usual. After distillation of most of the ethanol, the mixture was diluted with water and extracted with petroleum ether (30–60°). The extracts contained 5.4 g. of 2,3-dimethylthianaphthene. The alkaline layer was acidified with dilute hydrochloric acid in the presence of petroleum ether and extracted repeatedly with the solvent. The combined extracts were dried with magnesium sulfate and concentrated by distillation to a total weight of 31.6 g. When 10.4 g. of this solution was distilled *in vacuo*, only 2,3-dimethylthianaphthene (3.3 g.) was obtained. The solution reacted *instantly* (much more rapidly than the acetate) with ethanolic mercuric chloride, and 10.8 g. of it gave 5.34 g. of *o*-(α-methylallenyl)-thiophenoxymercuric chloride. Dilution of the mother liquors with water and extraction yielded 1.2 g. of 2,3-dimethylthianaphthene. These data indicate the presence of a 15% yield (based on I) of *o*-(α-methylallenyl)-thiophenol and a 28% yield of 2,3-dimethylthianaphthene in the concentrated solution.[12] Neither of the compounds obtained in the earlier run could be isolated in this case. As always, polymeric material remained in the still-pot.

In the best of another series of runs, using 27.3 g. of halide, the mixture after addition of the "reagent" to ethyl chlorocarbonate was heated under reflux for 2 hours, the excess reactant was hydrolyzed, then the ether layer was washed, dried and distilled at 0.4 mm., giving four cuts: 91–102° (5.35 g., $n^{20}D$ 1.5773), 102° (6.81 g., $n^{20}D$ 1.5727), 102–108° (9.24 g., $n^{20}D$ 1.5749), 108–180° (flamed, 1.90 g., dark amber). The first three fractions distilled very largely at 101–103° (a total of 21.4 g., 66%); a sample of ethyl S-*o*-(α-methylallenyl)-phenyl thiolcarbonate was taken from the center cut.

Anal. Calcd. for $C_{13}H_{14}O_2S$: C, 66.63; H, 6.02. Found: C, 66.46; H, 6.06.

The third fraction was light amber and after a day became quite viscous with $n^{20}D$ 1.5834. The center cut did not polymerize noticeably in a week.

The thiolcarbonate very slowly absorbed only 23% of the theoretical amount of hydrogen over platinum oxide in ethanol; it did not react with mercuric chloride in ethanol and was recovered from heating under reflux with either methanol or acetic acid, both containing several drops of concentrated hydrochloric acid.

When 5.26 g. of the ester was heated under reflux for 12 hours with 5 g. of potassium hydroxide in 25 ml. of 95% ethanol, diluted with several volumes of water, and extracted with petroleum ether, 2.98 g. (82%) of 2,3-dimethylthianaphthene was obtained. After reduction of 2.0 g. of ester with 1 g. of lithium aluminum hydride in ether, hydrolysis by pouring the mixture directly on ice, and acidification with sulfuric acid, 1.1 g. (87%) of 2,3-dimethylthianaphthene was isolated.

The last fraction in the original distillation was saponified with ethanolic alkali and the oily acidific material, which deposited only a trace of crystals from hexane, was desulfurized[8] with about 9 g. of Raney nickel in 40 ml. of ethanol; however, the resulting gum could not be resolved by sublimation.

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(12) Distillations were carried out in Pyrex ware, which might, of course, have acted catalytically; however, solutions expected to contain the thiophenol were tested routinely with mercuric chloride with negative results except in this experiment. The reason for the stability of the thiophenol under these conditions is obscure in view of the ease of closure under other circumstances which seemed less drastic. Perhaps solvent effects were responsible.

[CONTRIBUTION FROM THE RESEARCH LABORATORIES OF JOSEPH E. SEAGRAM & SONS, INC.]

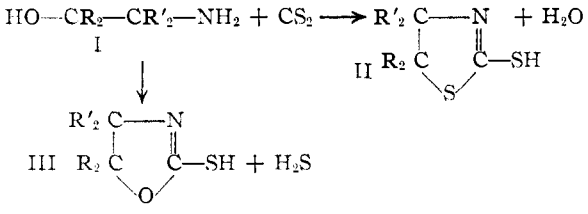
Synthesis of Oxazoline-2-thiols from 2-Aminoalcohols[1]

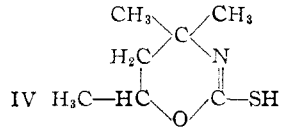
BY A. A. ROSEN[2]

RECEIVED DECEMBER 19, 1951

2-Aminoalcohols are combined with carbon disulfide at low temperature, through the oxidizing action of iodine, to form dialkanol thiuram disulfides. The thiuram disulfides decompose to yield oxazoline-2-thiols. The synthetic method generally employed to prepare these heterocyclic compounds (heating the aminoalcohol with carbon disulfide) results in some instances in the formation of thiazoline-2-thiols. Factors which determine the manner of heterocyclic ring formation by this latter method are considered.

Some 2-aminoalcohols (I), notably ethanolamine, yield thiazoline-2-thiols (II) when heated with carbon disulfide.[3,4] The reaction is usually accomplished in the presence of alkali. Several other 2-aminoalcohols, however, yield the corresponding oxazoline-2-thiols (III) under the same reaction conditions.[5,6] These compounds may be construed either as the thiones or as the tautomeric thiols[7]; the latter basis for nomenclature is the one most frequently encountered in the literature and is accordingly employed in this paper. The analogous 3-aminoalcohol, 4-amino-4-methyl-2-pentanol, yields the corresponding 6-membered oxygen–nitrogen heterocycle, 4,4,6-trimethyl-5,6-dihydro-1,3,4-oxazine-2-thiol[8] (IV).





The procedures whereby aminoalcohols which ordinarily yield the thiazoline derivatives can be converted to oxazoline-2-thiols have been summarized by Ettlinger.[4] The same methods, when applied to primary alkylamines, yield the corresponding alkyl isothiocyanates, R-NCS.[9] Probably

(1) Portions of this paper were presented before the Division of Organic Chemistry at the St. Louis Meeting of the American Chemical Society, 1941, and at the Boston Meeting, 1951.

(2) This paper is taken in part from a dissertation submitted by the author to the Graduate School of Arts and Sciences of the University of Cincinnati in partial fulfillment of the requirements for the degree of Ph.D., 1938.

(3) (a) L. Maquenne and E. Roux, *Compt. rend.*, **134**, 1589 (1902); (b) L. Knorr and P. Roessler, *Ber.*, **36**, 1278 (1903); (c) E. Roux, *Ann. chim.*, [8] **1**, 72 (1904).

(4) M. G. Ettlinger, THIS JOURNAL, **72**, 4792 (1950).

(5) H. A. Bruson and J. W. Eastes, *ibid.*, **59**, 2011 (1937).

(6) C. Y. Hopkins, *Can. J. Research*, **B20**, 268 (1942).

(7) M. G. Ettlinger, THIS JOURNAL, **72**, 4699 (1950).

(8) H. L. Fisher, U. S. Patent 2,326,732 (1944).

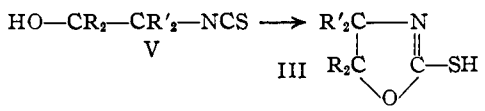
(9) (a) W. Rudneff, *Ber.*, **11**, 987 (1878); (b) J. von Braun, *ibid.*, **33**, 2726 (1900); (c) M. Delépine, *Compt. rend.*, **144**, 1125 (1907).

TABLE I

REACTION PRODUCTS OF 2-AMINOALCOHOLS WITH CARBON DISULFIDE

Aminoalcohol used	Thiuram disulfide method		Reflux with CS_2 and alc. KOH
	Mole ratio, amine/I_2	Products, 2-thiol	Products, 2-thiol
HO—CH_2—CH_2—NH_2	4.0	Oxazoline-	Thiazoline-
HO—CH(CH_3)—CH_2—NH_2	4.0	5-Methyloxazoline-	5-Methyloxazoline- and 5-Methylthiazoline-
HO—C(CH_3)$_2$—CH_2—NH_2	4.0	5,5-Dimethyloxazoline-	5,5-Dimethyloxazoline-
HO—CH_2—CH(C_2H_5)—NH_2	3.9	4-Ethyloxazoline-	4-Ethylthiazoline-
HO—CH_2—C(CH_3)$_2$—NH_2	...	4,4-Dimethyloxazoline-	4,4-Dimethyloxazoline- and 4,4-Dimethylthiazoline-
HO—CH(CH_3)—CH_2—C(CH_3)$_2$—NH_2	...	4,4,6-Trimethyl-5,6-dihydro-1,3,4-oxazine-	4,4,6-Trimethyl-5,6-dihydro-1,3,4-oxazine-

the oxazoline-2-thiols (III) result from ring closure of the intermediate hydroxyalkyl isothiocyanates (V).[10]



The present paper describes a method of synthesis of oxazoline-2-thiols based on the decomposition with ring closure of thiuram disulfides derived from 2-aminoalcohols. As von Braun[11] has reported, primary aliphatic amines and carbon disulfide combine at low temperatures through the action of oxidizing agents to yield unstable thiuram disulfides (Equation 1), which decompose at higher temperatures with formation of isothiocyanates (Equation 2) and thioureas (Equation 3).

$$4RNH_2 + 2CS_2 + I_2 \longrightarrow (RNH—CS_2—)_2 + 2RNH_2\cdot HI \quad (1)$$

$$(RNH—CS_2—)_2 \longrightarrow 2RNCS + H_2S + S \quad (2)$$

$$(RNH—CS_2—)_2 \longrightarrow (RNH)_2CS + CS_2 + S \quad (3)$$

The mode of decomposition indicated by Equation 2 predominates in the case of thiuram disulfides derived from amines of low molecular weight.

For use as intermediates in the synthesis of oxazoline-2-thiols, thiuram disulfides were prepared from five 2-aminoalcohols and one 3-aminoalcohol. The procedure consisted of titrating a solution of the aminoalcohol and excess carbon disulfide in methanol, held at 0°, with a methanolic solution of iodine. The reaction was rapid and the molar proportions of amine to iodine satisfactorily approximated the value of 4 to 1, in accordance with Equation 1, in the four instances in which the position of the amino group was a primary or secondary carbon atom. In each of the final two examples the amino group was sufficiently hindered by its position on a tertiary carbon atom that the slow rate of combination of carbon disulfide with the amino group prevented the determination of a precise end-point in the iodine titration. In these instances the theoretical quantity of iodine was added and the reaction proceeded slowly to completion.

The thiuram disulfide from ethanolamine was the only one isolated and identified by analysis. It precipitated from the reaction solution in 92% theoretical yield as a white powder, m.p. 98° (dec.). A portion was decomposed in boiling water and the evolved hydrogen sulfide was determined iodimetrically. It amounted to 0.95 mole per mole of thiuram disulfide, therefore the extent of the decomposition reaction yielding isothiocyanate was 95%. The other thiuram disulfides were soluble in the reaction mixture and were not isolated. The solvent was removed by evaporation at low temperature and the thiuram disulfide was decomposed to the corresponding oxazoline-2-thiol by heating in water.

Decomposition of the five thiuram disulfides derived from 2-aminoalcohols always resulted in the formation of the corresponding oxazoline-2-thiols; the thiuram disulfide from the single 3-aminoalcohol studied yielded the analogous oxazine derivative, IV. No identifiable side-reaction products were recovered, although the yields of oxazoline 2-thiols ranged from 35 to 65% of the theoretical.

The products obtained by the decomposition of the thiuram disulfides derived from each aminoalcohol studied are listed in Table I. The products obtained by refluxing the same aminoalcohols with carbon disulfide and alcoholic potassium hydroxide[5] are also listed. Two of the aminoalcohols, which yielded III by the thiuram disulfide route, yielded only II by the reflux procedure. In the case of the four other aminoalcohols, the oxygen–nitrogen heterocyclic compound was the sole or predominant product resulting from either method of preparation.

That two different classes of heterocyclic compounds are obtained by heating aminoalcohols with carbon disulfide merits consideration. Ettlinger[4] considered that the thiazoline derivative is formed from ethanolamine because of the presence of an unhindered primary hydroxyl group. He thus implied that the effect of secondary or tertiary hydroxyl groups should be to form the oxazoline derivatives. In apparent contrast to this explanation are the results of Hopkins.[6] From isopropanolamine he synthesized both the oxazoline and thiazoline derivatives, by procedures which differed significantly only in the reflux time. The oxazoline derivative was obtained after 2.5 hours whereas the thiazoline derivative was obtained in poor yield after six hours. These facts suggested a possible course of reaction in which the more rapidly produced oxazoline compound is converted by further heating in the reaction mixture to the corresponding thiazoline compound.

(10) P. G. Sergeev and S. N. Ivanova, *J. Gen. Chem.* (*U. S. S. R.*), **7**, 1495 (1937); *C. A.*, **32**, 2534 (1938).

(11) J. von Braun, *Ber.*, **35**, 817 (1902).

In the present research, this possible reaction sequence was tested in several ways. Table I shows that two of the aminoalcohols, ethanolamine and 2-amino-1-butanol, yielded only the thiazoline-2-thiol products when refluxed for six hours with carbon disulfide. When the reaction time for these two aminoalcohols was limited to one and a half hours there was still no evidence of oxazoline-2-thiol formation and the products recovered were the same as those resulting from the usual six hours of reflux. Hopkins' preparation of 4-methylthiazoline-2-thiol was repeated. A very small quantity of this product was obtained. It was accompanied, however, by a much greater quantity of the oxazoline analog, thus showing that this aminoalcohol containing a secondary hydroxyl group yielded as principal product the oxygen–nitrogen heterocycle. In the final test of the possible reaction sequence described above, 4-methyloxazoline-2-thiol was refluxed for four hours in the usual reaction mixture of carbon disulfide and alcoholic potassium hydroxide. No 4-methylthiazoline-2-thiol was obtained by this method. It thus appears that the two types of ring closure reactions are independent and are not consecutive steps of a reaction sequence.

Among the aminoalcohols listed in Table I, there is only one example of a primary hydroxyl group entering into the oxazoline ring closure on being heated with carbon disulfide. In this case, 2-amino-2-methyl-1-propanol, the position of the amino group is a tertiary carbon atom, which structure presumably hinders the primary hydroxyl group sufficiently to influence the manner of ring closure. These facts are thus in agreement with the explanation of Ettlinger, that only aminoalcohols with an unhindered primary hydroxyl group yield thiazoline-2-thiols. If the hydroxyl group is not primary or is otherwise hindered by extensive substitution of the alkane chain, then the predominant course of reaction leads to the corresponding oxazoline-2-thiol, when the reflux procedure is employed.

The reaction temperature, as well as the structure of the aminoalcohol, may influence the manner of ring closure. When the reaction is carried out at 130° to 170° under pressure, thiazoline-2-thiols are obtained[12] from substituted aminoalcohols which yield the corresponding oxazoline-2-thiols by the usual reflux procedure.

Experimental[13]

Bis-(2-hydroxyethyl)-thiuram Disulfide.—Ethanolamine (Eastman Kodak Co.), 19.7 g., was dissolved in 50 ml. of methanol, cooled in an ice-bath. With the temperature held at 0°, 20 ml. of carbon disulfide was added in small portions, then a methanolic solution of iodine (1 ml. contained 0.150 g. I_2) was added from a buret to a faint permanent yellow color. The white thiuram disulfide which precipitated during the titration was washed several times with methanol, then air-dried, to give 20.1 g. of bis-(2-hydroxyethyl)-thiuram disulfide (92% theoretical), m.p. 98° (dec.).

Anal. Calcd. for $C_6H_{12}N_2O_2S_4$: N, 10.28; S, 47.08. Found: N, 9.99; S, 45.96.

The same procedure was utilized to prepare the thiuram disulfide derivatives of the other aminoalcohols; the other thiuram disulfides, however, failed to precipitate. The solutions were evaporated in a stream of air, during which time partial decomposition of the thiuram disulfide occurred so that the thiuram was not isolated.

Oxazoline-2-thiol.—A suspension of 10.0 g. of the thiuram disulfide in 150 ml. of water was gradually heated to boiling in a period of an hour. The hot solution, made slightly acidic with dilute sulfuric acid and cooled, was filtered from suspended sulfur and saturated with sodium chloride, then it was extracted five times with 60-ml. portions of ethyl acetate. The extract, evaporated on a steam-bath, yielded 3.2 g. of the crude oxazoline-2-thiol (42% theoretical) which was recrystallized twice by throwing out of ethyl acetate solution with petroleum ether, to yield 1.4 g. of white crystals, m.p. 98–99° (lit.[4] 98–99°).

Anal. Calcd. for C_3H_5NOS: N, 13.58; S, 31.09. Found: N, 13.51; S, 30.00.

Thiazoline-2-thiol.—The product of the reaction of ethanolamine with carbon disulfide by the method of Bruson and Eastes[5] was thiazoline-2-thiol, m.p. 105.5–107° (lit.[3] 106–107°).

5-Methyloxazoline-2-thiol.—Isopropanolamine (Eastman Kodak Co.), 19.0 g., was converted into the soluble thiuram disulfide, in the manner described above for ethanolamine. Evaporation of the reaction solution in a stream of air resulted in a yellow oil containing suspended sulfur. The oil, dissolved in 125 ml. of water and acidified with sulfuric acid, was heated to boiling to complete the decomposition of the thiuram disulfide. The resulting suspension was cooled, filtered to remove sulfur, saturated with salt, and extracted with ethyl acetate. Evaporation of the solvent on a steam-bath left a light yellow oil which crystallized on cooling to yield 6.8 g. of nearly white crystals (46% theoretical), m.p. 73–75°. When purified by being thrown out of benzene solution by the addition of petroleum ether, 6.2 g. of creamy-white powder was obtained, m.p. 74.5–75° (lit.[6] 72–73°).

Anal. Calcd. for C_4H_7NOS: N, 11.96; S, 27.37. Found: N, 11.97; S, 27.30.

Products from Isopropanolamine by Reflux Method.—The procedure of Bruson and Eastes[5] was applied to 21.0 g. of isopropanolamine, using the same proportions of reagents. After acidification with 1:1 sulfuric acid and cooling, a white precipitate (largely inorganic) formed, which was leached with hot benzene. The benzene solution was concentrated and cooled, yielding 1.05 g. of impure 5-methylthiazoline-2-thiol. The product was purified twice by throwing out of benzene solution with petroleum ether, recrystallized from hot water, and once again precipitated from benzene solution by the addition of petroleum ether. Only 0.12 g. of the pure product was obtained, m.p. 94° (lit.[6] 93–94°).

The aqueous filtrate, separated from the crystalline precipitate formed in the acidification step, was extracted three times with 35-ml. portions of ethyl acetate. Evaporation of the solvent yielded 12 g. of waxy solid, from which by repeated recrystallization there was obtained 1.8 g. of 5-methyloxazoline-2-thiol, m.p. 72–73°.

In another trial the reflux time was limited to 2.5 hours. From 25.0 g. of the amine there was obtained 19.9 g. of the crude oxazoline derivative which, after two recrystallizations from hot benzene, yielded 5.6 g. of the pure product, m.p. 74–74.5°.

5,5-Dimethyloxazoline-2-thiol.—1-Amino-2-hydroxyisobutane (Shell Development "isobutanolamine," b.p. 150–150.5°), 8.1 g., was converted to the thiuram disulfide. When the solvent was evaporated, 11.2 g. of the pale yellow, granular thiuram disulfide was recovered. An odor of hydrogen sulfide and the presence of free sulfur indicated that partial decomposition had occurred, therefore identification by analysis of the compound was not attempted. The thiuram disulfide was readily soluble in methanol and insoluble in benzene or water; it was suspended in 100 ml. of water in which it dissolved, after two days, with evolution of hydrogen sulfide. Three grams (50% theoretical) of 5,5-dimethyloxazoline-2-thiol was recovered in the same manner described above for the corresponding product from isopropanolamine. When purified by throwing out of benzene solution with petroleum ether and recrystallization from water, the product melted at 107–109° (lit.[5] 107–109°) and was identical with the product obtained by the reflux procedure.

(12) B. M. Sturgis and J. J. Verbanc, U. S. Patent 2,273,424 (1942).

(13) Some of the analyses are by Clark Microanalytical Laboratory, Urbana, Illinois.

4-Ethyloxazoline-2-thiol.—When prepared by the usual thiuram disulfide procedure, 7.5 g. (65% theoretical) of slightly impure product was obtained from 15.7 g. of 2-amino-1-butanol (Commercial Solvents, b.p. 178–179°). Fractional precipitation from benzene solution by the addition of petroleum ether, the first oily fraction being discarded, resulted in pure 4-ethyloxazoline-2-thiol, m.p. 74–75°.

Anal. Calcd. for C_5H_9NOS: N, 10.68; S, 24.44. Found: N, 11.06; S, 25.48.

4-Ethylthiazoline-2-thiol.—Treatment of 2-amino-1-butanol by the reflux procedure yielded a viscous yellow oil which, on standing almost a year at room temperature, largely crystallized. Previous attempts at other methods of crystallization of the oil had not been successful. The crystalline product was purified by three recrystallizations from 40% ethanol and then was thrown out of ether solution by the addition of petroleum ether. It melted at 51–52° and gave no m.p. depression when mixed with an authentic sample,[14] m.p. 53–54°.

4,4-Dimethyloxazoline-2-thiol.—The thiuram disulfide was formed from 15.0 g. of 2-amino-2-methyl-1-propanol (Eastman Pract., redistilled, b.p. 163.5–164.5°). The reaction with iodine was too slow for determination of the titration end-point, therefore the theoretical volume of iodine solution was added in 10-ml. portions during a period of 1.25 hours. Each addition was made when the previous one had become decolorized. After the usual decomposition and recovery steps, there was obtained 6.0 g. (59% theoretical) of impure 4,4-dimethyloxazoline-2-thiol. Precipitation from benzene solution by the addition of petroleum ether yielded 5.6 g. of creamy-white needles, m.p. 123–124.5° (lit.[6] 123–125°).

Products from 2-Amino-2-methyl-1-propanol by Reflux Method.—Twenty-five grams of the aminoalcohol, refluxed with carbon disulfide and alcoholic potassium hydroxide by the method of Bruson and Eastes,[5] yielded 40 g. of the crude oxazoline derivative. The pale yellow solid, when boiled with 200 ml. of water, largely dissolved, leaving a heavy yellow oil from which the hot solution was decanted. When cooled, the aqueous solution deposited 10.8 g. of slightly impure 4,4-dimethyloxazoline-2-thiol, m.p. (after purification) 121.5–123°.

The yellow oil remaining from the hot water extraction consisted mainly of the same oxazoline compound, contaminated with 4,4-dimethylthiazoline-2-thiol. The oil was recrystallized from 80 ml. of 75% ethanol. The mother liquor was evaporated to dryness; the residue was leached twice with boiling water, recrystallized from 10 ml. of 50% ethanol, and twice precipitated from benzene solution by addition of petroleum ether. The product was 0.6 g. of 4,4-dimethylthiazoline-2-thiol, m.p. 116–117.5°, no m.p. depression when mixed with an authentic sample,[14] m.p. 115–116° (uncor.).

4,4,6-Trimethyl-5,6-dihydro-1,3,4-oxazine-2-thiol.—The theoretical quantity of iodine was added in preparing the thiuram disulfide from 17.7 g. of 4-amino-4-methyl-2-pentanol (Shell Development), because the reaction proceeded too slowly to permit titration, as in the example above. Decomposition by heating with water in the usual manner resulted in precipitation of 9 g. of a mixture of the heterocyclic product and sulfur. Recrystallization from acetone yielded 6.6 g. (55% theoretical) of nearly pure 4,4,6-trimethyl-5,6-dihydro-1,3,4-oxazine-2-thiol. A single precipitation from ethyl acetate solution by the addition of petroleum ether purified the product, m.p. 212–213° (lit.[8] 210–211° uncor.). The same compound was recovered as the sole product of reaction under reflux conditions, m.p. 211–212°.

Acknowledgment.—The author is indebted to the late Professor H. S. Fry at whose suggestion and under whose guidance a part of this problem was undertaken. Some of the aminoalcohols were generously supplied by the Commercial Solvents Corp. and the Shell Development Co.

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(14) Sample and melting point value kindly supplied by L. Onanian, American Cyanamid Company.

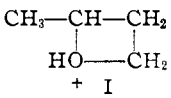
[CONTRIBUTION FROM HAVEMEYER LABORATORY, COLUMBIA UNIVERSITY]

Configurational Interrelationships of Some Secondary Carbinols

BY W. VON E. DOERING AND RICHARD W. YOUNG[1]

With optically active γ-methoxyvaleric acid as the common reference compound, the configurational interrelationships of 2-butanol, 6-methyl-2-heptanol, 2-octanol and 2-methoxypentane have been established, dextrorotatory compounds having identical configuration. The relationship of the first two carbinols has been established with considerably less jeopardization of the optically active center than the interrelationship previously reported, and is placed on a firmer chemical basis.

The significance of the stereochemistry of the partially asymmetric Meerwein–Ponndorf–Verley reduction depends upon the reliability of the assignment of stereochemical configuration to the secondary carbinols employed as reducing carbinol and reduction product, respectively.[2] The relationship of 2-butanol and 6-methyl-2-heptanol, one of the pairs used in this study has been established by chemical methods through 4-hydroxypentanoic acid by Levene and co-workers.[3–6] However, the individual reactions often proceeded with a loss of optical activity, so extensive as to cast considerable doubt on the validity of the conclusions. Indeed, a number were displacement reactions in which the possibility of 4-membered, neighboring group interaction was not remote and, if operative, could have led either to retention or inversion or both, in varying degree. Particularly suspect in this connection were the reactions of 1-amino-3-butanol with nitrous acid and 1,3-dihydroxybutane with hydrogen iodide, both of which involved extensive racemization and might reasonably have proceeded through the cyclic intermediate (I), the stereochemistry of the formation and of the further reaction of which would be uncertain. It seems



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desirable, therefore, to confirm the stereochemical interrelationship by an alternative scheme, using reactions, the stereochemical integrities of which are much more certain and where involvement

(1) From a dissertation submitted in partial fulfillment of the requirements for the Degree of Doctor of Philosophy in the Faculty of Pure Science, Columbia University. R. Melville Cramer Fellow from Dartmouth College, 1947–1949; American Cyanamid Fellow, 1949–1950.

(2) W. von E. Doering and R. W. Young, THIS JOURNAL, **72**, 631 (1950).

(3) P. A. Levene and H. L. Haller, *J. Biol. Chem.*, **69**, 165 (1926).

(4) P. A. Levene and H. L. Haller, *ibid.*, **69**, 569 (1926).

(5) P. A. Levene, A. Walti and H. L. Haller, *ibid.*, **71**, 465 (1926).

(6) P. A. Levene and H. L. Haller, *ibid.*, **83**, 177 (1929).