J = 7 Hz, H-3'), 1.88 (3H, *s*, H-10), 1.90 (6H, *s*, H-4 and H-2'), 3.21 (1H, *s*, H-9), 3.48 (1H, *d*, J = 12 Hz, H-5), 4.00, 4.51 (1H, *d*, J = 8 Hz, CH_2O), 4.20 (1H, *m*, H-12), 4.29 (1H, *d*, J = 8 Hz, H-1), 4.60 (1H, *m*, H-2), 4.98 (1H, *d*, J = 2 Hz, H-7), 5.45 (1H, *d*, J = 9 Hz, H-15), 5.82 (1H, *s*, H-3), 5.99 (1H, *dd*, J = 2, 11 Hz, H-6), 7.10 (1H, *d*, J = 7 Hz, H-3'); MS: *m/z* (rel. abundance) 494 $[M]^+$ (0.01), 424 (5), 414 (32), 394 (11), 247 (5), 256 (68), 187 (73), 151 (15), 149 (74), 135 (53), 100 (68), 83 (95), 55 (100).

Hydrolysis of **3**. A soln of **3** (20 mg) in MeOH–H_2O (1 : 1) was maintained at pH 9 at room temp. for 1 hr. After neutralization, the mixture was concd and the reaction products were purified by prep. TLC on silica gel ($CHCl_3$–MeOH, 19 : 1). The more polar 15-desacetylundulatone was isolated (yield 10%) and shown to be identical to **4** by UV, IR, MS and by TLC on silica gel.

Oxidation of **5**. A CH_2Cl_2 soln of pyridinium chlorochromate (10 mg in 1 ml) was added to 1 ml of a saturated CH_2Cl_2 soln of **5** and then stirred at room temp. for 1 hr. The reaction products were then separated by prep. TLC on silica gel ($CHCl_3$–MeOH, 9 : 1); the major product (9 mg) was identical to **4** (TLC on silica gel, UV, IR and MS).

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ALKALOIDS FROM *HAPLOPHYLLUM SUAVEOLENS*

AYHAN ULUBELEN

Faculty of Pharmacy, University of Istanbul, Istanbul, Turkey

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Key Word Index—*Haplophyllum suaveolens*; Rutaceae; alkaloids; flindersine; γ-fagarine; kokusaginine; haplophylline.

Abstract—Flindersine, γ-fagarine, kokusaginine and one new alkaloid of the flindersine-type were isolated from the aerial parts of *Haplophyllum suaveolens*. Spectral methods were used to determine the structures of the alkaloids.

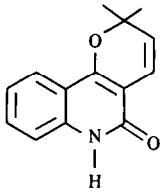
INTRODUCTION

A literature survey revealed that new and known quinoline and other types of alkaloids have been isolated from various *Haplophyllum* species and their structures determined [1–8]. In the present study, benzene and chloroform extracts of the arial parts of *Haplophyllum suaveolens* (DC.) G. Don yielded four alkaloids, one of which was a new compound. The main alkaloid of the plant was flindersine (**1**) [1], the second known alkaloid was γ-fagarine (**2**) [2] and the third kokusaginine (**3**) [9] which has also been obtained from various species of Rutaceae. The new alkaloid has an angular pyranoquinoline structure like flindersine.

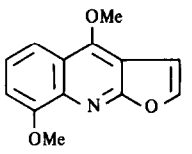
RESULTS AND DISCUSSION

H. suaveolens yielded three known and a new alkaloid of furoquinoline and angular pyrano-quinoline types. The identity of the known alkaloids was established by spectral comparison with literature data [1, 2, 9–12].

The structure of the new alkaloid named haplophylline (**4**) was determined by means of UV, IR, ^{1}H NMR and mass spectra. The UV spectrum of **4** was similar to that of flindersine (**1**) (see Experimental), but its IR spectrum however, showed an extra carbonyl band at 1720 cm^{-1}. In addition to flindersine peaks the ^{1}H NMR spectrum of **4** showed peaks for a senecioyloxy moiety at δ 1.88 (3H, *d*, J = 2 Hz), 2.2 (3H, *d*, J = 2 Hz), 5.67 (1H, *t*, J = 1 Hz) and a downfield peak for a methylene group at δ 6.37 (2H, *br s*). The lack of an amidic proton (N–H) signal at δ 11.28 indicated that the substitution could only be on the nitrogen atom. The mass spectrum showed the presence of senecioyloxy and methylene groups on the nitrogen atom. The base peak at *m/z* 324 $[M-15]^+$ corresponds to the base peak of **1** $[212\,[M-15]^+]$, the peak at *m/z* 227 $[M-C_6H_9O_2]^+$ shows the flindersine part of the molecule,



1



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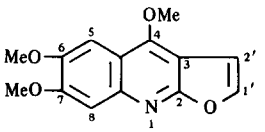

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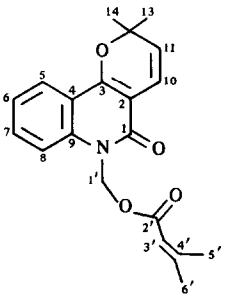

4

and the peak *m/z* 212 $[M-C_6H_9O_2-Me]$(95%) corraborates the flindersine skeleton. Other peaks at *m/z* 240 $[M-C_5H_7O_2]^+$ and 256 $[M-C_5H_7O]^+$ are derived from degradation of the senecioyloxy moiety, whereas the peak at *m/z* 83 (C_5H_7O) (70%) corresponds to the senecioyl moiety. All the spectral data confirm that haplophylline is a new derivative of flindersine.

EXPERIMENTAL

Plant material was collected from the Aegean section of Turkey (Denizli) in June 1982 and identified by E. Tuzlaci (Istanbul). A voucher specimen is deposited in the Herbarium of the Faculty of Pharmacy, University of Istanbul (ISTE 48925)

Dried and powdered plant material (500 g) was successively extracted with C_6H_6, $CHCl_3$ and EtOH in a Soxhlet Since C_6H_6 and $CHCl_3$ extracts showed the presence of the same alkaloids by TLC, they were combined The EtOH extract which had no alkaloids was set aside for future investigation.

Isolation of alkaloids The C_6H_6–$CHCl_3$ extracts of the plant material were evapd under vacuum. The residue (18.5 g) was dissolved in $CHCl_3$, 5% NH_4OH added to form a suspension and this was concd to a small vol and exhaustively extracted with $CHCl_3$. The combined $CHCl_3$ extracts were washed with H_2O, dried (Na_2SO_4), filtered and concd under vacuum. The $CHCl_3$ concentrate was extracted with 5% HCl until no further alkaloids were obtained The aq acid phase was made alkaline by the addition of conc NH_4OH, extracted with $CHCl_3$, washed with H_2O, dried (Na_2SO_4), filtered and evapd to dryness *in vacuo* to yield 1.8 g of crude alkaloid mixture (yield 0.36%). The alkaloid mixture was chromatographed on a neutral Al_2O_3 (activity III) column (3 × 50 cm), elution of the column started with $CHCl_3$ and continued by gradient addition of EtOH.

Identification of alkaloids: *flindersine* (**1**) Mp 185° (lit. [12] 185–186°), yield 74 mg UV λ_{max}^{EtOH} nm: 366, 348, 282 (sh), 260 (sh), 224. IR ν_{max}^{KBr} cm^{-1}: 3050, 1720 (sh), 1650, 1620, 1590, 1550 (sh), 1495, 1475, 1425, 1405, 1355, 1270, 1250, 1125, 1115, 870, 745. ^1H NMR (200 MHz, $CDCl_3$): δ 1.50 (6H, *s*, Me-13, Me-14), 5.55 (1H, *d*, *J* = 9 Hz, H-10), 6 75 (1H, *d*, *J* = 9 Hz, H-11), 7.18 (1H, *dt*, *J* = 2 Hz and 7 Hz, H-6*), 7.34 (1H, *br d*, *J* = 8 Hz, H-5†), 7.47 (1H, *dt*, *J* = 2 Hz and 7 Hz, H-7*), 7.88 (1H, *dd*, *J* = 2 Hz and 7 Hz, H-8†) and 11.28 (1H, *br s*, N–H). MS 70 eV, *m/z* (rel. int.): 227 $[M]^+$ (75), 212 $[M-15]^+$ (100), 198 $[M-29]^+$ (22), 183 $[M-44]^+$ (22) (Found: C, 73.94; H, 5.74; N, 6.18 %. $C_{14}H_{13}O_2N$ requires: C, 74.00; H, 5.68; N, 6.16%.)

γ-Fagarine (**2**). Yield 4 mg, mp 138° (lit. [10] 138–140°). UV λ_{max}^{EtOH} nm: 334, 320, 308, 297 (sh), 252 (sh), 245, 209. IR ν_{max}^{KBr} cm^{-1}: 3115, 1620, 1580, 1550, 1500, 1480, 1430, 1370, 1320, 1260, 1210, 1150, 1090, 940, 850. ^1H NMR (200 MHz, $CDCl_3$): δ 4 20 (3H, *s*, C_8-OMe), 4.45 (3H, *s*, C_4-OMe), 7.05 (1H, *d*, *J* = 2.5 Hz, H-1'), 7.57 (1H, *d*, *J* = 2.5 Hz, H-2'), 8.00 (1H, *dd*, *J* = 2 Hz and 7 Hz, H-5*), 7.45 (1H, *dt*, *J* = 2 Hz and 7 Hz, H-6), 7.18 (1H, *dd*, *J* = 2 Hz and 7 Hz, H-7*). MS 70 eV, *m/z* (rel. int.): 229 $[M]^+$ (100), 228 $[M-1]^+$ (78), 214 $[M-15]^+$ (17), 200 $[M-29]^+$ (68) (Found: C, 68.15; H, 4.82; N, 6.13%. $C_{13}H_{11}O_3N$ requires: C, 68.07; H, 4.80; N, 6.11%.)

Kokusaginine (**3**). Yield 10 mg, mp 160° (lit. [9] 164°). UV λ_{max}^{EtOH} nm: 334, 320, 308, 297 (sh), 252 (sh), 245, 209. IR ν_{max}^{KBr} cm^{-1}: 3115, 1620, 1585, 1545, 1500, 1480, 1430, 1365, 1320, 1255, 1210, 1150, 1090, 1050, 1010, 940, 850, 790, 770. ^1H NMR (200 MHz, $CDCl_3$): δ 4.04 (6H, *s*, C_6-OMe and C_7-OMe), 4.45 (3H, *s*, C_4-OMe), 7.05 (1H, *d*, *J* = 2 5 Hz, H-1'), 7.58 (1H, *d*, *J* = 2.5 Hz, H-2'), 7.35 (1H, *s*, H-5*), 7.48 (1H, *s*, H-8*). MS 70 eV, *m/z* (rel. int.): 259 $[M]^+$ (100), 244 $[M-15]^+$ (75), 229 $[M-30]^+$ (10), 216 $[M-43]^+$ (30), 201 $[M-58]^+$ (25), 186 $[M-73]^+$ (30). (Found: C, 64.92; H, 5.05; N, 5.43%. $C_{14}H_{13}O_4N$ requires: C, 64.86; H, 5.02, N, 5.40%.)

Haplophylline (**4**). Yield 15 mg, amorphous. UV λ_{max}^{EtOH} nm: 366, 348, 336, 322, 305 (sh), 254 (sh), 224. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3000, 2920, 1720, 1650, 1605, 1570, 1500, 1460, 1360, 1220, 1185, 1130, 1070, 970, 850. ^1H NMR (200 MHz, $CDCl_3$): δ 1.52 (6H, *s*, Me-13 and Me-14), 1.88 (3H, *d*, *J* = 2 Hz, Me-5'), 2.2 (3H, *d*, *J* = 2 Hz, Me-6'), 5.54 (1H, *d*, *J* = 9 Hz, H-10), 5.67 (1H, *t*, *J* = 1 Hz, H-3'), 6.37 (2H, *br s*, N–CH_2–O), 6.74 (1H, *d*, *J* = 9 Hz, H-11), 7.92 (1H, *dd*, *J* = 2 Hz and 10 Hz, H-8*), 7.48 (1H, *dt*, *J* = 2 Hz and 10 Hz, H-7†), 7.34 (1H, *br d*, *J* = 11 Hz, H-5†), 7.25 (1H, *dt*, *J* = 2 Hz and 10 Hz, H-6†, partially under $CDCl_3$ peak). MS 70 eV, *m/z* (rel. int): 339 $[M]^+$ (75), 324 $[M-15]^+$ (100), 256 $[M-83]^+$ (27), 240 $[M-99]^+$ (45), 227 $[M-112]^+$ (55), 212 $[M-127]^+$ (95), 167 (68), 149 (80), 83 (70). (Found: C, 70.82; H, 6.22; N, 4.18%. $C_{20}H_{21}O_4N$ requires: C, 70.79; H, 6.19; N, 4.13%.)

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*†, Interchangeable.

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