The Preparation of 2,2-Bis(hydroxymethyl)-3-butene-1-ol and 2-(Hydroxymethyl)-2-methyl-3-butene-1-ol and Their Acetates and Nitrates

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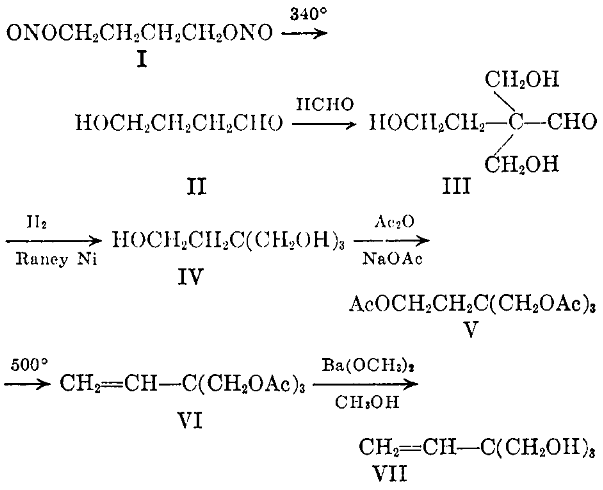
2,2-Bis(hydroxymethyl)-3-butene-1-ol (VII) was prepared by the following sequence of reactions:



II was prepared by adapting the pyrolysis of 1,4-butanediol dinitrite[1] as a synthetic method. Yields were lower than those reported by Kuhn and DeAngelis since the nitrite was pyrolyzed more rapidly and in large quantities, causing an increase in side reactions.

Attempted preparation of IV from II by condensation with formaldehyde followed by a crossed Cannizzaro reaction (as in the well-known synthesis of pentaerythritol[2]) led to the formation of uncrystallizable sirups and large amounts of gummy solid. IV was successfully prepared by condensing II with formaldehyde to form III, then hydrogenating[3] III catalytically to give IV. The crude IV was not isolated as such but was acetylated to give V, which was distilled. This was found to be the best way to work up the reaction mixture without large losses. Also, the next step, introduction of the double bond, required that IV be in the form of its acetate, since the trimethylol configuration is thermally unstable[4] and IV probably could not be dehydrated as such to give VII in reasonable yield. A small sample of IV was prepared and characterized by catalytic deacetylation of V.

2-(Hydroxymethyl)-2-methyl-3-butene-1-ol (VIII) was prepared from 4-hydroxy-3-(hydroxymethyl)-3-methyl-2-butanone[5] through reactions analogous to those used to prepare VII. The overall yields of VIII and VII (based on methyl ethyl ketone and on II) were 16.1 and 11.1%, respectively.

The nitrate esters of VII and VIII were prepared in a fairly pure state and their physical properties determined. In order to avoid the formation of nitro compounds and other side reactions it was found necessary to keep the reaction time to a minimum and to dilute the nitrating mixture with more acetic acid than is customary. The nitrates had negligible infrared absorption at 5.8 and 6.4 microns (carbonyl and nitro regions) and retained the absorption at 3.24 microns characteristic of C—H stretching in vinyl compounds.

EXPERIMENTAL

Preparation of 2,2-bis(hydroxymethyl)-3-butene-1-ol (VII).

γ-Hydroxybutyraldehyde. The pyrolysis of I was carried out in a vertical pyrex tube, 3 × 57 cm., with a side arm near the top for admitting nitrogen. The central 23-cm. portion of the tube was packed with glass helices and kept at 340° by means of an electric furnace, and a slow stream of nitrogen swept the pyrolyzate into two traps, the first cooled with ice and the second with Dry Ice. The system was maintained at 10–20 mm. by means of a water pump, and liquid I was added at a rate of 1 drop per 3 sec. The pyrolyzate was taken up in twice its volume of ether, washed with 5% sodium carbonate solution and dried over magnesium sulfate. After removal of the ether the product was distilled through a Vigreux column. The average yield of hydroxybutyraldehyde, b.p. 55–60° (9 mm.), was 43%.

2,2-Bis(hydroxymethyl)-4-hydroxybutyraldehyde (III). Into a 1-l., three necked flask equipped with a stirrer, thermometer, and gas inlet and outlet tubes were added 119 g. (1.35 moles) γ-hydroxybutyraldehyde, 232 g. 36% formaldehyde (2.79 moles), and 210 ml. of water. The mixture was cooled to 15° and 49.7 g. of sodium carbonate was added in small portions over 35 min. The solution was allowed to come to room temperature and after 1 hr. was heated to 45° and stirred at this temperature overnight. The reaction was carried out in a nitrogen atmosphere. The reaction mixture was then cooled and brought to a *p*H of 8 with 6*N* HCl. The water was distilled off under vacuum, leaving a paste which was treated with acetone and filtered to remove sodium chloride. The filtrate was evaporated to a small volume and treated with 700 ml. of acetone. The solution was kept cold overnight. More solid precipitated, which was filtered off. Evaporation of the filtrate yielded 179 g. crude III, whose infrared spectrum has no band in the carbonyl region, indicating that it exists in the form of its cyclic hemiacetal.

2,2-Bis(acetoxymethyl)-1,4-diacetoxybutane (V). The crude III was dissolved in 380 ml. absolute alcohol, 60 ml. W-7 Raney nickel catalyst was added, and the solution was hydro-

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[1] L. P. Kuhn, R. Wright, and L. DeAngelis, *J. Am. Chem. Soc.*, **78**, 2719 (1956).

[2] Gilman and Blatt, ed., *Org. Syntheses*, Coll. Vol. I, 2nd ed., 425 (1941).

[3] An alternate procedure would be to reduce the III with sodium borohydride and then acetylate.

[4] R. W. Brown and G. Dougherty, *J. Org. Chem.*, **13**, 173 (1948).

[5] W. Grimme and J. Wöllner, German Patent 924,803 (1955); *Chem. Abstr.*, **52**, 3853a (1958).

genated at 150° and 1000 p.s.i. for 3 hr. The catalyst was filtered off and the alcohol was removed at reduced pressure to leave a thick sirup (presumably IV) which was acetylated by refluxing for 2 hr. with 650 ml. of acetic anhydride and 70 g. freshly fused sodium acetate. After cooling, the reaction mixture was poured into 4 l. of ice water. The oily layer was separated and the aqueous layer, after standing 2 hr., was neutralized with sodium carbonate and extracted with ether. Extract and oil were washed acid free with 10% sodium carbonate solution and dried over calcium chloride. Removal of the ether and distillation of the product through a spinning band column gave 3 fractions: 16.5 g. b.p. < 125° (0.07 mm.), 28.4 g. impure acetate b.p. 125–147° (0.07 mm.), $n_D^{19.5}$ 1.4480, and 124 g. pure V, b.p. 153–156° (0.07 mm.), $n_D^{19.5}$ 1.4501, $d^{19.5°}$ 1.164. Calcd. MR, 73.46. Found, 73.47. The yield of pure product is 29%, based on the hydroxybutyraldehyde.

Anal. Calcd. for $C_{14}H_{22}O_8$: C, 52.81; H, 6.97. Found: C, 52.65; H, 6.83.

2,2-Bis(hydroxymethyl)-1,4-butanediol (IV). A solution of 1.3 g. V in 50 ml. dry methanol containing 3 ml. 0.2 *M* methanolic barium methylate was refluxed for 15 min., then cooled, neutralized with Dry Ice, and the methanol evaporated. It was necessary to repeat the entire process in order to secure complete deacetylation.

The residue was dissolved in acetone and centrifuged to remove barium salts. Evaporation of the acetone left crude product, m.p. 74–87°. One recrystallization from acetone gave 0.5 g. IV (82% yield), m.p. 87–88°.

Anal. Calcd. for $C_6H_{14}O_4$: C, 47.98; H, 9.39. Found: C, 48.02; H, 9.33.

4-Acetoxy-3,3-bis(acetoxymethyl)-1-butene (VI). Using the same apparatus described in the preparation of hydroxybutyraldehyde, 119 g. V were introduced at a rate of 1 drop per 3 sec. The temperature was 500° and a slow stream of nitrogen was passed through the system at atmospheric pressure. The pyrolyzate was taken up in ether, washed with 10% sodium carbonate solution until acid free and then with water and dried over calcium chloride. After removal of the ether the product was distilled through a spinning band column. The yield of VI was 51 g. (53% yield), b.p. 99–103° (0.1 mm.), $n_D^{20°}$ 1.4504, d^{20} 1.119. MR Calcd., 62.06. Found, 62.11.

Anal. Calcd. for $C_{12}H_{18}O_6$: C, 55.79; H, 7.02. Found: C, 56.09; H, 6.85.

2,2-Bis(hydroxymethyl)-3-butene-1-ol (VII). VI (8.9 g.) was deacetylated in the same manner as was V, using 80 ml. dry methanol and 4 ml. 0.2*M* methanolic barium methylate, and repeating the entire process. After removal of the barium salts and evaporation of the acetone, the residue was dissolved in 80 ml. hot chloroform and the solution was allowed to cool and set in the refrigerator overnight. The crystals which had formed were separated from the solvent by decantation of the solvent, and washed with cold chloroform and dried at reduced pressure. The yield of VII was 3.3 g. (72%), m.p. 16–19°, n_D^{20} 1.4980.

Anal. Calcd. for $C_6H_{12}O_3$: C, 54.51; H, 9.15. Found: C, 54.21; H, 9.34.

Proof of structure of 2,2-bis(hydroxymethyl)-3-butene-1-ol. One gram of VII was dissolved in 50 ml. absolute alcohol and hydrogenated for 3 hr. at 40 p.s.i., using 0.15 g. 10% Pd on charcoal catalyst. Filtration and evaporation left 1.0 g. crude 1,1,1-trimethylolpropane, m.p. 48–57°. After recrystallization from a mixture of acetone and ether, the product melted at 54–58° and showed no depression when mixed with a commercial sample of trimethylolpropane, m.p. 54–58°.

4-Nitrato-3,3-bis(nitratomethyl)-1-butene. With the temperature kept below 10°, 11.4 ml. (0.27 mole) 100% nitric acid was added slowly to a mixture of 8.1 ml. acetic anhydride and 19.5 ml. acetic acid. To this nitrating mixture 2.3 g. (0.0174 mole) VII dissolved in 7 ml. acetic acid were added slowly and with good stirring over a 5-min. period, the temperature being kept at −5 to −10°. After stirring for an additional 10 min. at this temperature the solution was poured into 200 ml. ice water. The mixture was extracted with ether and the extract was washed free of acid with 10% sodium carbonate solution, then was washed several times with water and dried over calcium chloride. Removal of the ether left 4.2 g. nitrate (91% yield), n_D^{21} 1.4876.

Anal. (of crude nitrate). Calcd. for $C_6H_9N_3O_9$: C, 26.98; H, 3.40; N, 15.73. Found: C, 26.33; H, 3.12; N, 15.31.

Preparation of 2-(hydroxymethyl)-2-methyl-3-butene-1-ol (VIII).

4-Hydroxy-3-(hydroxymethyl)-3-methyl-2-butanone (IX). This compound was prepared by a modification of the method of Grimme and Wöllner.[5] To 1.89 g. calcium hydroxide in 1290 ml. water were added simultaneously over a 5-min. period 600 g. (6 moles) 30% formaldehyde solution and 216 g. (3.0 moles) methyl ethyl ketone. The mixture was stirred vigorously and held at 10–15° for an additional 12 hr. After 6 hr. no free calcium hydroxide remained so an additional 0.4 g. were added. After 12 hr. the calcium hydroxide was neutralized with Dry Ice and the calcium carbonate was removed by filtration. The filtrate was concentrated at reduced pressure to a sirup which, upon distillation, gave 224 g. IX (57%), b.p. 138–140° (16 mm.), lit. 138–140° (16 mm.).[6]

2-(Hydroxymethyl)-2-methyl-1,3-butanediol (X). Two hundred twenty-four g. of IX were dissolved in 350 ml. absolute alcohol and hydrogenated for 2 hr. at 150° and 1300 p.s.i., using 24 g. copper chromite catalyst. Filtration to remove the catalyst and evaporation of the solvent at reduced pressure left crude X, which was used directly in the next step.

2-(Acetoxymethyl)-2-methyl-1,3-diacetoxybutane (XI). X was acetylated in the same manner as was IV. Distillation gave 253 g. XI (57% yield based on IX), b.p. 108° (0.1 mm.), n_D^{20} 1.4382, d^{20} 1.097. MR Calcd., 62.58. Found, 62.31.

Anal. Calcd. for $C_{12}H_{20}O_6$: C, 55.35; H, 7.74. Found: C, 55.11; H, 7.61.

4-Acetoxy-3-(acetoxymethyl)-3-methyl-1-butene (XII). XI (252.8 g.) was pyrolyzed in the same manner as was V. Distillation gave 149 g. of XII (76% yield), b.p. 64–66° (0.6 mm.), n_D^{21} 1.4378, d^{21} 1.026, MR Calcd., 51.22; Found, 51.19.

Anal. Calcd. for $C_{10}H_{16}O_4$: C, 59.99; H, 8.04. Found: C, 59.96; H, 7.80.

2-(*Hydroxymethyl)-2-methyl-3-butene-1-ol* (VIII). XII (70 g.) was deacetylated in the same manner as was V, using 320 ml. methanol and 12 ml. 0.2*M* barium methylate. The residue was distilled directly after removal of the methanol, giving 28 g. VIII (69% yield), b.p. 88–90° (2.4 mm.), m.p. 24–26°.

Anal. Calcd. for $C_6H_{12}O_2$: C, 62.07; H, 10.33. Found: C, 62.13; H, 10.36.

3-Methyl-4-nitrato-3-(nitratomethyl)-1-butene. VIII was nitrated in the same manner as was VII, using 13.1 ml. (0.311 mole) 100% nitric acid, 8.7 ml. acetic anhydride, and 19.8 ml. acetic acid. Three g. (0.0259 mole) of VIII in 9 ml. acetic acid were added. The yield of nitrate was 5.3 g. or 100%. Distillation gave two fractions: (1) 1.5 g., b.p. < 75° (0.05 mm.), n_D^{26} 1.4620; and (2) 2.3 g., b.p. 75° (0.05 mm.), n_D^{26} 1.4633. Fraction (2) had d^{22} 1.285, n_D^{22} 1.4648. MR Calcd., 45.21. Found: 44.35.

Anal. Calcd. for $C_6H_{10}N_2O_6$: C, 34.95; H, 4.89; N, 13.59. Found: (crude nitrate) C, 34.53; H, 4.77; N, 13.46. Fr. 2 dist. nitrate: C, 34.46; H, 4.80; N, 13.58.

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(6) N. M. Tilichenko, *J. Gen. Chem.* (*U.S.S.R.*), **10**, 718 (1940); *Chem. Abstr.*, **35**, 2471³ (1941).