

A dark green color formed and faded slowly with formation of a white precipitate. The mixture was stirred overnight, water was added, and the separated ether phase was taken to dryness. Crystallization of the crude product from aqueous ethanol gave 0.63 g. (two crops, 57%) of 6 as colorless plates, m.p. 57.8–58.0° (lit.⁷ 57–58°), $\lambda_{\text{max}}^{\text{cyclohexane}}$ 257 μ (ϵ 17,000), identical (infrared and ultraviolet spectra, gas chromatography) with authentic material.⁷

2-Bromo-1,1-diphenylcyclopentane (9) was prepared by the action of hydrogen bromide on 7 according to the published procedure⁷; our product was obtained in 83% yield with m.p. 91–93° (lit.⁷ 93–94°) and $\lambda_{\text{max}}^{\text{cyclohexane}}$ 255 μ (ϵ 510), 262 (550), and 270 (370).

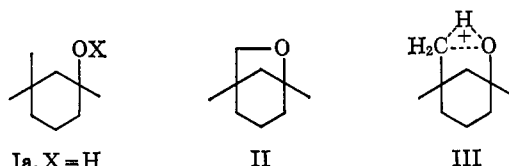
Evidence for a Radical Process in the Dark Cyclization Reaction of Aliphatic Alcohols with Silver Oxide and Bromine

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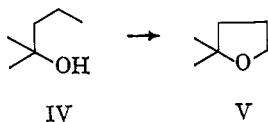
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In 1958 Corey and White¹ reported that treatment of peroxide Ib with *p*-nitrobenzenesulfonyl chloride in cold pyridine–methylene chloride produced some bicyclic ether II. They suggested that the transformation, Ib \rightarrow II, proceeded *via* a cationic transition state such as III. More recently, Sneen and Matheny^{2a}



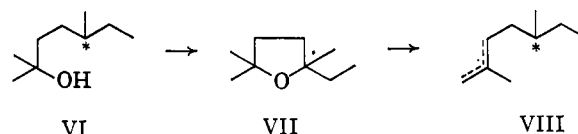
Ia, X = H
b, X = OH
c, X = Br
d, X = OTs
e, X = O-*p*-NB

have published a rather extensive study of this cyclization reaction under a variety of conditions and have speculated on the several mechanisms involved. The most useful procedure described for use in synthesis was the conversion, Ia \rightarrow II, employing silver oxide and bromine in pentane in the dark. Indeed, using these conditions, 2-methylpentanol-2 (IV) could be converted in reasonable yield to 2,2-dimethyltetrahydrofuran (V).²

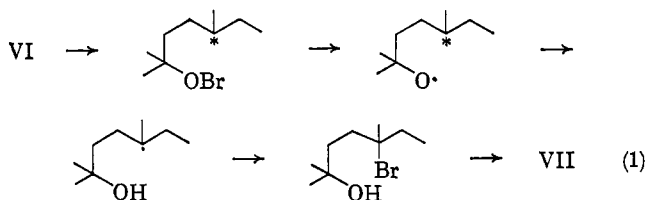


In this note, we concern ourselves with the mechanism of this dark cyclization reaction. We found that treating a pentane solution of (+)-(*S*)-2,5-dimethylhexanol-2 (VI) in the dark with silver oxide and bromine^{2a} gave an approximately equal mixture of optically inactive 2-ethyl-2,5,5-trimethyltetrahydrofuran (VII) and optically active olefins VIII, as well as about 70% recovered alcohol VI. We believe that the formation of optically inactive VII is inconsistent with a

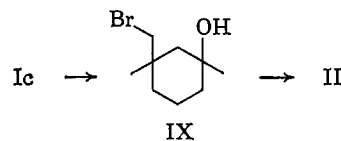
(1) E. J. Corey and R. W. White, *J. Am. Chem. Soc.*, **80**, 6686 (1958).
(2) (a) R. A. Sneen and N. P. Matheny, *ibid.*, **86**, 5503 (1964); (b) *ibid.*, **86**, 3905 (1964).



concerted cyclization mechanism.^{1,2} This result cannot readily be explained by a process involving the intermediacy of a monovalent cationic oxygen species⁸ which abstracts a hydride ion from the δ -carbon atom to form a carbonium ion, and then lives long enough in pentane solution to rotate about a C–C bond before reacting with the nearby hydroxyl group. We feel a mechanism such as the following multiple-step process (eq. 1) to be more reasonable.⁵ Indeed,



Sneen and Matheny^{2a} showed that formation of hypobromite Ic from alcohol Ia is possible by the action of bromine in the presence of a base such as silver oxide, and further showed that light-induced rearrangement of Ic to bromohydrin IX, which cyclized to ether II, on reaction with silver oxide.

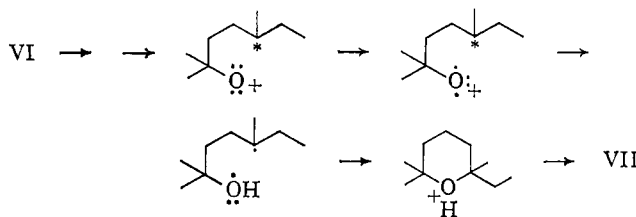


The results from the silver oxide–bromine induced cyclization reaction should be compared with the findings from three similar substitution reactions at unactivated carbon atoms: reaction of lead tetraacetate with optically active alcohol X gave inactive ether XI⁷; photoinduced cyclization of optically active *N*-iodoamide XII gave inactive imine XIII⁸; and, finally, nitrene (XIV and XVI) cyclizations at optically active

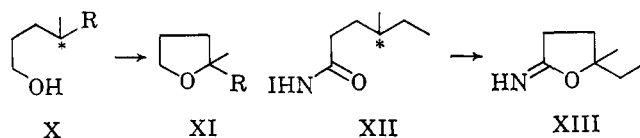
(3) Sneen and Matheny^{2a} concluded that the silver oxide–bromine cyclization, Ia \rightarrow II, in the dark, was not a radical process mainly on the basis that, when this reaction was carried out in the presence of thiophenol, no diphenyl disulfide formation could be detected by infrared analysis. However, when the light-induced rearrangement of hypobromite Ic to bromohydrin IX was run with thiophenol present, again no diphenyl disulfide could be detected, yet this rearrangement is very likely a radical-like process.⁴

(4) C. Walling and A. Padwa, *J. Am. Chem. Soc.*, **85**, 1597 (1963).

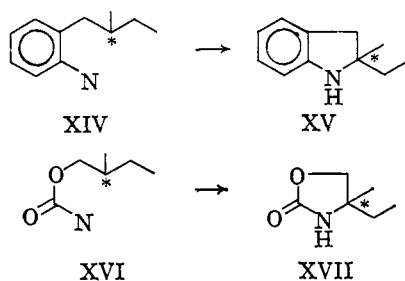
(5) An alternative, but we feel less likely explanation for the loss of optical activity during this reaction, would be to invoke the triplet state of the supposed cationic oxygen intermediate. (For a discussion of triplet-state nitrene and carbene reactions see ref. 6 and W. Kirmse, "Carbene Chemistry," Academic Press Inc., New York, N. Y., 1964.)



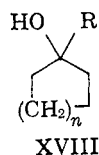
(6) G. Smolinsky and B. I. Feuer, *J. Am. Chem. Soc.*, **86**, 3085 (1964).
(7) D. Hauser, K. Schaffner, and O. Jeger, *Helv. Chim. Acta*, **47**, 1883 (1964).
(8) D. H. R. Barton, A. L. J. Beckwith, and A. Goosen, *J. Chem. Soc.*, 181 (1965).



centers gave optically active products⁶ (XV and XVII, respectively). Both the lead tetraacetate⁷ and N-iodoamide⁸ 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.



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 Dewhurst⁹ 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 hypochlorites⁴ and by the cyclization reaction of long-chain secondary chloramines¹⁰ (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.

Experimental

(+)-(S)-2,5-Dimethylhexanol-2 (VI).—Commercially available (–)-(S)-2-methylbutanol-1 was homologated⁶ to (+)-(S)-3-methylpentanol-1. The chloride (b.p. 126°, 80% from a thionyl chloride reaction in pyridine¹¹) 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_D^{20} 1.42756, α_D^{20} +5.72°.

Anal. Calcd. for $\text{C}_9\text{H}_{20}\text{O}$: 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 Sneed and Matheny,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. \times $\frac{3}{8}$ 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_{18} : 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 $\text{C}_9\text{H}_{18}\text{O}$: 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°.

(12) In their more recent paper^{2a} on this subject, Sneed and Matheny use a mixture of mercuric oxide and silver oxide to effect cyclization. In a private communication, Dr. Sneed 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

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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

(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).

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

(2) J. Marhold and J. Cizek, *Pracovní 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).