The bromide ions are located in such a manner that a very strong interaction exists with the basic nitrogen of the piperidyl ring. The quaternizing N-proton is directed from the nitrogen in the general direction of a single bromide anion, with the short N···Br approach distance of 3.17[10] A. The N–H···Br ionic bond angle is 107° with N–H and H···Br distances of 1.08 and 2.13 A, respectively. The errors in the bond distances are estimated at ±0.02 A, and those in the valency angles as ±3°.

All other short intermolecular distances seem to give rise to only the expected van der Waals contacts (see Table VII). Apart from the above described van der Waals bonding and the ionic N–H···Br interactions no strong intermolecular forces seem to hold the lattice together. This may explain the relatively high thermal motion which is ascribed to the terminal atoms of the functional groups.

Absolute Configuration Determination

The absolute configuration was established using the anomalous dispersion of the bromide ions, which causes the reflections (h, k, l) and $(\bar{h}, \bar{k}, \bar{l})$ to be different in both phase and scattering amplitude, in violation of Friedel's law. Two methods were used: first, the more obvious one in which the structure was refined first with the observed crystal planes assigned as (hkl) and then as $(-h, -k, -l)$. Even though no dramatic difference in over-all R was observed (0.078 and 0.084, respectively) a simple review of the data showed that for *most* of the reflections no large changes were calculated, but that *some* showed dramatic differences between $F_c(hkl)$ and $F_c(-h, -k, -l)$. For all reflections where this difference was more than 10% in $|F_o|$ it was obvious that the hand originally chosen was the correct one; for *these* planes $R(+++)$ and $R(---)$ were 0.107 and 0.152, respectively. In order to confirm this result the intensities of the $(-h, -k, -l)$ reflections were measured.[14] The data are shown in Table VIII, and they confirm the other work.

In all figures the absolute configuration has been depicted.

Table VIII. Anomalous Scattering Data for 19-Propylthevinol

h	k	l	$F_o(+++)/$ $F_o(---)$	$F_c(+++)/$ $F_c(---)$
8	1	1	1.061	1.112
8	2	4	1.053	1.101
7	2	1	1.115	1.110
2	1	3	1.100	1.101
7	5	5	0.948	0.877
9	7	2	1.055	1.103
1	2	2	1.080	1.102
1	2	5	1.096	1.108
5	12	2	1.027	1.110
5	12	3	0.887	0.880
6	15	1	0.903	0.896
4	10	4	0.909	0.885
4	10	5	0.858	0.853
4	15	2	0.889	0.859
2	11	3	1.121	1.108
2	12	5	1.084	1.105
1	12	4	1.047	1.115

(13) W. Fulmor, J. E. Lancaster, G. O. Morton, J. J. Brown, C. F. Howell, C. T. Nora, and R. A. Hardy, Jr., *J. Am. Chem. Soc.*, in press.

(14) J. M. Bijvoet, *Proc. Koninkl. Ned. Akad. Wetenschap.*, **B52**, 313 (1949); A. F. Peerdeman, A. J. van Bommel, and J. M. Bijvoet, *ibid.*, **54**, 3 (1951).

The Crystal and Molecular Structure of N-Brosylmitomycin A

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Contribution from the Sterling Chemistry Laboratory, Yale University, New Haven, Connecticut, and Lederle Laboratories, a Division of American Cyanamid Company, Pearl River, New York. *Received January 19, 1967*

Abstract: The structure of N-brosylmitomycin A, a crystalline derivative of an anticancer antibiotic extracted from soil isolates of *Streptomyces verticillatus* strains, has been determined using X-ray crystallographic techniques. The crystals are monoclinic with $a = 19.70$, $b = 8.24$, $c = 16.05$ A, $\beta = 95.80°$, space group C2, and there are four molecules per unit cell. The structure was solved using the heavy atom method and refined using Fourier and least-squares techniques. The mitomycin molecule contains four fused ring systems, one of which is an aziridine. Evidence was found indicating an interaction between the lone electron pairs of the two ring nitrogen atoms. The molecules are held in the crystal by continuous chains of N–H···O hydrogen bonds and a strong affinity between bromine atoms and the components of quinoid rings of adjacent molecules. The crystals are solvated with 0.5 mole of benzene/mole of antibiotic located in voids of the structure. The absolute configuration of the molecule has been determined from the comparision of observed and calculated structure factors utilizing the anomalous scattering contribution of bromine and sulfur for Cu Kα radiation with respect to alternative atomic positions.

Three soil isolates of *Streptomyces verticillatus*, Lederle strains AA-849, AB-286, and AB-929, were found to produce mixtures of ethyl acetate extractable antibiotics which were active in bacterial mouse protection tests.[2] When purified preparations made

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(2) D. V. Lefemine, M. Dann, F. Barbatschi, W. K. Hausmann, V. Zbinovsky, P. Monnikendam, J. Adam, and N. Bohonos, *J. Am. Chem. Soc.*, **84**, 3184 (1962).

from these cultures were compared by paper chromatography they appeared to contain the same groups of antibiotics, five of which were isolated in crystalline form. The characterization of several of these compounds showed that they were identical with mitomycin A, B, and C and porfiromycin, and were of a new and unusual structural type, representing the first naturally occurring examples of an aziridine elaborated by a microorganism.[3a] A considerable amount of chemical degradation and related studies had correctly identified all atoms and their interconnections, but several details which were of interest, such as the relative stereochemistry of the asymmetric carbons, could not be established *via* classical means.

The present paper deals with the structure elucidation using single-crystal, X-ray diffraction methods of the N-brosyl derivative of one of the components of the antibiotic mixture, mitomycin A, of which a preliminary report has appeared elsewhere.[4]

Experimental Section

Crystals of N-brosylmitomycin A suitable for X-ray examination were obtained by the slow evaporation of a solution of methylene chloride and benzene (1:4).[5] The crystals were deeply colored red laths and occasionally they displayed end-face development. The crystal chosen for X-ray examination also proved to be of sufficient quality for intensity data collection and its dimensions were approximately 0.8 × 0.3 × 0.05 mm.

The X-ray work was carried out with Cu Kα radiation and a General Electric XRD-5 equipped with a single-crystal orienter and a scintillation counter assembly. A preliminary survey of the diffraction pattern indicated that the crystal system was monoclinic with $a = 19.70$, $b = 8.24$, $c = 16.05$ A, $\beta = 95.80°$. The only reflections that were systematically absent were of the type $h + k = (2n + 1)$. Therefore, the space group was either C2, Cm, or C2/m. The latter was eliminated because it is centrosymmetrical and Cm was rejected because it contains a mirror plane (mitomycin A is an optically pure isomer). The space group C2 was verified upon examining the Patterson function of the crystal. The bromine–bromine and the sulfur–sulfur vectors and their cross vectors could be interpreted only in terms of the equivalent positions of space group C2.

A chemical analysis of the crystals (dried at 78° under vacuum) indicated an empirical formula corresponding to $C_{25}H_{25}N_3O_8SBr$. This carbon content is high by three with respect to the formula of the antibiotic derivative and suggested 0.5 mole of benzene solvate/mole of N-brosylmitomycin A.[6] The solvation was corroborated by flotation density measurements in aqueous potassium iodide solution ($d_{\text{obsd}} = 1.55$ g cm^{-3}; $d_{\text{calcd}} = 1.554$ g cm^{-3}, based on four N-brosylmitomycin A and two benzene molecules per unit cell).

Before initiating three-dimensional, intensity-data collection, the quality of the crystal was assessed by measuring the mosaic spreads of several reflections at different ϕ and χ values. The spreads were found to be single peaked and symmetrical, and varied from 0.4 to 0.7° in width as a function of ω (background to background). The quadrant of reciprocal space that included the narrowest and most symmetrical spreads was selected for intensity measurements. The intensities were obtained using the stationary crystal–stationary counter technique with balanced Ni–Co filters. Of the 1481 reflections accessible to $d_{\min} = 1.0$ A ($2\theta_{\max} = 100°$), 1352 (91.3%) were taken to be observable.

Throughout the data collection, the intensities of three convenient reflections were monitored as a function of X-ray exposure to the crystal. During the first 6 hr of exposure, the monitored reflections remained essentially constant but during the last 6 hr of data collection, they showed a continuous and slow decrease in intensity (maximum decrease of 6% after 12 hr of exposure). Consequently, the latter half of the intensity data was corrected for this fall off. The intensities were also corrected approximately for absorbtion (as a function of azimuthal angle ϕ).[7] The absorption correction was found to be 2θ dependent, and it was approximated with a weighted mean correction that was more appropriate for the higher order reflections. The maximum: minimum ratio of the correction was 2.4. Finally, Lorentz and polarization factors were applied to the modified intensities converting them into relative structure amplitudes.

The Structure Determination

The structure was solved using the phase-determining, heavy-atom method.[8] A three-dimensional Patterson function was computed sharpened with $(z_{\text{Br}}/f_{\text{Br}})^2$, where z_{Br} and f_{Br} are, respectively, the atomic number of bromine and the scattering form factor of bromine at rest. The effect of such a sharpening procedure is to enhance the bromine–bromine vectors to point bromine atom interactions with thermal motion. The sulfur atom interactions are also enhanced by this procedure, but not as much, while the light atom interactions are sharpened least of all. The bromine–bromine and sulfur–sulfur interactions were readily recognized in the Harker section at $v = 0$. From the (x, z) coordinates thus obtained, the bromine–sulfur interactions in general positions were identified. The latter also gave the relative y coordinates of bromine and sulfur.

Before proceeding with a structure factor computation, the positions of the two carbon atoms of the brosyl group that are bonded to the bromine and the sulfur atoms were inferred. The procedure was relatively straightforward and involved only the assumptions: (1) that all four atoms lie on a straight line and (2) the bond distances of C–Br and C–S. The crucial point of the procedure proved to be the correct identification of the Br–S vector belonging to a single molecule. There were two vectors of approximately the correct length; however, one could be eliminated because of its close proximity to a twofold rotation axis, thus giving rise to packing problems.

Structure factors were now computed based on the positions of the bromine, the sulfur, and the two inferred phenyl carbon atoms and an isotropic thermal parameter of $B = 3.0$ A^2. The calculated phases were then assigned to the observed structure amplitudes and a three-dimensional electron density (ρ_1) was computed. This electron density contained 45 peaks greater than 1.7 eA^{-3} (carbons included in the structure-factor computation are also included in this count). Of these peaks, 30 were shown to belong to the molecule, seven were eliminated because of close approaches to the brosyl system or the bromine atom, and two others were disregarded because they were situated too close to a twofold rotation axis.[9] The remaining six peaks were all positionally isolated from the main body of peaks and eventually were shown to be spurious. At this

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[3] J. S. Webb, D. B. Cosulich, J. H. Mowat, J. B. Patrick, R. W. Broschard, W. E. Meyer, R. P. Williams, C. F. Wolf, W. Fulmor, C. Pidacks, and J. E. Lancaster, *J. Am. Chem. Soc.*, **84**, 3185 (1962); (b) *ibid.*, **84**, 3186 (1962).

[4] A. Tulinsky, *ibid.*, **84**, 3188 (1962).

[5] We thank Dr. J. H. Mowat of Lederle Laboratories for preparing the N-brosyl derivative and for growing the crystals.

[6] This observation was also supported with gas chromatographic measurements. We should like to thank Mr. A. Mistretta of Lederle Laboratories for carrying out these measurements.

[7] S. Silvers and A. Tulinsky, *Acta Cryst.*, **16**, 579 (1963).

[8] J. M. Robertson and I. Woodward, *J. Chem. Soc.*, 219 (1937); 36 (1940).

[9] Symmetry-related peaks in the present instance belong to independent molecules unless the molecule itself has twofold rotation symmetry and additionally utilizes the crystallographic twofold rotor. Since the latter was not applicable to the antibiotic, the two peaks near the twofold rotation axis would give rise to unacceptably short van der Waals contacts. At a later stage of the work, these peaks were, in fact, shown to belong to the structure, and the way in which they are will be indicated below.

stage, the brosyl system was easily identified and it was linked to a three-membered ring (known to be aziridine) which in turn was fused to two fused five-membered rings (see Figure 1). From ring B, the density was somewhat ambiguous; either ring B was fused to a six-membered ring bearing short side chains (shown partially broken in Figure 1) or a long side chain emanated from B. Also, there was a two-atom chain at the bridgehead position between rings A and B (X) and a seemingly longer chain at Y.

At this point, consultation with the Lederle group engaged in the chemical structure determination of the mitomycins revealed a general agreement between their chemical structure and the one described above. Using the additional chemical information and the location of three smaller peaks (1.3–1.6 eA^{-3}, marked by asterisks in Figure 1) the remainder of the structure shown in Figure 1 (as broken lines) was recognized. Two of the smaller peaks proved to be part of a quinone system (C) bearing methyl and methoxyl groups. The other small peak formed part of a carbamoyloxymethyl side chain (CH_2OCONH_2) (side chain Y, partially broken). Finally, the fused five-membered rings were chemically known to be a pyrrolizine system (contained a bridgehead nitrogen).

Two structure factor and electron-density computations were now carried out: (1) the first (ρ_2) based on the complete structure including atoms of correct chemical identity, and (2) the second (ρ_3) included bromine, sulfur, and 25 carbon atoms (the crystallographically unambiguous structure; solid line structure of Figure 1). Both computations included an over-all isotropic parameter of $B = 3.0$ A^2. The latter computation was performed as a precautionary measure and also to confirm the results of including the complete structure. The R factors for these structure factor computations were 0.22 and 0.28, respectively.

A comparison of the two resulting electron densities verified 32 of the atoms included in the computation of ρ_2. All included atoms (except two in ρ_2) in both densities increased 2.5 times or more. The two atoms which remained stationary in ρ_2 (the methyl of the bridgehead methoxyl and the carbamate nitrogen) had other reasonable peaks ($\sim$1.6 eA^{-3}) within bonding distance of these groups. In the end, it was shown that an incorrect choice was originally made in both instances.

The atoms not included in structure factor computations remained essentially unchanged or increased in peak height in ρ_3. Nitrogen and oxygen atoms, included as carbon, appeared 1–3 eA^{-3} greater than included carbon atoms in this density and confirmed the chemical identities employed to obtain ρ_2. Finally, all spurious peaks of ρ_1 decreased or became vanishingly small in both ρ_2 and ρ_3.

The two peaks ignored in ρ_1 because they were too near a twofold rotation axis ($\simeq$1.2 A) persisted and increased in height in both ρ_2 and ρ_3. Furthermore, two other peaks developed significantly in this region (2.0–3.0 eA^{-3}) and they were located *on the twofold axis.* It now became apparent that these peaks represented benzene molecules which were utilizing twofold rotation symmetry to accommodate along the crystallographic twofold rotor. Thus, the 0.5 mole of benzene of solvation was satisfactorily accounted for since the multiplicity of the twofold position in space group C2 is two.[10]

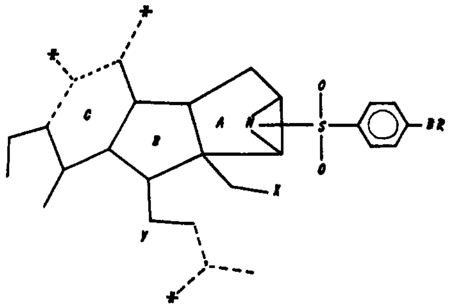

Figure 1. Atomic arrangement identifiable from ρ_1 and inferred from chemical considerations.

Refinement of the structure, including a half-benzene molecule, was now commenced through electron- and difference-density computations. After one cycle, individual isotropic thermal parameters were obtained from the difference density and these were included into structure factor computations. In all, six cycles of refinement were carried out in this manner and R decreased to 0.146. At this stage, refinement by the method of least squares was initiated.

The Least-Squares Refinement

The structure was first refined by conventional diagonal least-squares techniques. The weighting scheme adopted assigned unit weights ($w = 1.0$) to all reflections with $4|F_{\min}| < |F| < 10|F_{\min}|$; $w = |F|/4|F_{\min}|$ when $|F| \leq 4|F_{\min}|$; and $w = 10|F_{\min}|/|F|$ for reflections with $|F| \geq 10|F_{\min}|$. This scheme resembles the Hughes weighting and simultaneously takes into account variations in the measured intensity data due to the counting statistics. Isotropic refinement converged after three cycles in which only the non-zero structure amplitudes were included and an R of 0.109 was obtained. A three-dimensional electron density map was calculated at this stage and it clearly indicated a large amount of anisotropy for both the bromine and sulfur atoms. This was allowed for in some additional refinement by introducing both heavy atoms as slightly separated, but thermally coupled half-atoms. A considerable improvement in bond distances and valency angles resulted but R was not affected much.

Inclusion of all atoms with anisotropic correction factors and subjecting the data to additional refinement yielded a large change in R, which became stationary at 0.087, and caused significant changes in some of the bond distances. A difference density map was computed, but in general the regions in which the hydrogen atoms were expected to be located were poorly defined. Therefore, the refinement process was terminated. The final positional and anisotropic thermal parameters are given in Table I, and the standard errors of the positional parameters are given in Table II. (The observed and calculated structure factors are available from the authors.)

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(10) It should be remarked here that from the onset of the work, the one half mole of benzene of solvation was puzzling, especially in view of the fact that the crystal proved to be an excellent X-ray scatterer (91.3% of the data was observable to 1-A resolution). Such behavior was not consistent with disordered benzene of solvation as the one half mole would suggest.

Table I. Final Positional and Anisotropic Thermal Parameters[a]

Atom	x/a	y/b	z/c	B_{11}	B_{22}	B_{33}	B_{12}	B_{13}	B_{23}
Br	0.51422	0.50000	0.13205	281	1613	455	66	137	−120
S	0.22439	0.16162	0.15784	227	1028	221	34	36	−9
Ph1	0.30650	0.25157	0.14812	188	269	171	310	−134	51
Ph2	0.34954	0.27258	0.22431	211	1388	321	85	166	−7
Ph3	0.32259	0.31170	0.07327	258	981	151	386	42	70
Ph4	0.41411	0.34954	0.21744	147	1718	328	185	−12	317
Ph5	0.38493	0.38562	0.06751	379	1024	276	135	21	38
Ph6	0.42783	0.40172	0.13849	245	3325	97	−511	66	170
C1	0.17730	0.47555	0.14156	331	1173	245	−251	176	−297
C2	0.18842	0.43940	0.23212	251	1593	240	−363	73	260
C3	0.10817	0.55605	0.11861	147	1082	231	680	91	287
C4	0.12667	0.51127	0.27368	214	217	339	21	−14	−48
C5	0.08848	0.40434	0.33459	189	1405	169	−115	−17	90
C6	0.02029	0.37873	0.28454	165	252	282	134	−38	39
C7	0.01826	0.44726	0.20879	171	39	151	345	−52	369
C8	−0.03995	0.28770	0.30701	178	1345	307	284	23	−307
C9	−0.09885	0.28665	0.24291	115	1815	395	239	29	58
C10	−0.10110	0.34542	0.16691	104	265	252	606	−72	18
C11	−0.04241	0.43837	0.14456	222	1503	87	−61	−107	31
C12	−0.16063	0.32536	0.09958	275	2282	474	−286	−62	56
C13	−0.18431	0.24511	0.34415	283	2948	512	−118	164	−113
C14	0.10441	0.77575	0.32587	213	1152	318	153	69	57
C15	0.11997	0.24511	0.36145	113	86	335	169	−42	232
C16	0.21795	0.16369	0.45709	44	261	413	447	67	323
O1	0.20237	0.09838	0.07938	239	1294	433	144	35	−234
O2	0.23069	0.06661	0.23145	225	2128	474	284	72	87
O3	0.15177	0.65270	0.30881	134	798	383	91	98	−120
O4	0.18707	0.28912	0.40933	135	656	320	115	10	11
O5	0.19117	0.03085	0.45591	296	153	618	279	−51	−168
O6	−0.03849	0.21898	0.37502	179	2241	542	7	−25	106
O7	−0.04248	0.50850	0.07902	259	2299	196	129	−49	139
O8	−0.15546	0.20054	0.26759	209	1716	542	−34	−10	−9
N1	0.16834	0.30736	0.17228	167	299	268	326	110	−108
N2	0.07523	0.53547	0.20003	148	235	88	546	82	−6
N3	0.27685	0.21003	0.49369	167	1368	490	14	63	−180
B1	0.50000	0.06325	0.50000	436	1396	286	−196	288	−122
B2	0.50000	0.40322	0.50000	399	2792	276	−389	273	−284
B3	0.44802	0.14945	0.45348	439	2993	575	−327	372	−198
B4	0.44798	0.31978	0.45204	332	3502	223	−118	115	306

[a] The anisotropic temperature factors which were used in the calculations were of the form $T = e^{-(B_{11}h^2 + B_{22}k^2 + B_{33}l^2 + 2B_{12}hk + 2B_{13}hl + 2B_{23}kl)}$. All B values are multiplied by a factor of 10^5.

Structure of the Molecule

An inspection of the interatomic distances (Figure 2) shows that there are few anomalies present in the structure of N-brosylmitomycin A. Major interest lies with the aziridine ring system, which consists of three bonds of equal length. The C–N distances of 1.48 and 1.49 A are normal for single carbon-to-nitrogen bonds. The exocyclic bond angles N(1)–C(1)–C(3) of 110.7° and N(1)–C(2)–C(4) of 112.8° (Figure 3; see Figure 4 for labeling) indicate that the carbon atoms tend to retain their tetrahedral configuration despite the considerable shortening of the C–C bond to 1.48 A. The atoms C(4), C(2), C(1), and C(3) of ring A are coplanar. The angle between the plane defined thusly and the aziridine ring is 104°, and the distance between the indole nitrogen N(2) and N(1) is 2.69 A.

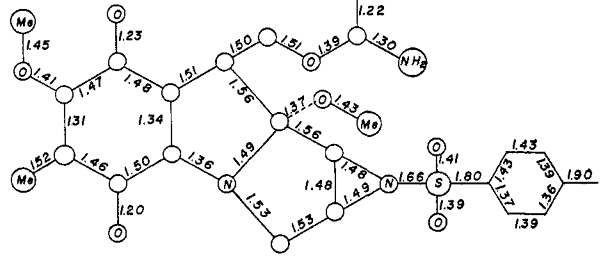

Figure 2. Final bond distances.

As one would expect, N(2) behaves much like an amide nitrogen owing to its ability to participate in the conjugation of the quinoid system. However, it is observed in ultraviolet absorption spectra that mitomycin A is bathochromic with respect to model compounds[3b] and that its extinction coefficient is considerably smaller, which is indicative of a lower energy system.

This may be accounted for by the fact that N(2) is observed to be nonplanar and thus is impaired in its ability to take part in the conjugation. N(2) is 0.3 A out of the plane defined by C(3), C(4), and C(7), and on the opposite side of that plane as the aziridine nitrogen, N(1). Furthermore, an inspection of the bond angles shows that it is more tetrahedral than trigonal. Even though one could ascribe this to the fact that

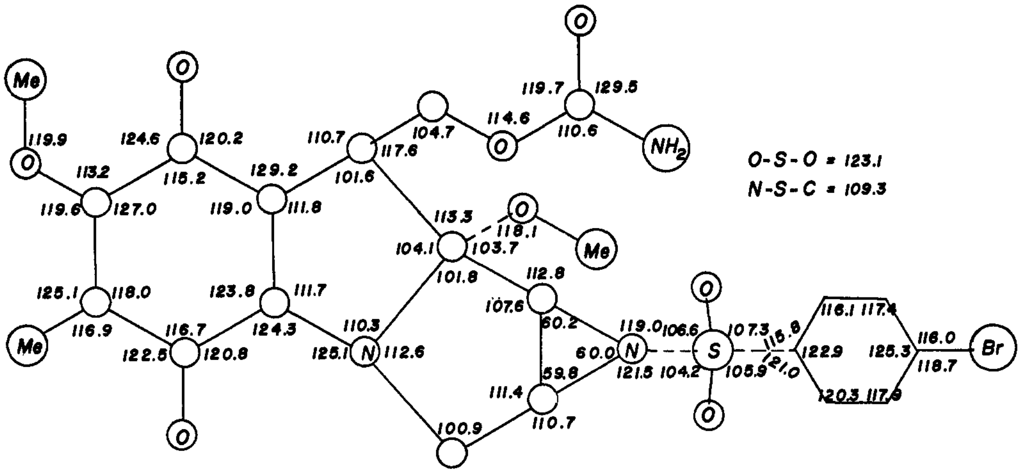

Figure 3. Final bond angles.

N(2) is part of two five-membered rings and therefore subject to distortion of its valency angles, a more plausible reason becomes obvious upon inspecting the orientation and position of the orbitals occupied by the free pairs of electrons of N(1) and N(2). If N(2) were planar these would be subject to overlap, and the observed deformation of N(2) is sufficient to avoid this to a great extent, as is indicated in Figure 5.

Table II. Standard Deviations of the Positional Parameters, in A, as Obtained from Least-Squares Residuals

Atom	$\sigma(x)$	$\sigma(y)$	$\sigma(z)$
Br	0.001	0.001	0.001
S	0.003	0.003	0.003
Ph1	0.010	0.010	0.010
Ph2	0.011	0.012	0.012
Ph3	0.012	0.012	0.011
Ph4	0.011	0.014	0.012
Ph5	0.014	0.013	0.013
Ph6	0.009	0.013	0.010
C1	0.011	0.010	0.011
C2	0.009	0.010	0.010
C3	0.012	0.014	0.012
C4	0.010	0.009	0.011
C5	0.010	0.011	0.010
C6	0.010	0.010	0.011
C7	0.010	0.009	0.009
C8	0.012	0.013	0.012
C9	0.011	0.015	0.013
C10	0.011	0.011	0.011
C11	0.010	0.011	0.009
C12	0.011	0.014	0.014
C13	0.012	0.016	0.015
C14	0.011	0.013	0.012
C15	0.009	0.008	0.010
C16	0.010	0.010	0.011
O1	0.008	0.009	0.009
O2	0.009	0.012	0.010
O3	0.007	0.007	0.008
O4	0.007	0.007	0.008
O5	0.009	0.007	0.010
O6	0.008	0.011	0.010
O7	0.008	0.010	0.008
O8	0.008	0.009	0.010
N1	0.008	0.008	0.009
N2	0.008	0.008	0.007
N3	0.009	0.011	0.012
B1	0.02	0.02	0.02
B2	0.02	0.03	0.02
B3	0.01	0.02	0.01
B4	0.01	0.02	0.01

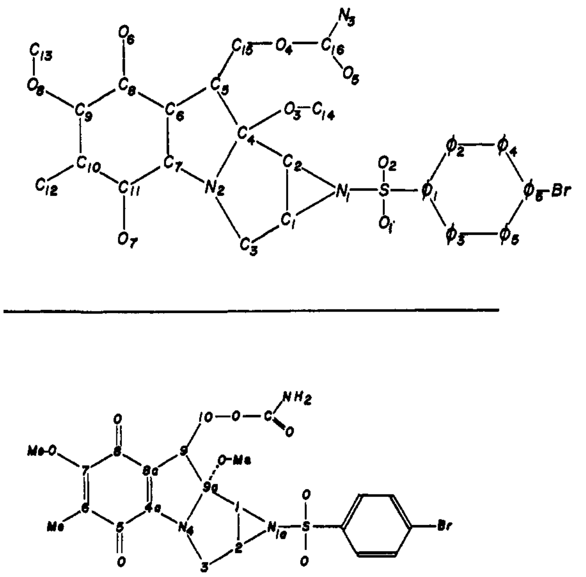

Figure 4. Key to X-ray (top) and chemical labelings (bottom).

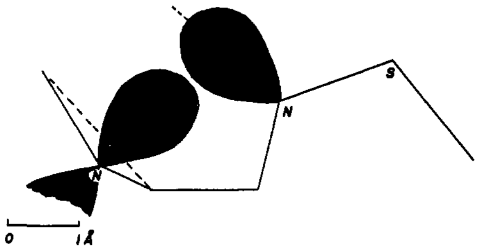

Figure 5. Schematic view of interaction of unshared electrons.

The nonplanarity of N(2) also affects other parts of the molecule. The substitution of an amide-type nitrogen at C(7) and an O–Me group at C(9) would, in the case of a normal planar molecule, be expected to result in: (a) a shortening of the C–N single bond owing to its participation in the conjugated system, (b) a simultaneous lengthening of the double bond C(7)–C(6), and, possibly, (c) a shortening of the C–O–Me bond due to the influence of the *p*-mide group.

It is observed that the C–N bond is indeed shortened. However, no shortening of the C–O bond is observed,

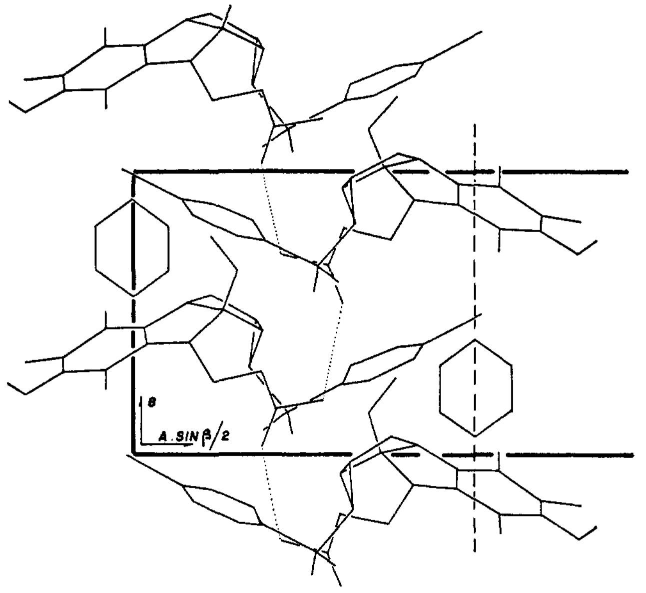

Figure 6. Projection of crystal structure as viewed along the *c* axis (one-half unit cell shown).

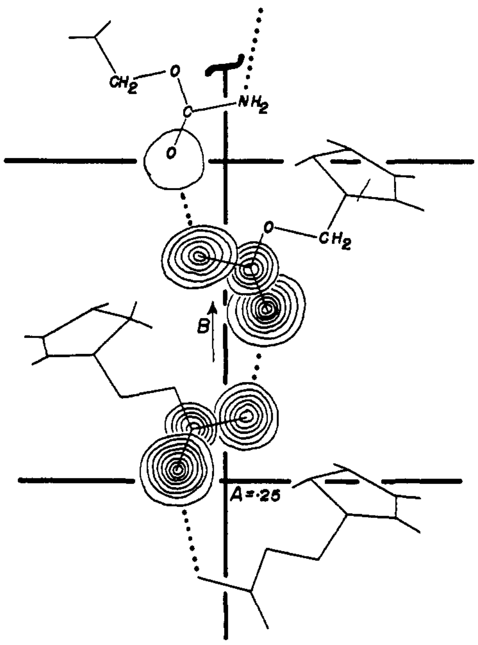

Figure 7. Hydrogen-bonding scheme.

Table III. Short Intermolecular Approaches[a]

A1–A2 A1	A2	Type	*d*, A	A1–A2 A1	A2	Type	*d*, A
O6	B4	a3	3.53	Br	C8	f3	3.91
O8	C2	a3	3.75	Br	C9	f3	3.81
O7	C3	b2	3.33	Br	C10	f3	3.72
C13	C16	c2	3.39	Br	C11	f3	3.79
C13	N3	c2	3.34	Br	C14	f3	3.89
O6	B3	c3	3.78	Br	N1	f3	3.96
C6	B3	c3	3.89	Ph1	O7	f3	3.84
C8	B3	c3	3.82	Ph2	O7	f3	3.96
C14	B4	c3	3.87	Ph2	O8	f3	3.60
O2	O3	d1	4.00	Ph3	O7	f3	3.60
O2	C14	d1	3.87	Ph4	O8	f3	3.33
O5	C14	d1	3.31	Ph4	C8	f3	3.96
S	C12	d3	3.76	Ph4	C9	f3	3.64
Ph1	C10	d3	3.81	Ph5	O7	f3	3.42
Ph1	C11	d3	3.94	Ph5	C12	f3	3.78
Ph1	C12	d3	3.67	Ph6	O7	f3	3.44
Ph2	C10	d3	3.79	Ph6	O8	f3	3.71
Ph2	C11	d3	3.78	Ph6	C9	f3	3.65
Ph4	C7	d3	3.91	Ph6	C10	f3	3.74
Ph4	C11	d3	3.71	Ph6	C12	f3	3.92
Ph6	C11	d3	3.86	O3	O8	f3	3.94
O1	C12	d3	3.50	O3	C13	f3	3.31
O2	O8	d3	3.77	O6	B1	f3	3.51
O2	C12	d3	3.73	C2	C13	f3	3.87
O2	C13	d3	3.53	C5	B1	f3	3.57
O5	C13	d3	3.03	C6	B1	f3	3.84
O6	B2	d3	3.33	C8	B1	f3	3.86
O5	N3	d4	2.817	C14	B2	f3	3.78
O5	B4	d4	3.68	O3	N3	f4	3.37
O6	B2	d4	3.33	O4	O5	f4	3.65
C16	N3	d4	3.82	O4	N3	f4	3.84
O1	C12	e2	3.46	O6	B1	f4	3.51
O7	O7	e2	3.18	C5	B1	f4	3.57
Ph3	O1	e4	3.40	C6	B1	f4	3.84
Ph5	O1	e4	3.28	C8	B1	f4	3.86
Ph2	B4	f1	3.98	C14	N3	f4	3.58
N3	B3	f1	3.53	C14	B2	f4	3.78
N3	B4	f1	3.62	C14	B3	f4	3.93
O4	C13	f2	3.98	C14	B4	f4	3.83
O5	C13	f2	3.68	O3	O5	g1	3.94
Br	O1	f3	3.97	C14	C15	g1	3.92
Br	C6	f3	3.96				
Br	C7	f3	3.88				

[a] Type refers to the following positions: 1 = x, y, z; 2 = $-x, y, -z$; 3 = $x + 0.5, y + 0.5, z$; 4 = $-x + 0.5, y + 0.5, -z$, located in the cell whose origin is displaced from the reference unit cell by: a = $-a, -b, 0$; b = $-a, 0, -c$; c = $-a, 0, 0$; d = $0, -b, 0$; e = $0, 0, -c$; f = $0, 0, 0$; g = $0, b, 0$.

which may be attributed to the fact that N(2) is not coplanar with the quinoid system, so that hyperconjugation with O(7) is not expected to occur.

From the above it may also be concluded that the nonbasic behavior of N(1) which is atypical for an aziridine nitrogen atom, even when part of a [3.1.0] bicyclo system, is due to the steric interference of its fourth valence pair with the free p orbital of N(2). In the free base this should also inhibit its ability to invert, as is indicated in nuclear quadrupole measurements. N(1) may therefore actually be considered as an optically active site produced by steric interference.

Some interesting observations may also be made about the brosyl group. First, the sulfonyl group is nearly tetrahedral with the exception of the angle between the O–S–O bond, which is 123°. Second, the bromine atom is nearly equidistant to the carbon atoms forming the quinoid ring of another molecule (see Table III). From the foregoing, it is reasonable to conclude that there is a negative charge present on the oxygen atoms of the sulfonyl group causing the increased O–S–O angle (SO_2 is a more electron-withdrawing group than bromine). The bromine atom in turn compensates for this by interacting with the quinoid system.

The observed N–S distance of 1.663 A shows that this bond contains some double bond character. No comparison is possible with similar systems since the literature contains only one reference to a N–S bond, that in $SO_2(N(CH_3)_2)_2$, where it is found to be 1.623 A.[11] A single bond would probably have a length of about 1.73 A [derived from atomic radii of S (1.04 A), N (0.74 A), and an electronegativity correction for N–S of −0.05 A].

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(11) T. Jordan, W. Smith, and W. N. Lipscomb, *Tetrahedron Letters*, 37 (1962).

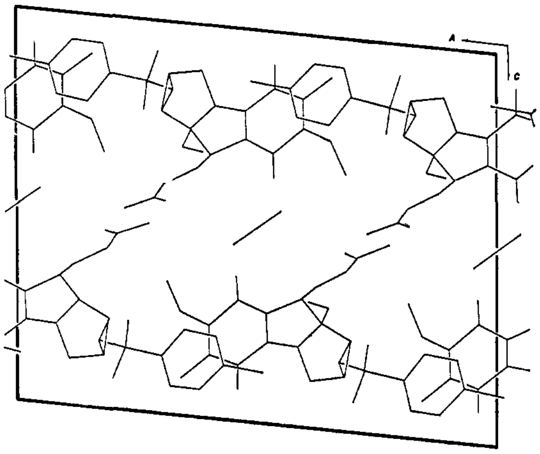

Figure 8. Arrangement of the molecules as viewed along the *b* axis.

Molecular Packing in the Crystal Lattice

The structure is held together *via* infinite chains of hydrogen bonds in the direction of the *b* axis between the amide functional groups of different molecules, as may be seen from Figures 6 and 7. The N–H···O distance of 2.817 A indicates a fairly strong interaction. This hydrogen-bonding scheme provides within each unit cell parts of two sets of these chains which seem to be joined together by the donor–acceptor relationship of the bromine and quinoid groups already discussed. It is within this framework that the benzene molecules of solvation are located in such a way as to provide the largest number of possible van der Waals contacts. A complete listing of all intermolecular distances smaller than 4 A is given in Table III. Figure 8 provides a schematic view of the molecular packing as viewed in the direction of the *b* axis and clearly delineates the solvate-containing channels.

Absolute Configuration Determination

At the time when the absolute configuration of the molecule became of interest, the crystal used for data collection was no longer available for intensity measurement of the reflections for which the largest deviations from Friedel's law could be expected. However, it is possible to determine the hand of the molecule without knowledge of these data by computing *R* values for selected sets of reflections with large differences between the calculated structure amplitudes for the two enantiomorphs.[12]

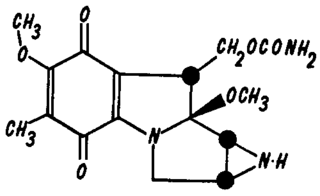

Figure 9. Absolute configuration.

For the 67 reflections with differences of more than 10% $|F_c|$, and magnitudes larger than 15 (electron-scattering units), it was found that when the reflections were assigned as (hkl), *R* was calculated as 0.150; however, if they were considered to be of the type $(\bar{h}\bar{k}\bar{l})$, *R* was 0.122. This procedure was repeated for all reflections with $|F_o|$ larger than 25, in which case the results were 0.153 and 0.109, respectively. This clearly suggests that the hand which was originally chosen was incorrect,[13] and the absolute configuration of mitomycin A determined in this manner is depicted in Figure 9. In addition to the two *R* values for the large differences it was found that the over-all *R* values (0.094 and 0.087) were also consistent with the above.

Acknowledgment. A. T. is grateful to the National Institutes of Health, U. S. Public Health Service (USPHS 3698), and Lederle Laboratories, Division of the American Cyanamid Company, for supporting this research.

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[12] J. H. van den Hende and N. R. Nelson, *J. Am. Chem. Soc.*, **89**, 2901 (1967).

[13] Originally, the reflections were assigned (hkl) in a right-handed coordinate system.