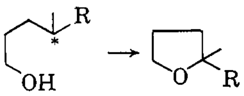
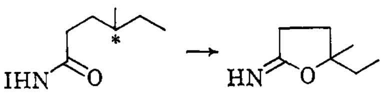
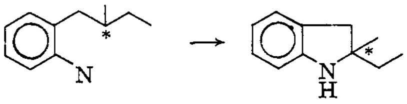


X XI

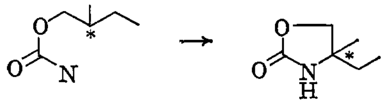


XII XIII

centers gave optically active products[6] (XV and XVII, respectively). Both the lead tetraacetate[7] and N-iodoamide[8] cyclization reactions have been explained as multiple-step radical mechanisms; only in the case of the nitrene cyclizations,[6] where optical activity is retained during the reaction process, has a concerted three-centered transition state been proposed.

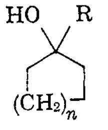


XIV XV



XVI XVII

It thus seems most reasonable to conclude that silver oxide–bromine induced cyclization of tertiary aliphatic alcohols to ethers proceeds *via* a multiple-step radical process. This conclusion is further supported by the recent findings of Akhtar, Hunt, and Dewhurst[9] on the action of silver acetate and bromine in the dark on a series of cyclic alcohols XVIII, which were especially chosen for study because the alkoxy radical derived from each of them undergoes a characteristic mode of decomposition. In addition, our conclusion is supported by the study of intramolecular chlorination with long-chain hypochlorites[4] and by the cyclization reaction of long-chain secondary chloramines[10] (the Hofmann–Löffler–Freitag reaction). Both these reactions are believed to involve radical species—in the first an alkoxy and in the second an imino—which transfer a chlorine atom to the 5-carbon in the chain, *via* extraction of a hydrogen atom, to give an essentially trigonal alkyl radical. Ultimately, cyclization takes place by displacement of the halide by oxygen or nitrogen, respectively.



XVIII

Experimental

(+)-(*S*)-2,5-Dimethylhexanol-2 (VI).—Commercially available (−)-(*S*)-2-methylbutanol-1 was homologated[6] to (+)-(*S*)-3-methylpentanol-1. The chloride (b.p. 126°, 80% from a thionyl chloride reaction in pyridine[11]) of the methylpentanol was converted to a Grignard reagent in ether. An excess (1.1 equiv.) of acetone in ether was then added dropwise to the Grignard solution. The reaction was boiled for 1 additional hr., cooled, and decomposed with ice–water and glacial acetic acid. The ether phase was washed with water and then carbonate solution, dried over anhydrous potassium carbonate, and distilled at reduced pressure. Pure 2,5-dimethylhexanol-2 (76% based on chloride) was obtained by a fractionation through a 2-ft. spinning-band column, b.p. 96° (45 mm.), n^{25}_{D} 1.42756, α^{27}_{D} +5.72°.

Anal. Calcd. for $C_9H_{20}O$: C, 74.93; H, 13.98. Found: C, 74.65; H, 14.08.

Reaction of (+)-(*S*)-2,5-Dimethylhexanol-2 (VI) with Silver Oxide and Bromine.—Using the method of Sneen and Matheny,[2b,12] VI was converted to 2-ethyl-2,5,5-trimethyltetrahydrofuran (VII) as follows. To a well-stirred mixture of 65 g. (0.45 mole) of alcohol VI, 2 l. of pentane, and 209 g. (0.9 mole) of silver oxide protected from light with aluminum foil and maintained in a nitrogen atmosphere, was added dropwise over a period of 15 min. 26 ml. (80 g., 0.5 mole) of bromine. After 4 hr., the reaction was filtered; the filtrate was successively washed, first with sulfurous acid to destroy unreacted bromine, then with water, and finally with saturated bicarbonate solution. After drying over anhydrous sodium sulfate the solution was distilled through a 2-ft. spinning-band column. The pentane was removed at atmospheric pressure and the residue was fractionated at reduced pressure. The fraction boiling at 57–85° (30 mm.) weighed about 45 g. and consisted mainly of unreacted starting alcohol. The fraction boiling at 44–48° (30 mm.) consisted of a mixture of olefins and cyclic ether VII. A refractionation of this mixture at atmospheric pressure gave a new mixture boiling at 124–137° which was readily separated by g.p.c. [using a 20 ft. × 3/8 in. column packed with 25% poly-*m*-phenyl ether (five rings) on 60–80-mesh Chromosorb W, at a column temperature of 120°] into two essentially equal components. The first was a mixture (as concluded from the n.m.r. spectrum) of olefinic hydrocarbons which was optically active, α_D +9.5°.

Anal. Calcd. for C_9H_{10}: C, 85.63; H, 14.37. Found: C, 85.68; H, 14.46.

The second component obtained from the g.p.c. was concluded to be the desired cyclic ether VII from the following evidence. The n.m.r. spectrum (in CCl_4, TMS standard determined on a Varian A-60) exhibited the following absorptions: a triplet centered at 0.93 p.p.m. (3H), J = 7 c.p.s.; a singlet at 1.07 p.p.m. (3H); a singlet at 1.12 p.p.m. (3H); a singlet at 1.17 p.p.m. (3H); a quartet centered at 1.42 p.p.m. (2H), J = 7 c.p.s.; and a relatively broad band centered at 1.72 p.p.m. (4H).

Anal. Calcd. for $C_9H_{18}O$: C, 75.99; H, 12.76. Found: C, 76.08; H, 12.84.

The optical rotation of VII was determined at several wave lengths on a Jasco optical rotatory dispersion spectrometer and found to be as follows: α_D 0.00°, α_{450} 0.00°, α_{350} +0.05°, α_{300} +0.1°.

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[9] M. Akhtar, P. Hunt, and P. B. Dewhurst, *J. Am. Chem. Soc.*, **87**, 1807 (1965).

[10] E. J. Corey and E. R. Hertler, *ibid.*, **82**, 1657 (1960).

[11] H. C. Brown and C. Groot, *ibid.*, **64**, 2566 (1942).

[12] In their more recent paper[2a] on this subject, Sneen and Matheny use a mixture of mercuric oxide and silver oxide to effect cyclization. In a private communication, Dr. Sneen informed us that still better results were obtained by a slow addition of bromine to the reaction mixture so that bromine is never present in too large an excess.

O,S-Dialkyl Phosphorothioates

A. E. LIPPMAN

Monsanto Company, Agricultural Division,
Research Department, St. Louis, Missouri

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O,S-Diethyl O-*p*-nitrophenyl phosphorothioate has been reported in the literature[1,2] in connection with this compound's reported increased toxicity over that of parathion, from which it is formed by rearrangement.[3,4] Though no physical constants or analysis have been

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[1] H. Martin, *J. Sci. Food Agr.*, **1**, 163 (1950).

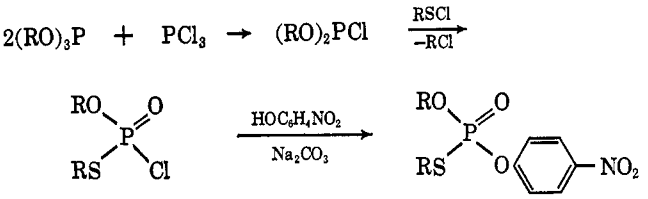
[2] J. Marhold and J. Cizek, *Pracovni Lekar.*, **9**, 390 (1957).

[3] B. Topley, *Chem. Ind.* (London), 859 (1950).

[4] J. B. McPherson and G. A. Johnson, *J. Agr. Food Chem.*, **4**, 42 (1956).

reported, Gage[5] states that it is obtained from ethyl *p*-nitrophenyl phosphorochloridate and sodium ethyl mercaptide.

This compound and the previously unreported methyl analog have now been synthesized from *p*-nitrophenol and the corresponding O,S-dialkyl phosphorochloridothioates. The latter were obtained from the interaction between ethane- or methanesulfenyl chloride and the corresponding dialkyl phosphorochloridite by the following series of reactions.



$R = CH_3$ or C_2H_5

The reaction between ethanesulfenyl chloride and diethyl phosphorochloridite has been reported by Petrov, *et al.*[6] It proceeds smoothly at −30 to −60° to give almost quantitative yield. The chief difficulty was the preparation of the dialkyl phosphorochloridite free from alkyl phosphorodichloridite and unreacted trialkyl phosphite. This was particularly so in the methyl series, where the intermediates and final product have limited thermal stability. The purity of these compounds has been followed by P^{31} and H^1 n.m.r. analysis.

The proton magnetic resonance of the methyl and methylene hydrogen coupled through sulfur was found to have a less negative chemical shift, and a larger P–H coupling constant, than when coupled through oxygen. This result is in agreement with similar data previously obtained in this laboratory from the H^1 n.m.r. spectra of O,O,S-triethyl and trimethyl phosphorodithioates, and is consistent throughout this series. Since the latter compounds contain twice as many hydrogen atoms adjoining oxygen than adjoining sulfur, the bands due to each are clearly recognizable, thus providing a basis for the assignment of resonance peaks in the O,S-dialkyl series of compounds.

Experimental

All H^1 n.m.r. spectra were obtained on the Varian A-60 spectrometer and referenced against external TMS. No solvent was used.

Diethyl Phosphorochloridite.—Phosphorus trichloride (69 g., 0.5 mole) was added to 166 g. (1 mole) of triethyl phosphite at 85° over a period of 0.5 hr. The product was distilled at 34–57° (20 mm.), then redistilled at atmospheric pressure through a 40-cm. Widmer column. A fraction (14 g.) boiling at 148–151° proved to be 95% pure by P^{31} n.m.r. analysis (chemical shift referred to 85% H_3PO_4) −165 p.p.m., n^{25}_{D} 1.4352 (lit. b.p. 143–148°,[7] 153–155°,[8] n^{20}_{D} 1.4350[8]).

Dimethyl Phosphorochloridite.—This material was prepared as above, but at 60°. After vacuum distillation of the product, it was refractionated five times *in vacuo* and at atmospheric pressure to give 12 g. of product of b.p. 30° (35 mm.), n^{25}_{D} 1.4370, P^{31} n.m.r. chemical shift (referred to 85% H_3PO_4) −169 p.p.m.; H^1 n.m.r. chemical shift $\delta = -3.93$ p.p.m., $J_{\mathrm{P-H}} =$ 11 c.p.s.; the latter analysis showed this product to contain 4% $(CH_3O)_3P$ (lit. b.p. 103–105°,[9] 39° (40 mm.),[10] n^{20}_{D} 1.4356). On one occasion the distillation residue decomposed violently at 145°.

O,S-Diethyl Phosphorochloridothioate.—Diethyl phosphorochloridite (10.2 g., 0.065 mole) in 20 ml. of toluene was added at −30 to −40° to ethane sulfenyl chloride prepared from 4 g. (0.033 mole) of ethyl disulfide and 4.4 g. (0.033 mole) of sulfuryl chloride, in 20 ml. of toluene. After stripping off volatile products and solvent, the resulting material was distilled twice through a short Vigreux column, giving 10.1 g. (82%) of O,S-diethyl phosphorochloridothioate: b.p. 78° (1.5 mm.); n^{25}_{D} 1.4803; P^{31} n.m.r. chemical shift −34.1 p.p.m.; H^1 n.m.r. $\delta = -1.87$ p.p.m., $J_{\mathrm{H-H}} = 7$ (CH_3 coupled through O) and 7.5 c.p.s. (CH_3 coupled through S); $\delta = -3.51$ p.p.m., $J_{\mathrm{H-H}}$ (SCH_2) = 7.5 c.p.s., $J_{\mathrm{P-H}}$ (SCH_2) = 19.4 c.p.s.; $\delta = -4.79$ p.p.m., $J_{\mathrm{H-H}}$ (OCH_2) = 7 c.p.s., $J_{\mathrm{P-H}}$ (OCH_2) = 11 c.p.s. Petrov, *et al.*,[6] report b.p. 98–99° (7–8 mm.), n^{20}_{D} 1.4847.

Anal. Calcd. for $C_4H_{10}ClO_2PS$: Cl, 18.8; P, 16.4; S, 17.0. Found: Cl, 18.98; P, 16.75; S, 17.25.

O,S-Dimethyl Phosphorochloridothioate.—Dimethyl phosphorochloridite (9.2 g. 0.724 mole) in 10 ml. of chloroform was added to methanesulfenyl chloride made from 3.4 g. (0.0362 mole) of methyl disulfide and 4.9 g. (0.0362 mole) of sulfuryl chloride in 30 ml. of the same solvent by the above procedure. Vacuum straight take-over distillation gave 7.3 g. (63%) of crude product. On redistillation through a short Vigreux column a fraction was obtained: b.p. 63–66° (3 mm.); n^{25}_{D} 1.4928; P^{31} n.m.r. shift −37.1 p.p.m. (85% H_3PO_4 reference); H^1 n.m.r. $\delta = -3.00$ p.p.m., $J_{\mathrm{P-H}}(SCH_3) = 19$ c.p.s.; $\delta = -4.26$ p.p.m., $J_{\mathrm{P-H}}$ (OCH_3) = 15 c.p.s. The latter analysis showed the sample to be about 70% pure. It turned brown on standing.

Anal. Calcd. for $C_2H_6ClO_2PS$: Cl, 22.1; P, 19.3; S, 19.96. Found: Cl, 23.23; P, 20.14; S, 21.05.

O,S-Diethyl *p*-Nitrophenyl Phosphorothioate.—O,S-Diethyl phosphorochloridothioate (2 g. 0.01 mole) was refluxed for 2 hr. with 1.5 g. (0.01 mole) of *p*-nitrophenol and 1.2 g. of anhydrous sodium carbonate in 25 ml. of dry acetone. After removal of solvent, water and methylene chloride were added, and the product layer was washed with 3% sodium carbonate and water until practically free from unreacted *p*-nitrophenol. The resulting, light brown liquid had P^{31} n.m.r. chemical shift at −24.0 p.p.m.; H^1 n.m.r. $\delta = -1.5$ and −1.6 p.p.m., $J_{\mathrm{H-H}} =$ 7.5 (CH_3CH_2SP) and 7.0 c.p.s. (CH_3CH_2OP); $\delta = -3.2$ p.p.m. (CH_2SP), $J_{\mathrm{H-H}} = 7.0$ and 7.5 c.p.s., $J_{\mathrm{P-H}} = 16.0$ c.p.s.; $\delta = -4.6$ p.p.m. ($-CH_2OP$), $J_{\mathrm{H-H}} = 7.2$ c.p.s., $J_{\mathrm{P-H}} = 9.5$ c.p.s.; $\delta = -7.64$ p.p.m.; $\delta = -8.41$ p.p.m. (aromatic H), $J_{\mathrm{H-H}} = 9$ c.p.s.

Anal. Calcd. for $C_{10}H_{14}NO_5PS$: N, 4.81; P, 10.64; S, 11.01. Found: N, 4.89; P, 10.74, S, 11.15.

O,S-Dimethyl *p*-Nitrophenyl Phosphorothioate.—O,S-Dimethyl phosphorochloridothioate (1.7 g., 0.011 mole) was treated with 1.1 g. of anhydrous sodium carbonate and 1.47 g. (0.011 mole) of *p*-nitrophenol in 10 ml. of dry acetone, as described previously. The light brown liquid product (1.35 g., 48% yield) appeared to be about 70% pure from n.m.r. spectra. P^{31} n.m.r. spectrum showed chemical shift at −25.2 with a broad impurity band at +6.2 p.p.m.; H^1 n.m.r. $\delta = -2.53$ p.p.m., $J_{\mathrm{P-H}} = 16$ c.p.s. (CH_3SP); $\delta = -4.11$ p.p.m., $J_{\mathrm{P-H}} = 13$ c.p.s. (CH_3OP); $\delta = -7.60$ and −8.35 p.p.m., $J_{\mathrm{H-H}} = 9$ c.p.s. (aromatic H).

Anal. Calcd. for $C_8H_{10}NO_5PS$: N, 5.33; P, 11.77; S, 12.19. Found: N, 4.89; P, 10.74; S, 11.15.

H^1 N.m.r. Spectra of Reference Compounds.—O,O,S-Triethyl phosphorodithioate gave $\delta = -1.80$ p.p.m., $J_{\mathrm{H-H}} = 7$ c.p.s. (CH_3); $\delta = -3.32$ p.p.m., $J_{\mathrm{H-H}} = 7.5$ c.p.s., $J_{\mathrm{P-H}} = 16$ c.p.s. (CH_2SP); $\delta = -4.56$ p.p.m., $J_{\mathrm{H-H}} = 7.1$ c.p.s., $J_{\mathrm{P-H}} = 9.5$ c.p.s. (CH_2OP). O,O,S-Trimethyl phosphorodithioate gave $\delta =$ −2.83 p.p.m., $J_{\mathrm{P-H}} = 16$ c.p.s. (CH_3SP); $\delta = -4.31$ p.p.m., $J_{\mathrm{P-H}}$ 15 c.p.s. (CH_3OP).

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[7] H. G. Cook, J. D. Ilett, B. C. Saunders, G. J. Stacey, H. G. Watson, I. G. E. Wilding, and S. J. Woodcock, *J. Chem. Soc.*, 2924 (1949).

[8] G. M. Kosolapoff, "Organophosphorus Compounds," John Wiley and Sons, Inc., New York, N. Y., 1950.

[9] A. R. Stiles (to Shell Development Co.), U. S. Patent 2,895,982 (July 21, 1959).

[10] M. Baudler, *Z. Elektrochem.*, **59**, 173 (1955).