Attempted Duplication of the Methyl Shift in Eremophilane Biosynthesis

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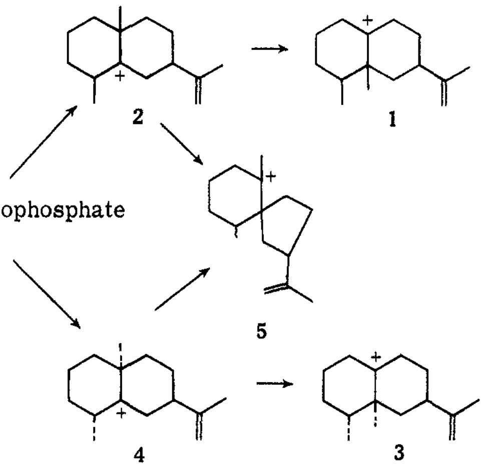
In an attempt to duplicate the proposed biosynthetic conversion of a 10-epieudesmane to a nootkatane derivative, 10-epieudesm-3-en-2-on-5β-ol (**10**) was prepared from 10-epieudesm-4-en-3-one by a four-step sequence patterned on the synthesis of α-agarofuran. Dehydration of **10** with phosphoryl chloride–pyridine gave as the only product the linear dienone, 10-epieudesma-3,5-dien-2-one (**15**). Hydrogenation of **10** gave 10-epieudesman-3-on-5β-ol (**16**), which on dehydration with boron trifluoride etherate–acetic acid gave 10-epieudesm-5-en-2-one (**20**), 10-epieudesm-3-en-2-one (**19**), and 5-epi-10-epieudesm-3-en-2-one (**18**). Dehydration of **16** with aqueous sulfuric acid gave only **18** and **19**. The factors governing the course of these reactions and the CD curves of compounds **10**, **16**, **18**, **19**, and **20** are discussed.

It was suggested a number of years ago by Robinson that the eremophilane (**1**) group of sesquiterpenes could be derived biosynthetically from a eudesmane (**2**) precursor.[1] In recent years this proposal has been modified slightly to give the currently accepted scheme for the biosynthesis of these sesquiterpenes and the closely related nootkatanes (**3** from a 10-epieudesmane **4**) and vetispirans (**5**).[2]

Although the conversions outlined in Scheme I can be represented as simple carbonium ion rearrangements, with one exception they have yet to be duplicated in the laboratory. The rearrangements of several epoxides of gross structure **6** have been investigated,[3] while the apparent methyl migration encountered in the rearrangement of **7**[4] has been shown to proceed *via* spiro intermediates.[5] The only chemical analogy to the biochemical interconversions described in Scheme I is the rearrangement on dehydration of β-rotunol (**8**) to a spirovetivane derivative **9**.[6]

SCHEME I



In an attempt to duplicate the biosynthetic methyl shift it was felt that the conversion of a 10-epieudesmane to a nootkatane derivative (**4** → **3**) would be more favorable than the conversion of **2** → **1**, since it would result in a net conversion of an axial to equatorial isopropyl group. Also, by analogy with the β-rotunol rearrangement, it seemed desirable to design a model which would afford a conjugated system on rearrangement. The simplest compound which fulfills these requirements is the hydroxy enone **10**, which could afford a dehydronootkatone derivative **11** on dehydration and rearrangement.

The synthesis of **10** as outlined in Scheme II followed the general procedure utilized by Büchi for the synthesis of α-agarofuran.[7] The only significant modification of Büchi's method was the use of the Dauben–Shapiro method[8] for the preparation of homoannular diene **12**. As expected, photosensitized oxidation of **12** gave a dienone **14** as well as the desired peroxide **13**. The stereochemistry of **13**, and the derived hydroxy ketone (**10**), was assigned by analogy with the agarofuran series[7] and confirmed by the CD curve of **10**, which showed a positive Cotton effect for the n → π* transition ($[\theta]_{363}$ + 799) which is of the same magnitude, but of opposite sign, to that of α-rotunol (**8**, with the hydroxyl α) and a 5α-androst-3-en-2-one derivative.[6]

Treatmentof **10** with phosphoryl chloride–pyridine under a variety of conditions gave a single product, although in mediocre yield. The spectral data for this compound (see Experimental Section) were not those predicted for the rearranged dienone **11**, but indicated that dehydration to a linear dienone (**15**), a reaction which has some precedent in the steroid series,[9] had occurred. After standing at room temperature for a number of hours, the original aqueous phase from the isolation of the products of this reaction gave significant quantities of recovered **10**. Apparently, **10** under the conditions of the reaction is converted to a phosphoric acid ester, which is soluble in the mildly basic aqueous pyridine solution, and slowly hydrolyzes to give recovered **10**.

In order to attempt to avert the formation of a simple conjugated system, **10** was reduced catalytically to give a single, saturated hydroxy ketone **16**. The stereochemistry assigned to **16** is based on the nmr spectrum,

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[1] R. Robinson in A. R. Penfold and J. L. Simonsen, *J. Chem. Soc.*, 87 (1939).

[2] (a) W. Parker, J. S. Roberts, and R. Ramage, *Quart. Rev., Chem. Soc.*, 331 (1971); (b) N. H. Andersen, M. S. Falcone, and D. D. Syrdal, *Tetrahedron Lett.*, 1759 (1970).

[3] (a) G. Mehtu, G. L. Chetty, U. R. Nayak, and S. Dev, *Tetrahedron*, **24**, 3775 (1967); (b) H. Hikino, T. Kohana, and T. Takemoto, *ibid.*, **25**, 1037 (1968).

[4] C. H. Heathcock and T. R. Kelly, *ibid.*, **24**, 3753 (1968).

[5] D. T. Dunham and R. G. Lawton, *J. Amer. Chem. Soc.*, **93**, 2075 (1971). These authors have proposed a mechanistically plausible alternative to Scheme I, which, however, suffers from a severe phytochemical flaw in that it predicts the existence of two new groups of sesquiterpenes, and is in addition based on the incorrect assumption that 10-epieudesmanes are not encountered in nature.

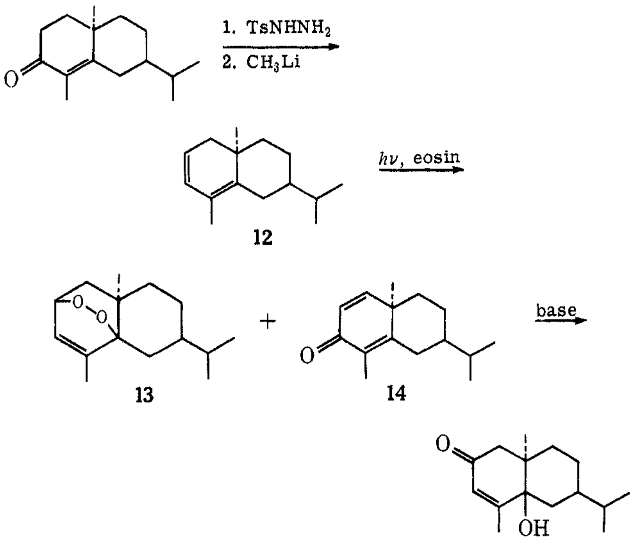
[6] H. Hikino, K. Aota, D. Kuwano, and T. Takemoto, *Tetrahedron Lett.*, 2741 (1969); *Tetrahedron*, **27**, 4831 (1971).

[7] H. C. Barrett and G. Büchi, *J. Amer. Chem. Soc.*, **89**, 5665 (1967). More recently this route has been used by J. A. Marshall, R. A. Ruden, L. K. Hirsch, and M. Phillipe, *Tetrahedron Lett.*, 3795 (1971), for the synthesis of a number of compounds similar to **10**.

[8] W. G. Dauben, M. E. Lorber, N. D. Vietmeyer, R. H. Shapiro, J. H. Duncan, and K. Tomer, *J. Amer. Chem. Soc.*, **90**, 4762 (1968).

[9] R. J. Conca and W. Bergman, *J. Org. Chem.*, **18**, 1104 (1953).

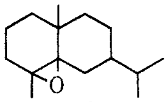
Scheme II



12

13 14

10



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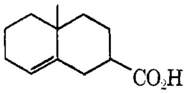

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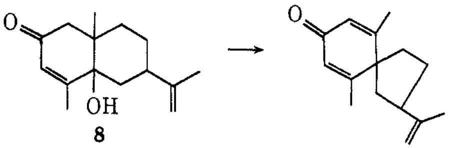

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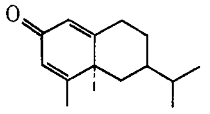

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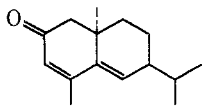

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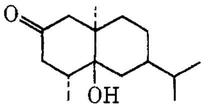
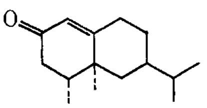
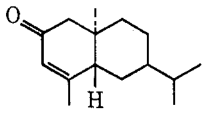


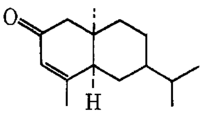
16



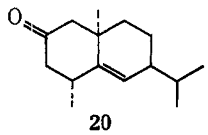
17



18



19



20

which shows a doublet (J = 7 Hz) with the coupling constant indicative of an axial methyl group.[10] Also, the chemical shift of the secondary methyl is nearly the same as that of the angular methyl in both benzene-d_6 and deuteriochloroform, indicating that both methyl groups have a similar spatial relationship to the ketone carbonyl. The ORD and CD curves of **16** show the expected negative Cotton effect curve; however, rather than the usual smooth curve obtained for ketones of this type,[11] a curve with two inflections and an amplitude (ORD) of −63 is obtained. This is almost the same amplitude as that of several model compounds, which however lack the secondary methyl group at C-4.[11] This methyl group should make a contribution of +20 to +25[12] to the amplitude of the Cotton effect of **16**, giving a predicted amplitude of about −40 to −50 for **16** assuming a normal, undistorted, all-chair conformation. On the basis of the ORD data, it seems probable that the ring containing the carbonyl group is either considerably flattened, or in a twist conformation, caused by the interaction of the axial secondary methyl group, with the angular methyl.

Reaction of **16** with phosphoryl chloride–pyridine gave no dehydration product, but only material soluble in aqueous pyridine which afforded starting hydroxy ketone on standing in solution. Treatment with aqueous sulfuric acid gave a mixture of two ketones, neither of which was dihydronootkatone (**17**).[13] By varying the reaction time it was found that one ketone could be obtained as the principal reaction product (Table I) and that this compound was probably not that initially formed. Separation and characterization indicated that the products were α,β-unsaturated ketones, and were both isomeric with dihydronootkatone. In the nmr each ketone showed a vinyl proton as a broadened singlet, a vinyl methyl group, an angular methyl, and an isopropyl group. The mass spectra of these compounds were very similar to that of dihydronootkatone (see Experimental Section), and on the basis of these data it was apparent that these compounds were the stereoisomeric eudesmenones, **18** and **19**. The ketone of shorter retention time, which is the more stable isomer, must be the cis isomer (**19**), which can exist in a nonsteroid conformation with an equatorial isopropyl group. The trans isomer, **18**, must be formed initially, *via* a hydride shift from C-4, and is then isomerized to **19** on prolonged treatment with acid. Further evidence for these structural assignments was obtained when it was found that treatment of **18** with acid or base gave predominantly **19**, and the CD curves of **18** and **19** provided additional evidence for the assigned stereochemistry. The CD curve of trans ketone **18** showed a positive Cotton effect for the n → π^* transition ($[\theta]_{356}$ +146) which is opposite in sign to that of α-rotunol and a 5α-androst-3-en-2-one derivative.[6] The cis isomer also exhibits a positive Cotton effect curve ($[\theta]_{353}$ +440), which is that predicted by the inverse octant rule[14] for a ketone of structure **19**, having a nonsteroid conformation.

In an effort to probe the course of this reaction, and also to effect the desired methyl migration, hydroxy ketone **16** was treated with boron trifluoride etherate in acetic acid under a variety of conditions. Prolonged treatment at room temperature gave essentially the

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[10] (a) F. Johnson, N. A. Starkowsky, and W. D. Gurowitz, *J. Amer. Chem. Soc.*, **87**, 3492 (1965). (b) The nmr spectrum of **16** is quite complex in the methyl region, and, in order to assign the position of the signals, the spectrum was run at both 60 and 90 MHz. We would like to thank Dr. G. B. Savitsky of this department for the 90-MHz spectra.

[11] (a) C. Djerassi and D. Marshall, *Tetrahedron*, **1**, 238 (1957); (b) W. Klyne, *ibid.*, **13**, 29 (1961).

[12] W. Klyne in G. Snatzke, "Optical Rotatory Dispersion and Circular Dichroism in Organic Chemistry," Heyden and Son, London, 1967, pp 139–152.

[13] Dihydronootkatone was prepared from (±)-nootkatone by hydrogenation using a homogeneous catalyst (see Experimental Section).

[14] G. Snatzke in G. Snatzke, "Optical Rotatory Dispersion and Circular Dichroism in Organic Chemistry," Heyden and Sons, London. 1967. pp 208–223.

same mixture of **18** and **19** obtained with sulfuric acid; however, 3% of a new compound could be detected by glc. By carrying out the dehydration for a short time, a mixture containing 16% of the new product plus 37 and 47% of **19** and **18**, respectively, was obtained. Separation of this minor reaction product and characterization by spectral methods (see Experimental Section) showed that it contained a saturated cyclohexanone carbonyl, an angular methyl group, a secondary methyl, an isopropyl group, and an isolated trisubstituted double bond. The only structure consistent with these data is that of the direct dehydration product **20**. The CD curve of **20** exhibits a weak negative Cotton effect (θ_{306} −680), and, although a negative Cotton effect is predicted by the octant rule, the small amplitude was unexpected. A study of models suggests that the most favorable conformation of **20** has a twist conformation for ring A which balances groups in positive and negative octants in such a manner that the amplitude of the Cotton effect will be minimal.

Although it was not anticipated that dihydronootkatone would be the exclusive product of the dehydration of **16**, it is *a priori* surprising that no trace of this compound was formed. The most probable explanation for the failure to observe any methyl migration is that the direct dehydration of **16** to **20** with the loss of the isopropyl–hydroxyl axial–axial interaction and relief of the methyl–methyl interaction is a much more rapid process. Protonation of **20** from the less hindered α face with migration of the β hydrogen at C-4 would lead to **18**, which is subsequently isomerized to the more stable cis isomer **19**.[15]

Experimental Section[16]

10-Epieudesm-4-en-3-one.—This compound was prepared from 10-epieudesm-11-en-3-on-5α-ol[17] by a modification of the method of Hikino.[8b]

10-Epieudesma-2,4-diene (12).—To a solution of 2.98 g of *p*-toluenesulfonylhydrazine in 35 ml of tetrahydrofuran was added 3.51 g of 10-epieudesm-4-en-3-one and 3 drops of concentrated hydrochloric acid. The reaction mixture was stirred and heated at reflux for 6 hr, benzene was added, and the solvents were distilled off until the boiling point reached 80°. The reaction flask was cooled with an ice bath and 30 ml of 1.91 *M* methyllithium was added dropwise over 30 min. Water was added cautiously, the mixture was extracted with two portions of hexane which were combined and dried, and the solvent was removed at reduced pressure to give 2.72 g of pale yellow oil. The crude product was taken up in hexane and filtered through a column of 75 g of Merck alumina to give 2.22 g (68%) of diene **12** as a rather unstable colorless oil, which was homogeneous to tlc (hexane, silica gel G) and glc: mass spectrum *m/e* (rel intensity) 204 (52), 189 (74), 145 (17), 132 (98), 131 (72), 118 (40), 117 (100); nmr δ 0.88, 0.90 (d, *J* = 6 Hz, isopropyl), 0.92 (s, 3 H, CH_3), 1.72 (d, *J* = 1 Hz, $CH_3C{=}CH-$), 5.68 (m, 2 H, HC=CH); uv 269 nm (log ε 3.73).

Photooxygenation of 12.—A solution of 0.81 g of homoannular diene was dissolved in 160 ml of a 1:1 mixture of benzene–ethanol and 0.020 g of eosin was added. The reaction mixture was irradiated with a Westinghouse 275W sun lamp while oxygen was bubbled through the reaction mixture. Analysis of aliquots by glc showed that no diene remained after 12 hr and the reaction mixture was filtered through Celite and charcoal and concentrated to a small volume *in vacuo*. The residue was taken up in benzene, washed with water until the washings were colorless, and dried, and the benzene was removed to give 0.73 g of yellow oil which partially crystallized. The crude product was taken up in hexane and chromatographed on 25 g of Merck acid-washed alumina. Elution with hexane–benzene (2:1) gave 0.216 g (23%) of endo peroxide **13** as white crystals, mp 72–73°. Recrystallization from aqueous methanol gave the analytical sample: mp 73–74°; nmr δ 0.88, 0.90 (d, *J* = 7 Hz, isopropyl), 0.92 (s, 3 H, CH_3), 1.85 (d, 3 H, *J* = 2 Hz, $CH_3C{=}CH$), 4.48 (m, 1 H, HCO), 6.20 (q, 1 H, $HCCH{=}CCH_3$); mass spectrum *m/e* (rel intensity) 236 (12), 204 (52), the balance of the spectrum was identical with that of the starting diene.

Anal. Calcd for $C_{15}H_{24}O_2$: C, 76.23 H, 10.24. Found: C, 76.00 H, 9.94.

Elution with benzene gave 0.035 g (4%) of **10-epieudesma-2,4-dien-3-one (14)** as a colorless oil, which was homogeneous to tlc [benzene–acetone (10:1), silica gel G]: ir 6.03 and 6.14 μ; nmr δ 0.88, 0.90 (d, *J* = 7 Hz, isopropyl), 1.09 (s, 3 H, CH_3), 1.95 (s, 3 H, $CH_3C{=}C$), 6.21, 6,83 (2 H, AB, *J* = 10 Hz, –CH=CH–); mass spectrum *m/e* (rel intensity) 219 (62), 218 (23), 204 (18), 175 (100), 161 (41), 147 (75).

Elution with methylene chloride gave 0.115 g (12%) of 10-epieudesm-3-en-2-on-5β-ol (**10**) as white crystals, mp 140–142°. The analytical sample, mp 143–144°, was prepared by recrystallization from hexane: ir 2.94 and 6.04 μ; nmr δ 0.91, 0.98 (d, *J* = 6 Hz, isopropyl), 1.05 (s, 3 H), CH_3), 1.96 (d, *J* = 1 Hz, 3 H, $\mathbf{CH_3}C{=}CH$), 5.76 (br s, 1 H, $\mathbf{H}C{=}CCH_3$); mass spectrum *m/e* (rel intensity) 236 (2), 208 (5), 193 (15), 175 (12), 126 (13), 123 (18), 111 (100), 110 (76); uv 237 nm (log ε 4.12); CD (*c* 0.00205, 25°) $[\theta]_{396}$ 0, $[\theta]_{379}$ +418, $[\theta]_{373}$ +351, $[\theta]_{363}$ +799, $[\theta]_{354}$ +351, $[\theta]_{348}$ +684, $[\theta]_{340}$ 0, $[\theta]_{339}$ −57, $[\theta]_{336}$ 0, $[\theta]_{333}$ +38, $[\theta]_{332}$ 0, $[\theta]_{326}$ −380, $[\theta]_{320}$ −285, $[\theta]_{314}$ −380.

Anal. Calcd for $C_{15}H_{24}O_2$: C, 76.23 H, 10.24. Found: C, 76.38 H, 10.40.

10-Epieudesm-3-en-2-on-5β-ol (10). A.—A solution of 0.117 g of peroxide **13** in 6 ml of 1 *M* ethanolic sodium hydroxide was heated at reflux for 15 min, cooled, acidified with glacial acetic acid, and diluted with water. The aqueous suspension was extracted with three portions of methylene chloride, which were combined, washed with water and 5% aqueous sodium hydroxide, and dried, and the solvent was removed at reduced pressure to give 0.077 g (66%) of white crystals, mp 138–140°, identical (ir, mixture melting point) with the material obtained as described above.

B.—The crude product from the photooxygenation of 1.36 g of diene **12** was dissolved in 60 ml of 1 *N* sodium hydroxide and treated as described in part A. Recrystallization of the crude product from hexane gave 0.415 (26%) of **10**, mp 136–139°. Concentration of the mother liquors gave 0.52 g of yellow oil which on tlc showed the presence of dienone **14**, hydroxy ketone **10**, and traces of two other compounds. By chromatography of the mother liquors and sublimation (0.5 mm, 100°) of the fractions eluted with methylene chloride, an additional 0.078 g (5%) of **10** could be obtained.

10-Epieudesma-3,5-dien-2-one (15).—To a solution of 0.078 g of hydroxy ketone **10** in 5 ml of pyridine was added 0.15 ml of phosphoryl chloride; the reaction mixture was heated at reflux for 1 hr, cooled, and poured into water; and the aqueous solution was extracted with three portions of ether. The ethereal extracts were combined, washed with two portions of water, 5% hydrochloric acid, and again with water and dried, and the solvent was removed at reduced pressure to give 0.021 g (29%) of yellow oil which gave essentially one spot on tlc (silica gel G,

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[15] A study of models of **20** show that with ring A in the twist conformation mentioned above the steric relationship between the double bond and the β hydrogen at C-4 should favor this reaction path.

[16] All melting points were determined on a Kofler hot stage apparatus and are uncorrected. Infrared spectra were taken as potassium bromide disks or liquid films on sodium chloride plates using a Perkin-Elmer Model 137 spectrophotometer and are reported in microns. Ultraviolet spectra were taken in methanol using a Perkin-Elmer Model 202 spectrophotometer and are reported as λ_{max} in nanometers (log ε). Nuclear magnetic resonance spectra were obtained using a Varian Associates A-60 nuclear magnetic resonance spectrophotometer with deuteriochloroform as a solvent unless stated otherwise. All spectra are reported in parts per million relative to tetramethylsilane (δ). Gas–liquid chromatography was carried out on an F & M Model 810 analytical gas chromatograph using helium as the carrier gas at a flow rate of 35 ml/min through a 10 ft × 0.125 in. copper column of 20% Carbowax on 'HP' Chromosorb W (80–100 mesh). Preparative glc was carried out on an Aerograph Autoprep, Model A-700, using helium as a carrier gas at a flow rate of 300 ml/min using a 25 ft × 0.375 in. copper column of 25% Carbowax on Chromosorb W. Optical rotatory dispersion and circular dichroism measurements were made in dioxane solution using a Jasco ORD/UV-5 spectropolarimeter. Mass spectra were determined using a Du Pont 21-490 mass spectrometer at 70-eV ionization potential. Elemental analyses were performed by Galbraith Laboratories, Knoxville, Tenn.

[17] The author would like to thank Professor A. R. Pinder for the gift of a generous sample of this material.

benzene–acetone, 10:1). Preparative tlc using the same system gave 0.010 g of **12** as a colorless oil: ir 6.02, 6.18, 6.30 μ; mass spectrum *m/e* (rel intensity) 218 (46), 203 (11), 175 (100), 161 (46), 147 (43), 133 (29), 131 (43); nmr δ 0.92, 0.99 (d, $J = 7$ Hz, isopropyl), 1.10 (s, 3 H, CH_3), 2.05 (d, $J = 1$ Hz, 3 H, $C\mathbf{H}_3C{=}CH$), 5.85 (br s, 1 H, $\mathbf{H}C{=}CCH_3$), 6.15 (d, 1 H, $J = 3$ Hz, $CHC\mathbf{H}{=}C-$); uv 284 nm (log ε 4.27).

After standing overnight at room temperature, the original aqueous pyridine solution deposited 0.034 g (43%) of starting hydroxy ketone, mp and mmp 140–142°.

Similar results were obtained at steam bath temperature for 1–2 hr and at reflux for 2 hr.

10-Epieudesman-3-on-5β-ol (16).—A solution of 0.040 g of hydroxy ketone **10** in 10 ml of 95% ethanol was hydrogenated at 30 psig using 0.010 g of 5% rhodium on alumina catalyst. The reaction mixture was filtered through Celite, and the solvent was removed at reduced pressure to give 0.027 g (68%) of white crystals, mp 157–159°, which were homogeneous to tlc.[18] Recrystallization from hexane gave the analytical sample: mp 161–162°; ir 2.89 and 5.91 μ; mass spectrum *m/e* (rel intensity) 238 (35), 223 (4), 220 (4), 203 (13), 193 (33), 154 (100); nmr ($CDCl_3$) δ 0.98, 1.00 (d, $J = 6$ Hz, isopropyl), 1.09 (d, $J = 7$ Hz, 3 H, $C\mathbf{H}_3CH$), 1.10 (s, 3 H, CH_3); nmr (C_6H_6); nmr (C_6D_6) δ 0.77 (d, $J = 7$ Hz, isopropyl), 0.83 (s, 3 H, CH_3), 0.89 (d, $J = 7$ Hz, $C\mathbf{H}_3CH$); CD (*c* 0.000212) θ_{332} 0, θ_{314} −2020, θ_{304} −3520, θ_{295} −3710; ORD ϕ_{380} −795°, ϕ_{322} −3640; ϕ_{314} −3060°, ϕ_{302} −900°, ϕ_{298} 0°, ϕ_{286} +2700°.

Anal. Calcd for $C_{15}H_{26}O_2$: C, 75.58; H, 10.99. Found: C, 75.57; H, 11.04.

Dehydration of 10-Epieudesman-2-on-5β-ol. A.—To a solution of 0.164 g of hydroxy ketone **16** in 4 ml of acetic acid was added with stirring 0.20 ml of redistilled boron trifluoride etherate. The reaction mixture was stirred at room temperature for 15 min, poured into ice water, and extracted with three portions of ether. The ethereal extracts were washed with water, 10% sodium hydroxide, and saturated brine and dried, and the solvent was removed *in vacuo* to give 0.074 g of pale brown oil. Analytical glc showed three compounds listed in order of increasing retention time in a ratio of 14:54:32, and the mixture was separated by preparative glc to give respectively, **20**, **19**, and **18**.

10-Epieudesm-5-en-2-one (20) (0.004 g) had ir 5.85 μ; mass spectrum *m/e* (rel intensity) 220 (34), 205 (23), 193 (18), 178 (49), 163 (21), 151 (25), 139 (70), 138 (100); nmr δ 0.91, 0.93 (d, $J = 7$ Hz, isopropyl), 1.12 (s, 3 H, CH_3), 1.20 (d, $J = 7$ Hz, 3 H, $C\mathbf{H}_3CH$); CD (*c* 0.0014) θ_{370} 0, θ_{316} −528, θ_{306} −680. Glc indicated that this material contained 15% of cis ketone **19** and 5% of the trans isomer **16**.

10-Epieudesm-3-en-2-one (19) (0.008 g) had ir 6.01 and 6.10 μ; mass spectrum *m/e* (rel intensity) 220 (100), 205 (25), 178 (87), 177 (64), 136 (42), 135 (43); nmr δ 0.88, 0.90 (d, $J = 6$ Hz, isopropyl), 0.98 (s, 3 H, CH_3), 1.98 (d, $J = 1$ Hz, CH_3-$C\mathbf{H}_3C{=}CH$), 5.82 (br s, 1 H, $\mathbf{H}C{=}CCH_3$); CD (*c* 0.0029) θ_{380} 0, θ_{369} +302, θ_{361} +176, θ_{353} +440, θ_{344} 0, θ_{338} +137, θ_{335} 0, θ_{330} −274, θ_{325} −176, θ_{318} −376, θ_{310} −274, θ_{306} −302; uv 243 nm (log ε 4.00). Glc indicated that this material contained less than 5% of the other two isomers.

5-Epi-10-epieudesm-3-en-2-one (18) (0.007 g) had ir 6.00 and 6.10 μ; mass spectrum *m/e* (rel intensity) 220 (96), 205 (25), 178 (100), 177 (73), 135 (91); nmr δ 0.92, 0.96 (d, $J = 6$ Hz), 1.02 (s, 3 H, CH_3), 1.89 (d, 3 H, $J = 1$ Hz, $C\mathbf{H}_3C{=}CH$), 5.88 (br s, 1 H, $\mathbf{H}C{=}CCH_3$); CD (*c* 0.0021) θ_{384} 0, θ_{372} +90, θ_{363} +42, θ_{356} +146, θ_{350} 0, θ_{347} −35, θ_{344} 0, θ_{341} +49, θ_{338} 0, θ_{333} −167, θ_{325} −28, θ_{320} −167, θ_{310} 0; uv 244 nm (log ε 3.79) Glc indicated that this compound contained less than 5% of the other two isomers. The retention time of **18** was the same (two columns) as that of 11,12-dihydronootkatone.

When the boron trifluoride catalyzed dehydration was carried out for varying periods and the mixture of ketones was isolated as described above and subjected to analytical glc, the results recorded in Table I were obtained.

TABLE I

DEHYDRATION OF 10-EPIEUDESMAN-2-ON-5β-OL (16)

Time, hr	Catalyst	Compd, % **20**	**19**	**18**
0.25[a]	Boron trifluoride	16	37	47
1	Boron trifluoride	8	51	41
18	Boron trifluoride	3	64	33
1.5	Sulfuric acid	0	47	53
3[a]	Sulfuric acid	0	67	33
18	Sulfuric acid	0	76	24

[a] Product were isolated, separated, and characterized.

B.—To 0.042 g of hydroxy ketone **16** at 0° was added with efficient stirring 4.0 ml of cold (0°) 50% aqueous sulfuric acid. The reaction mixture was allowed to warm to room temperature, stirred for 3 hr, and poured into ice water, and the aqueous suspension was extracted with three portions of methylene chloride. The organic extracts were combined, washed with water, and dried and the solvent was removed to give 0.039 g of yellow oil. Although this material was homogeneous to tlc (silica gel G, benzene–acetone 10:1), glc indicated the presence of two compounds in a ratio of 2:1. Preparative glc as described in part A gave 0.010 g of **19** and 0.004 g of **18**, the infrared, nmr, and mass spectra of which were identical with those of the compounds obtained in part A.

C.—A solution of 0.031 g of **16** in 2 ml of dry pyridine was treated with 0.10 ml of phosphoryl chloride and the product was isolated as described above to give 0.003 g (10%) of impure hydroxy ketone. The initial aqueous extracts after standing overnight gave an additional 0.015 g (48%) of **16**.

Isomerizations of 5-Epi-10-epieudesm-3-en-2-one. A.—To a solution of 0.001 g of **18** in 0.5 ml of dioxane was added 1 drop of concentrated hydrochloric acid, and the mixture was heated on the steam bath for 12 hr. Analysis by glc indicated a ratio of **19** to **18** of 7:1.

B.—To a solution of 0.001 g of **18** in 1 ml of methanol was added 0.050 g of sodium methoxide, and the mixture was heated at reflux for 18 hr. Glc indicated only the presence of cis ketone **19**.

(±)-11,12-Dihydronootkatone (17).—To a solution of 0.281 g of (±)-nootkatone[19] in 30 ml of dry benzene was added 0.147 g of tris(triphenylphosphine)rhodium chloride. The reaction flask was swept with hydrogen, sealed, and stirred overnight at room temperature. The reaction mixture was filtered through a short column of Merck alumina and the solvent was removed to give 0.234 g (83%) of **17** as a colorless oil, the infrared spectrum of which was identical with that of a sample prepared from (+)-nootkatone by Pinder:[20] mass spectrum *m/e* (rel intensity) 220 (81), 205 (12), 178 (100), 177 (21), 135 (95); nmr δ 0.90 (d, $J = 6$ Hz, isopropyl), 0.97 (d, $J = 6$ Hz, 3 H, $C\mathbf{H}_3CH$), 1.09 (s, 3 H, CH_3), 5.75 (br s, $\mathbf{H}C{=}C$). Glc indicated the presence of trace amounts of unreduced nootkatone and tetrahydronootkatone.

Registry No.—**10**, 34996-35-5; **12**, 34996-36-6; **13**, 34969-20-5; **14**, 34996-37-7; **16**, 34996-38-8; **18**, 34996-39-9; **19**, 34996-40-2; **20**, 34996-41-3.

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(18) Both this material and hydroxy enone **10** sublime readily at 100° and atmospheric pressure, which undoubtedly contributes to the mediocre yields encountered in their preparation.

(19) The author would like to thank Professor A. R. Pinder for making available a sample of (±)-nootkatone which had been supplied to him by Dr. P. Schudel.

(20) A. R. Pinder, unpublished work.