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WITHASOMNINE. A PYRAZOLE ALKALOID FROM *WITHANIA SOMNIFERA* DUN.*

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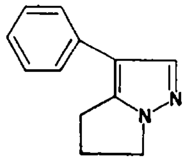
Abstract—The pyrazole alkaloid (I) has been isolated from the roots of *Withania somnifera* Dun. (*Solanaceae*), which are used medicinally in India. The structure was deduced by physical methods.

Withania somnifera Dun. (*Solanaceae*) is indigenous to the Mediterranean region, in South Africa and in India; the plant is also cultivated, and used medicinally.[1] Schwarting *et al.*[2] have investigated thoroughly the alkaloids of various types.

We isolated from the roots of plants grown in Halle a crystalline base which was not identical with any of the *Withania* alkaloids yet described. The base has been named Withasomnine and from its IR, UV, NMR and mass spectra and pK value, we propose that it is 4-phenyl-1,5-trimethylenepyrazole (I).



I

We believe that the sole pyrazole derivative previously found in the higher plants is β-1-pyrazolylalanine, described by Noe and Fowden[3] from *Cucurbitaceae* species.

Withasomnine gives a red colour with Munier's reagent. It does not react with hydrogen iodide and cannot be acetylated. Withasomnine hydrochloride absorbs hydrogen very slowly over a platinum oxide catalyst; the UV spectrum thereby undergoes a hypsochromic shift to λ_{max} 241 mμ.

The IR spectrum (Fig. 1) showed aromatic (ν3000 cm^{-1}) and aliphatic (ν2900 cm^{-1}) CH in the CH-stretching region. A mono-substituted benzene ring was indicated by bands at 1610, 1505, 770, 690 cm^{-1}. Further bands at 1570 and 1420 cm^{-1} suggested the presence of conjugated C=N and CH_2 respectively.

The NMR spectrum (Fig. 2) in carbon tetrachloride showed bands at 2·41, singlet (1H); 2·75, singlet (5H); 5·99, triplet J = 6·0 c/s (2H); and *ca.* 7·20, multiplet (4H). In benzene, the multiplet was partially resolved into a triplet, (lower field), and a pentuplet. Assignments are given in (II).

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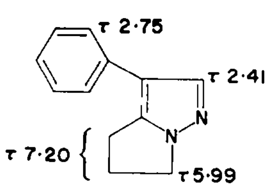
* Applications of Proton Resonance Spectroscopy, Part XXV. For Part XXIV see A. R. Katritzky and J. Musierowicz, *J. Chem. Soc.*, in press.

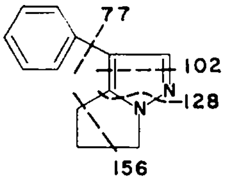
[1] C. K. Atal and A. E. Schwarting, *Econ. Bot.* **15**, 256 (1961).

[2] A. E. Schwarting, J. M. Bobbitt, A. Rother, C. K. Atal, K. L. Khanna, J. D. Leary and W. G. Walter, *Lloydia* **26**, 258 (1963).

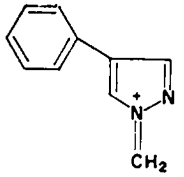
[3] F. F. Noe and L. Fowden, *Nature* **184**, 69 (1959).



II



III



IV

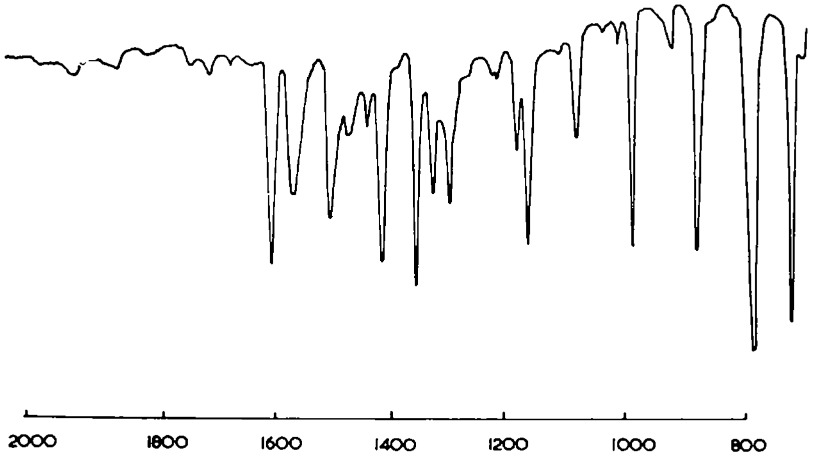


FIG. 1. IR Spectrum of Withasomnine.

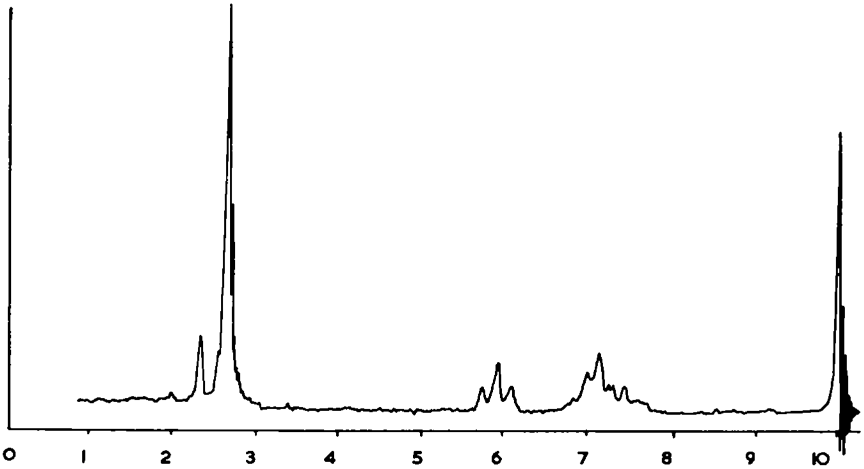


FIG. 2. NMR Spectrum of Withasomnine, in CCl_4.

The mass spectrum confirms the cryoscopically determined molecular weight as 184. The fragmentation scheme is given in III. The fragment of mass 156 probably is formed by the reaction I → IV, and this was supported by the appearance of metastable peaks at 105 and 80.

The pK_a value was determined spectrophotometrically as 2·01 ± 0·04 (cf. N-methylpyrazole, pK_a 2·04[4]).

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[4] G. Dedichen, *Ber.*, 39, 1831 (1906).

EXPERIMENTAL

M.ps are corrected.

Spectroscopic measurements. UV spectra were determined with a UVispek spectrophotometer in EtOH. IR spectra were determined on a Unicam SP 200 spectrophotometer in KBr disc or nujol mull. The mass spectrum was measured on an Atlas mass spectrometer CH4; oven ion source TO4, electron energy 70 eV. NMR spectra were determined on a Perkin-Elmer 40 Mc/s permanent magnet spectrometer with sample spinning; $SiMe_4$ was used as an internal standard and peaks measured in ppm on the τ scale.

Extraction and purification. Ground roots (15 kg) which had been grown under controlled conditions at Halle, were first extracted with pet. ether, then dampened with aq ammonia, and finally exhaustively extracted with ether. The ether was evaporated and the residue taken up in MeOH. This crude extract was run through a cation-exchange resin (Wofatit KPS in the H^+ form). MeOH was then evaporated and the residue fractionated on Al_2O_3 (Riedel de Haen, Grade II activity). Elution was carried out with solvents of gradually increasing polarity. From the pet. ether/ether fraction, repeated recrystallization from pet. ether gave *Withasomnine* (440 mg) m.p. 117–118°, $[\alpha]^D_{20°}$ 0° ($c = 5$, $CHCl_3$), (Found: C, 78·2; H, 6·6; N, 15·2; M, 184 (micro Rast). $C_{12}H_{12}N_2$ requires C, 78·2; H, 6·5; N, 15·2%; M, 184). The base was homogeneous on paper and thin-layer chromatography.

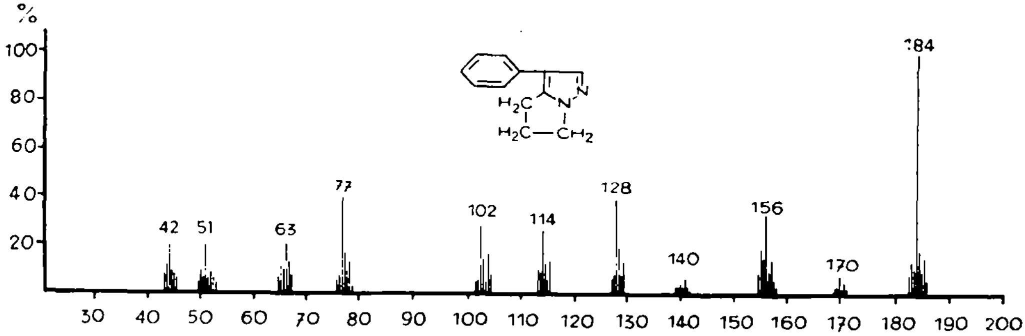

FIG. 3. Mass Spectrum of Withasomnine.

The *picrate* (prepared in $CHCl_3$) had m.p. 170–173° (from water), The very hygroscopic *hydrochloride* (prepared in ether with anhydrous HCl) had m.p. 115–117° (dried *in vacuo*). The *aurichloride* had m.p. 203° (from water).

Paper chromatography was carried out: (a) circular on filter paper impregnated with borate buffer at pH 7·8, developed with n-butanol saturated with water, $R_f = 0{\cdot}98$; (b) ascending, isopropanol/HCl/water (62:22:12), $R_f = 0{\cdot}8$; (c) descending, n-butanol saturated with water, $R_f = 0{\cdot}8$.

Thin-layer chromatography was carried out on Stahl's Silica G (Merck): EtOH/25% ammonia (8:2), $R_f = 0{\cdot}9$; EtOH/formic acid (8:2), $R_f = 0{\cdot}95$; pet. ether/n-propanol (95:5), $R_f = 0{\cdot}3$.

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