STRUCTURES OF MONTRIFOLINE AND DELBINE: TWO NEW FUROQUINOLINE ALKALOIDS FROM MONNIERIA TRIFOLIA L.

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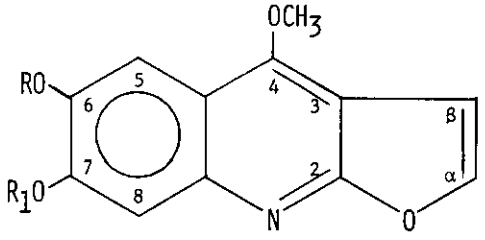
Abstract: Two novel furoquinoline alkaloids were isolated from Monnieria trifolia and their structures were determined on the basis of spectral characteristics and chemical transformation.

Monnieria trifolia L. (N.O. Rutaceae) popularly known as "Alfavaca-de-cobra", is a herb which grows throughout northeastern Brazil. The leaves of M. trifolia has been used in the popular medicine as a febrifuge, diaphoratic, antipyretic and antiinflammatory agent[2]. The well known rutaceous alkaloids, arborinine[3], skimmianine[4], and dictamnine[5] have been reported earlier from this plant. The basic fraction of the hexane extract of the leaves of M, trifolia, upon column chromatography, TLC and crystallization yielded two new alkaloids, montrifoline, $C_{18}H_{21}NO_6$ (M^+ 347), mp 191-193° and delbine, $C_{13}H_{11}NO_4$ (M^+ 245)[6], mp 229-231°, in addition to the alkaloids already reported. In this communication, we wish to report the structures of montrifoline and delbine as (1) and (2) respectively, based on spectral evidence and chemical transformation. Although a C_5-unit attached at various positions of the ring system has been encountered rather frequently in furoquinolines[7], montrifoline represents the first example of the occurrence of such an unit at C-6.



(1) R = $-CH_2CH(OH)C(OH)(CH_3)_2$; R_1 = CH_3

(2) R = H; R_1 = CH_3

(3) R = CH_3; R_1 = $-CH_2CH(OH)C(OH)(CH_3)_2$

(4) R = R_1 = CH_3

(5) R = CH_3; R_1 = H

The UV spectrum of montrifoline in methanol showed λ max (log ε) at 244(4.68), 252(4.73), 309(3.99), 321(3.99), and 333(3.82)nm. The IR spectrum of montrifoline in KBr showed peaks at 3350(OH), 3130(Ar-H), 1630, 1590(Ar), 1268, 1210, 845 and 820cm^{-1}. The UV and the IR spectra of montrifoline are typical[8,9] of furoquinolines, in general, and of kokusaginine, in particular. In addition to the molecular ion peak at 347, the MS of montrifoline showed important fragmentations at m/e 332 (M-15), 304(M-43), 288(M-59), 258(M-89), and the parent peak at 245(M-102) characteristic of furoquinolines having a $OCH_2CH(OH)C(OH)(CH_3)_2$ moiety.

The ^{1}H NMR spectrum of montrifoline in DMSO-d_6 with TMS as internal standard showed signals at 1.26(6H, s, broadened at the top, two C-CH_3), 3.96(3H, s, Ar-OCH_3) and 4.46(3H, s, Ar-OCH_3), two characteristic proton doublets at 7.28(1H, J=3Hz) and 7.82(1H, J=3Hz) and two para aromatic proton singlets at 7.28 and 7.53 ppm. The spectrum also showed multiplets which integrated for two protons around 4,30 and for one proton around 4,00 ppm overlapped by the two singlets for two OCH_3 groups. The proton doublets at 7.28 and 7.82 ppm are characteristic of α and β furan protons as in the furo(2,3-b)quinoline system. The OCH_3 signal at 4.46 ppm is certainly due to the C-4-OCH_3 in furoquinoline system as in dictamnine[10]. Therefore, all the above evidence can only by accomodated in the alternative structures (1) and (3) for montrifoline. However, (3) represents evolatine[11], an alkaloid isolated from the Australian Rutaceous plant Evodia alata. Evolatine has properties similar but not same with those of montrifoline. Therefore, montrifoline should be represented by (1). The structure of montrifoline was confirmed by its chemical transformation to delbine (vide infra).

The UV absorption maxima of delbine in methanol showed λ max (log ε) at 241 (4.17), 250 (4.19), 310 (3.51), 326 (3.50), 336 (3.88) nm. The IR spectrum in KBr showed important peaks at 3400-3100 (broad, OH), 3165 (Ar-H), 1623, 1585 (Ar), 1265, 1210, 1088, 1080, 865 and 850 cm^{-1} indicative of a furoquinoline system.

The MS of delbine showed, in addition to the molecular ion peak at m/e 245 (100%) significant fragments at m/e 230 (M-15) and 202(M-43), characteristic of the furoquinoline alkaloids[12]. The ^{1}H NMR spectrum of delbine in DMSO-d_6 with TMS as internal standard showed signals at 3.95(3H, s, Ar-OCH_3) and 4.37(3H, s, Ar-OCH_3), two typical doublets at 7.32(1H, J=3Hz) and 7.90(1H J=3Hz) for the α and β furan protons of the furo(2,3-b)quinoline system, two para aromatic proton singlets at 7.29 and 7.48 and a broad signal at 9.60 ppm for a OH proton which disappeared upon addition of D_2O. Methylation of delbine with CH_2N_2 gave 6,7-di-

methoxydictamnine (kokusaginine, 4). As the downfield OCH_3 signal at 4.37 ppm is definitely due to C-4-OCH_3[10], delbine must be either 6-hydroxy-7-methoxydictamnine (2) or 7-hydroxy-6-methoxydictamnine (5). The later compound (5), heliparvifoline (lit. mp 245-47°) was isolated[13] from a South American Rutaceae plant, Helietta parvifolia and it was also prepared[11] from evolatine by alkaline fusion. Delbine was found to be quite different (mp, TLC and IR) from heliparvifoline and the mmp[14] was depressed. Also, alkaline fusion of montrifoline gave delbine under identical condition in which evolatine furnished heliparvifoline[11]. Therefore, delbine must be represented by (2) and, consequently, montrifoline must have structure (1).

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14. Determined with an authentic sample of heliparvifoline supplied generously by Dr. G.A. Cordell, Professor of Pharmacognosy, Department of Pharmacognosy and Pharmacology, University of Illinois at the Medical Center, Chicago, Illinois, 60612, U.S.A., which is gratefully acknowledged.

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