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AROMATIC MONOTERPENES FROM *LAVANDULA GIBSONII**

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Key Word Index—*Lavandula gibsonii*; Labiatae; aromatic monoterpenes; 3-hydroxy-α,α,4-trimethyl benzyl alcohol; 3-hydroxy-α,α,4-trimethyl benzyl methyl ether; 3-hydroxy-α,4-dimethyl styrene.

Abstract—Three aromatic monoterpenes, not reported previously as natural products, together with ursolic acid, were isolated from *Lavandula gibsonii*. They were characterized as 3-hydroxy-α,α,4-trimethyl benzyl alcohol, 3-hydroxy-α,α,4-trimethyl benzyl methyl ether and 3-hydroxy-α,4-dimethyl styrene.

In continuation of our work on *L. gibsonii* [1] we report here the isolation and characterization of a new aromatic monoterpene, 3-hydroxy-α,α,4-trimethyl benzyl methyl ether (**2**) along with two other similar compounds, 3-hydroxy-α,α,4-trimethyl benzyl alcohol (**1**) and 3-hydroxy-α,4-dimethyl styrene (**3**). These compounds do not appear to have been reported previously as natural products but have been synthesized [2]. Column chromatography (Si gel) of the crude acetone extract of *L. gibsonii* resulted in isolation of compounds **1**–**3**. Compound **1**, mp 105–108°, analysed for $C_{10}H_{14}O_2$ (M^+ at *m/z* 166). The IR spectrum showed the presence of only a hydroxyl group (3226 cm^{-1}) and no other functional group containing oxygen. Bands at 1613, 1515 and 1451 cm^{-1} in the IR spectrum and the ^1H NMR spectral pattern indicated the aromatic nature of the compound. A 1,3,4-substitution pattern of an aromatic ring was indicated by the following signals in the ^1H NMR spectrum at δ6.65 (1H, *dd*, *J* = 8, 2 Hz), 6.91 (1H, *d*, *J* = 7 Hz) and 6.93 (1H, *d*, *J* = 2 Hz). Three methyls were indicated by a 3H singlet at 2.16 and a 6H singlet at 1.53. Acetylation of **1** yielded three products. A hydroxy aromatic monoacetate (**6**) [δ2.03 (Ar–OCOMe), 3571 cm^{-1} (OH)], a diacetate (**5**) [δ1.90 (–OCOMe) and 2.18 (Ar–OCOMe)] and the third product characterized as **4** [δ2.16 (2 × Me), 2.25 (Ar–OCOMe) and 4.90, 5.18 (=CH_2)]. Considering all these data, the two structures **1** and **1a**, analogous to carvacrol and thymol, respectively, seem to be biogenetically possible. Structure **1**, 3-hydroxy-α,α,4-trimethyl benzyl alcohol, was confirmed by its synthesis from 3-hydroxy-4-methyl-acetophenone [3] by alkylation with methyl magnesium iodide.

Compound **2**, mp 89–92°, $C_{11}H_{16}O_2$ (M^+ at *m/z* 180), showed an additional methyl signal at δ3.08 (–OMe) in its ^1H NMR spectrum by comparison with that of **1**, along with a hydroxyl band (3400 cm^{-1}) in the IR spectrum. Acetylation of **2** gave an acetate **9** (δ2.30) and methylation yielded an ether (**8**) which exhibited an additional –OMe (δ3.51). Compound **1** also gave the diether **8** in addition to a monoether **7**. This data clearly indicates that the isopropanolic hydroxyl of **1** is selectively methylated in nature to produce **2**. Thus, **2** was identified as 3-hydroxy-α,α,4-trimethyl benzyl methyl ether.

Compound **3**, a pale yellow viscous liquid, bp 120–125°/0.6 mm, $C_{10}H_{12}O$ (M^+ at *m/z* 148), possessed an aromatic methyl (δ2.00), one methyl at δ1.88, a methylene group (δ4.46, 4.73) and a hydroxyl (3448 cm^{-1}). Compound **4** on hydrolysis produced **3** and, hence, **3** was characterized as 3-hydroxy-α,4-dimethyl styrene.

In our first attempt to methylate **1** with dimethyl sulphate, instead of a mono- or diether, a solid, mp 104–105° was obtained which was identified as 4-methoxy-1,1,3,5-tetramethyl-3-(3-methoxy-4-methyl phenyl) indane (**10**) [4]. It has been observed that **1**, on keeping in deuterochloroform solution for a long time, dimerized to give the corresponding hydroxyl compound **11**, mp 170–171°.

EXPERIMENTAL

General exptal details have been described previously [1].

Earlier fractions (C_6H_6), in the chromatography of fraction B_3 (35 g) [1] eluted methyl-3-acetoxy-16-methyl-heptadecanoate. A white solid (2 g), obtained from the later fractions (C_6H_6), was acetylated (Ac_2O and pyridine), esterified (CH_2N_2) and characterized as acetyl methyl ursolate mp 235–238° (C_6H_6–petrol) (lit. 239–241° [5]).

C_6H_6–Me_2CO (98:2 and 96:4) gave a viscous dark material (10 g) which showed three spots in TLC (C_6H_6–EtOAc, 75:25). These were separated by passing through a Si gel column. C_6H_6–Me_2CO (98:2) eluted **3** [0.550 g, bp 120–125° (bath-temp.)/0.6 mm] [lit. [2] 60–100° (bath)/0.01 mm]; ^1H NMR: δ1.88 (3H, *s*), 2.00 (3H, *s*), 4.46, 4.73 (2H), 6.10 (1H), 6.25 (2H). MS *m/z* (rel. int.): 148 $[M]^+$ (100), 133 (75), 131 (44), 115 (44), 108 (66), 107 (55), 105 (58), 91 (32), 77 (41), 51 (44). C_6H_6–Me_2CO (94:6) gave a white solid **2** (2 g) mp 89–92° (petrol). (Found: C, 72.91; H, 8.88. Calc. for $C_{11}H_{16}O_2$: C, 73.30; H, 8.95%.) IR ν_{max}^{Nujol} cm^{-1}: 3400, 2994, 1590, 1449, 1408, 1267, 1117, 1058, 893, 805. ^1H NMR: δ1.56 (6H, *s*), 2.18 (3H, *s*), 3.08 (3H, *s*), 6.53 (1H, *dd*, *J* = 7, 2 Hz), 6.88 (1H, *d*, *J* = 7 Hz) 7.05 (1H, *d*, *J* = 2 Hz). MS *m/z* (rel. int.): 180 $[M]^+$ (98), 165 (100), 150 (41), 149 (91), 135 (82), 133 (25), 121 (52), 107 (23), 91 (38), 77 (54.5). Acetate **9**, (Ac_2O pyridine); bp 130–135°/1.0 mm; ^1H NMR: δ1.53 (6H, *s*), 2.16 (3H, *s*), 2.30 (3H, *s*), 3.03 (3H, *s*), 6.93 (1H), 7.10 (2H).

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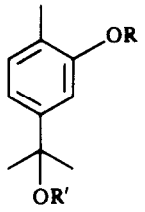
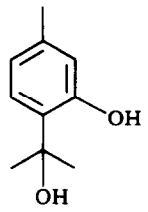
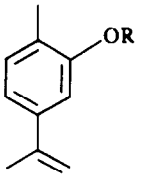


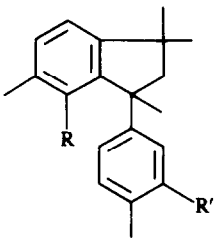
1 R = R′ = H
2 R = H, R′ = Me
5 R = R′ = Ac
6 R = Ac, R′ = H
7 R = Me, R′ = H
8 R = R′ = Me
9 R = Ac, R′ = Me



1a



3 R = H
4 R = Ac



10 R = R′ = OMe
11 R = R′ = OH

C_6H_6–Me_2CO (90:10) yielded a white solid **1** (4 g), mp 105–108° (lit. [2] 105–106°) UV λ_{max}^{MeOH} nm (log ε): 207 (4.56), 221 (4.49), 277 (3.97). ^{1}H NMR: δ1.53 (6H, *s*), 2.16 (3H, *s*), 6.65 (1H, *dd*, *J* = 8, 2 Hz), 6.91 (1H, *d*, *J* = 7 Hz), 6.97 (1H, *d*, *J* = 2 Hz). MS *m/z* (rel. int.): 166 $[M]^+$ (66), 151 (100), 149 (20), 148 (40), 135 (20), 133 (26), 108 (33), 107 (15), 91 (26), 77 (40). Acetylation of **1** (0.2 g), with Ac_2O–pyridine gave **4** (0.02 g); bp 120–125°/1.0 mm; ^{1}H NMR: δ2.16 (6H, *s*) 2.25 (3H, *s*) 4.90, 5.18 (2H), 6.85 (1H), 6.95 (2H). Compound **5** (0.09 g), bp 145–150°/0.9 mm. ^{1}H NMR: δ1.71 (6H, *s*), 1.90 (3H, *s*), 2.08 (3H, *s*), 2.18 (3H, *s*), 6.73 (1H), 6.90 (2H). Compound **6** (0.03 g), bp 135–140°/0.8 mm. ^{1}H NMR: δ1.43 (6H, *s*), 2.03 (3H, *s*), 2.16 (3H, *s*), 6.83 (1H), 6.90 (2H). Etherification (NaH, DMSO, MeI) of 0.2 g of **1** gave **8** (0.082 g), bp 90–95°/1.0 mm, ^{1}H NMR: δ1.5 (6H, *s*), 2.20 (3H, *s*), 3.03 (3H, *s*), 3.85 (3H, *s*), 6.75 (1H, *dd*, *J* = 8, 2 Hz), 6.85 (1H, *d*, *J* = 2 Hz), 6.98 (1H, *d*, *J* = 8 Hz) and **7** (0.1 g), mp 62° (petrol) [6] Methylation (Me_2SO_4, Me_2CO, K_2CO_3) of **1** (0.01 g) yielded **10**, mp 104–105° (lit. [4] mp 95–96°). ^{1}H NMR: δ1.01 (3H, *s*), 1.26 (3H, *s*), 1.56 (3H, *s*), 1.98, 2.03 (2H, 2*ds*, *J* = 12 Hz), 2.05 (3H, *s*), 2.1 (3H, *s*), 3.58 (3H, *s*), 3.75 (3H, *s*), 6.26 (2H, *s*), 6.28–6.66 (3H). Compound **11** was isolated from a $CDCl_3$ soln of **1** by chromatography over Si gel as a white crystalline solid, mp 170–171° (petrol–C_6H_6) ^{1}H NMR: δ1.0 (3H, *s*), 1.25 (3H, *s*), 1.56 (3H, *s*), 1.98, 2.31 (2H, 2*ds*, *J* = 10 Hz), 2.16 (3H, *s*), 2.21 (3H, *s*), 4.43 (2H, *br*, exchanges with D_2O) 6.4 (2H, *s*), 6.53–6.83 (3H, *m*). MS *m/z* (rel. int.): 296 $[M]^+$ (48), 281 (100), 266 (9.5), 265 (9.5), 251 (11.5), 189 (22.5), 173 (66.5), 157 (27), 133 (14), 128 (30).

Synthesis of **1**. 3-Hydroxy-4-methyl-acetophenone (1.5 g, THF 20 ml) with Me MgI (from 2 g Mg and 9.7 g MeI in Et_2O) yielded, after work-up with aq. NH_4Cl, **1** (1.29 g), mp, mmp 103–105° (Petrol–C_6H_6).

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