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Can One Predict Changes from S_N1 to S_N2 Mechanisms?

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Abstract: The reactions of substituted benzhydryl bromides Ar_2CHBr with primary and secondary amines in DMSO yield benzhydryl amines Ar_2CHNRR', benzophenones $Ar_2C{=}O$, and benzhydrols Ar_2CHOH. Kinetic investigations at 20 °C revealed the rate law $-d[Ar_2CHBr]/dt = (k_1 + k_2[HNRR'])[Ar_2CHBr]$, where the amine independent term k_1 gave rise to the formation of $Ar_2C{=}O$ and Ar_2CHOH and the amine-dependent term $k_2[HNRR']$ was responsible for the formation of Ar_2CHNRR'. Clear evidence for concomitant S_N1 and S_N2 processes was obtained. While the rate constants of the S_N1 reactions correlate with Hammett's σ^+ constants ($\rho = -3.22$), the second-order rate constants k_2 for the S_N2 reactions are not correlated with the electron releasing abilities of the substituents, indicating that the transition states of the S_N2 reactions do not merge with the transition states of the S_N1 reactions. The correlation equation $\log k_{20°C} = s(E + N)$, where nucleophiles are characterized by N and s and electrophiles are characterized by E (*J. Am. Chem. Soc.* **2001**, *123*, 9500−9512), was used to calculate the lifetimes of benzhydrylium ions in the presence of amines and DMSO. The change from S_N1 to S_N2 mechanism occurred close to the point where the calculated rate constant for the collapse of the benzhydrylium ions with the amines just reaches the vibrational limit; that is, the concerted S_N2 mechanism was only followed when it was enforced by the lifetime of the intermediate. The nucleophile-specific parameters N and s needed for this analysis were determined by studying the kinetics of the reactions of a variety of amines with amino-substituted benzhydrylium tetrafluoroborates ($Ar_2CH^+BF_4^-$) of known electrophilicity E in DMSO. Analogously, the rates of the reactions of laser flash photolytically generated benzhydrylium ions Ar_2CH^+ with DMSO in acetonitrile were employed to determine the nucleophile-specific parameters N and s of DMSO, and it is reported that DMSO is a significantly stronger O-nucleophile than water and ordinary alcohols.

Introduction

Nucleophilic displacement reactions at C(sp^3) centers[1] proceed either with simultaneous breaking and forming of the involved bonds (S_N2 or A_ND_N)[2] or via a mechanism where breaking of the old bond precedes formation of the new bond (S_N1 or D_N+A_N).[1] The borderline between these two mechanisms has been the subject of considerable controversy. In contrast to Ingold who considered S_N1 and S_N2 as discrete processes,[1b] it has been suggested that a clear-cut distinction between these two mechanisms is impossible because there is a gradual transformation of an S_N2 into an S_N1 mechanism as the transition state develops more carbocation character.[3−6] Winstein's concept of different types of ion pairs[4] was extended by Sneen who suggested that the entire S_N1-S_N2 mechanistic spectrum could be fitted into a simple scheme involving ion-pair intermediates.[5] Schleyer and Bentley criticized this concept and suggested that there is a gradation of transition states between the S_N1 and S_N2 extremes with varying degrees of nucleophilic participation by the solvents.[6,7] The intermediates in the borderline region were considered as "nucleophilically solvated ion pairs"[6] which look like the transition states of S_N2 reactions

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but are energy minima not maxima. They coined the term "S_N2 intermediate" mechanism.[6]

Support for the operation of concurrent S_N1 and S_N2 reactions in the borderline cases came from kinetic investigations of nucleophilic substitutions under nonsolvolytic conditions, where the concentration of the nucleophile could be varied.[8] Nucleophilic displacement reactions of benzhydryl thiocyanates with labeled $^*SCN^-$ in acetonitrile and acetone,[9] of benzhydryl chlorides with labeled Cl^- and Br^-, and of benzhydryl bromide with Br^-, Cl^-, and N_3^- as well as with amines followed the rate law 1 with a nucleophile-independent term k_1 and a nucleophile-dependent term k_2.[10,11]

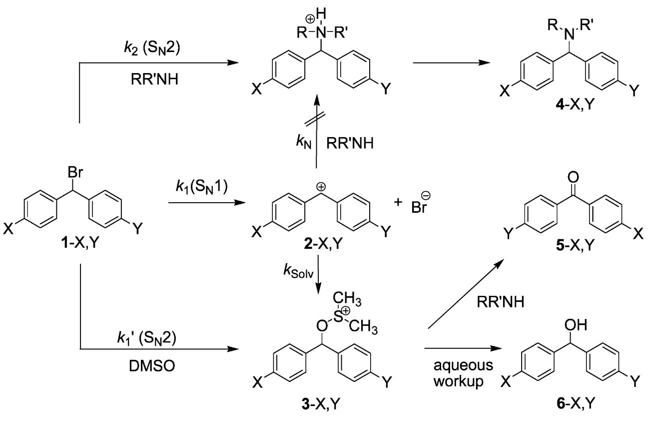
$$-\mathrm{d}[\text{R-X}]/\mathrm{d}t = [\text{R-X}](k_1 + k_2[\text{Nu}]) \qquad (1)$$

Yoh and Fujio et al. studied the kinetics of the reactions of benzyl halides and tosylates with amines.[12,13] While acceptor-substituted benzyl derivatives reacted exclusively by the S_N2 mechanism, donor-substituted benzyl derivatives, such as *p*-methoxybenzyl bromide, followed the rate law eq 1. This observation was considered "convincing evidence for the occurrence of simultaneous S_N1 and S_N2 mechanisms".[14a,b] Concurrent stepwise and concerted substitutions have also been reported by Amyes and Richard for the reactions of azide ions with 4-methoxybenzyl derivatives in trifluoroethanol/water mixtures.[14c]

Analogous rate laws have been observed by Katritzky for alkyl and benzyl group transfers from *N*-alkyl and *N*-benzyl pyridinium ions to various nucleophiles.[15] Because of the manifold of examples which demonstrate the duality of the two mechanisms the question arises whether the change from one to the other mechanism can be predicted.

Jencks and Richard based the differentiation of the mechanistic alternatives on the lifetimes of the potential intermediates.[16] It has been argued that nucleophilic aliphatic substitutions generally occur by the stepwise S_N1 mechanism when the intermediate carbocations exist in energy wells for at least the time of a bond vibration ($\approx 10^{-13}$ s) and that the change to the S_N2 mechanism is "enforced" when the energy well for the intermediate disappears. Convincing support for this hypothesis has been derived from the selectivities of carbocations ($k_{\text{azide}}/k_{\text{ROH}}$), which were solvolytically generated in alcoholic solutions of ionic azides.[16c,d,17]

Scheme 1. Reactions of Benzhydryl Bromides with Amines in DMSO



We have reported that the rates of the reactions of carbocations with nucleophiles can be calculated by eq 2, where E is a carbocation-specific electrophilicity parameter and s and N are solvent-dependent nucleophile specific parameters.[18−20]

$$\log k_{20\,°\mathrm{C}} = s(N + E) \qquad (2)$$

While the confidence limit of eq 2 is generally a factor of 10−100 in the presently covered reactivity range of 40 orders of magnitude, the predictive power of eq 2 is much better for reactions of benzhydrylium ions (factor 2−3) because benzhydrylium ions were used as reference electrophiles for deriving the nucleophile-specific parameters s and N. We now set out to examine whether the rate constants calculated by eq 2 can be used to predict the change from S_N1 to S_N2 mechanism on the basis of the lifetime criterion by Jencks and Richard. For that purpose, we investigated rates and products of the reactions of benzhydryl bromides with amines in DMSO, which yield benzhydryl amines **4**, benzophenones **5**, and benzhydrols **6**.

Scheme 1 shows that for each of the products **4**−**6** formation via the S_N1 process (k_1) or the S_N2 process (k_2 and k_1') has to be considered. In the following, it will be shown that the pathways k_1' and k_N can be excluded.

Experimental Section

Conductimetric Measurements of Nucleophilic Substitutions. Dissolution of the benzhydryl bromides **1**-X,Y in DMSO or in solutions of amines in DMSO led to an increase of conductivity due to the generation of HBr, which reacted with excess amine to give the hydrobromide salt. The rates of these reactions were followed by conductimetry (conductimeters: Tacussel CD 810 or Radiometer Analytical CDM 230; Pt electrode: WTW LTA 1/NS), while the temperature of the solutions was kept constant (20.0 ± 0.1 °C) by using a circulating bath thermostat. The correlation between conductance and the concentration of liberated HBr was determined by injecting 0.25 mL portions of 0.11 M acetonitrile solutions of the rapidly ionizing benzhydryl bromide **1**-Me,H into 30.0 mL of a 0.34 M solution of piperidine in DMSO. After the

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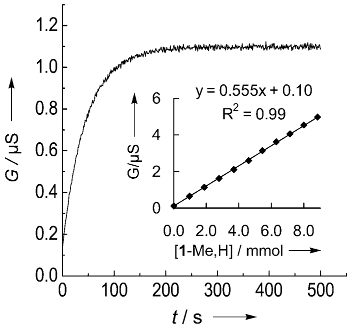


Figure 1. Exponential increase of conductivity during the reaction of 4-methylbenzhydryl bromide **1**-Me,H with 0.2 M piperidine in DMSO. Calibration in the inset: conductivity at t_∞ is proportional to the concentration of substrate.

conductivity had reached a constant value (typically 300 s), another portion of benzhydryl bromide was added. As depicted in the inset of Figure 1, the conductivity increased linearly with the concentration of released HBr, even at higher concentrations than used for the kinetic experiments.

Photometric Measurements of the Reactions of the Benzhydrylium Tetrafluoroborates with Amines. The rates of the reactions of benzhydrylium tetrafluoroborates with amines were studied in DMSO solutions. All amines were used as free bases. As the reactions of the colored benzhydrylium ions with amines gave rise to colorless products, the reactions could be followed by employing UV−vis spectroscopy at the absorption maxima of the benzhydrylium ions (Supporting Information Table S1). The rates were determined by using a Hi-Tech SF-61DX2 stopped-flow spectrophotometer system (controlled by Hi-Tech KinetAsyst2 software). Amine concentrations at least 10 times higher than the benzhydrylium ion concentrations were usually employed, resulting in pseudo-first-order kinetics with an exponential decay of the concentrations of the benzhydrylium ions Ar_2CH^+. First-order rate constants k_{obs} (s^{-1}) were obtained by least-squares fitting of the absorbance data (averaged from at least five kinetic runs at each amine concentration) to the single-exponential eq 3.

$$dA/dt = A_0\exp(-k_{obs}t) + C \tag{3}$$

Laser-Flash Photolysis. Laser-flash photolysis was employed for determining the rates of the reactions of Ar_2CH^+ with DMSO in acetonitrile. For that purpose, benzhydrylium ions were generated by irradiation of Ar_2CH-Cl in DMSO/acetonitrile with an Innolas SpitLight 600 Nd:YAG laser (fourth harmonic at $\lambda = 266$ nm; power/pulse of 40−60 mJ, pulse length = 6.5 ns) in a quartz cell. The rate constants were determined by observing the time-dependent decay of the UV−vis absorptions of the benzhydrylium ions. The pseudo-first-order rate constants were obtained by fitting the decay of the UV−vis absorptions to the exponential function of eq 3.

Product studies were carried out for several representative systems. For that purpose, 0.2 M solutions of the amines in DMSO were combined with 0.1 equiv of benzhydryl bromide **1**-X,Y. After 24 h, the reaction mixtures were quenched with water and extracted with diethyl ether. After evaporation, the residue was diluted with acetone containing a defined amount of *n*-hexadecane (internal standard, $\approx 10^{-3}$ M). Aliquots of the solutions were analyzed with a Thermo Focus GC equipped with a FID detector (column: Macherey-Nagel Optima-17, 25 m, 0.25 mm i.d.; carrier gas: N_2) for the determination of the absolute yields. In addition, GC−MS analysis (Agilent 6890 GC with an Agilent 5973 MS detector) was used for identifying the individual peaks. For the calculation of the absolute product concentrations, the products were synthesized individually, and GC calibrations were carried out to obtain the relative molar response factors (RMR).

Results and Discussion

Kinetics of the Nucleophilic Substitutions in DMSO. When solutions of the benzhydryl bromides **1**-X,Y in DMSO were treated with a high excess of amines (>10 equiv), the amine concentrations remained almost constant during the reactions, and the increase of conductivity followed the exponential function 4, as illustrated in Figure 1.

$$dG/dt = G_{max}[1 - \exp(-k_{obs}t)] + C \tag{4}$$

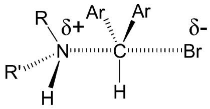
Plots of k_{obs} versus the concentrations of the amines were linear (Figure 2) but did not go through the origin. As expressed by eq 5, the observed rate constants k_{obs} (Supporting Information, pp S16−S29) can be regarded as the sum of an amine-independent term k_1 and an amine-dependent term k_2[amine], which are collected in Table 1.

$$k_{obs} = k_1 + k_2[\text{amine}] \tag{5}$$

The second-order rate constants k_2 can easily be assigned to the S_N2 reactions of the amines with the benzhydryl bromides. The amine-independent term k_1, which equals the directly measured solvolysis rate constant in DMSO in the absence of a nucleophilic amine, reflects either the rate of the S_N1-type process (k_1, Scheme 1) or the rate of an S_N2 reaction with DMSO as the nucleophile (k_1', Scheme 1), or a combination of both processes.

Comparison of the rate constants k_1 in the first line of Table 1 with previously published solvolysis rates in alcohols[21] shows that the solvolysis rates in DMSO are comparable to those in pure ethanol but considerably smaller than those in ethanol−water mixtures and in 2,2,2-trifluoroethanol. Creary et al. published kinetic data for the solvolysis of adamantyl mesylates and 3-aryl-3-hydroxy-β-lactams in DMSO.[22] In agreement with these data, our measurements confirm that DMSO is a solvent with a relatively high ionizing power.

The horizontal lines in Table 1 show that variation of the substituents of the benzhydryl bromides from **1**-CH_3,H to **1**-CF_3,CF_3 affects the second-order rate constants k_2 for the reactions with amines by less than a factor of 10. Accordingly, plots of log k_2 versus $\Sigma\sigma$ (Figure 3) or any other of Hammett's substituent constants (e.g., σ^+) illustrate that variation of the para-substituents in the benzhydryl bromides has only a marginal effect on the rate constants of the S_N2 reactions, indicating transition states **7**, where only little positive charge is developed at the benzhydryl center.



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Because of the small dependence of the second-order rate constants on the nature of the substituents, the poor correlations in Figure 3 are not surprising, particularly because substituent effects in diarylmethyl compounds have been reported not to be additive.[23] The poor correlation in Figure 3 is also in line

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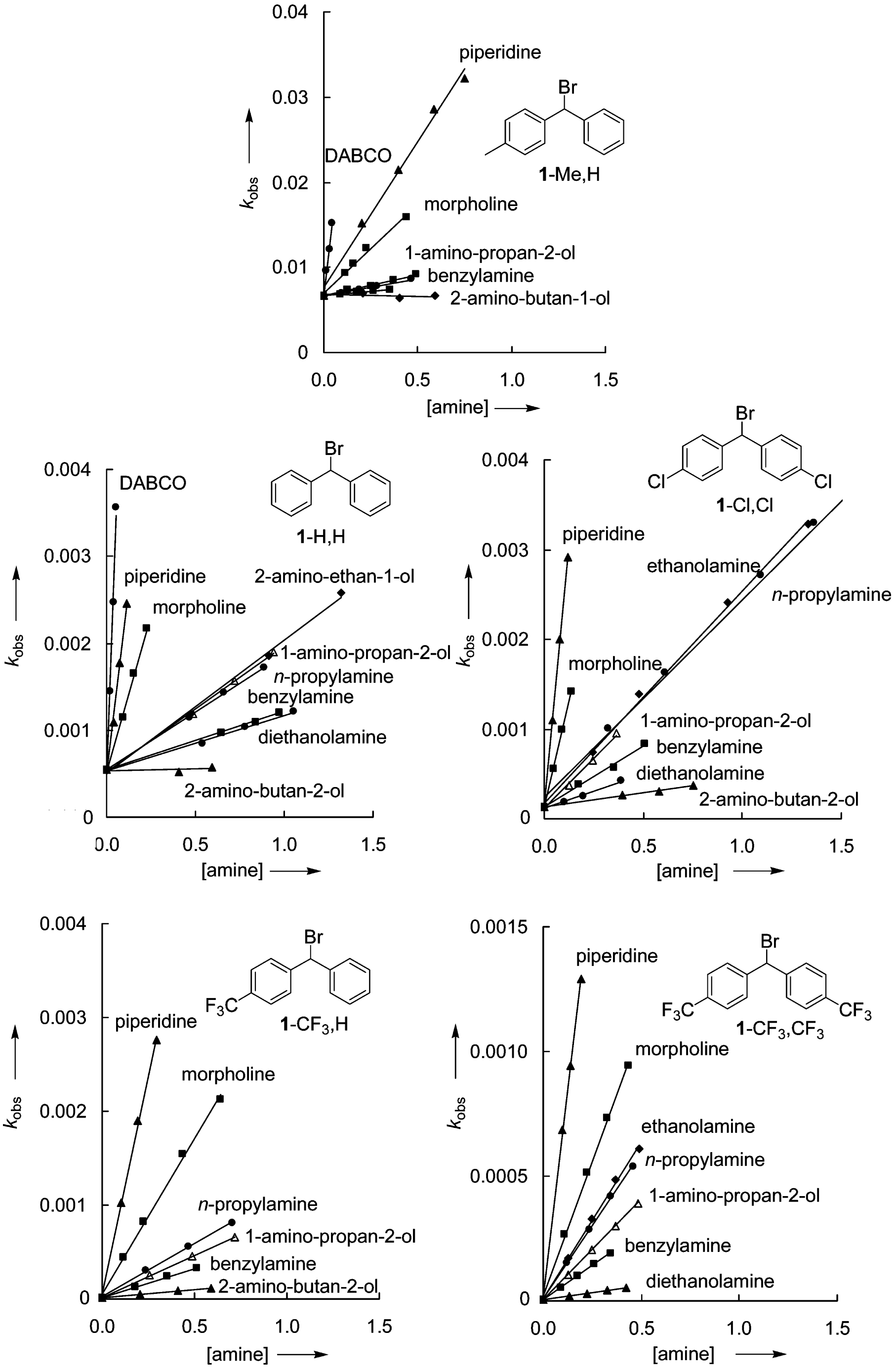

Figure 2. Plots of k_{obs} (s^{-1}) of the reactions of different benzhydryl bromides with amines in DMSO vs the concentrations of the amines (mol L^{-1}) (note the different calibration of the various *y*-axes).

with previous findings by Baker,[24] Jencks,[25] and Bordwell[26] that nucleophilic substitutions at substituted benzyl halides do not follow simple Hammett correlations.

On the other hand, the S_N2 reactions of substituted arylethyl bromides show a continuous increase of the ρ value as the electron-donating ability of the substituents is increased, indicating a continuous change of the transition state from very tight for acceptor-substituted systems to loose transition states with more positive charge on the benzylic carbon for the S_N2 reactions of the *p*-methoxy-substituted systems.[12]

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Table 1. Rate Constants (at 20° C) for the Solvolysis Reactions of the Benzhydryl Bromides **1**-X,Y in DMSO (s^{-1}) and for Their Reactions with Amines in DMSO ($M^{-1}\ s^{-1}$)

nucleophiles	**1**-Me,H	**1**-H,H	**1**-Cl,Cl	**1**-CF_3,H	**1**-CF_3,CF_3
DMSO (k_1)	6.71×10^{-3}	5.45×10^{-4}	1.36×10^{-4}	1.25×10^{-5}	2.76×10^{-6}
DABCO (k_2)	1.92×10^{-1}	5.45×10^{-2}	*a*	*a*	*a*
piperidine (k_2)	3.57×10^{-2}	1.69×10^{-2}	2.33×10^{-2}	9.36×10^{-3}	6.66×10^{-3}
morpholine (k_2)	2.16×10^{-2}	7.30×10^{-3}	9.51×10^{-3}	3.29×10^{-3}	2.17×10^{-3}
ethanolamine (k_2)	*a*	1.54×10^{-3}	2.37×10^{-3}	1.13×10^{-3}	1.25×10^{-3}
1-aminopropan-2-ol (k_2)	4.93×10^{-3}	1.45×10^{-3}	2.23×10^{-3}	8.92×10^{-4}	7.96×10^{-4}
n-$PrNH_2$ (k_2)	3.98×10^{-3}	1.33×10^{-3}	2.19×10^{-3}	1.13×10^{-3}	1.17×10^{-3}
benzylamine (k_2)	1.90×10^{-3}	6.76×10^{-4}	1.35×10^{-3}	6.30×10^{-4}	5.50×10^{-4}
diethanolamine (k_2)	*a*	6.37×10^{-4}	7.46×10^{-4}	2.55×10^{-4}	1.19×10^{-4}
2-aminobutan-1-ol (k_2)	*b*	*b*	3.13×10^{-4}	1.77×10^{-4}	*a*

[a] Not determined. [b] The k_{obs} was independent of the amine concentration (see Figure 2).

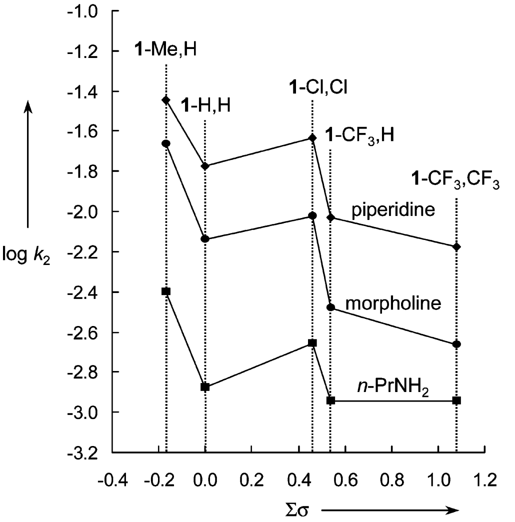

Figure 3. Plot of log k_2 of the reactions of the benzhydryl bromides with amines vs Hammett's substituent constants σ (from ref 27).

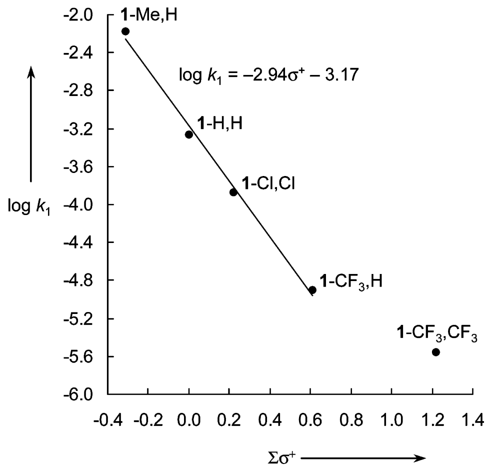

Figure 4. Plot of log k_1 for the solvolysis reactions of the benzhydryl bromides in DMSO vs Hammett's substituent constants σ^+ (σ^+ from ref 27; k_1 for **1**-CF_3,CF_3 not used for the correlation; see text).

Table 2. Products of the Reactions of the Benzhydryl Bromides **1**-X,Y ($c = 0.02$ mol L^{-1}) with Amines (10 equiv) in DMSO (20 °C)

1-X,Y	amine	[**5**-X,Y]/%	[**6**-X,Y]/%	[**4**-X,Y]/%	[**4**-X,Y]/([**5**-X,Y] + [**6**-X,Y])
1-CF_3,CF_3	piperidine	0	0	only	
	morpholine	0	0	only	
	propylamine	0	0	only	
1-H,CF_3	piperidine	0	0	only	
	morpholine	0	0	only	
	propylamine	0	0	only	
1-Cl,Cl	piperidine	1.5	0.6	77.0	36.7
	morpholine	2.6	2.0	50.5	11.0
	propylamine	alcohol cannot be separated from amine by GC			
1-H,H	piperidine	7.5	0.6	70.0	8.6
	morpholine	16.1	2.7	70.0	3.7
	propylamine	26.7	16.6	48.4	1.1
1-Me,H	piperidine		35.4[a]	41.8	1.2
	morpholine		49.8[a]	27.1	0.5
	propylamine		80.5[a]	14.6	0.2

[a] As the ketone **5**-Me,H and the alcohol **6**-Me,H could not be separated on the GC (see text), the yield refers to the sum of both compounds.

In contrast to the behavior of the second-order rate constants in Figure 3, the first-order rate constants k_1 (first line of Table 1) strongly depend on the para-substituents. From the plot of log k_1 versus $\Sigma\sigma^+$, one derives a Hammett reaction constant of $\rho = -2.94$ (Figure 4).

The magnitude of the reaction constant ρ suggests that the amine-independent term k_1 corresponds to the ionization step of an S_N1 reaction and not to an S_N2-type attack of DMSO at the benzhydryl bromides. The bis-trifluoromethyl-substituted compound **1**-CF_3,CF_3 deviates from this correlation, however, and reacts approximately 40 times faster than extrapolated from the linear log k_1 versus σ^+ correlation; we will discuss later that this deviation may be due to an S_N2-type reaction of **1**-CF_3,CF_3 with DMSO.

The 4,4′-dimethyl-substituted benzhydryl bromide **1**-Me,Me reacted so fast that analogous experiments, as described in Figure 2, could not be performed. From the Hammett correlation given in Figure 4, one can extrapolate a first-order solvolysis rate constant of 0.045 s^{-1} for the 4,4′-dimethyl-substituted benzhydryl bromide (**1**-Me,Me).

Reaction Products. As summarized in Table 2, the reactions of benzhydryl bromides **1**-X,Y with 0.2 M amines in DMSO give the benzhydryl amines **4**-X,Y, accompanied by the benzophenones **5**-X,Y and the diarylmethanols **6**-X,Y.

The exclusive formation of the benzhydryl amines **4**-X,Y in the reaction of **1**-CF_3,CF_3 and **1**-CF_3,H with morpholine, piperidine, and *n*-propylamine is in line with the kinetics

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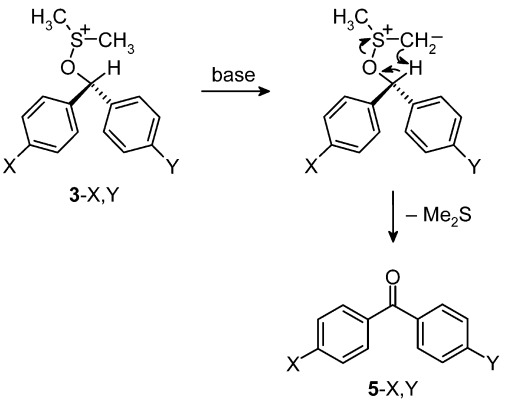
(24) Hammett plots of the second-order rate constants of the reactions of substituted benzyl bromides with pyridine (20 °C, in acetone) are shown in the Supporting Information: (a) Baker, J. W. *J. Chem. Soc.* **1936**, 1448–1451. (b) Baker, J. W. *Trans. Faraday Soc.* **1941**, *37*, 632–644.

(25) Young, P. R.; Jencks, W. P. *J. Am. Chem. Soc.* **1979**, *101*, 3288–3294.

(26) (a) Bordwell, F. G.; Hughes, D. L. *J. Org. Chem.* **1980**, *45*, 3320–3325. (b) Bordwell, F. G.; Hughes, D. L. *J. Am. Chem. Soc.* **1986**, *108*, 7300–7309.

(27) Hansch, C.; Leo, A.; Taft, R. W. *Chem. Rev.* **1991**, *91*, 165–195.

Scheme 2



described in Figure 2: The amine-independent terms are negligible in comparison to the amine-dependent terms. Therefore, at amine concentrations of 0.2 M, S_N2 reactions with amines take place exclusively.

Analogously, the predominant formation of amine **4**-Cl,Cl by reaction of **1**-Cl,Cl with piperidine can be explained by the high S_N2 reactivity of the amine at a concentration of 0.2 M. In the reactions with the less nucleophilic morpholine, the amounts of benzhydrol **6**-Cl,Cl and benzophenone **5**-Cl,Cl rise. Unfortunately, it was not possible to measure the product ratio obtained by the reaction of **1**-Cl,Cl with *n*-propylamine because the GC signals of the benzhydrol and the amine overlapped.

In the reactions of **1**-H,H with these amines, considerable amounts of benzophenone **5**-H,H and benzhydrol **6**-H,H were generated along with the benzhydryl amines **4**-H,H, and their quantities increase with decreasing nucleophilicities of the amines.

In the reaction of the monomethyl-substituted benzhydryl bromide **1**-Me,H, an even larger amount of diarylmethanol **6**-Me,H and benzophenone **5**-Me,H was found, while less of the benzhydryl amine **4**-Me,H was formed. As with the other substrates, the yield of the amine **4**-Me,H decreased in the series piperidine > morpholine > propylamine. While it was not possible to distinguish between diarylmethanol **6**-Me,H and benzophenone **5**-Me,H by our GC analysis because both compounds had the same retention times, the GC−MS spectra showed that benzophenones **5**-Me,H are the major products. Because the relative molar response (RMR) constant was nearly the same for the benzophenone **5**-Me,H and the benzhydrol **6**-Me,H (experiment with pure compounds), their sum could be determined.

As illustrated in Scheme 1, the benzophenones **5**-X,Y as well as the benzhydrols **6**-X,Y are formed through the intermediacy of the oxysulfonium ions **3**-X,Y. In accordance with previous reports on the mechanism of the Kornblum oxidation,[28] we assume that deprotonation of the oxysulfonium ion **3**-X,Y at a methyl group yields a sulfur ylide, which undergoes a proton shift and cleavage of the O−S bond to yield the benzophenone **5**-X,Y (Scheme 2). In line with this mechanism, benzhydrol **6**-H,H was not oxidized when treated with equimolar amounts of 2,6-lutidine and 2,6-lutidine hydrobromide under the conditions of the solvolysis reactions. The formation of oxysulfonium ions from alkyl halides[22] and their subsequent reactions with bases has been studied NMR spectroscopically by other groups.[29,30]

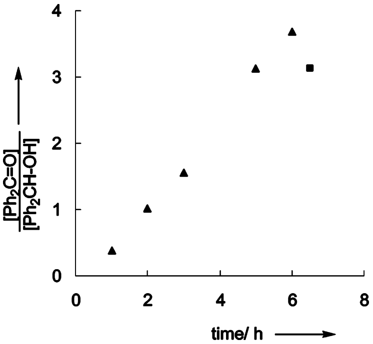


Figure 5. Plot of the ratios of $[Ph_2C{=}O]/[Ph_2CH{-}OH]$ vs time for the reaction of benzhydryl bromide **1**-H,H with 0.2 M 2,6-lutidine in DMSO after aqueous workup. Square indicates the workup with methanol (ratio equals $[Ph_2C{=}O]/([Ph_2CH{-}OH] + [Ph_2CH{-}OMe])$).

Benzhydrol **6**-H,H and benzophenone **5**-H,H were formed exclusively when benzhydryl bromide **1**-H,H (0.02 M) was dissolved in a 0.2 M solution of the weakly nucleophilic 2,6-lutidine in DMSO. Figure 5 illustrates that the ratio [**5**-H,H]/[**6**-H,H] obtained after aqueous workup of the solvolysis products from **1**-H,H increases with reaction time. From the observation that the increase of this ratio continues after complete consumption of **1**-H,H, one can derive that a precursor of **5**-H,H (e.g., the oxysulfonium ion **3**-H,H) accumulates in the reaction mixture before it is slowly converted into benzophenone **5**-H,H.

When the mixture obtained from **1**-H,H (0.02 M) and 0.2 M 2,6-lutidine in DMSO was worked up with methanol, the benzophenone **5**-H,H was accompanied by benzhydryl methyl ether, which may be formed by nucleophilic attack of methanol at the oxysulfonium ion **3**. Nucleophilic attack of impurities of water, amine, or methanol at the sulfur atom of **3**-H,H may account for the small amount of benzhydrol **6**-H,H (6.7%) obtained under these conditions. The ratio $[Ph_2C{=}O]/([Ph_2CH{-}OH] + [Ph_2CH{-}OMe])$ was similar to the ratio $[Ph_2C{=}O]/[[Ph_2CH{-}OH]$ observed after aqueous workup at comparable reaction times (□ in Figure 5).

Differentiation of S_N1 and S_N2 Processes. For each of the products (**4**−**6**)-X,Y drawn in Scheme 1, formation through an S_N1 (k_1) or S_N2 (k_2 and k_1') process has to be considered. With the data presented so far, it is possible to eliminate some of these reaction pathways. If the benzhydryl amines **4**-X,Y would be formed by an S_N1 reaction via the carbenium ions **2**-X,Y, which are subsequently trapped by the amines, an amine-independent rate law would result because the formation of the benzhydryl cations **2**-X,Y would be rate-determining. Pathway k_N of Scheme 1 can, therefore, be eliminated. This conclusion is confirmed by the comparison of the kinetic data with the product ratios in Table 3. For the reactions of different benzhydryl bromides **1**-X,Y with piperidine, morpholine, and propylamine, the product ratios [**4**]/([**5**] + [**6**]) divided by the concentrations of the amines, [**4**]/([amine]([**5**] + [**6**])), are almost equal to the ratios k_2/k_1.

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(28) (a) Kornblum, N.; Jones, W. J.; Anderson, G. J. *J. Am. Chem. Soc.* **1959**, *81*, 4113–4114. (b) Kornblum, N.; Powers, J. W.; Anderson, G. J.; Jones, W. J.; Larson, H. O.; Levand, O.; Weaver, W. M. *J. Am. Chem. Soc.* **1957**, *79*, 6562–6562. (c) Dave, P.; Byun, H.-S.; Engel, R. *Synth. Commun.* **1986**, *16*, 1343–1346.

(29) (a) Torssell, K. *Tetrahedron Lett.* **1966**, *7*, 4445–4451. (b) Torssell, K. *Acta Chem. Scand.* **1967**, *21*, 1–14.

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Table 3. Comparison of Rate Constant Ratios with the Product Ratios for the Reactions of Benzhydryl Bromides **1**-X,Y with 0.2 M Piperidine, Morpholine, and Propylamine in DMSO at 20 °C

	1-Me,H	**1**-H,H	**1**-Cl,Cl	**1**-CF_3,H
k_1/s^{-1}	6.71×10^{-3}	5.45×10^{-4}	1.36×10^{-4}	1.25×10^{-5}
reaction with piperidine (0.2 M)				
$k_2/M^{-1}\ s^{-1}$	3.57×10^{-2}	1.69×10^{-2}	2.33×10^{-2}	9.36×10^{-3}
k_2/k_1	5.3	31	1.7×10^2	7.5×10^2
[**4**]/0.2([**5**] + [**6**])	5.9	43	1.8×10^2	only amine **4**
reaction with morpholine (0.2 M)				
$k_2/M^{-1}\ s^{-1}$	2.16×10^{-2}	7.30×10^{-3}	9.51×10^{-3}	3.29×10^{-3}
k_2/k_1	3.2	13	70	2.6×10^2
[**4**]/0.2([**5**] + [**6**])	2.7	19	55	only amine **4**
reaction with *n*-propylamine (0.2 M)				
$k_2/M^{-1}\ s^{-1}$	3.98×10^{-3}	1.33×10^{-3}	2.19×10^{-3}	1.13×10^{-3}
k_2/k_1	0.59	2.4	16	90
[**4**]/0.2([**5**] + [**6**])	0.91	5.6	–	only amine **4**

Table 4. Comparison of the Rate Constants and Product Ratios for the Reaction of Benzhydryl Bromide **1**-Cl,Cl (0.02 M) with Morpholine (0.2 M) at Different Temperatures in DMSO

T/°C	20	35	50
k_1/s^{-1}	1.36×10^{-4}	3.85×10^{-4}	1.45×10^{-3}
$k_2/M^{-1}\ s^{-1}$	9.51×10^{-3}	2.10×10^{-2}	4.20×10^{-2}
[**4**-Cl,Cl]/M	1.01×10^{-2}	1.07×10^{-2}	8.52×10^{-3}
[**5**-Cl,Cl]/M	5.26×10^{-4}	1.27×10^{-3}	1.83×10^{-3}
[**6**-Cl,Cl]/M	3.95×10^{-4}	2.26×10^{-4}	2.33×10^{-4}
[**4**]/0.2([**5**]+[**6**])	55	36	21
k_2/k_1	70	55	29

If the amines **4**-X,Y would be formed via the pathway k_N in addition to the S_N2 pathway k_2, a higher percentage of the amines [**4**-X,Y] would be expected. We will demonstrate later that the trapping of the benzhydrylium ions **2**-X,Y by the solvent DMSO is so fast that the pathway k_N cannot compete with k_{solv} at amine concentrations of 0.2 M.

Formal kinetics do not allow differentiation between pathways k_1 and k_1' for the formation of **5**-X,Y and **6**-X,Y; that is, the oxysulfonium ion **3**-X,Y may be formed via either an S_N1 (k_1) or an S_N2 process (k_1') with the solvent DMSO. The linear Hammett plot for log k_1 (i.e., k_{obs} in pure DMSO) with a slope of −2.94 (Figure 4) indicates the operation of the S_N1 pathway for most systems. If the S_N2 pathway indicated by k_1' would be operating, a similar reactivity pattern as shown in Figure 3 would be expected for the different benzhydryl bromides. The significant deviation of **1**-CF_3,CF_3 from the linear Hammett correlation in Figure 4 may be indicative of an S_N2 participation in the reaction of this acceptor-substituted benzhydryl bromide with DMSO (k_1', nucleophilic solvent participation). Further support for this interpretation will be given below.

Temperature Effect on Rate Constants and Product Ratios. When the kinetics of the reaction of **1**-Cl,Cl with morpholine in DMSO were studied at variable temperature and evaluated as described above, the rate constants summarized in Table 4 were obtained. Raising the temperature from 20 to 50 °C increased the first-order rate constant k_1 by a factor of 11, while the second-order rate constant k_2 increased only by a factor of 4. In accordance with the previous discussion, the stronger increase of k_1 compared with k_2 resulted in a decrease of the yield of the amine **4**-X,Y (Table 4). The ratios of the products [**4**]/([amine]([**5**] + [**6**])) and the ratios of the rate constants k_2/k_1 again agreed within experimental error (Table 4), indicating that also, at elevated temperatures, amines **4** are produced through the S_N2 pathway (k_2) while **5** and **6** are formed via the S_N1 route (k_1).

Table 5. Eyring and Arrhenius Activation Parameters for the Reaction of the Benzhydryl Bromide **1**-Cl,Cl with Morpholine in DMSO

	for k_1	for k_2
$\Delta H^‡$/kJ mol^{-1}	59.4 ± 6.1	36.5 ± 0.6
$\Delta S^‡$/J mol^{-1} K^{-1}	-116.7 ± 19.8	-159.0 ± 1.8
E_a/kJ mol^{-1}	62.0 ± 6.1	39.0 ± 0.5
ln *A*	16.4 ± 2.4	11.4 ± 0.2

Table 6. Second-Order Rate Constants for the Reactions of Amino-Substituted Benzhydrylium Ions with Amines in DMSO at 20 °C

amine	*N*/*s*	Ar_2CH^+	$k_N/M^{-1}\ s^{-1}$
2-aminobutan-1-ol	14.39/0.67	$(ind)_2CH^+$	6.08×10^3
		$(jul)_2CH^+$	2.23×10^3
		$(lil)_2CH^+$	8.33×10^2
benzylamine	15.28/0.65	$(thq)_2CH^+$	3.91×10^4
		$(jul)_2CH^+$	6.60×10^3
		$(lil)_2CH^+$	2.51×10^3
1-aminopropan-2-ol	15.47/0.65	$(ind)_2CH^+$	2.27×10^4
		$(jul)_2CH^+$	9.31×10^3
		$(lil)_2CH^+$	3.29×10^3
diethanolamine	15.51/0.70	$(ind)_2CH^+$	4.83×10^4
		$(jul)_2CH^+$	1.74×10^4
		$(lil)_2CH^+$	6.19×10^3
ethanolamine	16.07/0.61	$(ind)_2CH^+$	2.87×10^4
		$(jul)_2CH^+$	1.19×10^4
		$(lil)_2CH^+$	4.71×10^3

Eyring and Arrhenius plots of high quality ($r^2 = 0.9998$, Supporting Information) were obtained for the second-order rate constants k_2, from which the activation parameters listed in Table 5 were obtained. The highly negative activation entropy (−159 J mol^{-1} K^{-1}) is in agreement with previous reports on alkylations of amines.[31]

Because of the small contribution of the first-order term k_1 to the overall rate constant, the rate constants k_1 are less precise, and the resulting Eyring and Arrhenius plots are of lower quality ($r^2 = 0.990$). The calculated activation entropy (−117 J mol^{-1} K^{-1}) is slightly more negative than typically observed for S_N1 reactions in alcoholic and aqueous solutions.[32]

Nucleophilicity Parameters *N* and *s* for Amines in DMSO. While *N* and *s* parameters for numerous amines have previously been determined in aqueous[33] and in methanolic solution,[34] only few amines have so far been characterized in DMSO.[35] Because amine nucleophilicities in DMSO will be needed for the mechanistic analysis below, we have now determined *N* and *s* values for the amines which were used in this investigation in DMSO. For that purpose, we have measured the rates of reactions of amino-substituted benzhydrylium ions with amines in DMSO (eqs 6 and 7) under pseudo-first-order conditions (excess of amine) using the photometric method described previously.[18−20] Comparison of the rate constants listed in Table 6 with those reported in water[33] shows that the amines react roughly 100 times faster

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[31] (a) Arnett, E. M.; Reich, R. *J. Am. Chem. Soc.* **1980**, *102*, 5892–5902. (b) Duty, R. C.; Gurne, R. L. *J. Org. Chem.* **1970**, *35*, 1800–1802.

[32] (a) Cowie, G. R.; Fitches, H. J. M.; Kohnstam, G. *J. Chem. Soc.* **1963**, 1585–1593. (b) Fox, J. R.; Kohnstam, G. *J. Chem. Soc.* **1963**, 1593–1598.

[33] Brotzel, F.; Chu, Y. C.; Mayr, H. *J. Org. Chem.* **2007**, *72*, 3679–3688.

[34] Phan, T. B.; Breugst, M.; Mayr, H. *Angew. Chem.* **2006**, *118*, 3954−3959; *Angew. Chem., Int. Ed.* **2006**, *45*, 3869−3874.

[35] Minegishi, S.; Mayr, H. *J. Am. Chem. Soc.* **2003**, *125*, 286–295.

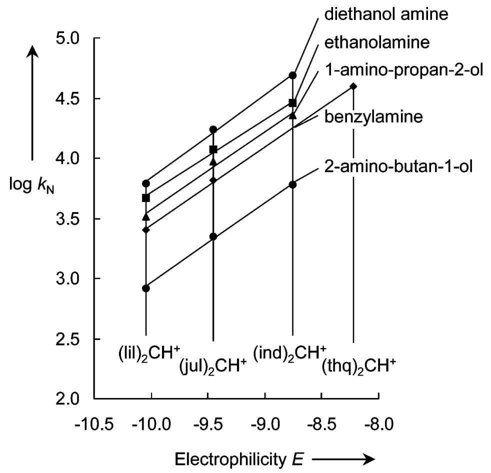
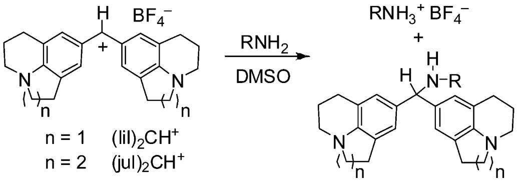
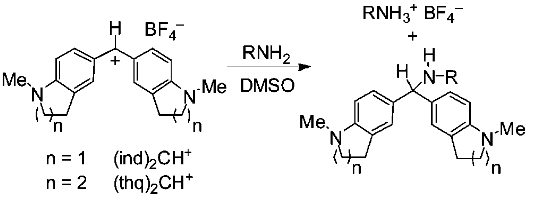


Figure 6. Plot of the rate constants k_N for the reactions of amines with benzhydrylium ions (DMSO, 20 °C) vs their electrophilicity parameters E ($E = -10.04$ for $(lil)_2CH^+$, -9.45 for $(jul)_2CH^+$, -8.76 for $(ind)_2CH^+$, and -8.22 for $(thq)_2CH^+$; from ref 18).

in DMSO than in water due to the weaker solvation in the nonprotic solvent.



(6)



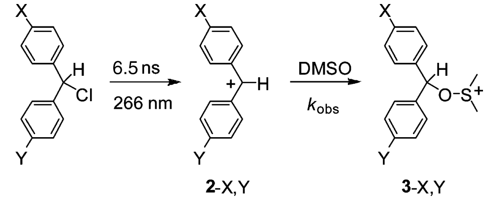
(7)

Plots (Figure 6) of the second-order rate constants given in Table 6 versus the electrophilicity parameters E of the benzhydrylium ions were linear as required by eq 2, and yielded the N and s parameters for amines in DMSO which are given in Table 6.

Solvent Nucleophilicity of DMSO. Dimethyl sulfoxide may react with electrophiles either at sulfur or at oxygen.[36] The formation of benzophenones and benzhydrols reported above indicates that the benzhydrylium ions employed in this work react at oxygen to yield the oxysulfonium ions **3** (Scheme 3).

The rates of these reactions were determined by laser-flash photolysis of solutions of benzhydryl chlorides in MeCN/DMSO mixtures and UV−vis spectrometric monitoring of the decay of the resulting benzhydrylium ions in the presence of variable concentrations of DMSO. Plots of the observed rate constants versus the concentrations of DMSO (Figure 7) give rise to the second-order rate constants of the reactions (Table 7).

Scheme 3. Laser Flash Photolytic Generation of Benzhydrylium Ions in MeCN/DMSO Mixtures



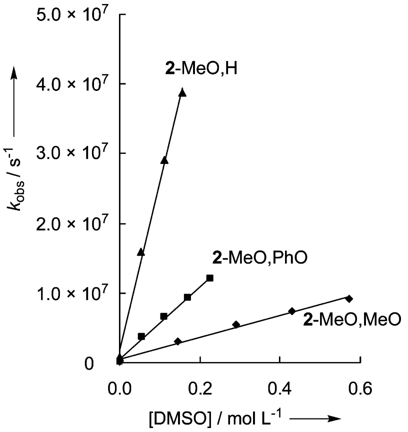


Figure 7. Plot of k_{obs} of the reactions of the benzhydrylium ions **2**-X,Y with DMSO in MeCN vs [DMSO].

Table 7. Second-Order Rate Constants for the Reactions of Benzhydrylium Ions (**2**-X,Y) with DMSO (O-Attack) in Acetonitrile

2-X,Y	E^a	k_2/M^{-1} s^{-1}
2-MeO,MeO	0.00	1.69×10^7
2-MeO,PhO	0.61	5.00×10^7
2-MeO,H	2.11	6.13×10^8
2-PhO,Me	2.16	7.04×10^8
2-PhO,H	2.90	8.60×10^8
2-Me,Me	3.63	2.63×10^9
2-Me,H	4.59	3.50×10^9
2-F,H	5.60	4.78×10^9
2-H,H	5.90	3.34×10^9
2-Cl,Cl	6.02	4.79×10^9

[a] Empirical electrophilicity parameter from ref 18.

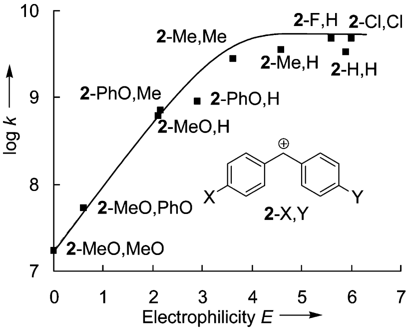


Figure 8. Plot of log k (second-order rate constants, M^{-1} s^{-1}) for the reactions of DMSO with the benzhydrylium ions **2**-X,Y in MeCN at 20 °C vs their electrophilicity parameters E.

Figure 8 shows that the rate constants (Table 7) for the reactions of DMSO with benzhydrylium ions increase with the electrophilicity parameters of the benzhydrylium ions and become diffusion-controlled at $E > 4$. For that reason, all benzhydrylium ions **2**-X,Y generated in DMSO from benzhydryl bromides **1**-X,Y of Table 1 are immediately trapped by the solvent DMSO. It can thus be explained that trapping of **2**-X,Y by amines (k_N, Scheme 1) does not occur despite the higher

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(36) (a) Ho, T.-L. *Hard and Soft Acids and Bases Principle in Organic Chemistry*; Academic Press: New York, 1977. (b) Smith, S. G.; Winstein, S. *Tetrahedron* **1958**, *3*, 317–318. (c) Rasul, G.; Prakash, G. K. S.; Olah, G. A. *J. Org. Chem.* **2000**, *65*, 8786–8789. (d) da Silva, R. R.; Santos, J. M.; Ramalho, T. C.; Figueroa-Villar, J. D. *J. Braz. Chem. Soc.* **2006**, *17*, 223–226.

Table 8. Calculated Lifetimes τ (1/*k*, s) of Benzhydrylium Ions in DMSO and in 1 M Solutions of Various Amines in DMSO

nucleophiles (*N*/*s*)	**2**-Me,H ($E = 4.59$)	**2**-H,H ($E = 5.90$)	**2**-Cl,Cl ($E = 6.02$)	**2**-CF_3,H ($E \sim 9.7$)[a]	**2**-CF_3,CF_3 ($E \sim 13.6$)[a]
DMSO ($N_1 = 11.3/0.74$)[b]	2×10^{-12}	2×10^{-13}	2×10^{-13}	3×10^{-16}	4×10^{-19}
2-aminobutan-1-ol (14.39/0.67)[c]	2×10^{-13}	3×10^{-14}	2×10^{-14}	7×10^{-17}	2×10^{-19}
benzylamine (15.28/0.65)[c]	1×10^{-13}	2×10^{-14}	1×10^{-14}	6×10^{-17}	2×10^{-19}
1-aminopropan-2-ol (15.46/0.65)[c]	9×10^{-14}	1×10^{-14}	1×10^{-14}	4×10^{-17}	1×10^{-19}
diethanolamine (15.51/0.70)[c]	9×10^{-15}	1×10^{-15}	8×10^{-16}	2×10^{-18}	4×10^{-21}
n-propylamine (15.70/0.64)[d]	1×10^{-13}	1×10^{-14}	1×10^{-14}	6×10^{-17}	2×10^{-19}
ethanolamine (16.07/0.61)[c]	2×10^{-13}	4×10^{-14}	3×10^{-14}	2×10^{-16}	8×10^{-19}
morpholine (16.96/0.67)[d]	4×10^{-15}	5×10^{-16}	4×10^{-16}	1×10^{-18}	3×10^{-21}
piperidine (17.19/0.71)[d]	3×10^{-16}	4×10^{-17}	3×10^{-17}	8×10^{-20}	1×10^{-22}
DABCO (18.80/0.70)[e]	4×10^{-17}	5×10^{-18}	4×10^{-18}	1×10^{-20}	2×10^{-23}

[a] Extrapolated from σ constants (from ref 27) using the correlation $\sigma^+ = 0.134E - 0.767$ reported in ref 18b. [b] N_1 for the calculation of first-order rate constants with DMSO in DMSO (see text). [c] From Table 6. [d] *N* and *s* parameters were taken from ref 35. [e] *N* and *s* parameters in acetonitrile from ref 40.

nucleophilicity of the amines. From the linear left part of Figure 8 ($k_2 < 8 \times 10^8$ M^{-1} s^{-1}), one can derive the nucleophilicity parameters $N = 9.75$ and $s = 0.742$ for the O-reactivity of DMSO, showing that DMSO is considerably more nucleophilic than water and ordinary alcohols.[37,38] With the assumption that the change of solvent polarity in MeCN/DMSO mixtures of different compositions does not affect the rate constants significantly, one can multiply the rate constants in Table 7 with 14.1 mol L^{-1}, that is, the concentration of DMSO in 100% DMSO to obtain the first-order rate constants of the decay in 100% DMSO. From the plot of the first-order rate constants versus *E*, one derives the solvent nucleophilicity $N_1 = 11.3$ for DMSO ($N_1 = N + (\log 14.1)/s$).[39]

Calculation of Hypothetical Lifetimes of Benzhydrylium Ions in DMSO Solution in the Presence of Amines. The *N* and *s* parameters of the amines (Table 6 and refs 33, 35, and 40) and N_1 of DMSO (Figure 8) can now be combined with the electrophilicity parameters *E* of the benzhydrylium ions to calculate rate constants for the reactions of benzhydrylium ions with these nucleophiles by eq 2. Many of the resulting rate constants exceed the diffusion limit. In these cases, the values 1/*k* (s), which are listed in Table 8, have to be considered as hypothetical lifetimes.

The upper diagram of Figure 2 shows that, at a concentration of [morpholine] = 0.3 M, the observed pseudo-first-order rate constant is two times the magnitude of the intercept ($k_{obs} \approx 2k_1$); that is, at this concentration, the reaction of the methyl-substituted benzhydrylium bromide (**1**-Me,H) with morpholine follows the S_N1 and the S_N2 mechanisms to equal extent. The calculated lifetime of 4×10^{-15} s for the reaction of the benzhydrylium ion **2**-Me,H with morpholine (Table 8) is shorter than a bond vibration ($\approx 10^{-13}$ s). According to Jencks and Richard, this relationship implies that the S_N2 mechanism will be enforced; that is, the benzhydrylium ion **2**-Me,H cannot exist in an encounter complex with morpholine. From the relationship $k_2 \approx 3k_1$ (Table 1), one can derive that nucleophilic assistance for breaking the C−Br bond (→S_N2) is very weak and ionization (k_1) may also occur in the absence of a morpholine molecule. Only at morpholine concentrations > 0.3 M will the S_N2 process override the S_N1 process. If ionization occurs in the absence of a morpholine molecule (S_N1), the intermediate *p*-methyl-substituted benzhydrylium ion (**2**-Me,H) is rapidly trapped by the solvent DMSO (lifetime $\approx 2 \times 10^{-12}$ s), and the diffusion-controlled reaction with morpholine cannot compete.

Piperidine ($k_2 \approx 5k_1$) and DABCO ($k_2 \approx 28k_1$) are stronger nucleophiles and, therefore, provide a stronger nucleophilic assistance for breaking the C−Br bond of **1**-Me,H. As shown in Figure 2, now the S_N2 process overrides the S_N1 process already at low amine concentrations, and the calculated lifetimes of 3×10^{-16} and 4×10^{-17} s are in line with Jencks' enforced concerted mechanism. Lifetimes $\tau > 10^{-14}$ s are calculated for the *p*-methylbenzhydrylium ion **2**-Me,H in 1 M solutions of the other amines, and Figure 2 shows that, in the reactions with benzylamine, 1-aminopropan-2-ol, and *n*-propylamine, the S_N1 mechanism generally dominates.

For the unsubstituted benzhydrylium ion **2**-H,H, 9-times shorter lifetimes are calculated; as a consequence, the S_N2 reactions gain more weight. Morpholine ($k_2 = 13k_1$), piperidine ($k_2 = 31k_1$), and DABCO ($k_2 = 100k_1$) prefer the S_N2 mechanism already at low amine concentrations (> 0.08−0.01 M), in accord with calculated lifetimes of $\tau < 10^{-15}$ s. No S_N2 contribution was found for the reaction of **1**-H,H with 2-aminobutan-1-ol ($\tau = 3 \times 10^{-14}$ s). For the reactions of **1**-H,H with diethanolamine ($\tau = 1 \times 10^{-15}$ s), ethanolamine ($\tau = 4 \times 10^{-14}$ s), benzylamine ($\tau = 2 \times 10^{-14}$ s), 1-aminopropan-2-ol ($\tau = 1 \times 10^{-14}$ s), and *n*-propylamine ($\tau = 1 \times 10^{-14}$ s), lifetimes similar to the vibrational limit are calculated, and the S_N2 reactions overrated the S_N1 process only at high amine concentrations.

Despite calculated lifetimes for the dichloro-substituted benzhydrylium ion **2**-Cl,Cl which closely resemble those of the parent compound **2**-H,H, Figure 2 shows that almost all amines prefer the S_N2 process at concentrations > 0.2 M. Only 2-aminobutan-1-ol ($\tau = 2 \times 10^{-14}$ s) allows the S_N1 mechanism to dominate at amine concentrations < 0.4 M.

In agreement with calculated lifetimes $\tau < 2 \times 10^{-16}$ s, all reactions of amines with the CF_3-substituted benzhydryl bromides **1**-CF_3, H and **1**-CF_3,CF_3 studied in this work preferentially follow the S_N2 process, and the intercepts of the correlations in Figure 2 are negligible compared with the pseudo-first-order rate constants k_{obs} in the presence of amines. The very short lifetimes estimated for **2**-CF_3,H and **2**-CF_3,CF_3 in DMSO suggest that the first-order rate constants for the solvolyses of **1**-CF_3,H and **1**-CF_3,CF_3 in DMSO may not be due to S_N1 reactions with formation of the carbocations **2**-CF_3,H and **2**-CF_3,CF_3 because

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(37) McClelland, R.; Kanagasabapathy, V. M.; Banait, N. S.; Steenken, S. *J. Am. Chem. Soc.* **1989**, *111*, 3966–3972.

(38) Minegishi, S.; Kobayashi, S.; Mayr, H. *J. Am. Chem. Soc.* **2004**, *126*, 5174–5181.

(39) Measurements of the nucleophilic reactivity of DMSO in neat DMSO are not possible with our equipment because the laser radiation at 266 nm, which is needed for the photoionization of the benzhydryl chlorides, is absorbed by DMSO.

(40) Baidya, M.; Kobayashi, S.; Brotzel, F.; Schmidhammer, U.; Riedle, E.; Mayr, H. *Angew. Chem.* **2007**, *119*, 6288−6292; *Angew. Chem., Int. Ed.* **2007**, *46*, 6176−6179.

the direct nucleophilic attack of DMSO at these benzhydryl bromides should be enforced. The positive deviation of **1**-CF_3,CF_3 from the correlation of log k_1 versus $\Sigma\sigma^+$ in Figure 4 is in line with a significant nucleophilic solvent participation by DMSO (k_1', S_N2). The fact that the first-order rate constant for **1**-CF_3,H matches the correlation with σ^+ in Figure 4 implies that in this case nucleophilic solvent participation by DMSO cannot be large.

Conclusion

In their seminal 1984 paper,[16d] Richard and Jencks concluded that a reaction can proceed concurrently through stepwise, monomolecular and concerted, bimolecular reaction mechanisms when the intermediate has a long lifetime in the solvent, but no lifetime when it is in contact with an added nucleophilic agent. This situation has now been found when benzhydryl bromides **1**-X,Y were treated with amines in DMSO. In several cases, first-order rate constants k_1 (s^{-1}) for the formation of the carbocations are of similar magnitude as the second-order rate constants k_2 (L mol^{-1} s^{-1}) for the concerted S_N2 reactions of the benzhydryl bromides with amines. For that reason, carbocations with short lifetimes were generated when amine molecules were not present in the vicinity, while in the same solution, concerted S_N2 reactions were enforced when amine molecules were present. The relationship $k_2/k_1 = [Ar_2CHNRR']/([amine]([Ar_2C{=}O] + [Ar_2CHOH]))$ implies that the benzhydryl amines Ar_2CHNRR' are formed exclusively through the S_N2 process and not through trapping of the intermediate carbocations by amines. As calculated from the nucleophilicity parameters N_1 and s of DMSO, the intermediate benzhydrylium ions Ar_2CH^+ (**2**-X,Y), formed by the S_N1 process, are quantitatively trapped by DMSO to give the benzhydryloxysulfonium ions **3**-X,Y, the precursors of the benzhydryl alcohols **6**-X,Y and the benzophenones **5**-X,Y. Because the change from S_N1 to S_N2 mechanisms was observed when the lifetimes of the carbocations in the presence of amines (1 M) were calculated to be approximately 10^{-14} s by eq 2, the E, N, and s parameters proved to be suitable for predicting the preferred mechanism of the nucleophilic substitutions of benzhydryl bromides. So far, our analysis, based on Jencks' lifetime criterion, did not include the role of the leaving groups. One can expect, however, that the S_N1/S_N2 ratio for a certain substrate R-X will also depend on the leaving group and will increase with increasing nucleofugality of X. Systematic investigations of these effects are in progress.

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Supporting Information Available: Details of kinetic experiments and product studies. This material is available free of charge via the Internet at http://pubs.acs.org.

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