1206 BULLETIN OF THE CHEMICAL SOCIETY OF JAPAN, VOL. 50 (5), 1206—1216 (1977) [Vol. 50, No. 5

Rishitin. II. Synthesis[1)]

Akio Murai, Kouichi Nishizakura, Nobukatsu Katsui, and Tadashi Masamune

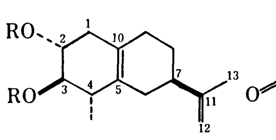
Department of Chemistry, Faculty of Science, Hokkaido University, Sapporo 060

(Received November 1, 1976)

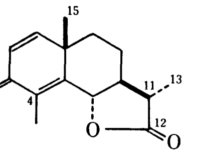
The regio- and stereo-selective synthesis of rishitin (**1**) from (−)-α-santonin (**2**) is described. The transformation involves twelve steps including two known processes, the overall yield amounting to 2.9% from the santonin (**2**).

In the preceding paper[2)] a report was given on the details of isolation and structure elucidation of rishitin (**1**), a representative member of a group of sesquiterpenes qualified as "phytoalexin" from diseased potatoes. As a result of continuing studies on the phytoalexins, we reported[3)] the regio- and stereo-selective synthesis of rishitin (**1**) from (−)-α-santonin[4)] (**2**). Details of the transformation are given in this paper.

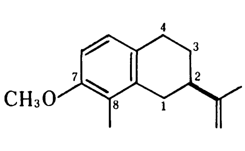
The structure and configuration of rishitin (**1**) are characterized by an eudesmane skeleton with a double bond intervening between the two rings as well as three asymmetric centers in the flexible A ring. After many attempts starting with (2*R*)-2-isopropenyl-7-methoxy-8-methyl-1,2,3,4-tetrahydronaphthalene (**3**), bp 89—91 °C (0.07 Torr), obtained from "desmethyl-6-epidesmotroposantonin"[5)] (**4**) *via* several steps (see Experimental), we functionalized the rigid A ring of a compound with a *trans*-decalin system, derivable from santonin **2**, as stereoselectively as possible and then introduce a double bond between both the A and B rings.



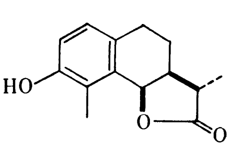
1 R=H
1a R=Ac



2

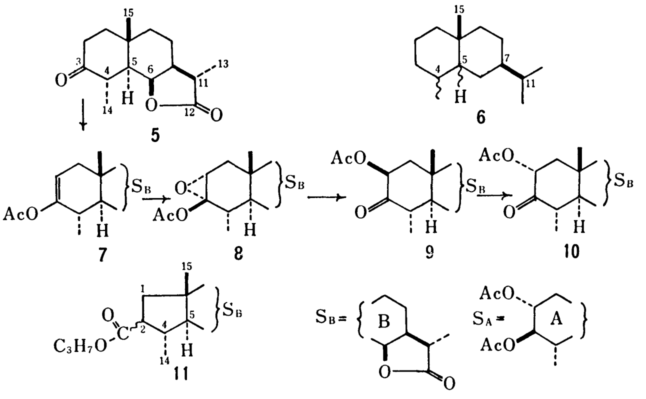


3



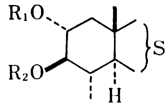
4

(−)-α-Santonin (**2**) was converted into (11*S*)-3-oxo-4β,5α-eudesman-6β,12-olide[6)] (**5**) by the two-step pro cedure,[7)] which on treatment with isopropenyl acetate in the presence of acid under reflux for 3 h[8)] gave the corresponding Δ^2-3-ol acetate (**7**), mp 140—141 °C, in a 99% yield. The spectral data [*m/e* 292 (M^+) and 250 (M^+-CH_2CO);[9)] ν_{max} 1773, 1755, and 1682 cm^{-1}; δ 2.17 (3H, s, $OCOC\underline{H}_3$) and 5.28 (1H, do t, *J*=5.5, 2.5, and 2.5 Hz)] were in good accord with the structure. Oxidation of enol acetate (**7**) with perbenzoic acid in chloroform at 0 °C for 24 h afforded 2α,3α-epoxy 3β-acetate (**8**), mp 156—156.5 °C, in a 91% yield, which was rearranged by heating at 170 °C for 10 min to 3-oxo 2β-acetate (**9**), mp 128—129 °C, and then epimerized with hydrobromic acid in acetic acid at room temperature[10)] to give 3-oxo 2α-acetate (**10**), mp 204—205 °C, in a 72% yield from **8**. The oxo acetate (**10**) could be obtained in a 74% overall yield from **5**, when the afore-mentioned four-step reactions (**5**→**10**) were carried out without isolation of the intermediates (**7**, **8**, and **9**). The mass [*m/e* 308 (M^+) and 266] and IR (ν_{max} *ca.* 1780 and 1740 cm^{-1}) spectra of the oxo acetates (**9** and **10**) were consistent with the assigned structures. The spectral patterns due to the C_2-proton in the respective NMR spectra clearly determined the configurations of the 2-acetoxyl groups [$\underline{H}$ at C_2, δ 5.35 (1H, do d, *J*=9 and 6 Hz) for **9**, and δ 5.45 (1H, do d, *J*=13 and 7 Hz) for **10**], as compared with those of the corresponding protons of 2-acetoxycholestan-3-ones[11)] [$\underline{H}$ at C_2, δ 5.12 (1H, do d, *J*=9.5 and 7.4 Hz) for 2β-acetate, and δ 5.07 (1H, do d, *J*=13.1 and 6.6 Hz) for 2α-acetate]. On the other hand, the 2α,3α-epoxy configuration of epoxide **8** was assigned on mechanistic considerations on transformation of **8** into unstable 3-oxo 2β-acetate (**9**).[10,11)]

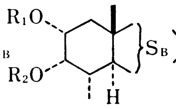


One-step oxidation of 3-ketone (**5**) to 3-oxo 2α-acetate (**10**) was carried out under various conditions. Treatment of **5** with lead tetraacetate in benzene containing boron trifluoride and 2-propanol at room temperature[12)] produced a mixture, from which 3-oxo 2α-acetate(**10**), 3-oxo 2β-acetate (**9**), and a new compound (**11**), mp 112.5—113 °C, were isolated after chromatography in 41, 9, and 14% yields, respectively. Compound **11**, $C_{18}H_{28}O_4$, gave the following spectra: MS, *m/e* 308 (M^+), 249 ($M^+-C_3H_7O$) and 221 ($M^+-C_3H_7OCO$); IR, ν_{max} 1772, 1728, 1213, 1200, 1184, 1163, and 1111 cm^{-1}; NMR, δ 0.91 (3H, s, 15-$C\underline{H}_3$), 1.04 and 1.32 (each 3H, d, *J*=7 and 7.5 Hz, 14- and 13-$C\underline{H}_3$), 1.26 [6H, d, *J*=6 Hz, $(C\underline{H}_3)_2CHOCO$], 1.68 (2H, br d, *J*=8.5 Hz, 2$\underline{H}$ at C_1), 2.39 (1H, q, *J*=7.5 Hz, $\underline{H}$ at C_{11}), 2.51 (1H, m, $\underline{H}$ at C_4), 3.05 (1H, do t, *J*=10.5, 8.5, and 8.5 Hz, $\underline{H}$ at C_2), 4.68 (1H, t, *J*=4 Hz, $\underline{H}$ at C_6), and 5.01 [1H, sep, *J*=6 Hz, $(CH_3)_2C\underline{H}OCO$]. These spectra indicated that (i) the B ring, including the γ-lactonic group, and one secondary methyl group in the original A ring remained unchanged, and (ii) an isopropoxycarbonyl group was newly formed. Assignment of formula **11** was made from these data together with those of spin decoupling studies. It is interesting that the ring contraction occurred in the presence of 2-propanol, in contrast to the corresponding reaction of 5α-cholestan-3-one.[12c)]

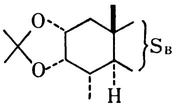
Reduction of 3-oxo 2α-acetate (**10**) with sodium borohydride in methanol at 0 °C afforded a mixture of diastereoisomeric 3-alcohols, which was separated by preparative TLC to give 3β-alcohol (**12**), mp 251—252 °C, and 3α-alcohol (**13**), mp 191—192 °C, in 41 and 48% yields, respectively. Each of these alcohols, when oxidized with the Jones reagent, was reconverted into the original 3-ketone (**10**) in 85—90% yields, indicating the configurational retention during the course of reduction. The C_3 configuration in question in these alcohols is evident from the NMR spectra. The former (**12**) showed two one-proton signals (1H, t, J=9 Hz and 1H, do do d, J=11.5, 9, and 5 Hz) due to the protons at C_3 and C_2 at δ 3.13 and 4.93, respectively, and the latter (**13**) the corresponding signals (1H, br s, W_H=6.5 Hz, and 1H, do do d, J=11, 5.5, and 3 Hz) at δ 3.91 and 5.01. These hydroxy acetates (**12** and **13**) were converted into the diacetates (**12a** and **13a**), mp 189.5—190.5 °C and 150—151 °C, and were hydrolyzed quantitatively to the glycols (**12b** and **13b**), mp 184—185 °C and 94.5—95 °C, respectively. In line with the assigned configurations, *cis*-glycol (**13b**) readily formed the acetonide (**14**), mp 131—132 °C, on treatment with acetone over silica gel (Wakogel Q-23), whereas *trans*-glycol (**12b**) was recovered unchanged under the same conditions.



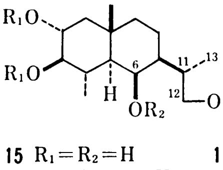
12 R_1=Ac, R_2=H
12a R_1=R_2=Ac
12b R_1=R_2=H



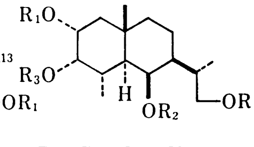
13 R_1=Ac, R_2=H
13a R_1=R_2=Ac
13b R_1=R_2=H



14



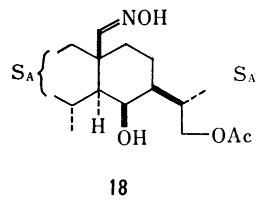
15 R_1=R_2=H
15a R_1=Ac, R_2=H
17 R_1=Ac, R_2=NO



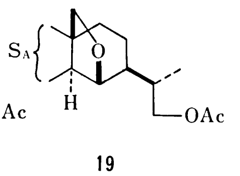
16 R_1=R_2=R_3=H
16a R_1=R_3=Ac, R_2=H
16b R_1=Ac, R_2=R_3=H

Further reduction of 2α-acetoxy 3β-hydroxy γ-lactone (**12**) with lithium aluminium hydride under reflux gave tetraol (**15**), amorphous, which was isolated as the triacetate (**15a**), mp 96.5—98 °C, almost quantitatively after acetylation at room temperature. The triacetate (**15a**) showed a broad singlet (W_H=6.5 Hz) due to the C_6-proton at δ 4.08, and the steric interaction between 1,3-diaxial methyl and hydroxyl groups at C_{10} and C_6 evidently hindered acetylation of the hydroxyl group. By the same treatment the 3α-hydroxy epimer (**13**) gave the 3-epimeric tetraol (**16**), mp 174—174.5 °C, which was also converted into the triacetate (**16a**), mp 80—81 °C, showing a broad singlet (W_H=7 Hz) due to the C_6-proton at δ 4.00, in an 80% yield, along with the 2,12-diacetate (**16b**), oil (15%). The same hydride reduction of 3-oxo 2α-acetate (**10**) followed by acetylation produced a mixture of **15a** and **16a**, from which the desired 2α, 3β,12-triacetate (**15a**) could be isolated in an 80% yield with the epimer (**16a**) (9%). The triacetate (**15a**) was then transformed quantitatively into the 6-nitrite (**17**), mp 103.5—105.5 °C, by treatment with nitrosyl chloride in pyridine, whose NMR spectrum was in line with the structure; δ 4.72 (1H, t, J=10 Hz, $\underline{H}$ at C_3), 5.05 (1H, do do d, J=11.5, 10, and 5 Hz, $\underline{H}$ at C_2), and 5.94 (1H, br s, W_H=5 Hz, $\underline{H}$ at C_6).

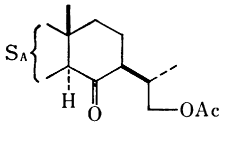
Irradiation of the 6-nitrite (**17**) by a 200 watt high pressure Hanovia lamp in benzene at room temperature for 2 h followed by reflux in a 1 : 1 mixture of tetrahydrofuran and 2-propanol[13)] resulted in functionalization at C_{15}, giving a three-component mixture, which was separated by chromatography over Florisil to yield 15-oxime (**18**), amorphous, as a major product (78%) with 6,15-oxolane and 6-ketone (**19** and **20**), mp 100—101 °C and 109.5—111 °C (5 and 7%). The 6-ketone (**20**) could readily be identified by oxidation of **15a** with the Jones reagent. The structure of oxime **18** was deduced from the following spectra. The mass spectrum indicated fragmentation peaks at *m/e* 410 ($M^+$$-$OH), 367 ($M^+-C_2H_4O_2$), and 350. The NMR spectrum revealed, instead of a singlet peak due to the 15-methyl protons, a doublet (J= 9 Hz) and two singlet peaks at δ 6.56, 7.18, and 10.45, which were ascribed to 6-hydroxy, hydroxyimino methylidene and oxime-hydroxy protons, respectively. The structure was further supported by oxidation of **18** with the Jones reagent to γ-lactone (**21**), mp 126—127 °C, in a 56% yield. The γ-lactone (**21**) was characterized by fragmentation peaks at *m/e* 382 (M^+-CO), 350 ($M^+-C_2H_4O_2$), and 322 (350$-$CO) as well as absorption maxima at 1780 and 1745 cm^{-1} and at δ 4.49 (1H, br s, W_H=2.5 Hz, $\underline{H}$ at C_6) in the mass, IR, and NMR spectra. Similarly, the structure of oxolane (**19**) was assigned as shown in the formula on the basis of the following spectral data: *m/e* 396 (M^+) and 336 ($M^+-C_2H_4O_2$); ν_{max} 1743, 1478, and 862 cm^{-1};[14)]



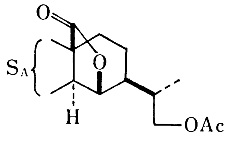
18



19



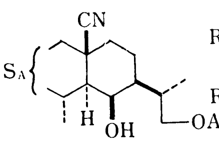
20



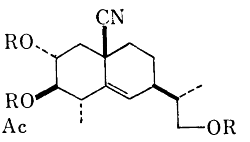
21

δ 3.62 and 3.86 (each 1H, ABq, J=8 Hz, 2$\underline{H}$ at C_{15}),[14] and 4.18 (1H, s, $\underline{H}$ at C_6). The oxolane (**19**) was also obtained by direct hypoiodite reaction[15] of **15a** in a 73% yield, confirming the structure for oxolane **19**. However, the oxolane resisted further oxidation to **21** and/or its analogues under various conditions, giving only multi-component intractable materials.

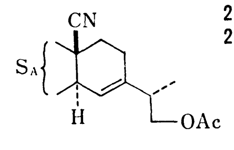
Treatment of 15-oxime (**18**) with acetic anhydride in pyridine at room temperature led to only dehydration of the hydroxyimino group to give 6β-hydroxy 10-nitrite (**22**), mp 175—176 °C in an 89% yield, whose functional groups were characterized by absorption maxima at 3530, 2230, 1739, and 1728 cm^{-1} in the IR spectrum. Compound **22**, when treated with methanesulfonyl chloride in pyridine at room temperature and then with collidine under reflux, underwent further dehydration to yield an oily mixture of olefins, from which Δ^5- and Δ^6-10-nitriles (**23** and **24**), mp 106—107 °C and 81—82 °C, were isolated after chromatography in 78 and 9% yields, respectively. Alternately, the hydroxy nitrile (**22**) was obtained by prolonged treatment of **18** with phosphoryl chloride at room temperature in 60—70% yields with a small amount of **23** (4%). However, attempted double dehydration of 15-oxime (**18**) with methanesulfonyl chloride under the afore-mentioned conditions resulted in formation of an intractable material, from which the desired nitrile (**23**) could be isolated only in a 15% yield.



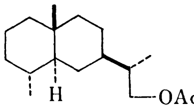
22



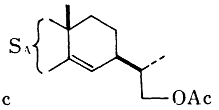
23 R=Ac
23a R=H
23b R=CH_2OCH_3



24



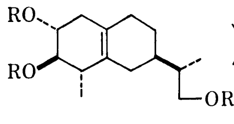
25



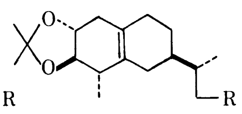
26

Both the olefins (**23** and **24**) exhibited almost the same mass [m/e 331 ($M^+-C_2H_4O_2$) and 211], IR (ν_{max} $ca.$ 2230 and 1745 cm^{-1}), and NMR spectra [δ $ca.$ 5.55 (1H, br s, W_H=5 Hz, olefinic $\underline{H}$)], indicating that the olefins are isomers differing only in the double bond position (Δ^5 or Δ^6). The position was assigned on the basis of the following considerations. i) In the NMR spectra of normal[16] and modified steroids,[17] the shielding effects of various substituents on the chemical shift of 19-methyl protons are additive. The additivity is expected to hold for the present 4β,5α-eudesmanes, in which the A and B rings are regared as the A and B rings in normal steroids, and the 15-methyl protons as the 19-methyl protons. The chemical shifts of 15-methyl protons were then estimated, by assuming the relevant shift of 4β,5α-eudesman-12-ol acetate[6] (**25**), a hypothetical compound, to be δ 0.18 (reference chemical shift) and by using well-established contributions of functional groups in the A and B rings of normal steroids.[16] The calculated values were in good accord with the observed: δ_{calcd} (δ_{obsd}) 1.18 (1.18), 1.15 (1.15), 1.14 (1.13), and 0.90 (0.88) for **15a**, **16a**, **16b**, and **20**, respectively. Compound **15a**, a 10-methyl analogue of **22**, when treated with methanesulfonyl chloride under the above conditions, underwent dehydration to give an olefin (**26**), oil, in a 97% yield, as the only isolatable product, whose 15-methyl protons appeared as a singlet at δ 1.18 in the NMR spectrum. The chemical shift coincided with the calculated value, δ 1.18, only when the compound (**26**) was assigned Δ^5-triacetate formula ($cf.$, δ_{calcd} 0.92 for Δ^6-triacetate). The result indicates that dehydration of the 6β-hydroxyeudesmanes would proceed regioselectively to form the corresponding Δ^5-eudesmanes, and hence the major dehydration product (**23**) would be represented by Δ^5-10-nitrile structure rather than Δ^6-10-nitrile. (ii) Tori and co-workers[16b] discussed the chemical shifts of the A ring protons in normal steroids in terms of the effects of functional groups in the A and B rings. The discussion apparently applies to eudesmanes; $e.g.$, the axial 3α-proton (δ 4.60) of Δ^5-triacetate (**26**) was observed at a field 0.10 ppm higher than that (δ 4.70) of 6β-hydroxy triacetate (**15a**), as expected by their presumption. The 3α-proton of the relevant major olefin (**23**) appeared as a double doublet (J= 11 and 9.5 Hz) at 0.13 ppm higher field, δ 4.56, as compared with the corresponding proton of 6β-hydroxy-10-nitrile (**22**), δ 4.69, and that of the minor olefin (**24**) as a triplet (J=9.5 Hz) at 0.09 ppm lower field, δ 4.78.

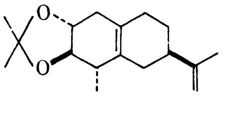
Δ^5-10-Cyano triacetate (**23**) was saponified to the triol (**23a**), oil, which was converted into Δ^5-10-cyano tris(methoxymethyl ether) (**23b**), oil, in a 56% yield from **23**, showing absorption maxima at 2255 cm^{-1} and at δ 3.38, 3.41, 3.46 (each 3H, s, 3OC$\underline{H}_3$), and 5.57 (1H, br s, W_H=4 Hz, $\underline{H}$ at C_6) in the IR and NMR spectra. Hydrolysis of the cyano group of **23** followed by decarboxylation with concomitant migration of the 5,6-double bond was unsuccessful, giving a tarry material. However, treatment of Δ^5-10-nitrile (**23**) with sodium in toluene containing ethanol under reflux[18] effected reductive decyanation with concurrent migration of the double bond to give $\Delta^{5(10)}$-triol (**27**), oil, which was converted into the triacetate (**27a**), oil, showing no olefinic proton in the NMR spectrum, in a 71% yield from **23**. The structure of olefin **27a** was identified by comparison with an authentic sample obtained from natural rishitin (**1**) via a four-step process (formation of the acetonide, hydroboration, acid hydrolysis, and acetylation). On the other hand, $\Delta^{5(10)}$ 2,3,10-triol (**27**), when treated with acetone over silica gel (Wakogel Q-23), formed the 2,3-acetonide (**28**), oil, ν_{max} 3390, 1380, and 1371 cm^{-1} and δ 1.46 [6H, s, $(C\underline{H}_3)_2CO$], in a 75% yield from **23**. The 2,3-acetonide (**28**) was treated successively with tosyl chloride in pyridine at room temperature and then with sodium iodide in acetone under reflux to give the 12-iodide (**29**), semi-soild, *m/e* 390 (M^+) and ν_{max} 1380 and 1371 cm^{-1}, in a 92% yield. Further treatment of the 12-iodide (**29**) with potassium hydroxide in refluxing methanol led to formation of a mixture of two compounds, which were separated by chromatography to give the 12-methoxy derivative (**30**), oil, *m/e* 294 (M^+), ν_{max} 1105 and 1088 cm^{-1}, and δ 3.32 (3H, s, $OC\underline{H}_3$), and $\Delta^{5(10),11}$-2,3-diol acetonide (**31**), oil, in 14 and 70% yields, respectively. The latter (**31**) exhibited parent and fragmentation peaks at *m/e* 262 (M^+) and 131 (base) in the mass spectrum and absorption maxima at 3080, 1643, and 888 cm^{-1} and δ 1.72 (3H, s, 13-$C\underline{H}_3$), 4.63 and 4.74 (each 1H, br s, W_H=4 Hz, 2$\underline{H}$ at C_{12}) in the IR and NMR spectra, and was identical with an authentic specimen[2] derived from natural rishitin (**1**). Hydrolysis of the acetonide (**31**) with 0.5% phosphoric acid in ethanol under reflux afforded $\Delta^{5(10),11}$-2,3-diol, mp 58—60 °C and $[\alpha]_D$ −30.4°, in a 78% yield, which was converted into the diacetate, mp 66—68 °C and $[\alpha]_D$ −14.1°. The glycol and diacetate were identical with natural rishitin[2] (**1**) and the diacetate[2] (**1a**), respectively. The present transformation from (−)-α-santonin (**2**) into rishitin (**1**) completes the first and total[4] synthesis of rishitin. The overall yield of rishitin amounted to 12.0% from compound **5** and 2.9% from (−)-α-santonin.



27 R=H
27a R=Ac



28 R=OH
28a R=OTs
29 R=I
30 R=OCH₃



31

Experimental

All the melting points were uncorrected. The homogenity of each compound was checked by TLC on silica gel (Wakogel B-5) with various solvent systems, and the spots were developed with cerium(IV) sulfate in dil sulfuric acid. The optical rotations, ORD curves, IR, and NMR (100 MHz) spectra were measured in chloroform, methanol, Nujol, and chloroform-*d*, respectively, unless otherwise stated. Abbreviations "s, d, t, q, m, br, and do" in the NMR spectra denote "singlet, doublet, triplet, quartet, multiplet, broad, and double," respectively.

(2R)-2-Isopropenyl-7-methoxy-8-methyl-1,2,3,4-tetrahydronaphthalene (3). *(i)* A soln of 2-(7-acetoxy-8-methyl-1,2,3,4-tetrahydro-2-naphthyl)propanoic acid[2] (12.63 g) in dry tetrahydrofuran (THF, 200 ml) was stirred with lithium aluminium hydride (LAH, 3.15 g) under reflux for 17 h. After addition of water to decompose an excess of the reagent, the suspended mixture was mixed with chloroform and stirred vigorously. The insoluble substance was removed by filtration and washed with chloroform and water. The filtrate and all the chloroform and water washings were combined and evaporated to dryness to leave an oily residue, which was again dissloved in chloroform. The chloroform soln was washed with water, dried, and evaporated to leave a crystalline residue (1.50 g), which was collected and recrystallized from ethyl acetate-hexane to give 2-(7-hydroxy-8-methyl-1,2,3,4-tetrahydro-2-naphthyl)-1-propanol[2] (1.26 g), mp 125—126 °C. The water washings were acidified (pH<4.0) with 6 M hydrochloric acid and extracted with chloroform repeatedly. The extracts were washed with water, dried, and evaporated to leave an amorphous substance (7.35 g), showing a single spot, which was identified as the corresponding saponified product, 2-(7-hydroxy-8-methyl-1,2,3,4-tetrahydro-2-naphthyl)-propanoic acid on the basis of the spectral data: IR ($CHCl_3$), ν_{max} 3585, 1704, 1598, 1486, 1271, and 1063 cm^{-1}; NMR, δ 1.27 (3H, d, J=6.5 Hz), 2.09 (3H, s), 5.85 (2H, br, 2O$\underline{H}$), 6.59 and 6.81 (each 1H, d, J=8 Hz). The hydroxy acid was dissolved in ether (150 ml), without further purification, and treated with diazomethane, prepared from nitrosomethylurea (20.6 g), in ether (230 ml) at room temp for 22 h. The soln was concentrated to give the corresponding methyl ester (6.72 g), oil, showing a single spot on TLC, which was purified by distillation at 168—172 °C (bath temp) under reduced pressure (1 Torr) and crystallized on standing: mp 43—45 °C and $[\alpha]_D$ +92.5°; MS, *m/e* 248 (M^+); IR ($CHCl_3$), ν_{max} 3410, 1722, 1597, 1483, 1267, 1162, and 1060 cm^{-1}; NMR, δ 1.27 (3H, d, J=7 Hz), 2.11 (3H, s), 3.74 (3H, s), 6.57 and 6.80 (each 1H, d, J=8 Hz). Found: C, 72.26; H, 8.11%. Calcd for $C_{15}H_{20}O_3$: C, 72.55; H, 8.12%.

(ii) A soln of methyl 2-(7-hydroxy-8-methyl-1,2,3,4-tetrahydro-2-naphthyl)propanoate (6.61 g) in methanol (250 ml) was treated with diazomethane, prepared from nitrosomethylurea (20.6 g), in ether (220 ml) at room temp for 13 h. After addition of the same amount of diazomethane in ether (220 ml), the soln was allowed to stand at room temp for 66 h and then evaporated below 36 °C to leave an oily residue (7.34 g), which was purified by column chromatography over silica gel (70 g) and celite (30 g) followed by distillation to give methyl 2-(7-methoxy-8-methyl-1,2,3,4-tetrahydro-2-naphthyl)propanoate in pure state: bp 143—148 °C (bath temp) (1 Torr) and $[\alpha]_D$ +89.3°; MS, *m/e* 262 (M^+); IR ($CHCl_3$), ν_{max} 1727, 1599, 1483, 1262, 1163, and 1088 cm^{-1}; NMR, δ 1.26 (3H, d, J=7 Hz), 2.13 (3H, s), 3.75 and 3.83 (each 3H, s), 6.67 and 6.93 (each 1H, d, J=8.5 Hz). Found: C, 73.10; H, 8.35%. Calcd for $C_{16}H_{22}O_3$: C, 73.25; H, 8.45%.

(iii) A soln of the methoxy methyl ester (6.14 g) in THF (160 ml) was mixed with LAH (3 g) in THF (250 ml), and the whole mixture was stirred at room temp for 18 h. After careful addition of water (40 ml), the resulting suspension was submitted to filtration to remove insoluble materials, and the filtrate was evaporated to dryness to leave an oily residue, which was extracted in ether. The ether soln was washed with saturated brine, dried, and evaporated to give an oil (5.69 g), showing a single spot, which was identical with an authentic sample of 2-(7-methoxy-8-methyl-1,2,3,4-tetrahydro-2-naphthyl)-1-propanol prepared from the corresponding 7-hydroxy analogue as described in the following.

A soln of 2-(7-hydroxy-8-methyl-1,2,3,4-tetrahydro-2-naphthyl)propanol[2] (896 mg), mp 125—126 °C, in acetone (40 ml) was stirred with dimethyl sulfate (1.6 ml) and potassium carbonate (4.8 g) under reflux for 9 h, cooled and then filtered. The ppts were washed with chloroform, and the filtrate and washings were combined and evaporated to leave an oily residue, which was again dissolved in chloroform. The chloroform soln was washed with water, dried, and evaporated to leave an oily substance (1.82 g), which was purified by chromatography over silica gel (Merck 30 g). Eluates with benzene-ether (3 : 1) (100 ml) afforded the methyl ether (800 mg), which was distilled for analysis: bp 97—102 °C (bath temp) (1 Torr) and $[\alpha]_D$ +70.9°; MS, *m/e* 234 (M^+), 216, 201, 186, 175, and 173 (base); IR (film), ν_{max} 3360, 1601, 1485, 1463, 1441, 1260, 1103, 1031, 812, and 794 cm^{-1}; NMR, δ 1.00 (3H, d, J=7 Hz), 1.83 (1H, s, $O\underline{H}$), 2.13 (3H, s), 3.69 (2H, m), 3.81 (3H, s), 6.69 and 6.93 (each 1H, d, J=8 Hz). Found: C, 76.69; H, 9.43%. Calcd for $C_{15}H_{22}O_2$: C, 76.88; H, 9.46%.

(iv) The methoxy-propanol (730 mg), described in *(iii)*, was treated with *p*-toluenesulfonyl chloroide (660 mg) in pyridine (Py, 8 ml) at room temp for 20 h, and then poured into ice-water (300 ml). The resulting ppts were collected by filtration, washed with water, dried in a desiccator, and triturated with isopropyl ether to yield a crystalline substance (980 mg). Recrystallization from isopropyl ether afforded 2-(7-methoxy-8-methyl-1,2,3,4-tetrahydro-2-naphthyl)-1-propanol tosylate, mp 86.5—87 °C and $[\alpha]_D$ +56.3°; MS, *m/e* 388 (M^+), 216, 201, and 174 (base); IR, ν_{max} 1598, 1485, 1355, 1261, 1188, 1180, 1171, 1106, 1096, 957, 929, 850, and 792 cm^{-1}; NMR, δ 0.97 (3H, d, J=6.5 Hz), 2.04, 2.45, and 3.78 (each 3H, s), 4.05 (2H, d, J=5 Hz), 6.65 and 6.87 (each 1H, d, J=8.5 Hz), 7.31 and 7.78 (each 2H, ABq, J=8 Hz). Found: C, 68.01; H, 7.23; S, 8.30%. Calcd for $C_{22}H_{28}O_4S$: C, 68.01; H, 7.26; S, 8.25%.

(v) The tosylate (650 mg) was stirred with sodium iodide (3 g) in acetone (30 ml) under reflux for 20 h. After removal of the insoluble substance by filtration, the mixture was evaporated to dryness and extracted with ether (50 ml). The extracts were washed with 5% aq sodium thiosulfate and saturated brine, dried, and evaporated to leave a crystalline substance (617 mg), which was recrystallized from hexane to give the corresponding iodide (570 mg), mp 73.5—75.5 °C. This was recrystallized from hexane for analysis: mp 75.5—77.5 °C and $[\alpha]_D$ +95°; MS, *m/e* 344 (M^+), 217, 175, and 161 (base); IR, ν_{max} 1599, 1587, 1479, 1258, 1105, and 801 cm^{-1}; NMR, δ 1.09 (3H, d, J=6.5 Hz), 2.14 (3H, s), 3.37 (2H, d, J=5 Hz, $C\underline{H}_2I$), 3.82 (3H, s), 6.70 and 6.94 (each 1H, d, J=8 Hz). Found: C, 52.32; H, 6.20; I, 37.21%. Calcd for $C_{15}H_{21}OI$: C, 52.33; H, 6.15; I, 36.87%.

(vi) The iodide (4.97 g) was refluxed in methanol (300 ml) containing potassium hydroxide (17.6 g) under nitrogen for 2.5 h. The reaction mixture was concentrated below 40 °C under reduced pressure (90 Torr), and then shaken with water (150 ml), ether (100 ml), and sodium chloride (40 g). The aqueous layer was separated and washed with ether (4×50 ml). The ether layer and washings were combined, washed with saturated brine (2×50 ml), dried, and evaporated to leave an oily residue (3.19 g), which was purified by column chromatography over silica gel (Mallinckrodt, 21 g) and celite (9 g). Eluates with hexane (1.6 l), after distillation, afforded (2*R*)-2-isopropenyl-7-methoxy-8-methyl-1,2,3,4-tetrahydronaphthalene (**3**, 2.68 g), bp 89—91 °C (bath temp) (0.07 Torr) and $[\alpha]_D$ +76.6°; MS, *m/e* 216 (M^+), 201, and 173 (base); IR (CCl_4), ν_{max} 3080, 1645, 1601, 1484, 1260, 1114, 1090, and 890 cm^{-1}; NMR, δ 1.83, 2.13, and 3.79 (each 3H, s), 4.80 (2H, s, $=C\underline{H}_2$), 6.69 and 6.94 (each 1H, d, J=8.5 Hz). Found: C, 83.52; H, 9.25%. Calcd for $C_{15}H_{20}O$: C, 83.28; H, 9.32%.

(11S)-3-Oxo-4β,5α-eudesman-6β,12-olide[6,7] *(**5**)*. Compound **5** was prepared by a modification of the procedure of Cocker *et al.*[7b] A soln of "6-epi-(−)-α-santonin"[7,19] (3 g), mp 102—103 °C, in acetic acid (AcOH, 400 ml) was hydrogenated over 10% palladium charcoal (200 mg) at room temp for 2 h, when 590 ml of hydrogen had been absorbed. The reaction mixture was worked up as usual to leave neutral crystalline substances (1.64 g), showing two 1 : 1 overlapped spots on TLC. The mixture, dissolved in AcOH (150 ml) at 50 °C, was stirred with *p*-toluenesulfonic acid (PTS, 1.5 g) at room temp for 18 h, evaporated to dryness, and diluted with water (500 ml). The resulting ppts were separated, collected by filtration and washed with water. Recrystallization from aq ethanol gave **5** (1.16 g), mp 164—165 °C. This was recrystallized from ethanol for analysis: mp 164—165 °C and $[\alpha]_D$ −106.0° (lit,[7] mp 177—178° and $[\alpha]_D$ −91°); ORD, $[\Phi]_{304}^{peak}$ +800°, $[\Phi]_{265}^{trough}$ −4790°, *a*=+55.9°; IR, ν_{max} 1762, 1703, 1420, 1210, 1178, 1153, 975, and 937 cm^{-1}; NMR, δ 1.14 (3H, d, J=7 Hz, 14-$C\underline{H}_3$), 1.22 (3H, s, 15-$C\underline{H}_3$), 1.33 (3H, d, J=8 Hz, 13-$C\underline{H}_3$), and 4.66 (1H, t, J=4 Hz, $\underline{H}$ at C_6). Found: C, 72.10; H, 9.07%. Calcd for $C_{15}H_{22}O_3$: C, 71.97; H, 8.86%.

*(11S)-3-Acetoxy-4β,5α-eudesm-2-en-6β,12-olide (**7**)*. A soln of **5** (67.2 g) in isopropenyl acetate (250 ml) containing concd sulfuric acid (0.7 ml) was refluxed for 3 h with stirring in a stream of argon gas. The mixture was cooled, concentrated, mixed with water, and extracted with dichloromethane. The extracts were worked up as usual to leave a crystalline residue, which on trituration with a 2 : 1 mixture of acetone and water followed by filtration afforded **7** (63.4 g), mp 139—140 °C. The filtrate (15.2 g), still containing the unreacted ketone (**5**) (TLC), was again treated with isopropenyl acetate (62 ml) and concd sulfuric acid (10 drops) for 3 h under reflux. The resulting crystalline residue, subjected to the same treatment as above, yielded **7** (14.3 g), mp 139—140 °C. The samples (**7**) were recrystallized from aq acetone for analysis: mp 140—141 °C and $[\alpha]_D$ −74.3 °C; MS, *m/e* 292 (M^+), 250 (base), and 177; IR, ν_{max} 1773, 1755, 1682, 1214, 1207, 1063, and 1021 cm^{-1}; NMR, δ 1.07 (3H, s, 15-$C\underline{H}_3$), 1.10 and 1.32 (each 3H, d, J=7 and 8 Hz, 14- and 13-$C\underline{H}_3$), 2.17 (3H, s, $OCOC\underline{H}_3$), 2.41 (1H, q, J=8 Hz, $\underline{H}$ at C_{11}), 2.74 (1H, br, W_H=24 Hz, $\underline{H}$ at C_4), 4.76 (1H, t, J=4 Hz, $\underline{H}$ at C_6), and 5.28 (1H, do t, J=5.5, 2.5, and 2.5 Hz, $\underline{H}$ at C_2). Found: C, 69.97; H, 8.47%. Calcd for $C_{17}H_{24}O_4$: C, 69.83; H, 8.27%.

*(11S)-3β-Acetoxy-2α,3α-epoxy-4β,5α-eudesman-6β,12-olide (**8**)*. A soln of **7** (2.45 g) in chloroform (40 ml) was treated with peroxybenzoic acid (purity 99.3%, 2 g) at 0 °C for 24 h. The mixture was washed with 5% aq sodium thiosulfate, 5% aq sodium hydrogencarbonate and water, dried, and evaporated to leave a crystalline substance, which was collected with acetone to give **8** (2.34 g), mp 153—154 °C. This was recrystallized from acetone for analysis: mp 156—156.5 °C and $[\alpha]_D$ −58.7°; MS, *m/e* 308 (M^+), 266 (base), 248, and 193; IR, ν_{max} 1771, 1750, 1223, 1158, 1050, and 976 cm^{-1}; NMR, δ 1.20 (3H, s, 15-$C\underline{H}_3$), 1.24 and 1.30 (each 3H, d, J=6.5 and 7.5 Hz, 14- and 13-$C\underline{H}_3$), 2.10 (3H, s, $OCOC\underline{H}_3$), 2.37 (1H, q, J=7.5 Hz, $\underline{H}$ at C_{11}), 2.67 (1H, do q, J=10.5, 6.5, 6.5, and 6.5 Hz, $\underline{H}$ at C_4), 3.45 (1H, d, J=5 Hz, $\underline{H}$ at C_2), and 4.67 (1H, t, J=4 Hz, $\underline{H}$ at C_6). Found: C, 66.15; H, 7.79%. Calcd for $C_{17}H_{24}O_5$: C, 66.21; H, 7.85%.

*(11S)-2β-Acetoxy-3-oxo-4β,5α-eudesman-6β,12-olide (**9**)*. Compound **8** (1.27 g) was heated in an oil-bath maintained at 170 °C for 10 min. The mixture, when cooled, crystallized spontaneously and showed a single spot on TLC. This was recrystallized from acetone-isopropyl ether to give **9** (1.187 g), mp 127—129 °C. Further recrystallization from the same solvent mixture afforded an analytical sample: mp 128—129 °C and $[\alpha]_D$ −7.7°; ORD, $[\Phi]_{304}^{peak}$ +3040°, $[\Phi]_{270}^{trough}$ −3790°, *a*=+68.3°; MS, *m/e* 308 (M^+), 266 (base), 248, and

193; IR, ν_{max} 1782, 1737, and 1229 cm^{-1}; NMR, δ 1.06 (3H, s, 15-C$\underline{H}_3$), 1.26 and 1.33 (each 3H, d, J=7 and 8 Hz, 14- and 13-C$\underline{H}_3$), 2.14 (3H, s, OCOC$\underline{H}_3$), 2.43 (1H, q, J=8 Hz, $\underline{H}$ at C_{11}), 2.92 (1H, do q, J=12, 7, 7, and 7 Hz, $\underline{H}$ at C_4), 4.69 (1H, t, J=4 Hz, $\underline{H}$ at C_6), and 5.35 (1H, do d, J=9 and 6 Hz, $\underline{H}$ at C_2). Found: C, 65.91; H, 7.82%. Calcd for $C_{17}H_{24}O_5$: C, 66.21; H, 7.85%.

*(11S)-2α-Acetoxy-3-oxo-4β,5α-eudesman-6β,12-olide (**10**).* *(i)* A soln of **9** (1.76 g) in glacial AcOH (35 ml) containing 47% hydrobromic acid (0.25 ml) was allowed to stand at room temp for 41 h. The soln was concentrated, diluted with water, and extracted with chloroform. The chloroform soln was worked up as usual to leave an oily residue, which on trituration with acetone-isopropyl ether followed by filtration afforded slightly crude **10** (1.24 g), mp 191—193 °C. The filtrate (0.35 g) was purified by chromatography over silica gel (25 g) to give an another sample of **10** (0.1 g), mp 193—195 °C, from ether-benzene (1 : 4) eluates. Recrystallization of both samples repeated twice yielded an analytical sample of **10**: mp 204—205 °C and $[\alpha]_D$ −32.8°; ORD, $[\Phi]_{305}^{\mathrm{peak}}$ +2570°, $[\Phi]_{269}^{\mathrm{trough}}$ −5010°, a=+75.8°; MS, *m/e* 308 (M^+), 266 (base), 248, and 193; IR, ν_{max} 1779, 1747, 1718, and 1244 cm^{-1}; NMR, δ 1.19 (3H, d, J=7 Hz, 14-C$\underline{H}_3$), 1.32 (3H, s, 15-C$\underline{H}_3$), 1.34 (3H, d, J=8 Hz, 13-C$\underline{H}_3$), 2.17 (3H, s, OCOC$\underline{H}_3$), 2.45 (1H, q, J=8 Hz, $\underline{H}$ at C_{11}), 2.89 (1H, do q, J=12, 7, 7, and 7 Hz, $\underline{H}$ at C_4), 4.63 (1H, t, J=4 Hz, $\underline{H}$ at C_6), and 5.45 (1H, do d, J=13 and 7 Hz, $\underline{H}$ at C_2). Found: C, 65.98; H, 7.83%. Calcd for $C_{17}H_{24}O_5$: C, 66.21; H, 7.85%.

*Oxidation of Compound **5** with Lead Tetraacetate.* A soln of **5** (1.44 g, 5.8 mmol) and lead tetraacetate (3.2 g, *ca.* 6.4 mmol) in a mixture of benzene (154 ml, 1.73 mol) and 2-propanol (4 ml, 57 mmol) containing boron trifluoride etherate (BF_3 5 ml, 39.6 mmol) was stirred at 25 °C under argon gas for 3.5 h, when the starch-iodide test for lead tetraacetate showed negative, an appreciable amount of **5** remaining unreacted (TLC). After addition of fresh lead tetraacetate (1.6 g, *ca.* 3.2 mmol), the soln was further stirred for 20 h under the same conditions. The reaction mixture was washed with 1 M hydrochloric acid, 5% aq sodium hydrogencabonate and water, dried, and evaporated to leave a crystalline residue (1.79 g), which was separated into three fractions by chromatography over silica gel (60 g) with ether-benzene (1 : 5) as eluents. The most mobile fraction gave A-nor-ester (**11**, 0.25 g), mp 111—112 °C, on trituration with hexane-isopropyl ether. Recrystallization from the same solvent mixture yielded an analytical sample of **11**: mp 112.5—113 °C and $[\alpha]_D$ −116.8°; MS, *m/e* 308 (M^+), 293, 249, 221, and 193 (base); IR and NMR, in the text. Found: C, 69.77; H, 9.05%. Calcd for $C_{18}H_{28}O_4$: C, 70.10; H, 9.15%.

The middle and least mobile fractions were triturated with acetone-isopropyl ether to give **10** (0.73 g), mp 202—203 °C, and **9** (0.16 g), mp 127.5—128.5 °C, respectively, which were identical with the corresponding authentic specimens.

*(11S)-2α,3β- and (11S)-2α,3α-Dihydroxy-4β,5α-eudesman-6β,12-olides (**12b** and **13b**), their 2-acetates (**12** and **13**), and their 2,3-diacetates (**12a** and **13a**).* *(i)* A soln of **10** (200 mg) in methanol (6 ml) was stirred with sodium borohydride (14 mg) at 0 °C for 14 min. After addition of AcOH (0.2 ml), the mixture was worked up as usual to leave a crystalline residue, showing two spots on TLC, which was separated into two fractions by preparative TLC over silica gel (Wakogel B-5) with a 2 : 3 mixture of ether and benzene. The more mobile fraction (117 mg), when triturated with acetone-isopropyl ether, gave **13** (96 mg), mp 190—191 °C. This was recrystallized from the same solvent mixture for analysis: mp 191—192 °C and $[\alpha]_D$ −77.6°; MS, *m/e* 250 (base, $M^+-C_2H_4O_2$), 235, 232, 217, and 204; IR, ν_{max} 3440, 1755, 1741, 1243, 1214, 1025, and 1018 cm^{-1}; NMR, δ 1.03 (3H, s, 15-C$\underline{H}_3$), 1.13 and 1.29 (each 3H, d, J=6 and 7.5 Hz, 14- and 13-C$\underline{H}_3$), 1.93 (1H, br s, O$\underline{H}$), 2.07 (3H, s, OCOC$\underline{H}_3$), 2.35 (1H, q, J=7.5 Hz, $\underline{H}$ at C_{11}), 3.91 (1H, br s, W_H=6.5 Hz, $\underline{H}$ at C_3), 4.59 (1H, t, J=4 Hz, $\underline{H}$ at C_6), and 5.01 (1H, do do d, J=11, 5.5, and 3 Hz, $\underline{H}$ at C_2). Found: C, 65.59; H, 8.53%. Calcd for $C_{17}H_{26}O_5$: C, 65.87; H, 8.44%.

The less mobile fraction (94 mg) on trituration with acetone-isopropyl ether afforded **12** (82 mg), mp 249—249.5 °C. This was recrystallized from the same solvent mixture for analysis: mp 251—252 °C and $[\alpha]_D$ −88.2°; MS, *m/e* 250 (base, $M^+-C_2H_4O_2$), 235, 232, 217, and 204; IR, ν_{max} 3435, 1742, 1732, 1243, and 1055 cm^{-1}; NMR, δ 1.06 (3H, s, 15-C$\underline{H}_3$), 1.16 and 1.31 (each 3H, d, J=6 and 7.5 Hz, 14- and 13-C$\underline{H}_3$), 2.07 (3H, s, OCOC$\underline{H}_3$), 2.36 (1H, q, J=7.5 Hz, $\underline{H}$ at C_{11}), 2.45 (1H, br s, O$\underline{H}$), 3.13 [(1H, do t, J=9, 9, and 5 Hz, $\underline{H}$ at C_3) (1H, t, J=9 Hz, on addition of D_2O)], 4.65 (1H, t, J=4 Hz, $\underline{H}$ at C_6), and 4.93 (1H, do do d, J=11.5, 9, and 5 Hz, $\underline{H}$ at C_2). Found: C, 65.58; H, 8.46%. Calcd for $C_{17}H_{26}O_5$: C, 65.78; H, 8.44%.

(ii) A soln of **12** (40 mg) in methanol (1 ml) containing 5% potassium hydroxide was stirred at room temp for 1 h. The reaction mixture was worked up as usual to leave a crystalline substance (32 mg), which was recrystallized from acetone-isopropyl ether to yield **12b** (29 mg), mp 182—183 °C. This was recrystallized from the same solvent mixture for analysis: mp 184—185 °C and $[\alpha]_D$ −93 °C; MS, *m/e* 268 (M^+), 250, 235, 232, 224 (base), 217, 209, and 206; IR, ν_{max} 3380, 3220, 1764, 1204, 1164, 1047, and 968 cm^{-1}; NMR, δ 0.99 (3H, s, 15-C$\underline{H}_3$), 1.14 and 1.30 (each 3H, d, J=6 and 7.5 Hz, 14- and 13-C$\underline{H}_3$), 2.37 (1H, q, J=7.5 Hz, $\underline{H}$ at C_{11}), 2.93 (1H, do d, J=9.5 and 8.5 Hz, $\underline{H}$ at C_3), 3.03 (2H, br s, 2O$\underline{H}$), 3.73 (1H, do do d, J=11, 8.5, and 5 Hz, $\underline{H}$ at C_2), and 4.66 (1H, t, J=4 Hz, $\underline{H}$ at C_6). Found: C, 66.97; H, 8.95%. Calcd for $C_{15}H_{24}O_4$: C, 67.13; H, 9.02%.

Compound **13** (139 mg) was hydrolyzed in methanol (4 ml) in the same manner as described above, giving a crystalline glycol (141 mg), which on recrystallization from ethyl acetate-isopropyl ether afforded **13b** (101 mg), mp 90—92 °C. This was recrystallized from the solvent mixture for analysis: mp 94.5—95 °C and $[\alpha]_D$ −90.1°; MS, *m/e* 268 (M^+), 250, 235, 232, 224, 217, and 206; IR, ν_{max} 3480, 3440, 1763, 1213, 1177, 1063, 1036, 1013, 999, and 971 cm^{-1}; NMR, δ 0.96 (3H, s, 15-C$\underline{H}_3$), 1.13 and 1.29 (each 3H, d, J=6.5 and 7.5 Hz, 14- and 13-C$\underline{H}_3$), 2.35 (1H, q, J=7.5 Hz, $\underline{H}$ at C_{11}), 2.65 (2H, br s, 2O$\underline{H}$), 3.84 (1H, br s, W_H=7 Hz, $\underline{H}$ at C_3), 3.91 (1H, br, W_H=20 Hz, $\underline{H}$ at C_2), and 4.62 (1H, t, J=4 Hz, $\underline{H}$ at C_6). Found: C, 65.00; H, 9.09%. Calcd for $C_{15}H_{24}O_4 \cdot 1/2CH_3COOC_2H_5$: C, 65.36; H, 9.03%.

(iii) Compound **12** (41 mg) was treated with acetic anhydride (Ac_2O, 1 ml) and Py (1 ml) at room temp for 12 h. The mixture was worked up as usual to leave a crystalline substance (47 mg), which on recrystallization from acetone-isopropyl ether gave **12a** (33.5 mg), mp 189.5—190.5 °C and $[\alpha]_D$ −82.0°; MS, 292 ($M^+-C_2H_4O_2$), 250 (base), 235, 232, and 217; IR, ν_{max} 1769, 1750, 1245, 1219, 1043, and 1030 cm^{-1}; NMR, δ 0.99 (3H, d, J=6.5 Hz, 14-C$\underline{H}_3$), 1.07 (3H, s, 15-C$\underline{H}_3$), 1.31 (3H, d, J=7.5 Hz, 13-C$\underline{H}_3$), 1.99 and 2.08 (each 3H, s, 2OCOC$\underline{H}_3$), 2.39 (1H, q, J=7.5 Hz, $\underline{H}$ at C_{11}), 4.66 (1H, t, J=4 Hz, $\underline{H}$ at C_6), 4.70 (1H, t, J=10 Hz, $\underline{H}$ at C_3), and 5.12 (1H, do do d, J=11, 9.5, and 5 Hz, $\underline{H}$ at C_2). Found: C, 64.70; H, 8.00%. Calcd for $C_{19}H_{28}O_6$: C, 64.75; H, 8.01%. Compound **12b** (14.5 mg) was acetylated in the same manner as **12** to give **12a** (crude 18.7 mg, pure 13.5 mg), mp 189—189.5 °C.

Compound **13** (84 mg) was treated with Ac_2O (1 ml) and Py (1 ml) at room temp for 24 h. The mixture was worked up as usual to leave a crystalline substance (97 mg), which was recrystallized from acetone-isopropyl ether to give **13a** (87 mg), mp 149.5—150.5 °C. Recrystallization from the same solvent mixture afforded an analytical sample: mp 150—151 °C and $[\alpha]_D$ −59.9 °; MS, *m/e* 292 ($M^+-C_2H_4O_2$), 250 (base), 235, 232, and 217; IR, ν_{max} 1772, 1741, 1260, 1248, 1233, and 1030 cm^{-1}; NMR, δ 1.01 (3H, d, $J=8$ Hz, 14-$C\underline{H}_3$), 1.05 (3H, s, 15-$C\underline{H}_3$), 1.30 (3H, d, $J=7.5$ Hz, 13-$C\underline{H}_3$), 1.97 and 2.11 (each 3H, s, 2OCOC$\underline{H}_3$), 2.39 (1H, q, $J=7.5$ Hz, $\underline{H}$ at C_{11}), 4.60 (1H, t, $J=4$ Hz, $\underline{H}$ at C_6), 5.11 (1H, do do d, $J=11$, 6, and 3 Hz, $\underline{H}$ at C_2), and 5.33 (1H, br, $W_H=6.5$ Hz, $\underline{H}$ at C_3).

Found: C, 64.52; H, 7.97%. Calcd for $C_{19}H_{28}O_6$: C, 64.75; H, 8.01%. Compound **13b** (37.5 mg) was acetylated in the same manner as **13** to give **13a** (crude 48.5 mg, pure 31.8 mg), mp 150—151 °C.

*(11S)-2α,3α-Dihydroxy-4β,5α-eudesman-6β,12-olide 2,3-acetonide (**14**).* (*i*) Silica gel (Wakogel Q-23, 25 g) packed in a column was washed twice with methanol, thrice with acetone, and once with hexane. Compound **13b** (100 mg) dissolved in hexane–acetone (1 : 1) was adsorbed onto the column and eluted with hexane–acetone (92 : 8) to give a crystalline material (112 mg), which was collected with hexane-isopropyl ether to yield **14** (57 mg), mp 115—117 °C. Recrystallization from the same solvent mixture afforded an analytical sample: mp 131—132 °C and $[\alpha]_D$ −53.9°; MS, *m/e* 293 (M^+-CH_3), 251, 233, 187, and 159 (base); IR (CCl_4), ν_{max} 1782, 1380, 1368, 1240, 1213, 1171, 1151, 1051, 1030, 1010, and 977 cm^{-1}; NMR, δ 0.90 (3H, s, 15-$C\underline{H}_3$), 1.19 and 1.30 (each 3H, d, $J=7$ and 7.5 Hz, 14- and 13-$C\underline{H}_3$), 1.35 and 1.48 [each 3H, s, $(C\underline{H}_3)_2CO$], 2.37 (1H, q, $J=7.5$ Hz, $\underline{H}$ at C_{11}), 4.23 (2H, br m, 2$\underline{H}$ at C_2 and C_3), and 4.70 (1H, t, $J=4$ Hz, $\underline{H}$ at C_6). Found: C, 70.09; H, 9.06%. Calcd for $C_{18}H_{28}O_4$: C, 70.10; H, 9.15%.

(*ii*) Compound **12b** (22.6 mg) was treated with silica gel (Wakogel Q-23, 25 g) and acetone in the same manner as **13b**. The crystalline eluate (22.8 mg) was triturated with acetone-isopropyl ether to give a crystalline material (13.7 mg), mp 170.5—172 °C, which was identical with the unreacted starting glycol (**12b**).

*Oxidation of Compounds **12** and **13** to **10**.* (*i*) A soln of **12** (25 mg) in acetone (3 ml) was stirred with the Jones reagent (0.3 ml) at 0 °C for 1 h. After addition of ethanol, the mixture was evaporated *in vacuo* below 40 °C, diluted with water, and extracted with chloroform. The chloroform soln was worked up as usual to leave a crystalline residue (27.4 mg), showing a single spot, which on recrystallization from acetone-isopropyl ether yielded **10** (22 mg), mp 203.5—204 °C, identical with an authentic sample.

(*ii*) Compound **13** (25 mg) was oxidized with the Jones reagent (0.3 ml) in the same manner as **12** to yield **10** (21 mg), mp 203—204 °C, on recrystallization from acetone-isopropyl ether.

*(11S)-4β,5α-Eudesmane-2α,3β,6β,12-tetraol (**15**) and Its 2,3,12-Triacetate (**15a**).* A soln of **12** (403 mg) in dry THF (40 ml) was stirred with LAH (400 mg) under reflux for 24 h and cooled. After successive addition of ethyl acetate, methanol and water, the mixture was filtered to remove insoluble materials, which were washed with hot ethanol. The filtrate and ethanol washings were combined, evaporated below 40 °C, diluted with water, and extracted with chloroform with a Soxhlet apparatus for 5 d. The chloroform soln was concentrated to dryness to leave an oily substance (**15**, 410 mg), showing a single spot, which was treated with Ac_2O (2.7 ml) in Py (4 ml) at room temp for 19 h. The reaction mixture was worked up as usual to leave an oily residue (654 mg), which on trituration with isopropyl ether gave **15a** (427 mg), mp 96.5—98 °C. This was recrystallized from isopropyl ether for analysis: mp 96.5—98 °C and $[\alpha]_D$ −7.6 °C; MS, *m/e* 338 ($M^+-C_2H_4O_2$), 279, 278, 236, 219 (base), and 218; IR, ν_{max} 3535, 1733, 1241, 1050, 1033, and 1027 cm^{-1}; NMR, δ 0.92 and 1.02 (each 3H, d, $J=6.5$ and 7 Hz, 14- and 13-$C\underline{H}_3$), 1.18 (3H, s, 15-$C\underline{H}_3$), 1.99 and 2.08 (3H and 6H, each s, 3OCOC$\underline{H}_3$), 3.89 and 4.21 (each 1H, do d, $J=11$, 6 and 11, 5 Hz, 2$\underline{H}$ at C_{12}), 4.08 (1H, br s, $W_H=6.5$ Hz, $\underline{H}$ at C_6), 4.70 (1H, t, $J=10$ Hz, $\underline{H}$ at C_3), and 5.11 (1H, do do d, $J=11.5$, 10, and 5 Hz, $\underline{H}$ at C_2). Found: C, 63.21; H, 8.74%. Calcd for $C_{21}H_{34}O_7$: C, 63.29; H, 8.60%.

Compound **15a** (132 mg) was refluxed in methanol (5 ml) containing 5% potassium hydroxide under nitrogen for 1 h. The soln was worked up as usual to give **15** (84 mg), amorphous; $[\alpha]_D$ −3.2° (EtOH). Found: C, 64.00; H, 10.17%. Calcd for $C_{15}H_{28}O_4 \cdot 1/2H_2O$: C, 64.02; H, 10.39%.

*(11S)-4β,5α-Eudesmane-2α,3α,6β,12-tetraol (**16**) and Its 2,3,12-Triacetate and 2,12-Diacetate (**16a** and **16b**).* A soln of **13** (211 mg) in dry THF (21 ml) was stirred with LAH (300 mg) under reflux for 24 h. The reaction mixture was worked up in almost the same manner as that for **12** to leave a crystalline substance (118 mg), showing a single spot, which was recrystallized from acetone–isopropyl ether to give **16** (76 mg), mp 170—171 °C. Recrystallization twice from the same solvent mixture afforded an analytical sample: mp 174—174.5 °C and $[\alpha]_D$ −14.6° (EtOH); IR, ν_{max} 3410, 3290, 1077, 1053, 1038, 1022, and 1000 cm^{-1}. Found: C, 66.16; H, 10.32%. Calcd for $C_{15}H_{28}O_4$: C, 66.14; H, 10.36%.

The tetraol (**16**, 133 mg) was treated with Ac_2O (1.3 ml) and Py (1.5 ml) at room temp for 17 h. The mixture was worked up as usual to leave an oily residue (231 mg), showing two spots, which was separated into two fractions by column chromatography over silica gel (20 g) with a 3 : 1 mixture of benzene and ether. The more mobile fraction (175 mg) was crystallized and recrystallized from hexane-isopropyl ether to give **16a** (127 mg), mp 78.5—80 °C. This was recrystallized from the same solvent mixture for analysis: mp 80—81 °C and $[\alpha]_D$ +7.2°; MS, *m/e* 338 ($M^+-C_2H_4O_2$), 296, 279, 278, 263, 260, 236, 219, 218, 203, 200, 176, 161, and 107 (base); IR, ν_{max} 3590, 1743, 1253, 1226, and 1024 cm^{-1}; NMR, δ 0.97 and 1.02 (each 3H, d, $J=7$ Hz, 14- and 13-$C\underline{H}_3$), 1.15 (3H, s, 15-CH_3), 1.97, 2.08, and 2.11 (each 3H, s, 3OCOC$\underline{H}_3$), 3.87 and 4.22 (each 1H, do d, $J=11$, 6 and 11, 5 Hz, 2$\underline{H}$ at C_{12}), 4.00 (1H, br s, $W_H=7$ Hz, $\underline{H}$ at C_6), 5.10 (1H, do do d, $J=11.5$, 5.5, and 3 Hz $\underline{H}$ at C_2), and 5.33 (1H, t, $J=3$ Hz, $\underline{H}$ at C_3). Found: C, 63.42; H, 8.65%. Calcd for $C_{21}H_{34}O_7$: C, 63.29; H, 8.60%. The less mobile fraction afforded **16b** (29 mg), oil and $[\alpha]_D$ −1.2°; MS, *m/e* 338 (M^+-H_2O), 296 ($M^+-C_2H_4O_2$), 278, 254, 236, 221, 218, and 203; IR ($CHCl_3$), ν_{max} 3610, 3500, 1733, 1246, and 1023 cm^{-1}; NMR, δ 1.00 and 1.07 (each 3H, d, $J=7$ Hz, 14- and 13-$C\underline{H}_3$ or *vice versa*), 1.13 (3H, s, 15-$C\underline{H}_3$), 2.08 (6H, s, 2OCOC$\underline{H}_3$), 3.88 and 4.21 (each 1H, do d, $J=11$, 6 and 11, 5 Hz, 2$\underline{H}$ at C_{12}), 3.97 (2H, m, 2$\underline{H}$ at C_3 and C_6), and 5.06 (1H, do do d, $J=11.5$, 5, and 3 Hz, $\underline{H}$ at C_2).

*Reduction of **10** with LAH and Subsequent Acetylation to **15a**.* To a cold suspension of LAH (15 g) in dry THF (1000 ml) was added dropwise a soln of **10** (30 g) in THF (200 ml) at 0 °C during a period of 15 min with stirring. The mixture, after further addition of THF (200 ml), was stirred under reflux for 24 h and cooled. After successive addition of ethyl acetate (100 ml), ethanol (200 ml), and water (100 ml), the resulting suspension was stirred overnight at room temp and then filtered to remove an insoluble substance, which was washed with ethanol. The filtrate and ethanol washings were combined and evaporated to dryness to leave an oily residue (40.9 g), which was treated with Ac$_2$O (170 ml) and Py (260 ml) at room temp for 13 h. After being worked up as usual, the mixture left oily substances (40 g), which on trituration with isopropyl ether gave **15a** (25.2 g), mp 95.5—96.5 °C, identical with the authentic sample described in the previous section. The mother liquors, obtained by removal of the pure sample of **15a**, were dissolved in methanol (150 ml), refluxed with 10% potassium hydroxide in methanol (150 ml) for 1 h under nitrogen and then allowed to stand overnight at room temp. The reaction mixture was concentrated at 50 °C, diluted with water (50 ml), neutralized with 6 M hydrochloric acid at 0 °C, and extracted with chloroform with a Soxhlet apparatus for 5 d. The chloroform extracts afforded a foamy residue (9.4 g), showing two spots, which was separated into two fractions by chromatography over silica gel (500 g) with ethyl acetate. The more mobile fraction (3.1 g) crystallized on trituration with acetone-isopropyl ether to yield **16** (2.6 g), mp 174—174.5 °C, identical with an authentic sample. The less mobile fraction (5.1 g), amorphous, was again treated with Ac$_2$O (36 ml) and Py (50.5 ml) at room temp for 17 h to give **15a** (5.8 g) on trituration with isopropyl ether.

*(11S)-2α,3β,12-Triacetoxy-4β,5α-eudesman-6-one (**20**).* A soln of **15a** (103 mg) in acetone (11 ml) was stirred with the Jones reagent (0.6 ml) at 0 °C for 1 h. After addition of ethanol, the mixture was concentrated, diluted with water, and extracted with chloroform. The chloroform extracts, after being worked up as usual, left a crystalline residue, which was recrystallized from isopropyl ether to give **20** (87.5 mg), mp 109—109.5 °C. Recrystallization from isopropyl ether afforded an analytical sample: mp 109.5—111 °C and $[\alpha]_D$ −44.7°; MS, *m/e* 396 (M$^+$), 336, 276, and 216 (base); IR, ν_{max} 1751, 1738, 1703, 1253, 1235, 1222, 1080, 1038, and 1025 cm^{-1}; NMR, δ 0.88 (3H, s, 15-C$\underline{\text{H}}_3$), 0.89 and 0.93 (each 3H, d, *J*=7 and 6.5 Hz, 14- and 13-C$\underline{\text{H}}_3$ or *vice versa*), 2.00, 2.05, and 2.06 (each 3H, s, 3OCOC$\underline{\text{H}}_3$), 3.96 (2H, d, *J*=5 Hz, 2$\underline{\text{H}}$ at C$_{12}$), 4.72 (1H, t, *J*=10 Hz, $\underline{\text{H}}$ at C$_3$), and 5.03 (1H, do do d, *J*=11, 10, and 4.5 Hz, $\underline{\text{H}}$ at C$_2$). Found: C, 63.72; H, 8.28%. Calcd for C$_{21}$H$_{32}$O$_7$: C, 63.61; H, 8.14%.

*Photolysis of (11S)-2α,3β,12-Triacetoxy-4β,5α-eudesman-6β-ol 6-Nitrite (**17**).* To a soln of **15a** (2.94 g) in Py (30 ml) cooled at −20—−30 °C was added dropwise excess nitrosyl chloride in Py during a period of 20 min, the yellow color of nitrosyl chloride remaining unchanged and the starting alcohol (**15a**) disappearing on TLC. The mixture was poured into ice-water (800 ml), and the resulting crystalline ppt was collected by filtration, washed with water, and dried over phosphorus pentaoxide for 18 h in a vacuum desiccator to yield **17** (3.13 g), mp 103.5—105.5 °C; IR, ν_{max} 1748, 1653, 1643, 1253, 1050, and 768 cm^{-1}; NMR, δ 0.89 and 0.91 (each 3H, d, *J*=6.5 Hz, 14- and 13-C$\underline{\text{H}}_3$ or *vice versa*), 1.01 (3H, s, 15-C$\underline{\text{H}}_3$), 1.98, 2.04, and 2.06 (each 3H, s, 3OCOC$\underline{\text{H}}_3$), 3.99 (2H, d, *J*=5 Hz, 2$\underline{\text{H}}$ at C$_{12}$), 4.72 (1H, t, *J*=10 Hz, $\underline{\text{H}}$ at C$_3$), 5.05 (1H, do do d, *J*=11.5, 10, and 5 Hz, $\underline{\text{H}}$ at C$_2$), and 5.94 (1H, br s, W_H=5 Hz, $\underline{\text{H}}$ at C$_6$).

The 6β-nitrite (**17**, 3.00 g) in dry benzene (thiophene-free, 200 ml) in a Pyrex vessel, without further purification, was irradiated with a 200 watt Hanovia high pressure mercury arc lamp at room temp for 2 h under a stream of argon. The reaction mixture was evaporated to dryness to leave a foamy residue, which was dissolved in THF (50 ml) and 2-propanol (50 ml) and refluxed for 1 h to decompose the nitroso dimer. The soln was evaporated below 50 °C to leave an oily residue, which was purified by chromatography over Florisil (100 g). Elution with benzene (180 ml), benzene–dichloromethane (5 : 1, 300 ml), and dichloromethane (570 ml) afforded oily materials (884 mg), which were purified as described later. Further elution with dichloromethane (280 ml) and dichloromethane-methanol (4 : 1, 240 ml) gave 15-oxime (**18**, 2.22 g), amorphous, resisting crystallization: $[\alpha]_D$ +12.1°; MS, *m/e* 410 (M$^+$−OH), 395, 382, 367, 350 (base), 335, 322, and 308; IR (CHCl$_3$), ν_{max} 3235, 3135, 1739, 1250, 1048, and 1032 cm^{-1}; NMR, δ 0.98 and 0.99 (total 6H, each d, *J*=7 and 6 Hz, 14- and 13-C$\underline{\text{H}}_3$ or *vice versa*), 2.00 and 2.07 (3H and 6H, each s, 3OCOC$\underline{\text{H}}_3$), 4.04 (3H, m, 3$\underline{\text{H}}$ at C$_6$ and C$_{12}$), 4.77 (1H, do d, *J*=8.5 and 7.5 Hz, $\underline{\text{H}}$ at C$_3$), 4.85 (1H, br m, W_H=10 Hz, $\underline{\text{H}}$ at C$_2$), 6.56 (1H, d, *J*=9 Hz, O$\underline{\text{H}}$), 7.18 (1H, s, C$\underline{\text{H}}$=N), and 10.45 (1H, s, N–O$\underline{\text{H}}$).

The oily material (884 mg) described above was separated by rechromatography over silica gel (30 g). Elution with ether–benzene (1 : 5, 50 ml) afforded a crystalline substance (186 mg), which was recrystallized from isopropyl ether to give **20** (70 mg), mp 109—109.5 °C, identical with an authentic sample. Further elution with ether-benzene (1 : 2, 75 ml) afforded an oily substance (131 mg), which crystallized on standing, giving 6,15-oxolane (**19**, 80 mg), mp 72.5—74 °C, on trituration with hexane–isopropyl ether. Recrystallization twice from the same solvent mixture yielded an analytical sample: mp 100—101 °C and $[\alpha]_D$ −8.9°; MS, *m/e* 396 (M$^+$), 336, 294 (base), 277, 276, 251, 234, and 216; IR, ν_{max} 1741, 1244, 1230, and 1032 cm^{-1}; IR (liquid), ν_{max} 1743, 1478, 1240, 1229, 1035, and 862 cm^{-1}; NMR, δ 0.96 (6H, d, *J*=6.5 Hz, 14- and 13-C$\underline{\text{H}}_3$), 2.00, 2.05, and 2.07 (each 3H, s, 3OCOC$\underline{\text{H}}_3$), 3.62 and 3.86 (each 1H, ABq, *J*=8 Hz, 2$\underline{\text{H}}$ at C$_{15}$), 4.04 (2H, d, *J*=5.5 Hz, 2$\underline{\text{H}}$ at C$_{12}$), 4.18 (1H, s, $\underline{\text{H}}$ at C$_6$), 4.76 (1H, t, *J*=10 Hz, $\underline{\text{H}}$ at C$_3$), and 5.01 (1H, do t, *J*=5, 10, and 10 Hz, $\underline{\text{H}}$ at C$_2$). Found: C, 63.65; H, 8.24%. Calcd for C$_{21}$H$_{32}$O$_7$: C, 63.61; H, 8.14%. Further elution with ether–benzene 1 : 2, 175 ml) gave 15-oxime (**18**, 125 mg), amorphous, identical with the afore-mentioned sample.

*Hypoiodite Reaction of **15a** to **19**.* A suspection of lead tetraacetate (7.1 g) and calcium carbonate (4 g), precipitated and dried, in benzene (100 ml) was stirred under reflux for 40 min. To the mixture were added iodine (1.95 g), freshly sublimed, and **15a** (1.22 g) in benzene (50 ml), and the whole mixture was refluxed for 1.3 h and then stirred at room temp for 1.5 h under nitrogen. This was filtered through celite to remove an insoluble substance and the filtrate was washed with 30% aq sodium thiosulfate (200 ml) and water, dried, and evaporated to leave an oily residue (1.43 g), showing a single spot on TLC, which was purified by chromatography over silica gel (30 g). Eluates with benzene-ether (5 : 1) afforded an oily substance (893 mg), which crystallized on standing. This was recrystallized from hexane-isopropyl ether to give 6,15-oxolane (**19**), mp 99—100 °C, identical with an authentic sample.

*(11S)-2α,3β,12-Triacetoxy-4β,5α-eudesman-6β,15-olide (**21**).* Compound **18** (100 mg) was stirred with the Jones reagent (0.25 ml) in acetone (2 ml) at 0 °C for 30 min. The reaction mixture was worked up as usual to leave an oily residue (112 mg), showing an almost single spot on TLC, which was purified by preparative TLC over silica gel (Wakogel B-5) with ether–benzene (1 : 2). Elution with methanol gave a crystalline substance (54 mg), which was recrystallized from acetone-isopropyl ether to yield **21** (36 mg), mp 125—126 °C. This was recrystallized from the same solvent

mixture for analysis: mp 126—127 °C and $[\alpha]_D$ −1.5°; MS, *m/e* 382 (M^+-CO), 350, 322, 308, 290, 280, 262, 248, 230, 202, and 186; IR, ν_{max} 1780, 1745, 1242, 1229, 1116, 1047, and 1028 cm^{-1}; NMR, δ 0.96 and 1.00 (each 3H, d, J=6.5 and 5.5 Hz, 14- and 13-CH_3 or *vice versa*), 1.97, 2.03, and 2.04 (each 3H, s, $3OCOCH_3$), 2.42 (1H, do d, J=13 and 5 Hz, H at C_1), 3.92 and 4.10 (each 1H, do ABq, J=5 and 11 Hz, 2H at C_{12}), 4.49 (1H, br s, W_H= 2.5 Hz, H at C_6), 4.68 (1H, t, J=10 Hz, H at C_3), and 4.74 (1H, do t, J=5, 10, and 10 Hz, H at C_2). Found: C, 60.89; H, 7.38%. Calcd for $C_{21}H_{30}O_8$: C, 61.45; H, 7.37%.

*(11S)-4β,5α-Eudesm-5-ene-2α,3β,12-triol Triacetate (**26**).* Compound **15a** (855 mg) was treated with methanesulfonyl chloride (MsCl, 1.5 ml) in Py (4 ml) at room temp for 44 h. The mixture was poured into ice–water and extracted with chloroform. The chloroform soln, after being worked up as usual, left an oily residue (928 mg), showing a single spot on TLC. This was purified by column chromatography over silica gel (50 g) with benzene–ether (5 : 1) to yield **26** (801 mg), bp 121—123 °C (bath temp) (5 Torr) and $[\alpha]_D$ −35.1°; MS, *m/e* 380 (M^+), 320, 260, and 200; IR (liquid), ν_{max} 1743, 1651, 1240, and 1041 cm^{-1}; NMR, δ 0.86 and 1.02 (each 3H, d, J=7 and 6.5 Hz, 13- and 14-CH_3), 1.18 (3H, s, 15-CH_3), 2.00 and 2.06 (3H and 6H, each s, $3OCOCH_3$), 3.98 (2H, br d, J=7 Hz, 2H at C_{12}), 4.60 (1H, do d, J=11 and 9.5 Hz, H at C_3), 5.16 (1H, do do d, J=12, 9.5, and 5 Hz, H at C_2), and 5.27 (1H, br s, W_H= 5 Hz, H at C_6). Found: C, 65.75; H, 8.50%. Calcd for $C_{21}H_{32}O_6$: C, 66.30; H, 8.48%.

*Dehydration of (11S)-15-Hydroxyimino-4β,5α-eudesmane-2α,3β,6β,12-tetraol 2,3,12-Triacetate (**18**).* (*i*) A soln of **18** (1.24 g) in Py (20 ml) was stirred with phosphoryl chloride (8.5 ml) at room temp for 70 h, cooled, poured into ice-water (1 l) and extracted with chloroform. The chloroform soln, after being worked up as usual, left a foamy residue (1.13 g), which was separated by chromatography over silica gel (36 g). Eluates with benzene–ether (2 : 1) afforded an oily substance, which was crystallized on trituration with isopropyl ether and collected to give Δ^5-10-nitrile (**23**, 44 mg), mp 101—103 °C. Recrystallization from the same solvent afforded an analytical sample: mp 106—107 °C and $[\alpha]_D$ −90.3°; MS, *m/e* 331 ($M^+-C_2H_4O_2$), 289, 271, 262, 244, 229, 211 (base), 202, and 184; IR, ν_{max} 2225, 1745, 1252, 1227, 1052, and 1038 cm^{-1}; NMR, δ 0.87 and 1.09 (each 3H, d, J=7 and 6.5 Hz, 14- and 13-CH_3 or *vice versa*), 2.01, 2.06, and 2.08 (each 3H, s, $3OCOCH_3$), 3.98 (2H, br d, J=6.5 Hz, 2H at C_{12}), 4.56 (1H, do d, J=11 and 9.5 Hz, H at C_3), 5.21 (1H, do do d, J=11.5, 9.5, and 4.5 Hz, H at C_2), and 5.58 (1H, br s, W_H=5 Hz, H at C_6). Found: C, 64.30; H, 7.51; N, 3.53%. Calcd for $C_{21}H_{29}O_6N$: C, 64.43; H, 7.47; N, 3.58%.

Eluates with benzene–ether (1 : 1) afforded a crystalline substance (751 mg), which on recrystallization from acetone–isopropyl ether gave 6β-hydroxy-10-nitrile (**22**, 606 mg), mp 174.4—175.5 °C. This was recrystallized from the same solvent mixture for analysis: mp 175—176 °C and $[\alpha]_D$ +21.5°; MS, *m/e* 409 (M^+), 366, 350 (base), 308, and 248; IR, ν_{max} 3530, 2230, 1739, 1728 (shoulder), 1240, 1050, and 1030 cm^{-1}; NMR, δ 0.98 and 1.02 (each 3H, d, J= 6.5 Hz, 14- and 13-CH_3 or *vice versa*), 1.79 (1H, s, OH), 1.98, 2.04, and 2.06 (each 3H, s, $3OCOCH_3$), 4.00 (3H, br m, 3H at C_6 and C_{12}), 4.69 (1H, do d, J=10.5 and 9.5 Hz, H at C_3), and 5.11 (1H, do do d, J=11.5, 9.5, and 5 Hz, H at C_2). Found: C, 61.62; H, 7.65; N, 3.46%. Calcd for $C_{21}H_{31}O_7N$: C, 61.59; H, 7.63; N, 3.42%.

(*ii*) Compound **18** (566 mg) was treated with Ac_2O (6 ml) and Py (10 ml) at room temp for 26 h. The mixture was worked up as usual to leave a foamy residue, showing a single spot on TLC, which was purified by chromatography over silica gel (25 g). Elution with ether–benzene (1 : 2) afforded a crystalline substance (484 mg), which on recrystallization from acetone-isopropyl ether yielded 6β-hydroxy-10-nitrile (**22**, 331 mg), mp 171.5—173.5 °C, identical with an authentic sample.

(*iii*) A soln of **18** (308 mg) in Py (2 ml) was treated with MsCl (0.5 ml) at room temp for 47 h. The mixture was worked up as usual to leave an amorphous residue (321 mg), which was dissolved in collidine (6 ml) and refluxed in a silicon-bath kept at 190 °C for 3 h. The mixture was cooled and diluted with chloroform. The whole soln gave an amorphous substance after the usual work-up, showing at least seven spots on TLC, which were purified by chromatography on silica gel (15 g). Elution with benzene–ether (2 : 1, 50 ml) afforded Δ^5-10-nitrile (**23**, 42 mg), mp 104—105 °C, on recrystallization from isopropyl ether. The other fractions were not examined further.

*Dehydration of (11S)-2α,3β,12-Triacetoxy-6β-hyrdoxy-15-nor-4β,5α-eudesmane-10β-carbonitrile (**22**).* A soln of **22** (4.24 g) in Py (20 ml) was stirred with MsCl (6.5 ml) at room temp for 47 h. The mixture was worked up as usual to leave an amorphous residue (5.00 g), which was refluxed in collidine (60 ml) for 3 h. The mixture was worked up in the same manner as that for **18** to give an oily residue (4.90 g), which was separated by chromatography over silica gel (100 g). Eluates with benzene–ether (2 : 1, 240 ml) afforded an oily substance (4.18 g), which was crystallized and recrystallized from isopropyl ether to give Δ^5-10-nitrile (**23**, 2.19 g), mp 106—107 °C, identical with an authentic sample. The mother liquors, obtained on crystallization and recrystallization, were concentrated to dryness and rechromatographed over silica gel (80 g). Eluates with benzene–ether (5 : 1, 180 ml) gave a crystalline substance (0.97 g), which on recrystallization from isopropyl ether yielded **23** (0.84 g), mp 106—106.5 °C. Further elution with benzene–ether (5 : 1, 240 ml) afforded an oily substance (0.38 g), which was crystallized and recrystallized from isopropyl ether to give Δ^6-10-nitrile (**24**), mp 80.5—82 °C. Recrystallization from the solvent gave an analytical sample: mp 81—82 °C and $[\alpha]_D$ −18°; MS, *m/e* 391 (M^+), 349, 331, 289, 271, 262, 244, 229, 211 (base), 202, 196, and 184; IR, ν_{max} 2230, 1742, 1242, 1224, 1051, and 1033 cm^{-1}; NMR, δ 1.04 and 1.09 (each 3H, d, J=5.5 and 7 Hz, 14- and 13-CH_3), 2.02, 2.05, and 2.10 (each 3H, s, $3OCOCH_3$), 3.92 and 4.16 (each 1H, do d, J=11, 6.5 and 11, 7.5 Hz, 2H at C_{12}), 4.78 (1H, t, J=9.5 Hz, H at C_3), 5.24 (1H, do do d, J=11.5, 9.5, and 5 Hz, H at C_2), and 5.51 (1H, br s, W_H= 5 Hz, H at C_6). Found: C, 64.31; H, 7.49; N, 3.47%. Calcd for $C_{21}H_{29}O_6N$: C, 64.43; H, 7.47; N, 3.58%.

*(11S)-2α,3β,12-Trihydroxy-15-nor-4β-eudesm-5-ene-10β-carbonitrile (**23a**) and Its 2,3,12-Trimethoxymethyl Ether (**23b**).* A soln of **23** (2.53 g) in methanol (60 ml) was stirred with 10% potassium hydroxide in methanol (60 ml) at room temp overnight. The mixture was concentrated below 40 °C, diluted with water (100 ml), salted out, and extracted with ethyl acetate (4×250 ml). The ethyl acetate soln was washed with saturated brine (4×50 ml), dried, and evaporated to leave an amorphous substance (**23a**, 1.79 g), showing a single spot on TLC; NMR, δ 0.87 and 1.23 (each 3H, d, J=7 Hz, 14- and 13-CH_3), 2.94 (1H, do d, J=10 and 8 Hz, H at C_3), 3.58 (2H, br d, J=6.5 Hz, 2H at C_{12}), 3.72 (1H, br m, H at C_2), and 5.58 (1H, br s, W_H=4 Hz, H at C_6). Compound **23a** (32 mg) was treated with Ac_2O (0.5 ml) in Py (0.5 ml) at room temp overnight to give **23** (38 mg), mp 102—104 °C, identical with the starting triacetate.

To a stirred soln of **23a** (269 mg) in dry chloroform (10 ml) and dimethoxymethane (10 ml), cooled at 0 °C, was added in portions phosphorus pentaoxide (5.7 g) during a period of 20 min.[20] The mixture was poured into cold 10 % aq sodium carbonate (400 ml) and extracted with chloroform. The chloroform extracts were washed with water, dried, and evaporated to leave an oily residue (362 mg), showing two spots on TLC, which was separated into two fractions by chromatography over alumina (Merck, standard, activity II-III, 40 g). Elution with benzene (460 ml) afforded an oily substance (55 mg), which would be the 2,3-methylenedioxy-12-methoxymethyl ether but was not further exmined: IR ($CHCl_3$), ν_{max} 2255, 1141, 1114, 1093 (shoulder), 1040, and 917 cm^{-1}; NMR, δ 0.87 and 1.20 (each 3H, d, J=7 and 6.5 Hz, 14- and 13-C$\underline{H}_3$), 2.94 (1H, do d, J=10 and 8 Hz, $\underline{H}$ at C$_3$), 3.37 (3H, s, OC$\underline{H}_3$), 3.45 (2H, br d, J=6.5 Hz, 2$\underline{H}$ at C$_{12}$), 3.82 (1H, do do d, J=12, 8, and 4 Hz, $\underline{H}$ at C$_2$), and 5.59 (1H, br s, W_H=6 Hz, $\underline{H}$ at C$_6$).

Eluates with benzene-ether (2 : 1, 400 ml) gave **23b** (235 mg), oil; MS, *m/e* 304 (M^+-3OCH_3); IR ($CHCl_3$), ν_{max} 2255, 1150, 1105, 1039, 1030, and 915 cm^{-1}; NMR, δ 0.87 and 1.23 (each 3H, d, J=7 and 6 Hz, 14- and 13-C$\underline{H}_3$), 3.02 (1H, do d, J=11 and 9 Hz, $\underline{H}$ at C$_3$), 3.38, 3.41, and 3.46 (each 3H, s, 3OC$\underline{H}_3$), 3.42 (2H, br d, J=6 Hz, 2$\underline{H}$ at C$_{12}$), 3.89 (1H, do do d, J=12, 9, and 4 Hz, $\underline{H}$ at C$_2$), 4.81 (6H, br m, 3OC$\underline{H}_2$O), and 5.57 (1H, br s, W_H=4 Hz, $\underline{H}$ at C$_6$).

*(11S)-15-Nor-4β-eudesm-5(10)-ene-2α,3β,12-triol (**27**), Its Triacetate (**27a**), and 2,3-Acetonide (**28**).* (*i*) To a suspension of sodium metal (1 g) in refluxing dry toluene (15 ml) was added dropwise a soln of **23** (125 mg) in dry ethanol (1.5 ml) and dry toluene (1.5 ml) during a period of 2 min. After 2 min, dry ethanol (4 ml) was again added, and the mixture was refluxed for 10 min and cooled. After addition of ethanol to decompose an excess of the sodium, the mixture was concentrated below 50 °C, diluted with water, salted out, and extracted with ethyl acetate. The acetate extracts were worked up as usual to leave **27** (79 mg), showing a single spot on TLC: NMR ($CDCl_3$ at 50 °C), δ 0.94 and 1.14 (each 3H, d, J=7 Hz, 13- and 14-C$\underline{H}_3$), 3.21 (1H, do d, J=9.5 and 8 Hz, $\underline{H}$ at C$_3$), and 3.60 (4H, br m, 3$\underline{H}$ at C$_2$ and C$_{12}$, and O$\underline{H}$). Compound **27** (79 mg), without further purification, was treated with Ac_2O (2 ml) in Py (2 ml) at room temp overnight. The mixture was worked up as usual to give an oily residue (106 mg), which was purified by chromatography over silica gel (5 g). Elution with benzene-ether (5 : 2) yielded **27a** (83 mg) in pure state, oil and $[\alpha]_D$ +1.7°; MS, *m/e* 306 ($M^+-C_2H_4O_2$), 264, 246, 204, 203, 186, 171, 157, 144 (base), and 143; IR (CCl_4), ν_{max} 1748, 1242, 1228, and 1031 cm^{-1}; NMR, δ 0.95 and 1.05 (each 3H, d, J=6.5 and 7 Hz, 13- and 14-C$\underline{H}_3$), 2.03 and 2.08 (3H and 6H, each s, 3OCOC$\underline{H}_3$), 3.91 and 4.11 (each 1H, do d, J=11, 6 and 11, 5.5 Hz, 2$\underline{H}$ at C$_{12}$), and 4.98 (2H, br m, 2$\underline{H}$ at C$_2$ and C$_3$). Found: C, 65.27; H, 8.41%. Calcd for $C_{20}H_{30}O_6$: C, 65.55; H, 8.25%.

(*ii*) To a suspension of sodium metal (16.1 g) in refluxing dry toluene (240 ml) was added dropwise a soln of **23** (1.99 g) in dry ethanol (24 ml) and dry toluene (24 ml) during a period of 7 min. After 5 min, dry ethanol (64 ml) was again added over a period of 8 min, and the whole mixture was stirred under reflux for 10 min. The reaction mixture was worked up in the same manner as described above to yield triol (**27**, 1.20 g), showing a single spot on TLC. A soln of the triol was immediately dissolved in a 1 : 1 mixture of acetone and hexane and passed through silica gel (Wakogel Q-23, 240 g), which had been packed in a column with chloroform and washed successively with methanol, acetone and hexane. Elution with acetone-hexane (1 : 3) afforded crude acetonide (**28**, 1.15 g), which was purified twice by chromatography over alumina (60 g). Eluates with ether-benzene (1 : 2) gave **28** (1.07 g) in pure state, oil and $[\alpha]_D$ −54.7°; MS, *m/e* 280 (M^+), 265, 222, 145, and 131 (base); IR (CCl_4), ν_{max} 3390, 1380, 1371, 1229, 1152, 1089, and 1034 cm^{-1}; NMR, δ 0.94 and 1.14 (each 3H, d, J=6.5 Hz, 13- and 14-C$\underline{H}_3$), 1.46 [6H, s, (C$\underline{H}_3$)$_2$CO], 3.20 (1H, t, J=9.5 Hz, $\underline{H}$ at C$_3$), and 3.57 (3H, br m, 3$\underline{H}$ at C$_2$ and C$_{12}$).

(*iii*) To a soln of rishitin acetonide[2] (**31**, 388 mg), obtained from natural rishitin (**1**), in dry ether (40 ml) was bubbled at room temp excess diborane, generated by dropwise addition of boron trifluoride etherate (1.2 ml) in dry diglyme (10 ml) to a soln of sodium borohydride (450 mg) in dry diglyme (15 ml), with stirring over a period of 25 min. The soln was stirred at room temp for 2 h, while the generator flask of diborane was allowed to stand at room temp for 1 h and then heated at 70—80 °C for 1 h. After removal of the generator and subsequent careful addition of water to decompose an excess of the diborane, the whole mixture was treated with 30% aq hydrogen peroxide (2 ml) and 3 M aq sodium hydroxide (2 ml) at 30—50 °C for 1 h with stirring. The mixture was cooled and extracted with ether repeatedly. The ether extracts were worked up as usual to leave an oily residue (500 mg), which was, without further purification, refluxed with 10% aq phosphoric acid (5 ml) in ethanol (30 ml) for 1 h. The reaction mixture was concentrated and extracted with ethyl acetate. The acetate extracts were worked up as usual to leave an oily residue (320 mg), showing two spots on TLC. A part (230 mg) of the residue was treated with Ac_2O (3 ml) in Py (6 ml) at room temp for 8 h to give oily materials, showing two spots on TLC, which were separated into two fractions by chromatography over silica gel (15 g) with benzene-ether (5 : 1). The less polar fraction (140 mg) was found to be identical with the diacetylrishitin[2] by comparison with an authentic sample. The more polar fraction (83 mg), oil, was identical with the triacetate (**27a**), derived from **23**, described above (TLC, Mass, IR, and NMR).

*(11S)-15-Nor-4β-eudesm-5(10)-ene-2α,3β,12-triol 2,3-Acetonide 12-Methyl Ether (**30**) and Rishitin Acetonide (**31**).* (*i*) Compound **28** (1.00 g) was treated with *p*-toluenesulfonyl chloride (1.03 g) in Py (10 ml) at room temp for 20 h. The soln was poured into ice-water (400 ml), salted out, and extracted with ether (4×200 ml). The ether extracts were worked up as usual to leave 12-tosylate (**28a**, 1.52 g), oil and $[\alpha]_D$ −5.8°; IR (CCl_4), ν_{max} 1600, 1377, 1371, 1229, 1189, 1180, 1100, 1087, 1044, 1032, 970, 842, and 815 cm^{-1}; NMR, δ 0.91 and 1.06 (each 3H, d, J=6 and 6.5 Hz, 13- and 14-C$\underline{H}_3$), 1.45 [6H, s, (C$\underline{H}_3$)$_2$CO], 2.44 (3H, s, C$\underline{H}_3$C$_6$H$_4$SO$_2$), 3.18 (1H, t, J=9 Hz, $\underline{H}$ at C$_3$), 3.51 (1H, m, $\underline{H}$ at C$_2$), 3.89 and 3.97 (each 1H, do ABq, J=5 and 9.5 Hz, 2$\underline{H}$ at C$_{12}$), 7.30 and 7.75 (each 2H, d, J=8 Hz, CH$_3$C$_6\underline{H}_4$SO$_2$).

(*ii*) A soln of 12-tosylate (**28a**, 1.49 g) in acetone (80 ml) was stirred with sodium iodide (8 g) under reflux for 22 h. The mixture was evaporated and extracted with ether (100 ml). The ether extracts were washed with 5% aq sodium thiosulfate (yellow color disappeared) and saturated brine, dried, and evaporated to leave 12-iodide (**29**, 1.26 g), showing a single spot, oil, which crystallized on cooling at −15 °C, and had mp 58—61 °C and $[\alpha]_D$ −28.5°; MS, *m/e* 390 (M^+), 375, 332, 315, 263, 262, 247, 205, 187, 163, 145, and 131; IR (CCl_4), ν_{max} 1380, 1371, 1230, and 1098 cm^{-1}; NMR, δ 0.99 and 1.15 (each 3H, d, J=6 and 6.5 Hz, 13- and 14-C$\underline{H}_3$), 1.45 [6H, s, (C$\underline{H}_3$)$_2$CO], 3.25 (3H, br m, 3$\underline{H}$ at C$_3$ and C$_{12}$), and 3.59 (1H, do t, J=7, 9, and 9 Hz, $\underline{H}$ at C$_2$).

(*iii*) 12-Iodide (**29**, 1.21 g) was refluxed with 5% potassium hydroxide in methanol (100 ml) for 2.5 h under nitrogen.

The mixture was worked up as usual to leave an oily residue (0.82 g), showing two spots on TLC, which was separated into two fractions by chromatography over alumina (60 g). Elution with hexane-benzene (1 : 1, 50 ml) afforded **31** (0.57 g), oil and $[\alpha]_D$ −71.7° (EtOH); MS, *m/e* 262 (M^+), 247, 205, 204, 203, 187, and 131 (base); IR (liquid), ν_{max} 3080, 1643, 1378, 1370, 1229, 1100, 1083, 1042, and 888 cm^{-1}; NMR, δ 1.14 (3H, d, J=6.5 Hz, 14-C$\underline{\text{H}}_3$), 1.44 [6H, s, $(\text{C}\underline{\text{H}}_3)_2$CO], 1.72 (3H, s, 13-C$\underline{\text{H}}_3$), 3.20 (1H, t, J=9 Hz, $\underline{\text{H}}$ at C_3), 3.58 (1H, do t, J=7, 9, and 9 Hz, $\underline{\text{H}}$ at C_2), 4.63 and 4.74 (each 1H, br s, W_H=4 Hz, 2$\underline{\text{H}}$ at C_{12}). This was identical with an authentic sample derived from natural rishitin. Further elution with hexane-benzene (1 : 1, 100 ml) gave **30** (0.13 g), oil and $[\alpha]_D$ −43.1°; MS, *m/e* 294 (M^+), 279, 236, and 131 (base); IR (liquid), ν_{max} 1378, 1371, 1105, and 1088 cm^{-1}; NMR, δ 0.92 and 1.14 (each 3H, d, J=6 and 6.5 Hz, 13- and 14-C$\underline{\text{H}}_3$), 1.45 [6H, s, $(\text{C}\underline{\text{H}}_3)_2$CO], 3.32 (3H, s, OC$\underline{\text{H}}_3$), and 3.41 (4H, br m, 4$\underline{\text{H}}$ at C_2, C_3 and C_{12}).

Rishitin (1) and Its Diacetate (1a). A soln of **31** (96 mg) in ethanol (24 ml) was stirred with 10% aq phosphoric acid (1.2 ml) under reflux for 1 h. After being worked up as usual, the soln gave an oily residue (84 mg), which was purified by chromatography over silica gel (9 g). Eluates with ether afforded an oily substance (**1**, 63 mg), which was further purified by distillation at 100—115 °C (bath temp) under reduced pressure (1 Torr) to yield crystalline rishitin (**1**), mp 58—60 °C and $[\alpha]_D$ −30.4° (EtOH) (lit,[2] mp 65—67 °C and $[\alpha]_D$ −35.1°); MS, *m/e* 222 (M^+), 204, and 189; IR (CCl_4), ν_{max} 3370, 3080, 1642, 1075, 1039, 1017, and 890 cm^{-1}; NMR, δ 1.14 (3H, d, J=6.5 Hz, 14-C$\underline{\text{H}}_3$), 1.75 (3H, s, 13-C$\underline{\text{H}}_3$), 3.18 (1H, t, J=9 Hz, $\underline{\text{H}}$ at C_3), 3.63 (1H, br do d, J=9 and 7 Hz, $\underline{\text{H}}$ at C_2), 4.64 and 4.74 (each 1H, br s, W_H=4 Hz, 2$\underline{\text{H}}$ at C_{12}). The synthetic rishitin (33 mg) was treated with Ac_2O (1 ml) and Py (1 ml) at room temp overnight. The mixture, after being worked up as usual, gave an oily substance, which was crystallized and recrystallized from hexane to give the diacetate (**1a**, 15 mg), mp 66—68 °C and $[\alpha]_D$ −14.1° (EtOH) (lit,[2] mp 70—71 °C and $[\alpha]_D$ −14.1°); Mass, *m/e* 246 ($M^+-C_2H_4O_2$), 204, 186, and 171; IR (CCl_4), ν_{max} 3070, 1749, 1642, 1242, 1225, 1030, and 890 cm^{-1}; NMR, δ 1.06 (3H, d, J=6.5 Hz, 14-C$\underline{\text{H}}_3$), 1.75 (3H, s, 13-C$\underline{\text{H}}_3$), 2.03 and 2.08 (each 3H, 2OCOC$\underline{\text{H}}_3$), 4.64 and 4.74 (each 1H, br s, W_H=4 Hz, 2$\underline{\text{H}}$ at C_{12}), and 4.98 (2H, br m, 2$\underline{\text{H}}$ at C_2 and C_3). These synthetic rishitin and diacetylrishitin were identical with the corresponding authentic specimens of natural rishitin (**1**) and its diacetate (**1a**) in all respects, respectively.

References

1) Part III of "Synthetic Studies of Rishitin and Related Compounds;" Part II, Ref 3.

2) T. Masamune, A. Murai, M. Takasugi, A. Matsunaga, N. Katsui, N. Sato, and K. Tomiyama, *Bull. Chem. Soc. Jpn.*, **50**, 1201 (1977).

3) A. Murai, K. Nishizakura, N. Katsui, and T. Masamune, *Tetrahedron Lett.*, **1975**, 4399.

4) For the total synthesis of (−)-α-santonin, *cf.*, Y. Abe, T. Harukawa, H. Ishikawa, T. Miki, M. Sumi, and T. Toga, *J. Am. Chem. Soc.*, **78**, 1422 (1956).

5) S. M. Sharif, S. Nozoe, K. Tsuda, and N. Ikekawa, *J. Org. Chem.*, **28**, 793 (1963).

6) In this paper we define eudesmane as 4,10β-dimethyl-7β-isopropyldecahydronaphthalene (**6**) and use the same nomenclature as that for steroids; *J. Org. Chem.*, **34**, 1517 (1969).

7) a) E. Piers and K. F. Cheng, *Can. J. Chem.*, **46**, 377 (1968); H. Ishikawa, *J. Pharm. Soc. Jpn.*, **76**, 504 (1956). b) W. Cocker, H. Gobinsingh, T. B. H. McMurry, and M. A. Nisbet, *J. Chem. Soc.*, **1962**, 1432.

8) *Cf.*, K. Kato, Y. Hirata, and S. Yamamura, *Tetrahedron*, **27**, 5987 (1971).

9) For the mass spectra of santonin derivatives, *cf.*, N. Wasada, T. Tsuchiya, E. Yoshii, and E. Watanabe, *Tetrahedron*, **23**, 4623 (1967).

10) *Cf.*, K. L. Williams and W. S. Johnson, *J. Org. Chem.*, **26**, 4563 (1961).

11) K. L. Williams and W. S. Johnson, *J. Am. Chem. Soc.*, **83**, 4623 (1961).

12) a) H. B. Henbest, D. N. Jones, and G. P. Slater, *J. Chem. Soc.*, **1961**, 4472; b) J. D. Cocker, H. B. Henbest, G. H. Phillipps, G. P. Slater, and D. A. Thomas, *J. Chem. Soc.*, **1965**, 6; c) H. B. Henbest, D. N. Jones, and G. P. Slater, *J. Chem. Soc., C*, **1967**, 756.

13) *Cf.*, D. H. R. Barton, J. M. Beaton, L. E. Geller, and M. M. Pechet, *J. Am. Chem. Soc.*, **83**, 4076 (1961).

14) *Cf.*, J. F. Bagli, P. F. Marand, and R. Gaudry, *J. Org. Chem.*, **28**, 1207 (1965).

15) *Cf.*, R. M. Moriarity and T. D. J. D'Silva, *Tetrahedron*, **21**, 547 (1965).

16) a) N. S. Bhacca and D. H. Williams, "Application of NMR Spectroscopy in Organic Chemistry," Holden-Day, Inc., San Francisco (1964), p. 13; b) K. Tori and T. Komeno, *Terahedron*, **21**, 309 (1965); K. Tori and K. Ando, *Ann. Rept Shionogi Res. Lab.*, **14**, 136 (1964).

17) T. Masamune, A. Murai, K. Nishizakura, T. Orito, S. Numata, and H. Sasamori, *Bull. Chem. Soc. Jpn.*, **49**, 1622 (1976), and refs cited therein.

18) *Cf.*, R. Gardi, C. Pedrali, and A. Ercoli, *Gazz. Chim. Ital.*, **93**, 525 (1963).

19) M. Nakazaki and K. Naemura, *Bull. Chem. Soc. Jpn.*, **37**, 1842 (1964).

20) *Cf.*, K. Fuji, S. Nakano, and E. Fujita, *Synthesis*, **1975**, 276.