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Furoquinoline Alkaloids in *Dictamus albus* Root Bark

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Abstract—From the root bark of *Dictamnus albus* (Rutaceae) five furoquinoline alkaloids, robustine, dictamine, γ-fagarine, skimmianine and haplopine were isolated and characterized by spectral data.

Keywords—*Dictamnus albus* · Rutaceae · furoquinoline alkaloid · robustine·dictamine· γ-fagarine · skimmianine · haplopine

Dictamnus albus L. (Rutaceae) has been used for jaundice, leprosy, headache, colds, rheumatism[1] and antifertility.[2] Phytochemical studies on this plant have demonstrated the presence of furoquinoline alkaloids,[3] limonoids,[4-8] amines,[9] monoterpenes,[10] flavonoids,[10-12] coumarins,[13] and saponins.[14]

Although the root bark of this plant is used as a crude drug, limited reports in the literature on the constituents of this part were found.[5,9] The present investigation was undertaken to determine the identity of any alkaloidal constituents in the root bark of this plant.

All the compounds (**I**—**V**) isolated from the alkaloidal fraction were indicated the positive Dragendorff's test.

Compound **I**, mp 144~5°, showed a maximum peak at 246.5nm and fine bands in the region of 302~340nm in UV spectrum which were shifted to a longer wavelength accompanied by loss of fine structure in acidic medium, typical of the furo [2, 3-b] quinoline system in its structure[15].

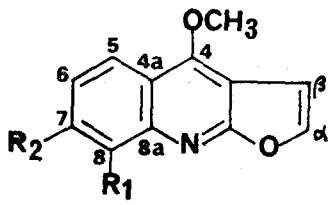
The appearance of peaks for furan ring system at 3160, 3130 and 1092cm^{-1} in its IR spectrum[16] and signals for furanoid protons at δ7.03 (1H, d, J=2.8Hz, H-β) and 7.56 (1H, d, J=2.8Hz, H-α)[17] and carbons at δ104.8(C-β) and 143.3(C-α)[18] in NMR spectra, respectively, strongly supported the above suggestion.

A methoxy signal at δ4.42 indicated the presence of 4-methoxy group.[17] Moreover, its NMR spectrum showed three aromatic proton signals at δ7.12 (1H, dd, J=2 and 7.4Hz), 7.33(dd, J=7.4 and 8.1 Hz) and 8.03(dd, J=2 and 8.1 Hz). Since the lower field double doublet can be interpreted as the resonance of H-5, a hydroxyl group should be located at C-8.

Methylation of Compound **I** with CH_2N_2 at room temperature afforded a methylether, mp 142~3°, which showed a molecular ion peak at m/z 229 as a base peak in its mass spectrum. The high intensity of fragment ions at m/z 214 (M^+-15) and 186(M^+-43), and at m/z 228 (M^+-1) and 200(M^+-29) supported that the methoxy groups were located at C-4 and C-8, respectively[19].

From the above results, Compound **I** was identified as 8-hydroxy dictamine (=robustine)[20] and its methylether as γ-fagarine.[21]

Compound **II**, mp 133~2°, was very similar to Compound **I** in its UV and IR spectra. The NMR spectrum showed a methoxy signal at δ4.42, furan ring proton signals at δ7.01 and 7.57 and overlapping signals for 4 protons in



	R_1	R_2
I	OH	H
II	H	H
III	OCH_3	H
IV	OCH_3	OCH_3
V	OCH_3	OH

the aromatic region indicating the simple 4-methoxy furoquinoline nature.[17] This suggestion was established by means of mass spectrum of this compound which showed a molecular ion peak at *m/z* 199 (100%) and the high intense peaks for M^+-15 and M^+ -43 ions at *m/z* 184 and 156, respectively.[19] The identity of Compound **II** as dictamine was obtained by comparison of its physical and spectral data with those appeared in literature.[15,17,19,22,23]

Compound **III**, mp 142~3°, was identified as γ-fagarine by direct comparison with the methylated Compound **I** coupled with physical and spectral data appeared in literature.[21]

Compound **IV**, mp 177~8°, was also very similar to Compound **I** in its UV and IR spectra. However, the NMR spectrum of this compound showed three methoxy signals at δ4.02, 4.11, and 4.42, the latter downfield signal being due to the C-4 methoxy group.[17] Two sets of doublets at δ7.18 (J=9.5Hz) and 7.97 (J=9.5Hz), and δ6.99 (J=2.8Hz) and 7.53 (J=2.8Hz), each integrating for one proton, were assigned to two ortho-coupled aromatic protons and furan ring protons, respectively.[17]

The downfield aromatic signal should be assigned to H-5. Therefore, the second aromatic proton must be located at H-6. Hence the other two methoxy groups were located at H-7 and 8. Therfore, Compound **IV** was identified as skimmianine.

All the physical and spectral data were identical those appeared in literature.[23]

Compound **V**, mp 204~5°, was virtually identical to skimmianine (IV) in UV and IR spectra. The NMR spectrum of Compound **V** exhibited the presence of two methoxy groups (δ4.22 and 4.42), which were allocated at C-4 and C-8, respectively, because of the intense peaks for M^+-15 and M^+-43, and for M^+-1 and M^+-29 in its mass spectrum. The orthro-coupled two aromatic proton signals at δ7.13 and 7.93 with J=9.3Hz were assigned to H-6 and H-5, respectively, as in skimmianine. Methylation with CH_2N_2 gave skimmianine which was confirmed by direct comparison with the natural material. Therefore, an additional hydroxy group must be located at C-7. From the above results, Compound **V** was identified as haplopine(**V**).[24]

Robustine (**I**) and haplopine (**V**) have not been isolated from this plant by any of the earlier authors from this plant.

Experimental

Nine kgs of the root bark of *D. albus* (purchased from a drug market) was powdered and extracted with $CHCl_3$. The $CHCl_3$ extract yielded 317g of residue after evaporation in vacuo. The residue was taken up in ether, and 5%HCl solution was added. After thorough partitioning, the ether was removed. The resulting acidic solution was made alkaline with c-NH_4OH and extracted several times with ether and then chloroform until the chloroform extract gave a negative alkaloid test with Mayer's reagent. The organic fractions were combined, dried over

anhydrous Na_2SO_4, filtered and concentrated in vacuo to yield a residue (12.65g).

The crude alkaloidal fraction was subjected to SiO_2 column chromatography eluting with benzene-ether (9 : 1, 6 : 1 and then 4 : 1) to yield 10 subfractions based on the similarity of their TLC patterns. Subfraction No. 3 yielded, after recrystallization from MeOH, Compound **I** as stout plates.

Subfraction No. 4 was crystallized from MeOH to give Compound **II** as stout plates. Fractional recrystallization of subfraction No. 6 from MeOH afforded Compound **III** and Compound **IV**, as needles.

The subfractions No. 7 and 8 gave Compounds **IV** and **V**, as needles, respectively.

Compound **I** (robustine)—Mp 144～5° [Lit.[20] mp 147～8°]

uv, λmax(MeOH) nm(log ε) : 246.5(4.36), 302 (3.30), 315(3.40), 330(3.40), 340(3.36); (MeOH-HCl) 252.5(4.37), 349(3.36).

ir, νmax(KBr) cm^{-1} : 3270(OH), 3160, 3130 (furan), 1618(C=C), 1255(ether), 1092(=COC).

H^1-nmr($CDCl_3$, TMS)δ:4.42(3H, s, 4-OCH_3), 7.03(1H, d, J=2.8Hz, furan β-H), 7.12(1H, dd, J=7.4 and 2Hz, H-7), 7.33(1H, dd, J=7.4 and 8.1Hz, H-6), 7.56 (1H, d, J=2.8 Hz, furan α-H), 8.03(1H, dd, J=8.1 and 2Hz, H-5).

C^{13}-nmr($CDCl_3$, TMS) δ : 59.0(OCH_3), 104.0 (C-4a), 104.8(furan β-C), 110.2(C-7), 112.9 (C-5), 118.8(C-3), 124.1(C-6), 135.8(C-8), 143.3(furan α-C), 151.1(C-8a), 157.5(C-4), 162.5(C-2).

ms, m/z(rel. int.): 215(M^+, 100), 200(M^+-CH_3, 60.1), 186(M^+-HCO, 24.4), 172[M^+-(CH_3+CO), 26.7], 144[M^+-(CH_3+2CO), 13.4], 116(144-CO, 13.1), 89(116-HCN, 15.3).

Compound **II** (dictamine)—Mp 132～3° [Lit.[23] mp 130～2°]

uv, λmax(MeOH) nm(log ϵ): 238(4.73), 243 (4.69), 309(3.93), 331(3.88); (MeOH-HCl), 241.5(4.84), 312(3.93), 329(3.91).

ir, νmax(KBr) cm^{-1}: 3140, 3112(furan), 1618 (C=C), 1259(ether), 1079(=COC).

nmr($CDCl_3$, TMS)δ: 4.42(3H, s, OCH_3), 7.01 (1H, d, J=2.9Hz, furan β-H), 7.57(1H, d, J=2.9Hz, furan α-H), 7.26～7.70(2H, m, H-6 and H-7), 7.84(1H, dd, J=2 and 8Hz, H-8), 8.19(1H, dd, J=2 and 8Hz, H-5).

ms, m/z(rel. int.): 199(M^+, 100), 184(M^+-CH_3, 75.5), 156[M^+-(CH_3+CO), 38.6], 128(156-CO, 46.7), 101(128-HCN, 27.2),

Compound **III**(γ-fagarine)—Mp 142～3° [Lit.[21] mp 140～2°]

uv, λmax(MeOH) nm(log ϵ): 245(4.63), 301 (sh, 3.64), 312(3.74), 326(3.72), 339 (3.67); (MeOH-HCl) 251(4.61), 343(3.69).

ir, νmax(KBr) cm^{-1}: 3150, 3122(furan), 1622 (C=C), 1266(ether), 1097(=COC).

nmr($CDCl_3$, TMS)δ: 4.06(3H, s, 8-OCH_3), 4.42(3H, s, 4-OCH_3), 7.03(1H, dd, J=7.6 and 1.3Hz, H-7), 7.05(1H, d, J=2.8Hz, furan β-H), 7.34(1H, dd, J=7.6 and 8.3Hz, H-6), 7.62(1H, d, J=2.8Hz, furan α-H), 7.84(1H, dd, J=8.3 and 1.3Hz, H-5).

ms, m/z(rel. int.): 229(M^+, 100), 228(M^+-H, 74.1), 214(M^+-CH_3, 33.3), 200(M^+-HCO, 77.8), 199(M^+-CH_2O, 35.2), 186[M^+-(CH_3+CO), 16.7], 184(199-CH_3, 31.5), 156(186-HCHO, 35.2), 128(156-CO, 24.1).

Compound **IV** (skimmianine)—Mp 177～8° [Lit.[23] mp 174～6°]

uv, λmax(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); (MeOH-HCl) 254(4.77), 322 (3.85), 351(3.90).

ir, νmax(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 β-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), 258(M^+-H, 13.6), 244(M^+-CH_3, 100), 230(M^+-CHO, 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).

Compound **V** (haplopine)—Mp 204~5° [Lit.[24] mp 209~210°]

uv, λmax(MeOH) nm(log ϵ) : 242(sh, 4.65), 250(4.79), 304(sh, 3.71), 318(3.84), 331 (3.84), 341(sh, 3.80); (MeOH-HCl) 239(sh, 4.32), 254(4.71), 322(3.85), 349(3.91).

ir, νmax(KBr) cm^{-1}: 3165, 3140(furan), 1626 (C=C), 1261(ether), 1096(=COC).

nmr($CDCl_3$, TMS)δ: 4.22(3H, s, 8-OCH_3), 4.42 (3H, s, 4-OCH_3), 7.01(1H, d, J=2.8Hz, furan β-H), 7.13(1H, d, J=9.3Hz, H-6) 7.53 (1H, d, J=2.8Hz, furan α-H), 7.93(1H, d, J=9.3Hz, H-5).

ms, m/z(rel. int.): 245(M^+, 69.5), 244(M^+-H, 15.9), 230(M^+-CH_3, 20.3), 227(M^+-H_2O, 100), 216(M^+-HCO, 23.3), 202[$M^+-(CH_3+CO)$, 61.3], 199(227−CO, 58.5), 187(202−CH_3, 42.8), 184(199−CH_3, 33.9) 172(202−CH_2O, 13.1).

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