Pergamon 0031-9422(95)00416-5

Phytochemistry, Vol. 40, No. 5, pp. 1473–1475, 1995

0031-9422/95 $9.50 + 0.00

DITERPENOIDS FROM *SALVIA HELDRICHIANA*

AYHAN ULUBELEN,*† ‡GÜLAÇTI TOPCU† and NUR TAN*

*Faculty of Pharmacy, University of Istanbul, 34452, Istanbul, Turkey; †TUBITAK, Marmara Research Center, Department of Chemistry, PK 21, 41470, Gebze, Kocaeli, Turkey

(*Received* 7 *February* 1995)

Key Word Index—*Salvia heldrichiana*; Labiatae; diterpenoids; a new aromatic compound; salvigenine.

Abstract—From the roots of *Salvia heldrichiana*, one new and five known diterpenes were isolated, together with a large amount of salvigenine and a new aromatic compound di(4,4′-hexyloxycarbonylphenyl) ether. The structures of the new and the known compounds were established by spectral data.

INTRODUCTION

Salvia heldreichiana Boiss. ex Bentham in DC. is a branched shrub, 1.5 ml tall, erect and leafy with short hairs, endemic to the eastern Mediterranean. In the present study, we have isolated and characterized five known diterpenes isopimaric acid (**1**) [1], 7*β*-hydroxysandaracopimaric acid (**2**) [1], 7-oxo-13-epi-pimara-8,15-dien-18-oic acid (**3**) [2], wiedelactone (**4**) [3] and wiedemannic acid (**5**) [4], in addition to a new abietane diterpene heldrichinic acid (**6**) and a new dimeric aromatic compound di(4,4′-hexyloxycarbonylphenyl) ether (**7**) as well as salvigenine [5], from the roots of the plant.

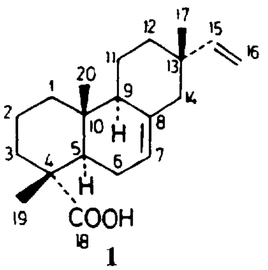
RESULTS AND DISCUSSION

The high resolution EI mass spectrum of **6** indicated the molecular formula $C_{20}H_{28}O_4$ (*m/z* 332.1980, calc. 332.1987). The IR spectrum showed the presence of hydroxyl (3400 cm^{-1}), acid [2600–2800 (sh) and 1693 cm^{-1}], carbonyl [1710 (sh) cm^{-1}] and vinylic group (1640, 980, 910 cm^{-1}) bonds. The ^{13}C NMR (APT) spectrum of **6** indicated the presence of three methyl, seven methylene, three methine and seven quaternary carbon singlets. The signal of a carbonyl group was at δ214.2 ppm and that of a carboxyl at δ182.3; two downfield signals at δ148.7 (*s*) and 110.3 (*t*) indicated an exomethylene group and two other downfield signals at δ111.2 (*s*) and 110.5 (*d*) showed the presence of a trisubstituted double bond. A signal at δ76.5, together with the absence of a carbinol proton in the ^1H NMR spectrum, indicated the presence of a tertiary hydroxyl group.

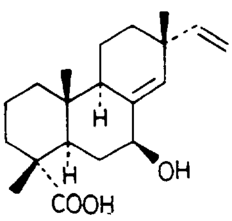
In the ^1H NMR spectrum the signals for an isopropenyl group were observed at δ4.81 (2H, *br s*, C-16 exo CH_2) and 1.72 (3H, *s*, Me-17). A signal at δ5.12 (1H, *dd*, $J = 4$ and 7 Hz, H-11) indicated the presence of a vinylic proton, while two methyl signals were observed as singlets at δ1.27 (Me-19) and 0.94 (Me-20). The mass fragmentation of compound **6** was similar to that of compactone (**8**) [6] (Fig. 1) with fragment ions at *m/z* 195 (a), 168 (b), 153 (c), 109 (d) and 165 (e). Therefore, the trisubstituted double bond in compound **6** had to be in ring C, and in one of the following positions Δ^{13-14}, Δ^{12-13}, Δ^{9-11} or Δ^{8-14}. The first two positions would cause a conjugation with the isopropenyl group, and the UV maximum would be *ca* 230–250 nm and not at 207 nm as observed. On the other hand, if the double bond was at Δ^{8-14} the signal for proton at C-14 would be shifted to δ_H 7.6–7.9 due to the presence of a carbonyl group at C-7, also its UV spectrum should show conjugation between the double bond and the carbonyl group. Therefore, the only possible place for the double bond was at Δ^{9-11}. Spin decoupling experiments showed a vicinal coupling between the signal at δ5.12 (H-11) and the signals at δ2.57 (1H, *br dd*, $J = 4$ and 10 Hz, H-12a) and 2.26 (1H, *br dd*, $J = 7$ and 10.0 Hz, H-12b). The position of the hydroxyl group should be at C-8 as observed in compound **8**. The stereochemistry of the hydroxyl group at C-8 was established by the pyridine-induced solvent shifts; thus, the methyl group at C-10 (Me-20) was shifted 0.25 ppm downfield due to the *syn*-diaxial relationship between the *β*-hydroxyl and Me-20, and downfield shifts were also observed for Me-17 (Δ 0.18) and 6*β*-H (Δ 0.19) [7], indicating the presence of a C-8 *β*-hydroxyl group. These results and biogenetic considerations, as well as the isolation of 7-oxygenated

---

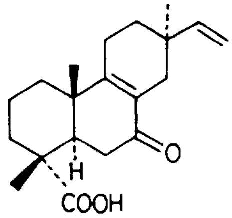
‡Author to whom correspondence should be addressed.



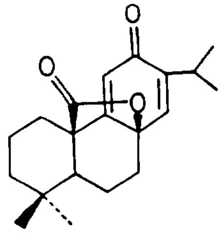
1



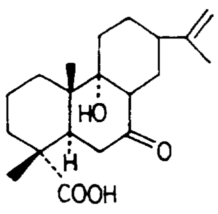
2



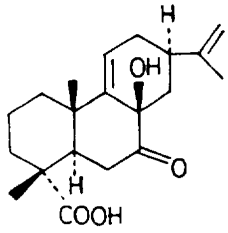
3



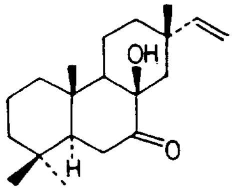
4



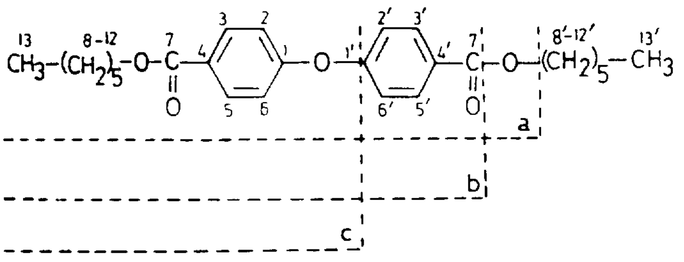
5



6



8



7

Fig. 1. Fragments of compound **6**.

diterpenoids **2**, **3** and **5** from the extract, supported a similar skeleton for compound **6**.

The HR mass spectrum of the new dimeric aromatic compound **7** indicated a molecular formula $C_{26}H_{34}O_5$ (*m*/*z* 426.2411; calc. 426.2406). The UV spectrum of **7** showed a substituted aromatic system giving a maximum at 278 nm. The IR signals were at 1730 cm^{-1} (carbonyl), 3050, 1616, 1558, 1520 cm^{-1} (aromatic). The ^{1}H NMR spectrum clearly indicated the structure: δ7.07 (4H, *d*, $J = 8$ Hz, H-3,5,3′,5′), 6.76 (4H, *d*, $J = 8$ Hz, H-2,6,2′,6′), 4.23 (4H, *t*, $J = 7$ Hz, CH_2-8 and CH_2-8′), 2.85 (4H, *t*, $J = 7$ Hz, CH_2-9 and CH_2-9′), 2.28 (4H, *br t*, $J = 7$ Hz, CH_2-10 and CH_2-10′), 1.58 (4H, *br t*, $J = 7$ Hz, CH_2-11 and CH_2-11′), 1.15 (4H, *br t*, $J = 7$ Hz, CH_2-12 and CH_2-12′) and 0.9 (6H, *t*, $J = 7$ Hz, Me-13 and Me-13′). The ^{13}C NMR spectrum of **7** was in agreement with the given structure (see Experimental). The mass spectrum showed ions at *m*/*z* 340 $[M - C_6H_{13} - H]^+$ (a), 323 $[M - C_6H_{13}O - 2H]^+$ (b) and 221 $[M - C_{13}H_{17}O_2]^+$ (c) which corroborated the assigned structure.

EXPERIMENTAL

General. IR: $CHCl_3$; ^{1}H NMR: 200 MHz (^{1}H) and 50.32 MHz (^{13}C) in $CDCl_3$; HRMS, VG ZapSpec; TLC: Kieselgel 60 F_{254} (E. Merck) precoated plates; CC Sephadex LH-20 (Fluka).

Plant material. *Salvia heldreichiana* was collected from Central Turkey (Niğde) in 1983 and identified by Dr E. Tuzlaci (Istanbul); a voucher specimen is deposited in the Herbarium of Faculty of Pharmacy, University of Istanbul, ISTE 50885.

Extraction and isolation of the compounds. The dried and powdered roots of *S. heldreichiana* (1 kg) was extracted with Me_2CO in a Soxhlet. The solvent was evapd *in vacuo* to give 9.5 g of a residue which was fractionated by silica gel CC (4 × 60 cm). The column was eluted with petrol, a gradient of EtOAc was added up to 100%, followed by EtOH. The following compounds were isolated; wiedelactone (7 mg), heldrichinic acid (8 mg), isopimaric acid (12 mg), di(4,4′-hexyloxycarbonylphenyl) ether (8 mg), wiedemannic acid (5 mg), 7β-hydroxysandracopimaric acid (13 mg), salvigenin (82 mg) and 7-oxo-13-epi-pimara-8,15-dien-18-oic acid (9 mg).

Heldrichinic acid (**6**). IR $\nu_{\max}^{\mathrm{CHCl_3}}$ cm^{-1}: 3400, 2800–2600 (sh), 1710 (sh), 1693, 1640, 1468, 1439, 1376, 1318, 1269, 1213, 1160, 1070, 1040, 850; UV $\lambda_{\max}^{\mathrm{MeOH}}$ nm: 207 (3.9); ^{1}H NMR ($CDCl_3$: see text; ^{13}C NMR (APT) ($CDCl_3$): δ43.1 C-1, 19.6 C-2, 41.2 C-3, 35.4 C-4, 58.0 C-5, 46.1 C-6, 214.2 C-7, 76.5 C-8, 111.2 C-9, 39.8 C-10, 110.5 C-11, 30.0 C-12, 40.0 C-13, 43.1 C-14, 148.7 C-15, 18.3 C-16, 110.3 C-17, 182.3 C-18, 29.7 C-19, 15.6 C-20; HREIMS *m/z* (rel. int.): 332.1980 $[M]^+$ (45), ($C_{20}H_{28}O_4$), 314 $[M - H_2O]^+$ (20), 287 $[M - CO_2H]^+$ (20), 258 (30), 195 (a) (40), 168 (b) (55), 153 (c) (65), 109 (d) (100), 165 (e) (42), 83 (98), 67 (80).

Di(4,4′-*hexyloxycarbonylphenyl*) *ether* (**7**). IR $\nu_{\max}^{\mathrm{CHCl_3}}$ cm^{-1}: 3050, 2915, 2847, 1730, 1616, 1558, 1520, 1472, 1190, 1180, 1109, 826; UV $\lambda_{\max}^{\mathrm{MeOH}}$ nm: 278 (2.9), 223 (3.8); ^{1}H NMR: see text; ^{13}C NMR (APT) ($CDCl_3$): δ154.2 (C-1, C-1′), 130.0 (C-2, C-2′, C-6, C-6′), 115.3 (C-3, C-3′, C-5, C-5′), 142.2 (C-4, C-4′), 174.0 (C-7, C-7′), 64.9 (C-8, C-8′), 34.3 (C-9, C-9′), 31.0 (C-10, C-10′), 24.9 (C-11, C-11′), 22.6 (C-12, C-12′), 14.0 (C-13, C-13′); HREIMS *m/z* (rel. int.): 426.2411 $[M]^+$ ($C_{26}H_{34}O_5$) (25), 411 $[M - Me]^+$ (45), 340 $[M - C_6H_{13}H]^+$ (a) (90), 323 $[M - C_6H_{13}O - 2H]^+$ (b) (100), 221 $[M - C_{13}H_{17}O_2]^+$ (c) (25), 199 (95), 152 (73), 121 (80), 103 (65), 85 (98), 71 (67).

REFERENCES

1. Mihashi, S., Yanagisawa, I., Tanaka, O. and Shibata, S. (1969) *Tetrahedron Letters* **1**, 1683.
2. de Pascual Teresa, J., Barrero, A. F., Muriel, L., San Feliciano, A. and Grande, M. (1980) *Phytochemistry* **19**, 1153.
3. Ulubelen, A., Topcu, G., Chen, S., Cai, P. and Snyder, J. K. (1991) *J. Org. Chem.* **56**, 7354.
4. Topcu, G. and Ulubelen, A. (1990) *Phytochemistry* **29**, 2346.
5. Ulubelen, A., Öztürk, S. and Doğanca, S. (1968) *J. Pharm. Sci.* **57**, 1037.
6. Pinto, A., Silva, A. J. R., Mayer, L. M. U. and Braz-Filho, R. (1979) *Phytochemistry* **18**, 2036.
7. Demarco, F. V., Farkas, E., Doddrell, D., Mylari, B. L. and Wenkert, E. (1968) *J. Am. Chem. Soc.* **90**, 5480.