SCIADOLINE, A NEW TYPE OF BISBENZYLISOQUINOLINE ALKALOID

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Sciadoline, a new alkaloid from Sciadotenia toxifera Krukoff and A. C. Smith (Menispermaceae), has been assigned structure II. It is the first example of a head-to-tail bisbenzylisoquinoline base which contains a completely aromatic isoquinoline unit.

We recently reported the isolation of the new bisbenzylisoquinoline alkaloid sciadenine (I) from a countercurrent fraction of the bases from Sciadotenia toxifera Krukoff and A. C. Smith.[1] Another base fraction from this plant has now yielded the related new alkaloid sciadoline (II), the first example of a head-to-tail bisbenzylisoquinoline in which one of the head units is a completely aromatic isoquinoline system.

Sciadoline (II) crystallized from chloroform-acetone as colorless needles, mp 225-228° (decomp.), $[\alpha]_D^{22}$ = +46° (c = 0.46, $CHCl_3$). The mass spectrum of II indicates the composition $C_{36}H_{34}N_2O_6$, showing a strong molecular ion at m/e 590, and fragment ions at m/e 589 (base peak), 576, 575, 483, 296, 295.5, 295, 204 and 190. The nmr spectrum of II ($CDCl_3$) showed one N-methyl at δ 2.35 (3 H) and three methoxyls at 3.55 (3 H), 3.83 (3 H) and 4.02 (3 H). In the aromatic region, two pyridine-type protons appeared as a low-field

AB quartet (J = 5.5 Hz) centered at 7.48 and 8.40, in addition to a one-proton singlet at δ 7.05 and nine additional protons in the range δ 5.50—6.85. The uv absorption spectrum of II showed maxima (log ε) at 275 (3.94) and 335 nm (3.78), and shoulders at 283 (3.88) and 326 nm (3.77); the spectrum resembles that of the simple isoquinoline alkaloid crykonisine (III).[2] The isoquinoline chromophore of II shows a marked bathochromic shift not only in acid (323 and 368 nm) but also in base (300 and 373 nm), indicating the presence of a phenolic hydroxyl in the isoquinoline nucleus. Acetic anhydride in pyridine effected acetylation of this hydroxyl with the formation of the O-monoacetate (IV), mp 236-237°, ir (KBr) 5.57 μ, mass spectrum m/e 632 (M^+, base peak). No deuterium was introduced into II by D_2O under basic conditions, showing that no aromatic proton is present ortho to the phenolic function.[3]

Reaction of II with excess diazoethane afforded O-ethylsciadoline (V), mp 192-194° (decomp.), m/e 618 (M^+, base peak). Reductive cleavage of V with sodium in liquid ammonia gave, as the only isolable product, R-armepavine (VI), identical with an authentic sample.[4]

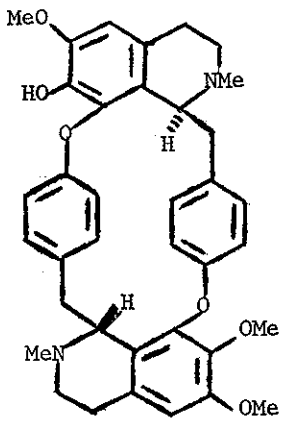
The results described above lead to the assignment of structure II to sciadoline, which is therefore a more highly unsaturated analog of its companion alkaloid sciadenine (I). Sciadoline is also the first example of a head-to-tail bisbenzylisoquinoline alkaloid which contains a fully aromatic isoquinoline system. A head-to-head bisbenzylisoquinoline structure containing an aromatic isoquinoline unit has been proposed for the alkaloid thalfine.[5]

Nmr Values (δ, $CDCl_3$) for Sciadoline and Its Derivatives

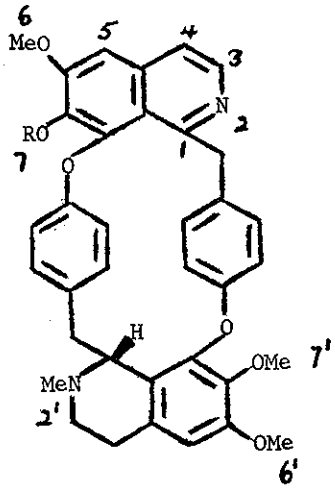
Compound	II	IV	V	VII
C_3-H [a]	8.40	8.55	8.41	8.48
C_4-H [a]	7.48	7.55	7.47	7.48
C_5-H [b]	7.05	7.10	7.02	7.03
Aromatic protons [c]	5.50∿6.85	5.58∿6.92	5.55∿6.85	5.54∿6.80
C_6-OMe [b]	4.02	3.93	3.90	3.95
C_7-OR	—	1.82 (MeCO) [b]	0.98 (CH_3CH_2) [d]	3.63 (Me) [b]
C_6'-OMe [b]	3.83	3.84	3.80	3.83
C_7'-OMe [b]	3.55	3.55	3.53	3.57
C_2'-NMe [b]	2.35	2.43	2.40	2.42

a: doublet, J = 5.5∿6.0 Hz, b: singlet, c: multiplet

d: triplet, J = 7 Hz



I

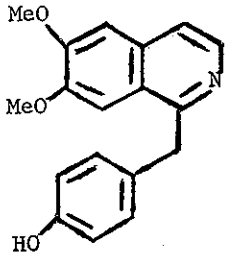


II R = H

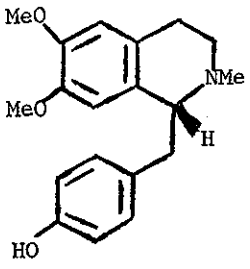
IV R = Ac

V R = Et

VII R = Me



III



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