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Phenyl Glycofuranosides

1. Synthesis of Phenyl β-D-Xylofuranoside and Phenyl α-L-Arabinofuranoside

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Phenyl β-D-xylofuranoside and phenyl α-L-arabinofuranoside have been prepared by condensation of the corresponding furanosidic sugar acetates with phenol in the presence of *p*-toluene sulphonic acid.

Most of the methyl and phenyl glycosides of the common sugars have been prepared and characterised (*cf.* Ref.[1]). Only a few phenyl glycofuranosides are, however, known. Vis and Fletcher [2] synthesised phenyl β-D-ribofuranoside from tri-*O*-benzoyl-D-ribofuranosyl bromide and sodium phenolate in 1,2-dimethoxyethane. The diacetates of 2-naphthyl [3] and phenyl [4] β-D-glucofurano-sidurono-γ-lactone were prepared by Tsou and Seligman by condensation of D-glucofuranurono-γ-lactone triacetate with the phenol in the presence of p-toluene sulphonic acid. This method had been devised by Helferich and Schmitz-Hillebrecht [5] for the synthesis of phenyl glycosides. Deacetylation of these glycosides by the Zemplén procedure was accompanied by cleavage of the glycosidic linkage. The 2-naphthyl furanoside could however be prepared by treatment of its acetate with ammonia in methanol and transformation of the resulting amide into the lactone.

As phenyl glycofuranosides are of potential interest in several respects, *e.g.* in connection with enzymatic studies, the synthesis of some phenyl furanosides of the more common sugars was investigated. In the present communication the syntheses of phenyl β-D-xylofuranoside and phenyl α-L-arabinofuranoside are reported.

Tetra-*O*-acetyl-D-xylofuranose was prepared from 1,2-*O*-isopropylidene-D-xylose diacetate [6] by acetylation under acidic conditions. Treatment of the tetraacetate with phenol in the presence of *p*-toluene sulphonic acid and deacetylation of the reaction product with sodium methoxide in methanol yielded the phenyl β-D-xylofuranoside, m.p. 114–116°, $[\alpha]_D$ −128° (water). The substance gave correct elemental analyses and on acid hydrolysis yielded phenol and xylose. It was different from the known phenyl D-xylopyranosides

and was more readily hydrolysed than these in acid solution. The final optical rotations observed after periodate oxidation of equimolar proportions of the substance and of phenyl β-D-glucopyranoside were the same. This confirms the β-configuration of the xylofuranoside, also indicated by its high negative specific optical rotation.

The phenyl α-L-arabinofuranoside was analogously prepared from crude L-arabinofuranose tetraacetate. The tetraacetate was prepared from L-arabinose by acetylation with acetic anhydride in dimethyl formamide and pyridine at high temperature, which favours the formation of furanosidic acetates. The crude arabinoside acetate was deacetylated as above and fractionated by chromatography on a silica gel column. The phenyl α-L-arabinofuranoside crystallised from its syrup, m.p. 63—66°, $[\alpha]_D$ −159° (water) but could not be recrystallised. It was therefore converted to its crystalline tribenzoate, m.p. 93—95°, $[\alpha]_D$ −28° (chloroform). The structure was confirmed by elemental analysis, acid hydrolysis to phenol and arabinose and by its distinction from the known phenyl L-arabinopyranosides. The final optical rotations, after periodate oxidation of an equimolar amount of the L-arabinofuranoside and phenyl α-D-glucopyranoside were numerically the same, although of opposite signs, thus confirming the α-configuration of the former. Small amounts of phenyl β-L-arabinopyranoside and impure phenyl α-L-arabinopyranoside were also obtained after the chromatographic separation of the reaction mixture.

Vis and Fletcher [7] obtained a low yield of 1,5-anhydro-β-D-ribofuranose on treatment of phenyl β-D-ribofuranoside with sodium alkoxide in 2-propanol. Alkaline treatment of phenyl β-D-xylofuranoside, which could be expected to give an analogous anhydride, yielded only traces of neutral reaction products. The xyloside was very labile; after 15 min in 0.44 M sodium hydroxide at 100° most of the starting material had been degraded. This is similar to the high alkali lability compared with other methyl glycosides of methyl β-D-xylofuranoside [8].

EXPERIMENTAL

Thin layer chromatography was performed on silica gel G.[9] Paper chromatography on dimethyl sulphoxide impregnated paper was performed according to Wickberg [10]. Concentrations were performed at water pump pressure and with a bath temperature of 40°, unless otherwise stated. Melting points are corrected.

Phenyl β-D-xylofuranoside. 3,5-Di-*O*-acetyl-1,2-*O*-isopropylidene-D-xylose [6] (23.4 g) was dissolved in a mixture of acetic acid (230 ml) and acetic anhydride (25 ml). Concentrated sulphuric acid (14 ml) was added with stirring and external cooling with ice. The solution was kept 18 h at 38° and then poured into ice-water (300 ml). The aqueous solution was extracted with chloroform (2 × 100 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 syrup (21.8 g). This was assumed to consist of D-xylofuranose tetraacetate and after distillation at 0.1 mm Hg and a bath temperature of 160—165° it was obtained as a colourless syrup, $[\alpha]_D^{20}$ + 37° (*c*, 3.0, ethanol). Chang and Lythgoe [11] report $[\alpha]_D^{19}$ + 56° in the same solvent. The product gave a single spot on paper chromatography (isopropyl ether) and thin layer chromatography (ethyl acetate).

A mixture of the tetraacetate (32 g), phenol (47 g) and *p*-toluene sulphonic acid (0.30 g) was melted to a homogeneous mixture and heated, under water pump pressure, to 100° for 25 min. Benzene (60 ml) was added to the hot mixture and after cooling a further quantity (100 ml) was added. The benzene solution was washed with 1 M aqueous sodium hydroxide (4 × 10 ml) and with water until washings were neutral. It was dried

over magnesium sulphate and concentrated to a yellow syrup (40 g). Thin layer chromatography (ethyl acetate-chloroform, 1:1) revealed the presence of a main component, together with smaller amounts of unchanged starting material.

The syrup (20.8 g) was dissolved in anhydrous methanol (1700 ml) to which sodium methoxide (from 0.37 g sodium) in methanol (50 ml) was added. After 3 h at room temperature the methanol was distilled off, the residue dissolved in water, passed through columns of Dowex 50 (H^+) and Dowex 3 (free base) and concentrated to a small volume (100 ml). The solution which contained a phenyl xyloside and smaller amounts of xylose was washed with chloroform (3 × 25 ml) and then extracted with ethyl acetate (8 × 100 ml), which removed the xyloside but not the xylose. The ethyl acetate was dried over magnesium sulphate and concentrated to a syrup. Crystallisation from ethyl acetate yielded colourless needles (3.9 g). Further crystallisations from the same solvent yielded the pure substance, m.p. 114–116°, $[\alpha]_D^{20}$ −128° (*c*, 2.5, water). (Found: C 58.6; H 6.29; O 35.2. $C_{11}H_{14}O_5$ requires C 58.4; H 6.24; O 35.4).

*Alkaline treatment of phenyl β-*D*-xylofuranoside.* Phenyl β-D-xylofuranoside was treated with 0.44 M aqueous sodium hydroxide at 100° and the reaction was followed by thin layer chromatography (butanol-ethanol-water, 10:3:5). After 15 min only traces of starting material remained. The xyloside (1.0 g) was treated with 0.44 M aqueous sodium hydroxide (30 ml) at 100° for 15 min, after which the solution was deionised and concentrated to a syrup (87 mg), which contained starting material, xylose and an unidentified component. The syrup was dissolved in 10 % aqueous ethanol and filtered through a short carbon-Celite column. This treatment removed the starting material. The residue was concentrated to a yellow syrup (14 mg), containing the unidentified component and xylose.

*Phenyl α-*L*-arabinofuranoside.* L-Arabinose (50 g) was dissolved with stirring in boiling dimethyl formamide (1000 ml). Pyridine (100 ml) and acetic anhydride (125 ml) were added and after 5 min at boiling temperature the mixture was poured into ice-water (2500 ml) and stirred for 30 min. It was then extracted with chloroform (3 × 250 ml), the chloroform solution was dried over calcium chloride and concentrated under reduced pressure (1 mm) and 70° to a dark brown syrup (65 g). Most of the coloured impurities were removed by chromatography through a short silica gel column with ethyl acetate-chloroform, 1:1. The decolourised syrup (51 g), which on examination by thin layer chromatography in the same solvent was found to contain both fully and partially acetylated products, was partitioned between carbon tetrachloride (700 ml) and water (2 × 100 ml). The carbon tetrachloride solution was dried over magnesium sulphate and concentrated to a lightcoloured syrup (29 g). Investigation of the syrup by paper chromatography showed the presence of a main component, believed to be the furanosidic acetate, some α-pyranose acetate and traces of other products.

A mixture of this syrup (28.7 g), phenol (43 g) and *p*-toluene sulphonic acid (0.30 g) was treated as described above for the synthesis of the xylofuranoside. The dark brown syrup containing the acetylated glycoside (31.4 g) was decolourised by chromatography on a short silica gel column. Thin layer chromatography (chloroform) of the yellow syrup (27.4 g) obtained, showed that most of the starting material had reacted.

Deacetylation of this syrup (6.0 g) as described above and partition between ethyl acetate and water yielded a yellow syrup, which was shown by thin layer chromatography to contain one major component, smaller amounts of phenyl arabinopyranosides and traces of other components. This syrup was fractionated by chromatography on a silica gel column (ethyl acetate), yielding a chromatographically pure fraction of the major component (2.0 g), followed by a non-resolved mixture of the two phenyl L-arabinopyranosides. The β-pyranoside, m.p. 175–179°, $[\alpha]_D^{20}$ + 246°, was obtained from this mixture by crystallisation from ethyl acetate.

The syrup containing the main component crystallised after some days at room temperature but the product could not be recrystallised. The crystals were washed with ethyl ether, yielding a colourless product, m.p. 63–66°, $[\alpha]_D^{20}$ −159° (*c*, 2.0, water). (Found: C 58.1; H 6.19; O 35.5. $C_{11}H_{14}O_5$ requires C 58.4; H 6.24; O 35.4).

*Phenyl tri-*O*-benzoyl-α-*L*-arabinofuranoside.* Phenyl α-L-arabinofuranoside (210 mg) was treated for two days at room temperature with benzoyl chloride (2 ml) in pyridine (4 ml) and chloroform (1 ml) and the mixture worked up as usual. Crystallisation from ethanol yielded the tribenzoate as colourless crystals, m.p. 93–95°, $[\alpha]_D^{20}$ −28° (*c*, 2.0, chloroform). (Found: C 71.2; H 5.17; O 24.0. $C_{32}H_{26}O_8$ requires C 71.4; H 4.87; O 23.8).

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