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SESQUITERPENOIDS—IV[1]

ACID-CATALYZED METHYL MIGRATION IN 9-METHYL DECALINS

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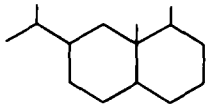
Abstract—Treatment of unsaturated acid **1** with refluxing formic acid leads to an equilibrium mixture of lactones **2** and **3** in a ratio of 2:1. The stereostructure of γ-lactone **2** is secured by its synthesis from epoxy-ester **6**, the stereochemistry of which is deduced from reactivity arguments. The structure of δ-lactone **3** was proven by correlation with the *trans*-9-methoxy-10-methyl decalin **29**, of unambiguous stereochemistry. The merits of such a "methyl-migration" route to eremophilanes are discussed.

THE sesquiterpenoid ketone eremophilone was first isolated in 1932.[2] Extensive subsequent investigations established that the material, as well as its congeners hydroxyeremophilone and hydroxydihydroeremophilone, possess the non-isoprenoid carbon skeleton indicated in formula i.[3] In subsequent years numerous members of



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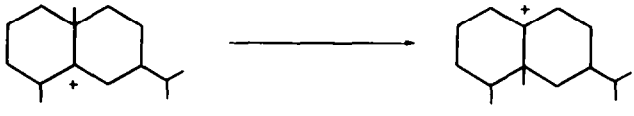
what may be termed the "eremophilane family" of sesquiterpenoids have been identified.‡

In order to account for the obvious departure of the eremophilanes from the normal isprene rule, Sir Robert Robinson suggested that the eremophilanes are formed in nature from eudesmanoid precursors *via* a route involving methyl migration in a cation of the type ii.[19]



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Such diangular 1,2-Me migrations are common in steroids (e.g. iv → v),[20] and in triterpenes (e.g. vi → vii).[21,22] At least one example of such a rearrangement has

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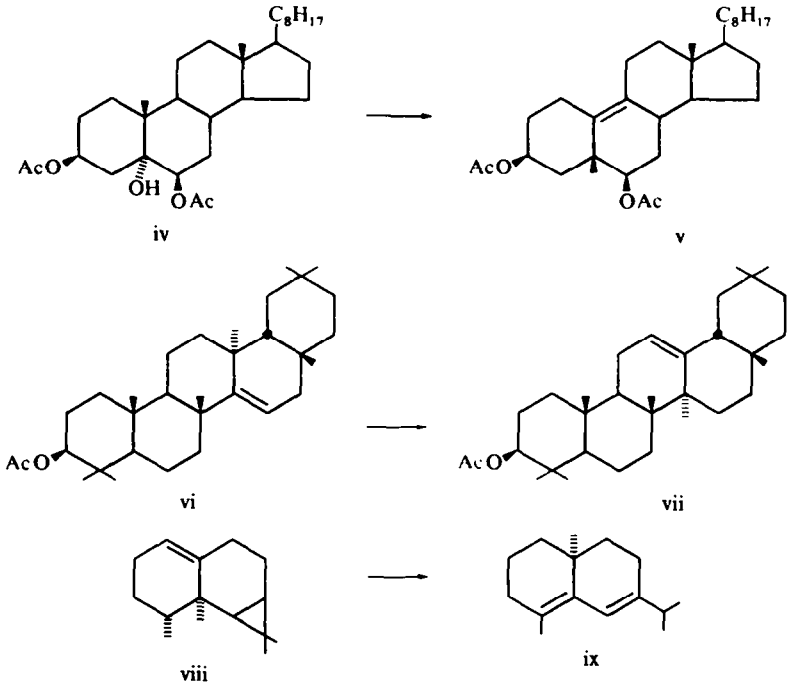
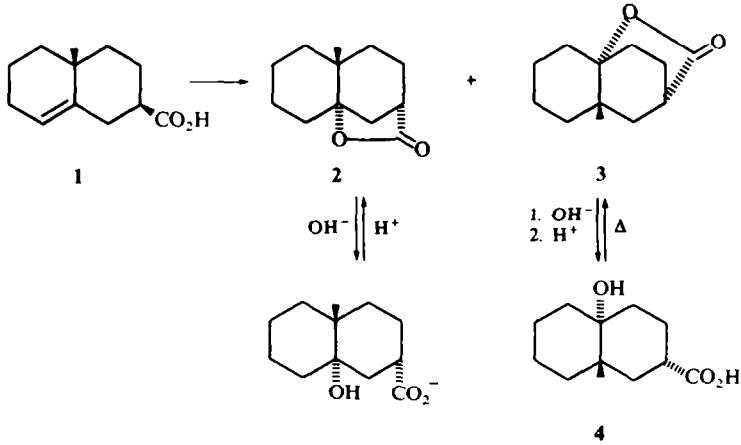
‡ *Inter alia*: Eremophilenolide;[4] petasin, isopetasin, and S-petasin;[5] β-gurjunene (calarene);[6] aristolene;[6a] α-ferulene;[7] aristolone;[8] valencene;[9] nootkatone;[9a] nootkatene;[10] valerianol;[11] ligularol, eremoligenol, furanoeremophilane, ligularone, and 6β-hydroxyeremophilenolide;[12] euryopsonol;[13] nardostachone;[14] α-vetivone (isonootkatone);[15] furanoligularanone;[16] warburgin;[17] and warburgiadione.[18]

been noted in a simple decalin (e.g. viii → ix).[6b] In connection with our interest in devising general methods for the total synthesis of various sesquiterpenoid systems, we have examined the possibility of a biogenetically styled eremophilane synthesis, involving such a diangular methyl migration. In the present paper, we present the



results of one phase of this investigation, which demonstrates the feasibility of the approach for the preparation of relatively inaccessible intermediates. Further papers in this series will be concerned with our attempts to develop the "methyl migration method" into a generally useful route to the eremophilane skeleton.

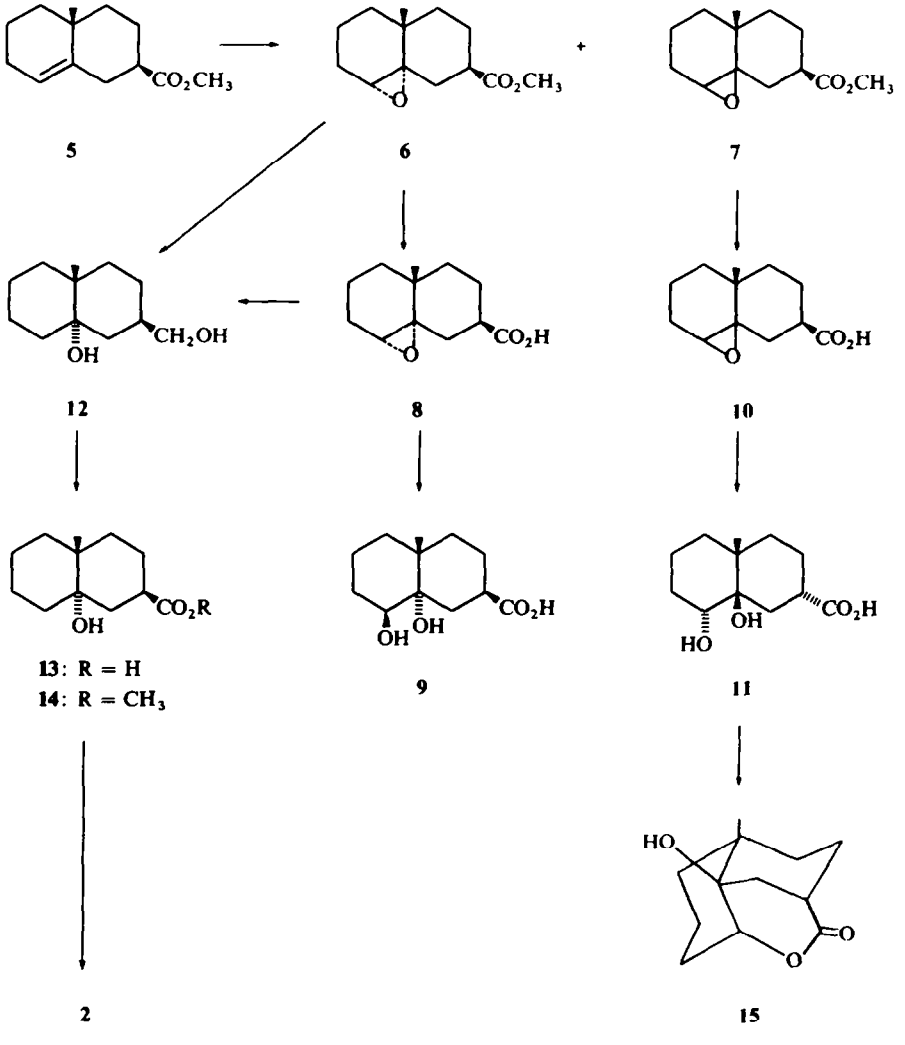
When the readily-available unsaturated acid **1**[1] is refluxed in anhydrous formic acid, there is produced a mixture of the γ-lactone **2** ($\gamma_{C=O}$ 1780 cm^{-1}) and δ-lactone



3 ($\gamma_{C=O}$ 1755 cm^{-1}) in an equilibrium ratio of 2:1. Similar treatment of pure **2** or pure **3** produces a mixture of **2** and **3** in the identical ratio. The conversion of acid **1** to the lactone mixture is essentially quantitative, and is remarkably clean. Only trace amounts of other products could be detected when the reaction product was analyzed by VPC.

Basic hydrolysis of the mixture of lactones **2** and **3**, followed by acidification of the reaction mixture, produces a mixture of lactone **2** and hydroxy-acid **4**. These compounds are conveniently separable, due to solubility differences. Continued resubmission of the recovered lactone **2** to the formolysis conditions allows large-scale conversion of acid **1** into hydroxy-acid **4**. Compound **4** spontaneously dehydrates, forming lactone **3**, on being heated to its m.p.

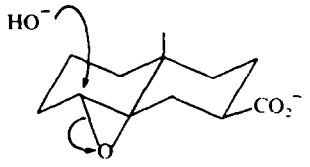
The structure of γ-lactone **2** was established in the following manner. Oxidation of the unsaturated ester **5**[1] with meta-chloroperbenzoic acid yields a mixture of the two epoxy-esters **6** and **7** in a ratio of 3:1. Compounds **6** and **7** are also produced, in



a ratio of 1:3, when acid **1**, is treated successively with hypobromous acid, base, and diazomethane.

The stereochemistry of the oxirane ring in compounds **6** and **7** was indicated by the vast difference in reactivity of these two compounds toward aqueous base. Ester **6** is hydrolyzed to the corresponding acid **8**, on exposure to dilute, aqueous base. Acid **8** is further transformed into the dihydroxy-acid **9** on treatment with 2 N aqueous sodium hydroxide solution at 100° for 24 hr. On the other hand, epoxy-acid **10** resists these conditions, and is only partially converted to a diol (**11**) after treatment with 6·5N NaOH at 170° for 96 hr. That epimerization of the carboxyl group has occurred in the transformation of **10** to **11** is shown by the fact that **11** dehydrates on heating, with the formation of a δ-lactone, **15** (ν_{max} 1725 cm^{-1}).

The difference in reactivity between **8** and **10** is easily rationalized by assuming the indicated structures. Approach of hydroxide ion to the secondary oxirane carbon in **8** should be relatively unhindered. However, in **10**, the attacking hydroxide ion would encounter severe steric hindrance.



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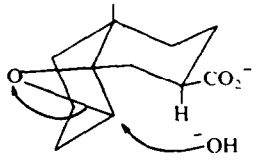

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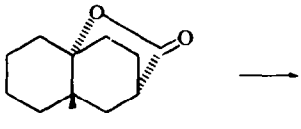
With the stereo-structures of **6** and **8** secured, we then completed the correlation of these materials with lactone **2**. Hydride reduction of pure epoxy-acid **8**, or the 3:1 ratio of epoxy-esters **6** and **7**, gave us the crystalline diol **12**. Compound **12** was oxidized to hydroxy-acid **13**, which was converted by diazomethane into the ester **14**. Treatment of **14** with methanolic sodium methoxide afforded lactone **2**.*

The structure assigned to lactone **3** was more difficult to prove. We initially envisioned the degradation of this material to the known *trans*-10-methyl-9-decalol[23] by removal of the carboxyl group from hydroxy-acid **4**. Since only one δ-lactone may be derived from *trans*-10-methyl-9-decalol, such a conversion would constitute a rigorous proof.

Initial attempts to decarboxylate **4** by various modifications of the Hunsdiecker reaction[24] were unsuccessful. Attempted application of the Barbier-Wieland degradation to lactone **3** was also unsuccessful. Treatment of **3** with phenylmagnesium bromide gave diol **16**, which could be partially dehydrated to an unsaturated alcohol, but attempts to oxidize this material failed.



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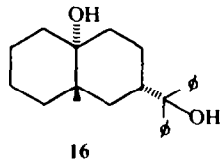

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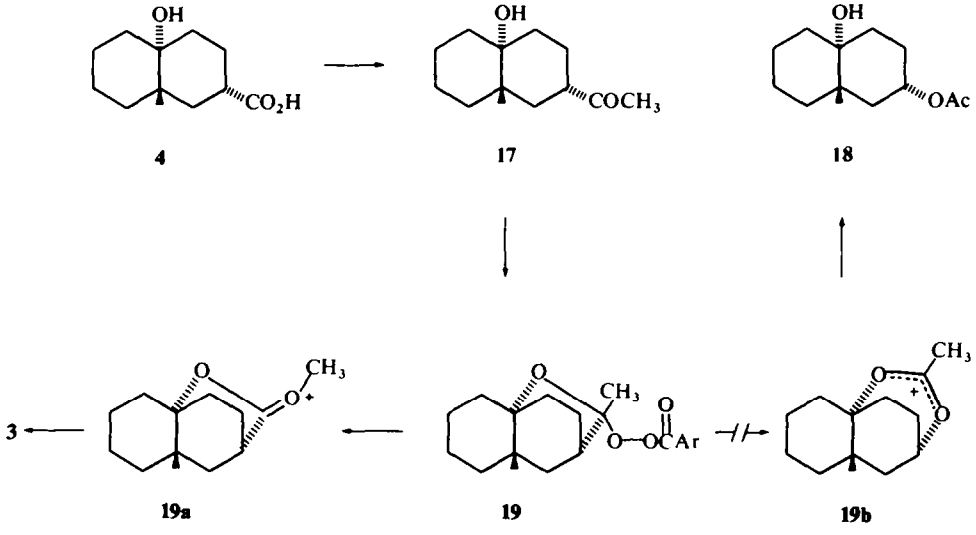
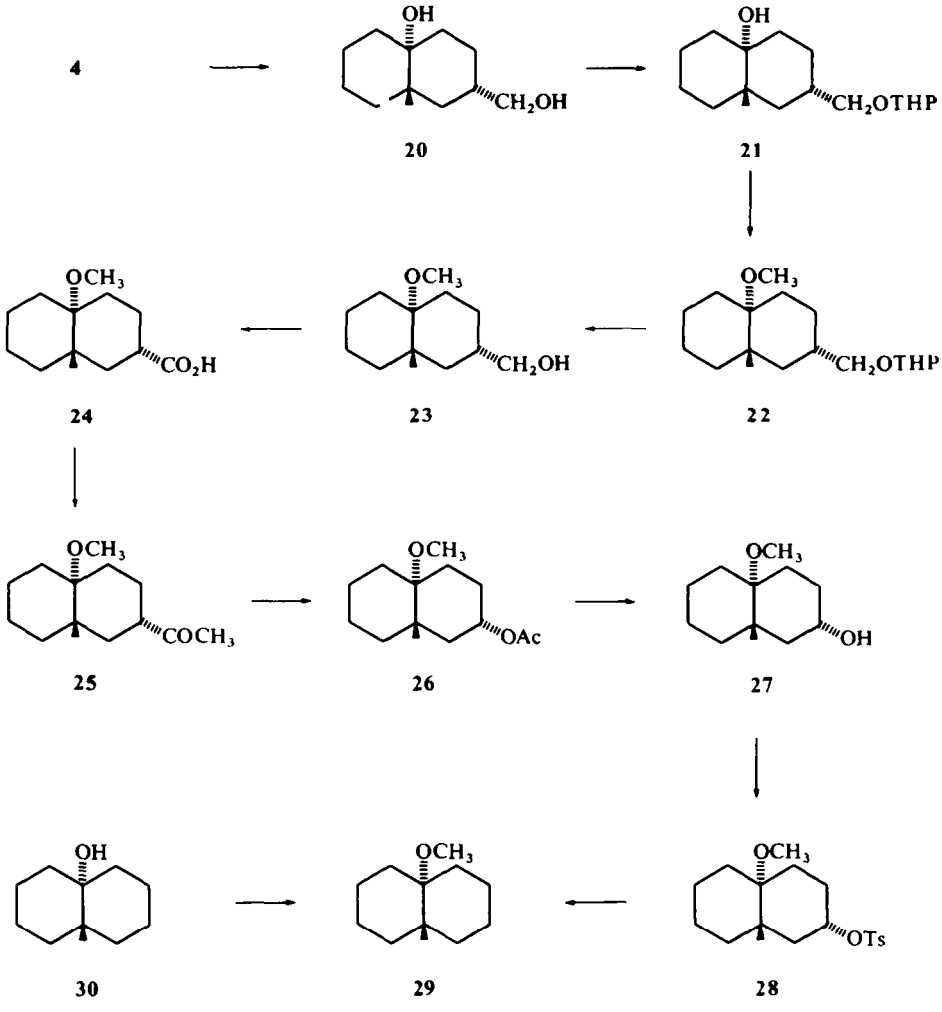
* The stability of lactone **2**, relative to hydroxy-ester **14**, had previously been indicated by the observation that compound **14** remains unchanged when submitted to these reaction conditions.

We then attempted the removal of the carboxyl group from hydroxy-acid **4** by the Baeyer–Villiger oxidation of the derived methyl ketone. Our first attempts along these lines were also thwarted. Acid **4** reacts smoothly with methyllithium in ether to afford the hydroxy-ketone **17** in 78% yield. However, attempted Baeyer–Villiger oxidation of **17** to the hydroxy-ester **18** led only to the formation of lactone **3**, in excellent yield. This reversal of the normally observed migratory aptitudes of methyl and secondary carbon in the Baeyer–Villiger oxidation is relatively unprecedented,[25] and may be explained by invoking the intermediacy of the peroxyketal **19**, which decomposes to form **3**, *via* ion **19a**, rather than **16**, *via* ion **19b**.



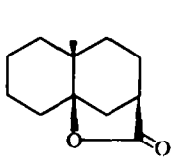
This hypothesis led us to protect the OH group in **4** as the methyl ether, in order to preclude the formation of the hypothetical peroxyketal **19**. Reduction of hydroxy-acid **4** with LAH in ether affords the diol **20**, which reacts with dihydropyran to yield the tetrahydropyranyl ether **21**. Methylation of **21**, with sodium hydride and methyl iodide in dimethoxyethane yields the ether **22**, which undergoes hydrolysis to hydroxy–ether **23**. Oxidation of **23** then affords methoxy-acid **24**. Compound **24** reacts smoothly with MeLi in ether to give the methyl ketone **25**, which undergoes normal Baeyer–Villiger oxidation to afford the methoxy-acetate **26**. Hydride reduction of **26**, yields alcohol **27**, which is converted into the *p*-toluenesulfonate **28**. Finally, lithium aluminum hydride reduction of **28** affords *trans*-10-methyl-9-decalyl methyl ether (**29**), identical with a sample prepared by methylation of the known alcohol **30**.[23]



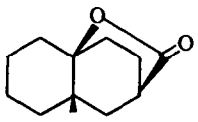
At this point, it is necessary to briefly discuss the conversion of **1** into **2** and **3**, along with the interconversion of **2** and **3**, and assess the implications of these reactions on our plans to use a Me-migration route to eremophilanes. The fact that **1**, **2** and **3** all yield the same mixture of **2** and **3** under identical conditions indicates that the observed equilibrium ratio of 3:1 must reflect the relative thermodynamic stabilities of the two lactones. Furthermore, the fact that the *cis*-lactone x is not found suggests that this lactone is much less stable than **2** or **3**.

Other lactones which could conceivably be produced (i.e. xi–xiii) might likewise be thermodynamically unstable relative to **2** and **3**, or might be precluded by the intervention of an unusually high activation barrier in going from **1** to any of these compounds. If free equilibrating carbonium ions are involved, there would seem to be no need to adopt this latter argument. Therefore, it is likely that **2** and **3** represent

the more stable of the various lactones which can be formed from **1** by no more than a single alkyl shift in the protonated olefin.



x



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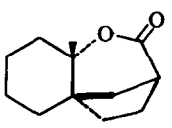
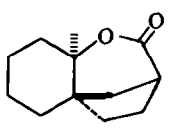
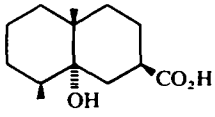


xii



xiii

The fact that lactone **3** is formed in major amounts from **1** is encouraging, since this lactone possesses 12 of the C atoms of the eremophilane skeleton and also has the proper relative stereochemistry between the angular Me group and the carboxyl group (potential isopropyl moiety) for the synthesis of certain members of the eremophilane class (valencene,[9] nootkatone,[9a] nootkatene,[10] and valerianol[11]). Since these compounds possess a secondary Me group adjacent to the angular Me group, and disposed *cis* relative to this group (a feature shared by all known members of the eremophilane family), we considered the preparation and formolysis of hydroxy-acid **31**. Our results in this phase of the investigation will be communicated separately.



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EXPERIMENTAL

IR spectra were determined on a Perkin–Elmer 237 IR Spectrometer. NMR spectra were determined on a Varian A-60 instrument. Chemical shifts are given in ppm downfield from internal TMS. VPC analyses were performed with an Aerograph A-90-P instrument. Unless otherwise noted, the column used was a 10 ft × 0·25 in UCON 75HB, 90,000 polar column. Microanalyses were performed by the University of California Microanalytical Laboratory, Berkeley, California.

4aβ-Methyl-8aα-hydroxydecahydronaphth-2α-oic acid, lactone (**2**) *and 4aβ-methyl-8aα-hydroxydecahydronaphth-3α-oic acid, lactone* (**3**)

A soln of 5·00 g of **1**[1] in 100 ml 98% formic acid was refluxed for 15 hr. The solvent was removed at reduced press to afford 5·54 g of brown oil, which was chromatographed on 20 g silica gel. Elution of the column with 250 ml $CHCl_3$ containing 0·75% EtOH gave 5·41 g yellow oil composed almost entirely of two lactones, (**2** and **3**), in a ratio of approximately 2:1.* That this is an equilibrium mixture was established by subjecting each pure lactone (*vide infra*) to the conditions given above, whereupon identical mixtures of **1** and **2** were again produced.

The major isomer (**2**) is obtained by crystallization of the mixture from hexane. Several recrystallizations from the same solvent yielded the analytical sample, m.p. 70·7–71·9°; NMR in CCl_4: δ 1·04 (Me); IR in CCl_4; ν_{max} 1780 cm^{-1} (C=O). (Found: C, 73·87; H, 9·18. Calc. for $C_{12}H_{18}O_2$: C, 74·19; H, 9·34%).

The mixture of lactones was conveniently separated in the following manner. A mixture of 5·41 g of the

* The mixture was analyzed by VPC (retention times at 182° He flow 45 ml/min: **2**, 87 min; **3**, 105 min), or by assessing the relative areas of the angular methyl singlets at δ 1·04 and δ 1·16 in the NMR spectrum of the mixture.

lactone mixture (*vide supra*) and 1·25 g NaOH in 150 ml H_2O was heated on a steam bath until a homogeneous soln resulted. The cooled soln was layered with ether and the aqueous phase was carefully neutralized by the dropwise addition of 2M H_2SO_4aq. The aqueous layer was saturated with NaCl and the layers were separated. After extracting the aqueous phase 4 times with ether, the combined ether layers were dried and evaporated at room temp under vacuum to yield 5·59 g of oil. Trituration of this oil with 15 ml benzene, followed by filtration, afforded 1·23 g (22·5%) of **4**, m.p. 132–143°. An analytical sample, m.p. 145–146° (evolution of H_2O) was obtained by washing the above crude acid with anhyd ether. NMR in MeOH: δ 1·04 (Me); IR in $CHCl_3$: ν_{max} 1705 cm^{-1} (C=O). (Found: C, 67·92; H, 9·43. Calc. for $C_{12}H_{20}O_3$: C, 68·06; H, 9·38%).

Concentration of the mother liquors from the above crystallization gave 4·3 g of an oil, whose spectra revealed it to be essentially pure **2**. Resubmission of this oil to the formic acid treatment allowed more of **4** to be obtained.

Upon heating above its m.p., **4** lactonizes. Thus, 1·57 g of **4** was heated at 150° for 45 min. After cooling, the crude lactone was dissolved in ether and filtered through a chromatography column prepared from 10 g of silica gel, topped with a layer of activated charcoal. The eluent was evaporated to afford 1·33 g (92·5%) of a white oil which crystallized upon addition of a seed crystal. Recrystallization from pentane at −80° gave analytically pure **3**, m.p. 65–68·3°. NMR in $CHCl_3$: δ 1·16 (Me); IR in CCl_4: ν_{max} 1755 cm^{-1} (C=O). (Found: C, 74·19; H, 9·25. Calc. for $C_{12}H_{18}O_2$: C, 74·19; H, 9·34%).

Methyl 4aβ-*methyl*-8α,8aα-*oxidodecahydronaphth*-2β-*oate* (**6**) *and methyl* 4aβ-*methyl*-8β,8aβ-*decahydronaphth*-2β-*oate* (**7**)

To a soln of 1·50 g of **5**, in 40 ml $CHCl_3$ was added over 15 min a soln of 2·30 g 85% *m*-chloroperbenzoic acid in 40 ml $CHCl_3$. The soln was stirred at room temp for 2 hr, then washed twice with Na_2CO_3aq. After drying over $MgSO_4$, the $CHCl_3$ soln was evaporated to yield 1·64 g of a mixture of **6** and **7**. The NMR spectrum of the mixture (in CCl_4) showed resonances due to angular Me groups at δ 1·09 (**6**) and δ 1·03 (**7**) in a ratio of 3:1. A single resonance due to OMe appeared at δ 3·55. IR in CCl_4: ν_{max} 1735 cm^{-1}. An analytical sample of the mixture was obtained by preparative VPC (5 ft × 0·25 in in SF-96 on Chromosorb W at 180°, He flow 60 ml/min, retention time 13 min). (Found: C, 69·42; H, 9·15. Calc. for $C_{13}H_{20}O_3$: C, 69·61; H, 8·99%).

The behavior of the two epoxy-esters toward base was used to assign the stereochemistry of the oxirane ring, as discussed in the text.

4aβ-*Methyl*-8α,8aα-*oxidodecahydronaphth*-2β-*oic acid* (**8**)*

A mixture of 13·81 g of the 3:1 mixture of **6** and **7** and 9·4 g KOH in 110 ml H_2O was refluxed until the mixture became homogeneous (40 min). The cooled soln was washed with ether, then carefully acidified with dil H_2SO_4aq. The resulting mixture was extracted with ether. After drying, the ethereal soln was evaporated to obtain 10·70 g of orange oil. Crystallization was effected from a mixture of 20 ml pentane and 2 ml ether. There was obtained 3·28 g of **8**, m.p. 86–88°, in 3 crops. Sublimation afforded the analytical sample, m.p. 78–80°. NMR in C_5H_5N: δ 1·04 (Me); IR in KBr: ν_{max} 3500, 1710 cm^{-1}. (Found: C, 68·38; H, 8·78. Calc. for $C_{12}H_{18}O_3$: C, 68·55; H, 8·65%).

4aβ-*Methyl*-8β,8aα-*dihydroxydecahydronaphth*-2β-*oic acid* (**9**)

To 1·01 g of a 3:1 mixture of **6** and **7** (*vide supra*, from peracid oxidation of **5**) was added 12 ml 40% NaOHaq and 36 ml H_2O. The mixture was stirred under reflux for 18 hr, cooled, and then diluted with 50 ml H_2O. After layering the basic soln with ether, it was carefully acidified by the dropwise addition of dil H_2SO_4aq. The layers were separated and the aqueous layer was extracted well with ether and with CH_2Cl_2. The combined organic layers were dried and evaporated to yield 910 mg yellow solid. After washing this solid with benzene, there remained 620 mg which was recrystallized from acetone to afford 385 mg of crystalline **9** in two crops, m.p. range 201–212°. Further recrystallization from acetone gave analytically pure **9**, m.p. 210·5–211·5°. NMR in MeOH: δ 1·23 (Me); IR in KBr: ν_{max} 3550, 3480, 3320, 3000–2300, 1705 and 1675 cm^{-1}. (Found: C, 63·16; H, 8·76. Calc. for $C_{12}H_{20}O_4$: C, 63·16; H, 8·77%).

Compound **9** was also obtained in the following manner. A soln of 80 mg of **8** (m.p. 86–88°) in 25 ml 8% NaOHaq was refluxed for 20 hr. After an analogous work-up, there was obtained 75 mg of crude **9**, which was triturated with ether to yield 43 mg of crystalline **9**, m.p. 201–209°. Recrystallization from

* This experiment was performed by Mr. Young Amano of these laboratories.

acetone gave material, m.p. 208·5–211·5°, which did not depress the m.p. of the dihydroxy-acid obtained by base treatment of the 3:1 mixture of **6** and **7**.

4aβ-Methyl-8α,8aβ-dihydroxydecahydronaphth-2α-oic acid (**11**)

A soln of 2·11 g of **1** and 2·30 g N-bromosuccinimide in 12 ml 50% aq THF was stirred at room temp for 3·5 hr. The mixture was then poured into 15 ml water and the resulting 2-phase soln was evaporated to yield 3·31 g of a mixture of bromohydrins. To this oil was added 60 ml water and 2 ml 50% NAOH aq. After stirring the alkaline soln for 30 min,* an additional 18 ml 40% NaOH aq was added and the resulting soln was refluxed for 20 hr. The soln was allowed to cool overnight, layered with ether, and acidified at 5° by the cautious addition of dil H_2SO_4 aq. The layers were separated and the aqueous phase extracted with 4 portions ether. The combined ether layers were dried and evaporated to yield 2·31 g oil. Trituration of this oil with benzene gave a solid which was collected by filtration. The crude solid so obtained was recrystallized from acetone–EtOAc to afford 190 mg of **9**, m.p. 200–210°.

The benzene soln from the above trituration was evaporated to yield 1·81 g of brown oil. Approximately 700 mg of this oil was dissolved in 10 ml 25% NaOH aq. The resulting soln was heated in a closed stainless steel tube at 170° for 96 hr. After cooling, the tube was emptied and rinsed with water. The combined aqueous solns were then layered with ether and carefully acidified with dil H_2SO_4 aq at 5°. The ether layer was separated and the aqueous phase was extracted further with ether. After drying, the combined ether layers were evaporated to yield 510 mg of an oil. Trituration of this oil with ether gave a solid, which was collected by filtration. The crude material obtained weighed 175 mg, m.p. 177–185° with evolution of gas. Recrystallization from acetone gave 110 mg, m.p. 190–194° (gas evolution). Further recrystallization from acetone gave analytically-pure material, m.p. 194–198° (gas evolution, heating rate 30°/min) or 184–190° (gas evolution, heating rate 10°/min). NMR in MeOH: δ 0·96 (Me); IR in Nujol: ν_{max} 3550–2300, 1705 cm^{-1}. (Found: C, 62·90; H, 8·64. Calc. for $C_{12}H_{20}O_4$: C, 63·16; H, 8·77%).

4aβ-Methyl-8α,8aβ-dihydroxydecahydronaphth-2α-oic acid, δ-lactone (**15**)

Compound **11** (50 mg, m.p. 190–194°) was heated at 195° for 15 min. After cooling, the resulting solid was recrystallized from benzene–hexane. There was obtained 36 mg of lactone in two crops, m.p. 118–128°. The analytical sample, m.p. 134–136·5° was obtained after sublimation and a further recrystallization from benzene–hexane. NMR in $CHCl_3$: δ 1·05 (Me) and δ 4·25 (C_8—H, partially resolved quartet, $W^{\frac{1}{2}}$ = 7 c/s, equatorial).[27] (Found: C, 68·38; H, 8·63. Calc. for $C_{12}H_{18}O_3$: C, 68·57; H, 8·57%).

4aβ-Methyl-2β-(hydroxymethyl)decahydronaphth-8aα-ol (**12**)

To 1·03 g LAH, in 40 ml ether, was added a soln of 1·53 g of a 3:1 mixture of **6** and **7** in 25 ml ether. After stirring overnight, 3·7 ml 5% KOH aq was added gradually to the soln. The solid was filtered off and washed with ether. The ethereal filtrate was evaporated to give 1·32 g oil. Crystallization of this oil from hexane gave 1·10 g (82%) crude diol, m.p. 60–100°. The NMR spectrum of this mixture showed angular Me resonances at δ 0·92 and δ 1·01 in a ratio of 1:3. Additional crystallizations from benzene gave analytically pure **12**, m.p. 103–104°. NMR in $CHCl_3$: δ 1·01 (Me), δ 3·50 (CH_2OH, doublet, J = 6 c/s); IR in $CHCl_3$: ν_{max} 3630 (free OH), 3450 cm^{-1} (associated OH). (Found: C, 72·40; H, 11·01. Calc. for $C_{12}H_{22}O_2$: C, 72·67; H, 11·19%).

4aβ-Methyl-8aα-hydroxydecahydronaphth-2β-oic acid (**13**)

A soln of 1·58 g crude **12** (m.p. 65–105°) in 50 ml 90% aqueous acetone was oxidized at room temp with 4 ml Jones oxidant.[28] Water was added, the aqueous layer was saturated with NaCl, and the mixture was extracted with ether (four 50 ml portions). The combined ether extracts were twice extracted with dil NaOH aq. The basic extracts were combined, layered with ether and carefully acidified with dil H_2SO_4 aq. After saturating the aqueous layer with NaCl, the ether layer was removed and the aqueous phase extracted twice more with ether. The combined ether extracts were dried and evaporated to yield 1·13 g white solid. One crystallization from benzene gave 630 mg of analytically pure **13**, m.p. 169–170·5°. A similar oxidation of 135 mg pure **12** (m.p. 103–104°) yielded 100 mg (70%) of **13**, m.p. 168·5–171°. NMR in MeOH: δ 1·03 (Me); IR in KBr: 2400–3500 (OH), 1705 cm^{-1} (C=O). (Found: C, 68·13; H, 9·38. Calc. for $C_{12}H_{20}O_3$: C, 67·92; H, 9·43%).

* In one run, the reaction was worked up at this point to yield a mixture of **8** and **10**. Methylation of this mixture with ethereal diazomethane[26] gave a mixture of **6** and **7** in a ratio of 1:3, as judged by the NMR spectrum of the mixture.

Methyl 4aβ-*methyl*-8aα-*hydroxydecahydronaphth*-2β-*oate* (**14**)

A soln of 384 mg pure **13** in 20 ml ether was esterified with distilled ethereal diazomethane soln.[26] After evaporation of the ether, crystallization from hexane furnished 325 mg of **14**, m.p. 81·5–85°. Sublimation (90° at 0·1 mm Hg) and recrystallization from pentane gave analytically pure **14**, m.p. 84–85°. NMR in CCl_4: δ 1·03 (Me), δ 3·59 (OMe); IR in CCl_4: ν_{max} 3610, 3500 (OH), 1725 cm^{-1} (C=O). (Found: C, 69·30; H, 10·04. Calc. for $C_{13}H_{22}O_3$: C, 69·03; H, 9·73%).

Preparation of lactone **2** *from hydroxy-ester* **14**

A soln of 33 mg of **14** and 50 mg NaOMe in 10 ml MeOH was heated in a sealed tube at 100° for 40 hr. After cooling, the methanolic soln was poured into 50 ml sat NaCl aq containing 1 ml AcOH. The 2-phase mixture was extracted 3 times with ether and the combined ether extracts were dried and evaporated to give 25 mg oil. Preparative VPC of this oil, which showed only one peak on the aforementioned column, gave 8 mg of clear oil, identical by IR to crystalline **2**, which instantaneously crystallized when a minute crystal of **2** was added. One recrystallization from hexane gave **2**, m.p. 68–70·5°.

3α-(*Diphenylhydroxymethyl*)-4aβ-*methyldecahydronaphth*-8aα-*ol* (**16**)

To a soln of 1·33 g **3** in 40 ml ether was added 20 ml 2M PhLi in benzene–ether. After stirring at room temp for 3 hr, the excess PhLi was destroyed by addition of 25 ml H_2O. The ether layer was separated and the aqueous layer further extracted with ether. The combined ether layers were dried and evaporated to afford 3·45 g solid which was chromatographed on 20 g silica gel. Elution with 300 ml benzene gave 2·19 g solid which partially crystallized. The semisolid was washed well with hexane to afford 0·46 g of white, crystalline **16**. Further elution of the above column with 300 ml ether gave 1·36 g crystalline **16**, for a total yield of 1·82 g (76%). The analytical sample, m.p. 171·5–172°, was obtained by recrystallization from hexane. NMR in $CDCl_3$: δ 1·04 (Me), δ 7·1–7·6 (aromatic). IR in $CHCl_3$: ν_{max} 3600, 3450, 1600, 1490 cm^{-1}. (Found: C, 82·52; H, 8·47. Calc. for $C_{24}H_{30}O_2$: C, 82·29; H, 8·57%).

3α-*Acetyl*-4aβ-*methyldecahydronaphth*-8aα-*ol* (**17**)

To 500 mg of **4**, dissolved in 70 ml dry ether, was added 10 ml 1·6M MeLi in ether. The resulting cloudy soln was refluxed 1·5 hr and then cooled. Water (25 ml) was added and the 2-phase mixture was stirred for a few min. The ether layer was separated, washed once with sat NaCl aq, dried and evaporated to yield 390 mg (78%) white solid. Recrystallization from hexane afforded an analytical sample, m.p. 104–106°. NMR in $CHCl_3$: δ 1·03 (Me), δ 2·10 (COMe); IR in CCl_4: ν_{max} 3600, 3500, 1710 cm^{-1}. (Found: C, 74·30; H, 10·86. Calc. for $C_{13}H_{22}O_2$: C, 74·04; H, 10·58%).

Baeyer–Villiger oxidation of ketol **17**

A soln of 220 mg of **17** and 470 mg (2·5 equiv) of 85% *m*-chloroperbenzoic acid in 35 ml CH_2Cl_2 was refluxed with stirring for 40 hr. The CH_2Cl_2 was removed and the residue chromatographed on silica gel. Elution with $CHCl_3$, containing 0·75% EtOH, failed to effect separation, affording 650 mg white solid. This solid was dissolved in ether and washed twice with Na_2CO_3 aq, once with sat NaCl aq, and dried. Evaporation of the ether gave 180 mg (88%) of oily **3**, essentially pure by NMR, which showed no discernable resonance due to acetyl or acetoxy protons. Crystallization of this oil from hexane gave a first crop of 50 mg of **3**, m.p. 62–66°, whose NMR and IR spectra were superimposable with those of the authentic material.

3α-(*Hydroxymethyl*)-4aβ-*methyldecahydronaphth*-8α-*ol* (**20**)

To a suspension of 2·35 g of **4** in 100 ml ether was added 1·20 g LAH. After the resulting suspension was stirred for 24 hr, 7 ml of 10% KOH aq was added and the mixture was stirred for 2 hr. The white solid was removed by filtration and washed with ether. The ether fractions were combined and evaporated, yielding 2·06 g (94%) of **20**, m.p. 121–126°. Several recrystallizations from benzene afforded pure material, m.p. 124·5–126°. NMR in C_5H_5N: δ 1·03 (Me), δ 3·65 (CH_2OH); IR in KBr: ν_{max} 3350 cm^{-1}. (Found: C, 72·48; H, 10·99. Calc. for $C_{12}H_{22}O_2$: C, 72·67; H, 11·19%).

3α-(*Hydroxymethyl*)-4aβ-*methyl*-8aα-*methoxydecahydronaphthalene* (**23**)

A soln of 2·65 g of **20** and 5 g dihydropyran in 50 ml ether containing 5 drops conc HCl was stirred at room temp for 2 days. The resulting clear soln was poured into sat NaCl aq containing 5 ml 10% KOH aq.

The aqueous layer was separated and twice extracted with ether. The combined ether layers were dried and evaporated to yield 4·26 g of oily **21**.

The above oil (4·26 g), in 75 ml anhyd 1,2-dimethoxyethane, was added to 5·00 g of NaH suspension (59·4% NaH in mineral oil). The slurry was refluxed for a few min with stirring and 15 ml MeI was added as rapidly as possible. After refluxing overnight, the cooled soln was diluted with 400 ml pentance and the resulting mixture filtered. Evaporation of solvents gave an oil, which contained a small amount of solid. The material was dissolved in CCl_4, filtered and the solvent removed to give 7·19 g of **22** as a slightly yellow oil.

To a soln of the above oil (7·19 g) in 200 ml MeOH, was added 5 drops conc HCl. After stirring at 30° for 16 hr, 1 g solid K_2CO_3 was added and the MeOH was evaporated. The total crude reaction mixture was chromatographed on 100 g silica gel. After eluting with 500 ml benzene, the column was eluted with 1 l. of 9:1 benzene–ether, to obtain 2·43 g pure **23** (86%, based on **20**). The analytical sample was collected by preparative VPC on the aforementioned column (retention time 38 min at 200°, He flow 55 ml/min). NMR in CCl_4: δ 1·01 (Me), δ 2·97 (OMe), and δ 3·24 (CH_2OH, doublet, J = 6 c/s); IR in CCl_4: ν_{max} 3650, 3400, 1080 cm^{-1}. (Found: C, 73·18; H, 11·63. Calc. for $C_{13}H_{24}O_2$: C, 73·33; H, 11·43%).

4aβ-*Methyl*-8aα-*methoxydecahydronaphth*-3α-*oic acid* (**24**)

Over the course of several hr, 6 ml Jones oxidant[28] was added to a soln of 2·43 g of **23** in 100 ml 80% aq acetone. After oxidation was complete, 250 ml sat NaCl aq was added and the resulting 2-phase mixture was extracted 4 times with ether. The ether extracts were combined and thrice extracted with dil KOH aq. After layering the basic soln with fresh ether, the aqueous phase was carefully acidified with dil H_2SO_4 aq and then saturated with NaCl. The layers were separated and the aqueous phase was extracted 4 times with ether. The combined ether extracts were dried and evaporated, giving 1·96 g of slightly damp solid. Sublimation of this material (100° at 20 μ) afforded 1·50 g of **24**, m.p. 118–126°. Recrystallization from hexane raised the m.p. to 126–127·4°. NMR in $CHCl_3$: δ 1·03 (Me), δ 2·92 (OMe). IR in CCl_4: ν_{max} 3500–2400 (COOH), 1705 (C=O) and 1080 cm^{-1}. (Found: C, 68·97; H, 9·77. Calc. for $C_{13}H_{22}O_3$: C, 68·75; H, 9·82%).

3α-*Acetyl*-4aβ-*methyl*-8aα-*methoxydecahydronapthalene* (**25**)

To a soln of 227 mg of **24** in 15 ml ether was added 2 ml of 1·3M MeLi in ether. After refluxing for 1 hr, the reaction mixture was cooled, diluted with ether and 10 ml water was added. The ether layer was separated, dried and evaporated, to yield 200 mg almost pure **25**. The analytical sample was collected by preparative VPC on the aforementioned column (retention time, 55 min at 180°, He flow 55 ml/min). NMR in CCl_4: δ 1·02 (Me), δ 1·95 (COMe) and δ 3·00 (OMe); IR in CCl_4: ν_{max} 1710, 1080 cm^{-1}. (Found: C, 75·31; H, 10·72. Calc. for $C_{14}H_{24}O_2$: C, 75·00; H, 10·71%).

4aβ-*Methyl*-8aα-*methoxydecahydronaphth*-3α-*yl acetate* (**26**)

A soln of 950 mg of **25** (approximately 90% pure, as judged by its NMR spectrum) and 1·90 g of 85% *m*-chloroperbenzoic acid in 100 ml CH_2Cl_2 was refluxed for 64 hr. After cooling, the soln was washed with dil KOH aq, dried and evaporated to yield 890 mg of **26**. Analytically pure material was obtained by preparative VPC (retention time, 21 min at 200°, He flow 50 ml/min). NMR in CCl_4: δ 1·04 (Me). δ 1·91 (OAc), and δ 3·06 (OMe), δ 4·85 ($W^{\frac{1}{2}}$ = 25 c/s, axial proton at C_3);[27] IR in CCl_4: ν_{max} 1735, 1240 and 1080 cm^{-1}. (Found: C, 70·31; H, 10·33. Calc. for $C_{14}H_{24}O_3$: C, 70·00; H, 10·00%).

4aβ-*Methyl*-8aα-*methoxydecahydronaphth*-3α-*ol* (**27**)

To a soln of 500 mg LAH in 20 ml ether was added 285 mg of **26** in 30 ml ether. The reaction mixture was stirred at room temp for 16 hr and then quenched by the dropwise addition of 3 ml 10% KOH aq. After stirring the resulting mixture for a few min, the solid was removed by filtration and washed with ether. The combined ether solns were evaporated, affording 190 mg (83%) of **27**. NMR in CCl_4: δ 0·99 (Me), δ 2·98 (OMe), and δ 3·65 (C_3—H, $W^{\frac{1}{2}}$ 20 c/s, axial);[27] IR in CCl_4: ν_{max} 3600, 3400 and 1080 cm^{-1}.

To 510 mg of **27** in 20 ml acetone, at 0°, was added 0·75 ml Jones reagent.[28] After the oxidation was complete, 75 ml of sat NaCl aq was added and the 2-phase soln was extracted with ether. The combined ether extracts were washed with sat NaCl aq containing a small amount of KOH. After drying over $MgSO_4$, the ethereal soln was evaporated to afford 400 mg 4aβ-methyl-8aα-methoxy-1,4,4a,5,6,7,8,8a-octahydronaphthalen-3(2H)-one. NMR in CCl_4: δ 0·95 (Me), δ 3·15 (OMe); IR in CCl_4: ν_{max} 1710,

080 cm^{-1}), characterized as its semicarbazone, m.p. 220–222·5° after recrystallization from aq MeOH. Found: C, 61·61; H, 9·21; N, 16·71. Calc. for $C_{13}H_{23}O_2N_3$: C, 61·66; H, 9·09; 16·60%).

Attempted Wolff-Kishner reduction of this semicarbazone dissolved in diethylene glycol afforded only traces of **29**.

4aβ-Methyl-8aα-methoxydecahydronaphth-3α-yl p-toluenesulfonate (**28**)

A soln of 190 mg of **27** and 190 mg *p*-toluenesulfonyl chloride in 10 ml dry pyridine was kept at room temp for 3 hr, then stored overnight at 5°. The soln was then poured into 50 ml water and the resulting mixture extracted with CH_2Cl_2. The extracts were dried and evaporated at room temp under a stream of N_2. There was obtained 265 mg of a semi-solid mass. Crystallization from EtOAc–hexane gave a total of 167 mg of crystalline tosylate in 2 crops. Recrystallization from the same solvent yielded analytically pure material, m.p. 106–108°. NMR in CCl_4: δ 0·96 (Me), δ 2·30 (ArMe), δ 2·90 (OMe), δ 7·18 and δ 7·64 (Aromatic protons, doublets, J = 8 c/s); IR in CCl_4: ν_{max} 1590, 1485 and 1085 cm^{-1}. (Found: C, 64·49; H, 7·97. Calc. for $C_{19}H_{28}O_4S$: C, 64·75; H, 8·01%).

Methyl 4aβ-methyldecahydronaphth-8aα-yl ether (**29**)

a. *From p-toluenesulfonate* **28**. To a soln of 58 mg of pure **28** in 20 ml dry ether was added 200 mg LAH. The mixture was refluxed for a total of 18·5 hr. After cooling, 20 ml ether was added, followed by 1·5 ml 10% KOH aq. The resulting mixture was stirred for 1 hr, then filtered. The collected solid was washed with ether and the ether layers were combined, dried and evaporated. There was obtained 30 mg of semi-solid which was purified by preparative VPC (5 ft × 0·25 in SF-96 on Chromosorb W at 118°, He flow 50 ml/min, retention time 37 min). There was obtained in this manner 4 mg of pure **29**. The IR spectrum of this material was superimposable upon the spectrum of authentic **29**, prepared as outlined below. The *cis*-isomer of **29** was also prepared and was shown to have a different IR spectrum (*vide infra*). The low yield in this experiment is largely due to inefficient collection because of the high volatility of this material. A similar run on less pure tosylate afforded a higher yield of **29**.

b. *From 4aβ-methyldecahydronaphth-8aα-ol* (**30**). To 1·00 g of NaH suspension (59·4% NaH), which had been washed with dry benzene, was added 40 ml 1,2-dimethoxyethane and a soln of 115 mg of **30**[23] in 10 ml dimethoxyethane. After heating to reflux, 10 ml MeI was added and the mixture was refluxed for 16 hr, then cooled and diluted with 300 ml pentane. The mixture was filtered and the filtrate was evaporated to yield 230 mg material which was extracted with 15 ml hexane. The filtered hexane soln was evaporated to leave an oil, which was purified by preparative VPC. There was obtained 25 mg of **30**, m.p. 84–88°, which was recrystallized from aq MeOH to afford material, m.p. 89–90°. (Found: C, 79·14; H, 12·44. Calc. for $C_{12}H_{22}O$: C, 79·12; H, 12·09%). NMR in CCl_4: δ 1·00 (Me), δ 3·01 (OMe); IR in CCl_4: ν_{max} 1085 cm^{-1}.

Methyl 4aβ-methyldecahydronaphth-8aβ-yl ether (cis-**29**)

This methyl ether was prepared from the *cis*-decalol[23] in a manner strictly analogous to that reported above for the synthesis of **29** from **30**. The analytically pure material (liquid) was obtained by preparative VPC on the aforementioned UCON column. NMR in CCl_4: δ 0·90 (Me), δ 3·02 (OMe); IR in CCl_4: ν_{max} 1085 cm^{-1}. The spectra of this material are distinctly different from those of the *trans*-isomer **29**. (Found: C, 79·24; H, 12·30. Calc. for $C_{12}H_{22}O$: C, 79·12; H, 12·09%).

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