The Synthesis of Methyl 2,4-Diacetamido-2,4,6-trideoxy Hexopyranosides[1]

URI ZEHAVI* AND NATHAN SHARON

Department of Biophysics, The Weizmann Institute of Science, Rehovoth, Israel

Received June 24, 1971

Acetylation of methyl 6-deoxy-3,4-*O*-isopropylidene-α-L-galactopyranoside gave methyl 2-*O*-acetyl-6-deoxy-3,4-*O*-isopropylidene-α-L-galactopyranoside (**1**). The isopropylidene residue could be selectively hydrolyzed by means of a weak acidic ion-exchange resin, leading to the formation of methyl 2-*O*-acetyl-6-deoxy-α-L-galactopyranoside (**2**). Reaction of compound **2** with methyl sulfonyl chloride in pyrdine yielded methyl 2-*O*-acetyl-6-deoxy-3,4-di-*O*-methylsulfonyl-α-L-galactopyranoside (**3**) which was converted by treatment with sodium methylate into methyl 2,3-anhydro-6-deoxy-4-*O*-methylsulfonyl-α-L-gulopyranoside (**4**). Treatment of **4** with sodium azide in dimethylformamide followed by catalytic reduction and acetylation afforded a mixture of two products which could be separated by chromatography on alumina. One of these was shown by nmr to be methyl 3-*O*-acetyl-2,4-diacetamido-2,4,6-trideoxy-α-L-altropyranoside (**5**), the major product expected from trans-diaxial epoxide ring opening and methylsulfonate replacement in compound **4**. The other product has been tentatively identified as methyl 3-*O*-acetyl-2,4-diacetamido-2,4,6-trideoxy-α-L-idopyranoside (**6**). It was assumed that it is formed as a result of an epoxide ring migration occurring during the treatment of compound **4** with sodium azide.

In 1959, Sharon and Jeanloz described the isolation from *Bacillus licheniformis* (then known as *Bacillus subtilis*) of an unusual diamino sugar, to which they ascribed the structure of a 4-acetamido-2-amino-2,4,6-trideoxyhexose[2] (*N*-acetylbacillosamine[3]). Since then, several other reports have appeared on the occurrence of derivatives of 2,4-diamino-2,4-dideoxyhexoses in natural products. Distler, Kaufman, and Roseman[4] isolated from extracts of *Diplococcus pneumoniae* a uridine diphosphate derivative of a 2,4-diamino-2,4,6-trideoxyhexose. Brundish and Baddiley[5] found a closely similar, or perhaps identical, diamino sugar in acid hydrolysates of the C-substance of *D. pneumoniae*. Another compound of this class, methyl 2,4-diamino-2,-3,4,6-tetradeoxy-α-D-mannopyranoside, was isolated by Suhara, Maeda, and Umezawa following degradation of the antibiotic Kasugamycin.[6]

The first synthesis of a 2,4-diamino sugar was accomplished in 1963 by Jeanloz and Rapin, who prepared 2,4-diacetamido-2,4-dideoxy-D-glucose.[7] In 1964 we described in a preliminary note[1] the synthesis of two related 2,4-diamino hexose derivatives from methyl 6-deoxy-α-L-galactopyranoside. Here we present evidence that one of the compounds obtained is methyl 2,4-diacetamido-2,4,6-trideoxy-α-L-altropyranoside (**5**) and the other probably methyl 2,4-diacetamido-2,4,6-trideoxy-α-L-idopyranoside (**6**).

Results and Discussion

Methyl 6-deoxy-3,4-isopropylidene-α-L-galactopyranoside, prepared by a modification of the method of Percival and Percival,[8] was acetylated with acetic anhydride in pyridine, yielding crystalline methyl 2-*O*-acetyl-6-deoxy-3,4-*O*-isopropylidene-α-L-galactopyranoside (**1**). The isopropylidene residue was removed selectively by a weak acidic ion-exchange resin, since it was more sensitive to acid hydrolysis than the acetate or the methyl glycoside. The product, methyl 2-*O*-acetyl-6-deoxy-α-L-galactopyranoside (**2**), consumed 1 equiv of periodate[9] as expected from a vicinal diol system. The nmr and ir spectra were in agreement with the assigned structure. Compound **2** was treated with methylsulfonyl chloride in pyridine to yield the dimethylsulfonyl derivative **3** possessing the typical methylsulfonyl absorption at 1170 cm^{-1}.[10] The nmr spectrum was also in accordance with the proposed structure. Treatment of compound **3** with base gave the epoxide **4** which still exhibited the absorption at 1170 cm^{-1}.

The formation of an epoxide takes place readily when the groups participating in the elimination are trans diaxial[10] and is also known to occur in sugar derivatives where those groups are trans diequatorial in the most stable conformation.[11,12] In the latter case, however, a change in conformation to produce a trans-diaxial arrangement is presumed to precede the reaction. In the nmr spectrum of compound **4** (Figure 1) a satisfactory resolution of the ring protons was achieved except for H-2 and H-3 both in chloroform-*d* and in methyl sulfoxide-*d*. Double resonance experiments, carried out in chloroform-*d*, supported the assignment of the ring protons. Irradiation at the C-5 CH_3 signal caused the collapse of the H-5 octet to a narrow doublet ($J_{4,5}$ = 1.5 Hz) and irradiation at the center of the H-5 octet converged the C-5 CH_3 doublet to a singlet and the H-4 triplet to a narrow doublet ($J_{3,4}$ = 1.5 Hz). Irradiation in methyl sulfoxide-*d*, at the H-2,H-3 multiplet caused the collapse of H-1 to a singlet and H-4 to an apparent singlet. It is of interest to note that the nmr spectrum of compound **4** in chloroform-*d* differs from that in methyl sulfoxide-*d* in some of the chemical shifts. For instance, taking the spectrum in chloroform-*d* allows the separation of the methyl ether and the methylsulfonyl signals (τ 6.60 and 6.90, respectively) that do not separate in methyl sulfoxide-*d* (broad peak, centered at τ 6.66).

(1) Preliminary communications have appeared: U. Zehavi and N. Sharon, *Israel J. Chem.*, **2**, 322 (1964); Abstracts, 149th National Meeting of the American Chemical Society, Detroit, Mich., April 1965, p 7C.

(2) N. Sharon, *Nature (London)*, **179**, 919 (1957); N. Sharon and R. W. Jeanloz, *Biochim. Biophys. Acta*, **31**, 277 (1959); N. Sharon and R. W. Jeanloz, *J. Biol. Chem.* **235**, 1 (1960).

(3) U. Zehavi and N. Sharon, *Israel J. Chem.*, **2**, 324 (1964); Abstracts, 149th National Meeting of the American Chemical Society, Detroit, Mich., April 1965, p 7C.

(4) J. Distler, B. Kaufman, and R. Roseman, *Arch. Biochem. Biophys.*, **116**, 466 (1966).

(5) D. E. Brundish and J. Baddiley, *Biochem. J.*, **105**, 30c (1967); **110**, 573 (1968).

(6) Y. Suhara, K. Maeda, and H. Umezawa, *Tetrahedron Lett.*, 1239 (1966).

(7) R. W. Jeanloz and A. M. C. Rapin, *J. Org. Chem.*, **28**, 2978 (1963).

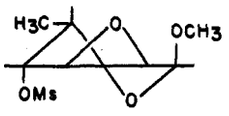
(8) E. E. Percival and E. G. V. Percival, *J. Chem. Soc.*, 690 (1950).

(9) G. O. Aspinall and R. J. Ferrier, *Chem. Ind. (London)*, 1216 (1957).

(10) E. J. Reist, R. R. Spencer, B. R. Baker, and L. Goodman, *ibid.*, 1794 (1962).

(11) F. H. Newth, *Quart. Rev., Chem. Soc.*, **13**, 30 (1959).

(12) G. J. Robertson and C. F. Griffith, *J. Chem. Soc.*, 1193 (1935).



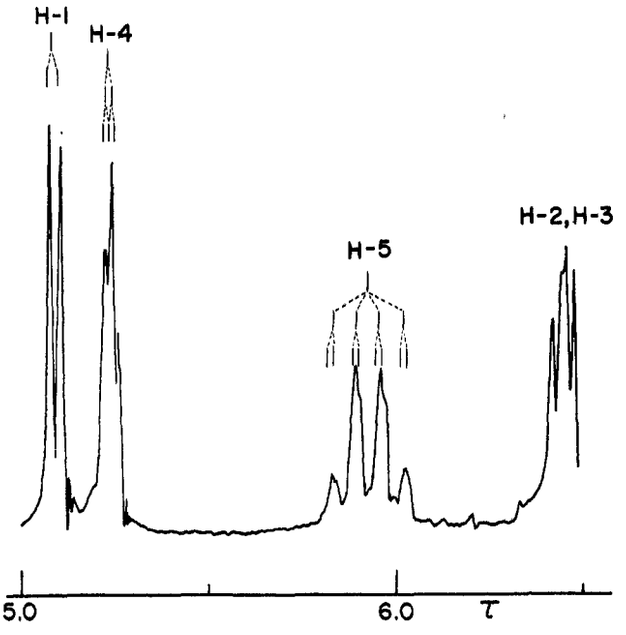
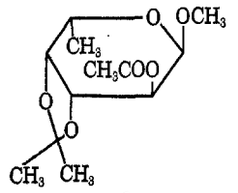


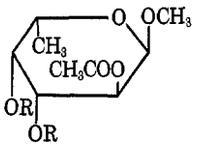
Figure 1.—The low-field portion of the 100-MHz spectrum of methyl 2,3-anhydro-6-deoxy-4-*O*-methylsulfonyl-α-L-gulopyranoside (**4**) in chloroform-*d*.

Compound **4** was treated with sodium azide in *N*,*N*-dimethylformamide at 130°, since extensive decomposition was observed to take place at reflux temperature. The products were not isolated at this stage. They were reduced with Adams platinum catalyst, acetylated, and then separated to give two major products, compounds **5** and **6**. These compounds possess a rather limited solubility in many organic solvents, including chloroform. As a result, most nmr information was derived from spectra of saturated solutions of these products in methyl sulfoxide.

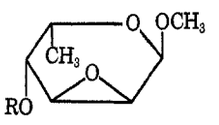
The use of azide ions for the opening of sugar epoxides was first described by Guthrie and Murphy.[13] In analogy to the opening of sugar epoxides with other nucleophiles the formation of two products can be envisaged, with the product of trans-diaxial opening of the more stable conformation of the sugar epoxide being the major one.[11] Since in our case the sugar derivative **4** contains also a methylsulfonyloxy group, another reaction can take place, namely the displacement of this group by azide ion that is known to be a bimolecular nucleophilic substitution occurring with Walden inversion.[10,13] The two products expected from epoxide opening and methylsulfonyloxy substitution in compound **4**, followed by reduction and acetylation, are therefore methyl 3-*O*-acetyl-2,4-diacetamido-2,4,6-trideoxy-α-L-altropyranoside and methyl 2-*O*-acetyl-3,4-diacetamido-3,4,6-trideoxy-α-L-glucopyranoside. The nmr spectrum of compound **5** is in agreement with the first structure. The acetyl resonances are those of an axial acetate, and an axial and an equatorial acetamido group (τ 7.88, 8.04, and 8.07, respectively, in chloroform-*d*). The H-3 resonance deshielded by the acetate is moved downfield and the low coupling constants ($J_{1,2}$ = 3.0, $J_{2,3}$ = 3.0, $J_{3,4}$ = 3.0 Hz) are in accordance with the altro *1C* conformation. Comparable data, although with lower $J_{1,2}$ values, were recorded by Coxon[14] for penta-*O*-acetyl-α-D-altropyranoside.



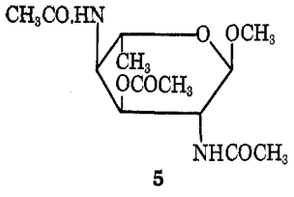
1



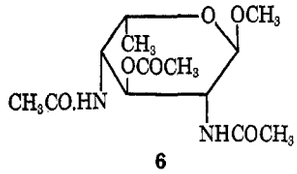
2, R = H
3, R = methylsulfonyl



4, R = methylsulfonyl



5



6

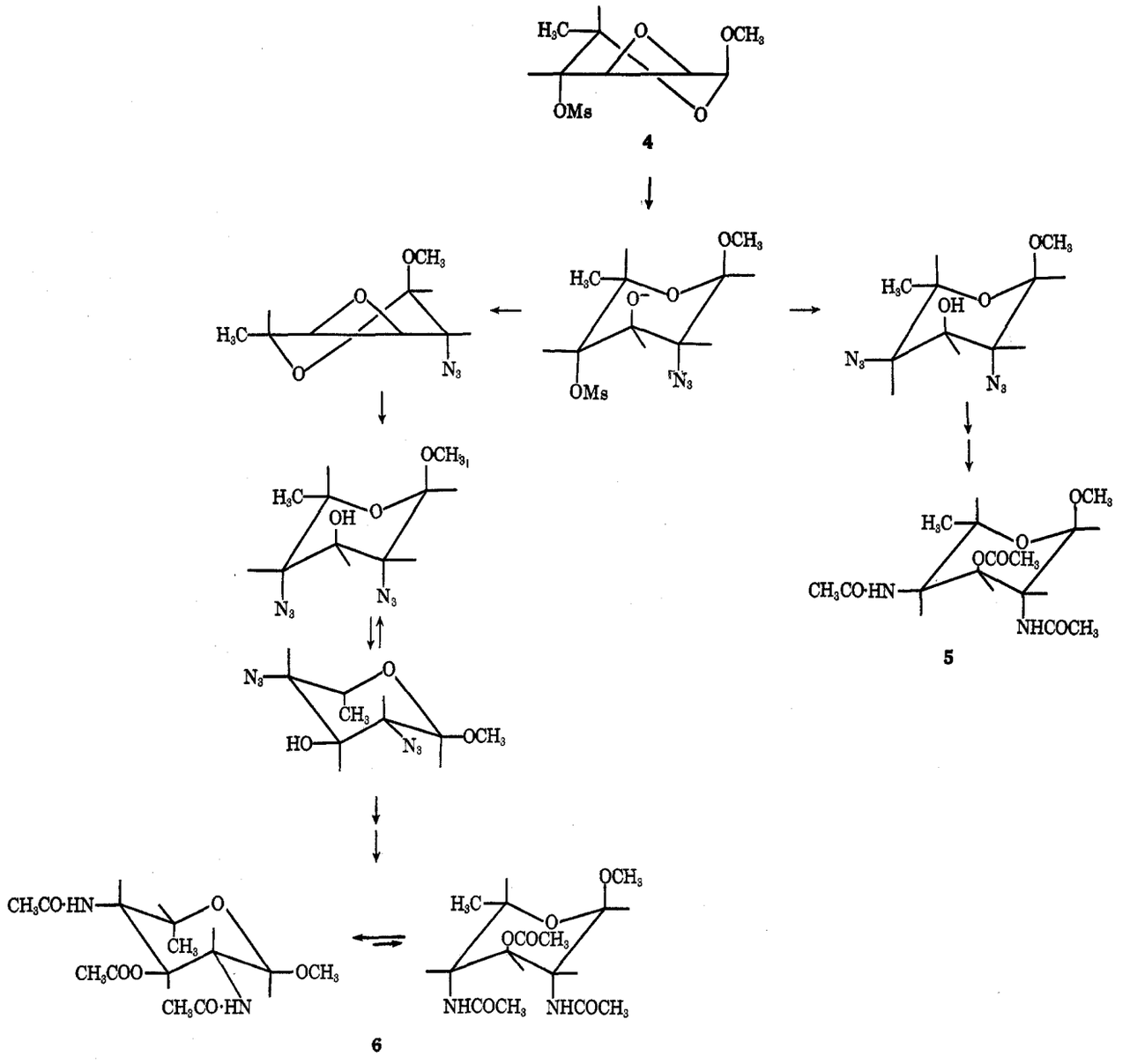
The structure of compound **6** was originally tentatively assigned as methyl 2-*O*-acetyl-3,4-diacetamido-3,4,6-trideoxy-α-L-glucopyranoside.[1] This was also suggested by the chemical shifts of the acetyl resonances measured in chloroform-*d* at 60 MHz which corresponded to those of an equatorial acetate and of two equatorial acetamido substituents. Since then, however, the study of the ring protons of compound **6** became possible from the 100-MHz nmr spectrum and the structure of methyl 3-*O*-acetyl-2,4-diacetamido-2,4,6-trideoxy-α-L-idopyranoside seems preferable. Double irradiation experiments on compound **6** in methyl sulfoxide-*d* supported the assignment of the ring protons. Irradiation at the H-2, H-4 multiplet caused the collapse of the H-1 and H-3 signals to singlets. Irradiation at the H-5 octet caused the collapse of the C-5 CH_3 doublet to a singlet and irradiation at the C-5 CH_3 resonance brought about the collapse of the H-5 octet to a doublet. The intermediate coupling constants for this compound probably represent a weighted time-average for the two chair conformers in rapid equilibrium with a larger proportion of the *C1* conformer. Such an equilibrium seems reasonable keeping in mind that, while energetic consideration supported the *1C* (D) conformation for α-D-idopyranose pentaacetate, it was actually found to favor the *C1* (D) conformation,[15] a fact that was attributed to polar factors whose importance is difficult to assess. The observed $J_{4,5}$ = 4.0 Hz is somewhat high for axial–equatorial interactions while $J_{1,2}$ = 4.0, $J_{2,3}$ = 6.0, and $J_{3,4}$ = 6.0 Hz are rather low for axial–axial interactions expected in the *C1* conformation.

(13) R. D. Guthrie and D. Murphy, *Chem. Ind. (London)*, 1473 (1962).

(14) B. Coxon, *Carbohyd. Res.*, **1**, 357 (1966).

(15) N. S. Bhacca, D. Horton, and H. Paulsen, *J. Org. Chem.*, **33**, 2484 (1968).

SCHEME I



The ido configuration proposed for compound **6** may result from the reaction mechanism shown in Scheme I.

The epoxide ring in compound **4** is first attacked in a trans-diaxial fashion. This is followed by an intramolecular displacement of the adjacent methyl sulfonate at C-4, thus forming the 3,4-altro-epoxide intermediate. Finally, nucleophilic attack at C-4 leads to the L-ido configuration with the nitrogen substituents at carbons 2 and 4.

Optical rotation considerations also support the assignment of the L-ido rather than the L-gluco configuration to compound **6** ($[\alpha]_D$ −60°, M_D −181). The specific rotation recorded for methyl 3-acetamido-2,4-di-*O*-acetyl-3,6-dideoxy-α-L-idopyranoside[16] is −62° (M_D −187). These values differ markedly from those recorded for related compounds of the gluco series: for methyl 4-acetamido-2,3-di-*O*-acetyl-4,6-dideoxy-α-D-glucopyranoside[17] ($[\alpha]_D$ +190°, M_D +576) and for methyl 3-acetamido-2,4-di-*O*-acetyl-3,6-dideoxy-α-L-glucopyranoside[18] ($[\alpha]_D$ −128°, M_D −388). (All the above-cited rotations were taken in chloroform.)

Another support for the proposed structures of compounds **5** and **6** comes from the mass spectra of these compounds. The molecular peak (M, *m/e* 302) and M + 1 are present; the major fragmentation is through the loss of 31 and 32 mass units (methoxy radical and methanol) and through the elimination of 59 and 60 mass units (acetate and acetamide or acetic acid). No peak was detected at *m/e* 216, which would arise by the elimination of $CH_3CONHCHCH_3$[19] if ring contraction to a furanoside had occurred during the reaction with sodium azide.

Acid hydrolysis of compound **5** led to extensive degradation, probably as a result of the formation of a pyrrolidene derivative.[10] Repeated attempts to diminish the extent of degradation by modifying the conditions of hydrolysis had only limited success.

(16) J. Jarý, K. Čapak, and J. Kovac, *Collect. Czech. Chem. Commun.*, **28**, 2171 (1962).

(17) C. L. Stevens, P. Blumbergs, F. A. Daniher, D. H. Otterbach, and C. G. Taylor, *J. Org. Chem.*, **31**, 2822 (1966).

(18) A. C. Richardson and K. A. McLauchlan, *J. Chem. Soc.*, 2499 (1962).

(19) N. K. Kochetkov and O. S. Chizhov, *Advan. Carbohyd. Chem.*, **21**, 39 (1966).

Experimental Section

All melting points are corrected. Optical rotation was determined with a Bendix polarimeter. Spectra were measured with a Perkin-Elmer Infracord spectrometer in chloroform or in KBr discs. Nmr spectra were recorded on a Varian A-60 or HA-100 instrument with tetramethylsilane as an internal standard, unless otherwise mentioned. The uv spectra were taken on a Zeiss model PMQ II spectrometer. Mass spectra were measured on an Atlas CH4 mass spectrometer with 70 eV ionizing current. The samples were introduced through a direct inlet system and heating was applied until the vapor pressure was sufficient to obtain usable mass spectra. Column chromatography was routinely done on silica gel "Grace," Davison Chemical Corp., grade 950, 60–200 mesh. Thin layer chromatography was carried out on silica gel G (E. Merck, Germany); R_{SR} refers to mobility relative to sudan red, a component of the test mixture supplied by C. Desaga, Heidelberg, Germany. The plates were prepared using a Desaga applicator set for a thickness of 0.25 mm.

6-Deoxy-L-galactose (L-fucose) was purchased from Pfanstiehl Laboratories, Waukegan, Ill.

Methyl 6-Deoxy-α-L-galactopyranoside.—6-Deoxy-L-galactose (80 g) and methanol-washed Amberlite IR-120 resin (H^+ form, 80 g) were refluxed in absolute methanol (800 ml) under a calcium chloride seal for 18 hr. The reaction mixture was filtered and evaporated *in vacuo*, and the solid residue was recrystallized from ethanol to yield 38 g (44%) of platelike crystals, mp 158°, $[\alpha]^{24}D$ −197.5 ± 0.3° (*c* 0.6, water).[20]

Anal. Calcd for $C_7H_{14}O_5$: C, 47.18; H, 7.92. Found: C, 47.27; H, 7.86.

Methyl 6-Deoxy-3,4-*O*-isopropylidene-α-L-galactopyranoside.—Methyl 6-deoxy-α-L-galactopyranoside (27 g) was shaken at room temperature with anhydrous copper sulfate (300 g) in dry acetone for 18 hr.[8] The oil obtained, in quantitative yield, after filtration and evaporation was found by tlc to be chromatographically pure, R_{SR} 0.23 (benzene–ethyl acetate, 2:1) and R_{SR} 0.73 (ethyl acetate), and was used directly for the next reaction.

Methyl 2-*O*-Acetyl-6-deoxy-3,4-*O*-isopropylidene-α-L-galactopyranoside (1).—Methyl 6-deoxy-3,4-isopropylidene-α-L-galactopyranoside (10.7 g) was dissolved in dry pyridine (42 ml). Acetic anhydride (6.3 ml) was added to the solution and the reaction mixture was sealed and left at room temperature. Ice was added (4 g) and after 2 hr the solution was evaporated *in vacuo* from a bath of 40°. The residue was crystallized from petroleum ether (bp 30–60°), yielding 9.1 g (79%) of crystals, mp 100–101°, $[\alpha]^{26}D$ −230.1 ± 0.8° (*c* 0.62, benzene). The product moved as a single spot with R_{SR} 0.74 (benzene–ethyl acetate, 2:1) and R_{SR} 0.93 (ethyl acetate). The OH absorption present in the ir spectrum of the starting material has disappeared, and a carbonyl absorption was present at 1730 cm^{-1}: nmr (60 MHz, chloroform-*d*) τ 4.98 (1-proton doublet, H-1, $J_{1,2}$ = 3.4 Hz), 5.15 (1-proton quartet, H-2, $J_{2,3}$ = 4.8 Hz), 5.5–6.1 (multiplets, 3 protons, H-3,4,5), 6.61 (3-proton singlet, OCH_3), 7.86 (3-proton singlet, $OCOCH_3$), 8.45 and 8.64 [two 3-proton singlets, $C(CH_3)_2$], 8.62 (3-proton doublet, C-5 CH_3, $J_{5,6}$ = 6.5 Hz).

Anal. Calcd for $C_{12}H_{20}O_6$: C, 55.37; H, 7.75. Found: C, 55.54; H, 7.76.

Methyl 2-*O*-Acetyl-6-deoxy-α-L-galactopyranoside (2).—The isopropylidene derivative 1 (9.0 g) in water (1100 ml) was heated to boiling in the presence of Amberlite IRC 50 (H^+ form, 5.6 g) for 2 hr. The resin was filtered off and the solution was evaporated *in vacuo* from a bath of 40° to give a syrup that solidified when placed in a desiccator. The material was recrystallized from benzene–petroleum ether, yielding 2.61 g (31%) of a chromatographically pure product, R_{SR} 0.47 (ethyl acetate), mp 82°. A second yield was obtained from the mother liquor after fractionation on a silica gel column (200 g, 4 cm diameter). The column was first washed with ethyl acetate (430 ml) and the product was subsequently removed by additional ethyl acetate (600 ml). The latter fraction was then evaporated and the solid residue was recrystallized as above, total yield 5.31 g (63%), mp 82–83°, $[\alpha]^{23}D$ −196 ± 0.3° (*c* 0.4, chloroform). The material, pure according to tlc, and giving as expected a positive color eaction for vicinal diols,[21] consumed 1.2 equiv of periodate (5% $NaIO_4$, 37°, oxidation completed after 2 hr). In the ir it had a carbonyl absorption at 1730 cm^{-1} and an OH absorption at 3450 cm^{-1}; nmr (60 MHz, chloroform-*d*) τ 4.88 (1-proton doublet, H-1, $J_{1,2}$ = 3.5 Hz), 5.10 (1-proton quartet, H-2, $J_{2,3}$ = 5.0 Hz), 5.8–6.2 (multiplets, 3 protons, H-3,4,5), 6.62 (3-proton singlet, OCH_3), 7.22 (2-proton singlet, disappears upon addition of deuterium oxide, OH), 7.87 (3-proton singlet, $OCOCH_3$), 8.70 (3-proton doublet, C-5 CH_3, $J_{5,6}$ = 6.5 Hz).

Anal. Calcd for $C_9H_{16}O_6$: C, 49.08; H, 7.32. Found: C, 49.08; H. 7.37.

Methyl 2-*O*-Acetyl-6-deoxy-3,4-di-*O*-methylsulfonyl-α-L-galactopyranoside (3).—A solution of compound **2** (13.5 g) in dry pyridine (130 ml) containing methylsulfonyl chloride (15.3 ml) was stirred overnight at 0° in a sealed tube. Ice water (100 ml) was added in small portions for 30 min and the stirring was continued for an additional 2 hr at 0°. Water (200 ml) was added and the mixture was extracted with chloroform (2 × 1 l.). The extracts were, in turn, washed with water (400 ml), combined, dried over sodium sulfate, and evaporated *in vacuo* to yield a chromatographically pure oil. The product was crystallized from benzene–petroleum ether, yielding 20.4 g (88.5%) of colorless crystals, mp 144°, $[\alpha]^{23}D$ −168 ± 0.4° (*c* 0.75, chloroform), R_{SR} 0.87 (ethyl acetate), 0.77 (benzene–ethyl acetate, 1:9). In the ir the material has a methylsulfonate band at 1170 cm^{-1}: nmr (60 MHz, chloroform-*d*) τ 4.8–5.1 (multiplets, 4 protons), 5.86 (1-proton multiplet), 6.59 (3-proton singlet, OCH_3), 6.79 and 6.88 (two 3-proton singlets, methylsulfonyl), 7.87 (3-proton singlet, $OCOCH_3$), 8.67 (3-proton doublet, C-5 CH_3, $J_{5,6}$ = 6.5 Hz).

Anal. Calcd for $C_{11}H_{20}O_{10}S_2$: C, 35.15; H, 5.33; S, 17.01. Found: C, 35.51; H, 5.13; S, 16.75.

Methyl 2,3-Anhydro-6-deoxy-4-*O*-methylsulfonyl-α-L-gulopyranoside (4).—Compound **3** (25 g) in 0.3 *N* sodium methoxide in methanol (250 ml) was refluxed for 45 min under a calcium chloride seal. The reaction mixture was cooled to room temperature and filtered, and the filtrate was passed through a column (2 cm diameter) containing methanol-washed Amberlite IR-120 (H^+ form to a height of 30 cm) and below it Amberlite 4B (OH^- form, to a height of 30 cm). Methanol (600 ml) was then passed through the column and the combined eluates were evaporated *in vacuo*. The product, 15.9 g (100%), contained only traces of impurities (as determined by tlc). It was crystallized from methanol (mp 98°) and recrystallized from benzene–petroleum ether, mp 101–102°, $[\alpha]^{23}D$ −3.7 ± 0.8° (*c* 0.25, chloroform), R_{SR} 0.86 (ethyl acetate), 0.69 (benzene–ethyl acetate, 1:9). The material turned brownish-red immediately after the tlc plates were sprayed with sulfuric acid. No heating of the plates was required. In the ir it possessed a typical methylsulfonyl absorption at 1170 cm^{-1}; nmr (100 MHz, chloroform-*d*) τ 5.09 (1-proton doublet, H-1, $J_{1,2}$ = 3.0 Hz), 5.24 (1-proton triplet, H-4, $J_{3,4}$ = 1.5 Hz, $J_{4,5}$ = 1.5 Hz), 5.91 (1-proton octet, H-5, $J_{5,6}$ = 6.5 Hz), 6.41–6.55 (2-proton multiplet, H-2 and H-3), 6.60 (3-proton singlet, OCH_3), 6.90 (3-proton singlet, methylsulfonyl) 8.80 (3-proton doublet, C-5 CH_3); nmr (60 MHz, methyl sulfoxide-*d*, TMS as external standard) τ 5.01 (1-proton doublet, H-1, $J_{1,2}$ = 2.0 Hz), 5.11 (1-proton quartet, H-4, $J_{3,4}$ = 3.0 Hz, $J_{4,5}$ = 1.5 Hz), 6.06 (1-proton octet, H-5, $J_{5,6}$ = 6.5 Hz), 6.41–6.46 (2-proton multiplet, H-2,3), 6.66 (6-proton singlet, OCH_3 and methylsulfonyl), 8.87 (3-proton doublet, C-5-CH_3).

Anal. Calcd for $C_8H_{14}O_6S$: C, 40.34; H, 5.92; S, 13.45. Found: C, 40.44; H, 5.71; S, 13.55.

Methyl 3-*O*-Acetyl-2,4-diacetamido-2,4,6-trideoxy-α-L-altropyranoside (5) and Methyl 3-*O*-Acetyl-2,4-diacetamido-2,4,6-trideoxy-α-L-idopyranoside (6).—Compound **4** (1.9 g) and sodium azide (3.1 g) in absolute dimethylformamide (165 ml) were stirred mechanically in a three-necked flask equipped with a condenser and a calcium chloride tube. The reaction was carried out in an oil bath of 130° for 18 hr. The reaction mixture when analyzed by tlc gave three spots, R_{SR} 0.81, 0.97, 1.04 (ethyl acetate). The material migrating with R_{SR} 0.81 appeared as a bluish-gray spot immediately after spraying with sulfuric acid and without heating the plate.

The spot of R_{SR} 0.97 was fainter than the other two spots. The reaction mixture was then filtered and the precipitate was washed with a little dimethylformamide. The combined filtrates were evaporated *in vacuo*. The residue was extracted with ethyl acetate (50 ml) and filtered, and the filtrate was evaporated. The residue was dissolved in methanol (50 ml),

(20) J. Minsaas, *Recl. Trav. Chim. Pays-Bas*, **51**, 475 (1932), reported mp 157.5–158.5°, $[\alpha]^{20}D$ −197.45°.

(21) A. Yoda, *J. Chem. Soc. Jap.*, **73**, 18 (1952); *Chem. Abstr.*, **47**, 3185 (1953).

filtered, and reduced under pressure (38 psi) with Adams platinum catalyst (1.8 g of platinum oxide) for 4 hr. The catalyst was filtered off, and the basic solution obtained was then evaporated *in vacuo*.

The residue was examined by descending paper chromatography on Whatman No. 1 paper with *n*-butyl alcohol–acetic acid–water (25:6:25, upper phase), revealing two ninhydrin positive spots at $R_{2\text{-Amino-2-deoxy-D-glucose}}$ 1.57 (brown) and 2.38 (pink). When checked by high-voltage paper electrophoresis on Whatman No. 1 paper in 1.2 *M* pyridine adjusted to pH 6.5 with acetic acid at 60 V/cm for 20 min, the first spot had an $M_{2\text{-Amino-2-deoxy-D-glucose}}$ value of 1.24 and the second 1.02.

Dry pyridine (30 ml) was added to the residue and evaporated. The oily material was redissolved in pyridine (2 ml) and after cooling to 0° acetic anhydride (2 ml) was added. The acetylation mixture was left overnight at room temperature. Water (0.3 ml) was then added and the mixture was kept for an additional 2 hr at room temperature. The mixture was evaporated *in vacuo*, extracted with ethyl acetate (5 ml), filtered, and placed on an alumina column (Merck, acid washed, 30 g, 1.5 cm diameter). The column was monitored by tlc on alumina G using acetone as solvent. The column was washed with ethyl acetate (150 ml) and the first compound which emerged (0.12 g) was eluted with the first portion of 1% methanol in ethyl acetate (90 ml). It did not contain nitrogen and had a R_{SR} of 0.87. It was not further investigated. Compound **5**, R_{SR} 0.67 (0.26 g, 10.8%), started to emerge after an additional volume (110 ml) of the same solvent, and its elution was completed with 200 ml of 2% methanol in ethyl acetate. The last fraction, compound **6**, R_{SR} 0.56 (0.156 g, 6.5%), started to emerge after an additional volume (200 ml) of 2% methanol in ethyl acetate and was eluted with the same solvent (300 ml).

On a small scale the mixture of compounds **5** and **6** was obtained also through acetylation in pyridine of the material of $R_{2\text{-Amino-2-deoxy-D-glucose}}$ 1.57 isolated by preparative paper chromatography.

Compound **5** was obtained from ethyl acetate as an amorphous white solid, mp 272°, $[\alpha]^{24}D$ −168 ± 1.6° (*c* 0.29, chloroform). It had the expected ir spectrum; nmr (100 MHz, methyl sulfoxide-*d*, hexamethylsiloxane as an external standard) τ 5.09 (1-proton triplet, H-3, $J_{2,3}$ = 3.0 Hz, $J_{3,4}$ = 3.0 Hz), 5.23 (1-proton doublet, H-1, $J_{1,2}$ = 3.0 Hz), 5.5–6.3 (3 protons, unresolved multiplets), 6.50 (3-proton singlet, OCH_3), 7.82 (3-proton singlet, $OCOCH_3$), 8.04 and 8.06 (two 3-proton singlets, $NCOCH_3$), 8.74 (3-proton doublet, C-5 CH_3, $J_{5,6}$ = 6.0 Hz); nmr (60 MHz, chloroform-*d*) τ 6.55 (3-proton singlet, OCH_3), 7.88 (3-proton singlet, $OCOCH_3$), 8.04 and 8.07 (two 3-proton singlets, $NCOCH_3$), 8.75 (3-proton doublet, C-5 CH_3).

Anal. Calcd for $C_{13}H_{22}N_2O_6$: C, 51.64; H, 7.34; N, 9.27. Found: C, 52.08; H, 7.61; N, 8.93.

Compound **6** was crystallized from ethyl acetate as colorless needles, mp 261° dec, $[\alpha]^{22}D$ −60 ± 1.3° (*c* 0.38, chloroform). It also had the expected ir spectrum; nmr (100 MHz, methyl sulfoxide-*d*, hexamethyl siloxane as an external standard) τ 5.05 (1-proton triplet, H-3, $J_{2,3}$ = 6.0 Hz, $J_{3,4}$ = 6.0 Hz), 5.19 (1-proton doublet, H-1, $J_{1,2}$ = 4.0 Hz), 5.61 (1-proton octet, H-5, $J_{4,5}$ = 4.0 Hz, $J_{5,6}$ = 6.5 Hz), 5.8–6.1 (2-proton multiplet, H-2, H-4), 6.51 (3-proton singlet, OCH_3), 7.81 (3-proton singlet, $OCOCH_3$), 7.91 and 7.97 (two 3-proton singlets, $NCOCH_3$), 8.68 (3-proton doublet, C-5 CH_3); nmr (100 MHz, chloroform-*d*) τ 6.61 (3-proton singlet, OCH_3), 7.92 (3-proton singlet, $OCOCH_3$), 8.07 and 8.10 (two 3-proton singlets, $NCOCH_3$), 8.79 (3-proton doublet, C-5 CH_3).

Anal. Calcd for $C_{13}H_{22}N_2O_6$: C, 51.64; H, 7.34; N, 9.27. Found: C, 51.77; H, 7.64; N, 9.14.

Registry No.—**1**, 34388-70-0; **2**, 34388-71-1; **3**, 34402-58-9; **4**, 34388-72-2; **5**, 34388-73-3; **6**, 34388-74-4; methyl 6-deoxy-α-L-galactopyranoside, 14687-15-1.

Acknowledgments.—This investigation was supported by a research grant (AI-03528) from the National Institute of Allergy and Infectious Diseases, National Institutes of Health, U. S. Public Health Service. We thank Mrs. Edna Meshulam of Bar-Ilan University and Miss Ronit Pinko of Tel Aviv University for measuring the spectra on HA-100 Varian nmr spectrometers. Our thaks are extended to Dr. Asher Mandelbaum for his help in the interpretation of mass spectra.

The Crystal and Molecular Structure of (2*S*,3*S*)-1-Cyano-2-hydroxy-3,4-epithiobutane-α-naphthylurethane

R. B. BATES,* R. A. GRADY, AND T. C. SNEATH

Department of Chemistry, University of Arizona, Tucson, Arizona 85721

Received September 8, 1971

The constitution, relative configuration, and partial conformation proposed for (2*S*,3*S*)-1-cyano-2-hydroxy-3,4-epithiobutane and its acetate on the basis of spectral evidence were confirmed by an X-ray study on its α-naphthylurethane. The structure was solved by symbolic addition and refined to an *R* of 0.048. The shortness of the carbon–carbon single bond joining the episulfide ring to the other atoms supports the view that the carbons in an episulfide ring are between sp^3 and sp^2 in hybridization. The naphthalene ring and urethane group form a dihedral angle of 55°; this unexpected lack of coplanarity probably occurs to allow intermolecular hydrogen bonding between N–H and carbonyl oxygen.

Enzymic hydrolysis of the thioglucosides progoitrin and epiprogoitrin produces four compounds formulated as the stereoisomeric 1-cyano-2-hydroxy-3,4-epithiobutanes; this unusual reaction probably involves episulfide formation by intramolecular transfer of thioglucoside sulfur to an isolated olefinic bond.[1] An ir–nmr study of these episulfides and their acetates permitted complete stereochemical assignments to be made, and further suggested that the hydrogens attached to the asymmetric carbons are trans to one another in the most stable conformation of each stereoisomer.[2] To check the constitution, relative configuration, and conformation of one of these substances and to gain further information about bond parameters in episulfide groups, we undertook an X-ray study on the title compound.[3]

(1) M. E. Daxenbichler, C. H. VanEtten, and I. A. Wolff, *Phytochemistry*, **7**, 989 (1968), and references cited therein.

(2) K. D. Carlson, D. Weisleder, and M. E. Daxenbichler, *J. Amer. Chem. Soc.*, **92**, 6232 (1970).

(3) This derivative, mp 134–136°, was kindly provided by M. E. Daxenbichler and I. A. Wolff. It was prepared by reacting episulfide B from epiprogoitrin with α-naphthyl isocyanate in the presence of dicyclohexylethylamine.