

Partial Synthesis of *ent*-Kaur-16-ene-15 β ,18-diol and *ent*-Kaur-16-ene-7 α ,15 β ,18-triol

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Treatment of *ent*-15 β ,16 β -epoxykauran-18-ol (V) with boron trifluoride-ether complex in dimethyl sulphoxide or direct photo-oxygenation of *ent*-kaur-15-en-18-ol (IV) gave the expected *ent*-kaur-16-ene-15 β ,18-diol (I). This product is suggested to be identical with natural candidiol. Treatment of *ent*-15 β ,16 β -epoxykaurane-7 α ,18-diol (VIII) (natural sideroxol) with boron trifluoride-ether complex in dimethyl sulphoxide or photo-oxygenation of *ent*-kaur-15-ene-7 α ,18-diol (II) (natural sideridiol) gave *ent*-kaur-16-ene-7 α ,15 β ,18-triol (VII).

CANDIDIOL, a diterpenoid diol extracted from *Sideritis candicans* Ait. var. *eriocephala* Webb (Labiatae), a mountain shrub of the Canary Islands, has been assigned structure (I), that of *ent*-kaur-16-ene-15 β ,18-diol.¹ We now report a partial synthesis of compound (I) and suggest that it is identical with natural candidiol.

ent-Kaur-15-ene-7 α ,18-diol (II) (natural sideridiol) was transformed, as described previously,² into *ent*-kaur-15-en-18-oic acid (III), which was reduced with lithium aluminium hydride to give *ent*-kaur-15-en-18-ol (IV). This was treated with *p*-nitroperbenzoic acid to form the epoxide (V), and the epoxide ring of (V) was cleaved with boron trifluoride-ether complex in dimethyl sulphoxide³ to yield *ent*-kaur-16-ene-15 β ,18-diol (I). Photo-oxygenation of *ent*-kaur-15-en-18-ol in the presence of haematoporphyrin^{4,5} also gave (I) as the main product.

Synthetic (I) had m.p. 172—173° (m.p. for natural

candidiol,¹ 183.5—184°). Its mass spectrum was identical (*m/e* values and peak intensities) with that recorded⁶ for natural candidiol. The i.r. spectra (Nujol) of the synthetic and natural products were identical, as were the n.m.r. spectra [60 MHz, (CD₃)₂SO]; a better resolved n.m.r. spectrum of (I) was recorded in CDCl₃ solution. The only remarkable difference between the synthetic and the natural material lay in their optical rotations; the synthetic product had $[\alpha]_D^{20} -65^\circ$ (EtOH; *c* 0.30) whilst natural candidiol had $[\alpha]_D^{24} -91.3^\circ$ (EtOH; *c* 1.05).

During work on the partial synthesis of *ent*-kaur-15-ene-7 α ,17,18-triol (VI) (natural sideritriol), we obtained a compound which we tentatively identified⁷ as *ent*-kaur-16-ene-7 α ,15 β ,18-triol (VII). We were unable to confirm this structure, in particular the stereochemistry at C-15, owing to lack of material. When *ent*-15 β ,16 β -epoxykaurane-7 α ,18-diol (VIII) (natural sideroxol⁸) was

⁴ M. F. Barnes and J. MacMillan, *J. Chem. Soc. (C)*, 1967, 361.

⁵ E. Fujita, T. Fujita, and H. Katayama, *Tetrahedron*, 1970, **26**, 1009.

⁶ B. Rodríguez González, *Anales de Quim.*, 1971, **67**, 85.

⁷ F. Piozzi, P. Venturella, A. Bellino, and A. Selva, *Gazzetta*, 1969, **99**, 582.

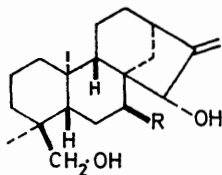
⁸ F. Piozzi, P. Venturella, A. Bellino, and R. Mondelli, *Ricerca sci.*, 1968, **38**, 462.

¹ B. Rodríguez González, S. Valverde, and J. M. Rocha, *Anales de Quim.*, 1970, **66**, 503.

² F. Piozzi, P. Venturella, A. Bellino, and R. Mondelli, *Tetrahedron*, 1968, **24**, 4073.

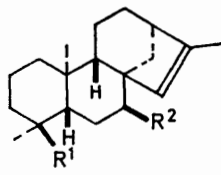
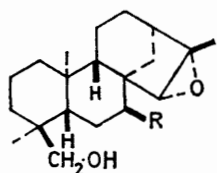
³ K. M. Baker, L. H. Briggs, J. G. St. C. Buchanan, R. C. Cambie, B. R. Davis, R. C. Hayward, G. A. S. Long, and P. S. Rutledge, *J.C.S. Perkin I*, 1972, 190.

treated with boron trifluoride-ether complex in dimethyl sulphoxide, the epoxide ring was cleaved to give compound (VII) in high yield. The photo-oxygenation of *ent*-kaur-15-ene-7 α ,18-diol (II) (natural sideridiol²) also



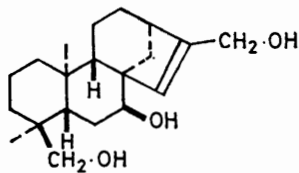
(I) R = H

(VII) R = OH

(II) R¹ = CH₂·OH, R² = OH(III) R¹ = CO₂H, R² = H(IV) R¹ = CH₂OH, R² = H

(V) R = H

(VIII) R = OH



(VI)

afforded (VII) together with traces of (VI). The product was identical with the sample obtained previously.⁷

EXPERIMENTAL

M.p.s were determined in capillary tubes. I.r. spectra were determined for Nujol mulls on Perkin-Elmer Infracord 137 and 157 spectrophotometers; n.m.r. spectra were registered for solutions in CDCl₃ unless otherwise stated, on a JEOL C-60H machine with Me₄Si as an internal standard. Mass spectra were determined on a Perkin-Elmer 270 spectrometer through the courtesy of Dr. A. Selva, Polytechnic School, Milano. Optical rotations were determined on a Perkin-Elmer 141 polarimeter. Silica gel (Merck; 0.05–0.20 mm) was used for column chromatography, and Kieselgel G (Merck) for t.l.c. Light petroleum refers to the fraction with b.p. 40–60°.

ent-Kaur-15-en-18-ol (IV).—*ent*-Kaur-15-en-18-oic acid² (III) (550 mg) was dissolved in ether (250 ml) and treated with lithium aluminium hydride (1 g) for 12 h. Excess of reagent was decomposed with ethyl acetate, and the solution was acidified with dilute hydrochloric acid and extracted with ethyl acetate. The solvent was evaporated off to give a crystalline residue which was chromatographed on silica gel. Elution with benzene gave the *alcohol* (IV) which crystallized from light petroleum as needles, m.p. 134–135° (Found: C, 83.1; H, 11.1. C₂₀H₃₂O requires C, 83.3; H, 11.2%), *m/e* 288 (M⁺), 273, 259, 257, 229, 123, 105, and 94, ν_{\max} 3200 (OH), 1640 (C=C), and 818 (C=CH) cm⁻¹, δ 0.76 (3H, s, 4-CH₃), 1.08 (3H, s, 10-CH₃), 1.70 (3H, d, *J* 1.5 Hz, 16-CH₃), 3.15 and 3.42 (2H, d, *J* 11 Hz, 4-CH₂·OH), and 5.08 [1H, q, *J* 1.5 Hz, C(15)-H]. The compound was homogeneous by t.l.c. in benzene-ethyl acetate (3 : 7).

ent-15 β ,16 β -Epoxykauran-18-ol (V).—*ent*-Kaur-15-en-

18-ol (IV) (200 mg) in ether (80 ml) was treated with *p*-nitroperbenzoic acid (200 mg) at room temperature for 24 h. The solution was washed with aqueous sodium carbonate, dried, and evaporated. The residue was chromatographed on silica gel. Elution with benzene-ethyl acetate (3 : 1) gave the *epoxide* (V) which crystallized from ethyl acetate as needles, m.p. 179–180° (Found: C, 78.75; H, 10.4. C₂₀H₃₂O₂ requires C, 78.9; H, 10.6%), *m/e* 304 (M⁺), 289, 273, 255, 123, and 107, ν_{\max} 3400 (OH) cm⁻¹, δ 0.75 (3H, s, 4-CH₃), 1.04 (3H, s, 10-CH₃), 1.42 (3H, s, 16-CH₃), 2.66 [1H, s, C(15)-H], and 3.12 and 3.40 (2H, d, *J* 11 Hz, 4-CH₂·OH).

Photo-oxygenation of ent-Kaur-15-en-18-ol (IV).—Product (IV) (200 mg) and haematoporphyrin (8 mg) were dissolved in anhydrous pyridine (10 ml). The solution was irradiated in a vertical glass tube (int. diam. 2.0 cm) by four fluorescent tubes (Philips TL 4W/33) mounted 2–3 cm away for 5 days while a stream of dry oxygen was passed through the solution. The pyridine was evaporated off below 40° and the resultant crude hydroperoxide was reduced with a solution of potassium iodide (400 mg) and acetic acid (0.1 ml) in ethanol (10 ml) overnight. The solution was evaporated and the residue was extracted with ether. The extract was washed with aqueous sodium thiosulphate and aqueous sodium carbonate and evaporated, and the residue was chromatographed on silica gel. Elution with cyclohexane-benzene (1 : 1) gave traces of unidentified products; elution with benzene gave unchanged (IV) (20 mg); elution with benzene-ethyl acetate (1 : 1) gave *ent*-kaur-16-ene-15 β ,18-diol (I) (30 mg) which crystallized from cyclohexane as needles, m.p. 172–173° (candidiol¹ has m.p. 183.5–184°) (Found: C, 78.7; H, 10.5. C₂₀H₃₂O₂ requires C, 78.9; H, 10.6%), $[\alpha]_D^{20}$ -65° (EtOH; *c* 0.30), *m/e* 304 (M⁺), 289, 286, 273, 255, 246, 123, and 109 (identical with the spectrum reported for candidiol⁶), ν_{\max} 3230 (OH), 1645 (C=C), and 900 (C=CH₂) cm⁻¹ (identical with a spectrum of natural candidiol), δ [(CD₃)₂SO] 0.66 (3H, s, 4-CH₃), 1.00 (3H, s, 10-CH₃), 3.25br (2H, 4-CH₂·OH), 3.76 [1H, s, C(15)-H], and 5.05br and 5.15br (2H, 2s, C=CH₂) {identical with a spectrum of candidiol in the same solvent; reported¹ for candidiol: 0.67, 1.05, 3.30br (s), 3.75, and 5.10 (apparent d, *J* 6 Hz)}; δ (CDCl₃) 0.75 (3H, s, 4-CH₃), 1.05 (3H, s, 10-CH₃), 3.09 and 3.41 (2H, d, *J* 11 Hz, 4-CH₂·OH), 3.78 [1H, s, C(15)-H], and 5.04br and 5.18br (2H, s, C=CH₂).

Rearrangement of ent-15 β ,16 β -Epoxykauran-18-ol (V).—The epoxide (V) (50 mg) in dry dimethyl sulphoxide (10 ml) was treated with two drops of freshly distilled boron trifluoride-ether complex and heated at 100° for 20 h. The solution was diluted with water and extracted with ether. The extract was washed with aqueous sodium carbonate, dried, and evaporated. The residue gave *ent*-kaur-16-ene-15 β ,18-diol (I) (30 mg) which crystallized from cyclohexane as needles, m.p. 172–173°. The i.r. and n.m.r. spectra and the optical rotation were identical with those of the product described above.

Rearrangement of ent-15 β ,16 β -Epoxykaurane-7 α ,18-diol (VIII) (Sideroxol).—Sideroxol⁸ (100 mg) was dissolved in dry dimethyl sulphoxide (20 ml) and treated with boron trifluoride-ether complex as described above. The product was crystallized from ethyl acetate to give *ent*-kaur-16-ene-7 α ,15 β ,18-triol (VII) (75 mg), as prisms, m.p. 193–194° (lit.⁷ 192–193°) (Found: C, 75.1; H, 10.15. Calc. for C₂₀H₃₂O₃: C, 75.0; H, 10.1%). The product was identical (t.l.c., mixed m.p., and i.r. and n.m.r. spectra) with

the substance obtained previously and assigned structure (VII).

Photo-oxygenation of ent-Kaur-15-ene-7 α ,18-diol (II) (*Sideridiol*).—Sideridiol² (250 mg) was photo-oxygenated as described for (IV). The final residue was chromatographed on silica gel. Elution with benzene gave traces of unidentified products. Elution with benzene-ethyl acetate (3:1) gave unchanged sideridiol (60 mg). Elution with benzene-ethyl acetate (1:3) gave *ent-kaur-16-ene-7 α ,15 β ,18-triol* (VII) (40 mg) which crystallized from ethyl acetate as

prisms, m.p. 193—194°. Elution with ethyl acetate gave *ent-kaur-15-ene-7 α ,17,18-triol* (VI) (*sideritriol*⁷) (5 mg), m.p. 224—225°, identified by t.l.c., mixed m.p., and i.r. spectrum.

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