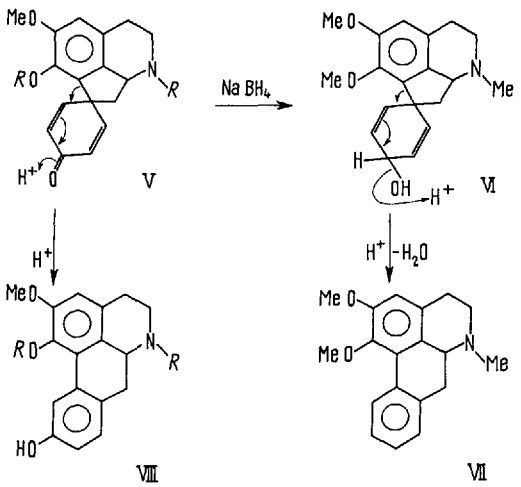
This evidence is capable of interpretation in terms of a cyclohexadienone structure for fugapavine (IV) similar to that put forward by BERNAUER[3] for pronuciferine (V, R=Me) from *Nelumbo nucifera* Gaertn., and by BARTON, KIRBY, HAYNES, and STUART[3,4] for crotonosine (V, R=H) and for Base A (pronuciferine) from *Croton linearis* Jacq. These latter alkaloids also show IR-peaks in the carbonyl region similar to fugapavine[3,4]; pronuciferin is reduced by sodium borohydride to an alcohol (VI)



which on dehydration gives the aporphine alkaloid nuciferin[3] (VII), while both pronuciferine and crotonosine on treatment with methanolic hydrochloric acid are isomerized to aporphines[4] which presumably have structures (VIII, R=H) and (VIII, R=Me) respectively. On this basis, fugapavine is (IV), and its conversion to isofugapavine (I, R=H), laureline (I, R=Me) and isoroemerine (II) takes place as shown.

The cyclodienone type of structure in (IV) and (V) was first suggested by BARTON and COHEN[5] as a hypothetical intermediate in the biosynthesis of aporphines from benzylisoquinoline alkaloids.

Zusammenfassung. Fugapavin, das Alkaloid von *Papaver fugax* aus Sowjetasien besitzt nach publizierten Eigenschaften und Reaktionen die pronuciferinartige Cyclohexadienonstruktur (IV) anstatt die ihm zugeschriebene Struktur (III).

I. R. C. BICK

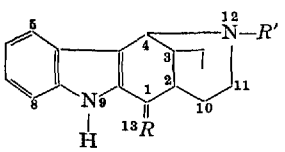
Chemistry Department, University of Tasmania, Hobart (Australia), February 25, 1964.

[3] K. BERNAUER, Helv. chim. Acta *46*, 1783 (1963).
[4] L. J. HAYNES and K. L. STUART, J. chem. Soc. *1963*, 1784, 1789. – L. J. HAYNES, K. L. STUART, D. H. R. BARTON, and G. W. KIRBY, Proc. chem. Soc. *1963*, 280.
[5] D. H. R. BARTON and T. COHEN, *Festschrift Arthur Stoll* (Birkhäuser, Basel 1957), p. 117.

The Structures of Five New *Aspidosperma* Alkaloids Related to Uleine[1]

Uleine (I), first isolated by SCHMUTZ et al.[2] from *Aspidosperma ulei* Mgf., is one of the most interesting indole alkaloids, since its skeleton[3] is devoid of the almost ubiquitous tryptamine bridge. In connection with our extensive survey[4] of the alkaloids of the genus *Aspidosperma*, we have become interested[5] in the chemistry of uleine as well as in uncovering 'missing links' in its biogenesis. In the present note we describe briefly the constitution of five new alkaloids related to uleine, which we have isolated from the (cork-covered) bark of *Aspidosperma dasycarpon* A. DC.[6].

Aside from the known alkaloids (+)-guatambuine[7], N-methyltetrahydroellipticine[7a,8] and uleine (I)[2,3] we have now isolated and identified the following new alkaloids: des-N-methyluleine (II), dasycarpidone (III), des-N-methyldasycarpidone (IV), dasycarpidol (V) and 1,13-dihydro-13-hydroxyuleine (VI). In all instances, the new alkaloids were characterized by ultraviolet, infrared, NMR and mass spectral measurements, the latter being



	R	R'
I	CH_2	CH_3
II	CH_2	H
III	O	CH_3
IV	O	H
V		CH_3
VI		CH_3

[1] Paper XLVII in the series *Alkaloid Studies*. For paper XLVI see K. S. BROWN JR. and C. DJERASSI, J. Am. chem. Soc. *86*, in press (1964).
[2] J. SCHMUTZ, F. HUNZIKER, and R. HIRT, Helv. chim. Acta *40*, 1189 (1957).
[3] G. BÜCHI and E. W. WARNHOFF, J. Am. chem. Soc. *81*, 4433 (1959).
[4] For first paper see B. GILBERT, L. D. ANTONACCIO, A. A. P. G. ARCHER, and C. DJERASSI, Exper. *16*, 61 (1960). For most recent communication see J. M. FERREIRA, B. GILBERT, R. J. OWELLEN, and C. DJERASSI, Exper. *19*, 585 (1963).
[5] J. A. JOULE and C. DJERASSI, J. chem. Soc., in press (1964).
[6] Collected by A. DUARTE and one of the authors (B.G.) in the Facenda da Mâe Dágua, Varzea da Palma Valley, Minas Gerais, through the cooperation of Dr. J. V. GONCALVEZ PINTO of the Belgo-Mineira Iron Company. This tree is used among others by the company for the production of charcoal.
[7] (a) J. SCHMUTZ and F. HUNZIKER, Helv. chim. Acta *41*, 288 (1958). – (b) M. A. ONDETTI and V. DEULOFEU, Tetrahedron Letters No. 7, 1 (1959) and Tetrahedron *15*, 160 (1961). – (c) P. CARVALHO-FERREIRA, G. B. MARINI-BETTOLO, and J. SCHMUTZ, Exper. *15*, 179 (1959).
[8] S. GOODWIN, A. F. SMITH, and E. C. HORNING, J. Am. chem. Soc. *81*, 1903 (1959). – R. B. WOODWARD, G. A. IACOBUCCI, and F. A. HOCHSTEIN, J. Am. chem. Soc. *81*, 4434 (1959).

especially characteristic[5] of the uleine skeleton. The molecular weights and hence empirical formulae were obtained by mass spectral measurements, where necessary (e.g. V and VI) by the direct inlet procedure[9].

Des-N-methyluleine (II) (m.p. 143–144°, $[\alpha]_D$ −20° (EtOH), mol. weight 252 = $C_{17}H_{20}N_2$) upon refluxing with methyl iodide in acetone-benzene for 30 min. provided uleine (I) methiodide (m.p. 196–198°), identified with an authentic sample, while treatment of the evaporated filtrate with alkali and crystallization from methanol gave authentic (+)-uleine (I).

The ketone dasycarpidone (III) was obtained in an amorphous state ($[\alpha]_D$ +65° ($CHCl_3$), $\lambda_{max}^{CHCl_3}$ 6.10 μ, λ_{max}^{EtOH} 237 mμ (log ε 4.15) and 316 mμ (log ε 4.29)[10], mol. weight 268 = $C_{17}H_{20}N_2O$) and its structure confirmed by careful low-temperature ozonolysis of uleine (I), which afforded III in ca. 15% yield. The lower homolog, des-N-methyldasycarpidone (IV) (m.p. 208–210°, $\lambda_{max}^{CHCl_3}$ 6.08 μ, same ultraviolet spectrum as III, mol. weight 254 = $C_{16}H_{18}N_2O$) was converted into dasycarpidone (III) by treatment with methyl iodide in the same manner as described above for the synthesis of uleine (I) from its des-N-methyl analog II.

The structure of dasycarpidol (V) (m.p. 118–122°, $[\alpha]_D$ −54° (EtOH), λ_{max}^{EtOH} 220 mμ (log ε 4.54), 282 mμ (log ε 3.89) and 290 mμ (log ε 3.81), no infrared carbonyl band, mol. weight 270 = $C_{17}H_{22}N_2O$) was indicated by the NMR spectrum, which contained all of the relevant signals[3,5] of uleine (I), except for the absence of the methylene proton signals and the presence of a one-proton doublet at 5.1 p.p.m. (J = 6 cps.) due to CHOH. Full confirmation was provided by oxidation with chromium trioxide in pyridine which afforded dasycarpidone (III).

The constitution of the amorphous 1,13-dihydro-13-hydroxyuleine (VI) ($[\alpha]_D$ −96°, λ_{max}^{EtOH} 221 mμ (log ε 4.56), 282 mμ (log ε 3.91) and 289 mμ (log ε 3.87), mol. weight 284 = $C_{18}H_{24}N_2O$) followed from the NMR spectrum, which was completely consistent with expression VI, and especially from its partial synthesis in 79% yield by hydroboration of uleine (I). The high yield and stereospecific course of the hydroboration reaction constitutes good evidence for the equatorial orientation of the hydroxymethyl substituent in VI.

The characterization of additional alkaloids from *Aspidosperma dasycarpon* A. DC. as well as the details and biogenetic implications of the presently outlined results will be reported in a full paper[11].

Zusammenfassung. Aus der Rinde des brasilianischen Baumes *Aspidosperma dasycarpon* A. DC. wurden fünf neue Alkaloide (II–VI) isoliert, die das selten vorkommende Uleinskelett besitzen. Die Strukturen wurden durch chemische Korrelation mit Ulein (I) sichergestellt.

M. OHASHI, J. A. JOULE,
B. GILBERT, and C. DJERASSI

Department of Chemistry, Stanford University, Stanford (California, USA) and Centro de Pesquisas de Produtos Naturais, Faculdade de Farmacia, Universidade do Brasil, Rio de Janeiro (Brazil), March 9, 1964.

[9] J. F. LYNCH, J. M. WILSON, H. BUDZIKIEWICZ, and C. DJERASSI, Exper. *19*, 211 (1963).

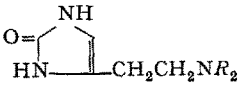
[10] For relevant infrared and ultraviolet data of 2-acylindoles, see J. A. BALLANTINE, C. B. BARRETT, R. J. S. BEER, B. G. BOGGIANO, S. EARDLEY, B. E. JENNINGS, and A. ROBERTSON, J. chem. Soc. *1957*, 2227.

[11] Financial support from the Rockefeller Foundation and the National Institutes of Health of the U.S. Public Health Service (grant No. GM 11309) is gratefully acknowledged, as are Fulbright travel grants to two of us (J.A.J. and M.O.).

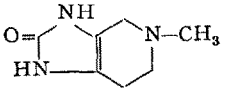
2-Imidazolone Analogues of Histamine

The problem of investigating the physiological activity of histamine is complicated by its spectacular peripheral effects which tend to mask any central function of the amine. In cooperation with a study designed mainly to elucidate the central effects of histamine and its derivatives[1] we sought to prepare analogues of histamine lacking in peripheral effects and which might be considered either as antimetabolites of histamine capable of crossing the blood-brain barrier or as hypothetical metabolites of this compound. It was considered that analogues of histamine which could be thought of as arising from a biological oxidative mechanism would be worthy of study.

4-β-aminoethyl-2-imidazolone hydrochloride, (I) m.p. 255° (prev. dec.) was obtained crystalline from ethanol by heating 1,4-diaminobutanone-2-dihydrochloride[2] with potassium cyanate in water as a thick syrup. The reaction product obtained in this way was contaminated with inorganic salts which were difficult to remove due to the amphoteric nature of the compound. Separation of I from inorganic material could be effected by forming the benzoyl derivative, m.p. 270–272° (MeOH) followed by acid hydrolysis (conc. HCl) to afford the imidazolone hydrochloride or preferably by conversion to the carbobenzyloxy derivative, m.p. 242–244° (EtOH) followed by hydrogenolysis.



I R = H; II R = Me



III

In an attempt to form 4-β-N,N-dimethylaminoethyl-2-imidazolone (II) by reductive alkylation of (I) with methanolic formaldehyde and hydrogen in the presence of a palladium-carbon catalyst, 5-methyl-4,5,6,7-tetrahydroimidazo (4,5,c)pyridin-2-one-hydrochloride (III) vac. m.p. 175° (EtOH), was obtained. The cyclic structure was demonstrated by the nuclear magnetic resonance spectrum which lacked the characteristic signal at 6.33

[1] L. GOLDSTEIN, C. C. PFEIFFER, and C. MUNOZ, Fed. Proc. *22*, 424 (1963).

[2] M. M. FRASER and R. A. RAPHAEL, J. chem. Soc. *1952*, 226.