TABLE I

CRYSTALLINE FORMS OF XYLITOL

| Form | Metastable | Stable |
|---|---|---|
| M. p., °C. | 61-61.5 | 93-94.5 |
| $\alpha$ | 1.519 | 1.549 |
| $\gamma$ | 1.548 | 1.566 |
| $\beta$ | 1.521 | 1.551 |
| Crystal system | Monoclinic | Rhombic |
| Axial angle and dispersion | $2V = 32 \pm 5°$<br>$(r > v)$ weak | $2V = 38 \pm 5°$<br>$(r < v)$ weak |
| Optical character | (+) | (+) |

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## Suggested Method for Replaceable Hydrogen

BY HERMAN A. LIEBHAFSKY

Dilute sodium amalgams react rapidly neither with acetonitrile nor with water dissolved therein at low concentrations. If silicon tetrachloride is added, however, the amalgam will, upon violent shaking, rapidly liberate hydrogen derived from the water initially present. Unfortunately, the reaction is not quantitative even under conditions chosen after considerable experimentation: the hydrogen is liberated in amounts ranging from one to two gram atoms for each mole of water.

Samples of known water (or alcohol) content were prepared with acetonitrile that had been distilled from phosphorus pentoxide; the solvent gave a negligible blank. 50 cc. of such a sample was measured into a 100-cc. acetylation flask attached to a mercury-filled gas buret. Ten drops of freshly distilled silicon tetrachloride was added with a dropper and dissolved by shaking the closed flask; 10 cc. of sodium amalgam (about 0.05% by weight) was now poured in, and the closed flask shaken violently for three ten-second periods; a gas buret reading was taken after each period had elapsed, the final reading being taken when temperature equilibrium had been re-established. At water concentrations below 0.05% by weight, more hydrogen could not be liberated by this procedure when amalgam or silicon tetrachloride was subsequently added. At the higher concentrations, these substances had to be added alternately in the amounts given above until no more hydrogen was evolved. Some of the results obtained are given in Table I; here all percentages are by weight, and water is assumed to have two replaceable hydrogens.

Two samples of acetonitrile in which 0.013 and 0.07% water had been obtained with the Karl Fischer reagent by Mr. Stanley Mills, Niacet Chemical Company, gave only 0.003 and 0.02% by the present method when the results were calculated as in the last column of the table. (An empirical correction would, of course, improve the agreement.) Whether the Karl Fischer reagent reacted with substances other than water in these samples is not known.

TABLE I

REPLACEABLE HYDROGEN IN ACETONITRILE SOLUTIONS

| No. | Solute | % Solute added | % Solute found |
|---|---|---|---|
| 1 | Water | 0.008 | 0.004 |
| 2 | Water | .015 | .010 |
| 3 | Water | .030 | .019 |
| 4 | Water | .045 | .031 |
| 5 | Water | .060 | .045 |
| 6 | Water | .075 | .055 |
| 7 | Water | .13 | .08 |
| 8 | Water | .13 | .08 |
| 9 | Water | .13 | .12 |
| 10 | Ethyl alcohol | .13 | .17 |
| 11 | Ethyl alcohol | .13 | .17 |
| 12 | Methyl alcohol | .13 | .12 |

The method suggested here is subject to complications. Silicon tetrachloride and sodium amalgam are both consumed in side reactions. Table I shows that the stoichiometry is not simple; water gives lower results than the alcohols, but this is not surprising because water (or an —OH group) is the more likely to be retained in an inactive condition by the reaction products. The amalgam becomes covered almost instantly by a film, presumably siliceous, that bars it from reacting when its surface is at rest; this simplifies the manipulation. Sodium amalgam can be slowly oxidized by the air in the system; the occurrence of this reaction, the rate of which is usually negligible, can be turned to account as a signal that the hydrogen chloride has been consumed with amalgam still present.

In spite of these complications, the proposed method may find its place where other methods are inapplicable or too slow. No doubt other substances that react like silicon tetrachloride could be used. One experiment showed that dioxane could replace acetonitrile.

The method grew out of experiments being carried on here by Dr. C. E. Reed. I am grateful also to Dr. R. O. Sauer for supplying the silicon tetrachloride, and to Mr. L. B. Bronk for helping with the determinations.

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## The Preparation of $\beta$-Primeverose Heptaacetate and $\beta$-Vicianose Heptaacetate

BY CHESTER M. MCCLOSKEY[1] AND GEORGE H. COLEMAN

Recently in this Laboratory we have had occasion to prepare primeverose and vicianose in con-

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nection with the work on the azoyl derivatives of sugars. The previous methods of preparation have been modified and increased yields obtained. The triacetylxylosyl bromide used in the preparation of the primeverose derivative was prepared by a modified procedure which is also described.

The synthesis of β-primeverose heptaacetate was reported by Helferich and Rauch.[2] They condensed 1,2,3,4-tetraacetyl-β-D-glucose with triacetyl-α-D-xylosyl bromide by the use of silver oxide in a chloroform solution and obtained a yield of 22%. Zemplén and Bognar[3] have since reported the condensation of 2,3,4-triacetyl-α-D-glucosyl chloride with triacetyl-α-D-xylosyl bromide in the presence of mercuric acetate and obtained the hexaacetyl α-primeverosyl chloride in 50% yield.

Helferich and Bredereck[4] synthesized β-vicianose heptaacetate by the method used previously to prepare β-primeverose heptaacetate. They reported a yield of only 3.5%.

β-Gentiobiose octaacetate had been synthesized by Helferich and Klein[5] in 1926 in 23.4% yield, using the method subsequently employed by Helferich and co-workers in the synthesis of the heptaacetates of primeverose and vicianose. Reynolds and Evans reasoned that the low yield of Helferich and Klein was largely due to the decomposition of the glucosyl bromide by the water liberated in the reaction. Working on that assumption they used a large quantity of drierite (anhydrous calcium sulfate) in the reaction medium to remove the water as it was formed. By this method they were able to obtain yields as high as 82% of β-gentiobiose octaacetate.[6]

The method of Reynolds and Evans has been applied by us to the preparation of β-primeverose heptaacetate and β-vicianose heptaacetate, as this presented a direct means of obtaining the sugars. The yields obtained were substantially increased over those reported by Helferich and co-workers.

## Experimental

**Alcohol-free chloroform** was prepared by extracting U. S. P. chloroform three times with one-third its volume of concentrated sulfuric acid. The chloroform was then washed successively with water, bicarbonate solution and water. It was dried first with calcium chloride then finally over drierite.

**2,3,4-Triacetyl-β-D-xylosyl Bromide.**[7]—Crystalline tetraacetylxylose (25 g.) was placed in a 250-ml. round-bottom flask and 25 ml. of acetic anhydride added. The flask was immersed in an ice-bath and anhydrous hydrogen bromide[8] was passed into the mixture until the acetate had all dissolved. To the solution was added 25 g. more of the tetraacetate and hydrogen bromide passed in until the solution was saturated at 0°. A calcium chloride drying tube was attached to the flask and it was allowed to stand for three hours in a hood at room temperature.

Reduced pressure was applied from an aspirator to the flask which was immersed in a water-bath. The temperature of the water-bath was gradually raised to 45°. When the hydrogen bromide had been largely removed the material in the flask crystallized. The crystals were mixed well with 100 ml. of absolute ether and then cooled in a freezing bath. After fifteen minutes the crystals were filtered and washed with a little cold absolute ether. The ethereal solution was evaporated and worked up as before. In this fashion several crops of crystals were obtained. Over three-fourths of the total yield was obtained in the first crop. The product was recrystallized by dissolving in the minimum amount of hot chloroform, adding four times the volume of absolute ether, and cooling in a freezing bath; yield 47–48 g., 88–90%; m. p. of crude product 98–99°.

**β-Primeverose Heptaacetate.**—1,2,3,4-Tetraacetyl-β-D-glucose[9] (25 g.), 18 g. of silver oxide,[5] 70 g. of drierite previously heated to 500° for five hours and cooled over phosphorus pentoxide, and 70 ml. of alcohol-free chloroform, were placed in a 500-ml. three-necked flask. The flask was equipped with a mechanical stirrer, a mercury seal and a dropping funnel. The mixture in the flask was stirred for one hour. Three grams of iodine was added and a solution of 25 g. of triacetyl-α-D-xylosyl bromide in 110 ml. of alcohol-free chloroform was added dropwise over a period of one hour. The resulting mixture was stirred for twenty-four hours.

The silver salts were filtered from the chloroform solution and washed well with 400 ml. of acetone. The filtrates were evaporated to dryness, the crystalline mass was dissolved in the minimum amount of chloroform and the solution was diluted with five volumes of methyl alcohol. The primeverose heptaacetate crystallized readily in granular form. Two recrystallizations in like manner yielded 21 g.; m. p. 216–217° (cor.). By working up the solvents, 2–3 g. more was obtained; yield 57%. Two additional crystallizations in the same manner did not change the melting point and produced only a slight change in the specific rotation. Final value was $[\alpha]^{24}\text{D}$ −26.2° in chloroform ($c$, 2).

**β-Vicianose Heptaacetate.**—Using triacetyl-β-L-arabinosyl bromide[10] instead of xylosyl bromide, the preparation was similar to that of primeverose heptaacetate up to

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[2] Helferich and Rauch, *Ann.*, **455**, 168 (1927).

[3] Zemplén and Bognar, *Ber.*, **72**, 47 (1939).

[4] Helferich and Bredereck, *Ann.*, **465**, 166 (1928).

[5] Helferich and Klein, *ibid.*, **450**, 219 (1926).

[6] Reynolds and Evans, THIS JOURNAL, **60**, 2561 (1938).

[7] Hudson and Johnson, *ibid.*, **37**, 2748 (1915); Levene and Sobotka, *J. Biol. Chem.*, **65**, 463 (1925).

[8] Ruhoff, Barnett and Reid, "Organic Syntheses," Vol. 15, p. 35.

[9] Reynolds and Evans, *ibid.*, Vol. 22, p. 56.

[10] Gehrke and Aichner, *Ber.*, **60**, 918 (1927); Meisenheimer and Jung, *ibid.*, **60**, 1462 (1927).

the isolation of the acetate. The residue from the chloroform–acetone filtrates was dissolved in 300 ml. of alcohol and to this was added 1–2 liters of water. An oil formed which settled out permitting the aqueous layer to be removed. After standing overnight the oil crystallized. The crystals were dissolved in 300 ml. of hot methyl alcohol from which the β-vicianose heptaacetate crystallized slowly in clusters of small needles. After two recrystallizations the product weighed 12.3 g., m. p. 158–159° (cor.), $[\alpha]^{24}_{D}$ 9.4° in chloroform (*c*, 2). Additional recrystallizations produced no change in either the melting point or the specific rotation. By working up filtrates an additional 2.2 g. was obtained; yield 34%. Six grams of a much lower melting product (144–149°) was isolated from residues.

**Acknowledgment.**—The authors wish to thank Dr. Giffin D. Jones and Mr. Harold Baker of this Laboratory for the preparation of the 1,2,3,4-tetraacetyl-β-D-glucose used in this investigation.

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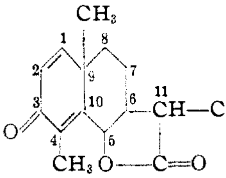
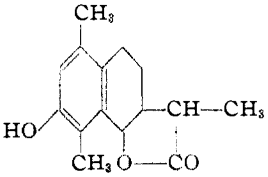
## Studies in the Santonin Series. I. The Two New Desmotropo-santonins and the Two New Desmotropo-santonous Acids[1]

BY HUANG MINLON, CHIEN-PEN LO AND LUCY JU-YUNG CHU

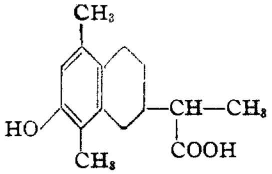
When santonin (I) is treated with mineral acids, a molecular rearrangement reaction takes place resulting in an aromatic compound, the desmotropo-santonin (II).[2,3,4] By an analogous reaction some transformation products of cholesterol with the dienone structure have been easily converted into the corresponding phenolic compounds by means of acetic anhydride and a drop of concentrated sulfuric acid.[5] The conversion is believed to be effected through an *enol*-acetylation reaction although the intermediate acetate has never been isolated. In the process of acetylation, the equilibrium between the enol- and the keto-forms is disturbed in favor of the former form. Now we have found that when santonin was subjected to the same treatment, in the cold or slightly warmed on a water-bath, it was almost quantitatively converted into an acetate of m. p. 156–157°[6a] which upon saponification yielded *l*-desmotropo-santonin (m. p. 194–195°).[6b]



I



II



III

It is also known that *l*-desmotropo-santonin (m. p. 194°) can be transformed into its stereoisomer, *d*-desmotropo-santonin (m. p. 260°) by prolonged heating with dilute sulfuric acid at 100°[4] and that the latter isomer in turn can be transformed into *d*-isodesmotropo-santonin (m. p. 194°), the enantiomorph of the former isomer by fusion with alkali.[7,8,9] Evidently, the dilute sulfuric acid is able to change the low-melting *l*-desmotropo-santonin into the high-melting *d*-desmotropo-santonin with an inversion of rotation, while the alkali is able to change the high-melting *d*-isodesmotropo-santonin with the direction of rotation unaltered. We therefore believe that the *d*-isodesmotropo-santonin, when treated with dilute sulfuric acid, will be transformed, not as was reported by Bargellini and Mannino[4] into the *d*-desmotropo-santonin, but into its high-melting levorotatory stereoisomer.

In fact, when *d*-iso-desmotropo-santonin was heated with dilute sulfuric acid on the water-bath, there were obtained colorless prisms melting at 260–261° and possessing the same physical and chemical properties but a specific rotation ($[\alpha]^{20}_{D}$ $-106.2°$) equal and opposite in sign to that of the *d*-desmotropo-santonin.[10] This new isomer formed with the latter compound a new racemic desmotropo-santonin (colorless plates, m. p. 231–232°) which yielded an inactive acetyl derivative (m. p. 182–183°) from which the original racemic mixture was recovered by saponification. Reduction

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[1] Original manuscript received July 17, 1942.

[2] Andreocci, *Gazz. chim. ital.*, **23**, II, 469 (1893).

[3] Andreocci and Bertolo, *Ber.*, **31**, 3131 (1898).

[4] Bargellini and Mannino, *Gazz. chim. ital.*, **39**, II, 103 (1909).

[5] Inhoffen and Huang Minlon, *Naturwissenschaften*, **26**, 756 (1938); *Ber.*, **73**, 451 (1940).

[6] (a) Gave no depression when mixed with *l*-desmotropo-santonin acetate prepared from *l*-desmotropo-santonin by acetylation. (b) Gave no depression by admixture with a specimen obtained directly from santonin.

[7] Cannizzaro, *Ber.*, **26**, 2311 (1893).

[8] Andreocci, *Gazz. chim. ital.*, **23**, II, 484 (1893); **25**, I, 476 (1895).

[9] Clemo, Haworth and Walton, *J. Chem. Soc.*, 1110 (1930).

[10] Three measurements by us gave the same value +106.2°. However, a value of +112.7° was reported by Andreocci.[2]