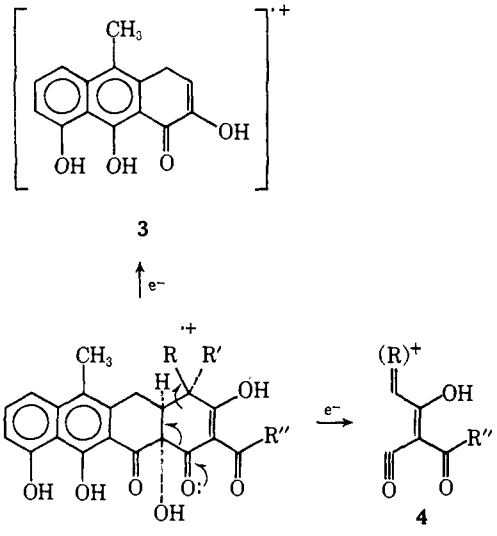
multiple polar groups available for solvation. This point is under further investigation.

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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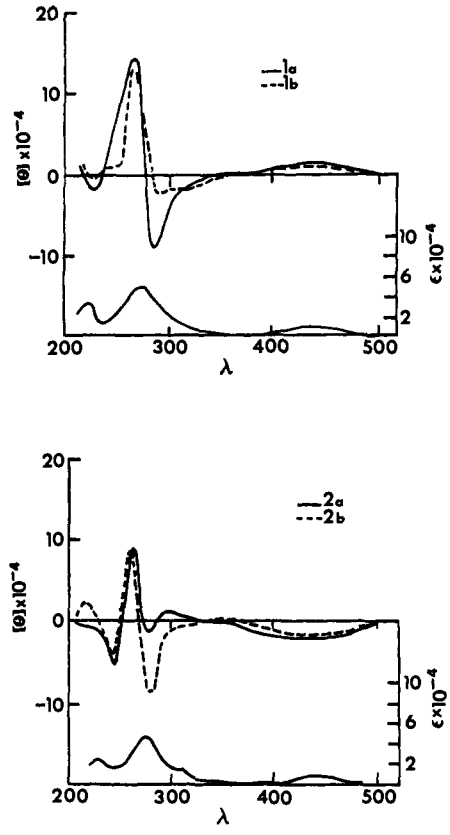

Figure 1. Circular dichroism spectra of **1a**, **1b**, **2a**, and **2b**.

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.

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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

routes to many cyclobutadiene–metal complexes.[1,2] This communication reports the first *intra*molecular cyclizations of macrocyclic diacetylenes in the presence of transition-metal derivatives. These unusual reactions give novel cyclopentadienylcobalt complexes of tricyclic cyclobutadiene derivatives.

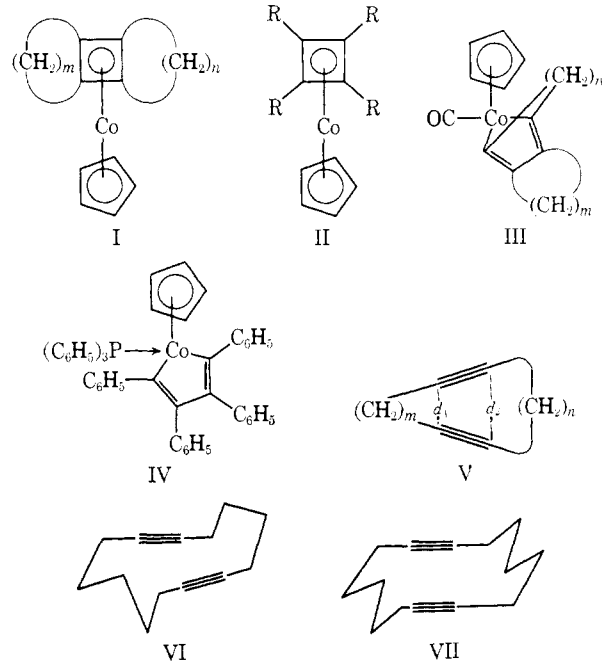
Reaction of equimolar quantities of cyclopentadienyldicarbonylcobalt and 1,7-cyclotridecadiyne in boiling *n*-octane for 17 hr gave a 65% yield of yellow crystalline monomeric $C_5H_5CoC_{13}H_{18}$, mp 75°, after isolation by chromatography in pentane solution on Florisil followed by sublimation at 65° (0.05 mm). *Anal.* Calcd for $C_{18}H_{23}Co$: C, 72.5; H, 7.8; Co, 19.8; mol wt, 298. Found: C, 72.9: H, 7.7; Co, 19.6; mol wt, 281 (vapor pressure osmometer in CH_2Cl_2 solution). The same compound could be obtained in 40% yield by the reaction of the 1,5-cyclooctadiene complex $C_5H_5CoC_8H_{12}$[3] with a 30% excess of 1,7-cyclotridecadiyne in boiling cyclooctane.

The infrared and proton nmr spectra were consistent with formulation of the cobalt complex $C_5H_5CoC_{18}H_{18}$ as the cyclobutadiene derivative I ($m = 4$, $n = 5$). The infrared spectrum showed no absorptions in the region 2200–1500 cm^{-1} where ν(CC) of various types of complexed and uncomplexed carbon–carbon multiple bonds might occur. In the region 1500–750 cm^{-1}, the infrared spectrum exhibited bands corresponding to those found in the similar complex $C_5H_5CoC_4H_4$ (II, R = H),[4,5] as well as additional absorptions around 1400 cm^{-1} arising from the δ(CH) of the nine methylene groups. The proton nmr spectrum ($CDCl_3$ solution) exhibited a sharp singlet C_5H_5 resonance at τ 5.52 and a broad resonance in the range τ 8.2–8.4 corresponding to the 18 CH_2 protons.

Similar reactions of the 14-membered ring macrocyclic diacetylene 1,8-cyclotetradecadiyne with the cyclopentadienylcobalt derivatives gave an analogous yellow monomeric complex $C_5H_5CoC_{14}H_{20}$ (I, $m = n = 5$), mp 103–105°, but in much lower yield (4% from $C_5H_5Co(CO)_2$ and 10% from $C_5H_5CoC_8H_{12}$) than was obtained for the preparation of $C_5H_5CoC_{13}H_{18}$ (I, $m = 4$; $n = 5$) from 1,7-cyclotridecadiyne. The intramolecular transannular cyclization of 1,8-cyclotetradecadiyne with $C_5H_5Co(CO)_2$ or $C_5H_5CoC_8H_{12}$ to form the substituted cyclobutadiene derivative $C_5H_5CoC_{14}H_{20}$ (I, $m = n = 5$) contrasts with the previously reported[6] intramolecular transannular cyclization of 1,8-cyclotetradecadiyne with $Fe(CO)_5$ to form the substituted π-cyclopentadienyl derivative $[C_{14}H_{19}Fe(CO)_2]_2$. This difference in behavior may be a consequence of the stability of the C_5H_5Co unit which, in order to achieve the favored 18-electron rare-gas configuration,[7] requires only four electrons, one less than the number donated by a neutral substituted π-cyclopentadienyl ligand.

The much higher yield in the formation of the substituted cyclobutadiene derivative of structure I from 1,7-cyclotridecadiyne than from 1,8-cyclotetradecadiyne is consistent with a cobaltacyclopentadiene (cobaltole) intermediate of type III analogous to the cobaltacyclopentadiene derivative $C_5H_5Co(C_6H_5C_2C_6H_5)_2P(C_6H_5)_3$ (IV) prepared by Yamazaki and Hagihara[8] and demonstrated by them to be an intermediate in the formation of the tetraphenylcyclobutadiene complex $C_5H_5CoC_4(C_6H_5)_4$ (II, R = C_6H_5). Formation of a cobaltacyclopentadiene derivative III from a macrocyclic diacetylene requires insertion of a cobalt atom between the pair of carbon atoms at one end of the carbon–carbon triple bonds and formation of a direct bond between the pair of carbon atoms at the other end of the carbon–carbon triple bonds. This type of process will take place most readily in a macrocyclic diacetylene V with relatively short minimum distances (d_1 and d_2 in V) between each pair of ends of the carbon–carbon triple bonds, but with one of these distances significantly longer than the other to accommodate the inserted cobalt atom. 1,7-Cyclotridecadiyne appears[9] to have a conformation (VI) meeting these requirements, whereas 1,8-cyclotetradecadiyne has a conformation (VII) with distances d_1 and d_2 (V) equivalent[9] and relatively long for facile carbon–carbon bond formation without extensive distortion. For this reason 1,7-cyclotridecadiyne can cyclize to form a cobaltacyclopentadiene intermediate more readily than 1,8-cyclotetradecadiyne.

This work demonstrates how subtle changes in the relative spatial orientations of the carbon–carbon triple bonds in macrocyclic di- and polyacetylenes can have significant effects on their reactions with transition-metal derivatives. Studies on reactions of transition-



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metal derivatives with such macrocyclic di- and polyacetylenes provide a novel means for investigating mechanisms of acetylene di- and oligomerizations; further studies of this type are in progress in this laboratory.

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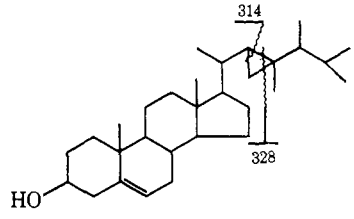
New Marine Sterol Possessing a Side Chain Cyclopropyl Group: 23-Demethylgorgosterol[1]

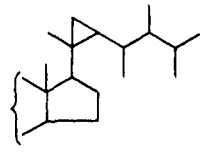
Sir:

A recent report[2] emanating from several laboratories showed that the marine sterol, gorgosterol,[3] possesses a biogenetically unprecedented side chain including the unusual features of carbon substitution at positions 22 and 23 and a cyclopropane ring located at either C-22,23 or C-20,22 as shown in **1** or **2**, respectively. An X-ray diffraction analysis[4] of 3β-bromogorgostene has subsequently shown that gorgosterol is (22*R*,23*R*,-24*R*) - 22,23 - methylene - 23,24 - dimethylcholest - 5 - en-3β-ol, in agreement with the nonstereochemical formula **1**. Discovery of the cyclopropane ring in gorgosterol was cited[2] as the first evidence in support of the postulate[5] that cyclopropanes may be intermediates in the introduction of methyl groups into the side chain of sterols, although it was also emphasized[2] that cyclopropanation might be only a terminal step in the biosynthesis of gorgosterol. We wish to report the isolation of a new marine sterol for which mass spectral and nmr data support a structure which includes a cyclopropane moiety bridging positions 22 and 23 of the sterol side chain but lacks the methyl group at C-23 present in gorgosterol.

The new sterol was isolated by gas-phase chromatography (2% OV-17)[6] from the complex mixture of sterols, including gorgosterol, extracted from either of the coelenterates *Gorgonia flabellum* L.[7a] or *G. ventilina* L.[7a,b] The recrystallized sterol, mp 162–163°, $C_{29}H_{48}O$ (high-resolution mass spectrometry[8]), exhibits a rotation, $[\alpha]^{21}D$ −34.5°, in the range characteristic of 3β-hydroxy-Δ^5-sterols.[9] A conventional C-19 steroid nucleus is indicated for this sterol by the series of peaks found at *m/e* 299–301, 271–273, 255–257, 231, 229, 217, 215, and 213 which are characteristic of the common sterols with an unsaturated side chain.[10] The presence of fragment ions at *m/e* 369 ($M^+ - C_3H_7$), 351 [$M^+ - (C_3H_7 + H_2O)$], and 341 ($M^+ - C_5H_{11}$) support the formulation of the terminal portion of the side chain as a $-CH(CH_3)CH(CH_3)_2$ moiety. The base peak in the mass spectrum of the new sterol is found at *m/e* 314 ($C_{22}H_{34}O$) and a second odd-electron fragment (relative intensity 32%) appears at *m/e* 328-($C_{23}H_{36}O$). The base peak in the spectrum of gorgosterol[2,11] also occurs at *m/e* 314 and is ascribed[2] to a cleavage of the cyclopropane ring as shown in **1**. Alternate fragmentation of the cyclopropane ring as shown in **1** would give rise to an *m/e* 328 ion. The occurrence of a *m/e* 328 peak in the spectrum of both gorgosterol,[11] **1**, and **3** coupled with the fact that nmr data (see below) exclude the C-20,22 positions for the cyclopropane ring in **3** leads us to conclude that the new C-29 sterol is 23-demethylgorgosterol.



1



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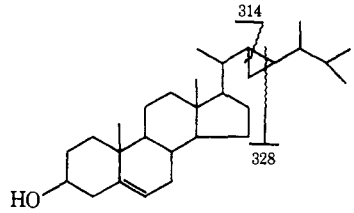

3

The two C-24 ethylidene sterols, fucosterol and Δ^5-avenasterol ($C_{29}H_{48}O$), would also be expected[10,12] to give rise to intense *m/e* 314 ions, but these sterols were excluded from structure considerations by nmr data (see below) and by the failure to obtain any low molecular weight carbonyl compounds upon attempted ozonolysis of the new sterol. Furthermore the infrared spectrum of **3** lacked the absorption bands at 12.14 and 12.30 μ characteristic of the 24-ethylidene sterols.[12]

The 220-MHz nmr spectrum[13] of **3** exhibits signals at δ 0.20 (2 H, distorted triplet,[14] $J \simeq 6$ cps), 0.28–0.41

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