7-OAc, 96690-21-0; 7-OH, 96690-22-1; 7-OMs, 96690-23-2; 7-Cl, 96745-37-8; 8-OAc, 3123-86-2; *endo*-9-Cl, 96690-09-4; *exo*-9-Cl, 96745-27-6; 9-OH, 96745-30-1; 9-NHAc, 96745-31-2; *endo*-10-Cl, 96745-28-7; *exo*-10-Cl, 96745-29-8; 10-OH, 96690-10-7; 10-NHAc, 96690-11-8; *endo*-11-Cl, 96745-25-4; *exo*-11-Cl, 96745-26-5; *endo*-12-Cl, 96690-07-2; *exo*-12-Cl, 96745-24-3; 13-OAc, 96690-15-2; 13 (ketone), 96690-17-4; 13-NHAc, 96690-19-6; 14-OAc, 96690-16-3; 14 (ketone), 96690-18-5; 15-OAc, 96745-32-3; 15-OH, 96745-33-4; 16-OAc, 96690-24-3; 16-OH, 96690-25-4; 16 (ketone), 96690-26-5; 16-Cl, 96690-32-3; 17-OAc, 96690-27-6; 17-OH, 96690-28-7; 17 (ketone), 96690-29-8; 17-Cl, 96690-31-2; 33, 87637-76-1; 2,3-dimethoxyanthracene, 51790-19-3; vinyl acetate, 108-05-4.

Neighboring Group Participation by Oxygen in the Solvolysis of Acyclic γ-Alkoxy Substituted *p*-Toluenesulfonates

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Methanolysis of branched 3-(benzyloxy)propyl *p*-toluenesulfonates, $PhCH_2OCR^1R^2CR^3R^4CHR^5OTs$ (R^1 = Me, R^2–R^5 = H; R^1 = R^2 = Me, R^3–R^5 = H; R^1 = R^2 = R^5 = Me, R^3 = R^4 = H; R^1 = R^2 = R^4 = R^5 = H, R^3 = Me; R^1 = R^2 = R^5 = H, R^3 = R^4 = Me) proceeds with partial rearrangement, implying neighboring group participation, only when there are geminal methyl groups in the 2- or 3-position (R^3 = R^4 = Me or R^1 = R^2 = Me). Addition of lithium perchlorate enhances the extent of rearrangement. No or negligible anchimeric assistance is manifest either in the absence or in the presence of the salt. Participation thus seems to occur past the transition state. The primary 3-substituted alcohol precursors of the *p*-toluenesulfonates are synthesized by solvomercuration–borohydride reduction of α,β-unsaturated acids followed by reduction with lithium aluminum hydride or diborane; the corresponding secondary alcohol is similarly obtained from 4-methyl-3-penten-2-ol, $(CH_3)_2C{=}CHCHOHCH_3$, by solvomercuration–borohydride reduction.

In a previous paper[2] we presented evidence, from both product and kinetic studies, that whereas the methanolysis of $PhCH_2SCH_2CH_2CH_2OTs$ and $PhCH_2SCH_2CH_2CH$-MeOTs proceeds without neighboring group participation, both rearrangement and anchimeric assistance occur when the tosylate is substituted at the 2- or 3-position with one or more alkyl groups. Moreover, neighboring group participation with rearrangement is found even in the unbranched primary and secondary tosylates shown above when the solvolysis is carried out in 2,2,2-trifluoroethanol, CF_3CH_2OH.

The present study was designed to probe whether similar participation might occur in the corresponding oxygen analogues, $C_6H_5CH_2OC$–C–COTs. RO participation involving five- and six-membered rings has been demonstrated repeatedly in the literature[3] and RO-3 participation is also known,[4] though it occurs less readily than RS-3 participation and apparently only in relatively highly branched compounds. The requirement for branching suggests that a Thorpe–Ingold effect[5,6] is at work, as we had also postulated in RS-4 participation.[2] RO-4 participation, has, to the best of our knowledge, not been demonstrated in acyclic systems but does occur in some cyclic[7] and bicyclic[8] systems where the participating group is located close to the reaction center in space and entropic considerations are therefore favorable.

Table I. Percentage of Rearranged Product in Methanolysis of 3-(Benzyloxy)propyl *p*-Toluenesulfonates

entry	compound	% rearranged product	sulfur series[a]
1	$PhCH_2OCMe_2CH_2CHMeOTs$	45	100
2	$PhCH_2OCMe_2CH_2CH_2OTs$	3.5	100
3	$PhCH_2OCHMeCH_2CH_2OTs$	0	20
4	$PhCH_2OCH_2CMe_2CD_2OTs$	33[b]	50[c]
5	$PhCH_2OCH_2CHMeCHDOTs$	0	12[d]

[a] Corresponding results with S in place of O, from ref 2. [b] This corresponds to 66% cyclic intermediate. [c] This corresponds to 100% cyclic intermediate. [d] This corresponds to 24% cyclic intermediate.

Table II. Methanolysis Rates[a]

entry	compound	k^a	k_{rel}[b]	k_O/k_{model}[c]	k_S/k_{model}[d]
1	$XCHMeCH_2CH_2OTs$	4.71	1	0.67	3.6
2	$XCMe_2CH_2CH_2OTs$	1.91	0.41	0.79	90.7
3	$XCMe_2CH_2CHMeOTs$	39.1	8.3	0.63	8.0

[a] $\times 10^6$ s^{-1} at 60 °C; X = $PhCH_2O$. [b] Relative to $PhCH_2OCHMeCH_2CH_2OTs$. [c] Rates for X = $PhCH_2O$ relative to X = CH_3.[2] [d] Rates for X = $PhCH_2S$ relative to X = CH_3, from ref 2.

Results and Discussion

Product studies in the methanolysis of variously substituted 3-(benzyloxy)propyl *p*-toluenesulfonates are summarized in Table I. Corresponding percentages from the 3-benzylthio series (S in place of O) are given in the last column.

Not unexpectedly the extent of neighboring group participation, as indicated by the extent of rearrangement, is considerably less in the oxygen than in the sulfur series. In fact, the 3-(benzyloxy)propyl compounds rearrange only if there are geminal methyl substituents at the 2- or 3-

(1) Knox, David E. Ph.D. Thesis, University of North Carolina, Aug, 1984.
(2) Eliel, E. L.; Knox, D. E. *J. Am. Chem. Soc.* **1985**, *107*, 2946.
(3) For example: Winstein, S.; Allred, E.; Heck, R.; Glick, R. *Tetrahedron* **1958**, *3*, 1.
(4) Cf. Capon, B.; McManus, S. P. "Neighboring Group Participation"; Plenum Press: New York, 1976; Chapter 4.
(5) Beesley, R. M.; Ingold, C. K.; Thorpe, J. F. *J. Chem. Soc.* **1915**, *107*, 1080. Ingold, C. K. *J. Chem. Soc.* **1921**, *119*, 305.
(6) See also: Eliel, E. L. "Stereochemistry of Carbon Compounds"; McGraw-Hill Book Co., Inc.: New York, 1962; p 197.
(7) Paquette, L. A.; Scott, M. K. *J. Am. Chem. Soc.* **1972**, *94*, 6760.
(8) Gassman, P. G.; Marshall, J. L.; Macmillan, J. G. *J. Am. Chem. Soc.* **1973**, *95*, 6319.

0022-3263/85/1950-2707$01.50/0

positions; a single methyl substituent is insufficient. The relative tendency of oxygen and sulfur participation via four-membered rings thus parallels that involving three-membered rings[4] (RS > RO) and reflects the much greater ease of sulfonium over oxonium ternary salt formation. This, in turn, has been explained[9] in terms of the hard/soft acid/base concept:[10] sulfur, being the softer base, is a better nucleophile toward an organic moiety CX (X = leaving group) which functions as a soft acid.

Because of the very slow solvolysis rates of the 3-(benzyloxy)propyl tosylates, particularly the ones with 2-substituents, kinetic studies were performed for the first three compounds (entries 1–3 in Table I) only. In Table II are given the first-order methanolysis rates of these species, both actual and relative to those of model compounds[2] CH_3C–C–COTs (model for $PhCH_2OC$–C–COTs) and the corresponding relative rates for the sulfur analogues ($PhCH_2SC$–C–COTs).

The fact that the 3-benzyloxy compounds all react slower than the oxygen-free models does not necessarily exclude anchimeric assistance. Unlike in the case of sulfur, which has but a trivial inductive effect from the 3-position,[2] the inductive effect of oxygen in position 3 on solvolysis rate is not negligible; for primary species ($ROCH_2CH_2CH_2X$) it may amount to a factor of 3.[11] If one multiplies the rates relative to the model (column 5, Table II) for the primary tosylates (entries 1, 2) by 3, one obtains numbers in the 2.0–2.5 range. Even if these values are taken at face value, they are too small to imply with any kind of certainty that anchimeric assistance occurs; in fact, taken together with the product data (Table I, entries 2, 3) they rather suggest that anchimeric assistance is absent in entry 1 (Table II) and negligible in entry 2. For the secondary tosylate (entry 3) the situation is not so clear; unfortunately data for $PhCH_2OCH_2CH_2CHMeOTs$ vs. $CH_3CH_2CH_2CHMeOTs$ are not available and it is conceivable that the rate retardation caused by the ether function in the secondary series would outbalance and thereby mask potential anchimeric assistance. However, for reasons to be discussed in the sequel, we consider this unlikely.

In the work on the sulfur analogues[2] we found substantial solvent and salt effects on both product ratio and solvolysis rates. We therefore tested the effect of adding water to the methanol in the solvolysis of $PhCH_2OCMe_2CH_2CH_2OTs$, but the effect was minor: percent rearrangement increased from 3.5% in presumably pure methanol to 6.6% in the presence of 10% water. The effect on product ratio of adding lithium perchlorate to the methanol solvent, on the other hand, was quite large for the 3,3-dimethyl substituted compounds, though negligible for the monomethyl substituted one, as shown in Table III. Table III also displays the effects of added salt on solvolysis rate: no kinetic salt effect is observed.

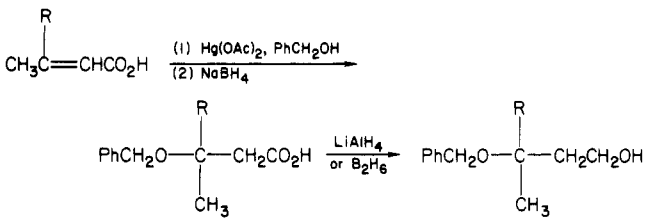
The fact that, in the case of the 3,3-dimethylated compounds (entries 2 and 3), the amount of rearranged product increases appreciably as the salt concentration is increased, whereas there is no significant rate increase, supports the assumption that there is no anchimeric assistance in these reactions, for if there were, reaction rate should increase parallel with the amount of rearrangement. Rather it appears that neighboring group participation occurs *after* the transition state is traversed. The increased amount

Table III. Effect of Added $LiClO_4$ on Product Ratio and Rate

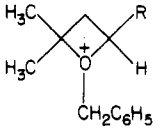
		concentration of added $LiClO_4$[a]			
entry	compound	0	0.001 N	0.050 N	0.10 N
1	$PhCH_2OCHMeCH_2CH_2OTs$	0/4.71	0/[b]	0/[b]	0/[b]
2	$PhCH_2OCMe_2CH_2CH_2OTs$[c]	3.4/1.91	13/1.97	21[d]/2.05	[e]/2.00
3	$PhCH_2OCMe_2CH_2CHMeOTs$	45/39.1	68/38.0	63/43.6	75/43.3

[a] First figure in column is percent rearrangement product, second figure is solvolysis rate $\times 10^6$ in s^{-1} at 60 °C. [b] Not determined. [c] The substantial increase in percent rearranged product upon addition of relatively small amounts of $LiClO_4$ is perhaps surprising. Similarly large effects have been seen with the sulfur analogues[2] and dramatic effects of $LiClO_4$ on ionization of (secondary) tosylates have been reported: Takeuchi, K.; Kato, Y.; Moriyama, T.; Okamoto, K. *Chem. Lett.* **1981**, 935. Nonetheless, the formation of a capturable intermediate in the solvolysis of a primary tosylate is unusual. [d] This figure may be slightly too large since a small amount of an unidentified third product was found in the proton NMR spectrum. [e] The product was mainly rearranged; however, a large amount of a byproduct was formed, possibly at the expense of unrearranged product, so the percentage of rearranged product is not significant.

Scheme I



of rearrangement with increased $LiClO_4$ concentration suggests that either neighboring group participation is enhanced at increased salt concentration or that opening of the cyclic oxetanonium intermediate 1 at the tertiary (as distinct from the primary or secondary) site is enhanced by the salt. This would be reasonable, since opening at the tertiary site is more "S_N1-like" and that at the secondary or primary site more "S_N2-like" and salt effects favor S_N1 over S_N2 reactions.[12] The fact that the increase in amount of rearranged product plateaus in entry 3 after the addition of only 0.001 N salt (which also causes a nearly 4-fold increase in entry 2) might suggest a special salt effect.[13]



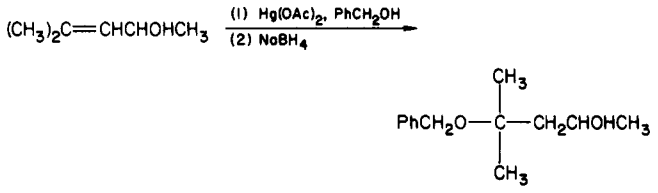
1, R=H or CH_3

Synthesis

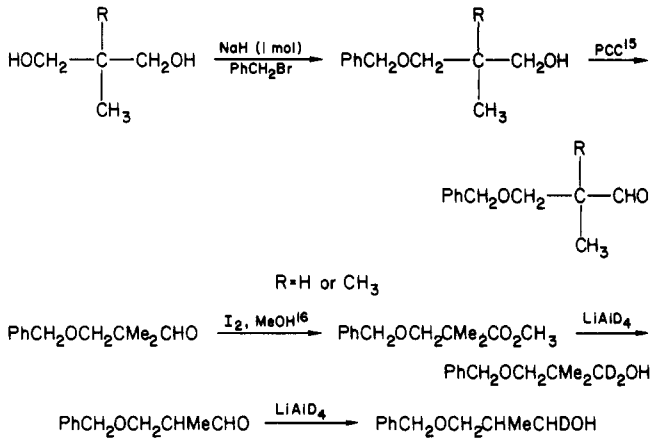
Tosylates were obtained from the precursor alcohols; the 3-substituted alcohols were, in turn, prepared by solvomercuration–reduction.[14] Thus, for the primary alcohols addition of benzyl alcohol to the appropriate α,β-unsaturated acid precursor in the presence of mercury(II) acetate

(9) Cf. Perst, H. "Oxonium Ions in Organic Chemistry"; Academic Press, Inc.: New York, 1971; p 11.
(10) Pearson, R. G. *J. Am. Chem. Soc.* **1963**, *85*, 3533.
(11) Cf. Isaacs, N. S. "Reactive Intermediates in Organic Chemistry"; John Wiley & Sons, Inc.: New York, 1974; p 200.
(12) Cf. Ingold, C. K. "Structure and Mechanism in Organic Chemistry", 2nd ed.; G. Bell & Sons, Ltd.: London, 1969; p 485.
(13) Winstein, S.; Clippinger, E.; Fainberg, A. H.; Robinson, G. C. *J. Am. Chem. Soc.* **1954**, *76*, 2597.
(14) Brown, H. C.; Rei, M.-H. *J. Am. Chem. Soc.* **1969**, *91*, 5646. See also: Carter, H. E.; West, H. D. "Organic Syntheses"; Wiley: New York, 1955; Collect. Vol. III, p 485.

Scheme II



Scheme III



gives an intermediate alkyl mercury species which is cleaved by sodium borohydride to give 3-benzyloxy substituted acids. These acids were reduced to alcohols with lithium aluminum hydride (Scheme I). Solvomercuration–reduction of the α,β-unsaturated ketone, mesityl oxide, on the other hand, was not successful, so the ketone was first reduced to the corresponding alcohol which was then subjected to solvomercuration–reduction (Scheme II). The 2-methyl and 2,2-dimethyl compounds were obtained by monobenzylation of the corresponding diols, $HOCH_2CRMeCH_2OH$ (R = H or Me) followed by tosylation. To obtain labeled compounds in this series, the benzyloxy alcohols ($PhCH_2OCH_2CRMeCH_2OH$) were oxidized to the corresponding aldehydes with pyridinium chlorochromate.[15] In the dimethyl case, (R = Me), the aldehyde was then converted to the methyl ester by the method of Inch;[16] the ester was reduced to the dideuterated alcohol with $LiAlD_4$. For the monomethyl compound attempts at oxidizing the aldehyde to the acid, or using the procedure of Inch to obtain the methyl ester were unsuccessful.[17] The aldehyde was therefore reduced to a monodeuterated alcohol by $LiAlD_4$ (Scheme III).

Authentic unrearranged methyl ethers were prepared by methylation (NaH/CH_3I) of the corresponding alcohols. Authentic rearranged ethers were obtained by substituting methanol for benzyl alcohol in the solvomercuration procedure. Reduction of the acids by $LiAlH_4$ followed by benzylation yielded the desired product. The products of the methanolysis of $PhCH_2OCH_2C(CH_3)_2CD_2OTs$ and $PhCH_2OCH_2CH(CH_3)_3CHDOTs$ were analyzed by ^1H NMR. The ^1H peaks for the 2,2-dimethyl compounds appeared at 3.21 ($PhCH_2OCH_2$) and 3.16 ppm (CH_2OCH_3), respectively. The peaks for the monomethyl compound appeared at 3.33 ($PhCH_2OCH_2$) and 3.20 ppm (CH_2OCH_3), respectively. (Unfortunately, ^2H NMR could not be used in the analysis of these compounds due to overlap of the signals.)

(15) Corey, E. J.; Schmidt, G. *Tetrahedron Lett.* **1979**, 399.
(16) Inch, T. D.; Ley, R. V.; Rich, P. *J. Chem. Soc. C* **1968**, 1693.
(17) The compound eliminates benzyl alcohol when the Inch oxidation[16] is attempted.

Experimental Section

Spectral and other measurements of physical properties were performed as described elsewhere.[2]

3-(Benzyloxy)-3-methylbutanoic Acid. To a vigorously stirred mixture of 9.63 g (30 mmol) of mercuric acetate in 30 mL of benzyl alcohol was added 2.97 g (29.7 mmol) of β,β-dimethylacrylic acid. Stirring was continued overnight; then 30 mL of 3 N sodium hydroxide was added over a 5–10-min period after cooling the flask to 0 °C. This was followed by 30 mL of 0.5 M sodium borohydride in 3 N aqueous NaOH added at a rate to maintain the solution between 0 and 10 °C (3–10 min). The resulting solution was decanted from any precipitated mercury and extracted twice with 75-mL portions of ether to remove excess benzyl alcohol. The aqueous layer was acidified with 10% hydrochloric acid to pH 2 and extracted with six 50-mL portions of ether which were combined, dried over $MgSO_4$, and concentrated, and the residue was distilled: bp 135–145 °C (0.5 torr); yield 2.79 g (45%); ^1H NMR δ 1.15 (s, 6 H), 2.16 (s, 2 H), 4.41 (s, 2 H), 7.14–7.38 (m, 5 H), 10.74 (bs, 1 H).

3-(Benzyloxy)butanoic acid was synthesized similarly from crotonic acid: yield 86%; ^1H NMR δ 1.28 (d, J = 6.5 Hz, 3 H), 2.49 (d of d, J = 5.5, 15 Hz, 1 H), 2.68 (d of d, J = 7.3, 15 Hz, 1 H), 4.00 (sextet, J = 6 Hz, 1 H), 4.54 (AB, J = 10.5 Hz, 2 H), 7.18–7.38 (m, 5 H), 9.90 (bs, 1 H); ^{13}C NMR δ 19.73, 41.76, 70.94, 71.73, 127.70, 127.78, 128.43, 138.19, 177.07.

3-(Benzyloxy)-3-methyl-1-butanol was prepared by standard lithium aluminum hydride reduction of the corresponding acid (vide supra): yield 83%; bp 122–125 °C (0.1 torr); ^1H NMR δ 1.23 (s, 6 H), 1.76 (t, J = 6.8 Hz, 2 H), 3.71 (t, J = 6.8 Hz, 2 H), ca. 3.70 (bs, 1 H), 4.36 (s, 2 H), 7.13–7.32 (m, 5 H); ^{13}C NMR δ 25.35, 42.91, 59.03, 63.78, 75.94, 127.25, 128.29, 139.32 (one aryl peak not resolved).

3-(Benzyloxy)-1-butanol was similarly prepared: yield 91%; bp 109–112 °C (0.1 torr); ^1H NMR (60 MHz) δ 1.14 (d, J = 6.5 Hz, 3 H), 1.70 (q, J = 6 Hz, 2 H), 3.33–3.85 (m, 4 H), 4.37 (d, J = 3 Hz, 2 H), 7.17 (s, 5 H); ^{13}C NMR δ 19.53, 39.208 59.73, 70.38, 73.55, 127.49, 127.61, 128.35, 138.78.

4-(Benzyloxy)-4-methyl-2-pentanol. The precursor of this compound, 4-methyl-3-penten-2-ol was obtained from mesityl oxide by lithium aluminum hydride reduction. The unsaturated alcohol was solvomercurated as described above except that, after borohydride reduction, the product, along with benzyl alcohol, was extracted with six 75-mL portions of ether which were combined, dried ($MgSO_4$), and concentrated. The residue was fractionally distilled with benzyl alcohol coming over in the first fraction. The main product boiled at 132–135 °C (0.1 torr): yield 53%; ^1H NMR δ 1.15 (d, J = 6.8 Hz, 3 H), 1.30 (s, 3 H), 1.37 (s, 3 H), 1.84 (d of d, J = 9.8, 15.4 Hz, 2 H), 4.10–4.29 (m, 2 H), 4.46 (d, J = 1.9 Hz, 2 H), 7.20–7.36 (m, 5 H).

The following *p*-toluenesulfonates were prepared from the corresponding alcohols by the standard procedure.[18]

3-(Benzyloxy)-3-methyl-1-butyl *p*-toluenesulfonate: yield 83%; ^1H NMR (60 MHz) δ 1.23 (s, 6 H), 1.96 (t, J = 6.5 Hz, 2 H), 2.40 (s, 3 H), 4.18 (t, J = 6.5 Hz, 2 H), 4.30 (s, 2 H), 7.19–7.42 (AA'BB' pattern + singlet, J = 5 Hz, 9 H). Anal. Calcd for $C_{19}H_{24}O_4$: C, 65.48; H, 6.96. Found: C, 65.29; H, 6.95.

3-(Benzyloxy)-1-butyl *p*-toluenesulfonate: yield 62%; ^1H NMR δ 1.16 (d, J = 6 Hz, 3 H), 1.81 (q, J = 6 Hz, 2 H), 2.38 (s, 3 H), 3.62 (sextet, J = 6.1 Hz, 1 H), 4.15 (m, 2 H), 4.25 (d, J = 8.6 Hz, 1 H), 4.26 (d, J = 8.6 Hz, 1 H), 7.16–7.82 (AA'BB' pattern + multiplet, J = 4.9 Hz, 9 H); ^{13}C NMR δ 19.50, 21.52, 36.21, 67.60, 70.57, 71.05, 125.55, 127.88, 128.32, 129.83, 133.29, 138.60, 144.70. Anal. Calcd for $C_{18}H_{22}O_4S$: C, 64.64; H, 6.64. Found: C, 64.88; H, 6.72.

4-(Benzyloxy)-4-methyl-2-pentyl *p*-toluenesulfonate: yield 63%; ^1H NMR δ 1.18 (s, 6 H), 1.31 (d, J = 5.5 Hz, 2 H), 1.88 (q of d, J = 5.5, 15 Hz, 2 H), 2.34 (s, 3 H), 4.32 (s, 2 H), 4.94 (sextet, J = 5.5 Hz, 1 H), 7.14–7.80 (AA'BB' pattern + multiplet, J = 5.8 Hz, 9 H); ^{13}C NMR δ 21.49, 22.71, 24.89, 26.53, 47.82, 63.59, 73.91, 78.03, 127.13, 127.16, 127.68, 129.71, 134.90, 139.54, 144.39.

Authentic Methyl Ether Products. Authentic, unrearranged, methyl ether products were prepared via methylation of

(18) Fieser, L. F.; Fieser, M. "Reagents for Organic Synthesis"; Wiley: New York, 1967; Vol. 1, p 1180.

the starting alcohols.[19] Rearranged ether products were prepared via a solvomercuration procedure (using methanol) of the precursor acids, or mesityl alcohol, similarly as described above. The acids were converted to alcohols via $LiAlH_4$ reduction as described. The alcohols were then benzylated in a Williamson synthesis by using benzyl bromide. The following compounds were prepared in this fashion.

3-(Benzyloxy)-3-methyl-1-butyl methyl ether: yield 78%; bp 121–139 °C (0.19 torr); ^{1}H NMR δ 1.29 (s, 6 H), 1.90 (t, J = 7 Hz, 2 H), 3.33 (s, 3 H), 3.53 (t, J = 7 Hz, 2 H), 4.43 (s, 2 H), 7.18–7.38 (m, 5 H); ^{13}C NMR δ 26.00, 40.00, 58.52, 63.70, 74.35, 127.11, 127.25, 128.25, 139.81.

3-(Benzyloxy)-1-butyl methyl ether: yield 49%; bp 107–115 °C (0.1 torr); ^{1}H NMR δ 1.20 (d, J = 6 Hz, 3 H), 1.61–1.89 (m, 2 H), 3.26 (s, 3 H), 3.46 (sextet, J = 6 Hz, 2 H), 3.67 (sextet, J = 6 Hz, 1 H), 4.50 (AB, J = 12 Hz, 2 H), 7.18–7.36 (m, 5 H); ^{13}C NMR δ 19.85, 37.00, 58.50, 69.46, 70.55, 72.26, 127.40, 127.64, 128.31, 139.22.

4-(Benzyloxy)-2-methyl-2-pentyl methyl ether: yield 55%; bp 139–144 °C (0.1 torr); ^{1}H NMR δ 1.19 (s, 3 H), 1.21 (s, 3 H), 1.26 (d, J = 6 Hz, 3 H), 1.64 (d of d, J = 4 Hz, 1 H), 1.85 (d of d, J = 6.5, 14 Hz, 1 H), 3.18 (s, 3 H), 3.75 (m, 1 H), 4.47 (AB, J = 11 Hz, 2 H), 7.2–7.38 (m, 5 H); ^{13}C NMR (25.2 MHz) δ 21.16, 25.32, 26.12, 47.52, 49.32, 70.80, 72.60, 74.52, 128.00, 128.48, 129.08, 139.76.

3-Methoxy-3-methyl-1-butyl benzyl ether: yield 55%; bp 124–132 °C (0.2 torr); ^{1}H NMR δ 1.16 (s, 6 H), 1.84 (t, J = 6 Hz, 2 H), 3.15 (s, 3 H), 3.56 (t, J = 6 Hz, 2 H), 4.47 (s, 2 H), 7.18–7.39 (m, 5 H); ^{13}C NMR δ 25.35, 39.35, 49.05, 66.73, 72.08, 72.99, 127.43, 127.55, 128.31, 138.66.

4-Methoxy-2-methyl-2-pentyl benzyl ether: yield 84%; bp 131–142 °C (0.1 torr); ^{1}H NMR δ 1.18 (d, J = 6.4 Hz, 3 H), 1.29 (s, 3 H), 1.31 (s, 3 H), 1.68 (d of d, J = 3.8, 13.9 Hz, 1 H), 1.83 (d of d, J = 6.8, 13.9 Hz, 1 H), 3.29 (s, 3 H), 3958 (m, 1 H), 4.45 (AB, J = 10.9 Hz, 2 H), 7.17–7.38 (m, 5 H); ^{13}C NMR (25.2 MHz) δ 20.44, 25.60, 26.80, 48.20, 55.80, 64.04, 74.28, 75.12, 127.68, 127.96, 128.96, 140.76.

3-(Benzyloxy)-2-methyl-1-propanol. 2-Methyl-1,3-propanediol (10 g, 0.11 mole) in 50 mL of THF was added dropwise to a suspension of NaH (5.3 g as a 50% oil dispersion, washed with pentane, 0.11 mol of active hydride) in 100 mL of THF. The reaction mixture was refluxed for 1 h to insure complete formation of the alkoxide, then benzyl bromide (19.8 g, 0.12 mol) was added and refluxing continued for 16 h. Water (10 mL) was added followed by removal of THF at reduced pressure. The residue was taken up in 200 mL of ether, the water layer separated, and the ether layer dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was vacuum distilled to yield precursor diol, benzyl bromide, and product, leaving a residual solid whose ^{1}H NMR spectrum was consistent with that of a bis benzylated species. Yield of monobenzyl ether 9.7 g (49%); bp 120–122 °C (0.2 torr) (lit.[20] 78 °C (0.06 torr); ^{1}H NMR (100 MHz) δ 0.88 (d, J = 7.4 Hz, 2 H), 2.0 (sextet, J = 7.4 Hz, 1 H), 3.04 (bs, 1 H), 3.36–3.68 (overlapping multiplets, 4 H), 4.48 (s, 2 H), 7.31 (s, 5 H) (lit.[21] 0.89, 4.51 ppm); ^{13}C NMR (25.2 MHz) δ 13.64, 35.88, 66.88, 73.35, 74.70, 127.56, 127.62, 128.41, 138.36.

3-(Benzyloxy)-2,2-dimethyl-1-propanol was prepared analogously to the monomethyl compound above: yield 11.5 g (54%); bp 129–132 °C (0.2 torr); ^{1}H NMR δ 0.92 (s, 6 H), 2.84 (bs, 1 H) 3.30 (s, 2 H), 3.44 (s, 2 H), 4.49 (s, 2 H), 7.30 (m, 5 H); ^{13}C NMR δ 21.87, 36.36, 71.36, 73.61, 79.13, 125.50, 127.65, 128.44, 138.39. Anal. Calcd for $C_{12}H_{18}O_2$: C, 74.19; H, 9.34. Found: C, 73.98; H, 9.30.

3-(Benzyloxy)-2-methylpropanal.[15,21] 3-(Benzyloxy)-2-methylpropanol (1.5 g, 8.3 mmol) dissolved in 3 mL of dry CH_2Cl_2 was added all at once to pyridinium chlorochromate (3.6 g, 16.7 mmol) and 0.25 g of anhydrous sodium acetate suspended in an additional 12 mL of dry CH_2Cl_2. The solution turned dark after about 10 s. It was refluxed for 2 h and then stirred overnight. Ether (50 mL) was then added and the brown precipitate filtered by successively passing the solution through a 50/50 $MgSO_4$/Celite pad and through a $^1/_4$ inch pad of silica. The ether layer was washed with 10 mL of saturated NaCl solution, dried over $MgSO_4$, and filtered, the solvent removed, and the resulting oil distilled to give 630 mg (43%) of aldehyde: bp 128–131 °C (0.3 torr); ^{1}H NMR δ 1.09 (d, J = 7.2 Hz, 3 H), 2.60 (m, 1 H), 3.59 (s, 1 H), 3.62 (d, J = 1.4 Hz, 1 H), 4.48 (s, 2 H), 7.29 (s, 5 H), 9.68 (d, J = 1.8 Hz, 1 H).

3-(Benzyloxy)-2,2-dimethylpropanal was prepared in a fashion similar to the monomethyl analogue above, except that the initial boiling period was 10 h and the solution was stirred for an additional 16 h at room temperature prior to workup: yield 3.6 g (54%); ^{1}H NMR δ 0.98 (s, 6 H), 3.32 (s, 2 H), 4.36 (s, 2 H), 7.15 (s, 5 H), 9.38 (s, 1 H).

Methyl 3-(benzyloxy)-2,2-dimethylpropionate was prepared according to the method of Inch:[16] yield 0.78 g (67%); bp 161–169 °C (0.5 torr); ^{1}H NMR δ 1.20 (s, 6 H), 3.43 (s, 2 H), 3.65 (s, 3 H), 4.49 (s, 2 H), 7.20–7.38 (m, 5 H); ^{13}C NMR δ 22.50, 43.73, 52.74, 73.33, 77.06, 127.44, 128.32, 138.60, 176.79 (one aryl peak is not resolved). Anal. Calcd for $C_{13}H_{18}O_3$: C, 70.23; H, 8.18. Found: C, 70.47; H, 8.36.

3-(Benzyloxy)-2-methyl-1-propanol-*1*-*d* and 3-(benzyloxy)-2,2-dimethyl-1-propanol-*1*,*1*-d_2 were synthesized by lithium aluminum deuteride reduction of the above aldehyde and ester, respectively.

3-(Benzyloxy)-2-methylpropyl *p*-toluenesulfonate[18] and its 1-deuterio analogue were prepared[18] in 72% yield. Protio compound: ^{1}H NMR δ 0.89 (d, J = 7.0 Hz, 3 H), 2.06 (quintet, J = 5.5 Hz, 1 H), 2.33 (s, 3 H), 3.28 (m, 2 H), 3.98 (d of d, J = 5, 15 Hz, 1 H), 4.34 (s, 2 H), 7.14–7.34 (AA'BB' pattern + multiples, J = 9 Hz, 9 H). Deuterio compound: ^{2}H NMR δ 3.98.

3-(Benzyloxy)-2,2-dimethylpropyl *p*-toluenesulfonate and its 1,1-dideuterio analogues were prepared[18] in 38% yield: ^{1}H NMR δ 0.91 (s, 6 H), 2.39 (s, 3 H), 3.16 (s, 2 H), 4.12 (s, 2 H), 4.37 (s, 2 H), 7.16–7.38 and 7.76 (AA'BB' pattern + multiplet, J = 8.5 Hz, 9 H). Deuterio compound: ^{2}H NMR δ 4.12.

3-Methoxy-2-methylpropyl benzyl ether was synthesized from the alcohol by Williamson's method[18] in 77% yield: bp 111–119 °C (0.1 torr); ^{1}H NMR δ 0.96 (d, J = 8.5 Hz, 3 H), 2.05 (sextet, J = 6.5 Hz, 1 H), 3.20–3.46 (overlapping multiplets, 7 H), 4.47 (s, 2 H), 7.30 (m, 5 H); ^{13}C NMR δ 14.47, 34.33, 58.84, 72.94, 73.15, 75.43, 127.47, 127.53, 128.35, 138.90.

3-Methoxy-2,2-dimethylpropyl benzyl ether was similarly synthesized from the corresponding alcohol in 52% yield: bp 120–131 °C (0.1 torr); ^{1}H NMR δ 0.92 (s, 6 H), 3.16 (s, 2 H), 3.21 (s, 2 H), 3.28 (s, 3 H), 4.46 (s, 2 H), 7.26 (m, 5 H); ^{13}C NMR δ 22.26, 36.33, 59.23, 73.27, 76.58, 79.25, 127.32, 127.56, 128.26, 139.18. Anal. Calcd for $C_{13}H_{20}O_2$: C, 74.94; H, 9.70. Found: C, 75.08; H, 9.68.

Preparative Solvolysis Reactions. The methanolysis of 4-(benzyloxy)-4-methyl-2-pentyl *p*-toluenesulfonate is described as representative. A solution of 0.5 g (1.3 mmol) of the tosylate in 25 mL of methanol containing 0.109 g (1.3 mmol) of sodium bicarbonate in suspension was heated under reflux for one week. The methanol was removed under reduced pressure, water was added, and the aqueous suspension was extracted with three 20-mL portions of ether which were combined, dried ($MgSO_4$), and concentrated. The residue was distilled in a Kugelrohr at 110–130 °C (0.5 torr), yield 0.24 g (89%). Analysis was effected by ^{1}H and ^{13}C NMR spectroscopy (cf. Table I).

Kinetics. The kinetic studies were performed as previously described.[2]

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Registry No. $PhCH_2OCMe_2CH_2CHMeOTs$, 96556-27-3; $PhCH_2OCMe_2CH_2CH_2OTs$, 96556-28-4; $PhCH_2OCHMeCH_2CH_2OTs$, 96556-29-5; $PhCH_2OCH_2CMe_2CD_2OTs$, 96556-30-8; $PhCH_2OCH_2CHMeCHDOTs$, 96556-31-9; 3-(benzyloxy)-3-methylbutanoic acid, 96556-32-0; β,β-dimethylacrylic acid, 541-47-9; 3-(benzyloxy)butanoic acid, 1135-38-2; crotonic acid, 3724-65-0; 3-(benzyloxy)-3-methyl-1-butanol, 96556-33-1; 3-(benzyloxy)-1-butanol, 52657-84-8; 4-(benzyloxy)-4-methyl-2-pentanol, 96556-34-2; 3-(benzyloxy)-3-methyl-1-butyl methyl ether,

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96556-35-3; 3-(benzyloxy)-1-butyl methyl ether, 96556-36-4; 4-(benzyloxy)-2-methyl-2-pentyl methyl ether, 96556-37-5; 3-methoxy-3-methyl-1-butyl benzyl ether, 96556-38-6; 4-methoxy-2-methyl-2-pentyl benzyl ether, 96556-39-7; 3-(benzyloxy)-2-methyl-1-propanol, 56850-59-0; 2-methyl-1,3-propanediol, 2163-42-0; 3-(benzyloxy)-2,2-dimethyl-1-propanol, 66582-32-9; 3-(benzyloxy)-2-methylpropanol, 73814-73-0; 3-(benzyloxy)-2,2-dimethylpropanal, 38216-93-2; mehyl 3-(benzyloxy)-2,2-dimethylpropionate, 96556-40-0; 3-(benzyloxy)-2-methyl-1-propanol-*1-d*, 96556-41-1; 3-(benzyloxy)-2,2-dimethyl-1-propanol-*1,1-d*$_2$, 96556-44-4; 3-(benzyloxy)-2-methylpropyl *p*-toluenesulfonate, 96556-45-5; 3-(benzyloxy)-2,2-dimethylpropyl *p*-toluenesulfonate, 96556-46-6; 3-methoxy-2-methylpropyl benzyl ether, 96556-42-2; 3-methoxy-2,2-dimethylpropyl benzyl ether, 96556-43-3.

Steric Effects on Hydrogen Bonding of 4-Nitro-2,6-diarylphenols with Bases

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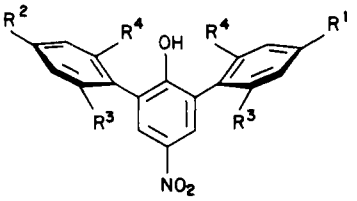
The thermodynamics of hydrogen bonding of 4-nitro-2,6-diarylphenols with a variety of proton acceptor bases have been studied by examining the hydroxyl stretching IR absorption spectra in CCl_4 solution. Their IR spectra show the existence of competitive interaction between intramolecular OH···π and intermolecular OH···B (B = base) hydrogen bonding. For the intermolecular OH···B hydrogen bond formation, the ^{1}H NMR study suggests that the hydroxyl group is approximately coplanar with the phenol ring, even in these sterically hindered phenols. The variation of the thermodynamic parameters caused by the steric effects can be well understood on the basis of this model. The steric effects on the hydrogen bond formation are found to affect not only the enthalpy but also the entropy changes. In the correlation between $-\Delta H$ and $-\Delta S$ values, anomalous behavior is observed for hydrogen bonding with Me_2SO.

There is little thermodynamic data available on hydrogen bonding between sterically hindered phenols and bases, in contrast to the extensive investigations of simple hydrogen bonded systems.[1] As to steric effects on hydrogen bonding, some discrepancies have appeared in the literature. Singh and Rao[2] reported that the enthalpies of hydrogen bonding are nearly equal for both unhindered and hindered systems. On the other hand, Yoshida and Ishibe[3] found that the steric effects on hydrogen bonding could influence not only the enthalpy but also the entropy factors. In most studies of the hindered hydrogen bonded systems, 2,6-dialkylphenols (like 2,6-dimethyl-[3] or 2,6-di-*tert*-butylphenols[2]) were used to investigate the steric effects on the hydrogen bonding. For this study, we have selected 4-nitro-2,6-diarylphenols[4] **1**–**6** in which the steric



1, $R^1 = R^2 = R^3 = R^4 = H$
2, $R^1 = R^2 = CH_3$; $R^3 = R^4 = H$
3, $R^1 = R^2 = C(CH_3)_3$; $R^3 = R^4 = H$
4, $R^1 = R^2 = H$; $R^3 = CH_3$; $R^4 = H$
5, $R^1 = R^2 = H$; $R^3 = R^4 = CH_3$
6, $R^1 = C(CH_3)_3$; $R^2 = R^3 = R^4 = H$

effects seem to be more serious than 2,6-dialkylphenols; the IR spectra of these phenols indicate a single hydroxyl stretching band (without a free OH band) due to an intramolecular OH···π bond in CCl_4 solution.[5,6]

In this paper, the thermodynamic values, $-\Delta G$, $-\Delta H$, and $-\Delta S$, for the competitive interaction between the intramolecular OH···π and the intermolecular OH···B (B = base) hydrogen bonding were determined by the use of IR spectroscopy. The steric effects on these hindered hydrogen bonds are discussed in relation to the variation of the thermodynamic values obtained. The probable geometry for these hydrogen bonded systems is deduced roughly on the basis of the results of the steric effects and of their ^{1}H NMR spectra. The thermodynamic values obtained for the hindered systems are used to test the correlations of $-\Delta H$ vs. $-\Delta S$ and $-\Delta H$ vs. $\Delta\nu$ [ν(OH···π) − ν(OH···B)].

Experimental Section

Materials. Most of the solvents were spectrograde reagents and were distilled from calcium hydride immediately before use. Cyclohexanone and benzonitrile were purified by a known method.[7] Compounds **1**–**4** were prepared as previously.[6]

4-Nitro-2,6-bis(2′,6′-dimethylphenyl)phenol (5). 1-Methoxy-2,6-diiodo-4-nitrobenzene[8] (3 g, 7.4 mmol), 2,6-dimethylbromobenzene (6.8 g, 37 mmol), and copper bronze (15 g) were mixed and heated at 180 °C for 1–2 h; after the reaction set in, the temperature was then raised to 250 °C. The reaction mixture was cooled to room temperature and extracted with acetone. The extract was concentrated and chromatographed on a silica gel column to give the crude product of 1-methoxy-2,6-bis(2′,6′-dimethylphenyl)-4-nitrobenzene, which was used in the following demethylation without further purification. To a solution of the crude anisole derivative (0.32 g) in acetic acid (10 mL), aqueous hydrogen bromide (10 mL, 47%) and acetic anhydride (2 mL) were added, after which the mixture was heated for 6 h. The mixture was then poured onto ice water and extracted with chloroform. The recrystallization of the acidic part from CCl_4–hexane gave 0.22 g of **5**: mp 180–182 °C; ^{1}H NMR ($CDCl_3$) δ 2.06 (s, 12 H), 5.17 (s, 1 H), 7.08–7.20 (m, 6 H), 8.01 (s, 2 H). Anal. Calcd for $C_{22}H_{21}O_3N$: C, 76.06; H, 6.09; N, 4.03. Found: C, 76.11; H, 6.13; N, 4.01.

4-Nitro-2-phenyl-6-(4′-*tert*-butylphenyl)phenol (6). This phenol was formed as a byproduct (ca. 5%) in the preparation

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