Biosynthesis of Natural Products. Part 2.[1] Syntheses of ^{14}C- or ^{3}H-Labelled *ent*-Kaur-16-ene Derivatives oxygenated at C-7, or at C-7 and C-15, from Epicandicandiol

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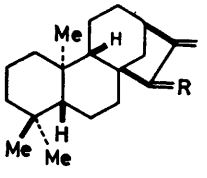
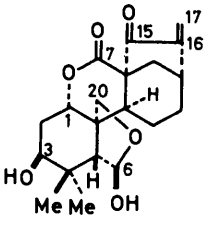
ent-Kaur-16-en-7α-ol (12a), *ent*-kaur-16-en-7-one (14a), *ent*-kaur-16-en-7β-ol (15a), *ent*-15-oxokaur-16-en-7α-ol (22a), and *ent*-kaur-16-ene-7,15-dione (23a), and the labelled compounds (12b), (14b), (14c), (15b), (22b), (23b), and (23c), which are required for the investigation on the biosynthetic route from *ent*-kaur-16-ene (1) into enmein (3) and oridonin (4), were synthesised from epicandicandiol (5).

RECENTLY, we reported the incorporations of *ent*-kaur-16-ene (1) and *ent*-kaur-16-en-15-one (2) into enmein (3) and oridonin (4) in *Isodon japonicus* Hara.[1] All the diterpenoids which have been isolated from *Isodon* species so far bear oxygen functions at C-7 and C-15[2] except for inflexin;[3] hence these carbon atoms seem to be oxidised at an early stage in the biosynthetic route from *ent*-kaur-16-ene (1). We are interested in investi-



(1) R = H_2
(2) R = O



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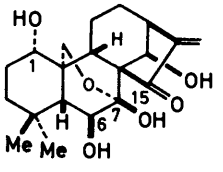
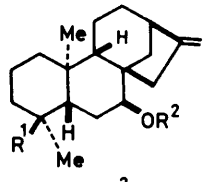


(4)

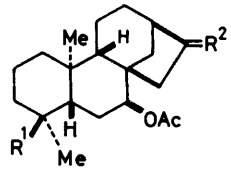
gating whether *ent*-kaur-16-ene derivatives oxygenated at C-7 are also incorporated into the *Isodon* diterpenoids and which of C-7 and C-15 is oxidised in the earlier step. This paper deals with the syntheses of the potential labelled precursors needed for this investigation. In all cases, epicandicandiol (5) was used as the starting material.

RESULTS AND DISCUSSION

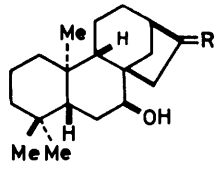
Syntheses of the Compounds oxygenated at C-7.—Epicandicandiol diacetate[4,5] (6) was subjected to partial hydrolysis on alumina to give the monoacetate (7a) in 58% yield accompanied by 36% recovery of the starting material. The tosylate (8) was treated with sodium benzylmercaptide in dimethylformamide to afford the benzyl sulphide (9), which on desulphurisation with Raney nickel afforded *ent*-kaur-16-en-7α-ol acetate (10a)[4,5] in 93% overall yield [based on (7a)]. Treatment of (10a) in methanol with ozone and subsequent decomposition of the ozonide with dimethyl sulphide resulted in the formation of 17-nor-16-one (11) in 85% yield. Wittig reaction of (11) with [17-^{14}C]methyltriphenylphosphonium iodide provided [17-^{14}C]-labelled compound (10b) in good yield, accompanied by a small amount of (12b). The tritium-labelled alcohol (7c) was derived from (7a) by Jones oxidation to aldehyde (13) and subsequent reduction of (13) with sodium borotritiide. Treatment of (10a) with lithium aluminium hydride in ether gave the known alcohol (12a),[5] which



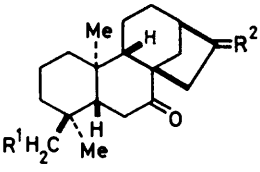
(5) R^1 = CH_2OH, R^2 = H
(6) R^1 = CH_2OAc, R^2 = Ac
(7a) R^1 = CH_2OH, R^2 = Ac
(7c) R^1 = CH^3HOH, R^2 = Ac
(8) R^1 = $CH_2OSO_2C_6H_4Me$-*p*, R^2 = Ac
(9) R^1 = CH_2SCH_2Ph, R^2 = Ac



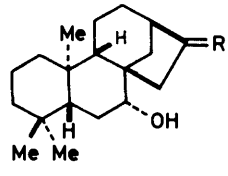
(10a) R^1 = Me, R^2 = CH_2
(10b) R^1 = Me, R^2 = $^{14}CH_2$
(10c) R^1 = $CH_2{}^3H$, R^2 = CH_2
(11) R^1 = Me, R^2 = O
(13) R^1 = CHO, R^2 = CH_2



(12a) R = CH_2
(12b) R = $^{14}CH_2$



(14a) R^1 = H, R^2 = CH_2
(14b) R^1 = H, R^2 = $^{14}CH_2$
(14c) R^1 = ^3H, R^2 = CH_2



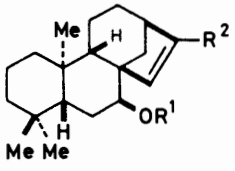
(15a) R = CH_2
(15b) R = $^{14}CH_2$

was oxidised with Jones reagent to (14a). On sodium borohydride reduction the ketone (14a) gave the alcohol (15a), which was shown to have an α-hydroxy group, and

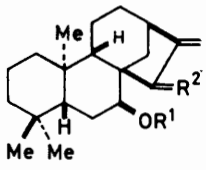
to be free from (12a), by n.m.r. spectroscopy, although both (12a) and (15a) had the same R_F value on thin-layer chromatography. In the same manner as above, (10b) was converted into (12b), (14b), and (15b), and (7c) was transformed into (14c) *via* (10c).

ent-[17-^{14}C]Kaur-16-en-7α-ol (12b), -7-one (14b), and -7β-ol (15b), and *ent*-[18-$^{3}H_1$]kaur-16-en-7-one (14c) thus obtained served effectively for the biosynthetic investigation, which will be published in a later paper.

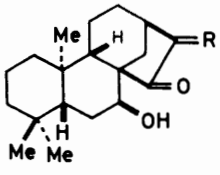
Syntheses of the Compounds oxygenated at C-7 *and* C-15.—For the introduction of an oxygen function into C-15, the photosensitised oxygenation of *ent*-kaur-15-ene derivatives has been useful.[1,6] In the present case also, we applied this procedure to compound (16a)



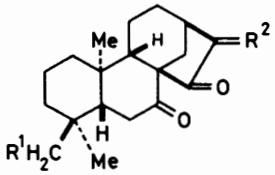
(16a) R^1 = Ac, R^2 = Me
(16b) R^1 = Ac, R^2 = $^{14}CH_3$
(20) R^1 = H, R^2 = Me



(17) R^1 = Ac, R^2 = O
(18) R^1 = Ac, R^2 = α-H, β-OH
(19) R^1 = H, R^2 = α-H, β-OH
(21) R^1 = H, R^2 = α-OH, β-H



(22a) R = CH_2
(22b) R = $^{14}CH_2$



(23a) R^1 = H, R^2 = CH_2
(23b) R^1 = H, R^2 = $^{14}CH_2$
(23c) R^1 = ^{3}H, R^2 = CH_2

derived from (10a) by treatment with iodine in benzene. Thus, (16a) was subjected to photo-oxygenation in the presence of haematoporphyrin in dry pyridine. The reaction mixture was then treated with acetic anhydride [7] to afford the 15-oxo-compound (17) in 50% yield. The ketone (17) on sodium borohydride reduction in methanol and subsequent treatment with lithium aluminium hydride gave the 7β,15β-diol (19) as a pure product *via* the 7β-acetate (18). For reference, the 15α-epimeric diol (21) was prepared by photo-oxygenation of (20), a hydrolysate of (16a). As a minor product, the 15-one (22a) was obtained. The diol (19) on treatment with 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ) in t-butanol gave the αβ-unsaturated ketone (22a) in good yield. Jones oxidation converted the ketone (22a) into the diketone (23a). However, oxidation of (21) with chromic anhydride–pyridine to (23a) was unsuccessful. In the same manner as above, (22b) and (23b) were prepared from (10b) *via* (16b), and (23c) was prepared from (7c) *via* (10c).

Thus *ent*-[17-^{14}C]-15-oxokaur-16-en-7α-ol (22b), *ent*-[17-^{14}C]kaur-16-ene-7,15-dione (23b), and *ent*-[18-^{3}H]-kaur-16-ene-7,15-dione (23c) were synthesised and used in the biosynthetic investigation. The tracer experiments using these materials will be reported elsewhere.

EXPERIMENTAL

General details are given in ref. 1.

ent-*Kaur*-16-*ene*-7α,18-*diol* 7-*Acetate* (7a).—A solution of diacetate (6) (695 mg) in benzene (30 ml) was adsorbed on Merck chromatographic basic alumina (44 g). After 5 d the column was eluted with benzene–ethyl acetate (95 : 5), to recover the starting material (250 mg). Elution with benzene–ethyl acetate (85 : 15—80 : 20) afforded a crystalline product (360 mg), which was recrystallised from n-hexane to give colourless needles of the monoacetate (7a),[4,5] m.p. 138—140 °C; $\nu_{max.}$ 3 460, 1 708, and 880 cm^{-1}; δ 4.78 (3 H, m, 17-H_2 and 7α-H), 3.33, 3.02 (2 H, AB quartet, *J* 11 Hz, 18-H_2), 2.03 (3 H, s, COMe), and 1.07 and 0.70 (each 3 H, s, 2 Me) (Found: C, 76.2; H, 10.0. Calc. for $C_{22}H_{34}O_3$: C, 76.26; H, 9.89%).

ent-*Kaur*-16-*ene*-7α,18-*diol* 7-*Acetate* 18-*Toluene*-p-*sulphonate* (8).—The alcohol (7a) (30 mg) and toluene-*p*-sulphonyl chloride (50 mg) in pyridine (0.5 ml) were set aside at room temperature for 3 d. The mixture was poured into dilute hydrochloric acid, then extracted with benzene. The organic layer was washed with dilute hydrochloric acid and water, and dried. Evaporation of the solvent left the *toluene*-p-*sulphonate* (8) (43 mg) as needles, m.p. 157 °C (from n-hexane); δ 7.83—7.28 (4 H, aromatic-H), 4.80 (3 H, m, 17-H_2 and 7α-H), 3.64, 3.33 (2 H, AB quartet, *J* 9.5 Hz, 18-H_2), 2.46 (3 H, s, Ar-Me), 2.16 (3 H, s, COMe), and 1.06 and 0.72 (each 3 H, s, 2 Me) (Found: C, 69.5; H, 8.35. $C_{29}H_{40}O_5S$ requires C, 69.57; H, 8.05%).

ent-18-*Benzylthiokaur*-16-*en*-7α-*ol Acetate* (9).—Sodium benzyl sulphide [prepared from benzyl hydrogensulphide (0.19 ml) and sodium (35 mg)] was dissolved in dimethylformamide (0.5 ml) and to the solution was added a solution of (8) (75 mg) in dimethylformamide (1.5 ml). The mixture was heated at 100 °C for 1.5 h under dry nitrogen. The cold solution was added to 5% KOH (20 ml) and extracted with ether, which was washed successively with 5% KOH, 5% HCl, 1% $NaHCO_3$, and then dried. The residue obtained after distilling off the ether was subjected to preparative thin-layer chromatography [benzene–ether (9 : 1)] to afford a crystalline product (67 mg) which was recrystallised from ether–methanol to give the *benzyl sulphide* (9) as needles, m.p. 116—117 °C; δ 7.33 (5 H, s, aromatic-H), 4.80 (3 H, m, 17-H_2 and 7α-H), 3.67 (2 H, s, 18-H_2), 2.03 (3 H, s, COMe), and 1.04 and 0.83 (each 3 H, s, 2 Me) (Found: M^+, 452.271. $C_{29}H_{40}O_2S$ requires *M*, 452.275).

ent-*Kaur*-16-*en*-7α-*ol Acetate* (10a).—The sulphide (9) (60 mg) in acetone (6 ml) and ethanol (2 ml) was refluxed for 50 min with Raney nickel (W-2) (*ca.* 500 mg). After filtration, the solvent was evaporated off. The crystalline residue (42 mg) was recrystallised from methanol to give (10a) [4,5] as needles, m.p. 101—102 °C; $\nu_{max.}$ 1 730 and 880 cm^{-1}; δ 4.80 (3 H, m, $W_{1/2}$ 6 Hz, 17-H_2 and 7α-H), 2.07 (3 H, s, OCOMe), 1.05 (3 H, s, Me), and 0.79 (6 H, s, 2 Me) (Found: C, 79.95; H, 10.4. Calc. for $C_{22}H_{34}O_2$: C, 79.95, H, 10.37%).

ent-16-*Oxo*-17-*norkauran*-7α-*ol Acetate* (11).—Ozone was introduced to a solution of (10a) (94 mg) in chloroform (4 ml) and methanol (4 ml) at −30 °C. When all the (10a)

had been consumed (t.l.c.) the reaction was stopped. After removal of ozone by passing through nitrogen, a few drops of dimethyl sulphide were added and the mixture was stirred overnight at room temperature. Evaporation *in vacuo* left a residue which was chromatographed [SiO_2, benzene–ethyl acetate (95 : 5)] to afford the 17-*norkauranone* (11) (80 mg) as colourless needles, m.p. 129—131 °C (from chloroform–methanol); $\nu_{max.}$ 1 745 and 1 730 cm^{-1}; δ 4.90 (1 H, m, $W_{1/2}$ 6 Hz, 7α-H), 2.05 (3 H, s, OCOMe), 1.11 (3 H, s, Me), and 0.82 (6 H, s, 2 Me) (Found: M^+, 332.233; C, 75.25; H, 9.75. $C_{21}H_{32}O_3$ requires M, 332.235; C, 75.86; H, 9.70%).

ent-[17-^{14}C]*Kaur*-16-*en*-7α-*ol Acetate* (10b).—A solution (0.67 ml) of potassium t-butoxide [from potassium (0.2 g) and t-butanol (5 ml)] was added to a stirred suspension of [^{14}C]methyltriphenylphosphonium iodide (4.68×10^9 disintegration min^{-1} $mmol^{-1}$; 272 mg) in dry tetrahydrofuran (THF) (3 ml) under nitrogen, and the mixture was stirred for 20 min. Then a solution of (11) (107 mg) in THF (3 ml) was added. The stirring was continued for further 20 min. The solvent was evaporated off *in vacuo*, and the residue was extracted with n-hexane–80% aqueous MeOH. The n-hexane layer was washed with brine, dried, and evaporated to dryness to yield a crude product (102 mg), which was subjected to preparative thin layer chromatography [benzene–ethyl acetate (85 : 15)] to afford the [17-^{14}C]*labelled compound* (10b) (4.6×10^9 disintegration min^{-1} $mmol^{-1}$; 91 mg), accompanied by the 7β-*alcohol* (12b) (4 mg). Each compound was identical with an authentic sample and showed a single radioactive peak on t.l.c. [benzene–ethyl acetate (85 : 15)].

ent-18-*Formylkaur*-16-*en*-7α-*ol Acetate* (13).—The alcohol (7a) (186 mg) dissolved in acetone (*ca.* 5 ml) was treated dropwise with a slight excess of Jones reagent and left at room temperature for only 5 min. Methanol was added to destroy excess of reagent, and the mixture was poured into water and extracted with ethyl acetate. The usual work-up gave a crude crystalline product, which was chromatographed [SiO_2, benzene–ethyl acetate (85 : 15)] to afford the acetoxy-aldehyde (13) (125 mg) as needles, m.p. 113—115 °C (from methanol), (lit.,[4] liquid); δ 9.20 (1 H, s, CHO), 4.80 (3 H, m, $W_{1/2}$ 7 Hz, 17-H_2 and 7α-H), 2.10 (3 H, s, OCOMe), 1.10 and 1.05 (each 3 H, s, 2 Me) (Found: C, 76.4; H, 9.6. Calc. for $C_{22}H_{32}O_3$: C, 76.70; H, 9.36%).

ent-[18-^{3}H]*Kaur*-16-*ene*-7α,18-*diol* 7-*Acetate* (7c).—A drop of 1% sodium hydroxide was added to a solution of (13) (110 mg) in methanol (10 ml); the mixture was then treated with sodium borotritiide (*ca.* 70 mCi $mmol^{-1}$; 14 mg) at 0 °C for *ca.* 1 h, and then evaporated to dryness *in vacuo*. The residue was extracted with benzene (150 ml). The usual work-up gave a crude product, which was subjected to preparative thin-layer chromatography [benzene–ethyl acetate (85 : 15)] to afford the *labelled alcohol* (7c) (2.85×10^{10} disintegration min^{-1} $mmol^{-1}$; 67.4 mg), identical with an authentic sample (7a) and showing a single radioactive peak on t.l.c. [benzene–ethyl acetate (85 : 15)].

ent-*Kaur*-16-*en*-7α-*ol* (12a).—To a solution of (10a) (36 mg) in ether (6 ml) was added lithium aluminium hydride (25 mg). After stirring at 0 °C for 40 min the excess reagent was destroyed by adding ice–water and the mixture was extracted with ether. The usual work-up gave a crystalline product (32 mg), which was recrystallised from methanol to afford the alcohol (12a) [5] as columnar crystals, m.p. 135.5—137 °C; δ 4.83 (2 H, m, $W_{1/2}$ 6 Hz, 17-H_2), 3.64 (1 H, m, $W_{1/2}$ 6 Hz, 7α-H), 1.05, 0.85 and 0.82 (each 3 H, s, 3 × Me), (Found: C, 83.05; H, 11.05. Calc. for $C_{20}H_{32}O$: C, 83.27; H, 11.18%).

ent-[17-^{14}C]*Kaur*-16-*en*-7α-*ol* (12b).—In the same manner as above, the labelled acetate (10b) (4.20×10^9 disintegration min^{-1} $mmol^{-1}$; 37 mg) was converted into the *alcohol* (12b) (4.01×10^9 disintegration min^{-1} $mmol^{-1}$; 27 mg), identical with an authentic sample (12a) and showing a single radioactive peak on t.l.c. [benzene–ethyl acetate (85 : 15)].

ent-*Kaur*-16-*en*-7-*one* (14a).—The alcohol (12a) (14 mg) dissolved in acetone (2 ml) was treated dropwise with Jones reagent at 0 °C for 5 min, and then methanol was added to destroy excess of reagent. The mixture was extracted with chloroform and the usual work-up gave crystals of the *ketone* (14a) (10 mg), m.p. 63—64.5 °C (from methanol); $\nu_{max.}$ 1 700 and 864 cm^{-1}; δ 4.90 (2 H, m, $W_{1/2}$ 5 Hz, 17-H_2) and 0.88 (9 H, s, 3 Me) (Found: M^+, 286.234. $C_{20}H_{30}O$ requires M, 286.230).

ent-[17-^{14}C]*Kaur*-16-*en*-7-*one* (14b).—Under the same conditions as above, the labelled alcohol (12b) (24.4 mg) was subjected to Jones oxidation. The resulting *product* (14b) (3.90×10^9 disintegration min^{-1} $mmol^{-1}$; 20 mg) was identical with an authentic sample of the ketone (14a) and showed a single radioactive peak on t.l.c. [benzene–ethyl acetate (85 : 15)].

ent-[18-^{3}H]*Kaur*-16-*en*-7-*one* (14c).—In the same manner as described for the preparation of (10a) from (7a) *via* (8) and (9), labelled monoacetate (7c) (2.85×10^{10} disintegration min^{-1} $mmol^{-1}$; 67.4 mg) was converted to (10c) (32.7 mg), identical with an authentic sample (10a) on t.l.c. [SiO_2 impregnated with silver nitrate (10%); benzene–light petroleum (8 : 2)] and showing a single radioactive peak (specific activity was not measured). Subsequent treatment of (10c) with lithium aluminium hydride followed by Jones oxidation gave the *labelled ketone* (14c) (2.80×10^{10} disintegration min^{-1} $mmol^{-1}$; 23.4 mg) as needles, identical with an authentic sample (14a) and showing a single radioactive peak on t.l.c. [benzene–ethyl acetate (85 : 15)].

ent-*Kaur*-16-*en*-7β-*ol* (15a).—The ketone (14a) (12 mg) in dry methanol (5 ml) was treated with sodium borohydride (20 mg) at room temperature for 30 min. Evaporation *in vacuo* left a residue which was extracted with ethyl acetate. The usual work-up gave a crystalline product, which was recrystallised from methanol to afford the *alcohol* (15a) (7 mg), m.p. 103—105 °C; δ 4.83 (2 H, m, $W_{1/2}$ 6 Hz, 17-H_2), 3.50 (1 H, dd, J 11 and 4 Hz, 7β-H), and 1.04, 0.88, and 0.83 (each 3 H, s, 3 Me) (Found: M^+, 288.246. $C_{20}H_{32}O$ requires M, 288.245).

ent-[17-^{14}C]*Kaur*-16-*en*-7β-*ol* (15b).—Labelled ketone (14b) (3.90×10^9 disintegration min^{-1} $mmol^{-1}$; 11.8 mg) was reduced by sodium borohydride (20 mg) under the same conditions as above. The resulting *product* (15b) (3.98×10^9 disintegration min^{-1} $mmol^{-1}$; 9.2 mg) was identical with an authentic sample of the alcohol (15a) and showed a single radioactive peak on t.l.c. [benzene–ethyl acetate (85 : 15)].

ent-*Kaur*-15-*en*-7α-*ol Acetate* (16a).—To a solution of (10a) (85 mg) in dry benzene (9.5 ml) was added iodine (20 mg), and the mixture was refluxed for 8 h. The solution was washed with 5% sodium thiosulphate and water, dried and evaporated to give a crystalline residue, which was chromatographed on a silica gel column impregnated with silver nitrate (10%). Elution with n-hexane–benzene (1 : 1)

recovered the starting material (10a) (24.7 mg). Elution with n-hexane–benzene (1 : 4) gave (16a) (49.7 mg) as crystals, m.p. 104—105 °C (from methanol) (lit.,[4] m.p. 106—108 °C); δ 5.28 (1 H, br s, 15-H), 4.75 (1 H, m, $W_{1/2}$ 6 Hz, 7α-H), 2.06 (3 H, s, OCOMe), 1.70 (3 H, d, J 2 Hz, 17-Me), 1.05 (3 H, s, Me), and 0.80 (6 H, s, 2 Me).

ent-[17-^{14}C]*Kaur*-15-*en*-7α-*ol Acetate* (16b).—The [17-^{14}C]acetate (10b) (3.70×10^9 disintegration min^{-1} mmol^{-1}; 63.3 mg) was treated with iodine (15 mg) in dry benzene (7 ml) in the same manner as above. The resulting mixture was subjected to preparative t.l.c. [SiO_2 impregnated with silver nitrate (10%); benzene–ethyl acetate (9 : 1)] to give the starting material (10b) (14.8 mg) and the *isomer* (16b) (3.70×10^9 disintegration min^{-1} mmol^{-1}; 40.4 mg), identical with an authentic sample of (16a) and showing a single radioactive peak on t.l.c.

ent-15-*Oxokaur*-16-*en*-7α-*ol Acetate* (17).—Oxygen was passed through a solution of (16a) (30.5 mg) and haematoporphyrin (5 mg) in dry pyridine (2.5 ml) under irradiation with fluorescent lamps (4 × 20 W) for 120 h. To the mixture was added acetic anhydride (0.2 ml), and it was set aside at room temperature for 24 h. The mixture was then evaporated to dryness *in vacuo* to leave a residue, which was extracted with chloroform. The usual work-up gave a crude product, which was purified by preparative t.l.c. [benzene–ethyl acetate (85 : 15)] to give the αβ-*unsaturated ketone* (17) (16 mg) as crystals, m.p. 129—131 °C (from methanol); δ 5.88 and 5.23 (each 1 H, br s, 17-H_2), 5.15 (1 H, t, J 2.5 Hz, 7α-H), 2.18 (3 H, s, OCOMe), 1.15 (3 H, s, Me), and 0.85 (6 H, s, 2 Me) (Found: M^+, 344.232. $C_{22}H_{32}O_3$ requires M, 344.235).

ent-*Kaur*-16-*ene*-7α,15α-*diol* 7α-*Acetate* (18).—A solution of the ketone (17) (12 mg) in dry methanol (2 ml) was treated with sodium borohydride (10 mg) at 0 °C for 35 min, then extracted with chloroform. The extract was washed with brine, dried, and evaporated below 30 °C to give the *product* (18) (10 mg) as crystals, m.p. 99—101 °C (from methanol); δ 5.13 (1 H, d, J 2.5 Hz, 17-H), 5.00 (1 H, m, $W_{1/2}$ 4 Hz, 17-H), 4.77 (1 H, m, $W_{1/2}$ 6 Hz, 7α-H), 4.10 (1 H, m, $W_{1/2}$ 6 Hz, 15α-H), 2.10 (3 H, s, OCOMe), 1.07 (3 H, s, Me), and 0.80 (6 H, s, 2 Me) [Found: *m/e* 286.226. $C_{20}H_{30}O$ (M − AcOH) requires 286.230].

ent-*Kaur*-16-*ene*-7α,15α-*diol* (19).—The crude monoacetate (18) (9 mg) in dry ether (2 ml) was treated with lithium aluminium hydride (10 mg) at room temperature for 30 min. Ice–water was added and the mixture was extracted with ethyl acetate. The extract was treated as usual to give the *diol* (19) (7.5 mg), m.p. 185—188 °C (from methanol); δ 5.15 (1 H, m, $W_{1/2}$ 4 Hz, 17-H), 5.02 (1 H, m, $W_{1/2}$ 5 Hz, 17-H), 4.26 (1 H, m, $W_{1/2}$ 6 Hz), 3.72 (1 H, m, $W_{1/2}$ 7 Hz), and 1.07, 0.87, and 0.85 (each 3 H, s, 3 Me) (Found: M,$^+$ 304.237. $C_{20}H_{32}O_2$ requires M, 304.240).

ent-*Kaur*-15-*en*-7α-*ol* (20).—The acetate (16a) (46 mg) in methanol (6 ml) was refluxed with a solution (0.6 ml) of sodium methoxide [from sodium (100 mg) and dry methanol (2 ml)] for 3.5 h. Evaporation *in vacuo* left a residue, which was extracted with ethyl acetate. The usual work-up gave a crystalline product (32 mg), which was recrystallised from methanol to afford the *alcohol* (20), m.p. 131—132 °C; δ 5.30 (1 H, br s, 15-H), 3.63 (1 H, m, $W_{1/2}$ 6 Hz, 7α-H), 1.70 (3 H, d, J 2 Hz, 17-Me), and 1.04, 0.85, and 0.82 (each 3 H, s, Me) (Found: M^+, 288.248. $C_{20}H_{32}O$ requires M, 288.245).

Photosensitised Oxygenation of (20).—Through a solution of (20) (30 mg) and haematoporphyrin (5 mg) in dry pyridine (2.5 ml), oxygen was passed under irradiation with fluorescent lamps (4 × 20 W) for 94 h. The usual work-up [1,6] gave a crude mixture which was separated by preparative t.l.c. [benzene–ethyl acetate (85 : 15)] to yield ent-15-*oxokaur*-16-*en*-7α-*ol* (22a) (4 mg); m.p. 106—108 °C; δ 6.02 and 5.33 (each 1 H, br s, 17-H_2), 3.93 (1 H, t, J 2.5 Hz, 7α-H), and 1.13, 0.92, and 0.83 (each 3 H, s, 3 Me) (Found: M^+, 302.230. $C_{20}H_{30}O_2$ M, 302.225): and ent-*kaur*-16-*ene*-7α,15β-*diol* (21), m.p. 202—204 °C (from methanol); δ 5.31 and 5.13 (each 1 H, br s, 17-H_2), 4.16 (1 H, br s, 15β-H), 3.94 (1 H, m, $W_{1/2}$ 6 Hz, 7α-H), and 1.05, 0.90, and 0.82 (each 3 H, s, 3 Me) (Found: M^+, 304.241. $C_{20}H_{32}O_2$ requires M, 304.240).

ent-15-*Oxokaur*-16-*en*-7α-*ol* (22a).—To a solution of DDQ (9 mg) in t-butanol (1.5 ml) was added diol (19) (7 mg) and the mixture was stirred for 19 h at room temperature. After addition of chloroform (10 ml), the solution was washed with 1% sodium hydroxide and brine. The usual work-up gave a crystalline product (5 mg), which was recrystallised from methanol to yield colourless crystals of (22a), m.p. 106—108 °C, identical with an authentic sample obtained by photosensitised oxygenation of (20).

ent-[17-^{14}C]-15-*Oxokaur*-16-*en*-7α-*ol* (22b).—In the same manner as described for the preparation of (22a) from (16a), labelled acetate (16b) (3.70×10^9 disintegration min^{-1} mmol^{-1}; 40 mg) was converted to *labelled hydroxyketone* (22b) (3.71×10^9 disintegration min^{-1} mmol^{-1}; 11 mg), which was identical with an authentic sample (22a) and showed a single radioactive peak on t.l.c. [benzene–ethyl acetate (85 : 15)].

ent-*Kaur*-16-*ene*-7,15-*dione* (23a).—The hydroxyketone (22a) (11.4 mg) dissolved in acetone (1.5 ml) was oxidised with Jones reagent at 0 °C for 30 min to give crystals of the *diketone* (23a) (10 mg), which was recrystallised from acetone–methanol, m.p. 137—139 °C; δ 5.93 and 5.40 (each 1 H, br s, 17-H_2), 0.90 (6 H, s, 2 Me), and 0.84 (3 H, s, Me) (Found: M^+, 300.210. $C_{20}H_{28}O_2$ requires M, 300.209).

ent-[17-^{14}C]*Kaur*-16-*ene*-7,15-*dione* (23b).—Labelled hydroxyketone (22b) (16.7 mg) prepared from (10b) (4.6×10^9 disintegration min^{-1} mmol^{-1}) was subjected to Jones oxidation under the same conditions as above. The *resulting product* (23b) (4.40×10^9 disintegration min^{-1} mmol^{-1}; 10.5 mg) was identical with an authentic sample (23a) and showed a single radioactive peak on t.l.c. [benzene–ethyl acetate (85 : 15)].

ent-[18-^{3}H]*Kaur*-16-*ene*-7,15-*dione* (23c).—Labelled acetate (10c) (133 mg) prepared from (7c) (3.8×10^{10} disintegration min^{-1} mmol^{-1}) was converted to the *labelled diketone* (23c) (3.76×10^{10} disintegration min^{-1} mmol^{-1}; 22.5 mg) in the same manner as described for the preparation of (23a) from (10a). This compound (23c) was identical with an authentic sample and showed a single radioactive peak on t.l.c. [benzene–ethyl acetate (85 : 15)].

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REFERENCES

[1] Part 1, T. Fujita, I. Masuda, S. Takao, and E. Fujita, *J.C.S. Perkin I*, 1976, 2098.

[2] E. Fujita, Y. Nagao, and M. Node, *Heterocycles*, 1976, **5**, 793.
[3] I. Kubo, K. Nakanishi, T. Kamikawa, T. Isobe, and T. Kubota, *Chem. Letters*, 1977, 99.
[4] A. G. González, B. M. Fraga, M. G. Hernández, and J. G. Luis, *Tetrahedron*, 1973, **29**, 561.
[5] A. G. González, B. M. Fraga, M. G. Hernández, and J. G. Luis, *Phytochemistry*, 1973, **12**, 2721.
[6] M. F. Barnes and J. MacMillan, *J. Chem. Soc.* (*C*), 1967, 361.
[7] W. P. Schneider and D. F. Ayer, *Proc. 2nd Internat. Congress Hormones and Steroids*, Milan, 1966, p. 254—260.