Studies on the Chemical Decomposition of Simple Sugars. XV. The Synthesis of 1-O-Benzoyl-3, 4 ; 5, 6-di-O-isopropylidene-L-xylo-2-hexulose

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Syntheses of keto-hexuloses have been made by many investigators since 1941. For instance, some synthetic procedures working through the condensation of acetylated aldonyl chlorides with diazomethane[1] and the oxidation of substituted hexitols with chromium trioxide[2,3] have been reported. However, the synthesis of diisopropylidene-keto-L-sorbose has not been reported. In accordance with the research program in our laboratory studying the decomposition mechanism of simple sugars, 1-*O*-benzoyl-3, 4 ; 5, 6-di-*O*-isopropylidene-L-*xylo*-2-hexulose, i. e., 1-*O*-benzoyl-3, 4 ; 5, 6-di-*O*-isopropylidene-keto-L-sorbose, has been synthesized. As the starting compound 1, 2-*O*-isopropylidene-D-sorbitol was used.

The benzoylation of 1, 2-*O*-isopropylidene-D-sorbitol[4] (I) with an equimolar amount of benzoyl chloride in anhydrous pyridine gave 1,2-*O*-isopropylidene-6-*O*-benzoyl-D-sorbitol (II). When II was treated with acetone in the presence of anhydrous copper sulfate, diacetone-monobenzoyl-D-sorbitol (III) was obtained. After the debenzoylation of III, one mole of di-*O*-isopropylidene-D-sorbitol obtained consumed one mole of sodium periodate. Therefore, III was confirmed to be 1, 2 ; 3, 4-di-*O*-isopropylidene-6-*O*-benzoyl-D-sorbitol, and the presence of 1, 2 ; 4, 5-di-*O*-isopropylidene isomer was excluded.

Compound II has three adjacent hydroxyl groups, attached to the carbons 3, 4 and 5. The adjacent hydroxyl groups attached to C_4 and C_5 have an erythro-, and those attached to C_3 and C_4 have a threo-configuration. In order to condense with acetone to form a five-membered ring, the two hydroxyl groups must have an eclipsed conformation. In such circumstances, the twist around the C_4–C_5 bond axis causes a large steric repulsion between the bulky groups (R_2 and $R_1 + C_3$ in Fig. 1), while that around the C_3–C_4 bond axis makes the steric repulsion (Fig. 2) so small that the condensation with acetone may take place and 1, 2 ; 3, 4-di-*O*-isopropylidene-6-*O*-benzoyl-D-sorbitol is produced exclusively.

The oxidation of 1, 2 ; 3, 4-di-*O*-isopropylidene-6-*O*-benzoyl-D-sorbitol (III) with chromium trioxide gave 1-*O*-benzoyl-3, 4 ; 5, 6-di-*O*-isopropylidene-keto-L-sorbose (IV) in a 49% yield. The deacetonation of ketose (IV) was effected by using the ion-exchange resin, Amberlite IR-120 (H-form). The crystalline 1-*O*-benzoyl-L-sorbose (V) obtained was debenzoylated by transesterification with methanol in the presence of sodium methoxide to give crystalline L-sorbose (VI).

Further investigations related to those described in this communication are in progress.

Experimental

1, 2-*O*-Isopropylidene-6-*O*-benzoyl-D- sorbitol (II).—To an ice-cooled solution of 1, 2-*O*-isopropylidene-D-sorbitol (18 g.) in 130 ml. of anhydrous pyridine, benzoyl chloride (12 ml.) was added with vigorous stirring drop by drop. After standing overnight at

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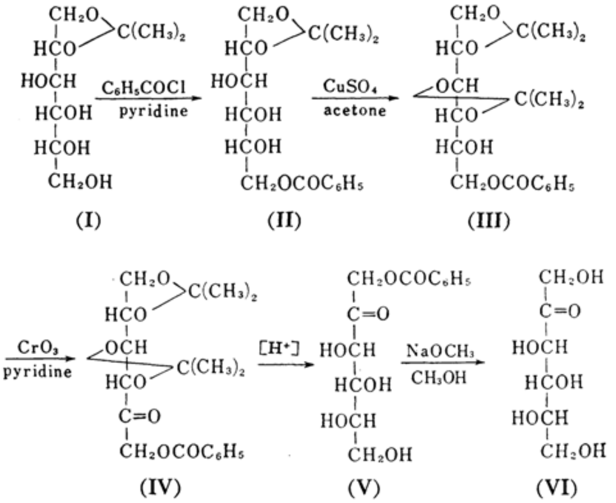
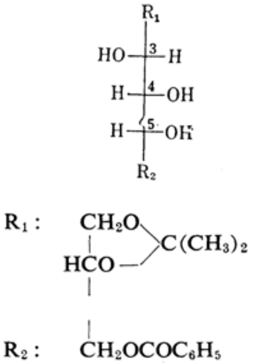
[1] W. Pigman, "The Carbohydrates," Academic Press, New York (1957), p. 111.

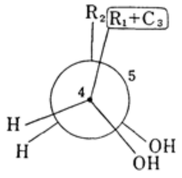
[2] W. R. Sullivan, *J. Am. Chem. Soc.*, **67**, 837 (1945).

[3] J. M. Sugihara and G. U. Yuen, ibid., **79**, 5780 (1957) ; G. U. Yuen and J. M. Sugihara, *J. Org. Chem.*, **26**, 1598 (1961).

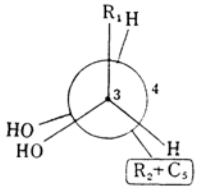
[4] L. Anderson, B. C. Pressmann and H. A. Lardy, *J. Am. Chem. Soc.*, **72**, 2404 (1950).







(Fig. 1.)
eclipsed
erythro-form



(Fig. 2.)
eclipsed
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room temperature, the solution was concentrated under reduced pressure. The resulting sirup was poured into 300 ml. of ice and water, and the crystalline precipitate was filtered and recrystallized from isopropyl ether containing a small amount of ethanol. 1,2-*O*-Isopropylidene-6-*O*-benzoyl-D-sorbitol(II) (m. p. 120.0~124.6°C) was obtained. After several recrystallizations, the compound had a m. p. of 124.7~125.1°C (13.5 g.), $[\alpha]_D^{25}$ +3° (*c* 1, pyridine).

Found: C, 58.91; H, 6.88; C_6H_5CO, 34.14, 33.17. Calcd. for $C_{16}H_{22}O_7$: C, 58.86; H, 6.74; C_6H_5CO, 32.21%.

Infrared spectrum: ν_{OH}, 3540, 3450; $\nu_{C=O}$, 1709; $\nu_{C=C}$, 1604, 1589 cm⁻¹.

Moles of periodate consumed/one mole of II: 2.08 (15 min.), 2.09 (20 min.), 2.09 (30 min.) and 2.13 (45 min.). Moles of formic acid produced/one mole of II: 1.05 (17 min.), 1.12 (1 hr.), 1.16 (2 hr.) and 1.24 (4 hr.).

1,2; 3,4-Di-*O*-isopropylidene-6-*O*-benzoyl-D-solbitol (III).—To a solution of 1,2-*O*-isopropylidene-6-*O*-benzoyl-D-sorbitol (II) (2 g.) in 70 ml. of anhydrous acetone, 5 g. of anhydrous copper sulfate was added, and the mixture was gently refluxed for 30 hr. After the inorganic salt had been filtered off, the filtrate was concentrated under reduced pressure to a sirup, which crystallized slowly when 10 ml. of isopropyl ether was added. The crude material (1.3 g.) had a m. p. of 66.7~67.1°C. After several recrystallizations from isopropyl ether, 1,2; 3,4-di-*O*-isopropylidene-6-*O*-benzoyl-D-sorbitol (III) showed a m. p. of 68.2~68.5°C, $[\alpha]_D^{25}$ +19.3° (*c* 1.03, pyridine).

Found: C, 62.19; H, 7.14. Calcd. for $C_{19}H_{26}O_7$: C, 62.28; H, 7.15%.

Infrared spectrum: ν_{OH}, 3550; $\nu_{C=O}$, 1713 cm⁻¹.

After the benzoyl residue of III had been removed, the product was oxidized with sodium periodate in aqueous dioxane. Moles of periodate consumed/one mole of 1,2; 3,4-di-*O*-isopropylidene-D-sorbitol; 1.18 (10 min.), 1.21 (20 min.), 1.25 (40 min.) and 1.28 (50 min.).

When copper sulfate was replaced with zinc chloride in the above procedure, 1,2-*O*-isopropylidene-6-*O*-benzoyl-D-sorbitol was recovered unchanged (90%).

1-*O*-Benzoyl-3,4; 5,6-di-*O*-isopropylidene-L-*xylo*-2-hexulose (IV). — Chromium trioxide (9 g.) was added to anhydrous pyridine while being agitated mechanically. To this mixture, 1,2; 3,4-di-*O*-isopropylidene-6-*O*-benzoyl-D-sorbitol (III) (7 g.) was added quickly, and the mixture was kept at 60°C for 7 hr. while being continuously stirred. The mixture was then poured into 300 ml. of ice and water and extracted with ether (200 ml. × 7). The ethereal solution was washed successively with dilute hydrochloric acid, aqueous sodium hydrogen carbonate, and water, and then dried over anhydrous magnesium sulfate. The removal of the solvent gave white crystalline needles (3.4 g.; m. p. 69~70°C). After several recrystallizations from aqueous ethanol, 1-*O*-benzoyl-3,4; 5,6-di-*O*-isopropylidene-L-*xylo*-2-hexulose (IV), (m. p. 75.0°~75.4°C) was obtained. $[\alpha]^{25}_{D}$ −38.4° (*c* 1, pyridine).

Found: C, 62.70; H, 6.86. Calcd. for $C_{19}H_{24}O_7$: C, 62.62; H, 6.64%. Infrared spectrum: $\nu_{C=O}$, 1742, 1724; $\nu_{C=C}$, 1604, 1588 cm^{-1}. No absorption peak was observed near 3550 cm^{-1}, where the parent compound had an absorption peak.

1-*O*-Benzoyl-L-sorbose (V).—Amberlite IR-120 (H-form) (7 g.) was added to a solution of 1-*O*-benzoyl-3,4; 5,6-di-*O*-isopropylidene-L-*xylo*-2-hexulose (IV) (3 g.) in 100 ml. of acetone and water (3 : 1 by volume). The mixture was kept at 40°C for 30 hr. After the resin had been removed by filtration, the filtrate was concentrated under reduced pressure. A crude material (2.2 g.) was obtained (m. p. 122~125°C). After several recrystallizations from isopropyl ether containing a small amount of ethanol, 1-*O*-benzoyl-L-sorbose (V) showed a m. p. of 132.5~133.0°C. $[\alpha]^{9}_{D}$ −2.1° (*c* 5, methanol). (Reported[2] m. p. 133.5°C, $[\alpha]^{26}_{D}$ −3.4° in methanol (*c* 5)).

Found: C, 54.66; H, 5.74. Calcd. for $C_{13}H_{16}O_7$: C, 54.93; H, 5.67%.

Infrared spectrum: ν_{OH}, 3540, 3350 (broad); $\nu_{C=O}$, 1709, 1697; $\nu_{C=C}$, 1610, 1595 cm^{-1}.

L-Sorbose (VI).—1-*O*-Benzoyl-L-sorbose (V) (1.7 g.) was dissolved in 25 ml. of anhydrous methanol, and the solution was cooled with an ice-bath. Into the cold solution, 6 ml. of 0.1 N sodium methoxide in anhydrous methanol was added. After 2 hr., the cooling bath was removed and the solution allowed to stand overnight at room temperature. The solvent was then distilled off under reduced pressure to a sirup, which crystallized spontaneously (900 mg.; m. p. 158~161°C). After several recrystallizations from aqueous ethanol, L-sorbose showed a m. p. of 164~165°C; it was undepressed when the substance was admixed with an authentic specimen of L-sorbose. $[\alpha]^{9}_{D}$ −42.9° (*c* 2.4, water).

Found: C, 40.14; H, 6.83. Calcd. for $C_6H_{12}O_6$: C, 40.00; H, 6.71%.

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