

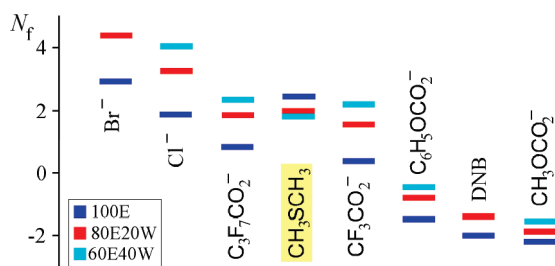
Leaving Group Property of Dimethyl Sulfide

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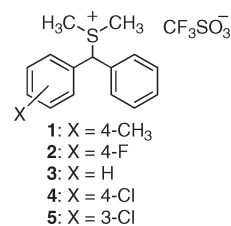
The LFER equation $\log k = s_f(E_f + N_f)$ was used to derive the nucleofuge specific parameters (N_f and s_f) for dimethyl sulfide in the series of aqueous alcohols, using the S_N1 solvolysis rate constants obtained for X-substituted benzhydryl dimethyl sulfonates **1–5**. The slope parameters (s_f) are practically independent of the solvent used, while N_f parameters slightly decrease as the polarity of the solvent increases.

Alkyl- or benzyldimethylsulfonium salts subjected to S_N1 -type solvolysis reactions produce the dimethyl sulfide molecule (Me_2S) as a leaving group in the initial step. Unlike in the neutral substrates, the separation of the positive and negative charge does not occur in the transition state, but to some extent transfer of the existing positive charge from sulfur to carbon takes place. Because of this specific feature, such substrates have widely been used to study reaction mechanisms, e.g., to distinguish the solvation and the solvent nucleophilic participation,¹ to estimate the importance of solvent nucleophilicity,² to create a solvent nucleophilicity scale,³ to investigate the solvation effects of alkyl and aryl substituents,⁴ to describe the detailed hydrolysis reaction,⁵ etc.

In this work, we have examined if it is justified to relate the leaving group ability of dimethyl sulfide with other commonly used negatively charged leaving groups generated from neutral substrates, i.e., to estimate the nucleofugality of Me_2S quantitatively in S_N1 reactions using the scale established and applied for charged leaving groups only. Numerous leaving groups have been compared and characterized using the scale developed on substituted benzhydryl derivatives as substrates.⁶ While the previous Noyce's scale,⁷ which is based on solvolysis rates of 1-phenylethyl derivatives in 80% aqueous ethanol, covers only 6 orders of magnitude (extended to 14 orders of magnitude by including substituted 1-phenylethyl derivatives and assuming constant reactivity ratios), the scale based on X,Y-substituted benzhydryl derivatives so far covers 16 orders of magnitude. Because of the linear relationship between the logarithms of the first-order rate constants for solvolysis and the electrofugalities in a given solvent, the reaction rates of heterolysis can be correlated according to the following three-parameter LFER eq 1

$$\log k(25^\circ\text{C}) = s_f(E_f + N_f) \quad (1)$$

in which k is the first-order rate constant (s^{-1}) and E_f is the electrofugality parameter, while the two variables that determine the nucleofuges in a given solvent are the nucleofuge-specific slope parameter (s_f) and the nucleofugality parameter (N_f) representing the negative intercept on the abscissa.



In this work, X-substituted benzhydryldimethylsulfonium trifluoromethanesulfonates (triflates) (**1–5**), prepared from the corresponding chlorides, were subjected to solvolysis in the series of aqueous alcohols. The reactions were monitored by titration of the liberated acid with an automatic pH-stat. Activation parameters were calculated from rate constants determined at least at three different temperatures. The measured and the extrapolated rate constants (to 25 °C) and the activation parameters are presented in Table 1. It should be mentioned that our rate constants obtained with **3** are the same in the limits of experimental error to those previously measured by Kevill, using different methods.^{4b}

The logarithms of the first-order rate constants (at 25 °C) for **1–5** in a given aqueous alcohol were plotted against E_f . The linear correlations obtained in the series of aqueous

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TABLE 1. Solvolysis Rate Constants of X-Substituted Benzhydryldimethylsulfonium Trifluoromethanesulfonates in Aqueous Alcohols and Activation Parameters

substrate	solvent ^a	temp (°C)	k (s ⁻¹) ^b	ΔH^\ddagger (kJ mol ⁻¹) ^c	ΔS^\ddagger (J K ⁻¹ mol ⁻¹) ^c
1	M	-4.7	$(1.55 \pm 0.01) \times 10^{-4}$	111 ± 1	95 ± 4
		0.0	$(3.61 \pm 0.10) \times 10^{-4}$		
		5.1	$(9.36 \pm 0.06) \times 10^{-4}$		
		10.1	$(2.15 \pm 0.06) \times 10^{-3}$		
		25.0	$(2.40 \pm 0.10) \times 10^{-2d}$		
	80M20W	5.0	$(4.03 \pm 0.14) \times 10^{-4}$	112 ± 3	94 ± 10
		10.0	$(9.31 \pm 0.09) \times 10^{-4}$		
		15.0	$(2.25 \pm 0.04) \times 10^{-3}$		
		25.0	$(1.10 \pm 0.10) \times 10^{-2d}$		
		5.0	$(2.20 \pm 0.04) \times 10^{-4}$		
	60M20W	10.0	$(5.29 \pm 0.05) \times 10^{-4}$	114 ± 1	94 ± 3
		14.8	$(1.21 \pm 0.02) \times 10^{-3}$		
		25.0	$(6.37 \pm 0.01) \times 10^{-3d}$		
		0.0	$(2.04 \pm 0.07) \times 10^{-4}$		
		5.0	$(5.12 \pm 0.15) \times 10^{-4}$		
	E	10.0	$(1.16 \pm 0.02) \times 10^{-3}$	109 ± 3	86 ± 9
		25.0	$(1.28 \pm 0.07) \times 10^{-2d}$		
		10.0	$(5.42 \pm 0.02) \times 10^{-4}$		
		15.0	$(1.22 \pm 0.04) \times 10^{-3}$		
		20.0	$(2.63 \pm 0.03) \times 10^{-3}$		
	80E20W	25.0	$(5.59 \pm 0.05) \times 10^{-3d}$	107 ± 1	69 ± 2
9.8		$(3.81 \pm 0.07) \times 10^{-4}$			
15.0		$(9.19 \pm 0.18) \times 10^{-4}$			
20.1		$(2.12 \pm 0.03) \times 10^{-3}$			
25.0		$(4.60 \pm 0.03) \times 10^{-3d}$			
60E40W	25.0	$(2.14 \pm 0.04) \times 10^{-3}$	113 ± 1	88 ± 1	
	25.0	$(1.24 \pm 0.02) \times 10^{-3}$			
	25.0	$(8.43 \pm 0.04) \times 10^{-4}$			
	25.0	$(1.52 \pm 0.03) \times 10^{-3}$			
	25.0	$(5.52 \pm 0.08) \times 10^{-4}$			
2	M	25.0	$(4.36 \pm 0.09) \times 10^{-4}$	111 ± 1 ^e	64 ± 1 ^e
		25.0	$(8.43 \pm 0.07) \times 10^{-4}$		
		25.0	$(4.40 \pm 0.09) \times 10^{-4}$		
		25.0	$(3.18 \pm 0.14) \times 10^{-4}$		
		25.0	$(4.85 \pm 0.03) \times 10^{-4}$		
3	80M20W	25.0	$(2.55 \pm 0.03) \times 10^{-4}$	111 ± 1 ^e	64 ± 1 ^e
		25.0	$(2.55 \pm 0.03) \times 10^{-4}$		
		25.0	$(1.82 \pm 0.02) \times 10^{-4}$		
		25.0	$(5.83 \pm 0.10) \times 10^{-4}$		
		25.0	$(2.92 \pm 0.13) \times 10^{-4}$		
4	60M40W	25.0	$(2.18 \pm 0.06) \times 10^{-4}$	127 ± 3	92 ± 10
		25.0	$(2.18 \pm 0.06) \times 10^{-4}$		
		25.0	$(3.46 \pm 0.02) \times 10^{-4}$		
		25.0	$(1.32 \pm 0.04) \times 10^{-4}$		
		25.0	$(1.06 \pm 0.02) \times 10^{-4}$		
5	M	25.0	$(4.23 \pm 0.10) \times 10^{-5}$	127 ± 3	92 ± 10
		30.0	$(5.01 \pm 0.09) \times 10^{-5}$		
		40.1	$(2.47 \pm 0.11) \times 10^{-4}$		
		50.1	$(1.23 \pm 0.15) \times 10^{-3}$		
		25.0	$(2.07 \pm 0.12) \times 10^{-5d}$		
	80M20W	40.1	$(1.87 \pm 0.10) \times 10^{-4}$	126 ± 2	87 ± 6
		44.8	$(3.81 \pm 0.04) \times 10^{-4}$		
		50.1	$(8.65 \pm 0.02) \times 10^{-4}$		
		25.0	$(1.52 \pm 0.07) \times 10^{-5d}$		
		30.0	$(6.59 \pm 0.10) \times 10^{-5}$		
	E	40.1	$(3.74 \pm 0.06) \times 10^{-4}$	128 ± 3	98 ± 9
		50.1	$(1.66 \pm 0.04) \times 10^{-3}$		
		25.0	$(2.81 \pm 0.16) \times 10^{-5d}$		
		40.0	$(1.55 \pm 0.01) \times 10^{-4}$		
		45.0	$(3.45 \pm 0.01) \times 10^{-4}$		
	80E20W	50.0	$(6.89 \pm 0.06) \times 10^{-4}$	127 ± 3	88 ± 10
		55.0	$(1.55 \pm 0.10) \times 10^{-3}$		
		25.0	$(1.26 \pm 0.11) \times 10^{-5d}$		
		45.0	$(2.61 \pm 0.06) \times 10^{-4}$		
		50.0	$(5.33 \pm 0.06) \times 10^{-4}$		
	60E40W	55.0	$(1.13 \pm 0.01) \times 10^{-3}$	125 ± 3	77 ± 9
25.0		$(1.03 \pm 0.10) \times 10^{-5d}$			

^aBinary solvents are on a volume–volume basis at 25 °C. E = ethanol, M = methanol, W = water. ^bErrors shown are standard deviations. ^cErrors shown are standard errors. ^dExtrapolated from data at different temperatures by using the Eyring equation. ^eTaken from ref 4b.

ethanols are presented in Figure 1. The nucleofuge-specific parameters derived for Me₂S are presented in Table 2. The

results presented in Table 2 showed that previous attempts to estimate the N_f values for dimethyl sulfide should be

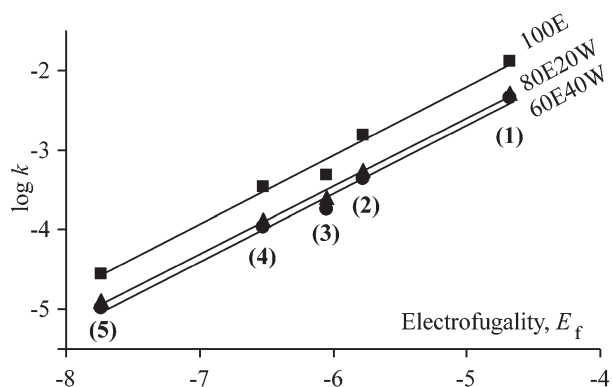


FIGURE 1. Correlation plots of $\log k$ vs E_f for the solvolysis of X-substituted benzhydryldimethylsulfonium triflates in aqueous ethanol. Solvent mixtures are given as v/v; E = ethanol, W = water.

TABLE 2. Nucleofugality Parameters N_f and s_f for Dimethyl Sulfide in Aqueous Alcohols

solvent ^a	N_f^b	s_f^b
100M	2.78 ± 0.21	0.89 ± 0.05
80M20W	2.43 ± 0.22	0.88 ± 0.05
60M40W	2.11 ± 0.23	0.85 ± 0.05
100E	2.44 ± 0.25	0.86 ± 0.06
80E20W	1.95 ± 0.15	0.85 ± 0.03
60E40W	1.87 ± 0.23	0.86 ± 0.05

^aBinary solvents are v/v at 25 °C. E = ethanol, M = methanol, W = water. ^bErrors shown are standard errors.

revised.^{6b} These values were obtained by applying Kevill's^{4b} rate constants obtained for solvolysis of benzhydryldimethylsulfonium salt (**3**) in various solvents to eq 1, assuming that $s_f = 1$. Because of the overestimated slope parameter, the derived N_f values are somewhat higher than those obtained by correlation presented here. Values of $s_f < 1$ indicate a smaller amount of positive charge transferred from sulfur into the benzhydrylium system in the TS than is developed in solvolysis of the reference chlorides on the way from the substrate to TS.

The most important trends that can be derived from Tables 1 and 2 are as follows: the changes of the N_f parameters with the solvent composition are in opposite directions compared to those obtained for anionic leaving groups,⁶ i.e., N_f values decrease as the water content in binary solvent increases (increase of polarity); the slope parameters are the same in the limits of error, so the $\log k$ vs E_f plots are nearly parallel; and finally, the high, favorable entropies of activation for all substrates are in a narrow range and the differences are close to the limits of the experimental error.

Decrease of the rate constants, and therefore decrease of the N_f parameters with polarity, is in accord with most of the results obtained with dimethylsulfonium ions as substrates.^{2,3} It has repeatedly been discussed that this phenomenon is due to solvation effects in the ground state. The decreasing trend of the solvolysis rates is rather mild, so the $\log k$ vs E_f lines are close to each other and the N_f parameters differ less with changing polarity than N_f for negatively charged leaving groups.

The major factor that controls the variation of the rates with solvent composition for substrates **1–5** is the solvation of the starting benzhydryldimethylsulfonium salt. Small shifts of the transition state toward the substrate in faster reactions or toward the benzhydrylium ion in slower

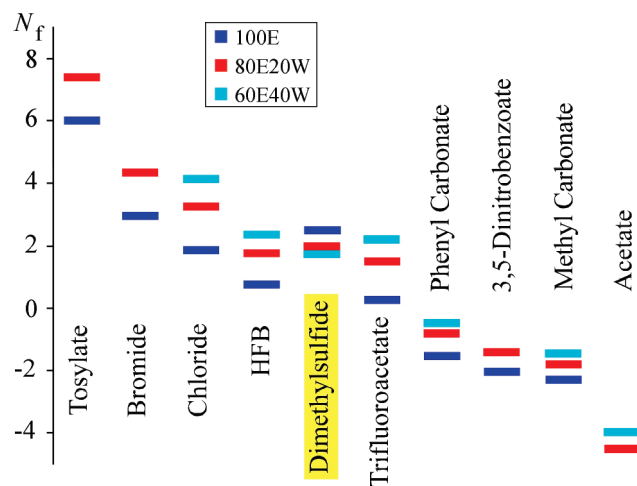


FIGURE 2. Nucleofugality parameters N_f of some leaving groups in aqueous ethanol. Solvent mixtures are given as v/v; E = ethanol, W = water.

reactions have little effect on the overall stabilization by solvation, so the changes of the water content similarly influence the reactivity of all substrates, producing nearly parallel $\log k$ vs E_f plots, i.e., almost the same s_f parameters in all solvents examined.

Practically invariant entropies of activation with the structures (Table 1) are in accord with this presumption. Solvation of the positive charge in the ground state requires a high degree of order. Since the positive charge is located mainly on the sulfur (the calculated NBO charges of the Me_2S moiety in ethanol for **3** and **5** are +0.92 and +0.94, respectively (for details of the calculation see below and the Supporting Information)), variation of X substituent on the benzhydryl backbone does not influence the overall solvation effect substantially. The two major variables that give considerable rise to the overall value of ΔS^\ddagger for all substrates are the gain of translational and vibrational freedom because of the elongated C–S bond and the diminished solvation. Thus, the solvolytic reactivity of benzhydryldimethylsulfonium salts **1–5** is determined with relatively high ΔH^\ddagger and also favorable ΔS^\ddagger , which enables the rates of these substrates to be measured by conventional kinetic methods.

Because of the reasonably good $\log k$ vs E_f correlation ($R > 0.99$, eq 1), it is possible to relate the leaving group ability of dimethyl sulfide to other commonly used leaving groups quantitatively (Figure 2).^{6,8–11} It turns out that dimethyl sulfide falls in the middle of the hitherto-established nucleofugality scale, and its N_f values are comparable with those of fluorinated carboxylates.

It may be advantageous to relate the results obtained for dimethylsulfonium ions to results obtained for other substrates. Besides similar reactivity (see Figure 2), heptafluorobutyrate (HFB) also produce almost parallel $\log k$ vs E_f lines, which make them suitable references.⁸ The two important parameters that are useful to be compared are the slope parameters and the affinities of the benzhydrylium ions toward a given leaving group.

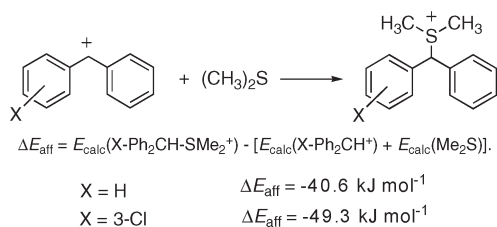
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SCHEME 1. Affinities of Some Benzhydrylium Cations toward Dimethyl Sulfide at PCM-B3LYP/6-311+G(2d,p) Level in Ethanol



It has been shown on several occasions that the slope parameter (s_f) can be related to the Hammett–Brown ρ^+ parameter.^{11,12} The s_f parameters of HFBs are essentially the same as those obtained with **1–5** in the limits of error. Even though the reactants' charge states are different, the values of s_f may indicate a similar quantity of positive charge transferred from sulfur in the reactant to benzhydrylium system in the TS of **1–5** as it is developed on the benzhydrylium system in heterolysis of HFB from the route from the reactant to TS.

To estimate the affinities of benzhydrylium ions toward Me_2S in ethanol, we carried out quantum chemical calculations using the Gaussian 03 program suite.¹³ We applied the polarizable continuum solvent model (PCM) with dielectric constant for ethanol and fully optimized the geometries of **3** and **5**, as well as the corresponding benzhydrylium ions and Me_2S at PCM-B3LYP/6-311+G(2d,p) level. The results are presented in Scheme 1.

Even though benzhydryl heptafluorobutyrate and dimethylsulfonium salts solvolyze via similar barriers, the calculated affinities of benzhydrylium ion toward heptafluorobutyrate ions ($E_{\text{aff}}^{\text{HFB}} = -75 \text{ kJ mol}^{-1}$) are considerably higher than toward dimethyl sulfide. The results indicate that dimethylsulfonium salts solvolyze through an earlier transition state producing less stable intermediates than those produced in solvolysis of HFB via later TS.

Finally, it should be discussed whether eq 1 can be applied to estimate the S_N1 reactivity of any dimethylsulfonium salt. Experimental data of Kevill and Anderson showed that unlike other sulfonium ions (e.g., *tert*-butyl-,² arylmethyl-,^{4b} and methoxybenzyl dimethylsulfonium^{4a} ion, etc.) the solvolytic reactivity of adamantyldimethylsulfonium ion in the series of aqueous ethanols and methanols increases very slightly as the water content increases.¹ The authors stated that this behavior is due to specific solvation caused with the cage structure. Evidently, eq 1 cannot be applied successfully to predict the solvolytic reactivity of adamantyldimethylsulfonium ion. Nevertheless, it can be concluded that the reactivity of a vast number of aryl- or alkyl dimethylsulfonium salts can indeed be semiquantitatively determined using the special LFER eq 1 and that only substrates with bulk cage structure might behave differently than the above LFER approach would predict.

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Experimental Section

General Procedure. Dimethyl sulfide (20.1 mmol) and the appropriate benzhydryl chloride (7.4 mmol) were added to 20 mL of nitromethane and stirred for 30 min in an ice bath. A solution of silver triflate (7.4 mmol) in nitromethane was then added dropwise over a 10 min period. Acetonitrile was added, and the stirring was continued for 1 h. The solid silver chloride was removed by filtration, and removal of solvent on rotary evaporator yielded brown oil, which crystallized in the ice bath. Filtration and washing with small portions of petroleum and ether led to 45–73% of the desired products.

4-Methylbenzhydryldimethylsulfonium triflate (1): mp 58.5–60.5 °C; ¹H NMR (300 MHz, CDCl_3) δ = 2.34 (s, 3H, ArCH_3), 2.90 [s, 6H, $(\text{CH}_3)_2\text{S}$], 6.12 (s, 1H, Ar_2CH), 7.20–7.55 (m, 9H, ArH); ¹³C NMR (75 MHz, CDCl_3) δ = 20.9 (ArCH_3), 24.3 [$(\text{CH}_3)_2\text{S}$], 65.5 (Ar_2CH), 125.3, 127.1, 128.5, 128.9, 130.9, 133.4, 137.5, 141.5 (Ar).

4-Fluorobenzhydryldimethylsulfonium triflate (2): mp 94.0–95.5 °C; ¹H NMR (300 MHz, CDCl_3) δ = 2.89 [s, 3H, $(\text{CH}_3)_2\text{S}$], 2.91 [s, 3H, $(\text{CH}_3)_2\text{S}$], 6.23 (s, 1H, Ar_2CH), 7.14 (t, 2H, $J_{\text{HF}} = 8.4$ Hz, ArH), 7.44–7.68 (m, 7H, ArH); ¹³C NMR (75 MHz, CDCl_3) δ = 24.3 [$(\text{CH}_3)_2\text{S}$], 64.4 (Ar_2CH), 126.4, 128.4, 128.6, 129.6, 130.2, 130.8, 131.0, 161.7 (Ar).

Benzhydryldimethylsulfonium triflate (3): mp 118.5–121.5 °C; ¹H NMR (300 MHz, CDCl_3) δ = 2.88 [s, 6H, $(\text{CH}_3)_2\text{S}$], 6.17 (s, 1H, Ar_2CH), 7.42–7.64 (m, 10H, ArH); ¹³C NMR (75 MHz, CDCl_3) δ = 24.0 [$(\text{CH}_3)_2\text{S}$], 65.1 (Ar_2CH), 127.2, 128.4, 129.8, 132.7 (Ar).

4-Chlorobenzhydryldimethylsulfonium triflate (4): mp 111.5–113.0 °C; ¹H NMR (300 MHz, CDCl_3) δ = 2.89 [s, 3H, $(\text{CH}_3)_2\text{S}$], 2.91 [s, 3H, $(\text{CH}_3)_2\text{S}$], 6.22 (s, 1H, Ar_2CH), 7.27–7.61 (m, 9H, ArH); ¹³C NMR (75 MHz, CDCl_3) δ = 24.6 [$(\text{CH}_3)_2\text{S}$], 65.1 (Ar_2CH), 126.6, 127.4, 128.6, 129.7, 129.9, 130.4, 131.2, 136.5 (Ar).

3-Chlorobenzhydryldimethylsulfonium triflate (5): mp 93.5–95.5 °C; ¹H NMR (300 MHz, CDCl_3) δ = 2.93 [s, 3H, $(\text{CH}_3)_2\text{S}$], 2.97 [s, 3H, $(\text{CH}_3)_2\text{S}$], 6.28 (s, 1H, Ar_2CH), 7.26–7.63 (m, 9H, ArH); ¹³C NMR (75 MHz, CDCl_3) δ = 24.50 [$(\text{CH}_3)_2\text{S}$], 64.5 (Ar_2CH), 118.0, 122.3, 125.7, 127.2, 128.4, 129.6, 130.8, 132.2, 134.9, 135.6 (Ar).

Kinetic Methods. Solvolysis rate constants were measured titrimetrically by means of a TIM 856 titration manager using a Red Rod combined pH electrode. Typically, 20–50 mg of substrate was dissolved in 0.10–0.20 mL of dichloromethane and injected into the solvent that was thermostated at the required temperature (± 0.01 °C). The liberated acid was continuously titrated at pH = 7.00 by using a 0.016 M solution of NaOH in the appropriate solvent mixture. Rate constants were averaged from at least three measurements.

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Supporting Information Available: Correlations of $\log k$ vs E_f in the series of aqueous methanol, NMR spectra (¹H, ¹³C and COSY) of X-substituted benzhydryl dimethylsulfonium triflates, quantum chemical calculation data, and a complete ref 13. This material is available free of charge via the Internet at <http://pubs.acs.org>.