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CARBAZOLE ALKALOIDS FROM THE LEAVES OF *MURRAYA EUCHRESTIFOLIA*

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Key Word Index—*Murraya euchrestifolia*; Rutaceae; carbazole alkaloid; murrayamine-I; murrayamine-J; murrayamine-K; murrayamine-M; murrayamine-N.

Abstract—Five new carbazole alkaloids, murrayamine-M, murrayamine-J, murrayamine-N, murrayamine-I and murrayamine-K, together with 10 known compounds were isolated from the leaves of *Murraya euchrestifolia* collected in November. Their structures were elucidated by spectral analyses.

INTRODUCTION

In continuation of our examination of the acetone extract of the leaves of *Murraya euchrestifolia* Hayata collected in Taiwan [1–3], five new carbazole alkaloids, murrayamine-M (**1**), murrayamine-J (**2**), murrayamine-N, (**3**), murrayamine-I (**4**) and murrayamine-K (**5**), were isolated from the leaves of *M. euchrestifolia* collected in November. Ten known compounds were also obtained from the leaves of the same plant. We report the structural elucidation of compounds **1**–**5**. These alkaloids were different from those which occurred in the same plants collected in February [3].

RESULTS AND DISCUSSION

The acetone extract of the leaves of *M. euchrestifolia* collected in November was repeatedly chromatographed to provide five new carbazole alkaloids: murrayamine-M (**1**), murrayamine-J (**2**), murrayamine-N (**3**), murrayamine-I (**4**) and murrayamine-K (**5**), which were isolated as colourless oils, except for **5** which crystallized. Eight known carbazoles (murrayamine-D (**6**) [3], girinimbine (**7**) [1, 3], mahanimbine (**8**) [2, 3], (+)-mahanine (**9**) [2], isomahanine (**10**) [4], murrayamine-E (**11**) [3], bicyclomahanimbine (**12**) [3], murrayamine-A (**13**) [2, 3]), a triterpenoid (friedelin (**14**) [2]) and sitosterol (**15**) were also found from the same plant. The structures of the compounds were characterized by spectroscopic analyses or direct comparison with authentic samples.

Murrayamine-M (**1**), with the molecular formula as $C_{23}H_{25}NO_2$, was thought to be an 7-oxygenated carbazole alkaloid by the UV absorptions at 243, 254 (sh), 292, 325 nm. A characteristic aldehydic singlet at δ 10.08 in ^1H NMR spectrum together with the strong carbonyl band at 1675 cm^{-1} revealed a formyl group attached to C-3 instead of a methyl group. In the aromatic region of the ^1H NMR spectrum, a relative downfield ABX type system at δ 7.48 (*d*, $J = 8.4$ Hz), 7.89 (*dd*, $J = 8.4$, 1.7 Hz) and 8.48 (*d*, $J = 1.7$ Hz) belonged to H-1, H-2 and H-4, respectively, which were deshielded by aldehyde substituent at C-3 on the C-ring. An AB pattern of protons at δ 6.88 and 7.86 (each *d*, $J = 8.4$ Hz) for H-6 and H-5, respectively, was affected by an oxygenated substituent on C-7. Thus, an 8-substituted-7-alkoxy-3-formylcarbazole was established. Conversely, the signals in the upfield region containing a benzylic doublet at δ 3.31 ($J = 9.4$ Hz, H-1′), three methyl singlets at δ 0.79, 1.47 and 1.59 along with two methylene and two methine protons between δ 0.8 and 2.8 suggested the existence of a 10-carbon tricyclic unit combined with the carbazole nucleus. This part was in accord with that of bicyclomahanimbine (**12**). Based on the above analyses and comparison with **12**, the structure of **1** was assigned for murrayamine-M.

Murrayamine-J (**2**) was determined to have molecular formula $C_{23}H_{23}NO_2$. Examination of the aromatic region of the ^1H NMR spectrum suggested that **2** was also an 8-substituted-7-alkoxy-3-formylcarbazole derivative. In the olefinic portion, three signals could be identified as 5.11 (*tq*, $J = 6.7$, 1.3 Hz, H-6′), 5.72 (*d*, $J = 10.1$ Hz, H-2′), 6.81 (*d*, $J = 10.1$ Hz, H-1′). The first vinyl proton exhibited complicated splitting owing to an adjacent methylene at δ 2.16 (*m*) which neighboured another methylene

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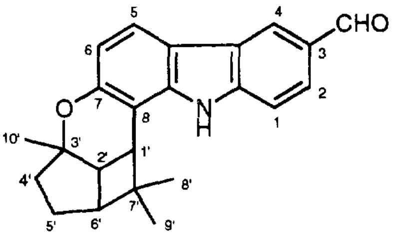
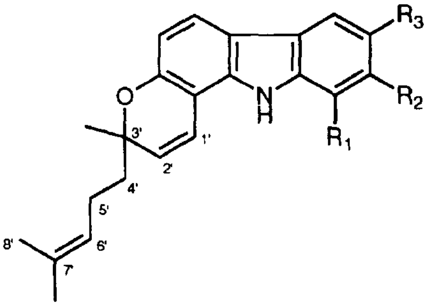
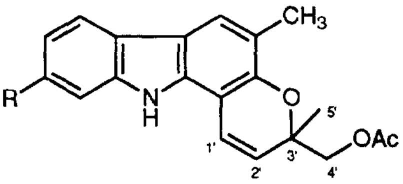


1



2 : R_1 =H, R_2 = H, R_3 =CHO
3 : R_1 = OCH_3, R_2 = H, R_3 =CHO



4 : R =OH
5 : R = H

at δ 1.77 (*m*) and a long-range coupling with geminal dimethyls at δ 1.56 and 1.65. The last two vinyl CH were coupling partners with the *cis* configuration. As no further coupling could be detected, this group, CH = CH, was apparently situated between two quaternary carbon atoms. Hence, the remaining methyl singlet at δ 1.47, together with the methylpentenyl side-chain, established a methyl,methylpentenylpyran ring fused to carbazole; therefore, murrayamine-J possessed the structure **2**.

By comparison of the ^{1}H NMR spectrum and mass spectrum of compound **3** with those of **2**, compound **3** contained a 2-methyl-2-(4′-methyl-3′-pentenyl) pyran ring owing to the presence of one *cis* double bond, an isolated methyl and a $(CH_3)_2C{=}CHCH_2CH_2$- side-chain as well as the base peak representing $[M - C_6H_{11}]^+$. The difference between **2** and **3** was the type and location of substituents on the carbazole.

Murrayamine-N (**3**) was shown to have the molecular formula, $C_{23}H_{25}NO_3$ and it was indicated to be a 1,7-dioxygenated carbazole alkaloid by its UV absorptions [2, 5]. Compound **3** presented an aldehydic group at δ 10.03 (*s*, 3-CHO), an AB-type spin system at δ 6.81 (*d*, *J* = 8.5 Hz, H-6) and 7.81 (*d*, *J* = 8.5 Hz, H-5), two broad singlet protons at δ 7.41 (H-2) and 8.07 (H-4), and a methoxyl singlet at δ 4.07 (1-OMe) for an 8-substituted-3-formyl-1-methoxycarbazole structure. Irradiation of the signal at δ 10.03 (3-CHO) provoked signal sharpness at δ 7.41 (H-2) and 8.07 (H-4) which supported the CHO group being close in space to H-2 and H-4. On the basis of the above analyses, structure **3** was inferred for murrayamine-N.

Murrayamine-I (**4**), $C_{20}H_{19}NO_4$, was suggested to be a 2,7-dioxygenated carbazole alkaloid according to its UV spectrum [2, 6]. The structure of **4** was very close to that of murrayamine-A (**13**) [2, 3] as revealed by the

Table 1. ^{1}H NMR spectral data of compounds **1**–**5*** (200 MHz, in $CDCl_3$, TMS as internal standard)

	1	**2**	**3**	**4**	**5**
H-1 or 1-OMe	7.48, *d* (8.4)	7.44, *d* (8.4)	4.07, *s*		
H-2 or 2-OH	7.89, *dd* (8.4,1.7)	7.89, *dd* (8.4,1.7)	7.41, *s*		
3-Me or 3-CHO	10.08, *s*	10.07, *br. s*	10.03, *s*	2.30, *s*	2.31, *d* (0.7)
H-4	8.48, *d* (1.7)	8.46, *br. d* (1.7)	8.07, *s*	7.56, *br. s*	7.67, *br. s*
H-5	7.86, *d* (8.4)	7.84, *d* (8.4)	7.81, *d* (8.5)	7.72, *d* (8.4)	7.91, *br. d* (7.7)
H-6	6.88, *d* (8.4)	6.81, *d* (8.4)	6.81, *d* (8.5)	6.72, *dd* (8.4, 2.2)	7.18, *td* (7.7, 1.1)
H-7 or 7-OH				4.82, *br. s*	7.31, *d* (7.7, 1.1)
H-8				6.84, *d* (2.2)	7.37, *d* (7.7)
NH	7.78, *br. s*	8.30, *br. s*	8.48, *br. s*	7.78, *br. s*	7.92, *br. s*
H-1′	3.31, *d* (9.4)	6.81, *d* (10.1)	6.69, *d* (9.8)	6.75, *d* (9.8)	6.76, *d* (9.9)
H-2′	2.74, *dd* (9.4, 7.7)	5.72, *d* (10.1)	5.71, *d* (9.8)	5.64, *d* (9.8)	5.63, *d* (9.9)
3′-Me (H-10′)	1.47, *s*	1.47, *s*	1.46, *s*	1.50, *s*	1.51, *s*
H-4′	1.70, *m* and 2.55, *dd* (8.4, 6.0)	1.77, *m*	1.81, *m*	4.17, *d* (11.5) and 4.26, *d* (11.5)	4.18, *d* (11.7) and 4.27, *d* (11.7)
H-5′	1.70, *m* and 2.08, *m*	2.16, *m*	2.14, *m*		
H-6′	2.08, *m*	5.11, *tq* (6.7, 1.3)	5.10, *m*		
7′-Me (H-8′ and H-9′)	0.79 and 1.59, *s*	1.56 and 1.65, *s*	1.56 and 1.66, *s*		
OAc				2.02, *s*	2.01, *s*

* *J* (Hz) value in parentheses.

comparison of their spectra. An ABX spin system at δ 6.72 (*dd*, $J = 8.4$, 2.2 Hz, H-6), 6.84 (*d*, $J = 2.2$ Hz, H-8) and 7.72 (*d*, $J = 8.4$ Hz, H-5) together with a broadened singlet at δ 7.56 (H-4) revealed a 1,2,3,7-tetrasubstituted carbazole. In addition, an aromatic methyl and a D_2O exchangeable hydroxyl signal at δ 4.82 identified two of those substituents. The location of the methyl group at C-3 was suggested by the H-4 signal (δ 7.56) changing sharpness during the irradiation of the methyl signal at δ 2.30. The remaining signals of two *cis*-olefinic protons at δ 5.64 and 6.75 (each *d*, $J = 9.8$ Hz) represented a pyran ring annulated to a carbazole moiety with two geminal substituents, one for a quaternary methyl at δ 1.50, the other for an acetoxymethyl. Two diasterotopic protons at δ 4.17 and δ 4.26 (each *d*, $J = 11.5$ Hz, H-4′) belonged to the same methylene group that neighboured an acetoxyl group at δ 2.02. This proposition was supported by the mass molecular ion and fragment ion at *m/z* 337 $[M]^+$ and 264 $[M - CH_2OCOCH_3]^+$. Thus, the above analyses led to the structure of murrayamine-I being determined as **4**.

The molecular formula of murrayamine-K (**5**) was $C_{20}H_{19}NO_3$, an oxygen less than that of **4**. The ^1H NMR spectrum was very similar to that of **4** and the only difference was the presence of an unsubstituted A-ring in the carbazole, which was proved by the four mutually coupled protons at δ 7.18 (*td*, $J = 7.7$, 1.1 Hz), 7.31 (*td*, $J = 7.7$, 1.1 Hz), 7.37 (*d*, $J = 7.7$ Hz) and 7.91 (*br d*, $J = 7.7$ Hz). In a NOE experiment, the signal of H-4 (δ 7.67) was found to be enhanced by 6.8% when the methyl signal at δ 2.31 (3-Me) was irradiated. Murrayamine-K was revealed to possess the structure **5**.

EXPERIMENTAL

General. The mps were measured on a Yanagimoto MP-S_3 micromelting point apparatus. ^1H and ^{13}C NMR spectra were recorded on Bruker AC-200 and Varian-300XL spectrometers in $CDCl_3$. Chemical shifts are shown in δ values (ppm) with tetramethylsilane (TMS) as internal reference. EI-MS and HR-MS were produced with VG 70-250 S spectrometer by direct inlet system. UV spectra were recorded on a Hitachi UV-3210 double-beam spectrophotometer in MeOH. IR spectra were recorded on Jasco IR Report-100 spectrophotometer in $CHCl_3$ except where otherwise noted.

Plant material. The leaves of *M. euchrestifolia* were collected in Kuantaochi, Nantou Hsien, Taiwan in November, 1986 and identified by Prof. C. S. Kuoh. The specimen of the plant has been deposited at the herbarium of the National Cheng Kung University, Tainan, Taiwan.

Extraction and isolation. The air-dried leaves (1.73 kg) of *M. euchrestifolia* were extracted (3 ×) with Me_2CO at room temp. The combined Me_2CO extracts were concd under red. pres. to yield a brown syrup (135 g) which was subjected to CC over silica gel and eluted with C_6H_6–Me_2CO (9: 1) to give six frs. Frs 1 and 2 were combined and rechromatographed over a silica gel column eluted with hexane–EtOAc (6:1) or TLC plate to yield **14** (20 mg), **7** (2.7 g), **8** (0.4 g) and **12** (10 mg). Fr. 3 was also rechromatographed on silica gel using C_6H_6–Me_2CO (9:1) as eluent or TLC plate to give an unknown **A** (1.0 mg), **2** (20 mg), **5** (7 mg), **3** (4 mg), **15** (134 mg), an unknown dimer **D** (5 mg) and **1** (6 mg). In a similar manner, **11** (5 mg) and **6** (3 mg), **13** (6 mg) and **9** (9 mg) were obtained from fr. 4; an unknown **B** (3 mg), **10** (4 mg), **4** (3 mg) were obtained from frs 5 and 6 by TLC separation using $CHCl_3$–Me_2CO (25:1) as eluent.

Murrayamine-M (**1**). Oil. HR-MS: calcd for $C_{23}H_{23}NO_2$, *m/z* 345.1730 $[M]^+$, found 345.1716. UV λ_{max} nm 243, 254 (sh), 292, 325 (sh). IR ν_{max} cm^{-1}: 3300, 2930, 2850, 1675, 1605. EI-MS *m/z*: 345 $[M]^+$, 330, 302, 262 (100%), 234, 233.

Murrayamine-J (**2**). Oil. HR-MS: calcd for $C_{23}H_{23}NO_2$, *m/z* 345.1730 $[M]^+$, found 345.1717. UV λ_{max} nm 243, 267, 290, 311, 346 (sh). IR ν_{max} cm^{-1}: 3331, 2856, 2739, 1667, 1646, 1611, 1575. EI-MS *m/z* (rel. int): 345 $[M]^+$ (52), 330 (5), 302 (7), 262 (100), 234 (23), 233 (15), 204 (17).

Murrayamine-N (**3**). Oil. UV λ_{max} nm 248, 264, 271 (sh), 289, 300, 313, 337, 358. IR ν_{max} cm^{-1}: 3333, 1750, 1668, 1590, 1492. EI-MS *m/z* (rel. int.): 375 (M^+, 18), 293 (20), 292 (100), 262 (11), 225 (13), 83 (21), 71 (37).

Murrayamine-I (**4**). Oil. HR-MS: calcd for $C_{20}H_{19}NO_4$, *m/z* 337.1315 $[M]^+$, found 337.1339. UV λ_{max} nm 222, 240, 281 (sh), 295, 324, 360. IR ν_{max} cm^{-1}: 3330, 3270, 1695, 16050. EI-MS *m/z* (rel. int.) 337 $[M]^+$ (15), 264 (100).

Murrayamine-K (**5**). Needles (Me_2CO), mp 127–128°. HR-MS: calcd for $C_{20}H_{19}NO_3$, *m/z* 321.1366 $[M]^+$, found 321.1348. UVλ_{max} nm 237, 279 (sh), 288, 327, 344, 359. IR ν_{max}^{KBr} cm^{-1}: 3388, 1728, 1646, 1613, 1495. EI-MS *m/z*: 321 $[M]^+$, 306, 292, 279, 278, 262, 261, 260, 248 (100%). ^{13}C NMR ($CDCl_3$): δ 15.90 (*q*), 20.78 (*q*), 23.32 (*q*), 67.94 (*t*), 76.6 (*s*), 103.94 (*s*), 110.42 (*d*), 117.20 (*s*), 118.41 (*s*), 119.40 (*d*), 119.62 (*d*), 119.81 (*d*), 121.72 (*d*), 123.84 (*d*), 124.42 (*s*), 124.45 (*d*), 134.83 (*s*), 139.54 (*s*), 149.33 (*s*), 170.83 (*s*).

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