

Summary

The keto acids, 5-cyclopentyl-5-oxopentanoic acid and 6-cyclohexyl-6-oxohexanoic acid, have been synthesized by a new method. Bromination of these keto acids gives dibromo keto acids which are readily hydrolyzed to give the γ - and δ -lactones, respectively, of 5-(1-hydroxycyclopentyl)-

5-oxo-4-hydroxypentanoic acid and 6-(1-hydroxycyclohexyl)-6-oxo-5-hydroxyhexanoic acid. The structures of the latter have been established by periodic acid titration and cleavage with one mole of periodate to give cyclopentanone and cyclohexanone, respectively.

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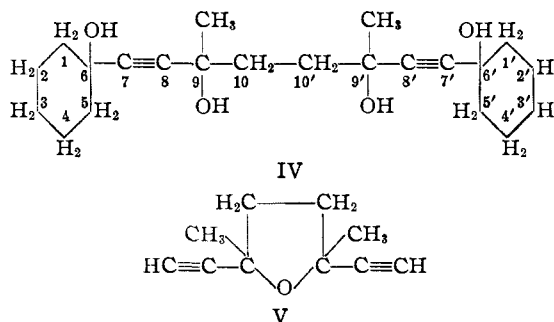
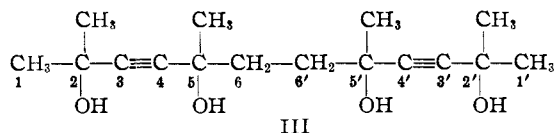
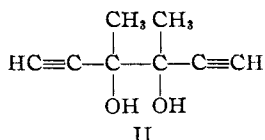
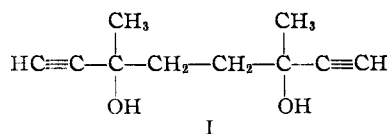
[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, MASSACHUSETTS INSTITUTE OF TECHNOLOGY]

The Synthesis of Diethynyl Glycols and their Condensation with Ketones

BY NICHOLAS A. MILAS, ROBERT J. BROWN¹ AND OLIVERIO PHILLIPS²

With the exception of diacetylene³ and dipropargyl,⁴ no true diacetylenes are known in which each acetylene group bears a reactive hydrogen atom. Diacetylene has been used in this Laboratory⁵ for the synthesis of certain carotenoids containing twelve carbon atoms between two β -ionone nuclei. In the present investigation, the synthesis of diethynyl glycols in which the acetylene groups are separated by two or more carbon atoms was undertaken to provide intermediates in the synthesis of carotenoids containing longer chains between the two β -ionone nuclei. When acetylacetone or diacetyl was allowed to react with sodium acetylide in liquid ammonia, 3,6-dimethyl octa-1,7-diynediol-3,6 (I) and 3,4-dimethyl hexa-1,5-diynediol-3,4 (II) were formed, respectively. A condensation of these diethynyl glycols via the Grignard reaction with excess acetone or cyclohexanone yielded compounds of the type III and IV.

The tetrol (IV) was obtained in two isomeric crystalline forms which may be the *meso* and race-



mic modifications. The yield of the tetrols was somewhat low possibly because of the unfavorable solubility properties of the Grignard derivatives of the glycols.

Wilson and Hyslop⁶ prepared the diphenyl derivative of the glycol (I) from phenylacetylene and acetylacetone. When heated with 60% sulfuric acid in a sealed tube this derivative yielded a substituted tetrahydrofuran. Similarly in an attempt to dehydrate the diethynyl glycol (I) at 290–300° over aluminum phosphate on pumice⁷ the diethynyl substituted tetrahydrofuran (V) was mainly formed.

Experimental

3,6-Dimethyl-octa-1,7-diynediol-3,6 (I).—Into a 5-liter 3-necked round-bottomed flask equipped with a Hershberg stirrer was condensed 2 liters of ammonia. The liquid ammonia was then saturated with dry acetylene and while the latter was allowed to bubble through the solution with stirring, 50.6 g. (2.2 g.-atoms) of sodium was added slowly in the course of five hours. When the blue color of the solution had completely disappeared, 114 g. (1 mole) of acetylacetone dissolved in an equal volume of ether was added dropwise in the course of three hours. Stirring was continued overnight while the temperature was allowed to rise slowly. The ammonia was then removed and to the residue was added 500 cc. of ether and the mixture cooled to 0° and acidified with a tartaric acid solution (250 cc.) containing 165 g. of tartaric acid. The ether layer was separated and the aqueous layer extracted with 3 × 100 cc. of ether, whereby a pale yellowish solid (127.2 g., 77% yield) separated out. This was further purified either by vacuum sublimation or by recrystallization from a 2:1 mixture of *n*-heptane and benzene; m. p. 92–92.5°.

(6) Wilson and Hyslop, *J. Chem. Soc.*, **126**, 707 (1924).

(7) Milas, MacDonald and Black, *THIS JOURNAL*, **70**, 1829 (1948).

(1) M. S. Thesis, Massachusetts Institute of Technology, June, 1946.

(2) B. S. Thesis, Massachusetts Institute of Technology, January, 1948.

(3) Noyes and Tucker, *Am. Chem. J.*, **19**, 128 (1897); Straus and Kollek, *Ber.*, **59**, 1672 (1926).

(4) Iotsitch, *J. Russ. Phys.-Chem. Soc.*, **38**, 656 (1906); *Bull. soc. chim.*, **4**, 1208 (1908).

(5) Rivers, Ph.D. Thesis, Massachusetts Institute of Technology, 1941.

Anal. Calcd. for $C_{10}H_{14}O_2$: C, 72.26; H, 8.49; unsaturation, 4.0 $\overline{=}$; A. H. (Zerewitinoff), 4.0. Found: C, 72.5; H, 8.54; unsaturation, 4.75 $\overline{=}$ (Pt); A. H. (Zerewitinoff), 4.06.

The high hydrogenation value is probably due to slow hydrogenolysis of the tertiary hydroxyl groups.

3,4-Dimethyl-hexa-1,5-diyndiol-3,4 (II).—Using the same technique the diethynyl glycol (II) was prepared in liquid ammonia (600 cc.) from sodium acetylide (using 29.3 g. of sodium) and 50 g. of diacetyl dissolved in 50 cc. of ether. A yield of 32.6 g. (41%) of the crude diethynyl glycol was obtained. Several attempts to crystallize this glycol were unsuccessful. It was then fractionated under reduced pressure and the fraction boiling at 76–78° (3 mm.) collected and analyzed; n_D^{20} 1.4852.

Anal. Calcd. for $C_8H_{10}O_2$: C, 69.54; H, 7.29; unsaturation, 4.0 $\overline{=}$; A. H. (Zerewitinoff), 4.0. Found: C, 69.5, 69.3; H, 7.23, 7.26; unsaturation, 4.14 $\overline{=}$ (Pt); A. H. (Zerewitinoff), 3.93.

With alcoholic ammoniacal silver nitrate, it forms an insoluble white precipitate which detonates on heating.

2,2',5,5'-Tetramethyl-dodeca-3,3'-diynetetrol-2,2',-5,5' (III).—A Grignard was prepared from 9.73 g. of magnesium and 43.6 g. of ethyl bromide in 250 cc. of ethyl ether. To this was added dropwise with stirring at 0° a solution of 16.6 g. of the diethynyl glycol (I) in 200 cc. of ethyl ether in the course of one hour. At first a white precipitate was formed which turned into sticky grey lumps which impeded stirring. More ether (150 cc.) was then added and the lumps broken up by means of a glass rod. Stirring was continued for one-half hour longer while the mixture was gently refluxed. The mixture was again cooled to 0° and to it added dropwise 11.6 g. of acetone, in 50 cc. of ether, then gently refluxed for one hour. Finally, the mixture was cooled and hydrolyzed with a mixture of ice and ammonium sulfate (50 g.). The ether layer was separated and the aqueous layer extracted with 2 × 100 cc. of ether and the combined ether layers dried over magnesium sulfate. The ether was then concentrated to a small volume and *n*-heptane was added until a slight turbidity was observed. On cooling to 0° for three hours a white crystalline product separated out which had a m. p. of 162–166°. This was recrystallized from dioxane to a constant m. p. of 169.5–170°.

Anal. Calcd. for $C_{16}H_{26}O_4$: C, 68.05; H, 9.28. Found: C, 67.66; H, 9.35.

9,9'-Dimethyl-7,7'-dicyclohexyl-octa-7,7'-diynetetrol-6,6',9,9' (IV).—Using the same technique as in the previous case, the tetrol (IV) was prepared from 29 g. of cyclohexanone in 350 cc. of anhydrous ether. When the mixture was hydrolyzed a solid separated out in the interface which was collected and recrystallized from dioxane to constant m. p., 190–192° (1.2 g.).

Anal. Calcd. for $C_{22}H_{34}O_4$: C, 72.85; H, 9.45. Found: C, 72.21; H, 9.43.

From the ether solution was separated a second crystalline product which was recrystallized from dioxane to a constant m. p. of 167–168.5° (1 g.). A mixed m. p. with the previous product gave 169–181° showing that the two products were not identical.

Anal. Calcd. for $C_{22}H_{34}O_4$: C, 72.85; H, 9.45. Found: C, 72.01; H, 9.45.

Neither of the two crystalline products gave a test for free acetylene groups with ammoniacal alcoholic silver nitrate. It is therefore possible that the higher melting tetrol is the racemic form while the lower one is the *meso* form.

In addition to the two crystalline products a brownish viscous liquid was obtained which, when distilled at 10⁻⁴ mm. yielded 3 g. of the original diethynyl glycol and a dark brown resin.

2,5-Dimethyl-2,5-diethynyldihydrofuran (V).—When the diethynyl glycol was passed upward through aluminum phosphate on pumice⁷ (140 g. pumice, 78 g. aluminum phosphate) maintained at 290–300° and 50 mm. pressure at the rate of about 12 g. per hour, a condensate was obtained in a carbon dioxide ice trap which yielded 13.5 g. of a liquid soluble in *n*-heptane and much of the original diethynyl glycol. The liquid was fractionated and the fraction boiling at 63.5–65° (28 mm.) was collected and analyzed; n_D^{20} 1.4790. The final product gives a voluminous precipitate with ammoniacal alcoholic silver nitrate solution.

Anal. Calcd. for $C_{10}H_{12}O$: C, 82.12; H, 8.16; unsaturation, 4.0 $\overline{=}$; A. H. (Zerewitinoff), 2.0. Found: C, 82.22; H, 8.15; unsaturation, 4.94 $\overline{=}$ (Pt); A. H. (Zerewitinoff), 2.06.

The high hydrogenation value indicates the possible hydrogenolysis of the tetrahydrofuran ring.

Summary

1. 3,6-Dimethyl-octa-1,7-diyndiol-3,6 (I) and 3,4-dimethyl-hexa-1,5-diyndiol-3,4 (II) have been synthesized and some of their properties determined.

2. The diethynyl glycol (I) was condensed *via* the Grignard reaction with acetone and cyclohexanone and the expected tetrols were isolated in low yields.

3. The diethynyl glycol (I) was dehydrated at 290–300° over aluminum phosphate to 2,5-dimethyl 2,5-diethynyldihydrofuran (V).

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