Registry No. **2**, 768-95-6; **3**, 77418-99-6; **4**, 768-93-4; **5**, 22635-62-7; **6**, 762-72-1; **7**, 6651-36-1; **8**, 22922-62-9; **9**, 41031-34-9; **10**, 13361-64-3; **11**, 74203-26-2; **12**, 36960-53-9; **13**, 16104-50-0; **14**, 22922-66-3; **15**, 5001-18-3; **16**, 70017-41-3; **17**, 770-70-7; **18**, 82112-68-3; **19**, 82112-69-4; **21**, 27011-47-8; **22**, 2094-72-6; **23**, 82094-36-8; **24**, 14579-08-9; **25**, 19752-23-9; **26**, 82094-37-9; **27**, 82094-38-0; **29**, 2170-06-1; **30**, 1578-33-2; **31**, 18245-28-8; **32**, 82094-39-1; **33**, 82094-40-4; **34**, 82094-41-5; **35**, 7450-03-5; **36**, 1459-55-8; **37**, 82094-42-6; **38**, 19980-43-9; **39**, 82094-43-7; **40**, 13735-81-4; **41**, 82094-44-8; **42**, 62889-07-0; **43**, 82094-45-9; **44**, 6651-34-9; **45**, 82094-46-0; **46**, 82094-47-1; **47**, 82094-48-2; **48**, 82094-49-3; **49**, 82094-50-6; **50**, 82094-51-7; **51**, 82094-52-8; **52**, 82094-53-9; **53**, 2094-74-8; **54**, 1660-04-4; **55**, 82094-54-0; **56**, 82094-55-1; **57**, 82094-56-2; **58**, 24053-96-1; **59**, 82094-57-3; **60**, 82094-58-4; **61**, 64741-22-6; **62**, 24886-73-5; silver triflate, 2923-28-6; 1-phenyl adamantane, 780-68-7; trimethylsilyl triflate, 27607-77-8; bis(trimethylsilyl)acetamide, 10416-58-7; 2-(1-adamantyl)vinyl bromide, 57040-44-5; trimethyl silyl chloride, 75-77-4; acetyl chloride, 75-36-5.

Thiol Acidities and Thiolate Ion Reactivities toward Butyl Chloride in Dimethyl Sulfoxide Solution. The Question of Curvature in Brønsted Plots

Frederick G. Bordwell* and David L. Hughes

Department of Chemistry, Northwestern University, Evanston, Illinois 60201

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Acidities of 15 benzenethiols and 5 aliphatic thiols have been measured in dimethyl sulfoxide solution. Homohydrogen bonding of the type $PhS^- \cdots HSPh$, which is strong for phenols in Me_2SO, is absent from thiophenols. On the other hand, evidence for strong intramolecular hydrogen bonding was found for the $2\text{-}HOC_6H_4S^-$ anion. A Brønsted plot for the rates of reaction of nine ArS^- ions with BuCl in Me_2SO vs. pK_a for ArSH was found to give an excellent correlation extending over 9 pK units ($\beta = 0.409 \pm 0.003$; $R^2 = 0.9998$). This is contrasted with a Hammett plot for ArSH acidities, which gave a poorer correlation ($R^2 = 0.988$) despite the selection of the five "best" points. A Brønsted plot for log k vs. pK_a for five RS^- ions reacting with BuCl gave a poor correlation over a 5-pK-unit range with a much smaller slope ($\beta = 0.19 \pm 0.03$; $R^2 = 0.91$). The strict linearity of Brønsted plots in Me_2SO solution when basicities are changed by remote substitution is contrasted with the apparent curvature of some Brønsted plots in hydroxylic solvents. It is concluded that the curvature in the latter instances may be an artifact caused by the necessity of using several different families of bases in order to construct the extended Brønsted plots and by the failure to control proximity effects. Attempts to displace a thianion or carbanion by S_N2 attack of a strongly basic anion on the benzyl carbon atom of $PhCH_2SPh$ or $9\text{-}PhCH_2\text{-}9\text{-}PhFl$ were unsuccessful. It is concluded that the intrinsic barriers for these reactions ($\Delta G_0^{\ddagger}$) must be high (>25 kcal/mol) and that homolytic bond dissociation energies are of little use in predicting their size. The general conclusion is drawn that for many reactions there is relatively little variation in transition-state structure for an appreciable change in the thermodynamics of the overall reaction and that theoretical postulates such as the generalized Hammond postulate, the reactivity–selectivity principle, or the variable transition-state theory can have little or no applicability for such reactions.

The question of curvature in Brønsted plots for proton transfers and other types of reactions[1] has evoked considerable discussion in recent years.[4-8] The question is of fundamental import since linearity means that β in the rate-equilibrium relation (eq 1) remains constant, whereas

$$\delta(\Delta G^{\ddagger}) = \beta\delta(\Delta G^{\circ}) \qquad (1)$$

curvature indicates that β in eq 1 is variable. The assumption that the size of β in eq 1 varies with changes in ΔG°, approaching zero for highly exoenergetic reactions and approaching unity for highly endoenergetic reactions, is the basis for a number of widely used theoretical postulates, including the generalized Hammond postulate,[9]

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(1) The Brønsted equation, e.g., log $k_B = \beta$ log $K_{BH} + C$, is a general relationship that can be applied to all kinds of reactions between donors and acceptors. For example, the equation can be used for reactions of a series of bases (donors) not only with an acid but also with an alkyl halide,[2] an electron acceptor,[3] or any other kind of electrophile.

(2) (a) Smith, G. F. *J. Chem. Soc.* **1943**, 521–523. (b) Hudson, R. F.; Klopman, G. *J. Chem. Soc.* **1962**, 1062–1067. (c) Hudson, R. F. "Chemical Reactivity and Reaction Paths"; Klopman, G., Ed.; Wiley-Interscience: New York, 1974; Chapter 5.

(3) Bordwell, F. G.; Clemens, A. H. *J. Org. Chem.* **1981**, *46*, 1035–1036.

(4) Eigen, M. *Angew. Chem., Int. Ed. Engl.* **1964**, *3*, 1–19. These fast proton transfers are not strictly comparable with slow proton transfers because the mechanisms are different. In the fast proton transfers the formation of the encounter complex and the proton transfer occur at rates of the same order of magnitude and either step may be rate limiting. In the slow proton transfers the encounter complex is formed rapidly and reversibly whereas the proton transfer step is much slower.

(5) (a) Kreevoy, M. M.; Konasevich, D. E. *Adv. Chem. Phys.* **1971**, *21*, 243–252. (b) Kreevoy, M. M.; Oh, S.-W. *J. Am. Chem. Soc.* **1973**, *95*, 4805–4810. (c) Kreevoy, M. M.; Albery, W. J. *Adv. Phys. Org. Chem.* **1978**, *16*, 87–157.

(6) Bell, R. P. "The Proton in Chemistry", 2nd ed.; Cornell University Press: Ithaca, NY, 1973; Chapter 10.

(7) (a) Kresge, A. J. *Chem. Soc. Rev.* **1973**, *2*, 475–503. (b) Kresge, A. J. *Acc. Chem. Res.* **1975**, *8*, 354–360.

(8) Bell, R. P. "Correlation Analysis in Chemistry"; Chapman, N. B., Shorter, J. Eds.; Plenum Press: New York, 1978; Chapter 2, pp 55–84.

(9) Hammond, G. S. *J. Am. Chem. Soc.* **1955**, *77*, 334–338. In its restrictive form the Hammond postulate refers to transition states and intermediates of nearly the same energy and does not require β to change. However, Hammond suggested that the value of the postulate derives from its application to highly endothermic reactions where the products will provide the best models for the transition states or to highly exothermic reactions where the reactants will provide the best models. It is this generalized form, which requires β to change, that is most commonly invoked. Evidence for an increase in β in a series of deprotonations as ΔG° was made more positive had been observed some years earlier by Bell and Lidwell.[10]

(10) The changes in β observed by Bell and Lidwell for the deprotonation of a series of β-diketone, β-keto ester, and ketone substrates by RCO_2^- bases[11] was the principal experimental evidence cited by Leffler and Grunwald for the assumption that β in eq 1 would vary between the limits of 0 and 1.[12] They recognized the generality of Brønsted-type relationships and believed that changes in β would also be general. This idea was formulated into the reactivity–selectivity principle (RSP). In a recent extensive review of the reactivity–selectivity principle, Pross concludes that "despite many apparent failures the RSP is fundamentally valid".[13]

(11) Bell, R. P.; Lidwell, O. M. *Proc. R. Soc. London, Ser. A* **1940**, *176*, 88–113.

0022-3263/82/1947-3224$01.25/0

Table I. Acidities of Benzenethiols in Dimethyl Sulfoxide, Water, Methanol, and Aqueous Ethanol at 25 °C

G	pK_a			
	Me_2SO[a]	H_2O[d]	MeOH[f]	48% $EtOH/H_2O$[g]
4-NH_2	12.51			
2-MeO	11.35	6.89		
4-MeO	11.19	6.775	8.95	7.99
4-Me	10.82	6.82	8.96	8.03
2-Me	10.70	6.995		
3-Me	10.55	6.60		7.96
H	10.28 (9.8)[b]	6.615, 6.52[e]	8.65	7.76
4-Br	8.98	6.02		6.99
3-Cl	8.57	5.78		6.74
2-Cl	8.55	5.675		
3-CF_3	8.09			
2-OH	8.05			
2,4,5-Cl_3	6.03			
4-NO_2	5.5 (5.6)[c]	4.715		5.11
2,3,4,5,6-Cl_5	3.3			

[a] Present work, reproducible to ±0.05 pK_a unit; 4-NO_2 and perchloro to ±0.1 unit. [b] Courtot-Coupez, J.; Le De'me'zet, M. *Bull. Soc. Chim. Fr.* **1969**, 1033–1040. [c] Clare, B. W.; Cook, D.; Ko, E. C. F.; Mac, Y. C.; Parker, A. J. *J. Am. Chem. Soc.* **1966**, *88*, 1911–1916. [d] De Maria, P.; Fini, A.; Hall, F. M. *J. Chem. Soc., Perkin Trans. 2* **1973**, 1969–1971. [e] Kreevoy, M. M.; Harper, E. T.; Duvall, R. E.; Wolgus, H. S.; Ditsch, L. T. *J. Am. Chem. Soc.* **1960**, *82*, 4899–4902. [f] Reference 2b. [g] Bordwell, F. G.; Andersen, H. M. *J. Am. Chem. Soc.* **1953**, *75*, 6019–6022.

the reactivity–selectivity principle,[13] and the variable transition-state theory.[14]

Equation 1 was first derived almost simultaneously by Polanyi[15] and by Bell[16] by making assumptions concerning the shapes and interactions of potential-energy curves representing the bonding of the proton in its initial and final states. Bell has pointed out that the range over which β in eq 1 can be treated as a constant will depend on the range over which the intersecting potential-energy curves may be regarded as linear, which can only be determined by experiment.[8] Changes in β for proton transfer with (a) variations in the substrate, (b) variations in the bases (or acids) and substrate, and (c) variations in the bases (or acids) with a single substrate have been observed for a number of reactions.[4-8] Most current investigators appear to have accepted these changes in β as evidence of the generality of curvature in Brønsted plots for proton transfers in hydroxylic solvent, although Bell has warned that "in some instances the curvature barely exceeds the scatter" and that "a large extension of the range of catalysts (or substrates) is often incompatible with the requirement that they should be chemically similar, so that it becomes uncertain whether observed deviations represent true curvature of the Brønsted plot or are due to structural factors".[8] In recent years curvature in Brønsted plots has been explained by application of Marcus' theory[17] to proton transfers and other reactions.[5,7,8,13,18] The size of the intrinsic barrier, ΔG_0^*, i.e., the kinetic barrier at $\Delta G° = 0$, determines the magnitude of curvature, with small intrinsic barriers causing large curvature over a small pK_a range. One of the surprising implications drawn from these analyses, which assume an Eigen two-step mechanism for proton transfer,[4] is that the making and breaking of chemical bonds is often *less* important to the overall barrier than the solvent reorganization and/or the molecular distortion and orientation that presumably occur in the encounter complex.[7,18] A few skeptics remain, however, who question the reality of curvature, and a few questions concerning curvature remain unanswered. For example, the explanation as to why some Brønsted plots fail to exhibit curvature over extended ranges, even under expert scrutiny,[19] in terms of "anti-Hammond" effects balancing Hammond effects[13,42] is not very satisfying. Also, it has been pointed out that the failure of Hammett ρ values that relate rate and equilibrium processes to show curvature is contrary to the Hammond postulate.[20] Our study of the reactions of 9-substituted fluorenyl carbanion families, 9-G-Fl^-, with benzyl chloride in Me_2SO solution, wherein we found that 9-CO_2Me-Fl^-, 9-PhS-Fl^-, 9-Me-Fl^-, and like family lines could be joined into essentially a single line of constant slope that extends over 16 p*K* units, has placed us on the side of the skeptics.[21] Our skepticism has now been reenforced by a study of a single family of bases, the benzenethiolate ions (ArS^-), reacting with butyl chloride in Me_2SO solution that reveals an excellent Brønsted line extending over a range of 9 p*K* units with no trace of curvature.

Results and Discussion

Equilibrium Acidities of Benzenethiols. Equilibrium acidity data in H_2O, MeOH, 48% aqueous EtOH, and Me_2SO solution for benzenethiol (thiophenol) and 14 of its derivatives with one or more substituents in the 2-, 3-, and 4-positions are summarized in Table I.

A Hammett plot for data in Me_2SO constructed by using the 3-Me, H, 4-Br, 3-Cl, and 3-CF_3 points, which are relatively free of resonance effects, is shown in Figure 1 ($\rho = 4.84 \pm 0.31$; $R^2 = 0.988$). Examination of Figure 1 shows

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(12) Leffler, J. E.; Grunwald, E. "Rates and Equilibria of Organic Reactions"; Wiley: New York, 1963.

(13) Pross, A. *Adv. Phys. Org. Chem.* **1977**, *14*, 69–132.

(14) The variable transition-state theory is essentially the application of extended Hammond postulate or the rate-equilibrium relationship, with variable β values, to reactions such as S_N2 and E2. In essence, it assumes that the kinetic activation energy, ΔG^*, has a thermodynamic component. For example, as these reactions become more endoenergetic, β will approach unity, and the influence of the thermodynamic component will increase. See: Lowry, T. H.; Richardson, K. S. "Mechanism and Theory in Organic Chemistry"; Harper and Row: New York, 1976, for discussions.

(15) Ogg, R. A.; Polanyi, M. *Trans. Faraday Soc.* **1935**, *31*, 604–620. Evans, M. G.; Polanyi, M. *Nature (London)* **1936**, 137, 530, 531.

(16) Bell, R. P. *Proc. R. Soc. London, Ser. A* **1936**, *154*, 414–429.

(17) Marcus, R. A. *J. Phys. Chem.* **1968**, *72*, 891–899.

(18) Murdoch, J. R. *J. Am. Chem. Soc.* **1980**, *102*, 71–78. The author cites five types of reactions and gives references to 16 papers where curvature has been reported.

(19) Kemp, D. S.; Casey, M. L. *J. Am. Chem. Soc.* **1973**, *95*, 6670–6680.

(20) (a) Johnson, C. D. "The Hammett Equation"; Cambridge University Press: New York, 1973; pp 152–158. (b) Johnson, C. D. *Chem. Rev.* **1975**, *75*, 755–765.

(21) Bordwell, F. G.; Hughes, D. L. *J. Org. Chem.* **1980**, *45*, 3314–3320. This observation has since been supported by studies of several other families, including the 9-$PhCH_2$-Fl^- and ArC(Me)CN^- families (unpublished results).

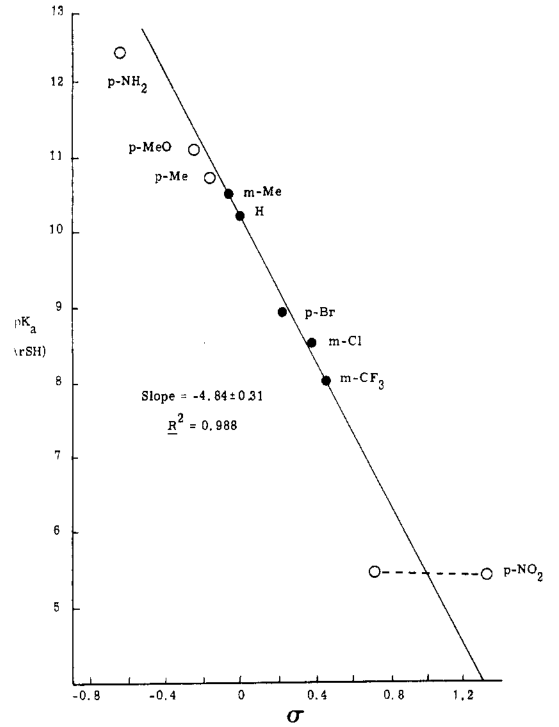
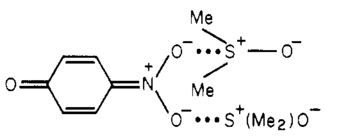


Figure 1. Hammett plot for the equilibrium acidities of benzenethiols in dimethyl sulfoxide solution.

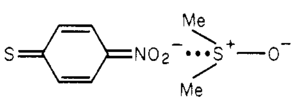
that points for the 4-Me, 4-MeO, and 4-NH_2 functions fall progressively farther below the line, indicating that donor-resonance effects increase in the same way as for benzoic acids but are less acid weakening. On the other hand, the 4-NO_2 point falls above the line with an apparent $\sigma^-_{p\text{-}NO_2}$ of 1.0.

A plot of the pK_a values for ArSH in Me_2SO vs. ArOH in Me_2SO, based on these same five points (Figure 2) shows slightly more scatter (slope = 1.11 ± 0.09; $R^2 = 0.98$) but now the 4-Me, 4-MeO, and 4-NH_2 points fall close to the line, showing that donor-resonance effects in ArSH and ArOH are similar.

The large deviation of the 4-NO_2 point in Figure 2 is likely to be associated with the greater enhancement of negative charge on the oxygen atoms of the nitro group induced by solvation in 4-$NO_2C_6H_4O^-$ than in 4-$NO_2C_6H_4S^-$. The smaller size of oxygen than sulfur allows a stronger interaction in 4-$NO_2C_6H_4O^-$, as depicted by 1.



1



2

Analysis of acidity data for substituted phenols in water and the gas phase has shown that the resonance-accepting ability of the nitro group is greatly enhanced in water by hydrogen bonding to the oxygen atoms of the nitro group.[22] A similar analysis of acidity data for substituted phenols in Me_2SO and in the gas phase has shown that the resonance accepting ability of the *p*-nitro group is also greatly enhanced in Me_2SO by solvation.[23] In this medium it must be specific electrostatic solvation of the oxygen atoms of the nitro group in the anion, as shown in 1, that leads to the enhanced resonance effect. The larger sulfur atom delocalizes the negative charge to carbon and thence to the nitro group to a much lesser degree (2).

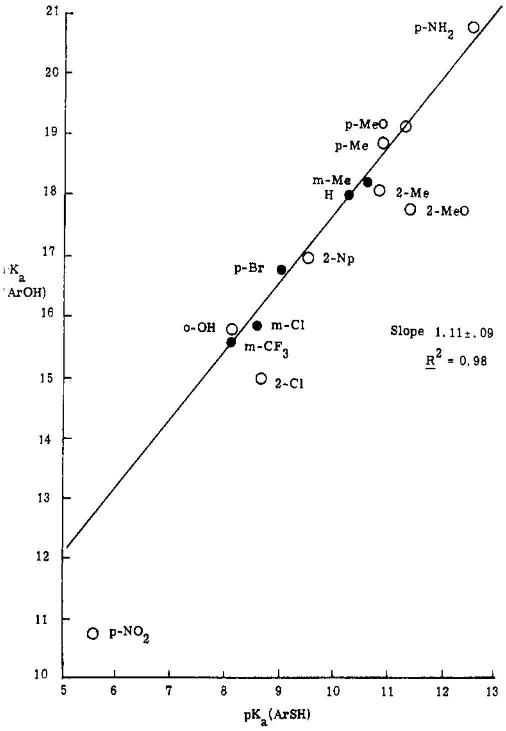


Figure 2. Plot of the acidities of phenols vs. benzenethiols in dimethyl sulfoxide solution.

The smaller size of oxygen, its greater solvation requirements, and its shorter bond to carbon result in a stronger interaction with ortho functions in phenoxide ions than in benzenethiolate ions, which causes the points for 2-Cl, 2-MeO, and 2-Me to fall below the line in Figure 2. The acidities of 2- and 4-methoxybenzenethiols differ by only 0.16 pK_a unit and those of 2- and 4-methylbenzenethiols differ by only 0.12 unit, indicating that steric effects for ortho substituents are small in benzenethiols.

Hydrogen Bonding (H Bonding) Effects on Acidities. The acidity of benzenethiol increases by 3.8 pK_a units in changing the solvent from Me_2SO to H_2O, whereas for phenol the acidity increase is 8 pK_a units. These increases in the degree of dissociation in changing from Me_2SO to H_2O, which correspond to 5.2 and 11 kcal/mol, respectively, are caused primarily by stabilization of the PhS^- and PhO^- anions through H bonding. The smaller size and higher concentration of the charge on oxygen makes PhO^- a much better H-bond acceptor than PhS^-. The relatively high basicity of PhO^- in Me_2SO enhances its H-bond acceptor properties to the point where it competes effectively with Me_2SO solvent for PhOH, despite the strong H-bond-accepting properties of the medium. As a consequence equilibrium 2 is established in Me_2SO with log K_{HB}

$$\mathrm{PhO^- + PhOH \overset{K_{HB}}{\rightleftharpoons} PhO^-\cdots HOPh} \qquad (2)$$

= 3.36.[23] There is no evidence that homohydrogen bonding of this type occurs for PhS^- in Me_2SO. Evidently H bonding of PhSH with Me_2SO is stronger than with PhS^-. A similar situation exists for PhO^- in H_2O where strong H bonding with water precludes the type of homohydrogen bonding shown in eq 2.

In Me_2SO 2-hydroxybenzenethiol is a stronger acid than benzenethiol by 2.2 pK_a units whereas 2-methoxybenzenethiol is a weaker acid by 1.05 units. (2-Methoxybenzenethiol is 0.1 pK_a unit less acidic than 4-$MeOC_6H_4SH$

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[22] Fujio, M.; McIver, R. T., Jr.; Taft, R. W. *J. Am. Chem. Soc.* **1981**, *103*, 4017–4029.

[23] (a) Olmstead, W. N.; Bordwell, F. G., unpublished results. (b) Olmstead, W. N.; Margolin, Z.; Bordwell, F. G. *J. Org. Chem.* **1980**, *45*, 3295–3299.

Table II. Comparison of Acidities of Aliphatic Thiols in Dimethyl Sulfoxide and Water at 25 °C

thiol	$pK_a(Me_2SO)^a$	$pK_a(H_2O)$	$\Delta pK_a{}^g$
PhSH	10.3	6.5	3.2
MeO_2CCH_2SH	12.9 (13.0)[b]	7.80[c]	4.5
$3\text{-}NO_2C_6H_4CH_2SH$	14.15		
$PhCH_2SH$	15.4	9.43[d]	5.4
PrSH	17.05[b]		
BuSH	17.03	10.88[e]	5.5
t-BuSH	17.90	11.14[e] (11.22)[f]	6.2

[a] Present work; pK_a's reproducible to ±0.1 pK_a unit; $ArCH_2SH$ to ±0.2 unit. [b] Ritchie, C. D., private communication. Ritchie, C. D.; Van Werth, J. E.; Virtanen, P. O. J. *J. Am. Chem. Soc.* **1982**, *104*, 3491-3497. [c] Calvin, M. "Glutathione" Colowick, S., Ed.; Academic Press: New York, 1954; Chapter 1. [d] Kreevoy, M. M.; Harper, E. T.; Duvall, R. E.; Wilgus, H. S.; Ditsch, L. T. *J. Am. Chem. Soc.* **1960**, *82*, 4899-4902. [e] Yabroff, D. L. *Ind. Eng. Chem.* **1940**, *32*, 257-262. [f] Irving, R. J.; Nelander, L.; Wadso, I. *Acta Chem. Scand.* **1964**, *18*, 769-787. [g] $\Delta pK_a = pK_a(Me_2SO) - pK_a(H_2O) - 0.6$.

Table III. Rates of Reaction of Benzenethiolate Anions and Aliphatic Thiolate Anions with Butyl Chloride in Dimethyl Sulfoxide Solution at 25 °C

anion	$pK_a(ArSH)$	k_2, $M^{-1}\ s^{-1}$
substituent in benzenethiolate		
$4\text{-}NH_2$	12.5	0.366 ± 0.020
2-MeO	11.3_5	$(7.57 \pm 0.38) \times 10^{-2}$
4-MeO	11.2	0.100 ± 0.007
2-Me	10.7	$(4.57 \pm 0.17) \times 10^{-2}$
H	10.3	$(4.26 \pm 0.07) \times 10^{-2}$
4-Br	9.0	$(1.33 \pm 0.06) \times 10^{-2}$
2-Cl	8.5_5	$(8.77 \pm 0.78) \times 10^{-3}$
$3\text{-}CF_3$	8.1	$(5.78 \pm 0.20) \times 10^{-3}$
2-OH	8.0_5	$(1.44 \pm 0.20) \times 10^{-3}$
$2,4,5\text{-}Cl_3$	6.0	$(8.52 \pm 0.13) \times 10^{-4}$
$4\text{-}NO_2$	5.5	$(2.79 \pm 0.01) \times 10^{-4}$
$2,3,4,5,6\text{-}Cl_5$	3.3	$(5.81 \pm 0.44) \times 10^{-5}$
2-naphthalenethiol	9.5_3	$(2.54 \pm 0.17) \times 10^{-2}$
aliphatic thiolate		
$t\text{-}BuS^-$	17.9	1.95 ± 0.15
$n\text{-}BuS^-$	17.0	2.58 ± 0.07
$PhCH_2S^-$	15.4	0.83 ± 0.08
$3\text{-}NO_2C_6H_4CH_2S^-$	14.1_5	0.65 ± 0.03
$MeO_2CCH_2S^-$	12.9	0.251 ± 0.03

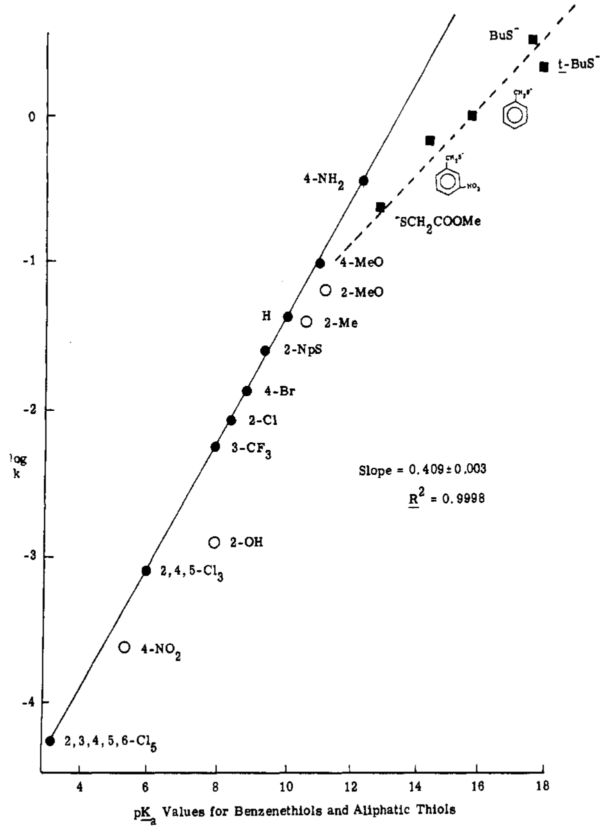
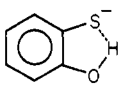
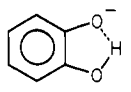


Figure 3. Brønsted plots for the rates of reaction vs. equilibrium acidities of butyl chloride reacting with benzenethiols (solid line) and with aliphatic thiols (dashed line).



3



4

in both Me_2SO and in H_2O, but in H_2O $2\text{-}MeOC_6H_4SH$ is only 0.3 unit less acidic than benzenethiol itself.) The acidifying effect of the 2-OH group in $2\text{-}HOC_6H_4SH$ points to strong intramolecular H bonding in $2\text{-}HOC_6H_4S^-$, as depicted in **3**. A comparable effect is observed in 2-hydroxyphenol, which is a stronger acid than phenol by 2.2 units in Me_2SO.[23a] In the phenol series $4\text{-}HOC_6H_4OH$ is a *weaker* acid than phenol by 1.8 units, indicating that the intramolecular H bond in **4** has a strength of about 5.5 kcal mol^{-1}. The H-bonding effect in **3** must be of the same order of magnitude, which suggests that the larger size of sulfur compensates for its poorer H-bond-accepting ability. Similarly, in neutral 2-hydroxybenzenethiol, theoretical and physical studies show that the hydrogen bond of the hydroxyl proton to sulfur is strong.[24]

Equilibrium Acidities of Aliphatic Thiols. Acidities for benzenethiol and four aliphatic thiols in Me_2SO are compared in Table II with acidities in H_2O. Examination of Table II shows that acidities of the thiols in Me_2SO decrease progressively as one proceeds down the list, the range being 7.6 pK_a units from PhSH to *t*-BuSH. In H_2O the corresponding decrease is only 4.7 units. The increase in charge density in changing from PhS^- to $t\text{-}BuS^-$ is no doubt accompanied by increased dipole stabilization of the ions in Me_2SO and by increased H bonding in H_2O. The smaller acidity decrease in water illustrates the leveling effect of H bonding. A similar leveling effect is observed for alkoxide ions where the change from PhOH to *t*-BuOH results in an acidity decrease of 14 pK_a units in Me_2SO, compared to about 8 or 9 units in H_2O.[23]

2-Methyl-2-propanethiol is a weaker acid than 1-butanethiol by 0.9 pK_a unit in Me_2SO and 0.55 unit in H_2O (Table II). The acidity order *n*-BuSH > *t*-BuSH in solution is noteworthy since in the gas phase the order is MeSH < EtSH < *i*-PrSH < *t*-BuSH.[25] It would appear that the gas-phase and solution acidity order for these thiols is reversed, just as is true for the gas-phase and solution acidity order for the corresponding alcohols.[23b]

Brønsted Correlations of Rates of Reactions of Thiolate Ions with Butyl Chloride. Rate data for the reactions of 12 benzenethiolate ions with butyl chloride in Me_2SO are summarized in Table III. Also included are rate data for 2-naphthalenethiolate and five aliphatic thiolate ions. Brønsted correlations for these data are presented in Figure 3.

Examination of Figure 3 shows that an excellent Brønsted correlation extending over 9 pK_a units is obtained

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(24) Schaefer, T.; Wildman, T. A.; Salman, S. R. *J. Am. Chem. Soc.* **1980**, *102*, 107-110.

(25) Bartmess, J. E.; McIver, R. T., Jr. "Gas Phase Ion Chemistry"; Bowers, M. T., Ed.; Academic Press: New York, 1979; Vol. 2, Chapter 11.

by plotting the rate data for nine ArS$^-$ ions, including 2-naphthalenethiolate ion (2-NpS$^-$) vs. the pK_a values for the corresponding thiols. All of these points fall on the line ($\beta = 0.409 \pm 0.003$; $R^2 = 0.9998$). It is noteworthy that the points for 2-$ClC_6H_4S^-$, 2,4,5-$Cl_3C_6H_2S^-$, and 2,3,4,5,6-$Cl_5C_6S^-$ fall on this line since ortho points often deviate in linear free energy plots. In a previous section we presented evidence to show that ortho steric effects on equilibrium acidities of benzenethiols are small. The rate data indicate that proximity effects on rates and equilibria for the 2-Cl substituent are comparable in size. On the other hand, this is not true for the 2-MeO and 2-Me substituents, the points for which fall below the line by 1.5-fold in rate.[26] The largest deviation from the line (4-fold in rate) was observed with the 2-OH point. This must be associated with the strong H bonding in 2-$HOC_6H_4S^-$ (**3**). Slowing of rates in proton transfer by intramolecular H bonding in the base has been observed in a number of proton transfers.[7]

The deviation of the 4-NO_2 point is the result of direct resonance in the 4-$NO_2C_6H_4S^-$ anion (**2**). In the equilibrium acidity this effect is offset to some degree by a similar, but smaller, effect in the undissociated acid, 4-$NO_2C_6H_4SH$; this effect is absent in the S_N2 reaction. Deviations of this type have been observed for 4-Ph, 4-CO_2Me, and 4-$MeSO_2$ points in a Brønsted correlation of the reactions of ArO$^-$ with $PhCH_2Cl$.[27]

Aliphatic thiolate ions, RS$^-$, reacting with BuCl gave a poor Brønsted correlation ($\beta = 0.19 \pm 0.03$; $R^2 = 0.91$) over a 5 pK range (Figure 3). The scatter of the points is caused in part because of experimental problems (the error in measuring the pK_a's was ±0.2 for $PhCH_2SH$ and p-$NO_2C_6H_4CH_2SH$) and in part because structural changes have been made close to the reaction site. The latter may lead to differences in steric effects in the reactions, including steric hindrance to the approach of the nucleophile and steric hindrance to solvation. The importance of solvation is made clear by the substantial differences found for acidities in Me_2SO vs. H_2O (ΔpK_a) for RSH vs. ArSH. The ΔpK_a values for MeO_2CCH_2SH, $C_6H_5CH_2SH$, BuSH, and *t*-BuSH are 4.5, 5.4, 5.5, and 6.2 units, respectively, as compared to 3.2 for PhSH (Table II). The larger ΔpK_a for RSH suggests that the more concentrated negative charge in RS$^-$ causes stronger hydrogen bonding in water than for PhS$^-$. Stronger solvation of RS$^-$ than ArS$^-$ in Me_2SO could lead to a decrease in β if the effect is felt more in the rates than in the equilibria. It is also possible that the smaller β may reflect an inherent difference in the two types of thiolate ions such as the degree of charge delocalization.

Comparison of the reactivities of RS$^-$ ions toward BuCl with those of ArS$^-$ ions of the same basicity in Figure 3 shows that the latter are more reactive. However, if the lines cross, as seems likely, the RS$^-$ ions would then be more reactive than ArS$^-$ ions of the same basicity. A study of the reaction of thianions reacting with disulfides in hydroxylic solvents showed ArS$^-$ ions to be more reactive than RS$^-$ ions of the same basicity.[28] Here the lines were considered to be parallel, although both plots were poor ($r = 0.93$–0.97).

Hammett and Brønsted Relationships. The Hammett equation (eq 3) and Brønsted equation (eq 4) can both be considered to be examples of the rate-equilibrium equation (eq 1).

$$\log (k/k_0)^{S}{}_{ArYX} = \rho \log(K/K_0)^{H_2O}{}_{ArCO_2H} \qquad (3)$$

$$\log k_B = \beta \log K_{HB} + C \qquad (4)$$

The Hammett equation is applicable to any reaction at an aliphatic site, YX, adjacent to an aromatic nucleus, Ar, when carried out in a solvent, S. The price for this generality is imprecision. The Hammett plot in Figure 2 is typical. The meta points give a fair correlation ($R^2 = 0.988$) over a range of 0.5 log units in σ, but the points for *p*-Me, *p*-MeO, and *p*-NH_2 substituents fall progressively farther below the line as their donor capacity increases, partly because the SH group in the ArSH substrate is a poorer acceptor than the CO_2H group in the reference substrate ($ArCO_2H$) and partly because the substituents are one atom closer to the acidic site in ArSH, which makes the polar effects larger. On the other hand, the *p*-NO_2 point deviates from the line about equally below or above the line, depending on whether $\sigma_{p\text{-}NO_2}$ or $\sigma^-{}_{p\text{-}NO_2}$ is used (Figure 1). In contrast we see in Figure 3 that nine points fit on the Brønsted plot, which covers a much wider range (about 9 pK units). The much better correlation ($R^2 = 0.9998$) results primarily because in the Brønsted relationship substituent effects are not referred to an arbitrary reference standard in a different solvent and, in part, because a much wider basicity range is covered.

Interpretation of the slope in the Brønsted equation is also less complex than in the Hammett equation. For example, the ρ of 4.84 in Figure 1 tells us that the acidities of benzenethiols are 4.84 times as sensitive to substituent effects as those in benzoic acids. This greater sensitivity is due to (1) the change in solvent, (2) the change in the donor atom (O vs. S), and (3) the change in the distance of the reactive site from the aromatic ring. It is difficult to decide the relative magnitudes of these effects. In the Brønsted plot (Figure 3) these effects are absent, and we have a direct comparison of the effect of substituents on rates as compared to their effect on basicity. In other words, β tells us what fraction of the change in basicity caused by substituent changes ($\Delta G°$) can be utilized in the transition state to effect a change in rate in a given reaction. At present, we do not know what factor (or factors) determines the size of β, but it seems certain that β will, in time, provide us with valuable mechanistic information.

Brønsted Plots in Hydroxylic and Dipolar Nonhydroxylic Solvents—The Question of Curvature. It was recognized by Brønsted that curvature must occur as rates approach the encounter-controlled limit,[29] but no evidence of curvature was obtained in the early work. The much-cited study of Bell and Lidwell published in 1940 provided the first evidence for curvature, i.e., changes in β with substrate variation,[10,11] but no further examples were forthcoming for over 20 years. Eigen's studies of fast proton transfers revealed plots that curved sharply over a range of about 4 pK units as the diffusion-controlled limit was approached.[4] Eigen also observed curvature in Brønsted plots for slow proton transfers, for example in the reaction of $(CH_3CO)_2CH_2$ with a series of bases covering a pK range of about 16 units[30] and concluded that

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(26) Methyl and methoxyl groups have been observed to exert as large or larger proximity effects than Cl in other instances. For example, the *A* values derived from cyclohexane equilibria for Me, MeO, and Cl are 1.8, 0.60, and 0.53, respectively.

(27) Hughes, D. L., Ph.D. Dissertation, Northwestern University, Evanston, IL, 1981.

(28) Freter, R.; Pohl, E. R.; Wilson, J. M.; Hupe, D. J. *J. Org. Chem.* **1979**, *44*, 1771–1774. Hupe, D. J. Abstracts of the 5th IUPAC Conference on Physical Organic Chemistry, University of California, Santa Cruz, CA, Sept. 1980.

(29) Brønsted, J. N.; Pedersen, K. J. *Z. Phys. Chem.* **1924**, *108*, 185–225. Brønsted, J. N.; Guggenheim, E. A. *J. Am. Chem. Soc.* **1927**, *49*, 2554–2584.

(30) Ahrens, M. L.; Eigen, M.; Kruse, W.; Maass, G. *Ber. Bunsenges. Phys. Chem.* **1970**, *74*, 380–385. Jones, J. R. "The Ionization of Carbon Acids"; Academic Press: New York, 1973; p 132.

a linear Brønsted plot represents only part of a continuous curve having slopes of 0 and 1 at the two extremities.[4,30] Other reactions where curvature in Brønsted plots has since been observed include the reaction of hydronium ion with aromatic hydrocarbons (guaiazulene, azulene, 1,3,5-trimethoxybenzene, 2,4-dimethoxytoluene, anisole, and benzene),[31] the protonation of diazo compounds by a series of acids,[5] the deprotonation of a ketonic substrate, $MeCOCH_2CH_2OC_6H_4NO_2$, by reaction with a series of bases,[32] and the cleavage of disulfides by reaction with ArS^- and RS^-.[28] Examples of reactions in hydroxylic solvents extending over a considerable range where the investigators observed no evidence for curvature include the reaction of substituted benzisoxazoles with bases,[19] the acid-catalyzed dehydration of acetaldehyde hydrate,[33] the deprotonation of ethyl nitroacetate,[34] and the detritiation of *tert*-butylmalonitrile.[35]

Before accepting curvature in Brønsted plots as inherent in the reaction, one must be sure that it is not caused by the failure to keep the catalysts "chemically similar".[8] Unfortunately, in hydroxylic solvents it is impossible to fulfill this requirement if the reaction is to be studied over an extended pK range. Traditionally Brønsted plots for base-catalyzed reactions are constructed by using a variety of bases. For example, in the study of the deprotonation of $(CH_3CO)_2CH_2$ Eigen used 13 oxygen bases, including H_2O, $ClCH_2CO_2^-$, HCO_2^-, $HO_2CCH_2CO_2^-$, $(CH_3)_2AsO_2^-$, ArO^-, gluconate ion, and hydroxide ion, as well as amine and sulfur bases.[30] With such diverse structures deviations from linearity are to be expected. For example, the hydroxide rate in water is almost always much slower than expected, apparently because of unusually strong solvation.[7b] Also, bases of the same strength but with different kinds of donor atoms often do not fit on the same Brønsted line,[6] which is one of the reasons that considerable scatter is often observed in Brønsted plots. This donor-atom effect is exaggerated in Me_2SO solution for S_N2 reactions of $PhCH_2Cl$ with various kinds of delocalized anions, where points for oxanions and nitranions fall on lines about 1 and 2 log units, respectively, below a carbanion line adopted as a standard, whereas points for thianions fall on a line 3 log units *above* this carbanion line.[36,37] In the present study we have seen that points for ArS^- and RS^- fall on different Brønsted lines even though the donor atom is the same. Besides this donor-atom effect, which may have its origin in a solvation effect or intrinsic electronic effect, the principal cause of deviations leading to apparent curvature are proximity effects of various kinds. The examples of apparent curvature of Brønsted plots cited above each contain one or both of these causes of curvature. There are large differences in proximity effects between the various β-diketone, β-keto ester, and ketone substrates used by Bell and Lidwell.[11] In fact, an analysis by Kemp and Casey led to the conclusion that the data could be fitted at least as well by two separate lines, one for β-diketone and β-keto ester functions and a second for monoketone functions.[19] (This explanation appears to have been accepted by Bell.[8]) In the study of the deprotonation of acetylacetone by Eigen et al.[30] donor-atom and proximity effects are both present. In the deprotonation of $MeCOCH_2CH_2OC_6H_4NO_2$ studied by Hupe and Wu a variety of oxygen bases were used.[32] The pK_a range 4.8–8 was covered by three diverse bases, AcO^-, $C_6F_5O^-$, and $(F_3C)_2C(OH)O^-$, the range from pK_a 7.7 to 10.1 by ArO^- bases, that from 10 to 12 by oxime bases, $ArCH{=}NO^-$, and that from 12 to 16, which accounts for most of the curvature, by alkoxide bases. Our analysis suggests that the data may follow a pattern similar to that in Figure 3, i.e., an essentially linear region from pK_a 4.8 to 12 (with considerable scatter caused by the use of several oxygen base families) and a second "linear" region from 12 to 16 with greater scatter caused by proximity effects and uncertainty in the data (pK_a values in this region are difficult to measure in water).

Our conclusion that curvature in Brønsted plots extending over about 12 pK_a units may be an artifact caused by the presence of donor-atom and proximity effects is supported by evidence that there are instances where curvature fails to be observed. The example of base-catalyzed elimination of benzisoxazoles has already been mentioned.[19] Another example is the base-catalyzed detritiation of *tert*-butylmalonitrile studied by Hibbert et al.[38] and extended by Pratt and Bruice.[35] The latter study covers a range of 9 pK_a units extending from pK_a 3 to 12 by using several kinds of bases, RCO_2^-, RNH_2, and HO_2^-. The β is about 0.8[39] with no indication of curvature except for the ever deviant HO^- point. It is noteworthy that this large β holds even near the thermoneutral point (with $k = 1.5 \times 10^5$)[35] where the assumption of a variable β would suggest a substantial decrease in its size. This result is somewhat similar to that of Barnes and Bell for the deprotonation of ethyl nitroacetate by RCO_2^-, pyridine, and ArO^- bases, where there is no evidence for curvature over the ΔpK_a range of 4 to −4, except for the HO^- point ($\beta \simeq 0.55$). Here the reaction goes from the endoenergetic side through the thermoneutral point to the exoenergetic side, k reaching $10^{4.5}$.[34] The failure of β to decrease in these instances on the exoenergetic side is consistent with the results obtained by Ritchie for cation–anion combination reactions where the slope in his N_+ plots remain constant up to near the encounter-controlled limit and then suddenly flatten out.[40]

The difficulties in determining whether or not curvature is present in Brønsted plots for reactions in hydroxylic solvents is evident from the various treatments of the data for the acid-catalyzed dehydration of acetaldehyde hydrate where over 50 RCO_2H, $ArCO_2H$, and ArOH acids were studied. The original authors, Bell and Higginson,[33] presented a linear plot showing the usual scatter for plots where catalysts of differing structure are used,[6] and Wiberg later cited this an an example of a Brønsted plot that was linear over an extended region (10 pK units).[41] Eigen accepted the linearity of the plot, although this was contrary to his belief that such plots should be curved. He explained the lack of curvature as being the result of a "coupled mechanism".[4] More recently a curved plot has been assumed and the data analyzed by use of the Marcus equation.[7b]

The problems sometimes encountered in determining accurate values of β in hydroxylic solvents, even when remote substitution is used to vary basicities, can be il-

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(31) Kresge, A. J.; Mylonakis, S. G.; Sato, Y.; Votullo, V. P. *J. Am. Chem. Soc.* **1971**, *93*, 6181–6188.

(32) Hupe, D. J.; Wu, D. *J. Am. Chem. Soc.* **1977**, *99*, 7653–7659.

(33) Bell, R. P.; Higginson, W. C. E. *Proc. R. Soc. London, Ser. A* **1949**, *197*, 141–159.

(34) Barnes, D. J.; Bell, R. P. *Proc. R. Soc. London, Ser. A* **1970**, *318*, 421–440.

(35) Pratt, R. F.; Bruice, T. C. *J. Org. Chem.* **1972**, *37*, 3563–3564.

(36) Bordwell, F. G.; Hughes, D. L. *J. Org. Chem.* **1981**, *46*, 3570–3571.

(37) D. L. Hughes has found that points for thianions, oxanions, nitranions, and carbanions fall on different lines for deprotonation of butenonitrile (unpublished results).

(38) Hibbert, F.; Long, F. A.; Walters, E. A. *J. Am. Chem. Soc.* **1971**, *93*, 2829–2835.

(39) The three-point β determined with RCO_2^- is 0.98.[38]

(40) Ritchie, C. D. *Acc. Chem. Res.* **1972**, *5*, 348–354.

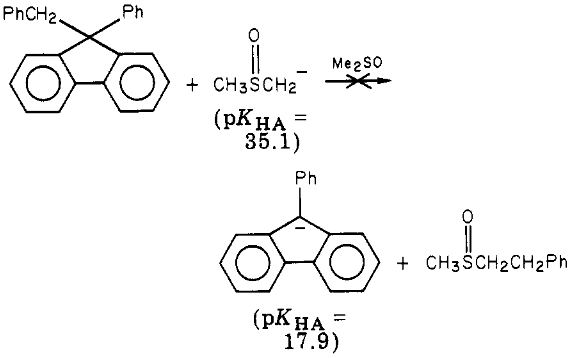
(41) Wiberg, K. B. "Physical Organic Chemistry"; Wiley: New York, 1964; p 402.

lustrated by examining the data for the reaction of a series of p-$GC_6H_4S^-$ anions with a series of benzyl bromides, p-$G'C_6H_4CH_2Br$, in MeOH solution.[2b] The slopes of the Brønsted lines increase as the G′ substituent in the benzyl bromide is changed from a donor to an acceptor: p-MeO, 0.15; p-Me, 0.21; H, 0.20; p-Br, 0.26; p-NO_2, 0.36. The trend in these slopes is real since it has been observed for benzyl halides in a number of other instances,[21,42] but there is appreciable scatter of the points as is apparent from the poor R^2 values for the plots (0.80, 0.89, 0.88, 0.91, and 0.86, respectively—compare $R^2 = 0.9998$ for the plot in Figure 3). The scatter is caused in part by the short range of acidities covered by six of the benzenethiols (1.13 pK_a units), which means that rate and equilibrium data of high accuracy are needed to eliminate scatter. The slopes of the lines are determined to an inordinate degree by the seventh point, which extends the pK range by another 0.91 unit. This is unfortunate because the seventh point is that for p-CH_3CO, which is expected to be deviant by analogy with the deviant behavior of the p-NO_2 point in Figure 3. The accuracy of the slopes determined from these seven ArS^- points is clearly questionable. Let us suppose that we wished to extend this study with one of the benzyl bromides in order to test curvature in the Brønsted plot. To do this we must use other families of stronger bases such as ArO^- and amines. It would certainly be difficult to decide whether the points from such a composite plot should be fitted to a curve or a line. The advantage of Brønsted plots in Me_2SO or other dipolar nonhydroxylic solvents is that a wide range of basicities can be covered with minimal structural variation. We see no evidence for curvature in any of the Brønsted plots for S_N2 reactions in Me_2SO studied to date. These include reactions of carbanions, nitranions, oxanions, and thianions that cover pK ranges as large as 16 pK units. It is possible, of course, that different results will be obtained for proton-transfer reactions in Me_2SO solution since the activation barriers are lower. Nevertheless, these results, and the analysis of the experimental evidence for curvature made above in light of these results, cast serious doubt on the reality of curvature in composite Brønsted plots for proton transfer constructed from data obtained in hydroxylic solvents. Furthermore, these results cast serious doubt on the variation of β in eq 1 for other reactions where the barriers are likely to be of the same order of magnitude as those for S_N2 reactions.

Application of the Marcus Equation to S_N2 Reactions. Curved Brønsted plots imply that there is a thermodynamic component present in the kinetic activation barrier. For very fast reactions the intrinsic activation barrier, $G_0^{\ddagger}$, i.e., the barrier at $\Delta G^\circ = 0$, will be small, and the presence of a thermodynamic component should cause sharp curvature, as was observed by Eigen for very fast proton transfers. For slow proton transfers, which have higher barriers, β is assumed to change gradually over a wide pK range. Analysis of the curvature has been made by several investigators using a form of the Marcus equation in which two parameters are used, ω^r, to define the energy required to orient the reactants in an encounter complex, and $\Delta G_0^{\ddagger}$, to define the intrinsic barrier. A surprising feature of such analyses is that ω^r is often larger than $\Delta G_0^{\ddagger}$,[7b,18] which could mean that the analysis of the experimental results has overestimated the degree of curvature. A recent hypothesis that the curvature in Brønsted plots may be hyperbolic in nature has been advanced by Lewis et al.[43] It leads to conclusions similar to those of the Marcus theory, i.e., that more curvature is expected for reactions with low activation barriers.

So that the Marcus theory can be used, the overall free-energy change for the reaction, ΔG°, and the free energy of activation at $\Delta G^\circ = 0$, $\Delta G_0^{\ddagger}$, must both be known. For calculation of these quantities, either the reverse rate or the equilibrium constant for the reaction in question is required. For thianions, the slowest reaction with n-BuCl, that with $C_6Cl_5S^-$ ion, goes to completion, signifying that ΔG° is still negative. Since $\Delta G^{\ddagger}$ for that reaction is 22 kcal/mol,[27] $\Delta G_0^{\ddagger}$ for these S_N2 reactions must be greater than this number. The same must be true for the carbanion reactions, where the slowest reaction with $PhCH_2Cl$, that with 9-CN-Fl^- ion, has $\Delta G^{\ddagger} = 21$ kcal/mol and goes to completion.[27]

In an attempt to measure reverse rates for these S_N2 reactions, several reactions where a strongly basic anion attacks carbon to displace a thianion or carbanion were tried. The reactions shown in eq 5–7 were all too slow to measure ($<10^{-5}$ M^{-1} s^{-1}) at room temperature, however, despite the fact that the differences in anion basicities provide potential driving forces of 23.5, 16, and 19.7 kcal/mol, respectively.



(5)

$$\underset{(pK_{HA} = 22.3)}{PhCH_2SPh + 9\text{-Me-Fl}^-} \xrightarrow[\times]{Me_2SO} \underset{(pK_{HA} = 10.3)}{PhS^-} + 9\text{-}PhCH_2\text{-}9\text{-MeFl} \quad (6)$$

$$\underset{(pK_{HA} = 17.7)}{PhCH_2SC_6Cl_5 + 2,7\text{-}Br_2\text{-}9\text{-MeFl}^-} \xrightarrow[\times]{Me_2SO} \underset{(pK_{HA} = 3.3)}{C_6Cl_5S^-} + 9\text{-}PhCH_2\text{-}2,7\text{-}Br_2\text{-}9\text{-MeFl} \quad (7)$$

The failure of reactions 5–7 to be realized under these conditions shows that the bond energies derived from homolytic scissions are likely to be deceptive for the prediction of heterolytic reactivities. For example, the C–S bond dissociation energy in CH_3SPh is about 24 kcal/mol less than the C–Cl bond dissociation energy in CH_3Cl,[44,45] yet the $C_6Cl_5S^-$ ion is displaced from $PhCH_2SC_6Cl_5$ at a rate at least 10^6 times slower than Cl^- ion in Me_2SO solution at 25 °C, even though the two ions have roughly the same basicity. As a consequence, estimating the intrinsic barriers for S_N2 reactions involving thianion and carbanion

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

(43) Lewis, E. S.; Shen, C. C.; More O'Ferrall, R. A. *J. Chem. Soc., Perkin Trans. 2* **1981**, 1084–1088.

(44) Caspapier, P.; Swart, E. R. *J. Chem. Soc.* **1963**, 1254–1262.

(45) Cox, J. D.; Pilcher, G. "Thermochemistry of Organic and Organometallic Compounds"; Academic Press: New York, 1970.

nucleophiles is impossible from the present data. We can only say that $\Delta G_0^{\ddagger}$ is greater than 25 kcal/mol. It does not seem likely that the barrier is much higher than 25 kcal/mol since elimination of Cl^- in the reaction of a carbanion base with $PhCH_2CH_2Cl$ is only about 10^4 times faster than elimination of PhS^- from $PhCH_2CH_2SPh$.[46]

The Marcus Theory predicts less curvature for reactions with high intrinsic barriers (eq 8). If the intrinsic barrier

$$\frac{\delta\beta}{\delta(\Delta G^\circ)} = \frac{1}{8\Delta G_0^{\ddagger}} \tag{8}$$

is of the order of 30 kcal/mol for reactions of ArS^- ions with *n*-BuCl, a change in β of 0.004 per kcal/mol in ΔG° is expected. From assumption that ΔpK_a provides at least a rough measure of the change in ΔG°, the calculated change in β would then be 0.051 for the 9-unit pK_a range covered by our data. For a carbanion reacting with $PhCH_2Cl$, $\Delta G^{\ddagger}$ is estimated to be about 20 kcal/mol higher than for a thianion of the same basicity.[27] From assumption that $\Delta G_0^{\ddagger} = 50$ kcal for this reaction, a change in β of 0.055 is expected for the 16-unit pK_a range covered. While there is no change in β observable for either of these reactions, the possibility of a small change cannot be excluded if the barriers are of this order of magnitude.

Summary and Conclusions. The strict linearity in the Brønsted plot for reactions of ArS^- ions with *n*-BuCl in Me_2SO solution (Figure 3) has reenforced our earlier conclusions, derived from a study of carbanion families reacting with benzyl chlorides, that such plots are linear over extended pK_a ranges when basicities are changed by remote substitution and the donor atom in the base is kept constant.[21] Variation of the donor atom in the base (S^-, C^-, N^-, O^-) can cause apparent deviations of as much as 5 log units in the plots.[36,37] These results suggest that the much discussed deviations from linearity commonly observed for Brønsted plots in hydroxylic solvents arise because different base families have been used. Hydroxide, azide, and like ions, which do not belong to a family, can be considered to be "orphans" with unique properties. The small range of basicities available in hydroxylic solvents necessitates the use of such "orphans", as well as different families of bases, if an extended pK_a range is to be covered in the Brønsted plot. A review of the data in hydroxylic solvents from this standpoint has caused us to question the curvature claimed for a number of such extended plots. In any event, our data show that β in the rate-equilibrium equation (eq 1) remains constant for changes in ΔG° of at least 20 kcal/mol for S_N2 reactions, (assuming ΔpK_a reflects the overall change in ΔG°) and suggests that this may be true also for many other types of reactions. It follows that theoretical postulates such as the generalized Hammond postulate,[10] the reactivity–selectivity principle,[12,14] and the variable transition-state theory,[15] are inapplicable to reactions for at least changes in ΔG° of this magnitude. (A somewhat similar conclusion has been drawn by Johnson from the constancy of Hammett ρ values.[20]) The apparent qualitative success of these theoretical postulates for reactions where ΔG° has been changed over relatively small ranges is likely to be the result of insufficient control of reaction variables.[20] For quantitative tests of the variation of β in eq 1 it is required that (a) the nature of the bonds formed and broken, as well as medium effects, be kept constant and (b) reactivities be changed by remote substitution in order to minimize proximity effects. We conclude that for many reactions there is relatively little variation in transition-state structure for an appreciable change in the thermodynamics of the overall reaction.

Experimental Section

Thiols. The thiols were all commercially available. The liquids were distilled before use. The solids were purified to literature melting points by dissolution of the sample in aqueous NaOH, filtration, and acidification with dilute HCl followed by recrystallization from hexane under a nitrogen atmosphere.

Acidity measurements were performed as described previously.[24,47] A generous supply of dimethyl sulfoxide was provided by the Chemical Products Division of Crown Zellerbach Co., Camas, WA.

Rate Measurements. The rates of reaction were measured by two methods.

Method 1. This method is the same as that previously described,[21] wherein the decrease in absorbance of the thiophenoxide anion is monitored at a fixed wavelength.

Method 2. This method was used for all of the rate measurements of the aliphatic thianions, which have no absorbance in the visible region and for some of the thiophenoxide anions. The thiol was equilibrated with an indicator anion (In^-) whose conjugate acid (HIn) had a pK_a within 1 unit of the thiol (eq 9).

$$In^- + RSH \xrightleftharpoons{K_{eq}} HIn + RS^- \tag{9}$$

$$RS^- + R'X \xrightarrow[k_2]{} RSR' + X^- \tag{10}$$

Then the alkyl halide (RX) was added and the rate of reaction followed by monitoring the decrease in absorbance of the colored In^- anion caused by the reaction in eq 10 shifting the equilibrium in eq 9 to the right. The procedure was as follows. First a standard pK_a measurement was performed exactly as described in ref 47, establishing the equilibrium shown in eq 9 and generating known concentrations of In^-, RSH, HIn, and RS^-. The solution was equilibrated at 25 °C. Next, the alkyl halide was added in greater than 10-fold excess over the RS^- concentration, and the cuvette was weighed in order to determine how much RX was added. As the thianion reacted to form the inert sulfide (eq 10), the equilibrium in eq 9 was shifted to the right, causing a decrease in In^- concentration, which was monitored spectrophotometrically. The calculations needed to determine the k_2 rate constant for eq 10 are available.[48] Calculations were performed on an Olivetti Model 6060 minicomputer.

Methods 1 and 2. The $2,4,5\text{-}Cl_3C_6H_2S^-$ anion absorbed in the visible so that the rate could be followed both by the direct method (1) and indirect method (2). Two runs were made by following the decrease of absorbance at a fixed wavelength for the reaction with $PhCH_2Cl$,[21] and two runs were made with $2,7\text{-}Br_2\text{-}9\text{-}CO_2Me\text{-}FlH$ as the indicator (method 2). The agreement in rates for the four runs was ±3%.

Product Study. Reaction of $2,4,5\text{-}Cl_3C_6H_2S^-$ with BuCl in Me_2SO solution for 12 h by the procedure described previously[21] gave a 90% yield of $2,4,5\text{-}Cl_3C_6H_2SBu$: mp 18–19 °C; NMR ($CDCl_3$) δ 0.8–1.2 (3 H, m CH_3), 1.2–1.9 (4 H, m, $CH_3\mathbf{CH_2CH_2}CH_2$), 2.9 (2 H, br t, SCH_2), 7.2 (1 H, s, aromatic H) 7.4 (1 H, s, aromatic H); mass spectrum (peak, % abundance) 212, (100), 214, (99), 216 (33) ($Cl_3C_6H_2S$ fragments); parents 268 (49.6) (3 Cl^{35}), 270 (47.5), ($^{35}Cl_2{}^{37}Cl$), 272 (16.7), ($^{35}Cl^{37}Cl_2$), 274 (2.3) ($^{37}Cl_3$).

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(48) These calculations are available from the author.

Registry No. 4-$NH_2C_6H_4SH$, 1193-02-8; 2-$MeOC_6H_4SH$, 7217-59-6; 4-$MeOC_6H_4SH$, 696-63-9; 4-MeC_6H_4SH, 106-45-6; 2-MeC_6H_4SH, 137-06-4; 3-MeC_6H_4SH, 108-40-7; PhSH, 108-98-5; 4-BrC_6H_4SH, 106-53-6; 3-ClC_6H_4SH, 2037-31-2; 2-ClC_6H_4SH, 6320-03-2; 3-$CF_3C_6H_4SH$, 937-00-8; 2-OHC_6H_4SH, 1121-24-0; 2,4,5-$Cl_3C_6H_2SH$, 3773-14-6; 4-$NO_2C_6H_4SH$, 1849-36-1; 2,3,4,5,6-Cl_5C_6SH, 133-49-3; MeO_2CCH_2SH, 2365-48-2; 3-$NO_2C_6H_4CH_2SH$, 77472-39-0; $PhCH_2SH$, 100-53-8; BuSH, 109-79-5; *t*-BuSH, 75-66-1; BuCl, 109-69-3; 4-$NH_2C_6H_4S^-$, 35337-61-2; 2-$MeOC_6H_4S^-$, 82044-19-7; 4-$MeOC_6H_4S^-$, 26971-83-5; 2-$MeC_6H_4S^-$, 24309-25-9; PhS^-, 13133-62-5; 4-$BrC_6H_4S^-$, 26972-20-3; 2-$ClC_6H_4S^-$, 82044-20-0; 2-$CF_3C_4H_4S^-$, 78232-02-7; 2-$OHC_6H_4S^-$, 58728-63-5; 2,4,5-$Cl_3C_6H_2S^-$, 78232-01-6; 4-$NO_2C_6H_4S^-$, 45797-13-5; 2,3,4,5,6-$Cl_5C_6S^-$, 46012-16-2; 2-naphthylS^-, 29869-27-0; *t*-BuS^-, 20733-19-1; *n*-BuS^-, 20733-16-8; $PhCH_2S^-$, 1492-49-5; 3-$NO_2C_6H_4CH_2S^-$, 82044-21-1; $MeO_2CCH_2S^-$, 64743-45-9; 9-$PhCH_2$-9-PhFl, 35377-96-9; $CH_3S(O)CH_2^-$, 13810-16-7; $PhCH_2SPh$, 831-91-4; 9-$MeFl^-$, 31468-21-0; $PhCH_2SC_6Cl_5$, 82044-22-2; 2,7-Br_2-9-$MeFl^-$, 73872-46-5.

Studies on Organic Fluorine Compounds. 38.[1] Ring-Opening Reactions of *gem*-Difluorocyclopropyl Ketones with Nucleophiles

Yoshiro Kobayashi,* Takeo Taguchi, Tsutomu Morikawa, Toyohiko Takase, and Hiroshi Takanashi

Tokyo College of Pharmacy, 1432-1 Horinouchi, Hachioji, Tokyo 192-03, Japan

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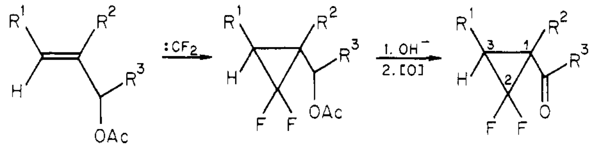
Syntheses of *gem*-difluorocyclopropyl ketones (**3a–d**) and their reactions with nucleophiles are described. Ring-opening reaction of **3a,c,d** having a hydrogen substituent at C_1 adjacent to the carbonyl group with a methanolate anion gave carboxylic acid derivatives derived from C_1–C_2 bond scission (between the carbon atom with an acyl group and the carbon atom with fluorine substituents). On the other hand, reaction of **3a–c** with a thiolate anion resulted in the C_1–C_3 bond cleavage (carbon–carbon bond opposite to the difluoromethylene group).

Introduction

Ring-opening reactions of dihalocyclopropanes, formed by the addition of dihalocarbene to carbon–carbon double bonds, are useful methods for homologation of carbon chain and ring enlargement in synthetic chemistry.[2] Although dichloro- and dibromocyclopropanes have been well investigated, a limited number of reports on the difluoro analogues, which would be expected to have unique features compared with those of dichloro or dibromo analogues due to the characteristic properties of carbon–fluorine bonds, have appeared.[3]

We have already reported our results on the ring-opening reaction of acetoxydifluorocyclopropanes with various nucleophiles[2] and its application to a synthesis of 24,24-difluoro-25-hydroxyvitamin D_3.[4] In our preliminary paper we have demonstrated that the ring-opening reaction of *gem*-difluorocyclopropyl ketones possessing a hydrogen substituent at the carbon atom adjacent to the carbonyl group with a methanolate anion and a thiolate anion occurred by a different course.[5] In this paper we will describe in detail the ring-opening reaction of *gem*-difluorocyclopropyl ketones with nucleophiles and its application to the construction of heterocyclic compounds by the reaction of *gem*-difluorocyclopropanes with two functional nucleophiles.

Scheme I



1 **2** **3**

1a, **2a**, **3a**, R^1 = Ph; R^2 = H; R^3 = CH_3
1b, **2b**, **3b**, R^1 = Ph; R^2 = CH_3; R^3 = CH_3
1c, **2c**, **3c**, R^1 = H; R^2 = H; R^3 = *n*-Bu
1d, **2d**, R^1 = Ph; R^2 = H; R^3 = H; **3d** R^1 = Ph; R^2 = H; R^3 = OCH_3

Results and Discussion

Syntheses of *gem*-Difluorocyclopropyl Ketones. It is known that the addition reaction of difluorocarbene generated by pyrolysis of sodium chlorodifluoroacetate to α,β-unsaturated carbonyl compounds usually proceeds in low yields due to the low reactivity of the electron-deficient carbon–carbon double bond toward electrophilic difluorocarbene and causes the formation of the side reaction products.[6] Therefore, we synthesized *gem*-difluorocyclopropyl ketones (**3**) by the following three-step procedure: (1) addition of difluorocarbene to the allyl acetate (**1**), (2) alkaline hydrolysis, and (3) Jones oxidation. Compound **3d** was prepared by treatment of the resulting carboxylic

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