Approach to the Synthesis of Side-chain Eudesmanediols: Synthesis of Kudtriol from 1-(α)-Santonin

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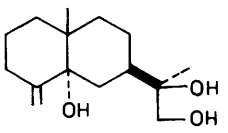
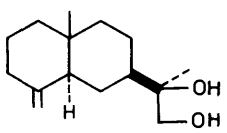
The synthesis of an eudesmanic alcohol, kudtriol (**1**), is described along with its 11-deoxy analogue (**19**) starting from 1-(α)-santonin in ten steps. The known intermediate methyl (11*S*)-3-oxoeudesm-4-en-12-oate (**5b**) was taken through the new intermediates methyl (11*S*)-eudesm-4-en-12-oate (**6**), (11*S*)-eudesm-4-en-12-al (**17**), 11-hydroxyeudesm-4-en-12-al (**18**), and eudesm-4-ene-11,12-diol (**8**). The construction of side-chain diol moiety in the last mentioned intermediate was achieved by the application of Vedejs' enolate hydroxylation on (**17**). The sensitised photo-oxygenation cum reduction sequence transformed the ene diol (**8**) into the title compound (**1**). A similar sequence on (11*S*)-eudesm-4-en-12-ol (**16**) resulted in 11-deoxykudtriol (**19**).

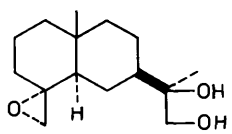
Recently, Teresa *et al.* reported[1] the occurrence of some new eudesmanic sesquiterpenols from the hot benzene extracts of a medicinal plant *Jasonia glutinosa* D.C. (Compositae, subfamily Inulae), namely kudtriol (**1**), kudtdiol (**2**), and α-epoxykudtdiol (**3**). Even though the proposed structures were based on spectral data and chemical correlation with the known sesquiterpene



(**1**)



(**2**)



(**3**)

(+)-β-eudesmol it was deemed necessary to confirm them by means of unequivocal synthesis. The present paper hence deals with our first synthesis of one of the natural products namely kudtriol (**1**) and its 11-deoxy analogue (**19**) from 1-(α)-santonin (**4**), a well known starting material for sesquiterpenes. As the total synthesis of santonin[2] has been accomplished, the present synthesis is a formal total synthesis of kudtriol (**1**).

A preliminary route (Scheme 1) was devised *via* the known key intermediate keto ester (**5b**) obtainable from santonin in two steps. Its conversion into deoxy ester (**6**) was brought about by the thioacetal–desulphurisation method.[3] The dithioacetal ester (**13**) hence prepared showed conspicuous absence of ketone absorption in its i.r. spectrum and the presence of ^{1}H n.m.r. signals in the region δ 3.3—3.4 assignable to the four methylene protons of a dithioacetal moiety. Desulphurisation of (**13**) was effected smoothly by special grade Raney nickel prepared as per the procedure of Slazwski and Wajatala,[4] and afforded the ene ester (**6**) in satisfactory yield. It showed in its i.r. spectrum an ester absorption at 1 730 cm^{-1} and an olefinic stretching band at 1 610 cm^{-1}, and its ^{1}H n.m.r. spectrum was conspicuously clear in the olefinic region, indicating that the sole product formed was the desired Δ^4-ene ester (**6**).

Interestingly the two earlier methods of deoxygenation which we tried on the keto ester (**5b**) had resulted in undesired isomers of compound (**6**). The Wolff–Kishner reduction[5] of keto acid (**5a**) and the modified Huang–Minlon procedure had resulted in a deoxy acid, the methyl ester of which was characterised to be an intimate mixture of Δ^3 and Δ^4 ene esters (**10**) based on the facts that an undesired olefinic signal at δ 5.40 was observed, integrating for 0.6 H, and that the g.l.c. analysis also showed the presence of two isomers. Subsequently a milder and better alternative to Wolff–Kishner reduction was tried on compound (**5b**) in the form of Kabalka's tosylhydrazone reduction sequence.[6] The tosylhydrazone (**11**) prepared from (**5b**) was reduced with catecholborane and the purified oily product exhibited homogeneity in g.l.c. analysis and absence of keto carbonyl absorption in its i.r. spectrum, although the ^{1}H n.m.r. spectrum showed an olefinic signal again at δ 5.35 integrating for 1 H, unlike the partial integration observed earlier for the product of Wolff–Kishner reduction. However, the product did not have a retention time equal to that of one of the isomers of (**10**), indicating that even though it was a Δ^3-ene ester it had a *cis* ring fusion[7] and was thus assigned structure (**12**). This observation was in conformity with Kabalka's findings that the reduction of α,β-unsaturated tosylhydrazones is generally associated with double-bond migration.

As evident from the proposed Scheme 2, success of the reaction sequence very much depended upon two important structural changes, namely (i) transforming the $\Delta^{4(5)}$ bond into a 5α-hydroxy-$\Delta^{4(14)}$-moiety and (ii) modifying the C-7 side-chain to introduce an additional hydroxy function at C-11. One method of bringing about the former task was *via* the sensitised photo-oxygenation of olefins.[8] This was initially tried on the ene ester (**6**) as a model substrate for the method, since it was to be ultimately employed in the penultimate step of the Scheme. The photo-oxygenation of compound (**6**) in ethanol containing a catalytic amount of Methylene Blue furnished, after chromatography, the expected ene hydroperoxide (**14**) along with a minor product (**15**). Both structures were confirmed by i.r. and ^{1}H n.m.r. data. The ene hydroperoxide (**14**) showed in its ^{1}H n.m.r. spectrum, besides the usual signals, two olefinic signals at δ 4.45 and 5.10 for the $\Delta^{4(14)}$-exomethylene group, whereas compound (**15**) did not show any olefinic signal.

After successful completion of this model study our efforts were concentrated on C-11 hydroxylation of the ene ester (**6**). Of various methods for enolate hydroxylation[9] we chose to employ the one propounded by Vedejs,[10] since we were impressed by the fact that his mild conditions of hydroxylation furnished the desired products free from undesired over-oxidation products. The ene ester (**6**), however, did not

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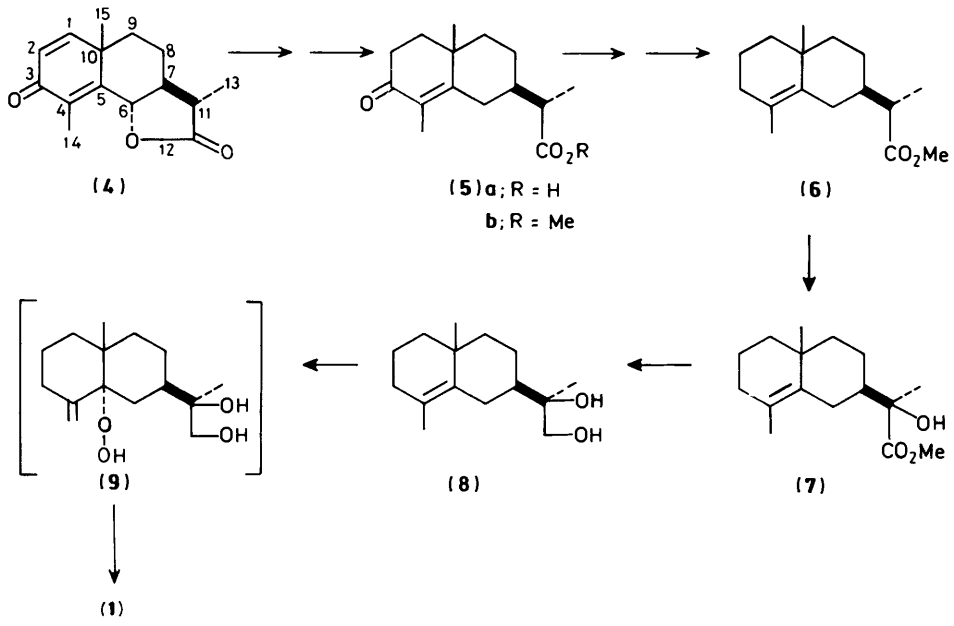


Scheme 1. Proposed approach for the synthesis of the title compound from santonin (**4**)

undergo α-hydroxylation to produce the hydroxy ester (**7**) despite repeated attempts under varied reaction conditions and reagent stoicheiometry; this was attributable to the fact that its C-11 hydrogen was not acidic enough to become enolised under the experimental conditions. The aldehyde (**17**) however, underwent smooth α-hydroxylation to furnish hydroxy aldehyde (**18**), though initially an undesired 1,2-carbonyl addition product of butyl-lithium was formed in major amounts. By the proper adjustment of stoicheiometry, when complete formation of lithium di-isopropylamide was ensured, formation of this by-product was suppressed.

The aldehyde (**17**) itself was not obtained directly by controlled reduction of ester (**6**) by either di-isobutyl-aluminium hydride[11] or sodium bis-(β-methoxyethoxy)-aluminium dihydride;[12] instead a fully reduced diol (**16**) was isolated. This, however, furnished the required aldehyde (**17**) upon oxidation by one of the polymer-supported reagents,[13,14] namely chromic acid supported on silica gel.[15]

The ene aldehyde (**17**) showed in its i.r. spectrum the presence of two bands, at 2 720 and 1 720 cm^{-1}, and absence of any band in the hydroxy region, and its ^1H n.m.r. spectrum contained a characteristic aldehyde proton signal at δ 9.20 besides other signals. The hydroxy aldehyde (**18**) exhibited in its i.r. spectrum bands at 3 350, 2 710, and 1 700 cm^{-1} and in its ^1H n.m.r. spectrum signals at δ 1.05 and 9.50 for the C-11 methyl and aldehyde proton respectively. The successful hydroxylation of aldehyde (**17**) clearly revealed that the enolate-hydroxylation procedure of Vedejs is applicable to aldehydes too, an aspect not covered by him.

The g.l.c. analysis of hydroxy aldehyde (**18**) showed, as expected, two peaks in the relative ratio 9:1, for the two C-11 epimers formed during the reaction. The fact that incoming groups at C-11 prefer to approach from the β-side in the 6,13-lactone analogues prompted us to propose the stereostructure as depicted in (**18**) for the major isomer, even though it depended very much on the preferred population of the rotamers. This was later confirmed when the optical rotation of synthetic kudtriol compared very well with the value reported for the natural isomer. The reduction of aldehyde (**18**) with DIBAL furnished the ene diol (**8**) which showed in its i.r. spectrum distinct absence of the carbonyl absorption.

Table. ^1H N.m.r. spectral data (δ_H) of natural and synthetic kudtriols[a]

Natural kudtriol[1]	Synthetic kudtriol	Assignments
0.83	0.90	3 H, s, 15-H_3
1.16	1.20	3 H, br s, 13-H_3
3.40, 3.56 (*J* 12 Hz)	3.55, 3.60 (*J* 16 Hz)	2 H, two doublets, 12-H and 12-H′
4.65	4.72	1 H, m, 14-H
4.76	4.83	1 H, m, 14-H′

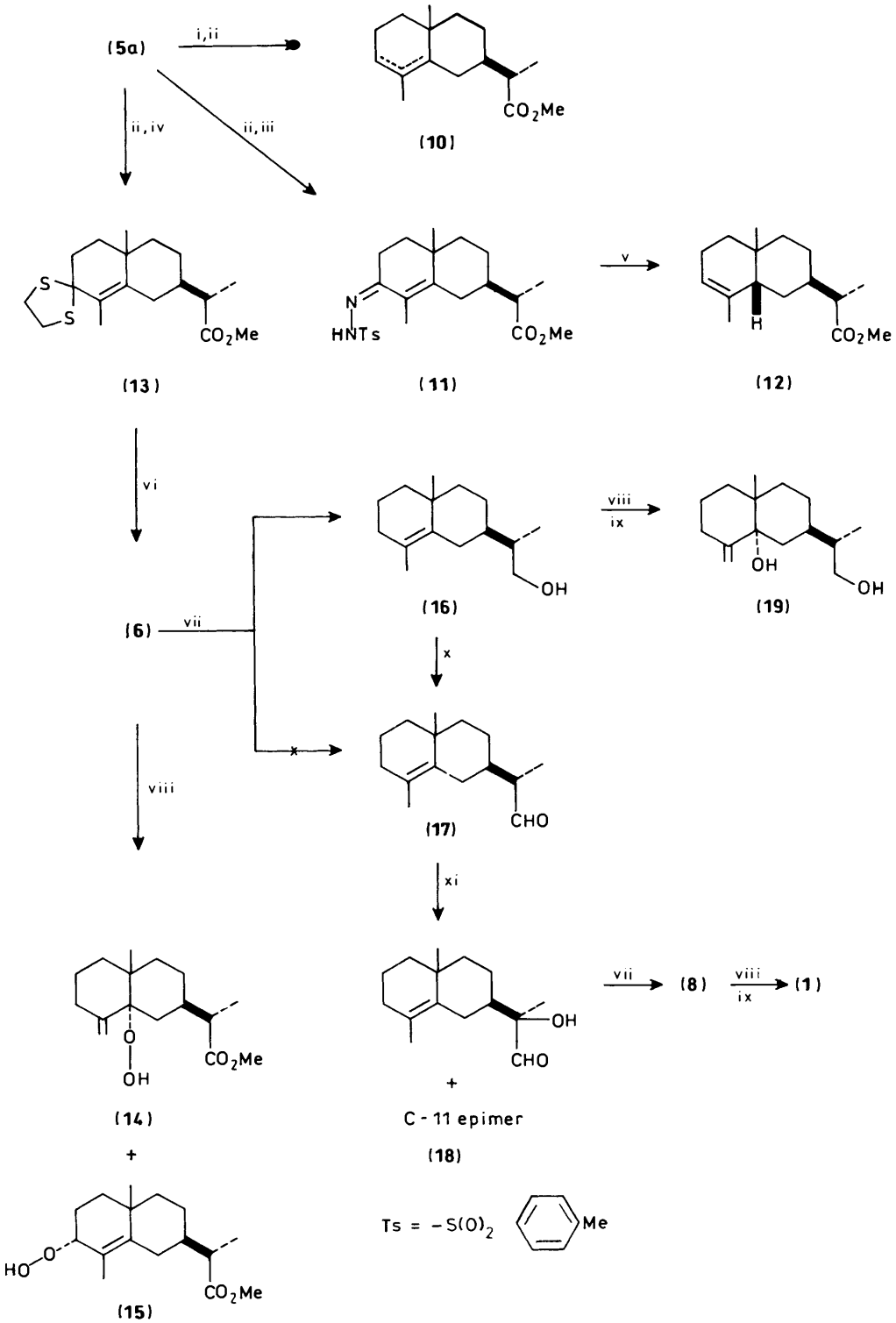
[a] Owing to different conditions under which the spectrum of synthetic kudtriol was recorded, there is a uniform chemical-shift difference downfield for the synthetic form *vs.* the natural form.

Sensitised photo-oxygenation was carried out by employing the same conditions used earlier for the ene ester (**6**). The photo-oxygenated product, *viz.* the hydroperoxide (**9**), was reduced *in situ* with sodium borohydride to give the title compound, kudtriol (**1**), matching the natural isomer in all respects of physicochemical data and, as can be seen from the Table, a fair comparison of ^1H n.m.r. data was obtained. The ene alcohol (**16**) upon photo-oxygenation under similar conditions resulted in the hypothetical analogue 11-deoxykudtriol (**19**) after reductive work-up with sodium borohydride.

To summarise, kudtriol (**1**) and its 11-deoxy analogue (**19**) have been synthesized for the first time through transformation studies on 1-(α)-santonin (**4**).

Experimental

All m.p.s (determined on a Tempo Electrothermal instrument) and b.p.s are uncorrected. Dry tetrahydrofuran (THF) was obtained by distillation from potassium. Dry di-isopropylamine and dichloromethane were obtained by distillation from calcium hydride. Light petroleum refers to the fraction boiling in the range 60—80 °C. Anhydrous sodium sulphate was used for drying all organic extracts, which were evaporated at reduced pressure below 50 °C. The homogeneity of all compounds reported was checked by g.l.c. on an Aimil-Nucon



Scheme 2. *Reagents:* i, N_2H_4, KOH, Digol; ii, MeOH, HCl; iii, *p*-$TsNHNH_2$, THF, BF_3·Et_2O; iv, MeOH, $(CH_2SH)_2$, BF_3·Et_2O; v, THF, catecholborane, then $NaOAc·3H_2O$; vi, Raney nickel, Pr^iOH; vii, DIBAL, THF; viii, EtOH, Methylene Blue, $^1O_2$; ix, $NaBH_4$; x, CrO_3 supported on silica, CH_2Cl_2; xi, LDA, MoOPH, THF

Engineers-Gas chromatograph series 5500 instrument using Carbowax (2%) as the stationary phase. U.v. spectra were recorded on a Varian Superscan-3 instrument, with ethanol as solvent. I.r. spectra were recorded on a Perkin-Elmer 237-B grating spectrophotometer for neat samples unless stated otherwise. N.m.r. data were obtained at 60 MHz from a Hitachi R-6000, at 100 MHz from a Varian XL-100A, and at 500 MHz from a Brucker-500 instrument. Spectra were recorded in $CDCl_3$ solution with $SiMe_4$ as internal standard. Mass spectra were recorded on a Varian MAT 112-S instrument. They were

run with electron impact (e.i.) at 70 eV. The optical rotation of synthetic kudtriol was measured on a Perkin-Elmer 141 polarimeter as a solution in chloroform.

(11S)-3-*Oxoeudesm*-4-*en*-12-*oic Acid* (**5a**).—The procedure of Rao [16] was followed in reducing santonin (**4**) (10 g, 40.65 mmol), and the crude keto acid (**5a**) was crystallised from acetone–light petroleum (8.3 g, 82%), m.p. 122—123 °C (lit.,[16] 123—124 °C); $\nu_{max.}$(Nujol) 3 250 (CO_2H), 1 710 (C=O of acid), and 1 670 cm^{-1} (α,β-unsaturated C=O).

Methyl (11S)-3-*Oxoeudesm*-4-*en*-12-*oate* (**5b**).—The acid (**5a**) (8.5 g, 34.0 mmol) was dissolved in methanol (200 ml) and conc. hydrochloric acid (5.0 ml) was added. After the mixture had been refluxed gently for *ca.* 1.5 h, methanol was removed under reduced pressure and the reaction mixture was diluted with cold water and extracted with dichloromethane. The extract was washed successively with aqueous sodium hydrogen carbonate, water, and brine, and was dried and evaporated to dryness. Chromatography on silica gel with ethyl acetate–light petroleum (15:75) as eluant yielded the keto ester (**5b**) as a pale gum (8.17 g, 91%), b.p. 170—172 °C/0.65 Torr (lit.,[16] b.p. 170—180 °C/0.30 Torr) (Found: C, 72.85; H, 9.9. Calc. for $C_{16}H_{24}O_3$: C, 72.72; H, 9.09%); $\lambda_{max.}$ 255 nm (ε 4 500); $\nu_{max.}$ 1 740 (methyl ester), 1 675 (α,β-unsaturated ketone), and 1 620 cm^{-1} (tetrasubstituted olefin); δ_H(100 MHz) 1.13 (3 H, s, 15-H_3), 1.19 (3 H, d, *J* 6 Hz, 13-H_3), 2.15 (3 H, s, 14-H_3), 2.30—2.45 (2 H, m, 2-H_2), and 3.70 (3 H, s, CO_2Me).

Methyl (11S)-5α*H*-*Eudesm*-3-*en*-12-*oate and Methyl* (11S)-*Eudesm*-4-*en*-12-*oate* (**10**).—The keto acid (**5a**) (2.0 g, 8.0 mmol) was dissolved in a solution of KOH (2 g, 35.71 mmol) and hydrazine hydrate (80%; 2.0 ml, 57.15 mmol) in diethylene glycol (10 ml). The entire solution was gently set to reflux for 1 h. Water and excess of hydrazine hydrate were distilled off until the temperature reached 200 °C. After being gently refluxed at this temperature for a further 1 h, the reaction mixture was cooled, diluted with water (30 ml), and extracted with diethyl ether (2 × 50 ml) so as to separate neutral organic components from the aqueous solution. The aqueous layer was acidified with hydrochloric acid (10%) at 0—5 °C, and the precipitate was extracted with dichloromethane; the extract was evaporated to dryness to afford a dark red gummy acid (1.2 g). This acid gum was esterified in the way described above for compound (**5b**). The crude ester, after work-up, was purified by chromatography over silica gel. Elution with 1.5% ethyl acetate in light petroleum afforded *pure ester mixture* (**10**) as a gum (0.9 g, 45%) (Found: C, 76.8; H, 10.0. $C_{16}H_{26}O_2$ requires C, 76.8; H, 10.4%); $\nu_{max.}$ 1 735 cm^{-1} (methyl ester); δ_H(100 MHz) 0.96 (1.8 H, s, 15-H_3 of Δ^3-isomer), 1.05 (1.2 H, s, 15-H_3 of Δ^4-isomer), 1.10 (1.75 H, d, *J* 6 Hz, 13-H_3 of Δ^3-isomer), 1.20 (1.15 H, d, *J* 6 Hz, 13-H_3 of Δ^4-isomer), 1.6 (3 H, m, 14-H_3), 3.70 (3 H, br s, CO_2Me), and 5.40 (0.6 H, br s, 3-H of Δ^3-isomer).

Methyl (11S)-3,3-*Ethylenedithioeudesm*-4-*en*-12-*oate* (**13**).—Keto ester (**5b**) (5.0 g, 18.93 mmol) was dissolved in dry methanol. To this cooled solution (0—5 °C) were added successively ethane-1,2-dithiol (1.88 g, 20.0 mmol) followed by freshly distilled BF_3·Et_2O (2.84 g, 20.0 mmol). The resulting reaction mixture was left in a refrigerator for 4 h and worked up. Methanol was removed under reduced pressure and the residual gum was passed through a short alumina column packed in light petroleum. Elution with light petroleum–chloroform (60:40) furnished pure *dithioacetal* (**13**) (5.52 g, 92.3%), m.p. 51—52 °C (Found: C, 68.45; H, 8.55; S, 20.1. $C_{18}H_{28}O_2S$ requires C, 68.35; H, 8.86; S, 20.25%); $\nu_{max.}$ 1 735 cm^{-1} (methyl ester C=O); δ_H(500 MHz) 1.04 (3 H, s, 15-H_3), 1.14 (3 H, d, *J* 7.2 Hz, 13-H_3), 1.85 (3 H, s, 14-H_3), 3.10—3.66 (4 H, m, SCH_2CH_2S), and 3.68 (3 H, s, CO_2Me); *m/z* 316 (M^+).

Methyl (11S)-*Eudesm*-4-*en*-12-*oate* (**16**).—The dithioacetal ester (**13**) (5 g, 15.82 mmol) was dissolved in propan-2-ol (200 ml) and the solution was cooled to 10 °C. To this stirred solution was added freshly prepared Raney nickel (40 g) in three lots. The entire heterogeneous mixture was stirred as such for 30 min, then for another 2 h at 40 °C. It was then filtered through a sintered glass funnel and the residue was washed twice with propan-2-ol (20 ml). The combined filtrate and washings were evaporated under reduced pressure and the crude product was purified by silica gel chromatography with ethyl acetate–light petroleum (1:10) and the *ene ester* (**6**) was obtained as a gum (2.6 g, 65%) (Found: C, 76.6; H, 10.7. $C_{16}H_{26}O_2$ requires C, 76.8; H, 10.40%); $\nu_{max.}$ 1 785 cm^{-1} (methyl ester C=O); δ_H(100 MHz) 1.20 (3 H, s, 15-H_3), 1.22 (3 H, d, *J* 6 Hz, 13-H_3), 1.75 (3 H, br s, 14-H_3), 2.30—2.50 (3 H, m, 11-H and 3-H_2), and 3.70 (3 H, s, CO_2Me); *m/z* 250 (M^+).

Sensitised Photo-oxygenation of Compound (**6**). *Formation of Methyl* (11S)-5α-*Hydroperoxyeudesm*-4(14)-*en*-12-*oate* (**14**) *and Methyl* (11S)-3α-*Hydroperoxyeudesm*-4-*en*-12-*oate* (**15**).—The Δ^4-ester (**6**) (0.5 g, 2.0 mmol) was dissolved in absolute ethanol (50 ml) and Methylene Blue (10 mg) was added. The resulting dark blue solution was transferred to a double-walled, immersion-well Pyrex photoreactor with the bottom built of sintered glass to allow for smooth bubbling of oxygen. With a steady flow of oxygen, the entire reactor was immersed in a cold-water bucket and cold water was also circulated through the inner jacket. This was irradiated with a tungsten–halogen lamp (125 W, 25 V) and photo-oxygenation was allowed to proceed until a photostationary state was reached (as inferred from unchanged composition on g.l.c. analysis, in this case 10 h). The photo source was extinguished, ethanol was removed under reduced pressure, and the crude blue syrup obtained was chromatographed rapidly over a short alumina column. Gradient elution with chloroform–light petroleum ether gave the following components. Elution with chloroform–light petroleum (1:9) furnished the starting material (**6**) (0.045 g). Elution with a 4:6 mixture afforded the *hydroperoxide* (**15**) as a gum (0.11 g, 20.1%) (Found: C, 67.8; H, 9.1. $C_{16}H_{26}O_4$ requires C, 68.08; H, 9.22%); $\nu_{max.}$(neat) 3 420 (O–OH) and 1 735 cm^{-1} (methyl ester C=O); δ_H(100 MHz) 1.0 (3 H, s, 15-H_3), 1.16 (3 H, d, *J* 6 Hz, 13-H_3), 2.21 (3 H, s, 14-H_3), 3.4 (1 H, t, *J* 8 Hz, 3-H), and 3.7 (3 H, s, CO_2Me). Further elution with a 6:4 mixture provided the $\Delta^{4,(14)}$-hydroperoxide (**14**) as a gum (0.31 g, 55.2%) (Found: C; 67.55; H, 9.5%); $\nu_{max.}$ 3 400 (O–OH) and 1 735 cm^{-1} (methyl ester C=O); δ_H(100 MHz) 1.13 (3 H, s, 15-H_3), 1.25 (3 H, d, *J* 7 Hz, 13-H_3), 3.72 (3 H, s, CO_2Me), 4.45 (1 H, m, 14-H), and 5.10 (1 H, m, 14-H′).

(*Hexamethylphosphoric Triamide*)*oxodiperoxo*(*pyridine*)-*molybdenum*(VI) [*MoOPH*].—The original procedure of Mimoun *et al.*[17] as modified by Vedejs [10] was followed, and gave the reagent complex as a pale yellow powder, $\nu_{max.}$(KBr) 1 210 (P→O), 960 (Mo=O), 850 (O–O), and 760 cm^{-1} (N–P–O).

Attempted Hydroxylation of Ene Ester (**6**) *using MoOPH*.—In a flame-dried, well guarded three-necked flask (50 ml) with a steady flow of dry nitrogen were placed anhydrous THF (10 ml) and dry di-isopropylamine (0.51 g, 5.0 mmol). The solution was magnetically stirred, and cooled to −20 °C and butyl-lithium (1.4M hexane solution; 3.43 ml, 4.8 mmol) was added during 10 min and the mixture was stirred for a further 20 min at −78 °C before a solution of ene ester (**6**) (0.1 g, 0.4 mmol) in dry THF (10 ml) was gradually added. After being stirred for a further 20 min the mixture was treated with solid MoOPH (0.65 g, 1.5

mmol) added in one lot; the temperature was raised from −78 to −50 °C, and the mixture was stirred for 30 min before being quenched with saturated aqueous sodium sulphite (10 ml), and temperature was then allowed to rise to 0 °C. Water and ether (each 20 ml) were added and the reaction mixture was extracted with the ether. Usual processing furnished a pale yellow gum, which on t.l.c. and g.l.c. was revealed to be starting material. Although a feeble polar spot appeared on t.l.c. it was too meagre to be isolated. Temperature and time variations did not seem to improve the yield of polar material.

(11S)-*Eudesm*-4-*en*-12-*ol* (**16**).—In a flame-dried, well guarded three-necked round-bottom flask under nitrogen atmosphere were placed dry THF (30 ml) and ene ester (**6**) (2.0 g, 8.0 mmol). To this stirred and cooled (−78 °C) solution was added DIBAL (20% solution in toluene; 11.36 ml, 16 mmol) very slowly through a dropping funnel. The mixture was stirred at this temperature for 1 h and then the temperature was gradually raised to 0 °C. The reaction was quenched by addition of 10% hydrochloric acid and the mixture was extracted with ether. The extract was washed successively with aqueous sodium hydrogen carbonate, water, and brine, dried, and evaporated to dryness. Chromatographic purification over silica gel with ethyl acetate–light petroleum (1:9) afforded the *ene alcohol* (**16**) (1.53 g, 86.2%) (Found: C, 80.85; H, 11.6. $C_{15}H_{26}O$ requires C, 81.08; H, 11.71%); $\nu_{max.}$ 3 340 (OH) and 1 650 cm^{-1} (C=C); δ_H(100 MHz) 1.01 (3 H, s, 15-H_3), 1.12 (3 H, d, *J* 7 Hz, 13-H_3), 1.82 (3 H, br s, 14-H_3), and 3.70–3.85 (2 H, m, 12-H_2).

Preparation of Reagent Chromic Acid Adsorbed on Silica Gel.—The procedure of Santaniello *et al.*[15] was followed. To a stirred solution of chromium trioxide (2.0 g) in water (50 ml) was added silica gel (20 g). After evaporation under reduced pressure, the resultant yellow solid was dried overnight at 100 °C. The reagent so formed could be kept for a week *in vacuo* in the dark.

(11S)-*Eudesm*-4-*en*-12-*al* (**17**).—Ene alcohol (**16**) (1.5 g, 6.75 mmol) was dissolved in dry dichloromethane (100 ml). To this stirred and cooled (10 °C) solution was added the freshly prepared supported reagent CrO_3/silica (40 g) in four lots during 2 h and the resulting heterogeneous mixture was stirred for a further 1 h, and filtered over a sintered glass funnel. The residual material was washed with copious quantities of CH_2Cl_2. The combined filtrate and washings were evaporated, and chromatographic purification of the residue over silica gel (2% ethyl acetate–light petroleum as eluant) furnished the *pleasant smelling aldehyde* (**17**) (0.765 g, 51.5%) (Found: C, 81.50; H, 10.45. $C_{15}H_{24}O$ requires C, 81.82; H, 10.9%); $\nu_{max.}$ 2 720 (CHO) and 1 720 cm^{-1} (C=O); δ_H(500 MHz) 1.05 (3 H, s, 15-H_3), 1.18 (3 H, d, *J* 6.5 Hz, 13-H_3), 1.68 (3 H, br s, 14-H_3), and 9.20 (1 H, s, 12-H).

11-*Hydroxyeudesm*-4-*en*-12-*al*-(**18**).—An attempted hydroxylation, similar to that for the ene ester (**6**), was carried out on ene aldehyde (**17**) (0.6 g, 2.7 mmol) using BuLi (1.4M; 17.85 ml, 25 mmol), di-isopropylamine (3.03 g, 30 mmol), and MoOPH (3.51 g, 8.1 mmol) and the crude product after work-up was chromatographed over silica gel. Elution with ethyl acetate–light petroleum (5:95) furnished unchanged starting material (**17**) (0.12 g, 20% recovery). Further elution with a 20:80 mixture provided the *title polar hydroxy aldehyde* (**18**) (0.31 g, 49.2%) as an oil (Found: C, 75.85; H, 10.0. $C_{15}H_{24}O_2$ requires C, 76.27; H, 10.17%); $\nu_{max.}$ 3 350 (OH), 2 710 (CHO), and 1 700 cm^{-1} (C=O); δ_H(100 MHz) 0.80 (3 H, s, 15-H_3), 1.05 (3 H, s, 13-H_3), 1.60 (3 H, br s, 14-H_3), 2.50 (2 H, m, 6-H_2), and 9.50 (1 H, s, 12-H).

Eudesm-4-*ene*-11,12-*diol* (**8**).—To a cooled (−70 °C) and stirred solution of ene hydroxy aldehyde (**18**) (0.25 g, 1.05 mmol) in dry THF (20 ml) under nitrogen was added a solution of DIBAL (20% in toluene; 1.5 ml, 2.10 mmol) in one lot. After the mixture had been stirred at this temperature for 30 min, it was allowed to warm to 0 °C and was then stirred for 15 min. The reaction was quenched by slow addition of 10% HCl (5 ml) and the mixture was extracted with ether. Usual processing of extract furnished a gum, which upon chromatographic purification (silica gel; ethyl acetate–light petroleum, 2:8) furnished pure *ene diol* (**8**) as a gum (0.12 g, 51%) (Found: C, 75.2; H, 10.7. $C_{15}H_{26}O_2$ requires C, 75.63; H, 10.92%); $\nu_{max.}$ 3 390 (OH), 1 650, and 1 605 cm^{-1} (C=C).

Sensitised Photo-oxygenation of the Ene Diol (**8**). *Synthesis of Kudtriol* (**1**).—The procedure as described for ene ester (**6**) was followed. Ene diol (**8**) (0.10 g, 0.42 mmol) was photo-oxygenated for 9 h, the reaction mixture was concentrated to 25 ml, sodium borohydride (0.100 g, 2.64 mmol) was added, and reduction was allowed to proceed for 30 min. Excess of borohydride was decomposed by addition of 50% aqueous acetic acid slowly to the cooled mixture. Most of the ethanol was removed under reduced pressure and the residue was extracted with dichloromethane after dilution with water (20 ml). Usual processing and chromatography (silica gel; ethyl acetate–light petroleum, 2:8) furnished kudtriol (**1**) (0.052 g, 49.5%) (Found: C, 70.45; H, 10.0. $C_{15}H_{26}O_3$ requires C, 70.86; H, 10.23%); $[\alpha]_D$ ($CHCl_3$) +75.650° (*c*, 1.02) {lit.,[1] $[\alpha]_D$ 76.5° (*c*, 1.03 in $CHCl_3$)}; $\nu_{max.}$ 3 400 (OH), 1 650, and 1 625 cm^{-1} (C=C); δ_H(100 MHz) 0.90 (3 H, s, 15-H_3), 1.20 (3 H, br s, 13-H_3), 3.55 (1 H, d, *J* 16 Hz, 12-H), 3.60 (1 H, d, *J* 16 Hz, 12-H′), 4.72 (1 H, m, 14-H), and 4.83 (1 H, m, 14-H′); *m/z* 254 (M^+, 100%) and 236 (M^+ − 18).

Synthesis of 11-*Deoxykudtriol* (**19**).—A similar photo-oxygenation–borohydride reduction sequence on ene alcohol (**16**) (0.1 g, 0.45 mmol) furnished, after chromatography, 11-*deoxykudtriol* (**19**) (0.056 g, 52%) (Found: C, 75.2; H, 10.25. $C_{15}H_{26}O_2$ requires C, 75.63; H, 10.92%); $\nu_{max.}$ 3 400 (OH) and 1 625 cm^{-1} (C=C); δ_H(100 MHz) 1.06 (3 H, s, 15-H_3), 1.15 (3 H, d, *J* 5 Hz, 13-H_3), 3.60 (2 H, m, 12-H_2), 4.75 (1 H, d, *J* 12 Hz, 14-H), and 4.90 (1 H, d, *J* 12 Hz, 14-H′).

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