

### Note

## A novel synthesis of ( $\pm$ )-8-hydroxy-5-isopropylnonan-2-one

Ajay K Arora, Jaswinder Singh, Sangeeta Chaudhary, Vasundhara Singh & G L Kad  
Department of Chemistry, Panjab University  
Chandigarh 160 014, India

Received 13 May 1996;  
accepted (revised) 7 November 1996

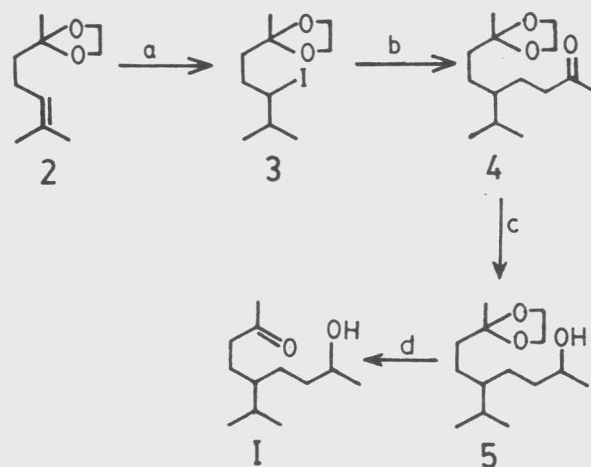
An irregular terpenoid, ( $\pm$ )-8-hydroxy-5-isopropylnonan-2-one **1** has been synthesized utilising hydroboration-iodination and ultrasonically promoted 1,4-conjugate addition of alkyl iodide to 3-buten-2-one as the key steps.

Demole *et al.*<sup>1</sup> have isolated ( $\pm$ )-8-hydroxy-5-isopropylnonan-2-one **1** from the Burley tobacco condensate *Nicotiana glauca* Linn. It is responsible for the characteristic flavour of Burley tobacco. Literature records a few syntheses<sup>2</sup> of the title compound. We report herein a simple and elegant synthesis of compound **1** utilising hydroboration-iodination<sup>3</sup> and zinc-copper catalysed<sup>4</sup> conjugate addition of alkyl halides to  $\alpha,\beta$ -unsaturated compound under sonochemical aqueous conditions as the two key reactions. The spectral data of the synthetic **1** was comparable to those reported in the literature<sup>2</sup>.

6-Methyl-2,2-ethylenedioxy-hept-5-ene<sup>5</sup> **2** on hydroboration-iodination utilising acetoxyborohydride/ $I_2$  in dry THF afforded **3**. Its 1,4-conjugate addition to 3-buten-2-one under ultrasound and in the presence of zinc-copper couple as the catalyst furnished 8,8-ethylenedioxy-5-propylnonan-2-one **4**. LAH reduction of **4** in dry ether followed by deketalisation with *p*-toluenesulphonic acid (PTSA) in aqueous acetone gave title compound **1** (cf. Scheme I).

### Experimental Section

The glass apparatus and syringes were dried at 140°C for 2 hr and assembled hot under nitrogen. <sup>1</sup>H NMR spectra were recorded in CDCl<sub>3</sub> or CCl<sub>4</sub> on a Varian EM 390 (90 MHz) spectrometer using TMS as internal reference (chemical shifts in 100, ppm) and IR spectra as liquid films on a Perkin-Elmer



### Reagents:

- (a)  $CH_3COOB^-H_3$ ,  $I_2$ , THF
- (b) Zn(Cu),  $\alpha,\beta$ -unsaturated ketone, EtOH:H<sub>2</sub>O
- (c) LAH, anhyd. Et<sub>2</sub>O.
- (d) PTSA, Acetone, H<sub>2</sub>O

### Scheme I

infrared 337 spectrophotometer ( $\nu_{max}$  in  $cm^{-1}$ ). Unless otherwise stated all organic extracts were dried over anhydrous sodium sulphate. Purity of all the samples was checked by TLC.

### 2,2-Ethylenedioxy-5-iodo-6-methylheptane(3).

To a well stirred and cooled slurry of sodium borohydride (20 mmoles, 0.76 g) in dry THF (40 mL), under a blanket of nitrogen was added mercuric acetate (10 mmoles, 3.18 g). The reaction mixture was stirred for 1 hr at 0°C and then brought to room temperature. A solution of **2** (20 mmoles, 3.40 g) in anhydrous THF (5 mL) was added dropwise. The mixture was allowed to stir for 16 hr at room temperature for complete hydroboration. Iodine (25 mmoles, 6.35 g) was added all at once at room temperature to the above solution followed by dropwise addition of 3M solution of NaOH (10 mL) in EtOH (30 mL). The reaction mixture was stirred for 10 min at room temperature, decanted and poured into cold water (50 mL) containing sodium thiosul-

fate (1 g) to remove the excess iodine. The aqueous layer extracted with ether (3x25 mL) and dried. Solvent evaporation gave the crude product which was purified by column chromatography over silica-gel using pet. ether as eluent to furnish **3**, yield 5.28 g, (88.6%) (Found :C, 40.1, H, 6.3; C<sub>10</sub>H<sub>19</sub>O<sub>2</sub>I requires C, 40.3, H, 6.4%); IR : 2930, 1380, 1040, 880 and 660 cm<sup>-1</sup>, <sup>1</sup>H NMR : 3.95 (s, 4H, ketal methylenes), 2.9-3.2 (m, 1H, CHI), 1.3-1.5 (m, 5H, 2 x CH<sub>2</sub> + CH), 1.2 (s, 3H, -CH<sub>3</sub>), 0.90 (d, 6H, *J* = 7Hz, -CH(CH<sub>3</sub>)<sub>2</sub>).

**8,8-Ethylenedioxy-5-isopropylnonan-2-one 4.** Zinc-copper couple was prepared by sonicating [model XL 2015 (20 KHz)] Zn (24 mmoles, 1.56 g) and CuI (5 mmoles, 0.95 g) in ethanol-water mixture (9:1, 30 mL) under N<sub>2</sub>. 3-Buten-2-one (10 mmoles, 0.70 g) and the iodide **3** (15 mmoles, 4.47 g) were added to it and the mixture was sonicated further for 1 hr. The reaction was quenched with saturated brine and the contents filtered through sintered funnel. After removing the solvent, the residue was extracted with ether (3x25 mL). The ether extract was washed twice with brine and concentrated to give the crude material which on chromatography over silica-gel using pet. ether as eluent gave **4**, yield 1.76 g (72.7%) (Found : C, 69.2; H, 10.5. C<sub>14</sub>H<sub>26</sub>O<sub>3</sub> requires C, 69.4; H, 10.8%); IR: 2980, 1730, 1460, 1040, 970 and 880 cm<sup>-1</sup>, <sup>1</sup>H NMR : 3.95 (s, 4H, ketal methylenes), 2.3 (t, 2H, *J* = 7 Hz, -CH<sub>2</sub>CO-), 2.1 (s, 3H, CH<sub>3</sub>CO-), 1.25-1.35 (m, 8H, 3 x -CH<sub>2</sub>- + 2 x CH<sub>3</sub>), 1.2 (s, 3H, -CH<sub>3</sub>), 0.85 (d, 6H, -CH(CH<sub>3</sub>)<sub>2</sub>).

**8,8-Ethy 8,8-Ethylenedioxy-5-isopropylnonan-2-ol 5.** To a stirred suspension of LAH (5 mmoles, 0.19 g) in dry ether (100 mL) was slowly added the keto-acetal **4** (7 mmoles, 1.60 g) in dry ether (30 mL) at such a rate as to maintain a gentle reflux. After stirring and refluxing for 5 hr, the contents were decomposed with saturated sodium potassium tartrate solution, extracted with ether, dried and the extract concentrated to obtain a viscous oily liquid, yield 1.22 g (75.7%) (Found: C, 68.6; H, 11.3.

C<sub>14</sub>H<sub>28</sub>O<sub>3</sub> requires C, 68.9; H, 11.5%); IR: 3400, 2990, 1550, 1380, 1040 and 870 cm<sup>-1</sup>, <sup>1</sup>H NMR : 3.5 (s, 4H, ketal methylenes), 3.8 (bs, 1H, -OH, D<sub>2</sub>O exchangeable), 3.5 (m, 1H, -CH(OH)CH<sub>3</sub>), 1.25-1.35 (m, 10H, 4 x -CH<sub>2</sub>- + 2 x -CH), 1.1 (d, 3H, *J* = 7Hz, -CH(OH)CH<sub>3</sub>), 0.85 (d, 6H, *J* = 7 Hz, -CH(CH<sub>3</sub>)<sub>2</sub>).

**((±)-8-Hydroxy-5-isopropylnonan-2-one 1.** A solution of PTSA (0.2g) and water (1 mL) was added to **5** (4 mmoles, 0.98 g) in acetone (50 mL). The mixture was stirred for 3 hr at room temperature, diluted with ether (50 mL), washed with brine and dried. Solvent was evaporated under reduced pressure and the residue chromatographed over silica-gel using pet. ether-ethyl acetate (4:1) as eluent, yield 0.58 g (72.0%) (Found : C, 71.9; H, 11.8. C<sub>12</sub>H<sub>24</sub>O<sub>2</sub> requires C, 72.0; H, 12.1%); IR: 3400, 2900, 1730, 1530 and 870 cm<sup>-1</sup>; <sup>1</sup>H NMR : 3.7 (bs, 1H, -OH, D<sub>2</sub>O exchangeable), 3.5 (m, 1H, -CH(OH)CH<sub>3</sub>), 2.35 (t, 2H, *J* = 6 Hz, -CH<sub>2</sub>CO-), 2.1 (s, 3H, CH<sub>3</sub>CO-), 1.2-1.4 (m, 8H, 3 x -CH<sub>2</sub>- + 2 x CH), 1.1 (d, 3H, *J* = 7 Hz, -CH(OH)CH<sub>3</sub>), 0.85 (d, 6H, *J* = 7 Hz, -CH(CH<sub>3</sub>)<sub>2</sub>).

#### Acknowledgement

The authors gratefully acknowledge the financial assistance from CSIR, New Delhi to carry out this work.

#### References

- 1 Demole E & Demole C, *Helv Chim Acta*, 58, 1975, 1867.
- 2 (a) Vig O P, Sharma S D, Bari S S & Handa V K, *Indian J Chem*, 15B, 1977, 89.  
(b) Vig O P, Sood O P, Bari S S & Rana S S, *Indian J Chem*, 15B, 1977, 391.
- 3 Gautam V K, Singh J & Dhillon R S, *J Org Chem*, 53, 1988, 187.
- 4 Luche J L, Allevina C, Dupuy C & Petrier C, *Tetrahedron Lett*, 29, 1988, 5373.
- 5 Wesley G Taylor, *J Org Chem*, 44, 1979, 1020.