Carbohydrate Research, 205 (1990) 45–51
Elsevier Science Publishers B.V., Amsterdam

Synthesis of sweet-tasting methylthio derivatives of D-fructose and sucrose*

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(Received September 6th, 1989; accepted for publication, December 14th, 1989)

ABSTRACT

1,6-Di-*S*-methyl-1,6-dithio-D-fructofuranose and its bis(*S*-oxide) and bis(*S*,*S*-dioxide) are described. On examination for sweetness, the oxygenated compounds were neutral but the parent compound was 15–20 times sweeter than sucrose, and 1′,6′-di-*S*-methyl-1′,6′-dithiosucrose was slightly less sweet than sucrose.

INTRODUCTION

Halogens alone should not uniquely possess the property of sterically and electronically producing enhanced sweetness in carbohydrates[1]. On the basis of a comparison of molecular volumes and dipole moments with those of chlorine, several substituents have been identified that should induce molecular effects similar to those of chlorine. We now report on the replacement by methylthio of the primary hydroxyl groups of D-fructofuranose and the β-D-fructofuranosyl component of sucrose; the sweetness of chlorodeoxysucroses identifies the D-fructosyl moiety of sucrose as contributing most to sweetness.

RESULTS AND DISCUSSION

D-Fructose (**1**) was treated with *p*-toluenesulfonyl chloride and the product was heated with dry acetone and sulfuric acid to yield 2,3-*O*-isopropylidene-1,6-di-*O*-tosyl-β-D-fructofuranose (**2**). The tosyl groups in **2** were displaced by methylthio groups by reaction with sodium methanethiolate in *N*,*N*-dimethylformamide. Acid hydrolysis of the product **4** yielded 1,6-di-*S*-methyl-1,6-dithio-D-fructofuranose (**5**), which was judged by a taste panel to be 15–20 times sweeter than an isomolar solution of sucrose. Compound **5** was unstable and soon began to evolve a sulfurous aroma and develop a straw color. Detection of methylthio and dimethyl disulfide ions in the headspace of the

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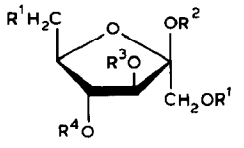
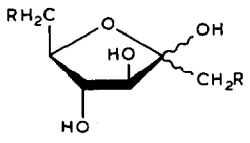
0008-6215/90/$ 03.50

sample container and of methylthio and acetyl ions from the syrup of an aged sample by mass spectrometry suggested that a displacement of MeS-1 had occurred, reminiscent of reactions in the first stages of non-enzymic browning. The instability of **5** relative to D-fructose may be due to the fact that MeS-1 is a much better leaving group than OH.

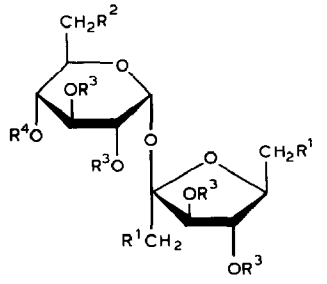
Oxidation of **5** with m-chloroperoxybenzoic acid gave the bis(*S*-oxide) **6** and the bis(*S,S*-dioxide) **7**, neither of which was sweet.



2 R^1 = OTs, R^2, R^3 = CMe_2, R^4 = H
3 R^1 = OTs, R^2, R^3 = CMe_2, R^4 = Ac
4 R^1 = MeS, R^2, R^3 = CMe_2, R^4 = H



5 R = MeS
6 R = MeSO
7 R = $MeSO_2$



8 R^1 = R^2 = OH, R^3 = R^4 = H
9 R^1 = R^2 = OTr, R^3 = R^4 = Ac
10 R^1 = OH, R^2 = OAc, R^3 = Ac, R^4 = H
11 R^1 = OTs, R^2 = OAc, R^3 = Ac, R^4 = H
12 R^1 = OTs, R^2 = OAc, R^3 = R^4 = Ac
13 R^1 = Br, R^2 = OAc, R^3 = R^4 = Ac
14 R^1 = MeS, R^2 = OAc, R^3 = R^4 = Ac
15 R^1 = MeS, R^2 = OH, R^3 = R^4 = H

Tritylation of sucrose (**8**) followed by acetylation gave the 1′,6,6′-tri-*O*-trityl derivative **9**. Mild acid hydrolysis of **9** removed the trityl groups and caused 4→6 acetyl migration to yield **10**, which was tosylated in pyridine to give **11** and then acetylated to yield the 1′,6′-ditosylate derivative **12**. Reaction of **12** with lithium bromide in hexamethylphosphoramide gave the 1′,6′-dibromo derivative **13**. Subsequent displacement of the bromide substituents with sodium methanethiolate in *N,N*-dimethylformamide produced **14** which was deacetylated (Zemplén) to yield 1′,6′-di-*S*-methyl-1′,6′-dithiosucrose (**15**).

The taste properties of **4**–**7** are explained easily by the conventional AH, B, X sweetness theory[2,3]. Compound **4** is not sweet because AH (HO-2) is blocked by the isopropylidene group. Compound **5** is sweeter than sucrose because S-1 is a better B group than O-1. The idea that an atom other than H, O, N, or F can participate in a hydrogen bond was initially promulgated by Hough and Khan[1], who suggested that chlorine may act as the B group in chlorinated sucroses. Hence, we suggest that S-1 of **5** acts as a good B group. However, the ability to act in this manner depends on the presence of free pairs of electrons and the polarizability of the B group. That this is so is

shown by the tastelessness of the bis(*S*-oxide) **6** and the bis(*S*,*S*-dioxide) **7** which do not have a "good" B group.

The sucrose derivative **15** is slightly sweet, but less than sucrose, which may be due to the larger size of the methylthio group (relative to hydroxyl or chloro) and consequent steric interference with binding to the sweet receptor.

EXPERIMENTAL

General methods. — Melting points were determined on a Fisher–Johns apparatus and the boiling point was determined by Emich's method[4]; the values are uncorrected. Optical rotations were measured with a Perkin–Elmer 241 polarimeter. Column chromatography at 25° was performed on silica gel (230–400 mesh, Merck). T.l.c. at 25° was performed on Silica Gel 60 or 60 F_{254} (Merck) with detection by charring with sulfuric acid or by short-wavelength u.v. light. The ^{1}H- and ^{13}C-n.m.r. spectra were recorded on Nicolet NT 200 or NT 470 spectrometers with internal Me_4Si or sodium 3-(trimethylsilyl)propionate-*2,2,3,3-d*$_4$ (D_2O). Chemical shift data were converted to the Me_4Si scale where 1,4-dioxane (δ 67.4) and $CDCl_3$ (δ 77.0) were used as internal references for the ^{13}C-n.m.r. spectra.

*2,3-*O*-Isopropylidene-1,6-di-*O*-tosyl-β-*D*-fructofuranose* (**2**). — Prepared from D-fructose (**1**) by the literature procedures[5–8], **2** (19%) had m.p. 131–132°, $[\alpha]_D^{25}$ +19° (*c* 0.2, ethanol); lit.[8] m.p. 132–133°, $[\alpha]_D^{20}$ +14.5° ±0.8° (ethanol). Conventional treatment of **2** with acetic anhydride–pyridine gave the 4-acetate **3**, m.p. 79–80°, $[\alpha]_D^{25}$ +20° (*c* 2.2, chloroform); lit.[7] m.p. 80–82°, $[\alpha]_D$ +20° (chloroform).

*2,3-*O*-Isopropylidene-1,6-di-*S*-methyl-1,6-dithio-β-*D*-fructofuranose* (**4**). — A mixture of **2** (5.28 g, 10.0 mmol) and sodium methanethiolate (2.10 g, 30 mmol) in *N,N*-dimethylformamide (60.0 mL) was stirred at 25° for 1 h and then heated for 1 h at 80°. The mixture was cooled to 25°, poured into ice and water, and extracted with ether, and the extract was washed with water, dried (Na_2SO_4), and concentrated under reduced pressure to dryness. Column chromatography (ethyl acetate–light petroleum, 1:4) of the residue gave **4** (2.42 g, 86%), m.p. 85–86° (from methanol–acetone), $[\alpha]_D^{25}$ +22° (*c* 1.3, chloroform). N.m.r. data ($CDCl_3$): ^{1}H (200 MHz), δ 4.46 (s, 1 H, H-3), 4.26, 3.80 (ABq, 2 H, *J* 9.5 Hz, H-4 and HO-4), 4.19 (d, 1 H, *J* 7.5 Hz, H-5), 3.10, 2.85 (ABq, 2 H, *J* 15.0 Hz, H-1a,1b), 2.84 (d, 2 H, *J* 7.5 Hz, H-6a,6b), 2.27, 2.18 (2 s each, 3 H, 2 MeS), 1.53, 1.35 (2 s each, 3 H, CMe_2) (these assignments were confirmed by decoupling and exchange with D_2O); ^{13}C (50.3 MHz), δ 116.8 (*C*Me_2), 112.2 (C-2), 89.1 (C-3), 88.2 (C-5), 77.0 (C-4), 39.9 (C-6), 36.8 (C-1), 26.9, 25.7 (2 SCH_3), 17.8, 15.8 (C*Me*).

Anal. Calc. for $C_{11}H_{20}O_4S_2$: C, 47.14; H, 7.14; S, 22.86. Found: C, 47.03; H, 7.48; S, 22.96.

*1,6-Di-*S*-methyl-1,6-dithio-*D*-fructofuranose* (**5**). — To a solution of **4** (1.12 g, 4.0 mmol) in aqueous 95% ethanol (10 mL) was added M sulfuric acid (4 mL). The mixture was stirred and boiled under reflux for 7 h, cooled, diluted with water (10 mL), neutralized ($BaCO_3$), and centrifuged, and the clear supernatant solution was concentrated under reduced pressure at <50°. Column chromatography (ethyl acetate–

toluene, 3:2) of the residue, then treatment with activated charcoal in water, gave **5** (0.59–0.67 g, 61–70%), isolated as a colorless syrup with the β anomer preponderant; b.p. 174° (dec.), $[\alpha]_D^{25}$ +35.5° (*c* 1.4, water). N.m.r. data: ^{1}H (D_2O, 200 MHz), δ 3.85–4.20 (m, 3 H, H-3,4,5), 2.62–3.00 (m, 4 H, H-1a,1b,6a,6b), 2.15, 2.18 (2 s, each 3 H, 2 Me); ^{13}C (CD_3OD, 200 MHz), δ 102.8 (C-2), 80.7 (C-5), 78.7 (C-3), 77.5 (C-4), 39.5 (C-6), 38.0 (C-1), 16.1, 14.8 (2 SCH_3). The signals for the α anomer, present in minor amounts, are not listed.

Anal. Calc. for $C_8H_{16}O_4S_2$: C, 40.00; H, 6.67; S, 26.67. Found: C, 39.82; H, 7.04; S, 26.58.

*1,6-Di-*S*-methyl-1,6-dithio-*D*-fructofuranose bis(*S*-oxide)* (**6**). — To a stirred solution of **5** (1.48 g, 6.1 mmol) under nitrogen in acetone (15 mL) maintained at 0–5° was added a solution of 85% *m*-chloroperoxybenzoic acid (2.09 g, 12.2 mmol) in acetone (40 mL) at such a rate that the temperature did not exceed 5°. After stirring for 20 min at 0–5°, the mixture gave a negative starch–iodide test and the solvent was evaporated under reduced pressure. Column chromatography (chloroform–methanol–water, 8:4:1, lower layer) of the residue followed by treatment with activated charcoal in water gave **6** (0.78 g, 47%), isolated as a colorless, hygroscopic, amorphous solid, $[\alpha]_D^{25}$ +54° (*c* 1, water). ^{1}H-N.m.r. data (D_2O, 200 MHz): δ 4.86–4.40 (m, 3 H, H-3,4,5), 3.10–3.60 (m, 4 H, H-1a,1b,6a,6b), 2.81, 2.79 (2 s, each 3 H, 2 MeSO).

Anal. Calc. for $C_8H_{16}O_6S_2 \cdot 0.5H_2O$: C, 34.16; H, 6.05; S, 22.78. Found: C, 33.99; H, 6.21; S, 22.69.

*1,6-Di-*S*-methyl-1,6-dithio-*D*-fructofuranose bis(*S,S*-dioxide)* (**7**). — To a stirred solution of **5** (740 mg, 3.08 mmol) in acetone (5 mL) at 0–5° under nitrogen was added a solution of 85% *m*-chloroperoxybenzoic acid (2.86 g, 16.6 mmol) in acetone (40 mL) at such a rate that the temperature did not exceed 5°. The mixture was stirred for 2 h, saturated aqueous sodium hydrogen sulfite (1.5 mL) and solid sodium hydrogen sulfite (216 mg) were added, stirring was continued until the mixture had a negative starch–iodide test, and the acetone was then evaporated under reduced pressure. Column chromatography (chloroform–methanol, 85:15) of the residue gave **7** (600 mg, 64%), m.p. 130–131° (from methanol–acetone), $[\alpha]_D^{25}$ +30° (*c* 1, water). ^{1}H-N.m.r. data (D_2O, 200 MHz): δ 4.51–4.03 (m, 3 H, H-3,4,5), 3.81–3.57 (m, 4 H, H-1a,1b,6a,6b), 3.21 and 3.19 (2 s, each 3 H, 2 $MeSO_2$).

Anal. Calc. for $C_8H_{16}O_8S_2$: C, 31.58; H, 5.26; S, 21.05. Found: C, 31.85; H, 5.54; S, 20.88.

*2,3,6,3′,4′-Penta-*O*-acetyl-1′,6′-di-*O*-tosylsucrose* (**11**). — To a solution of 2,3,6,3′,4′-penta-*O*-acetylsucrose[9–11] (**10**; 4.0 g, 7.24 mmol) in dry pyridine (40 mL) at 0° was added tosyl chloride (3.17 g, 16.6 mmol) with stirring. The mixture was kept for 4 days at 0°, then poured onto ice and water, and the syrupy product was extracted with ethyl acetate–ether (1:1). The extract was washed successively with water, aqueous 5% cupric sulfate, and water, dried (Na_2SO_4), and concentrated under reduced pressure. Column chromatography (chloroform–acetone–light petroleum, 4:1:3) of the residue gave **11** (4.1 g, 66%), isolated as an amorphous solid, $[\alpha]_D^{25}$ +42° (*c* 1.1, chloroform). ^{1}H-N.m.r. data ($CDCl_3$, 470 MHz): δ 7.81–7.79 (m, 4 H, Ar-H), 7.39–7.36 (m, 4 H,

Ar-H), 5.40 (d, 1 H, *J* 6.0 Hz, H-3'), 5.28 (d, 1 H, *J* 2.5 Hz, H-1), 5.23 (t, 1 H, *J* 10.2 Hz, H-3), 5.19 (t, 1 H, *J* 6.0 Hz, H-4'), 4.73 (dd, 1 H, *J* 2.5 and 10.2 Hz, H-2), 4.28–3.98 (m, 8 H, H-5,5',6a,6b,1'a,1'b,6'a,6'b), 3.46 (ddd, 1 H, *J* 6.6, 7.3, and 10.2 Hz, H-4), 3.01 (d, 1 H, *J* 6.6 Hz, HO-4), 2.47 (s, 6 H, 2 ArMe), 2.10 (6 H), 2.07 (3 H), 2.06 (3 H), 2.00 (3 H) (4 s, 5 Ac).

Anal. Calc. for $C_{36}H_{44}O_{20}S_2$: C, 50.23; H, 5.12; S, 7.44. Found: C, 50.30; H, 5.39; S, 7.34.

2,3,4,6,3',4'-Hexa-O-*acetyl-1',6'-di*-O-*tosylsucrose* (**12**). — Conventional treatment of **11** (5.31 g, 6.17 mmol) with pyridine (12 mL) and acetic anhydride (3.0 mL) for 15 h at 25° gave a crude product (5.50 g), a solution of which in acetone was treated with activated charcoal and then concentrated to give **12** (5.48 g, 98%), isolated as a colorless amorphous solid, $[\alpha]_D^{25}$ +49° (*c* 1.45, chloroform). N.m.r. data ($CDCl_3$): ^1H (470 MHz), δ 7.80–7.75 (m, 4 H, Ar-H), 7.41–7.35 (m, 4 H, Ar-H), 5.42 (d, 1 H, *J* 6.5 Hz, H-3'), 5.31 (t, 1 H, *J* 9.9 Hz, H-3), 5.23 (d, 1 H, *J* 3.2 Hz, H-1), 5.19 (t, 1 H, *J* 6.5 Hz, H-4'), 4.93 (t, 1 H, *J* 9.9 Hz, H-4), 4.76 (dd, 1 H, *J* 3.2 and 10.0 Hz, H-2), 4.06, 3.90 (ABq, 2 H, *J* 11.0 Hz, H-1'a,1'b), 4.20–4.04 (m, 6 H, H-5,5',6a,6b,6'a,6'b), 2.47 (s, 6 H, 2 Ar-*Me*), 2.10 (3 H), 2.07 (6 H), 2.03 (3 H), 2.02 (3 H), 2.00 (3 H) (6 s, each 3 H, 6 Ac); ^{13}C (50.3 MHz), δ 170.6, 169.9, 169.9, 169.9, 169.5, 169.5, 169.3, 169.3 (2 Ar*C*OO and 6 CH_3*C*OO), 102.7 (C-2'), 89.6 (C-1), 78.5 (C-5'), 75.1 (C-3'), 74.2 (C-4'), 69.6 (C-3), 69.5 (C-5), 69.0 (C-2), 68.5 (C-4), 68.2 (C-6'), 67.3 (C-1'), 62.2 (C-6), 21.7, 21.7 (2 × Ar-*C*H_3), 20.6, 20.6, 20.6, 20.6, 20.4, 20.4 (6 × CH_3*C*OO). Chemical shifts for the carbon atoms of the benzene ring are not listed.

Anal. Calc. for $C_{38}H_{46}O_{21}S_2$: C, 50.55; H, 5.10; S, 7.10. Found: C, 50.84; H, 5.31; S, 6.98.

2,3,4,6,3',4'-Hexa-O-*acetyl-1,6-dibromo-1,6-dideoxysucrose* (**13**). — A mixture of lithium bromide (4.35 g, 50 mmol), **12** (2.25 g, 2.5 mmol), toluene (125 mL), and hexamethylphosphoramide (8.96 g, 50 mmol) was stirred and heated to reflux under nitrogen, and ~60 mL of the solvent were removed by distillation. After 20 h at reflux, more solvent (45 mL) was distilled and boiling under reflux was continued for 3 h. The mixture was cooled (ice bath), diluted with toluene (100 mL), washed with water (3 × 50 mL), dried ($MgSO_4$), filtered, and concentrated under reduced pressure. Column chromatography (chloroform–acetone–light petroleum, 4:1:10) of the residue, followed by treatment with activated charcoal in acetone, gave **13** (1.54 g, 86%), isolated as a colorless amorphous solid, $[\alpha]_D^{25}$ +38° (*c* 1.8, chloroform). N.m.r. data ($CDCl_3$): ^1H (200 MHz), δ 5.72 (d, 1 H, *J* 6.0 Hz, H-3'), 5.64 (d, 1 H, *J* 3.7 Hz, H-1), 5.44 (t, 1 H, *J* 10.0 Hz, H-3), 5.38 (t, 1 H, *J* 6.0 Hz, H-4'), 5.07 (t, 1 H, *J* 10.0 Hz, H-4), 4.92 (dd, 1 H, *J* 3.7 and 10.0 Hz, H-2), 4.35–4.18 (m, 4 H, H-5,5',6a,6b), 3.62, 3.49 (ABq type, 2 H, *J* 11.4 Hz, H-1'a,1'b), 3.62 (d, 2 H, *J* 6.6 Hz, H-6'a,6'b), 2.18 (3 H), 2.11 (6 H), 2.10 (3 H), 2.05 (3 H), 2.02 (3 H) (5 s, 6 Ac); ^{13}C (50.3 MHz), δ 170.6, 170.0, 170.0, 169.8, 169.5, 169.5 (6 *C*H_3COO), 103.9 (C-2'), 90.3 (C-1), 80.9 (C-5'), 76.9 (C-3'), 76.9 (C-4'), 70.0 (C-3), 69.5 (C-5), 68.6 (C-2), 68.1 (C-4), 61.9 (C-6), 32.5 (C-6'), 31.3 (C-1'), 20.7, 20.7, 20.7, 20.7, 20.7, 20.7 (6 CH_3*C*OO).

Anal. Calc. for $C_{24}H_{32}Br_2O_{15}$: C, 40.00; H, 4.44; Br, 22.22. Found: C, 40.18; H, 4.58; Br, 22.44.

*2,3,4,6,3',4'-Hexa-*O*-acetyl-1',6'-di-*S*-methyl-1',6'-dithiosucrose* (**14**). — A mixture of sodium methanethiolate (350 mg, 5 mmol), **13** (1.44 g, 2 mmol), and *N,N*-dimethylformamide (10 mL) was stirred and heated at 100–105° under nitrogen for 4 h, then cooled, poured into ice and water, and extracted with ethyl acetate. The extract was washed with water, dried (Na_2SO_4), filtered, and concentrated under reduced pressure to dryness. The residue was treated with acetic anhydride (2 mL) and pyridine (5 mL) at 25°, and then worked-up as described above. Column chromatography (chloroform–acetone–light petroleum, 4:1:5) of the product gave **14** (0.91 g, 70%), isolated as a colorless hygroscopic amorphous solid, $[\alpha]_D^{25}$ +53° (*c* 1.3, chloroform). N.m.r. data ($CDCl_3$): ^{1}H, (200 MHz), δ 5.81 (d, 1 H, *J* 7.4 Hz, H-3'), 5.61 (d, 1 H, *J* 3.5 Hz, H-1), 5.47 (t, 1 H, *J* 9.6 Hz, H-3), 5.42 (t, 1 H, *J* 7.4 Hz, H-4'), 5.07 (t, 1 H, *J* 9.6 Hz, H-4), 4.92 (dd, 1 H, *J* 3.5 and 9.6 Hz, H-2), 4.34–4.18 (m, 4 H, H-5,5',6a,6b), 2.93–2.78 (m, 4 H, H-1'a,1'b,6'a,6'b), 2.21 (3 H), 2.18 (3 H), 2.12 (3 H), 2.11 (6 H), 2.09 (3 H), 2.05 (3 H), 2.02 (3 H) (7 s, 24 H, 2 SMe and 6 Ac); ^{13}C (50.3 MHz), δ 170.6, 170.2, 170.2, 170.0, 170.0, 169.5 (6 CH_3COO), 106.5 (C-2'), 89.9 (C-1), 80.4 (C-5'), 77.2 (C-3'), 76.8 (C-4'), 70.2 (C-3), 69.7 (C-5), 68.3 (C-4), 68.3 (C-2), 61.9 (C-6), 39.7 (C-6'), 37.4 (C-1'), 20.8, 20.8, 20.7, 20.7, 20.7, 20.7 (6 CH_3COO), 17.8, 16.3 (2 SCH_3).

Anal. Calc. for $C_{26}H_{38}O_{15}S_2$: C, 47.71; H, 5.81; S, 9.79. Found: C, 47.77; H, 6.07; S, 9.41.

*1',6'-Di-*S*-methyl-1',6'-dithiosucrose* (**15**). — A mixture of **14** (910 mg, 1.39 mmol), sodium methoxide (54 mg, 1 mmol), and methanol (25 mL) was stirred for 1 h at 25° and then concentrated under reduced pressure to dryness. Column chromatography (chloroform–methanol, 8:2) of the residue followed by treatment with activated charcoal in water gave **15** (0.43 g, 77%), isolated as a colorless, hygroscopic, amorphous solid, $[\alpha]_D^{25}$ +87° (*c* 0.4, ethanol). N.m.r. data (D_2O): ^{1}H (200 MHz), δ 5.41 (d, 1 H, *J* 3.4 Hz, H-1), 4.43 (d, 1 H, *J* 8.0 Hz, H-3'), 4.05 (t, 1 H, *J* 8.0 Hz, H-4'), 3.93 (m, 1 H, H-5), 3.81 (m, 2 H, H-6a,6b), 3.75 (t, 1 H, *J* 10.4 Hz, H-3), 3.68 (t, 1 H, *J* 7.5 Hz, H-5'), 3.51 (dd, 1 H, *J* 3.4 and 10.4 Hz, H-2), 3.45 (t, 1 H, *J* 10.4 Hz, H-4), 3.08, 2.85 (ABq, 2 H, *J* 14.5 Hz, H-1'a,1'b), 2.90 (d, 2 H, *J* 7.5 Hz, H-6'a,6'b), 2.20, 2.17 (2 s, each 3 H, 2 SMe); ^{13}C (50.3 MHz), δ 105.3 (C-2'), 92.2 (C-1), 79.7 (C-5'), 77.1 (C-3'), 76.7 (C-4'), 72.6 (C-3), 72.4 (C-5), 71.1 (C-2), 69.3 (C-4), 60.1 (C-6), 37.6 (C-6'), 36.3 (C-1'), 16.4, 14.6 (2 SCH_3).

Anal. Calc. for $C_{14}H_{26}O_9S_2 \cdot 2.5H_2O$: C, 37.58; H, 6.94; S, 14.32. Found: C, 37.76; H, 6.87; S, 13.94.

To a solution of **15** (50 mg, 0.12 mmol) in water (1 mL) was added M sulfuric acid (1 mL). After heating for 3 h at 95° the mixture was diluted with water (2 mL), neutralized ($BaCO_3$), and concentrated under reduced pressure to dryness. T.l.c. of the residue revealed glucose and **5**.

ACKNOWLEDGMENTS

We thank Michael A. Madson and William Cook for the mass spectrometry.

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