Communications to the Editor

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STRUCTURES OF MURRAFOLINE-B AND -C, NEW BINARY CARBAZOLE ALKALOIDS FROM MURRAYA EUCHRESTIFOLIA[1)]

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The structures of murrafoline-B (1) and -C (5), new binary carbazole alkaloids from Murraya euchrestifolia Hayata (Rutaceae), have been determined by spectral experiments, and dimerization of the monomeric carbazole alkaloids is discussed.

KEYWORDS — murrafoline-B; murrafoline-C; Murraya euchrestifolia; Rutaceae; carbazole alkaloid; binary; dimerization; Nafion

In the studies of the constituents of Murraya euchrestifolia Hayata[2-7)] (Rutaceae), we reported the isolation and structure determination of three binary carbazole alkaloids, bismurrayafoline-A[3)] and -B,[3)] and murrafoline-A.[4)] Further studies of the components of the same plant led to the characterization of two new binary carbazole alkaloids named murrafoline-B and -C.

Murrafoline-B (1), $C_{32}H_{30}N_2O_2$, [m/z 474.2325 (M^+ found); 474.2305, calcd] was obtained as colorless needles from methanol [mp 234-237°C; CD (in methanol, 200-350 nm): no absorption; MS m/z: 474 (M^+, 100%), 419, 278, 263, 248, 237 (M^{++}), and 211], and gave UV spectral data typical of a carbazole nucleus[8,9)] [λ_{max} (MeOH): 208, 226, 240, 292, 304, and 330 nm]. The ^{1}H-NMR spectrum (Table I) contained signals attributable to one methoxy (δ 3.87), and two aryl methyl groups (δ 2.48 and 2.49) as well as three 1H singlets at δ 6.62, 7.44, and 7.79. An appearance of ABX-type signals at δ 2.30, 2.38 and 4.69 accompanied by two oxygen-linked tertiary methyl groups (δ 1.46, and 1.56) suggested the presence of a 4-substituted 2,2-dimethyldihydropyran ring system in the molecule. The decoupling experiments of aromatic protons indicated the presence of carbazole nuclei having a non- and an 8-substituted A-ring in the molecule. In NOE experiments, irradiation of the aryl methyl protons (δ 2.48 and 2.49) revealed 8.4, 10.2 and 14.4% enhancements of the signals at δ 6.62 (H-2'), 7.44 (H-4 or 4'), and 7.79 (H-4 or 4'), respectively. Irradiation of the methoxy protons at δ 3.87 gave a 21.3% area increase of the signal at δ 6.62 (H-2').

These spectral results coupled with the observation of mass fragment peaks at m/z 263 and 211 assignable to fragments corresponding to upper (R part in the Figure) and lower halves in the molecule, respectively, showed that the structural components of this alkaloid were the previously known monomeric carbazoles, murrayafoline-A (4)[2,5)] and girinimbine (7),[11)] and the structure of murrafoline-B was proposed as the racemic form of 1.

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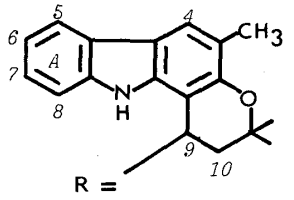
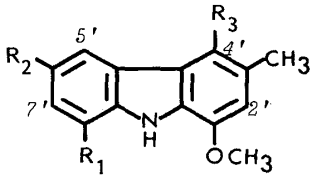
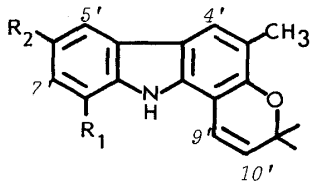
Treatment of 4 and 7 with Nafion 117 (Aldrich)[10] in refluxing aqueous methanolic solution for 48 h gave three dimeric products, I, II, and III. The UV absorptions of these products showed good similarities to each other as follows: I: UV λ_{max} (EtOH): 228, 242, 293, 302, 332, and 346 nm; II: λ_{max} (EtOH): 230inf, 240, 253sh, 296, 331, and 345inf; III: λ_{max} (EtOH): 239sh, 292, 304, 331, 360 nm. The ^{1}H-NMR spectra (Table I) revealed that one of the structural components of these compounds was dihydrogirinimbine having a substituent at C-9. Another component was murrayafoline-A (4)[2,5] in the molecule of I and II, and girinimbine (7)[11] in that of III. Furthermore, the analysis of the three-spin system of the aromatic protons in the spectra of I and III indicated the location of the linkage of one carbazole nucleus at C-6.





(1) R_1=R, R_2=R_3=H
(2) R_2=R, R_1=R_3=H
(3) R_3=R, R_1=R_2=H
(4) R_1=R_2=R_3=H



(5) R_1=R, R_2=H
(6) R_2=R, R_1=H
(7) R_1=R_2=H

Table I. ^{1}H-NMR (400MHz) Spectra of Natural and Synthetic Binary Carbazoles

	1	2	3	5	6
CH_3	1.46(s)	1.40(s)	1.55(s)	1.38(s)	1.40(s)
	1.56(s)	1.51(s)	1.58(s)	1.41(s)	1.48(s)
				1.42(s)	1.49(s)
				1.54(s)	1.51(s)
Ar-CH_3	2.48(s)	2.41(s)	1.79(s)	2.24(s)	2.30(s)
	2.49(s)	2.50(s)	2.42(s)	2.47(s)	2.40(s)
OCH_3	3.87(s)	3.99(s)	3.97(s)		
H-4#	7.79(s)	7.73(s)	7.71(s)	7.79(s)	7.73(s)
H-5	7.85(br d,8)	7.85(dd,1,8)	7.87(dd,1,8)	7.83(br d,8)	7.86(dd,1,8)
H-6	7.06(dt,1,8)	7.04(dt,1,8)	7.05(dt,1,8)	7.04(dt,1,8)	7.05(dt,1,8)
H-7	7.11(dt,1,8)	7.08(dt,1,8)	7.10(dt,1,8)	7.09(dt,1,8)	7.09(dt,1,8)
H-8	6.93(br d,8)	6.90(dd,1,8)	6.87(dd,1,8)	6.95(br d,8)	6.92(dd,1,8)
H-9	4.69(dd,7,11)	4.47(dd,7,12)	5.74(dd,7,12)	4.63(dd,7,11)	4.45(dd,7,13)
H-10	2.30(dd,7,11)	2.14(t,12)	2.31(t,12)	2.27(dd,7,11)	2.13(t,13)
	2.38(t,11)	2.27(dd,7,12)	2.39(dd,7,12)	2.31(t,11)	2.26(dd,7,13)
H-2'#	6.62(s)	6.73(s)	6.56(s)		
H-4'#	7.44(s)*	7.43(s)	....	7.55(s)	7.62(s)
H-5'	7.98(d,8)	8.04(br s)	8.31(br d,8)	7.85(d,8)	7.89(br s)
H-6'	7.24(t,8)	....	7.23(dt,1,8)	7.24(t,8)	....
H-7'	7.44(br s)*	7.24(br d,8)	7.47(dt,1,8)	7.43(br d,8)	7.18(br d,8)
H-8'	....	7.34(d,8)	7.59(br d,8)	....	7.29(d,8)
H-9'				6.07(br s)**	6.62(d,10)
H-10'				5.56(d,10)	5.70(d,10)
NH	7.01(s)	6.95(s)	6.80(s)	7.2(br s)	6.96(br s)
	7.70(s)	8.18(s)	8.45(s)	7.4(br s)	7.93(br s)

Values are in ppm. Figures in parentheses are coupling constants in Hz. Recorded in $CDCl_3$. * Overlapped each other. # Can be interchanged. ** The broadening of this signal ($W_{1/2}$ = 16 Hz) seems to be due to slow interconversion between the conformations of the molecule.

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And in the spectrum of II, the presence of two four-spin systems in the aromatic proton region and lack of the lower field signal due to H-4 in the carbazole nucleus suggested the location of a linkage at C-4' of 4.

On the basis of these results, the structures of 2, 3, and 6 were assigned to compounds I, II, and III, respectively.[12]

Murrafoline-C (5), $C_{36}H_{34}N_2O_2$ [m/z 526.2611 (M^+, found); 526.2618 calcd] was isolated as colorless oil, and gave the following spectral data: CD (200-350 nm, in EtOH): no absorption; IR ν_{max} ($CHCl_3$): 3460 and 1610 cm^{-1}; UV λ_{max} (EtOH): 224, 242, 251, 291, 328, and 342 nm; MS m/z: 526 (M^+), 511 (100), 469, 263, 256 (M^{++}), 248, and 227. The observation of an ABX-type (δ 2.27 , 2.31, and 4.63) and an AB-type signal (δ 5.56, and 6.07) together with four oxygen-linked tertiary methyl groups (δ 1.38, 1.41, 1.42, and 1.54) suggested the presence of a 4-substituted 2,2-dimethyldihydropyran ring, the same as 1, and a 2,2-dimethylpyran ring system in the molecule, respectively. Close resemblance between the ^{1}H-NMR spectra of murrafoline-C and 1, save for the signals due to H-2' and a methoxy group in the latter and the dimethylpyran moiety in the former, suggested that both alkaloids had the same linkage (between C-9 and C-8') of the two carbazole nuclei.

These spectral data led us to propose the racemic structure 5 to murrafoline-C.

Dimerization of 7, the structural component of murrafoline-C (5), was carried out as described above to afford a colorless oil, which was found to be identical with compound III (6) by the comparison of UV, IR, and ^{1}H-NMR spectra and by TLC.[12]

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REFERENCES AND NOTES

1) This work was presented at the 105th Annual Meeting of the Pharmaceutical Society of Japan, Kanazawa, April 4, 1985.
2) T.-S. Wu, T. Ohta, H. Furukawa, and C.-S. Kuoh, Heterocycles, 20, 1267 (1983).
3) H. Furukawa and T.-S. Wu, Chem. Pharm. Bull., 31, 4202 (1983).
4) A. T. McPhail, T.-S. Wu, T. Ohta, H. Furukawa, Tetrahedron Lett., 24, 5377 (1983).
5) H. Furukawa, T. Ohta, T.-S. Wu, and C.-S. Kuoh, Chem. Pharm. Bull., 33, (1985). "in press".
6) H. Furukawa, M. Yogo, C. Ito, T.-S. Wu, and C.-S. Kuoh, Chem. Pharm. Bull., 33, 1320 (1985).
7) H. Furukawa and T.-S. Wu, Heterocycles, "in press".
8) W. Otting and G. Staiger, Chem. Ber., 88, 828 (1955).
9) H. J. Teuber and G. Staiger, Chem. Ber., 89, 489 (1956).
10) Perfluorinated ion-exchange powder, 5 wt.% solution in mixture of lower aliphatic alcohols and 10% water.
11) D. P. Chakraborty, B. K. Barman, and P. K. Bose, Science and Cult. (India), 30, 445 (1964).
12) This is the first example of the application of ion-exchange resin (H^+) (Nafion) for this kind of reaction. However, the isolation of the products having the same linkage as natural 1 and 5 was unsuccessful.

ADDED IN PROOF (May 10, 1985) After submission of the present manuscript, one more binary carbazole alkaloid, murrafoline-D was isolated from the same plant source, and was shown to be identical (^{1}H-NMR, IR, MS, and TLC) with synthetic compound I (2).

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