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THE SYNTHESIS OF FURTHER ANALOGUES OF TREHALOSE CONTAINING AMINO AND FLUORO SUBSTITUENTS*

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ABSTRACT

Syntheses of 4,6-diacetamido-4,6-dideoxy-α-D-galactopyranosyl, 4-amino-4,6-dideoxy-6-fluoro-α-D-galactopyranosyl, and a derivative of 4,6-diacetamido-4,6-dideoxy-α-D-glucopyranosyl α-D-glucopyranoside, *via* nucleophilic displacement reactions of appropriate sulphonic esters or chlorodeoxy derivatives, are described. The synthesis of the symmetrical derivative 4-amino-4,6-dideoxy-6-fluoro-α-D-galactopyranosyl 4-amino-4,6-dideoxy-6-fluoro-α-D-galactopyranoside is also described. The ^{19}F-n.m.r. spectra of the salts of the 4-amino-6-fluorides reveal an unexpected conformation about the C-5–C-6 bond, due to the dipolar attraction between the 6-C–F and 4-C–N$^+$ bonds.

INTRODUCTION

Some fluorinated derivatives of α,α-trehalose function as reversible inhibitors of inset trehalase[1–3], and we now report on syntheses of other fluoro and amino derivatives of trehalose.

RESULTS AND DISCUSSION

The reaction of 2,3-di-*O*-benzyl-4,6-di-*O*-mesyl-α-D-glucopyranosyl 2,3-di-*O*-benzyl-4,6-*O*-benzylidene-α-D-glucopyranoside[2] (**2**) with sodium azide in hexamethylphosphoric triamide at 90° afforded the syrupy 4,6-diazide **6** in 56% yield. Subsequent catalytic hydrogenation of **6**, using palladium-on-charcoal in the absence of acid, reduced only the azido groups, to give the crystalline diamine **7**. Alternatively, addition of acetic anhydride to the reaction mixture gave the di-*N*-acetyl derivative **8**, catalytic hydrogenolysis of which, in the presence of mineral acid, removed the protecting groups, to give crystalline 4,6-diacetamido-4,6-dideoxy-α-D-galactopyranosyl α-D-glucopyranoside (**12**), which was further characterised as its crystalline hexaacetate **13**.

*Chemical Modification of Trehalose: Part XXII. For Part XXI, see ref. 1.

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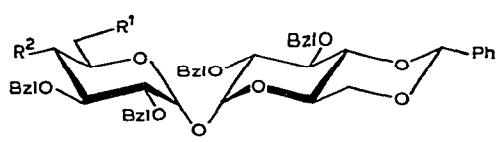
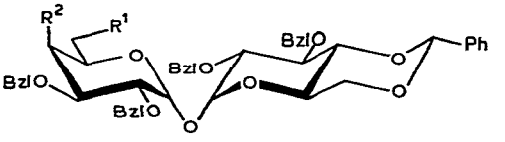
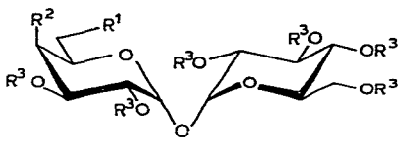


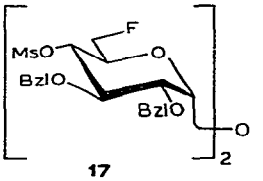
1 $R^1 = R^2 = OH$
2 $R^1 = R^2 = OMs$
3 $R^1 = R^2 = N_3$
4 $R^1 = R^2 = NHAc$
5 $R^1 = F, R^2 = OMs$



6 $R^1 = R^2 = N_3$
7 $R^1 = R^2 = NH_2$
8 $R^1 = R^2 = NHAc$
9 $R^1 = F, R^2 = N_3$
10 $R^1 = F, R^2 = NHAc$
11 $R^1 = R^2 = Cl$



12 $R^1 = R^2 = NHAc, R^3 = H$
13 $R^1 = R^2 = NHAc, R^3 = Ac$
14 $R^1 = F, R^2 = NHAc, R^3 = H$
15 $R^1 = F, R^2 = NHAc, R^3 = Ac$
16 $R^1 = F, R^2 = NH_3Cl\ R^3 = H$



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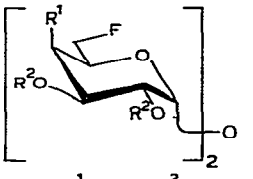

18 $R^1 = N_3, R^2 = Bzl$
19 $R^1 = NH_2, R^2 = Bzl$
20 $R^1 = NHAc, R^2 = Bzl$
21 $R^1 = NH_3Cl\ R^2 = H$

Attempted, simultaneous reduction of the azido groups in **6** and removal of the *O*-benzyl and *O*-benzylidene substituents by conducting the hydrogenation in the presence of acid led to incomplete reaction, and the required 4,6-diamine could not be obtained. It is well known that the catalytic hydrogenolysis of *O*-benzyl groups requires the presence of acid, presumably because the reactive species is the protonated *O*-benzyl group. In the case of **6**, the azido groups would almost certainly be reduced very rapidly to give the diamine salt, which would inhibit protonation elsewhere in the molecule.

In common with other trehalose derivatives, the mass spectrum of **13** was dominated by fragments formed *via* the A-series[1], that is cleavage of the two glycosidic bonds. Thus, the dominant fragments had *m/e* 331 (glucopyranosyl ring) and 329 (galactopyranosyl ring), both of which sequentially lost the elements of acetic acid and ketene, to give fragments having *m/e* 271, 269 and 229, 227.

Access to the *gluco,gluco*-analogue (**4**) of the 4,6-diamino derivative **7** required a double inversion at C-4, starting from the 4,6-diol **1**. This reaction was accomplished by treatment of **1** with sulphuryl chloride, which gave the 4,6-dichloride **11** in 48% yield as a syrup. Subsequent nucleophilic displacement of the two chloro substituents with azide afforded the crystalline 4,6-diazido-*gluco*-isomer **3** in 63% yield. Reduction of the azido groups in **3** with hydrazine–Raney nickel gave the diamine, which was isolated as its di-*N*-acetyl derivative **4**. The mass spectrum of **4** displayed the expected fragmentation pattern.

The reaction of the 6-fluoro-4-mesylate[2] **5** with sodium azide in either hexamethylphosphoric triamide or *N,N*-dimethylformamide resulted in nucleophilic displacement of the sulphonyloxy group to give the 4-azide **9**. Reduction of the latter, followed by *N*-acetylation, afforded the crystalline 4-acetamido-6-fluoride **10** in 50% yield. Catalytic hydrogenolysis of **10** yielded the deblocked disaccharide 4-acetamido-4,6-dideoxy-6-fluoro-α-D-galactopyranosyl α-D-glucopyranoside (**14**), which was characterised as its crystalline hexa-acetate **15**. The 4-amino-6-fluoride **16** was obtained from the 4-azide **9** by first removing the *O*-benzylidene group with acid followed by catalytic hydrogenolysis in the presence of mineral acid. Although the simultaneous reduction of azide and *O*-benzyl groups had not been successful for the diazide **6**, it worked well with the azide **9**, giving the 4-amine **16** in 35% overall yield as a hygroscopic hydrochloride.

The ^{19}F-n.m.r. spectra of the 4-acetamido-6-fluoride **14** and its hexa-acetate **15** (Table I) were consistent with the *galacto* configuration of the ring carrying the fluorine substituent, with the F-6 resonances appearing as double triplets. Notably, the $J_{F\text{-}6,H\text{-}5}$ value (~15 Hz) was within the range (12–15 Hz) normally found for 6-deoxy-6-fluorogalactopyranosides[4] (*cf.* 27–29 Hz for glucopyranosides). The difference in the $J_{F\text{-}6,H\text{-}5}$ values is due to the differences in rotamer population about the C-5–C-6 bond. For the glucopyranosides, the large value for $J_{F\text{-}6,H\text{-}5}$ is indicative of an antiperiplanar arrangement (Fig. 1*a*). An axial group at C-4 destabilises this arrangement, and consequently the favoured rotamer in galactopyranosides is one in which the fluorine is gauche to H-5 (Fig. 1*b* or Fig. 1*c*, or both). The reason for the destabilisation of rotamer *a* in galactopyranosides is either steric or polar repulsion between the 6-substituent and the axial substituent at C-4. The greater importance of the polar factor is suggested by the ^{19}F-n.m.r. parameters obtained for the 4-amino-6-fluoride hydrochloride **16**, and the corresponding symmetrical analogue **21** (Table I). The values (30 and 33 Hz, respectively) of $J_{F\text{-}6,H\text{-}5}$ are strongly indicative of the antiperiplanar arrangement between H-5 and F-6 (Fig. 1*a*), and this unusual arrangement for galactopyranosides must be due to attractive dipolar interactions between the 6-C-F and the 4-C-N$^+$ bonds.

TABLE I

^{19}F-N.M.R. PARAMETERS[a]

Compound	*Solvent*	*F-6*	$J_{F-6,H-5}$	$J_{F-6,H-6}$
9	$CDCl_3$	−68.4	~10	~49
10	$CDCl_3$	−69.8[b]		
14	$CDCl_3$	−70.1	~15	~48
15	$CDCl_3$	−67.8	~15	~50
16	D_2O	−70.2	30	47
18	$CDCl_3$	−69.8	10	45
21	D_2O	−71.4	33	52
20	$CDCl_3$	−67.2	15	46

[a]First-order chemical shifts (p.p.m. relative to external hexafluorobenzene) and coupling constants (Hz) at 56.45 MHz. [b]Second-order multiplet.

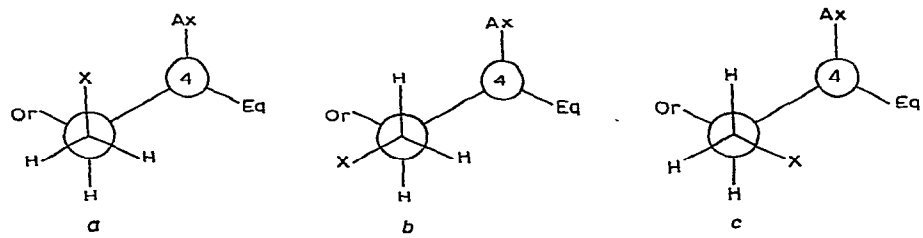

Fig. 1. Rotamers about the C-5–C-6 bond, showing the relationship of the 6-substituent (X) to the axial and equatorial substituents at C-4.

Synthesis of the symmetrical analogue 4-amino-4,6-dideoxy-6-fluoro-α-D-galactopyranosyl 4-amino-4,6-dideoxy-6-fluoro-α-D-galactopyranoside dihydrochloride (**21**) was accomplished in an analogous manner from the 6,6′-difluoro-4,4′-dimesylate[2] **17**. Sequential azidolysis and catalytic hydrogenation under acidic conditions afforded the diamine dihydrochloride **21** as a crystalline trihydrate in an overall yield of 24%.

The 4-acetamido-6-fluoride **14** and the 4,6-diacetamide **12** were assayed for inhibitory activity against trehalase from the flight muscle of the greenbottle fly (*Lucilia sericata*). The diacetamide **12** showed no inhibition, but the 4-acetamido-6-fluoride **14** was weakly inhibitory, producing 25% inhibition at a concentration of 31mM.

EXPERIMENTAL

For general methods, see ref. 1.

*4,6-Diazido-2,3-di-*O*-benzyl-4,6-dideoxy-α-*D*-galactopyranosyl 2,3-di-*O*-benzyl-4,6-*O*-benzylidene-α-*D*-glucopyranoside* (**6**). — To a solution of the 4,6-dimesylate[2] **2** (4 g, 4.23 mmol) in hexamethylphosphoric triamide (20 cm^3) was added sodium azide (1 g, 15.4 mmol). The mixture was heated at 90° for 48 h, and t.l.c. (light petroleum–ethyl acetate, 3:1) then indicated completion of the reaction. The cooled mixture was diluted with ethyl acetate (50 cm^3) and extracted with water (3 × 50 cm^3). The combined aqueous extracts were then extracted with ethyl acetate (2 × 25 cm^3), and the combined organic layers were dried ($MgSO_4$) and evaporated to dryness. Chromatography of the product on dry-packed silica gel with ethyl acetate–light petroleum (1:3) afforded **6** (2 g, 56%) as a chromatographically pure, hard glass, $[\alpha]_D$ +96° (*c* 0.5) (Found: C, 67.3; H, 5.7; N, 10.2. $C_{47}H_{48}N_6O_9$ calc.: C, 67.2; H, 5.7; N, 10.0).

*4,6-Diamino-2,3-di-*O*-benzyl-4,6-dideoxy-α-*D*-galactopyranosyl 2,3-di-*O*-benzyl-4,6-*O*-benzylidene-α-*D*-glucopyranoside* (**7**) *and the di-*N*-acetyl derivative* **8**. — To a solution of the 4,6-diazide **6** (4 g, 4.76 mmol) in ether (50 cm^3) and ethanol (100 cm^3) was added palladium-on-charcoal. The mixture was hydrogenated at 50 p.s.i. for 34 h, filtered, and then evaporated, to give **7**, m.p. 110–111.5°, $[\alpha]_D$ +117° (*c* 1) (Found: C, 71.8; H, 6.9; N, 3.4. $C_{47}H_{52}N_2O_9$ calc.: C, 71.6; H, 6.6; N, 3.55).

The above hydrogenation was repeated and, after filtration of the reaction mixture, acetic anhydride (2 g, 19.6 mmol) was added; immediate crystallisation took place to give **8** (1.8 g, 39%), m.p. 283–284.5°, $[\alpha]_D$ +102° (*c* 1) (Found: C, 69.6; H, 6.5; N, 3.3. $C_{51}H_{56}N_2O_{11}$ calc.: C, 70.2; H, 6.4; N, 3.2). Mass spectrum: *m/e* 447 (2.8), 441 (44.7), 431 (12.6), 425 (35.5), 341 (2.8), 339 (7.1), 333 (17.8), 325 (2.4), 323 (5.6), 317 (39.0), 233 (17.8), 217 (4.8), and 181 (100%, PhC^+HCH_2Ph).

*4,6-Diacetamido-4,6-dideoxy-α-*D*-galactopyranosyl α-*D*-glucopyranoside* (**12**). — To a suspension of **8** (1.5 g, 1.72 mmol) in ethanol (120 cm^3) was added conc. hydrochloric acid (1 cm^3). The mixture was hydrogenated over palladium-on-charcoal at 52 p.s.i. for 18 h, and t.l.c. (ethyl acetate–methanol, 1 : 1) then indicated completion of the reaction. After neutralisation ($PbCO_3$) and evaporation, the product was eluted from a short column of silica gel with ethyl acetate–methanol (1 : 1), to give **12** (0.35 g, 46%), m.p. 175–176.5° (ethyl acetate–ethanol), $[\alpha]_D$ +179° (*c* 1, methanol) (Found: C, 43.0; H, 7.0; N, 6.4. $C_{16}H_{28}N_2O_{11} \cdot H_2O$ calc.: C, 43.4; H, 6.8; N, 6.35). Mass spectrum of hexakis(Me_3Si) derivative: *m/e* 451 (0.4), 389 (25.1), 361 (7.9), 331 (1.3), 299 (6.9), 271 (2.2), 217 (11.2), 204 (5.0), and 73 (100%, Me_3Si^+).

The hexa-acetate **13**, prepared in the usual manner (acetic anhydride–pyridine) in 50% yield, had m.p. 260–261°, $[\alpha]_D$ +141° (*c* 1) (Found: C, 50.1; H, 6.3; N, 4.05. $C_{28}H_{40}N_2O_{17}$ calc.: C, 49.7; H, 5.9; N, 4.1). Mass spectrum: *m/e* 331 (12.6), 329 (31.6), 271 (1.7), 269 (7.1), 229 (3.6), 227 (14.2), 211 (1.6), 169 (56.3), and 43 (100%, CH_3CO^+).

*2,3-Di-*O*-benzyl-4,6-dichloro-4,6-dideoxy-α-*D*-galactopyranosyl 2,3-di-*O*-benzyl-4,6-*O*-benzylidene-α-*D*-glucopyranoside* (**11**). — A solution of the 4,6-diol[2] **1** (1 g, 1.26 mmol) in pyridine (5 cm^3) was cooled to ~ −10° and sulphuryl chloride (1 g, 7.4 mmol) was added. The mixture was kept at 0° for 72 h, and t.l.c. (light petroleum–ethyl acetate, 2 : 1) then indicated completion of the reaction. The solution was diluted with chloroform (10 cm^3) and extracted with cold, dilute hydrochloric acid. The dried ($MgSO_4$) chloroform layer was then evaporated and the residue fractionated on a dry-packed column of silica gel with light petroleum–ethyl acetate (8 : 1). The resulting, syrupy 4,6-dichloride **11** (0.5 g, 48%) had $[\alpha]_D$ +105° (*c* 1) (Found: C, 68.1; H, 6.1. $C_{47}H_{48}Cl_2O_9$ calc.: C, 68.2; H, 5.8). Mass spectrum: *m/e* 447 (1.1), 431 (2.2), 395 (1.3), 341 (2.0) 339 (1.8), 325 (0.4), 323 (0.7), 287 (2.8), 251 (2.2), 233 (3.2), 217 (1.8), and 181 (100%, $PhCH^+CH_2Ph$).

*4,6-Diazido-2,3-di-*O*-benzyl-4,6-dideoxy-α-*D*-glucopyranosyl 2,3-di-*O*-benzyl-4,6-*O*-benzylidene-α-*D*-glucopyranoside* (**3**). — To a solution of the 4,6-dichloride **11** (6 g, 7.26 mmol) in hexamethylphosphoric triamide (25 cm^3) was added sodium azide (3 g, 46 mmol). The mixture was heated at 95° for 48 h, and t.l.c. (light petroleum–ethyl acetate, 3 : 1) then indicated that the reaction was complete. The mixture was processed as described for **6**, and the product was eluted from a dry-packed column of silica gel with light petroleum–ethyl acetate (2 : 1). The resulting diazide (3.8 g, 62%) was recrystallised from methanol, to give **3**, m.p. 92–94°, $[\alpha]_D$ +165° (*c* 1) (Found: C, 66.9; H, 5.9; N, 9.7. $C_{47}H_{48}N_6O_9$ calc.: C, 67.2; H, 5.7; N, 10.0).

*4,6-Diacetamido-2,3-di-*O*-benzyl-4,6-dideoxy-α-*D*-glucopyranosyl 2,3-di-*O*-ben-*

zyl-4,6-O-benzylidene-α-D-glucopyranoside (**4**). — To a solution of the 4,6-diazide **3** (2.5 g, 3 mmol) in ethanol (100 cm^3) was added a spatula load of Raney nickel. The mixture was heated under reflux, and aliquots (1 cm^3) of hydrazine hydrate were periodically added until t.l.c. (ethyl acetate–methanol, 20:1) indicatedc ompletion of the reaction. After cooling, excess of acetic anhydride was added and the mixture was kept at room temperature for 16 h. After filtration, evaporation of the solvent gave a syrupy product that crystallised from ethanol–light petroleum, to afford **4** (1 g, 39%), m.p. 91–93°, $[\alpha]_D$ +117° (*c* 1) (Found: C, 70.1; H, 6.2; N, 2.9. $C_{51}H_{56}N_2O_{11}$ calc.: C, 70.2; H, 6.4; N, 3.2). Mass spectrum: *m/e* 447 (0.7), 441 (11.2), 431 (5.6), 425 (15.0), 341 (1.9), 339 (2.4), 333 (8.9), 325 (1.6), 323 (1.7), 317 (25.1), 233 (7.1), 217 (5.6), and 181 (100%, $PhC^+H{\cdot}CH_2PH$).

4-Azido-2,3-di-O-benzyl-4,6-dideoxy-6-fluoro-α-D-galactopyranosyl 2,3-di-O-benzyl-4,6-O-benzylidene-α-D-glucopyranoside (**9**). — To a solution of the 4-mesylate[2] **5** (4 g, 4.6 mmol) in *N,N*-dimethylformamide (30 cm^3) was added sodium azide (2 g, 30.8 mmol). The mixture was kept at 110° for 18 h, and t.l.c. (light petroleum–ethyl acetate 3:1) then indicated completion of the reaction. The product was then processed as described for **6** and finally purified by elution from a dry-packed column of silica gel with light petroleum–ethyl acetate (2:1), to give syrupy **9** (3 g, 80%), $[\alpha]_D$ +96° (*c* 0.8) (Found: C, 69.1; H, 5.9; N, 5.3. $C_{47}H_{48}FN_3O_9$ calc.: C, 69.0; H, 5.9; N, 5.15).

4-Acetamido-2,3-di-O-benzyl-4,6-dideoxy-6-fluoro-α-D-galactopyranosyl 2,3-di-O-benzyl-4,6-O-benzylidene-α-D-glucopyranoside (**10**). — To a solution of the 4-mesylate[2] **5** (7.8 g, 9 mmol) in hexamethylphosphoric triamide (30 cm^3) was added sodium azide (2 g, 30.8 mmol). The mixture was kept at 90° for 2 days, and t.l.c. (light petroleum–ethyl acetate, 3:1) then indicated the formation of one product. The mixture was processed as described for **6**, and the syrupy product was hydrogenated over palladium-on-charcoal and subsequently *N*-acetylated (acetic anhydride–ethanol) in the usual way. Purification of the product by elution from a dry-packed column of silica gel with ethyl acetate afforded **10** (3.4 g, 50%), which crystallised from ethyl acetate–light petroleum; m.p. 74–75.5°, $[\alpha]_D$ +119° (*c* 1) (Found: C, 70.5; H, 6.3; N, 1.7. $C_{49}H_{52}FNO_{10}$ calc.: C, 70.6; H, 6.2; N, 1.7). Mass spectrum: *m/e* 447 (5.0), 431 (6.9), 402 (15.8), 386 (63.1), 382 (31.6), 366 (35.5), 341 (6.3), 339 (6.3), 325 (5.5), 323 (4.4), 294 (6.9), 278 (21.9), 274 (7.8), 258 (56.3), 233 (12.6), 217 (7.8), and 181 (100, $PhCH_2C^+HPh$).

4-Acetamido-4,6-dideoxy-6-fluoro-α-D-galactopyranosyl α-D-glucopyranoside (**14**). — To a solution of the 4-acetamido derivative **10** (1 g, 1.2 mmol) in ethanol (100 cm^3) was added conc. hydrochloric acid (1 cm^3). The mixture was hydrogenated over palladium-on-charcoal for 16 h, and t.l.c. (ethyl acetate–methanol, 1:1) then indicated completion of the reaction. The mixture was then processed in the usual way and the product purified by elution from a column of silica gel with ethyl acetate–methanol (1:1). The eluate was diluted with light petroleum, to give amorphous **14** (0.25 g, 55%). Mass spectrum of hexakis(Me_3Si) derivative: *m/e* 451 (0.3), 361 (7.1),

350 (12.9), 330 (1.0), 271 (1.8), 260 (8.9), 240 (1.4), 217 (20.0), 204 (10.0), and 73 (100, Me_3Si^+).

The hexa-acetate **15**, prepared (68%) with acetic anhydride–pyridine, had m.p. 111–113°, $[\alpha]_D$ +176° (*c* 1) (Found: C, 49.4; H, 5.9; N, 1.9. $C_{26}H_{36}FNO_{16}$ calc.: C, 49.0; H, 5.65; N, 2.2).

*4-Amino-4,6-dideoxy-6-fluoro-α-*D*-galactopyranosyl α-*D*-glucopyranoside hydrochloride* (**16**). — A solution of the 4-azide **9** (3.0 g, 3.67 mmol) in methanol (30 cm^3) containing hydrochloric acid (1 cm^3) was boiled under reflux until t.l.c. (light petroleum–ethyl acetate, 3:1) indicated that methanolysis was complete. The solution was neutralised ($PbCO_3$) and evaporated, to give a syrupy product that was purified by elution from a dry-packed column of silica gel with ethyl acetate–methanol (1:1), to give the hygroscopic hydrochloride **16** (0.5 g, 35%), which was chromatographically pure, but did not give a satisfactory analysis, presumably because of its hygroscopic nature.

*4-Azido-2,3-di-*O*-benzyl-4,6-dideoxy-6-fluoro-α-*D*-galactopyranosyl 4-azido-2,3-di-*O*-benzyl-4,6-dideoxy-6-fluoro-α-*D*-galactopyranoside* (**18**). — To a solution of the 4,4′-dimesylate[3] **17** (8.6 g, 10 mmol) in hexamethylphosphoric triamide (20 cm^3) was added sodium azide (6.2 g, 100 mmol). The mixture was kept at 90° for 16 h, and t.l.c. (light petroleum–ethyl acetate, 3:1) then indicated one major product. The mixture was then processed in the usual way and the product purified by elution from a column of silica gel with light petroleum–ethyl acetate (3:1), to give **18** (5.4 g, 72%) as a thick syrup, $[\alpha]_D$ +148° (*c* 0.5, chloroform) (Found: C, 63.4; H, 5.9; N, 11.4. $C_{40}H_{42}F_2N_6O_7$ calc.: C, 63.5; H, 5.6; N, 11.1).

*4-Acetamido-2,3-di-*O*-benzyl-4,6-dideoxy-6-fluoro-α-*D*-galactopyranosyl 4-acetamido-2,3-di-*O*-benzyl-4,6-dideoxy-6-fluoro-α-*D*-galactopyranoside* (**20**). — A solution of the 4,4′-diazide **18** (5 g, 6.6 mmol) in ether (20 cm^3) and ethanol (70 cm^3) was hydrogenated and acetylated in the usual way. The product was then purified by elution from a dry-packed column of silica gel with light petroleum–ethyl acetate (4:1), to give **20** (3 g, 60%), m.p. 99–100°, $[\alpha]_D$ +192° (*c* 1) (Found: C, 67.4; H, 6.0; N, 3.3. $C_{44}H_{50}F_2N_2O_9$ calc.: C, 67.0; H, 6.3; N, 3.5). Mass spectrum: *m/e* 402 (10.0), 386 (77), 382 (79), 366 (63), 294 (7.8), 278 (55.0), 274 (7), 258 (79.5), and 181 (100%, PhC^+HCH_2Ph).

*4-Amino-4,6-dideoxy-6-fluoro-α-*D*-galactopyranosyl 4-amino-4,6-dideoxy-6-fluoro-α-*D*-galactopyranoside dihydrochloride* (**21**). — To a solution of the 4,4′-diazide, **18** (4.4 g, 5.8 mmol) in ether (20 cm^3) was added methanol (100 cm^3) and conc. hydrochloric acid (2 cm^3). The mixture was hydrogenated over palladium-on-charcoal for 24 h, and t.l.c. (ethyl acetate–methanol, 1:1) then indicated completion of the reaction. The solution was neutralised ($PbCO_3$), filtered, and evaporated, to give **21** (0.9 g, 33%), which crystallised from ethanol–2-propanol; the salt decomposed above 320° without melting, and had $[\alpha]_D$ +175° (*c* 1, water) (Found: C, 30.6; H, 6.8; N, 5.8. $C_{12}H_{24}Cl_2F_2N_2O_7 \cdot 3H_2O$ calc.: C, 30.6; H, 6.4; N, 5.95).

REFERENCES

1 A. F. HADFIELD, L. HOUGH, AND A. C. RICHARDSON, *Carbohydr. Res.*, 71 (1979) 95–102.
2 A. F. HADFIELD, L. HOUGH, AND A. C. RICHARDSON, *Carbohydr. Res.*, 63 (1978) 51–60.
3 L. HOUGH, A. K. PALMER, AND A. C. RICHARDSON, *J. Chem. Soc., Perkin Trans. 1*, (1973) 2513–2517.
4 L. PHILLIPS AND V. WRAY, *J. Chem. Soc., B*, (1971) 1618–1624; L. EVELYN AND L. D. HALL, *Chem. Ind. (London)*, (1968) 183–184.