hydrolyzed by the addition of water.[9] After complete hydrolysis, the reaction mixture was poured into 50 ml. of ice–water and the organic layer was separated. Gas chromatographic analysis of the organic phase on a silicone rubber column showed the presence of 88 mmoles (88%) of 1-hydro-2-chlorohexafluorocyclopentene, 4 mmoles (4%) of 1,2-dihydrohexafluorocyclopentene, and 4 mmoles (4%) of unreacted 1-chloroheptafluorocyclopentene. The 1-hydro-2-chlorohexafluorocyclopentene was isolated by fractionation in a 36-in. spinning-band column.

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(9) In this reaction only 4 mmoles of hydrogen (corrected to S.T.P.) was evolved on hydrolysis. In the reactions of the olefins containing the -CF=CF- and the -CCl=CCl- groupings, much larger amounts of hydrogen were generated on hydrolysis, and the addition of water should be carried out cautiously.

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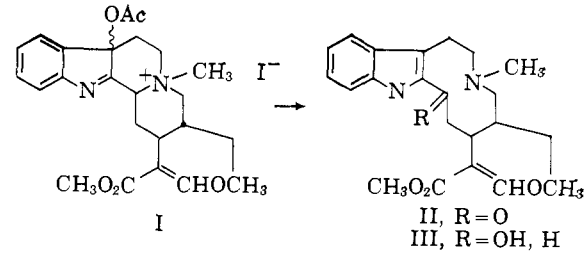
A New C–D Ring Cleavage of Dihydrocorynantheine Derivatives. The Partial Synthesis of the Dihydroburnamicine Ring System[1]

Sir:

Several examples of 2-acylindole alkaloids have recently been found and a 2-acylindole alkaloid has been suggested as an intermediate in the biogenesis of echitamine.[2–4] We wish to report a new C–D ring cleavage of dihydrocorynantheine which produces the 2-acylindole chromophore and has been used in the partial synthesis of dihydroburnamicine.

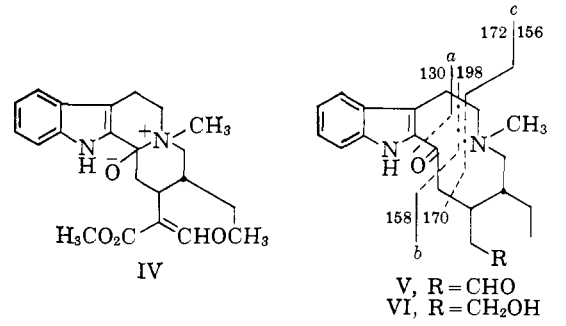
The action of lead tetraacetate in benzene solution transforms dihydrocorynantheine to the expected 7-acetoxy-7H-dihydrocorynantheine, m.p. 180–181°, in 23% yield based on unrecovered dihydrocorynantheine.[5] The acetoxyindolenine afforded the corresponding N_b-methiodide, I, m.p. 206° dec., upon exposure to methyl iodide. Hydrolysis of 7-acetoxy-7H-dihydrocorynantheine methiodide in refluxing aqueous acetic acid containing sodium acetate afforded in 55% yield the 2-acylindole compound II, obtained in two crystalline modifications from ether solution. One form melted at 153–155° (needles) and the other form (prisms) had m.p. 208–209°; they had identical infrared spectra in chloroform solution.

The structure of II is supported by the following observations. The ultraviolet spectrum in ether solutions shows normal 2-acylindole absorption [λ_{max}^{ether} 307 mμ (ε 14,800)] which was changed to normal indole absorption by the addition of acetic acid. In ethanol solution the compound shows only the absorption expected for a normal indole and α-methoxymethylenecarbonyl chromophores. This striking solvent effect



is ascribed to the formation of an ionic species such as IV in polar solvents. The infrared spectrum (chloroform solution) of II has a strong band at 1640 cm.$^{-1}$ consistent with the 2-acylindole structure. The n.m.r. spectrum of II exhibits a sharp signal at τ 8.36 attributed to the N-methyl group. That the N-methyl group should appear at such high field is not unexpected since the N-methyl group of protopine appears τ 8.08.[6] Compound III has a pK_a of 9.02 (50% aqueous methanol) which is very close to that reported for burnamicine.[2]

The 3-keto compound, III, was quite resistant to reduction with sodium borohydride in aqueous methanol. This inertness is ascribed to the formation of the ionic species IV in polar solvents. In accord with this hypothesis, II is smoothly reduced to the corresponding alcohol, III, m.p. 179–180°, in 1,2-dimethoxyethane. The alcohol shows the expected infrared and ultraviolet spectra and its n.m.r. spectrum shows the N-methyl group shifted downfield to τ 7.76.



Saponification and acid-catalyzed hydrolysis of the 2-acyindole III was accompanied by decarboxylation to give in 60% yield the ketoaldehyde V which was used without deliberate purification. The infrared spectrum in chloroform solution showed absorption at 1720 and 1640 cm.$^{-1}$. The ketoaldehyde was converted in 50% yield to dihydroburnamicine[7] VI by the action of sodium borohydride in aqueous methanol. The dihydroburnamicine obtained in this manner melted at 101–103° after crystallization from benzene. The crystalline material retains benzene which is shown by combustion analysis and its n.m.r. spectrum. The benzene is removed by extended drying at 80° under reduced pressure. The ultraviolet spectrum in ether shows 2-acylindole absorption [λ_{max} 307 mμ (ε 13,900)] changed to a normal indole spectrum upon addition of acetic acid. The ultraviolet spectrum in ethanol

(1) The authors gratefully acknowledge financial support from the National Science Foundation (Grant GP-252) and the National Institutes of Health (Grant NB 03232-03).

(2) M. F. Bartlett and W. I. Taylor, *J. Am. Chem. Soc.*, **85**, 1203 (1963).

(3) U. Renner, D. A. Prins, A. L. Burlingame, and K. Bieman, *Helv. Chim. Acta*, **46**, 2186 (1963); M. P. Cava, S. K. Talapatra, J. A. Weisbach, B. Douglas, and G. O. Dudek, *Tetrahedron Letters*, **No. 2**, 53 (1963).

(4) G. F. Smith, *Chem. Ind.* (London), 1120 (1961).

(5) N. Finch, C. Gemeden, I. Hsu, and W. I. Taylor, *J. Am. Chem. Soc.*, **85**, 1520 (1963).

(6) N. S. Bhacca, L. F. Johnson, and J. N. Shoolery, "NMR Spectra Catalog," Varian Associates, Palo Alto, Calif., 1962, No. 339.

(7) A direct comparison of our material with the reduction product of authentic burnamicine was not possible since no burnamicine remained from structural studies.[2] We wish to thank Dr. Taylor for a helpful discussion of this problem. It is not certain that dihydroburnamicine prepared from dihydrocorynantheine has the same absolute configuration at C-15 as authentic burnamicine but biogenetic considerations suggest that this should be the case.

appears to be a combination of indole and 2-acylindole chromophores: λ_{max} (mμ) 291 (ϵ 7230), 282 (8400), 274 (8120), and 220 (39,100), λ_{sh} 310 mμ (ϵ 2020). The infrared spectrum (chloroform solution) shows carbonyl absorption at 1640 cm.$^{-1}$ and the n.m.r. spectrum exhibits a sharp signal at τ 8.06 ascribed to the N-methyl group. Dihydroburnamicine has a pK_a of 9.02 (50% methanol–water) which is very close to that reported for burnamicine.[2]

The mass spectrum of dihydroburnamicine[8] provides further confirmation for the proposed structure. The parent mass peak at m/e = 328 was also the most intense line in the spectrum. The anticipated fragmentations along lines a, b, and c are those observed for burnamicine.[2] The expected fission along a gave medium intensity peaks at m/e = 128, 129, and 130 from the indole fragment. A medium intensity peak at m/e = 170 is considered to arise by cleavage along b and by loss of carbon monoxide (mass 28) from the fragment of mass 198 formed from fission along a. The peak at m/e = 170 thus corresponds to the strong peak at m/e = 168 in the mass spectrum of burnamicine. The second strongest peak in the spectrum, m/e = 143, and a peak at m/e = 144 correspond to the intense peaks at the same m/e in the mass spectrum of burnamicine and could have arisen as previously suggested for burnamicine. The mass spectrum of dihydroburnamicine also shows a peak at m/e = 310 which corresponds to the peak at m/e = 308 in the mass spectrum of burnamicine resulting from the loss of the elements of water in both cases.[2] The synthesis of other indole alkaloids from compound II is under investigation.[9]

(8) We are indebted to Dr. Taylor for the mass spectrum and his helpful interpretation.

(9) Satisfactory analytical data were obtained for all new compounds described in this communication.

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Viomycin. I. The Structure of Viomycidine

Sir:

On complete acid hydrolysis, the tuberculostatic *streptomyces* antibiotic viomycin[1] yields carbon dioxide, ammonia, urea L-serine, L-α,β-diaminopropionic acid,[1,2] L-β-lysine,[3,4] and a basic amino acid[1,2] which we have named viomycidine (I). Ion-exchange separation of viomycin hydrolysate followed by charcoal chromatography of the fraction containing strongly basic amino acids gave I as a crystalline hydrochloride, m.p. 200–208° dec., $[\alpha]^{30}D$ −78° (c 1.78, water). *Anal.* Calcd. for $C_6H_{10}O_2N_4 \cdot HCl$: C, 35.00; H, 5.36; O, 15.48; N, 27.65; Cl, 17.18. Found: C, 35.07; H, 5.31; O, 14.20; N, 27.49; Cl, 16.97. C-Methyl, O-methyl, N-methyl, and primary amino groups were shown to be absent. Viomycidine had pK_a values of 2.8, 5.87, and 13.4 (in 66% dimethylformamide) and 1.3 (estimated), 5.50, and 12.6 (in water)[5]; it gave positive Sakaguchi, Weber, and ninhydrin tests and negative Tollens, Benedict, and Benedict–Behre tests. Viomycidine hydrochloride showed strong infrared absorption at (μ) 2.98, 3.18, 3.50, 5.91, 6.06, 6.87, and 7.10, among others; it displayed only end absorption in the ultraviolet region. The n.m.r. spectrum of I-hydrochloride in deuterium oxide solution showed five nonexchangeable protons present. Absorptions were present at τ 4.37 (1H, triplet, J = 2.4 c.p.s.), 5.38 (2H, multiplet), and 7.43 (2H, triplet, J = 1.9 c.p.s.).

Guanidine was detected as a product of nitric acid oxidation of I; the strongly basic group present in I was assigned to a monosubstituted guanidine function because of the strongly positive Sakaguchi reaction. The nonguanidine nitrogen of I was characterized as an imine due to (i) its weakly basic nature, (ii) its differential ultraviolet spectrum (λ_{max} 212 mμ (ϵ 2530), pH 9.80 *vs.* 3.82),[5] characteristic of tertiary amines,[6] and (iii) a positive *o*-aminobenzaldehyde test.[7,8] I consumed 1 mole of hydrogen (platinum–acetic acid). Thus viomycidine contains a strongly acidic carboxyl group, a monosubstituted guanidine function, one reducible double bond, and, therefore, one ring. Because I is stable to vigorous acid hydrolysis, three- and four-membered rings containing nitrogen are excluded and I must contain a Δ^1-pyrroline ring.

Hydrolysis of I by hot barium hydroxide solution furnished nearly 3 moles of ammonia[10]; no other volatile base was formed. From the hydrolysate pyrrole-2-carboxylic acid[11] was isolated in 21% yield. Sodium hydroxide fusion of I gave 2-aminopyrimidine,[11,12] pyrrole-2-carboxylic acid,[11] and glycine[11,12]; no volatile base other than ammonia was formed. The products of alkaline hydrolysis of viomycidine place the carboxyl group at an α-position of the Δ^1-pyrroline nucleus.

The n.m.r. spectra of viomycidine and related compounds[13] indicate the absence of an olefinic-type proton in I.

(1) T. H. Haskell, S. A. Fusari, R. P. Frohardt, and Q. R. Bartz, *J. Am. Chem. Soc.*, **74**, 599 (1952).

(2) L. H. Mason, Ph.D. Thesis, University of Illinois, 1953.

(3) H. E. Carter, W. R. Hearn, E. M. Lansford, Jr., A. C. Page, Jr., N. P. Salzman, D. Shapiro, and W. R. Taylor, *J. Am. Chem. Soc.*, **74**, 3704 (1952).

(4) E. E. van Tamelen and E. E. Smissman, *ibid.*, **74**, 3713 (1952).

(5) We are grateful to Dr. Harold Boaz, Eli Lilly and Co., for obtaining these data.

(6) G. W. Stevenson and D. Williamson, *J. Am. Chem. Soc.*, **80**, 5943 (1958).

(7) W. B. Jakoby and J. Fredericks, *J. Biol. Chem.*, **234**, 2145 (1959).

(8) In this test, I showed λ_{max} 301 mμ. Δ^1-Pyrroline showed λ_{max} 288 mμ; 2-methyl-Δ^1-pyrroline-5-carboxylic acid[9] showed λ_{max} 296 mμ. Viomycidine and all imines and Δ^1-pyrrolines tested showed broad shoulders of low extinction in the region 420–480 mμ, responsible for the yellow color of the positive test.

(9) We are grateful to Dr. H. Gershon, Pfister Chemical Works, Inc., for a sample of this compound.

(10) Under these conditions arginine gives only 2 moles of ammonia.

(11) Identified by comparison with an authentic sample, melting point, mixture melting point, infrared, ultraviolet, and n.m.r. spectra, color reactions, and paper chromatographic behavior. The transformation of I into this substance and the structural inferences derived therefrom will be fully developed in the complete paper.

(12) The formation of 2-aminopyrimidine and glycine on base fusion is considered to proceed through a derivative of β-guanidopropionaldehyde, derivable from I by isomerization, ring opening, and cyclization.

(13) The n.m.r. spectrum of I in trifluoroacetic acid showed absorptions at τ 4.07 (1H), 5.05 (2H), and 7.23 (2H); guanidinium absorptions were present from τ 1.5 to 3.0. The n.m.r. spectrum of Δ^1-pyrroline in trifluoroacetic acid solution showed absorptions at τ 1.20 (position 2, 1H), 6.75 (position 3, 2H), 7.58 (position 4, 2H, quintet, J = 4.0 c.p.s.), and 5.73 (position 5, 2H); no absorption was present that might be assigned to the protonated imine. The olefinic proton of isobutylideneethylamine absorbs at τ 2.47 (neat liquid) and at 1.66 (trifluoroacetic acid solution); the olefinic proton of isobutylideneazine absorbs at τ 2.32 (neat liquid); the olefinic proton of 5,5-dimethyl-Δ^1-pyrroline absorbs at τ 3.1 (neat liquid).[14]

(14) R. Bonnett and D. E. McGreer, *Can. J. Chem.*, **40**, 177 (1962).