Synthesis of Some 3-*O*, 4-*O*, and 3,4-Di-*O*-glycosyl-substituted Methyl α-D-Galactopyranosides

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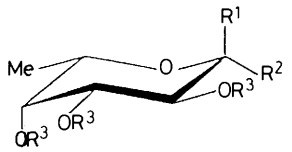
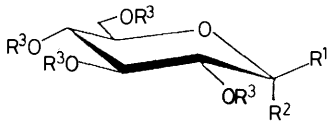
Seven disaccharide and eight trisaccharide methyl glycosides required for n.m.r. and conformational studies have been synthesized. They are all derivatives of methyl α-D-galactopyranoside which has been 3-*O*-, 4-*O*-, or 3,4-di-*O*-glycosylated with either L-fuco- or D-gluco-pyranosyl groups. All anomeric forms were synthesized, either *via* thioglycosides and methyl triflate promotion or *via* glycosyl bromides and silver triflate promotion.

Branched oligo- and poly-saccharides are an important group of naturally occurring carbohydrates. When the branching originates from two vicinally substituted hydroxy groups steric crowding could occur. This may have profound effects on conformation and on the ^1H and ^{13}C n.m.r. chemical shifts of signals for those atoms involved in the branching. In order to understand the underlying principles of these effects a number of 'branched' trisaccharides were chosen as models for the branching region in oligo- and poly-saccharides. The present work is part of a continuous project in which a number of disaccharides have previously been synthesized, their conformations calculated, and n.m.r. data recorded.[1-4] We now report the synthesis of seven disaccharides and eight 'branched' trisaccharides. The disaccharides include both anomeric forms of L-fuco- or D-gluco-pyranose linked to either the 3- or 4-position of methyl α-D-galactopyranoside; the trisaccharides are composed of methyl α-D-galactopyranoside 3,4-di-*O*-substituted with different anomeric forms of either L-fuco- or D-gluco-pyranosyl groups.

Results and Discussion

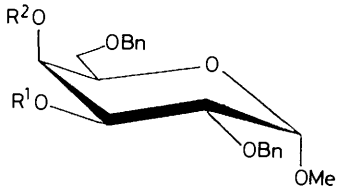
The synthesis of a series of similar compounds is facilitated by the use of as few starting materials as possible, and therefore





(**1**) R^1 = –, R^2 = H, R^3 = Bn
(**2a**) R^1 = H, R^2 = –, R^3 = Ac
(**2b**) R^1 = H, R^2 = –, R^3 = Bz
(**3**) R^1 = H, R^2 = SEt, R^3 = Bn
(**4a**) R^1 = H, R^2 = SEt, R^3 = Bz
(**4b**) R^1 = H, R^2 = SEt, R^3 = Ac
(**5**) R^1 = H, R^2 = –, R^3 = Bn
(**6a**) R^1 = –, R^2 = H, R^3 = Bz
(**6b**) R^1 = –, R^2 = H, R^3 = Bn
(**7**) R^1 = SEt, R^2 = H, R^3 = Bn
(**8**) R^1 = H, R^2 = Br, R^3 = Bz

methyl 2,6-di-*O*-benzyl-α-D-galactopyranoside[5] (**9**) and its derivatives (**10**) and (**11**)[6] were chosen as key compounds in all glycosidation reactions. Thioglycosides are versatile as intermediates in the synthesis of both 1,2-*trans*- and 1,2-*cis*-glycosides,[7] and were the glycosyl donors of choice in most of the glycosidation reactions. Thus for the formation of α-glycosides, fully benzylated glycosyl donors were employed: fully acylated glycosyl donors were used when neighbouring group participation to yield β-glycosides was desired. The ready availability of per-*O*-benzoylated glucosyl bromide for



(**9**) R^1 = H, R^2 = H
(**10**) R^1 = H, R^2 = Ac
(**11**) R^1 = Bz, R^2 = H
(**12a**) R^1 = (**1**), R^2 = Ac
(**12b**) R^1 = (**1**), R^2 = H
(**13a**) R^1 = (**2a**), R^2 = Ac
(**13b**) R^1 = (**2b**), R^2 = H
(**14**) R^1 = Bz, R^2 = (**1**)
(**15**) R^1 = Bz, R^2 = (**2a**)
(**16a**) R^1 = (**5**), R^2 = Ac
(**16b**) R^1 = (**5**), R^2 = H
(**17**) R^1 = (**6a**), R^2 = H
(**18**) R^1 = H, R^2 = (**5**)
(**19**) R^1 = H, R^2 = (**6b**)
(**20**) R^1 = (**1**), R^2 = (**1**)
(**21**) R^1 = (**1**), R^2 = (**2b**)
(**22**) R^1 = (**2b**), R^2 = (**1**)
(**23**) R^1 = (**2b**), R^2 = (**2b**)
(**24**) R^1 = (**5**), R^2 = (**5**)
(**25**) R^1 = (**5**), R^2 = (**6**)
(**26**) R^1 = (**6**), R^2 = (**5**)
(**27**) R^1 = (**6**), R^2 = (**6**)

(**28**) β-L-Fuc*p*-(1 ⟶ 3)-α-D-Gal*p*
(**29**) α-L-Fuc*p*-(1 ⟶ 4)-α-D-Gal*p*
(**30**) β-L-Fuc*p*-(1 ⟶ 4)-α-D-Gal*p*
(**31**) α-D-Glc*p*-(1 ⟶ 3)-α-D-Gal*p*
(**32**) β-D-Glc*p*-(1 ⟶ 3)-α-D-Gal*p*
(**33**) α-D-Glc*p*-(1 ⟶ 4)-α-D-Gal*p*
(**34**) β-D-Glc*p*-(1 ⟶ 4)-α-D-Gal*p*

(**35**)
α-L-Fuc*p*-(1 ⟶ 4)
|
α-D-Gal*p*
|
α-L-Fuc*p*-(1 ⟶ 3)
|
β-L-Fuc*p*-(1 ⟶ 4)

(**36**)
α-D-Gal*p*
|
α-L-Fuc*p*-(1 ⟶ 3)
|
α-L-Fuc*p*-(1 ⟶ 4)

(**37**)
α-D-Gal*p*
|
β-L-Fuc*p*-(1 ⟶ 3)
|
β-L-Fuc*p*-(1 ⟶ 4)

(**38**)
α-D-Gal*p*
|
β-L-Fuc*p*-(1 ⟶ 3)

(**39**)
α-D-Glc*p*-(1 ⟶ 4)
|
α-D-Gal*p*
|
α-D-Glc*p*-(1 ⟶ 3)
|
β-D-Glc*p*-(1 ⟶ 4)

(**40**)
α-D-Gal*p*
|
α-D-Glc*p*-(1 ⟶ 3)
|
α-D-Glc*p*-(1 ⟶ 4)

(**41**)
α-D-Gal*p*
|
β-D-Glc*p*-(1 ⟶ 3)
|
β-D-Glc*p*-(1 ⟶ 4)

(**42**)
α-D-Gal*p*
|
β-D-Glc*p*-(1 ⟶ 3)

Scheme 1. Compounds (**28**)—(**42**) are the methyl glycosides of the above di- and tri-saccharides

the synthesis of β-D-glucosides made it the choice as glycosyl donor in some of the glycosidations.

Scheme 2 shows routes to compounds (**29**), (**30**), (**33**), (**34**), and (**39**), starting from methyl 3-*O*-benzoyl-2,6-di-*O*-benzyl-α-D-galactopyranoside (**11**). No selectivity for the 4-position could be obtained under any of the glycosidation conditions tested and the 4-linked disaccharides (**29**), (**30**), (**33**), and (**34**) were therefore synthesized *via* the galactopyranoside (**11**) which is also protected in the 3-position. Coupling reactions gave the disaccharides in 30—80% yield (see Table 1a). An indication of the anomeric configuration of the product was obtained from the chemical shifts of the anomeric carbons in the protected oligosaccharides and later verified from the coupling constants, $J_{1,2}$, of the deprotected oligosaccharides (Table 1b). Notable in the synthesis of compound (**34**) is that coupling of compound (**11**) with the per-*O*-benzoylated glucosyl bromide (**8**) under β-coupling conditions only gave a low yield (~10%) of the desired product. However, in the synthesis of compound (**18**) using α-coupling conditions the β-glycoside (**19**) was obtained in 32% yield as a 'by-product'. The trisaccharide (**39**) was obtained from compound (**18**) by glycosidation with compound (**7**). Attempted glycosidation of compound (**9**) to trisaccharide directly gave a complex reaction mixture with several products; the reaction was not further investigated.

Scheme 3 shows routes to compounds (**28**), (**31**), (**36**), and (**40**) starting from methyl 4-*O*-acetyl-2,6-*O*-benzyl-α-D-galactopyranoside (**10**). For example, glycosidation of compound (**10**) with the ethylthio glycopyranoside (**7**) under methyl trifluoromethanesulfonate promotion yielded the protected compound (**16a**) in 48% yield. De-*O*-acetylation followed by glycosidation with the bromosugar (**8**) promoted by silver trifluoromethanesulfonate yielded the trisaccharide (**25**) in 77% yield, for which signals at δ 99.2 and 102.6 for the anomeric carbons in the glycosyl groups indicated the correct stereochemistry. Deprotection of compound (**25**) yielded the trisaccharide (**40**), for which the ^{1}H n.m.r. spectrum showed two signals in the anomeric region with small coupling constants (3.9 Hz) and one signal with a large coupling constant (8.0 Hz).

The glycosidations starting from methyl 2,6-di-*O*-benzyl-α-D-galactopyranoside (**9**) are shown in Scheme 4. Selective β-glucosidation of compound (**9**) to give the disaccharide (**17**) was accomplished in 55% yield. The selectivity of the reaction for the 3-position was demonstrated by n.m.r. spectroscopy of the deprotected disaccharide. The chemical shift of the C-3 signal was significantly shifted indicating that the linkage was at the 3-position. Condensation of compound (**17**) with compound (**7**) gave the trisaccharide (**26**) in 76% yield. Deprotection yielded compound (**41**) for which the ^{1}H n.m.r. spectrum showed signals for anomeric protons with two small and one large coupling constants. When an excess of compound (**8**) was used in the glycosidation of compound (**9**), the diglucosyl derivative (**27**) was formed in 65% yield. The ^{1}H n.m.r. spectrum of the deprotected compound (**42**) showed signals for three anomeric protons with expected chemical shifts and coupling constants. The analogous disubstitution with α- and β-fucopyranosyl groups could also be performed on condensation of compound (**9**) with the fucosyl derivatives (**3**) or (**4a**), respectively. N.m.r. spectroscopy of the protected (**20**) and deprotected (**35**) trisaccharide [from (**9**) and (**3**)] demonstrated the configurations of the α-fucosyl groups, and n.m.r. spectra of the protected (**23**) and deprotected (**38**) trisaccharide [from (**9**) and (**4a**)] that of the β-fucosyl groups. In the synthesis of compound (**37**) we noticed that for β-coupling conditons of the 3-position of the de-*O*-benzoylated disaccharide (**14**) only the α-glycoside was obtained. The trisaccharide (**37**) was therefore synthesized by selective β-coupling to the 3-position followed by α-coupling to the 4-position.

Experimental

General Methods.—The coupling reactions were not optimized. Melting points are corrected. Evaporations were performed under reduced pressure at bath temperatures <40 °C. Optical rotations were recorded using a Perkin-Elmer 241 polarimeter. ^{1}H (400 MHz) and ^{13}C n.m.r. spectra (100 and 25 MHz) were recorded for D_2O or $CDCl_3$ solutions with JEOL GX-400 or JEOL FX-100 instruments. Chemical shifts are given relative to sodium 3-[2,2,3,3-$^2H_4$]-(trimethylsilyl)-propanoate (TSP, δ_H 0.00) and tetramethylsilane (TMS, δ_H 0.00) for ^{1}H n.m.r. spectra of D_2O and $CDCl_3$ solutions, respectively. Dioxane (δ_C 67.40) or TMS (δ_C 0.0) were used as internal references for ^{13}C n.m.r. spectra of D_2O and $CDCl_3$ solutions, respectively. Column chromatography was performed on silica gel (Matre Silica Si 60 Å, 35–70 μ, Amicon).

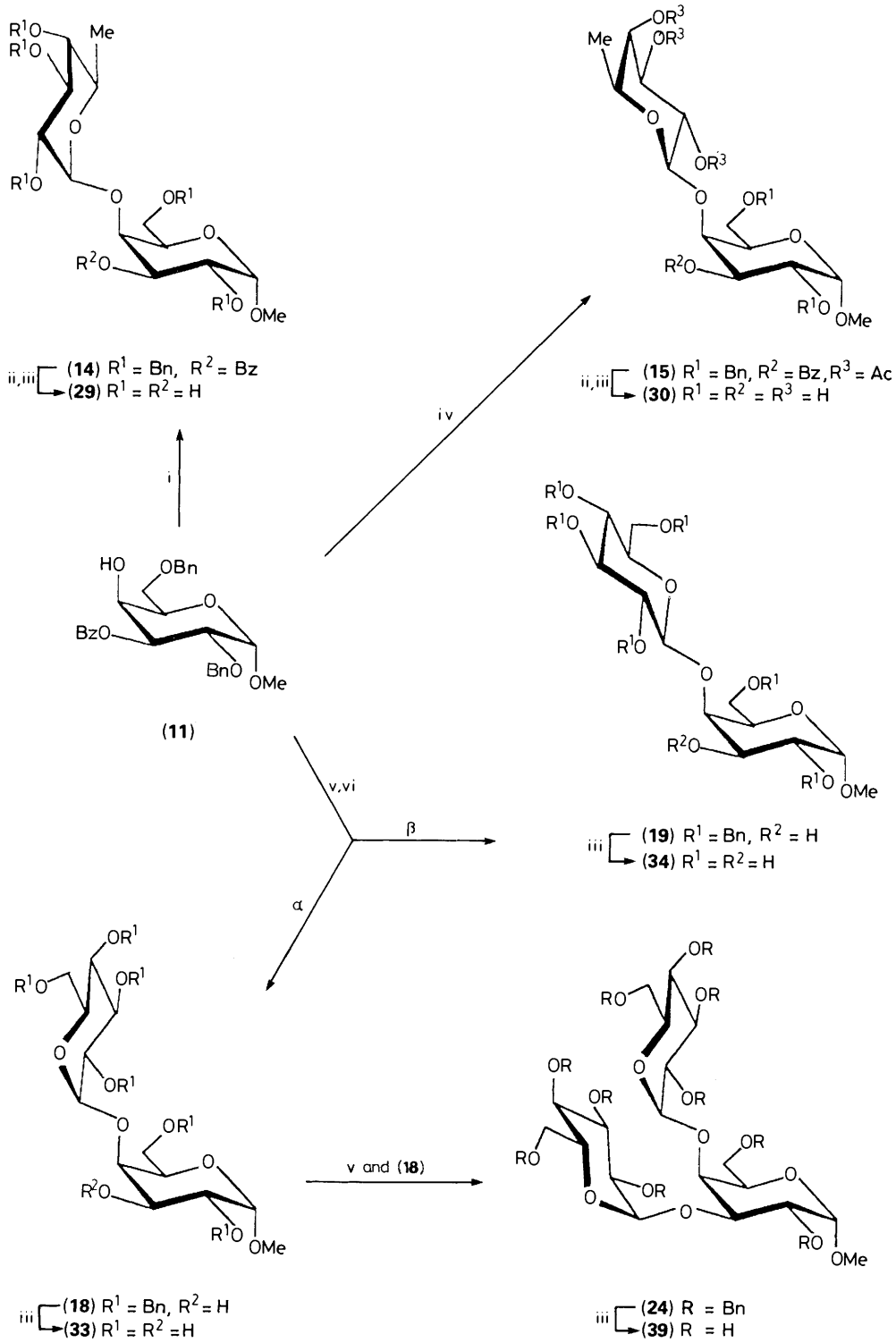
The purity of intermediates was initially analysed by t.l.c., where they showed only one spot; from ^{13}C n.m.r. spectroscopy the intermediates were estimated to be more than 95% pure. The number and chemical shifts of signals in the ^{13}C n.m.r. spectrum were consistent with the postulated structures, and the chemical shift and $^1J_{C,H}$ values from the C-1 signals showed the anomeric configurations.

In the ^{1}H n.m.r. spectra of the deprotected oligosaccharides, signal integrals from contaminating components were less than 5% of those of the anomeric protons. The position of substitution of the glycosyl groups was determined in most cases by the synthetic route. When diols were monoglycosylated, the determination of an n.O.e. between the anomeric proton and the proton on the linkage carbon, or a methylation analysis, established the linkage position. The number and chemical shifts of signals in the ^{1}H and ^{13}C n.m.r. spectra were in agreement with the postulated structures. Anomeric configurations were deduced from the coupling patterns ($^3J_{H,H}$, $^1J_{C,H}$) of signals from anomeric protons and carbons.

Glycosidation Methods.—Method A. Methyl trifluoromethanesulfonate (5 equiv.) was added to a stirred solution at 0 °C of thioglycoside (1.3 equiv.) and aglycon (1.0 equiv.) in diethyl ether containing ground molecular sieves (4 Å, 1—2 g).[7] The mixture was then allowed to warm to 20 °C. When the reaction was complete by t.l.c. analysis (2—20 h), triethylamine (10 equiv.) was added and stirring continued for 30 min. The mixture was then diluted with dichloromethane, filtered through a layer of Celite, and washed successively with aqueous 10% H_2SO_4, aqueous $NaHCO_3$, and water. The organic layer was dried (Na_2SO_4) and evaporated to dryness, and the product was then purified on a silica gel column using the solvents given in Table 1.

Method B. A solution of silver trifluoromethanesulfonate (2.25 equiv.) and 2,4,6-trimethylpyridine (2.25 equiv.) in dichloromethane was added to a stirred solution of per-*O*-benzoylated glucosylbromide (1.5 equiv.), aglycon (1.0 equiv.), and ground molecular sieves (4 Å, 1 g) in dichloromethane at −20 °C under nitrogen.[8,9] When the reaction was complete (by t.l.c.) the mixture was allowed to warm to 20 °C, filtered through a layer of Celite and washed successively with aqueous 10% $Na_2S_2O_3$, water, 2M H_2SO_4, H_2O, and aqueous $NaHCO_3$. The organic layer was dried (Na_2SO_4) and evaporated, and the crude product was then purified on a silica gel column using the solvents given in Table 1.

Deblocking and Purification Procedures.—Method C. The oligosaccharide derivative (100—600 mg) in aqueous acetic acid (90%, 20—40 ml) was hydrogenolysed at ~350 kPa over Pd/C (10%, 200—400 mg) for 6—18 h. The solution was filtered and evaporated to dryness, then the residue was chromatographed on a silica gel column (10 × 2 cm) (ethyl acetate–acetic acid–methanol–water, 12:3:3:2) and then on a Bio-Gel P-2 column



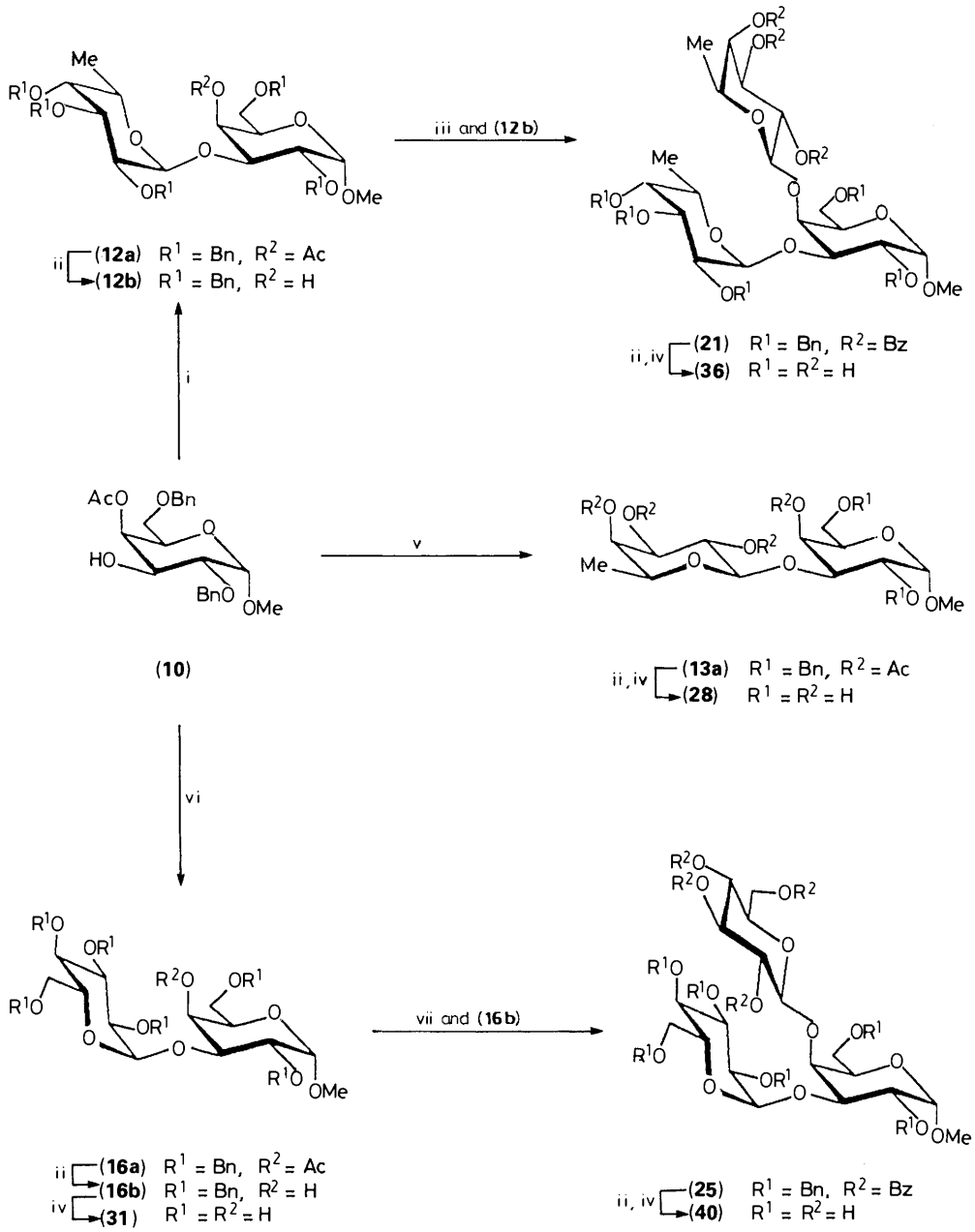
Scheme 2. Syntheses starting from compound (**11**); *Reagents and conditions:* i, glycosyl donor (**3**), $F_3CSO_3CH_3$, Et_2O, room temp.; ii, NaOMe, MeOH–CH_2Cl_2; iii, H_2, Pd; iv, glycosyl donor (**4b**), $F_3CSO_3CH_3$, Et_2O, room temp.; v, glycosyl donor (**7**), $F_3CSO_3CH_3$, Et_2O, room temp.; vi, NaOMe, MeOH–CH_2Cl_2, SiO_2 chromatography

(80 × 2.5 cm) with water as eluant. After freeze-drying, the product was obtained as an amorphous powder.

Method D. The oligosaccharide derivative was de-*O*-acylated with sodium methoxide in 1:1 dichloromethane–methanol (0.025M; 10—30 ml). The solution was neutralized with acetic acid or Dowex 50 (H^+) then evaporated and hydrogenolysed as described in Method C.

The syntheses of substances not fully covered in the Table were performed as follows:

Methyl 4-O-*Acetyl*-2,6-*di*-O-*benzyl*-α-D-*galactopyranoside* (**10**).—A mixture of compound (**9**) (3.55 g), *p*-toluenesulphonic acid monohydrate (100 mg), and trimethyl orthoacetate (2.4 ml) was dissolved in acetonitrile (35 ml) by stirring.[10] The solvent

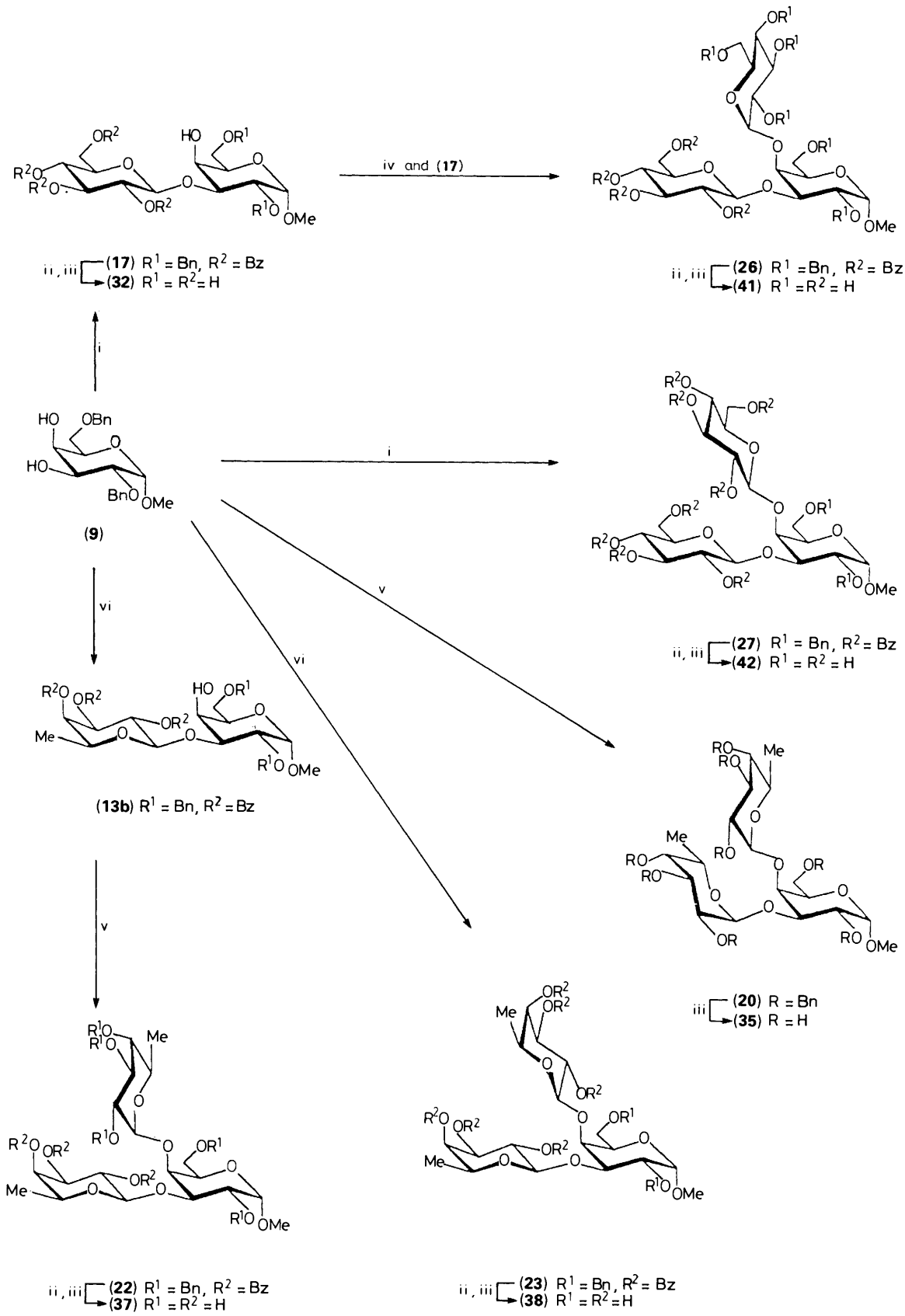


Scheme 3. Syntheses starting from compound (**10**); *Reagents and conditions:* i, glycosyl donor (**3**), $F_3CSO_3CH_3$, Et_2O, room temp.; ii, NaOMe, MeOH–CH_2Cl_2; iii, glycosyl donor (**4a**), $F_3CSO_3CH_3$, Et_2O, room temp; iv, H_2, Pd; v, glycosyl donor (**4b**), $F_3CSO_3CH_3$, Et_2O, room temp.; vi, glycosyl donor (**7**), $F_3CSO_3CH_3$, Et_2O, room temp.; vii, glycosyl donor (**8**), F_3CSO_3Ag, CH_2Cl_2, collidine, −20 °C

was evaporated and the residue was dissolved in acetonitrile (20 ml) and treated with aqueous 90% trifluoroacetic acid (1 ml) for 5 min at 25 °C. The solvent was evaporated, then the product was dissolved in dichloromethane, washed with aqueous sodium bicarbonate, dried (Na_2SO_4), filtered, and concentrated to dryness. Chromatography on a silica gel column (toluene–ethyl acetate, 4:1) gave compound (**10**) (2.65 g, 67%) which was crystallized from toluene–iso-octane, m.p. 83—84 °C; $[\alpha]_{578}^{22}$ (*c* 1.0, CH_2Cl_2); δ_H 4.71 (1-H), 3.69 (2-H), 4.16 (3-H), 5.43 (4-H), 4.06 (5-H), 3.49 (6-H and 6′-H), and 3.36 (OMe); δ_C 98.2 (C-1), 76.8 (C-2), 71.0 (C-4), 67.8, 68.0, 68.8 (C-3, C-5, and C-6), and 55.4 (OMe).

Methyl 2,6-*Di*-O-*benzyl*-3-O-(2,3,4-*tri*-O-*benzyl*-α-L-*fucopyranosyl*)-α-D-*galactopyranoside* (**12b**).—Disaccharide derivative (**12a**) (625 mg) was de-*O*-acetylated by treatment with sodium methoxide in methanol (0.025M; 10 ml) for 16 h at 25 °C. The solution was neutralized with Dowex 50 (H^+), filtered, and evaporated to dryness. Purification on a silica gel column (toluene–ethyl acetate, 4:1) gave compound (**12b**) as a solid (515 mg, 87%, R_f 0.31), δ_C 98.8 (C-1), 99.3 (C-1′).

Methyl 2,6-*Di*-O-*benzyl*-4-O-(2,3,4,6-*tetra*-O-*benzyl*-α-D-*glucopyranosyl*)-α-D-*galactopyranoside* (**18**) *and Methyl* 2,6-*di*-O-*benzyl*-4-O-(2,3,4-6-*tetra*-O-*benzyl*-β-D-*glucopyranosyl*)-α-D-*galactopyranoside* (**19**).—Methyl trifluoromethanesulphonate (1 ml) was added to a stirred mixture of thiosugar (**7**) (1.5 g), compound (**11**) (0.88 g), and ground molecular sieves (4 Å, 4 g) in diethyl ether at 0 °C, then the mixture was allowed to warm to 20 °C. After 20 h at this temperature triethylamine (2 ml) was added and stirring continued for 30 min. The solution was diluted with dichloromethane, filtered through a layer of



Scheme 4. Syntheses starting from compound (**9**); *Reagents and conditions:* i, glycosyl donor (**8**), F_3CSO_3Ag, CH_2Cl_2, collidine, −20 °C; ii, NaOMe, MeOH–CH_2Cl_2; iii, H_2, Pd; iv, glycosyl donor (**7**), $F_3CSO_3CH_3$, Et_2O, room temp.; v, glycosyl donor (**3**), $F_3CSO_3CH_3$, Et_2O, room temp.; vi, glycosyl donor (**4a**), $F_3CSO_3CH_3$, Et_2O, room temp.

Table 1. Data on coupling reactions and deprotection procedures, yields, physical constants, and selected n.m.r. chemical shifts

(a)

Compd.	Aglycone precursor (mg)	Glycosyl donor (mg)	Glycosidation method[a] (time/h)	T.l.c. R_f (solvent)[b]	Column chromatography solvent	Yield mg (%)	δ_C C-1	C-1′	C-1″
(**12a**)	(**10**) (1 000)	(**3**) (1 500)	A (2)	0.48 (T–E, 4:1)	T–E, 6:1	1 710 (85)	98.4	98.4	
(**13a**)	(**10**) (500)	(**4b**) (600)	A (5)	0.29 (T–E, 3:1)	T–E, 3:1	700 (85)	99.3	99.3	
(**13b**)	(**9**) (740)	(**4a**) (1 100)	A (16)	0.31 (T–E, 4:1)	T–E, 4:1	480 (29)	98.6	101.0	
(**14**)	(**11**) (215)	(**3**) (330)	A (2)	0.43 (T–E, 6:1)	T–E, 6:1	315 (78)	98.6	97.4	
(**15**)	(**11**) (260)	(**4b**) (270)	A (16)	0.18 (T–E, 6:1)	T–E, 4:1	250 (61)	98.8	100.4	
(**16a**)	(**10**) (1 040)	(**7**) (1 700)	A (2)	0.52 (T–E, 4:1)	T–E, 6:1	1 120 (48)	98.3	92.3	
(**17**)	(**9**) (650)	(**8**) (1 100)	B (2)	0.28 (T–E, 6:1)	T–E, 6:1	910 (55)	98.4	101.8	
(**18**)[e]	(**11**) (880)	(**7**) (1 500)	A (20)	0.41 (I–E, 1:1)	I–E, 1:1	610 (37)[c]	98.4	100.1	
(**19**)[e]	(**11**) (880)	(**7**) (1 500)	A (20)	0.47 (I–E, 1:1)	I–E, 1:1	530 (32)[c]	98.3	103.9	
(**20**)	(**9**) (400)	(**3**) (1 500)	A (2)	0.46 (T–E, 6:1)	T–E 6:1	450 (35)	98.6	95.2	99.6
(**21**)	(**12b**)[f] (150)	(**4a**) (150)	A (16)	0.56 (T–E, 5:1)	T–E 5:1	150 (63)	98.8	98.4	100.2
(**22**)	(**13b**) (480)	(**3**) (360)	A (4)	0.41 (T–E, 4:1)	T–E 4:1	515 (71)	98.9	99.6	95.8
(**23**)	(**9**) (100)	(**4a**) (420)	A (4)	0.33 (T–E, 4:1)	T–E 4:1	150 (40)	98.9	101.3	103.3
(**24**)	(**18**) (340)	(**7**) (375)	A (20)	0.47 (T–E, 4:1)	T–E 6:1	410 (77)	98.0	98.1	99.2
(**25**)	(**16b**) (390)	(**8**) (430)	B (4)	0.42 (T–E, 4:1)	T–E 6:1	500 (77)	98.1	99.2	102.6
(**26**)	(**17**) (265)	(**7**) (240)	A (20)	0.59 (T–E, 4:1)	T–E 6:1	310 (76)	98.5	99.4	103.0
(**27**)	(**9**) (200)	(**8**) (660)	B (2)	0.64 (T–E, 4:1)	T–E 4:1	530 (65)	97.9	99.1	102.0

(b)

Compd.	Protected precursor (mg; deprotection method)[d]	Yield mg (%)	Optical rotation $[\alpha]_{578}^{22}$ (c in H_2O)	$\delta_{1\text{-H}}$ ($J_{1,2}$/Hz) 1-H	1′-H	1″-H	δ_C C-1	C-1′	C-1″
(**28**)	(**13a**) (600; D)	240 (81)	153 (1.1)	4.90 (3.6)	4.50 (7.7)		100.1	101.5	
(**29**)	(**14**) (380; D)	110 (77)	18 (1.0)	4.85 (3.0)	5.12 (3.5)		100.4	102.3	
(**30**)	(**15**) (243; D)	75 (68)	127 (1.0)	4.86 (3.2)	4.36 (7.7)		100.5	104.2	
(**31**)	(**16a**) (390; D)	100 (68)	217 (1.0)	4.87 (3.9)	5.11 (3.8)		100.4	96.0	
(**32**)	(**17**) (480; D)	120 (68)	106 (1.0)	4.86 (3.8)	4.67 (7.8)		100.2	104.4	
(**33**)[e]	(**18**) (195; C)[e]	70 (90)	210 (1.0)	4.88 (2.9)	4.96 (3.9)		100.4	101.1	
(**34**)[e]	(**19**) (150; C)[e]	50 (82)	104 (0.9)	4.86	4.64 (7.9)		100.4	104.6	
(**35**)	(**20**) (440; C)	110 (61)	−74 (0.7)	4.89 (3.9)	5.19 (2.5)	5.40 (4.0)	100.5	101.4	99.4
(**36**)	(**21**) (150; D)	40 (68)	23 (0.9)	4.88 (3.8)	5.23 (4.0)	4.36 (7.5)	100.4	101.0	104.1
(**37**)	(**22**) (443; D)	140 (82)	32 (1.0)	4.93 (3.2)	4.51 (7.7)	5.38 (4.0)	100.1	102.3	100.5
(**38**)	(**23**) (150; D)	45 (79)	131 (0.8)	4.93 (3.6)	4.54 (7.7)	4.46 (7.6)	100.0	102.6	103.8
(**39**)	(**24**) (225; C)	60 (75)	223 (0.9)	4.91 (3.8)	5.16 (3.8)	5.07 (3.6)	100.4	96.9	101.4
(**40**)	(**25**) (460; D)	120 (74)	160 (1.1)	4.88 (3.9)	5.15 (3.9)	4.77 (8.0)	100.5	96.4	103.6
(**41**)	(**26**) (245; D)	55 (85)	150 (1.0)	4.90 (3.8)	4.65 (8.0)	5.00 (3.7)	100.3	105.1	100.0
(**42**)	(**27**) (200; D)	60 (88)	76 (1.0)	4.88 (3.8)	4.67 (7.8)	4.84 (7.9)	100.3	104.8	103.3

[a] Two coupling methods were used: A and B. See Experimental for details. [b] T.l.c. R_f values are given for the solvent system used: T = toluene; E = ethyl acetate, I = iso-octane. [c] Calculated from amount of aglycone. [d] Two deprotection methods were used: C and D. See Experimental for details. [e] See Experimental for details. [f] Second order.

Celite, and then washed successively with aqueous 10% H_2SO_4, aqueous $NaHCO_3$, and water. The organic layer was dried (Na_2SO_4) and evaporated, and column chromatography of the residue on silica gel (toluene–ethyl acetate, 4:1) gave the 3-*O*-benzoylated title compounds as a mixture (1.5 g). De-*O*-benzoylation with sodium methoxide in 1:1 methanol–dichloromethane (0.025M; 50 ml), neutralization with Dowex 50 (H^+), and then separation on two silica gel columns (iso-octane–ethyl acetate, 1:1) gave compound (**18**) (610 mg, 37%, R_f 0.41) δ_C 98.4 (C-1), 100.1 (C-1′), and compound (**19**) (530 mg, 32%, R_f 0.47), δ_C 98.3 (C-1), 103.9 (C-1′).

Methyl 4-O-(α-D-*glucopyranosyl*)-α-D-*galactopyranoside* (**33**).—The protected disaccharide (**18**) (195 mg) was dissolved in ethyl acetate–90% aqueous acetic acid (1:1, 30 ml) and hydrogenolysed at 350 KPa over Pd/C (10%, 200 mg) for 16 h. The solution was filtered and evaporated, and the residue was then chromatographed on silica gel (ethyl acetate–acetic acid–methanol–water, 12:3:3:2) followed by purification on a column (80 × 2.5 cm) of Bio-Gel P-2 with water as eluant. After freeze-drying, disaccharide (**33**) was obtained as an amorphous powder (70 mg, 90%), $[\alpha]_{578}^{22}$ 210 ° (c 1.0, H_2O); δ_C 100.4 (C-1) and 101.1 (C-1′); δ_H 4.88 (d, $J_{1,2}$ 2.9 Hz 1-H) and 4.96 (d, $J_{1,2}$ 3.9 Hz 1′-H).

Methyl 4-O-(β-D-*glucopyranosyl*)-α-D-*galactopyranoside* (**34**).—The protected disaccharide (**19**), (150 mg) was deprotected as above to give disaccharide (**34**) (50 mg, 82%) $[\alpha]_{578}^{22}$ 104 ° (c 0.9, H_2O); δ_C 100.4 (C-1) and 104.6 (C-1′); δ_H 4.86 (m, $J_{1,2}$ second order, 1-H) and 4.64 (d, $J_{1,2}$ 7.9 Hz, 1′-H).

Acknowledgements

This work was supported by grants from the Swedish Natural Science Research Council and the Swedish National Board for Technical Development.

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Received 3rd *October* 1988; *Paper* 8/03929A