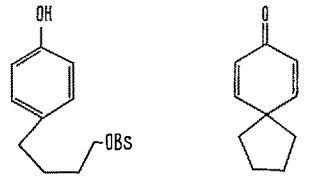
We have chosen to represent the formation of the spiro intermediate (5) from (3) by way of an anionic process, an intramolecular C-arylation of the chalcone by the phenolic ring-A, an Ar_1-3 mechanism in WINSTEIN's notation[11], analogous to the formation of (7) from (6)[12]. However, Ar_1 participation may equally well occur in a radical process[11] and the intermolecular C-arylation of chalcones by phenols has been reported to occur under acid-oxidizing[13] as well as alkaline conditions[14].



(6) (7)

The net effect of Scheme c is to generate the neoflavanoid skeleton from (3) by way of a single 1,3-aryl migration of the polyketide derived ring-A, rather than by the two 1,2-aryl migrations of the shikimate-prephenate derived ring-B previously considered.

The new hypothesis requires that [3-^{14}C] phenylalanine should lead to a neoflavanoid labelled specifically at C-4. In contrast to OLLIS's hypothesis, the dalbergiones are not visualized as precursors of the 4-arylcoumarins. An attractive feature of the new hypothesis is that is preserves a close biosynthetic relationship between the neo- and other flavanoids.

Discrimination between the biogenetic routes suggested by SESHADRI, by OLLIS, and that given here will have to await the results of further experiments.

Zusammenfassung. Eine neue Hypothese für die Biogenese der Neoflavanoide wird vorgeschlagen, indem dasselbe Chalkon als Zwischenstufe wie für die Flavanoide postuliert wird. Nach dieser Hypothese sollte sich nach Verabreichung von [3-^{14}C]-Phenylalanin die Markierung an C-4 des Neoflavanoids befinden, wie es beim Calophyllolid[6] tatsächlich der Fall ist.

M. H. BENN

Dyson Perrins Laboratory, South Parks Road, Oxford (England), 19 June 1967.

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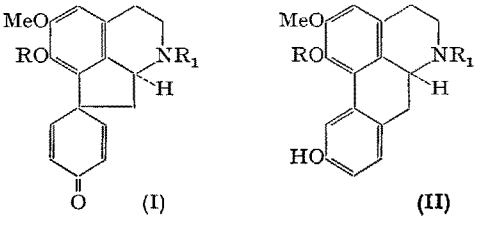
Crotsparine, a New Proaporphine Alkaloid from *Croton sparsiflorus* Morong

Reinvestigation of the alkaloids of *Croton sparsiflorus* Morong (N. O. Euphorbiaceae) has resulted in the isolation of a new proaporphine base ($C_{17}H_{17}NO_3$), m.p. 193–195 °C, $(\alpha)_D$ – 30° (c, 1.22 $CHCl_3$) from extracts of the whole plant and is now designated as crotsparine. Crotsparine is different to sparsiflorine[1], an amorphous base previously isolated from the same plant but a second base m.p. 125–127 °C, $C_{19}H_{21}NO_3$ isolated with crotsparine proved to be identical with pronuciferine[2–6] (IR- and mass-spectra).



(I) (II)

Crotsparine has been assigned the structure (I, $R = R_1 = H$). It is susceptible to aerial oxidation and forms a crystalline hydrochloride m.p. 278 °C (decomp.). The presence of a secondary >NH group and a bound -OH group in the crotsparine molecule is suggested by bands at 3490 and 2896 cm^{-1} respectively in its IR-spectrum and is confirmed by the formation of a *N,O*-diacetyl derivative, m.p. 185–186 °C. The IR-spectrum of this derivative also has absorption bands at 1772, 1260 (phenolic OAc), 1642 (amide) and at 1670 cm^{-1} (dienone C=O). Further, IR-bands in the spectrum of crotsparine at 1664 and 1624 cm^{-1} in conjunction with an UV-absorption maxima at 235 nm (log ε, 3.37) are indicative of a cross-conjugated dienone system[7]. The mass-spectrum of crotsparine shows a molecular ion peak (M^+) at m/e 283 and other prominent peaks are m/e 282, 254, 211, 165, 118 and 87. The NMR-spectrum of crotsparine is in agreement with the proposed formula (I, $R = R_1 = H$). Singlets at 3.40 (1 H), at 6.21 (3 H) τ and multiplets centred around 2.9 (2 H) and 3.6 (2 H) τ are due to an aromatic proton, an OMe group and 4 olefinic protons respectively.

N-methylation of crotsparine with formic acid-formaldehyde affords *N*-methyl crotsparine (I, $R_1 = Me$, $R = H$) ($C_{18}H_{19}NO_3$), m.p. 223–225 °C, $(\alpha)_D$ – 113° (c, 1.52 $CHCl_3$). The mass spectrum of this compound shows a molecular ion peak at m/e 297 and other significant peaks at m/e 296, 268, 254, 225, 165, 115 and 97. This fragmentation pattern is the same as has been observed for glaziovine[4]. The IR-spectrum of the *N*-methyl derivative still has a band at 2860 cm^{-1} (bonded OH) but the >NH band at 3490 cm^{-1}, which is present in the spectrum of crotsparine is absent. The dienone system is unaffected during methylation as the compound shows IR-absorption at 1672 cm^{-1}, an UV-maximum at 235 nm and the loss of 28 mass units in the mass spectrum.

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[7] D. H. R. BARTON and A. I. SCOTT, J. chem. Soc. 1767 (1958).

The NMR-spectrum of *N*-methylcrotsparine exhibited sharp singlets at 7.64 (3H), 6.17 (3H), 3.35 (1H) τ on account of a *N*-Me, OMe and one aromatic proton respectively. The 4 vinylic protons are responsible for the signals at 3.40–3.75 τ and 3.30–2.70 τ.

When treated with 3*N* hydrochloric acid, crotsparine is rearranged to apocrotsparine (II, R_1 = R = H) ($C_{17}H_{17}NO_3$). Apocrotsparine hydrochloride does not melt below 300 °C and maxima at 266, 276 and 305 nm (log ε, 1.02, 1.3, 0.9) in the UV-spectrum of apocrotsparine are characteristic of an aporphine oxygenated at position 3, 5 and 6[5,8]. Similarly, *N*-methyl crotsparine furnishes apo-*N*-methyl crotsparine (II, R_1 = Me, R = H) ($C_{18}H_{19}NO_3$), $(\alpha)_D$ + 30 °C (c, 0.2 $CHCl_3$) under acidic conditions. This compound is also obtained from apocrotsparine on treatment with formaldehyde-formic acid. The hydrochloride of this aporphine melts at 284–286 °C (decomp.). The UV-spectrum of the product is identical with that of 3,5-dihydroxy-6-methoxy aporphine[4,8] (II, R_1 = Me, R = H).

Direct comparison of the samples on thin layer chromatography established the identity of *N*-methylcrotsparine with that of glaziovine[4]. *N*-methyl crotsparine is, therefore, an enantiomer of glaziovine.

The proaporphine bases, crotonosine[5], glaziovine[4], pronuciferine[2], and stepharine[6] have positive rotation and D-configuration. The isomerized aporphines of these bases having the same configuration are laevorotatory. *N*-methylcrotsparine is laevorotatory and the isomerized aporphine is dextrorotatory. Crotsparine should, therefore, have the L-configuration.

It is of interest that *C. sparsiflorus* Morong collected around Calcutta (Eastern India), yielded crotsparine with negative rotation whereas the same plant collected in Lucknow (North-Central, India) gave crotsparine with positive rotation[9].

Zusammenfassung. Ein neues Proaporphin Alkaloid, Crotsparine genannt, wurde von *Croton sparsiflorus* Morong isoliert. Es wurde ihm die Formel (I, R = R_1 = H) angewiesen.

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Central Drug Research Institute, Lucknow (India), 26 June 1967.

[8] T. Kitamura, J. pharm. Soc. Japan *80*, 1104 (1960).

[9] We thank Dr. K. L. Stuart for samples of Crotonosine and Base A, Dr. G. Gilbert for a sample of glaziovine and Dr. R. S. Kapil for mass- and NMR-spectral determinations.

Flavomycoin, ein neues antifungales Polyenantibiotikum

Die soeben erschienene Arbeit über die Mycoticine A und B[1] veranlasst uns, einige Ergebnisse mitzuteilen, die wir bei der Untersuchung eines Antibiotikums desselben Strukturtyps, dem Flavomycoin, erhielten.

Flavomycoin ist in bestimmten Eigenschaften, wie der UV-Absorption, der gelbgrünen Farbe, der Luft- und Lichtempfindlichkeit sowie dem antibiotischen Verhalten (Tabelle) den Antibiotika Mycoticin[2] und Flavofungin[3] vergleichbar.

Flavomycoin wird von dem Streptomyces Stamm JA 5068[4] gebildet, der zur Species *Streptomyces roseoflavus* Arai, 1951 gehört, und aus dessen Mycel durch Extraktion mit Methanol gewonnen. Es kristallisiert aus wässrigem Alkohol in gelbgrünen Nadeln, die bei 161–163 °C schmelzen. Die spezifischen Drehungen wurden zu $[\alpha]_D^{23} = -45° \pm 2°$ ($c = 1$; Dioxan) und $[\alpha]_D^{23} = -4° \pm 2°$ ($c = 4$; Pyridin) bestimmt. Das IR-Spektrum (KBr-Pressling) zeigt Banden bei 750, 850, 940, 1010, 1100, 1235, 1440, 1580, 1620, 1705, 2940, 3020 und 3400 (breit) cm^{-1}. Massenspektrographisch wurde nach der Elektronenanlagerungsmethode[5] ein Molgewicht von 721 ermittelt, woraus nach den analytischen Daten die Bruttoformel $C_{41}H_{68}O_{10} \times 2H_2O$ resultiert.

Ber.: C = 65,05%, H = 9,58%, O = 25,36%

Gef.: C = 64,49%, H = 9,35%, O (Diff.) = 26,16%

Auf Grund der genannten Daten ist Flavomycoin von den Mycoticinen und von Flavofungin zu differenzieren und demzufolge ein neuer Vertreter dieser Antibiotikagruppe.

Bei der katalytischen Hydrierung in Eisessig über Adams-Katalysator nimmt das Antibiotikum fünf Mole Wasserstoff auf.

Flavomycoin absorbiert bei Raumtemperatur im UV mit 2 Maxima bei 262 und 363 nm ($E_{1cm}^{1\%}$ 150 bzw. 860).

Vorläufige Ergebnisse eines Vergleiches der antimikrobiellen Wirksamkeiten von Flavomycoin und Flavofungin[8] im Reihenverdünnungstest auf Agarplatten[9]

Testorganismen	Minimale Hemmkonzentration µg/ml	
	Flavomycoin	Flavofungin
E. coli SG 458[a]	> 125	> 125
B. subtilis ATCC 6633[a]	125	62
S. cerevisiae[b]	16	31
Hansenula anomala SG 908[b]	31	31
Candida albicans SG 916[b]	31	31
Candida albicans SG 942[b]	31	31
Candida krusei SG 937[b]	31	31
Candida tropicalis SG 938[b]	62	31
Aspergillus niger[b]	16	31
Trichophyton mentagrophytes var. interdigitale SG 955[b]	16	16
Microsporum gypseum SG 956[b]	16	16
Microsporum canis SG 959[b]	4	8

[a] auf Peptonagar; [b] auf Malzagar.

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