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SESQUITERPENE LACTONES FROM *CARPESIUM ABROTANOIDES*

MASAO MARUYAMA, AKIO KARUBE* and KIYOKO SATO†

Department of Chemistry, Miyagi University of Education, Sendai, Japan 980; *Department of Chemistry, Akita Technical College, Akita, Japan 011; †Department of Chemical Engineering, Ichinoseki Technical College, Ichinoseki, Japan 021

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Key Word Index—*Carpesium abrotanoides*; Compositae; carabrol; ivaxillin; 11(13)-dehydroivaxillin; eriolin.

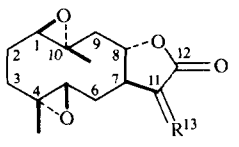
Abstract—Carabrol, ivaxillin and 11(13)-dehydroivaxillin were obtained from *Carpesium abrotanoides*, and the structures of carabrol and 11(13)-dehydroivaxillin were elucidated. The structure of eriolin was also elucidated by interconversion from 11(13)-dehydroivaxillin.

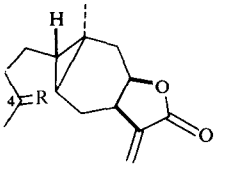
INTRODUCTION

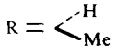
In the course of a continuing search for antifungal and antibacterial material from *Carpesium abrotanoides* L. we have reported the isolation and stereochemistry of granilin [1], the isolation of ivalin [2] and carabrone [3], and the isolation and structure of carpesiolin [3]. This paper reports the isolation of ivaxillin (**1**), the isolation and structure elucidation of carabrol (**2**) and 11(13)-dehydroivaxillin (**3**), and the structure of eriolin (**4**).

RESULTS AND DISCUSSION

One of the active fractions obtained from the chromatography of the active extract afforded a non-crystalline, viscous substance, carabrol (**2**), bp 110° (bath temperature)/0.2 mm Hg, $[\alpha]_D$ +74.9°, $C_{15}H_{22}O_3$. The ^{1}H NMR spectrum of **2** was similar to that of carabrone (**5**) [4]; their only difference was that a methyl singlet at δ2.13 in the spectrum of **5** was replaced by a 3H doublet at 1.17, and a 1H multiplet was present at δ3.7 in the spectrum of **2** which shifted to 5.3 in the spectrum of its 3,5-dinitrobenzoate (**6**), mp 123–126°, $C_{22}H_{24}O_8N_2$. The IR spectrum of **2** lacked a carbonyl absorption which was present at 1714 cm^{-1} in **5**, and instead showed a hydroxyl absorption at 3610 cm^{-1}. These facts suggested that **2** had a secondary hydroxyl group in place of the carbonyl group of **5**. This was proved by oxidation of **2** which afforded **5**.



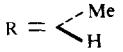


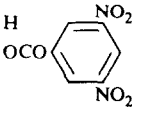
1 R = 

2 R = 

3 R = CH_2

5 R = O

4 R = 

6 R = 

This fraction also yielded an inactive crystalline substance, mp 177–178°, $[\alpha]_D$ −130°, $C_{15}H_{22}O_4$. The ^{1}H NMR and ^{13}C NMR spectral data of this substance were very similar to those of ivaxillin (**1**) [5], and their IR spectra were superimposable. Therefore, this substance was identified as compound **1**.

Another active fraction afforded an antibacterial crystalline compound **3**, mp 166–167°, $[\alpha]_D$ −57.0°, $C_{15}H_{20}O_4$. Compound **3** had an α-methylene-γ-lactone [ν_{max} 1770 cm^{-1}; λ_{max} 214 nm (ε17600); δ5.71 (*d*, *J* = 3 Hz) and 6.36 (*d*, *J* = 3 Hz)] instead of the secondary methyl group (δ1.25, *d*, *J* = 9 Hz) and γ-lactone (ν_{max} 1779 cm^{-1}) found in compound **1**. The rest of its ^{1}H NMR spectrum was very similar to that of compound **1**. Hydrogenation of **3** over platinum catalyst afforded two products, one of which was identified as compound **1**. Therefore, compound **3** was established as 11(13)-dehydroivaxillin. The other product **4**, mp 218–220°, $[\alpha]_D$ −46.5°, $C_{15}H_{22}O_4$, was a C-11 epimer of ivaxillin.

Eriolin [6] has been reported to have the same planar structure as compounds **1** and **4**, and Herz and his coworkers [5] have mentioned that eriolin may be the C-11 epimer of compound **1**. Although neither a sample nor the IR spectrum of eriolin was obtained and compound **4** and eriolin were not compared directly, their ^{1}H NMR spectra [7] were superimposable. Therefore, compound **4** was identical with eriolin and its structure was determined as the C-11 epimer of compound **1**.

Furthermore, the diepoxygermacranolidei obtained by Romo de Vivar from *Schkuhria pinnata* and mentioned by Herz [5] is identical with compound **3**.

EXPERIMENTAL

Mps are uncorr. ^{1}H NMR spectra were measured in $CDCl_3$ with TMS as int. standard.

Isolation of carabrol (**2**) *and ivaxillin* (**1**). Fraction G (4.98 g) obtained from the silica gel CC of the partitioned extract of *C. abrotanoides* [1] was repeatedly chromatographed over silica gel in C_6H_6–EtOAc (5:1) followed by $CHCl_3$ to give an oily fraction (1.10 g) and a crystalline fraction (0.10 g). The oily fraction was chromatographically homogeneous and a small portion was distilled to give a viscous, colourless oil, carabrol (**2**), bp 110° (bath temp.)/0.2 mm Hg; $[\alpha]_D^{18}$ +74.9°, *c* 0.41 ($CHCl_3$). (Found: C, 71.35; H, 8.94. Calc. for $C_{15}H_{22}O_3$: C, 71.97; H, 8.86%.) MS:

m/z 232 $[M-H_2O]^+$; IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3610, 1755, 1655; UV λ_{max}^{MeOH} nm (ε): 213 (8300); ^1H NMR (60 MHz): δ0.4 (2H, *m*, H-1 and H-5), 1.03 (3H, *s*, C-10 Me), 1.17 (3H, *d*, J = 3 Hz, C-4 Me), 3.2 (1H, *m*, H-7), 3.7 (1H, *m*, H-4), 4.72 (1H, *ddd*, J = 12, 8 and 6 Hz, H-8), 5.47 (1H, *d*, J = 3 Hz, H-13), 6.12 (1H, *d*, J = 3 Hz, H-13). Carabrol (**2**) is unstable and deteriorates on storage, and the yield from the distillation was poor. The crystalline fraction was recrystallized from EtOH to give colourless prisms of ivaxilline (**1**, 0.03 g), mp 177–178°; $[\alpha]_D^{18}$ −130°, *c* 0.28 ($CHCl_3$). (Found: C, 67.34; H, 8.30. Calc. for $C_{15}H_{22}O_4$: C, 67.64; H, 8.33%.) Compound **1** was identified by comparison of its IR spectrum with that of an authentic sample.

Isolation of 11(13)*-dehydroivaxillin* (**3**). Fraction E (0.79 g) from the chromatography mentioned above was repeatedly chromatographed over silica gel in C_6H_6–EtOAc (5:1) followed by recrystallization from MeOH to give colourless needles of 11(13)-dehydroivaxillin (**3**, 0.088 g), mp 166–167°; $[\alpha]_D^{18}$ −57.0°, *c* 0.33 ($CHCl_3$). (Found: C, 67.96; H, 7.60. Calc. for $C_{15}H_{20}O_4$: C, 68.16; H, 7.63%.) IR ν_{max}^{KBr} cm^{-1}: 1770, 1665; UV λ_{max}^{MeOH} nm (ε): 214 (17 600); ^1H NMR (100 MHz): δ1.31 (3H, *s*, C-4 or C-10 Me), 1.47 (3H, *s*, C-4 or C-10 Me), 2.9 (3H, *m*, H-1, H-5 and H-7), 4.23 (1H, *ddd*, J = 10, 7 and 1 Hz), 5.71 (1H, *d*, J = 3 Hz), 6.36 (1H, *d*, J = 3 Hz); ^{13}C NMR (25 MHz): δ15.95 (C-4 Me), 17.95 (C-10 Me), 23.60 (C-2), 32.09 (C-6), 35.91 (C-3), 45.86 (C-9), 46.35 (C-7), 57.75 (C-10), 60.73 (C-4), 63.40 and 64.37 (C-1 and C-5), 82.14 (C-8), 121.88 (C-13), 139.17 (C-11), 168.66 (C-12).

Preparation of carabrol 3,5*-dinitrobenzoate* (**6**). Treatment of **2** (200 mg) in pyridine (3 ml) with 3,5-dinitrobenzoyl chloride (400 mg) followed by recrystallization of the product from EtOH afforded the 3,5-dinitrobenzoate (**6**, 87 mg) as yellow prisms, mp 123–126°. (Found: C, 59.44; H, 5.49; N, 6.20. Calc. for $C_{22}H_{24}O_8N_2$: C, 59.45; H, 5.44; N, 6.30%.) IR ν_{max}^{KBr} cm^{-1}: 1750, 1730, 1625, 1550, 1350; UV λ_{max}^{MeOH} nm (ε): 211 (32 000); ^1H NMR (60 MHz): δ0.35 (2H, *m*, H-1 and H-5), 1.10 (3H, *s*, C-10 Me), 1.40 (3H, *d*, J = 7 Hz, C-4 Me), 3.2 (1H, *m*, H-7), 4.74 (1H, *m*, H-8), 5.3 (1H, *m*, H-4), 5.55 (1H, *d*, J = 3 Hz, H-13), 6.23 (1H, *d*, J = 3 Hz, H-13), 9.17 (3H, *br s*, aromatic).

Oxidation of carabrol (**2**). To a soln of **2** (200 mg) in DMF (16 ml) was added CrO_3 (250 mg) and H_2SO_4 (3 drops). The reaction mixture was kept overnight at room temp., then poured on ice H_2O. The product was extracted with Et_2O and usual work-up of the extract afforded a crystalline mass which was recrystallized from Et_2O–petrol to give carabrone (**5**, 78 mg), which was characterized by mmp, co-TLC and IR comparison with an authentic sample.

Hydrogenation of **3**. Compound **3** (106 mg) in EtOH (28 ml) was hydrogenated over Pt catalyst prepared from PtO_2 (50 mg) to absorb 9.55 ml (19°, 745 mm Hg) of H_2. After removal of the catalyst, the soln was evapd *in vacuo* to dryness to give 105 mg of crystals which showed two spots on TLC (silica gel, Et_2O). Fractional recrystallization of the product from EtOH gave ivaxillin (**1**, 20 mg), mp 165–168°, which was characterized by mmp, co-TLC and IR comparison with an authentic sample, and the epimer (**4**, 37 mg), mp 218–220°, $[\alpha]_D^{18}$ −46.5°, *c* 0.2 ($CHCl_3$); (Found: C, 67.67; H, 8.34. Calc. for $C_{15}H_{22}O_4$: C, 67.64; H, 8.33%); IR ν_{max}^{KBr} cm^{-1}: 1763; ^1H NMR (60 MHz): δ1.27 (3H, *s*, C-4 Me), 1.27 (3H, *d*, J = 7 Hz, C-11 Me), 1.38 (3H, *s*, C-10 Me), 4.1 (1H, *br t*, H-8), which was identified as eriolin by comparison of its ^1H NMR spectra.

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