(c 1.5, $CHCl_3$); IR ($CHCl_3$) 3682, 1751, 1522, 1425 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$, 25 °C) δ 6.08 (d, J = 1.2, 1 H, H-1), 5.39 (td, J = 3.8, 0.9, 1 H, H-4), 5.29 (t, J = 3.6, 1 H, H-3), 5.07 (ddd, J = 3.9, 1.5, 0.9, 1 H, H-2), 4.81 (d, J = 10.2, 1 H, NH), 4.67 (t, J = 9.6, 1 H, H-6), 4.11 (m, 1 H, H-5), 3.74 (s, 3 H, CO_2Me), 2.16, 2.15, 2.12, and 2.00 (four s, each 1 H, OAc), 1.39 (s, 9 H, Bu^t); ^{13}C NMR (75.4 MHz, $CDCl_3$, 25 °C) δ 171.5, 170.1, 169.8, 169.7, 167.7, 154.1, 91.3, 80.8, 71.3, 66.2, 65.3, 63.7, 52.7, 52.1, 28.1, 20.8, 20.6, 20.5, 20.4; MS m/z 505 (M^+). Anal. Calcd for $C_{21}H_{31}NO_{13}$: C, 49.90; H, 6.18; N, 2.77. Found: C, 50.07; H, 6.24; N, 2.91.

Methyl α-D-*glycero*-D-*talo*-Heptopyranuronate D-9. This was obtained by starting with D-7 (0.12 g, 0.23 mmol) according to the above three-reaction protocol: yield 75 mg (64%); glassy solid; $[\alpha]_D$ +59.06° (c 1.27, $CHCl_3$). Anal. Calcd for $C_{21}H_{31}NO_{13}$: C, 49.90; H, 6.18; N, 2.77. Found: C, 49.69; H, 6.34; N, 2.40.

Methyl β-L-*glycero*-L-*allo*-Heptopyranuronate L-10. The reaction was conducted as described for L-9 by starting with 0.15 g (0.29 mmol) of heptopyranose L-8. Flash chromatography eluting with 1:1 hexane/ethyl acetate gave 95 mg (65% yield) of pure L-10 as a glass: $[\alpha]_D$ −5.0° (c 0.47, $CHCl_3$); IR ($CHCl_3$) 3682, 1753, 1524, 1425 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$, 25 °C) δ 5.93 (d, J = 9.0, 1 H, H-1), 5.70 (t, J = 3.0, 1 H, H-3), 5.08 (dd, J = 10.5, 2.7, 1 H, H-4), 4.96 (dd, 9.0, 2.8, 1 H, H-2), 4.58 (d, J = 6.6, 1 H, NH), 4.30 (dd, J = 10.5, 2.7, 1 H, H-5), 4.15 (dd, J = 6.5, 3.0, 1 H, H-6), 3.76 (s, 3 H, CO_2Me), 2.17, 2.16, 2.14, and 2.05 (four s, each 1 H, OAc), 1.46 (s, 9 H, Bu^t); ^{13}C NMR (75.4 MHz, $CDCl_3$, 25 °C) δ 172.43, 170.4, 169.,9, 168.8, 167.7, 154.2, 90.8, 81.2, 75.5, 66.4, 65.3, 63.4, 52.8, 52.3, 28.8, 20.8, 20.6, 20.5, 20.3; MS m/z 505 (M^+). Anal. Calcd for $C_{21}H_{31}NO_{13}$: C, 49.90; H, 6.18; N, 2.77. Found: C, 49.61; H, 6.40; N, 2.43.

Methyl β-D-*glycero*-D-*allo*-Heptopyranuronate D-10. This was obtained by starting with D-8 (100 mg, 0.19 mmol) according to the previous protocol: yield 63 mg (65%); a glass; $[\alpha]_D$ +5.6° (c 0.9, $CHCl_3$). Anal. Calcd for $C_{21}H_{31}NO_{13}$: C, 49.90; H, 6.18; N, 2.77. Found: C, 50.02; H, 6.06; N, 2.59.

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Registry No. 1, 61550-02-5; D-2, 95715-87-0; L-2, 102308-32-7; D-3, 127997-05-1; L-3, 131613-93-9; D-4, 127997-06-2; L-4, 131613-94-0; D-5, 135086-50-9; L-5, 136597-86-9; D-6, 136597-87-0; L-6, 136597-85-8; D-7, 135086-52-1; L-7, 136597-88-1; D-8, 136597-89-2; L-8, 136598-84-0; D-9, 135086-55-4; L-9, 136489-91-3; D-10, 136489-92-4; L-10, 136523-34-7; citric acid, 27-92-9.

Horsfiline, an Oxindole Alkaloid from *Horsfieldia superba*

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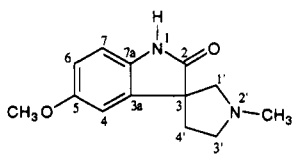
Horsfiline (1), a new oxindole alkaloid, was isolated from *Horsfieldia superba* together with the known alkaloids 6-methoxy-2-methyl-1,2,3,4-tetrahydro-β-carboline **2** and 5-methoxy-*N*,*N*-dimethyltryptamine. The structure of 1 was determined by spectral analysis and confirmed by partial synthesis from **2**.

Introduction

Several Myristicaceae are used as sources of intoxicating snuffs, and some of them have been shown to contain hallucinogenic alkaloids, especially those from *Virola*, which contain tryptamine derivatives.[1] The *Horsfieldia* genus, which encompasses several woody species growing in South East Asia, is sometime used as a medicinal plant.[2] Previous phytochemical investigations of the group led to isolation of trimyristin,[3] arylalkanones,[4] and lignans.[5,6] Alkaloids were not previously reported in the genus. From *H. superba*, a small tree indigenous to Malaysia, we isolated from the leaves three bases including a new oxindole alkaloid, horsfiline (1).



Horsfiline 1

Results and Discussion

Extraction of alkaloids was carried out in the usual way and the three main constituents of the alkaloid fraction were separated by column chromatography and further purified by TLC or crystallization. Two known compounds, 6-methoxy-2-methyl-1,2,3,4-tetrahydro-β-carboline (**2**) and 5-methoxy-*N*,*N*-dimethyltryptamine (**3**), were identified on the basis of their spectral data. Horsfiline (1) was obtained as colorless crystals from acetone, mp 125–126 °C, optically active, $[\alpha]^{20}_D$ −7.2° (MeOH).

The molecular formula $C_{13}H_{16}N_2O_2$ for horsfiline (1) was determined by HRMS. The ^{13}C NMR spectrum displayed signals of 13 carbon atoms: two methyl and three methylene groups, six sp^2 carbons, three among them protonated, one carbonyl at δ_C 183.32, and one quaternary carbon atom at δ_C 54.17 (Table I). The ^1H NMR spectrum revealed one methoxyl (δ_H 3.732) and one *N*-methyl group (δ_H 2.412), three aromatic protons of an ABX spin system, and six protons analyzed from the ^1H–^1H and ^1H–^{13}C COSY data as one methylene and two vicinal methylene groups; one exchangeable proton, detected at lower field (δ_H 9.52), was assigned to an NH group. The NMR chemical shifts of two of the three methylene groups in-

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0022-3263/91/1956-6527$02.50/0

Table I. ^{13}C (75.47 MHz) and ^{1}H (300.13 MHz) NMR Data of 1 and 4 ($CDCl_3$, TMS as Internal Reference)

	1				4		
C	δ_C	δ_H	J (Hz)	LR, J_{CH} = 7 Hz, correlations with H:	δ_C	δ_H	J (Hz)
1		9.52 br s					
2	183.32 s			1'a; 1'b; 4'a; 4'b	181.45 s		
3	54.17 s			1; 4; 1'a; 1'b; 4'a	49.0 s		
3a	137.51 s			1; 7; 1'a; 4'a	135.86 s		
4	110.00 d	6.971 d	2.6		111.48 d	7.221 s	
5	155.98 s			4; OMe	158.13 s		
6	112.30 d	6.668 dd	8.4; 2.6	4; 6	115.34 d	6.885 s	
7	110.08 d	6.780 d	8.4	7	111.94 d	6.885 s	
7a	133.73 s			1; 4; 6	132.84 s		
1'a	66.18 t	2.806 d	9.5	NMe	74.07 t	4.072 d	13.0
1'b		2.846 d	9.5			3.839 d	13.0
3'a	56.64 t	2.746 ddd	8.8; 7.6; 7.4	1'a; 1'b; NMe	67.41 t	4.064 m	
3'b		2.961 ddd	8.8; 7.4; 5.0			4.064 m	
4'a	37.92 t	2.048 ddd	12.8; 7.4; 7.4	1'a	37.53 t	2.707 dt	14.2; 7.0
4'b		2.363 ddd	12.8; 7.6; 5.0			2.616 dt	14.2; 7.0
NMe	41.71 q	2.412 s			55.09 q	3.504 s	
NMe					54.02 q	3.504 s	
OMe	55.73 q	3.732 s		OMe	56.56 q	3.807 s	

dicated that they were linked to a nitrogen atom. These substructures were connected from analysis of the cross peaks observed in the ^{1}H–^{13}C long-range COSY optimized for a J_{C-H} coupling constant value of 7 Hz. The quaternary carbon atom at δ_C 54.17 gave $^{3}J_{C-H}$ correlations with the aromatic proton at δ_H 6.971 (H-4) and the exchangeable proton (δ_H 9.52) and $^{2}J_{C-H}$ correlations with both the lower field methylene at δ_H 2.846 and 2.808 (C-1') and the methylene at δ_H 2.048 and 2.363 (C-4'). The carbonyl carbon showed $^{3}J_{C-H}$ correlations with the same methylene groups at C-1' and C-4'; it was assumed to be an amide carbonyl from its ^{13}C chemical shift and IR absorption (ν 1705 cm^{-1}).

Assignment of aromatic substituents arose from the following observations: the quaternary carbon atom at δ_C 137.51 (C-3a) showed $^{3}J_{CH}$ correlations with the NH group, the aromatic proton at δ_H 6.780 (C-7), and two methylene protons (H-1'a and H-4'a), whereas the quaternary carbon atom at δ_C 133.73 (C-7a) showed $^{2}J_{C-H}$ correlations with the same NH group and aromatic proton and $^{3}J_{C-H}$ correlations with two aromatic protons at δ_H 6.668 (C-6) and 6.971 (C-4). Hence, the methoxyl group was at C-5. This location was confirmed from NOE data, which further allowed assignment of the pyrrolidine ring protons: NOE enhancements were measured between H-4 and the methoxyl group (8.3%) as well as the three following protons: H-1'b (2.2%), H-3'b (1.4%), and H-4'a (3.1%), which are thus on the same side of the ring. These results are in agreement with structure 1 for horsfiline, the absolute configuration for the C-3 spiro asymmetric center remaining undetermined.

On methylation with methyl iodide, horsfiline gave a dimethylammonium iodide derivative (4), characterized by spectral measurements. The molecular cation was observed at m/z 247. Signals of the N-methyl groups at C-2' were not separated in the ^{1}H NMR spectrum (δ_H 3.504) but were distinguished in the ^{13}C NMR spectrum (δ_C 54.02 and 55.09).

The molecular formula $C_{13}H_{16}N_2O$ of alkaloid 2 was determined from mass spectral data. The ^{1}H NMR spectrum revealed spin systems that were connected by using ^{1}H–^{13}C long-range COSY data and established 2 as 6-methoxy-2-methyl-1,2,3,4-tetrahydro-β-carboline. Assignments were confirmed from NOE data. This tetrahydro-β-carboline 2 has been already described[7,8] and previously characterized in some *Virola* species[1] but ^{13}C NMR assignments were not described.

Compound 3 was identified as 5-methoxy-*N*,*N*-dimethyltryptamine (methylbufotenine), a hallucinogen, by spectral analysis and comparison of physical characteristics with published data.[9]

From a structural point of view, horsfiline appeared to be produced by an oxidative rearrangement of the β-carboline 2 into a 3,3-disubstituted-2-oxindole. Such rearrangements have been described especially in the heteroyohimboid and corynantheoid area.[10,11] A synthesis of horsfiline (1) from 2 was thus attempted.

Oxidation of 2 by *N*-chlorosuccinimide was first tried (Scheme I). However, the preparation of the expected intermediate 4a-chloroindolenine 5 failed and we isolated further chlorinated and dehydrogenated derivatives, 5-chloro- and 5,7-dichloro-6-methoxy-2-methyl-β-carbolinium chlorides 6 and 7, respectively.[10-12] The structure of compound 6 was confirmed by a molecular cation at m/z 247/249 and NMR. The benzene ring was tetrasubstituted, bearing two ortho aromatic protons (J = 9.1 Hz). The additional chlorine was thus introduced at C-5 during the reaction. The heterocyclic six-membered ring was aromatic according to NMR data: all the carbon atoms were clearly sp^2 from their chemical shifts, and the three protons belonging to this cycle were ortho/para with low field shifted chemical shift value in agreement with the pyridinium structure 6. NMR assignments arose from ^{1}H–^{1}H and ^{1}H–^{13}C COSY and ^{1}H–^{13}C long-range COSY (optimized for J_{C-H} = 7 Hz). Spectral data indicated compound 7 to differ from 6 by substitution of H-7 by a chlorine. Noteworthy is that the H-3 and H-4 reciprocal assignment was deduced from ^{1}H–^{13}C COSY of 6 and 7 and NOE measurements: irradiation of the N-Me group of 6 induced enhancement of the signal at δ_H 8.438 (9%, H-3) and not of that at δ_H 8.766 (H-4). Upon borohydride reduction, this dichlorocarbolinium 7 afforded the 5,7-dichloro-6-methoxy-2-methyl-1,2,3,4-tetrahydro-β-carboline (8).

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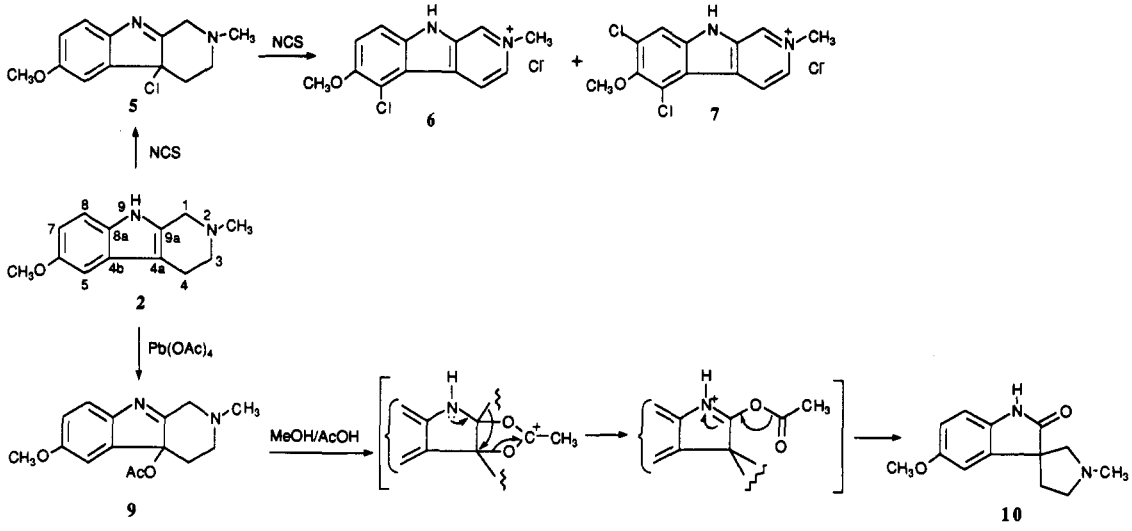
Scheme I. Synthesis of Horsfiline



The reaction of tetrahydro-β-carboline **2** with lead tetraacetate, following the Finch et al. method,[11] furnished a 4a-acetoxyindolenine (**9**) isolated by silica gel chromatography. The IR spectrum showed acetoxyl bands at 1750 and 1220 cm^{-1}. In the ^{13}C NMR spectrum a sp^3 quaternary carbon atom bearing an oxygen atom was observed at δ_C 84.12 and the quaternary sp^2 carbon (C-4a), detected at δ_C 107.37 in the spectrum of **2**, was absent. The ^{13}C NMR spectral assignments were deduced from ^1H–^{13}C COSY and ^1H–^{13}C long-range (J = 7 Hz) COSY data.

The 4a-acetoxyindolenine **9** was further converted into the oxindole (±)-horsfiline (**10**) by an acid-catalyzed rearrangement (Scheme I); **10** was obtained as a racemic mixture, mp 156–157 °C. The identity of (–) natural (**1**) and (±) synthetic (**10**) horsfilines was deduced from comparison of mass and NMR spectral data. A compound such as **10** was supposed to be formed in trace amounts during the reaction of formaldehyde with *N*-methyl-5-methoxytryptamine, but neither physical nor spectral data were given.[13]

Only one other simple natural spiropyrrolidinyl-oxindole has been described in the literature: a 6-hydroxy-1′-isobutyl derivative isolated from *Eleagnus commutata*.[14]

Experimental Section

The leaves of *Horsfieldia superba* (Hk. f. et Th.) Warb. were collected at Sandakan (Sabah, Malaysia) in September 1986. A voucher specimen (David 255) was deposited at the Laboratoire de Phanérogamie, Muséum National d'Histoire Naturelle, Paris France. The dried and powdered material (2.8 kg) was made basic with aqueous NH_3 (10%) and extracted with CH_2Cl_2 in a Soxhlet apparatus until the Mayer test was negative. The organic phases were extracted with HCl (5%) and the acidic solutions were made basic with aqueous NH_3 (25%) and extracted with CH_2Cl_2. Concentration of the organic layer to dryness gave the crude alkaloids (1.9 g). A rough separation was obtained by column chromatography (SiO_2; CH_2Cl_2/MeOH/aqueous NH_3, 92/8/0.5). Further purification, on preparative TLC or crystallization, afforded pure compounds, **1** (1.050 g, 0.037%), **2** (0.230 g, 0.008%), and **3** (0.020 g, 0.0007%).

(–)-Horsfiline (5-methoxy-2′-methylspiro[3*H*-indole-5,5′-pyrrolidin]-2(1*H*)-one, 1): $C_{13}H_{16}N_2O_2$; mp 125–126 °C (acetone); $[\alpha]^{20}_D$ –7.2° (MeOH, c = 1). UV (MeOH), λ_{max} nm (log ϵ): 207 (4.35), 260 (3.96), 305 (3.31). IR (KBr, ν cm^{-1}): 3061, 2940, 2851, 2793, 2656, 1705, 1609, 1495, 1446, 1424, 1347, 1324, 1298, 1219, 1199, 1165, 1030, 900, 812, 765, 680, 610. EIMS (70 eV, 200 °C) m/z (rel intensity): 232 ([M]$^{+\bullet}$, 77), 215 (10), 189 (16), 176 (14), 175 (100), 160 (12), 132 (7), 117 (9), 84 (16), 57 (91), 42 (10). HRMS: 232.1200, calcd for $C_{13}H_{16}N_2O_2$ 232.1212.

2-*N*-Methylhorsfilinium iodide (4): $C_{14}H_{19}N_2O_2^+I^-$; molecular cation = 247; mp 281 °C (MeOH). IR (KBr, ν cm^{-1}): 3142, 1704, 1658, 1606, 1497, 1436, 1403, 1308, 1208, 1136, 1081, 1034, 848, 819. EIMS (70 eV, 200 °C) m/z (rel intensity): 247 (M^+, 1), 246 (9), 232 (16), 215 (2), 203 (3), 189 (27), 175 (42), 160 (9), 142 (100), 132 (3), 127 (41), 117 (4), 89 (1), 77 (2), 57 (20).

6-Methoxy-2-methyl-1,2,3,4-tetrahydro-β-carboline (2): $C_{13}H_{16}N_2O$; mp 217–218 °C (MeOH), lit. mp 183–184 °C,[8] 215.5–216.5 °C.[7] IR (KBr, ν cm^{-1}): 3138, 3045, 2945, 2881, 2834, 2787, 2755, 1598, 1486, 1468, 1399, 1372, 1280, 1244, 1218, 1151, 1131, 1058, 1034, 915, 827, 785, 699, 641. EIMS (70 eV, 200 °C) m/z (rel intensity): 216 ($M^{+\bullet}$, 23), 173 (100), 158 (64), 140 (3), 130 (20), 115 (11), 103 (12), 89 (12), 77 (21), 63 (5), 51 (2). ^1H NMR (CD_3OD) δ: 3.652 (2 H, s; H_2-1), 2.839 (4 H, s; H_2-3 and 4), 6.888 (1 H, dd, J = 2.3, 0.5 Hz; H-5), 6.693 (1 H, dd, J = 8.7, 2.3 Hz; H-7), 7.146 (1 H, dd, J = 8.7, 0.5 Hz; H-8), 2.519 (3 H, s; NMe), 3.789 (3 H, s; OMe). ^{13}C NMR (CD_3OD) δ: 53.19 (t; C-1), 54.09 (t; C-3), 22.11 (t; C-4), 107.37 (s; C-4a), 128.46 (s; C-4b), 101.00 (d; C-5), 154.96 (s; C-6), 111.71 (d; C-7), 112.40 (d; C-8), 132.97 (s; C-8a), 132.58 (s; C-9a), 45.52 (q; NMe), 56.28 (q; OMe).

5-Methoxy-*N*,*N*-dimethyltryptamine (3): $C_{13}H_{18}N_2O$. ^1H NMR ($CDCl_3$) δ: 8.187 (1 H, s; NH), 7.205 (1 H, d, 8.8 Hz), 7.027 (1 H, d, 2.4), 6.955 (1 H, d, 1.5), 6.824 (1 H, dd, J = 8.8, 2.4 Hz), 3.843 (3 H, s; OMe), 2.910 (2 H, m), 2.638 (2 H, m), 2.349 (6 H, s; NMe_2). EIMS (70 eV, 200 °C) m/z (rel intensity): 218 ($M^{+\bullet}$, 66), 216 (1), 188 (6), 174 (16), 173 (10), 160 (36), 145 (23), 130 (12), 117 (28), 103 (5), 89 (7), 83 (5), 77 (9), 58 (100).

Reaction of 1,2,3,4-Tetrahydro-β-carboline (2) with *N*-Chlorosuccinimide. 1,2,3,4-Tetrahydro-β-carboline **2** (21.6 mg) and NCS (20 mg) in CCl_4 (10 mL) were refluxed for 15 min. TLC of the reaction mixture showed the major part of β-carboline **2** unchanged. NCS (40 mg) was added and the mixture refluxed for 15 min. Removal of the solvent in vacuo gave an orange foam. Chromatography on silica gel and elution with CH_2Cl_2/MeOH (8/2) yielded 5-chloro-β-carbolinium **6** and of 5,7-dichloro-β-carbolinium **7**.

5-Chloro-6-methoxy-2-methyl-β-carbolinium chloride (6): $C_{13}H_{12}ClN_2O^+Cl^-$, pseudo M^+ = 247/249; amorphous yellow solid. EIMS (70 eV, 200 °C) m/z (rel intensity): 249 (3), 248 (22), 247 (14), 246 (60), 233 (40), 232 (22), 231 (100), 203 (21). ^1H NMR (CD_3OD) δ: 9.189 (1 H, s; H-1), 8.438 (1 H, d, 6.5; H-3), 8.766 (1 H, d, 6.5; H-4), 7.632 (2 H, s; H-7 and H-8), 4.531 (3 H, s; N^+Me), 3.997 (3 H, s; OMe). ^{13}C NMR (CD_3OD) δ: 131.31 (d; C-1), 133.82 (d; C-3), 120.27 (d; C-4), 132.46 (s; C-4a), 118.21 (s) and 119.28 (s) C-4b and C-5, 152.02 (s; C-6), 113.01 (d) and 120.69 (d) C-7 and C-8, 141.13 (s; C-8a), 137.37 (s; C-9a), 48.73 (q; NMe), 58.30 (q; OMe).

5,7-Dichloro-6-methoxy-2-methyl-β-carbolinium chloride (7): $C_{13}H_{11}Cl_2N_2O^+Cl^-$, pseudo M^+ = 281/283/285; amorphous orange solid. EIMS (70 eV, 200 °C) m/z (rel intensity): 285 (2),

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284 (10), 283 (9), 282 (50), 281 (14), 280 (70), 270 (3), 269 (17), 268 (15), 267 (80), 266 (23), 265 (100), 240 (4), 239 (26), 238 (7), 237 (38). ^{1}H NMR ($CDCl_3$) δ: 8.830 (1 H, d, 1.2; H-1), 7.530 (1 H, dd, 6.4, 1.2; H-3), 8.494 (1 H, d, 6.4; H-4), 7.409 (1 H, s; H-8), 4.301 (3 H, s; NMe), 3.934 (3 H, s; OMe).

5,7-Dichloro-6-methoxy-2-methyl-1,2,3,4-tetrahydro-β-carboline (8). Reduction of **7** with $NaBH_4$ (EtOH) afforded a tetrahydro-β-carboline as a colorless solid: $C_{13}H_{14}Cl_2N_2O$, $M^{+\cdot}$ = 284/286/288. ^{1}H NMR ($CDCl_3$) δ: 3.576 (2 H, s; H_2-1), 3.124 (2 H, t, 5.9; H_2-3), 2.741 (2 H, t, 5.9; H_2-4), 6.816 (1 H, s; H-8), 8.021 (1 H, s; NH), 2.481 (3 H, s; NMe), 3.868 (3 H, s; OMe).

4a-Acetoxy-6-methoxy-2-methyl-2,3,4,4a-tetrahydro-1*H*-pyrido[3,4-*b*]indole (9). 1,2,3,4-Tetrahydro-β-carboline **2** (21.6 mg) and lead tetraacetate (66.5 mg) in CH_2Cl_2 (10 mL) were stirred at 20 °C for 10 min. The dichloromethane solution was washed with water and dried (Na_2SO_4) and the solvent was removed. TLC of the residue on silica gel was eluted by CH_2Cl_2/MeOH (9/1). The zone of R_f 0.8 afforded 4a-acetoxyindolenine **9** (14 mg). IR (KBr, ν cm^{-1}): 1750 (C=O), 1220 (C–O–C). ^{1}H NMR ($CDCl_3$) δ: 3.089 (d, 12.0) and 3.700 (d, 12.0), H_2-1, 2.732 (m) and 2.60 (m), H_2-3, 2.60 (m) and 1.514 (m), H_2-4, 6.952 (d, 2.6; H-5), 6.855 (dd, 8.4, 2.6; H-7), 7.465 (d, 8.4; H-8), 2.405 (s; NMe), 3.790 (s; OMe), 2.036 (s; Ac). ^{13}C NMR ($CDCl_3$) δ: 55.02 (t; C-1), 49.35 (t; C-3), 36.09 (t; C-3), 84.12 (s; C-4a), 138.58 (s; C-4b), 109.52 (d; C-5), 158.55 (s, C-6), 113.84 (d; C-7), 121.71 (d; C-8), 147.60 (s; C-8a), 175.56 (s; C-9a), 44.66 (q; NMe), 55.68 (q; OMe), 20.94 (q; Ac), 168.65 (s; Ac).

(±)-Horsfiline (10). 4a-Acetoxyindolenine **9** (14 mg) in methanol (1 mL), water (0,2 mL), and acetic acid (1 drop) was refluxed for 1.5 h. The solution was evaporated to dryness, basified with ammonia, extracted with CH_2Cl_2, and purified by silica gel TLC, eluting with CH_2Cl_2/MeOH (9/1), to yield (±)-horsfiline (**10**) (R_f 0.4, 4.5 mg), mp 156–157 °C (acetone). The ^{1}H NMR spectrum was identical with that of **1**.

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Synthetic Studies on the Macrodiolide Elaiophylin

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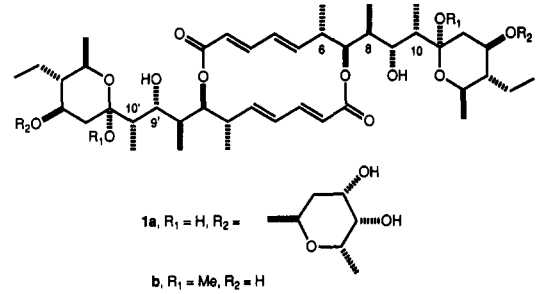
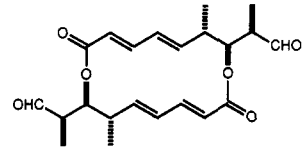
An approach to the synthesis of the monomeric fragment of the macrodiolide elaiophylin is reported. The absolute stereochemistry of C_5–C_{10} is contained in fragment **5** and that of C_{13}–C_{15} is incorporated in aldehyde **6b**. A method for the union of these fragments is outlined.

The antibiotic elaiophylin (**1**) was first isolated in 1959 by Arcamone and co-workers[1] from cultures of *Streptomyces melanosporus*. A year later, Arai et al.[2] reported the isolation of the same compound (azalomycin B) from *S. hygroscopicus* var. *azalomyceticus*. Subsequently, elaiophylin (azalomycin B) was isolated from several other strains of *Streptomyces*.[3] After early structural work by Takahashi,[4] Kaiser and Keller-Schierlein[5] were able to elucidate the gross structure of elaiophylin through the use of ^{1}H and ^{13}C NMR spectroscopy and chemical degradations. Their efforts confirmed the earlier assignment of the carbohydrate residues as 2-deoxy-L-fucose (L-oliose).[4b] In the following year, Neupert-Laves and Dobler[6] published the X-ray crystal structure of elaiophylin, which not only confirmed the efforts of Kaiser and Keller-Schierlein but also defined the relative and absolute stereochemistry of elaiophylin. Ley et al.[3c] were able to define hydrogen bonding in both the solid state and in solution by analysis of X-ray data and NOE studies, respectively.





2

Elaiophylin is a member of a group of C_2-symmetrical, 16-membered macrodiolides that includes pyrenophorin,[7a-c]

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