2981, 2929, 1728, 1613, 1523, 1475, 1445, 1394, 1332, 1279, 1256, 1089, 1012, 947, 819, 751, 666 cm^{-1}.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.6b02844.

Details of the kinetic experiments, correlation line (log k_2 vs E) for **1b**, and NMR spectra of all characterized compounds (PDF)

Crystallographic data (CIF)

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Notes

The authors declare no competing financial interest.

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