ribonic acid tetraacetate, its amide, chloride and methyl ester. The latter is recorded for the first time and improved directions for the preparation of the chloride are cited.

2. Reaction of D-ribonyl chloride tetraacetate with diazomethane yielded 1-diazo-1-desoxy-*keto*-D-psicose tetraacetate (II).

3. *keto*-D-Psicose pentaacetate and 1-desoxy-*keto*-D-psicose tetraacetate have been synthesized from II.

4. D-Psicose has been prepared in amorphous form from its *keto*-acetate and characterized as its crystalline phenylosazone and phenyl osotriazole.

1-Desoxy-D-psicose (amorphous) likewise has been synthesized from its *keto*-acetate and characterized as its crystalline phenylosazone.

5. The 1-chloro-, 1-bromo- and 1-iodo- derivatives of *keto*-D-psicose tetraacetate have been synthesized.

6. A systematic nomenclature for ketoses is proposed.

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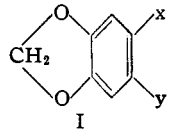
[CONTRIBUTION FROM THE SCHOOL OF CHEMISTRY OF THE UNIVERSITY OF MINNESOTA]

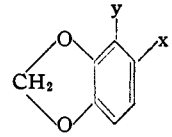
Orientation in the 1,3-Benzodioxole Series

BY RICHARD T. ARNOLD AND NEWMAN BORTNICK[1]

The unusual tendency for direct nuclear substitution to occur almost exclusively at the para positions in 1,3-benzodioxole to give 5,6-disubstituted-1,3-benzodioxoles (type I below) is well known.[2]



I



II

As a result of this preferred orientation, compounds related to type II are not readily accessible and are generally prepared by indirect methods.

In an earlier publication[3] dealing with the synthesis of comparable isomeric pairs in the veratrole series, it was shown that the Claisen thermal rearrangement of allyl phenyl ethers could be used for the synthesis of compounds related to substances I and II (x = hydroxyl; y = allyl) from a common intermediate (III). We have now proved that the procedure employed in the veratrole series[3] can be applied with equal success to the synthesis of 1,3-benzodioxoles as outlined in the reaction diagram (p. 1798).

Some interest has been shown in the possible analgesic action of the acetoxy acids ("aspirins") in the veratrole and 1,3-benzodioxole series.[5] These substances have been prepared by careful oxidation of the corresponding acetoxyaldehydes[2,4] although attempts to acetylate the hydroxy acids directly in the usual manner have been unsuccessful.[2,5]

Incidental to the main study reported in this paper, we have been able to show that the failures mentioned above are due to the remarkable rapidity with which the acetoxy acids undergo hydrolysis and not due to the inability of effecting the acetylation of the hydroxy acids. When the acetylation is brought about by acetic anhydride, good yields of the acetoxy acids are obtained if the excess acetic anhydride is hydrolyzed at low temperatures as described in the experimental section.

Acknowledgment.—The authors greatly appreciate the financial aid furnished by Sharp and Dohme, Incorporated, and the interest shown by Drs. James Sprague and M. L. Moore.

Experimental

6-Carbomethoxy-5-allyloxy-1,3-benzodioxole.—Allylation of 6-carbomethoxy-5-hydroxy-1,3-benzodioxole was effected with allyl bromide and potassium carbonate in acetone solution in a manner identical to that used in the veratrole series[3]; yield 96.5%; m. p. 73–73.5°. A mixture of ether and petroleum ether (b. p. 28–38°) was used as solvent in the recrystallization.

Anal. Calcd. for $C_{12}H_{12}O_5$: C, 61.06; H, 5.13. Found: C, 61.29; H, 5.33.

4-Allyl-5-hydroxy-6-carbomethoxy-1,3-benzodioxole.—The above allyloxy ester (20 g.) was heated at 180–215° for five hours in a nitrogen atmosphere. The product was distilled in a sausage flask at reduced pressure (16 mm.); yield 16.5 g.; m. p. 51–55°. Three recrystallizations from dilute methanol gave the analytical sample; m. p. 54–56°.

Anal. Calcd. for $C_{12}H_{12}O_5$: C, 61.06; H, 5.13. Found: C, 61.19; H, 5.45.

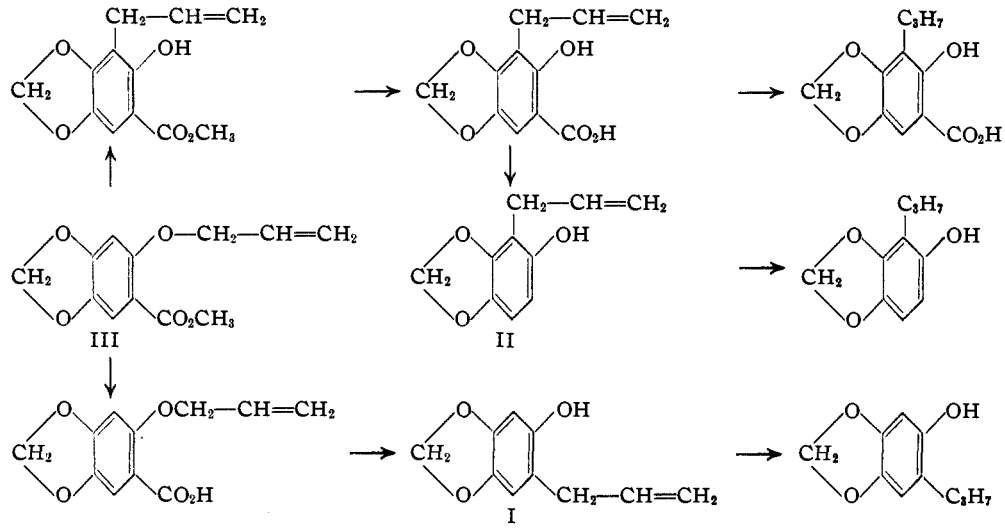
Saponification of this ester with dilute potassium hydroxide gave 5-allyl-6-hydroxypiperonylic acid; m. p. 169–170° (dec.).

Anal. Calcd. for $C_{11}H_{10}O_5$: C, 59.50; H, 4.55. Found: C, 59.45; H, 4.45.

4-Propyl-5-hydroxy-1,3-benzodioxole-6-carboxylic Acid.—When 4-allyl-5-hydroxy-6-carbomethoxy-1,3-benzodioxole (15 g.) was dissolved in methanol (100 cc.) and shaken with hydrogen at forty pounds pressure in the presence of Adams catalyst (100 mg.), the theoretical uptake of hydrogen required only four minutes. The precipitated propyl ester was redissolved by warming the solution. After removing the catalyst on a filter, the filtrate was boiled with excess potassium hydroxide (10%). During this time the methanol was slowly removed by distillation. Acidification and crystallization of the product from dilute acetic acid gave 12 g. of pure product; m. p. 168–169° (dec.).

Anal. Calcd. for $C_{11}H_{12}O_5$: C, 58.97; H, 5.40. Found: C, 58.78; H, 5.33.

(1) Sharp and Dohme Fellow, 1942–1944.
(2) Arnold and Bordwell, THIS JOURNAL, **64**, 2983 (1942).
(3) Arnold and Bortnick, *ibid.*, **67**, 806 (1945).
(4) Robertson and Head, *J. Chem. Soc.*, 2434 (1930).
(5) Bogert and Elder, THIS JOURNAL, **51**, 534 (1929).



4-Propyl-5-hydroxy-1,3-benzodioxole.—Decarboxylation of 4-allyl-5-hydroxy-1,3-benzodioxole-6-carboxylic acid was effected by heating the acid (3.5 g.) in dimethylaniline (5 cc.) at its boiling point for one hour. The cooled solution was dissolved in benzene and extracted with hydrochloric acid (10%). After removal of the benzene, the product was distilled in a sausage flask under reduced pressure (11 mm.); yield 2.4 g. (86%); m. p. 71.5–73.5°.

Anal. Calcd. for $C_{10}H_{10}O_3$: C, 67.41; H, 5.66. Found: C, 67.01; H, 5.40.

Hydrogenation of this product (1.5 g.) in methanol using Adams catalyst (10 mg.) was rapid. The solution was filtered, the solvent removed by distillation and the resulting 4-propyl-5-hydroxy-1,3-benzodioxole purified by distillation in a sausage flask at reduced pressure (11 mm.); m. p. 74–76°.

Anal. Calcd. for $C_{10}H_{12}O_3$: C, 66.64; H, 6.70. Found: C, 66.67; H, 6.72.

5-Allyloxy-1,3-benzodioxole-6-carboxylic Acid.—5-Allyloxy-6-carbomethoxy-1,3-benzodioxole (6 g.) was dissolved in a solution of potassium hydroxide (75 cc., 15%), and ethanol (25 cc.) and heated at the boiling point for one hour. The ethanol was removed by distillation and the cooled aqueous solution was acidified. The collected precipitate was recrystallized from dilute acetic acid; m. p. 115–116°; wt. 5.1 g.

Anal. Calcd. for $C_{11}H_{10}O_5$: C, 59.50; H, 4.55. Found: C, 59.45; H, 4.86.

5-Hydroxy-6-allyl-1,3-benzodioxole.—When 5-allyloxy-1,3-benzodioxole-6-carboxylic acid (2 g.) was boiled in dimethylaniline for one hour in an atmosphere of nitrogen, decarboxylation and rearrangement occurred simultaneously. Removal of the dimethylaniline in the usual manner and distillation of the residue gave a pure product; yield 84%; m. p. 71.5–73.5°. When admixed with 4-allyl-5-hydroxy-1,3-benzodioxole the melting point was below 58°.

Anal. Calcd. for $C_{10}H_{10}O_3$: C, 67.41; H, 5.66. Found: C, 67.44; H, 5.45.

Hydrogenation of this product at low pressure with platinum gave 5-hydroxy-6-propyl-1,3-benzodioxole; m. p. 71–72°.[6] When admixed with 5-hydroxy-6-allyl-1,3-benzodioxole, the resulting sample melted at 58–61°.

5-Methoxy-1,3-benzodioxole-6-carboxylic Acid.—5-Hydroxy-6-carbomethoxy-1,3-benzodioxole (5 g.), dimethyl sulfate (9 g.), potassium carbonate (14 g.) and dry benzene (100 cc.) were stirred and heated under reflux for forty-eight hours. The warm solution was filtered and upon evaporation of the solvent methyl 6-methoxypiperonylate separated in large prisms; m. p. 73–75°. Saponification with methanolic potassium hydroxide gave the acid; yield 80%; m. p. 148–149°.

Anal. Calcd. for $C_9H_8O_5$: C, 55.15; H, 4.11. Found: C, 55.43; H, 4.11.

6-Acetoxyveratric Acid.—6-Hydroxyveratric acid (5.0 g.) was dissolved in acetic anhydride (20 cc.) with heating. After cooling the solution to room temperature, two drops of concentrated sulfuric acid were added and the solution was allowed to stand for forty hours. Water (60 cc.) was added and the flask was placed in a refrigerator at 0° for twenty-four hours. The precipitate was removed by filtration and recrystallized from acetone–benzene; yield 3.0 g.; m. p. 160–160.5°.

Anal. Calcd. for $C_{11}H_{12}O_6$: C, 55.00; H, 5.04. Found: C, 54.85; H, 5.21.

5-Hydroxy-1,3-benzodioxole-6-carboxylic acid (4.4 g.) was acetylated in a similar manner. Acetylation was complete in a few hours; yield 5.5 g. (93%); m. p. 150–152° (dec.).

Summary

Two pairs of isomeric 4,5- and 5,6-disubstituted-1,3-benzodioxoles have been prepared from a common intermediate.

MINNEAPOLIS 14, MINN. RECEIVED MAY 17, 1945

(6) Thoms and Biltz, *Arch. Pharm.*, **242**, 90 (1904).