3,6-Thioanhydro Sugar Derivatives. An Enantiospecific Synthesis of (2*R*,3*R*,4*S*)-3-Benzyloxy-4-hydroxy-2-[(*R*)-1-benzyloxy-4-hydroxybutyl]thiolane as the Key Intermediate for Thioswainsonine [1]

Isidoro Izquierdo*, Maria T. Plaza, Antonio Ramírez, and Fida Aragón

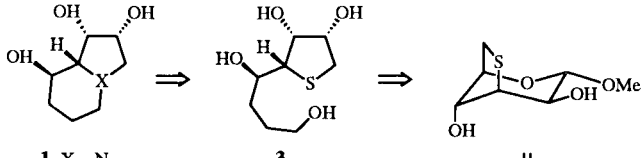
Department of Organic Chemistry, Faculty of Pharmacy, University of Granada, 18071 Granada, Spain

Received October 16, 1995

Methyl 2-*O*-benzyl-3,6-thioanhydro-α-D-mannopyranoside (**9**) was obtained in eight steps from the commercially available methyl α-D-glucopyranoside. Compound **9** was transformed into (2*R*,3*R*,4*S*)-3-benzyloxy-4-hydroxy-2-[(*R*)-1-benzyloxy-4-hydroxybutyl]thiolane (**14**) by acid hydrolysis of its 2,4-di-*O*-benzyl derivative **10** followed by reaction of the not isolated 2,4-di-*O*-benzyl-3,6-thioanhydro-D-mannose (**11**) with ethoxycarbonylmethylenetriphenylphosphorane to give an ≈ 1:1 *E*/*Z* mixture of the corresponding α,β-unsaturated ester (**12**). Finally, catalytic hydrogenation of **12** to ethyl (*R*)-4-benzyloxy-4-[(2'*R*,3'*R*,4'*S*)-3'-benzyloxy-4'-hydroxythiolan-2'-yl]butanoate (**13**) and subsequent reduction with lithium aluminum hydride gave the title compound **14**.

J. Heterocyclic Chem., **33**, 1239 (1996).

Methyl 2-*O*-benzyl-3,6-*thioanhydro*-α-*D*-mannopyranoside (**9**) was obtained in eight steps from the commercially available methyl α-*D*-glucopyranoside. Transformation of **9** into (2*R*,3*R*,4*S*)-3-benzyloxy-4-hydroxy-2-[(*R*)-1-benzyloxy-4-hydroxybutyl]thiolane (**14**) was achieved by acid hydrolysis of its 2,4-di-*O*-benzyl derivative **10** followed by reaction of the not isolated 2,4-di-*O*-benzyl-3,6-*thioanhydro*-*D*-mannose (**11**) with ethoxycarbonylmethylenetriphenylphosphorane to give an ≈ 1:1 *E*/*Z* mixture of the corresponding α,β-unsaturated ester **12**. Finally, catalytic hydrogenation of **12** to ethyl (*R*)-4-benzyloxy-4-[(2'*R*,3'*R*,4'*S*)-3'-benzyloxy-4'-hydroxythiolan-2'-yl]butanoate (**13**) and subsequent reduction with lithium aluminium hydride gave the title compound **14**. Polyhydroxyindolizidines such as (1*S*,2*R*,8*R*,8a*R*)-1,2,8-trihydroxyindolizidines (swainsonine, **1**) was shown to be a potent and specific inhibitor of lysosomal and some of the processing forms of α-mannosidase [2] and may have therapeutic value as an antimetastatic [3], anti-tumour-proliferative [4] or immunoregulatory agent [5]. On the other hand, some polyhydroxylated cyclic sulfonium salts are also inhibitors of different glycosidases [6]. On the basis of this knowledge, we are interested in the enantiospecific synthesis of the thioanalogue of swainsonine (**2**).



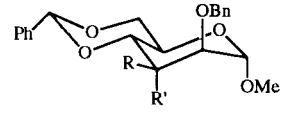
1 X = N
2 X = S^+A^-

3

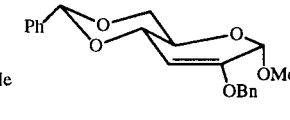
METHYL α-*D*-GLUCOPYRANOSIDE

The above retrosynthetic analysis clearly indicated that (2*R*,3*R*,4*S*)-3-benzyloxy-4-hydroxy-2-[(*R*)-1-benzyloxy-4-hydroxybutyl]thiolane (**14**) a dibenzyloxy derivative of **3**, could be an appropriate key intermediate for the synthesis of thioswainsonine (**2**). Compound **14** could be obtained from the commercially available methyl α-*D*-glucopyranoside through a 3,6-*thioanhydro* sugar derivative with the *D-manno* configuration. In addition, polyhydroxythiolanes as **3**, could be considered of interest since they are the thioanalogues of the important glycosidase inhibitors polyhydroxypyrrolidines [7]. We report herein the enantiospecific synthesis of **14** from the readily available methyl α-*D*-glucopyranoside.

Reaction of methyl 2-*O*-benzyl-4,6-*O*-benzylidene-α-*D*-altropyranose (**4**) [8] with trifluoromethanesulfonic anhydride, according to the Baer procedure [8], gave the corresponding 3-*O*-trifluoromethanesulfonyl derivative **5** that was not isolated but transformed (30% yield from **4**) into methyl 3-*S*-acetyl-2-*O*-benzyl-4,6-*O*-benzylidene-3-*thio*-α-*D*-mannopyranoside (**7**) by treatment with potassium thioacetate. The basic character of thioacetate anion also caused a 1,2-elimination reaction of **5** to afford methyl 2-*O*-benzyl-4,6-*O*-benzylidene-3-deoxy-α-*D*-*erythro*-hex-2-enopyranoside (**6**, 28% yield from **4**). The $J_{3,4}$ value (11 Hz) in **7** was in accordance with its *D-manno* configuration.



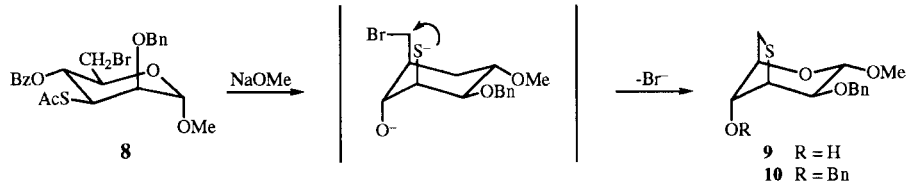
4 R = H; R' = OH
5 R = H; R' = OTf
7 R = SAc; R' = H



6

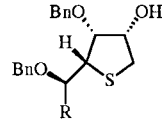
Reaction of **7** with *N*-bromosuccinimide in carbon tetrachloride gave a complex mixture from which methyl 3-*S*-acetyl-4-*O*-benzoyl-2-*O*-benzyl-6-bromo-6-deoxy-3-*thio*-α-*D*-mannopyranoside (**8**) could be isolated. The extremely low yield obtained, must be due to the partial loss of the benzyl protecting group during the reaction.

Treatment of compound **8** with methanolic sodium methoxide caused the loss of the protecting acyl groups and a ring closure to afford methyl 2-*O*-benzyl-3,6-



thioanhydro-α-*D*-mannopyranoside (**9**) by a favourable 5-*exo*-tet [9] nucleophilic displacement of the bromine at C-6 by the thiolate anion at C-3. The structure of **9** was established on the basis of its analytical and spectroscopic data.

Conventional benzylation of **9** gave the related 2,4-di-*O*-benzyl derivative **10** that was subjected to acid hydrolysis to produce the uninvestigated aldehyde **11**. Reaction of 2,4-di-*O*-benzyl-3,6-*thioanhydro*-*D*-mannose (**11**) with ethoxycarbonylmethylenetriphenylphosphorane gave an ≈ 1:1 *E*/*Z* unresolvable mixture of ethyl (*R*)-4-benzyloxy-4-[(2'*R*,3'*R*,4'*S*)-3'-benzyloxy-4'-hydroxythiolan-2'-yl]-2-butenoate (**12**). The stereochemistry of **12** was irrelevant since it was hydrogenated to ethyl (*R*)-4-benzyloxy-4-[(2'*R*,3'*R*,4'*S*)-3'-benzyloxy-4'-hydroxythiolan-2'-yl]butanoate (**13**). Finally, reduction of **13** with lithium aluminium hydride gave the required key intermediate (2*R*,3*R*,4*S*)-3-benzyloxy-4-hydroxy-2-[(*R*)-1-benzyloxy-4-hydroxybutyl]thiolane (**14**).



11, R = CHO
12, R = HC = $CHCO_2Et$
13, R = $(CH_2)_2CO_2Et$
14, R = $(CH_2)_3OH$

EXPERIMENTAL

Melting points were determined with a Gallenkamp apparatus and are uncorrected. Solutions were dried over magnesium sulfate before concentration under reduced pressure. The ^1H and ^{13}C nmr spectra were recorded with Bruker AM-360 spectrometer for solutions in deuteriochloroform (internal tetramethylsylane). The ir spectra were recorded with a Perkin-Elmer 9836 instrument and mass spectra with a Kratos MS-25 mass spectrometer. Optical rotations were measured for solutions in chloroform (1-dm tube) with a Perkin-Elmer 141 polarimeter. Analysis (tlc) was performed on precoated silica gel 60 F_{254} aluminium sheets and detection by charring with sulfuric acid. Column chromatography was performed on silica gel (Merck, 7734). The noncrystalline compounds, for which elemental analyses were not obtained were shown to be homogeneous by chromatography and characterized by nmr and mass spectrometry.

Methyl 3-*S*-Acetyl-2-*O*-benzyl-4,6-*O*-benzylidene-3-*thio*-α-*D*-mannopyranoside (**7**).

A solution of 18.5 g (49.73 mmoles) of methyl 2-*O*-benzyl-4,6-*O*-benzylidene-α-*D*-altropyranoside (**4**) [8], in 100 ml of dry pyridine and 100 ml of dichloromethane was treated with 10 ml (60 mmoles) of trifluoromethanesulfonic anhydride by the Baer method [8]. The residue (20.1 g) was taken-up in 75 ml of dry *N*,*N*-dimethylformamide and 8.8 g (75 mmoles) of potassium thioacetate were added at -40°. The mixture kept at room temperature for 48 hours. Analysis (tlc) (ethyl acetate-hexane 1:2, v/v) then revealed the presence of a sligltly lower-running compound. The mixture was concentrated and the residue dissolved in 150 ml of dichloromethane, washed with brine, water and then concentrated. Column chromatography (ethyl acetate-hexane 1:6, v/v) of the residue gave first 5 g (28% from **4**) of syrupy methyl 2-*O*-benzyl-4,6-*O*-benzylidene-3-deoxy-α-*D*-*erythro*-hex-2-enopyranoside (**6**), $[\alpha]_D^{25}$ -167 (c, 1); ir (neat): ν 749, 697 cm^{-1} (aromatic); ^1H nmr: δ 7.51-7.26 (m, 10H, phenyl protons), 5.63 (s, 1H, C*H*Ph), 5.43 (d, 1H, 3-H, J = 5.2 Hz), 4.82 (s, 1H, 1-H), 4.66 and 4.62 (2d, each, 1H, -CH_2-, J = 12 Hz), 4.41 (dd, 1H, 6*e*-H, J = 6.4, 9.5 Hz), 4.38-4.32 (m, 1H, 5-H), 3.93 (dd, 1H, 4-H, J = 1.7 Hz), 3.88 (t, 1H, 6*a*-H, J = 9.5 Hz), 3.46 (s, 3H, OCH_3); ^{13}C nmr: δ 154.6 (C-2), 138.1, 136.6, 129.5, 128.5, 128.4, 127.9, 127.8, and 126.3 (2 Ph), 102.8 (C-3), 101.3 (*C*HPh), 99.9 (C-1), 72.6 (C-5), 70.7 (CH_2Ph), 69.6 (C-6), 60.1 (C-4), 55.9 (OCH_3).

Syrupy **7** eluted second (6.3 g, 30% from **4**), $[\alpha]_D^{25}$ -36 (c, 1); ir (neat): ν 1694 (C=O, thioacetate), 770, 739 cm^{-1} (aromatic); ^1H nmr: δ 7.44-7.28 (m, 10H, phenyl protons), 5.51 (s, 1H, C*H*Ph), 4.68 (d, 1H, 1-H, J = 1.4 Hz), 4.66, 4.60 (2d, each, 1H, -CH_2-, J = 11.5 Hz), 4.28 (dd, 1H, 3-H, J = 3, 11 Hz), 4.22 (dd, 1H, 6*e*-H, J = 4.3, 10 Hz), 3.95 (dt, 1H, 5-H), 3.88 (dd, 1H, 4-H, J = 9 Hz), 3.78 (t, 1H, 6*a*-H, J = 10 Hz), 3.75 (dd, 1H, 2-H), 3.40 (s, 3H, OCH_3), 2.29 (s, 3H, $SCOCH_3$); ^{13}C nmr: δ 194.4 ($SCOCH_3$), 137.5, 128.9, 128.4, 128.2, 128.1, 128.0, 126.2 (2 Ph), 101.9 (*C*HPh), 98.3 (C-1), 78.7 (C-5), 76.0 (C-2), 73.8 (CH_2Ph), 69.0 (C-6), 65.6 (C-4), 55.0 (OCH_3), 45.4 (C-3), 30.7 ($SCOCH_3$); ms: (ci, *i*-BuH) m/z 431 (0.6), 429 (1.4), 415 (1.2), 387 (2.0), 355 (1.3), 105 (53.5), 91 (100).

Methyl 3-*S*-Acetyl-4-*O*-benzoyl-2-*O*-benzyl-6-bromo-6-deoxy-3-*thio*-α-*D*-mannopyranoside (**8**).

A stirred suspension of 690 mg (1.6 mmoles) of **7**, 310 mg (1.74 mmoles) of *N*-bromosuccinimide and 1.2 g of barium carbonate in 20 ml of dry carbon tetrachloride was heated under reflux for 2 1/4 hours then allowed to stand at room temperature overnight. Analysis (tlc, ethyl acetate-hexane 1:3, v/v) then revealed a new compound of slightly higher mobility. The reaction mixture was filtered through a Hyflo pad and the filtrate concentrated. The residue was dissolved in ether and washed with water, then concentrated. Column chromatography (ethyl acetate-hexane 1:6, v/v) of the residue gave 100 mg (14%) of **8**

as a syrup; $[\alpha]_D^{26}$ -44 (c, 0.5); ^{1}H nmr: δ 7.99-7.96 and 7.59-7.29 (2m, 10H, phenyl protons), 5.31 (dd, 1H, 4-H, J = 9.7, 11 Hz), 4.81 (d, 1H, 1-H, J = 1.3 Hz), 4.70, 4.58 (2d, each, 1H, -CH_2-, J = 11.7 Hz), 4.42 (dd, 1H, 3-H, J = 3 Hz), 4.14 (ddd, 1H, 5-H, J = 7.4 Hz), 3.71 (dd, 1H, 2-H), 3.50 (s, 3H, OCH_3), 3.49-3.39 (m, 2H, 6,6'-H), 2.13 (s, 3H, SCOCH_3); ^{13}C nmr: δ 194.2 (SCOCH$_3$), 165.7 (PhCO), 137.2, 133.5, 130.0, 129.0, 128.5, 128.4, 128.0, 127.9 (2 Ph), 97.2 (C-1), 78.4 (C-5), 73.1 (CH_2Ph), 71.7 (C-2), 70.0 (C-4), 55.2 (OCH_3), 45.4 (C-3), 32.0 (C-6), 30.5 (SCOCH_3); ms: (70 eV, electron impact) m/z 435 (0.3), 402 (1.3), 106 (19.4), 105 (95.9), 91 (100).

Unreacted **7** eluted second (76 mg).

Methyl 2-*O*-Benzyl-3,6-*thioanhydro*-α-*D*-mannopyranoside (**9**).

To a stirred solution of **8** (95 mg, 0.19 mmole) in dry methanol (5 ml), *M* methanolic sodium methoxide (2 ml) was added dropwise, and the mixture maintained at room temperature for 2 1/2 hours. Analysis (tlc, ethyl acetate-hexane 1:2, v/v) of the deep brown solution showed the absence of **8** and the presence of a slower-moving product. The mixture was neutralized with acetic acid, concentrated and the residue extracted with ethyl acetate. The combined extracts were washed with water, and then concentrated. Column chromatography (ethyl acetate-hexane 1:2, v/v) of the residue afforded **9** (33 mg, 62%) that crystallized on standing, mp 77-79°, $[\alpha]_D^{25}$ +67.5 (c, 1); ^{1}H nmr: δ 7.36-7.26 (m, 5H, phenyl protons), 4.89 (d, 1H, 1-H, J = 6.8 Hz), 4.77, 4.64 (2d, each, 1H, -CH_2-, J = 12.2 Hz), 4.38 (dd, 1H, 5-H, J = 2.8 Hz), 4.16 (ddd, 1H, 4-H, J = 5 Hz), 3.78 (dd, 1H, 2-H, J = 3 Hz), 3.54 (s, 3H, OCH_3), 3.43 (dd, 1H, 3-H), 3.02 (dd, 1H, 6-H, J = 4.7, 12.5 Hz), 2.85 (d, 1H, 6'-H), 2.76 (d, 1H, 4-OH, J = 8.6 Hz); ^{13}C nmr: δ 138.3, 128.4, 127.7, 127.6 (Ph), 102.5 (C-1), 76.5, 75.7, and 74.4 (C-2, 4, 5), 72.6 (CH_2Ph), 57.3 (OCH_3), 48.2 (C-3), 30.0 (C-6).

Anal. Calcd. for $C_{14}H_{18}O_4S$: C, 59.55; H, 6.43; S, 11.35. Found: C, 59.65; H, 6.66; S, 10.92.

Methyl 2,4-Di-*O*-benzyl-3,6-*thioanhydro*-α-*D*-mannopyranoside (**10**).

To a stirred solution of sodium dimethylsulfoxide (from 60 mg of a 60% dispersion of sodium hydride in oil) compound **9** (300 mg, 1.06 mmoles) in dry ether (5 ml) was added. The mixture was heated at 60° for 15 minutes and then cooled and benzyl bromide (0.15 ml) was added and then, refluxed for another 15 minutes. Analysis (tlc, ethyl acetate-hexane 1:1, v/v) then revealed the presence of a faster-moving product. The mixture was cooled and water was added carefully. The organic phase was separated, the aqueous phase was extracted with ether, and the combined extracts were washed with brine and water, and concentrated. Column chromatography (ethyl acetate-hexane 1:5, v/v) of the residue gave syrupy **10** (630 mg, 91%); $[\alpha]_D^{25}$ +42 (c, 1); ir (neat): ν 1450 (benzyl), 738, 696 cm^{-1} (aromatic); ^{1}H nmr: δ 7.37-7.24 (m, 10H, phenyl protons), 4.91 (d, 1H, 1-H, J = 6.8 Hz), 4.77, 4.58 (2d, each, 1H, -CH_2-, J = 12.2 Hz), 4.53-4.52 (m, 1H, 5-H), 4.51, 4.46 (2d, each, 1H, -CH_2-, J = 12 Hz), 3.82-3.79 (m, 2H, 2,4-H), 3.54 (s, 3H, OCH_3), 3.37 (dd, 1H, 3-H, J = 3.2, 4.5 Hz), 2.91 (dd, 1H, 6-H, J = 4.5, 12.2 Hz), 2.78 (d, 1H, 6'-H); ^{13}C nmr: δ 138.5, 137.3, 128.4, 128.3, 127.9, 127.9, 127.5 (2 Ph), 102.3 (C-1), 81.4 (C-4), 74.4, 73.5 (C-2,5), 72.6, 71.8 (2 CH_2Ph), 57.0 (OCH_3), 46.0 (C-3), 30.0 (C-6).

Anal. Calcd. for $C_{21}H_{24}O_4S$: C, 67.71; H, 6.50. Found: C, 67.37; H, 6.67.

Ethyl (*E/Z*)-(*R*)-Benzyloxy-4-[(2'*R*,3'*R*,4'*S*)-3'-benzyloxy-4'-hydroxythiolan-2'-yl]-2-butenoate (**12**).

A solution of **10** (340 mg, 0.9 mmole) in aqueous 70% trifluoroacetic acid (3 ml) was heated at 60° for 1 1/4 hours. Analysis (tlc, ethyl acetate-hexane 1:1, v/v) then revealed the presence of a new slower-moving product. The reaction mixture was concentrated and repeatly codistilled with dichloromethane. The residue was dissolved in dichloromethane (10 ml), ethoxycarbonylmethylenetriphenylphosphorane (370 mg, 0.92 mmole) was added and the mixture was allowed to stand at room temperature for 3 days. Analysis (tlc, ethyl acetate-hexane 1:1, v/v) then showed the presence of a new compound of higher mobility. The solvent was evaporated and the residue chromatographed (ethyl acetate-hexane 1:3 → 1:1, v/v) to afford syrupy **12** (245 mg, 64%) as a ≈ 1:1 *E/Z* mixture, $[\alpha]_D^{24}$ +49 (c, 1); ir (neat): ν 3416 (OH), 1715 (C=O, ester), 1651 (C=C), 1450 (benzyl), 735, 697 cm^{-1} (aromatic); ^{1}H nmr: δ 7.38-7.26 (m, 10H, phenyl protons), 6.82 (dd, 3-H (*E*-isomer), J = 15.7, 7.8 Hz), 6.26 (dd, 3-H (*Z*-isomer), J = 11.6, 8.8 Hz), 6.13 (dd, 2-H (*E*-isomer), J = 0.7 Hz), 5.94 (dd, 2-H (*Z*-isomer), J = 1.2 Hz); ^{13}C nmr: δ 165.8, 165.6 (2 C-1), 147.5, 145.23 (2 C-3), 125.1, 122.6 (2 C-2), 74.5, 73.6, 72.2, 71.2 (4 CH_2Ph), 60.7, 60.5 (2 CH_2CH$_3$), 50.6, 50.5 (2 C-2'), 34.8, 33.9 (2 C-5'), 14.21 (2 CH$_2$CH_3).

Anal. Calcd. for $C_{24}H_{28}O_5S$: C, 67.26; H, 6.59. Found: C, 67.41; H, 6.32.

Ethyl (*R*)-4-Benzyloxy-4-[(2'*R*,3'*R*,4'*S*)-3'-benzyloxy-4'-hydroxythiolan-2'-yl]butanoate (**13**).

A solution of **12** (190 mg, 0.44 mmole) in methanol (10 ml) was hydrogenated over Palladium hydroxide on carbon (100 mg) at 4 atmospheres for 1/2 hour. The mixture was filtered, the catalyst washed with methanol and the combined filtrate and washings concentrated. Column chromatography (1:3 ethyl acetate-hexane) of the residue afforded syrupy **13** (165 mg, 86%), $[\alpha]_D^{24}$ -12.3 (c, 1.2); ir (neat): ν 3469 (OH), 1726 (C=O, ester), 1450 (benzyl), 734, 697 cm^{-1} (aromatic); ^{1}H nmr: δ 7.37-7.26 (m, 10H, phenyl protons), 4.76, 4.66 (2d, each, 1H, -CH_2-, J = 11.8 Hz), 4.65, 4.38 (2d, each, 1H, -CH_2-, J = 11.1 Hz), 4.30-4.20 (m, 1H, 4-H), 4.18 (t, 1H, 3'-H, J = 3.7 Hz), 4.08 (q, 2H, CH_2CH$_3$, J = 7.1 Hz), 4.00 (m, 1H, 4'-H), 3.55 (dd, 1H, 2'-H, J = 9.4 Hz), 2.93 (dd, 1H, 5'-H, J = 6.8, 9.9 Hz), 2.86 (t, 1H, 5"-H, J = 9.9 Hz), 2.46-2.26, 1.95-1.83 (2m, 5H, H-2,2',3,3',OH, relative intensity 4:1), 1.22 (t, 3H, CH$_2$CH_3); ^{13}C nmr: δ 173.5 (C-1), 138.3, 138.0, 128.6, 128.4, 127.9, 127.6, 127.4 (2 Ph), 81.9, 77.3, 76.3 (C-4,3',4'), 74.3, 70.4 (2 CH_2Ph), 60.4 (CH_2CH$_3$), 49.1 (C-2'), 33.8 (C-5'), 28.3 (C-2), 25.1 (C-3), 14.1 (CH$_2$CH_3); ms: (70 eV, electron impact) m/z 415 (0.1%), 414 (1.0), 323 (4.9), 221 (14.5), 91 (100).

Anal. Calcd. for $C_{24}H_{30}O_5S$: C, 66.95; H, 7.02. Found: C, 66.72; H, 7.14.

(2*R*,3*R*,4*S*)-3-Benzyloxy-4-hydroxy-2-[(*R*)-1-benzyloxy-4-hydroxytyl]thiolane (**14**).

To a stirred solution of **13** (160 mg, 0.37 mmole) in anhydrous ether (5 ml), lithium aluminium hydride (45 mg) was added and the mixture refluxed for 3 hours. Analysis (tlc, ethyl acetate) then revealed the presence of a new slower-moving product. The excess of hydride was decomposed by addition of ether saturated with water, and water. The organic phase was separated, washed with brine and concentrated to give crude crystalline **14** (130 mg, 90%), mp 108-110° (from ether), $[\alpha]_D^{24}$ -20 (c, 1); ^{1}H nmr: δ 7.30-7.18

(m, 10H, phenyl protons), 4.71, 4.60 (2d, each, 1H, -CH_2-, J = 11.8 Hz), 4.57, 4.32 (2d, each, 1H, -CH_2-, J = 11.1 Hz), 4.15 (m, 1H, 1'-H), 4.11 (t, 1H, 3-H, J = 3.7 Hz), 3.95-3.91 (m, 1H, 4-H), 3.60-3.48 (m, 3H, 2,4',4"-H), 2.84 (dd, 1H, 5-H, J = 6.9, 9.8 Hz), 2.78 (t, 1H, 5'-H, J = 9.8 Hz), 2.25-1.50 (2m, 6H, 2',2",3',3"-H, 4,4'-OH); ^{13}C nmr: δ 138.3, 133.9, 128.6, 128.5, 127.9, 127.7, 127.6, 127.4 (2 Ph), 81.8, 78.0, 76.4 (C-3,4,1'), 74.3, 70.5 (2 CH_2Ph), 62.9 (C-4'), 49.2 (C-2), 33.6 (C-5), 26.6, 26.5 (C-2',3').

Anal. Calcd. for $C_{22}H_{28}O_4S$: C, 68.01; H, 7.27. Found: C, 68.33; H, 7.41.

REFERENCES AND NOTES

[1] Thioanhydro Sugar Derivatives, Part **V**. For Part **IV** see: I. Izquierdo, M. T. Plaza, and A. Saenz de Buruaga, *Carbohydr. Res.*, **230**, 145 (1996).

[2] I. Cenci di Bello, P. R. Dorling, and C. R. Huxtable, *Biochem. J.*, **215**, 693 (1983); D. R. P. Tulsiani, T. M. Harris, and O. Touster, *J. Biol. Chem.*, **257**, 7936 (1982).

[3] M. J. Humphries, K. Matsumoto, S. L. White, R. J. Molyneux, and K. Olden, *Cancer Res.*, **48**, 1410 (1988).

[4] J. W. Dennis, *Cancer Res.*, **46**, 5131 (1986).

[5] T. Kino, N. Inamura, K. Nakahara, S. Kiyoto, T. Goto, H. Terano, M. Kohsaka, H. Aoki, and H. Imanaka, *J. Antibiot.*, **38**, 936 (1985).

[6] A. H. Siriwardena, A. Chiaroni, C. Riche, S. El-Daher, B. Winchester, and D. S. Grierson, *J. Chem. Soc., Chem. Commun.*, 1531 (1992).

[7] A. Dondoni, P. Merino, and D. Perrone, *Tetrahedron*, **49**, 2939 (1993).

[8] H. H. Baer and B. Radatus, *Carbohydr. Res.*, **128**, 165 (1984).

[9] J. E. Baldwin, *J. Chem. Soc., Chem. Commun.*, 734 (1976).