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EFFECT OF A NUCLEOPHILIC SUBSTITUENT ON THE STEREOCHEMISTRY OF THE KOENIGS–KNORR REACTION. STEREOSPECIFIC SYNTHESIS OF SOME α- AND β-LINKED DISACCHARIDES OF L-FUCOSE

HAROLD M. FLOWERS
Department of Biophysics, The Weizmann Institute of Science, Rehovoth (Israel)
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ABSTRACT

Reaction of 2-*O*-benzyl-3,4-di-*O*-p-nitrobenzoyl-α-L-fucopyranosyl bromide with suitably protected benzyl α-L-fucopyranoside, methyl α- and β-L-fucopyranosides, and methyl α- and β-D-galactopyranosides afforded 2-*O*-α-L-linked disaccharides stereospecifically. Reaction of the same nucleophilic derivatives with 2,3,4-tri-*O*-acetyl-α-L-fucopyranosyl bromide generally led to the corresponding β-L-linked disaccharides. However, methyl 6-*O*-benzoyl-3,4-*O*-isopropylidene-β-D-galactopyranoside gave an appreciable proportion of α-L-disaccharide, whereas benzyl β-L-fuco- and β-D-galacto-pyranosides gave α-L-linked disaccharides stereospecifically.

INTRODUCTION

The Koenigs–Knorr reaction between peracetylglycopyranosyl bromides and protected saccharides in the presence of mercuric cyanide in nitromethane–benzene generally leads to β-D- or β-L-linked disaccharides. However, a number of examples have been described in which these conditions, or rather more polar media, have afforded considerable proportions of α-linked disaccharides[1]. In the majority of these cases[2–5], but not in all[6,7], glycosylation has been at OH-2 of a protected derivative, and the adjacent anomeric centre in the nucleophilic intermediate had either the α or β configuration. Stereospecific syntheses of α-linked disaccharides generally involve protected glycosyl halides that are less accessible than the peracetylglycopyranosyl bromides, and thus there might be considerable practical value in ascertaining conditions under which they can be prepared directly from these bromides.

Earlier work in this laboratory has demonstrated the stereospecific synthesis of β-linked disaccharides by treatment of several α-D-glycopyranosyl bromides with various nucleophilic intermediates in the presence of mercuric cyanide[8]. β-L-Disaccharides had previously been prepared from 2,3,4-tri-*O*-acetyl-α-L-fucopyranosyl bromide in a similar fashion[9,10]. The configuration of the compounds obtained was in contrast to that of the 2-*O*-α-L-linked disaccharides previously obtained by treatment of the same fucosyl bromide with a suitably protected benzyl β-L-fucopyranoside[11] and β-D-galactopyranoside[8,12]. The question may therefore be raised as to whether the structure of the nucleophilic intermediate or the site of substitution in the pyranose ring may have an effect on the configuration of the product of the Koenigs–Knorr reaction. Thus, suitably protected derivatives of L-fucose and D-galactose having OH-2 free for reaction and C-1 either in α- or β-configuration were prepared, and the effect of this configuration on the reaction at the vicinal OH-2 was investigated.

RESULTS AND DISCUSSION

Benzyl α-L-fucopyranoside (**1**), prepared by glycosylation of benzyl alcohol in the presence of an acidic resin, was acetonated in quantitative yield with 2,2-dimethoxypropane and *p*-toluenesulfonic acid to syrupy benzyl 3,4-*O*-isopropylidene-α-L-fucopyranoside (**4**). Methyl 6-*O*-benzoyl-3,4-*O*-isopropylidene-α-D-galactopyranoside (**9**) and -β-D-galactopyranoside[13] (**10**) were prepared by selective benzoylation of methyl 3,4-*O*-isopropylidene-α- and β-D-galactopyranoside[14,15].

A series of disaccharides were synthesized by condensation of benzyl 3,4-*O*-isopropylidene-β-L-fucopyranoside[11] (**5**), methyl 3,4-*O*-isopropylidene-α-L-fucopyranoside[16] (**6**) and -β-L-fucopyranoside[17] (**7**), methyl 6-*O*-benzyl-3,4-*O*-isopropylidene-α-D-galactopyranoside[18] (**8**), and **9** and **10** with 2,3,4-tri-*O*-acetyl-α-L-fucopyranosyl bromide[11] (**2**) and 2-*O*-benzyl-3,4-di-*O*-*p*-nitrobenzoyl-α-L-fucopyranosyl bromide[19] (**3**), respectively, in nitromethane–benzene solution in the presence of mercuric cyanide under essentially identical conditions. The reaction was quite rapid, several hours at room temperature being sufficient, and the yields were excellent. In the previous synthesis[11] of the α-linked disaccharide **16**, rather harsh conditions of temperature and prolonged reaction times were employed. In the present work, it was found that a somewhat better yield resulted after reaction for a shorter time at room temperature, but the configuration of the product was unaffected. Similarly, prolonged reaction at a higher temperature of **4** and **2** afforded the β-linked disaccharide **11** stereospecifically, but in rather reduced yield. The intermediate and final products were characterized, and the optical rotations and p.m.r. spectra compared. In addition, the gas–liquid chromatograms of some of the products were examined. Comparison of the optical rotations, and spectral and chromatographic properties of the pure, crystalline intermediate and final products with those of the crude materials (separated from other impurities by chromatography or solvent extractions without crystallization) gave an indication of the steric course of the condensation reaction. It was found that bromide **3** led to α-linked disaccharides irrespectively of the structure of the nucleophilic intermediate. This result is in agreement with previous findings, in which use of this bromide had always afforded α-linked disaccharides stereospecifically[19,20].

Bromide **2** generally gave β-linked disaccharides with high stereoselectivity. Thus, **4** was converted into benzyl 2-*O*-β-L-fucopyranosyl-α-L-fucopyranoside (**11**) and 2-*O*-β-L-fucopyranosyl-L-fucose (**12**), whereas **8** and **9** afforded methyl 2-*O*-β-L-fucopyranosyl-α-D-galactopyranoside (**30**) exclusively. These results are in contrast to the reaction of **2** with the β-L-fucopyranoside **5**, in which the α-linked disaccharide **17** was obtained exclusively[11]. A considerable proportion (~40%) of α-linked disaccharide was also formed in the reaction of **2** with the methyl β-D-galactopyranoside derivative **10**.

Complex equilibria are considered to be present in the reaction of peracetylglycopyranosyl halides with nucleophilic reagents, and the predominating course of reaction may depend on the polarity of the medium, the presence of bromide ions, and the possibility of participation of the 2-*O*-acetyl substituent[1,21]. The reactive entity may well differ, for example, in acetonitrile and in the less polar 1:1 benzene–nitromethane mixture. Furthermore, the addition of mercuric bromide in molar proportions[2,4,5] would facilitate the formation of the more reactive β-halide which could react *via* a β-ion-pair or a structure that is shielded at the "β-side" of C-1 to form α disaccharides. On the other hand, conditions favoring participation of the 2-*O*-acetyl group would facilitate the formation of β-disaccharide.

The possible influence of substituents on vicinal carbon atoms in the nucleophilic intermediates, especially at the anomeric center, in the course of reaction of OH-2 with peracetylglycopyranosyl halides was indicated by the rather large number of 2-*O*-α-linked disaccharides resulting from this reaction. No systematic studies have been performed on the effect of the orientation of this C-1 substituent. The different configurations resulting from the reaction of the benzyl α-and β-L-fucopyranosides described in this paper and the α-orientation of the disaccharides obtained previously from benzyl β-D-galactopyranoside are rather striking. It is not possible, at present, to distinguish between steric and polar effects of the benzyl group, which lead to a fine differentiation between the α and β configurations of the products.

EXPERIMENTAL

General methods. — See ref. 22. P.m.r. spectra were recorded either with a Varian A-60 n.m.r. (60 MHz) or a Bruker HFX-10 n.m.r. (90 MHz) spectrometer. The solvent employed, unless otherwise specified, was chloroform-*d*. The following solvent systems were used for chromatography (all v/v): (*A*) 4:1 benzene–methanol; (*B*) 4:1 benzene–ether; (*C*) 14:14:1 benzene–ether–methanol; (*D*) 65:15:2 chloroform–methanol–water; (*E*) 7:1:2 1-propanol–ethyl acetate–water; (*F*) 3:1:1 1-butanol–pyridine–water; (*G*) 4:1:5 1-butanol–acetic acid–water; and (*H*) 6:4:1 chloroform–methanol–water.

Glycosylation reactions. — A solution of the nucleophilic intermediate was dissolved in 1:1 (v/v) nitromethane–benzene (~60 ml/g) and ~25% of the solvent was removed by evaporation. The solution was cooled to room temperature (calcium chloride seal), and mercuric cyanide (1.5 mol) was added with stirring, followed by the appropriate bromide (1.5 mol) in 3–4 portions over 3–4 h, each addition being made after complete conversion of the bromide was shown by t.l.c. After the final addition of bromide, stirring was continued for an additional 4 h, and the mixture was processed by dilution with benzene, washing the organic layer with saturated sodium hydrogencarbonate solution, drying, and evaporation *in vacuo*. The crude product was directly deacylated.

Deacylations. — A solution of the aforementioned product, either in methanol or in 1:2 (v/v) chloroform–methanol (chloroform being added to facilitate solution in the case of products resulting from **3**), containing ~ 20% of the calculated quantity of sodium methoxide, was kept at room temperature until t.l.c. revealed complete deacylation. The solvent was evaporated *in vacuo*.

Deacetalation. — A solution of the acetal in 1:1 (v/v) 1,4-dioxane–1% aqueous sulfuric acid (10 ml reagent/g of compound) was kept for 18–40 h at room temperature, completion of the reaction being monitored by t.l.c. There was no evidence for hydrolysis of glycosidic linkages. The solution was then neutralized by the addition of excess barium carbonate, the filtrate evaporated, and the residue processed further as required.

Catalytic hydrogenolysis. — Debenzylation was achieved by treatment of a solution of the compound in 90% ethanol, in the presence of 10% palladium–charcoal, with hydrogen at 3 atm for 18–40 h at room temperature. (It was found that benzyl α-L-fucopyranosides were more resistant to hydrogenolysis than were the corresponding β-L-glycosides, so that longer reaction times were necessary to ensure their complete reduction). After removal of the catalyst by filtration, the solution was evaporated *in vacuo*, and the residue either purified by chromatography or directly crystallized.

Benzyl α-L-fucopyranoside (**1**). — A mixture of L-fucose (10 g) and Dowex 50 (H^+, 5 g) in benzyl alcohol (75 ml) was stirred for 4 h at 80°. After filtration and evaporation of the solution, a syrup was obtained that was purified by chromatography. Solvent *A* eluted fractions that crystallized from ethanol (5.0 g, 32%), m.p. 161–163°, $[\alpha]_D^{25}$ −152° (*c* 1.19, water); n.m.r. (90 MHz, Me_2SO): δ 1.09, 1.17, (3 H, C-Me), 4.38, 4.52, 4.60, and 4.75 (2 H, Bzl), 4.77 (S, 1 H, anomeric H), and 7.25–7.42 (5 H, Ph).

Anal. Calc. for $C_{13}H_{18}O_5$: C, 61.40; H, 7.14. Found: C, 61.74; H, 7.42.

Benzyl 3,4-O-isopropylidene-α-L-fucopyranoside (**4**). — A solution of **1** (2.54 g) in dry *N,N*-dimethylformamide (50 ml) containing 2,2-dimethoxypropane (5 ml) and *p*-toluenesulfonic acid (50 mg) was stirred for 2 h at room temperature. T.l.c. (*B*) showed a single product with complete disappearance of **1**. Neutralization with IR 45 (OH^-) anion-exchange resin, filtration, and evaporation of the solution gave an oil (2.97 g, 98%), $[\alpha]_D^{25}$ −125.8° (*c* 3.67, chloroform); the n.m.r. spectrum showed the expected absorptions: δ 4.84 (*J* 3 Hz, 1 H, anomeric).

Anal. Calc. for $C_{16}H_{22}O_5$: C, 65.30; H, 7.48. Found: C, 65.12; H, 7.29.

Benzyl 2-O-β-L-fucopyranosyl-α-L-fucopyranoside (**11**). — Reaction of **4** (1.2 g) with 2,3,4-tri-*O*-acetyl-α-L-fucopyranosyl bromide[11] (**2**) in 1:1 (v/v) nitromethane–benzene in the presence of mercuric cyanide, followed by the usual processing and catalytic deacetylation, gave an oil (1.6 g, 89%), $[\alpha]_D^{25}$ −96.0° (*c* 2.33, chloroform); n.m.r. (90 MHz, Me_2SO): δ 1.16–1.50 (12 H) and 4.95 (d, 1 H, *J* 3 Hz, anomeric), no peak in the δ 5–5.5 region expected from an α-linked disaccharide.

Deacetalation required 24 h at room temperature and, after neutralization with barium carbonate, a white crystalline solid was obtained (1.32 g, 81%); n.m.r. data (90 MHz, Me_2SO): δ 4.53 (d, 1 H, *J* 7 Hz, β-glycoside), 4.95 (d, 1 H, *J* 3 Hz, α-glycoside); m.p. 181–183° (from ethanol) $[\alpha]_D^{25}$ —140° (*c* 0.69, methanol).

Anal. Calc. for $C_{19}H_{28}O_9$: C, 56.99; H, 7.05. Found: C, 56.80; H, 7.12.

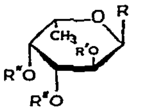
2-O-β-L-Fucopyranose-L-fucose (**12**). — Hydrogenolysis of **11** (0.50 g) for 2 days gave a single product that slowly crystallized from ethanol (0.35 g, 89%), m.p. 152–154°, $[\alpha]_D^{25}$ —58.6 → —50.2° (after 20 h, *c* 0.90, water).

Anal. Calc. for $C_{12}H_{22}O_9$: C, 46.45; H, 7.15. Found: C, 46.36; H, 7.05.

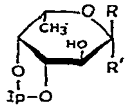
Benzyl 2-O-(2-O-benzyl-a-L-fucopyranosyl)-3,4-O-isopropylidene-a-L-fucopyranoside (**23**). — Reaction of **4** (0.88 g) and 2-*O*-benzyl-3,4-di-*O*-(*p*-nitrobenzoyl)-α-L-fucopyranosyl bromide[19] (**3**), followed by catalytic deacylation and purification by silica gel chromatography with solvent *C* as eluent, gave **23** as a crystalline solid (1.20 g, 75%), $[\alpha]_D^{25}$ —189° (*c* 0.81, chloroform). A portion of this material was recrystallized from ethanol, m.p. 143–145°, $[\alpha]_D^{25}$ —218° (*c* 1.14, chloroform).

Anal. Calc. for $C_{29}H_{38}O_9$: C, 65.64; H, 7.22. Found: C, 65.82; H, 7.29.

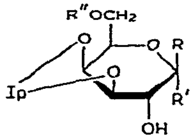
Benzyl 2-O-(2-O-benzyl-α-L-fucopyranosyl)-α-L-fucopyranoside (**16**). — A portion of **23** that had not been chromatographed and recrystallized was deacetalated. The solution obtained after neutralization with barium carbonate was concentrated to



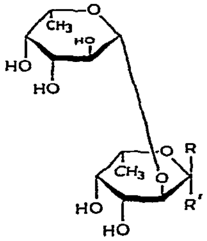
1 R = OBzl, R′ = R″ = H
2 R = Br, R′ = R″ = Ac
3 R = Br, R′ = Bzl, R″ = $OCC_6H_4NO_2$ (p)



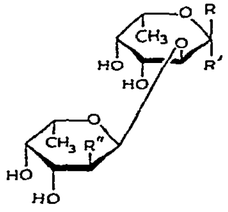
4 R = OBzl, R′ = H
5 R = H, R′ = OBzl
6 R = OMe, R′ = H
7 R = H, R′ = OMe



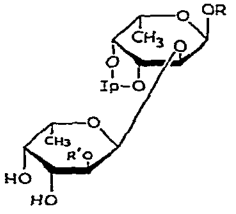
8 R = H, R′ = OMe, R″ = B
9 R = H, R′ = OMe, R″ = B
10 R = OMe, R′ = H, R″ =



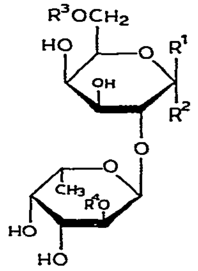
11 R = OBzl, R′ = H.
12 R, R′ = H, OH
13 R = H, R′ = OMe
14 R = OMe, R′ = H

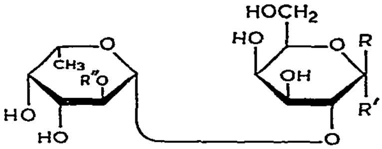


15 R, R′ = H, OH; R″ = OH
16 R = R″ = OBzl, R′ = H
17 R = H, R′ = OBzl, R″ = OH
18 R = OMe, R′ = H, R″ = OBzl
19 R = OMe, R′ = H, R″ = OH
20 R = H, R′ = OMe, R″ = OBzl
21 R, R′ = H, OH; R″ = OH
22 R = H, R′ = OMe, R″ = OH



23 R = R′ = Bzl
24 R = Me, R′ = Bzl





25 $R^1 = H, R^2 = OMe, R^3 = R^4 = Bzl$
26 $R^1 = R^3 = R^4 = H, R^2 = OMe$
27 $R^1 = R^3 = H, R^2 = OMe, R^4 = OBzl$
28 $R^1 = OMe, R^2 = R^3 = R^4 = H$

29 $R = H, R' = OMe, R'' = Bzl$
30 $R = R'' = H, R' = OMe$
31 $R = OMe, R' = R'' = H$

remove most of the 1,4-dioxane and extracted with chloroform to remove methyl *p*-nitrobenzoate resulting from the catalytic deacylation. The solution was evaporated to a syrup that was dissolved in solvent *D* and chromatographed to give a crystalline solid (1.0 g, 60% from **4**), $[\alpha]_D^{25}$ −178° (*c* 0.80, methanol); after recrystallization from ethanol, m.p. 186–188°, $[\alpha]_D^{25}$ −186° (*c* 0.77, methanol).

Anal. Calc. for $C_{26}H_{34}O_9$: C, 63.66; H, 6.99. Found: C, 63.83; H, 6.99.

2-O-α-L-Fucopyranosyl-L-fucose (**21**). — Hydrogenolysis of **16** (150 mg) for 2 days, followed by filtration and evaporation of the solvent, afforded 115 mg (97%) of a syrup that slowly crystallized from ethanol, m.p. 193–195°, $[\alpha]_D^{25}$ −168.5° (*c* 0.78, water); lit.[11] m.p. 189–192°, $[\alpha]_D$ −163°). The product was identical with an authentic specimen of 2-*O*-α-L-fucopyranosyl-L-fucose on t.l.c. (*D* and *E*) and on paper chromatography (*F* and *G*).

Methyl 2-O-β-L-fucopyranosyl-α-L-fucopyranoside (**13**). — Reaction of methyl 3,4-*O*-isopropylidene-α-L-fucopyranoside[16] (**6**), 0.60 g) with **2**, followed by catalytic deacetylation, afforded a syrup (0.80 g, 80%), $[\alpha]_D^{25}$ −87.6° (*c* 2.04, chloroform). Removal of the isopropylidene group of a part of this product (0.70 g) gave **13** as a crystalline solid (0.40 g, 51%); g.l.c. of the per(trimethylsilyl) ether of this material showed two peaks, $T_{sucrose}$ 0.52 (96%) and 0.56 (4%). After recrystallization from ethanol the m.p. was 236–238°, $[\alpha]_D^{25}$ −88.9° (*c* 0.90, methanol) and a single peak was obtained on g.l.c. of the per(trimethylsilyl) ether, $T_{sucrose}$ 0.52; n.m.r. (90 MHz, Me_2SO): δ 1.05 and 1.15 (6 H, C-Me), 3.21 (3 H, OCH_3), 4.20 (d, 1 H, *J* 7Hz, β-glycoside), and 4.93 (s, 1 H, α-glycoside).

Anal. Calc. for $C_{13}H_{24}O_9$: C, 48.18; H, 7.46. Found: C, 48.08; H, 7.56.

Methyl 2′-O-(2-O-benzyl-α-L-fucopyranosyl)-3,4-O-isopropylidene-α-L-fucopyranoside (**24**). — Reaction of **6** (1.10 g) with **3**, followed by catalytic deacylation and separation from methyl *p*-nitrobenzoate by silica gel chromatography, gave a crystalline solid (1.70 g, 74%), m.p. 155–157°, $[\alpha]_D^{25}$ −216° (*c* 0.79, chloroform); n.m.r.: δ 1.22–1.55 (12 H), 3.45 (3 H, OMe), 4.86 (d, 1 H, *J* 3 Hz, α-glycoside), 5.14 (d, 1 H, *J* 3 Hz, α-glycoside), and 7.47 (5 H, Ph).

Anal. Calc. for $C_{23}H_{34}O_9$: C, 61.01; H, 7.60. Found: C, 60.78; H, 7.54.

Methyl 2-O-(2-O-benzyl-α-L-fucopyranosyl-α-L-fucopyranoside (**18**). — The isopropylidene group of a portion of **24** (130 mg) was split off, and the product crystallized from ethanol (105 mg, 89%), m.p. 192–194°, $[\alpha]_{D}^{25}$ —201.2° (*c* 1.03, methanol); n.m.r. (90 MHz, Me_2SO): δ 3.20 (3 H, OMe), 4.77 (s, 1 H, α-glycoside), 5.01 (d, 1 H, *J* 2.5 Hz, α-glycoside), and 7.33 (5 H, Ph).

Anal. Calc. for $C_{20}H_{30}O_9$: C, 57.97; H, 7.30. Found: C, 58.25; H, 7.48.

A sample of crude **24**, isolated after the glycosylation and catalytic deacylation reactions, was partially hydrolyzed without previous chromatographic purification. The product was purified by chromatography in solvent *D* to give 0.80 g of a crystalline solid having an n.m.r. spectrum identical with that of authentic **18**. On recrystallization from ethanol, the product (0.60 g) had m.p. 192–194°, $[\alpha]_{D}^{25}$ —200° (*c* 0.77, methanol), and the mother liquors, on evaporation, gave a crystalline solid, $[\alpha]_{D}^{25}$ —196° (*c* 0.78, methanol).

Methyl 2-O-a-L-fucopyranosyl-a-L-fucopyranoside (**19**). — Hydrogenolysis of **18** (130 mg) overnight afforded 95 mg (93%) of a solid that was recrystallized from ethanol, m.p. 190–192°, $[\alpha]_{D}^{25}$ —227° (*c* 0.57, methanol); a single peak, $T_{sucrose}$ 0.56, was obtained on g.l.c. of the per(trimethylsilyl) ether.

Anal. Calc. for $C_{13}H_{24}O_9$: C, 48.14; H, 7.46. Found: C, 48.04; H, 7.58.

Methyl 2-O-(2-O-benzyl-a-L-fucopyranosyl)-β-L-fucopyranoside (**20**). — Reaction of methyl 3,4-*O*-isopropylidene-β-L-fucopyranoside[17] (**7**, 0.70 g) with **3**, followed by catalytic deacylation, removal of the isopropylidene group and chromatography gave crystalline **20** (0.60 g, 70%); recrystallization from 98% ethanol gave 0.50 g, m.p. 193–195°, $[\alpha]_{D}^{25}$ —100° (*c* 0.50, methanol); n.m.r. (90 MHz, Me_2SO): δ 5.03 (d, 1 H, *J* 3 Hz), assigned to the α-disaccharide H.

Anal. Calc. for $C_{20}H_{30}O_9$: C, 57.96; H, 7.30. Found: C, 57.80; H. 7.25.

Methyl 2-O-α-L-fucopyranosyl-β-L-fucopyranoside (**22**). — Catalytic hydrogenolysis of **20** gave a product that crystallized from 98% ethanol, m.p. 210–212°, $[\alpha]_{D}^{25}$ —91.4° (*c* 0.70, methanol); g.l.c. of the per(trimethylsilyl) ether gave a single peak, $T_{sucrose}$ 0.62.

Anal. Calc. for $C_{13}H_{24}O_9$: C, 48.14; H, 7.46. Found: C, 48.01; H, 7.25.

Methyl 2-O-β-L-fucopyranosyl-β-L-fucopyranoside (**14**). — Reaction of **7** (1.09 g) with **2**, followed by catalytic deacylation and removal of the isopropylidene group gave 0.92 g (88%), $[\alpha]_{D}^{25}$ + 1.2° (*c* 0.86, methanol); on recrystallization from 98% ethanol (yield 0.82 g), m.p. 188–190°, $[\alpha]_{D}^{25}$ —1.2° (*c* 1.0, methanol); n.m.r. (90 MHz, Me_2SO): δ 1.23 and 1.30 (6H, C-Me), 3.54 (3 H, OMe), 4.40 (d, 1H, *J* 7 Hz), and 4.60 (d, 1H, *J* 7 Hz). G.l.c. of the per(trimethylsilyl) ether of **14**, either before or after recrystallization from 98% ethanol; gave a single peak, $T_{sucrose}$ 0.50. Furthermore, **14** and **22** were clearly separated in t.l.c. in solvent *D*. No indication of the presence of any **22** in crude **14** was observed (R_{22}:R_{14} 0.9).

Anal. Calc. for $C_{13}H_{24}O_9$: C, 48.14; H, 7.46. Found: C, 48.02; H, 7.33.

Methyl 6-O-benzyl-2-O-(2-O-benzyl-α-L-fucopyranosyl)-α-D-galactopyranoside (**25**). — Reaction of methyl 6-*O*-benzyl-3,4-*O*-isopropylidene-α-D-galactopyranoside (**8**, 1.5 g) with **3** followed by catalytic deacylation and chromatography gave a syrup (1.9 g, 73%), $[\alpha]_D^{25}$ —23.0° (*c* 1.80, chloroform); n.m.r.: δ 1.35–1.55 (9 H), 3.50 (3 H, OMe), 4.95 (d, 1 H, *J* 3 Hz), 5.37 (d, 1 H, *J* 3 Hz), and 7.52 (10 H, Ph). Removal of the isopropylidene group of 1.6 g of this product gave a syrup (1.3 g, 90%), a portion of which crystallized from water, m.p. 137–139°, $[\alpha]_D^{25}$ —18.0° (*c* 0.86, methanol).

Anal. Calc. for $C_{27}H_{36}O_{10}$: C, 62.29; H, 6.97. Found: C, 62.15; H, 7.01.

Methyl 2-O-α-L-fucopyranosyl-α-D-galactopyranoside (**26**). — A portion (1.0 g) of the crude syrup just described (before crystallization of **25**) was directly hydrogenolyzed, and small amounts of impurity were removed by chromatography and elution with solvent *H* (yield 0.60 g, 92%), $[\alpha]_D^{25}$ + 1.3° (*c* 1.12, water); n.m.r. (90 MHz, D_2O): δ 1.12 (d, 3 H, *J* 7 Hz, C-Me), 3.42(3 H, OMe), 4.98 (d, 1 H, *J* 3 Hz, α-D-galactopyranosyl H), 5.09 (d, 1 H, *J* 3 Hz, α-L-fucopyranosyl H), no signal between 4.30 and 4.76. On crystallization from ethanol, m.p. 202–204°, $[\alpha]_D^{25}$ + 0.9° (*c* 1.15, water); n.m.r. spectrum unchanged after crystallization.

Anal. Calc. for $C_{13}H_{24}O_{10}$: C, 45.88; H, 7.11. Found: C, 45.60; H, 7.25.

Methyl 2-O-β-L-fucopyranosyl-α-D-galactopyranoside (**30**). — (*a*) *From* **8**. After reaction of **8** (0.60 g) with **2**, followed by catalytic deacetylation of the product and purification by chromatography, a syrup was obtained (0.70 g 80%), $[\alpha]_D^{25}$ + 35.8° (*c* 0.74, chloroform); n.m.r.: δ 1.30–1.55 (9 H), 3.54 (3 H, OMe), 4.95 (d, 1 H, *J* 3 Hz, α-galactopyranosyl H), and 7.50 (5 H, Ph).

After removal of the isopropylidene group, followed directly by hydrogenolysis, a solid was obtained (0.50 g, 80% from **8**), $[\alpha]_D^{25}$ + 109° (*c* 0.89, water); n.m.r. (90 MHz, D_2O): δ 1.27 (3 H, *J* 7 Hz, C-Me), 3.42 (3 H, OMe), 4.47 (d, 1 H, *J* 8 Hz, β-L-fucopyranosyl H), 5.00 (d, 1 H, *J* 3 Hz, α-D-galactopyranosyl H), and no peak > 5.00. On recrystallization of this solid from ethanol, the n.m.r. spectrum remained unchanged, m.p. 226–228°, $[\alpha]_D^{25}$ + 114.7° (*c* 0.75, water).

Anal. Calc. for $C_{13}H_{24}O_{10}$: C, 45.88; H, 7.11. Found: C, 46.02; H, 7.16.

(b). *From methyl 6-O-benzoyl-3,4-O-isopropylidene-α-D-galactopyranoside*[13] (**9**). — Reaction of **9** (0.60 g) with **2**, followed by catalytic deacylation and catalytic removal of the isopropylidene group, gave a syrup (0.50 g, 81%), $[\alpha]_D^{25}$ + 103° (*c* 1.0, water); the p.m.r. spectrum did not show a peak at δ 5.09 corresponding to α-L-fucopyranosyl H, but a doublet at 4.47 (*J* 8 Hz) was present; on crystallization from ethanol (yield 0.45 g); m.p. 225–227°, $[\alpha]_D^{25}$ + 112.5° (*c* 0.70, water).

Methyl 2-O-(2-O-benzyl-α-L-fucopyranosyl)-α-D-galactopyranoside (**27**). — Reaction of **9**, (0.50 g) with **3**, followed by catalytic deacylation, removal of the isopropylidene group, and column chromatography, gave a solid product (0.50 g, 79% overall), $[\alpha]_D^{25}$ —2.1° (*c* 1.90, water); a portion was recrystallized from ethanol, m.p. 193–195°, $[\alpha]_D^{25}$ —1.0° (*c* 0.4, water).

Anal. Calc. for $C_{20}H_{30}O_{10}$: C, 55.80; H, 7.03. Found: C, 55.61; H, 7.15.

Hydrogenolysis of a portion of **27** afforded a product that was identical with **26** (m.p., t.l.c., optical rotation, and p.m.r. spectrum).

Methyl 2-O-α- and -β-L-fucopyranosyl-β-D-galactopyranoside. — Reaction of methyl 6-*O*-benzoyl-3,4-*O*-isopropylidene-β-D-galactopyranoside[13] (**10**) with **2**, followed by catalytic deacylation and removal of the isopropylidene group, led to a syrup

(1.0 g, 90%), $[\alpha]_D^{25}$ —44.5° (*c* 0.67, water); n.m.r. (90 MHz, Me_2SO): δ 5.04 (0.4 H, α-disaccharide); on crystallization from 95% ethanol, a crystalline solid was obtained (0.367 g), m.p. 218–220°, $[\alpha]_D^{25}$ + 11.5° (*c* 1.04, water); n.m.r. (90 MHz Me_2SO): no peak > δ 4.60; g.l.c. of the per(trimethylsilyl)ether; $T_{sucrose}$ 1.22.

Anal. Calc. for $C_{13}H_{24}O_{10}$: C, 45.88; H, 7.11. Found: C, 45.98; H. 7.29.

To this compound was attributed the structure methyl 2-*O*-β-L-fucopyranosyl-β-D-galactopyranoside (**31**). On evaporation the mother liquor, gave an amorphous product (0.616 g, 55%), $[\alpha]_D^{25}$ —61.6° (*c* 1.68, water); g.l.c. of the per(trimethylsilyl) ether: $T_{sucrose}$ 1.30 and 1.22 (2:1). Thus, the syrupy reaction product contained ~40% of α-linked disaccharide.

Methyl 2-O-(2-O-*benzyl-α-*L-*fucopyranosyl*)-*β-*D-*galactopyranoside* (**27**). — Reaction of **10** (0.5 g) with **3**, followed by deblocking, led to **27** (0.50 g, 79%), $[\alpha]^{25}$ —109° (*c* 1.06, water). A portion (0.40 g) was crystallized from ethanol (yield 0.32 β); m.p. 192–194°, $[\alpha]_D^{25}$ —118° (*c* 0.69, water); n.m.r. (90 MHz, Me_2SO): the expected doublet at δ 5.03 (*J* 3Hz) characteristic of α-L-fucopyranosyl H.

Anal. Calc. for $C_{20}H_{30}O_{10}$: C, 55.80; H, 7.03. Found: C, 56.02; H, 7.08.

Methyl 2-O-*α-*L-*fucopyranosyl-β-*D-*galactopyranoside* (**28**). — Catalytic hydrogenolysis of **27** afforded an amorphous solid, $[\alpha]_D^{25}$ —70.1° (*c* 0.88, water); g.l.c. of per(trimethylsilyl) ether: $T_{sucrose}$ 1.30.

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