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DELPHIRINE, A NEW ALKALOID FROM DELPHINIUM STAPHISAGRIA L.

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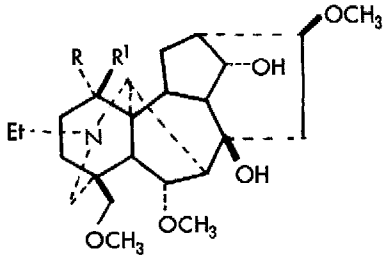
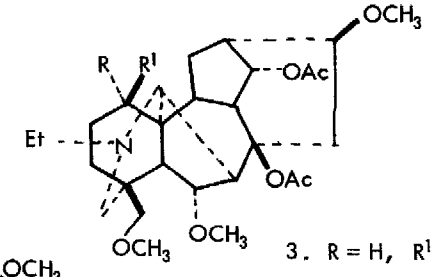
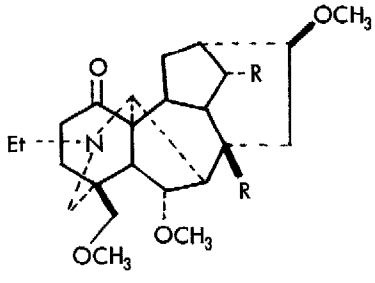
The seeds of Delphinium staphisagria L. on extraction with ligroin yield an alkaloid fraction of which delphinine[1] is the major component. The mother liquors accumulated during the isolation of a large quantity of delphinine, furnished an amorphous fraction which yielded delphisine,[2] delphidine[3] and several novel bis-diterpenoid alkaloids.[4-6] Further examination of the amorphous fraction by a combination of gradient pH separation technique, column chromatography and crystallization from benzene resulted in the isolation of delphirine, $C_{24}H_{39}NO_6$, mp 95-100°, $[\alpha]^{26}$ D + 3.8 (c 1.0, abs. EtOH). In this communication, we wish to report the structure of delphirine as 1. Except for talatizidine,[7] delphirine represents the only example of a C_{19} diterpenoid alkaloid possessing a 1β-OH function.



1. R = H, R^1 = OH
2. R = OH, R^1 = H



3. R = H, R^1 = OH
4. R = OH, R^1 = H



5. R = OAc
6. R = OH

Delphirine was obtained as a colorless crystalline material from the $CHCl_3$ extract of the bases at pH 10.5 by column chromatography and crystallization from benzene. It showed IR (KBr) bands at 3430 (OH), 1480, 1440, 1425, 1125 and 1100 (C-O) cm^{-1}. The ^1H NMR (100 MHz) spectrum of delphirine in $CDCl_3$ gave signals at δ 1.06 (3H triplet, J = 7 Hz, N-CH_2-CH_3), 3.32 and 3.38 (3H singlet and 6H

singlet, respectively, C-6, C-16 and C-18 OCH_3), 3.62 (1H broad multiplet, $W_{H/2}$ = 6H, C-1α H), 4.15 (1H doublet of doublets, J_1 = 1 Hz, J_2 = 7 Hz, C-6β H), and 4.26 (1 H doublet of doublets, $J_1 = J_2$ = 4.5 Hz, C-14β H) ppm. The ^{13}C NMR spectrum of delphirine resembles that of neoline (2)[7] except for the chemical shifts of carbons in ring A and C-19. The shifts of the carbons of ring A and of C-19 resemble those of 1-epidelphisine (3).[7] The above spectral characteristics of delphirine suggested its structure to be 1-epineoline which was confirmed by chemical correlation with neoline in the following way: Oxidation of delphisine (4) by Cornforth reagent gave 1-ketodelphisine (5) which upon alkaline hydrolysis afforded 1-ketoneoline (6). The latter when reduced with $NaBH_4$ gave a mixture of neoline (20%) and 1-epineoline (60%).[2] Comparison of delphirine with epineoline (IR, ^1H and ^{13}C NMR, TLC) proved identity. Because delphirine has been related to delphisine, the absolute configuration derived for delphisine by X-ray analysis[8] also applies to delphirine, except for the configuration at C-1.

It is interesting to note that delphirine reacts very slowly with Draggendorf's reagent giving a precipitate after several minutes while neoline reacts instantly with this reagent. The C-1-OH group in neoline has been shown[2] to be hydrogen bonded with the N-atom which requires ring A to be in the boat form. The C-1α-OH group in delphirine on the other hand cannot form a hydrogen bond with the N-atom in any conformation of ring A. The reduced basicity of the N-atom of delphirine (pK_a = 6.7) compared with that of neoline (pK_a = 7.6) is the reverse of what would be expected from the hydrogen bonding argument.[9] It appears that the difference in the basicity of delphirine and neoline is due to the orientation of the C-1-OH (β or α) group and the conformation of ring A. Further work in this area is in progress.

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9. A referee cites the case of the cinchona alkaloids where, when the OH and an amino group are suitably disposed, internal hydrogen bonding, possibly with participation of solvent molecule(s), stabilizes the conjugate acid form and thereby confers greater basicity on the corresponding base.