

of a unified theory of aging at the molecular level bearing on a group of diverse processes involved in secondary aging seems highly improbable.

The distinction between primary and secondary aging is believed to be fruitful both in experimental design and in theoretical explorations of the problem of aging<sup>77</sup>.

**Zusammenfassung.** Der Begriff des primären Alterns wird neu eingeführt und gegen den des sekundären Alterns abgegrenzt. Wesentliches Kennzeichen des primären Alterns ist eine fortschreitende Abnahme der Stoffwechselkapazität. Experimente belegen die Abnahme der Photosyntheserate, der Atmungsaktivität, der allgemeinen Biosyntheseaktivität und der Anhäufung verschiedener Substanzen im Verlauf der Zellentwicklung. Die unmittelbare Ursache des primären Alterns sind Verschiebungen im Zusammenspiel der Enzymsysteme. Mit dem Altern der Zelle nimmt allgemein die anabolische Aktivität ab, während die katabolische Aktivität zunimmt. Im Zeitpunkt der Zellteilung werden diese Veränderungen rückläufig und die Zelle erhält wieder ihre ursprüngliche Stoffwechselintensität. In reiner Form tritt das primäre Altern bei sich nicht differenzierenden Zellen auf, so z. B. bei Mikroorganismen.

Bei Zellen mit Differenzierungsvermögen wird das primäre Altern von sekundärem Altern zunächst begleitet und dann vielleicht überlagert, was für Gewebe der vielzelligen Organismen typisch ist. Die Kennzeichen des sekundären Alterns sind komplex und können bei verschiedenen Organismen und auch bei verschiedenen Geweben desselben Organismus voneinander ausgesprochen abweichen. Vieles, was über das Altern vielzelliger Organismen bekannt ist, beruht im Grunde auf dem Phänomen einer «Übervölkerung». Daraus resultieren: Konkurrenz, Unterernährung und Schädigung der Zellen. Obgleich das sekundäre Altern auf endogen gesteuerten Eigenschaften der Zellen beruhen dürfte, ist die Situation im vielzelligen Organismus so komplex, dass sich dies schwer beweisen lässt. Bei der Untersuchung des Alterns vielzelliger Organismen erweist sich der Begriff des primären Alterns besonders insofern als nützlich, als er zur folgenden Regel führt: Jedes sekundäre Altern setzt ein primäres Altern voraus oder wird von einem solchen begleitet, jedenfalls aber von ihm beeinflusst.

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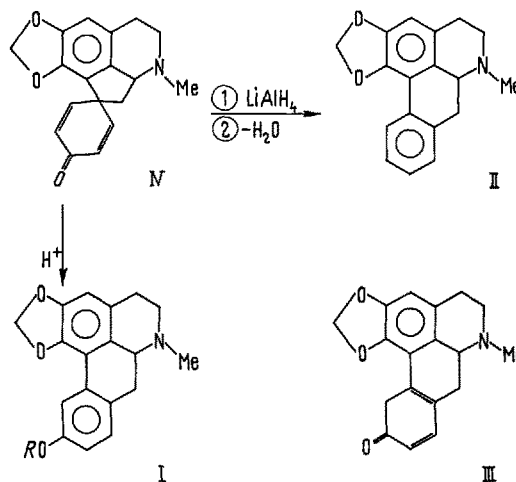
## Brèves communications – Kurze Mitteilungen – Brevi comunicazioni – Brief Reports

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### The Structure of Fugapavine

The alkaloid fugapavine was discovered by YUNUSOV, MNATSAKANYAN and AKRAMOV<sup>1</sup> in various parts of the plant *Papaver fugax* Poir. collected in the Armenian S.S.R. It was shown to have the formula  $C_{18}H_{17}O_3N$  with a methylenedioxy group and a tertiary nitrogen to which is attached a methyl group. The remaining oxygen atom was in a carbonyl group since the alkaloid gave a semicarbazone and an IR-absorption peak at  $1675\text{ cm}^{-1}$ ; the position of the latter also indicated that the carbonyl was conjugated with a double bond<sup>2</sup>. Hydrogenation with platinum black showed two double bonds to be present, and the hexahydro product had alcohol properties<sup>2</sup>.

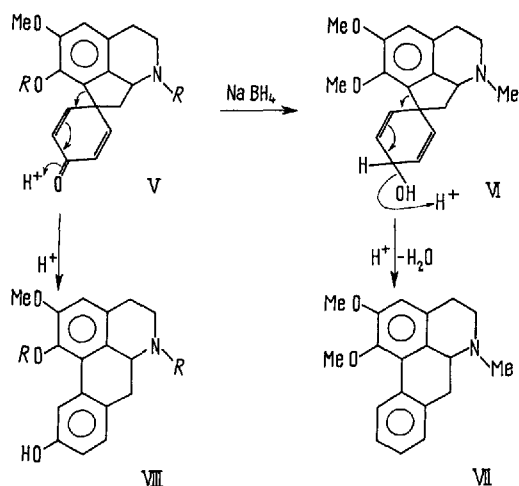
Fugapavine was shown, moreover, to be isomerized with mineral acid to a phenolic compound, isofugapavine (I,  $R=H$ ), which on methylation with diazomethane gave the dextro isomer of the known aporphine alkaloid laureline<sup>2</sup> (I,  $R=Me$ ). Furthermore, fugapavine could be reduced with lithium aluminium hydride to an alcohol which could be dehydrated to isoroemerine<sup>2</sup> (II), evidently a dimorphic form of roemerine<sup>1</sup>, and on the basis of this evidence the structure (III) was put forward for fugapavine<sup>2</sup>.



<sup>1</sup> S. YU. YUNUSOV, V. A. MNATSAKANYAN, and S. T. AKRAMOV, Doklady Acad. Nauk UzSSR No. 8, 43 (1961).

<sup>2</sup> V. A. MNATSAKANYAN and S. YU. YUNUSOV, Doklady Acad. Nauk UzSSR No. 12, 36 (1961).

This evidence is capable of interpretation in terms of a cyclohexadienone structure for fugapavine (IV) similar to that put forward by BERNAUER<sup>3</sup> for pronuciferine (V,  $R=Me$ ) from *Nelumbo nucifera* Gaertn., and by BARTON, KIRBY, HAYNES, and STUART<sup>3,4</sup> 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<sup>3,4</sup>; pronuciferin is reduced by sodium borohydride to an alcohol (VI)



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

The cyclodienone type of structure in (IV) and (V) was first suggested by BARTON and COHEN<sup>5</sup> as a hypothetical intermediate in the biosynthesis of aporphines from benzyloquinoline 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).

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

<sup>3</sup> K. BERNAUER, *Helv. chim. Acta* **46**, 1783 (1963).

<sup>4</sup> 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.

<sup>5</sup> 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<sup>1</sup>

Uleine (I), first isolated by SCHMUTZ et al.<sup>2</sup> from *Aspidosperma ulei* Mgf., is one of the most interesting indole alkaloids, since its skeleton<sup>3</sup> is devoid of the almost ubiquitous tryptamine bridge. In connection with our extensive survey<sup>4</sup> of the alkaloids of the genus *Aspidosperma*, we have become interested<sup>5</sup> 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.<sup>6</sup>

Aside from the known alkaloids (+)-guatambuine<sup>7</sup>, N-methyltetrahydroellipticine<sup>7a,8</sup> and uleine (I)<sup>2,3</sup> we have

now isolated and identified the following new alkaloids: des-N-methyluleine (II), dasycarpidone (III), des-N-methyladasycarpidone (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

<sup>1</sup> 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).

<sup>2</sup> J. SCHMUTZ, F. HUNZIKER, and R. HIRT, *Helv. chim. Acta* **40**, 1189 (1957).

<sup>3</sup> G. BÜCHI and E. W. WARNHOFF, *J. Am. chem. Soc.* **81**, 4433 (1959).

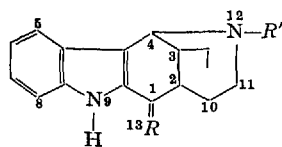
<sup>4</sup> For first paper see B. GILBERT, L. D. ANTONACCIO, A. A. P. G. ARCHER, and C. DJERASSI, *Exper.* **16**, 61 (1960). For most recent communication see J. M. FERREIRA, B. GILBERT, R. J. OWELLEN, and C. DJERASSI, *Exper.* **19**, 585 (1963).

<sup>5</sup> J. A. JOULE and C. DJERASSI, *J. chem. Soc.*, in press (1964).

<sup>6</sup> Collected by A. DUARTE and one of the authors (B.G.) in the Fazenda da Mãe D'água, Varzea da Palma Valley, Minas Gerais, through the cooperation of Dr. J. V. GONCALVES PINTO of the Belgo-Mineira Iron Company. This tree is used among others by the company for the production of charcoal.

<sup>7</sup> (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).

<sup>8</sup> 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).



|     | R                                              | R'              |
|-----|------------------------------------------------|-----------------|
| I   | CH <sub>2</sub>                                | CH <sub>3</sub> |
| II  | CH <sub>2</sub>                                | H               |
| III | O                                              | CH <sub>3</sub> |
| IV  | O                                              | H               |
| V   | $\begin{matrix} H \\   \\ OH \end{matrix}$     | CH <sub>3</sub> |
| VI  | $\begin{matrix} H \\   \\ CH_2OH \end{matrix}$ | CH <sub>3</sub> |