Carbohydrate Research, 156 (1986) 218–224
Elsevier Science Publishers B.V., Amsterdam – Printed in The Netherlands

Note

Chemical modification of melibiose: synthesis of 6′-acetamido derivatives

SINICHI OTANI, SHIRO HASHIMOTO, AND KIYOSHI MATSUMOTO
Department of Chemistry, College of Liberal Arts and Sciences, Kyoto University, Nihonmatsu-cho, Yoshida, Sakyo-ku, Kyoto 606 (Japan)

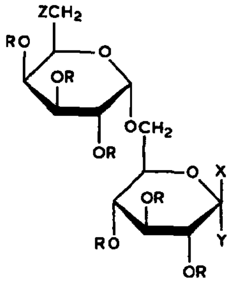
(Received October 9th, 1985; accepted for publication in revised form, January 30th, 1986)

Several papers have been published concerning the chemical modification of melibiose[1–7] (**1**), but no amino derivative has been synthesized. The present work describes the synthesis of 6′-acetamido-6′-deoxy derivatives of melibiose.

Methyl β-melibioside (**5**) was first synthesized as an amorphous product by Levene *et al.*[1] by Koenigs–Knorr reaction of hepta-*O*-acetylmelibiosyl bromide and silver carbonate with methanol, followed by deacetylation. They arbitrarily described the glycoside as the β anomer, but without supporting evidence. Samples of amorphous **5**, obtained similarly from hepta-*O*-benzoylmelibiosyl bromide and hepta-*O*-acetylmelibiosyl bromide, were identical[8,9] and homogeneous by t.l.c., and by g.l.c.[10] (after trimethylsilylation). Elemental analysis showed the product to be a methyl melibioside monohydrate. The ^{13}C-n.m.r. spectrum in D_2O showed the C-1 peak at 104.2 and methyl carbon peak at 58.1 p.p.m., indicating the glycoside to be β.

For introduction of the amino group, the 6′-azido-6′-deoxy derivative was prepared from the 6′-*O-p*-tolylsulfonyl derivative and sodium azide in hexamethylphosphoric triamide. For the selective sulfonylation of the group at C-6′, methyl β-melibioside was treated with chlorotriphenylmethane and then peracetylated to give methyl 2,2′,3,3′,4,4′-hexa-*O*-acetyl-6′-*O*-trityl-β-melibioside (**6**). Compound **6** was detritylated[3] to methyl 2,2′,3,3′,4,4′-hexaacetate (**7**), which was treated with *p*-toluenesulfonyl chloride in pyridine to give the desired 6′-*O-p*-tolylsulfonyl derivative[11] (**8**). This synthetic route, however, was laborious and resulted in poor yields (19% for **8**). Therefore, the *p*-tolylsulfonyloxy group was introduced directly at C-6′ by treatment of **5** with *p*-toluenesulfonyl chloride in pyridine at −15°. Compound **8** was obtained, after peracetylation, in 47% yield.

Compound **8** was converted into the corresponding 6′-azido-6′-deoxy derivative (**9**) in 53% yield by treatment with sodium azide in hexamethylphosphoric triamide[12], and this product was then reduced with hydrogen and 5% palladium-on-carbon, and subsequently acetylated with acetic anhydride in pyridine to give the 6′-acetamido-6′-deoxy derivative (**10**) in 91% yield[12]. Treatment of **10** with methanolic sodium methoxide gave amorphous methyl 6′-acetamido-6′-deoxy-β-



1 R = H, X,Y = H, OH, Z = OH
2 R = Bz, X = Z = OBz, Y = H
3 R = Bz, X = OMe, Y = H, Z = OBz
4 R = Ac, X = OMe, Y = H, Z = OAc
5 R = Y = H, X = OMe, Z = OH
6 R = Ac, X = OMe, Y = H, Z = OTr
7 R = Ac, X = OMe, Y = H, Z = OH
8 R = Ac, X = OMe, Y = H, Z = OTs
9 R = Ac, X = OMe, Y = H, Z = N_3
10 R = Ac, X = OMe, Y = H, Z = NHAc
11 R = Y = H, X = OMe, Z = NHAc
12 R = Ac, X = OBn, Y = H, Z = OAc
13 R = Bz, X = OBn, Y = H, Z = OBz
14 R = Y = H, X = OBn, Z = OH
15 R = Ac, X = OBn, Y = H, Z = OTs
16 R = Ac, X = OBn, Y = H, Z = N_3
17 R = Ac, X = OBn, Y = H, Z = NHAc
18 R = Y = H, X = OBn, Z = NHAc

Ac = acetyl, Bn = benzyl, Bz = benzoyl, Tr = trityl, Ts = *p*-tolylsulfonyl

melibioside monohydrate (**11**), whose structure was confirmed by its ^{13}C-n.m.r. spectrum and elemental analysis.

Benzyl melibioside derivatives were synthesized analogously. Benzyl β-melibioside monohydrate (**14**), prepared from the octabenzoate and the octa-acetate via the Koenigs–Knorr reaction of the corresponding hepta-*O*-acyl-melibiosyl bromide, with subsequent deacylation, was directly *p*-toluenesulfonated at C-6′, acetylated (**15**), treated with sodium azide (**16**), reduced with sodium borohydride[13], *N*-acetylated (**17**), and deacetylated with sodium methoxide, to give benzyl 6′-acetamido-6′-deoxy-β-melibioside (**18**) as a monohydrated, amorphous product, whose structure was proved by ^{13}C-n.m.r. spectroscopy.

EXPERIMENTAL

General methods. — Melting points were measured in capillary tubes with a Yamato melting-point apparatus MP-21 and are uncorrected. Column chromatography was performed on Wakogel C-200 (100–200 mesh). G.l.c. was performed for the trimethylsilylated sugars with a Shimadzu gas chromatograph GC-4CMPF equipped with a hydrogen flame-ionization detector. The carrier gas was nitrogen, with flow rates between 30 and 50 mL/min at 250°. Glass columns containing 5% silicone GESE-30 on Shimalite W (60–80 mesh) were 2 m × 0.32 cm (i.d.). I.r. spectra were recorded with a Hitachi 215 grating infrared spectrophotometer. ^{1}H-N.m.r. spectra (90 MHz) were recorded with a Hitachi R-40 n.m.r. spectrometer and ^{13}C-n.m.r. spectra (22.5 MHz) with a JEOL FX-90Q spectrometer. Optical rotations were determined with a Jasco DIP-140 digital polarimeter.

Methyl hepta-O-benzoyl-β-melibioside (**3**). — To β-melibiose octabenzoate[2] (**2**, 80 g) in chloroform (160 mL) was added hydrogen bromide in acetic acid (32%, 320 g). The solution was stirred for 5 h at room temperature, and evaporated to a syrup. After stirring a mixture of the syrup in toluene (400 mL) with Drierite (40.0 g) and silver carbonate (44.0 g) for 10 min, methanol (160 mL) was added and the mixture was stirred for 48 h at room temperature[14]. The filtrate from the mixture was evaporated, and the residue triturated with ethanol to give an amorphous precipitate (48.6 g) that was chromatographed on a column of silica gel with 19:1 (v/v) benzene–ethyl acetate and crystallized from ethanol–ethyl acetate; yield, 23.3 g (31.5%), m.p. 165–166°, $[\alpha]_D^{27}$ +136° (*c* 2.02, chloroform); ^{1}H-n.m.r.($CDCl_3$): δ 3.44 (s, 3 H, CH_3) and 7.34–8.12 (m, 35 H, 7 Ph).

Anal. Calc. for $C_{62}H_{52}O_{18}$: C, 68.62; H, 4.84. Found: C, 68.12; H, 4.86.

Methyl β-melibioside monohydrate (**5**). — (*A*) A solution of **3** (10.0 g) in 0.5M methanolic sodium methoxide (125 mL) and methanol (375 mL) was boiled under reflux for 4 h, deionized with a column of Amberlite IR-120 resin (H^+, 250 mL), and then evaporated. A solution of the residue in water (250 mL) was washed with chloroform, treated with charcoal, and then evaporated to a syrup. The syrup was purified from ethanol–ether to give a white powder (3.0 g, 88%), that was homogeneous on g.l.c. in the trimethylsilylated form[8]. For t.l.c., silica gel plates were dipped in 0.5M aqueous sodium dihydrogenphosphate, air dried, and heated for 1 h at 105°. Compound **5** was developed with 2:2:1 (v/v) 2-propanol–acetone–0.1M aqueous lactic acid[9] and detected by heating at 100° with a reagent composed of diphenylamine (2 g) and aniline (2 mL) in acetone (100 mL) and 80% phosphoric acid (15 mL)[10]. The chromatogram showed **5** to be homogeneous, m.p. 102–105°, $[\alpha]_D^{21}$ +84.0° (*c* 1.93, water); ν_{max}^{Nujol} 3390 cm^{-1} (OH); ^{1}H-n.m.r. (D_2O): δ 3.52 (s, 3 H, CH_3); ^{13}C-n.m.r.: δ 104.2 (C-1), 98.8 (C-1′), 76.7, 75.0, 74.0, 71.7, 70.3, 70.2, 70.1, 69.2, 66.2 (C-6), 61.9 (C-6′), and 58.1 (CH_3).

Anal. Calc. for $C_{13}H_{24}O_{11}$: C, 41.70; H, 7.01. Found: C, 41.87; H, 7.11.

(*B*) Methyl hepta-*O*-acetyl-β-melibioside (**4**, 4.8 g), prepared by the method of Levene *et al.*[1], was dissolved in 0.5M methanolic sodium methoxide (125 mL) and methanol (300 mL). The solution was boiled under reflux for 5 h and treated as in the preceding experiment to give a white powder (2.3 g, 85%). By g.l.c. of trimethylsilylated product[8] and by t.l.c.[9,10], the product was indistinguishable from that obtained from **4**; m.p. 100–105°, $[\alpha]_D^{27}$ +83.0° (*c* 1.91, water); lit.[1] $[\alpha]_D^{27}$ +75.0°.

Methyl 2,2′,3,3′,4,4′-hexa-O-acetyl-6′-O-trityl-β-melibioside (**6**). — A solution of **5** (1.0 g) and chlorotriphenylmethane (1.0 g) in dry pyridine (20 mL) was stirred for 48 h at room temperature, and then treated with acetic anhydride (10 mL) and pyridine (10 mL) overnight at room temperature, poured into ice–water (400 mL), and the mixture filtered. The precipitate was chromatographed on a column of silica gel with 4:1 (v/v) benzene–ethyl acetate and the product recrystallized from ethanol; yield, 1.4 g (64%), m.p. 144–145°, $[\alpha]_D^{27}$ +46.9° (*c* 2.07, chloroform); ν_{max}^{Nujol} 1750 (C=O) and 1600 cm^{-1} (aromatic); ^{1}H-n.m.r. ($CDCl_3$): δ

1.86, 1.96, 2.03, 2.08 (4s, 12 H, 4 Ac), 2.00 (s, 6 H, 2 Ac), 3.47 (s, 3 H, MeO), and 7.31 (m, 15 H, 3 Ph).

Anal. Calc. for $C_{44}H_{50}O_{17}$: C, 62.12; H, 5.88. Found: C, 62.03; H, 6.01.

Methyl 2,2',3,3',4,4'-hexa-O-acetyl-β-melibioside (**7**). — A solution of **6** (1.0 g) in acetic acid (4 mL) and water (1 mL) was heated[3] for 1.5 h at 100°. After being kept at room temperature overnight, the mixture was cooled with an ice-bath, filtered, and the filtrate washed with 80% aqueous acetic acid. The filtrate and washings were combined, evaporated, and the resultant syrup was purified on a column of silica gel with 4:1 (v/v) chloroform–acetone. The product was recrystallized from ethanol; yield, 0.45 g (63%), m.p. 160–161.5°, $[\alpha]_D^{27}$ +107° (*c* 1.01, chloroform); ν_{max}^{Nujol} 3510 (OH) and 1750 cm^{-1} (C=O); ^{1}H-n.m.r. ($CDCl_3$): δ 1.98, 2.06 (2s, 6 H, 2 Ac), 2.03, 2.10 (2 s, 12 H, 2 × 2 Ac), and 3.46 (s, 3 H, MeO).

Anal. Calc. for $C_{25}H_{36}O_{17}$: C, 49.37; H, 5.92. Found: C, 49.17; H, 6.06.

Methyl 2,2',3,3',4,4'-hexa-O-acetyl-6'-O-p-tolylsulfonyl-β-melibioside (**8**). — (*A*) Solutions of **7** (0.5 g) in pyridine (4 mL) at −15° and of *p*-toluenesulfonyl chloride (0.5 g) in pyridine (3.5 mL) at −15° were mixed, and the resulting solution was kept for 4 h at −15°, overnight at 5°, and then for 24 h at room temperature, poured into ice–water (100 mL), and extracted with dichloromethane (3 × 20 mL). Conventional processing of the extract, and purification of the product on a column of silica gel with 2:1 (v/v) benzene–ethyl acetate gave a glassy solid (0.3 g, 48%), $[\alpha]_D^{28}$ +84.5° (*c* 2.01, chloroform); ν_{max}^{Nujol} 1750 (C=O), 1600 (aromatic), and 1180 cm^{-1} (SO_2); ^{1}H-n.m.r. ($CDCl_3$): δ 1.97, 2.09 (2s, 6 H, 2 Ac), 2.03 (s, 12 H, 4 Ac), 2.44 (s, 3 H, $CH_3C_6H_4SO_2$), 3.44 (s, 3 H, MeO), and 7.28–7.82 (m, 4 H, $CH_3C_6H_4SO_2$).

Anal. Calc. for $C_{32}H_{42}O_{19}S$: C, 50.38; H, 5.56. Found: C, 50.01; H, 5.49.

(*B*) Compound **5** (1.0 g) was directly *p*-toluenesulfonated as before, and then acetylated with acetic anhydride and pyridine to give **8** as a glassy solid (0.95 g, 47%).

Methyl 2,2',3,3',4,4'-hexa-O-acetyl-6'-azido-6'-deoxy-β-melibioside (**9**). — A solution of **8** (2.5 g) and sodium azide (1.9 g) in hexamethylphosphoric triamide (75 mL) was stirred[12] for 72 h at 55–60°, diluted with ethyl acetate (250 mL), washed with water, dried with sodium sulfate, and evaporated to a syrup. Purification on a column of silica gel with 2:3 (v/v) ether–benzene gave a glassy solid (1.1 g, 53%); $[\alpha]_D^{13}$ −101° (*c* 2.01, chloroform); ν_{max}^{Nujol} 2110 (N_3) and 1755 cm^{-1} (C=O); ^{1}H-n.m.r. ($CDCl_3$): δ 1.97, 2.01 (2s, 12 H, 2 × 2 Ac), 2.09, 2.11 (2 s, 6 H, 2 Ac), and 3.44 (s, 3 H, MeO).

Anal. Calc. for $C_{25}H_{35}N_3O_{16}$: C, 47.39; H, 5.57; N, 6.63. Found: C, 47.25; H, 5.55; N, 6.33.

Methyl 6'-acetamido-2,2',3,3',4,4'-hexa-O-acetyl-6'-deoxy-β-melibioside (**10**). — A solution of **9** (1.5 g) in ethanol (150 mL) was hydrogenated[12] with 5% palladium-on-carbon (0.6 g) and hydrogen at atmospheric pressure for 24 h, evaporated to a syrup, and acetylated with acetic anhydride (3 mL) and pyridine (15 mL) overnight at room temperature. Repeated evaporation of toluene from the product gave a syrup that was purified on a column of silica gel with 9:1 (v/v) ethyl acetate–methanol and crystallized from ethanol–petroleum ether; yield, 1.4 g (91%); m.p. 167–168.5°, $[\alpha]_D^{27}$ +95.8° (*c* 1.00, chloroform); ν_{max}^{Nujol} 3430 (NH), 1750 (CO in CH_3COO), and 1670 cm^{-1} (C=O in CH_3CON); ^{1}H-n.m.r. ($CDCl_3$): δ 1.93, 2.07, 2.12 (3s, 9 H, 3 Ac), 1.95, 2.01 (2s, 12 H, 2 × 2 Ac), 3.44 (s, 3 H, MeO), and 5.83 (m, 1 H, NH).

Anal. Calc. for $C_{27}H_{39}NO_{17}$: C, 49.92; H, 6.05; N, 2.16. Found: C, 49.74; H, 6.21; N, 1.88.

Methyl 6'-acetamido-6'-deoxy-β-melibioside monohydrate (**11**). — A solution of **10** (0.4 g) and methanolic 0.05M sodium methoxide (1 mL) in dry methanol (6 mL) was stirred for 30 min at room temperature, deionized with Amberlite IR-120 resin (H^+, 5 mL) for 30 min, evaporated to a syrup, and treated with ethanol–ether to give a hygroscopic, amorphous powder (0.2 g, 79%), which was homogeneous on g.l.c. in the trimethylsilylated form[8]; m.p. 120–130°, $[\alpha]_D^{27}$ +146° (*c* 0.96, water); ν_{max}^{Nujol} 3340 (NH, OH) and 1640 cm^{-1} (C=O); ^{1}H-n.m.r. (dimethyl sulfoxide-d_6): δ 1.81 (s, 3 H, Ac), 3.35 (s, 3 H, MeO); ^{13}C-n.m.r. (pyridine-d_5): δ 171.5 (C=O), 104.5 (C-1), 100.0 (C-1'), 77.9, 75.7, 75.5, 70.7, 70.6, 69.8 (overlapped), 67.3, 56.4 (MeO), 40.7 (C-6'), and 22.6 (CH_3CO).

Anal. Calc. for $C_{15}H_{27}O_{11}N \cdot H_2O$: C, 43.36; H, 7.05; N, 3.37. Found: C, 43.86; H, 7.63; N, 2.84.

Benzyl hepta-O-acetyl-β-melibioside (**12**). — To β-melibiose octaacetate (10.2 g) in acetic anhydride (16 mL) was added hydrogen bromide in acetic acid (30%, 35 mL). The solution was stirred for 5 h at room temperature, poured into ice–water (500 mL), and extracted with dichloromethane (3 × 100 mL). Conventional isolation gave a syrup. A mixture of the syrup in toluene (80 mL), benzyl alcohol (20 mL), silver carbonate (11.0 g) and Drierite (5 g) was stirred for 72 h at room temperature[13], filtered, and the filtrate evaporated to a syrup, which was purified on a column of silica gel with 2:1 (v/v) benzene–ethyl acetate to give a glassy solid (6.36 g, 58%), $[\alpha]_D^{31}$ +50.2° (*c* 1.00, chloroform); ^{1}H-n.m.r. ($CDCl_3$): δ 2.00 (s, 15 H, 5 CH_3), 2.10, 2.13 (2s, 6 H, 2 CH_3), 7.29 (s, 5 H, Ph); ^{13}C-n.m.r. (pyridine-d_5): δ 99.9 (C-1), 96.9 (C-1'), 73.6, 73.1, 72.0, 70.9, 69.5, 68.7 (overlapped), 68.2, 67.2, 66.5, and 62.1; 170.5, 170.2, 170.1, 169.8, and 169.5 (C=O); 137.9, 128.8, 128.1, and 128.0 (Ph); 20.5 and 20.3 (CH_3CO).

Anal. Calc. for $C_{33}H_{42}O_{18}$: C, 54.53; H, 5.84. Found: C, 54.41; H, 5.86.

Benzyl hepta-O-benzoyl-β-melibioside (**13**). — To β-melibiose octabenzoate[1] (30 g) in chloroform (60 mL) was added hydrogen bromide in acetic acid (24%, 90 mL), and the solution was stirred for 5 h at room temperature, washed successively with water, M aqueous sodium hydrogencarbonate, and water, dried with magnesium sulfate, and evaporated to a syrup. A mixture of the syrup, benzyl alcohol (50 mL), and silver carbonate (16.5 g) in toluene (150 mL) was stirred overnight at room temperature, filtered and the filtrate evaporated to a syrup. Crystallization from hot ethanol gave colorless crystals (16.5 g, 56%), m.p. 143–146°, $[\alpha]_D^{29}$ +116° (*c* 1.00, chloroform); ν_{max}^{Nujol} 1730 (C=O) and 1600 cm^{-1} (aromatic); ^{1}H-n.m.r. ($CDCl_3$): δ 7.29 (s, 5 H, $C_6H_5CH_2$) and 7.37–8.15 (m, 35 H, 7C_6H_5CO).

Anal. Calc. for $C_{68}H_{56}O_{18}$: C, 70.33; H, 4.86. Found: C, 70.15; H, 4.70.

Benzyl β-melibioside monohydrate (**14**). — (*A*) To **12** (13.53 g) in methanol (240 mL) was added sodium (2.4 g) in methanol (720 mL). The solution was boiled under reflux for 4 h, deionized with Amberlite IR-120 resin (H^+, 750 mL) and evaporated to a syrup. The syrup was dissolved in water (500 mL), washed with dichloromethane (2 × 100 mL), treated with charcoal, and evaporated to a glassy solid (7.5 g, 86%), which was homogeneous on g.l.c. in the trimethylsilylated form[8]; $[\alpha]_D^{31}$ +44.9° (c 0.96, water); ν_{max}^{Nujol} 3310 cm^{-1} (OH); ^1H-n.m.r. (D_2O): δ 7.40 (s, 5 H, Ph); ^{13}C-n.m.r.: δ 104.9 (C-1), 100.6 (C-1'), 78.5, 76.8, 75.7, 74.2, 73.4, 72.1 (overlapped), 71.8, 71.0, 68.1, and 63.6; 137.7, 130.0, 129.2, and 125.6 (Ph).

Anal. Calc. for $C_{19}H_{28}O_{11} \cdot H_2O$: C, 50.65; H, 6.73. Found: C, 50.71; H, 6.77.

(*B*) To **13** (10 g) was added sodium methoxide in methanol (1.2 g of sodium in 600 mL of methanol). The solution was boiled under reflux for 3 h and evaporated to give a partially crystalline syrup. The product was dissolved in 2.5% aqueous acetic acid (100 mL), and the solution was washed with chloroform (2 × 50 mL), deionized with a column of Amberlite IR-120 resin (H^+), 120 mL), evaporated, and treated with methanol–ethyl acetate to give a precipitate (3.46 g, 98%) that was homogeneous on g.l.c. in the trimethylsilylated form[8]. The ^1H-n.m.r. spectrum coincided with that of the product obtained from **12**; m.p. 128–131°, $[\alpha]_D^{29}$ +45.0° (c 0.96, water).

Anal. Calc. for $C_{19}H_{28}O_{11} \cdot H_2O$: C, 50.65; H, 6.73. Found: C, 50.72; H, 6.30.

Benzyl 2,2',3,3',4,4'-hexa-O-acetyl-6'-O-p-tolylsulfonyl-β-melibioside (**15**). — Solutions of **14** (1.0 g) in pyridine (10 mL) at −10°, and of *p*-toluenesulfonyl chloride (0.5 g) in pyridine (10 mL) at −10° were mixed and the resulting solution was kept for 4 h at −10°, overnight at 5°, and then for 24 h at room temperature. After treatment with acetic anhydride (10 mL) and pyridine (10 mL) overnight, the solution was poured into ice–water (200 mL) and extracted with dichloromethane (3 × 30 mL). Conventional isolation of the product with purification on a column of silica gel with 3:1 (v/v) benzene–ethyl acetate gave a glassy solid (0.75 g, 38%), $[\alpha]_D^{32}$ +47.5° (c 1.00, chloroform); ν_{max}^{Nujol} 1760 (C=O), 1600 (aromatic), and 1180 cm^{-1} (SO_2); ^1H-n.m.r. ($CDCl_3$): δ 1.95, 2.02, 2.04, 2.09 (4s, 12 H, 4 Ac), 1.98 (s, 6 H, 2 Ac), 2.43 (s, 3 H, $CH_3C_6H_4$), 7.27 (s, 5 H, Ph), and 7.32–7.78 (m, 4 H, $CH_3C_6H_4$).

Anal. Calc. for $C_{38}H_{46}O_{19}S$: C, 54.40; H, 5.54. Found: C, 54.36; H, 5.80.

Benzyl 2,2',3,3',4,4'-hexa-O-acetyl-6'-azido-6'-deoxy-β-melibioside (**16**). — A solution of **15** (1.0 g) and sodium azide (0.75 g) in hexamethylphosphoric triamide (30 mL) was stirred[12] for 72 h at 60–65°, diluted with ethyl acetate (100 mL), washed with water, and evaporated to a syrup, which was purified on a column of silica gel with 4:1 (v/v) benzene–ethyl acetate to give a glassy solid (0.74 g, 87%), $[\alpha]_D^{32}$ +58.2° (c 1.00, chloroform); ν_{max}^{Nujol} 2110 (N_3) and 1750 cm^{-1} (C=O); ^1H-n.m.r. ($CDCl_3$): δ 1.98 (s, 9 H, 3 CH_3), 2.01, 2.09, 2.13 (s, 9 H, 3 CH_3), and 7.28 (s, 5 H, Ph).

Anal. Calc. for $C_{31}H_{39}N_3O_{16}$: C, 52.46; H, 5.55; N, 5.92. Found: C, 52.39; H, 5.57; N, 5.83.

Benzyl 6'-acetamido-2,2',3,3',4,4'-hexa-O-acetyl-6'-deoxy-β-melibioside (**17**). — To **16** (1.1 g) in *N,N*-dimethylformamide (15 mL) was added sodium borohydride[13] (0.38 g) during 15 min with stirring at room temperature. After being kept for 3 h at 60°, the mixture was poured into ice–water (200 mL) and extracted with dichloromethane (3 × 30 mL). The extract was washed with water, evaporated, and acetylated with acetic anhydride (10 mL) and pyridine (10 mL) overnight at room temperature. Purification of the product on a column of silica gel with ethyl acetate gave a glassy solid (0.90 g, 81%), $[\alpha]_D^{31}$ +54.0° (*c* 1.00, chloroform); ν_{max}^{Nujol} 3380 (NH), 1750 (C=O in CH_3CO_2), and 1650 cm^{-1} (C=O in CH_3CON); ^1H-n.m.r. ($CDCl_3$): δ 1.92, 2.02, 2.08, 2.13 (4s, 12 H, 4 CH_3), 1.98 (s, 9 H, 3 CH_3), 5.83 (m, 1 H, NH), and 7.28 (s, 5 H, Ph).

Anal. Calc. for $C_{33}H_{43}NO_{17}$: C, 54.61; H, 5.98; N, 1.93. Found: C, 54.38; H, 6.18; N, 1.82.

Benzyl 6'-acetamido-6'-deoxy-β-melibioside monohydrate (**18**). — To **17** (1.8 g) in methanol (15 mL) was added 0.05M methanolic sodium methoxide (2.5 mL), and the solution was stirred for 30 min at room temperature, deionized with Amberlite IR-120 resin (H^+, 15 mL) for 30 min, and evaporated to amorphous powder (0.89 g, 69%), which was homogeneous on g.l.c. in the trimethylsilylated form[8]; m.p. 202–204°, $[\alpha]_D^{31}$ +47.6° (*c* 0.96, methanol); ν_{max}^{Nujol} 3330 (NH, OH) and 1620 cm^{-1} (C=O); ^1H-n.m.r. (dimethyl sulfoxide-d_6): δ 1.81 (s, 3 H, CH_3), 7.33 (s, 5 H, Ph); ^{13}C-n.m.r. (pyridine-d_5): δ 171.1 (C=O), 103.8 (C-1), 100.3 (C-1'), 78.4, 76.0, 74.9, 71.7, 71.2, 70.9 (overlapped), 70.3 (overlapped), 67.8, 41.2 (C-6'), and 23.0 (CH_3); and 138.6, 128.6, 128.4 and 127.7 (Ph).

Anal. Calc. for $C_{21}H_{31}NO_{11}\cdot H_2O$: C, 51.31; H, 6.78; N, 2.85. Found: C, 51.89; H, 6.69; N, 2.70.

REFERENCES

1 P. A. Levene and E. Jorpes, *J. Biol. Chem.*, 86 (1930) 403–415.
2 L. M. Lerner, *J. Org. Chem.*, 32 (1967) 3663–3665.
3 N. K. Kochetkov, A. F. Bochkov, and I. G. Yazlovetsky, *Carbohydr. Res.*, 5 (1967) 243–244; N. K. Kochetkov, A. F. Bochkov, I. G. Yazlovetsky, and V. I. Snyatkova, *Izv. Akad. Nauk SSSR, Ser, Khim.*, (1968) 1802–1812; *Chem. Abstr.*, 70 (1969) 4467a.
4 A. B. Zanlungo, J. O. Deferrari, and R. A. Cadenas, *J. Chem. Soc., C*, (1970) 1908–1911.
5 H. E. Gelpi, J. O. Deferrari, and R. A. Cadenas, *J. Chem. Soc., C*, (1971) 3354–3357.
6 G. O. Aspinall, T. N. Krishnamurthy, W. Mitura, and M. Funabashi, *Can. J. Chem.*, 53 (1975) 2182–2188.
7 R. Adachi and T. Suami, *Bull. Chem. Soc. Jpn.*, 50 (1977) 1901–1902.
8 S. A. Hansen, *J. Chromatogr.*, 107 (1975) 224–226.
9 R. W. Bailey and E. J. Bourne, *J. Chromatogr.*, 4 (1960) 206–213.
10 J. S. Sawardeker and J. H. Sloneker, *Anal. Chem.*, 37 (1965) 945–947.
11 S. Tejima and Y. Okamori, *Chem. Pharm. Bull.*, 20 (1972) 2036–2041.
12 Y. Okamori, M. Haga, and S. Tejima, *Chem. Pharm. Bull.*, 21 (1973) 2538–2544.
13 Y. Ali and A. C. Richardson, *Carbohydr. Res.*, 5 (1967) 441–448.
14 D. H. Leaback and P. G. Walker, *J. Chem. Soc.*, (1957) 4750–4760.