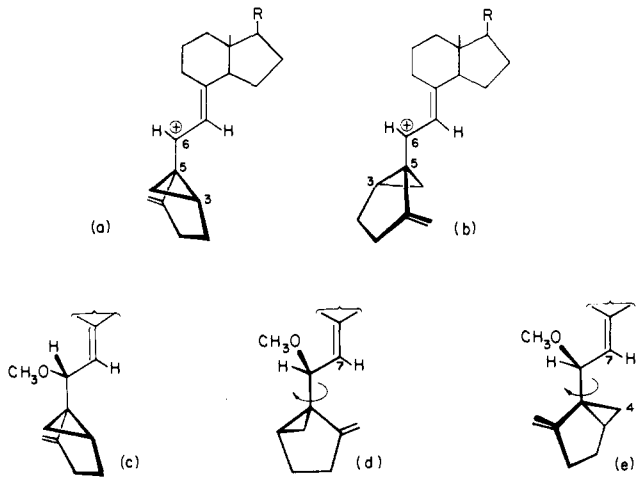

Figure 1. Perspective formulas of: (a) cyclopropylcarbinyl cation A, (b) cyclopropylcarbinyl cation B, (c) low energy conformation of (6*R*)-methyl ether **2a**, (d) low energy conformation of (6*S*)-methyl ether **2b**, (e) energetically strained conformation of (6*S*)-methyl ether **2b** with C_3-C_5 and C_6-OCH_3 bonds in antiparallel relation.

cyclopropylcarbinyl cation A (Figure 1a) from both these compounds is preferred.

We assume that the cyclopropylcarbinyl cation A has the bisected geometry in respect to the cyclopropane ring,[9] whose C_3-C_5 bond is in an anti relationship with the C_6-H bond.

The α-side attack of the methanol on the cation A (Figure 1a) is favored since it both involves C_3-C_5 bond participation and leads to the (6*R*)-methyl ether **2a** in its sterically more stable conformation (Figure 1c). In this conformation the methyl ether **2a** will also have suitable geometry for the creation of a low-energy transition state leading back to the carbonium ion A.[10]

On the other hand, the geometry of the stable conformation of the (6*S*)-methyl ether, **2b** (Figure 1d),[11] is not suitable for stereoselective formation of the cyclopropylcarbinyl cation B, whose C_3-C_5 and C_6-H bonds are in a syn relationship (Figure 1b). Conversely the transition state for a β-side attack of methanol on the cation B, which involves participation of the C_3-C_5 bond, will be less favored, since it leads to the (6*S*)-methyl ether, in its sterically strained conformation (Figure 1e).[12]

As expected, solvolysis of *trans*-cholecalciferyl tosylate, **3b**,[13] involving the intermediacy of the cation B, does not proceed stereoselectively.

Thus, heating of a solution of *trans*-cholecalciferyl tosylate, **3b** (2 mmol/cm^3), in 4:1 methanol:acetone (55°, 12 hr) yields three isomeric methyl ethers (in 60%) in a ratio of 6.5:4:1. The first two were found to be identical with (6*R*)- and (6*S*)-methyl ethers **2a** and **2b**, respectively, and the third one was the C_3-methyl ether of *trans*-cholecalciferol, **3c**, as shown by its uv and ^{1}H NMR spectra (λ_{max} 272 nm, ϵ 18.000; δ 4.96, 4.65 (=CH_2) and 6.51, 5.86 ppm, AB quartet J = 11.5 Hz (=C*H*—C*H*=)), which are typical of the (*EEZ*)-hexa-1,3,5-triene system of *trans*-cholecalciferol (**3a**).

It is to be noted that two different C_3-methyl ethers **1c** and **3c** were formed on solvolysis of cholecalciferyl and *trans*-cholecalciferyl tosylates, **1b** and **3b**, respectively, each retaining the original configuration of the tosyloxy group at C_3, confirming thus the noninterconvertibility of the cations A and B.

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(2) Mp 107–108° prepared from **1a** with TsCl and pyridine.
(3) Assigned structures are consistent with their analytical data and high resolution mass spectral data, the details of which will be published later.
(4) This ratio was established by integration of the ^{1}H NMR peaks of the OCH_3 protons in the total mixture of products.
(5) In addition to these compounds, cholecalciferyl acetate (5%) and a mixture of unsaturated hydrocarbons were isolated.
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(7) This ratio was established by high-pressure liquid chromatography using Corasil II column.
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(10) It is unlikely that *m/e* 540 is the molecular ion and that *m/e* 542 results from the addition of two hydrogens, since the absence of *m/e* 541 from the addition of one hydrogen would be most unusual.
(11) Where the cyclopropyl hydrogens are farthest from the hydrogen at C_7 and the methoxy group.
(12) In this conformation the cyclopropyl hydrogen at C_4 interacts severely with the hydrogen at C_7.
(13) On the relation between the stereochemistry of double bond formation and the conformation of cyclopropyl methyl system see M. Julia, C. Descoins, and C. Risse, *Tetrahedron Suppl.*, **8**, 443 (1966); S. F. Brady, M. A. Ilton, and W. S. Johnson, *J. Am. Chem. Soc.*, **90**, 2882 (1968); S. Sarel, J. Yovell, and M. Sarel-Imber, *Angew. Chem., Int. Ed. Engl.*, 7, 577 (1968).

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A Revised Structure for the Antibiotic Pillaromycin A

Sir:

Pillaromycin A,[1] an antibiotic obtained from cultures of *Streptomyces flavovirens*, is composed of a tetracyclic aglycone and a highly modified monosaccharide residue.[2] As with some other previously known members of the anthracycline group of antibiotics, daunomycin[3] and adriamycin,[4] pillaromycin A displays antitumor activity. However, it is less toxic[1b]—a circumstance which is of interest in developing structure-activity relationships for this group of antibiotics. In view of this aspect, we wish to report that the structure assigned to the sugar component[5] is incorrect. Thus the formulation of the antibiotic should be **1a**, not **1b** as originally proposed.[2] In this communication we report crystallographic and mass spectral evidence in support of this claim, and in the adjoining paper,[6] synthetic studies related to this problem are described.

The structure of pillaromycin A (**1**) was unambiguously deduced from a single-crystal X-ray diffraction experiment. The crystals of composition $C_{28}H_{30}O_{11}\cdot(C_2H_5)_2O$ belong to the common monoclinic space group $P2_1$ with a = 11.097 (2) Å, b = 7.794 (2) Å, c = 17.492 (3) Å, and β = 84.58 (1)°. A total of 1947 unique diffraction maxima with $\theta \leq$ 57° were recorded using a fully automated four-circle diffractometer and graphite monochromated Cu Kα radiation (1.5418 Å). After correction for background, Lorentz, and polarization effects all reflections were utilized in subsequent calculations.

A plausible trial structure was arrived at by a multiple solution, weighted tangent formula approach[7] coupled with the recycling of plausible molecular fragments. Full-matrix,

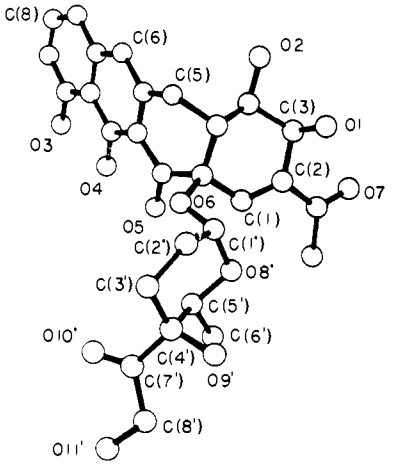
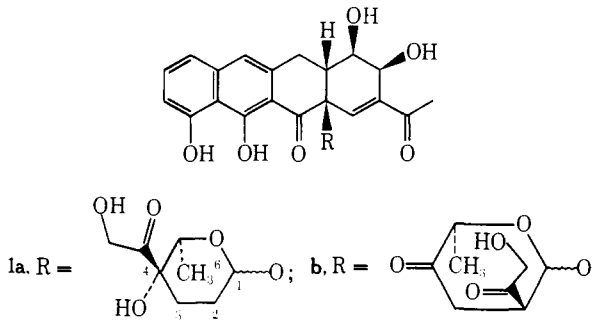


Figure 1. A computer generated perspective drawing of pillaromycin A (**1a**). No hydrogen atoms are shown.

Table I. Field Desorption Mass Spectrum of Pillaromycin A[a,b]

m/e	543	542	540	526	370	336	173
Per cent	29	100	2	2	2	2	1

[a] In ethyl acetate solution. [b] Source 68°; anode 10 kV, 20 mA.



least-squares refinement with anisotropic temperature factors for carbon and oxygen atoms and isotropic temperature factors for the hydrogens converged to a conventional discrepancy index of 0.038 for all of the reflections.[8] Figure 1 is a computer generated drawing of the final X-ray model. All bond distances and angles agree well with generally accepted values for given bond types.

The X-ray experiment, in the absence of anomalous scattering, defines only the relative configuration. The absolute stereochemistry rests upon the earlier crystallographic[9] work on the aglycone. As can be seen clearly in Figure 1 the previously published structure of the aglycone is correct but pillarose must now be reformulated as a 2,3,6-trideoxy-4-*C*-hydroxymethylcarbonyl-L-*threo*-aldohexose.

The molecular formulas for **1a** and **1b** ($C_{28}H_{30}O_{11}$ and $C_{28}H_{28}O_{11}$, respectively) differ by two units −542.2 vs. 540.2. The peaks from the field desorption mass spectrum of pillaromycin A shown in Table I, confirm the molecular weight at 542.[10] The *m/e* 543 peak for $^{13}C^{12}C_{27}H_{30}O_{11}$ is calculated to be 31% and *m/e* 370 represents the aglycone + H, while *m/e* 173 represents the sugar.

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Supplementary Material Available. The fractional coordinates (Table II), important bond distances (Table III), important bond angles (Table IV), and structure factors (Table V), will appear following these pages in the microfilm edition of this volume of the journal. Photocopies of the supplementary material from this paper only or microfiche (105 × 148 mm, 24× reduction, negatives) containing all of the supplementary material for the papers in this issue may be obtained from the Business Office, Books and Journals Division, American Chemical Society, 1155 16th St., N.W., Washington, D.C. 20036. Remit check or money order for $4.50 for photocopy or $2.50 for microfiche, referring to code number JACS-75-6250.

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Syntheses of "Supposed" and "Real" Pillarose

Sir:

In the accompanying paper,[1] crystallographic and mass spectral data are reported which indicate that the structure of pillarose, the sugar component of the antitumor agent pillaromycin A, is **1** and not **2** as originally proposed.[2] In this communication we complement the evidence by describing syntheses of the alkyl D-glycosides **3–6** which establish unequivocally that pillarose has the L-threo configuration of formulation **1**.[3] Of additional significance is the fact that the tricarbonyl structure **2** has no naturally occurring congeners, while **1** is obviously related to **7** which has recently been determined as the sugar component of the antibiotic, quinocyclin B.[5]

In the original investigation,[2] pillarose had been characterized as its benzoylated methyl glycoside whose salient physical constants and ^1H NMR parameters are shown in Table I. Our objective was therefore the synthesis of the epimeric benzoates related to formulation **2**, viz., **3** and **4**, one of which would possess the skeleton proposed for pillarose.[5]