At the end of some "cold" runs, the thymine was isolated as crystalline material but the radiothymine, after chromatographic purification, was handled in solution with less loss. Chromatographic behavior and ultraviolet absorption were relied upon for identification and assay. The specific activity of the product was identical, within the limits of error, to that of the propionate as reported by the supplier, ORNL.

Experimental

Ethyl propionate-3-C^{14} was prepared from 26.7 mg. (0.278 mmole) of powdered sodium propionate-3-C^{14} (0.452 μc./μmole) by reaction with 2.0 ml. of triethyl phosphate at 170–185° in an apparatus similar to that described by Melville, *et al.*,[5] and collected in a spiral trap with a sintered glass plate.[6]

Subsequent reactions were carried out in a 50-ml. spherical flask having a stoppered 8-mm. side-arm. The neck of the flask included a 3-mm. bore stopcock and terminated in a ball joint for attachment to the vacuum line.

Sodium Diethyl Methyl-C^{14}-oxosuccinate.—The ethyl propionate was condensed into the reaction flask which contained 0.48 mmole of dry sodium ethoxide, 0.49 mmole of diethyl oxalate and 0.3 ml. of diethyl ether. The flask was removed from the vacuum line, shaken mechanically for two hours, and then heated for a few minutes in a boiling water-bath while vented to the atmosphere through a liquid nitrogen-cooled trap. An orange-red solid, presumably sodium diethyl methyl-C^{14}-oxosuccinate, remained.

Diethyl β-Methyl-C^{14}-malate.—To the above solid in the reaction flask cooled to 0° was added a slurry of 10–20 mg. of Adams platinum oxide catalyst in 0.5 ml. of dil. acetic acid (0.63 meq.) and 1.5 ml. of ethanol. The flask side-arm was sealed off and the flask returned to the vacuum line. While immersed in liquid nitrogen to the level of the stopcock plug the flask was evacuated, flushed with hydrogen and then filled with one atmosphere of hydrogen. The stopcock was closed and secured and the flask placed on a shaker to warm to room temperature and to shake for two hours.[7] In large scale runs the yields were 85–95%.[4b]

Sodium β-Methyl-C^{14}-malate.—The flask was vented to release excess hydrogen, 1.0 ml. of 2.34 *N* sodium hydroxide was added, and the reaction mixture was shaken two hours at room temperature.[8] Volatile materials were removed at room temperature by pumping the flask slowly down to 50 μ to leave a white solid.

Thymine (Methyl-C^{14}).—Four ml. of 20% fuming sulfuric acid was cooled in an ice-salt-bath and one g. of urea was dissolved in portions so that the temperature remained below 10°. Two ml. of this solution was transferred to the reaction flask which then was heated on a steam-bath with occasional swirling for 2.5 hours. The product was taken up in water. Ultraviolet assay indicated the presence of 4.85 mg. of thymine (0.038 mmole, 14%). The solution was brought to *p*H 4.0 by adding anion exchange resin (Amberlite IRA-400, OH^- form). After removal of resin on a büchner funnel, assay of the filtrate gave 3.12 mg. of thymine. The resin was re-extracted by stirring with water and filtering again. These two filtrates were concentrated to small volumes and chromatographed in butanol-2 saturated with water on filter paper which had previously been chromatographically washed with butanol–water. The thymine-containing areas were cut from the paper and extracted with abs. ethanol. The thymine solutions thus obtained from the two resin filtrates exhibited good absorption curves so the solutions were combined; yield 2.24 mg. (0.018 mmole, 6.4%); radioactivity: 0.46 μc./μmole; yields ranged from 3.3 to 17.0%.

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[5] C. Melville, J. Rachele and E. Keller, *J. Biol. Chem.*, **169**, 419 (1947).

[6] M. Calvin, C. Heidelberger, J. C. Reid, B. M. Tolbert and P. E. Yankwich, "Isotopic Carbon," John Wiley and Sons, Inc., New York, N. Y., 1949, p. 133.

[7] Neither in macro-scale reductions, where the diethyl β-methylmalate was isolated by fractionation, nor in some micro-scale reactions, where aliquots of the reaction product after hydrolysis were chromatographed, was evidence obtained for the presence of diethyl α-methylsuccinate; *cf.* E. C. Jorgensen, J. A. Bassham, M. Calvin and B. M. Tolbert, THIS JOURNAL, **74**, 2418 (1952).

[8] Experiments using pure diethyl β-methylmalate indicated that hydrolysis was 98-100% complete in this time.

Pentaerythritol Derivatives. I. The Preparation of Pentaerythritol Monomethyl Ether[1]

BY C. H. ISSIDORIDES AND A. I. MATAR

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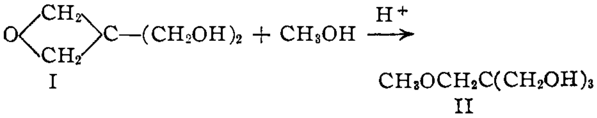
In a previous work on the preparation of pentaerythritol ethers[2] it was found that the trimethylene oxide ring of 3,3-bis-(hydroxymethyl)-oxetane (I) can be opened by the sodium salt of ethylene glycol to give pentaerythritol β-hydroxyethyl ether in satisfactory yield. Recently, Searles and Butler[3] have shown that trimethylene oxide reacts with alcohols in the presence of catalytic amounts of strong acids or bases or in the presence of water to give the corresponding monoalkyl ethers of trimethylene glycol. These reactions indicate that the behavior of 1,3-epoxides toward alcohols is similar to that of 1,2-epoxides.

The present paper describes the preparation of pentaerythritol monomethyl ether (II) from 3,3-bis-(hydroxymethyl)-oxetane (I) and methyl alcohol in the presence of catalytic amounts of sulfuric acid. This method, in contrast to the ones previously described in the literature,[4-6] gives II in good yield (80%).



I

II

A small amount of a side-product (probably a mixture of pentaerythritol and a higher polyether) which is also formed during this reaction can be separated easily from the main product by continuous extraction of the latter with dry ether. The monomethyl ether of pentaerythritol obtained by this method was further characterized as the triacetate and the tritrityl ether.

The starting material I in this investigation was obtained by the action of alcoholic potassium hydroxide on pentaerythrityl monobromide (III) according to the method of Govaert and Beyaert.[7] This procedure gives I in good yield, also small amounts of a side-product which we identified as 2-methylene-1,3-propanediol (IV) by its physical constants and by conversion to the corresponding diacetate and dichloride. The formation of IV is probably the result of an elimination reaction op-

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[1] Abstracted in part from the M.S. thesis of Afaf I. Matar, American University of Beirut, June, 1955.

[2] S. Wawzonek and C. H. Issidorides, THIS JOURNAL, **75**, 2373 (1953).

[3] S. Searles and C. F. Butler, *ibid.*, **76**, 56 (1954).

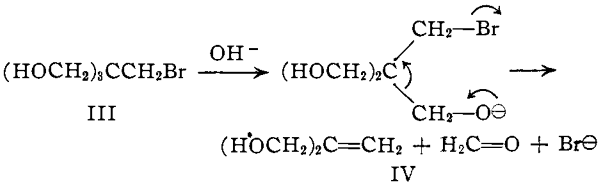
[4] L. Orthner and G. Freyss, *Ann.*, **484**, 131 (1930).

[5] S. Wawzonek and D. A. Rees, THIS JOURNAL, **70**, 2433 (1948).

[6] S. Wawzonek and J. P. Henry, *ibid.*, **75**, 1258 (1953).

[7] F. Govaert and M. Beyaert, *Proc. Acad. Sci. Amsterdam*, **42**, 790 (1939).

erating along the chain of the 1,3-bromohydrin moiety of III by a mechanism similar to the one postulated by Searles and Gortatowski[8] for the cleavage of 3-bromo-2,2-dimethyl-1-propanol by base.



It is interesting to note that while IV dissolved in carbon tetrachloride absorbs bromine readily, the bromine absorptive capacity of its dichloride is not appreciable, in agreement with the observation of Mooradian and Cloke.[9]

Experimental[10]

Pentaerythrityl Monobromide (III).—The procedure of Beyaert and Hansens[11] was modified using 48% in place of 66% hydrobromic acid. Recrystallization of the final product from a mixture of 2 parts by volume of ethyl acetate and 3 parts by volume of chloroform gave monobromopentaerythritol (III) melting at 75–76° (reported m.p. 70–72°,[11] 76°[12]); yield 54% of the theoretical based on pentaerythritol.

Reaction of Pentaerythrityl Monobromide (III) with Alcoholic Potassium Hydroxide.—The procedure was essentially based on the method of Govaert and Beyaert.[7] A solution of 13 g. of potassium hydroxide (0.23 mole) in 190 ml. of absolute ethyl alcohol was added to a solution of 39.8 g. (0.2 mole) of pentaerythrityl monobromide in 160 ml. of absolute ethyl alcohol. The mixture was stirred for two hours at room temperature, refluxed on the steam-bath for five minutes, cooled in an ice-bath, filtered from the precipitated potassium bromide, neutralized with acetic acid and concentrated *in vacuo* to a viscous residue. Fractionation through a Vigreux column at reduced pressure gave two fractions: fraction i, b.p. 85–100° (1–2 mm.), 4 g.; fraction ii, 3,3-bis-(hydroxymethyl)-oxetane, b.p. 135–138° (1–2 mm.), 16.5 g. (literature b.p. 128° (0.4 mm.)[7]).

Identification of Fraction (i).—Refractionation of this fraction gave a colorless liquid boiling at 93–95° (2 mm.), n^{25}_{D} 1.4731, d^{27}_{4} 1.077 (lit. b.p. for 2-methylene-1,3-propanediol 125–126° (18 mm.[9]), n^{20}_{D} 1.4758,[9] d^{20}_{4} 1.0791[9]). The compound gave positive tests for unsaturation with bromine in carbon tetrachloride and with a solution of potassium permanganate.

Acetylation was accomplished by heating on the steam-bath for 12 hours a mixture of 10 g. of 2-methylene-1,3-propanediol (IV) with 80 ml. of acetic anhydride and 1 ml. of dry pyridine. Removal of the excess acetic anhydride under reduced pressure was followed by the addition of ice and neutralization with sodium bicarbonate. Extraction with ether gave an oil which was fractionated through a Vigreux column. The yield of ester boiling at 85–87° (1 mm.) was 17.5 g. (90%), n^{25}_{D} 1.4335, d^{28}_{4} 1.072, sapon. equiv. 86 (calcd. for the diacetate of 2-methylene-1,3-propanediol, 86).

Conversion of IV to the dichloride was accomplished by addition over a period of 2 hours at 0° of 29 g. of thionyl chloride dissolved in 20 ml. of dry chloroform to a well-stirred solution of 8.8 g. of IV, 15 ml. of dry pyridine and 10 ml. of dry chloroform. The mixture was then refluxed for two hours, allowed to stand overnight and then poured onto ice and neutralized with solid sodium bicarbonate. Extraction with ether followed by washing the ether extracts with dilute sulfuric acid gave, after removal of the solvent, an oil which was fractionated to give 3.2 g. of 3-chloro-2-chloromethyl-1-propene, b.p. 137–138° (756 mm.), n^{28}_{D} 1.4720, d^{27}_{4} 1.178 (lit. b.p. 138–138.3°,[9] n^{20}_{D} 1.4754,[9] d^{20}_{4} 1.1782[9]).

Pentaerythritol Monomethyl Ether (II).—A solution of 22 g. (0.19 mole) of 3,3-bis-(hydroxymethyl)-oxetane in 60 ml. of methyl alcohol was added in the course of 5 minutes to 60 ml. of methyl alcohol containing 0.25 ml. of concentrated sulfuric acid. The mixture was kept at room temperature for 48 hours, neutralized with sodium bicarbonate, cooled in an ice-bath, filtered from the precipitated salt and concentrated *in vacuo* to a viscous residue which solidified upon standing. The crude product was dried in a vacuum desiccator, powdered and extracted exhaustively in a Soxhlet extractor with 100 ml. of dry ether. The ether extracts were cooled and filtered to give 23 g. (82%) of methyl pentaerythrityl ether (II) melting at 67–68°. One recrystallization from a mixture of 12 ml. of chloroform and 8 ml. of ethyl acetate raised the m.p. to 71–72°, recovery 90%. Two more recrystallizations raised the melting point to 72–73° (reported m.p. 72°,[4] 71–72°,[5] 70°,[6] 60–67°[13]).

The crude ether (m.p. 67–68°) was acetylated with acetic anhydride and pyridine by a procedure similar to the one described previously for the esterification of IV. The yield of ester boiling at 117–119° (1 mm.) was 71% of the theoretical based on the crude ether, n^{20}_{D} 1.4408, d^{28}_{4} 1.119.

Anal. Calcd. for $C_{12}H_{20}O_7$: C, 52.17; H, 7.30; sapon. equiv., 92. Found: C, 52.32; H, 7.23; sapon. equiv., 91.5.

Tritylation of the crude ether (1.2 g., 0.08 mole) with triphenylchloromethane (7.3 g., 0.026 mole) and dry pyridine (12 ml.) was carried out as previously reported for the monoethylene glycol ether of pentaerythritol.[2] Recrystallization from acetone gave 4.2 g. (60%) of product melting at 219–220°.

Anal. Calcd. for $C_{63}H_{56}O_4$: C, 86.26; H, 6.43. Found: C, 86.03; H, 6.50.

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[8] S. Searles and M. J. Gortatowski, THIS JOURNAL, **75**, 3030 (1953).

[9] A. Mooradian and J. B. Cloke, *ibid.*, **67**, 942 (1945).

[10] Melting points and boiling points are not corrected.

[11] M. Beyaert and M. Hansens, *Natuurw. Tijdschr.* (*Belg.*), **22**, 249 (1940).

[12] F. Govaert and M. Beyaert, *ibid.*, **21**, 29 (1939).

[13] R. H. Barth (to Heyden Chem. Corp.) U. S. Patent 2,644,013 (June 30, 1953); *C. A.*, **48**, 5211b (1954).

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On the Air Oxidation of 2-Phenylcyclopentanone

BY KURT MISLOW AND ALLAN K. LAZARUS

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We have had occasion to reëxamine the spectral properties[1] of 2-phenylcyclopentanone. While the infrared spectrum was identical with that earlier reported, the ultraviolet spectrum was distinctly different. We are now in a position to explain this discrepancy.

In agreement with the findings of Pascual and Crespo,[2] we have found that the ketone is rapidly oxidized by air to γ-benzoylbutyric acid. Comparison of the ultraviolet spectrum of the acid (Fig. 1, curve A) with that of freshly prepared and repeatedly crystallized ketone (Fig. 1, curve B) reveals that the acid has a maximum at 241.5 mμ, ε 1.2 × 10^4, precisely at a minimum point for the

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[1] K. Mislow and C. L. Hamermesh, THIS JOURNAL, **77**, 1590 (1955).

[2] J. Pascual and R. Crespo, *Anales real soc. españ. fis. y quim.*, **48B**, 273 (1952).