Neighboring Group Participation in the Conversion of β-Substituted Ethanesulfonate Salts to β-Substituted Ethanesulfonyl Chlorides

Samuel P. McManus,* Maurice R. Smith, and Frederick T. Herrmann

Department of Chemistry, The University of Alabama in Huntsville, Huntsville, Alabama 35807

Rudolph A. Abramovitch[1]

Department of Chemistry, The University of Alabama, University, Alabama 35486

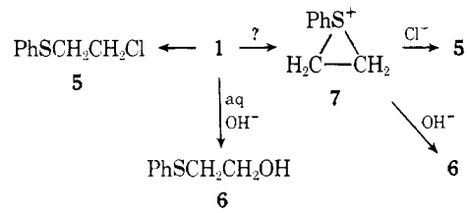
Received August 2, 1977

Reaction of the sulfonate **1** with either PCl_5, $POCl_3$, or $SOCl_2$ proceeds with desulfonation to give chloride **5** rather than the expected sulfonyl chloride **2**. This is in contrast to the results from similar reactions with the analogous β-substituted sulfonates containing neighboring bromine, oxygen, and sulfone groups which give the sulfonyl chlorides, e.g., **3**, **4**, and **9**, respectively. When **10** is reacted with $SOCl_2$, desulfonation occurs and a 60% distilled yield of a 41:59 mixture of the isomeric chlorides **15** and **16**, respectively, is obtained. One may infer that the sulfonium ion **11** is the intermediate which leads to **15** and **16**. Desulfonation of **1** also occurs in poor yield upon prolonged boiling in aqueous sodium hydroxide.

In connection with other studies, we attempted to convert the sulfonate **1** to the sulfonyl chloride **2** using reactions and conditions previously employed to successfully prepare similar β-substituted ethanesulfonyl chlorides, e.g., **3** and **4**.[2,3] However, the only product obtained upon treatment of **1** with either phosphorus pentachloride, phosphorus oxychloride, or thionyl chloride was **5**, the product of desulfonation.[4] Furthermore, upon heating **1** to reflux in aqueous sodium hydroxide, desulfonation occurred, giving the alcohol **6** in poor yield.

$PhSCH_2CH_2SO_3^-Na^+$ (1) $\quad PhSCH_2CH_2SO_2Cl$ (2)

$BrCH_2CH_2SO_2Cl$ (3) $\quad PhOCh_2CH_2SO_2Cl$ (4)



Since the driving force for neighboring-group participation is known to be greater for sulfur than for oxygen or bromine,[5,6] we suspected involvement by the β-phenylthio group and intermediacy of the sulfonium ion **7** in the desulfonation reactions of **1**.

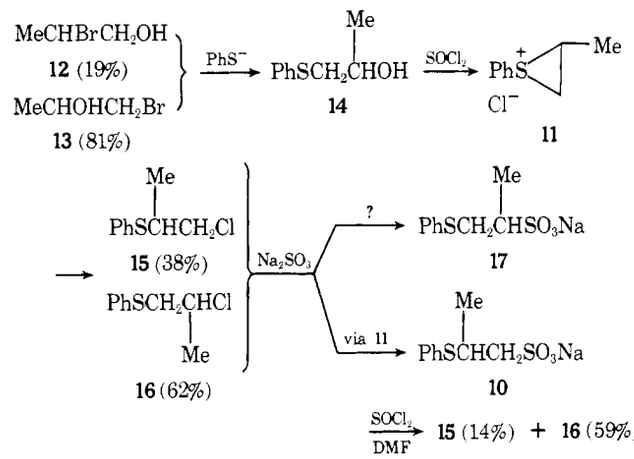
If nucleophilic participation by sulfur is occurring during the chlorination reaction of **1**, this participation should be absent in the chlorination of the corresponding sulfone. When **8** was subjected to the chlorination procedure, no abnormality in its conversion to **9** was observed.

$$PhSO_2CH_2CH_2SO_3^-Na^+ \xrightarrow{SOCl_2} PhSO_2CH_2CH_2SO_2Cl$$
8 **9**

To ascertain whether or not the sulfonium ion **7** is an intermediate in the reactions of **1** discussed above, it was decided to subject the sulfonate **10** to the chlorination reaction. The sulfonate **10**, which would provide an unsymmetrical cyclic sulfonium ion, i.e., **11**, was prepared according to the sequence of reactions shown in Scheme I.[7]

Reaction of thiophenoxide with the commercially available mixture of bromohydrins **12** and **13** afforded a single β-phenylthio alcohol **14** (see Experimental Section) owing to the greater relative reactivity of the primary bromide **13**.[8,9]

Scheme I



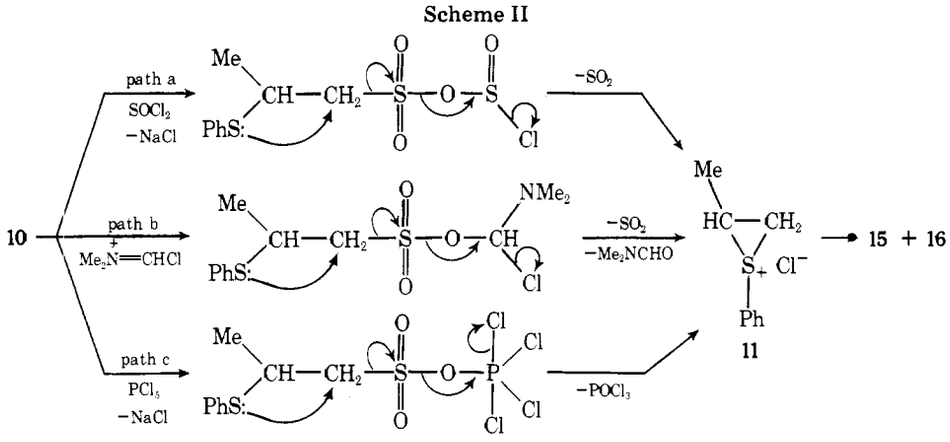
Chlorination of the secondary alcohol **14** proceeded, not unexpectedly,[6,10] with sulfur participation and gave a mixture of the chlorides **15** and **16** from ring opening of the sulfonium ion **11**.

Mueller and Butler[11] have shown that in methylene chloride at −75 °C the sulfonium ion **11** undergoes attack by chloride ion to give a 68:32 mixture of **15** and **16**, respectively. On standing at ambient temperature, the mixture of **15** and **16** equilibrated, presumably via **11**, giving a **15**/**16** ratio of 15:85. Thus, **15** is favored kinetically, while **16** is thermodynamically the more stable. Although the mixture of **15** and **16** which formed from **14** cannot be directly compared to the Mueller–Butler results, it seems reasonable to assume that the **15**:**16** ratio is approaching the thermodynamic composition for the conditions employed.

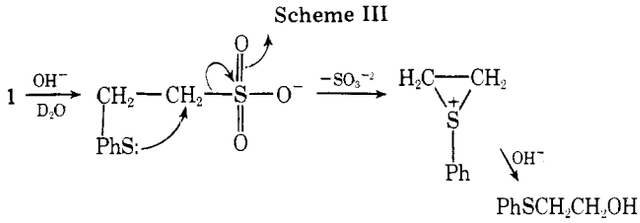
Reaction of the mixture of chlorides **15** and **16** with sodium sulfite allowed the isolation of the sodium sulfonate salt, which is assigned structure **10** on the assumption that it is formed in a kinetically controlled process from **11**.[12-14] Analysis of the sodium sulfonate salt by TLC on silica gel and on neutral alumina revealed a single spot, although a shoulder on the methyl doublet in the NMR spectrum suggests the possibility of 10–15% of the isomer **17**. Upon refluxing a dry benzene suspension of **10** with an excess of thionyl chloride and a catalytic amount of dimethylformamide,[15] concentrating in vacuo, and distilling the residue, a 60% yield of a 41:59 mixture of the chlorides **15** and **16**, respectively, was obtained. This ratio of the chlorides is similar to that obtained on conversion of **14** to **15** and **16**, further suggesting the approach to equilibrium.

0022-3263/78/1943-0647$01.00/0

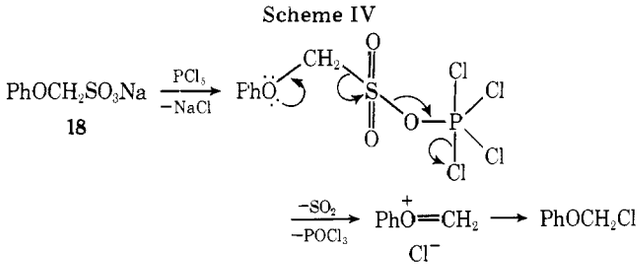
Scheme II



Scheme III



Scheme IV



It is interesting to consider possible mechanisms for the sulfite group-displacement reactions. The sulfonate group is known to be an excellent nucleophile,[16] but neither it nor the chlorosulfonyl group is generally treated among common leaving groups.[17] Since the sulfite group would presumably need activation for displacement in benzene, path a in Scheme II represents a mechanism which is consistent with the experimental data and is similar to the mechanism for other displacement reactions involving thionyl chloride.[18] Paths b and c are similar pathways for the Zollinger reagent[15] and phosphorus pentachloride.[19]

Because of the greatly different reaction conditions, the sluggish displacement of the sulfite group from **1** by hydroxide ion most likely involves the loss of the solvated sulfite group with no SO_2 evolution, Scheme III. The forcing conditions and the aqueous medium make loss of sulfite a relatively more facile process than the loss of sulfite ion (as SO_3^{-2}) from **10** with thionyl chloride in benzene.

Although there is no other known example of β participation in a desulfonation reaction, an apparently analogous reaction occurs on attempted chlorination of aryloxymethanesulfonic acids or their salts.[20] The parent salt **18**, for example, reacts readily with phosphorus pentachloride or thionyl chloride at room temperature and sulfur dioxide is eliminated. The probable driving force for this reaction is formation of the resonance-stabilized intermediate (Scheme IV).

Participation by the thioether group in these desulfonation reactions is, thus, additional evidence of this group's superiority relative to other similar neighboring groups when three-membered ring formation is involved.[5,6] Although we did not explore the conversion of the nitrogen derivative analogous to **1**, it seems likely, based on the relatively high tendency for nitrogen participation,[5,6] that it might undergo desulfonation upon chlorination.

Experimental Section

Melting points are uncorrected. Infrared spectra were determined on a Beckman Acculab I spectrometer, the NMR spectra on a Bruker HFX-10 90-MHz spectrometer using tetramethylsilane as an internal standard, and the refractive indexes on a Bausch and Lomb Abbe 3L refractometer. Elemental analyses were determined either by the Analytical Services Laboratory of the Department of Chemistry, The University of Alabama, Tuscaloosa, or by Galbraith Laboratories, Inc., Knoxville, Tenn.

Sodium 2-Phenylthioethanesulfonate (1). 2-Phenylthioethyl chloride[21] (100 g, 0.579 mol) was added to anhydrous sodium sulfite (100 g, 1.26 mol) in water (750 mL). The solution was boiled under reflux for 48 h and then cooled to room temperature to yield white platelets of the salt (125 g, 90.0%): mp >260 °C; IR (KBr) 1180 (γ_{as} SO_2), 1045 cm^{-1} (γ_{sym} SO_2); NMR (D_2O), δ 7.56 (m, 5 H, ArH), 3.52 (m, 4 H, SCH_2CH_2)

Anal. Calcd for $C_8H_9NaO_3S_2$: C, 40.00; H, 3.78. Found: C, 40.13; H, 3.90.

Reaction of Sodium 2-Phenylthioethanesulfonate (1) with Phosphorus Pentachloride. Phosphorus pentachloride (15 g, 72 mmol) was ground with **1** (22.5 g, 93.7 mmol) in a mortar. The solid reacted after a few seconds with gas evolution to yield a pasty liquid, which was poured into water (400 mL) and extracted with chloroform (3 × 70 mL). The organic layer was washed with sodium bicarbonate (5%, 3 × 100 mL) and water (2 × 150 mL), dried ($MgSO_4$), and concentrated in vacuo to leave a yellow oil that was distilled to yield 2-phenylthioethyl chloride (**5**) (12.5 g, 77.3%) which was identical with a sample prepared by the method of Ford-Moore et al.:[21] bp 95–97 °C (2 mm); $n^{21}D$ 1.5837; IR (film) 3060, 3010, 2970, 1580, 1475, 1435, 1370, 1295, 1270, 1205, 1160, 1115, 1080, 1060, 1020, 990, 850, 725, and 675 cm^{-1}; NMR ($CDCl_3$) δ 7.43 (m, 5 H, ArH), 3.67 (m, 2 H, CH_2Cl), 3.21 (m, 2 H, SCH_2).

In a separate experiment the phosphorus pentachloride was replaced by thionyl chloride in benzene with dimethylformamide as a catalyst;[15c] after a 24-h reflux period, **1** was converted to **5** in 13% yield.

Phenyl 2-Chloroethyl Sulfone. 2-Phenylthioethyl chloride[21] (8.50 g, 49.2 mmol) was added in one portion to glacial acetic acid (35 mL) containing 30% hydrogen peroxide (15 mL) and boiled under reflux for 0.5 h. Cold water (150 mL) was added to the reaction mixture to yield white platelets of the sulfone (6.00 g, 59.6%): mp 52 °C (from ethanol) (lit.[21] mp 52 °C); IR (KBr) 1315 (γ_{as} SO_2), 1140 cm^{-1} (γ_{sym} SO_2).

Sodium 2-Phenylsulfonylethanesulfonate (8). Phenyl 2-chloroethyl sulfone (5.00 g, 24.4 mmol) was boiled under reflux for 12 h with anhydrous sodium sulfite (6.20 g, 48.8 mmol) in water (40 mL). The reaction mixture was filtered and cooled to yield white crystals of the salt (6.60 g, 99.2%): mp >250 °C; IR (KBr) 1285 (γ_{as} SO_2), 1175 (γ_{as} SO_3Na), 1140 (γ_{sym} SO_2), 1030 cm^{-1} (γ_{sym} SO_3Na); NMR (D_2O) δ 7.56 (m, 5 H, ArH), 3.52 (m, 4 H, $CH_2CH_2SO_3Na$). The salt was used to prepare **9** without further purification.

2-Phenylsulfonylethanesulfonyl Chloride (9). Thionyl chloride (19.9 g, 167 mmol) was added dropwise to sodium 2-phenylsulfonylethanesulfonate (5.00 g, 18.4 mmol) in benzene (100 mL) containing dimethylformamide (10 drops) over a 1-h period. The solution was boiled under reflux for 14 h and then evaporated to dryness in vacuo.

The crude product was recrystallized three times from chloroform to yield white needles of the sulfonyl chloride (2.76 g, 55.8%): mp 173 °C; IR (KBr) 1405 (γ_{as} SO_2Cl), 1350 (γ_{as} SO_2), 1215 (γ_{sym} SO_2Cl), 1135 cm^{-1} (γ_{sym} SO_2); NMR ($CDCl_3$) δ 7.87 (m, 5 H, ArH), 4.07 (m, 2 H, $CH_2CH_2SO_2Cl$), 3.72 (m, 2 H, $CH_2CH_2SO_2Cl$).

Anal. Calcd for $C_8H_9ClO_4S_2$ C, 35.76; H, 3.38. Found: C, 35.99; H, 3.33.

Hydrolysis of (1). Compound 1 (10.0 g, 41.7 mmol) was added to sodium hydroxide (2.50 g, 62.5 mmol) in water (20 mL) at 90 °C and stirred at that temperature for 48 h. The reaction mixture was cooled to 5 °C and the white precipitate was recrystallized from acetone to give 1 (1.08 g) identical (IR spectrum) with starting material. Water (150 mL) was added to the above liquor, and the solution was acidified (6 N HCl) and extracted with ether (7 × 50 mL). The extract was dried ($MgSO_4$) and concentrated in vacuo to yield an oil, identified by comparison of its IR and GLC retention time (6 ft × 0.25 in. column of 10% OV-17 on Gas Chrom Q, 225 °C) with an authentic sample, as 2-phenylthioethanol (1.25 g, 19.5%).

1-Phenylthio-2-propanol (14). A 19:81 mixture of 2-bromo-1-propanol **12** and 1-bromo-2-propanol **13,** respectively (Eastman Yellow Label) (65.3 g, 470 mmol), was added dropwise to a solution of thiophenol (51.7 g, 470 mmol) and sodium hydroxide (19.0 g, 475 mmol) in water (180 mL). The solution was boiled under reflux for 48 h, the organic layer was then separated, and the aqueous layer was extracted with ether (2 × 50 mL). The combined organic and ether layers were concentrated in vacuo and the crude product was distilled to yield **14** (59.0 g, 74.5%) which proved to be a single isomer (>99%) by GLC: bp 105–106 °C (0.6 mm); $n^{25}D$ 1.5700; IR (film) 3360, 3080, 2980, 2920, 1580, 1480, 1440, 1120, 1060, 1010, 930, 730, 680 cm^{-1}; NMR ($CDCl_3$) δ 7.33 (m, 5 H, ArH), 1.28 (d, J = 6.5 Hz, 3 H, $CHCH_3$), 3.87 (br m, 1 H, $CH_2CHOHCH_3$), 3.11 (d, J = 13 Hz, of d, J = 4 Hz, 1 H, $HCHCHOHCH_3$), 2.84 (d, J = 13 Hz, of d, J = 8 Hz, 1 H, $HCHCHOHCH_3$), 2.58 (s, 1 H, OH).

Anal. Calcd for $C_9H_{12}OS$: C, 64.25; H, 7.19. Found: C, 64.40; H, 7.19.

1-Chloro-2- (15) and 2-Chloro-1-phenylthiopropane (16). Thionyl chloride (124 g, 1.04 mol) was added dropwise to **14** (51.7 g, 308 mmol) in benzene (250 mL) and then the mixture was boiled under reflux for 14 h. The solvent was removed in vacuo and the crude product distilled to yield a 38:62 mixture (as determined by NMR) of **15** and **16,** respectively (46.0 g, 80.2%): bp 98 °C (1.0 mm); $n^{25}D$ 1.5645; IR (film) 3080, 2980, 2940, 2860, 1580, 1480, 1440, 1380, 1270, 1180, 1090, 1030, 1010, 730, 690 cm^{-1}; NMR ($CDCl_3$) δ 1.66 (d, relative area 62, $CH_2CHClCH_3$), 1.48 (d, relative area 38, $CHCH_3CH_2Cl$), 2.95–3.90 (m, 2 H, CH_2 from **15** and **16**), 3.90–4.20 (m, 1 H, CH from **15** and **16**), 7,33 (m, 5 H, ArH from **15** and **16**).

Anal. Calcd for $C_9H_{11}ClS$: C, 57.90; H, 5.94. Found: C, 58.04; H, 5.96.

Sodium 2-Phenylthiopropanesulfonate (10). A 38:62 mixture of **15** and **16,** respectively (43.0 g, 231 mmol), was added to a solution of anhydrous sodium sulfite (62.0 g, 492 mmol) in water (150 mL) and boiled under reflux for 64 h. The reaction mixture was filtered hot and cooled to 0 °C to deposit white platelets, which were dried in vacuo to yield mainly **10** (21.6 g, 36.9%): mp > 260 °C; IR (KBr) 1180 (γ_{as} SO_3Na), 1060 cm^{-1} (γ_{sym} SO_3Na); NMR (D_2O) δ 7.78 (m, 5 H, ArH), 4.06 (br m, 1 H, CH_3CHCH_2), 3.69 (d, J = 14 Hz, of d, J = 5 Hz, 1 H, $HCHCHMeSPh$), 3.36 (d, J = 14 Hz, of d, J = 5 Hz, 1 H, $HCHCHMeSPh$), 1.83 (d, J = 6.5 Hz, 3 H, $CHCH_3$), 1.79 (shoulder).

Anal. Calcd for $C_9H_{11}O_3S_2Na$: C, 42.51; H, 4.36. Found: C, 42.49; H, 4.44.

Reaction of Sodium 2-Phenylthio-1-propanesulfonate (10) with Thionyl Chloride. Thionyl chloride (66.2 g, 556 mmol) was added dropwise to a stirred mixture of **10** (18.5 g, 72.8 mmol) in dry benzene (200 mL) containing dimethylformamide (10 drops). The mixture was boiled under reflux for 24 h, concentrated in vacuo, and distilled to yield a 41:59 mixture of **15** and **16,** respectively (8.2 g, 60%): bp 100–102 °C (3 mm); $n^{25}D$ 1.5645; IR (film) 3080, 2980, 2940, 1585, 1480, 1440, 1375, 1270, 1180, 1090, 1060, 1025, 1010, 750 and 680 cm^{-1}; NMR ($CDCl_3$) δ 1.66 (d, relative area 59, $CH_2CHClCH_3$), 1.47 (d, relative area 41, $CHCH_3CH_2Cl$).

Anal. Calcd for $C_9H_{11}ClS$: C, 57.90; H, 5.94. Found: C, 58.04; H, 5.77.

Acknowledgment. We thank the donors of the Petroleum Research Fund, administered by the American Chemical Society, for partial support of this work in Huntsville. The work in Tuscaloosa was supported by the National Science Foundation, Grant CH75-09309, for which we are grateful.

Registry No.—**1,** 64440-79-5; **5,** 5535-49-9; **8,** 64440-80-8; **9,** 64440-81-9; **10,** 64440-82-0; **12,** 598-18-5; **13,** 19686-73-8; **14,** 937-56-4; **15,** 19826-03-0; **16,** 5877-11-2; PCl_5, 10026-13-8; $SOCl_2$, 7719-09-7; phenyl 2-chloroethyl sulfone, 938-09-0.

References and Notes

(1) Current address: Department of Chemistry, Clemson University, Clemson, S.C. 29631.
(2) C. S. Marvel, C. F. Bailey, and M. S. Sparberg, *J. Am. Chem. Soc.*, **49,** 1833 (1927).
(3) F. M. Beringer and R. A. Falk, *J. Am. Chem. Soc.*, **81,** 2997 (1959).
(4) Recently, the preparation of the fluoride, i.e., $PhSCH_2CH_2SO_2F$, has been accomplished, Dr. J. A. Hyatt, personal communication; see: J. A. Hyatt and J. J. Krutak, *J. Org. Chem.*, **42,** 169 (1977).
(5) S. Winstein and E. Grunwald, *J. Am. Chem. Soc.*, **70,** 828 (1948).
(6) B. Capon and S. P. McManus, "Neighboring Group Participation", Vol. 1, Plenum Press, New York, N.Y. 1976.
(7) The percentages in parentheses refer to isomeric composition as determined by NMR analysis (methyl group intergration).
(8) With typical secondary/primary S_N2 reactivities (cf. ref 9) one calculates an isomer composition with >98% of isomer **14.**
(9) A. Streitweiser, Jr., "Solvolytic Displacement Reactions", McGraw-Hill, New York, N.Y., 1962, p 12.
(10) (a) R. C. Fuson, C. C. Price, and D. M. Burness, *J. Org. Chem.*, **11,** 475 (1946). (b) C. S. Marvel and E. D. Weil, *J. Am. Chem. Soc.*, **76,** 61 (1954).
(11) W. H. Mueller and P. E. Butler, *J. Am. Chem. Soc.*, **88,** 2866 (1966); cf.: G. H. Schmid and D. G. Garrett, in "Double Bonded Functional Groups", Suppl. A, S. Patai, Ed., Wiley, New York, N.Y., 1976, p 725. The sulfonium ion **11** may also collapse by chloride attack at sulfur, but the sulfurane probably would not survive under the conditions employed; cf.: W. A. Smit, M. Z. Krimer, and E. A. Vorob'eva, *Tetrahedron Lett.*, 2451 (1975); D. C. Owsley, G. K. Helmkamp, and S. N. Spurlock, *J. Am. Chem. Soc.*, **91,** 3606 (1969); D. C. Owsley, G. K. Helmkamp, and M. F. Rettig, *ibid.*, **91,** 5239 (1969); J. F. King, K. Abikar, D. M. Deaken, and R. G. Pews, *Can. J. Chem.*, **46,** 1 (1968); J. F. King and K. Abikar, *ibid.*, **46,** 9 (1968).
(12) Sulfite ion is known to react with cyclic sulfonium salts, e.g., the mustard cation; C. G. Swain and C. B. Scott, *J. Am. Chem. Soc.*, **75,** 141 (1953).
(13) Epoxides also undergo sulfonation, giving primary sulfonic acids, cf.: H. Schmitz, H. Grosspietsch, H. Kaltenhauser, and H. Wendt, *Angew. Chem., Int. Ed. Engl.*, **2,** 216 (1963).
(14) Should any of the reaction not proceed via the sulfonium cation **11, 10** is still predicted, as sulfonation proceeds much faster at primary as compared to secondary carbon; cf.: E. E. Gilbert, "Sulfonation and Related Reactions", Wiley-Interscience, New York, N.Y., 1965, pp 136–145.
(15) (a) C. A. Buehler and D. E. Pearson, "Survey of Organic Synthesis", Wiley-Interscience, New York, N.Y., 1970, pp 336–337. (b) L. F. Fieser and M. Fieser, "Reagents for Organic Synthesis", Vol. 1, Wiley, New York, N.Y., 1967, p 286. (c) H. H. Bosshard, R. Mory, M. Schmid, and H. Zollinger, *Helv. Chim. Acta,* **42,** 1653 (1959).
(16) R. G. Pearson, H. Sobel, and J. Songstad, *J. Am. Chem. Soc.*, **90,** 319 (1968).
(17) (a) S. R. Hartshorn, "Aliphatic Nucleophilic Substitution", Cambridge University Press, London, 1973, pp 52–53. (b) A. Streitwieser, Jr., "Solvolytic Displacement Reactions", McGraw-Hill, New York, N.Y., 1956, pp 81–82.
(18) J. March, "Advanced Organic Chemistry", 2nd ed, McGraw-Hill, New York, N.Y., 1977, pp 302–306.
(19) Phosphorus pentachloride was reacted with compound **1** but not with compound **10.** Based on the results with **1** it seems likely that **10** and phosphorus pentachloride will follow the course shown in path c of Scheme II.
(20) H. J. Barber, R. F. Fuller, M. B. Green, and H. T. Zwartouw, *J. Appl. Chem.*, **3,** 266 (1953).
(21) A. H. Ford-Moore, R. E. Peters, and R. W. Wakelin, *J. Chem. Soc.*, 1754 (1949).