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(−)-MAGLIFLOENONE, A NOVEL SPIROCYCLOHEXADIENONE NEOLIGNAN AND OTHER CONSTITUENTS FROM *MAGNOLIA LILIFLORA*

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Key Word Index—*Magnolia liliflora*; Magnoliaceae; tetrahydrofuranolignan; (+)-veraguensin; neolignans; futoenone; (−)-maglifloenone; aporphine derived alkaloid; taspine; β-sitosterol; mass spectral study.

Abstract—A new neolignan designated (−)-maglifloenone and the known one futoenone, both of which contain the rarely occurring spirocyclohexadienone skeleton, have been isolated together with the tetrahydrofuranolignan (+)-veraguensin, an optically inactive tertiary base taspine and β-sitosterol from the leaves and twigs of *Magnolia liliflora*. The structure and stereochemistry of (−)-maglifloenone have been deduced from the spectral data and the mass fragmentation of (−)-maglifloenone and futoenone have been rationalized. This is the first report of two neolignans of spirocyclohexadienone skeleton and of taspine from the Magnoliaceae family and the second report of the natural occurrence of futoenone.

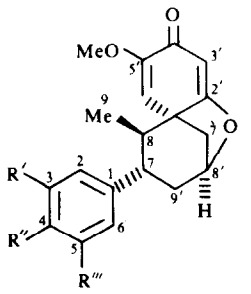
INTRODUCTION

Magnolia liliflora Desr., a large handsome tree native to Japan was collected in June, 1979 in Darjeeling where it has been naturalized. The wood of this species is used for lacquer ware in Japan [1]. The ether extract of *M. liliflora* depressed the spontaneous activity of mice and chicks and caused a distinct muscle weakness. In addition it suppressed convulsions induced by strychnine, picrotoxin and pentetrazole [2]. The bark of *M. liliflora* was found to contain two neolignans, magnolol and honokitol [3], and an alkaloid magnocuranine [1] whereas the leaves and roots were found to contain aporphine, benzylisoquinoline alkaloids [4] and quarternary alkaloids [5–7].

RESULTS AND DISCUSSION

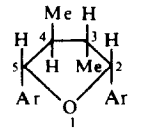
Extensive chromatography over Si gel of the petrol and chloroform extracts of the dried and milled leaves and twigs of *M. liliflora* led to the isolation of a new neolignan with a spirocyclohexadienone skeleton which we have designated (−)-maglifloenone (**1**), in addition to four other known compounds: futoenone (**2**), the only reported neolignan possessing a spirocyclohexadienone skeleton, (+)-veraguensin (**3**), a 2,5-diaryltetrahydrofuranolignan [8], the optically inactive *t*-base taspine (**4**) and β-sitosterol. To our knowledge, the present paper constitutes the first report of the alkaloid taspine and the above lignans except (+)-veraguensin [9], in the Magnoliaceae family and the second report of the natural occurrence of futoenone.

(−)-Maglifloenone, mp 232°, $C_{22}H_{26}O_6$ (M^+ 386), $[\alpha]_D = -90.12°$ ($CHCl_3$; *c* 0.081) has been assigned structure **1** from spectral evidence. Its IR spectrum (KBr) shows a conjugated carbonyl band at 1658 cm^{-1} but no hydroxyl absorption. A comparison of the ^1H NMR spectral data (Table 1) of (−)-maglifloenone with those obtained by us for the congener neolignan futoenone (**2**) [10–12], mp 192°, $[\alpha]_D = -60°$ ($CHCl_3$) leads to the structure and stereochemistry depicted in **1**. The difference in



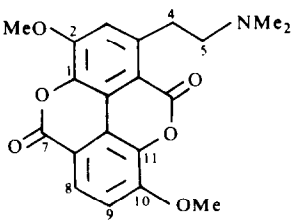
1 R′ = R″ = R‴ = OMe

2 R′ = R″ = CH_2 (−O− / −O−), R‴ = H



Ar = 3,4—Dimethoxyphenyl

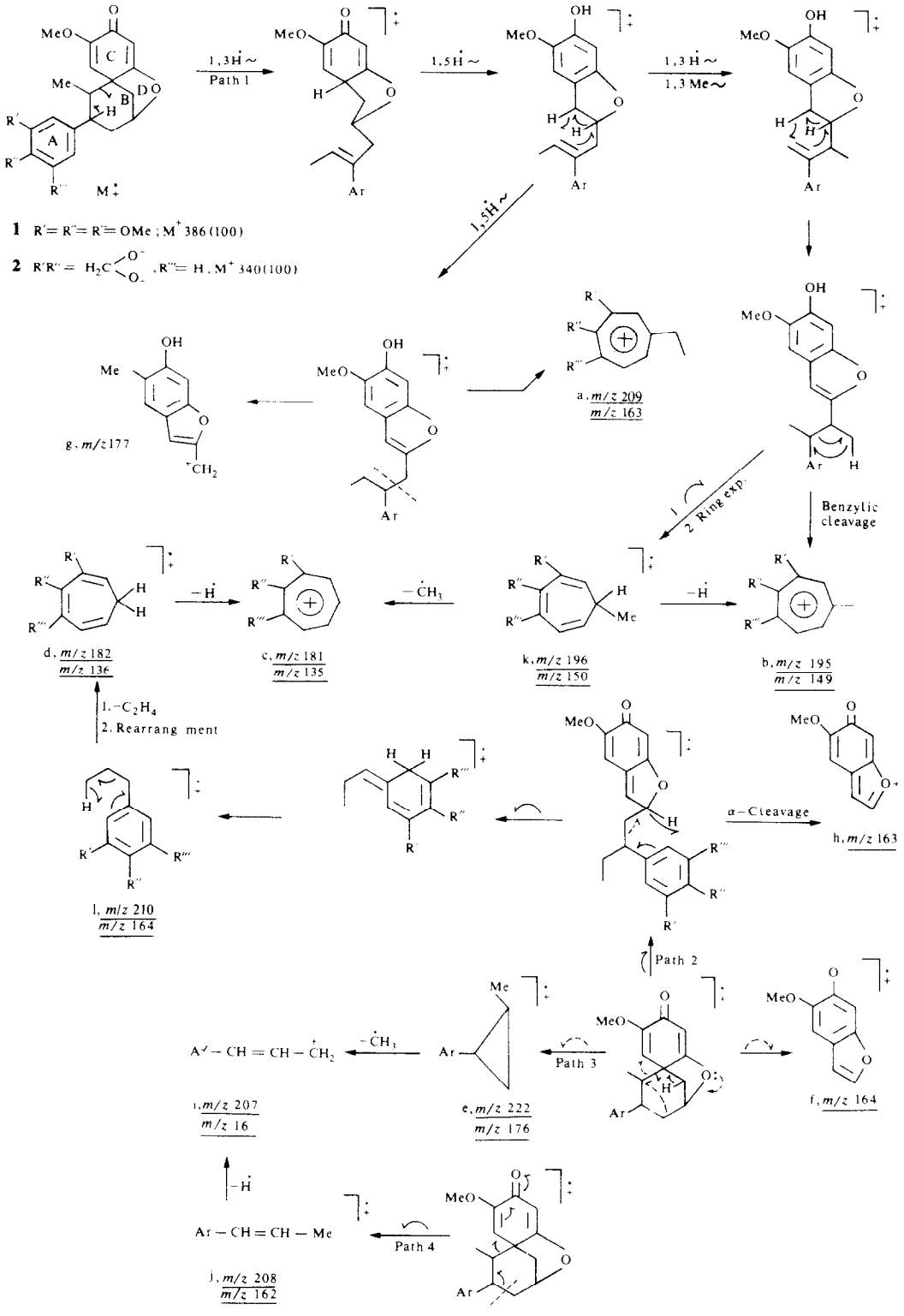
3



(Biogenetic numbering)

4

aromatic substitution patterns between **1** and **2** is clearly evident from Table 1. (−)-Maglifloenone (**1**) exhibits three aromatic methoxyl signals and a 2H singlet assignable to H-2 and H-6 whereas futoenone (**2**) shows one methylenedioxy singlet (2H) and a broad 3H signal due to H-2, H-5 and H-6. The signals due to the remaining 15 protons are almost identical in the spectra of **1** and **2**. Futoenone (**2**) has only been isolated from one other plant, *Piper futokadzura* Sieb et Zucc (Fam. Piperaceae) [10].



Scheme 1. Mass fragmentation of maglifloenone (**1**) and futoenone (**2**). In each case the ion with the higher *m/z* value is from **1** and the one with the lower *m/z* value is from **2**.

Table 1. ^{1}H NMR spectral data of compounds **1** and **2** [80 MHz (**1**) and 60 MHz (**2**), $CDCl_3$, TMS as int. standard]

Assignment	1	2
H_3C-8	0.63 *d*	0.62 *d*
	$J_{9,8} = 6.4$	$J_{9,8} = 6.4$
H-7, H-8, H-7′ and H-9′	1.5–3.0 *m(br)*	1.5–3.0 *m(br)*
H_3CO-5′	3.67 *s*	3.70 *s*
H-8′	5.04 *m*	5.05 *m*
H-6′	5.47 *s*	5.47 *s*
H-3′	5.78 *s*	5.80 *s*
CH_2O_2 at C-3 and C-6	—	5.96 *s*
H_3CO-4	3.82 *s*	—
H_3CO-3 and H_3CO-5	3.85 *s*	—
H-2 and H-6	6.37 *s*	—
H-2, H-5 and H-6	—	6.63–6.80 *s(br)*

The UV absorption of **1** [λ_{max}^{EtOH} nm (log ϵ): 258 (4.32) and 285 (inflection)] is also in accord with the presence of an α-methoxy-$\alpha,\beta,\alpha',\beta'$-dienone chromophore (calc. 262) [13].

The mass spectra of maglifloenone (**1**) and futoenone (**2**) are characteristic of the spirodienone skeleton and the genesis of the significant ions in both cases is given in Scheme 1. The four alternative pathways of the fission of the saturated spiro-ring B is noteworthy. In the mass spectrum of futoenone (**2**) (the genesis of its mass ions has not been reported earlier) the ions containing ring A are the same and those containing ring C appeared with the expected mass shifts (46 a.m.u. less than **1**).

The third lignan, mp 125°, $[\alpha]_D = +31.8°$, had similar UV, IR, ^{1}H NMR and MS spectral data as those reported for (+)-veraguensin (**3**) isolated from *Ocotea veraguensis* Mez. (Fam. Lauraceae) [14]. The basic fraction of the chloroform extract of *M. liliflora* upon usual work-up afforded taspine (**4**), mp 225°d, hydrochloride 251–252°d, $[\alpha]_D = \pm 0°$, isolated earlier from two Berberidaceae plants *Leontice eversmannii* Bunge and *Caulophyllum robustum* Maxim [15, 16].

EXPERIMENTAL

Mps are uncorr. Si gel (100–200 mesh) was used for chromatography, unless otherwise stated; spots were visualized under UV radiation and with I_2 vapour. Homogeneity of compounds was established by TLC and MS.

Extraction. Dried milled leaves and twigs of *M. liliflora* (1.2 kg) collected from Darjeeling, West Bengal during June 1979, were extracted exhaustively in a Soxhlet apparatus with hot petrol (60–80°) followed by $CHCl_3$ (40 hr each). The petrol extract on concn deposited a solid (fraction A) which was filtered. The filtrate (fraction B), residue (fraction A) and the neutral $CHCl_3$ portion (fraction C) obtained after separation of the basic constituents were separately chromatographed over Si gel (60–120 mesh) using solvents and solvent mixtures of increasing polarities. Compounds with the same R_fs (TLC) were combined. The $CHCl_3$ extract (positive Dragendorff's test) was concd under red. pres. to a thick gummy mass. The latter was extracted repeatedly by stirring with 5% citric acid soln (400 ml × 5). The combined acid soln (single spot in TLC) was carefully basified with NH_3 (pH ≥ 8) and the liberated base was taken up in CH_2Cl_2 (500 ml × 4). Evaporation of the solvent from the dried extract (dry Na_2SO_4) afforded a gummy residue which was chromatographed over neutral Al_2O_3 (Brockmann grade, BDH). The known compounds were characterized by spectroscopic methods (IR, UV, ^{1}H NMR, MS).

Isolation of (+)-veraguensin (**3**). The deep green residue from the C_6H_6–$CHCl_3$ (1 : 1) eluates of the main chromatography was subjected to repeated chromatography over Si gel. The later C_6H_6–$CHCl_3$ (1 : 1) eluates afforded (+)-veragyensin (**3**) [9, 14, 17]: colourless flakes (40 mg, $CHCl_3$–petrol), mp 125°, $[\alpha]_D = +31.83°$ ($CHCl_3$; *c* 0.1037), R_f 0.3 in $CHCl_3$ (Si gel); pink colouration with conc. H_2SO_4; UV λ_{max}^{EtOH} nm (log ϵ): 232 (4.26), 279 (3.79): IR ν_{max}^{KBr} cm^{-1}: 3120, 2940 2880, 1600 (aromatic), 1585, 1502, 1225 (*br*), 1155, 1015 (*br*), 805, 750; ^{1}H NMR (60 MHz, $CDCl_3$, TMS as int. standard): δ 3.90–3.95 (4 aromatic-OCH_3), 6.80–7.15 (6H, aromatic, *br*), 0.69 (3H, *d*, $J = 6.3$ Hz, H_3C-3), 1.08 (3H, *d*, $J = 6$ Hz, H_3C-4), 1.8–2.3 (2H, *m*, H-3 and H-4), 4.45 (1H, *d*, $J = 8.3$ Hz, H-5), 5.12 (1H, *d*, $J = 8$ Hz, H-2); MS 70 eV *m/z* (rel. int.): 372 [M]$^+$ (26.1), 206 (100), 191 (35.8), 175 (31.6), 158 (10.3).

Isolation of futoenone (**2**). The black gummy residue obtained from the earlier $CHCl_3$–MeOH (19 : 1) eluates having two spots on TLC, was repeatedly chromatographed over Si gel. The early $CHCl_3$–MeOH (49 : 1) eluates afforded futoenone (**2**): fine colourless needles (55 mg, $CHCl_3$–petrol), mp 192°, R_f 0.4 in $CHCl_3$–MeOH (97 : 3) (Si gel), $[\alpha]_D = -60.0°$ ($CHCl_3$; *c* 0.103), deep pink colouration with conc. H_2SO_4: UV λ_{max}^{EtOH} nm (log ϵ): 258 (4.26), 286 (3.95) IR ν_{max}^{KBr} cm^{-1}: 2920(w), 1635 (conjugated C=O), 1600 (aromatic), 1480, 1235(*br*), 1030, 925 (–OCH_2O–), 725; MS 70 eV: *m/z* (rel. int.): 340 [M]$^+$ (100), 178 (31.3), 177 (33.4), 176 (25.5), 164 (43.6), 163 (95.6), 162 (54.7), 150 (6.3), 149 (17.3), 148 (15.3), 147 (25.5), 135 (62.6 and 134 (17.7).

Isolation of (−)-maglifloenone (**1**). The mother liquor left after the removal of futoenone, and later $CHCl_3$–MeOH (49 : 1) eluates having another spot on TLC were subjected to rechromatography over Si gel. The later $CHCl_3$–MeOH (49 : 1) eluates afforded (−)-maglifloenone (**1**): colourless needles (25 mg, $CHCl_3$–petrol), mp 232°, R_f 0.35 in $CHCl_3$–MeOH (97 : 3), $[\alpha]_D = -90.12°$ ($CHCl_3$; *c* 0.081), deep pink colouration with conc. H_2SO_4; UV λ_{max}^{EtOH} nm (log ϵ): 258 (4.32) and 285 (inflection); IR ν_{max}^{KBr} cm^{-1}: 2938 (*br*), 1658 (conjugated C=O), 1608, 1590 (aromatic), 1506, 1240 (*br*), 1130 (*br*), 1000, 832; MS 70 eV *m/z* (rel. int.): 386 [M]$^+$ (100), 222 (41.8), 210 (53.7), 209 (54.7), 208 (26.4), 207 (17.3), 196 (38.8), 195 (18.6), 182 (29.1), 181 (16.3), 179 (19.2), 177 (20.9), 164 (23.4) and 163 (16.5).

Isolation of taspine (**4**). Elution of the combined basic fractions with C_6H_6–$CHCl_3$ (1 : 1) over neutral Al_2O_3

afforded taspine (**4**) which was further purified from CH_2Cl_2–petrol as an amorphous base (3 g), mp 225°d, R_f 0.6 in $CHCl_3$ (Al_2O_3 neutral), $[\alpha]_D = \pm 0°$, no colouration with conc. H_2SO_4 and alcoholic KOH; UV λ_{max}^{EtOH} nm (log ϵ): 247 (4.85), 285 (4.1) 333 (3.99) and 349 (4.07); UV $\lambda_{max}^{EtOH+NaOH}$ nm (log ϵ): 215 (4.51) and 235 (4.55); IR ν_{max}^{KBr} cm^{-1}: 2950(w), 1725 (>C=O), 1598 (aromatic), 1460, 1435, 1282, 1182, 1085 and 970; ^1H NMR (80 MHz, $CDCl_3$, TMS as int. standard): δ 2.39 [6H, *s*, $-N(CH_3)_2$], 2.66 (2H, *m*, H_2-5), 3.51 (2H, *m*, H_2-4), 4.10 (6H, *s*, H_3CO-2 and H_3CO-10), 7.19 (1H, *s*, H-3), 7.32 (1H, *d*, $J = 9$ Hz, H-9) and 8.21 (1H, *d*, $J = 9$ Hz, H-8); MS 70 eV *m/z* (rel. int.): 369 $[M]^+$ (1) and 58 $[CH_2{=}NMe_2]^+$ (100).

Taspine hydrochloride. A solution of taspine (50 mg) in CH_2Cl_2 containing a drop of conc. HCl (AR grade) was stirred for 2 hr and then cooled in ice. The separated solid crystallized from EtOH as colourless needles (7 mg), mp 251–252°d [18]. Its UV spectra [λ_{max}^{EtOH} nm (log ϵ): 248 (4.86), 285 (4.10), 333 (3.4) and 348 (4.08)] was similar to that reported in the literature [19].

Isolation of β-sitosterol. The earlier C_6H_6 fractions were combined and on chromatography over Si gel, C_6H_6 eluted β-sitosterol: flakes (50 mg, $CHCl_3$–MeOH), mp 138°, $[\alpha]_D = -37°$; β-sitosterol acetate, mp 132°.

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