of 4-bromo-1-methoxypentane (**1b**) 10.0 g of the ether yielded 13.14 g (89.6%) of distilled 5-bromo-2-pentyl trifluoroacetate. That the product was free of the isomeric (nonhalogen shifted) 4-bromo-1-pentyl trifluoroacetate was demonstrated by capillary column gas chromatography on DC-550, which gave excellent separation, showing 99.97 ± 0.03% isomeric purity. 2-Bromo-1-methoxypropane (**1c**) and 4-chloro-1-methoxypentane (**1a**) yielded 1-bromo-2-propyl trifluoroacetate (98.5 ± 1.5% isomeric purity) and 5-chloro-2-pentyl trifluoroacetate, respectively. 2-Chloro-1-methoxypropane (**1**, $n = 0$; X = Cl) has not yet been subjected to the reaction, but the corresponding three-membered chloronium ion has been generated by trifluoroacetolysis of 2-chloropropyl *p*-nitrobenzenesulfonate, which yielded 1-chloro-2-propyl trifluoroacetate, 99 ± 1% free of the product of "normal" solvolysis.

The reaction of 2-iodo-1-methoxypropane (**1d**), followed by nmr, proceeded with iodine shift, exhibiting formation of a methyl doublet at δ 1.50 at the expense of the original doublet at δ 1.88. The expected sextet at δ 4.9–5.5 appeared simultaneously.

3-Chloro-1-methoxybutane (**1**, $n = 1$; X = Cl) and 3-bromo-1-methoxybutane (**1**, $n = 1$; X = Br) did not undergo 1,3-halogen shifts with trimethyloxonium fluoroborate in trifluoroacetic acid. Following commonly expressed ideas pertaining to ring formation, we postulate that favorable entropy effects cannot compensate for strain in the formation of four-membered-ring halonium ions, in contrast with the balance of effects which results in relatively rapid three-membered-ring formation.

Dimethyl ether is at least moderately better than *p*-nitrobenzenesulfonate as a leaving group. Trimethyl- and triethyloxonium fluoroborates solvolyzed about 25 and 3 times as fast, respectively, as did ethyl *p*-nitrobenzenesulfonate.[5] Departure of dimethyl ether was not rate determining, yet the over-all reaction of 4-chloro-1-methoxypentane (**1a**) (0.8 *M* trimethyloxonium fluoroborate, 0.43 *M* **1a**) to form 5-chloro-2-pentyl trifluoroacetate occurred three times faster than trifluoroacetolysis of 4-chloro-1-pentyl *p*-nitrobenzenesulfonate[1] to give the same product.

(5) Ethyl *p*-nitrobenzenesulfonate was studied in our group by Mr. Joseph Coffey. Ethyl tosylate has been trifluoroacetolyzed by J. E. Nordlander and W. G. Deadman, *J. Am. Chem. Soc.*, **90**, 1590 (1968).

(6) NDEA predoctoral fellow, 1966 to present.

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Molecular Structure of Bisdethiodi(methylthio)acetylaranotin Including Absolute Configuration

Sir:

In the attempt to determine those metabolites responsible for the antiviral activity of the fungus *Arachniotus aureus* (Eidam) Schroeter, several new molecular species were isolated. These include the three similar substances aranotin, acetylaranotin, and bisdethiodi(methylthio)acetylaranotin (BDA). Structures have recently been proposed for these molecules without any steric assignments.[1] This communication will report the complete structure of BDA including the absolute configuration. The structures of aranotin and acetylaranotin follow from the relationships among these molecules.[1]

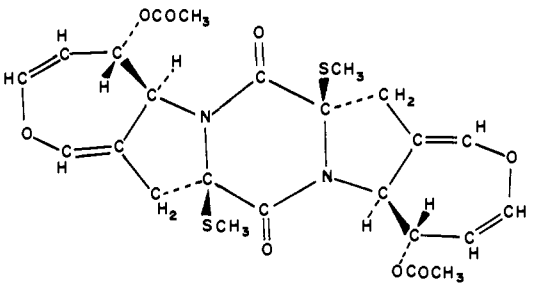

Figure 1. Conventional chemical representation of the stereochemistry of BDA.

Crystals of BDA ($C_{24}H_{26}O_8N_2S_2$) are monoclinic in space group $P2_1$. There are two molecules in the unit cell which has parameters $a = 14.53$ Å, $b = 12.41$ Å, $c = 6.85$ Å, and $\beta = 94.3°$. The data were collected about the *a* and *c* axes employing Cu Kα radiation with the use of a manually operated Buerger diffractometer. Bijvoet anomalous scattering pairs were collected for approximately one-half of the *a* axis. The data from the two axes were correlated after the usual corrections had been made for Lorentz and polarization factors. The structure was solved with the aid of a three-dimensional Fourier map whose terms were weighted by the method of Sim[2] and whose phases were taken to be determined solely by the positions of the two sulfur atoms in the asymmetric unit, the locations of which having been determined by the interpretation of a sharpened three-dimensional Patterson function. A three-dimensional minimum function superposition based on the sulfur positions and using a sharpened Patterson map was also calculated. Those peaks which the Sim-weighted Fourier and the superposition function shared in common and whose distances and angles relative to neighboring peaks were chemically reasonable where used as the starting point of successive Fourier analysis which eventually let to the solution of the structure. The absolute configuration was determined by comparing the calculated and observed signs of $I_{hKl} = I_{hKl} - I_{h\bar{K}\bar{l}}$[3] for all reflections on the first three levels of *a* for which $\Delta I/|F_o|^2 > 0.20$. The value of $R = \Sigma||F_o| - |F_c||/\Sigma|F_o|$ is 0.108 for 1434 observed reflections.

The molecular structure, stereochemistry, and absolute configuration are given in Figures 1 and 2. It will be noted that the previously proposed structure by Nagarajan, *et al.*,[1] is indeed correct. It should also be noted that the absolute configuration of BDA and thus of aranotin and acetylaranotin is identical with that of gliotoxin and sporidesmin[4] and that the steric conformations of those groups which both aranotin and gliotoxin share are identical.

Although BDA possesses a molecular twofold axis of symmetry, this symmetry element is not used by the

(1) R. Nagarajan, L. L. Huckstep, D. H. Lively, D. C. DeLong, M. M. Marsh, and N. Neuss, *J. Amer. Chem. Soc.*, **90**, 2980 (1968).

(2) G. A. Sim, *Acta Cryst.*, **12**, 813 (1959).

(3) J. M. Bijvoet, A. F. Peerdeman, and A. J. van Bommel, *Nature*, **168**, 271 (1951).

(4) J. Fridrichsons and A. M. Mathieson, *Acta Cryst.*, **23**, 439 (1967).

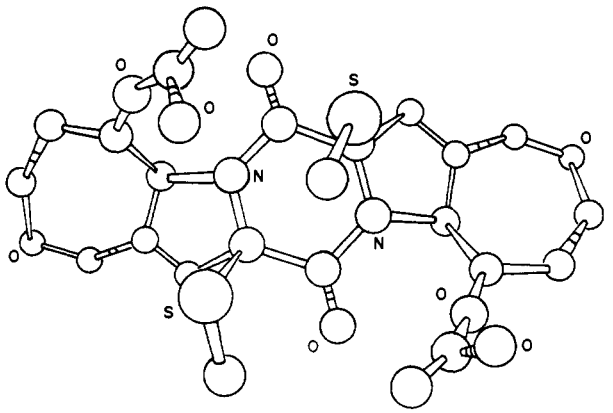

Figure 2. The BDA molecule as it appears in the crystal.

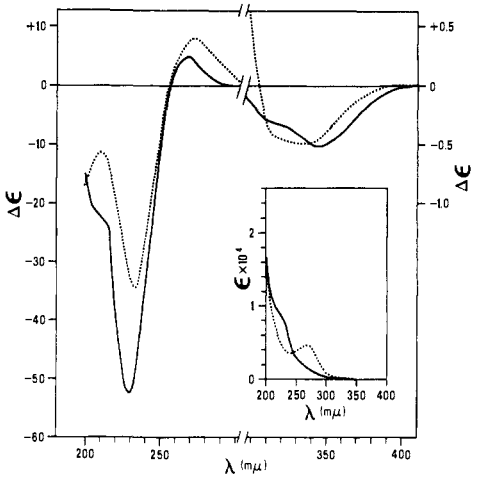

Figure 1. Circular dichroism and ultraviolet spectra of acetylaranotin (——) and gliotoxin (· · · · ·) determined in methanol solution.

crystal. While every other pair of atoms which could be so related is indeed closely related in the crystal by the twofold molecular axis, the methyl groups bonded to the sulfur atoms are not. This is indicated in Figure 2.

A study of the possibility of the more extensive use of the small effects of anomalous scattering by sulfur atoms to facilitate structure determination is continuing.

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Aranotin and Related Metabolites. III. Configuration and Conformation of Acetylaranotin[1]

Sir:

The metabolites from *Arachniotus aureus* are of interest due to their antiviral activity.[2] We present evidence to show that the configuration at the asymmetric centers in our key metabolite acetylaranotin, **1**, and gliotoxin[3] are identical. This evidence of configurational identity in acetylaranotin, gliotoxin,[3] and apoaranotin,[4] we hope, will stimulate work on the biogenetic correlation[4,6] between the cyclohexadiene and dihydrooxepin moieties in these metabolites.

The CD curve of acetylaranotin, **1**, consists of a high amplitude negative maximum at 229, a positive maximum at 268, and a low amplitude negative maximum at 345 with a negative inflection at ~310 mμ. This is qualitatively in good agreement with the CD curve of gliotoxin[7] (Figure 1) and shows that the absolute stereochemistry of the asymmetric carbon atom on the diketopiperazine moiety in gliotoxin[3] and acetylaranotin are identical.[8] Acetylaranotin lacks the diene chromophore of gliotoxin, and consequently the three Cotton effects at 268, 310, and 345 mμ should have their origins in the disulfide chromophore.[7,9]

Desulfurization of acetylaranotin with Raney nickel followed by reduction and deacetylation gave the diol[1] **2**. The CD spectrum of the diol **2** has a negative maximum at 222, a positive maximum at 210, and a negative maximum below 200 mμ. In the wavelength region under discussion, the diol **2** contains only the diketopiperazine chromophore, and therefore, all the three Cotton effects should have their origins in the diketopiperazine moiety. Since L-prolyl-L-proline and D-prolyl-D-proline diketopiperazines[10] are good model compounds for comparison with the diol **2** their CD spectra were determined[11] (Figure 2). A comparison of these CD spectra firmly established the L configuration at the asymmetric carbon in the diketopiperazine moiety in diol **2**. Obviously, Raney nickel desulfurization occurred with retention of configuration.[12] In

(1) R. Nagarajan, L. L. Huckstep, D. H. Lively, D. C. DeLong, M. M. Marsh, and N. Neuss, *J. Amer. Chem. Soc.*, 90, 2980 (1968).

(2) Biological properties will be described by D. C. DeLong, *et al.*

(3) J. Fridrichsons and A. M. Mathieson, *Acta Cryst.*, 23, 439 (1967).

(4) N. Neuss, R. Nagarajan, B. B. Molloy, and L. L. Huckstep, *Tetrahedron Lett.*, 4467 (1968). The configuration at the asymmetric centers of apoaranotin is identical[5] with gliotoxin.[3]

(5) R. Nagarajan, N. Neuss, and S. M. Nash, unpublished work.

(6) J. E. Baldwin, H. H. Basson, and H. Krauss, Jr., *Chem. Commun.*, 984 (1968).

(7) H. Herrmann, R. Hodges, and A. Taylor, *J. Chem. Soc.*, 4315 (1964).

(8) Professor J. W. Moncrief of the Department of Chemistry, Emory University, Atlanta, Ga., has established by X-ray analysis that the configuration at the three asymmetric centers in bisdethiodi(methylthio)-acetylaranotin[1] and gliotoxin are identical. Independently, Dr. J. H. van den Hende of American Cyanamid Company, Pearl River, N. Y., has found by X-ray analysis that acetylaranotin and gliotoxin have the same configuration at the three asymmetric centers. We wish to thank Professor J. W. Moncrief and Dr. J. H. van den Hende for permission to quote their results.

(9) (a) H. Ziffer, U. Weiss, and E. Charney, *Tetrahedron*, 23, 3881 (1967); (b) M. Carmack and L. A. Neubert, *J. Amer. Chem. Soc.*, 89, 7134 (1967); (c) A. F. Beecham, J. W. Loder, and G. B. Russell, *Tetrahedron Lett.*, 1785 (1968); (d) J. A. Barltrop, P. M. Hayes, and M. Calvin, *J. Amer. Chem. Soc.*, 76, 4348 (1954); (e) D. L. Coleman and E. R. Blout in "Conformation of Biopolymers," Vol. 1, G. N. Ramachandran, Ed., Academic Press, New York, N. Y., 1967, p 123.

(10) Obtained from Cyclo Chemical Corporation, Los Angeles, Calif.

(11) The uv spectra are not recorded in Figure 2 because the diketopiperazines gave end absorption: diol **2**, 200 (ε 11,140); prolylproline diketopiperazines, 200 mμ (ε 14,000).

(12) The X-ray result of Professor J. W. Moncrief on BDA,[1] and of Dr. J. H. van den Hende on acetylaranotin, **1**, in conjunction with our CD data proves conclusively that Raney nickel desulfurization of acetylaranotin and BDA occurred with retention of configuration. Our re-