(6). Ozonolysis of methyl 2,4,6-trideoxy-3(*R*)-(*tert*-butyldimethylsiloxy)-(5*R*)-6-(2-propenyl)-α-D-allopyranoside in methanol afforded, after workup with dimethyl sulfide,[20] an intermediate aldehyde (0.037 g, 0.12 mmol) which was immediately reacted with (±)-1-(triphenylphosphoranylidene)-2-oxo-5,6,8-decatriene (0.065 g, 0.16 mmol) in ca. 2 mL of CH_2Cl_2. Reaction over an 18-h period produced an intensely UV-active spot at R_f 0.51 (3 × 10% THF/hexanes). The reaction mixture was concentrated in vacuo and chromatographed over silica gel by eluting with 10% THF/hexanes. Appropriate fractions were combined to yield 0.038 g (74%) of material as a clear oil. Rechromatography via MPLC provided an analytical sample of what appeared to be a single diastereomer having the following spectral characteristics: 300-MHz ^{1}H NMR ($CDCl_3$) δ 6.84 (d(t), J = 15.8, 7.2 Hz, 1 H), 6.10 (d, J = 15.8 Hz, 1 H), 5.76 (m, 2 H), 5.62 (m, 1 H), 5.59 (m, 1 H), 4.66 (dd, J = 4.4, 2.23 Hz, 1 H), 4.03 (m, 2 H), 3.28 (s, 3 H), 2.62–1.72 (m, 6 H), 1.55 (m, 9 H), 0.85 (s, 9 H), 0.02 (s, 3 H), 0.01 (s, 3 H); 75-MHz ^{13}C NMR ($CDCl_3$) δ 206.7, 202.9, 200.0, 147.4, 130.8, 127.5, 127.4, 98.6, 95.1, 91.6, 64.0, 63.5, 55.0, 39.2, 38.9, 36.9, 34.2, 28.8, 25.8, 23.2, 18.1, −4.7, −4.9; IR (neat) 3020 cm^{-1} (w), 2920 (s), 2850 (s), 2220 (w), 1945 (w), 1720 (m), 1670 (m), 1630 (m), 1250 (s), 830 (s), 770 (s), 730 (s); mass spectrum (EI), m/z (relative intensity) 434 [M$^+$] (0.2), 324 (0.3), 270 (6.6), 167 (16.1), 138 (28.7), 110 (10.2), 97 (31.5), 96 (14.9), 85 (100.00), 74 (57.3), 69 (29.8), 55 (58.2).

Preparation of Diastereomers 28 and 29. Vinylallene **3** (0.1027 g, 0.23 mmol) was dissolved in 5 mL of toluene and placed in a resealable Dumas tube along with 25 mg of BHT. The mixture was thoroughly degassed with argon for 20 min, sealed, and thermolyzed at 140 °C for 1.25 h. Analytical TLC after this time indicated complete consumption of starting material and the formation of two UV-active products at R_f 0.65 and 0.57 (5 × 10% THF/hexanes). The reaction mixture was diluted with 5 mL of THF and cooled to 0 °C. Treatment with lithium tri-*sec*-butylborohydride (0.46 mmol, 30 min, 0 °C) afforded, after aqueous workup, two spots with R_f 0.50 and 0.39 (3 × 10% THF/hexanes). Acylation of the crude reaction mixture with (*S*)-(+)-2-methylbutyric anhydride (0.69 mmol, 0.1283 g) according to the procedure of Grieco[5c] (DMAP, 0.34 mmol, 0.0421 g; $N(Et)_3$, 0.92 mmol, 0.093 g; in CH_2Cl_2) provided after 38 h almost complete conversion to a mixture of UV-active diastereomers having R_f 0.43, 0.33 (3 × 10% THF/hexanes). Extractive isolation and chromatographic purification over silica gel by MPLC, eluting with a gradient of hexanes to 2.5% THF/hexanes, provided an analytical sample of each diastereomer (84% combined yield). The isomer with R_f 0.33 contains the correct absolute configuration present in the mevinic acids (vide supra). Isomer R_f 0.43: $[\alpha]^{25}_D$ −22.0° (*c* 0.0095, CH_2Cl_2); HPLC t_r 15.6 min [5μ Alltex silica gel column (4.6 mm × 25 cm) 2.5% THF/hexanes, 2 mL/min]; 300-MHz ^{1}H NMR ($CDCl_3$) δ 5.94 (d, J = 9.9 Hz, 1 H), 5.72 (dd, J = 9.9, 5.5 Hz, 1 H), 5.52 (m, 1 H), 5.25 (m, 1 H), 4.62 (dd, J = 4.2, 2.9 Hz, 1 H), 3.99 (m, 2 H), 3.27 (s, 3 H), 2.15 (m, 2 H), 1.95 (m, 2 H), 1.30 (m, 17 H), 1.12 (d, J = 5.7 Hz, 3 H), 0.92 (m, 12 H), 0.11 (s, 3 H), 0.07 (s, 3 H); 75-MHz ^{13}C NMR ($CDCl_3$) δ 177.0, 134.4, 133.5, 128.5, 123.8, 98.4, 67.8, 64.5, 64.1, 55.0, 41.6, 39.0, 37.6, 37.5, 37.0, 33.0, 31.0, 26.9, 26.2, 25.8, 24.1, 21.0, 18.1, 17.0, 13.9, 11.7, −4.7; IR (neat) 2940 cm^{-1} (s), 2880 (s), 2860 (s), 1730 (s), 1460 (s), 1250 (s), 1185 (s), 935 (m), 830 (s), 770 (s), 710 (w), 660 (w), 620 (w); mass spectrum (EI), m/z 522 (0.2), 520 [M$^+$] (0.5), 488 (7.2), 431 (2.0), 386 (4.8), 357 (46.7), 323 (15.6), 255 (39.8), 254 (33.3), 237 (28.4), 159 (76.2), 145 (61.0), 89 (50.0), 75 (100.0), 57 (83.4). Isomer R_f 0.33: $[\alpha]^{25}_D$ +53.63° (*c* 0.0031, CH_2Cl_2); HPLC, t_r 17.4 min [5μ Alltex silica gel column (4.6 mm × 25 cm) 2.5% THF/hexanes, 2 mL/min]; 300-MHz ^{1}H NMR ($CDCl_3$) δ 5.93 (d, J = 9.9 Hz, 1 H), 5.70 (m, 1 H), 5.50 (m, 1 H), 5.37 (m, 1 H), 5.23 (m, 1 H), 4.60 (m, 2 H), 3.25 (s, 3 H), 2.15 (m, 2 H), 1.95 (m, 2 H), 1.30 (m, 17 H), 1.12 (d, J = 5.7 Hz, 3 H), 1.92 (m, 12 H), 0.11 (s, 3 H), 0.07 (s, 3 H); IR (neat) 2925 cm^{-1} (s), 2860 (s), 1730 (s), 1460 (s), 1250 (s), 1185 (s), 940 (m), 830 (s), 770 (s), 715 (m), 660 (m); mass spectrum (EI), m/z 520 [M$^+$] (0.1), 357 (7.0), 299 (5.1), 255 (7.0), 225 (43.1), 197 (19.3), 159 (33.0), 123 (100.0), 105 (42.4), 89 (44.6), 57 (65.2).

Synthetic (+)-Compactin. A solution of compound **28** (0.0085 g, 0.16 mmol) in 1.5 mL of a 3:5 10% HCl/THF solution was heated at 45–55 °C for 20 min in a sealed tube. Analytical TLC analysis at this time indicated nearly complete selective hydrolysis to a diol having R_f 0.10 (35% THF/hexanes). Extractive isolation (CH_2Cl_2) provided the crude intermediate lactols, which were immediately oxidized with Fetizon's reagent (Ag_2CO_3/Celite, toluene, 95 °C/2 h). Analytical TLC of the crude reaction mixture provided a UV-active material having R_f 0.15 (35% THF/hexanes) that cospotted identically with natural (+)-compactin. Filtration through a Celite wafer and subsequent pipet chromatography over silica gel eluting with 10% THF/hexanes provided the analytical sample, which crystallized upon standing (0.0049 g, 77%). The synthetic (+)-compactin thus obtained proved indistinguishable from natural (+)-compactin by comparison of the following physical properties and spectral data: mp 148 °C; $[\alpha]^{25}_D$ +271.00° (*c* 0.002, CH_2Cl_2); 300-MHz ^{1}H NMR ($CDCl_3$) δ 5.98 (d, J = 9.8 Hz, 1 H), 5.73 (dd, J = 9.8, 5.8 Hz, 1 H), 5.56 (m, 1 H), 5.34 (m, 1 H), 4.46 (m, 1 H), 4.35 (m, 1 H), 2.70 (m, 3 H), 2.36 (m, 3 H), 2.14 (m, 3 H), 1.95 (m, 3 H), 1.68 (m, 4 H), 1.43 (m, 5 H), 1.12 (d, J = 6.9 Hz, 3 H), 0.90 (d, J = 7.2 Hz, 3 H); 75-MHz ^{13}C NMR ($CDCl_3$) δ 177.6, 171.4, 134.0, 133.1, 128.6, 124.1, 76.7, 67.9, 62.7, 41.9, 38.7, 37.6, 37.0, 36.1, 33.1, 31.0, 26.8, 26.3, 24.1, 21.0, 17.0, 13.9, 11.8; IR (neat) 3510 cm^{-1} (s), 3010 (w), 2960 (s), 2930 (s), 2840 (m), 1740 (s), 1695 (s), 1230 (s), 1200 (s), 1175 (s), 1080 (m), 1050 (m), 820 (m); mass spectrum (EI), m/z (relative intensity) 390 [M$^+$] (0.2), 270 (5.4), 255 (2.8), 210 (4.1), 184 (43.0), 169 (14.9), 158 (37.2), 145 (88.5), 143 (100.0), 129 (37.3), 91 (27.9), 57 (56.5).

Acknowledgment. We thank the National Institutes of Health for generous financial support through Grant GM 31556. We also thank Professor Brian Goh for a generous sample of natural compactin and Dr. F. Kathawala for generous samples of various intermediates used at Sandoz for the preparation of the lactone portion of compactin.

The Structure and Chemistry of Paulomycin[1]

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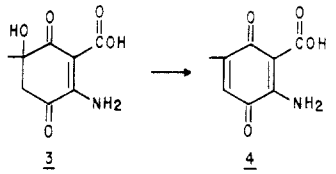
Received October 22, 1985

The gross structures and absolute stereochemistry of paulomycins A and B have been demonstrated to be those indicated in **1a** and **1b** by spectral studies on **1a** and **1b** and on their degradation products and by identity of degradation products with known compounds as well as by X-ray crystallographic studies.

Paulomycin was originally isolated as a mixture of paulomycins A and B[2] related to senfolomycins[3] and proceomycins.[4] Subsequently paulomycin was reisolated[5] and found to have excellent antibacterial properties. It

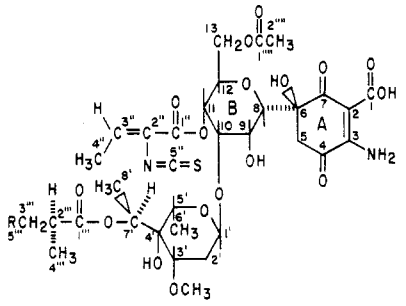
0022-3263/86/1951-2493$01.50/0

Scheme I



3 4

is now being investigated in depth as a possible clinically useful agent. The term paulomycin refers to the mixture of paulomycins A and B (**1a** and **1b**) evidence for whose structure is reported in this paper. Paulomycins are shown to be members of a new structural class hitherto unknown.



PAULOMYCIN A (1a) : R = CH_3

PAULOMYCIN B (1b) : R = H

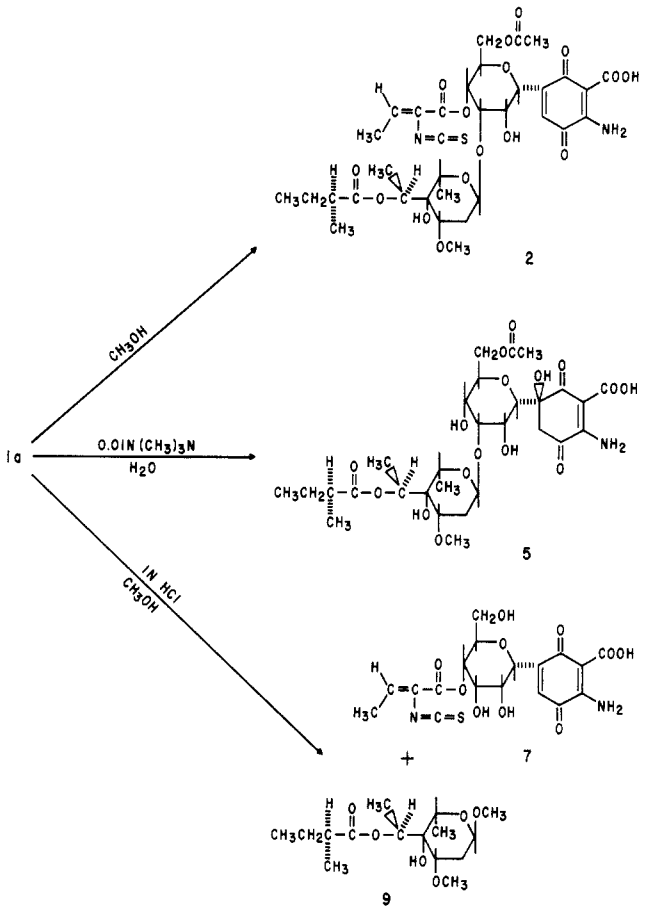
Argoudelis et al.[5] have published the physical properties of **1a** and **1b** with complete spectral data. The molecular formula of **1a** is $C_{34}H_{46}N_2O_{17}S$,[5] and it differs from **1b** by having a 2-methylbutyryl where **1b** has an isobutyryl group. Two titratable groups are present with pK_a's of 3.0 and 7.4. An isothiocyanate group, two ketone carbonyls, four other carbonyls, four olefinic carbons, an anomeric carbon, and twelve carbon atoms substituted by hydroxyl or ether oxygens are present.

The ^1H NMR spectrum of **1a** has a series of resonances coupled to each other in such a manner that a completely substituted tetrahydropyran ring is indicated which must have the stereochemistry of either β-D- or β-L-allose as shown by appropriate coupling constants. A CH_2O group is attached at a carbon attached to the ether oxygen.

Compound **1a** in solution in CH_3OH is slowly converted to a yellow solid (paulomycinone, **2**) having the molecular formula $C_{34}H_{44}N_2O_{16}S$, suggesting loss of one molecule of water from **1a**. The NMR spectra of **2** indicate that two new olefinic carbons are formed with one coming from a CH_2 adjacent to carbonyl and having a carbon on the other side having no hydrogen, suggesting loss of a tertiary OH. The spectra indicate the presence of quinone carbonyl, and the color with ready decolorization by $Na_2S_2O_4$ is in agreement with quinone formation. These data would be consistent with conversion of the moiety **3** to **4** or an alternate system in which the amino group and the carboxyl are interchanged (Scheme I).

The action of dilute base [0.01 N $(CH_3))_3N$] on **1a** gives a crystalline solid (paulomenol A, **5**) whose molecular formula is $C_{29}H_{43}NO_{16}$ (Scheme II). The loss of a C_5H_3-

Scheme II



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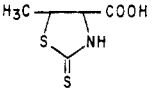
NO_2S moiety is consistent with NMR spectra showing five fewer carbons comprising CH_3 attached to an unsaturated carbon, two olefinic carbons, a carbonyl, and the NCS. The five carbons lost were isolated as 5-methyl-2-thioxo-4-thiazolinecarboxylic acid (**6**),[6] which must arise from a



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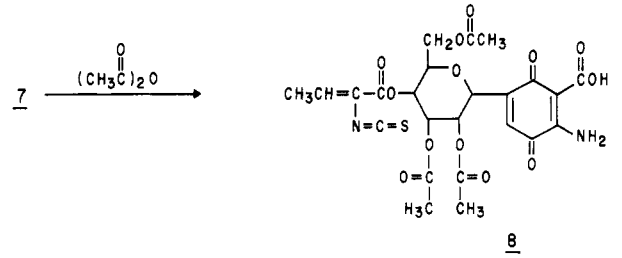
$CH_3CH{=}C(NCS)C{=}O$ moiety with H_2S being formed by hydrolysis of NCS and then reacting with the above pauloyl moiety. This acyl group (corresponding acid is paulic acid) must be attached at C-11 of **1a** as there is an upfield shift of H-11 on going from **1a** to **5**.

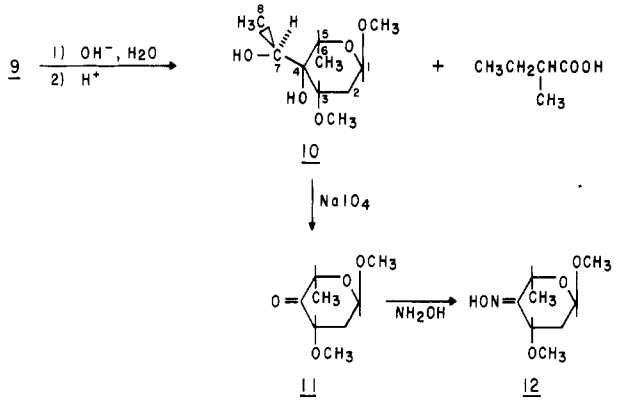
In the ^1H NMR of **1a** chemical shifts for the methyl group and the olefinic proton in the pauloyl moiety are δ 1.97 and 6.83, respectively, in CD_3COCD_3. in **2** these signals in $CDCl_3$ were δ 1.94 and 6.75. These are very similar to the analogous chemical shifts in ethyl α-thiocyanatocrotonate which were δ 1.97 and 6.75.[7] The work of Jackman and Wiley[8] suggests that there would be a substantial difference between the *Z* and *E* forms. These workers report that in methyl crotonate the chemical shift for the terminal methyl protons in the ^1H NMR in CCl_4 of the trans isomer is δ 1.89, while that of the cis isomer is δ 2.84. In the cases of the olefinic H-3 protons the values were δ 7.05 and 6.43, respectively. The close correspondence of values for resonances in the pauloyl moiety of **1a** and its degradation products with those from ethyl δ-

(1) A preliminary account of a part of this work has been published. See: Wiley, P. F.; Mizsak, S. A.; Baczynskyj, L.; Argoudelis, A. D. *J. Antibiot.* **1984**, *37*, 1273.
(2) Wiley, P. F. *J. Antibiot.* **1976**, *29*, 587.
(3) Mitscher, L. A.; McRae, W.; Devoe, S. E.; Shay, A. J.; Hausmann, W. K.; Bohonos, N. *Antimicrob. Agents Chemother.* **1965**, 828.
(4) Tsukiura, H.; Okanishi, N.; Koshiyama, H.; Ohmori, T.; Miyaki, T.; Kawagushi, H. *J. Antibiot.* **1964**, *17*, 223.
(5) Argoudelis, A. D.; Brinkley, T. A.; Brodasky, T. F.; Buege, J. A.; Meyer, H. F.; Mizsak, S. A. *J. Antibiot.* **1982**, *35*, 285.
(6) Doyle, F. P.; Holland, D. O.; Momolis, P.; Norman, A. *J. Chem. Soc.* **1958**, 4605.
(7) Volkmann, R. A. *Synth. Commun.* **1978**, *8*, 541.
(8) Jackman, L. M.; Wiley, R. H. *J. Chem. Soc.* **1960**, 2886.

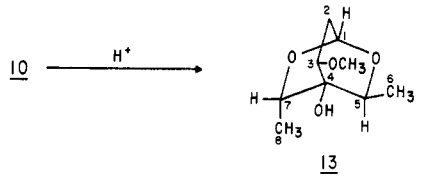
Scheme III



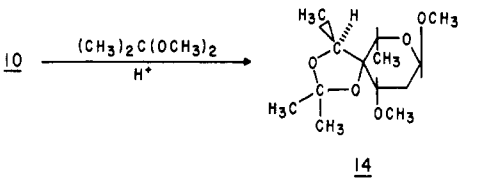
Scheme IV



Scheme V



Scheme VI



thiocyanatocrotonate and the indicated substantial difference between *E* and *Z* forms demonstrates that the pauloyl olefinic bond is *Z* as shown in **1a**.

Acidic methanolysis of **1a** forms an orange crystalline solid (11-*O*-pauloylpaulinone, **7**, $C_{18}H_{18}N_2O_{10}S$) and a colorless liquid [methyl 7-*O*-(2-methylbutyryl)paulomycoside, **9**, $C_{15}H_{28}O_6$]. The spectral data and color indicate that **7** has the quinone system of **2**, the tetrahydropyran ring and the pauloyl moiety. The H-8 proton now resonates at δ 5.06 rather than δ 3.70 as in **1a**, suggesting that C-8 is attached to the quinone ring at the carbon which was previously substituted by a tertiary OH. In the ^{1}H NMR of **7** the protons of CH_2O have moved upfield to δ 3.61, indicating loss of an acyl group from this oxygen. Acetylation to give **8** causes a downfield shift supporting this conclusion (Scheme III). Since **7** and **9** minus a CH_3O introduced into **9** by methanolysis account for all carbons but two of **1a**, and NMR spectra show that these are CH_3 and CO, an acetyl must be present at C-13. NMR data from **7** and **1a** and formation of **8** preclude the N not present as NCS being elsewhere than ring A. Then **7** must be the structure of 11-*O*-pauloylpaulinone or an isomer with NH_2 and COOH interchanged.

A mixture of **9** and its **1b** analogue is readily hydrolyzed by base to give **10** (methyl paulomycoside) as a colorless liquid and a mixture of isobutyric and 2-methylbutyric acids (Scheme IV). The NMR data show that a methoxyl group is present in **9** and **10** which was not present in **1a**. Reaction of **1a** with (*S*)-2-methylbutyryl chloride converted it back to **9**, establishing the stereochemistry of the chiral carbon in the acyl group.

Periodate oxidation of **10** formed acetaldehyde identified as its 2,4-dinitrophenylhydrazone and a liquid (**11**, $C_8H_{14}O_4$) which was converted to an oxime (**12**). Monneret et al. have reported the synthesis of a sugar and its oxime[9,10] whose ^{1}H NMR spectra were compared with those of **11** and **12** and found to be identical. The possibility of **11** and **12** being epimers of Monneret's compounds was ruled out by the similarity of rotations. The upfield shift of the proteon at C-7 in the ^{1}H NMR on going from **9** to **10** establishes that the acyl group of **9** is attached to the oxygen at C-7, requiring the indicated structure for **9**. The presence of an anomeric carbon in **1a** and introduction of a new CH_3O on acidic methanolysis indicate a glycosidic attachment of **9** to one of the hydroxyls of ring B in **1a**. Oxygens at C-11 and C-13 are acylated and NMR indicates a hydroxyl at C-9 so the sugar must be at C-10.

Hydrolysis of **10** by the method of Paulsen and Sinnwell[11] formed a bicyclic compounds (**13**) which differed from **10** in molecular formula by loss of the elements of CH_3OH (Scheme V). In the ^{1}H NMR of **13** a proton on a carbon to which CH_3 is attached is coupled by long range coupling (J = 2.1 Hz) to the proton of the carbon bearing CH_3O. This is a coupling requiring that the 1,3-protons involved are in a *W* conformation which can only arise if the protons are cis and equatorial. This necessitates identical conformations of the two carbon atoms substituted by CH_3.[10]

Treatment of **10** with 2,2-dimethoxypropane using an acidic catalyst formed an acetonide (**14**) (Scheme VI). This compound could have two possible structures according to the chirality of C-4 of **10**. A ^{1}H NMR spectrum of **14** with irradiation of H-6 resulted in enhancement of the signals for H-5 and H-7. Irradiation of H-8 resulted in enhancement of signals at H-7, H-5, and H-3. If C-4 had the opposite configuration to that indicated in **10**, irradiation of H-8 would not cause enhancement of the resonance of H-5. Therefore the absolute stereochemistry of **9** and **10** must be as shown.

It was originally proposed that the substituents on ring A at C-2 and C-3 were $CONH_2$ and OH,[1] but subsequent titration and NMR data indicated that this was not correct. Paulomycin has now been found to have two titratable groups, and ^{1}H NMR resonances at δ 14.39, 9.98, and 9.31 would be consistent with the view that these arrise from COOH and amino NH_2. The ^{13}C NMR spectrum of **7** with no proton decoupling gave resonances at δ 196.40 as a doublet for C-7 and δ 187.2 as a broad singlet for C-4. Irradiation of the three exchangeable protons at higher field than δ 9 caused no change in the signals for C-7 and C-4. In contrast, irradiation at δ 9.31 collapsed the C-4 signal to a doublet (J = 5.1 Hz). These changes in the C-4 signal require a three-bond connection from C-4 to the amino protons,[12] indicating the amino group is at C-3 in **1a**.

(9) Monneret, C.; Conreur, C.; Qui, K.-H. *Carbohydr. Res.* **1978**, *65*, 35.

(10) C. G. Chidester has provided X-ray crystallographic studies supporting the structures of **12** and **13**.

(11) Paulsen, H.; Sinnwell, V. *Chem. Ber.* **1978**, *111*, 869.

(12) Takeuchi, S.; Uzawa, J.; Seto, H.; Yonehara, H. *Tetrahedron Lett.* **1977**, 2943.

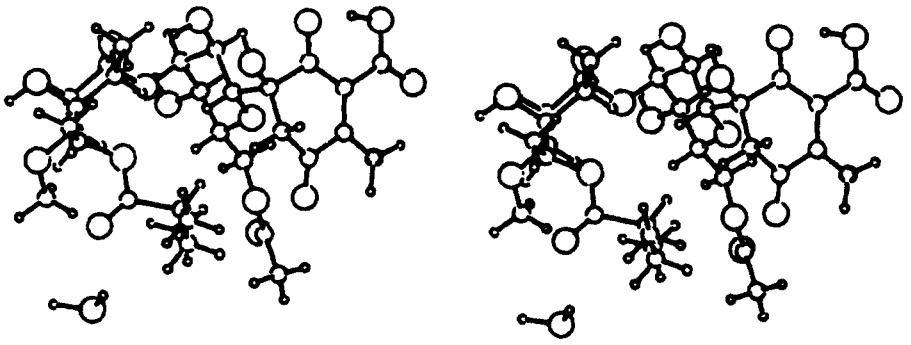


Figure 1. Stereoscopic view of paulomenol A.

As neither **1a** nor **5** are oxidized by periodate the C-4 carbonyl must behave as a vinylogous α-keto acid and the C-7 carbonyl as a vinylogous amide as seems possible with structure **3**. If the amino and carboxyl groups were interchanged, C-7 and C-6 would represent a periodate oxidizable system. Further support for **3** as the structure of ring A in **1a** is provided by the ^{13}C NMR spectrum of **7**. This spectrum shows that H-5 is coupled to C-3 requiring a three-bond connection and the arrangement of ring A depicted in **3**.[12] A ring system very similar to that of ring A in **1a** has been reported for enaminomycin A.[13]

Combining the above conclusions points very strongly to the structures depicted in **1a** and **1b** for paulomycins A and B, respectively, except for absolute stereochemistry of ring B and of C-6. X-ray crystallographic studies of paulomenol A (**5**) gives this information and in addition confirms many of the conclusions from the preceeding investigations. The crystal structure was determined by using full three-dimensional data, measured at low temperature, and refined to $R = 0.062$. Final atomic coordinates are given in Table I with numbering as in **1a**. A stereodrawing of the paulomenol A molecule is shown in Figure 1. Although the absolute configuration could not be determined by X-ray crystallography, this study showed the relative configuration of all chiral centers. Since the absolute configuration of the lower portion, **9**, is known, paulomenol A has the absolute configuration shown. The paulomenol molecule forms four intramolecular hydrogen bonds in the crystal: N-3 to O-1, O-1A to O-7, O-6 to O-9, and O-9 to O-6′. These hydrogen bonds appear to help stabilize the conformation found in the crystal. Bond distances and angles are as normally expected (see supplementary material), except at C-2‴, which appears to be poorly determined.

Experimental Section

Paulomycinone A (2). A solution of 2.0 g of **1a** in 200 mL of CH_3OH was allowed to stand at room temperature for 5 days. The solution was evaporated to dryness in vacuo, and the residue was chromatographed on 200 g of silica gel by eluting with $CHCl_3$–CH_3OH (94:6). Combination of fractions containing **2** by TLC (R_f 0.67; SiO_2; 9:1 $CHCl_3$–CH_3OH) and evaporation in vacuo gave 663 mg. This material was combined with 407 mg of similarly prepared material, and the chromatography was repeated, yielding 1.0 g: mp 57–73 °C; $[\alpha]^{25}_D$ +2° (*c* 0.694, CH_3OH); UV (CH_3OH) 232 nm (ϵ 15 250), 264 (18 400), 440 (2100); IR (Nujol) 3488, 3363, 3235, 3249, 2037, 1735, 1695, 1637, 1618, 1569, 1461, 1378, 1367, 1341, 1264, 1240, 1187, 1154, 1115, 1096, 1056, 1023, 998, 989, 890, 751, 722 cm^{-1}; ^1H NMR (CD_3COCD_3) δ 0.91 (3 H, t, J = 6.4 Hz, H-5‴), 1.15 (3 H, d, J = 8.4 Hz, H-4‴), 1.31 (3 H, d, J = 6.4 Hz, H-6′), 1.35 (3 H, d, J = 7.2 Hz, H-8′), 1.50, 1.73 (2 H, 2 m, H-3‴), 1.97 (3 H, d, J = 8.0 Hz, H-4″), 2.04 (3 H, s, H-2⁗), 1.90, 2.43 (2 H, 2 m, H-2′), 2.42 (1 H, m, H-2‴), 2.93 (1 H, s, exchangeable), 3.39 (3 H, s, CH_3O), 3.50 (1 H, m, H-9), 3.70 (2 H, m, H-13), 4.27, 4.46, 4.62 (5 H, 3 m, H-10, H-12, exchangeable), 5.06, 5.12 (3 H, 2 m, H-8, H-1′, exchangeable), 5.41 (1 H, m, H-11), 6.42 (1 H, q, J = 8.0 Hz, H-3″), 6.47 (1 H, s, H-5), 8.66, 10.00 (2 H, 2 br s, NH_2), 13.09 (1 H, s, COOH); ^{13}C NMR ($CDCl_3$) δ 185.12 (C-4), 180.50 (C-7), 175.79 (C-1‴), 170.60 (C-1⁗), 168.62 (C-1), 160.51 (C-1″),

(13) Itoh, Y.; Haneishi, T.; Arai, M.; Hata, T.; Aiba, K.; Tamura, C. *J. Antibiot.* **1978**, *31*, 838.

Table I. Fractional Coordinates ($\times 10^4$) and B_{eq} (Å^2)[a]

$B_{eq} = \frac{4}{3}(a^2B_{11} + b^2B_{22} + c^2B_{33} + ab\cos\gamma B_{12} + ac\cos\beta B_{13} + bc\cos\alpha B_{23})$

	x	y	z	B_{eq}
O(1A)	1704 (5)	−1957 (3)	5522 (1)	2.9 (2)
C(1)	1654 (6)	−2473 (5)	5169 (1)	2.4 (2)
O(1)	2021 (4)	−3483 (3)	5149 (1)	2.7 (2)
C(2)	1161 (6)	−1809 (4)	4822 (1)	1.7 (2)
C(3)	1132 (6)	−2312 (4)	4445 (1)	1.8 (2)
N(3)	1578 (6)	−3354 (4)	4365 (1)	2.4 (2)
C(4)	492 (6)	−1680 (4)	4088 (1)	1.8 (2)
O(4)	685 (5)	−2041 (3)	3757 (1)	2.4 (2)
C(5)	−465 (6)	−630 (4)	4179 (1)	1.9 (2)
C(6)	286 (6)	69 (4)	4505 (1)	1.7 (2)
O(6)	−872 (4)	904 (3)	4609 (1)	2.1 (2)
C(7)	720 (6)	−645 (4)	4871 (1)	2.0 (2)
O(7)	722 (4)	−151 (3)	5201 (1)	2.3 (2)
C(8)	1811 (6)	685 (4)	4349 (1)	1.7 (2)
C(9)	2667 (6)	1457 (5)	4643 (1)	1.9 (2)
O(9)	1628 (4)	2308 (3)	4800 (1)	2.1 (2)
C(10)	4140 (6)	1956 (4)	4435 (1)	1.8 (2)
O(10)	3637 (4)	2559 (3)	4080 (1)	1.8 (2)
C(11)	5250 (6)	1018 (4)	4292 (1)	1.8 (2)
O(11)	6614 (4)	1451 (3)	4085 (1)	2.1 (2)
C(12)	4299 (6)	214 (4)	4018 (1)	1.7 (2)
O(12)	2914 (4)	−196 (3)	4233 (1)	1.7 (2)
C(13)	5309 (6)	−785 (4)	3898 (1)	2.0 (2)
O(13)	4427 (4)	−1406 (3)	3604 (1)	2.6 (2)
C(1′)	3504 (6)	3746 (4)	4108 (2)	2.2 (2)
C(2′)	3785 (6)	4206 (5)	3693 (2)	2.5 (3)
C(3′)	2417 (6)	3916 (4)	3417 (1)	1.8 (2)
O(3′)	2679 (4)	4395 (3)	3034 (1)	2.7 (2)
C(3′M)	3537 (7)	3668 (5)	2771 (2)	3.4 (3)
C(4′)	798 (6)	4332 (4)	3580 (1)	2.0 (2)
O(4′)	868 (5)	5526 (3)	3637 (1)	2.4 (2)
C(5′)	585 (6)	3809 (4)	3994 (1)	2.2 (2)
C(6′)	−911 (8)	4146 (5)	4229 (2)	3.8 (3)
O(6′)	1947 (4)	4070 (3)	4254 (1)	2.4 (2)
C(7′)	−548 (7)	4067 (5)	3285 (2)	2.9 (3)
O(7′)	−815 (6)	2864 (3)	3327 (1)	4.5 (2)
C(8′)	−2166 (7)	4639 (7)	3342 (2)	5.9 (4)
C(1‴)	−115 (10)	2323 (5)	2998 (2)	5.6 (4)
O(1‴)	−1168 (7)	2710 (3)	2664 (1)	6.0 (3)
C(2‴)	−1768 (8)	1033 (6)	3118 (2)	5.0 (3)
C(3‴)	−725 (9)	362 (7)	2886 (2)	6.1 (4)
C(4‴)	−3562 (7)	987 (5)	3025 (2)	3.4 (3)
C(5‴)	1069 (8)	395 (5)	2986 (2)	4.8 (3)
C(1⁗)	5304 (7)	−2097 (5)	3376 (1)	3.0 (3)
O(1⁗)	6778 (5)	−2142 (4)	3397 (1)	4.5 (3)
C(2⁗)	4269 (9)	−2737 (5)	3096 (2)	3.8 (3)
O(W)	313 (6)	1749 (4)	1987 (1)	5.8 (3)

[a] Estimated standard deviations are in parentheses. The number in parentheses corresponds to an uncertainty in the least significant digit.

152.90 (C-3), 151.96 (C-6), 136.06 (C-3″), 129.59 (C-5), 123.44 (C-2″), 100.31 (C-1′), 97.25 (C-2), 80.03 (C-8), 79.64 (C-4′), 74.06 (C-10), 73.59 (C-3′), 72.47 (C-12), 70.82 (C-11), 70.58 (C-7′), 70.25 (C-9), 69.08 (C-5′), 62.64 (C-13), 57.65 (CH_3O), 41.56 (C-2‴), 30.85 (C-2′), 26.77 (C-3‴), 20.76 (C-2⁗), 16.65 (C-4‴), 15.73 (C-6′, C8′), 14.68 (C-4″), 11.75 (C-5‴); MS, m/z 768 (M^+); M_r 768. Anal. Calcd for $C_{34}H_{44}N_2O_{16}S$: C, 53.12; H, 5.77; N, 3.60; S, 4.17. Found: C, 52.43; H, 5.99; N, 3.58; S, 4.17.

Paulomenol A (5). A solution of 786 mg (1 mmol) of **1a** in 500 mL of 0.01 N $(CH_3)_3N$ was prepared by stirring a mixture of the two. The solution was allowed to stand at room temperature for 2 days followed by filtration. The filtrate was extracted with four 250-mL portions of $CHCl_3$. The aqueous phase was adjusted to pH 3 with concentrated HCl, and the extraction was repeated. All of the extracts were combined and evaporated to dryness in vacuo, yielding 449 mg. This was combined with 458 mg obtained similarly and chromatographed on 131 g of silica gel by eluting with $CHCl_3$–CH_3OH (85:15). The fractions containing **5** were determined by TLC (R_f 0.37; SiO_2; 78:20:2 $CHCl_3$–CH_3OH–H_2O), combined, and evaporated in vacuo, yielding 521 mg. This was recrystallized from $CHCl_3$–Skellysolve B and finally from $CHCl_3$, yielding 202 mg: mp 187–191 °C; UV (C_2H_5OH) 241 nm (ϵ 8590), 318 (8860); IR (Nujol) 3300, 3270, 1730, 1695, 1580, 1305, 1245, 1190, 1105, 1045, 995, 900, 760 cm^{-1}; ^1H NMR (CD_3COCD_3) δ 0.98 (3 H, t, J = 6.0 Hz, H-5‴), 1.21 (3 H, d, J = 8.0 Hz, H-4‴), 1.29 (3 H, d, J = 6.0 Hz, H-6′), 1.31 (3 H, d, J = 6.3 Hz, H-8′), 1.64 (2 H, m, H-3‴), 1.92, 2.27 (2 H, 2 m, H-2′), 2.04 (3 H, s, H-2⁗), 2.46 (1 H, m, H-2‴), 3.16 (2 H, dd, H-5), 3.34 (3 H, s, CH_3O), 3.41 (1 H, s, exchangeable), 3.49 (2 H, m, H-9, H-11), 3.65 (1 H, m, H-3′), 3.73 (2 H, m, H-13), 3.92 (1 H, d, J = 8.0 Hz, H-8), 4.08 (1 H, m, H-12), 4.10 (1 H, m, H-10), 4.30 (1 H, d, exchangeable), 4.49 (1 H, q, J = 6.0 Hz, H-5′), 5.06 (1 H, d, exchangeable), 5.17 (1 H, q, H-1′), 5.25 (1 H, s, exchangeable), 5.39 (1 H, q, J = 6.3 Hz, H-7′), 8.37, 9.88 (2 H, 2 br s, NH_2); ^{13}C NMR (CD_3COCD_3) δ 198.61 (C-4), 188.02 (C-7), 175.06 (C-1‴), 170.48 (C-1⁗), 169.40 (C-1), 159.46 (C-3), 99.40 (C-2), 99.66 (C-1′), 80.67 (C-10), 78.34 (C-4′), 78.25 (C-8), 75.04 (C-12), 74.34 (C-3′), 73.53 (C-6), 69.86 (C-7′), 69.72 (C-11), 67.90 (C-5′), 67.60 (C-9), 63.42 (C-13), 56.38 (CH_3O), 48.12 (C-5), 41.53 (C-2‴), 30.23 (C-2′), 26.71 (C-3‴), 20.08 (C-2⁗), 16.68 (C-4‴), 15.35 (C-6′, C-8′), 11.36 (C-5‴); MS, (Me_3Si derivative) m/z 949.4221, calcd for $C_{41}H_{75}NO_{16}Si_4$ 949.41636. Anal. Calcd for $C_{29}H_{43}NO_{16}$: C, 52.64; H, 6.55; N, 2.12. Found: C, 51.52; H, 6.44; N, 2.09.

Crystals of **5** suitable for X-ray crystallography were prepared by two recrystallizations from $CHCl_3$–Skellysolve B, one from $CHCl_3$, one from CH_3COCH_3, and two from $CH_3COOC_2H_5$.

5-Methyl-2-thioxo-4-thiazolidinecarboxylic Acid (6). A solution of 6.3 g of a mixture of **1a** and **1b** in 4 L of 0.01 N $(CH_3)_3N$ was allowed to stand at room temperature for 12 h. It was adjusted to pH 5.5 with HCl and passed over 500 mL of Amberlite XAD-2. The column was washed with 1 L of H_2O. The effluent and the wash were combined and adjusted to pH 3.0 with HCl and passed over 500 mL of Amberlite XAD-2. The resin was washed with 1.5 L of H_2O followed by elution with 4.34 L of CH_3OH–H_2O (7:3). The eluate was evaporated to dryness in vacuo, yielding 180 mg: ^1H NMR (CD_3COCD_3) δ 1.57 (3 H, d, J = 8.0 Hz, CH_3), 4.27 (1 H, dq, J = 8.0, 4.4 Hz, H-5), 4.56 (1 H, d, J = 4.4 Hz, H-4); ^{13}C NMR (CD_3COCD_3) δ 198.46 (C-2), 170.96 (C=O), 70.69 (C-4), 47.68 (C-5), 22.45 (CH_3); MS, m/z 176.9904, calcd for $C_5H_7NO_2S_2$ 176.9918.

11-*O*-Pauloylpaulinone (7). A mixture of **1a** and **1b** (1 g) was dissolved in 125 mL of 1 N methanolic HCl. After the solution had stood at room temperature for 3 h, it was neutralized by slow addition of 34.4 g of Ag_2CO_3 with stirring. The mixture was filtered, and the insoluble material was washed thoroughly with CH_3OH. The filtrate was evaporated to dryness in vacuo, and the residue was mixed with 100 mL of 60% CH_3OH. The insoluble material (**16**) was removed by filtration, and the filtrate was extracted with four 50-mL portions of cyclohexane to remove **9**. The aqueous phase was concentrated in vacuo until the CH_3OH was removed. The residue was filtered, giving 363 mg of an orange solid, which was chromatographed on 36 g of acid-washed silica gel by eluting with $CHCl_3$–CH_3OH (9:1). Fractions containing **7** were combined on the basis of TLC (R_f 0.59; SiO_2; 70:20:11 $C_2H_5COCH_3$–CH_3COCH_3–H_2O) and evaporated in vacuo. The residue was recrystallized from CH_3OH, yielding 100 mg: mp 157–160 °C; $[\alpha]^{25}_D$ +108° (c 0.2835, CH_3OH); UV (CH_3OH) 231 nm (ϵ 15400), 266 (18050), 438 (1700); IR (Nujol) 3511, 3436, 3417, 3327, 2050, 1722, 1696, 1682, 1644, 1634, 1617, 1568, 1512, 1268, 1247, 1181, 1166, 1120, 1075, 1072, 1049, 1039, 909, 900, 827, 751, 747, 622 cm^{-1}; ^1H NMR (CD_3COCD_3) δ 1.96 (3 H, d, J = 7.2 Hz, H-4′), 3.61 (3 H, m, H-9, H-13), 4.05 (1 H, m, H-12), 4.45 (1 H, m, H-10), 4.97 (2 H, m, H-11, exchangeable), 5.06 (1 H, d, J = 8.6 Hz, H-8), 6.85 (1 H, q, J = 7.2 Hz, H-3′), 7.06 (1 H, s, H-5), 8.56, 9.93 (2 H, 2 br s, NH_2), 13.40 (1 H, s, COOH); ^{13}C NMR (CD_3OD) δ 186.69 (C-4), 182.05 (C-7), 171.15 (C-1), 162.12 (C-1′), 154.79 (C-3), 153.03 (C-6), 144.1 (C-5′), 136.49 (C-3′), 131.83 (C-5), 125.10 (C-2′), 97.0 (C-2), 75.10 (C-8), 74.76 (C-10), 72.75 (C-12), 71.01 (C-11), 69.83 (C-9), 62.44 (C-13), 14.63 (C-4′); MS, m/z 454 (M^+), M_r 454. Anal. Calcd for $C_{18}H_{18}N_2O_{10}S$: C, 47.58; H, 4.00; N, 6.12; S, 7.06. Found: C, 47.58; H, 4.11; N, 5.99; S, 6.95.

9,10,11-Tri-*O*-acetyl-11-*O*-pauloylpaulinone (8). A mixture of 746 mg of **7**, 11 mL of CH_3COOH, 2.2 mL of $(CH_3CO)_2O$, and 110 mg of p-$CH_3C_6H_4SO_3H$·H_2O was stirred until solution occurred. After 18 h at room temperature a solution of 20 g of $NaHCO_3$ in 300 mL of H_2O was stirred while the reaction mixture was added slowly. The solid which precipitated was removed by extraction with three 100-mL portions of $CHCl_3$, which were combined and evaporated to dryness in vacuo, yielding 950 mg. The orange solid was chromatographed on 95 g of silica gel by eluting with $CHCl_3$–CH_3OH (92:8). Fractions containing **8** were combined on the basis of TLC (R_f 0.46; SiO_2; 92:8 $CHCl_3$–CH_3OH) and evaporated in vacuo, yielding 715 mg. Of this sample, 230 mg was rechromatographed as previously to give a material homogeneous by TLC in the above system: UV (CH_3OH) 227 nm (ϵ 15350), 265 (13950), 437 (1530); IR (Nujol) 3370, 3253, 3218, 2043, 1751, 1702, 1639, 1618, 1268, 1231, 1157, 1095, 1055, 1043, 1041, 949, 905, 750 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.92 (3 H, s, CH_3CO), 1.96 (3 H, d, J = 7.67 Hz, H-4′), 2.10 (3 H, s, CH_3CO), 2.29 (3 H, s, CH_3CO), 4.27 (3 H, m, H-12, H-13), 4.91 (1 H, dd, J = 2.65, 9.81 Hz, H-9), 5.13 (1 H, dd, J = 2.68, 10.0 Hz, H-11), 5.20 (1 H, d, J = 9.8 Hz, H-8), 5.76 (1 H, t, J = 2.65, 2.68 Hz, H-10), 6.67 (1 H, q, J = 7.6 Hz, H-3′), 6.94 (1 H, s, H-5), 7.34, 9.88 (2 H, 2 d, NH_2), 13.16 (1 H, s, COOH); ^{13}C NMR ($CDCl_3$) δ 184.54 (C-4), 180.56 (C-7), 170.57, 170.07, 169.52, 168.52 (4 C=O), 160.26 (C-1) 152.06 (C-3), 149.68 (C-6) 143.5 (C-5′), 136.32 (C-3′), 130.41 (C-5), 123.07 (C-2′), 97.06 (C-2), 72.46, 70.8, 68.66, 68.07, 67.73 (C-8, C-9, C-10, C-11, C-12), 62.25 (C-13), 20.99, 20.74, 20.46 (3 CH_3), 14.66 (C-4′); MS, m/z 580 (M^+), M_r 580. Anal. Calcd for $C_{24}H_{24}N_2O_{13}S$: C, 47.76; H, 4.16; N, 4.83; S, 5.53. Found: C, 47.56 H, 4.28; N, 4.73; S, 5.35.

Methyl 7-*O*-(2-Methylbutyryl)paulomycoside (9). The cyclohexane extracts from the preparation of **7** from 3 g of **1a** were combined and evaporated in vacuo to give 753 mg of liquid. This was chromatographed on 75 g of silica gel by eluting with $CHCl_3$–CH_3OH (95:5), with combination of those fractions containing a weight maximum and evaporation in vacuo, yielding 718 mg: R_f 0.76 (SiO_2; 9:1 $CHCl_3$–CH_3OH); $[\alpha]^{25}_D$ −76° (c 0.722, CH_3OH); IR (neat) 3503, 2970, 2940, 2880, 1734, 1644, 1463, 1382, 1361, 1300, 1294, 1264, 1238, 1187, 1153, 1134, 1112, 1090, 1055, 1027, 996, 985, 754, 666, cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.87 (3 H, t, J = 7.5 Hz, H-5′), 1.11 (3 H, d, J = 7.2 Hz, H-4′), 1.23 (3 H, d, J = 6.6 Hz, H-6), 1.26 (3 H, d, J = 6.6 Hz, H-8), 1.33–2.50 (4 H, m, H-2, H-3′), 3.27, 3.31 (6 H, 2 s, 2 CH_3O), 3.43 (1 H, m, CHO), 3.82 (1 H, m, CHO), 4.73 (1 H, m, H-1), 5.27 (1 H, q, J = 6.6 Hz, H-7); ^{13}C NMR ($CDCl_3$) δ 176.1 (C-1′), 97.90 (C-1), 73.94 (C-3), 73.42 (C-4), 70.21 (C-7), 65.67 (C-5), 56.73, 54.43 (2 CH_3O), 41.53 (C-2′), 30.23 (C-2), 26.48 (C-3′), 16.34 (C-4′), 15.69, 15.21 (C-6, C-8), 11.30 (C-5′); MS, m/z 304 (M^+), M_r 304. Anal. Calcd for $C_{15}H_{28}O_6$: C, 59.20; H, 9.30. Found: C, 59.26; H, 9.19.

Methyl Paulomycoside (10). A solution of 2.18 g of a mixture of **9** and its 7-*O*-isobutyryl analogue in 87 mL of 1:1 CH_3OH–1 N NaOH was refluxed for 4 h. The CH_3OH was removed by reduced pressure evaporation, and the residue was extracted with four 22-mL portions of $CHCl_3$. Evaporation of the combined extracts gave 1.75 g of liquid residue, which was chromatographed on 175 g of silica gel by eluting with $CHCl_3$–CH_3OH (95:5). Those fractions containing a weight maximum were combined and evaporated in vacuo, giving 1.61 g of colorless liquid. Rechromatography in the same fashion gave 1.43 g: R_f 0.47 (SiO_2; 95:5 $CHCl_3$–CH_3OH); $[\alpha]^{25}_D$ −80° (c 0.852, CH_3OH); IR (neat) 3479, 2978, 2943, 2907, 2831, 1458, 1421, 1379, 1326, 1203, 1161, 1128,

1095, 1078, 1053, 1026, 973, 923, 891, 679 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.14 (3 H, d, J = 7.8 Hz, H-6), 1.21 (3 H, d, J = 5.7 Hz, H-8), 1.84–2.08 (2 H, m, H-2), 3.17–4.05 (5 H, m, CHO, exchangeable), 3.31, 3.33 (6 H, 2 s, 2 CH_3O), 4.78 (1 H, m, H-1); ^{13}C NMR ($CDCl_3$) 98.37 (C-1), 76.40 (C-3), 73.78 (C-4), 71.95 (C-7), 66.96 (C-5), 55.17, 54.84 (CH_3O), 29.56 (C-2), 18.90 (C-6 or C-8), 13.58 (C-6 or C-8); MS, m/z 189.1153, calcd for $C_9H_{17}O_4$ ($M^+ - OCH_3$) 189.1126. Anal. Calcd for $C_{10}H_{20}O_5$: C, 54.53; H, 9.15. Found: C, 53.34; H, 9.33.

2-Methylbutyric Acid and Isobutyric Acid. From hydrolysis of 500 mg of a mixture of 7-*O*-acylpaulomycosides derived from **1a** and **1b** as in the preparation of **10**, 123 mg of acid was isolated by acidification of the extracted aqueous phase and extraction with $CHCl_3$. This material was found to contain the above acids by comparison of Me_3Si-derivatized samples with samples of Me_3Si derivatives of authentic acids by GC–mass spectra: ^1H NMR ($CDCl_3$) δ 0.93 (t, CH_3CH_2), 1.17 (d, CH_3CH), 1.20 (d, CH_3CH), 1.67 (m, CH_2), 2.42 (m, CH), 11.46 (s, acidic H); ^{13}C NMR ($CDCl_3$) δ 184.09 (C=O), 41.09 (CH of 2-methylbutyric acid), 34.05 (CH of isobutyric acid), 26.67 (CH_2), 18.79 (CH_3 of isobutyric acid), 16.40, 11.56 (2 CH_3 of 2-methylbutyric acid).

Synthetic Methyl 7-*O*-[(*S*)-2-Methylbutyryl]paulomycoside (9). A solution of 440 mg (2 mmol) of **10** in 20 mL of anhydrous pyridine was added slowly to 273 mg (2.27 mmol) of (*S*)-2-methylbutyryl chloride. The solution was allowed to stand at room temperature for 22 h followed by evaporation to dryness in vacuo. The residue was dissolved in 20 mL of $CHCl_3$, and the solution was washed successively with 10 mL of H_2O, 2 × 10 mL of 0.1 N HCl, 2 × 10 mL of saturated $NaHCO_3$, and 10 mL of H_2O. The $CHCl_3$ solution was dried over $MgSO_4$, filtered, and evaporated to a liquid residue in vacuo, yielding 411 mg. The residue was chromatographed on 41 g of silica gel by eluting with $CHCl_3$–CH_3OH (95:5) and analyzing by weight and TLC in the above solvent. The fractions containing **9** were combined and evaporated in vacuo, yielding 345 mg: $[\alpha]^{25}_D$ −70° (c 0.828, CH_3OH). TLC in $CHCl_3$–CH_3OH (95:5), ^1H NMR, and mass spectrum were identical with the same properties determined on **9** from **1a**.

Methyl 7-*O*-[(*R*,*S*)-2-Methylbutyryl]paulomycoside. This was prepared and purified in the same manner as was synthetic **9** except that racemic 2-methylbuturyl chloride was used, yielding 298 mg: $[\alpha]^{25}_D$ −92° (c 0.7035, CH_3OH). Its R_f, mass spectrum, and ^1H NMR were identical with those of natural and synthetic **9**. Attempts to separate the diastereomers by analytical chromatography in several systems were unsuccessful.

Methyl 2,6-Dideoxy-3-*O*-methyl-α-L-*threo*-hexopyranosid-4-ulose (11). A solution of 2.14 g (10 mmol) of $NaIO_4$ in 125 mL of H_2O was added to a solution of 1.10 g (5 mmol) of **10** in 125 mL of *t*-BuOH. After 18 h at room temperature, the *t*-BuOH was removed by evaporation in vacuo. The residue was extracted with four 50-mL portions of $CHCl_3$ which were combined and evaporated in vacuo, yielding 717 mg. Chromatography on 72 g of silica gel eluting with Skellysolve B–CH_3COCH_3 (7:3) gave 575 mg. This was rechromatographed on 58 g of silica gel by eluting with $CHCl_3$–CH_3OH (95.5), yielding 394 mg: R_f 0.33 (SiO_2; 7:3 Skellysolve B–CH_3COOCH_3); $[\alpha]^{25}_D$ −274° (c 1.005, $CHCl_3$); IR (neat) 2990, 2942, 2837, 1740, 1447, 1376, 1343, 1318, 1271, 1208, 1175, 1124, 1079, 1052, 1003, 966, 914, 839, 818, 800, 760 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.30 (3 H, d, J = 6.56 Hz, H-6), 2.07 (1 H, ddd, $J_{2a,2e}$ = 12.91 Hz, $J_{2a,1}$ = 3.59 Hz, $J_{2a,3}$ = 12.06 Hz), 2.56 (1 H, ddd, $J_{2e,2a}$ = 12.91 Hz, $J_{2e,1}$ = 1.55 Hz, $J_{2e,3}$ = 6.71 Hz), 3.46, 3.50 (6 H, 2 s, 2 CH_3O), 4.23 (1 H, dd, $J_{3,2e}$ = 6.7 Hz, $J_{3,2a}$ = 12.06 Hz), 4.31 (1 H, q, J = 6.56 Hz, H-5), 4.90 (1 H, dd, $J_{1,2e}$ = 1.55 Hz, $J_{1,2a}$ = 3.59 Hz); ^{13}C NMR ($CDCl_3$) δ 205.42 (C-4), 98.04 (C-1), 78.21 (C-3), 69.99 (C-5), 58.35, 55.40 (2 CH_3O), 39.41 (C-2) 13.85 (C-1); MS, m/z 173.0792, calcd for $C_8H_{13}O_4$ ($M^+ - H$) 173.0814. Anal. Calcd for $C_8H_{14}O_4$: C, 55.16; H, 8.10. Found: C, 53.84; H, 7.75.

Acetaldehyde from 10. The reaction was run as in the preparation of **11** except that 220 mg (1 mmol) of **10** was used. The reaction mixture was swept out with dry N_2 which was bubbled through 276 mL of Brady's reagent. The precipitate was removed by filtration and dried. Its ^1H and ^{13}C NMR were identical with those of an authentic sample of acetaldehyde 2,4-dinitrophenylhydrazone.

Methyl 2,6-Dideoxy-3-*O*-methyl-α-L-*threo*-hexopyranosid-4-ulose Oxime (12). This was prepared according to the procedure of Monneret et al.[10] From 1.086 g of **11**, 207 mg of **12** was obtained: mp 84–86 °C (lit.[10] mp 105–110 °C); $[\alpha]^{25}_D$ −222 °C (c 0.944, $CHCl_3$) [lit.[10] $[\alpha]^{25}_D$ −193° ($CHCl_3$)]; ^1H NMR δ 1.47 (3 H, d, J = 6.61 Hz, H-6), 1.90 (1 H, m, H-2), 2.39 (1 H, ddd, J = 2.1, 5.4, 14.8 Hz, H-2), 3.26, 3.38 (6 H, 2 s, 2 CH_3O), 3.82 (1 H, dd, J =2.1, 5.5 Hz, H-3), 4.84 (2 H, m, H-5), 8.65 (1 H, s, NOH); ^{13}C NMR ($CDCl_3$) δ 157.07 (C-4), 95.78 (C-1), 75.01 (C-3), 63.96 (C-5), 56.23, 55.71 (2 CH_3O) 37.35 (C-2), 17.33 (C-6); MS, m/z 190 (M^+ + H), M_r 189. Anal. Calcd for $C_8H_{15}NO_4$: C, 50.78; H, 7.98; N, 7.40. Found: C, 50.80; H, 8.11; N, 7.17.

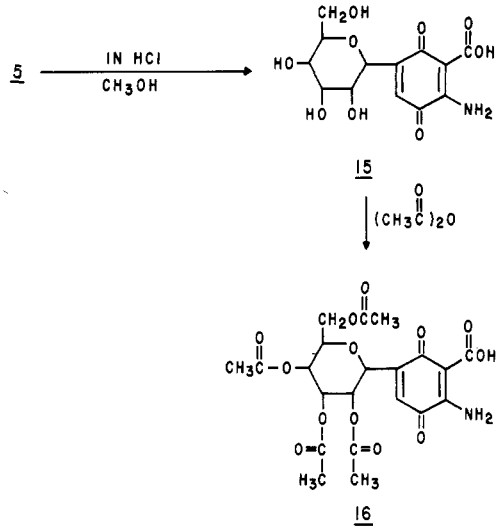
1,7-Anhydropaulomycose (13). A solution of 1.126 g of **10** in 94 mL of 0.5% (v/iv) of CF_3COOH was allowed to stand at room temperature for 1 day. The solution was neutralized with Dowex 2 (OH^-), filtered, and freeze-dried. The residue was chromatographed on 94 g of silica gel by developing with CH_2Cl_2–CH_3OH (100:3), collecting 5-mL fractions, which were analyzed by weight combining 76–85. Evaporation in vacuo gave 239 mg, which was recrystallized from Skellysolve B, yield 129 mg: mp 101–103 °C; R_f 0.57 (SiO_2; 95:5 $CHCl_3$–CH_3OH); $[\alpha]^{25}_D$ −37° (c 0.918, CH_3OH): IR (Nujol) 3345, 1380, 1350, 1320, 1285, 1230, 1205, 1185, 1120, 1085, 1075, 1045, 1030, 995, 980, 835 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.35 (3 H, d, J = 6.5 Hz), 1.38 (3 H, d, J = 6.5 Hz), 2.01 (1 H, ddd, $J_{2a,2b}$ = 13 Hz, $J_{1,2a}$ = 2 Hz, $J_{2a,3}$ = 3.3 Hz), 2.44 (1 H, ddd, $J_{1,2b}$ = 2 Hz, $J_{2b,3}$ = 9.7 Hz), 3.39 (3 H, s, CH_3O), 3.55 (1 H, ddd, $J_{3,5}$ = 2.1 Hz), 3.80 (1 H, q, J =6.5 Hz), 4.20 (1 H, dq, $J_{5,6}$ = 6.5 Hz, $J_{3,5}$ = 2.1 Hz), 4.98 (1 H, t, H-1); ^{13}C NM R ($CDCl_3$) δ 90.62 (d, C-1), 81.11 (d, C-3), 75.48 (d, C-5 or C-7), 69.41 (d, C-5 or C-7), 68.75 (s, C-4), 57.07 (q, CH_3O), 36.35 (t, C-2), 16.96, 14.59 (2 q, $2CH_3$); MS, m/z 188 (M^+), M_r 188. Anal. Calcd for $C_9H_{16}O_4$: C, 57.43; H, 8.57. Found: C, 57.67; H, 8.68.

Methyl Paulomycoside 4,7-Acetonide (14). A solution of 650 mg of **10** and 26 mg of p-$CH_3C_6H_4SO_3H$·H_2O in 13 mL of 2,2-dimethoxypropane was allowed to stand at room temperature for 18 h. The solution was diluted with 30 mL of $CHCl_3$ and washed with 10 mL of saturated $NaHCO_3$ and 10 mL of water. It was dried over $MgSO_4$, filtered, and evaporated to dryness in vacuo. The residue was chromatographed on 10 g of silica gel by eluting with Skellysolve B–CH_3COCH_3 (95:5) with a combination on a basis of weight analysis and TLC of those fractions containing **14**. Evaporation in vacuo gave 460 mg, which was rechromatographed in the same fashion, yielding 328 mg of a liquid: R_f 0.28 (SiO_2; 95:5 Skellysolve B–CH_3COCH_3); $[\alpha]^{25}_D$ −94° (c 0.8865, CH_3OH); IR (neat) 2375, 2330, 2280, 2215, 1145, 1075, 1065, 950, 915, 870, 810, 755, 720, 705, 685, 625, 585, 560, 450 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.06 (3 H, d, H-6), 1.12 (3 H, d, H-8), 1.19 (3 H, s, CH_3), 1.29 (3 H, s, CH_3), 1.63 (1 H, m, H-2a), 1.84 (1 H, m, H-2_b), 3.05, 3.08 (6 H, 2 s, 2 CH_3O), 3.77 (1 H, dd, H-3), 3.50 (1 H, q, H-5), 3.88 (1 H, q, H-7), 4.58 (1 H, t, H-1); ^{13}C NMR ($CDCl_3$) δ 108.60 (acetonide C), 98.56 (C-1), 83.93 (C-3), 74.77, 74.24, 66.51 (C-4, C-5, C-7), 54.92, 54.79 (2 CH_3O), 30.32 (CH_2), 27.02, 26.77 (2 CH_3C), 14.76, 14.37 (C-6, C-8); MS, m/z 260 (M^+), M_r 260. Anal. Calcd for $C_{13}H_{24}O_5$: C, 59.88; H, 9.29. Found: C, 59.77; H, 9.36.

Ammonia from 5. A solution of 330 mg (0.5 mmol) of **5** in 50 mL of 1 N NaOH was steam distilled into 20 mg of 0.155 N HCl. Titration of the distillate with 0.1 N NaOH indicated distillation of 0.30 mmol of volatile base. The titrated solution was made strongly basic and steam distilled into H_2O, to which was added 83 mg of p-hydroxyazobenzenesulfonic acid. The salt was isolated and found to be identical to an authentic sample of ammonium p-hydroxyazobenzenesulfonate by comparison of ^1H and ^{13}C NMR spectra.

Paulinone (15) (Scheme VII). A solution of 596 mg of **5** in 1 N methanolic HCl was allowed to stand at room temperature for 3 h. The mixture was neutralized by addition of 9.8 g of Ag_2CO_3 in small portions with vigorous stirring. The reaction mixture was filtered, washing the filtrate thoroughly with CH_3OH. The filtrate was evaporated to dryness in vacuo, and the residue was dissolved in 60 mL of 60% CH_3OH. This solution was extracted with four 30-mL portions of cyclohexane. The methanolic solution was evaporated in vacuo until the CH_3OH was removed and then refrigerated. The precipitate was removed by filtration and dried to yield 100 mg of red solid, which was chromatographed on 10 g of silica gel by eluting with $C_2H_5COCH_3$–CH_3COCH_3–H_2O (7:2:1), yielding 73 mg: R_f 0.24 (SiO_2; 70:20:1 $C_2H_5COCH_3$–CH_3COCH_3–H_2O); ^1H NMR DMF-d_7) δ 3.61, 3.73, 3.83, 4.16; ^{13}C

Scheme VII



NMR (DMF-d_7) δ 77.68, 72.54, 68.32, 62.52; MS, m/z 329.0805, calcd for $C_{13}H_{15}NO_9$ 329.0742. Anal. Calcd for $C_{13}H_{15}NO_9$: C, 47.42; H, 4.59; N, 4.25. Found: C, 47.29; H, 4.85; N, 4.44.

9,10,11,13-Tetra-*O*-acetylpaulinone (16). This was prepared by the same procedure used for **8** but 100 mg of **13** was used, yielding 141 mg. The material (230 mg) prepared in this way was chromatographed on 21.5 g of silica gel by eluting with $CHCl_3$–CH_3OH (9:1): UV (CH_3OH) 209 nm (ϵ 19 800), 259 (11 850), 446 (1900); IR (Nujol) 3270, 3130, 1765, 1715, 1710, 1635, 1585, 1250, 1110, 1065, 965, 930, 840, 750 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.89, 2.01, 2.09, 2.20 (4 CH_3), 4.07 (2 H, s, H-13), 4.79 (1 H, d, CHO), 4.90 (1 H, m, CHO), 5.12 (1 H, d, CHO), 5.18 (1 H, m, CHO), 5.67 (1 H, t, CHO), 6.96 (1 H, s, H-5), 7.34, 9.88 (2 H, 2 br s, NH_2), 13.19 (1 H, s, COOH); ^{13}C NMR ($CDCl_3$) 184.61 (C-4), 180.59 (C-7), 170.63, 169.94, 169.50, 169.25, 168.54 (5 C=O), 152.11 (C-3), 149.92 (C-6), 130.39 (C-5), 97.01 (C-3), 72.69, 71.11, 68.54, 66.06, 66.34 (C-8, C-9, C-10, C-11, C-12), 62.35 (C-13), 20.75 (2 CH_3), 20.50 (2 CH_3); MS, m/z 497, M_r 497. Anal. Calcd for $C_{21}H_{23}NO_{13}$: C, 50.70; H, 4.66; N, 2.82. Found: C, 49.43; H, 4.55; N, 2.58.

X-ray Study of Paulomenol A (5): $C_{29}H_{43}NO_{16}\cdot H_2O$, M_r 679.75, orthorhombic, $P2_12_12_1$, a = 8.268 (1) Å, b = 11.891 (2) Å, c = 33.581 (1) Å, V = 3301.5 (3) Å^3, Z = 4, D_m = 1.30 gm/cm^3, D_c 1.37 gm/cm^3, λ (Cu Kα) = 1.5418, μ(Cu Kα) = 0.9 cm^{-1}, T = 123 K, R = 0.062 for 2689 unique reflections.

A clear, thin plate of dimensions 0.05 × 0.16 × 0.36 mm was used for intensity measurements on a Syntex $P2_1$ diffractometer controlled by a Harris computer. Cu Kα radiation and a graphite monochromator were used for intensity measurement. The step–scan technique was used with a scan speed of 4 deg/min, a scan width of 3.4°, and a $2\theta_{max}$ = 138°. Ten reflections periodically monitored showed no loss of intensity during the data collection. Of the 2689 unique reflections measured, 2165 had intensities >3σ. Standard deviations in the intensities were approximated by the equation

$$\sigma^2(I) = \sigma^2(I)_{\text{counting statistics}} + (0.011I)^2$$

where the coefficient of I was calculated from the variations in intensities of the monitored reflections. Unit cell parameters were determined by least-squares fit of Kα_1 2θ values (λ (Cu Kα_1) = 1.5402) for 30 high 2θ values.[15] Lorentz and polarization corrections appropriate for a monochromator with 50% perfect character were applied. A partial trial solution, 26 atoms, was obtained by direct methods, using DIREC[16] and MULTAN80.[18] The remaining nine atoms were found by successive Fourier syntheses. Hydroxyl hydrogen positions found in difference maps were used; all other hydrogen atoms found in difference maps were very close to positions generated by using planar or tetrahedral geometry, so generated positions were used. The structure was refined by least squares with the coordinates and anisotropic thermal parameters for non-hydrogen atoms included in the refinement. Hydrogen parameters were included in the calculations but were not refined. Isotropic thermal parameters for hydrogen atoms were set 0.5 unit higher than the isotropic equivalent of the thermal parameters of the attached heavier atom. An enantiomer determination was attempted by calculating structure factors for both enantiomers and performing a computer search to find the reflections most significantly affected by anomalous dispersion, however, the list indicated that there was no discrimination between the two enantiomers. The function minimized in the refinement was $\sum w(F_o^2 - F_c^2)^2$, where weights w were $1/\sigma^2(F_o^2)$. Atomic form factors were from Doyle and Turner,[14] except for hydrogen which was from Stewart, Davidson, and Simpson.[19] In the final refinement cycle, all shifts were <0.80σ. The final R was 0.062, and the standard deviation of fit was 2.48. A final difference map showed no peaks were >0.5 e Å^{-3}. The CRYM system of computer programs was used.[17]

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Supplementary Material Available: Tables 2–6 consisting of interatomic distances and angles, torsion angles, intermolecular contacts, hydrogen bonds, and anisotropic temperature factors (6 pages). Ordering information is given on any current masthead page.

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