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APPLICATION OF THE IMIDATE PROCEDURE TO α-D-GALACTOSYLATION*

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ABSTRACT

Using the imidate procedure, 2,3,4,6-tetra-*O*-benzyl-1-*O*-(*N*-methylacetimidoyl)-β-D-galactopyranose was condensed with various monosaccharides to provide, in good yield and with high stereoselectivity, α-linked disaccharides.

INTRODUCTION

A few years ago, we reported, in preliminary form, a novel method of activation of the anomeric centre of carbohydrates and its application to the synthesis of various 1,2-*cis*-disaccharides[1,2]. Details of this reaction for α-D-glucosylation have been published[3,4], and we have applied the procedure for specific α-L-fucosylation[5–7,9] and α-D-galactosylation[7–9]. We now report details of the synthesis of various α-D-galactopyranosides by the imidate procedure.

RESULTS AND DISCUSSION

When a benzene solution of 2,3,4,6-tetra-*O*-acetyl-α-D-galactopyranosyl bromide was stirred at room temperature in the presence of a secondary amide, silver oxide, di-isopropylethylamine, and powdered 4 Å molecular sieve, an imidate of type **1** was formed. Similar compounds have previously been obtained in the D-*gluco* series[3]. Not unexpectedly[3], when an imidate of type **1** was condensed in benzene with 1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranose in the presence of *p*-toluenesulfonic acid, ortho ester **2** was obtained. A non-participating group at C-2 is necessary to provide an α-D-galactopyranoside.

Indeed, when the imidate **3**[7] was condensed at room temperature either in benzene or nitromethane with properly substituted monosaccharides in the presence of *p*-toluenesulfonic acid and powdered molecular sieve, an α-D-galactopyranoside was obtained in good yield, as demonstrated by the following examples.

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*Preliminary communication: ref. 2.
**To whom enquiries should be sent.

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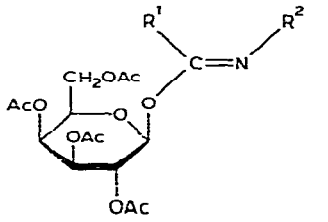
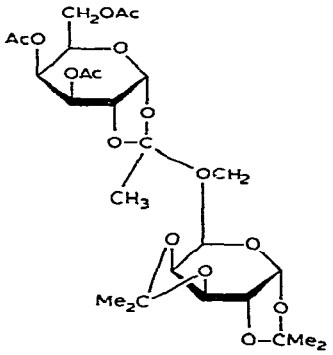


1a $R^1 = R^2 = Me$
1b $R^1 = Ph, R^2 = Me$
1c $R^1 = R^2 = Ph$
1d $R^1 = Me, R^2 = Ph$
1e $R^1 = Me, R^2 = o\text{-}Cl\text{—}Ph$



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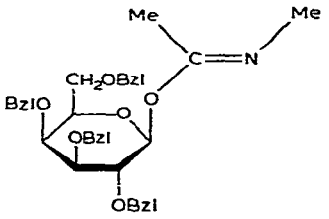

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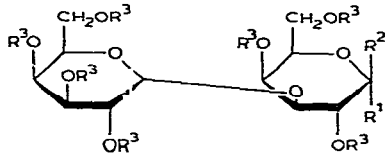
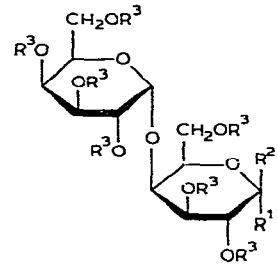
3-*O*-α-D-Galactopyranosyl-D-galactose, which is a building unit of the antigenic determinant for the B human blood-group, was isolated after partial, acid hydrolysis of B substance[10] and as a degradation product of λ-carrageenan[11]. An attempt[12] to synthesize this disaccharide by using quaternary ammonium salts derived from 2,3,4,6-tetra-*O*-benzyl-α-D-galactopyranosyl bromide failed, but it was obtained[13] by a non-specific route from 2,3,4,6-tetra-*O*-acetyl-α-D-galactopyranosyl bromide. 3-*O*-α-D-Galactopyranosyl-α,β-D-galactopyranose has been synthesized from 1,2:5,6-di-*O*-isopropylidene-α-D-galactofuranose by the oximino chloride[14] and the halide-ion catalyzed[15] methods, and from 2,2,2-trichloroethyl 2,4,6-tri-*O*-acetyl-β-D-galactopyranoside by the halide-ion catalyzed reaction[16]. When the imidate **3** was condensed with benzyl 2,4,6-tri-*O*-benzyl-β-D-galactopyranoside[17] during 4 days in benzene, benzyl 2,4,6-tri-*O*-benzyl-3-*O*-(2,3,4,6-tetra-*O*-benzyl-α-D-galactopyranosyl)-β-D-galactopyranoside (**4**) was obtained (78% after chromatography). The n.m.r. signal of H-1′ of **4** in $CDCl_3$ was a doublet having a small coupling constant (δ 5.22, $J_{1',2'}$ 3 Hz). Catalytic hydrogenolysis of **4** in acetic acid gave 3-*O*-α-D-galactopyranosyl-D-galactopyranose as an amorphous powder, whose optical rotation is close to those reported[11,13]. After borohydride reduction and trimethylsilylation, **5** showed a single peak in g.l.c.

4-*O*-α-D-Galactopyranosyl-D-galactopyranose has been isolated from okra mucilage[18], from the kidney of a patient suffering from Fabry's disease[19], and from a sheep hydated-cyst fluid[20]. This disaccharide was synthesized in moderate yield from 2,3-di-*O*-acetyl-1,6-anhydro-β-D-galactopyranose by a Koenigs–Knorr type condensation[12] and a halide-ion catalyzed reaction[21].

Treatment of benzyl 2,3,6-tri-*O*-benzyl-β-D-galactopyranoside[17] with an excess of imidate **3** for 3 days in nitromethane gave, after chromatography, benzyl 2,3,6-tri-*O*-benzyl-4-*O*-(2,3,4,6-tetra-*O*-benzyl-α-D-galactopyranosyl)-β-D-galactopyranoside (**6**) in 74% yield. The α configuration at the interglycosidic linkage was clear from the n.m.r. signal for H-1′ (δ 5.08, $J_{1',2'}$ 3 Hz). Catalytic hydrogenolysis of **6**



4 R^1 = H, R^2 = OBzl, R^3 = Bzl
5 R^1 = OH, R^2 = R^3 = H

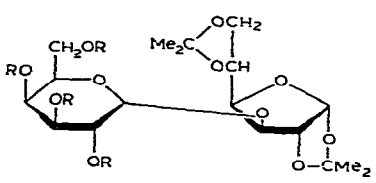


6 R^1 = H, R^2 = OBzl, R^3 = Bzl
7 R^1 = OH, R^2 = R^3 = H
8 R^1 = OAc, R^2 = H, R^3 = Ac
9 R^1 = H, R^2 = OMe, R^3 = Bzl
10 R^1 = R^3 = H, R^2 = OMe
11 R^1 = H, R^2 = OMe, R^3 = Ac

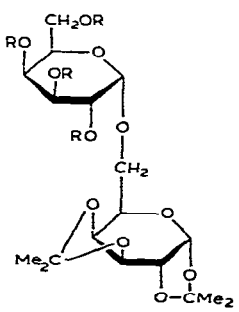
in acetic gave 4-*O*-α-D-galactopyranosyl-D-galactopyranose (**7**) in very high yield as an amorphous powder, whose optical rotation value is very close to that reported by Chacón-Fuertes and Martín-Lomas[13], and which gave the known[13] octa-acetate **8**.

Likewise, condensation of **3** in benzene during 3 days with methyl 2,3,6-tri-*O*-benzyl-β-D-galactopyranoside[22] gave, after chromatography, amorphous methyl 2,3,6-tri-*O*-benzyl-4-*O*-(2,3,4,6-tetra-*O*-benzyl-α-D-galactopyranosyl)-β-D-galactopyranoside (**9**) in 82% yield. Catalytic hydrogenolysis of **9** in acetic acid gave methyl 4-*O*-α-D-galactopyranosyl-β-D-galactopyranoside (**10**) in very high yield. The α-configuration at the newly established glycosidic bond is apparent from the n.m.r. signal for H-1′ (δ 5.55 in D_2O, $J_{1',2'}$ 3 Hz). Acetylation of **10** (acetic anhydride in pyridine) gave the amorphous acetate **11** which, on acetolysis with acetic anhydride containing a trace of sulfuric acid, gave 80% of the octa-acetate **8** which was identical with the product prepared from disaccharide **7**.

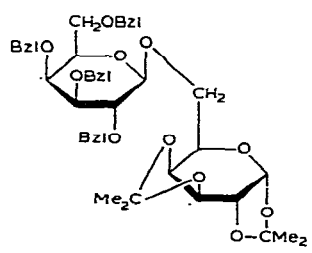
When the imidate **3** was treated with methyl 2,3,6-tri-*O*-benzoyl-α-D-galactopyranoside[23], a complex mixture resulted from which no condensation product could



12 R = Bzl
13 R = H



14 R = Bzl
15 R = H
16 R = Ac



17

be isolated. This result is in sharp contrast to the high-yielding* condensation[24] of this alcohol with 2,3,4,6-tetra-*O*-benzyl-α-D-galactopyranosyl chloride under halide-ion catalyzed conditions[15].

In order to broaden the scope of the procedure, the condensation of the imidate **3** with sugars partially protected by acid-sensitive groups was also studied. Thus, the reaction of **3** with 1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose[25] in nitromethane gave the amorphous disaccharide derivative **12** (79% after chromatography). Catalytic hydrogenolysis of **12** in ethanol gave amorphous 3-*O*-α-D-galactopyranosyl-1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose (**13**), identical with the compound previously synthesized by Lemieux *et al.*[14]. Finally, the reaction of **3** with 1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranose[25] in nitromethane gave, after chromatography, the α-linked disaccharide **14** (81%). In this case, a small proportion of the β anomer **17** was also isolated (17%). A similar loss of stereospecificity during the glucosylation of a primary hydroxyl group has been observed[2,3]. The disaccharide **14** was easily transformed first into the alcohol **15** and then into the acetate **16**, both products being identical with known compounds[14].

Together with other reported examples[5,7–9,26], this work demonstrates the utility of the imidate procedure for α-D-galactosylation reactions.

EXPERIMENTAL

General. — Melting points were determined with a Büchi apparatus. Optical rotations were determined at 22–24° with a Perkin–Elmer model 141 polarimeter. ^{1}H-N.m.r. spectra were recorded for solutions in $CDCl_3$ (internal Me_4Si) unless otherwise stated. Purity of products was determined by t.l.c. on Kieselgel 60 F_{254} (Merck) and detection by charring with sulfuric acid. Column chromatography was performed on Kieselgel 60 (0.063–0.200 mm, Merck). G.l.c. of the per-*O*-(trimethylsilyl) derivatives was performed with a Girdel 3000 apparatus provided with a flame-ionization detector and a 3.40-m Pyrex column (4% of OV 17 on Gas-Chrom Q, 80–100 mesh), programmed at 10°.min^{-1} from 150 to 300°; retention times (T_R) are given relative to that of per-*O*-(trimethylsilyl)-*myo*-inositol. Microanalyses were performed by the Service Central d'Analyse du C.N.R.S.

*2,3,4,6-Tetra-*O*-acetyl-1-*O*-(N-methylacetimidoyl)-β-D-galactopyranose* (**1a**). — A solution of 2,3,4,6-tetra-*O*-acetyl-α-D-galactopyranosyl bromide (2.05 g) in benzene was stirred for 24 h at room temperature under dry nitrogen in the presence of *N*-methylacetamide (0.515 g), freshly prepared silver oxide (2.32 g), di-isopropylethylamine (0.7 ml), and molecular sieve 4 Å (200 mg). In order to remove insoluble salts and the excess of *N*-methylacetamide, the solution was passed through a bed of neutral alumina, which was washed with benzene–ether (9:1) containing 0.1% of triethylamine. The filtrate was evaporated, to give the imidate **1a** (1.73 g, 85%), $[\alpha]_D$ +35° (*c* 1, chloroform). ^{1}H-N.m.r. data: δ 5.95 (d, 1 H, $J_{1,2}$ 8 Hz, H-1),

*In our hands, this reaction afforded the expected disaccharide in only 41% yield.

5.4 (dd, 1 H, $J_{2,3}$ 11 Hz, H-2), 5.15 (dd, 1 H, $J_{3,4}$ 4 Hz, H-3), 3.05 (s, 3 H, N-Me), 2.05–2.18 (3 s, 12 H, 4 OAc), and 1.90 (s, 3 H, CMe).

Anal. Calc. for $C_{17}H_{25}NO_{10}$: C, 50.61; H, 6.25; N, 3.47. Found: C, 50.65; H, 6.27; N, 3.20.

The following imidates were prepared by the same procedure:

*2,3,4,6-Tetra-*O*-acetyl-1-*O*-(*N*-methylbenzimidoyl)-β-*D*-galactopyranose* (**1b**). — From *N*-methylbenzamide (0.9 g), **1b** was obtained (1.9 g, 82%), m.p. 108–109° (from benzene–hexane), $[\alpha]_D$ +26° (*c* 1, chloroform). ^{1}H-N.m.r. data: δ 7.45 (m, 5 H, Ph), 6.15 (d, 1 H, $J_{1,2}$ 8 Hz, H-1), 5.5 (dd, 1 H, $J_{2,3}$ 11 Hz, H-2), 5.20 (dd, 1 H, $J_{3,4}$ 4 Hz, H-3), 3.18 (s, 3 H, N-Me), and 2.00–2.18 (3 s, 12 H, 4 OAc).

Anal. Calc. for $C_{22}H_{27}NO_{10}$: C, 56.77; H, 5.85; N, 3.01. Found: C, 57.07; H, 5.99; N, 2.87.

*2,3,4,6-Tetra-*O*-acetyl-1-*O*(*N*-phenylbenzimidoyl)-β-*D*-galactopyranose* (**1c**). — From benzanilide (1.3 g), **1c** was obtained (72%), $[\alpha]_D$ +5.5° (*c* 0.8, chloroform). ^{1}H-N.m.r. data: δ 6.7–7.4 (m, 10 H, Ph), 6.22 (dd, 1 H, $J_{1,2}$ 8 Hz, H-1), 5.60 (dd, 1 H, $J_{2,3}$ 11 Hz, H-2), 5.22 (dd, 1 H, $J_{3,4}$ 4 Hz, H-3), and 2.05–2.20 (3 s, 12 H, 4 OAc).

Anal. Calc. for $C_{27}H_{29}NO_{10}$: C, 61.48; H, 5.54; N, 2.65. Found: C, 61.52; H, 5.66; N, 2.55.

*2,3,4,6-Tetra-*O*-acetyl-1-*O*-(*N*-phenylacetimidoyl)-β-*D*-galactopyranose* (**1d**). — From acetanilide (0.9 g), **1d** was obtained (85%), $[\alpha]_D$ +75° (*c* 0.9, chloroform). ^{1}H-N.m.r. data: δ 6.12 (dd, 1 H, $J_{1,2}$ 8 Hz, H-1), 5.50 (dd, 1 H, $J_{2,3}$ 11 Hz, H-2), 5.18 (dd, 1 H, $J_{3,4}$ 4 Hz, H-3), 2.05–2.22 (3 s, 12 H, 4 OAc), and 1.90 (s, 3 H, CMe).

Anal. Calc. for $C_{22}H_{27}NO_{10}$: C, 56.77; H, 5.85; N, 3.01. Found: C, 57.39; H, 5.94; N, 2.92.

*2,3,4,6-Tetra-*O*-acetyl-1-*O*-(*N*-p-chlorophenylacetimidoyl)-β-*D*-galactopyranose* (**1e**). — From *N*-*p*-chlorophenylacetamide (1.15 g), **1e** was obtained (62%), $[\alpha]_D$ +84° (*c* 1, chloroform). ^{1}H-N.m.r. data: δ 6.75–7.35 (m, 4 H, Ph), 6.18 (dd, 1 H, $J_{1,2}$ 8 Hz, H-1), 5.15 (dd, 1 H, $J_{2,3}$ 11, $J_{3,4}$ 4 Hz, H-3), 2.05–2.20 (3 s, 12 H, 4 OAc), and 1.90 (s, 3 H, CMe).

Anal. Calc. for $C_{22}H_{26}ClNO_{11}$: C, 52.86; H, 5.24; N, 2.50. Found: C, 53.21; H, 5.50; N, 2.21.

*3,4,6-Tri-*O*-acetyl-α-D-galactopyranose 1,2-(1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranose-6-yl orthoacetate)* (**2**). — A solution of 1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranose (132 mg) and 2,3,4,6-tetra-*O*-acetyl-1-*O*-(*N*-methylbenzimidoyl)-β-D-galactopyranose (**1b**, 280 mg) in anhydrous benzene (3 mL) was boiled under reflux for 4 days in the presence of anhydrous *p*-toluenesulfonic acid (89 mg). The mixture was diluted with chloroform, washed with saturated aqueous sodium hydrogencarbonate and water, dried (Na_2SO_4), and evaporated. The residue was chromatographed on silica gel (10 g) with benzene–ether (2:1), to give syrupy **2** (273 mg, 77%). Although no correct elemental analysis has been obtained for this product, its structure was indicated by ^{1}H-n.m.r. spectroscopy: δ 5.88 (d, 1 H, $J_{1,2}$ 5 Hz, H-1), 5.55 (d, 1 H, $J_{1',2'}$ 5 Hz, H-1'), 2.10–2.12 (2 s, 9 H, 3 OAc), 1.72 (s, 3 H, CMe ortho ester), 1.35, 1.48, and 1.55 (3 s, 12 H, 2 CMe_2).

No disaccharide was formed in this reaction. The same ortho ester **2** was obtained with all the acetylated imidates of series **1**.

*Benzyl 2,4,6-tri-*O*-benzyl-3-*O*-(2,3,4,6-tetra-*O*-benzyl-α-*D*-galactopyranosyl)-β-*D*-galactopyranoside* (**4**). — A solution of benzyl 2,4,6-tri-*O*-benzyl-β-*D*-galactopyranoside (526 mg) and 2,3,4,6-tetra-*O*-benzyl-1-*O*-(*N*-methylacetamidoyl)-β-*D*-galactopyranose (**3**) (1.2 g) in anhydrous benzene (20 mL) was stirred at room temperature under nitrogen for 4 days in the presence of *p*-toluenesulfonic acid (175 mg) and powdered molecular sieve 4 Å (300 mg). The mixture was filtered, washed with saturated, aqueous sodium hydrogencarbonate and water, dried (Na_2SO_4), and evaporated. The residue was chromatographed on silica gel (200 g); elution with benzene–ether (12:1) gave syrupy **4** (823 mg, 78%), $[\alpha]_D$ +26.5° (*c* 2, chloroform). ^{1}H-N.m.r. data: δ 7.20–7.25 (m, 40 H, Ph) and 5.22 (d, 1 H, $J_{1',2'}$ 3 Hz, H-1').

Anal. Calc. for $C_{68}H_{70}O_{11}$: C, 76.81; H, 6.63; O, 16.55. Found: C, 76.65; H, 6.80; O, 16.40.

*3-*O*-α-*D*-Galactopyranosyl-*D*-galactose* (**5**). — A solution of **4** (344 mg) in acetic acid (10 mL) was hydrogenolysed with Pd/C (10%, 200 mg) for 48 h. The mixture was filtered and evaporated, to give **5** (93 mg, 84%) as an amorphous, hygroscopic powder, $[\alpha]_D$ +145° (*c* 1, water); lit.[11,13]: $[\alpha]_D^{25}$ +155° (*c* 0.3, water), $[\alpha]_D^{20}$ +149° (*c* 1.6, water). ^{1}H-N.m.r. data (D_2O): δ 5.81 (d, 1 H, $J_{1,2}$ 2.5 Hz, H-1), and 5.68 (d, 1 H, $J_{1',2'}$ 3 Hz, H-1').

This compound was homogeneous in g.l.c. (T_R 1.80) after reduction with sodium borohydride and per-*O*-(trimethylsilylation).

*Benzyl 2,3,6-tri-*O*-benzyl-4-*O*-(2,3,4,6-tetra-*O*-benzyl-α-*D*-galactopyranosyl)-β-*D*-galactopyranoside* (**6**). — A solution of benzyl 2,3,6-tri-*O*-benzyl-β-*D*-galactopyranoside (630 mg) and 2,3,4,6-tetra-*O*-benzyl-1-*O*-(*N*-methylacetimidoyl)-β-*D*-galactopyranose (**3**) (1.6 g) in anhydrous nitromethane (20 mL) was stirred at room temperature under nitrogen for 3 days in the presence of powdered molecular sieve 4 Å (300 mg) and anhydrous *p*-toluenesulfonic acid (195 mg). The mixture was filtered, washed with saturated aqueous sodium hydrogencarbonate and water, dried (Na_2SO_4), and evaporated. The residue was chromatographed on silica gel (200 g); elution with hexane–ethyl acetate (7:2) gave syrupy **6** (786 mg, 74%), $[\alpha]_D$ +38° (*c* 1, chloroform). ^{1}H-N.m.r. data: δ 7.20–7.30 (m, 40 H, Ph), and 5.08 (d, 1 H, $J_{1',2'}$ 3 Hz, H-1').

Anal. Calc. for $C_{68}H_{70}O_{11}$: C, 76.81; H, 6.63. Found: C, 76.96; H, 6.69.

*4-*O*-α-*D*-Galactopyranosyl-*D*-galactopyranose* (**7**). — A solution of **6** (284 mg) in acetic acid (15 mL) was hydrogenolysed with Pd/C (10%, 150 mg) for 48 h. The mixture was filtered and evaporated, to give **7** (82 mg, 94%) as an amorphous, hygroscopic powder, $[\alpha]_D$ +163° (*c* 1, water); lit.[13] $[\alpha]_D^{26}$ +170° (*c* 1, water). ^{1}H-N.m.r. data: δ 5.82 (d, 1 H, $J_{1,2}$ 3 Hz, H-1), and 5.50 (d, 1 H, $J_{1',2'}$ 3 Hz, H-1').

*1,2,3,6-Tetra-*O*-acetyl-4-*O*-(2,3,4,6-tetra-*O*-acetyl-α-*D*-galactopyranosyl)-α-*D*-galactopyranose* (**8**). — The disaccharide **7** (45 mg) was acetylated (acetic anhydride–pyridine). After the usual work-up, the residue was crystallized from ethanol to give **8** (70 mg, 78.5%), m.p. 155°, $[\alpha]_D$ +135° (*c* 0.4, chloroform); lit[13] m.p. 153–154°, $[\alpha]_D^{24}$ +138° (*c* 2, chloroform). ^{1}H-N.m.r. data: δ 6.42 (d, 1 H, $J_{1,2}$ 3.5 Hz, H-1).

Methyl 2,3,6-tri-O-benzyl-4-O-(2,3,4,6-tetra-O-benzyl-α-D-galactopyranosyl)-β-D-galactopyranoside (**9**). — A solution of methyl 2,3,6-tri-*O*-benzyl-β-D-galactopyranoside (1 g) and 2,3,4,6-tetra-*O*-benzyl-1-*O*-(*N*-methylacetimidoyl)-β-D-galactopyranose (**3**, 2 g) in anhydrous benzene (20 mL) was stirred at room temperature under nitrogen in the presence of powdered molecular sieve 4 Å (1 g) and anhydrous *p*-toluenesulfonic acid (300 mg). After 3 days, triethylamine (3.5 mL) was added, and the mixture was filtered and concentrated to dryness. The residue was eluted from a column of silica gel (150 g) with hexane–ethyl acetate (4:1), to give a crude disaccharide contaminated by an acetylated species. *O*-Deacetylation of this mixture (sodium methoxide in methanol) followed by elution of the product from a column of silica gel (100 g) with hexane–ethyl acetate (4:1) gave **9** (1.73 g, 81%), $[\alpha]_D$ +43° (*c* 1.24, chloroform).

Anal. Calc. for $C_{62}H_{66}O_{11}$: C, 75.43; H, 6.73. Found: C, 75.13; H, 6.67.

Methyl 4-O-α-D-galactopyranosyl-β-D-galactopyranoside (**10**). — A solution of **9** (1.4 g) in acetic acid (15 mL) was hydrogenolysed with Pd/C (10%, 0.5 g) for 12 h. The mixture was filtered and concentrated, and the residue was eluted from a column of silica gel (50 g) with methanol–chloroform (1:1), to give syrupy **10** (476 mg, 94%), $[\alpha]_D^{20}$ +73° (*c* 1.24, ethanol). ^{1}H-N.m.r. data (D_2O): δ 5.55 (d, 1 H, $J_{1',2'}$ 3 Hz, H-1'), 4.95 (d, 1 H, $J_{1,2}$ 9 Hz, H-1), and 3.95 (s, 3 H, OMe).

Anal. Calc. for $C_{13}H_{24}O_{11}$: C, 43.82; H, 6.78. Found: C, 43.59; H, 6.80.

Methyl 2,3,6-tri-O-acetyl-4-O-(2,3,4,6-tetra-O-acetyl-α-D-galactopyranosyl)-β-D-galactopyranoside (**11**). — Conventional acetylation of **10** (90 mg) with acetic anhydride (0.5 mL) in pyridine (2 mL) and elution of the product from a column of silica gel (10 g) with ethyl acetate–chloroform (1:1) gave syrupy **11** (120 mg, 73%), $[\alpha]_D^{20}$ +66° (*c* 1.14, chloroform).

Anal. Calc. for $C_{27}H_{38}O_{18}$: C, 49.84; H, 5.88. Found: C, 49.71; H, 6.09.

A solution of **11** (650 mg) in acetic anhydride (3 mL) containing concentrated sulfuric acid (0.1 mL) was kept at 0° for 10 min, neutralized at 0° with 5% aqueous sodium hydrogencarbonate, and extracted with chloroform. The chloroform layer was washed with water, dried (Na_2SO_4), and evaporated. The residue was crystallized from ethanol, to give the octa-acetate **8**, identical with the compound previously prepared.

3-O-1,2:5,6-Di-O-isopropylidene-(2,3,4,6-tetra-O-benzyl-α-D-galactopyranosyl)-α-D-glucofuranose (**12**). — A solution of 1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose (275 mg) and 2,3,4,6-tetra-*O*-benzyl-1-*O*-(*N*-methylacetimidoyl)-β-D-galactopyranose (1.4 g) in anhydrous nitromethane (10 mL) was stirred at room temperature under nitrogen for 3 days in the presence of powdered molecular sieve 4 Å (200 mg) and *p*-toluenesulfonic acid (180 mg). The mixture was filtered, washed with saturated aqueous sodium hydrogencarbonate and water, dried (Na_2SO_4), and evaporated. The residue was chromatographed on silica gel (120 g); elution with ether–hexane (7:6) gave syrupy **12** (822 mg, 79%), $[\alpha]_D$ +33° (*c* 0.9, chloroform). ^{1}H-N.m.r. data: δ 7.15 (m, 20 H, Ph), 5.87 (d, 1 H, $J_{1,2}$ 4 Hz, H-1), 5.20 (d, 1 H, $J_{1',2'}$ 3 Hz, H-1'), and 1.16–1.45 (4 s, 12 H, 2 CMe_2).

Anal. Calc. for $C_{46}H_{54}O_{11}$: C, 70.56; H, 6.95. Found: C, 70.52; H, 7.05.

3-O-α-D-Galactopyranosyl-1,2:5,6-di-O-isopropylidene-α-D-glucofuranose (**13**). — A solution of **12** (214 mg) in ethanol (20 mL) was hydrogenolysed with Pd/C (10%, 100 mg) for 12 h. The mixture was filtered and concentrated, to give amorphous **13** (110 mg, 90%), $[\alpha]_D$ +93° (*c* 1, *N,N*-dimethylformamide); lit.[14] $[\alpha]_D^{23}$ +94.4° (*N,N*-dimethylformamide).

1,2:3,4-Di-O-isopropylidene-6-O-(2,3,4,6-tetra-O-benzyl-α-D-galactopyranosyl)-α-D-galactopyranose (**14**). — A solution of 1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranose (121 mg) and 2,3,4,6-tetra-*O*-benzyl-1-*O*-(*N*-methylacetimidoyl)-β-D-galactopyranose (**3**, 466 mg) in anhydrous nitromethane (10 mL) was stirred at room temperature under nitrogen for 2 days in the presence of powdered molecular sieve 4 Å (200 mg) and *p*-toluenesulfonic acid (68 mg). The mixture was filtered, washed with saturated aqueous sodium hydrogencarbonate and water, dried (Na_2SO_4), and evaporated. The residue was chromatographed on silica gel (40 g); elution with diisopropyl ether–hexane (5:3) gave, first, syrupy **14** (290 mg, 81%), $[\alpha]_D$ +10.5° (*c* 1.2, chloroform). ^{1}H-N.m.r. data: δ 7.20 (s, 20 H, Ph), 5.40 (d, 1 H, $J_{1,2}$ 5 Hz, H-1), 4.95 (d, 1 H, $J_{1',2'}$ 4.5 Hz, H-1'), and 1.20–1.47 (4 s, 12 H, 2 CMe_2).

Anal. Calc. for $C_{46}H_{54}O_{11}$: C, 70.56; H, 6.95. Found: C, 70.56; H, 6.89.

Eluted second was 1,2:3,4-di-*O*-isopropylidene-6-*O*-(2,3,4,6-tetra-*O*-benzyl-β-D-galactopyranosyl)-α-D-galactopyranose (**17**) (64 mg, 17%) as a syrup, $[\alpha]_D$ −25° (*c* 1, chloroform). ^{1}H-N.m.r. data: δ 7.30 (m, 20 H, Ph), 5.75 (d, 1 H, $J_{1,2}$ 4 Hz, H-1), 4.42 (d, 1 H, $J_{1',2'}$ 9 Hz, H-1'), and 1.20–1.48 (4 s, 12 H, 2 CMe_2).

Anal. Calc. for $C_{46}H_{54}O_{11}$: C, 70.56; H, 6.95. Found: C, 70.44; H, 6.77.

6-O-α-D-Galactopyranosyl-1,2:3,4-di-O-isopropylidene-α-D-galactopyranose (**15**). — A solution of **14** (200 mg) in ethanol (20 mL) was hydrogenolysed with Pd/C (10%, 100 mg) for 12 h. The mixture was filtered and concentrated, to give syrupy **15** (99 mg, 96%), $[\alpha]_D$ +55° (*c* 0.64, *N,N*-dimethylformamide); lit.[14] $[\alpha]_D^{23}$ +55.4° (*N,N*-dimethylformamide).

1,2:3,4-Di-O-isopropylidene-6-O-(2,3,4,6-tetra-O-acetyl-α-D-galactopyranosyl)-α-D-galactopyranose (**16**). — Conventional acetylation of **15** (100 mg) with acetic anhydride (1 mL) in pyridine (4 mL) and the usual work-up gave **16** (138 mg, 95%), m.p. 82–85°, $[\alpha]_D$ +55° (*c* 0.46, chloroform); lit[14] m.p. 87–89°, $[\alpha]_D^{23}$ +54.5° (chloroform).

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