Denmark. Infrared spectra were obtained on either a Beckman IR-33 or a Perkin-Elmer 257 spectrophotometer and ultraviolet spectra were obtained on a Beckman Acta III spectrophotometer. The CD spectra were taken in methanol on a JASCO J-40 recording spectropolarimeter and optical rotation measurements were performed on a Perkin-Elmer 141 polarimeter. Mass spectra were obtained on a Du Pont CEC-492 mass spectrometer. ^{1}H NMR spectra were recorded on a JEOL C-60HL spectrometer using Me_4Si as internal standard. Coupling constants were calculated using first-order approximations. Column chromatography was carried out with silicic acid AR, 100 mesh (Mallinckrodt), activated by heating at 120 °C for 12 h or silica gel 60, 70–270 mesh (Brinkmann).

(15) I. R. C. Bick, R. B. Brown, and W. E. Hillis, *Aust. J. Chem.*, **25**, 449 (1972).
(16) S. Mongkolsuk and F. M. Dean, *J. Chem. Soc.*, 4654 (1964).
(17) P. J. Sawhney and T. R. Seshadri, *J. Sci. Ind. Res., Sect. B*, **13**, 5 (1954).
(18) Pinocembrin was synthesized from phloroglucinol and cinnamoyl chloride by the procedure of S. Fujise and H. Tatsuta, *Ber.*, **74B**, 275 (1941).
(19) K. Hess and H. Frahm, *Ber.*, **71**, 2627 (1938).
(20) Phloroglucinol monomethyl ether was prepared by treatment of phloroglucinol with diazomethane and had melting point[21] (68–71 °C), ^{1}H NMR, and molecular formula data (Anal. Calcd for $C_7H_8O_3$: mol wt, 140.0474. Found: mol wt, 140.0498) consistent with the structure.
(21) K. Weinges and F. Toribio, *Justus Liebigs Ann. Chem.*, **681**, 161 (1965).

Synthesis of Deoxy Sugar. Deoxygenation of an Alcohol Utilizing a Facile Nucleophilic Displacement Step

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Methyl 2-amino-2-deoxy-α-D-glucopyranoside was converted in good yield to the corresponding 3-deoxy analogue. The key steps include the facile nucleophilic displacement of a 3-*O*-trifluoromethylsulfonyl function by benzenethiolate under mild conditions and subsequent desulfurization with sodium in liquid ammonia. Desulfurization was also achieved, but in low yield, with Raney nickel or tributyltin hydride. The nucleophilic displacement step was accompanied by little, if any, neighboring group participation.

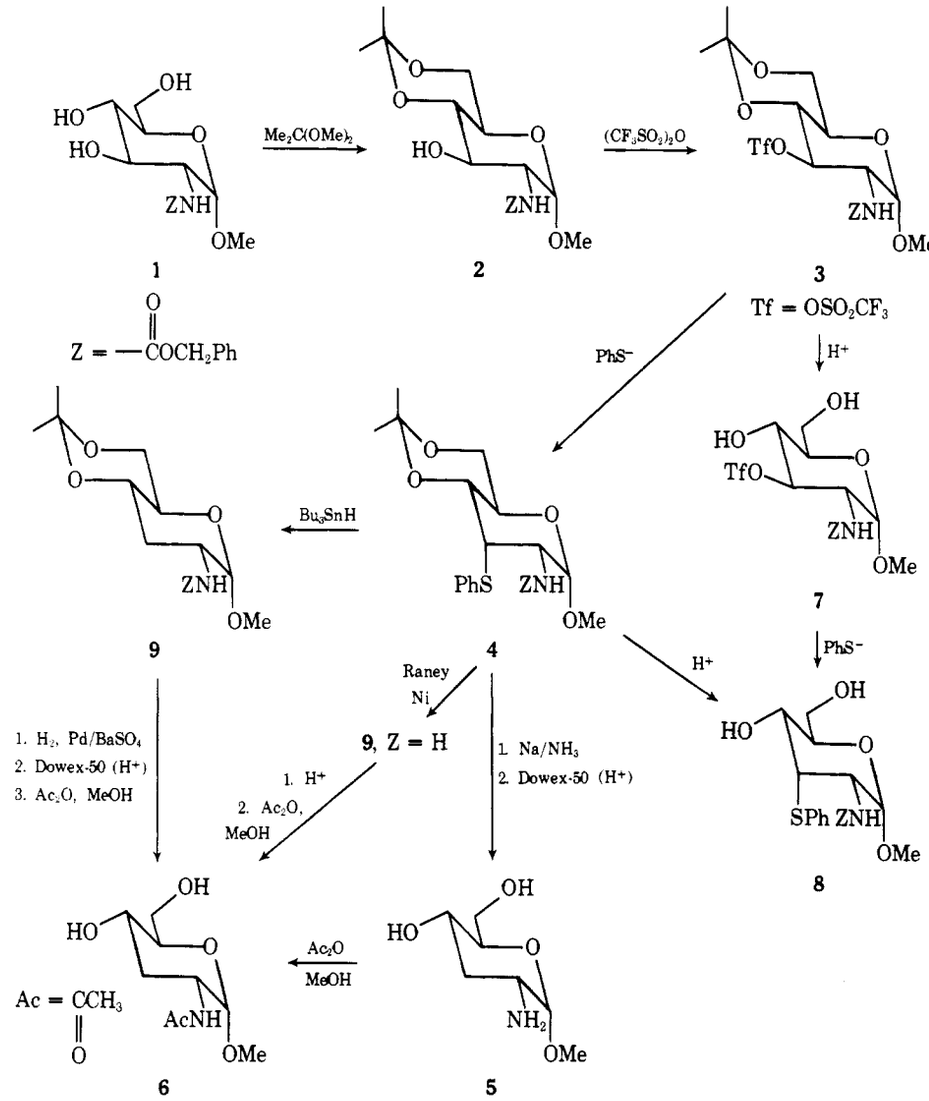
The conversion of an equatorial C-3 hydroxyl to the corresponding deoxy function in an α-linked D-hexopyranosyl glycoside, present in a number of prominent aminoglycoside antibiotics, has been of current interest because of the development of bacterial resistance by phosphorylation of this hydroxyl group.[1] Such a conversion, in several instances, was effected through the use of nucleophilic displacement as one of the key steps.[2] Recently, a reductive method proceeding through free-radical mechanism was also reported.[3] Generally speaking, nucleophilic displacement by presently available methods proceeds with difficulty, which may be accounted for by probable 1,3-diaxial interaction between the aglycone and the approaching nucleophile, as well as by complications arising from neighboring group participation. In the course of our synthetic modification studies of the antibiotic butirosin,[4] we have succeeded in such a conversion by devising a facile nucleophilic displacement. Through the combined use of the trifluoromethylsulfonyl (triflate) function, an exceedingly good leaving group,[5] and the benzenethiolate anion, one of the most powerful nucleophiles,[6] the nucleophilic displacement was achieved under extremely mild conditions. The study of this reaction in model compounds, together with subsequent desulfurization leading to the desired deoxy sugar, will be described in the present paper.

Methyl 2-deoxy-2-[[(phenylmethoxy)carbonyl]amino]-α-D-glucopyranoside (**1**) was converted to the corresponding 4,6-*O*-(1-methylethylidene) derivative (**2**) with 2,2-dimethoxypropane. Triflation of **2** with trifluoromethanesulfonic anhydride afforded the triflate (**3**) in 90% crude yield, which could be further purified by crystallization. Nucleophilic displacement of crude **3** with sodium benzenethiolate at 5 °C gave, almost exclusively (TLC evidence), the 3-(phenylthio)allopyranoside (**4**), which was subsequently isolated in crystalline form in 64% overall yield from **2**. The allo configuration of **4** was readily inferred from its 4,6-O-unsubstituted derivative **8** (cf. below). The conversion of **4** to **5** was conveniently realized by initial treatment with sodium in liquid ammonia,[8] which reductively removed both the phenylthio and the *N*-[(phenylmethoxy)carbonyl] groups, followed by hydrolytic cleavage of the 4,6-O-(1-methylethylidene) group on Dowex 50 × 4 (a strong cation exchange resin) in the hydrogen form. The product, compound **5**, was isolated by elution with aqueous ammonia and further converted to the crystalline *N*-acetyl derivative (**6**) in an overall yield of 81% from **4**. The 3-deoxy-D-ribo configuration in **6** was confirmed by NMR data, which showed a geminal coupling $J_{3a,3e}$ (ca. 11 Hz), two axial–axial couplings $J_{2a,3a}$ (ca. 12 Hz) and $J_{3a,4a}$ (ca. 11 Hz), and two axial–equatorial couplings $J_{1e,2a}$ (ca. 3.8 Hz) and $J_{2a,3e}$ (ca. 4.7 Hz each). The 4,6-di-*O*-acetate of **6** (**6**, OH = OAc) showed properties closely resembling those reported for an identical compound[9] and provided NMR data fully confirming the 3-deoxy-D-ribo configuration.

Other methods for the reductive cleavage of the phenylthio–sp^3 carbon bond in **4** were also examined. Treatment of **4** with nickel boride[10] in boiling ethanol for 12 h gave essentially unchanged starting material. Reaction of **4** with Raney nickel (previously neutralized to pH 7 with acetic acid) in boiling ethanolic solution yielded the corresponding 3-deoxy analogue, but in low yield; under these conditions the *N*-[(phenylmethoxy)carbonyl] group was preferentially hydrogenolyzed, generating the amine which was then irreversibly absorbed by the Raney nickel. Treatment of **4** with tributyltin hydride[11,12] in boiling toluene for 12 h in the presence of the radical initiator 2,2′-azobis(2-methylpropanenitrile) resulted in the isolation of the 3-deoxy compound **9** in less than 37% yield, which was characterized by eventual conversion to the crystalline compound **6**, together with ca. 12% of unreacted **4**. The side products of the reaction, showing much lower TLC mobilities, conceivably could be compounds having a free amino group at C-2 but were not further investigated.

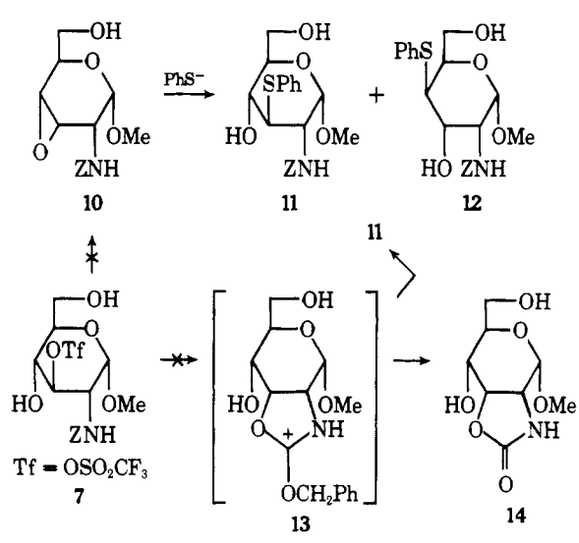
The presence of neighboring groups, such as a hydroxyl or a [(phenylmethoxy)carbonyl]amino group, in trans orientation to the triflate leaving group, may lead to possible complications in the nucleophilic displacement step. To resolve such possibilities, the attack of the benzenethiolate ion on **7**, the 4,6-dihydroxy analogue of **3**, was studied. The product, a 3-deoxy-3-phenylthio-D-allo derivative (**8**), was isolated in crystalline form in high yield (81%) and found to be identical with the product obtained by removal of the 4,6-*O*-(1-methylethylidene) group from **4**. The C-3 configuration in **8**

Scheme I



was ascertained by NMR data. The signal of H-2 in **8** and of H-3 in **8**, each showing two axial–equatorial couplings ($J_{1e,2a}$ = 3.5; $J_{2a,3e}$ = 4.8; $J_{3e,4a}$ = 4.7 Hz), and the signal of H-4 in the crystalline di-*O*-acetate of **8**, showing one axial–equatorial and one axial–axial couplings ($J_{3e,4a}$ = 4.5; $J_{4a,5a}$ = 8.7 Hz), all indicated the presence of an equatorial hydrogen atom, hence an axial phenylthio group at C-3. On the other hand, neighboring group participation by the C-4 hydroxyl would lead to the epoxide **10**, which would then further react with the nucleophile to give either a D-gluco derivative **11**, or a D-gulo derivative **12**, or a mixture of both, instead of the D-allo derivative **8** actually obtained in high yield. Neighboring participation by the 2-[[(phenylmethoxy)carbonyl]-amino] group would give rise to the oxazolinium intermediate **13**, which then may undergo elimination to give the oxazolone **14**, or nucleophilic attack to give the D-gluco derivative **11**, instead of **8** as actually obtained. Evidently then, under the experimental conditions used, the benzenethiolate displacement of triflate took place mostly as a straightforward S_N2 type reaction, with little, if any, neighboring group participation, thus constituting a promising reaction of synthetic utility.

Scheme II



Thus a simple reaction series for the conversion of a hydroxyl group to the deoxy function, utilizing a facile nucleophilic displacement step, has been devised. The application of this procedure to more complex systems, such as aminoglycoside antibiotics, will be the subject of further communications.[13]

Experimental Section

General. Thin layer chromatography (TLC) was performed using glass plates precoated with silica gel (Quanta Q1F, 10-cm length, Quantum Industries, Fairfield, N.J.) and aqueous solution of am-

monium molybdate containing 5% phosphoric acid and 5% sulfuric acid as spray. Column chromatography was performed using silica gel (E. Merck 60, 0.013–0.20 mm) packed by gravity as slurries in solvents. Melting points, unless otherwise specified, were determined in a silicone oil bath and were uncorrected. Nuclear magnetic resonance (NMR) spectra were determined with a Bruker WH-90 spectrometer by the pulsed Fourier transformation technique (except those for compounds **2, 3, 4,** and **7,** which were determined on a Varian A-60 spectrometrr). Chemical shift data are reported in δ (ppm) units relative to tetramethylsilane in the solvent chloroform-*d* and pyridine-d_5 and to sodium 3-(trimethylsilyl)propanoate-*2,2,3,3-d*$_4$ in deuterium oxide and methanol-d_4. Eu(fod$_3$)$_3$-d_{27}, i.e., tris-[6,6,7,7,8,8,8-heptafluoro-2,2-di(methyl-d_3)-3,5-octanedion-*1,1,1-d*$_3$-ate-*O,O'*]europium(3+), was used as a shift reagent. The triflates **3** and **7** were stable at −29 °C and were generally stored at this temperature.

Methyl 2-Deoxy-4,6-*O*-(1-methylethyldiene)-2-[[(phenylmethoxy)carbonyl]amino]-α-D-glucopyranoside (2). A solution of methyl 2-deoxy-2-[[(phenylmethoxy)carbonyl]amino]-α-D-glucopyranoside (**1**, 8.67 g) in 85 mL of dry *N,N*-dimethylformamide containing 0.89 g of *p*-toluenesulfonic acid and 17.5 mL of 2,2-dimethoxypropane was stirred for 36 h at room temperature. The mixture was neutralized with 0.72 mL of triethylamine and evaporated to a syrup in vacuo. A mixture of the syrup and 50 mL of water was stirred at 5 °C for 1 h, the aqueous phase decanted, and the residue extracted into 500 mL of chloroform. The chloroform extract was washed with water and saturated sodium chloride solution, dried over sodium sulfate, and evaporated in vacuo to give 7.34 g of a sticky semisolid containing some tenaciously held, residual *N,N*-dimethylformamide. The material was homogeneous by TLC (chloroform–methanol, 75:1), and its NMR spectrum was consistent with structure **2.**

Methyl 2-Deoxy-4,6-*O*-(1-methylethylidene)-2-[[(phenylmethoxy)carbonyl]amino]-3-*O*-[(trifluoromethyl)sulfonyl]-α-D-glucopyranoside (3). To a solution of 4.1 g (11.17 mmol) of **2** in 50 mL of 1,2-dichloroethane and 12 mL of dry pyridine cooled to 0 °C was added a solution of 2.0 mL (12.5 mmol) of trifluoromethanesulfonic anhydride in 15 mL of 1,2-dichloroethane dropwise with stirring over a 30-min period. After stirring for 1 h at 0 °C the reaction was complete according to TLC (1% methanol in benzene). Following the addition of another 100 mL of 1,2-dichloroethane the reaction mixture was washed with water, dilute hydrochloric acid, aqueous sodium bicarbonate, water, and saturated sodium chloride solution and dried over sodium sulfate. Solvent removal in vacuo afforded crude **3,** which was used directly in the next step. The yield, estimated from a similar run, was about 89%. Recrystallization of a small sample from toluene–petroleum ether gave pure **3,** mp 94–95 °C.

Anal. Calcd for $C_{19}H_{24}F_3NO_9S$ (499.5): C, 45.69; H, 4.84; N, 2.80; S, 6.41. Found: C, 45.68; H, 4.80; N, 2.75; S, 6.76.

Methyl 2,3-Dideoxy-4,6-*O*-(1-methylethylidene)-2-[[(phenylmethoxy)carbonyl]amino]-3-(phenylthio)-α-D-allopyranoside (4). To a suspension of 2.4 g (50 mmol) of sodium hydride (50% in mineral oil) in 20 mL of *N,N*-dimethylformamide was added 7.2 mL (70 mmol) of benzenethiol dropwise with stirring and cooling in a nitrogen atmosphere. Stirring was continued at room temperature for 3 h to give a solution of sodium benzenethiolate. The solution was cooled to 0 °C, and a solution of the crude, dried triflate **3,** prepared from 4.1 g (11.2 mmol) of **2** as described above, in slightly more than 5 mL of dry *N,N*-dimethylformamide was added in one portion. The mixture was stirred overnight at 5 °C, and TLC (0.5% methanol in benzene) showed the complete disappearance of starting material and the almost exclusive formation of a single product, with only minute traces of side products. The mixture was neutralized by adding 2.9 mL of acetic acid and 3 mL of water. After the addition of 100 mL of benzene, the mixture was washed four times with water, then with saturated sodium chloride solution, and dried over sodium sulfate. Solvent removal in vacuo afforded an oil which was chromatographed over silica gel using 5% ethyl acetate in toluene as eluent. The fractions containing pure **4** were combined, evaporated, and recrystallized from benzene–petroleum ether to give 3.127 g (6.8 mmol) of crystals, mp 115–116 °C, $[\alpha]^{23}D$ +46.8 (*c* 1, chloroform).

Anal. Calcd for $C_{24}H_{29}NO_6S$ (459.5): C, 62.73; H, 6.36; N, 3.05; S, 6.98. Found: C, 63.00; H, 6.49; N, 2.97; S, 7.06.

An additional 267 mg (0.58 mmol) of **4,** mp 114–115 °C, was obtained from the tailing chromatographic fractions.

Methyl 2-Amino-2,3-dideoxy-α-D-*ribo*-hexopyranoside (5) and Methyl 2-(Acetylamino)-2,3-dideoxy-α-D-*ribo*-hexopyranoside (6). To 50 mL of liquid ammonia was added 233 mg (0.51 mmol) of finely divided **4.** Small pieces of metallic sodium was added with stirring until a blue color persisted for 1 min. The excess sodium was removed by addition of ammonium chloride crystals, and the ammonia was evaporated to give a dry residue which was then extracted with methanol. Evaporation of the methanol extract gave a residue, which was then extracted with ethanol. Subsequent evaporation of the ethanol extract gave another residue, which was mixed with water and washed three times with benzene to remove benzenethiol. The aqueous layer was passed over a 10-mL column of Dowex 50 × 4 (hydrogen form),[14] and the column was washed thoroughly with water. Elution of the resin with 1 N aqueous ammonia followed by evaporation in vacuo afforded crude **5** as a white solid. The product was N-acetylated in a methanol–water (1:1) solution at room temperature by the addition of 0.2 mL of acetic anhydride. After 3 h evaporation to dryness afforded **6** as a crystalline residue. Recrystallization from ethanol gave 90 mg (0.41 mmol) of pure **6,** mp 211–212 °C, $[\alpha]^{23}D$ +138° (*c* 1, water).

Anal. Calcd for $C_9H_{17}NO_5$ (219.2): C, 49.30; H, 7.82; N, 6.39. Found: C, 49.30; H, 8.08; N, 6.26.

NMR (D_2O): H-2, δ 3.98 (d of t, $J_{1,2}$ = 3.8, $J_{2,3e}$ = 4.7, $J_{2,3}$ = 12.5 Hz, *J* values obtained by spin decoupling); H-3a, δ 1.79 (q with additional fine splittings, width 34.5 Hz, $J_{3a,3e} \simeq J_{3a,4} \simeq$ 11 Hz); H-3e, δ 2.1 (m, partially hidden by CH_3C=O). NMR (pyridine-d_5): H-1, δ 5.00 (d, $J_{1,2}$ = 3.5 Hz).

Acetylation of **6** with acetic anhydride in pyridine afforded the 4,6-di-*O*-acetate of **6,** mp 138 °C, $[\alpha]^{23}D$ +112° (*c* 0.38, methanol) (reported[9] +90°).

Anal. Calcd for $C_{13}H_{21}NO_7$ (303.31): C, 51.48; H, 6.98; N, 4.62. Found: C, 50.80; H, 6.74; N, 4.52.

NMR ($CDCl_3$): H-1, δ 4.58 (d, $J_{1,2}$ = 3.5 Hz); H-2, δ 4.22 (d of d of q, partly hidden, $J_{2,3e}$ = 4.6, $J_{2,3a}$ = 12.5 Hz); H-3e, δ 2.2 (d of t, $J_{3a,3e}$ = 11.5 Hz); H-3a, δ 1.64 (q, $J_{3a,4}$ = 11.0 Hz); H-4, δ 4.80 (d of t, $J_{3e,4}$ = 5.0, $J_{4,5}$ = 10.2 Hz); H-5, δ 3.82 (d of q, $J_{5,6}$'s = 4.5 and 3.0 Hz); H-6, δ 4.17 (q); $-OCH_3$, δ 3.39 (s); $-OC(:O)CH_3$'s, δ 1.97 (s), 2.02 (s), and 2.08 (s); NH, δ 5.56 (d, broad, $J \sim$ 9.6 Hz).

The spectrum is identical with that reported in the literature.[9]

Methyl 2-Deoxy-2-[[(phenylmethoxy)carbonyl]amino]-3-*O*-[(trifluoromethyl)sulfonyl]-α-D-glucopyranoside (7). Chromatographically pure **3,** 0.30 g, was warmed in 3 mL of moist toluene and cooled to room temperature. Needles separated, and the crystallization process was completed by gradual addition of petroleum ether. After standing overnight at 5 °C, the product was filtered from the mother liquor, which was strongly acidic to pH paper, and dried affording 0.18 g of **7,** mp 88–91 °C. The product was differentiated from the starting material **3** by the respective ^1H NMR spectra and by TLC, which showed that **7** had a much lower mobility than **3** in benzene containing 1% of methanol.

Anal. Calcd for $C_{16}H_{20}F_3NO_9S$ (543.5): C, 41.83; H, 4.38; N, 3.04; S, 6.97. Found: C, 42.24; H, 4.41; N, 3.11; S, 6.89.

Compound **7** formed a di-*O*-acetate with acetic anhydride–pyridine, needles from benzene–petroleum ether, mp 109–110 °C dec.

Anal. Calcd for $C_{20}H_{24}F_3NO_{11}S$ (543.5): C, 44.20; H, 4.45; N, 2.58; S, 5.90. Found: C, 44.12; H, 4.56; N, 2.81; S, 6.13.

Methyl 2,3-Dideoxy-2-[[(phenylmethoxy)carbonyl]amino]-3-(phenylthio)-α-D-allopyranoside (8). A. From Compound 7. A solution of sodium benzenethiolate was prepared from 240 mg (5 mmol) of sodium hydride (50% in mineral oil), 0.9 mL (9 mmol) of benzenethiol, and 5 mL of *N,N*-dimethylformamide (cf. preparation of **4,** above). Compound **7,** 0.30 g (0.65 mmol), was added with stirring at 5 °C. After additional stirring overnight at 5 °C, the solution was neutralized with 3 mL of 2 N acetic acid, and the solvent was removed in vacuo. The residue was dissolved in chloroform, washed with water (two times) and saturated sodium chloride, and dried over sodium sulfate. The filtered solution was passed over a column containing 9 g of silica gel. The column was washed well with chloroform and finally eluted with 5% methanol in chloroform. The fractions containing product were combined, evaporated, and crystallized from water to give 0.23 g (0.53 mmol) of **8.** Recrystallization from ethyl acetate–petroleum ether gave the analytical sample, mp 61–63 °C.

Anal. Calcd for $C_{21}H_{25}NO_6S \cdot H_2O$ (435.5): C, 57.65; H, 6.22; N, 3.20; S, 7.33. Found: C, 57.87; H, 5.97; N, 3.16; S, 7.39.

NMR (CD_3OD): H-1, δ 4.63 (d, $J_{1,2}$ = 3.5 Hz); H-2, δ 4.17 (t, $J_{2,3}$ = 4.8 Hz); relationship verified by spin decoupling. NMR [$CDCl_3$, 2.5% solution containing ca. 0.6% Eu(fod$_3$)d_{27}]: H-1, δ 5.02 (d, $J_{1,2}$ = 3.5 Hz); H-3, δ 4.18 (t, $J_{2,3} \simeq J_{3,4} \simeq$ 4.7 Hz).

Compound **8** formed a di-*O*-acetate with acetic anhydride in pyridine, needles from hexane, mp 96–97 °C.

Anal. Calcd for $C_{25}H_{29}NO_8S$ (503.6): C, 59.63; H, 5.81; N, 2.78; S, 6.37. Found: C, 59.89; H, 5.92; N, 2.76; S, 6.61.

NMR ($CDCl_3$): H-1, δ 4.69 (d, $J_{1,2}$ = 3.5 Hz); H-3, δ 4.12 (t, $J_{2,3} \simeq$

$J_{3,4} \simeq 4.5$ Hz); H-4, δ 4.98 (d of d, $J_{4,5} \simeq 8.7$, $J_{3,4} \simeq 4.5$ Hz; additional complex splittings at the lower field doublet, probably due to virtual coupling with H-5), H-2, H-5, and H-6, δ 4.20–4.46 (m, overlapping); all assignments verified by spin decoupling. NMR (pyridine-d_5): H-4, δ 5.4 [q, partly hidden by $-C(:O)OCH_2C_6H_5$, $J_{3,4} = 3.5$, $J_{4,5} \simeq 10$ Hz].

B. From Compound 4. Compound **4** (0.20 g) was heated on a steam bath in 10 mL of acetic acid–water (4:1) for 1 h and cooled. The solution was evaporated to dryness in vacuo. The residue was acetylated with acetic anhydride in pyridine to give needles from hexane, mp 96–97 °C, identical with the di-*O*-acetate of **8** by TLC (toluene–ethyl acetate, 8:2) and mixture melting point determination. The sample was de-*O*-acetylated with sodium methoxide in methanol at 5 °C to yield a crystalline product identified as **8** by NMR and TLC, mp 58–60 °C.

Studies on the Desulfurization of 4 by Other Methods. A. Nickel Boride. A solution of 480 mg (2.0 mmol) of nickel chloride hexahydrate in 10 mL of water was aerated for 10 min with nitrogen, then treated with a 2 N aqueous sodium borohydride solution added dropwise with stirring until the precipitation of nickel boride ceased (1.9 mL used). The precipitate was washed three times with ethanol and then heated under reflux with a solution of 20 mg (0.043 mmol) of **4** in 3.0 mL of ethanol for 12 h. TLC showed that no reaction had occurred.

B. Raney Nickel. A suspension of Raney nickel (W. R. Grace, Davison Chemical, No. 30) was neutralized with 2 N acetic acid from pH 10.8 to 7.0 with stirring. The catalyst was washed three times with water, five times with *N,N*-dimethylformamide, and finally three times with methanol and used in the following desulfurization reaction.

Compound **4** (273 mg 0.59 mmol) in 10 mL of methanol and 2.0 mL (ca. 2.4 g) of settled Raney nickel was stirred at room temperature for 2 h. TLC showed the presence of mostly the 2-amino analogue of **4**, i.e., **4** (Z = H) (R_f, 1% methanol in toluene, 0.0; 5% methanol in benzene, 0.27), in addition to some starting material (R_f, 1% methanol in toluene, 0.66) and a small amount of the 2-amino-3-deoxy analogue of **4**, i.e., **9** (Z = H) (R_f, 5% methanol in benzene, >0.06). The presence of a free amino group was detected by ninhydrin, and the presence of a phenylthio group by strong fluorescence quenching under UV at 2537 Å. The reaction mixture was filtered and evaporated to dryness giving 137 mg of residue [65% yield assuming all of the product to be **4** (Z = H)].

The above reaction product (125 mg) in 1.5 mL of methanol and 0.6 mL of settled Raney nickel was heated under reflux with stirring for 4 h. Another 0.7 mL of settled Raney nickel was added, and reflux with stirring was continued for 4 h. TLC showed that the major product was **9** (Z = H), with a minor amount of **4** (Z = H). The reaction mixture was filtered and evaporated to 75 mg of colorless oil [60% yield assuming all of the product to be **9** (Z = H)].

The 4,6-*O*-(1-methylethylidene) group was removed from crude **9** by treatment with 4.2 mL of acetic acid and 2.8 mL of water at 45 °C for 11 h. The reaction mixture was evaporated to dryness in vacuo, treated with 5 mL of methanol and 2 mL of acetic anhydride for 3 days at room temperature, and evaporated to give 72 mg of brown residue. Two recrystallization from methanol–acetone gave 16.7 mg of **6**, identified by IR, NMR, and melting point (215 °C, Fisher-Johns hot stage, uncorrected).

C. Tributyltin Hydride. To a solution of 0.28 g (0.25 mL, 0.96 mmol) of tributyltin hydride in 1.5 mL of dry toluene under an argon atmosphere was added a solution of 73.5 mg (0.156 mmol) of **4** in 2 mL of toluene. The clear solution was heated under reflux for 25 h. TLC (1% methanol in toluene) indicated the presence of largely unreacted **4** (R_f 0.50), together with minor amounts of **9** (R_f 0.33) and some decomposition products (R_f's 0.13, 0.08, 0.05, 0.00). A solution of 5.2 mg of 2,2′-azobis(2-methylpropanenitrile) (0.032 mmol) in 1 mL of toluene was then added and the reflux continued. After 2 h, TLC showed the presence of **4** and **9** in approximately equal intensities, a very weak spot at 0.28, and very small spots at R_f's less than 0.08. After an additional 7 h of reflux, the TLC spot for **9** became stronger relative to that for **4**, but the side product with R_f 0.05 had also increased. The solution was concentrated and applied to a 20 cm × 20 cm × 1000 μ silica gel plate (Quanta PQ1F), which was then developed two times with 1% methanol in benzene. Compound **9** (together with a trace of side product with R_f 0.28), 20 mg (less than 38%), was isolated, and the starting material **4**, 9.3 mg (12.7%), was recovered. The solvent front smelled very strongly of benzenethiol. Compound **9** was hydrogenolyzed for 1.5 h with a stream of hydrogen in methanol containing 2 N acetic acid and 26 mg of 20% palladium on barium sulfate catalyst. Addition of another 20 mg of catalyst and further treatment with hydrogen did not lead to any more hydrogenolysis, as evidenced by the lack of further evolution of carbon dioxide. The catalyst was filtered and washed with aqueous methanol, and solvent removal gave 17 mg of residue. An aqueous solution of the residue was percolated through a column containing 1.0 mL of Dowex 50 × 4 (hydrogen form).[12] The column was washed with water, allowed to stand for ca. 40 min, and eluted with 33 mL of 1 N aqueous ammonia. Evaporation of the eluate in vacuo gave 9.7 mg of residue. A solution of the residue in 0.35 mL of water was treated with 1.1 mL of methanol and 0.6 mL of acetic anhydride for 20 h. Evaporation gave 14 mg of residue which was recrystallized from hot ethanol to give 1.4 mg of **6**, identified by its infrared spectrum and melting point (215 °C, Fisher-Johns hot stage, uncorrected). Evaporation of the mother liquor gave an additional 4.3 mg of solid.

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Registry No.—**1**, 4704-15-8; **2**, 61348-62-7; **3**, 61364-33-8; **4**, 61348-63-8; **5**, 61348-64-9; **6**, 25541-56-4; **6** di-*O*-Ac, 61348-65-0; **7**, 61348-66-1; **7** di-*O*-Ac, 61348-67-2; **8**, 61348-68-3; **8** di-*O*-Ac, 61348-69-4; 2,2-dimethoxypropane, 77-76-9; trifluoromethanesulfonic anhydride, 358-23-6; sodium benzenethiolate, 930-69-8.

References and Notes

(1) (a) M. Yagisawa, H. Yamamoto, H. Naganawa, S. Kondo, T. Takeuchi, and H. Umezawa, *J. Antibiot.*, **25**, 748 (1972); (b) R. Benveniste and J. Davies, *Annu. Rev. Biochem.*, **42**, 471 (1973); (c) H. Umezawa, *Adv. Carbohydr. Chem. Biochem.*, **30**, 183 (1974).
(2) See, for example, D. Ikeda, T. Tsuchiya, S. Umezawa, and H. Umezawa, *J. Antibiot.*, **26**, 799 (1973), and references cited therein.
(3) D. H. R. Barton and S. W. McCombie, *J. Chem. Soc., Perkin Trans. 1*, 1574 (1976).
(4) (a) P. W. K. Woo, H. W. Dion, and Q. R. Bartz, *Tetrahedron Lett.*, 2625 (1971); (b) P. W. K. Woo, *J. Antibiot.*, **28**, 522 (1975).
(5) T. M. Su, W. F. Sliwinski, and P. v. R. Schleyer, *J. Am. Chem. Soc.*, **91**, 5386 (1969).
(6) R. G. Pearson, H. Sobel, and J. Sonstad, *J. Am. Chem. Soc.*, **90**, 319 (1968).
(7) K. Heyns and H. Paulsen, *Ber.* **8**, 188 (1955).
(8) R. C. Krug and S. Tocker, *J. Org. Chem.*, **20**, 1 (1955).
(9) T. Oda, T. Mori and Y. Kyōtani, *J. Antibiot.*, **24**, 503 (1971).
(10) (a) W. E. Truce and F. M. Perry, *J. Org. Chem.*, **30**, 1316 (1965), (b) J. Clark, R. K. Grantham, and J. Lydiate, *J. Chem. Soc. C*, 1122 (1968).
(11) H. G. Kuivila, *Synthesis*, 499 (1970).
(12) M. Pang and E. I. Becker, *J. Org. Chem.*, **29**, 1948 (1964).
(13) See, for example, P. W. K. Woo and T. H. Haskell, U.S. Patent 3 970 643 (July 20, 1976).
(14) A strong cation exchange resin from the Dow Chemical Co., Midland, Mich.