Di(hex-5-enyl)mercury was prepared from the corresponding Grignard reagent and $HgCl_2$. The remaining hexenyl metal derivatives were then all prepared by the reaction of $Hg[(CH_2)_4CH=CH_2]_2$ with the respective metal in a sealed tube under the conditions indicated in Table I. The independent existence of the hexenyl metal derivative was not established in all cases, and, in fact, attempts to prepare tri(hex-5-enyl)aluminum indicated that only the cyclic product was detectable after exchange of aluminum for mercury.

All compounds were characterized by hydrolysis with 10% HCl–H_2O, which gave methylcyclopentane, and by their nmr spectra. In addition the Al and Li derivatives yielded $H_2C=(c\text{-}C_5H_8)$ on pyrolysis. These products were characterized by their nmr spectra. The formation of the cyclic mercury compound indicated in eq 4 was shown both by its nmr spectrum and by its mass spectrum.

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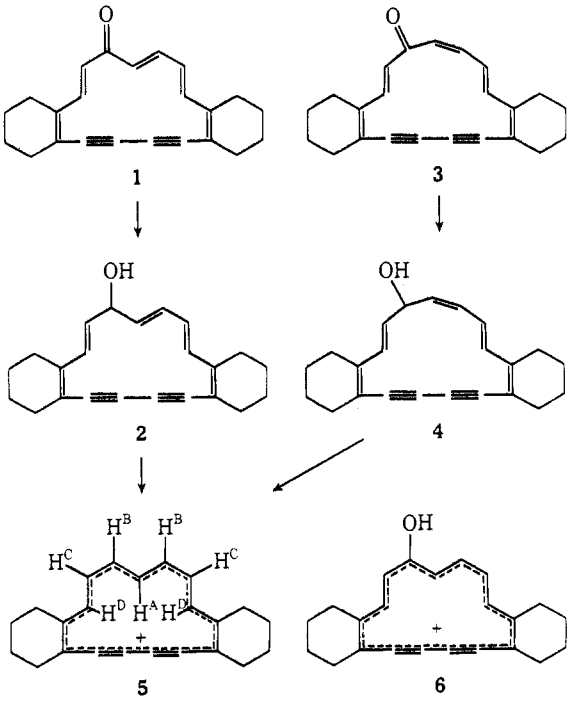
Synthesis of the 5,6:14,15-Bis(tetramethylene)-1,3-bisdehydro[15]annulenium Cation, an Aromatic 15-Membered Carbocyclic System[1]

Sir:

$(4n + 3)$-Membered conjugated carbocyclic cations contain $(4n + 2)$ π electrons and are therefore expected to be aromatic (diatropic),[2] provided they are reasonably coplanar. Well-known examples are the aromatic cyclopropenium ($n = 0$) and tropylium ($n = 1$) cations,[3] and recently some bridged derivatives of higher members ($n = 2, 3$) have been synthesized.[4] However, it has previously not been possible to prepare an unbridged macrocyclic annulenium cation. We now report the synthesis of the bisdehydro[15]annulenium cation **5** ($n = 3$) which, as expected, proved to be strongly diatropic.

Reduction of *all-trans*-4,5:10,11-bis(tetramethylene)-6,8-bisdehydro[15]annulenone (**1**)[5] in ether with ethanolic $NaBH_4$ for 2 hr at room temperature led to the orange-yellow alcohol **2**: λ_{max} (ether) 260 (ϵ 26,600), 269 (27,700), 285 sh (17,500), 354 (11,000), 375 sh (8300), 404 sh nm (2600).[6] Similar reduction of the mono-*cis*-bisdehydro[15]annulenone **3**[5] gave the lemon yellow alcohol **4**: λ_{max} (ether) 272 (ϵ 25,300), 283 sh (23,400), 312 sh (13,900), 340 sh nm (8600).[6] Both **2** and **4** were unstable substances which readily decomposed in the neat state at room temperature or on attempted chromatography on SiO_2 or Al_2O_3. Their structures were confirmed by the ir spectra (presence of OH bands, absence of C=O bands) and by oxidation in ether with MnO_2 to **1** and **3**, respectively, in high yield.

Several methods for converting **2** and **4** to the cation **5** were investigated. The best results were obtained by treatment of either **2** or **4** in the neat state with CF_3COOH or CF_3COOD at $\sim -78°$, followed by gradual warming to room temperature. Removal of the black insoluble polymer resulted in a deep violet solution of the trifluoroacetate of **5**: λ_{max} (CF_3COOH) 324 (ϵ 14,800), 387 (54,200), 550 sh (8400), 582 nm (22,200),[7] with absorption >700 nm. The structure of **5**, obtained from either **2** or **4**, follows unequivocally from the rather simple nmr spectrum (CF_3COOD, 100 MHz,



$-7°$[8]), which consisted of a 2 H double doublet at τ −0.31 (H^B; $J_{B,A}$ = 14, $J_{B,C}$ = 7.5 Hz), a 2 H double doublet at τ 0.13 (H^C; $J_{C,D}$ = 15, $J_{C,B}$ = 7.5 Hz), an 8 H multiplet at τ 5.65–6.05 (allylic CH_2), an 8 H multiplet at τ 7.3–7.7 (nonallylic CH_2), a 1 H triplet at τ 13.13 (H^A; $J_{A,B}$ = 14 Hz), and a 2 H doublet at τ 13.91 (H^D; $J_{D,C}$ = 15 Hz). Although the trifluoroacetate of **5** was relatively stable in CF_3COOH solution, it could not be isolated since decomposition occurred on removal of the solvent or on addition of water.

The nmr spectrum of **5** trifluoroacetate clearly shows the substance to be strongly diatropic, since the inner olefinic protons resonate at very high field and the outer olefinic, allylic, and nonallylic protons at low field (the downfield shift is much greater than could be explained by the positive charge). The diamagnetic ring current in the cation **5** is considerably greater than in **6** (obtained by protonation of **1** or **3** with CF_3COOH),[5] in which the inner olefinic protons resonate at τ 9.61–9.88, the outer olefinic protons at τ 0.37–1.49, the allylic protons at τ 6.2–6.8, and the nonallylic protons at τ

(1) Unsaturated Macrocyclic Compounds. XCVII. For part XCVI, see E. LeGoff and F. Sondheimer, *Angew. Chem.*, in press.
(2) See F. Sondheimer, *Accounts Chem. Res.*, 5, 81 (1972).
(3) See P. J. Garratt, "Aromaticity," McGraw-Hill, Maidenhead, Berkshire, England, 1971, Chapter 4.
(4) See E. Vogel, *Int. Congr. Pure Appl. Chem., 23rd, Suppl.*, 1, 275 (1971); H. Ogawa, M. Kubo, and H. Saikachi, *Tetrahedron Lett.*, 4859 (1971).
(5) P. D. Howes, E. LeGoff, and F. Sondheimer, *ibid.*, 3695 (1972).
(6) The ϵ values represent minimum ones due to the instability of the substance.
(7) Complete conversion of **2** and **4** to **5** has been assumed in calculating the ϵ values which represent minimum ones. The electronic spectrum of **5** derived from **2** was essentially identical with that derived from **4**, although some variations in ϵ values were naturally observed.
(8) The nmr spectrum at room temperature was essentially identical, but the lowest field band was obscured by the solvent peak.

7.3–7.9. This difference is presumably due to the fact that the nondelocalized O-protonated species is a contributor to the structure of **6**. The fact that the electronic spectrum of **5** is similar to that of **6** [λ_{max} (CF_3COOH) 375 (ϵ 66,700), 518 (15,200), 569 nm (25,700)], but bathochromically shifted by ~12 nm, is probably due to the same cause.

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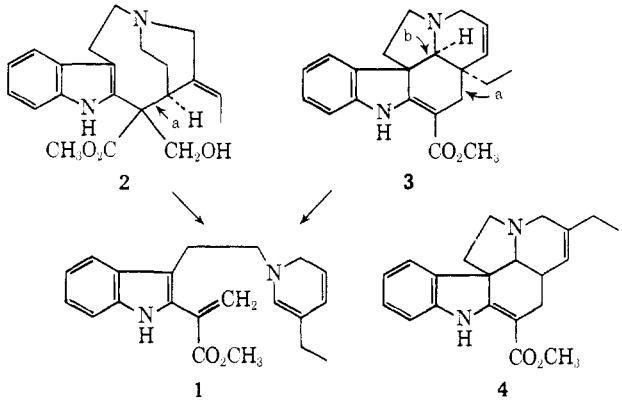
Regio- and Stereospecific Models for the Biosynthesis of the Indole Alkaloids. Prologue and Commentary

Sir:

In 1968 we proposed[1] a theoretical model for the enzymatic interconversions linking the *Corynanthe*, *Strychnos*, *Aspidosperma*, and *Iboga* alkaloids. Since the original disclosure of this hypothesis a large body of biochemical and structural evidence has accumulated[2] which supports in every detail the utilization of a dihydropyridine acrylic ester (**1**) as a highly reactive, pivotal biointermediate. This structure has since been named dehydrosecodine[3] and forms the nucleus of a new class of *chano* alkaloids corresponding formally



to the cleavage of the bonds marked a and b in stemmadenine (**2**) and tabersonine (**3**). The extended Mannich chemistry implicit in the formation and reactions of **1** not only bridges the major structural types of indole alkaloid but has also been employed in an elegant synthesis of *Aspidosperma* alkaloids.[4]

However, a discordant note in the proper and logical development of this field was sounded in 1969 by Smith, *et al.*,[5] who reported their inability to generate **1** from either **2** or **3** in hot acetic acid solution according to the general directions outlined[1b] in our preliminary note. In spite of extensive private communication in which the critical factors necessary for the success of these capricious but nevertheless authentic conversions were detailed to the best of our ability, the Anglo–French group elected to question the validity of our experiments. Thus there has arisen in the secondary literature[6] an erroneous impression that these transformations, which are of vital importance for the development of mechanistic models for the biosynthesis of indole alkaloids, cannot be effected. Due to the scarcity of the substrates **2** and **3** it has, until recently, been impossible for us to comment further except to note[7] that high external temperatures were efficacious. It should probably be pointed out that the manipulation of microgram quantities in biomimetic experiments is an art which, in our experience, has oft-times required *several hundred trials before declaring a negative result.*

The situation has now been resolved as a result of a series of expeditions to the tropical jungle in the state of Veracruz, Mexico, whereby a good source (*Stemmadenia Donnell-Smithii*) of stemmadenine (**2**) has become available after a 3-year interim. In the accompanying three communications we report on the complete vindication and extension of our original observations together with suggestions for the lack of corroboration elsewhere.[5,8]

Finally we are compelled to comment on what can only be described as an unfortunate breach of both the letter and spirit of scientific inquiry on the part of Smith, *et al.* For example Smith, *et al.*, state[5,8] that the reference compound used in all of their work to assay the extent of the conversions **2** or **3** → **1** is an amorphous levorotatory ($[\alpha]_D$ −60°) preparation to which they allude as pseudocatharanthine (**4**). In our hands (and in agreement with previous literature[9]) **4** is a crystalline racemic base ($[\alpha]_{300-600\ nm}$ 0°) and all of the products resulting from **1** are of course optically inactive. As will be seen from the accompanying communications, knowledge of the optical purity of the various preparations is a vital probe for the mechanisms in operation. Indeed, one of the most severe criticisms of our earlier work by Smith, *et al.*, concerned interconversion experiments with "pseudocatharanthine" ($[\alpha]_D$ −60°) to give[5] "catharanthine [(−) or (±)]. It is obvious from these statements that Smith, *et al.*, were utilizing mixtures of uncertain optical purity, thus formally vitiating many conclusions that can be drawn about their work. We would submit that in spite of the lack of explicit detail (occasioned by the then current scarcity of **2** and **3**) contained in our preliminary communication[1b] progress in this area of bioorganic chemistry has been unnecessarily hindered by the incontinent publication of these negative results.

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