Nitric oxide alone does not react with $NiCl_2L_2$ to produce this nickel nitrosyl halide.[13]

Acknowledgment. Acknowledgment is made to the donors of the Petroleum Research Fund, administered by the American Chemical Society, for support of this research.

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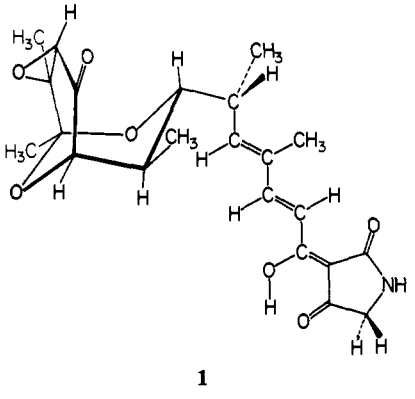
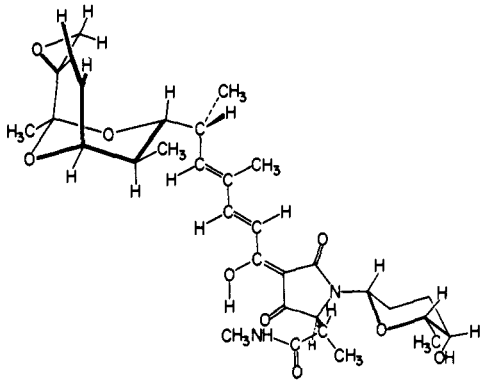
X-Ray Structure of Tirandamycic Acid *p*-Bromophenacyl Ester. Complete Stereochemical Assignments of Tirandamycin and Streptolydigin

Sir:

Gross structures have been assigned earlier to the two acyltetramic acid antibiotics tirandamycin[1] and streptolydigin,[2] which have stimulated considerable recent interest on account of their modes of action, especially their inhibition of RNA polymerase.[3] We report here the complete X-ray determination of the structure of the *p*-bromophenacyl ester of tirandamycic acid,[1] which completes the absolute stereochemical assignment of tirandamycin as **1**. We also report here the conversion of tirandamycic acid and streptolic acid[4] to a common derivative retaining the stereochemistry of both acids, as well as additional stereochemical data on the ydiginic acid[5] portion of streptolydigin; together, these results allow the complete stereochemical assignment of streptolydigin as **2**.



1



2

The *p*-bromophenacyl ester of tirandamycic acid (**3**) was prepared by reaction of the sodium salt of the acid with *p*-bromophenacyl bromide, purified over silica gel, and crystallized from ethanol: $C_{26}H_{29}BrO_7$;[6,7] mp 173–183°; $[\alpha]^{25}D$ +50° (*c* 1.09, $CHCl_3$). The crystals are monoclinic, space group $P2_1$ with a = 17.603, b = 8.400, and c = 8.673 Å, and β = 90.73°. Three-dimensional X-ray diffraction intensity data were gathered on a computer-controlled diffractometer using nickel-filtered Cu radiation. The data (2603 reflections) were corrected for systematic errors including absorption.[8] A trial Br position was obtained by computerized direct methods. A three-dimensional electron density map, phased using this Br, contained images of two superimposed molecules, as expected. The superimposed images were sorted out by analysis of distances and angles, and without reference to the previously assigned stereochemistry or structure of tirandamycic acid. In this manner a partial trial structure (17 atoms and Br) was obtained from the initial map. Full separation of the images required two more electron density calculations. Atomic positions and first isotropic, then anisotropic, thermal parameters refined by least squares to an agreement factor R ($=\Sigma||F_o| - |F_c||/\Sigma F_o$) of 0.102 without including anomalous dispersion. At this point, the correct enantiomer was determined by Bijvoet's method.[9] Structure factors were calculated for both enantiomers, and 15 reflections most affected by anomalous dispersion were selected for accurate measurement of $I(h,k,l)$, $I(-h,k,-l)$, $I(-h,-k,-l)$, and $I(h,-k,l)$. All 15 clearly indicated the enantiomer shown in Figure 1. Additional least-squares refinement, with anomalous dispersion effects included, reduced R to 0.083. Details of the crystallographic investigation will be published.[10]

The X-ray results agree perfectly with previous structural assignments on tirandamycic acid.[1] The assignment of the stereochemistry of the bromo ester as that shown in Figure 1 (6*R*,7*R*,8*R*,9*S*,11*R*,12*S*,13*S*) completes the absolute stereochemical assignment of tirandamycin as **1**.

The α-keto epoxide group of tirandamycic acid (**3**) was reduced by the procedure of Wharton and Bohlen[11]

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(6) Elemental analyses agree with the formula given.
(7) Low-resolution mass spectra, obtained on a Varian MAT CH5 mass spectrometer by the direct inlet technique, were in agreement with the formula cited.
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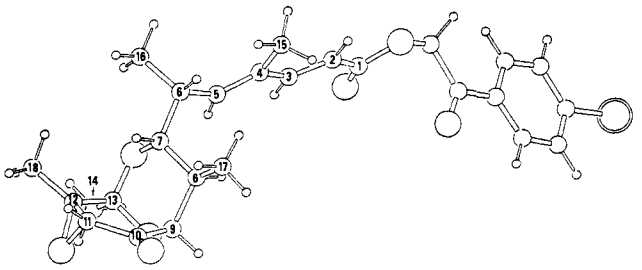
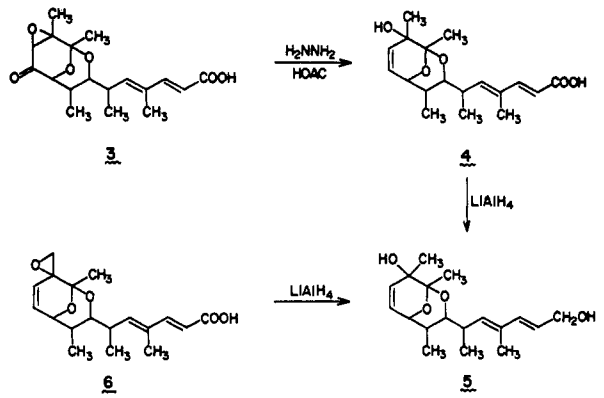
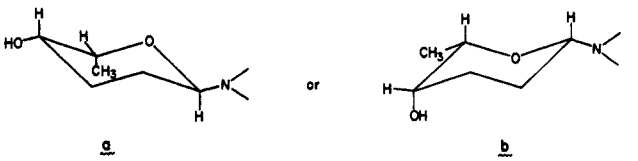


Figure 1. Computer-drawn X-ray structure showing the absolute configuration of the *p*-bromophenacyl ester of tirandamycic acid.

(hydrazine hydrate and ethanolic acetic acid) to an allyl alcohol (**4**), which was not isolated but reduced further by lithium aluminum hydride to streptolol (**5**),[4] isolated as its monoacetate: $C_{20}H_{30}O_5$;[12] $[\alpha]^{29}D$ +112° (*c* 0.998, $CHCl_3$). The same monoacetate, $[\alpha]^{29}D$ +108° (*c* 1.12, $CHCl_3$), was obtained by acetylation of an authentic sample of streptolol, the lithium aluminum hydride reduction product of streptolic acid (**6**).[4] The two samples of streptolol acetate were identical in their nmr, ir, and mass spectral as well as tlc behavior in three solvent systems. Thus, the absolute stereochemistry of streptolic acid is the same as that of tirandamycic acid.



The stereochemistry of the β-methylaspartic acid portion of streptolydigin was earlier assigned as L-threo.[5] Similarly, the stereochemistry of the 2,3,6-trideoxyhexose was assigned as L-threo by independent methods in two laboratories.[13,14] It only remains to assign the anomeric configuration of the sugar. With L-threo stereochemistry the substituents at C-4 and C-5 of the trideoxyhexose portion of the antibiotic cannot both be equatorial and the sugar will adopt whatever conformation makes the bulky anomeric substituent at C-1 equatorial. This is conformation **a** if the anomeric configuration is α-L or conformation **b** if it is β-L. In conformation **a** the C-4 hydroxyl would be equatorial; in conformation **b** the C-4 hydroxyl would be axial. In fact, the half-band width of the C-4 proton of ydiginic acid[5] is 7 Hz, appropriate only for an



equatorial[15] proton, while the acetoxyl methyl singlet appears at δ 2.15, appropriate only for an axial acetoxyl.[16] Thus, conformation **b** is indicated, in which the C-1 configuration is *S* (β-L).

With this point settled the total absolute configuration of streptolydigin can be assigned as **2**.

Acknowledgment. This work was supported in part by Public Health Service Grant No. AI 01278 from the National Institute of Allergy and Infectious Diseases.

(12) High-resolution mass spectral data, obtained on a Varian MAT SM-1B mass spectrometer, were in agreement with the formula cited. The high-resolution mass spectrometer and data processing equipment employed in the present study were provided by National Institutes of Health Grants CA 11388 and GM 16864, from the National Cancer Institute and the National Institute of General Medical Sciences, respectively.

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Structure of $C_2H_5^+$ at Low Vibrational Energies

Sir:

The structure of simple carbocations has been a matter of extensive discussion in the recent literature.[1-5] In this communication we demonstrate that randomization of hydrogen atoms in ethyl ion is rapid relative to intermolecular hydride transfer and estimate an upper limit of the activation energy for hydrogen atom scrambling.

Theoretical investigations of the ethyl cation have fluctuated between support of a classical ethyl ion structure favored by *ab initio* molecular orbital calculations and a nonclassical protonated ethylene structure favored by semiempirical calculations. In both cases the predicted structures are artificially favored. Hariharan, Lathan, and Pople have recently examined the structure of $C_2H_5^+$ by *ab initio* molecular orbital theory.[5] Their calculations used an extended basis set including polarization functions (d functions on carbon and p functions on hydrogen). These near Hartree–Fock results indicate the nonclassical form of ethyl ion to be more stable than the classical form by 0.9 kcal/mol. The inclusion of correlation energy, which was not explicitly considered by Hariharan, *et al.*, may favor the nonclassical structure even more.

From the available experimental evidence it now seems established that ethyl ion produced by radiolysis,

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