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Phenyl Glycofuranosides

2. Synthesis of Phenyl β-D-Glucofuranoside and Phenyl β-D-Galactofuranoside

PER JERKEMAN and BENGT LINDBERG

Institutionen för träkemi, Kungl. Tekniska Högskolan, Stockholm 70, Sweden

Phenyl β-D-glucofuranoside and phenyl β-D-galactofuranoside have been prepared by condensation of the corresponding furanosidic sugar acetates with phenol in the presence of *p*-toluene sulphonic acid. The two furanosides were degraded to phenyl β-D-xylofuranoside and phenyl α-L-arabinofuranoside, respectively, by controlled periodate oxidation followed by borohydride reduction.

In the preceding paper [1] the syntheses of phenyl β-D-xylofuranoside and phenyl α-L-arabinofuranoside were reported. In the present paper, the syntheses of phenyl β-D-glucofuranoside and phenyl β-D-galactofuranoside are reported. The mode of preparation described in the earlier paper was adopted, that is condensation of a furanosidic sugar acetate with phenol in the presence of *p*-toluene sulphonic acid. The furanosidic glucose pentaacetate was prepared from 3,5,6-tri-*O*-acetyl-1,2-isopropylidene-α-D-glucose [2] by acetylation under acidic conditions. The penta-*O*-acetyl-β-D-galactofuranose [3] was prepared from D-galactose by direct acetylation at high temperature. The phenyl glycofuranoside acetates were not characterised but directly deacetylated to the free glycosides.

The phenyl β-D-glucofuranoside, m.p. 79–80°, $[\alpha]_D$ −142° (water) was converted into the crystalline phenyl β-D-xylofuranoside by the method devised by Kjølberg [4]. This method involves preferential cleavage of the bond between C-5 and C-6 by oxidation with one mole of periodate and subsequent borohydride reduction of the aldehyde formed. By the same method, the phenyl β-D-galactofuranoside, m.p. 82–83°, $[\alpha]_D$ −148° (water), was converted into the phenyl α-L-arabinofuranoside, characterised as its tribenzoate. These reactions confirm the furanosidic structures of the hexosides as well as the configurations at their anomeric centres.

The four phenyl furanosides synthesised by condensation of a furanosidic sugar acetate with phenol and *p*-toluene sulphonic acid have the same configur-

ation at C-1. There was no evidence for the formation of the other furanosidic anomer, which, if present in traces only, may have escaped detection.

When the four furanosides were treated with a commercial sample of emulsin, it was found somewhat unexpectedly that they were all hydrolysed, although at a low rate.

The phenyl β-D-glucofuranoside was completely hydrolysed after 90 min in 2 M aqueous sodium hydroxide at 100°. Only traces of neutral reaction products were formed.

EXPERIMENTAL

Concentrations were performed at water pump pressure and a bath temperature of 40°. Melting points are corrected. The syntheses were followed by thin layer chromatography on silica gel G[5] and paper chromatography on Whatman No. 1 filter paper.

Phenyl β-D-glucofuranoside. 3,5,6-Tri-*O*-acetyl-1,2-*O*-isopropylidene-α-D-glucose [2] (74.5 g) was dissolved in a mixture of acetic acid (750 ml) and acetic anhydride (75 ml). Concentrated sulphuric acid (40 ml) was added with stirring and external cooling with ice. The solution was kept 24 h at room temperature and then poured into ice-water (2500 ml). The aqueous solution was extracted with chloroform (2 × 300 ml) and the chloroform solution washed with water, saturated aqueous sodium hydrogen carbonate solution and again with water, dried over magnesium sulphate and concentrated to a colourless syrup (70 g). This was assumed to consist of glucofuranose pentaacetates and on thin layer chromatography (ethyl acetate) the major component was shown to be different from the two glucopyranose pentaacetates. This procedure is analogous to that of Reist and coworkers [6] for the preparation of 1,2-di-*O*-acetyl-3-*O*-benzoyl-D-glucofuranose 5,6-*O*-carbonate from the corresponding 1,2-di-*O*-isopropylidene derivative.

The above syrup (70 g), phenol (70 g) and *p*-toluene sulphonic acid (0.50 g) were melted together and heated at 100° under water pump pressure for 30 min. Benzene (100 ml) was added to the hot mixture and after cooling a further quantity (150 ml) was added. The benzene solution was washed with water, 1 M aqueous sodium hydroxide (3 × 50 ml) and water until the washings were neutral, dried over magnesium sulphate and concentrated to a syrup (66 g). Thin layer chromatography (chloroform) revealed the presence of a major component and some unchanged starting material.

The syrup (20 g) was dissolved in anhydrous methanol (1500 ml) and a solution of sodium methoxide (from 0.5 g sodium) in methanol (50 ml) was added. After 4 h at room temperature the solution was concentrated, the residue dissolved in water and deionised (Dowex 50 (H^+) and Dowex 3 (free base)). The residue, which contained the glucoside, glucose and a small amount of phenol, was concentrated to 100 ml. Extraction with chloroform (2 × 25 ml) removed the phenol and the glucoside was separated from glucose by extraction with ethyl acetate (8 × 100 ml). The ethyl acetate solution was dried over magnesium sulphate and concentrated to a syrup (5 g), which crystallised spontaneously. Three crystallisations from butanone yielded the pure substance, m.p. 79—80°, $[\alpha]_D^{20}$ −142° (*c*, 2.0, water). (Found: C 56.2; H 6.48; O 37.6; $C_{12}H_{16}O_6$ requires C 56.2; H 6.29; O 37.5.)

Periodate oxidation of phenyl β-D-glucofuranoside. The glucofuranoside (0.15 mmole) was dissolved in water (1 ml) and 0.17 M aqueous periodic acid (1 ml) was added. The reaction was followed in the polarimeter and after about 1 h the optical rotation had reached a constant value (α_D −2.38, 10 cm tube). Sodium borohydride (20 mg) was added and after 1 h at room temperature, the borohydride was decomposed by bubbling carbon dioxide through the solution, which was then extracted with ethyl acetate. The extract was dried over magnesium sulphate and concentrated to a syrup. Hydrolysis of a sample of the syrup yielded phenol and xylose. The remaining syrup crystallised from butanone, yielding phenyl β-D-xylofuranoside, m.p. 108—111°, undepressed on admixture with an authentic sample [1].

Alkaline degradation of phenyl β-D-glucofuranoside. Phenyl β-D-glucopyranoside (1.0 g) was dissolved in 2 M aqueous sodium hydroxide (300 ml) and heated to 100°. The disappearance of the starting material was followed by paper chromatography (butanone, saturated with water). After 90 min, when no starting material could be detected, the solution

was cooled, deionised and concentrated to a dark-coloured syrup (20 mg), which was not further investigated.

Phenyl β-D-galactofuranoside. Penta-*O*-acetyl-β-D-galactofuranose (25 g) prepared according to Schlubach and Prochownick,[3] phenol (25 g) and *p*-toluene sulphonic acid were treated as described above for the synthesis of the glucofuranoside. The syrupy acetate mixture obtained (26 g) was also deacetylated and worked up in a similar manner. The galactofuranoside (8.5 g) crystallised spontaneously and was recrystallised twice from butanone yielding the pure substance m.p. 82–83° $[\alpha]_D^{20}$ −148° (*c* 2.0, water). (Found: C 56.0; H 6.21; O 37.6. $C_{12}H_{16}O_6$ requires C 56.2; H 6.29; O 37.5).

Periodate oxidation of phenyl β-D-galactofuranoside. The galactoside (0.15 mmole) was oxidised and worked up as described for the glucoside. After 35 min, the optical rotation had reached a constant value (α_D −0.596°, 1.5 cm tube). The resulting syrup on hydrolysis yielded phenol and arabinose. It did not crystallise but was converted into the crystalline benzoate m.p. 93–95°C, undepressed on admixture with authentic phenyl α-L-arabinofuranoside tribenzoate [1].

Enzymic hydrolysis of the phenyl glycofuranosides. Phenyl β-D-glucofuranoside, phenyl β-D-galactofuranoside, phenyl β-D-xylofuranoside and phenyl α-L-arabinofuranoside (0.1 g of each) were dissolved in water (20 ml) to which emulsin (0.4 g from Fluka AG) in water (10 ml) and 0.05 M acetate buffer (10 ml) of pH 5.3 were added and the mixture kept at 25° for 48 h. The solution was filtered, deionised, concentrated and investigated by paper chromatography (water-saturated butanone and ethyl acetate-pyridine-water 8:2:1). Approximately 25 % of each glycoside had been hydrolysed. The relative rates of hydrolysis were: glucoside > xyloside = arabinoside > galactoside.

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