

A NEW PENTASUBSTITUTED APORPHINE:
(+)-N-METHYLDANGUYELLINES. FAZAL HUSSAIN,¹ M. TARIQ SIDDIQUI,¹ HÉLÈNE GUINAUDEAU,² and MAURICE SHAMMA*

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ABSTRACT.—*Thalictrum pedunculatum* of Pakistan origin has yielded the aporphine (+)-N-methyldanguyelline (1). The firm assignment of ¹H-nmr chemical shifts to this alkaloid has allowed for the definition of the structure of the previously known (+)-danguyelline (2).

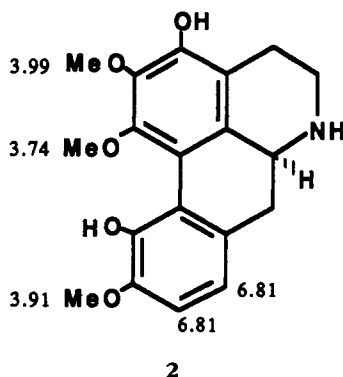
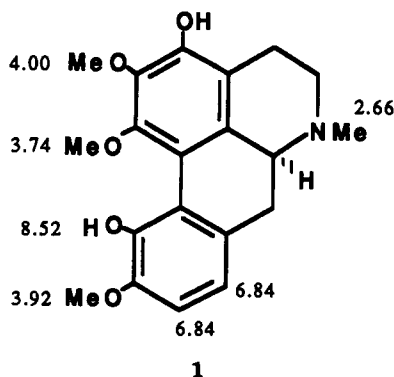
Thalictrum pedunculatum Edgew. (Ranunculaceae) is an herbaceous plant native to northern Pakistan. We are presently studying the alkaloidal content of the whole plant, an endeavor that has resulted in the isolation of the new aporphine (+)-N-methyldanguyelline [1]. This was accompanied by the aporphines (+)-norconovine, (+)-conovine, (+)-thalicsimidine, and (+)-isocorydine (1), the proaporphine (+)-pronuciferine, and the benzylisoquinoline (+)-reticuline.

The diphenolic (+)-N-methyldanguyelline [1], C₂₀H₂₃NO₅, displayed a mass spectrum with a molecular ion *m/z* 357 and base peak *m/z* 342 [M - Me]⁺. The uv spectrum, with λ max (MeOH) 219, 277, and 312 sh nm (log ε 4.40, 4.02, and 3.72), showed a strong bathochromic shift and an hyperchromic effect

in basic solution, suggesting the presence of a phenolic function.

The ¹H-nmr spectrum at 200 MHz in CDCl₃ solution indicated an N-methyl singlet at δ 2.66 and three methoxyls at δ 3.74, 3.92, and 4.00. The aromatic region included only a two-proton singlet at δ 6.84. There was also a very sharp downfield phenolic proton singlet at δ 8.52 that disappeared upon addition of D₂O.

The two-proton singlet at δ 6.84 is diagnostic of C-10, 11 substitution in an aporphine, with a phenolic group at C-11. To ascertain this point, the nmr spectrum was rerun first in DMSO-*d*₆, and then in DMSO-*d*₆/NaOD. In neutral medium, H-8 and H-9 appeared as two doublets, at δ 6.80 and 6.83, *J*_o = 8.1 Hz. After addition of NaOD, the H-8 signal had shifted to δ 5.82,



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while H-9 was at δ 6.31. This upfield shift of almost 1 ppm for H-8 indicated its *para* relationship to the phenolic group (2,3).

The upfield methoxyl singlet at δ

3.74 can be safely assigned to C-1 (2,3). In order to place with certainty the remaining three aromatic substituents, a detailed nmr NOE study was carried out. Irradiation of H-9 (δ 6.84) led to enhancement of the 10-OMe singlet (δ 3.92). Irradiation of the 1-OMe singlet (δ 3.74) affected the C-11 phenolic singlet (δ 8.52) as well as the 2-OMe (δ 4.00). In all of these instances, reciprocating enhancements were also observed. It follows that the second phenolic group must be located at C-3.

An important conclusion at this stage is that for 1,2,3-trisubstituted aporphines with a phenol at C-3 and methoxyls at C-1 and C-2, the 2-methoxyl signal will appear near δ 4.00. However, in the alternate situation, where the phenol is at C-2 and the methoxyls are at C-1 and C-3, the 3-methoxyl signal is found near δ 3.92.

The above observation now allows us to settle conclusively the structure of (+)-danguyelline. Originally it was suggested that the phenolic group of this pentasubstituted aporphine could be either at C-2 or C-3 (4). Since the downfield methoxyl signal in (+)-danguyelline is at δ 3.99, this substituent should be located at C-2, and the phenol at C-3. Thus, the complete structure and ^1H nmr chemical shift assignments for this alkaloid are given in structure 2.

EXPERIMENTAL

PLANT MATERIAL.—*T. pedunculatum* was col-

lected in Azad Kashmir in northern Pakistan, in July 1987. Specimen samples, identified by S. Farooq, Botanist, PCSIR Laboratories, Peshawar, were deposited in the herbarium of the PCSIR and at the National Herbarium in Islamabad. The whole plant (7.5 kg) was dried, powdered, and extracted with EtOH at room temperature. The solvent was removed in vacuo. The dried extract was taken up in 5% HCl, filtered, basified with NH_4OH and extracted with CHCl_3 . The organic extract was chromatographed on a column of Si gel (Merck) using a $\text{CHCl}_3/\text{MeOH}$ gradient. The fractions were monitored by tlc. Further purification was obtained by preparative tlc in $\text{C}_6\text{H}_6\text{-MeOH}$ (95:5) and NH_3 vapor. The alkaloids isolated were (+)-norconovine (2.5 mg), (+)-conovine (109 mg), (+)-thalicimidine (27.5 mg), (+)-isocorydine (72 mg), (+)-*N*-methyl-danguyelline (13 mg), (+)-pronuciferine (1.3 mg), and (+)-reticuline (9.8 mg). The known alkaloids were identified by uv, ^1H -nmr and mass spectra, and specific rotations.

(+)-*N*-METHYLDANGUYELLINE [1].— $\text{C}_{20}\text{H}_{23}\text{NO}_5$; eims $[M]^+$ 357 (60), 342 (100), 340 (37); 326 (61), 311 (13), 310 (13); $[\alpha]_D^{+96}$ ($c = 0.25$, CHCl_3).

ACKNOWLEDGMENTS

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