geometry about the double bonds,[23] and a similar preferred direction of decay might be expected for the excited complex I. We have observed substantial selectivity for the formation of trans dienes. In summary, the evidence suggests that the isomerization of the dienes occurs *via* the triplet excited state of the $[W(CO)_5(diene)]$ due to direct absorption of light by the complex. Further studies of the structure and reactivity of this complex are in progress.

Acknowledgment. This research was supported by the Directorate of Chemical Sciences, Air Force Office of Scientific Research (Contract No. AF49(638)-1479), and the National Science Foundation. We thank Professor J. H. Richards and Dr. Nancy Beach for useful discussions.

(23) This has been confirmed experimentally by selective triplet transfer to *s-cis,trans*-piperylene: J. Saltiel, L. Metts, and M. Wrighton, unpublished results.

(24) National Institutes of Health Trainee.

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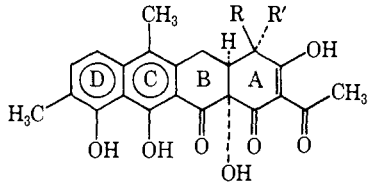
Received June 15, 1970

Structure of Chelocardin, a Novel Tetracycline Antibiotic

Sir:

Chelocardin, a broad-spectrum antibiotic produced by *Nocardia sulphurea*, was first described in 1962.[1] Based on further work, we conclude that chelocardin is 2-decarboxamido-2-acetyl-4-dedimethylamino-4-epiamino-9-methyl-5a,6-anhydrotetracycline (**1a**), a new member of the tetracycline family. This structure contains several features which are not commonly encountered among the tetracyclines but which are readily accommodated biogenetically.[2] Chelocardin, $C_{22}H_{21}NO_7$[3] (M^+ = 411, M − H_2O = 393.1273), possesses a typical anhydrotetracycline absorption spectrum[4] (λ_{max}^{MeOH} 226, 276, and 437 nm (log ϵ 4.51, 4.70, and 3.91)). Subtraction of the uv spectrum of 2-acetylnaphthalene-1,8-diol leaves a difference curve characteristic of the 2-acetyl-1,3-dione system[5] present in ring A. This finding is consistent with the presence of a single nitrogen atom, isolatable as ammonia on strong alkaline treatment, and the presence of ir carbonyl absorption at 1684 cm^{-1}.[6] The antibiotic gives naphthacene and anthracene derivatives on zinc dust distillation, establishing the carbon framework.



1a, R = NH_2; R′ = H
b, R = H; R′ = NH_2
c, R = $NHCOCH_3$; R′ = H
1d, R = H; R′ = $NHCOCH_3$
e, R = NMe_2; R′ = H
f, R = H; R′ = NMe_2

The pmr spectrum (60 MHz) of chelocardin hydrochloride in dimethyl-d_6 sulfoxide solution further emphasizes the similarity of chelocardin to model anhydrotetracyclines:[7,8] δ 2.56 (s, $COCH_3$, partly obscured by solvent resonance), 2.34 (s, 6-CH_3), 2.28 (s, 9-CH_3), 4.87 (d, H_4), 2.5–3.8 (m, H_{4a}, H_5, and $H_{5'}$), and 7.31 and 7.57 ppm (AB d, J = 8.0 Hz, ArH_2). The pmr spectrum (100 MHz) of **1c** in acetone-d_6 was much more clearly defined and allowed determination of chemical shifts and coupling constants: δ 2.10 (s, N–$COCH_3$), 2.31 (s, 6-CH_3), 2.34 (s, 9-CH_3), 3.08 (d of t, H_{4a}, $J_{4,4a}$ = 4.2 Hz, $J_{4a,5}$ = 12.3 Hz, $J_{4a,5'}$ = 4.4 Hz), 2.72 (d of d, H_5, $J_{5,5'}$ = 16.4 Hz), 3.53 (d of d, $H_{5'}$), 5.79 (d, H_4), 7.32 (d, H_7, $J_{7,8}$ = 8.5 Hz), 7.50 (d, H_8), and 2.50 ppm (s, C–$COCH_3$).

These assignments were confirmed by appropriate spin-decoupling experiments. Complete analysis of the spectrum affords corroboration of the structure, assignment of the relative stereochemistry, and establishment of the solution conformation (to be discussed in our full paper).

The occurrence of tetracyclines with an acetyl function at C-2 in place of the more common carboxamido group[5,6,9] and a primary amino function at C-4[10] has precedent, whereas the presence of a second aromatic *C*-methyl group is novel in this class of antibiotics. The position of the aromatic methyl group was ascertained from the ortho coupling of the two aromatic protons and the discovery that each aromatic proton is proximate to an aromatic methyl group. The latter was clearly demonstrated by a nuclear Overhauser effect[11] observed with derivative **1c**. Simultaneous irradiation of both aromatic methyl resonances results in a significant increase in the integrated intensity of both aromatic proton resonances (H-7, 16.5%; H-8, 11.5%) compared to the integrated intensity when the irradiation is off resonance.

Application of the method of aromatic-solvent-induced chemical shift differences in pyridine[12] fails with chelocardin derivatives. Neither the methyl nor the proton resonances associated with rings C and D in derivative **1c** move with respect to their positions in chloroform. Rules derived from studies with simple, monofunctional models may be unsatisfactory on occasion when dealing with complex substrates having

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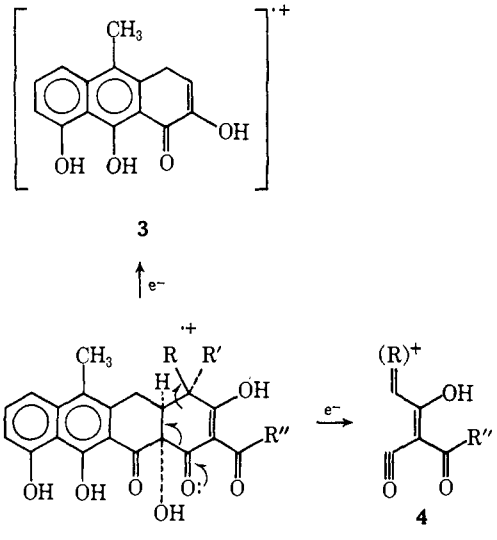
multiple polar groups available for solvation. This point is under further investigation.

Epimerization at C-4 is common among the tetracyclines,[13] and ageing solutions of chelocardin, its *N*-acetyl derivative (**1c**), and *N*-dimethyl analog (**1e**) produced mixtures from which **1b**, **1d**, and **1f** were isolated, respectively. Derivatives **1a**–**1f** have all been fully characterized by analyses, complete high-resolution mass spectroscopy, pmr, uv, etc. It is known that H_4 of anhydrotetracyclines is more deshielded when its orientation is β (epi) contrasted to α (normal).[8] This relationship holds for **1a** and **1b**. In confirmation, the circular dichroism spectra of **1a** and **1b** closely parallel those of anhydrotetracycline (**2a**) and 4-epi-anhydrotetracycline (**2b**) (Figure 1).[14] Furthermore, the apparent Davydov splitting[15] between the π to π^* transitions of the ring A and BCD chromophores (centered at approximately 275 nm) for **1a** and **2b**, but *not* **1b** and **2a**, indicate a common conformation fixing these chromophores at a discrete, close angle. Because the sign of the first transition (at 290 nm) is negative for both **1a** and **2b**, the same absolute configuration is indicated.[16,17]

Finally, detailed comparison of the complete high-resolution mass spectra of substances **1a**–**1f** with those of **2a**–**2d**[18,19] is in complete agreement with the assigned structures. The most significant fragmentation of tetracycline derivatives, for our purposes, is that illustrated in formulas **3** and **4**.[19] The chelocardin



2a, R = H; R′ = NMe_2; R″ = NH_2
b, R = NMe_2; R′ = H; R″ = NH_2
c, R = H; R′ = NMe_2; R″ = CH_3
d, R = H; R′ = NH_2; R″ = NH_2

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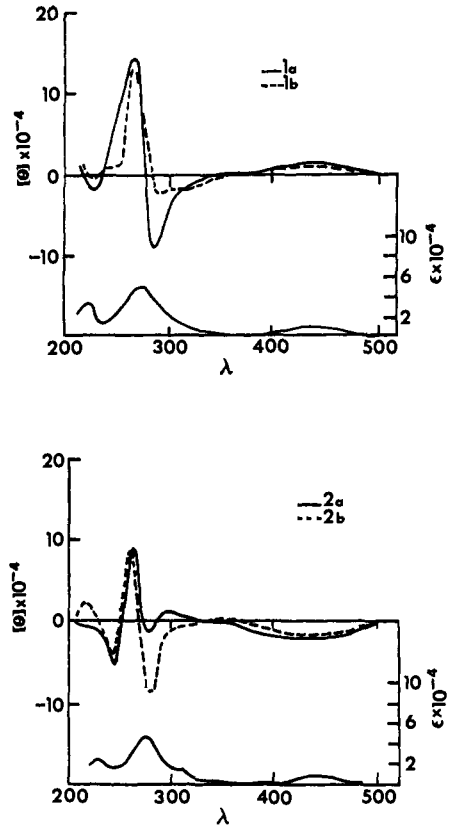

Figure 1. Circular dichroism spectra of **1a**, **1b**, **2a**, and **2b**.

derivatives all produce a prominent ion corresponding to **3** with *m/e* 14 mass units higher than those of models **2a**–**2d** (*m/e* 270.0885 ($C_{16}H_{14}O_4$) *vs.* 256.0752 ($C_{15}H_{12}O_4$)) and an ion corresponding to **4** whose mass varies as required by the changing identity of R (R′) and R″ (for example, the ion appears at *m/e* 141.0424 ($C_6H_7NO_3$) in the spectra of **1a** and **1b**).

Details of the fragmentation patterns, the means of preparing these derivatives, their biological properties, and other chemical transformations of chelocardin will be presented in a full paper in preparation.

Acknowledgment. The authors thank R. L. Foltz of the Battelle Memorial Institute and M. I. Levenberg and S. L. Mueller of Abbott Laboratories for the mass spectra. R. S. Stanaszek and M. Cirovic of Abbott Laboratories provided many pmr measurements.

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Received July 8, 1970

Intramolecular Transannular Cyclizations of Macrocyclic Diacetylenes to Form Cyclobutadiene Derivatives

Sir:

*Inter*molecular dimerizations of acetylenes in the presence of transition-metal derivatives provide useful