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ALKALOIDS FROM *HERNANDIA SONORA*

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Key Word Index—*Hernandia sonora*; Hernandiaceae; trunk bark; alkaloids; aporphine; dehydroaporphine; 7-formyldehydroovigerine; 7-formyldehydronornantenine; dehydrohernandaline.

Abstract—Three new aporphine alkaloids, 7-formyldehydroovigerine, 7-formyldehydronornantenine and dehydrohernandaline, along with 10 known compounds, (+)-ovigerine, (+)-hernangerine, (+)-*N*-methylhernangerine, *N*-methyl-6,7-dimethoxyisoquinolone, hernandonine, (+)-malekulatine, isovanillin, backebergine, atheroline and (+)-corytuberine, were isolated and characterized from the trunk bark of *Hernandia sonora*. The structures of these compounds were elucidated by spectral analyses.

INTRODUCTION

Hernandia sonora is an evergreen tree, distributed in tropics of the Old World. In Taiwan, it grows along the shores of the Hengchun peninsula and Green Island [1]. The chemical constituents of this plant have been reported extensively [2–24]. Recently, further investigation on the chemical constituents of the trunk bark of this species has led to the isolation of three new minor aporphine alkaloids, 7-formyldehydroovigerine (**1**), 7-formyldehydronornantenine (**2**) and dehydrohernandaline (**3**), together with 10 known compounds from the tertiary basic part of the chloroform-soluble fraction. The known compounds were four aporphines, (+)-ovigerine (**4**) [8], (+)-hernangerine (**5**) [9], (+)-*N*-methylhernangerine (**6**) [9] and (+)-corytuberine (**7**) [25], two oxoaporphines, hernandonine (**8**) [12] and atheroline (**9**) [26], one isoquinolone, *N*-methyl-6,7-dimethoxyisoquinolone (**10**) [10], one isoquinoline, backebergine (**11**) [27], one bis-benzylisoquinoline, (+)-malekulatine (**12**) [19], and one benzaldehyde, isovanillin (**13**). These were identified by comparison of their spectral data (UV, IR, ^{1}H NMR, mass) and/or mixed melting points with corresponding authentic samples. In this paper, we report on the isolation and structural elucidation of the three new aporphine alkaloids (**1**–**3**).

RESULTS AND DISCUSSION

7-Formyldehydroovigerine (**1**) was isolated as yellowish prisms. The molecular formula, $C_{19}H_{13}O_5N$, was determined by electron impact (EI) ($[M]^+$, *m/z* 335) and high-resolution (HR) mass spectrometry. The UV absorptions at 234, 270, 295*sh*, 345 and 429 nm suggested the presence of a dehydroaporphine skeleton [28]. The IR spectrum showed a carbonyl absorption at 1625 cm^{-1} and a methylenedioxy group at 1070 and 950 cm^{-1}. The ^{1}H NMR spectrum of **1** showed four protons [δ3.12 (2H, *t*, J = 6.8 Hz), δ3.62 (2H, *dt*, J = 6.8 Hz, 2.8 Hz)] assignable to the two methylene units at C-4 and C-5, and two methylenedioxy signals at δ6.07 and 6.16 (each 2H, *s*). The aromatic region of the spectrum showed the presence of three protons, one at δ6.92 (1H, *s*) was assigned to H-3, the other *ortho*-coupled protons at δ7.08 and 7.62 (each 1H, *d*, J = 8.7 Hz) to H-9 and H-8. A downfield singlet at δ10.42 was assigned to a formyl group at the C-7 position and a down-field broad singlet at δ11.04 to an NH group due to the formation of hydrogen-bonding with the neighbouring carbonyl group. According to the above data, the structure of **1** was elucidated as 7-formyldehydroovigerine; this was confirmed by NOE difference experiments (Fig. 1).

7-Formyldehydronornantenine (**2**) was obtained as yellowish prisms. The molecular formula, $C_{20}H_{17}O_5N$, was determined by EI ($[M]^+$, *m/z* 351) and HR mass spectrometry. The UV absorptions at 211, 261, 285, and 429 nm were similar to those of **1** and were characteristic of a 7-formyldehydroaporphine nucleus. The IR spectrum showed a carbonyl absorption at 1625 cm^{-1} and a methylenedioxy group at 1060 and 940 cm^{-1}. The ^{1}H NMR spectrum of **2** showed four methylene protons for C-4 and C-5 of ring B at δ3.16 (2H, *t*, J = 6.6 Hz) and δ3.64 (2H, *dt*, J = 6.6, 2.6 Hz), two methoxy signals at δ3.83 and 4.03 (each 3H, *s*) and a methylenedioxy signal at δ6.05 (2H, *s*). The aromatic signals which appeared at δ6.92, 7.60 and 8.96 (each 1H, *s*) were assigned to H-3, H-8 and H-11, respectively. In addition, one formyl group appeared downfield at δ10.46 as a singlet, which was assigned to the C-7 position. One NH group appeared downfield at δ10.89 (1H, *br s*, diappeared with D_2O) due to the formation of hydrogen-bonding with the neighbouring carbonyl group. The chemical shifts of the

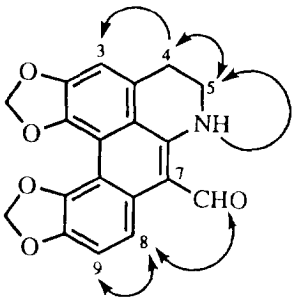
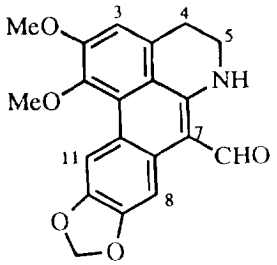


Fig. 1. NOE difference of compound 1.



2

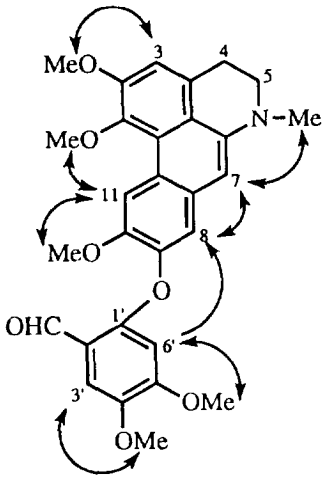


Fig. 2. NOE difference of compound 3.

protons of rings A, B and C of 2 were similar to those of 1 and dioxygenated substituents in ring A at the C-1 and C-2 positions was suggested. Because of the small quantity of 2, NOE–DIF experiments could not be done in order to locate the two methoxyl and methylenedioxy groups, but reviewing ^{1}H NMR data for aporphine alkaloids revealed that two methoxyl groups at the C-9 and C-10 positions, usually show a singlet (6H) or two singlets (each 3H) with a very small difference of chemical shift (within 0.01–0.04 ppm) [28–32]. The chemical shifts of the two methoxyl groups of 2 were δ3.83 and 4.03 with a 0.20 ppm difference and therefore do not agree with this observation. Therefore, it is reasonable to suggest that the two methoxyl groups are located at the C-1 and C-2 position with the methylenedioxy group at the C-9 and C-10 positions. Furthermore, according to the general features of ^{1}H NMR data of aporphines, the higher-field signal at δ3.83 (3H, *s*) was assigned to the C-1 methoxyl and the lower-field signal at δ4.03 (3H, *s*) to the C-2-methoxyl. From the above data, the structure of 2 as 7-formyldehydronornantenine is proposed.

Dehydrohernandaline (3) was obtained as yellowish needles. The molecular formula, $C_{20}H_{19}O_5N$, was determined by EI ([M]$^+$, *m/z* 503) and HR mass spectrometry. The presence of an aporphine–benzene dimeric nucleus was characterized by the UV spectrum showing absorptions at 266 and 333 nm [33]. The IR spectrum showed a carbonyl absorption at 1680 cm^{-1}. The ^{1}H NMR spectrum of 3 showed the presence of an *N*-methyl group at δ3.02 (3H, *s*) and four methylene protons for C-4 and C-5 of ring B at δ3.31 (4H, *m*), in addition to five methoxyl groups at δ3.79, 3.93, 3.96, 4.02 and 4.03 (each 3H, *s*) attributed to C-5′, C-1, C-4′, C-10 and C-2-OMe, respectively, six aromatic protons at δ6.41, 6.53, 7.01, 7.03, 7.44 and 9.26 (each 1H, *s*) assigned to C-7, C-6′, C-8, C-3, C-3′ and C-11-H, respectively, and a formyl group at δ10.38 (1H, *s*) assigned to the C-2′ position. The above assignments were further confirmed by NOE–DIF experiments (Fig. 2). From the above evidence, 3 was characterized as dehydrohernandaline. This is the first report of the occurrence of 3 from a natural source, although it has been synthesized by Mollov and Dutschewska [33].

EXPERIMENTAL

Mps are uncorr. ^{1}H (200 and 400 MHz) and ^{13}C NMR (50 MHz) were taken in $CDCl_3$. Chemical shifts are given in δ with TMS as int. standard. Ms were measured using a direct inlet system. UV spectra were determined in EtOH, IR in KBr discs.

Plant material. Trunk bark of *H. sonora* L. was collected from Green Island, Taitung Hsien, Taiwan, in August 1992. A voucher sample is deposited in the Herbarium of Kaohsiung Medical College, Kaohsiung, Taiwan.

Extraction and isolation. Dried trunk bark (7 kg) was powdered, extracted with MeOH, and the extract concd under red. pres. The MeOH extract when partitioned between H_2O–$CHCl_3$ (1:1) afforded a $CHCl_3$-soluble fr. Bases in the $CHCl_3$-soluble fr. were extracted with 2% H_2SO_4. The acid-soluble part was basified with NH_4OH and extracted with $CHCl_3$. The $CHCl_3$ soln was then treated with 2% aq. NaOH, then dried with K_2CO_3 to give crystalline tertiary non-phenolic bases (fr. B, 26.7 g). The NaOH soln was treated with NH_4Cl and extracted with $CHCl_3$. The $CHCl_3$ soln was dried with $MgSO_4$ and evapd *in vacuo* to afford tertiary phenolic bases (fr. A, 10.4 g). Fr. B (26.7 g) was washed with $CHCl_3$ and filtered to yield 8 (971 mg) after recrystallization ($CHCl_3$–MeOH). The washings (25.3 g) were chromatographed

over silica gel and elution with $CHCl_3$ and $CHCl_3$–MeOH mixts gave 9 frs (B1–B9). Fr. B3 (10.5 g) was rechromatographed on silica gel using $CHCl_3$ and $CHCl_3$–Me_2CO mixts to yield 15 frs (B3-1-B3-15). Fr. B3-3 (27.8 mg) was purified by prep. TLC ($CHCl_3$–Me_2CO, 10:1) to afford frs B3-3-a and B3-3-b. Fr. B3-3-a was further purified by prep. TLC (C_6H_6–EtOAc, 10:1) and recrystallization ($CHCl_3$–MeOH) to afford **1** (2.5 mg) and **2** (1.8 mg). Fr. B3-3-b was recrystallized repeatedly from Et_2O to obtain **13** (16.4 mg). Fr. B3-5 (403 mg) was rechromatographed on silica gel and eluted with $CHCl_3$ to give 3 frs and the first fr. (92.7 mg) further purified by prep. TLC ($CHCl_3$–Me_2CO, 10:1) to afford **3** (4.3 mg) (R_f 0.81) after recrystallization from $CHCl_3$–MeOH. Fr. B3-9 (271 mg) was washed with Et_2O, then purified by prep. TLC (C_6H_6–EtOAc, 10:1) and recrystallization ($CHCl_3$–MeOH) to obtain **10** (115 mg). Fr. B3-11 (22 mg) was rechromatographed on silica gel and elution with CH_2Cl_2–EtOAc (1:1) to obtain frs B3-11-1–B3-11-5. Fr. B3-11-4 (7.3 mg) was further purified by prep. TLC ($CHCl_3$–Me_2CO, 5:1) to give **11** (2.9 mg) (R_f 0.57) after recrystallization from Et_2O. Fr. B3-13 (3.595 g) was rechromatographed on a silica gel column and eluted with $CHCl_3$–Me_2CO (10:1) to afford frs B3-3-1–B3-13-6. Fr. B3-13-5 (1.042 g) was further purified by prep. TLC ($CHCl_3$–MeOH, 10:1) to give **4** (247 mg)(R_f 0.46) after recrystallization from Et_2O–MeOH. Fr. A (10.4 g) was rechromatographed on silica gel, eluting with $CHCl_3$–MeOH (9:1) and gradual increase in proportions of MeOH; 8 frs (A1–A8) were collected. Fr. A2 (134 mg) was purified by prep. TLC (CH_2Cl_2–MeOH, 10:1) to yield **6** (14.5 mg)(R_f 0.61) after recrystallization from Me_2CO. Fr. A4 (1.603 g) was rechromatographed on silica gel, eluting with $CHCl_3$–MeOH (5:1) to give frs A4-1–A4-3. Fr. A4-2 (1.032 g) was separated by prep. TLC ($CHCl_3$–MeOH, 9:1) to give frs A4-2-a–A4-2-d. Fr. A4-2-c (138 mg) was further purified by prep. TLC ($CHCl_3$–MeOH, 10:1) to obtain **9** (11.3 mg) (R_f 0.47) after recrystallization from MeOH. Fr. A4-2-d (685 mg) was also purified by prep. TLC ($CHCl_3$–MeOH, 5:1) to afford **5** (278 mg)(R_f 0.54). Fr. A5 (2.274 g) was rechromatographed on silica gel, and elution with EtOAc–MeOH (1:1) gave frs A5-1–A5-5. Fr. A5-5 (187 mg) was further purified by prep. TLC ($CHCl_3$–MeOH, 1:1) and recrystallization ($CHCl_3$–MeOH) to yield **12** (18.2 mg). Fr. A7 (382 mg) was purified by prep. TLC ($CHCl_3$–MeOH, 10:1) to give **7** (13.7 mg)(R_f 0.29) after recrystallization from MeOH.

7-Formyldehydroovigerine (**1**). Yellowish prisms ($CHCl_3$–MeOH), mp 247–249°. UV λ_{max} nm (log ε): 234 (4.47), 270 (4.48), 295*sh* (4.17), 345 (3.80), 429 (4.00). IR ν_{max} cm^{-1}: 1625 (C=O), 1070, 950 (OCH_2O). EIMS *m/z* (rel. int.): 335 $[M]^+$ (5), 249 (2), 220 (3), 190 (6), 163 (12); HRMS: $C_{19}H_{13}O_5N$, found: 335.0799, calcd: 335.0794. ^1H NMR (200 MHz): δ3.12 (2H, *t*, *J* = 6.8 Hz, H-4), 3.62 (2H, *dt*, *J* = 6.8, 2.8 Hz, H-5), 6.07, 6.16 (each 2H, *s*, $OCH_2O \times 2$), 6.92 (1H, *s*, H-3), 7.08 (1H, *d*, *J* = 8.7 Hz, H-9), 7.62 (1H, *d*, *J* = 8.7 Hz, H-8), 10.42 (1H, *s*, CHO), 11.40 (1H, *br s*, NH, disappeared after addition of D_2O).

7-Formyldehydronornantenine (**2**). Yellowish prisms ($CHCl_3$–MeOH), mp 213–214°. UV λ_{max} nm (log ε): 211 (4.60), 261 (4.62), 285 (4.45), 429 (3.99). IR ν_{max} cm^{-1}: 1625 (C=O), 1060, 940 (OCH_2O). EIMS *m/z* (rel. int.): 351 $[M]^+$ (100), 336 (31), 307 (12), 292 (10), 279 (9), 264 (12); HRMS: $C_{20}H_{17}O_5N$, found: 351.1110, calcd: 351.1107. ^1H NMR (200 MHz): δ3.16 (2H, *t*, *J* = 6.6 Hz, H-4), 3.64 (2H, *dt*, *J* = 6.6, 2.6 Hz, H-5), 3.83 (3H, *s*, OMe-1), 4.03 (3H, *s*, OMe-2), 6.05 (2H, *s*, OCH_2O), 6.92 (1H, *s*, H-3), 7.60 (1H, *s*, H-8), 8.96 (1H, *s*, H-11), 10.46 (1H, *s*, CHO), 10.89 (1H, *br s*, NH, disappeared after addition of D_2O).

Dehydrohernandaline (**3**). Yellowish needles ($CHCl_3$–MeOH), mp 151–153°. UV λ_{max} nm (log ε): 266 (4.66), 333 (4.26). IR ν_{max} cm^{-1}: 1680 (C=O). EIMS *m/z* (rel. int.): 503 $[M]^+$ (13), 488 (2), 308 (4), 292 (2), 280 (3), 264 (4); HRMS: $C_{29}H_{29}O_7N$, found: 503.1944, calcd: 503.1945. ^1H NMR (200 MHz): δ3.02 (3H, *s*, *N*-Me), 3.31 (4H, *m*, H-4, 5), 3.79 (3H, *s*, OMe-5′), 3.93 (3H, *s*, OMe-1), 3.96 (3H, *s*, OMe-4′), 4.02 (3H, *s*, OMe-10), 4.03 (3H, *s*, OMe-2), 6.41 (1H, *s*, H-7), 6.53 (1H, *s*, H-6′), 7.01 (1H, *s*, H-8), 7.03 (1H, *s*, H-3), 7.44 (1H, *s*, H-3′), 9.26 (1H, *s*, H-11), 10.38 (1H, *s*, CHO).

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