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Preparation and Properties of 1,3-Dioxep-5-enes

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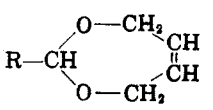
Several aldehydes and cyclohexanone were found to react with *cis*-2-butene-1,4-diol to give good yields of 1,3-dioxep-5-enes, whereas 4-methyl-2-pentanone did not react. Bromine added to 1,3-dioxep-5-ene to give 5,6-dibromo-1,3-dioxepane. Reaction of the dibromodioxepane with sodium methoxide produced 5-bromo-1,3-dioxep-5-ene, by means of a *cis* dehydrobromination, and a methoxy-1,3-dioxepene. No 1,3-dioxepin was found.

With the exceptions of a recent report that the reaction of *cis*-2-butene-1,4-diol with formaldehyde gives a cyclic acetal[1] and an earlier statement that *cis*-2-butene-1,4-diol forms polymerizable acetals,[2] there are no descriptions of 1,3-dioxep-5-enes (I) in the literature.



Ia R=H

I

We have found that the reaction of *cis*-2-butene-1,4-diol with formaldehyde in the presence of an acidic catalyst gives 1,3-dioxep-5-ene (Ia). That the product was indeed Ia, and not the isomeric 4-vinyl-1,3-dioxolane, was shown by hydrogenation to the known 1,3-dioxepane, which was converted to tetrahydrofuran by aqueous sulfuric acid solution.

Other aldehydes reacted with *cis*-2-butene-1,4-diol under similar conditions to give the corresponding 2-alkyl-1,3-dioxep-5-enes. The structures of the latter were assigned on the basis of analogy and the similarity of the infrared spectra of these materials to that of Ia.

Under the same conditions as were used for the aldehyde reactions, *cis*-2-butene-1,4-diol reacted with cyclohexanone to give the spiro ketal but did not react with 4-methyl-2-pentanone.

A high yield of Ia was obtained from the reaction of *cis*-2-butene-1,4-diol with formaldehyde if the product was distilled from the acidic reaction mixture. If the acidic catalyst was neutralized before distillation, the yield dropped to about 25%, and a large amount of viscous, nonvolatile residue was obtained. These results may be attributed to the formation, during the reaction, of an equilibrium mixture of cyclic acetal and linear polymeric acetal which, on distillation from the acidic medium, is converted to the volatile cyclic acetal. The effect of neutralizing the acidic catalyst prior to distillation was investigated only in the case of the preparation of Ia.

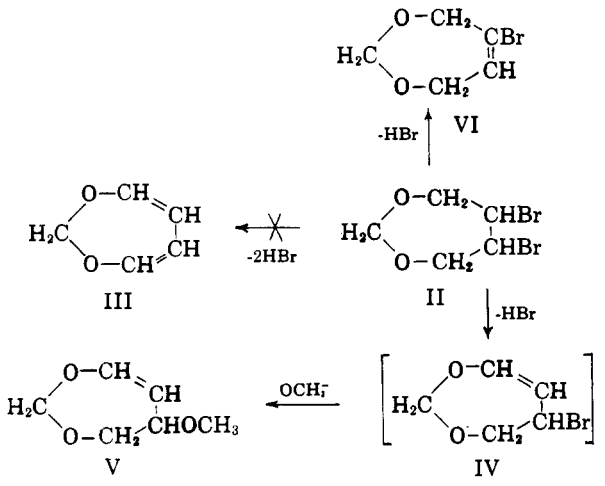
The addition of bromine to 1,3-dioxep-5-ene gave 5,6-dibromo-1,3-dioxepane (II) in high yield. That the addition occurred in the expected *trans* manner was shown by cleavage of II with methanolic hydrogen chloride to give the known *dl-threo*-2,3-dibromo-1,4-butanediol. It was hoped that *trans* dehydrobromination of II would lead to the unknown 1,3-dioxepin (III) in a manner analogous to the dehydrobromination of *trans*-1,2-dibromocyclohexane to 1,3-cyclohexadiene.[3] However, attempted dehydrobromination of II using quinoline or potassium *tert*-butoxide in tetralin gave no low-boiling products. Reaction of II with methanolic sodium methoxide gave two monodehydrobromination products, one a methoxy-1,3-dioxepene and one a bromo-1,3-dioxepene. The former is believed to be 6-methoxy-1,3-dioxep-4-ene (V) which may have been formed by a 4,5-dehydrobromination to the allylic bromide (IV) followed by substitution of methoxyl for bromine. This structure was not established conclusively, but it is consistent with the observed properties of the compound. The infrared spectra of the various 1,3-dioxep-5-enes and of the bromodioxepene showed many similarities. In particular, all had a strong band at 12.8 μ in the skeletal band region. This band, as well as others apparently characteristic of the 1,3-dioxep-5-ene structure, was absent from the spectrum of the methoxydioxepene. Therefore, the 1,3-dioxep-5-ene skeleton probably was not present in the methoxydioxepene but, because of the lack of model compounds, no conclusive infrared spectral evidence could be obtained to definitely establish the presence of the 1,3-dioxep-4-ene skeleton. The bromodioxepene was shown to be 5-bromo-1,3-dioxep-5-ene (VI) by its lack of reactivity toward sodium methoxide and by infrared spectral data.

Reaction of II with sodium isopropoxide gave a product which appeared to be a mixture of VI with an isopropoxy-1,3-dioxepene analogous to V, but the mixture could not be separated by fractional distillation. The formation of VI required an unexpected *cis* elimination of hydrogen bromide. This

(1) Reppe, *et al.*, *Ann.*, **596**, 1 (1956).

(2) Copenhaver and Bigelow, *Acetylene and Carbon Monoxide Chemistry*, Reinhold Publishing Corp., New York, N. Y., 1949, p. 143.

(3) Mousseron and Winternitz, *Bull. soc. chim.*, [5] **13**, 232 (1946).



is another example in the growing list of *cis* eliminations.[4]

EXPERIMENTAL

1,3-Dioxep-5-ene. A mixture of 176 g. (2 moles) of *cis*-2-butene-1,4-diol, 60 g. (2 moles) of paraformaldehyde, 25 ml. of benzene, and 0.25 g. of *p*-toluenesulfonic acid was refluxed under a Dean-Stark trap until the removal of water was complete (2 to 3 hours). Distillation of the reaction mixture through a short column gave, after removal of benzene, 172 g. (86%) of crude 1,3-dioxep-5-ene, b.p. 120–126.5°. The crude product, which contained a small amount of water and formaldehyde, was best purified by redistillation from solid sodium hydroxide or potassium hydroxide. Thus, 160 g. of pure 1,3-dioxep-5-ene was obtained, b.p. 127.8–128.2° (734 mm.), n_D^{20} 1.4570.

Anal. Calc'd for $C_5H_8O_2$: C, 59.98; H, 8.05. Found: C, 59.91; H, 8.17.

In another preparation, carried out as above, the acid catalyst was removed prior to distillation by shaking the reaction mixture with solid sodium hydroxide. Distillation gave only 56 g. of crude dioxepene along with 134 g. of a viscous residue. This residue was not further investigated but was presumed to be the linear polymeric acetal.

2-Isopropyl-1,3-dioxep-5-ene. In a like manner, *cis*-2-butene-1,4-diol and isobutyraldehyde gave an 84% yield of crude 2-isopropyl-1,3-dioxep-5-ene, which on redistillation boiled at 170–170.6° (735 mm.), n_D^{20} 1.4484.

Anal. Calc'd for $C_8H_{14}O_2$: C, 67.57; H, 9.92. Found: C, 67.46; H, 9.90.

2-(1-Methylpropyl)-1,3-dioxep-5-ene. In a like manner, *cis*-2-butene-1,4-diol and 2-methylbutyraldehyde gave a 75% yield of 2-(1-methylpropyl)-1,3-dioxep-5-ene, b.p. 190–193° (730 mm.), n_D^{20} 1.4514. The crude product was not redistilled.

Anal. Calc'd for $C_9H_{16}O_2$: C, 69.20; H, 10.33. Found: C, 69.18; H, 10.22.

2-Propenyl-1,3-dioxep-5-ene. The reaction mixture from *cis*-2-butene-1,4-diol and crotonaldehyde was flash-distilled at 4 to 5 mm. to give a fraction boiling at 50–80° and a considerable quantity of residue. Fractional distillation through an efficient column gave a 25% yield of 2-propenyl-1,3-dioxep-5-ene, b.p. 54–55° (4.5 mm.), n_D^{20} 1.4739.

Anal. Calc'd for $C_8H_{12}O_2$: C, 68.53; H, 8.63. Found: C, 68.69; H, 8.65.

Spiro[cyclohexane-1,2'-(1',3'-dioxep-5'-ene)]. A mixture of 49 g. (0.5 mole) of cyclohexanone, 44 g. (0.5 mole) of *cis*-2-butene-1,4-diol, and 45 ml. of benzene was prepared. When 0.25 g. of *p*-toluenesulfonic acid was added to the mixture, the temperature rose spontaneously to 40°. The mixture was refluxed under a Dean-Stark trap for 2 hours. Distillation of the reaction mixture through a short column gave, after removal of benzene, 6.5 g. of cyclohexanone, b.p. 40–43° (10 mm.), and 61 g. (73%) of spiro[cyclohexane-1,2'-(1',3'-dioxep-5'-ene)], b.p. 94° (10 mm.), n_D^{20} 1.4876.

Anal. Calc'd for $C_{10}H_{16}O_2$: C, 71.39; H, 9.59. Found: C, 70.97; H, 9.51.

Attempted reaction of cis-2-butene-1,4-diol with 4-methyl-2-pentanone. A mixture of 44 g. (0.5 mole) of *cis*-2-butene-1,4-diol, 60 g. (0.6 mole) of 4-methyl-2-pentanone, 45 ml. of benzene, and 0.25 g. of *p*-toluenesulfonic acid was refluxed under a Dean-Stark trap for 20 hours; during this time 9 ml. of water was collected. Distillation of the reaction mixture gave a quantitative recovery of 4-methyl-2-pentanone, some low-boiling products (presumably dihydrofuran and crotonaldehyde),[5] and a large amount of tarry residue.

1,3-Dioxepane. A solution of 90 g. (0.9 mole) of 1,3-dioxep-5-ene in 60 ml. of methanol was hydrogenated over 5 g. of Raney nickel at 1000 p.s.i. for 1 hour at 100°. The catalyst was removed by filtration and the filtrate was distilled to give, after removal of methanol, 78 g. (85%) of 1,3-dioxepane, b.p. 117.5–118°,[6] n_D^{20} 1.4303.[7]

A mixture of 20 g. of 1,3-dioxepane with a solution of 15 ml. of concentrated sulfuric acid in 30 ml. of water was heated under a short, glass bead-packed column. Formaldehyde was evolved rapidly. Over a period of 30 minutes 12.1 g. (86%) of tetrahydrofuran was collected at 63–66°. The distillate was dried over sodium hydroxide pellets and redistilled, b.p. 65°, n_D^{20} 1.4055. Its infrared spectrum was identical to that of an authentic sample of tetrahydrofuran.

5,6-Dibromo-1,3-dioxepane. A solution of 76 g. (0.76 mole) of 1,3-dioxep-5-ene in 100 ml. of carbon tetrachloride was cooled in an ice-bath. A solution of 120 g. (0.76 mole) of bromine in 100 ml. of carbon tetrachloride then was added dropwise with stirring. The solvent then was removed by distillation and the residue was recrystallized from ethanol to give 150 g. (76%) of 5,6-dibromo-1,3-dioxepane, m.p. 36–37°.

Anal. Calc'd for $C_5H_8Br_2O_2$: C, 23.15; H, 3.08; Br, 61.60. Found: C, 23.22; H, 3.12; Br, 61.60.

Reaction of 5,6-dibromo-1,3-dioxepane with sodium methoxide. A solution of sodium methoxide was prepared by dissolving 46.0 g. (2.0 g.-atoms) of sodium in 750 ml. of anhydrous methanol. This solution was heated to reflux and stirred, and to it was added during a period of 3 hours a solution of 260 g. (1.0 mole) of 5,6-dibromo-1,3-dioxepane in 250 ml. of anhydrous methanol. The mixture was refluxed for an additional 18 hours. Titration of an aliquot with acid indicated that approximately 1.3 moles of sodium methoxide had been consumed. Refluxing was continued for an additional 24 hours but no further consumption of sodium methoxide occurred. The excess sodium methoxide was destroyed by adding 100 g. of ethyl bromide and refluxing about 3 hours. The mixture then was cooled and filtered. Most of the methanol was removed from the filtrate by distillation. The residue was diluted with ether to precipitate the remaining sodium bromide and filtered. The solvent was removed from the filtrate under reduced pressure. The residue, 143 g., was distilled at reduced pressure through a short, packed column to give 126 g. of distillate, b.p. 62–66° (7 mm.). Fractionation of 120 g. of this distillate at 7 mm. pressure through a column having an efficiency of approximately 100 plates gave two main fractions. Fraction A weighed 29 g., b.p. 48.0–50.0°, n_D^{20} 1.4560; Fraction B weighed 43 g., b.p. 61.0–61.6°, n_D^{20} 1.5128. There was no

(4) Baddeley, *Ann. Repts. on Progr. Chem. (Chem. Soc. London)*, **51**, 154 (1954).

(5) Brace, *J. Am. Chem. Soc.*, **77**, 4157 (1955).

(6) Reppe, ref. (1), reports b.p. 117°

(7) Hill and Carothers, *J. Am. Chem. Soc.*, **57**, 925 (1935), report n_D^{20} 1.4310.

indication of the presence of any substance with as low a boiling point as 1,3-dioxepin should have.

Examination of Fraction A. Fraction A contained no halogen and rapidly added bromine in carbon tetrachloride to give a very unstable substance which could not be isolated. Treatment of Fraction A with methanolic hydrogen chloride gave methylal and tar. Elemental analysis of Fraction A indicated that it was a methoxy-1,3-dioxepene. The infrared spectral data were inconclusive but indicated the probability that this material did not have the 1,3-dioxep-5-ene skeleton. It is likely, therefore, that this fraction was 6-methoxy-1,3-dioxep-4-ene.

Anal. Calc'd for $C_6H_9O_3$: C, 55.8; H, 6.98. Found: C, 55.51; H, 7.15.

Examination of Fraction B. Fraction B contained bromine and rapidly added bromine in carbon tetrachloride solution to give a very unstable substance which could not be isolated. Treatment with methanolic hydrogen chloride gave methylal and tar. Elemental analysis indicated that this fraction was a bromo-1,3-dioxepene. Infrared spectral data established the presence of the 1,3-dioxep-5-ene skeleton, which was consistent with the assigned structure, 5-bromo-1,3-dioxep-5-ene.

Anal. Calc'd for $C_5H_7BrO_2$: C, 33.5; H, 3.91; Br, 44.4. Found: C, 33.29; H, 4.01; Br, 44.34.

Methanolysis of 5,6-dibromo-1,3-dioxepane. To 200 ml. of approximately 1 *N* methanolic hydrogen chloride solution was added 50 g. (0.19 mole) of 5,6-dibromo-1,3-dioxepane. The mixture was refluxed for 30 minutes and then was distilled through an efficient column to remove the methylal formed. The yield of methylal, b.p. 41–44°, was 14 g. (98%). The residual methanolic solution was neutralized with sodium bicarbonate, filtered, and distilled under reduced pressure to remove the methanol. The residue was distilled *in vacuo* to give 33 g. (72%) of *dl-threo*-2,3-dibromo-1,4-butanediol, b.p. 140–145° (0.5 mm.), m.p. 86–87° (after recrystallization from benzene). The reported melting point of *dl-threo*-2,3-dibromo-1,4-butanediol[8] is 87°.

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(8) Valette, *Ann. chim.* (*Paris*), [12] **3**, 644 (1948).