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GERMACRANE DERIVATIVES FROM THE FRUITS OF *SMYRNIUM CRETICUM*

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Key Word Index—*Smyrnium creticum*; Umbelliferae; germacranes; epoxygermacranes; germacranolides.

Abstract—Extracts of the fruits of *Smyrnium creticum* yielded seven known compounds, furodiene, germacrone, glechomafuran, 1β,10α-epoxy-4-methoxyglechomanolide, 1β,10α-epoxy-4-methoxy-8-hydroxyglechomanolide, 1β,10α-epoxygermacrone, 1β,10α;4α,5β-diepoxygermacrone, and two new compounds, 4α,5β-epoxygermacrone and 1β,10α-epoxy-4-hydroxyglechoma-8-enolide, were also characterized from the same extract. Their structures were established by spectral methods.

INTRODUCTION

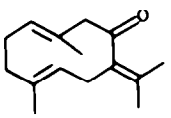
While studying the oxidation of furanosesquiterpenes to their corresponding lactones [1-5], we isolated germacrone (**1**) from the fruits of *Smyrnium creticum* Mill. in a high yield, and three epoxygermacrones (**2–4**), one of them being new, together with a new germacranolide, 1β,10α-epoxy-4-hydroxyglechoma-8-enolide (**5**). Other compounds were identified as furodiene (**6**), the main compound of the plant material, glechomafuran (**7**), 1β,10α-epoxy-4-methoxy-glechomanolide (**8**) and 1β,10α-epoxy-4-methoxy-8-hydroxyglechomanolide (**9**). In the course of this study we observed the oxidation of **1** to **2–4**. The structures of the known compounds were established by comparing their spectra with those of authentic samples as well as by TLC comparison, while the new compounds were established mainly by their ^{1}H NMR spectra.

RESULTS AND DISCUSSION

Although we obtained two eremophilanolides, istanbulins D and E, from the roots of *S. creticum* [6] in a previous study and eudesmanolides [3,4] and eremophilanolides [7, 8] from the roots and fruits of various *Smyrnium* species, in this study we only isolated germacrane derivatives from the fruits of *S. creticum*. 1β,10α-Epoxygermacrone and 1β,10α; 4α,5β-diepoxygermacrone, together with germacrone, were previously obtained from *S. olusatrum* [9].

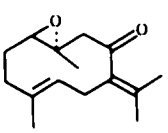
The mass spectrum of 4α,5β-epoxygermacrone (**2**) indicated the molecular formula $C_{15}H_{22}O_2$ ([M]$^+$, *m/z* 234). The IR spectrum showed a carbonyl group at 1730 cm^{-1}, while no hydroxyl or lactone bands were present. The ^{1}H NMR spectrum showed four methyl singlets at δ 1.81 and 1.79 (C-11 Me), 1.70 (C-10) and 1.22 (C-4 Me). A double doublet at 5.34 (*J* = 6 and 13 Hz, H-1) indicated a vinylic proton at C-1. An isolated methylene at C-9 was indicated by the peaks at 2.86 (*d*, *J* = 14 Hz, H-9) and 2.02 (*d*, *J* = 14 Hz, H-9'). Further signals were a double doublet at δ 2.42 (*J* = 2 and 11 Hz, H-6) and a broad doublet at 2.07 (*J* = 11 Hz, H-6'). The stereochemistry of the epoxy group at C-4 and C-5 was observed from the coupling constants between H-5 and H-6, H-6' (2.15, *br d J* = 11 Hz, H-5) and by studying Dreiding models. Although the conformational flexibility of a ten-membered ring system makes assignment of the stereochemistry of the epoxy group difficult, when alternative models were studied the *J* values were found to be *ca* 6–7 Hz; therefore the stereochemistry suggested is the only plausible one.

The mass spectrum of 1β,10α-epoxy-4-hydroxy-glechoma-8-enolide (**5**) indicated the molecular formula $C_{15}H_{20}O_4$ ([M]$^+$, *m/z* 264). Its IR spectrum showed a hydroxyl band at 3450 cm^{-1}, a lactone band at 1750 cm^{-1} and unsaturation at 1650 cm^{-1}. The ^{1}H NMR spectrum



1

[O]



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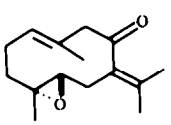

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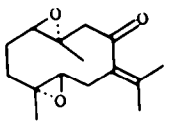

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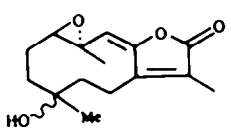

5

of **5** showed three methyl singlets at δ1.92 (C-13), 1.42 (C-15) and 1.73 (C-14). There were no signals either for a lactone proton or for an isolated methylene group, but a one-proton singlet at low field (δ5.92) suggested a vinylic proton which could only be at C-9. The coupling constants between H-1 and H-2, H-2' indicated the stereochemistry of the epoxy group at C-1 and C-10. The double doublet at δ2.86 (J = 2 and 14.5 Hz, H-1) and the Dreiding models indicated the suggested stereochemistry for the epoxy group. The studied J values of the alternative models were found to be different (5–7 Hz) from the measured values. The spectral data for compounds **2**–**5** were in agreement with the suggested structures.

In previous papers [2, 3] we suggested the oxidation of furodiene to various lactones through the epoxidation of the double bonds to form glechomafuran as a first step. The oxidation of germacrone to these three epoxygermacrones seems to be further proof for this oxidation pathway.

EXPERIMENTAL

The plant material was collected from Kirkareli (European section of Turkey) in August 1985. It was identified by Dr. E. Tuzlaci (University of Marmara, Istanbul). A voucher has been deposited at the Herbarium of the Faculty of Pharmacy, University of Istanbul (ISTE 43818).

Isolation and identification of the compounds. Air-dried and powdered fruits of *Smyrnium creticum* Mill. (1.4 g) were extracted with petrol–Et_2O (2:1) and evaporated to dryness under vacuum at room temp. The residue was treated with MeOH to remove long-chain saturated hydrocarbons. After filtration the MeOH soln was evaporated to dryness and the remaining residue fractionated on a silica gel column (5 × 70 cm). After crude separation on the column, **1**–**9** were further separated and/or purified on prep. TLC plates. The yields of the compounds were **1**, 400 mg; **2**, 5 mg; **3**, 7 mg; **4**, 5 mg; **5**, 10 mg; **6**, 800 mg; **7**, 10 mg; **8**, 50 mg; **9**, 150 mg.

4α,5β-Epoxygermacrone (**2**). UV λ_{max}^{EtOH} nm: 236, 217. IR ν_{max}^{KBr} cm^{-1}: 2910, 2850, 1730, 1670, 1435, 1370, 1290, 1250, 1190, 1140, 1070, 890, 840, 810, 730. ^{1}H NMR: see text. MS *m/z* (rel. int.): 234 [M]$^+$ $C_{15}H_{22}O_2$ (8), 219 [M − 15]$^+$ (5), 216 [M − 18]$^+$ (4), 167 (50), 121 (38), 68 (100).

1β,10α(Epoxy-4-hydroxyglechoma-8-enolide (**5**). UV λ_{max}^{EtOH} nm: 242, 217. IR ν_{max}^{KBr} cm^{-1}: 3450, 2930, 1750, 1650, 1440, 1375, 1260, 1230, 1120, 1090, 760. ^{1}H NMR: see text. MS *m/z* (rel. int.): 264 [M]$^+$ ($C_{15}H_{20}O_4$) (5), 246 [M − 18]$^+$ (28), 205 (40), 175 (60), 149 (62), 107 (56), 61 (100).

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