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SCIADOLINE, A NEW TYPE OF BISBENZYLISOQUINOLINE ALKALOID

Keiichi Takahashi and Michael P. Cava*

Department of Chemistry, University of Pennsylvania

Philadelphia, Pennsylvania 19174, U. S. A.

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.), $[\alpha]_D^{22} = +46^\circ$ (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)

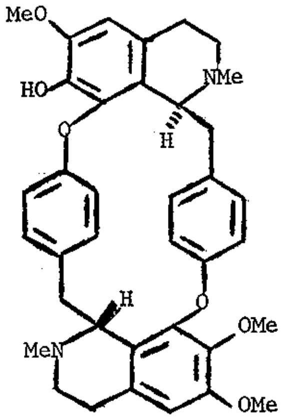
The results described above lead to the assignment of structure II to sciadoline, which is therefore a more highly unsaturated analog of its companion alkaloid sciadenine (I). Sciadoline is also the first example of a head-to-tail bisbenzylisoquinoline alkaloid which contains a fully aromatic isoquinoline 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

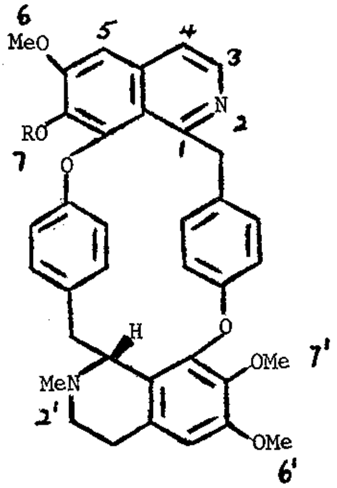
Compound	II	IV	V	VII
C_3-H [a]	8.40	8.55	8.41	8.48
C_4-H [a]	7.48	7.55	7.47	7.48
C_5-H [b]	7.05	7.10	7.02	7.03
Aromatic protons [c]	5.50∼6.85	5.58∼6.92	5.55∼6.85	5.54∼6.80
C_6-OMe [b]	4.02	3.93	3.90	3.95
C_7-OR	—	1.82 ($\underline{\mathrm{Me}}\mathrm{CO}$)[b]	0.98 ($\mathrm{C}\underline{\mathrm{H}_3}\mathrm{CH_2}$)[d]	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

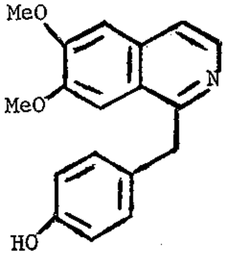


II R = H

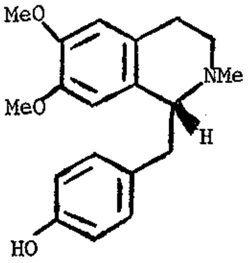
IV R = Ac

V R = Et

VII R = Me



III



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