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STRUCTURE AND SYNTHESIS OF MUKONINE, A NEW CARBAZOLE ALKALOID FROM *MURRAYA KOENIGII*

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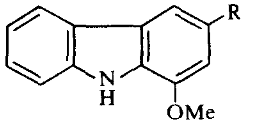
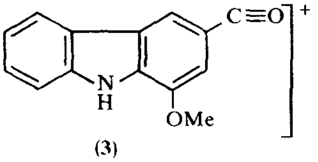
Key Word Index—*Murraya Koenigii*; Rutaceae; alkaloids; mukonine; synthesis.

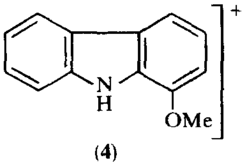
In continuation of our studies on carbazole alkaloids of Rutaceae [1, 2] we now report the structure and synthesis of a new carbazole alkaloid, mukonine mp 198–200° isolated from the stem bark of *Murraya koenigii* Spreng. Mukonine (**1**), $C_{15}H_{13}NO_3$, M^+ 255, was homogeneous by TLC and MS. The IR spectrum of the compound showed the presence of —NH and ester carbonyl functions on an aromatic system. The UV spectrum of (**1**) was similar to that of 1-methoxy carbazole. On alkaline hydrolysis (**1**) furnished a compound (**2**) mp 242° which was identical to mukoeic acid [3] from its UV, IR and mmp data. Mukonine is the Me ester of mukoeic acid and can be represented by the structure (**1**). The MS of (**1**) also supports this conclusion; the peak at (M-59) was readily suggestive of the presence of a carbomethoxy group in mukonine. The other significant peaks are at *m*/*e* 224, 196 and 153 which could be represented by the following ionic species (**3**–**6**).



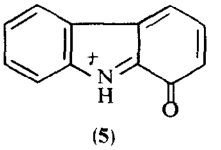
(**1**) R = CO_2Me
(**2**) R = COOH



(3)



(**4**)



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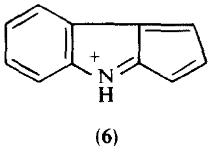
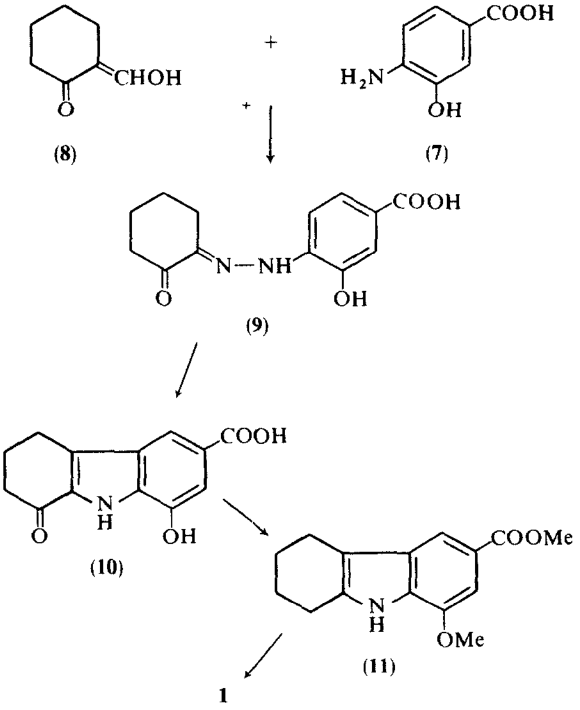


(**6**)

The structure of (**1**) for mukonine has been confirmed by synthesis as follows. 4-Amino-3-hydroxybenzoic acid [4] (**7**), mp 217° (prepared by nitration of *m*-hydroxybenzoic acid and then reducing the nitro compound) by the Japp–Klingemann reaction with formyl cyclohexanone (**8**) furnished cyclohexane 1,2-dione-1-(4′-carboxy-2′-hydroxy) phenyl hydrazone (**9**), $C_{13}H_{14}N_2O_4$, mp 178–179°. The hydrazone on cyclization with a mixture of HCl and HOAc by the usual procedure furnished 3-carboxy-1-hydroxy-8-oxo-5,6,7,8-tetrahydrocarbazole (**10**) $C_{13}H_{11}NO_4$, mp 190–192°.

The oxocompound (**10**) on Wolff–Kishner–Huang Minlon reduction in ethylene glycol followed by CH_2N_2 treatment produced 1-methoxy-3-carbomethoxy-5,6,7,8-tetrahydrocarbazole, (**11**), $C_{15}H_{17}NO_3$, mp 172–173°. The compound (**11**) was then dehydrogenated with 10% Pd/C when a compound mp 198–200° was obtained which was identical with natural mukonine (**1**) in all respects (UV, IR, TLC and mmp).

The occurrence of murrayanine, mukoeic acid and mukonine in *M. koenigii* shows that the aromatic C-Me group at C-3 of the carbazole nucleus is oxidised to a carboxylic acid group and methylated in the same plant to yield mukonine.



EXPERIMENTAL

All mps are uncorr. Petrol had bp 60–80° unless stated. Analytical samples were analysed after drying over P_2O_5 *in vacuo* usually at 80° for 10 hr. Si gel was supplied by Gouri Chemical Co. of India.

Isolation of mukonine (**1**). Finely powdered root of *M. koenigii* (1 kg) was extracted for 48 hr with petrol (40–60°) and the solvent removed by distillation. The residue left was dissolved in C_6H_6 and chromatographed over Si gel (400 g). Eluents were collected in fraction of 250 ml each. Petrol–C_6H_6 (1 : 4) furnished mukonine which was crystallized from $CHCl_3$–C_6H_6, mp 195°. Yield 0.0015%. UV: λ_{max}^{EtOH} 236, 245, 266, 274, 306, 320 nm with log ε 4.6, 4.57, 4.64, 4.73, 3.88, 3.78. IR: ν_{max}^{Nujol} 3431 (—NH), 1690, (ester carbonyl) 1635, 1613, 1609 cm^{-1} (aromatic). (Found: C, 70.56; H, 5.12; N, 5.48%. Calculated for $C_{15}H_{13}NO_3$: C, 70.58; H, 5.13; N, 5.49%).

Hydrolysis of mukonine to mukoeic acid (**2**). Mukonine (8 mg) was dissolved in 10% alcoholic KOH (5 ml) and refluxed at 100° for 5 hr. After the completion of the reaction, the alcohol was removed keeping the soln vol, constant by addition of H_2O. The soln was then cooled, acidified with HCl and filtrated. The residue was washed with H_2O, dried and crystallized from C_6H_6, when a compound mp 242°, identical with mukoeic acid was obtained (mmp, TLC, UV, IR). Yield 7 mg.

4-Amino-3-hydroxy benzoic acid (**7**). 4-Nitro-3-hydroxybenzoic acid (2.5 g) dissolved in EtOH (100 ml) was catalytically hydrogenated at atm. pres. and room temp. using 10% Pd–C and Raney Nickel catalyst (1:1, 0.5 g) with constant stirring. After completion of the reaction it was freed from catalyst and the solvent removed by distillation. The residue was crystallized from C_6H_6, mp 215° (lit. 216°). Yield 2 g.

Cyclohexane 1,2-dione-1-(4′-carboxy-2′-hydroxy) phenyl hydrazone (**9**). An aq. soln of NaOAc (5 g in 10 ml) was added to a soln of formyl cyclohexanone (3 g) in MeOH (35 ml). A diazotised soln of 4-amino-3-hydroxy benzoic acid (2 g) was added with mechanical agitation during 30 min, when crystals of compound (**9**) were obtained. This was further purified by crystallization from EtOH mp 178–179° (yield 2 g). UV: λ_{max}^{EtOH} 225, 270 nm with log ε 4.7, 4.6. IR: ν_{max}^{Nujol} 3480 (—NH), 3320 (—OH), 1700 ($\rangle$C=0), 1610, 890 cm^{-1} (aromatic residue). (Found: C, 59.50, H, 5.30, N, 10.58%. Calculated for $C_{13}H_{14}N_2O$: C, 59.54, H, 5.38, N, 10.68%).

3-Carboxy-1-hydroxy-8-oxo-5,6,7,8-tetrahydrocarbazole (**10**). Compound (**9**) (2 g) was added to boiling HOAc (13 ml) and conc HCl (4 ml) for 3 min. The reaction mixture was poured in ice–H_2O and filtered. The product obtained was washed, dried and crystallized from C_6H_6 when (**10**) was obtained, mp 190–192° (yield 1.5 g). UV: λ_{max}^{EtOH} 232, 285 nm with log ε 4.42, 4.16. IR: ν_{max}^{Nujol} 3480 (—NH), 3200 (—OH), 1700, 1630 ($\rangle$C=O), 1610, 870 cm^{-1} (aromatic residue). (Found: C, 63.58; H, 4.50; N, 5.68%; Calculated for $C_{13}H_{11}NO_4$: C, 63.67; H, 4.57; N, 5.71%)

1-Methoxy-3-carbomethoxy-5,6,7,8-tetrahydrocarbazole (**11**). Compound (**10**) (1.5 g) dissolved in freshly dist. ethylene glycol 25 ml) was heated with hydrazine hydrate (99–100%; 1 g) and KOH (0.9 g) at 190° for 1 hr and up to 200° under reflux for 3 hr. After the completion of the reaction the mixture was poured in ice-H_2O and extracted with Et_2O. On evapn of solvent an oily mass was obtained which was taken up in C_6H_6 and filtered through a Si gel column. The C_6H_6 soln on evapn furnished a semi solid product which could not be crystallized. A cold Et_2O soln of CH_2N_2 was added to a soln of the above tetrahydrocarbazole in MeOH (25 ml) kept at 0–5°. The mixture was then kept for 16 hr at 0°. After the decomposition of excess CH_2N_2 with HOAc and removal of solvent, a semisolid mass was obtained. This was taken up in Et_2O, washed with H_2O to free it from acid and then dried. After removal of Et_2O, (**11**) was obtained as colourless solid. On crystallization from C_6H_6–petrol (1:1), (**11**) was obtained, mp 172–173°. Yield 0.5 g. UV: λ_{max}^{EtOH} 240, 285, 300 nm with log ε 4.54, 4.12, 3.85; IR: ν_{max}^{Nujol} 3480 (—NH), 3220 (—OH), 1740 (—COOMe), 1200 cm^{-1} (aromatic ether). (Found: C, 69, H, 6.58; N, 5.35%; Calculated for $C_{15}H_{17}NO_3$; C, 69.48; H, 6.61; N, 5.40%).

1-Methoxy-3-carbomethoxy carbazole (**1**). The above compound (0.8 g) was dissolved in *p-cymene* (3 *ml*) and was intimately mixed with 10% palladized charcoal (50 mg) and the mixture heated in sealed tube at 200° for 5 hr. After the reaction, the solvent was separated from Pd/C by filtration and the solvent was evapd at 100°. An oily mass was obtained which on crystallization from C_6H_6–$CHCl_3$ yielded a compound mp 185–187°. This was identical in all respect with the natural and synthetic specimens stated above (mmp, TLC). Yield 0.5 g.

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ALKALOIDS OF *HAZUNTA MODESTA*

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Key Word Index—*Hazunta modesta*; Apocynaceae; indole alkaloids; voacangine; coronaridine; 19-isoheyneanine; 16-decarbomethoxy-20-epiervatamine; 6-oxosilicine; tabernaelegantine A.

In a previous paper [1] we reported the isolation of 3 alkaloids, dregamine, tabernaemontanine and ibogamine from the roots of *Hazunta modesta* (Apocynaceae) collected in Madagascar. In this note we have described the characterization of a further 6 alkaloids we have found in this plant.

Alkaloid 1, voacangine (mp, [α], UV, PMR and MS identical to those reported [2]). Alkaloid 2 coronaridine oily $[\alpha]_D^{20}$ −31.9 ($CHCl_3$ $c = 1$) UVλ_{max}^{MeOH} nm (log ε) 295 (3.88) 285 (3.98) 231 (4.28). ^{13}C-NMR identical with that reported [3]. Alkaloid 3 19-isoheyneanine, recently isolated from *Peschiera affinis* [4a] and *Pandaca mocquerysii* [4b] that we have isolated as solvated with a molecule of solvent of crystallization, mp 155–158° (EtOAc) $[\alpha]_D^{20}$ −34.2 (MeOH, $c = 0.5$) mp 170–172° (cyclohexane) [4a]; acetate mp 215° (C_6H_6) $[\alpha]_D^{20}$