[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF THE AMERICAN UNIVERSITY OF BEIRUT]

Pentaerythritol Derivatives. II. 3-Halomethyl-3-hydroxymethyl Oxetanes[1]

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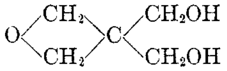
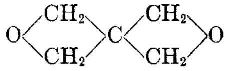
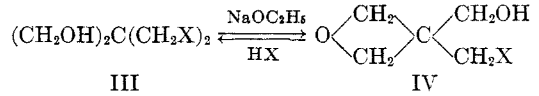
The reaction between pentaerythrityl dichloride or pentaerythrityl dibromide and sodium ethoxide in ethyl alcohol gives the corresponding 3-halomethyl-3-hydroxymethyl oxetanes (IV) in good yield. Evidence for the structure of these compounds is presented. The use of the compounds as intermediates in the preparation of some new mixed dihalides of pentaerythritol is described.

Pentaerythritol can form intramolecular ether linkages to give 3,3-bis-(hydroxymethyl)oxetane (I) or 2,6-dioxaspiro[3,3]heptane (II). Recent interest in these compounds stems from the fact that the trimethylene oxide ring is sensitive to attack by amines[2] and alcohols,[3] thus providing a possible route for the synthesis of amino and ether derivatives of pentaerythritol, not easily available by more direct methods. The general method for the preparation of these oxetane derivatives is by the action of potassium hydroxide on a pentaerythrityl halide.[4,5,6] While the yield of I by this method is satisfactory,[4] the yield of II is remarkably low.[5,6]

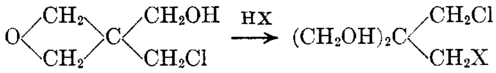

I


II

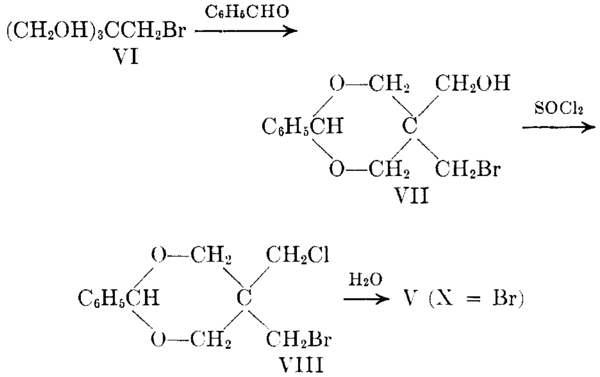
This paper describes the results of a search originally meant to improve the yield of II. The starting materials used were pentaerythrityl dichloride (III, X = Cl) or pentaerythrityl dibromide (III, X = Br). When either one of these compounds was treated with sodium ethoxide in ethyl alcohol, the product isolated was not the expected dioxaspiro compound (II), but a viscous liquid containing chlorine or bromine. The fact that substitution of methyl for ethyl alcohol gave the same products suggested the possibility of occurence of a preferential one-sided dehydrohalogenation of III to give the corresponding 3-hydroxymethyl-3-halomethyl oxetanes (IV, X = Cl or Br). Furthermore, when each liquid was treated with the corresponding halogen acid, even at room temperature, the starting material (III) was recovered in good yield.


III IV

As expected, the trimethylene oxide ring of IV is easily opened by other halogen acids. Thus, treatment of 3-chloromethyl-3-hydroxymethyl oxetane (IV, X = Cl) with concentrated hydrobromic acid or with concentrated hydriodic acid gave two mixed dihalides of pentaerythritol hitherto unavailable: 2-bromomethyl-2-chloromethyl-1,3-propanediol (V, X = Br) and 2-chloromethyl-2-iodomethyl-1-3-propanediol (V, X = I).


V

The structures assigned to these compounds are further supported by an independent synthesis of V (X = Br) from pentaerythrityl monobromide (VI). Compound VI was converted through its monobenzal derivative (VII), into VIII which then was hydrolyzed to give a compound identical with the one obtained by treatment of IV (X = Br) with hydrochloric acid or by treatment of IV (X = Cl) with hydrobromic acid.


VI VII VIII

In contrast to the low yield of II obtained by the action of potassium hydroxide on pentaerythrityl dichloride[5] or pentaerythrityl dibromide,[6] the action of sodium ethoxide on these dihalides gives the corresponding oxetanes (IV) in 70–76% yield.

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[1] Abstracted in part from the M.S. thesis of Riza C. Gulen, American University of Beirut, June 1955.

[2] Govaert and Cazier, *Bull. soc. chim. Belges*, **54**, 43 (1945).

[3] Issidorides and Matar, *J. Am. Chem. Soc.*, **77**, 6382 (1955).

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

[5] Wawzonek and Issidorides, *J. Am. Chem. Soc.*, **75**, 2373 (1953).

[6] Backer and Kenning, *Rec. trav. chim.*, **53**, 812 (1934); Furukawa, Wada, and Oda, *Repts. Chem. Research Inst., Kyoto Univ.*, **31**, 222 (1953) [*Chem. Abstr.*, **48**, 7596 (1954)].

EXPERIMENTAL[7]

Pentaerythrityl dibromide (III, X = Br). The procedure of Beyaert and Hansens[8] was modified using 48% in place of 66% hydrobromic acid. The yield of pentaerythrityl dibromide melting at 110–111° was 63% (based on pentaerythritol).

3-Bromomethyl-3-hydroxymethyl oxetane (IV, X = Br). A solution of 7.2 g. of sodium (0.31 g.-atom) in 350 ml. of absolute ethanol was added slowly to a solution of 80 g. of pentaerythrityl dibromide (0.31 mole) in 150 ml. of ethanol. The mixture was refluxed with stirring for 2.5 hours, cooled, filtered from the precipitated sodium bromide, and concentrated *in vacuo* to a viscous residue. Fractionation through a Vigreux column at reduced pressure gave 39 g. (71%) of IV (X = Br), boiling at 141–143° (1-2 mm), n^{20}_{D} 1.5101.

Anal. Calc'd for $C_5H_9BrO_2$: Br, 44.14. Found: Br, 44.50.

Conversion to pentaerythrityl dibromide was accomplished by refluxing for 2 hours 5 g. of IV (X = Br) with 50 ml. of 48% hydrobromic acid. Dilution of the mixture with 100 ml. of water was followed by extraction with several portions of ether. Evaporation of the ether gave a residue which was recrystallized from water to give 5.7 g. of pentaerythrityl dibromide (79%) melting at 110–111°. A similar procedure using 48% hydrobromic acid at room temperature for 2 days gave 70% yield of pentaerythrityl dibromide.

3-Chloromethyl-3-hydroxymethyl oxetane (IV, X = Cl). This compound was prepared from pentaerythrityl dichloride[5] and sodium ethoxide by a procedure similar to the one described above. Fractionation under reduced pressure gave a product boiling at 142–145° (4–5 mm.), n^{21}_{D} 1.4822; yield 76%.

Anal. Calc'd for $C_5H_9ClO_2$: Cl, 25.96. Found: Cl, 26.05.

Conversion to pentaerythrityl dichloride was accomplished by refluxing IV (X = Cl) with concentrated hydrochloric acid. The yield of pentaerythrityl dichloride melting at 80–81° was 70%.

2-Bromomethyl-2-chloromethyl-1,3-propanediol (V, X = Br). This compound was prepared from IV (X = Br) and concentrated hydrochloric acid by a method similar to the one described above. The crude product was recrystallized from a mixture of carbon tetrachloride (4 parts) and toluene (1 part) to give V (X = Br), melting at 95.5–96°; yield 71%.

Anal. Calc'd for $C_5H_{10}BrClO_2$: C, 27.62; H, 4.64; Cl-Br, 53.07. Found: C, 27.89; H, 4.73; Cl-Br, 53.80.

The same product was obtained from IV (X = Cl) and 48% hydrobromic acid.

2-Chloromethyl-2-iodomethyl-1,3-propanediol (V, X = I). A solution of 2.5 g. of IV (X = Cl) in 25 ml. of 45% hydriodic acid was refluxed for 1/2 hour and then diluted with 75 ml. of water. The mixture was neutralized with solid sodium carbonate and cooled in an ice-bath. The precipitated crude product (3.5 g.) was separated by filtration. An additional 1.5 g. of material was obtained by extracting the filtrate with ether. The combined crude product was recrystallized from carbon tetrachloride and a small amount of toluene to give 4.3 g. (78%) of V (X = I) melting at 95–95.5°.

Anal. Calc'd for $C_5H_{10}ClIO_2$: C, 22.70; H, 3.81; Cl-I, 61.38. Found: C, 22.70; H, 3.64; Cl-I, 61.70.

Preparation of V (X = Br) *from pentaerythrityl monobromide.* A solution of 20 g. of pentaerythrityl monobromide[3] (VI) (0.1 mole) in 50 ml. of water was treated with 10.6 g. of benzaldehyde (0.1 mole) and 0.6 ml. of concentrated hydrochloric acid and the mixture was stirred for 48 hours. The precipitate was dried and recrystallized from a mixture of benzene and 60–70° petroleum ether to give 20 g. of monobenzal pentaerythrityl monobromide (VII) (69%) melting at 73.5–74.5°.

Anal. Calc'd for $C_{12}H_{15}BrO_3$: C, 50.19; H, 5.26. Found: C, 50.14; H, 5.08.

Conversion of VII to V was accomplished by addition over a period of 2 hours at 0° of 7.2 g. of thionyl chloride dissolved in 8 ml. of dry chloroform to a well-stirred solution of 17.2 g. of VII, 4.7 g. of dry pyridine, and 8 ml. of dry chloroform. The mixture was refluxed and then hydrolyzed, as previously reported[5] for the preparation of pentaerythrityl dichloride. Recrystallization of the crude product from a mixture of carbon tetrachloride (20 ml.) and toluene (5 ml.) gave 7 g. of V (X = Br) (53%) melting at 94–95°. A mixture with a sample prepared by the action of hydrochloric acid on IV (X = Br) melted at the same point.

2,2-Bis(bromomethyl)-1,3-dichloropropane. This compound was prepared by the action of excess thionyl chloride on pentaerythrityl dibromide, by a method similar to the one described above. Removal of chloroform and excess thionyl chloride under reduced pressure gave a residue which was washed several times with hot water, dried and recrystallized from 80–100° petroleum ether. Yield 69%. The analytical sample was sublimed in vacuo; m.p. 116.5–118°.

Anal. Calc'd for $C_5H_8Br_2Cl$: Cl-Br, 77.21; Found: Cl-Br, 77.10.

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BEIRUT, LEBANON

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(7) Melting points and boiling points are not corrected.

(8) Beyaert and Hansens, *Natuurw. Tijdschr.* (*Belg.*), 22, 249 (1940).