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Reaction of Sugar Esters with Hydrogen Fluoride

IV. Isomerisation of Tetra-*O*-benzoyl-α-D-lyxopyranose

CHRISTIAN PEDERSEN

Organisk-kemisk Laboratorium, Polyteknisk Læreanstalt, Copenhagen, Denmark

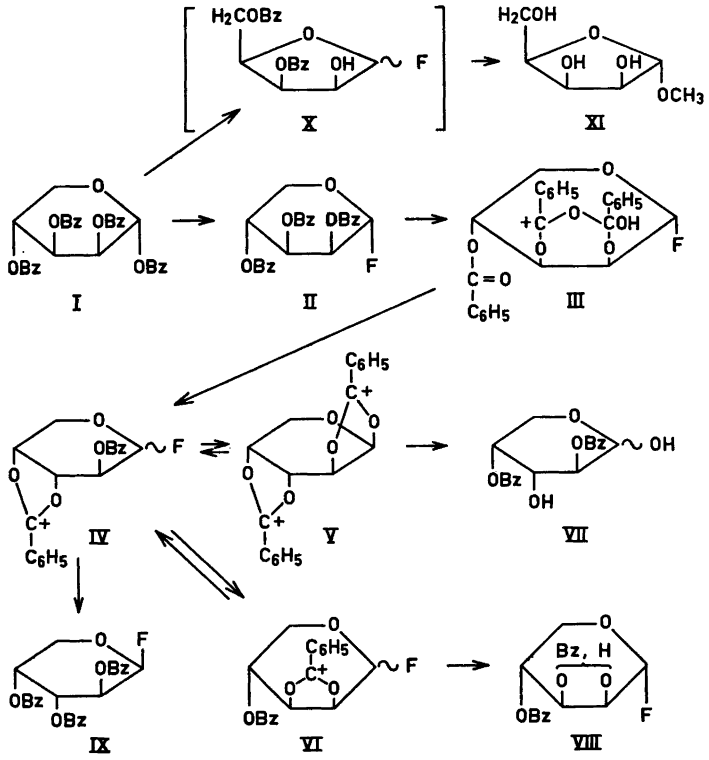
Prolonged treatment of tetra-*O*-benzoyl-α-D-lyxopyranose with anhydrous hydrogen fluoride leads to the formation of derivatives of D-arabinopyranose and D-lyxopyranose. Besides, a lyxofuranose derivative is formed, isolated as methyl α-D-lyxofuranoside. The nature of the products depends on the manner in which excess hydrogen fluoride is removed from the reaction mixture.

In part III of this series[1] it was shown that prolonged reaction of tetra-*O*-benzoyl-β-D-xylopyranose with anhydrous hydrogen fluoride led to the formation of derivatives of D-arabinose and D-lyxose. When excess hydrogen fluoride was removed by washing the reaction mixture with aqueous sodium hydrogen carbonate 2,4-di-*O*-benzoyl-D-arabinopyranose was the main product, but when hydrogen fluoride was removed by evaporation with air a lyxose derivative was obtained. It was suggested that the first step in this rearrangement is an attack of the carbonylgroup at C—3 upon C—2 leading to the formation of a cyclic carbonium ion.

In lyxose C—2 and C—3 are in a *cis* configuration and therefore tetra-*O*-benzoyl-α-D-lyxopyranose would not be expected to rearrange according to the mechanism proposed for the rearrangement of tetra-*O*-benzoyl-β-D-xylopyranose. However, lyxose tetrabenzoate has three benzoyloxygroups in a contiguous *cis-trans* arrangement and it may therefore be expected to react with hydrogen fluoride according to the mechanism proposed by Hedgley and Fletcher for the rearrangement of esters of cyclitols[2] or 1,5-anhydroglycitols.[3] The first step in the reaction of tetra-*O*-benzoyl-α-D-lyxopyranose (I) with hydrogen fluoride is the formation of tri-*O*-benzoyl-α-D-lyxopyranosyl fluoride (II) as shown in part III of this series.[1] Prolonged reaction of (II) with hydrogen fluoride will, according to the mechanism of Hedgley and Fletcher, give the cyclic carbonium ion (IV) *via* the ion (III). (IV) would be expected to be in equilibrium with (VI) and probably also (V) and since (IV), (V), and (VI) are the same ions as those assumed to be intermediates in the rearrangement of tetra-*O*-benzoyl-β-D-xylopyranose one would expect to get

the same products from the reaction of tetrabenzoyl lyxose (I) with hydrogen fluoride as those obtained from tetrabenzoyl xylose.

Treatment of (I) with anhydrous hydrogen fluoride for 20 h followed by removal of excess hydrogen fluoride by direct washing with aqueous sodium hydrogen carbonate gave a product from which was crystallised 2,4-di-*O*-



benzoyl-D-arabinopyranose (VII) in 16 % yield. Chromatography of the mother liquor on alumina gave a 6.7 % yield of tri-*O*-benzoyl-α-D-lyxopyranosyl fluoride (II). When the mother liquor material was benzoylated and then chromatographed on alumina small amounts of tri-*O*-benzoyl-β-D-arabinopyranosyl fluoride (IX) and tetra-*O*-benzoyl-β-D-arabinopyranose were obtained. No other crystalline compounds could be isolated. In a separate experiment the material remaining after crystallisation of 2,4-di-*O*-benzoyl-D-arabinose was treated with sodium methoxide. Paper chromatography of the resulting product gave spots corresponding to arabinose, lyxose, methyl α-D-arabinopyranoside, and methyl α-D-lyxopyranoside. Besides, another rather large spot was present and isolation of the material corresponding to this spot by chromatography on thick paper gave an 8.5 % yield of methyl α-D-lyxofuranoside (XI). The spot corresponding to methyl α-D-arabinopyranose

was also eluted and the product was benzoylated yielding 9.7 % of methyl tri-*O*-benzoyl-α-D-arabinopyranoside.

Reaction of tetra-*O*-benzoyl-α-D-lyxopyranose (I) with hydrogen fluoride for 20 h, followed by removal of excess hydrogen fluoride by evaporation with a stream of dry air, gave a product from which was crystallised 4.2 % of tri-*O*-benzoyl-α-D-lyxopyranosyl fluoride (II). No other crystalline compound could be obtained. When the product was benzoylated a 15 % yield of (II) was obtained after chromatography on alumina. Besides, a small amount of tetra-*O*-benzoyl-β-D-arabinopyranose was isolated. Treatment of the crude product with sodium methoxide gave material which on paper chromatography showed the same picture as the one obtained above. Methyl α-D-lyxofuranoside (XI) was isolated in a 10 % yield. The 4.2 % of (II) (or 6.7 % when hydrogen fluoride was removed by direct washing) which was isolated before the crude product was benzoylated is probably material which has not reacted with hydrogen fluoride. The increased amount of (II) obtained after benzoylation of the reaction mixture must be due to benzoylation of di-*O*-benzoyl-α-D-lyxopyranosyl fluoride (VIII).

Thus the reaction of tetra-*O*-benzoyl-α-D-lyxopyranose with hydrogen fluoride does give the same products as those obtained from tetra-*O*-benzoyl-β-D-xylopyranose and in the case of tri-*O*-benzoyl-α-D-lyxopyranosyl fluoride (II) the yield is nearly the same in the two cases. However, the yield of 2,4-di-*O*-benzoyl-D-arabinopyranose (VII) from tetrabenzoyl lyxose is much lower than from tetrabenzoyl xylose (16 % *versus* 45 %). The reaction of tetrabenzoyl lyxose with hydrogen fluoride is apparently more complex than the reaction of the corresponding xylosederivative since a lyxofuranose derivative is formed, isolated as methyl α-D-lysofuranoside (XI). No furanose derivative was found in the case of tetrabenzoyl xylose. Pedersen and Fletcher [4] found that prolonged treatment of tetra-*O*-benzoyl-β-D-ribopyranose with hydrogen fluoride gave a low yield of 3,5-di-*O*-benzoyl-D-ribofuranosyl fluoride and in analogy with this it may be assumed that the primary product from tetrabenzoyl lyxose is 3,5-di-*O*-benzoyl-D-lyxofuranosyl fluoride (X). The mechanism by which this compound is formed is at present unknown.

In order to make certain that the methyl α-D-lyxofuranoside does not arise from an impurity in the tetra-*O*-benzoyl-α-D-lyxopyranose which was used in these experiments the latter compound was treated with hydrogen fluoride for 30 min at −10° and the tri-*O*-benzoyl-α-D-lyxopyranosyl fluoride (II) was crystallised as described in part III of this series.[1] The material in the mother liquor was treated with sodium methoxide and the product thus obtained was chromatographed on paper. It gave a strong spot corresponding to methyl α-D-lyxopyranoside and two very weak spots, but no methyl α-D-lyxofuranoside could be detected indicating that no lyxofuranose derivative is present until a more vigorous reaction with hydrogen fluoride has taken place.

EXPERIMENTAL

Melting points are uncorrected.

Reaction of tetrabenzoyl lyxopyranose with hydrogen fluoride for 20 h. Hydrogen fluoride removed by washing. Tetra-*O*-benzoyl-α-D-lyxopyranose (5.0 g) was dissolved in anhydrous hydrogen fluoride (10 ml) and the solution was kept at room temperature for 20 h.

Methylene chloride (100 ml) was then added and the mixture was poured into 500 ml of saturated sodium hydrogen carbonate. The organic layer was separated and washed with aqueous sodium hydrogen carbonate and water. After drying the solvent was removed *in vacuo* leaving 3.5 g of a brown syrup which from ether-pentane deposited 500 mg (16 %) of 2,4-di-*O*-benzoyl-D-arabinopyranose (VII), m.p. 166–169°. After one recrystallisation from ethyl acetate-pentane the product melted at 169–172° and showed no depression when mixed with a sample prepared as previously described.[1] The infrared spectra of the two products were identical.

The syrupy material from the mother liquor was put on a column of alumina (75 g, 'Fluka' grade II, pH 6.5). Elution with benzene-hexane (1:1) gave a fraction from which was crystallised 275 mg (6.7 %) of tri-*O*-benzoyl-D-D-lyxopyranosyl fluoride (II), m.p. 141–143°, undepressed when mixed with an authentic sample. Further elution of the column with more polar solvents gave syrups only.

In a separate experiment the syrupy material was benzoylated and then chromatographed on alumina. The fraction eluted with benzene gave, after several recrystallisations from ethanol and ether-pentane, 100 mg of tri-*O*-benzoyl-β-D-arabinopyranosyl fluoride (IX), m.p. 155–157°, and 30 mg of tetra-*O*-benzoyl-β-D-arabinopyranose, m.p. 173–174°. Both compounds were identified by infrared spectra and mixed melting points with authentic samples.

Methyl α-D-lyxofuranoside. Tetra-*O*-benzoyl-α-D-lyxopyranose (2.0 g) was treated with hydrogen fluoride for 20 h as described above. The 2,4-di-*O*-benzoyl-D-arabinopyranose was crystallised from ether-pentane and the material from the mother liquor was dissolved in methanol (10 ml); 2 ml of 1 N sodium methoxide was added and the solution was kept at + 5° over night. The methanol was then evaporated and the residue was dissolved in water and deionized by passage through Amberlite IR–120 and IR–4B. The aqueous solution was evaporated leaving 430 mg of a syrup which on paper chromatography in ethyl acetate:propanol:water (5:2:3) or butanone saturated with water gave spots corresponding to arabinose, lyxose, methyl α-arabinopyranoside, and methyl α-lyxopyranoside. Besides, a spot with R_F-value equal to that of methyl α-lyxofuranoside was found. The compound corresponding to this spot was isolated by chromatographing 100 mg of the syrup on a sheet of Whatmann 3 MM paper using butanone saturated with water as solvent. The appropriate area was cut out and eluted with methanol; the methanol was removed and the residue was crystallised from ethyl acetate to give 12.3 mg (8.5 %) of methyl α-D-lyxofuranoside, m.p. 95–96°, $[\alpha]_D^{24}$ + 132° (*c* 0.18, CH_3OH). Mixed melting point and infrared spectrum proved that the compound was identical with an authentic sample prepared according to Nys and Verheijden.[5] The spot corresponding to methyl α-arabinopyranoside was eluted from the same sheet of paper. The material thus isolated was benzoylated and gave 9.7 % of methyl tri-*O*-benzoyl-α-D-arabinopyranoside, m.p. 143–144°, $[\alpha]_D^{24}$ −199° (*c* 0.56, $CHCl_3$), identical with an authentic sample.

In another experiment lyxose tetrabenzoate was treated with hydrogen fluoride for 72 h and then worked up as above. This gave the same amount of 2,4-di-*O*-benzoyl-D-arabinopyranose and a 12.2 % yield of methyl α-D-lyxofuranoside.

Hydrogen fluoride removed with dry air. Tetra-*O*-benzoyl-α-D-lyxopyranose (5.0 g) was kept in hydrogen fluoride (10 ml) for 20 h at room temperature. Methylene chloride (25 ml) was then added and the mixture was evaporated in a stream of dry air; this was repeated to remove as much hydrogen fluoride as possible. The residue was dissolved in methylene chloride and washed with sodium hydrogen carbonate and water. Removal of the solvent left 3.75 g of syrup which from ethanol gave 175 mg (4.2 %) of tri-*O*-benzoyl-α-D-lyxopyranosyl fluoride, m.p. 140–142°. The mother liquor material was chromatographed on alumina but no crystalline compound was obtained.

In a separate experiment the crude product was benzoylated to give 5.3 g of a syrup which was put on a column of alumina (75 g, 'Fluka' grade II, pH 6.5). Elution with hexane gave a fraction which from ethanol deposited 625 mg (15 %) of tri-*O*-benzoyl-α-D-lyxopyranosyl fluoride, m.p. 139–142°. Elution of the column with benzene-hexane (1:1) gave a large fraction (1119 mg) which from ether-pentane yielded 75 mg of tetra-*O*-benzoyl-β-D-arabinopyranose, m.p. 172–173°, $[\alpha]_D^{22}$ −320° (*c* 0.48, $CHCl_3$). Further elution with more polar solvents gave syrupy material only.

Isolation of methyl α-D-lyxofuranoside. Tetrabenzoyl lyxose (1.0 g) was treated with 2 ml of hydrogen fluoride for 20 h. The hydrogen fluoride was evaporated with air and the residue was washed. The product was treated with sodium methoxide, deionized and evaporated to give 330 mg of material. Paper chromatopraphy of this material gave spots corresponding to arabinose, lyxose, methyl α-arabinopyranoside, methyl α-lyxopyranoside, and methyl α-lyxofuranoside. Chromatography on 3 MM paper as described above gave 10 % methyl α-D-lyxofuranoside.

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REFERENCES

1. Pedersen, C. *Acta Chem. Scand.* **17** (1963) 1269.
2. Hedgley, E. J. and Fletcher, H. G., Jr. *J. Am. Chem. Soc.* **84** (1962) 3726.
3. Hedgley, E. J. and Fletcher, H. G., Jr. *J. Am. Chem. Soc.* **85** (1963) 1615.
4. Pedersen, C. and Fletcher, H. G., Jr. *J. Am. Chem. Soc.* **82** (1960) 941.
5. Nys, M. and Verheijden, J. P. *Bull. Soc. Chim. Belges* **69** (1960) 57.

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