Table I. Effects of Model Compound and Inert Solvent on Heats of Formation of Hydrogen Bonds of Phenol with Various Bases, Calculated by Process 2

Base	Inert solvent	$-\Delta H_2$,[a] kcal mol^{-1}	$-\Delta H_2$,[b] kcal mol^{-1}	$-\Delta H_1$, kcal mol^{-1}
Pyridine	Cyclohexane	7.5	8.5	8.0[c]
	n-Heptane	7.7	8.6	
	Carbon tetrachloride	7.3	7.7	7.2[d]
		7.3[d]		6.6[e]
THF	Cyclohexane	5.9	6.9	
	n-Heptane	6.1	7.0	
	Carbon tetrachloride	5.7	6.1	5.3[c]
		5.75[d]		5.7[d]
Acetone	Cyclohexane	5.5	6.6	
	n-Heptane	5.7	6.7	
	Carbon tetrachloride	5.3	5.8	4.9[c]
		5.6[g]		4.6[f]
p-Dioxane	Cyclohexane	5.3	6.3	
	n-Heptane	5.5	6.4	
	Carbon tetrachloride	5.0	5.6	
		5.1[h]		

[a] Model compound is anisole (M_1). [b] Model compound is toluene (M_2). [c] Reference 8. [d] Reference 3. [e] Reference 5. [f] Reference 2. [g] E. Mitchell, personal communication, 1970. [h] T. S. S. R. Murty, Ph.D. Thesis, University of Pittsburgh, 1967.

solvents. Since this heat has nothing to do with the actual formation of the hydrogen bond and enters the calculation primarily as an approximation, we wish to propose an alternate treatment by which this method can produce useful information.

By combination of eq 2 written for two different bases (B and B′) with the same acid, we eliminate all species dissolved in the inert solvent, as in process 3.

$$AB'(B') + B(B) + M(B) \longrightarrow AB(B) + B'(B') + M(B') \quad (3)$$

This necessarily removes any contribution of the inert solvent to the results. In the same way that the heat of process 2 can be considered as the heat of formation of the hydrogen bond in pure base, the heat of process 3 can be considered to represent the difference in heats of formation of hydrogen bonds of the acid with the two different bases. The heat for this process is calculated from the heats of solution of the acid and the model compound in the two basic solvents. With elimination of the inert solvent, the method can now be extended to acids for which strong self-association prevents accurate determination of standard heats of solution in inert solvents. To illustrate this point, we have also measured the heats of solution of acetic acid, benzoic acid, and their model compounds methyl acetate, acetone, methyl benzoate, and acetophenone, respectively. We have chosen THF as the reference base (B′) and report heats for process 3 in Table II as the heat of transfer of the hydrogen bond of the acid from THF to the other bases. These heats are shown to be virtually independent of the choice of model compound. In fact, acetophenone or methyl benzoate could have been used as the model compound for phenol without changing the calculated heats by more than 0.1 kcal.

The difference in the heats of formation of hydrogen bonds between an acid and different bases may also be calculated from the difference in heats determined for process 1. The contribution of the inert solvent is not necessarily eliminated in this combination. From Lamberts' data[2,5] we calculate 2.0 kcal for the difference between the phenol–pyridine and phenol–acetone interactions with carbon tetrachloride as solvent, compared with an average value of 1.94 kcal calculated by combination of our data for pyridine and acetone in Table II. Using his Method I, Arnett obtained a difference of 1.5 kcal between phenol–THF and phenol–pyridine in carbon tetrachloride compared with our average value of 1.59 kcal.

Table II. Heats of Transfer of Hydrogen Bonds from THF (B′) to Other Bases, Calculated by Process 3

Acid	Base (B)	ΔH_3, kcal mol^{-1} Model M_1	Model M_2
Phenol	Pyridine	−1.58	−1.60
	p-Dioxane	+0.67	+0.57
	Acetone	+0.43	+0.27
Acetic acid	Pyridine	−1.77	−1.79
	p-Dioxane	+0.77	+0.64
	Acetone	+0.79	+0.81
Benzoic acid	Pyridine	−2.08	−1.96
	p-Dioxane	+0.92	+0.98
	Acetone	+1.09	+1.18

From this study we conclude that "absolute" heats of formation of hydrogen bonds determined by process 2 may be in considerable error relative to reported uncertainties, but relative heats determined by this process are at least as reliable as, and possibly more accurate than, those determined by process 1. Heats of formation of hydrogen bonds determined by process 2 with carbon tetrachloride as "inert" solvent might more properly be considered in terms of process 3 with carbon tetrachloride as the reference base. Because of their greater dependence on the model compound, these heats should be recognized as somewhat less accurate than those determined with stronger bases.

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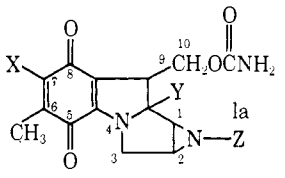
The Structure of Mitiromycin

Sir:

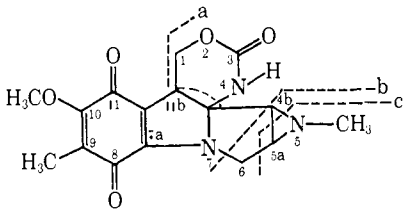
Mitiromycin, a compound of unknown structure in the mitomycin class of antibiotics I–IV,[1,2] was isolated and described in 1962.[1] From combustion analysis and ir, uv, and nmr spectra mitiromycin was indicated to have the molecular formula $C_{16}H_{19}N_3O_6$, the same as I and II, the same chromophore as I and II, and functional groups 1 OME, 1 NMe, and 1 CMe. Careful examination of the nmr spectra in the presence of CD_3OD also indicated two or three of the 19 protons readily exchanged with deuterium. Although one active proton was assigned as NH the remaining exchangeable protons were not unambiguously defined.

(1) D. V. Lefemine, M. Dann, F. Barbatschi, W. K. Hausmann, V. Zbinovsky, P. Monnikendam, J. Adam, and N. Bohonos, *J. Amer. Chem. Soc.*, **84**, 3184 (1962).
(2) 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, *ibid.*, **84**, 3185 (1962).

New spectroscopic evidence, including additional 60-MHz ^1H nmr, 100-MHz ^1H nmr, and high-resolution mass spectral data, has now provided a revised elemental formula $C_{16}H_{17}N_3O_5$ and a new proposed structure, 1,4b,5,5a,6,11b-hexahydro-10-methoxy-5,9-dimethylazirino[2′,3′:3,4]pyrrole[1,2-*a*][1,3]oxazino-[4,5-*b*]-indole-3(4H),8,11-trione (V). Thus mitiromycin is the first mitomycin antibiotic to contain the unusual "oxazinone" ring in place of the open-chain carbamate ester.



I–IV



V

I, mitomycin A; X = H_3CO; Y = OCH_3; Z = H
II, mitomycin B; X = H_3CO; Y = OH; Z = CH_3
III, mitomycin C; X = H_2N; Y = OCH_3; Z = H
IV, porfiromycin; X = H_2N; Y = OCH_3; Z = CH_3

A high-resolution mass spectrum of mitiromycin exhibited a molecular ion at *m/e* 331 with composition $C_{16}H_{17}N_3O_5$ (see Table I). Thus, the formula arrived at by combustion analysis is that of the molecular hydrate $C_{16}H_{17}N_3O_5 \cdot H_2O$. In addition, interpretation of the original nmr spectrum is indicated to have been complicated by the presence of water. To validate this point and arrive at a structure for mitiromycin the nmr spectrum of mitiromycin was reexamined in two solvent systems (see Table II).

Table I. Mass Spectral Peaks (High Resolution)[a]

Ion	Composition	Obsd mass	Calcd mass	Rel ab, %
$M\cdot^+$	$C_{16}H_{17}N_3O_5$	331.1174	331.1168	90
M − CH_3	$C_{15}H_{14}N_3O_5$	316.0952	316.0933	10
M − (a + H)	$C_{14}H_{13}N_2O_3$	257.0922	257.0926	28
M − (a + CH_3)	$C_{13}H_{11}N_2O_3$	243.0793	243.0769	26
b + H	$C_4H_8N_1$	70.0666	70.0657	100
b − H	$C_4H_6N_1$	68.0499	68.0500	20
c	$C_2H_4N_1$	42.0347	42.0344	32

[a] Accurate mass data was obtained at resolution 10,000 on an AEI MS-9 mass spectrometer. Spectra obtained on CEC-21-110 mass spectrometers were similar to those obtained on the MS-9.

The total number of protons observed in these nmr spectra was 19 which agreed with the analytical data. The two-proton singlet at δ1.6 was assigned to water on the basis of the following data. In the $CDCl_3$–C_6D_6 solvent system the δ1.60 peak underwent an upfield shift of δ 0.5 from its position in $CDCl_3$ while other peaks experienced shifts from δ 0.06 to 0.30. This fact suggests that the peak at δ 1.60 in $CDCl_3$ is from a molecule other than mitiromycin. The δ 1.60 peak also underwent exchange with deuterium in CD_3OD. An emulsion of H_2O in $CDCl_3$ exhibited a peak at δ 1.58 in its nmr spectrum which also offered further evidence for our water assignment in the mitiromycin spectra. Conclusive proof of the presence of water was obtained by dehydration of the $CDCl_3$–mitiromycin solution *via* molecular sieves.[3] The nmr spectrum of the dehydrated solution showed no peak at δ 1.60 while all other peaks remained unchanged. In addition, the spectrum integrated for a total of 17 protons which was consistent with the mass spectral data. Comparison of the nmr spectra of I and V and the mass spectral fragmentation properties of I–IV and V led to the proposed structure, V. The coupling constants observed for the H_9,H_{10}, and $H_{10'}$ three-spin system in the nmr spectra of I and the H_{11b}, H_1, and $H_{1'}$ three-spin system in V are: I, $J_{9,10} = 9.95$, $J_{9,10'} = 4.95$, $J_{10,10'} = -10.5$; V, $J_{1,11b} = 4.0$, $J_{1'11b} = 2.2$, $J_{1,1'} = -11$. The difference in coupling constants for the two compounds suggests a change in orientation for the carbamoyl side chain. The observance of only one NH proton in the spectrum of V *vs.* NH_2 in the spectra of I–IV prompted the choice of a cyclic carbamate or oxazinone ring in V. The $J_{1,1'}$ of −11 Hz is in agreement with the data for the $-CH_2$ next to O of a six-membered ring lactone also.[4]

Table II. Nmr Spectral Data

Assignment	Chemical shift[a]	Coupling constant[b]	Δδ[c]
H_4	6.75 (s)		−0.15
$H_{1'}$	4.75 (d,d)	$J_{1',11b} = 2.2$ $J_{1,1'} = 11$	−0.08
H_1	4.50 (d,d)	$J_{1,11b} = 4$ $J_{1,1'} = 11$	−0.20
C_{10}–OCH_3	4.07 (s)		−0.15
H_{11b}	3.97 (d,d)	$J_{1,11b} = 4$ $J_{1',11b} = 2.2$	−0.22
$H_{6'}$	3.88 (d)	$J_{6,6'} = 13$	−0.10
H_6	3.43 (d,d)	$J_{6,6'} = 13$ $J_{6,5a} = 1.5$	−0.18
H_{5a}	2.38 (d,d)	$J_{5a,6} = 1.5$ $J_{5a,4b} = 5$	−0.30
H_{4b}	2.27 (d)	$J_{4b,5a} = 5$	−0.30
N_5–CH_3	2.30 (s)		−0.23
C_9–CH_3	1.83 (s)		−0.06
H_2O	1.60 (s)		−0.50

[a] Chemical shift reported in δ from internal TMS using $CDCl_3$ as solvent. Spectra were run on a Varian A-60 coupled with a C-1024 time-averaging computer as well as on a Varian HA-100. Frequency spin decoupling confirmed the 3- and 4-spin systems ($H_{1,1',11b}$ and $H_{4b,5a,6,6'}$). [b] Coupling constants reported in hertz. [c] Upfield shift of peaks relative to $CDCl_3$ when C_6D_6 was added to the $CDCl_3$ solution.

The mass spectra of I–IV exhibited weak molecular ions and prominent M − HY, M − H_3NCO, and carbamylium ions.[5] The mass spectrum of mitiromycin exhibited an intense molecular ion and the ions M − HY, M − H_3NCO_2, and H_2NCO were either conspicuously absent or weak. However, ions at *m/e* 257, M − (a + H), and *m/e* 243, M − (a + CH_3), were observed as the prominent high mass ions and are consistent with the proposed structure. Other ions such

(3) Davidson molecular seives, Grade 564, 3A effective pore size, 8–12 mesh beads, Davidson Chemical, Baltimore, Md. 21226.
(4) R. C. Cookson, T. A. Crabb, J. J. Frankel, and J. Hudec, *Tetrahedron Suppl.*, 22 (7), 355 (1966).
(5) G. E. Van Lear, *ibid.*, in press.

as b + H, b − H, and c which are indicative of a N-methyl-substituted aziridine ring were also observed.

Confirmatory evidence for the oxazinone ring was obtained from the uv and ir spectra. A uv stability study of I–V in aqueous 0.1 *N* HCl established that the chromophore of V is more stable by at least a factor of 50 than I–IV. This observation suggested that any proposed structure for mitiromycin must not have a function at position 9a which could be readily eliminated to give the mitosene ("apo") chromophore.[2,6] The proposed structure V is in accord with this requirement.

In the ir spectra of II and V, the carbonyl maximum from the carbamate in II and the oxazinone in V was found in the 5-8-μ region as expected. However, in the solid state the carbonyl maximum in II exhibited intermolecular hydrogen bonding characteristics whereas V did not. Additionally, in the 7.50-μ region the maximum assigned to the ester (ROC(=O)R) portion of the carbamate in the spectrum of II was essentially missing in the ir spectrum of V. This change is completely analogous to that obtained in the spectral changes that occur in going from an ester to a lactone. In the 9.20-μ region the maximum assigned to the alcohol function (Y in II) was missing in the ir spectrum of V as would be expected for the structural changes proposed.

Additional work including an X-ray structure determination of a suitable derivative of mitiromycin is planned.[7]

Acknowledgments. The authors are indebted to Dr. T. Mead, J. C. Cook, and K. Angyal for aid in determining the mass spectra. Acknowledgment is also due to Dr. J. E. Lancaster for the 100-MHz ^{1}H nmr spectra and to Dr. E. Patterson for a sample of mitiromycin.

(6) J. B. Patrick, R. P. Williams, W. E. Meyer, W. Fulmor, D. B. Cosulich, R. W. Broschard, and J. S. Webb, *J. Amer. Chem. Soc.*, **86**, 1889 (1964).

(7) NOTE ADDED IN PROOF. The reason for the structure determination of V was that although structurally very similar to the potent antibiotics I–IV, compound V has no antibiotic activity. Also, to our knowledge, this the first report of a naturally occurring oxazinone or six-membered cyclic carbamate ring.

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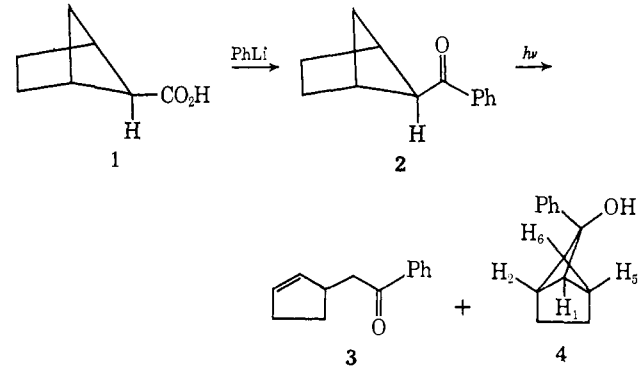
Photochemical Synthesis of the Tricyclo[3.2.0.0^{2,6}]heptane System[1]

Sir:

A recent report from this laboratory described a simple photochemical synthesis of phenylbicyclo[1.1.1]-pentan-2-ol.[2] The formation of the bicyclopentanol was proposed to occur by a novel transannular hydrogen abstraction by the excited n–π^* triplet state of cyclobutyl phenyl ketone.[3,4] We now wish to report an extension of the transannular hydrogen abstraction route which provides a convenient synthesis of the heretofore unknown tricyclo[3.2.0.0^{2,6}]heptane ring system.

exo-5-Benzoylbicyclo[2.1.1]hexane (**2**) was readily prepared by the reaction of bicyclo[2.1.1]hexane-*exo*-5-carboxylic acid[5] (**1**) with phenyllithium.[6] Its stereochemistry is clear from its nmr spectrum, which shows a 7.0-Hz long-range coupling constant between the distant *endo* C-5 and C-6 protons.[7] Irradiation of a 1% solution of **2** in benzene using a 450-W Hanovia lamp through a Pyrex filter for 8 hr led to the formation of two new photoisomers, shown to be Δ^2-cyclopentenylacetophenone (**3**, 66%) and 7-phenyltricyclo[3.2.0.0^{2,6}]-heptan-7-ol (**4**, 30%).[8]



The structure of the major product (**3**), analogous to the ketoolefin produced photochemically from cyclobutyl phenyl ketone,[2] is apparent from its spectral characteristics: uv $\lambda\lambda_{max}$ (95% ethanol) 238, 270, and 305 mμ (ϵ 11,700, 6000, 75); ir λ_{max} (CCl_4) 5.92, 6.02 μ; 60-MHz nmr (deuteriochloroform) multiplets at τ 2.18, 2.65, 6.90, and 8.75, singlet at τ 4.35, triplet at τ 7.73. The peak areas are in the ratio of 2:3:3:2:2:2. The mass spectrum of 3 included peaks with *m/e* 186 (M^+) and 105 (base peak). This product also has a prominent peak at *m/e* 120 corresponding to loss of cyclopentadiene in a McLafferty rearrangement. Structure **3** was further confirmed by an independent synthesis from Δ^2-cyclopentenylacetic acid and phenyllithium.

The structure of **4** (*p*-bromophenylurethan derivative, mp 137–138°) was elucidated on the basis of the physical and chemical data cited. The infrared spectrum shows hydroxyl bands at 2.86 and 3.04 μ and a carbon–oxygen stretching band at 8.32 μ. Its ultraviolet spectrum exhibited an absorption characteristic of an isolated benzene ring. The mass spectrum of **4** included peaks with *m/e* 186, 168, 120, 105, 91, and 77 and is very similar to that of **3**. Confirmation of the structure of **4** was available from its unique nmr spectrum. The 100-MHz nmr spectrum showed the aromatic hydrogens as a singlet at τ 2.75, the two bridgehead hydrogens (H_1 and H_6) as a singlet at τ 7.34, H_5 as a doublet at τ 6.45 (J = 7.0 Hz), H_2 as a doublet at τ 7.88 (J = 7.0 Hz), the hydroxyl proton as a broad singlet at τ 7.09, and the four methylenic hydrogens as

(1) Photochemical Transformations of Small Ring Carbonyl Compounds. XXV. For part XXIV, see A. Padwa, S. Clough, and E. Glazer, *J. Amer. Chem. Soc.*, **92**, 1778 (1970).

(2) A. Padwa and E. Alexander, *ibid.*, **89**, 6376 (1967).

(3) A. Padwa, E. Alexander, and M. Niemcyzk, *ibid.*, **91**, 456 (1969).

(4) A. Padwa and D. Eastman, *ibid.*, **91**, 462 (1969).

(5) J. Meinwald, C. B. Jensen, A. Lewis, and C. Swithenbank, *J. Org. Chem.*, **29**, 3469 (1964).

(6) Each new compound described gave satisfactory elemental analysis, as well as ir and nmr spectra compatible with the assigned structures.

(7) J. Meinwald and A. Lewis, *J. Amer. Chem. Soc.*, **83**, 2769 (1961).

(8) The reported yields were determined by vpc and have not been corrected for the small amount of thermal decomposition of **4** (~10%) on the vpc column.