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CORD-FACTOR ANALOGS: SYNTHESIS OF 6,6′-DI-*O*-MYCOLOYL- AND -CORYNOMYCOLOYL-(α-D-MANNOPYRANOSYL α-D-MANNOPYRANOSIDE)

AVRAHAM LIAV AND MAYER B. GOREN*
Department of Molecular and Cellular Biology, National Jewish Hospital and Research Center, Denver, Colorado 80206 (U.S.A.)
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ABSTRACT

Selective triflation of 4,6:4′,6′-di-*O*-benzylidene-α,α-trehalose gave 4,6:4′,6′-di-*O*-benzylidene-2,2′-di-*O*-triflyl-α,α-trehalose, the structure of which was confirmed by the ^{1}H-n.m.r. spectrum of its 3,3′-di-*O*-acetyl derivative (**4**). Treatment of **4** with sodium nitrite in hexamethylphosphoric triamide, followed by benzylation, afforded 2,3,2′,3′-tetra-*O*-benzyl-4,6:4′,6′-di-*O*-benzylidene-(α-D-mannopyranosyl α-D-mannopyranoside (**7**). Removal of the two benzylidene groups from **7**, and selective tosylation of the product, gave a mixture of the 6,6′-ditosylate (**11**) and the 6-monotosylate (**12**), which were separated by chromatography. Treatment of **11** with potassium corynomycolate or potassium mycolate afforded the corresponding 6,6′-diesters, **14** and **15**, respectively. Treatment of the monotosylate **12** with potassium corynomycolate gave the 6-monoester **18**. Catalytic hydrogenolysis of **14**, **15**, and **18** gave the respective cord-factor analogs.

INTRODUCTION

For the purpose of correlating their structures with their biological activities, our laboratory has been involved in the synthesis of cord-factors (6,6′-di-*O*-mycoloyl-α,α-trehalose) and cord-factor analogs, and several syntheses of this type of biologically important compound have been described (see ref. 1 and references cited therein). In these syntheses, diverse linkages between the disaccharide and the lipid moieties were investigated. In continuation of this study, and in order to probe stereochemical requirements for expression of various biological activities, we are now interested in synthesizing cord-factor analogs in which the natural sugar (α,α-trehalose) is replaced by the corresponding D-*galacto*- and D-*manno* disaccharides[2].

*Also, Department of Microbiology and Immunology, University of Colorado Health Sciences Center, Denver, Colorado, U.S.A. To whom correspondence should be addressed, at National Jewish Hospital.

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Although a per-*O*-benzylated D-*manno* analog of α,α-trehalose has been synthesized from suitable tetra-*O*-benzyl-D-mannopyranosyl derivatives[3,4], the methods reported did not provide the selective activation of O-6 and O-6′ necessary for introduction of the ester groups. We now describe the synthesis of a suitably blocked α-D-mannopyranosyl α-D-mannopyranoside derivative and its conversion into 6,6′-di-*O*-mycoloyl- and 6,6′-di-*O*-corynomycoloyl-(α-D-mannopyranosyl α-D-mannopyranoside). Also described is the synthesis of 6-*O*-corynomycoloyl-(α-D-mannopyranosyl α-D-mannopyranoside), analogous to 6-*O*-corynomycoloyl-α,α-trehalose[5].

RESULTS AND DISCUSSION

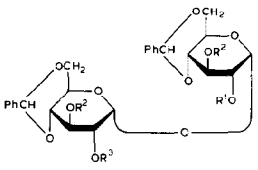
Treatment of 4,6:4′,6′-di-*O*-benzylidene-α,α-trehalose[6] (**1**) with trifluoromethanesulfonyl chloride in pyridine for 1 h gave a mixture of two components: 4,6:4′,6′-di-*O*-benzylidene-2,2′-di-*O*-trifluoromesyl-α,α-trehalose (**2**, 21% yield) and 4,6:4′,6′-di-*O*-benzylidene-2-*O*-trifluoromesyl-α,α-trehalose (**3**, 57% yield). The ditrifluoromethanesulfonate **2** could be obtained as the sole product (77% yield) when the reaction was conducted for 24 h with a slight excess of the chloride. The structure of **2** was confirmed by the ^{1}H-n.m.r. spectrum of the corresponding 3,3′-di-*O*-acetyl derivative: the signal of H-3 was shifted to lower field (δ 5.72, $J_{3,2} = J_{3,4} = 9.5$ Hz) owing to the deshielding effect of the adjacent *O*-acetyl group.

Before solvolyzing the trifluoromethanesulfonate groups in **2**, we found it necessary to block OH-3 in order to avoid complicating side-reactions, and the tetrahydropyran-2-yl group[7] was employed for this. The 3,3′-di-(tetrahydropyran-2-yl) ether **5** was obtained in 88% yield by treatment of **2** with dihydropyran in dichloromethane in the presence of pyridinium *p*-toluenesulfonate. Solvolysis of **5** with sodium benzoate in hexamethylphosphoric triamide then afforded the α-D-mannopyranosyl α-D-mannopyranoside derivative **6** in satisfactory yield. However, attempts to remove the benzylidene groups selectively from **6** were unsuccessful and this approach was abandoned. It should be noted that it is mandatory to keep OH-3 blocked during the ultimate conversion into the 6,6′-diester, in order to avoid 3,6-anhydro-ring formation; see ref. 8.

In a recent study[9], methyl 3-*O*-acetyl-4,6-*O*-benzylidene-α-D-glucopyranoside was converted into a mixture of 2-*O*-acetyl- and 3-*O*-acetyl-α-D-mannopyranoside derivatives (as a result of participation by the neighboring acetyl group) by treatment with tetrabutylammonium nitrite in acetonitrile. Similarly, when the acetate **4** was treated with sodium nitrite in hexamethylphosphoric triamide, a mixture of α-D-mannopyranosyl α-D-mannopyranoside acetates was obtained. Removal of the blocking groups from the mixture gave the known[10] α-D-mannopyranosyl α-D-mannopyranoside **8**, thus confirming that an epimerization of the α,α-trehalose derivative **4** had taken place.

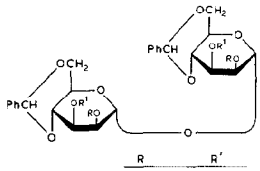
Although 4,6:4′,6′-di-*O*-benzylidene-(α-D-mannopyranosyl α-D-manno-

pyranoside) could be readily obtained from the solvolysis mixture by *O*-deacetylation, it was more convenient to benzylate the mixture directly by treatment with sodium hydride and benzyl chloride in *N,N*-dimethylformamide (DMF). The syrupy tetra-*O*-benzyl derivative **7** resulting was then treated with 80% aqueous acetic acid, to give 2,3,2′,3′-tetra-*O*-benzyl-(α-D-mannopyranosyl α-D-man-



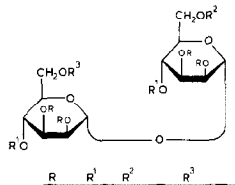
	R^1	R^2	R^3
1	H	H	H
2	Tf	H	Tf
3	Tf	H	H
4	Tf	Ac	Tf
5	Tf		Tf

Tf = F_3CSO_2



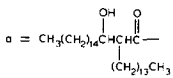
	R	R′
6	COPh	
7	Bn	Bn

Bn = $PhCH_2$



	R	R^1	R^2	R^3
8	H	H	H	H
9	Bn	H	H	H
10	Bn	H	H	Ac
11	Bn	H	Ts	Ts
12	Bn	H	H	Ts
13	Bn	Ac	Ts	Ts
14	Bn	H	a	a
15	Bn	H	mycoloyl	mycoloyl
16	H	H	a	a
17	H	H	mycoloyl	mycoloyl
18	Bn	H	H	a
19	H	H	H	a

Ts = $SO_2C_6H_4Me$-*p*

a = 

nopyranoside) (**9**). Compound **9** was accompanied by a minor by-product which was found by ^{1}H-n.m.r. spectroscopy to have the structure of a 6-*O*-acetyl derivative (compound **10**). Indeed, when the mixture of **9** and **10** was subjected to *O*-deacetylation, compound **9** was obtained as the sole product. Acetylation of a primary hydroxyl group with aqueous acetic acid, although considered unlikely, had already been reported by Duff[11] and by us[12].

Selective tosylation of **9** with *p*-toluenesulfonyl chloride gave a mixture that was separated by column chromatography. The ditosylate **11** was isolated in 62% yield, and the monotosylate **12** in 17% yield. For the synthesis of 6-*O*-corynomycoloyl-(α-D-mannopyranosyl α-D-mannopyranoside), the monotosylate **12** was obtained in higher yield (45%) by decreasing the proportion of tosyl chloride. The structure of the ditosylate **11** was confirmed by the ^{1}H-n.m.r. spectrum of its 4,4′-di-*O*-acetyl derivative **13**. The H-4,H-4′ signal was shifted to lower field (δ 5.20, $J_{4,3} = J_{4,5} = 9.5$ Hz) owing to the deshielding effect of the adjacent *O*-acetyl group. The monotosylate **12** could be converted into the ditosylate **11** by further treatment with *p*-toluenesulfonyl chloride.

Treatment of **11** with potassium corynomycolate[13] in hexamethylphosphoric triamide gave the 6,6′-diester **14**. Similarly, **11** was converted into the 6,6′-dimycolate **15** by treatment with potassium mycolate[12]. Removal of the benzyl groups from **14** and **15** by catalytic hydrogenolysis gave 6,6′-di-*O*-corynomycoloyl-(α-D-

mannopyranosyl α-D-mannopyranoside) (**16**) and 6,6′-di-*O*-mycoloyl (α-D-mannopyranosyl α-D-mannopyranoside) (**17**).

In order to obtain the D-*manno*-D-*manno* analog of 6-*O*-corynomycoloyl-α,α-trehalose[5], the monotosylate **12** was treated with potassium corynomycolate, and the resulting 6-monocorynomycolate **18** was hydrogenolyzed, to give 6-*O*-corynomycoloyl-α-D-mannopyranosyl α-D-mannopyranoside (**19**).

The chromatographic behavior of compounds **16**, **17** and **19** is similar to that of the analogous trehalose esters. The results of preliminary experiments suggest that some of the biological activities (*e.g.*, toxicity in mice) of these cord-factor analogs are dramatically abrogated.

EXPERIMENTAL

General methods. — Melting points were determined with a Fisher–Johns apparatus and are not corrected. Optical rotations were determined with a Jasco DIP-140 polarimeter. Thin-layer chromatograms were obtained on Eastman Kodak plates. Chromatography columns were packed with silica gel (Baker No. 3404 or 3405). Microanalyses were performed by Galbraith Laboratories, Knoxville, Tennessee. N.m.r. spectra were recorded at 60 MHz with a Varian EM 360A spectrometer, and at 360 MHz with an NT 360 spectrometer, with tetramethylsilane as the internal standard and $CDCl_3$ as the solvent.

4,6:4′,6′-Di-O-benzylidene-2,2′-di-O-(trifluoromethylsulfonyl)-α,α-trehalose (**2**) *and 4,6:4′,6′-di-O-benzylidene-2-O-(trifluoromethylsulfonyl)-α,α-trehalose* (**3**). — *Method a.* To a cold (ice-bath) suspension of 4,6:4′,6′-di-*O*-benzylidene-α,α-trehalose[6] (**1**) (293 mg, 0.57 mmol) in pyridine (2 mL) was added trifluoromethanesulfonyl chloride (0.25 mL, 2.34 mmol). The mixture was stirred for 30 min in an ice-bath and for an additional 2 h at room temperature. It was then cooled, the acid neutralized with cold, saturated sodium hydrogencarbonate solution, the mixture extracted with ethyl acetate, and the extract washed with water, dried (sodium sulfate), and evaporated, to give a syrupy residue which was chromatographed on silica gel. Elution with 1:1 ethyl acetate–hexane gave a homogeneous product that was found to have the structure of the ditriflate **2**; yield 103 mg (23%). An analytically pure sample was obtained by crystallization from acetone–hexane; m.p. 146–150° (dec.), $[\alpha]_D$ +75° (*c* 1.0, 3:1 chloroform–methanol).

Anal. Calc. for $C_{28}H_{28}F_6O_{15}S_2$: C, 42.97; H, 3.61; S, 8.19. Found: C, 42.74; H, 3.62; S, 8.34.

Continued elution with the same solvent-system afforded the major product, the monotriflate **3**; yield, 210 mg (57%). It crystallized from acetone–hexane; m.p. 135–138° (dec.), $[\alpha]_D$ +76° (*c* 1.0, 3:1 chloroform–methanol).

Anal. Calc. for $C_{27}H_{29}F_3O_{13}S$: C, 49.85; H, 4.49; S, 4.93. Found: C, 49.75; H, 4.65; S, 4.95.

Method b. To a cold (ice-bath) suspension of the dibenzylidene acetal **1** (520

mg, 1.0 mmol) in pyridine (5 mL) was added trifluoromethanesulfonyl chloride (0.3 mL, 2.8 mmol), and the mixture was stirred for 30 min in an ice-bath and for an additional 22 h at room temperature, more chloride (0.2 mL, 1.8 mmol) being added after 5 h. The mixture was cooled (ice-bath), made neutral with cold, saturated sodium hydrogencarbonate solution, and diluted with water. The crystalline product was filtered off, washed with water, dried, and purified by chromatography as already described, to give pure ditriflate **2**; yield: 610 mg (77%).

3,3'-Di-O-acetyl-4,6:4',6'-di-O-benzylidene-2,2'-di-O-(trifluoromethylsulfonyl)-α,α-trehalose (**4**). — The ditriflate **2** (990 mg) was acetylated in the usual way with acetic anhydride and pyridine. Evaporation of the mixture gave homogeneous product **4** (1.05 g, 95%). A small sample was recrystallized from ether–hexane; m.p.129–132° (dec.), $[\alpha]_D$ +66° (*c* 1.0, chloroform); ^{1}H-n.m.r. data (360 MHz): δ 7.33–7.48 (m, 10 H, aryl), 5.72 (t, 2 H, H-3,3', $J_{3,2} = J_{3,4} = 9.6$ Hz), 5.48 (s, 2 H, CH of benzylidene), 5.44 (d, 2 H, H-1,1', $J_{1,2}$ 4.5 Hz), 4.88 (dd, 2 H, H-2,2'), 4.40 (dd, 2 H, H-4,4', $J_{4,5}$ 6.5 Hz), 4.14 (m, 2 H, H-5,5'), 3.70 (m, 4 H, H_2-6, H_2-6'), and 2.12 (s, 6 H, 2 AcO).

Anal. Calc. for $C_{32}H_{32}F_6O_{17}S_2$: C, 44.35; H, 3.72; S, 7.40. Found: C, 44.51; H, 3.79; S, 7.35.

4,6:4',6'-Di-O-benzylidene-3,3'-di-O-(tetrahydropyran-2-yl)-2,2'-di-O-(trifluoromethylsulfonyl)-α,α-trehalose (**5**). — A mixture of the ditriflate **2** (340 mg) and pyridinium *p*-toluenesulfonate (40 mg) in dichloromethane (10 mL) was treated with dihydropyran (2 mL) for 2 h at room temperature. It was then washed successively with saturated sodium hydrogencarbonate solution and water, and evaporated, giving an amorphous residue which was purified by chromatography. The product **5** was eluted with 3:2 hexane–ether, yield 363 mg (88%); $[\alpha]_D$ +56° (*c* 0.9, chloroform).

Anal. Calc. for $C_{38}H_{44}F_6O_{17}S_2$: C, 48.00; H, 4.66; S, 6.74. Found: C, 47.84; H, 4.90; S, 7.00.

2,2'-Di-O-benzoyl-4,6:4',6'-di-O-benzylidene-3,3'-di-O-(tetrahydropyran-2-yl)-(α-D-mannopyranosyl α-D-mannopyranoside) (**6**). — The diester **5** (200 mg) was treated with sodium benzoate (480 mg) in hexamethylphosphoric triamide for 64 h at 110°, and the mixture cooled. Ice and water were added, and the solid product was filtered off, washed with water, dried, and purified by column chromatography. It was eluted with 3:2 hexane–ether, and isolated in amorphous form; yield, 88 mg (47%); $[\alpha]_D$ +11.5° (*c* 0.5, chloroform); ^{1}H-n.m.r. data: δ 7.44–8.28 (m, 2 OH, aryl), 5.75 (s, 2 H, CH of benzylidene), 5.62 (bd, 2 H, H-2,2', $J_{2,1}$ ~1.0, $J_{2,3}$ 4.5 Hz), 5.38 (bs, 2 H, H-1,1'), and 1.65 (v broad s, 18 H, 2 tetrahydropyranyl).

Anal. Calc. for $C_{50}H_{54}O_{15}$: C, 67.10; H, 6.08. Found: C, 66.97; H, 6.22

2,3,2',3'-Tetra-O-benzyl-4,6:4',6'-di-O-benzylidene-(α-D-mannopyranosyl α-D-mannopyranoside) (**7**). — Compound **4** (576 mg) was treated with sodium nitrite (1.3 g) in hexamethylphosphoric triamide (10 mL) for 16 h at 105°. The mixture was cooled, diluted with water, and extracted with ethyl acetate. The extract was washed with water (3 times), dried (sodium sulfate), and evaporated. The

syrupy residue, which contained several components (t.l.c.), was then dissolved in *N,N*-dimethylformamide (5 mL), and sodium hydride (57% oil dispersion; 200 mg) was added. The mixture was stirred for a few minutes at room temperature, benzyl chloride (2 mL) was added, and stirring was continued for an additional 2 h at room temperature. Acetic acid (a few drops) was added, and, after 5 min, the mixture was evaporated, and the residue was purified by chromatography. Elution with 2:1 hexane–ether removed residual benzyl alcohol and dibenzyl ether, and continued elution with the same solvent-system gave syrupy product **7**; yield, 211 mg (36% based on **4**); $[\alpha]_D$ +55° (*c* 1.1, chloroform); ^{1}H-n.m.r. data: δ 7.28–7.72 (30 H, aryl), 5.70 (s, 2 H, CH of 2 benzylidene), and 5.10 (bs, 2 H, H-1,1′).

Anal. Calc. for $C_{54}H_{54}O_{11}$: C, 73.78; H, 6.19. Found: C, 73.92; H, 6.36.

α-D-Mannopyranosyl α-D-mannopyranoside (**8**) *(from* **4**). — Compound **4** (100 mg) was treated with sodium nitrite in hexamethylphosphoric triamide as just described, and the crude product was hydrolyzed with 80% aqueous acetic acid (2 mL) for 4 h at 80°. The mixture was evaporated, and the residue was *O*-deacetylated with M sodium methoxide solution in methanol. After 90 min at room temperature, the mixture was made neutral with acetic acid, and evaporated. The residue was de-ionized by dissolving it in methanol and passing the solution through a column of AG-50W X8 (H^+) ion-exchange resin. Evaporation of the effluent gave an amorphous residue (25 mg; 83% based on **4**) which was practically homogeneous in t.l.c. It crystallized from absolute ethanol; m.p. 232–237°, $[\alpha]_D$ +123° (*c* 0.5, 1:1 methanol–water); lit.[10] m.p. 240–243°, $[\alpha]_D$ +124°.

2,3,2′,3′-Tetra-O-benzyl-(α-D-mannopyranosyl α-D-mannopyranoside) (**9**). — *Method a.* The tetra-*O*-benzyl derivative **7** (163 mg) was treated with 80% aqueous acetic acid (5 mL) for 3 h at 80°, the mixture cooled and evaporated, and the residue (which gave 2 spots in t.l.c.) chromatographed on silica gel. Elution with chloroform, followed by 25:1 chloroform–methanol, gave syrupy 6-*O*-acetyl-2,3,2′,3′-tetra-*O*-benzyl-(α-D-mannopyranosyl α-D-mannopyranoside) (**10**, 10%); $[\alpha]_D$ +29.5° (*c* 0.9, chloroform); ^{1}H-n.m.r. data: δ 7.38 (20 H, aryl), 5.18 (bs, 2 H, H-1,1′), and 2.10 (s, 3 H, AcO).

Anal. Calc. for $C_{42}H_{48}O_{12}$: C, 67.72; H, 6.49. Found: C, 67.51; H, 6.60.

Continued elution with 25:1 chloroform–methanol gave the major product, **9**; yield, 71.5%; $[\alpha]_D$ +41.5°, ^{1}H-n.m.r. data: δ 7.35 (20 H, aryl) and 5.12 (2 H, H-1,1′).

Anal. Calc. for $C_{40}H_{46}O_{11}$: C, 68.36; H, 6.59. Found: C, 68.27; H, 6.63.

Method b. The tetrabenzyl derivative **7** (250 mg) was treated with 80% aqueous acetic acid as just described, and the residue obtained on evaporation was treated with M sodium methoxide solution in methanol for 2 h at room temperature. T.l.c. then showed that the byproduct **10** had disappeared. The mixture was made neutral with acetic acid, and evaporated, and the product **9** was purified by chromatography as already described; yield, 167 mg (84%).

2,3,2′,3′-Tetra-O-benzyl-6,6′-di-O-p-tolylsulfonyl-(α-D-mannopyranosyl α-D-mannopyranoside) (**11**) *and 2,3,2′,3′-tetra-O-benzyl-6-O-p-tolylsulfonyl-(α-D-*

mannopyranosyl α-D-mannopyranoside) (**12**). — *Method a.* To a solution of **9** (153 mg) in pyridine (2 mL) was added *p*-toluenesulfonyl chloride (124 mg), and the mixture was stirred for 7 h at room temperature. T.l.c. then showed the presence of 3 components, which were separated by chromatography. Elution with chloroform gave the ditosylate **11** (41 mg, 18.5%); $[\alpha]_D$ +15° (*c* 1.3, chloroform); ^{1}H-n.m.r. data: δ 7.24–7.88 (28 H, aryl), 5.12 (bs, 2 H, H-1,1′), and 2.44 (s, 6 H, 2 Ar-CH_3 groups).

Anal. Calc. for $C_{47}H_{52}O_{13}S_2$: C, 64.14; H, 5.78; S, 5.78. Found: C, 64.10; H, 5.91; S, 6.31.

Continued elution with chloroform, followed by 20:1 chloroform–methanol gave the monotosylate **12** (84 mg, 45%); [α[$_D$ +25° (*c* 0.85, chloroform); ^{1}H-n.m.r. data: δ 7.25–7.88 (14 H, aryl), 5.10, 5.18 (2 d, $J_{1,2}$ 2.0 Hz, H-1,1′), and 2.44 (s, 3 H, Ar-CH_3 group).

Anal. Calc. for $C_{47}H_{52}O_{13}S$: C, 65.87; H, 6.11; S, 3.74. Found: C, 65.60; H, 6.11; S, 3.52.

Continued elution with 20:1 chloroform–methanol yielded unchanged starting-material **9** (41 mg, 27%).

Method b. To a solution of the tetrabenzyl derivative **9** (147 mg) in pyridine (2 mL) was added *p*-toluenesulfonyl chloride (123 mg), and the mixture was stirred. During 29 h at room temperature more tosyl chloride was added (42 mg after 5 h and 35 mg at 24 h). The mixture was worked up as just described, to give the ditosylate **11** (132 mg, 62.5%) and the monotosylate **12** (30 mg, 17%); only a trace of the starting material was recovered.

4,4′-Di-O-acetyl-2,3,2′,3′-tetra-O-benzyl-6,6′-di-O-p-tolylsulfonyl-(α-D-mannopyranosyl α-D-mannopyranoside) (**13**). — The ditosylate **11** (16 mg) was acetylated in the usual way with acetic anhydride and pyridine, and the amorphous product was purified by chromatography using elution with 3:2 hexane–ethyl acetate; yield, 13 mg (75%); $[\alpha]_D$ +25.5° (*c* 1.2, chloroform); ^{1}H-n.m.r. data (360 MHz): δ 7.22–7.55 (36 H, aryl), 5.20 (t, 2 H, H-4,4′, $J_{4,3} = J_{4,5}$ = 9.5 Hz), 5.07 (d, 2 H, H-1,1′, $J_{1,2}$ 2.0 Hz), 2.42 (s, 6 H, 2 Ar-CH_3 groups), and 2.08 (s, 6 H, 2 AcO).

Anal. Calc. for $C_{58}H_{62}O_{17}S_2$: C, 63.60; H, 5.70; S, 5.85. Found: C, 63.41; H, 5.84; S, 5.88.

2,3,2′,3′-Tetra-O-benzyl-6,6′-di-O-corynomycoloyl-(α-D-mannopyranosyl α-D-mannopyranoside) (**14**). — The ditosylate **11** (64 mg) was treated with potassium corynomycolate (130 mg) in hexamethylphosphoric triamide (2 mL) for 16 h at 120°. Ice and water were added to the cooled solution, and the mixture was acidified with dilute hydrochloric acid. The precipitate was filtered off, and washed with water, and the crude product was dried by dissolving it in chloroform and evaporating the solution. Treatment of the residue with Bio Rad AG-MP1 (OH^-) ion-exchange resin in 1:1 chloroform–methanol removed the excess of corynomycolic acid. Finally, the crude product was purified by chromatography, by elution with 2:1 hexane–ethyl acetate; yield 88 mg (84%). An analytically pure sample was obtained by rechromatography; $[\alpha]_D$ +13° (*c* 0.8, chloroform); ^{1}H-

n.m.r. data: δ 7.38 (20 H, aryl), 5.18 (bs, 2 H, H-1,1'), and 1.28 (s, corynomycoloyl).

Anal. Calc. for $C_{104}H_{170}O_{15}$: C, 75.22; H, 10.32. Found: C, 74.93; H, 10.25.

2,3,2',3'-Tetra-O-benzyl-6,6'-di-O-mycoloyl-(α-D-mannopyranosyl α-D-mannopyranoside) (**15**). — The ditosylate **11** was treated with potassium mycolate in hexamethylphosphoric triamide as already described, and waxy 6,6'-di-*O*-mycoloyl derivative **15** was obtained in 61% yield; $[\alpha]_D$ +8.5° (*c* 0.75, chloroform); ^{1}H-n.m.r. data: similar to those given for compound **14**.

Anal. Calc. for $C_{208}H_{370}O_{15}$: C, 80.29; H, 11.98. Found: C, 80.18; H, 12.12.

2,3,2',3'-Tetra-O-benzyl-6-O-corynomycoloyl-(α-D-mannopyranosyl α-D-mannopyranoside) (**18**). — The monotosylate **12** (78 mg) was treated with potassium corynomycolate (95 mg) in hexamethylphosphoric triamide (1.5 mL) as just described. De-ionization and chromatography gave the monocorynomycolate **18**; yield, 69 mg (64%); $[\alpha]_D$ +22° (*c* 0.6, chloroform).

Anal. Calc. for $C_{72}H_{108}O_{13}$: C, 73.18; H, 9.21. Found: C, 72.92; H, 9.48.

6,6'-Di-O-corynomycoloyl-(α-D-mannopyranosyl α-D-mannopyranoside) (**16**). — The dicorynomycolate **14** (64 mg) was dissolved in 1:1 ethyl acetate–ethyl alcohol mixture (50 mL), and hydrogenolyzed in the presence of 10% Pd–C catalyst (70 mg) at 344.5 kPa for 5 h. The catalyst was filtered off, and washed with chloroform, and the filtrate and washings were combined and evaporated, to give an amorphous residue which was chromatographed on silica gel. Elution with 20:1 chloroform–methanol removed fast-moving, minor byproducts, and elution with 10:1 chloroform–methanol gave the pure product; yield, 26 mg (52%); $[\alpha]_D$ +34.5° (*c* 0.6, chloroform).

Anal. Calc. for $C_{76}H_{146}O_{15}$: C, 70.22; H, 11.32. Found: C, 69.94; H, 11.24.

6,6'-Di-O-mycoloyl-(α-D-mannopyranosyl α-D-mannopyranoside) (**17**). — The dimycolate **15** (53 mg) was dissolved in 2:1 ethyl acetate–ethyl alcohol (60 mL), and hydrogenolyzed as already described. Chromatography of the crude product gave pure **17** (20 mg, 42%); $[\alpha]_D$ +34° (*c* 0.9, chloroform).

Anal. Calc. for $C_{180}H_{346}O_{15}$: C, 78.66; H, 12.60. Found: C, 78.40; H, 12.47.

6-O-Corynomycoloyl-α-D-mannopyranosyl α-D-mannopyranoside (**19**). — The benzylated monocorynomycolate **18** (59 mg) was hydrogenolyzed and chromatographed as already described, to give pure monomycoloyl derivative **19**; yield, 27 mg (66%); $[\alpha]_D$ +42° (*c* 0.5, chloroform).

Anal. Calc. for $C_{44}H_{84}O_{13}$: C, 64.36; H, 10.31. Found: C, 64.20; H, 10.44.

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