Syntheses of Some Polyfluoro-aromatic Derivatives of Carbohydrates and Polyols

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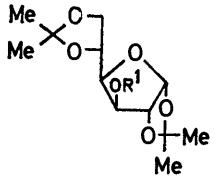
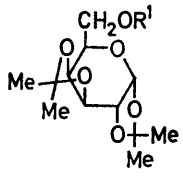
The reactions of partially substituted carbohydrates and polyols, *e.g.* 1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose (1), 1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranose (3), and 1,2:5,6-di-*O*-isopropylidene-D-mannitol (8) with sodium hydride followed by hexafluorobenzene in 1,2-dimethoxyethane yield the corresponding pentafluorophenyl ethers. Monoethers can be prepared from diols and these compounds on treatment with sodium hydride yield novel cyclic carbohydrate derivatives, *e.g.* methyl 4,6-*O*-benzylidene-2,3-*O*-(tetrafluoro-*o*-phenylene)-α-D-glucopyranoside (16). Reaction of the alkoxide of compound (3) with its 6-*O*-pentafluorophenyl ether (4) links the two sugar residues through the aryl nucleus. Arylation of 1,2-*O*-isopropylidene-α-D-glucofuranose (20) yields. besides the expected 1,2-*O*-isopropylidene-3,5,6-tri-*O*-pentafluorophenyl-α-D-glucofuranose (21), a second product, 1,2-*O*-isopropylidene-6-*O*-pentafluorophenyl-3,5-*O*-(tetrafluoro-*o*-phenylene)-α-D-glucofuranose (22).

ALTHOUGH aryl glycosides are abundant in nature and are readily prepared,[1] few aryl ether derivatives of carbohydrates have been described. 6-*O*-Phenyl ethers of hexoses have been obtained by the fusion of 5,6-anhydro-derivatives with phenols under basic catalysis,[2,3] but the reaction has not been widely applied. 2,4-Dinitrophenyl ethers of some alditols have been made,[4] and while the present work was in progress a few 2,4,6-trinitrophenyl ethers of carbohydrates were prepared as part of a solvolytic study.[5] The susceptibility of hexafluorobenzene to nucleophilic attack by the alkoxides of methanol and ethane-1,2-diol [6] suggested that carbohydrate pentafluorophenyl ethers might be easily synthesised and that novel cyclic structures might be obtained in certain cases. This paper reports our initial investigation into the preparation of polyfluoro-aromatic derivatives of substituted carbohydrates and polyols.

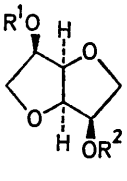
The alcohols were converted into their pentafluorophenyl ethers by treating their sodium salts (formed with sodium hydride) in 1,2-dimethoxyethane with an excess of hexafluorobenzene. The reaction generally proceeded to completion in 24 h at room temperature in reasonable yields; *e.g.* in the conversions of compounds (1), (3),



(1) $R^1 = H$
(2) $R^1 = C_6F_5$



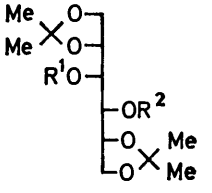
(3) $R^1 = H$
(4) $R^1 = C_6F_5$



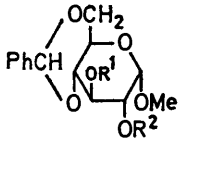
(5) $R^1 = R^2 = H$
(6) $R^1 = R^2 = C_6F_5$
(7) $R^1 = H$, $R^2 = C_6F_5$

and (8) into the ethers (2), (4), and (9), respectively. The preparation of the ether (6) from the diol (5), however, required heating under reflux and also proceeded in lower yield.

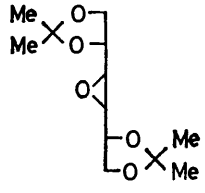
Reaction of methyl 4,6-*O*-benzylidene-α-D-glucoside (12) gave not the expected 2,3-di-*O*-aryl ether, but a mono-*O*-pentafluorophenyl derivative in 45% yield, which could be converted into an acetate and a methyl ether. The methyl ether was identical with that prepared by pentafluorophenylation of methyl 4,6-*O*-benzylidene-3-*O*-methyl-α-D-glucopyranoside; this confirmed that the reaction product from the diol (12) was methyl 4,6-*O*-benzylidene-2-*O*-pentafluorophenyl-α-D-glucoside (13). The partial etherification may be a



(8) $R^1 = R^2 = H$
(9) $R^1 = R^2 = C_6F_5$
(10) $R^1 = H$, $R^2 = C_6F_5$
(11) $R^1R^2 = o\text{-}C_6F_4$



(12) $R^1 = R^2 = H$
(13) $R^1 = H$, $R^2 = C_6F_5$
(14) $R^1 = Ac$, $R^2 = C_6F_5$
(15) $R^1 = Me$, $R^2 = C_6F_5$
(16) $R^1R^2 = o\text{-}C_6F_4$



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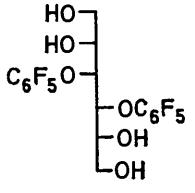

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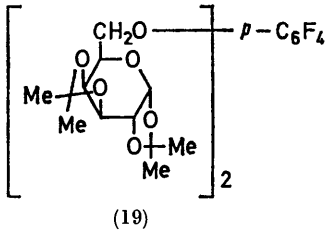


(19)

result of steric hindrance; the reaction illustrates a noteworthy difference in reactivity between 2- and 3-hydroxy groups. 1,4:3,6-Dianhydro-D-mannitol (5) and 1,2:5,6-di-*O*-isopropylidene-D-mannitol (8) could, by the use of only 1 mol. equiv. of sodium hydride, be partially converted into their mono-*O*-pentafluorophenyl derivatives (7) and (10), respectively, but the corresponding di-*O*-aryl ethers were formed concomitantly.

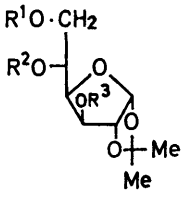
In view of the fact that 2-pentafluorophenoxyethanol is readily cyclised on treatment with base,[6] it was of interest to attempt intramolecular cyclisations with

[1] J. Conchie, G. A. Levvy, and C. A. Marsh, *Adv. Carbohydrate Chem.*, 1957, **12**, 157.
[2] H. Ohle, E. Euler, and R. Voulième, *Ber.*, 1938, **71**, 2250.
[3] J. Kocourek and V. Jiricek, *Coll. Czech. Chem. Comm.*, 1957, **22**, 806.
[4] M. L. Wolfrom, N. D. Juliano, M. S. Toy, and A. Chaney, *J. Amer. Chem. Soc.*, 1959, **81**, 1446.
[5] M. L. Sinnott and M. C. Whiting, *J. Chem. Soc.* (*B*), 1971, 965.
[6] J. Burdon, V. A. Damodaran, and J. C. Tatlow, *J. Chem. Soc.*, 1964, 763.

those of the foregoing aryl ethers containing hydroxy-groups. Treatment of compound (7) with 1 equiv. of sodium hydride in refluxing dimethoxyethane resulted in the disappearance of starting material, but the product was not homogeneous, and had a low mobility on t.l.c. compared to (7), a property not expected for the cyclised product.* The mannitol derivative (10) and the glucopyranoside derivative (13) on the other hand readily underwent cyclisations in high yields to give the tetrafluoro-*o*-phenylene derivatives (11) and (16), respectively. Molecular (Dreiding) models indicate that the latter two *O*-substituted arenes could be formed without strain, but this was not so for any 2,5-*O*-arylene derivative (*o*-, *m*-, or *p*-) of 1,4:3,6-dianhydro-D-mannitol (5). During the cyclisation of the ether (10), only a trace of 3,4-anhydro-1,2:5,6-di-*O*-isopropylidene-D-altritol (17) was detected, suggesting that pentafluorophenoxy is not a good leaving group under these conditions.† Also the pentafluorophenyl ether group is relatively stable under acidic conditions; the di-*O*-isopropylidene derivative (9) could be hydrolysed to the tetraol (18) and the latter then reacetonated [to (9)] in high overall yield.

In an attempt to link two carbohydrate residues through an aromatic ring, the alkoxide of 1,2:5,6-di-*O*-isopropylidene-α-D-galactopyranose (3) was treated with the corresponding aryl ether (4). Chromatographically homogeneous material was obtained which gave the expected analytical figures; however it showed a wide m.p. range. The singlet resonance in its ^{19}F n.m.r. spectrum suggested the product was predominantly the *para*-linked compound (19), but multiplets could just be detected which indicated the presence of *ortho*- and *meta*-isomers. The preferential formation of compound (19) is expected in view of the reaction of pentafluoroanisole with methoxide ion.[7]

Pentafluorophenylation of the triol 1,2-*O*-isopropylidene-α-D-glucofuranose (20) gave a product containing two major components (t.l.c.) in approximately equal



(20) $R^1 = R^2 = R^3 = H$ (23) $R^1 = R^2 = H$, $R^3 = C_6F_5$
(21) $R^1 = R^2 = R^3 = C_6F_5$ (24) $R^1 = H$, $R^2R^3 = o\text{-}C_6F_4$
(22) $R^1 = C_6F_5$, $R^2R^3 = o\text{-}C_6F_4$ (25) $R^1 = Bz$, $R^2R^3 = o\text{-}C_6F_4$

amounts. The faster-running was the expected 1,2-*O*-isopropylidene-3,5,6-tri-*O*-pentafluorophenyl-α-D-glucofuranose (21). The second component (X) had no hydroxy-absorption in its i.r. spectrum, and its analytical figures and ^{19}F n.m.r. spectrum, coupled with a peak at *m/e* 532 in its mass spectrum, suggested that it contained a pentafluorophenyl group and a tetrafluoro-*o*-phenylene system. Three such structures are possible in which the second aromatic ring is *ortho*-substituted by oxygen atoms at the 3,5-, 3,6-, or 5,6-positions of the sugar. A decision between these possibilities was reached as follows. 1,2:5,6-Di-*O*-isopropylidene-3-*O*-pentafluorophenyl-α-D-glucofuranose (2) was partially hydrolysed to 1,2-*O*-isopropylidene-3-*O*-pentafluorophenyl-α-D-glucofuranose (23), which on treatment with sodium hydride cyclised to yield a single product containing an *ortho*-substituted aromatic ring. The ^1H n.m.r. spectrum of this cyclised compound showed a two-proton multiplet at τ 6·02, which was absent in the spectrum of its benzoate derivative; the two-proton resonance in this case occurred as part of a multiplet at τ *ca.* 5·30.‡ The resonance at τ 6·02 can be assigned therefore to H-6 and H-6′, with C-6 carrying an hydroxy-group, and the cyclised product is therefore 1,2-*O*-isopropylidene-3,5-*O*-(tetrafluoro-*o*-phenylene)-α-D-glucofuranose (24). Treatment of this compound with sodium hydride–hexafluorobenzene in the usual manner yielded a compound identical with (X) obtained from the triol (20); this established the latter as 1,2-*O*-isopropylidene-6-*O*-pentafluorophenyl-3,5-*O*-(tetrafluoro-*o*-phenylene)-α-D-glucofuranose (22).

All the new derivatives are crystalline. Attempts made so far to remove selectively the polyfluorophenyl groups in these compounds (*e.g.* with sodium–liquid ammonia) have been unsuccessful. Investigation into the syntheses of other polyhalogenoaromatic derivatives of carbohydrates, including perfluorophenyl glycosides, is in progress.

EXPERIMENTAL

T.l.c. was performed on Kieselgel GF_{254} and preparative layer chromatography (p.l.c.) on Kieselgel PF_{254}. The polyfluoroaryl derivatives were readily detected under u.v. light. 1,2-Dimethoxyethane (DME) was dried by distillation from calcium hydride, and sodium hydride was freed from oil by a petroleum wash. Rotations were measured for solutions in chloroform unless stated otherwise, on a Perkin-Elmer 141 polarimeter (1 dm tubes). ^1H N.m.r. spectra were run at 60 or 100 MHz on a Perkin-Elmer R12 or a Varian HA-100 spectrometer, respectively. ^{19}F N.m.r. spectra were measured for solutions in chloroform at 94·1 MHz on the Varian spectrometer and reported chemical shifts are to high field of the internal standard, trichlorofluoromethane.

Pentafluorophenyl Ethers.—The ethers (2), (4), (6), and (9) were prepared from compounds (1),[8] (3),[9] (5),[10] and (8),[11] respectively by the following general method, except that preparation (c) required heating under reflux for 18 h.

To a stirred solution of the carbohydrate derivative

* The cyclic products (11) and (16) showed R_F values greater than those of their precursors (10) and (13), respectively.

† *Cf.* alkyl picrates, which are solvolysed with alkyl–oxygen fission at rates comparable with those of corresponding toluenesulphonates.[5]

‡ The n.m.r. spectra of 1,2-*O*-isopropylidene-3,5-*O*-benzylidene-α-D-glucofuranose and its 6-benzoate also showed similar features, and supported the assignments.

[7] J. Burdon, W. B. Hollyhead, and J. C. Tatlow, *J. Chem. Soc.*, 1965, 5152.
[8] D. J. Bell, *J. Chem. Soc.*, 1935, 1874.
[9] H. Ohle and G. Berend, *Ber.*, 1925, **58**, 2585.
[10] L. F. Wiggins, *J. Chem. Soc.*, 1945, 4.

(0·01 mol) in DME (10 ml), small portions of sodium hydride were added until a new addition produced no further effervescence. Hexafluorobenzene (0·012 mol per hydroxy-group) was then added, and the mixture was stirred with protection from moisture until a clear solution was obtained (18—72 h). The solution was poured into water (200 ml), and in cases where crystallisation occurred the solid was collected and dried; otherwise the aqueous solution was extracted with chloroform (4 × 50 ml) and the combined extracts were dried (Na_2SO_4) and concentrated. The products sometimes contained traces of materials which ran faster than the ethers on t.l.c. and were conveniently purified by p.l.c. Physical constants and analytical data for the ethers are as follows (the developer used in purification by p.l.c. is noted after the % yield).

(a) 1,2:5,6-*Di*-O-*isopropylidene*-3-O-*pentafluorophenyl*-α-D-*glucofuranose* (2) (89%), C_6H_6, b.p. 100° at 0·05 mmHg, m.p. 39—40°, $[\alpha]_D^{24}$ −27·7° (*c* 1·0) (Found: C, 50·6; H, 4·6; F, 22·2. $C_{18}H_{19}F_5O_6$ requires C, 50·7; H, 4·5; F, 22·3%). The ^{19}F n.m.r. spectrum showed signals at 155·9 (d) and 163·4 p.p.m. (m) characteristic of an ABB'XX' system (*cf.* spectrum of pentafluoroanisole [12]).

(b) 1,2:3,4-*Di*-O-*isopropylidene*-6-O-*pentafluorophenyl*-α-D-*galactopyranose* (4) (52%), C_6H_6, m.p. 75—76° (from MeOH), $[\alpha]_D^{25}$ −61·7° (*c* 1·9) (Found: C, 50·7; H, 4·6; F, 22·2. $C_{18}H_{19}F_5O_6$ requires C, 50·7; H, 4·5; F, 22·3%).

(c) 1,4:3,6-*Dianhydro*-2,5-*di*-O-*pentafluorophenyl*-D-*mannitol* (6) (36%), C_6H_6, m.p. 108—109° (from MeOH), $[\alpha]_D^{20}$ +123° (*c* 0·6) (Found: C, 45·0; H, 1·5; F, 39·6. $C_{18}H_{18}F_{10}O_4$ requires C, 45·2; H, 1·7; F, 39·7%).

(d) 1,2:5,6-*Di*-O-*isopropylidene*-3,4-*di*-O-*pentafluorophenyl*-D-*mannitol* (9) (45%), C_6H_6, m.p. 87—88° (from MeOH), $[\alpha]_D^{20}$ +27·4° (*c* 0·6) (Found: C, 48·4; H, 3·3; F, 31·65. $C_{24}H_{20}F_{10}O_6$ requires C, 48·5; H, 3·4; F, 32·0%).

Selective Pentafluorophenylation Reactions.—(a) 1,4:3,6-*Dianhydro*-2-O-*pentafluorophenyl*-D-*mannitol* (7). To a stirred solution of the diol (5) (1·46 g) in DME (150 ml) was added sodium hydride (0·3 g), and the mixture was heated under reflux with stirring while a solution of hexafluorobenzene (2·79 g) in DME (50 ml) was added dropwise (3 h). Heating and stirring were continued for 18 h, and after concentration to *ca.* 20 ml the mixture was poured into water. Extraction with chloroform followed by concentration of the extracts gave a product (1·1 g) containing [t.l.c. in benzene–ethyl acetate (9 : 1)] the starting diol, the diether (6), and a new component with R_F 0·14. Separation of this compound by p.l.c. gave, after vacuum sublimation and crystallisation from ethyl acetate–petroleum, the *pentafluorophenyl ether* (7) (0·7 g), m.p. 83—84°, $[\alpha]_D^{20}$ +91° (*c* 0·4) (Found: C, 45·9; H, 3·2; F, 30·1. $C_{12}H_9F_5O_4$ requires C, 46·2; H, 2·9; F, 30·4%).

(b) 1,2:5,6-*Di*-O-*isopropylidene*-3-O-*pentafluorophenyl*-D-*mannitol* (10). The diol (8) (0·42 g) in DME (50 ml) was treated with sodium hydride (0·05 g) and hexafluorobenzene (0·74 g) with stirring for 18 h at room temperature. T.l.c. [benzene–ethyl acetate (4 : 1)] showed the presence of the starting diol, the diether (9), and a new major component with R_F 0·28, which was isolated by p.l.c. The material (0·23 g) was distilled (distillate slowly crystallised) to yield the *pentafluorophenyl ether* (10), b.p. 115° (bath) at 0·04 mmHg, m.p. 58—59°, $[\alpha]_D^{20}$ 0·0° (*c* 0·6) (Found: C, 50·4; H, 5·1; F, 22·2. $C_{18}H_{21}F_5O_6$ requires C, 50·5; H, 4·9; F, 22·2%).

(c) *Methyl* 4,6-O-*benzylidene*-2-O-*pentafluorophenyl*-α-D-*glucopyranoside* (13). A stirred solution of the diol [13] (12) (1·41 g) in DME (5 ml) was treated with sodium hydride (0·3 g), and then hexafluorobenzene (1·86 g) in DME (15 ml) was added. After 48 h at room temperature, the mixture was poured into water (200 ml) and the crude product (1·5 g) was collected, dried, and crystallised from methanol to yield the *pentafluorophenyl ether* (13) (1 g, 45%), m.p. 138—139°, $[\alpha]_D^{20}$ +34·7° (*c* 0·96) (Found: C, 53·3; H, 4·0; F, 20·9. $C_{20}H_{17}F_5O_6$ requires C, 53·6; H, 3·8; H, 21·2%).

Treatment of the foregoing ether with acetic anhydride–pyridine yielded the *acetate* (14), m.p. 157—158° (from ethanol), $[\alpha]_D^{20}$ +18·6° (*c* 0·8) (Found: C, 54·2; H, 4·1; F, 19·4. $C_{22}H_{19}F_5O_7$ requires C, 53·9; H, 3·9; F, 19·4%).

Purdie methylation [14] (three treatments) of the ether (13) did not go to completion (t.l.c.), but p.l.c. in benzene yielded the expected *methyl ether* (15) (0·06 g), m.p. 139—140° (from petroleum), $[\alpha]_D^{20}$ +35·3° (*c* 0·7) (Found: C, 54·2; H, 4·2; F, 20·6. $C_{21}H_{19}O_6$ requires C, 54·55; H, 4·1; F, 20·55%). The same ether (15), m.p. 137—139°, $[\alpha]_D^{20}$ +34·6° (*c* 0·8), indistinguishable (i.r. spectrum and t.l.c.) from the foregoing sample, was obtained by pentafluorophenylation of methyl 4,6-*O*-benzylidene-3-*O*-methyl-α-D-glucoside. The latter was conveniently prepared by partial Purdie methylation of methyl 4,6-*O*-benzylidene-α-D-glucoside,* and had constants in agreement with reported values.[15]

Attempted Cyclisation of 1,4:3,6-*Dianhydro*-2-O-*pentafluorophenyl*-D-*mannitol* (7).—The ether (7) (0·6 g) in DME (15 ml) was converted into its alkoxide by addition of sodium hydride, and the solution was heated under reflux for 18 h. After concentration to *ca.* 5 ml, the mixture was poured into water and the product isolated by chloroform extraction. The product (0·06 g) was a gum, R_F 0·0 on t.l.c. in benzene–ethyl acetate (9 : 1); (starting material, R_F 0·14). T.l.c. in other solvents showed it to be inhomogeneous.

1,2:5,6-*Di*-O-*isopropylidene*-3,4-O-(*tetrafluoro*-o-*phenylene*)-D-*mannitol* (11).—A stirred solution of the ether (10) (0·35 g) in DME (5 ml) was treated with sodium hydride (0·03 g) for 18 h at room temperature. After dilution with water (100 ml) the mixture was extracted with chloroform (3 × 30 ml) and the extracts dried and concentrated to yield a crystalline solid (0·33 g). T.l.c. [benzene–ethyl acetate (4 : 1)] showed no starting material, a major product, and a trace of 1,2:5,6-di-*O*-isopropylidene-3,4-anhydro-D-altritol (17).[16] Crystallisation from methanol gave the *cyclised product* (11), m.p. 107—108°, $[\alpha]_D^{20}$ +1·2° (*c* 1·4) (Found: C, 52·9; H, 4·9; F, 18·3. $C_{18}H_{20}F_4O_6$ requires C, 52·9; H, 4·9; F, 18·6), showing no i.r. absorption near 3600 cm^{-1}. The ^{19}F n.m.r. spectrum showed a typical AA'XX' pattern centred on 164·7 and 169·3 p.p.m.

Methyl 4,6-O-*Benzylidene*-2,3-O-(*tetrafluoro*-o-*phenylene*)-α-D-*glucopyranoside* (16).—Treatment of the ether (13) (0·5 g) in DME (20 ml) with sodium hydride as before gave the *product* (0·4 g, 84%), m.p. 152—153° (from methanol), $[\alpha]_D^{20}$ −54·8° (*c* 0·8) (Found: C, 55·8; H, 3·9; F, 18·0. $C_{20}H_{16}F_4O_6$ requires C, 56·1; H, 3·8; F, 17·7%), showing no i.r. absorption near 3600 cm^{-1}. The ^{19}F n.m.r. spectrum

* P. J. Garegg, personal communication.

[11] E. Baer, *J. Amer. Chem. Soc.*, 1945, **67**, 338.
[12] I. J. Lawrenson, *J. Chem. Soc.*, 1965, 117.
[13] N. K. Richtmeyer, *Methods Carbohydrate Chem.*, 1962, **1**, 108.
[14] T. Purdie and J. C. Irvine, *J. Chem. Soc.*, 1904, 1049, 1071.
[15] H. R. Bolliger and D. A. Prins, *Helv. Chim. Acta*, 1946, **29**, 1116.
[16] B. R. Baker and A. H. Haines, *J. Org. Chem.*, 1963, **28**, 442.

showed absorptions at 161·9 (m), 162·7 (m), and 167·9 p.p.m. (m) of intensity ratios 1 : 1 : 2.*

3,4-*Di*-O-*pentafluorophenyl*-D-*mannitol* (18).—The acetal (9) (0·1 g) was dissolved in trifluoroacetic acid (2·7 ml) and water (0·3 ml) was added dropwise. After 5 min, the solution was concentrated to an oil which crystallised from ethyl acetate–light petroleum to give the *tetraol* (0·078 g, 91%), m.p. 125—126°, $[\alpha]_D^{19}$ +75·5° (*c* 0·55 in MeOH) (Found: C, 41·7; H, 2·3; F, 36·9. $C_{18}H_{12}F_{10}O_6$ requires C, 42·0; H, 2·55; F, 36·95%). The tetraol was reconverted into the acetal (9) in 87% on treatment for 18 h at room temperature with 2,2-dimethoxyethane containing a trace of trifluoroacetic acid.

Linking of Galactopyranosyl Residues through an Aromatic Ring.—1,2:3,4-Di-*O*-isopropylidene-α-D-galactopyranose (3) (0·65 g) in DME (10 ml) was converted into its sodium salt with sodium hydride, and a solution of the 6-*O*-pentafluorophenyl ether (4) (1·22 g) in DME (10 ml) was added dropwise. After 18 h at room temperature the solution was concentrated to 5 ml and poured into water (150 ml), and the aqueous suspension was extracted with chloroform. The material (1·66 g) obtained on concentration of the extract showed [t.l.c. in benzene–ethyl acetate (9 : 1)] complete conversion of starting materials into a new product which after p.l.c. and crystallisation from methanol yielded a solid (1·5 g), m.p. 110—125°, $[\alpha]_D^{20}$ −87·7° (*c* 0·65) (Found: C, 53·8; H, 6·0; F, 11·5. Calc. for $C_{30}H_{38}F_4O_{12}$: C, 54·05; H, 5·75; F, 11·4%). Its ^{19}F n.m.r. spectrum showed a singlet for the *para*-substituted ring at 158·2 p.p.m., but resonances were just detectable which were attributed to *ortho*- and *meta*-isomers.

Reaction of 1,2-O-*Isopropylidene*-α-D-*glucofuranose with Hexafluorobenzene.*—Sodium hydride (0·8 g) was added to a solution of the triol [17] (20) (2·2 g) in DME (20 ml), followed by hexafluorobenzene (6 g) in DME (10 ml). An exothermic reaction occurred during 30 min and the resulting yellow solution was stirred for 18 h. Work-up in the usual way gave a yellow syrup; t.l.c. (benzene) revealed two major and a number of minor components. A portion (0·4 g) of this mixture was subjected to p.l.c. (C_6H_6) and the materials having R_F 0·54 (0·1 g) and 0·45 (0·15 g) were isolated. The faster-running component crystallised from methanol to yield 1,2-O-*isopropylidene*-3,5,6-*tri*-O-*pentafluorophenyl*-α-D-*glucofuranose* (21), m.p. 123—124°, $[\alpha]_D^{20}$ +6° (*c* 0·6) (Found: C, 44·9; H, 2·0; F, 40·0. $C_{27}H_{13}F_{15}O_6$ requires C, 45·1; H, 1·8; F, 39·7%).

The slower-running component crystallised from methanol to yield 1,2-O-*isopropylidene*-6-O-*pentafluorophenyl*-3,5-O-(*tetrafluoro*-o-*phenylene*)-α-D-*glucofuranose* (22), m.p. 96—97°, $[\alpha]_D^{20}$ +118° (*c* 0·9) (Found: C, 47·1; H, 2·7; F, 32·3. $C_{21}H_{13}F_9O_6$ requires C, 47·4; H, 2·5; F, 32·1%). The ^{19}F n.m.r. spectrum, which showed signals at 156·9 (d), 159·6 (d), 160·6 (d), 163·5 (m), 164·7 (t), and 166·7 p.p.m. (t), was virtually a sum of the ABB′XX′ and ABXY spectra of compounds (2) and (24), respectively. Its mass spectrum showed a parent ion *m/e* 532 (70%).

Reactions leading to Proof of Structure of Compound (22).—(*a*) The ether (2) (0·85 g) in methanol (15 ml) was partially hydrolysed by portionwise addition of 0·1M-sulphuric acid (6 ml) during 6 h. The mixture was then stirred with barium carbonate, filtered, and poured into chloroform (150 ml). The organic solution was extracted with saturated aqueous sodium hydrogen carbonate (10 ml), dried, and concentrated to yield material (0·7 g) homogeneous by t.l.c. which crystallised from ethyl acetate–petroleum to give 1,2-O-*isopropylidene*-3-O-*pentafluorophenyl*-α-D-*glucofuranose* (23), m.p. 148—149°, $[\alpha]_D^{20}$ +7·9° (*c* 0·4) (Found: C, 46·8; H, 4·1; F, 24·5. $C_{15}H_{15}F_5O_6$ requires C, 46·6; H, 3·9; F, 24·6%).

(*b*) Treatment of compound (23) (0·44 g) in DME (150 ml) with sodium hydride (0·054 g) followed by storage for 3 days at room temperature gave a single product [t.l.c. in benzene–ethyl acetate (4 : 1)]. Work-up in the usual manner gave a product (0·41 g) which was sublimed at 130° (bath) and 0·04 mmHg to yield 1,2-O-*isopropylidene*-3,5-O-(*tetrafluoro*-o-*phenylene*)-α-D-*glucofuranose* (24), m.p. 72—74°, $[\alpha]_D^{20}$ +179° (*c* 0·4) (Found: C, 49·4; H, 4·1; F, 20·3. $C_{15}H_{14}F_5O_6$ requires C, 49·2; H, 3·85; F, 20·75%), τ ($CDCl_3$) 3·96 (d, H-1), 5·15 (d, H-2), 5·26 (d) and 5·39 (d) (H-3 and H-4), 5·59 (m, H-5), 6·02 (m, H-6,6′), 7·74br (OH), and 8·48 (s) and 8·65 (s) (CMe_2). The ^{19}F n.m.r. spectrum showed signals at 160·4 (d), 161·2 (d), 165·5 (t), and 166·6 p.p.m. (t), characteristic of any ABXY system, with *ortho*-coupling (22 Hz), large compared with *meta*- and *para*-coupling (≤4 Hz).

(*c*) The foregoing compound (24) on treatment with benzoyl chloride in pyridine yielded the 6-*benzoate* (25) (82%), m.p. 152—154° (from methanol), $[\alpha]_D^{20}$ +135° (*c* 0·75) (Found: C, 56·3; H, 4·0; F, 15·7. $C_{22}H_{18}F_4O_7$ requires C, 56·2; H, 3·9; F, 16·2%), τ ($CDCl_3$) 1·95 and 2·53 (m, aromatic H), 3·89 (d, H-1), 5·13 (d, H-2), 5·17—5·40 (complex, H-3,4,5,6,6′), and 8·48 (s) and 8·64 (s) (CMe_2).

(*d*) Compound (24) was treated with sodium hydride and hexafluorobenzene in the usual manner and gave a product, m.p. 96—98°, $[\alpha]_D^{24}$ +117° (*c* 1·55), which was indistinguishable (t.l.c., i.r. spectrum, mixed m.p. 96—98°) from the slower-running component [compound (22)] obtained in the reaction of 1,2-*O*-isopropylidene-α-D-glucofuranose with hexafluorobenzene.

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* Although the spectrum of the *meta*-isomer might also show these intensity ratios, they would be expected to be in the order (from low to high field) of 1 : 2 : 1, by analogy with the spectrum of 1,2,3,5-tetrafluoro-4,6-dimethoxybenzene.[7] Also steric considerations rule out the *meta*-isomer.

[17] R. E. Cramera, A. Park, and R. L. Whistler, *J. Org. Chem.*, 1963, **28**, 3230.