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Furoquinoline Alkaloids from the Leaves of *Melicope confusa*

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Abstract□In addition to the previous reported furoquinoline alkaloids, skimmianine, kokusaginine and confusameline, a rare furoquinoline alkaloid, heliparvifoline, mp 241-3°, was isolated from the leaves of *Melicope confusa* and characterized by spectral data.

Keywords□*Melicope confusa*, Rutaceae, Furoquinoline alkaloid, Skimmianine, Kokusaginine, Confusameline, Heliparvifoline.

This paper describes the results of our investigation on the furoquinoline alkaloids of *Melicope confusa* (Rutaceae), which is distributed in Taiwan.

Recrystallization of the alkaloidal fraction from the methanol extract afforded the major alkaloid as stout plates, mp 177-8°, which was identified as skimmianine (I) by direct comparison with an authentic sample.[1] The mother liquor was subjected to SiO_2 column chromatography eluting with benzene-ether mixture to give kokusaginine (II), mp 170°, confusameline (III), mp 250-2°, which were identified by comparison of their physical and spectral data with those appeared in literature,[2] and a minor alkaloid (IV), which has not been reported in this plant.

The minor compound (IV) crystallized from methanol to afford stout plates, mp 241-3°, exhibited a maximum peak at 248nm with fine bands in the region of 301-337 nm in uv spectrum which were shifted to a longer wavelength accompanied by loss of fine structure in acidic medium, typical of a furo [2,3-b] quinoline system in its structure.[3] Its ir spectrum also showed peaks for furan ring system at 3160, 3130 and 1096 cm^{-1}[4] which was supported by the presence of two sets of doublets at δ7.89 (J=2.8Hz) and 7.36 (J=2.8Hz) for furan protons[5] in its nmr spectrum. A methoxy signal at δ4.40 suggested the presence of 4-methoxy group[5] which was also supported by the intense peaks for M^+-15 and M^+-43 ions at *m/z* 230 and 202[6], respectively. Another methoxy signal singlet at δ3.90 and two singlets at δ7.42 and 7.16 indicated that 6 and 7 positions were oxygenated and one of them was methylated, which was supported by the fact that methylation of IV with CH_2N_2 afforded kokusaginine (II). In the presence of a drop each of D_2O and NaOD, the downfield proton (H-5) was shifted from δ7.42 to 7.33, while the upfield proton (H-8) was shifted from δ7.16 to 7.01. Thus, the hydroxyl group should be located at 7-position adjacent to the proton resonating at δ7.16. From the above facts and by comparison of its physical and spectral data with those appeared in literature[7], compound IV was identified as heliparvifoline, which has only been isolated from *Helietta parvifolia*.

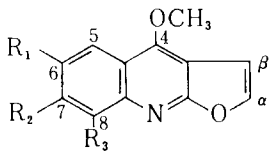
EXPERIMENTAL METHODS

The mps were taken on a Mitamura-Riken apparatus and are uncorrected. The ir spectra were determined in KBr tablets on a Perkin-Elmer model 283B spectrophotometer and the uv spectra were runned with Gilford System 2600 spectrophotometer. The nmr spectra were recorded at 80MHz on a Varian FT-80A with TMS as internal standard. Mass spectra were taken a Hewlett-Packard 5985B GC/MS spectrometer operating at 70eV.

Isolation of Alkaloids

Powdered leaves (650g) were extracted with MeOH and the MeOH extract was partitioned with 3% acetic acid and ether. The aqueous layer was basified with c-NH_4OH and exhaustively extracted with $CHCl_3$. The combined $CHCl_3$ extracts was recrystallized from MeOH to give skimmianine (I) (4.8g) as stout needles. The mother liquor was chromatographed over SiO_2 column eluting with benzene-ether mixture (9:1, 7:1, 5:1 and then 4:1) to yield kokusaginie (II), skimmianine (I), confusameline (III) and then heliparvifoline (IV) in the order

of elution.



I $R_1 = H$, $R_2 = R_3 = OCH_3$

II $R_1 = R_2 = OCH_3$, $R_3 = H$

III $R_1 = R_3 = H$, $R_2 = OH$

IV $R_1 = OCH_3$, $R_2 = OH$, $R_3 = H$

Skimmianine (I)

mp 177-8° [Lit.[1] mp 177-8°]

UV λ_{max}^{MeOH} nm (log ε); 242(sh, 4.66), 250(4.81), 305(sh, 3.69), 321(3.86), 333(3.88), 344(sh, 3.76); $\lambda_{max}^{MeOH+HCl}$ nm (log ε); 254(4.77), 322(3.85), 351(3.90).

IR ν_{max}^{KBr} cm^{-1}; 3150, 3121(furan), 1619(C=C), 1269(ether), 1093(=COC). NMR($CDCl_3$, TMS)δ; 4.02(3H, s, OCH_3), 4.11(3H, s, OCH_3), 4.42(3H, s, 4-OCH_3), 6.99(1H, d, J=2.8Hz, furan ß-H), 7.18(1H, d, J=9.5Hz, H-6), 7.53(1H, d, J=2.8Hz, furan α-H), 7.97(1H, d, J=9.5Hz, H-5).

MS, *m/z*(rel. int).: 259(M^+, 34.6), 248(M^+-H, 13.6), 244(M^+-CH_3, 100), 230(M^+-HCO, 65.4), 216[M^+-(CH_3+CO) 31.9], 201(216-CH_3, 51.3), 200(230-CH_2O, 16,8), 199 (200-H, 18.3), 188(216-CO, 4.7), 184(199-CH_3, 13.6), 173 (201-CO, 29.8), 158(173-CH_3, 8.4), 130(158-CO, 27.7).

Kokusaginine (II)

mp 170° [Lit.[2] mp 166-7°].

UV λ_{max}^{MeOH} nm (log ε); 246(4.85), 253(4.86), 298(4.04), 309(4.16), 321(4.14), 336(4.00); $\lambda_{max}^{MeOH+HCl}$ nm (log ε); 247(sh, 4.74), 252(4.77), 338(4.28).

IR ν_{max}^{KBr} cm^{-1}; 3160, 3125, 3075(furan), 1626(C=C), 1254 (ether), 1090(=COC).

UV λ_{max}^{MeOH} nm (log ε); 246(4.85), 253(4.86), 298(4.04), 309(4.16), 321(4.14), 336(4.00); $\lambda_{max}^{MeOH-HCl}$ nm (log ε); 247 (sh, 4.74), 252(4.77), 338(4.28).

NMR(DMSO-d_6, TMS)δ; 3.89(3H, s, OCH_3), 3.92(3H, s, OCH_3), 4.42(3H, s, 4-OCH_3), 7.26(1H, s, H-8), 7.40(1H, d, J=2.8Hz, furan ß-H), 7.42(1H, s, H-5), 7.93(1H, d, J=2.8Hz, furan α-H); ($CDCl_3$, TMS)δ; 4.02(6H, s, 2×OCH_3), 4.43(3H, s, 4-OCH_3), 7.03(1H, d, J=2.8Hz, furan ß-H), 7.34(1H, s, H-8), 7.48(1H, s, H-5), 7.56(1H, d, J=2.8Hz, furan α-H).

MS, *m/z* (rel. int.); 259(M^+, 100), 244(M^+-CH_3, 87.8), 216(244-CO, 36.8), 201(216-CH_3, 44.7), 188(216-CO, 15.4), 186(216-CH_2O, 49.3), 173(201-CO, 23.0), 158(173-CH_3, 7.6), 130(158-CO, 17.3).

Confusameline (III)

mp 250-2° [Lit.[2] mp 239-240°]

UV λ_{max}^{MeOH} nm (log ε); 238(sh, 4.76), 246(4.86), 299(3.93), 312(4.02), 327(3.99), 338(3.94); $\lambda_{max}^{MeOH+HCl}$ nm (log ε); 240(sh, 4.68), 246(4.76), 319(4.08), 339(4.12).

IR ν_{max}^{KBr} cm^{-1}; 3160, 3125(furan), 1626(C=C), 1090 (=COC).

NMR(DMSO-d_6, TMS) δ; 4.40 (3H, s, 4-OCH_3), 7.03(1H, dd, 1=2.4 and 9.0Hz, H-6), 7.11 (1H, d, J=2.4Hz, H-8), 7.37 (1H, d, J=2.8Hz, furan ß-H), 7.90(1H, d, J=2.8Hz, furan α-H), 8.06(1H,d, J=9.0Hz, H-5), 10.04 (OH).

MS, *m/z*(rel. int.); 215(M^+, 100), 200(M^+-CH_3, 42.1), 172 (200-CO, 25.6), 144(172-CO, 12.8).

Heliparvifoline (IV)

mp 241-3° [Lit.[7] mp 245-7°]

UV λ_{max}^{MeOH} nm (log ε); 248(4.87), 301(4.01), 313(4.16), 323 (4.18), 337(4.11); $\lambda_{max}^{MeOH+HCl}$ nm (log ε); 246(sh, 4.74), 251 (4.76), 334(4.32), 343(4.36).

IR ν_{max}^{KBr} cm^{-1}; 3160, 3130(furan), 1626(C=C), 1268 (ether), 1096(=COC).

NMR(DMSO-d_6, TMS) δ; 3.90(3H, s, 6-OCH_3), 4.40(3H, s, 4-OCH_3), 7.16(1H, s, H-8), 7.36(1H, d, J=2.8Hz, furan ß-H), 7.42(1H, s, H-5), 7.89(1H, d, J=2.8Hz, furan α-H); (DMSO-d_6 + D_2O + NaOD)δ; 3.87(3H, s, 6-OCH_3), 4.38 (3H, s, 4-OCH_3), 7.01(1H, s, H-8), 7.30(1H, d, J=2.8Hz, furan ß-H), 7.33(1H, s, H-5), 7.78(1H, d, J=2.8Hz, furan α-H).

MS, *m/z* (rel. int.); 245(M^+, 100), 230(M^+-CH_3, 94.5), 215(230-CH_3, 9.3), 202(230-CO, 30.5), 187(202-CH_3, 13.1), 172(202-CH_2O, 25.4), 159(187-CO, 11.1).

Methylation of IV

3mg of IV was methylated with CH_2N_2 in a usual manner and crystallized from MeOH to yield II as needles. The identity was confirmed by direct comparison with II.

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