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Note

Synthesis of solatriose

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A branched trisaccharide, 3-*O*-β-D-glucopyranosyl-2-*O*-α-L-rhamnopyranosyl-β-D-galactose (solatriose, **13**), is the carbohydrate moiety of such alkaloid glycosides as α-solanine[1], α-solasonine[2], and α-solamarine[3], from which it has been isolated[1–3] after partial hydrolysis with acid. The component disaccharides, 3-*O*-β-D-glucopyranosyl-D-galactose[4] (solabiose) and 2-*O*-α-L-rhamnopyranosyl-D-galactose[5,6], have previously been synthesized. The synthesis of **13** is now described.

Treatment of benzyl 3-*O*-allyl-β-D-galactopyranoside[7] (**1**) with α,α-dimethoxytoluene in acetonitrile in the presence of *p*-toluenesulfonic acid gave benzyl 3-*O*-allyl-4,6-*O*-benzylidene-β-D-galactopyranoside (**2**) in crystalline form in 87% yield. Condensation of **2** with 2,3,4-tri-*O*-acetyl-α-L-rhamnopyranosyl bromide (**3**) in dichloromethane, in the presence of silver trifluoromethanesulfonate (triflate) and 1,1,3,3-tetramethylurea[8], afforded a mixture that was shown by t.l.c. to contain benzyl 3-*O*-allyl-4,6-*O*-benzylidene-2-*O*-(2,3,4-tri-*O*-acetyl-α-L-rhamnopyranosyl)-β-D-galactopyranoside (**4**) as the major product, accompanied by traces of the marginally slower-moving, unreacted **2** that could not be removed by column chromatography. Therefore, the mixture was *O*-deacetylated with methanolic sodium methoxide, and the resulting mixture of products was fractionated by chromatography on a column of silica gel to give, in 85% yield, crystalline benzyl 3-*O*-allyl-4,6-*O*-benzylidene-2-*O*-α-L-rhamnopyranosyl-β-D-glucopyranoside (**5**). Acetylation of **5** produced **4** in crystalline form. The configuration at the newly introduced, inter-glycosidic linkage in **4** was confirmed by the ^{13}C-n.m.r. spectrum, which showed a signal for C-1' at** δ 97.9, with $^{1}J_{C,H}$ 176 Hz, consistent[9] with the α configuration at C-1'.

Removal of the benzylidene group from **5** with aqueous acetic acid afforded crystalline benzyl 3-*O*-allyl-2-*O*-α-L-rhamnopyranosyl-β-D-galactopyranoside (**6**) in 91% yield. Acetylation of **6** gave crystalline benzyl 4,6-di-*O*-acetyl-3-*O*-allyl-2-

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**The unprimed, single-primed, and double-primed numbers refer to the carbon atoms in the D-galactosyl, L-rhamnosyl, and D-glucosyl rings, respectively.

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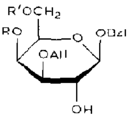
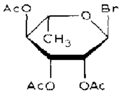


1 R = R′ = H

2 R, R′ = PhCH

Bzl = $PhCH_2$



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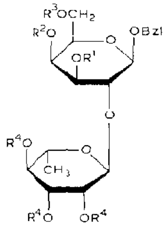


4 R^1 = All, R^2, R^3 = PhCH, R^4 = Ac

5 R^1 = All, R^2, R^3 = PhCH, R^4 = H

6 R^1 = All, R^2 = R^3 = R^4 = H

7 R^1 = All, R^2 = R^3 = R^4 = Ac

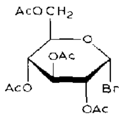
8 R^1 = All, R^2 = R^3 = R^4 = Bzl

9 R^1 = H, R^2 = R^3 = R^4 = Bzl

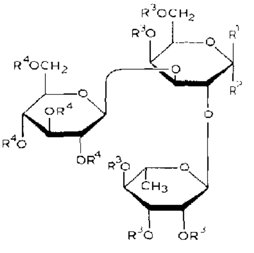
All = $H_2C{=}CH_2{-}CH_2$

O-(2,3,4-tri-*O*-acetyl-α-L-rhamnopyranosyl)-β-D-galactopyranoside (**7**). Benzylation of **6** with benzyl bromide and sodium hydride[10] in *N*,*N*-dimethylformamide provided, in 93% yield after column chromatography, benzyl 3-*O*-allyl-4,6-di-*O*-benzyl-2-*O*-(2,3,4-tri-*O*-benzyl-α-L-rhamnopyranosyl)-β-D-galactopyranoside (**8**) as a syrup. Isomerization of the allyl group in **8** with tris(triphenylphosphine)rhodium(I) chloride in the presence of 1,4-diazabicyclo[2.2.2]octane[11], followed by removal of the resulting 1-propenyl group with mercuric chloride and mercuric oxide[12], gave, in 76% yield after column chromatography, crystalline benzyl 4,6-di-*O*-benzyl-2-*O*-(2,3,4-tri-*O*-benzyl-α-L-rhamnopyranosyl)-β-D-galactopyranoside (**9**).

Compound **9** was condensed with 2,3,4,6-tetra-*O*-acetyl-α-D-glucopyranosyl



10



11 R^1 = OBzl, R^2 = H, R^3 = Bzl, R^4 = Ac

12 R^1 = OBzl, R^2 = R^4 = H, R^3 = Bzl

13 R^1, R^2 = H, OH, R^3 = R^4 = H

bromide (**10**) in dichloromethane in the presence of silver triflate and 1,1,3,3-tetramethylurea, to give, in 77% yield, crystalline benzyl 4,6-di-*O*-benzyl-3-*O*-(2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl)-2-*O*-(2,3,4-tri-*O*-benzyl-α-L-rhamnopyranosyl)-β-D-galactopyranoside (**11**), after column chromatography. The β configuration of the newly formed interglycosidic bond in **11** was indicated[9] by the ^{13}C-n.m.r. spectrum, which showed a signal for C-1″ at δ 100.9, with $^1J_{C,H}$ 160 Hz. *O*-Deacetylation of **11** gave, in 95% yield, benzyl 4,6-di-*O*-benzyl-3-*O*-β-D-glucopyranosyl-2-*O*-(2,3,4-tri-*O*-benzyl-α-L-rhamnopyranosyl)-β-D-galactopyranoside (**12**) as amorphous material. Catalytic hydrogenolysis of **12** in acetic acid in the presence of palladium-on-charcoal furnished, in 78% yield after column chromatography, the title compound **13**, having physical constants in good agreement with those reported[1,3] for this compound, obtained from the natural products.

EXPERIMENTAL

General methods. — Unless stated otherwise, the general experimental conditions were the same as those described previously[13]. ^{13}C-N.m.r. spectra were recorded with a Jeol JNM-FX 200 spectrometer operated at 50.10 MHz, and with tetramethylsilane as the internal standard.

Benzyl 3-O-allyl-4,6-O-benzylidene-β-D-galactopyranoside (**2**). — A solution of **1** (13.78 g), α,α-dimethoxytoluene (10 g), and *p*-toluenesulfonic acid (0.1 g) in anhydrous acetonitrile (100 mL) was stirred for 6 h at room temperature. The solution was made neutral with Amberlite IR-400 (OH) ion-exchange resin, and the resin filtered off and washed with methanol. The filtrate and washings were combined, and evaporated, to give a white, crystalline residue which was recrystallized from ethanol to afford **2** (15.39 g, 87%); m.p. 174–175°, $[\alpha]_D^{25}$ −6.3° (*c* 0.6, chloroform); n.m.r. data: δ_H (chloroform-*d*): 7.65–7.25 (m, 10 H, arom. H), 5.33 (s, 1 H, benzylic H), 4.81 (AB q, 2 H, *J* 12.0 Hz, PhCH_2), and 2.58 (broad s, 1 H, disappeared on deuteration, HO-2); δ_C (dimethyl sulfoxide-d_6): 99.6 (C-1, $^1J_{C,H}$ 162.0 Hz).

Anal. Calc. for $C_{23}H_{26}O_6$: C, 69.33; H, 6.58. Found: C, 69.47; H, 6.64.

Benzyl 3-O-allyl-4,6-O-benzylidene-2-O-α-L-rhamnopyranosyl-β-D-galactopyranoside (**5**). — A solution of **3** (11.65 g, 33 mmol) in dry dichloromethane (40 mL) was added dropwise during 40 min, with rigorous exclusion of moisture and light, to a stirred solution (cooled to −30°) of **2** (7.73 g, 19.4 mmol), silver triflate (10.17 g, 39.6 mmol), and 1,1,3,3-tetramethylurea (9.47 mL, 79.2 mmol) in dichloromethane (60 mL). After being stirred for 1 h at −30°, the mixture was allowed to reach room temperature gradually, and then stirred overnight. T.l.c. (1:1 benzene–ethyl acetate) showed the formation of **4** (R_F 0.52) as the major product, accompanied by traces of, marginally slower-migrating, unreacted **2** (R_F 0.48). The suspension was filtered off through a Celite pad, and the inorganic solid was washed with dichloromethane. The filtrate and washings were combined, washed successively with aqueous sodium hydrogencarbonate, and water, dried (sodium sulfate), and evaporated. A solution of the residue in anhydrous methanol (100 mL) was treated with methanolic M sodium methoxide (5 mL). The mixture was kept for 2 h at room temperature, made neutral with Amberlite IR-120 (H^+) ion-exchange resin, and the resin filtered off and washed with methanol. The filtrate and washings were combined, and evaporated to a syrup which was fractionated on a column of silica gel with 4:1 benzene–ethanol, to give **5** (8.98 g, 85%); m.p. 195–196° (ethanol), $[\alpha]_D^{25}$ −20.3° (*c* 1.3, methanol); ^{1}H-n.m.r. data (dimethyl sulfoxide-d_6): δ 7.50–7.20 (m, 10 H, arom. H), 5.63 (s, 1 H, benzylic-H), 4.98 (d, 1 H, $J_{1,2}$ 1.5 Hz, H-1′), and 0.97 (d, 3 H, $J_{5',6'}$ 6.0 Hz, CH_3-5′).

Anal. Calc. for $C_{29}H_{36}O_{10}$: C, 63.96; H, 6.66. Found: C, 64.13, H, 6.74.

*Benzyl 3-O-allyl-4,6-O-benzylidene-2-O-(2,3,4-tri-O-acetyl-α-*L*-rhamnopyranosyl)-β-*D*-galactopyranoside* (**4**). — A solution of **5** (1.12 g) in 1:1 (v/v) acetic anhydride–pyridine (15 mL) was kept overnight at room temperature. The solvents were removed by codistillation with toluene to give a syrup, which crystallized from ether–petroleum ether to afford **4** (1.27 g, 92%); m.p. 161–162°, $[\alpha]_D^{25}$ −40.0° (*c* 0.8, chloroform); n.m.r. data (chloroform-*d*): δ_H 7.63–7.22 (m, 10 H, arom. H), 5.53 (s, 1 H, benzylic-H), 2.08 (s, 3 H, OAc), 1.98 (s, 6 H, 2 OAc), and 0.89 (d, 3 H, $J_{5',6'}$ 6.0 Hz); δ_C 100.4 (C-1, $^1J_{CH}$ 155.3 Hz) and 97.9 (C-1′, $^1J_{CH}$ 175.8 Hz).

Anal. Calc. for $C_{35}H_{42}O_{13}$: C, 62.68; H, 6.31. Found: C, 62.82; H, 6.40.

*Benzyl 3-O-allyl-2-O-α-*L*-rhamnopyranosyl-β-*D*-galactopyranoside* (**6**). — A solution of **5** (7.16 g) in acetic acid (70 mL) was heated to 90°, water (46 mL) was added in small portions, and the mixture was stirred for 1 h at 90°. The solvents were evaporated, and the last traces of the solvents were removed with the aid of repeated addition and evaporation of toluene. The residue was recrystallized from ethanol, to give **6** (5.46 g, 91%); m.p. 131.5–132.5°, $[\alpha]_D^{25}$ −47.6° (*c* 1.4, methanol).

Anal. Calc. for $C_{22}H_{32}O_{10}$: C, 57.89; H, 7.07. Found: C, 57.78; H, 7.21.

*Benzyl 4,6-di-O-acetyl-3-O-allyl-2-O-(2,3,4-tri-O-acetyl-α-*L*-rhamnopyranosyl)-β-*D*-galactopyranoside* (**7**). — Acetylation of **6** (0.31 g), as described for **5**, gave **7** (0.42 g, 93%); m.p. 115–116° (ethanol), $[\alpha]_D^{25}$ −60.7° (*c* 1.2, chloroform); ^{1}H-n.m.r. data (chloroform-*d*): δ 7.35–7.31 (m, 5 H, arom. H), 2.10, 2.08, 2.07, 2.00, and 1.98 (s, each 3 H, 5 OAc), and 0.92 (d, 3 H, $J_{5',6'}$ 6.0 Hz, CH_3-5′).

Anal. Calc. for $C_{32}H_{42}O_{15}$: C, 57.65; H, 6.35. Found: C, 57.81; H, 6.29.

*Benzyl 4,6-di-O-benzyl-2-O-(2,3,4-tri-O-benzyl-α-*L*-rhamnopyranosyl)-β-*D*-galactopyranoside* (**9**). — Sodium hydride (2.5 g) was added to a solution of **6** (4.25 g) in *N,N*-dimethylformamide (90 mL), and the mixture was stirred for 1 h at room temperature, and then cooled to 0°. Benzyl bromide (14 mL) was added, and the mixture was stirred overnight at room temperature. Methanol was added to decompose the excess of the hydride, and most of the solvent was evaporated. A solution of the residue in chloroform was washed with water, dried (sodium sulfate), and evaporated to a syrup, which was eluted from a column of silica gel with 4:1 hexane–ethyl acetate, to give benzyl 3-*O*-allyl-4,6-di-*O*-benzyl-2-*O*-(2,3,4-tri-*O*-benzyl-α-L-rhamnopyranosyl)-β-D-galactopyranoside (**8**) as a syrup (7.86 g, 93%); $[\alpha]_D^{25}$ −28.8° (*c* 1.2, chloroform). A solution of **8** (6.13 g) in 8:3:1 ethanol–benzene–water (180 mL) containing tris(triphenylphosphine)rhodium(I) chloride (0.37 g) and diazabicyclo[2.2.2]octane (2.0 g) was boiled overnight under reflux, and evaporated to dryness. The residue was dissolved in chloroform, and the solution was washed successively with water, cold M hydrochloric acid, aqueous sodium hydrogencarbonate, and water, dried (sodium sulfate), and evaporated. The residue was dissolved in 9:1 acetone–water (60 mL), and mercuric oxide (2 g) was added, followed by the addition of a solution of mercuric chloride (2 g) in 9:1 acetone–water (60 mL). After the suspension had been stirred for 30 min at room temperature, the solids were removed by filtration, and the filtrate was evaporated to a syrup which was dissolved in ether. The solution was washed successively with water, aqueous potassium iodide, and water, dried (sodium sulfate), and evaporated. The residual syrup was chromatographed on a column of silica gel with 3:1 hexane–ethyl acetate, to give **9** (4.45 g, 76%); m.p. 82–83° (ether–hexane), $[\alpha]_D^{25}$ −20.6° (*c* 1.1, chloroform).

Anal. Calc. for $C_{54}H_{58}O_{10}$: C, 74.80; H, 6.74. Found: C, 74.93; H, 6.86.

*Benzyl 4,6-di-O-benzyl-3-O-(2,3,4,6-tetra-O-acetyl-β-*D*-glucopyranosyl)-2-O-(2,3,4-tri-O-benzyl-α-*L*-rhamnopyranosyl)-β-*D*-galactopyranoside* (**11**). — To a stirred solution (cooled to −30°) of **9** (3.15 g, 3.6 mmol), silver triflate (2.25 g, 8.8 mmol), and 1,1,3,3-tetramethylurea (2.1 mL, 17.6 mmol) in dichloromethane (30 mL) was added dropwise a solution of **10** (3.0 g, 7.3 mmol) in dichloromethane (20 mL) during 30 min. The mixture was stirred for 1 h at −30° and overnight at room temperature, and then processed as described previously. The resulting syrupy product was chromatographed on a column of silica gel with 2:1 hexane–ethyl acetate, to give **11** (3.35 g, 77%); m.p. 150–152° (ethanol), $[\alpha]_D^{25}$ −39.1° (*c* 1.0, chloroform); n.m.r. data (chloroform-*d*): δ_H 7.49–7.11 (m, 30 H, arom. H), 2.06 (s, 3 H, OAc), 2.02 (s, 6 H, 2 OAc), 1.88 (s, 3 H, OAc), and 1.12 (d, 3 H, $J_{5',6'}$ 6.0 Hz, CH_3-5'); δ_C 100.9 (C-1″, $^1J_{C,H}$ 159.7 Hz), 100.3 (C-1, $^1J_{C,H}$ 161.2 Hz), and 98.0 (C-1′, $^1J_{CH}$ 172.9 Hz).

Anal. Calc. for $C_{68}H_{76}O_{19}$: C, 68.21; H, 6.40. Found: C, 68.39; H, 6.53.

*Benzyl 4,6-di-O-benzyl-3-O-β-*D*-glucopyranosyl-2-O-(2,3,4-tri-O-benzyl-α-*L*-rhamnopyranosyl)-β-*D*-galactopyranoside* (**12**). — *O*-Deacetylation of **11** (2.95 g), as described previously, gave **12** as an amorphous solid (2.41 g, 95%); m.p. 93–97° (ethanol), $[\alpha]_D^{25}$ −12.9° (*c* 0.9, methanol).

Anal. Calc. for $C_{60}H_{68}O_{15}$: C, 70.02; H, 6.66. Found: C, 69.87; H, 6.81.

*3-O-β-*D*-Glucopyranosyl-2-O-α-*L*-rhamnopyranosyl-*D*-galactose* (**13**). — A solution of **12** (1.97 g) in acetic acid (20 mL) was hydrogenolyzed in the presence of 10% palladium-on-charcoal (1.7 g) at normal pressure for 3 days at room temperature. The catalyst was filtered off, and washed with methanol. The filtrate and washings were combined, and evaporated to a syrup, which was eluted from a column of silica gel with 3:2 chloroform–methanol, to give **13** (0.73 g, 78%); m.p. 195–197° (dec.) (methanol–ethanol) after slight foaming at 145–160°, $[\alpha]_D^{25}$ −7.2 (5 min) → −4.5° (1 h, constant; *c* 1.2, water); lit. m.p. 200° (dec.) (methanol–ethanol) after foaming at 150–160°, $[\alpha]_D^{20}$ −7.5 (5 min) → −4.4° (1 h; *c* 1.64, water)[1]; m.p.

~196° (dec.) after foaming at 145–160°, $[\alpha]_D^{27}$ −6.8 (5 min) → −3.9° (1 h; *c* 1.15, water)[3].

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