Total Synthesis of (±)-Copaene and (±)-Ylangene. A General Method for the Synthesis of Tricyclo[4.4.0.0^{2,7}]decanes[1,2]

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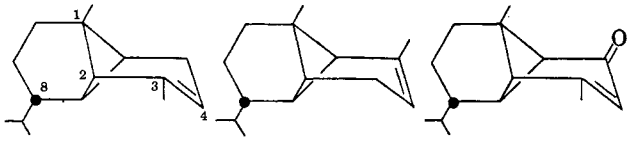
Abstract: A total synthesis of (±)-copaene (**1**) and (±)-ylangene (**2**) is described. The key reaction, base-catalyzed cyclization of the keto tosylate **36**, has also been applied to the related compounds **5, 35, 47,** and **48** and apparently constitutes a general method for the construction of tricyclo[4.4.0.0^{2,7}]decanes.

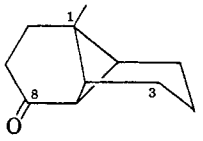
The naturally occurring sesquiterpenoids copaene (**1**),[4] ylangene (**2**),[5] and mustakone (**3**)[4b] have been shown to possess the unusual tricyclo[4.4.0.0^{2,7}]decane ring system.[6,7] An interest in the total synthesis of



1 **2** **3**

compounds **1–3**, prompted by the novel nuclear skeleton of these materials, led us to examine possible synthetic routes to 1-methyltricyclo[4.4.0.0^{2,7}]decanes. We here describe our investigations in this area, which have led to the development of an efficient method for the elaboration of this type of compound, culminating in the total synthesis of (±)-copaene and (±)-ylangene.

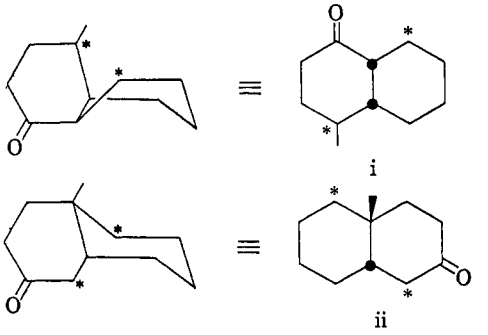
As a model for the more complicated 1-methyltricyclo[4.4.0.0^{2,7}]decanes which we eventually wished to synthesize, we chose 1-methyltricyclo[4.4.0.0^{2,7}]decan-8-one (**4**), which appeared ideally suitable from several



4

standpoints. Compound **4** is properly functionalized at the site where an isopropyl moiety must be introduced for the synthesis of compounds **1–3** and could thus be used in exploratory work on this phase of our projected synthesis. There appeared to be several possible routes to **4** from readily available synthetic intermediates, which could conceivably be modified in such a manner as to allow for the additional functionality necessary to introduce the C_3-methyl group and the $\Delta^{3,4}$ unsaturation inherent in **1** and **2**.

Inspection of compound **4** reveals that fission of either the C_1–C_2 bond or the C_2–C_7 bond leads to a *cis*-decalone (i or ii). Hence, the reverse of this process,



i

ii

namely, the cyclization of a suitably activated *cis*-decalone, recommends itself as a plausible mode for the production of **4**. Since decalones of the gross type ii are in general more easily preparable than those of type i, and since the former type of compound offers the additional advantage of having the carbonyl group adjacent to one terminus of the proposed bridging bond, we turned our immediate attention to the preparation of a derivative of ii with which to test our hypothesis.

The substrate for our exploratory experiments, the keto tosylate **5**, was synthesized by the following sequence of reactions. Selective borohydride reduction[8] of the readily available Wieland–Miescher ketone **6**[9] yields the oily ketol **7**, which has previously been converted, by a somewhat laborious method, to the *cis*-ketol **8**.[8] Compound **8** reacts with *p*-toluenesulfonyl chloride in pyridine to afford the desired keto tosylate **5**. A superior route to compound **5** became available when it was found that the unsaturated keto tosylate **9**, prepared from the ketol **7** in the normal manner, gives mainly (but not entirely) the highly crystalline *cis*-keto tosylate **5** upon hydrogenation in the presence of palladized strontium carbonate. Using this latter method, compound **5** can be obtained in 45–55% over-all yield from the diketone **6** (see Scheme I).

Compound **5** was found to react readily with potassium *t*-butoxide in *t*-butyl alcohol, affording a mixture of the desired tricyclic ketone **4** and its condensation product, the hexacyclic enone **10**, from which **4** could be isolated in 52% yield. Compound **10** was obtained,

(1) Preliminary communications of various portions of this work have appeared: (a) C. H. Heathcock, *Tetrahedron Letters*, 2043 (1966); (b) C. H. Heathcock, *J. Am. Chem. Soc.*, **88**, 4110 (1966).

(2) This work was supported by a grant from the Petroleum Research Fund, administered by the American Chemical Society (Grant No. 2381-A1).

(3) National Institutes of Health Predoctoral Fellow, 1965–1967.

(4) (a) P. de Mayo, R. E. Williams, G. Büchi, and S. H. Feairheller, *Tetrahedron*, **21**, 619 (1965); (b) V. H. Kapadia, B. A. Nagasampagi, V. G. Naik, and S. Dev, *ibid.*, **21**, 607 (1965).

(5) O. Motl, V. Herout, and F. Sorm, *Tetrahedron Letters*, 451 (1965).

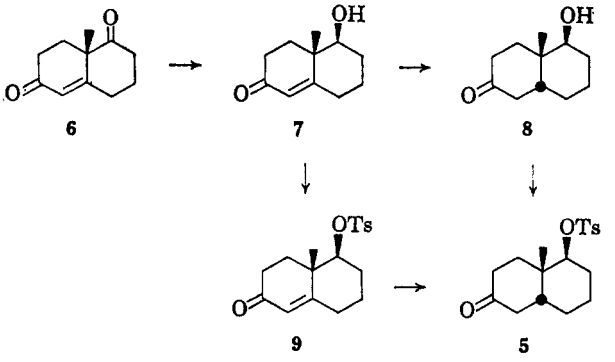
(6) For a suggested system of nomenclature for the copane sesquiterpenoids, see ref lb, footnote 4.

(7) Considerable confusion has existed in the literature concerning the identification of copaene and ylangene in various sources. This situation has now been largely clarified and will be reported upon in a forthcoming communication (R. Teranishi and C. H. Heathcock).

(8) C. B. C. Boyce and J. S. Whitehurst, *J. Chem. Soc.*, 2680 (1960).

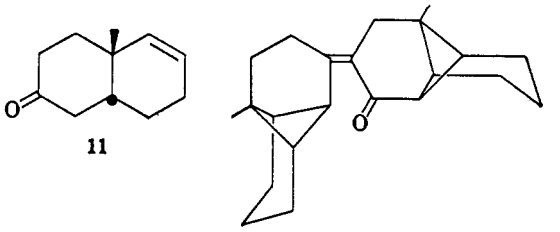
(9) (a) P. Wieland and K. Miescher, *Helv. Chim. Acta*, **33**, 2215 (1950); (b) S. Ramachandran and M. S. Newman, *Org. Syn.*, **41**, 38 (1961).

Scheme I



6 7 8 9 5

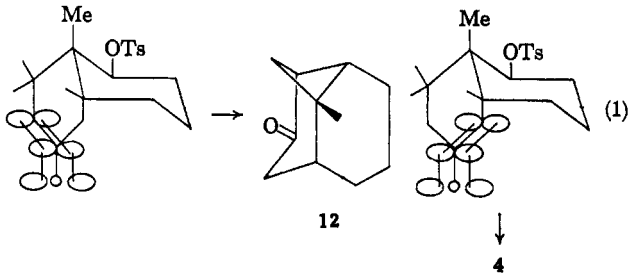
as a 50:50 mixture of the geometrical double bond isomers, even when keto tosylate **5** was present in 10% excess over the base. When an excess of base was used, compound **10** was the sole isolable product of the reaction. Treatment of **5** with 1 equiv of methylsulfinyl



11 10

carbanion in dimethyl sulfoxide[10] smoothly converted it to the tricyclic ketone **4** without the production of **10**. The product of this reaction is usually contaminated with variable amounts (2–5%) of the unsaturated ketone **11**, from direct dehydrotosylation of **5**.

A priori, there are two tricyclic ketones which might be formed from the self-alkylation of compound **5**, since there are two different enolate anions derivable from this ketone. We considered the alternative formulation (**12**) an unlikely one for our tricyclic ketone on mechanistic grounds. An examination of Dreiding stereomodels shows that the π orbital of the enolate which would lead to **12** is approximately orthoganol to the line of departure of the tosylate group, with that portion of the orbital associated with C_3 being on the same side of C_5 as the tosylate. The analogous orbital in the enolate leading to **4** is disposed directly to the rear of the tosylate-bearing carbon and is oriented at an angle of approximately 65° to the line of departure of this group (eq 1).

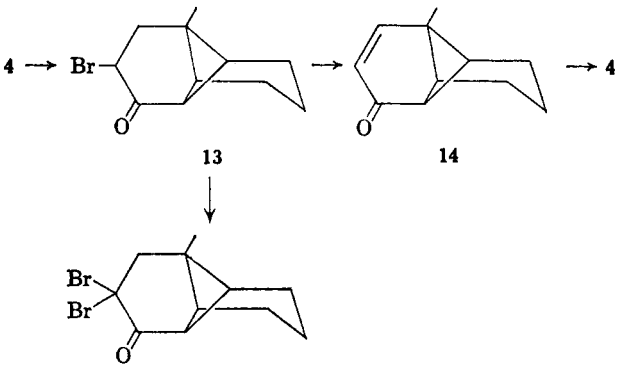


(1)

12 4

Nmr of the tricyclic ketone gave confirmatory evidence for this view. The angular proton adjacent to the carbonyl group was found as a sharp singlet at τ 7.40. In structure **4**, the dihedral angle between the C_7–H bond and both adjacent C–H bonds is 90°, and hence this proton should be only weakly coupled to its neighbors.[11] In the alternative structure **12**, the relevant angles are 30, 30, and 90°, and therefore the analogous proton should be appreciably coupled to two of its neighbors.[11]

In order to rigorously eliminate structure **12** from further consideration, we envisioned the conversion of the tricyclic ketone into an α,β-unsaturated ketone. Since no α,β-unsaturated ketones derived from **12** are geometrically capable of existence, such a transformation would eliminate this formulation. Our anticipations were realized when the α-bromo ketone **13** was dehydrobrominated with collidine to yield the enone **14**, which may be converted back to compound **4** by catalytic hydrogenation.[12]



13 14 15

The bromination of compound **4** is noteworthy, in that this ketone undergoes acid-catalyzed bromination more slowly than the bromo ketone **13**. Thus, when compound **4** is treated with 1 equiv of bromine in glacial acetic acid containing a catalytic amount of hydrogen bromide, and the reaction is quenched immediately, there is obtained a mixture of bromo ketone **13** and dibromo ketone **15** in a ratio of 2:1. If the reaction is allowed to proceed for several hours at room temperature after all the bromine is consumed, bromo ketone **13** is obtained in nearly quantitative yield. Dibromo ketone **15** may be obtained in high purity by a similar reaction utilizing 2 equiv of bromine.

The next synthetic problem facing us was that of converting the carbonyl group at C_8 into an isopropyl group. We anticipated several problems in this connection. Molecular models indicate that C_8 is expected to be relatively inaccessible on steric grounds. In addition, compound **4** might be more acidic than a normal cyclohexanone, due to the relief of the bowstern H–H interaction which occurs in enolization.

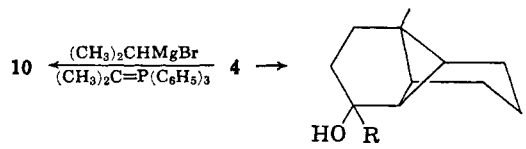
We were not surprised, then, to find that treatment of compound **4** with isopropylmagnesium bromide in ether leads only to a poor yield of the aldol dimer **10**, with none of the isopropylcarbinol **16** being produced. Similarly, isopr ylidinetriphenylphosphorane in either dimethyl sulfoxide or ether led only to the dimer **10**. Even isopropyllithium in pentane caused enolization of **4** to the extent of approximately 50%, the remainder of the product being the carbinol **16**. However, in the hydrocarbon solvent, aldolization did not occur, and

(10) E. J. Corey and M. Chaykovsky, *J. Am. Chem. Soc.*, **87**, 1345 (1965).

(11) M. Karplus, *J. Chem. Phys.*, **30**, 11 (1959).

(12) A conclusive proof of the structure of **4** has now been provided by an X-ray crystallographic analysis of the bromo ketone **13**; D. H. Templeton and David St. Clair, unpublished work.

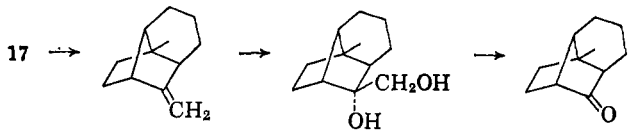
by repeating the alkylation several times, a good overall conversion of **4** to **16** could be achieved.



16, R = $(CH_3)_2CH$
17, R = CH_3

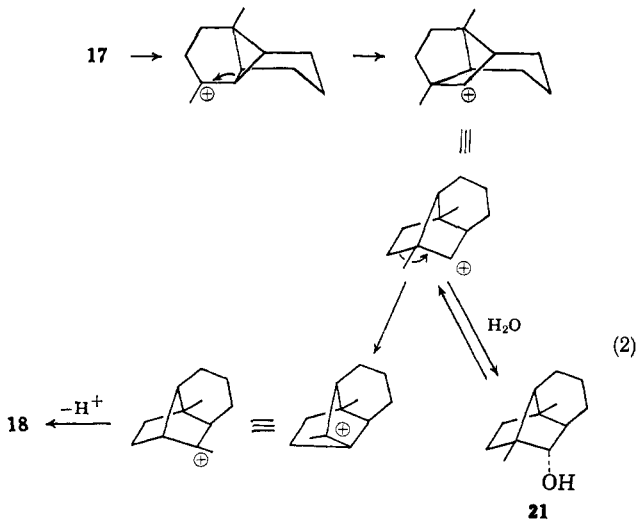
It was now necessary to remove the tertiary hydroxyl by dehydration. Since compound **16** is a cyclobutyl carbinol of the pinol type, it seemed likely that direct acid-catalyzed dehydration would lead to rearranged products. In order to test this point, the methyl carbinol **17**, prepared from **4** by four successive alkylations with methyllithium, was dehydrated in a two-phase system (pentane–50% sulfuric acid). The product of the reaction was an olefin, to which we have assigned structure **18** on the following grounds.

The presence of an exocyclic methylene group was apparent from both the infrared and nuclear magnetic resonance spectra of the hydrocarbon. Compound **18** reacts with osmium tetroxide to afford a crystalline diol (**19**), which is cleaved by periodic acid to the ketone **20**, shown to be a cyclopentanone by its infrared spectrum ($\nu_{C=O}$ at 1750 cm^{-1}).



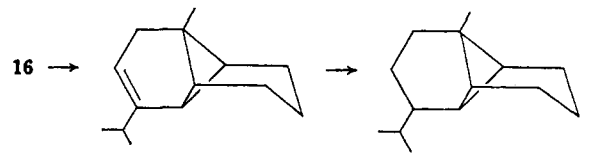
18 **19** **20**

A reasonable mechanistic path (eq 2), involving two Wagner–Meerwein shifts, may be invoked for the formation of **18** from **17**. This hypothesis is strengthened by the observation that during the course of the reaction, a rearranged alcohol gradually accumulates and then disappears. We have assigned structure **21** to this rearranged alcohol.



21 (2)

Since it was clear that direct dehydration would not suffice to bring about the desired transformation of carbinol **16**, we utilized a method less likely to involve rearrangement. Treatment of **16** with phosphorus oxychloride in pyridine gave mainly the olefin **22**. Catalytic hydrogenation of **22** then afforded (±)-norcopane (**23**).

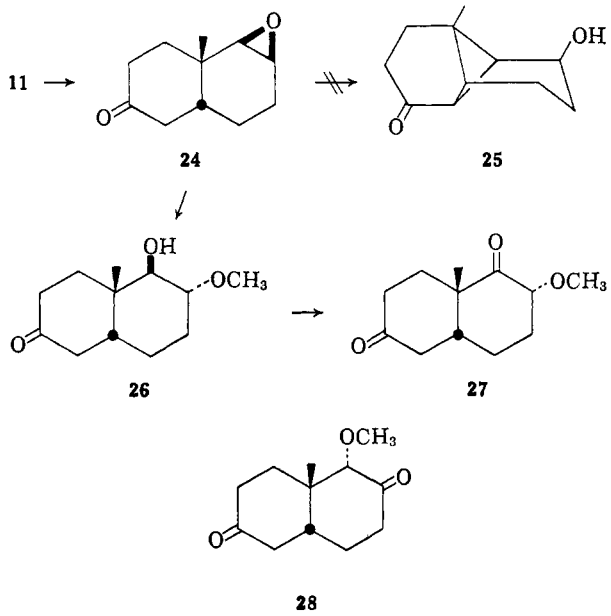


22 **23**

In order for the present tricyclo[4.4.0.$0^{2,7}$]decane synthesis to be useful for the preparation of compounds **1–3**, there is a need for functionality in the other cyclohexane ring of **23**. An attractive intermediate for this purpose appeared to be the *cis*-octalone **11**, which we had already encountered as a by-product in the cyclization of tosylate **5** (*vide supra*).

It was found that compound **1** can be prepared in high purity by direct dehydrotosylation of **5** with refluxing pyridine. Oxidation of **11** with *m*-chloroperbenzoic acid in chloroform led to the epoxide **24**, contaminated with lactones formed by Baeyer–Villiger oxidation of the ketone. Extensive purification afforded the crystalline oxide **24** in 40–45% yield. The stereochemistry of the oxirane ring is assigned on the basis of the well-known propensity of *cis*-decalins to suffer attack from the convex side.

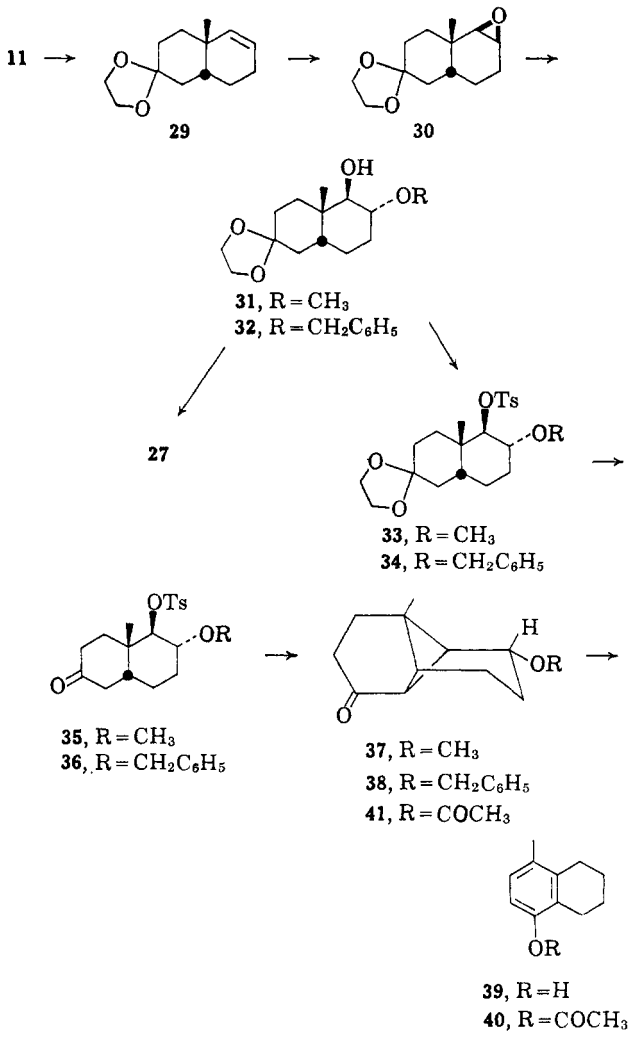
Many attempts to cause the keto epoxide **24** to undergo base-catalyzed cyclization to the tricyclic ketol **25** failed. However, we observed that **24** reacts smoothly with methanolic sodium methoxide to afford the methoxy alcohol **26**. The placement of the methoxyl group in **26** was confirmed by the finding that the compound may be oxidized to the dione **27**, whose nuclear magnetic resonance spectrum is clearly incompatible with the alternative structure **28**.



24 **25** **26** **27** **28**

Compound **26** appeared to be a solution to our problem, since the derived tosylate would contain the essential elements necessary for cyclization to a tricyclic methoxy ketone. However, the problem of Baeyer–Villiger oxidation in the transformation of **11** to **24** was troublesome, so steps were taken to circumvent this difficulty.

Ketalization of **11** yields the crystalline dioxolane **29**, which was oxidized in high yield to the oxide **30**. Compound **30** reacted with methanolic sodium methoxide in the expected manner to afford the methoxy alcohol **31**, which like **26** was oxidized, with concomitant hydrolysis to the dione **27**. Alcohol **31** reacted with *p*-toluenesulfonyl chloride in pyridine to afford the tosylate **33**, which was deketalized with sulfuric acid in aqueous acetone to give the methoxy keto tosylate **35**. Compound **35** reacted with methylsulfinyl carbanion in dimethyl sulfoxide to yield the tricyclic methoxy ketone **37**. The over-all yield for the ten steps from dione **6** to ketone **37** was 13%.



It should be noted here that the alkoxy group in **35** serves a purpose beyond that of adding functionality to the second ring of the tricyclic ketone. Since the tosylate **35** now contains no β-hydrogens *trans* to the tosylate moiety, the sole observable side reaction accompanying the conversion of **5** to **4** (β-dehydrotosylation) is eliminated (*vide supra*).

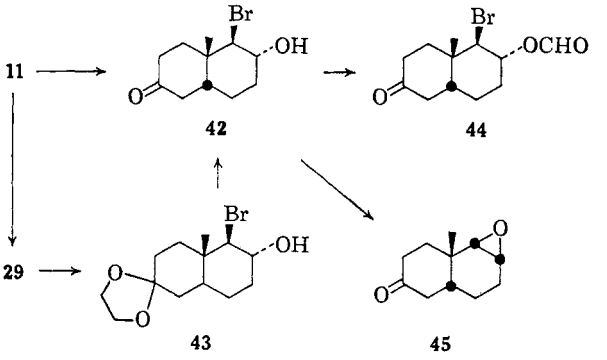
We had anticipated that the methoxyl group in **37** could eventually be cleaved by hydrogen bromide in acetic acid to generate a hydroxyl at that position, which could then be transformed by conventional methods in such a manner as to introduce the olefinic methyl group of copaene. We were led to this expectation by the observation of Burwell, *et al.*,[13] who found that optically active methyl *sec*-butyl ether is transformed by the above reagent to *sec*-butyl acetate of retained configuration. However, the fact that compound **37** is a cyclobutylcarbinyl ether apparently mitigates against this possibility, for when **37** was treated with 1 *N* hydrogen bromide in glacial acetic acid, under conditions sufficiently vigorous to cause any change to occur, the only products obtained were the phenol **39** and its corresponding acetate **40**.

Since the conjugate acid of **37** apparently dissociates with concomitant ring opening, in preference to displacement on the methyl group by bromide, we sought to prepare an analog of **37** in which the hydroxyl was protected by a more easily removable group. An obvious candidate was the corresponding benzyl ether. We then repeated the above sequence of reactions, converting the oxidodioxolane **30**, *via* intermediates **32**, **34**, and **36**, into the tricyclic benzyl ether **38**.

Compound **38** proved to be more amenable to dealkylation, undergoing cleavage to the acetoxy ketone **41** in 55% yield when treated with 1 *N* hydrogen bromide in glacial acetic acid at room temperature.

Although we had shown that additionally functionalized intermediates of the type **41** can be prepared by this method, a more direct route was desirable. To this end, we considered the following possibility. Since electrophilic attack on the double bond of either **11** or **29** occurs from the side *cis* to the angular methyl group, and since opening of the epoxide ring in both **24** and **30** occurs at the less hindered carbon, these olefins should form bromohydrins with the proper steric and structural features for further elaboration into compounds of the type **41**.

Our predictions were confirmed when it was found that both **11** and **29** react with N-bromosuccinimide in water to yield the derived bromohydrins **42** and **43**. Compound **43** could be conveniently deketalized by sulfuric acid in aqueous acetone to afford **42**.

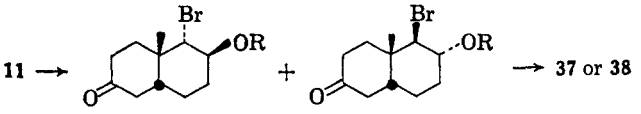


Attempts to prepare a tetrahydropyranyl ether from **42** failed. However, dissolution of this compound in anhydrous formic acid led to the production of the crystalline formate **44**. Attempts to cyclize the bromoformate **44** with methylsulfinyl carbanion in dimethyl sulfoxide or with triphenylmethylpotassium in ether led only to the formation of the keto epoxide **45**, which could also be prepared by direct cyclization of the bromohydrin **42**.

The problem was solved by the finding that octalone **11** reacts with N-bromosuccinimide in methanol to give the bromomethyl ether **47**, contaminated by a small amount of the isomeric adduct **46**. Compound **47** reacts with methylsulfinyl carbanion in dimethyl sulf-

(13) R. L. Burwell, Jr., L. M. Elkin, and L. G. Maury, *J. Am. Chem. Soc.*, 73, 2428 (1951).

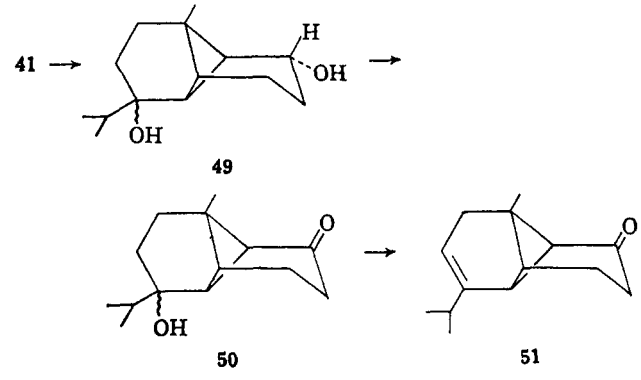
oxide to afford the tricyclic keto ether **37**, thus making this intermediate available in a much shorter route than that previously developed.



46, R = CH_3 **47**, R = CH_3
48, R = $CH_2C_6H_5$

Similar results were obtained when olefin **11** was treated with N-bromosuccinimide in benzyl alcohol. The product of this reaction is a mixture of bromobenzyl ether **48**, the corresponding dibenzyl ketal and benzyl enol ethers. However, after mild acid hydrolysis of the mixture, **48** may be obtained in reasonable yield. Normal cyclization of **48** then affords the tricyclic benzyl ether **38**.

At this point we were in a position to introduce the requisite isopropyl moiety into the molecule. Four successive treatments of the acetoxy ketone **41** with excess isopropyllithium gave the diol **49** as a mixture of C_8 epimers. This mixture was oxidized, after the method of Jones,[14] to the corresponding mixture of stereoisomeric ketols **50**, which was dehydrated, with phosphorus oxychloride in pyridine, to give the tricyclic unsaturated ketone **51**. The over-all yield for the three steps, in which no intermediates were purified, was 17%.



We were now at a juncture in our synthesis at which we were forced to concern ourselves with the sole stereochemical feature of the copaene and ylangene molecules. Catalytic saturation of the C_8 olefinic linkage leads to either of the natural configurations, depending on which side of the molecule is preferentially adsorbed to the catalyst surface.

Our initial experiments were done on the unsaturated alcohol **52**, obtained by treatment of **51** with methyllithium. Hydrogenation of **52** in ethyl acetate over 5% palladized carbon gave a mixture of the isomeric alcohols **53** and **54**. Dehydration of the mixture, again with phosphorus oxychloride in pyridine, yielded a 50:50 mixture of (±)-copaene (**1**) and (±)-ylangene (**2**), identified by comparison of their infrared spectra with those of authentic natural materials (see Scheme II and Experimental Section).

Direct hydrogenation of **51**, in ethyl acetate or methanol, gave a mixture of the saturated ketones **55** and **56**, in a ratio of 71:29. The major isomer, **55**, was converted, by methyllithium, into the carbinol **53** which was dehydrated to give (±)-ylangene (**2**). Ketone **56** was similarly converted, *via* carbinol **54**, into (±)-copaene (**1**). Hydrogenation of **51** in hexane gave a mixture of **55** and **56** in a ratio of 43:57.

Inspection of structure **51** shows that, save for the carbonyl group, the molecule contains a plane of symmetry, which passes through the plane of the double bond. Thus, any stereospecificity in the hydrogenation of **51** or derivatives thereof must arise through the influence of the carbonyl group or other groups which may be attached to C_3. Any group at that position could conceivably influence the stereochemistry of hydrogenation in two ways: by steric effect or by bonding to the catalyst surface. The former effect leads to the ylangene stereochemistry, the latter to copaene stereochemistry.

Hydrogenation of **51** in hexane gave a slight excess of copaene stereochemistry at C_8. In polar solvents which may compete with the carbonyl group of **51** for the catalyst surface, the steric effect of the group overcomes its bonding ability and the major product has the ylangene stereochemistry. However, in these same solvents, the alcohol **52** gives a 50:50 mixture of the two products. Since the combined size of the methyl and hydroxyl groups must be greater than that of a carbonyl group, we must conclude that the hydroxyl bonds to the catalyst much more effectively than does a carbonyl.

We were led by this analysis to prepare and hydrogenate the unsaturated alcohol **57**. Compound **57** was obtained by sodium borohydride reduction of the unsaturated ketone **51**. After oxidation of the hydrogenation mixture, we obtained a mixture of the saturated ketones **55** and **56** in a ratio of 9:91. Thus, by a judicious choice of hydrogenation substrates and conditions, the present synthesis can be made stereoselective for either copaene or ylangene.

Experimental Section

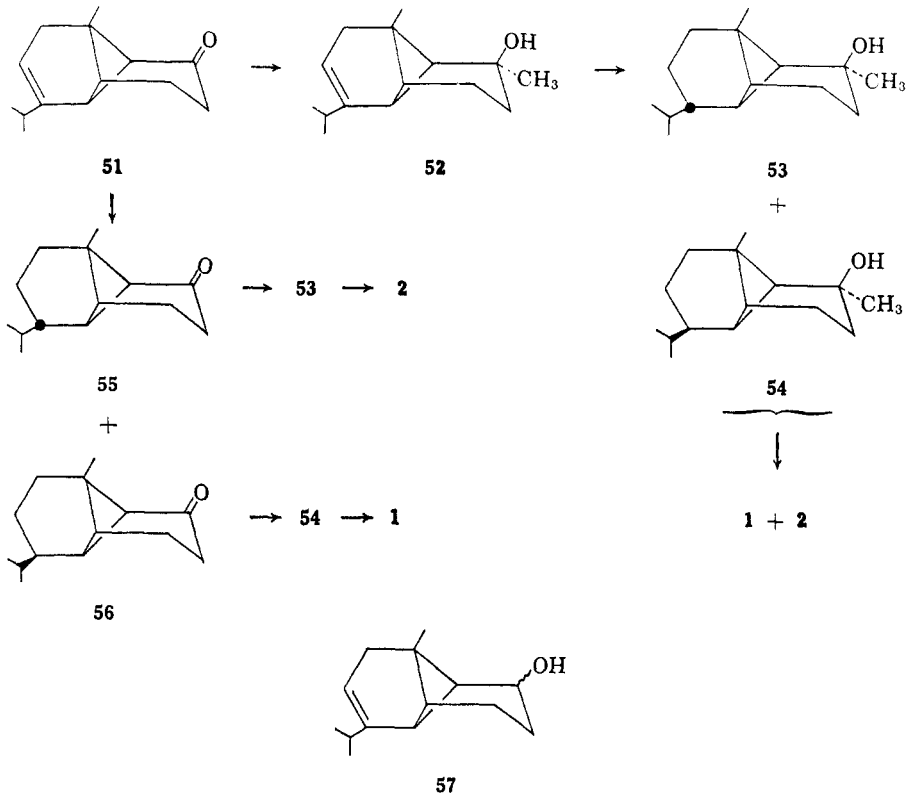
General Procedures. Proton magnetic resonance spectra were taken on a Varian A-60 spectrometer. Chemical shifts are relative to internal tetramethylsilane and are given on the τ scale. Infrared spectra were taken on a Perkin-Elmer 237 grating spectrometer. Spectra were determined in carbon tetrachloride unless otherwise indicated. Elemental analyses were performed by the Microanalytical Laboratory, operated by the Department of Chemistry, University of California, Berkeley, Calif.

4aβ-Methyl-4,4a,5,6,7,8-hexahydronaphth-5β-ol-2(3H)-one (7). To a solution of 178 g (1.0 mole) of 4a-methyl-4,4a,7,8-tetrahydronaphthalene-2,5(3H,6H)-dione (**6**) in 1350 ml of absolute ethanol at 0° was added dropwise a solution of 10.4 g of sodium borohydride in 2250 ml of ethanol. The addition required 4 hr. The purple solution was stirred in the cold for an additional hour, then neutralized by the addition of 25 ml of glacial acetic acid. The solvents were then evaporated *in vacuo* on the steam bath to yield a semisolid mass which was dissolved in 1000 ml of chloroform. The combined aqueous washes were extracted with 100 ml of chloroform which was added to the original organic layer. The combined chloroform layers were washed with saturated sodium chloride solution, dried over anhydrous magnesium sulfate, and evaporated to afford 179 g of crude ketol **7** as a viscous yellow oil.

4aβ-Methyl-4,4a,5,6,7,8-hexahydronaphth-5β-ol-2(3H)-one *p*-Toluenesulfonate (9). The crude ketol **7** was dissolved in 600 ml of anhydrous pyridine and added to a solution of 191 g (1.0 mole of freshly recrystallized *p*-toluenesulfonyl chloride in 400 ml of pyridine. The red solution was kept at room temperature for 18 hr, then poured into 2.5 l. of ice–water. The mixture was extracted with chloroform (500, 250, and 250 ml). The organic extracts were washed with water (two 250-ml portions), 10% sulfuric acid (cold, three 1-l. portions), water (500 ml), and saturated sodium chloride solution (500 ml). After drying the solution over anhydrous magnesium sulfate, it was evaporated *in vacuo* to yield 245 g of a viscous brown

(14) K. Bowden, I. M. Heilbron, E. R. H. Jones, and B. C. L. Weedon, *J. Chem. Soc.*, 39 (1946).

Scheme II



oil which solidified on cooling. A small portion of the material was recrystallized several times from ethyl acetate–pentane to afford the analytical specimen, melting at 117–118°.

Anal. Calcd for $C_{18}H_{22}SO_4$: C, 64.65; H, 6.64; S, 9.58. Found: C, 64.51, 64.62; H, 6.51, 6.58; S, 9.28.

4aβ-Methyl-3,4,4a,5,6,7,8,8aβ-octahydronaphth-5β-ol-2(1H)-one *p*-Toluenesulfonate (5). The crude unsaturated keto tosylate **9** (254 g) was dissolved in 1 l. of ethyl acetate, and the resulting solution was divided into three portions. Each aliquot was hydrogenated in a Parr apparatus with 5.0 g of 10% Pd–$SrCO_3$ at an initial hydrogen pressure of 50 psi. The individual hydrogenation runs required from 2 to 3 hr; the total hydrogen uptake was 0.84 mole. The catalyst was removed by filtration, and the combined filtrates were concentrated to *ca.* 500 ml. Pentane (700 ml) was added, and the solution was cooled to −20°. The white crystals of *cis*-keto tosylate (**5**) were collected by filtration and air-dried. The yield of material melting at 134–139° was 172 g (51% yield based on the dione **6**). This material was sufficiently pure to use in subsequent reactions. In a number of essentially identical runs, the over-all yield of *cis*-keto tosylate **5** ranged from 45 to 55%.

A portion of the crude *cis*-keto tosylate **5** was recrystallized several times from ethyl acetate–pentane to obtain the analytical sample, mp 139.5–140.5°. In subsequent runs, material melting as high as 142–143° was obtained.

Anal. Calcd for $C_{18}H_{24}SO_4$: C, 64.26; H, 7.19. Found: C, 64.53; H, 7.03.

Compound **4** displays infrared bands at 1715, 1600, 1500, 1200, and 1180 cm^{-1}. This material was identical, by infrared spectrum and mixture melting point, with a sample prepared by tosylation of 4aβ-methyl-3,4,4a,5,6,7,8,8aβ-octahydronaphth-5β-ol-2(1H)-one (**8**), prepared by the method of Boyce and Whitehurst.[8]

4aβ-Methyl-3,4,4a,7,8,8aβ-hexahydronaphthalen-2(1H)-one (11). A solution of 137 g of the *cis*-keto tosylate **5** in 1 l. of pyridine was refluxed under nitrogen for 22 hr. The solution was concentrated *in vacuo* on the steam bath to a semisolid mass, which was dissolved in 300 ml of chloroform and washed with water (two 200-ml portions), 10% hydrochloric acid (three 150-ml portions), and saturated sodium chloride solution (200 ml). After drying the solution, it was concentrated *in vacuo* to a brown oil which was fractionated through a 23-plate, spinning-band column. The yield of pure ketone **11**, bp 65° (0.15 mm), was 49.7 g (74%). In other runs, beginning with 20–70 g of tosylate **5**, the yield of compound **11** ranged from 82 to 97%. One run, utilizing 519 g of **5**, gave a 70% yield of **11**. It was found that the crude olefin was of sufficient purity to directly ketalize, as outlined below, without distillation. The compound shows infrared bands at 1715, 1650, 715, and 685 cm^{-1}.

Anal. Calcd for $C_{11}H_{16}O$: C, 80.43; H, 9.82. mol wt, 164. Found: C, 80.11; H, 9.49; mol wt (mass spectral), 164.

A yellow 2,4-dinitrophenylhydrazone derivative was prepared by the method of Shriner, Fuson, and Curtin.[15] After three recrystallizations from 95% ethanol, the derivative had mp 103.5–104.5°.

Anal. Calcd for $C_{17}H_{20}N_4O_4$: C, 59.27; H, 5.86; N, 16.28. Found: C, 59.50; H, 5.95; N, 16.21.

1-Methyltricyclo[4.4.0.0^{2,7}]decan-8-one (4). A solution of methylsulfinyl carbanion in dimethyl sulfoxide was prepared by the method of Corey and Chaykovsky[10] from 6.55 g of 55% sodium hydride emulsion (washed with pentane) and 100 ml of dimethyl sulfoxide. To the rapidly stirred solution, under nitrogen at 75°, was added in one portion, a solution of 50 g (0.149 mole) of the *cis*-keto tosylate **5** in 250 ml of warm dimethyl sulfoxide. The dark orange solution was stirred at 75° under nitrogen for 3 hr, then poured into 1 l. of ice–water. The mixture was extracted with ether (four 200-ml portions), and the combined ether extracts were washed with water (four 100-ml portions) and dried over anhydrous magnesium sulfate. Evaporation of the ether left 22.11 g of cloudy yellow oil which was distilled under reduced pressure. There was obtained 16.12 g of clear distillate, boiling at 73.5–75.5° (0.8 mm), 66%. Vapor phase chromatographic analysis (6 ft × 0.25 in. NPGS on Chromosorb, 220°, helium flow 100 cc/min) revealed that the material was 97% pure, the sole contaminant being olefin **11**, identified by comparison of its infrared spectrum with that of the authentic material (*vide supra*). The analytical sample was obtained by preparative gas chromatography.

Anal. Calcd for $C_{11}H_{16}O$: C, 80.43; H, 9.82. Found: C, 80.67; H, 9.87.

The infrared spectrum shows bands at 1715, 1475, 1418, 1380, 1250, and 1030 cm^{-1}. The nmr spectrum shows a three-proton singlet (methyl group) at τ 9.00, a one-proton singlet at τ 7.47 (C_7 bridgehead proton), and a two-proton multiplet centered at approximately τ 7.65 (C_9 protons). At both 60 and 100 Mc, the τ 7.47 band displays a ^{13}C satellite with $J = 146 \pm 2$ cps.

The dideuterated analog of ketone **4** was prepared by heating a mixture of 250 μl of the ketone and 10 ml of 1.4 *N* sodium deuterioxide in deuterium oxide in a sealed tube at 100° for 45 hr. The deuterated ketone was purified by preparative vpc on a 10 ft ×

(15) R. I. Shriner, R. C. Fuson, and D. Y. Curtin, "The Systematic Identification of Organic Compounds," John Wiley and Sons, Inc., New York, N. Y., 1956.

$^3/_8$ in. Carbowax 20 M column, previously equilibrated with 2.0 ml of 99.83% D_2O at 220°. Mass spectral analysis revealed that the material contained 1.47 atoms of deuterium per molecule, distributed in the following manner: 7% d_0, 38% d_1, 55% d_2, and 0% d_3. The infrared spectra of **4** and **4**-d_2 differ significantly in the fingerprint region. The 1420-cm^{-1} band is not present in **4**-d_2. The nmr spectrum of **4**-d_2 does not show the two-proton multiplet at τ 7.65.

The 2,4-dinitrophenylhydrazone derivative of **4**, melted at 174–175.5° after four recrystallizations from 95% ethanol.[15]

Anal. Calcd for $C_{17}H_{20}N_4O_4$: C, 59.27; H, 5.86; N, 16.28. Found: C, 58.98; H, 5.72; N, 16.23.

The semicarbazone derivative of **4** melted at 238–239° after two recrystallizations from 95% ethanol.[15]

Anal. Calcd for $C_{12}H_{19}N_3O$: C, 65.13; H, 8.65; N, 18.99. Found: C, 65.47; H, 8.44 N, 19.08.

The benzylidine derivative of **4** was prepared by adding 1.0 g of potassium hydroxide to a solution of 2.0 g of **4** and 2.0 g of benzaldehyde in 20 ml of 95% ethanol. After 15 min, the product separated as an oil, which soon crystallized. The resulting solid was recrystallized from aqueous ethanol to afford 2.78 g of the benzal ketone as white plates, mp 110–111° (87% of the theoretical).

Anal. Calcd for $C_{18}H_{20}O$: C, 85.67; H, 7.99. Found: C, 85.66; H, 7.89.

To a solution of 1.092 g of ketone **4** in 20 ml of absolute ethanol was added 0.250 g of sodium borohydride. The solution was stirred at room temperature for 19 hr. Water (30 ml) was added, and the resulting mixture was extracted with ether (three 20-ml portions). The ether extracts were combined, washed with water (two 20-ml portions) and saturated sodium chloride solution (50 ml), and dried over anhydrous magnesium sulfate. Evaporation of the solvent left a clear oil which solidified on standing. The yield of 1-methyltricyclo[4.4.0.$0^{2,7}$]decan-8-ol, melting at 55–58°, was 1.055 g (95%). Sublimation at 45° (0.2 min) gave 0.945 g, mp 59–61°.

Anal. Cacld for $C_{11}H_{18}O$: C, 79.47; H, 10.91. Found: C, 79.23; H, 10.96.

The infrared spectrum shows bands at 3600, 3300, 1470, 1070, 1030, 1000, and 970 cm^{-1}. The nmr spectrum displays a three-proton singlet at τ 9.17 (methyl), a broad one-proton triplet at τ 6.04 (C_8 hydrogen), and a one-proton doublet (J = 2.5 cps) at τ 7.95 (C_7 bridgehead proton).

The *p*-nitrobenzoate derivative of 1-methyltricyclo[4.4.0.$0^{2,7}$]-decan-8-ol was prepared by treating the alcohol with *p*-nitrobenzoyl chloride in pyridine. After the normal work-up, the ester was obtained as white crystals, mp 67–70°. The analytical sample, melting at 78–78.5°, was obtained by two recrystallizations from pentane

Anal. Calcd for $C_{18}H_{21}NO_4$: C, 68.56; H, 6.71; N, 4.44. Found: C, 68.30; H, 6.81; N, 4.56.

Compound **4** was also obtained from keto tosylate **5** in the following manner. To a solution of 3.60 g of potassium *t*-butoxide (27 mmoles) in 50 ml of anhydrous *t*-butyl alcohol was added 10.08 g (30 mmoles) of compound **5**. The solution was refluxed under nitrogen for 3 hr, then poured into 300 ml of ice-cold water. The resulting mixture was extracted with ether (two 100-ml portions). After washing the ether extracts with water (three 100-ml portions) and drying over magnesium sulfate, the solvent was evaporated to afford 4.64 g of brown oil. Distillation of this oil in a Hickman still gave 2.58 g (52%) of the tricyclic ketone **4**, identical by infrared and nmr with the material prepared by cyclization of **5** with methylsulfinyl carbanion in dimethyl sulfoxide (*vide supra*).

The distillation residue, 1.60 g, was identical by infrared and nmr with a sample of the hexacyclic enone **10**, prepared as outlined below.

9-(1′-Methyltricyclo[4.4.0.$0^{2,7}$]dec-8′-ylidine)-1-methyltricyclo-[4.4.0.$0^{2,7}$]decan-8-one (10). A solution of 2.72 g of the tricyclic ketone **4** and 2.0 g of potassium *t*-butoxide in 100 ml of *t*-butyl alcohol was refluxed under nitrogen for 16 hr. After this period, the reddish solution was poured into 300 ml of cold water and the resulting mixture extracted with ether (two 100-ml portions). The ether extracts were washed well with water (five 100-ml portions) and dried. Evaporation of the ether gave 2.23 g of a viscous yellow oil. A portion of this material (1.88 g) was chromatographed on 100 g of Woelm neutral alumina, activity I, to obtain 0.99 g of the enone **10** as a 1:1 mixture of the double-bond stereoisomers. The material was a clear, water-white glass which displayed thixotropic properties. An analytical sample was obtained by sublimation at 80° (0.2 mm).

Anal. Calcd for $C_{22}H_{30}O$: C, 85.09; H, 9.74. Found: C, 84.77; H, 9.85.

The mass spectrum of **10** contains a prominent molecular ion peak at *m/e* 310. The ultraviolet spectrum (95% ethanol) has λ_{max} 270 (log ϵ 4.18). The infrared spectrum has bands at 1678, 1595, 1475, 1447, 1379, 1351, 1339, 1307, 1299, 1242, 1205, 1186, 1163, 1124, 1075, 1047, and 1020 cm^{-1}. The nmr spectrum of the 1:1 mixture has the following features: a three-proton singlet at τ 9.12, a pair of 1.5-proton singlets at τ 9.00 and 9.02, a one-proton singlet at τ 7.48, and a pair of 0.5-proton singlets at τ 5.65 and 7.24. Apparently one of the angular methyl groups and one of the C_7-hydrogens has the same chemical shift in either isomer. The other angular methyl and the other C_7-hydrogen have different chemical shifts in the two isomers.

Compound **10** was also obtained when ketone **4** was treated with isopropylmagnesium bromide in ether, or with isopropylidinetriphenylphosphorane in either dimethyl sulfoxide or ether.

1-Methyl-9-bromotricyclo[4.4.0.$0^{2,7}$]decan-8-one (13) and 1-Methyl-9,9-dibromotricyclo[4.4.0.$0^{2,7}$]decan-8-one (15). To a solution of 3.28 g of ketone **4** in 50 ml of glacial acetic acid containing 0.5 ml of 48% hydrobromic acid, was added a solution of 3.20 g of bromine in 50 ml of acetic acid (dropwise over a period of 20 min). After the addition was completed, the yellow solution was stirred at room temperature for 4 hr, then poured into 500 ml of ice–water and the resulting solid collected by filtration. After air drying, the pale yellow solid weighed 4.610 g (95% of the theoretical) and had an nmr spectrum identical with that of the analytically pure material. One recrystallization from hexane afforded 3.027 g of dense white prisms, mp 93–95°. The analytical specimen was obtained from a similar run. After three recrystallizations from pentane the material melted at 94–95°.

Anal. Calcd for $C_{11}H_{15}BrO$: C, 54.33; H, 6.22; Br, 32.87. Found: C, 54.48; H, 5.99; Br, 32.74.

The infrared spectrum shows prominent bands at 1735, 1475, 1220, and 1020 cm^{-1}. The nmr spectrum contains the following distinctive features: a three-proton singlet at τ 8.98 (angular methyl), a one-proton singlet at τ 7.17 (C_7–H), a one-proton double doublet at τ 5.38 (C_9–H, the X portion of an ABX system, with J_{AX} = 10 cps and J_{BX} = 7 cps), a one-proton double doublet at τ 7.3 (C_{10}–H, the A portion of an ABX system, with J_{AX} = 10 cps and J_{AB} = 14.5 cps), and a one-proton double doublet at τ 7.90 (C_{10}–H, the B portion of an ABX system, with J_{BX} = 7 cps and J_{AB} = 14.5 cps, partially obscured by the broad envelope due to the protons on C_2, C_3, and C_4).

In a run similar to that described above, the reaction was quenched immediately after all the bromine had been added. The resulting tan solid weighed 2.58 g and melted at 69–85°. Analysis by nmr showed that the product consisted of a mixture of bromo ketone and dibromo ketone (*vide infra*) in a ratio of 2:1. Four recrystallizations of this material from hexane gave 0.50 g of pure dibromo ketone **15**, mp 125–126°.

The dibromo ketone was more conveniently prepared by the following method. To a solution of 1.64 g of ketone **4** in 25 ml of glacial acetic acid was added a solution of 3.20 g of bromine in 25 ml of acetic acid containing six drops of 48% hydrobromic acid. The solution was stirred at room temperature for 15 min, then poured into 300 ml of ice-cold water, containing 50 mg of sodium sulfite. The product was filtered and air-dried, whereupon there was obtained 2.716 g of gray solid, mp 106–116°. Two recrystallizations from hexane gave the pure material, mp 125–126°.

Anal. Calcd for $C_{11}H_{14}Br_2O$: C, 41.02; H, 4.38; Br, 49.56. Found: C, 41.01; H, 4.31; Br, 49.68.

The infrared spectrum has prominent bands at 1735, 1470, 1370, 1200, 1170, 1020, and 955 cm^{-1}. The nmr spectrum displays a three-proton singlet at τ 9.03 (angular methyl), a one-proton singlet at τ 7.00 (C_7–H), and a two-proton singlet at τ 6.61 (C_9–H).

1-Methyltricyclo[4.4.0.$0^{2,7}$]dec-9-ene (14). A solution of 1.205 g of bromo ketone **13** in 10 ml of γ-collidine (bp 169–170°) was refluxed for 90 min. After cooling to room temperature, the resulting dark mixture was poured into 40 ml of water, and the resulting mixture was extracted with ether (two 25-ml portions). The combined ether layers were washed with water (20 ml), 10% sulfuric acid (three 35-ml portions), water (50 ml), and saturated sodium chloride (25 ml) and dried over anhydrous magnesium sulfate. The product was 0.457 g of brown oil. This material was purified by preparative vpc (6 ft × 0.25 in. SE-30 on Chromosorb at 200°) to obtain 0.149 g of pure enone.

Anal. Calcd for $C_{11}H_{14}O$: C, 81.45; H, 8.70. Found: C, 80.96; H, 8.52; mol wt (mass spectral), 162.

The ultraviolet spectrum of **14** has λ_{max} 252 mμ (log ϵ 3.48) and strong end absorption (log ϵ_{210} 3.71). The infrared shows bands at 1700, 1475, 1380, 1250, 1235, 830, and 670 cm^{-1}. The nmr

spectrum shows a three-proton singlet at τ 8.91 (methyl), a one-proton doublet at τ 2.69 (J = 9 cps, C_{10}–H), a one-proton double doublet at τ 4.3 (J = 9 and 2 cps, C_9–H), and a one-proton doublet at τ 7.33 (J = 2 cps).

The 2,4-dinitrophenylhydrazone derivative of **14**, melted at 164–168° after three recrystallizations from 95% ethanol.[15]

Anal. Calcd for $C_{17}H_{18}N_4O_4$: C, 59.64; H, 5.30; N, 16.37. Found: C, 58.97; H, 5.28; N, 16.75.

To a solution of 59.6 mg of enone **14** in 3.0 ml of ethyl acetate was added 16 mg of 5% palladium on charcoal. The mixture was hydrogenated at atmospheric pressure for 25 min. The catalyst was removed by filtration, and the solution was analyzed by vpc. The chromatogram showed a single component. From three 50-μl injections of the ethyl acetate solution, 1.8 mg of the product was collected for infrared analysis. The infrared spectrum was superimposable with that of authentic ketone **4**.

1-Methyl-8-isopropyltricyclo[4.4.0.0^{2,7}]decan-8-ol (16). To a refluxing solution of 820 mg of ketone **4**, in 20 ml of olefin-free hexane, under nitrogen, was added 10 ml of 1 *M* isopropyllithium in pentane. After 24 hr, 10 ml of water was added, and the layers were separated. The aqueous layer was extracted with 10 ml of ether which was added to the original organic layer. This solution was washed with saturated sodium chloride solution, dried, and evaporated to yield 926 mg of viscous yellow oil. Vpc analysis showed only 50% conversion to alcohol. The above procedure was repeated twice more, with the reaction times being 14 and 3.5 hr, respectively. The final product was 818 mg of viscous yellow oil, containing 10% unreacted ketone by vpc. This material was purified by preparative vpc (6 ft × 0.25 in. SE-30 on Chromosorb at 200°, helium flow 50 cc/min) to yield 333 mg of pure alcohol **16**.

Anal. Calcd for $C_{14}H_{24}O$: C, 80.71; H, 11.61. Found: C, 80.94; H, 11.42.

The infrared spectrum shows prominent peaks at 3600, 3450, 1470, 1395, 1370, 1040, 1015, 970, 945, and 920 cm^{-1}. The nmr spectrum displays a three-proton singlet at τ 9.18 (C_1 methyl), a six-proton doublet at τ 9.12 (J = 7 cps, isopropyl), and a one-proton singlet at τ 8.02 (C_7 hydrogen).

1-Methyl-8-isopropyltricyclo[4.4.0.0^{2,7}]dec-8-ene (22). To a solution of 128.5 mg of alcohol **16** in 1.0 ml of pyridine was added 0.25 ml of phosphorus oxychloride. The solution was warmed to 90° and then allowed to cool to room temperature. The partially crystalline mixture was mixed with 25 ml of ice–water and extracted with ether (three 30-ml portions). The combined ether extracts were washed with 5% hydrochloric acid (50 ml), 10% potassium carbonate solution (10 ml), and saturated sodium chloride solution (50 ml) and dried. Evaporation of solvent gave 99.4 mg of brown oil which was purified by preparative vpc (5 ft × 0.25 in. NPGS on Chromosorb at 168°, helium flow 60 cc/min). The material consisted of two components, in the relative amounts 3:1 with relative retention times of 1:2. The major product was olefin **22**. The minor product was not identified.

Anal. Calcd for $C_{14}H_{22}$: C, 88.35; H, 11.65. Found: C, 88.45; H, 11.45.

The infrared spectrum has bands at 3060, 1655, 1470, 1380, 1365, 1005, and 860 cm^{-1}. The nmr spectrum has a three-proton singlet at τ 9.09 (methyl), a six-proton doublet at τ 9.01 (J = 7 cps, isopropyl), and a one-proton multiplet at τ 4.91 (olefinic hydrogen). The three bridgehead protons appeared as an overlapping multiplet at τ 8.00.

1-Methyl-8-isopropyltricyclo[4.4.0.0^{2,7}]decane [Norcopane (23)]. To a solution of 35.6 mg of olefin **22** in 5 ml of hexane was added 13.2 mg of 5% palladium on charcoal. The mixture was hydrogenated for 3.5 hr at atmospheric pressure. The catalyst was removed and the solvent evaporated to yield 25.3 mg of clear, water-white liquid, homogenous on a 5 ft × 0.25 in. NPGS column at 165°. The analytical sample was obtained by preparative vpc on the above column.

Anal. Calcd for $C_{14}H_{24}$: C, 87.42; H, 12.58. Found: C, 87.43; H, 12.70.

The infrared spectrum shows peaks at 1475, 1470, 1385, and 1370 cm^{-1}. The nmr spectrum has a three-proton singlet at τ 9.18 (methyl) and a six-proton doublet at τ 9.10 (J = 7 cps, isopropyl).

1,8-Dimethyltricyclo[4.4.0.0^{2,7}]decan-8-ol (17). To a solution of 5.0 g of ketone **4** in 50 ml of ether was added 35 ml of 1.7 *M* methyllithium. After 4 hr at room temperature, 10 ml of water was added, and the layers were separated. The ether layer was washed with water (three 20-ml portions), dried, and evaporated. Inspection of the nmr spectrum of the mixture indicated that it consisted of 64% alcohol **17** and 36% of ketone **4**. The foregoing procedure was repeated twice more to afford 4.77 g of clear oil, containing greater than 95% alcohol. This liquid was distilled (1.0 mm) from an oil-jacketed flask (bath temperature, 100°) to give 3.91 g of water-white liquid which partially crystallized. Low-temperature crystallization from pentane gave 1.40 g of pure alcohol, mp 35–37°.

Anal. Calcd for $C_{12}H_{20}O$: C, 79.94; H, 11.18. Found: C, 79.70; H, 10.87.

The infrared spectrum has bands at 3600, 3400, 1475, 1370, 925, and 900 cm^{-1}. The nmr spectrum has bands at τ 9.17 (C_1-methyl, three-proton singlet), τ 8.82 (C_8-methyl, three-proton singlet), and τ 8.10 (C_7–H, one-proton singlet).

2-Methylene-8-methyltricyclo[5.3.0.0^{3,8}]decane (18). To a solution of 2.06 g of alcohol **17** in 100 ml of olefin-free pentane was added 50 ml of 50% sulfuric acid. The flask was stoppered and stirred at 20° for 15 hr. The pentane layer was removed, washed with water, dried, and evaporated to obtain 1.75 g of a pale yellow liquid with a highly camphoraceous odor. This material was distilled in a Hickman microstill to obtain 1.10 g of water-white olefin, bp 42–43° (1.0 mm). The analytical sample was obtained by preparative vpc on a 5 ft × 0.25 in. Carbowax 20 M column at 120°, helium flow, 50 cc/min.

Anal. Calcd for $C_{12}H_{18}$: C, 88.82; H, 11.28. Found: C, 88.99; H, 11.09.

The infrared spectrum contains prominent peaks at 2980, 1670, 1380, and 885 cm^{-1}. The nmr spectrum bands at τ 8.94 (three-proton singlet, angular methyl), τ 5.45 (one-proton broad multiplet, $W_{1/2}$ = 4.5 cps), and τ 5.20 (one-proton broadened doublet, J = 3 cps, $W_{1/2}$ of each line = 2.5 cps).

2-Hydroxy-2-hydroxymethyl-8-methyltricyclo[5.3.0.0^{3,8}]decane (19). To a solution of 500 mg of osmium tetroxide in 20 ml of benzene containing 0.5 ml of pyridine was added 400 mg of olefin **18**. The black solution was kept at room temperature for 45 hr, then concentrated to a viscous oil on a rotary evaporator. The oil was dissolved in a solution of 1.0 g of potassium hydroxide and 1.0 g of mannitol in 65 ml of water. After being kept at room temperature for 4.5 hr, the alkaline solution was extracted with methylene chloride (two 50-ml portions). The extracts were washed with 25 ml of water and 100 ml of 5% hydrochloric acid, then dried over magnesium sulfate. Evaporation of the dried solution yielded 441 mg of brown oil which crystallized upon addition of pentane. The resulting mixture was filtered, and the crystals were washed with pentane and air-dried. There was obtained 235 mg of diol, mp 157–159°. The analytical sample, mp 163.5–164°, was obtained by recrystallization from acetone–pentane.

Anal. Calcd for $C_{12}H_{20}O_2$: C, 73.43; H, 10.27. Found: C, 73.50; H, 10.17.

The infrared spectrum has a broad band at 3400 cm^{-1}, and a richly detailed fingerprint region, with prominent bands at 1145, 1060, 1050, 1025, 1000, 980, 960, and 890 cm^{-1}. The nmr spectrum (in chloroform containing 10% pyridine) has bands at τ 9.17 (three-proton singlet, angular methyl), τ 6.18 (one-proton doublet, J = 10 cps), and τ 6.55 (one-proton doublet, J = 10 cps).

8-Methyltricyclo[5.3.0,0^{3,8}]decan-2-one (20). To a solution of 157 mg of diol **19**, in 5.0 ml of methanol, was added a solution of 450 mg of periodic acid (H_5IO_6) in 10 ml of water. After 20 hr at room temperature, the solution was extracted with ether (25 ml, two 15-ml portions). The ether extracts were washed with water, dried, and evaporated to afford 109 mg of the waxy ketone. Sublimation at 40° (2.0 mm) gave 100 mg of the ketone as waxy prisms, mp 151–152°. The analytical specimen, obtained by preparative vpc on a 5 ft × 0.25 in. NPGS column at 180°, melted at 161–162.5°.

Anal. Calcd for $C_{11}H_{16}O$: C, 80.44; H, 9.82. Found: C, 80.24; H, 9.78.

The infrared spectrum has bands at 1750, 1380, 1150, 980, and 965 cm^{-1}. No band appears at 1420 cm^{-1}. In the nmr spectrum, the angular methyl appears as a three-proton singlet at τ 8.83.

The 2,4-dinitrophenylhydrazone melted at 165–167° after three recrystallizations from 95% ethanol.[15]

Anal. Calcd for $C_{17}H_{20}N_4O_4$: C, 59.27; H, 5.86; N, 16.28. Found: C, 59.44; H, 5.81; N, 16.40.

4aβ-Methyl-5β,6β-oxido-3,4,4a,5,6,7,8,8aβ-octahydronaphthalen-2(1H)-one (24). To a rapidly stirring solution of 57.2 g of octalone **11** in 1500 ml of chloroform at 5°, was added dropwise over a period of 7 hr, a solution of 72.0 g of 85% *m*-chlorobenzoic acid in 800 ml of chloroform. The solution was kept at 5° for an additional 24 hr, then washed with 1 l. of 5% sodium hydroxide solution, 1 l. of water, and 300 ml of saturated sodium chloride solution. After drying over magnesium sulfate, the chloroform was evaporated to afford a slightly yellow oil, which was dissolved in 50 ml of petroleum ether (bp 100–110°) and cooled to −20°. Two crops of crystalline

epoxide, melting at 60–65° and weighing 15.35 g (24.5%), were collected in this manner. The mother liquors were concentrated to a viscous oil, which was distilled through a 23-plate, spinning-band column. Fraction 1, bp 56–72° (0.2 mm), weighed 3.07 g and was greater than 95% octalone **11**. Fraction 2, bp 74–77° (0.2 mm), weighed 3.11 g and contained 65% octalone **11**. Fractions 3–5, bp 73–77° (0.1 mm), weighed 25.55 g and contained an average of 75% of the epoxide **24**. These fractions were combined and dissolved in 25 ml of petroleum ether (bp 100–110°). An additional 8.11 g (12.9%) of crystalline epoxide, mp 63–65°, was deposited. The mother liquors were concentrated and once again fractionated to yield 11.0 g of liquid epoxide, of approximately 85% purity. This material yielded an additional 1.67 g (2.6%) of crystalline product, mp 62–65°. The total yield of crystalline epoxide **24** was 25.13 g (40%). A portion of this material was recrystallized twice from acetone–petroleum ether to afford the analytical sample, mp 67–68°.

Anal. Calcd for $C_{11}H_{16}O_2$: C, 73.29; H, 8.96. Found: C, 72.99; H, 8.95.

The infrared spectrum has prominent bands at 1720, 1475, 1464, 1451, 1435 1425, 1385, 1247, 1167, 1145, and 991 cm^{-1}. The nmr spectrum has a three-proton singlet at τ 8.67 (methyl), a one-proton doublet at τ 7.39 (J = 4 cps, C_5–H), and a one-proton multiplet at τ 6.96 (C_6–H). The mass spectrum displays a prominent molecular ion at *m/e* 180.

A portion of epoxy ketone **24** (196 mg) was reduced with 21.2 mg of sodium borohydride to a mixture of the corresponding epimeric alcohols, 4aβ-methyl-5β-6β-oxido-8aβ-decahydronaphth-2α- and -2β-ol; in a ratio of 2:1. The alcohols were separated for analysis by preparative vpc (10 ft × 0.25 in. SE-30 on Chromosorb at 180°). The major isomer melted at 125–127° and has distinctive bands in its infrared spectrum at 3600, 3420, 3005, 1228, 1170, 1100, 1055, 1038, 1000, and 970 cm^{-1}.

Anal. Calcd for $C_{11}H_{18}O_2$: C, 72.47; H, 9.95. Found: C, 72.60; H, 9.89.

The minor isomer was a liquid and has characteristic infrared absorptions at 3600, 3415, 2985, 1080, 1067, 1044, 1017, 995, 944, and 920 cm^{-1}.

Anal. Calcd for $C_{11}H_{18}O_2$: C, 72.47; H, 9.95. Found: C, 72.40; H, 9.93.

Both alcohols displayed substantial molecular ion peaks at *m/e* 182 in their mass spectra.

4aβ-Methyl-5β-hydroxy-6α-methoxy-3,4,4a,5,6,7,8,8aβ-octahydronaphthalen-2(1H)-one (26). A solution of 720 mg of epoxy ketone **24** in 5.0 ml of 1 *N* methanolic sodium methoxide was refluxed under nitrogen for 2.5 hr. The solution was concentrated to 3 ml by direct distillation and taken up in 25 ml of ether. Glacial acetic acid, 0.25 ml, was added dropwise, whereupon a gel formed. After adding 1.0 ml of water, the layers were separated and the ether layer was dried. Evaporation of the ether gave 806 mg of clear oil, which was chromatographed on 15 g of Woelm neutral alumina, activity I. Fractions 3 and 4, eluted with 2:1 pentane–ether, gave 353 mg of the methoxy alcohol **26** as a viscous, water-white oil. The material could not be induced to crystallize. The infrared spectrum (neat) has bands at 3472, 2820, 1706, 1120, 1101, 1079, and 770 cm^{-1}. This material was not further characterized, but was directly oxidized, by the method of Jones,[14] to the dione **27** (*vide infra*).

4aβ-Methyl-3,4,4a,7,8,8aβ-hexahydronaphthalen-2(1H)-one Ethylene Ketal (29). A mixture of 27.02 g of the octalone **11**, 30 g of ethylene glycol, and 2.0 g of *p*-toluenesulfonic acid monohydrate in 500 ml of benzene was refluxed under a water separator for 12 hr. The dark solution was washed with potassium carbonate solution, water, and saturated sodium chloride solution, then dried over magnesium sulfate. Evaporation of the benzene gave a brown oil which was distilled from an oil-jacketed flask [bath temperature 140° (0.5 mm)]. The distillate was a viscous, water-white liquid which solidified on cooling. This material was dissolved in 30 ml of pentane and cooled to −20°. Two crops of white prisms, totaling 24.46 g (72%) were obtained. The material melts at 34–36°. An analytical sample was obtained by preparative vapor phase chromatography on a 6 ft × 0.25 in. SE-30 column at 218°.

Anal. Calcd for $C_{13}H_{20}O_2$: C, 74.95; H, 9.68. Found: C, 74.97; H, 9.90.

The material shows infrared bands at 1105, 1093, 1075, 710, and 690 cm^{-1}. The mass spectrum contains a molecular ion peak at *m/e* 208.

The filtrate from the above crystallization was concentrated to an oil and again submitted to ketalizing conditions. In this manner there was obtained a further 3.5 g of ketal **29**. The total yield is thus 27.96 g (82%).

In subsequent runs, the crude ketal was directly epoxidized, without distillation. One run, beginning with 176 g of octalone **11**, 195 g of ethylene glycol, and 7 g of *p*-toluenesulfonic acid, gave 223 g of crude ketal, which contained less than 1% unreacted ketone, as judged by vpc.

4aβ-Methyl-5β,6β-oxido-3,4,4a,5,6,7,8,8aβ-octahydronaphthalen-2(1H)-one Ethylene Ketal (30). To a solution of 223 g of crude unsaturated ketal **29** in 1.5 l. of chloroform at 0°, (ice bath, vigorous mechanical stirring) was added dropwise a solution of 241 g of 85% *m*-chloroperbenzoic acid in 2.5 l. of chloroform. The addition required 3.5 hr. The solution was kept at 0° for an additional 3 hr and then at room temperature overnight. To the mixture was then added 500 ml of 20% aqueous sodium sulfite solution, and the heterogeneous mixture was stirred vigorously for 1 hr. The layers were separated, and the chloroform layer was washed with 1 l. of 10% sodium hydroxide and dried over anhydrous sodium sulfate. Evaporation of the chloroform gave a colorless, slightly cloudy residue which was distilled from an oil-jacketed flask [bath temperature 140–170° (0.2 mm)]. The distillate was 231 g of a water-white, viscous oil. The material was dissolved in 200 ml of hexane and cooled to −20°. Two crops of white crystals, weighing 183.5 g and melting from 38 to 41°, were obtained. The total yield was 77% of the theoretical. From a similar run, a portion of the first crop of crystals, mp 41.5–43°, was sublimed at 35° (0.2 mm) to obtain the analytical specimen, mp 42–43.5°.

Anal. Calcd for $C_{13}H_{20}O_3$: C, 69.62; H, 8.99. Found: C, 69.55; H, 8.72.

In subsequent runs, it was found that the liquid epoxide was of sufficient purity for further preparative use. The nmr spectrum contains bands at τ 8.92 (three-proton singlet, angular methyl), τ 7.47 (one-proton doublet, J = 4 cps, C_5–H), τ 6.98 (one-proton multiplet, C_6–H), and τ 6.20 (four-proton singlet, dioxolane methylenes).

4aβ-Methyl-5β-hydroxy-6α-methoxy-3,4,4a,5,6,7,8,8aβ-octahydronaphthalen-2(1H)-one Ethylene Ketal (31). A solution of 1.12 g of the ketal epoxide **30** in 10 ml of 1.0 *N* methanolic sodium methoxide solution was heated under reflux for 18 hr. The solution was then concentrated on a rotary evaporator to a foam which was dissolved in 10 ml of water and extracted with ether (20 and 10 ml). The ether solution was washed with saturated sodium chloride solution and dried over anhydrous sodium sulfate. Evaporation of the ether gave a viscous oil which solidified on scratching. The yield of material melting at 76–80° was 1.080 g (85%). From a similar run, an analytical sample was prepared by two recrystallizations from pentane. The pure material melts at 82–83°.

Anal. Calcd for $C_{14}H_{24}O_4$: C, 65.60; H, 9.44. Found: C, 65.77; H, 9.26.

The compound displays bands in its infrared spectrum at 3580, 3440, 2805, 1095, and 1060 cm^{-1}. The nmr spectrum contains bands at τ 9.08 (three-proton singlet, angular methyl), τ 6.67 (three-proton singlet, methoxyl), τ 6.40 (one-proton doublet, J = 9 cps, C_5–H), and τ 6.19 (four-proton singlet, dioxolane methylenes).

In larger scale runs, it was necessary to greatly prolong the base treatment in order to accomplish complete conversion of the epoxide to the methoxy alcohol. In a typical case, 16 g of epoxide **30** was refluxed in 150 ml of 1.0 *N* $NaOCH_3$–CH_3OH for 68 hr. The progress of the ring-opening reaction was conveniently monitored by thin layer chromatography on silica gel G using a solvent system 15% ethyl acetate in benzene. In one run, the product crystallized from pentane in two crystalline forms, dense prisms and slender needles. Both forms melted at 82–83°.

4aβ-Methyl-6-methoxy-3,4,4a,7,8,8aβ-hexahydronaphthalene-2,5-(1H,6H)-dione (27). To a solution of 1.0 g of compound **31**, in 40 ml of acetone at 0°, was added 2.0 ml of 8 *N* chromic acid solution (Jones reagent). After standing at 0° for 10 min, the mixture was poured into 100 ml of water. The aqueous solution was extracted with two 50-ml portions of chloroform. After washing the combined chloroform extracts with water, they were dried and evaporated. A yellow oil resulted, which was dissolved in 40 ml of hexane and cooled to −20°. The crystalline dione which separated weighed 598 mg and melted from 67 to 88°. Recrystallization from the same solvent raised the melting point to 87–88°. This material was identical by mixture melting point and infrared spectrum with that obtained from a similar oxidation of alcohol **26**. The analytical sample was obtained from the latter source and melted at 87–89°.

Anal. Calcd for $C_{12}H_{18}O_3$: C, 68.54; H, 8.63. Found: C, 68.36; H, 8.63.

The infrared spectrum contains bands at 2820, 1730 (with a shoulder at 1718), 1420, 1380, 1140, 1040, 1000, and 960 cm^{-1}. The nmr spectrum has a three-proton singlet at τ 8.7 (angular methyl), a three-proton singlet at τ 6.65 (methoxyl), and a broad multiplet centered at τ 6.20 (C_6–H).

The configuration of the methoxyl group is undetermined, since epimerization may have occurred during the oxidation. The alternative structural formulation, **28**, is excluded on the basis of the multiplicity of the band at τ 6.20 in the nmr spectrum of **27**.

4aβ-Methyl-5β-hydroxy-6α-methoxy-3,4,4a,5,6,7,8,8aβ-octahydronaphthalen-2(1H)-one Ethylene Ketal *p*-Toluenesulfonate (33). A solution containing 14.377 g (0.0562 mole) of methoxy alcohol **31** and 21.4 g of *p*-toluenesulfonyl chloride (0.112 mole) in 65 ml of pyridine was kept at 60–65° for 23 hr. The dark solution was poured into 250 ml of ice–water, and the resulting mixture was extracted with chloroform (150 ml, two 50-ml portions). The chloroform extract was washed with water (three 250-ml portions) and saturated sodium chloride solution (250 ml). After drying over anhydrous magnesium sulfate, the chloroform was evaporated to yield a tan solid. This solid was kept at 50° (1 mm) for 1 hr to remove residual pyridine. The yield of material melting at 145–154° was 21.10 g (92%). This material was of sufficient purity for further use. The analytical sample, melting at 159–160°, was prepared by three recrystallizations from ethyl acetate.

Anal. Calcd for $C_{21}H_{30}SO_6$: C, 61.44; H, 7.37. Found: C, 61.39; H, 7.19.

The infrared spectrum contains bands at 1600, 1500, 1370, 1220, 1190, 1180, 1095, 975, 940, and 670 cm^{-1}. The nmr spectrum has bands at τ 9.04 (three-proton singlet, angular methyl), τ 7.30 (three-proton singlet, methoxyl), τ 6.18 (four-proton broadened singlet, $W_{1/2}$ = 3 cps, dioxolane methylenes), and τ 5.31 (one-proton doublet, J = 9 cps, C_5–H), in addition to the resonances due to the *p*-toluenesulfonate group.

4aβ-Methyl-5β-hydroxy-6α-methoxy-3,4,4a,5,6,7,8,8aβ-octahydronaphthalen-2(1H)-one *p*-Toluenesulfonate (35). The crude ketal **33** (21.10 g) was dissolved in 200 ml of acetone at 50°. A solution of 36 ml of water and 4 ml of concentrated sulfuric acid was added, and the clear solution was kept at 50° for 45 min. The solution was then concentrated on a rotary evaporator to *ca.* 60 ml. The cold mixture was filtered, and the resulting white crystals were washed with 250 ml of cold water. The product was dried overnight (0.1 mm) to give 16.73 g of white needles, mp 174–176.5° (89%). The analytical sample, melting at 176–177°, was prepared by two recrystallizations from ethyl acetate.

Anal. Calcd for $C_{19}H_{26}SO_5$: C, 62.27; H, 7.15. Found: C, 62.03; H, 6.96.

The infrared spectrum contains peaks at 1715, 1600, 1500, 1380, 1370, 1185, 1180, 1110, 1095, 965, 940, and 665 cm^{-1}. The nmr spectrum (in chloroform) has bands at τ 8.92 (three-proton singlet, angular methyl), τ 7.10 (three-proton singlet, methoxyl), and τ 5.08 (two-proton doublet, J = 9 cps, C_5–H), in addition to the resonances of the *p*-toluenesulfonate group.

1-Methyl-3-*anti*-methoxytricyclo[4.4.0.0^{2,7}]decan-8-one (37). a. From Compound 35. A solution of methylsulfinyl carbanion in dimethyl sulfoxide was prepared by the method of Corey and Chaykovsky[10] from 2.18 g of 55% sodium hydride emulsion (washed with pentane) and 50 ml of dimethyl sulfoxide. To the solution, under nitrogen at 75°, was added a solution of 17.913 g of the methoxy keto tosylate **35** in 200 ml of dimethyl sulfoxide, preheated to 65°. The dark solution was stirred at 75° for 3 hr, cooled to room temperature and poured into 500 ml of water. The resulting mixture was extracted with ether (six 100-ml portions). The ether extracts were washed with water (two 100-ml portions) and saturated sodium chloride (100 ml), dried over anhydrous magnesium sulfate, and evaporated to obtain 8.605 g of yellow oil. This oil was distilled from an oil-jacketed flask (0.3 mm) and bath temperature of 130–145° to yield 6.391 g of water-white ketone (67%). The analytical sample was prepared by preparative vpc (10 ft × 0.25 in. SE-30 on Chromosorb at 200°).

Anal. Calcd for $C_{12}H_{18}O_2$: C, 74.19; H, 9.34. Found: C, 73.99; H, 9.09.

The infrared spectrum has bands at 2820, 1715, 1420, and 1100 cm^{-1}. The nmr spectrum has a three-proton singlet at τ 9.07 (methyl), a three-proton singlet at τ 6.80 (methoxyl), and a one-proton singlet at τ 7.40 (C_7–H).

The 2,4-dinitrophenylhydrazone derivative melted at 149–150° after four recrystallizations from ethanol at room temperature.[15] This derivative was orange. A bright yellow modification of this compound is obtained if the crystallization is conducted at −20°. The yellow form also melts at 149–150° when the oil bath is warmed from room temperature. If a sealed capillary containing the yellow form is inserted into the oil bath at 135°, the material immediately melts. The two forms gave similar analyses.

Anal. Calcd for $C_{18}H_{22}N_4O_5$: C, 57.79; H, 5.93; N, 14.98. Found (orange form): C, 58.07; H, 5.69; N, 15.12. Found (yellow form): N, 14.69.

b. From Compound 47. The above procedure was followed using 7.15 g of bromide **47**, adjusting the quantities of other reagents accordingly. After 1 hr, the reaction was worked up in the normal manner. Distillation of the crude product in a Hickman still gave 3.05 g of clear distillate (61%), identical in all respects with the material obtained from cyclization of tosylate **35**. The distillation residue afforded 150 mg of compound **46** (*vide infra*).

4aβ-Methyl-5β-hydroxy-6α-benzyloxy-3,4,4a,5,6,7,8,8aβ-octahydronaphthalen-2(1H)-one Ethylene Ketal (32). A mixture of 2.0 g of the ketal epoxide **30** and 10 ml of 1 *N* sodium benzyloxide in benzyl alcohol was sealed in a Pyrex tube and heated at 200° for 2 hr. The mixture was cooled to room temperature, and the semisolid residue was partitioned between water (50 ml) and ether (50 ml). The ether layer was washed with 50 ml of water and dried. Distillation of the ether at 100° and the benzyl alcohol at 120° (0.2 mm) left a viscous, pale yellow oil, 2.304 g, which was 90% pure, as judged by its nmr spectrum. This material was dissolved in 5 ml of hot ethyl acetate, and 50 ml of petroleum ether was added. After cooling overnight at −20°, 1.310 g of clear white prisms, mp 75–78°, were obtained by filtration. Two recrystallizations from the same solvent system raised the melting point to 79–80°.

Anal. Calcd for $C_{20}H_{28}O_4$: C, 72.26; H, 8.49. Found: C, 71.99; H, 8.33.

The infrared spectrum shows bands at 3600, 3420, 3070, 3040, 1600, 1500, 1095, and 697 cm^{-1}. The nmr spectrum has a five-proton singlet at τ 2.8, a two-proton AB system at τ 5.40, and τ 6.65 (J = 12 cps, benzyl CH_2), a four-proton singlet at τ 6.23 (dioxolane methylenes), and a three-proton singlet at τ 9.11 (methyl).

In subsequent, large-scale runs (up to 100 g of ketal **30**), the crude alcohol was used for conversion into its *p*-toluenesulfonate ester without further purification. In one such run, the over-all yield of crystalline *p*-toluenesulfonate **34**, mp 133–140°, was 76% of the theoretical for the two steps.

4aβ-Methyl-5β-hydroxy-6α-benzyloxy-3,4,4a,5,6,7,8,8aβ-octahydronaphthalen-2(1H)-one Ethylene Ketal, *p*-Toluenesulfonate (34). To a solution of 14.9 g of the alcohol **32** in 50 ml of pyridine was added 17 g of *p*-toluenesulfonyl chloride. The solution was kept at 65° for 17 hr, then poured into 250 ml of ice–water. Extraction of the mixture with chloroform (250 ml, two 100-ml portions) gave an organic solution which was washed with water (two 200-ml portions), dried, and evaporated to yield a semisolid. Removal of pyridine at 65° (0.5 mm) left a brown solid which was triturated with petroleum ether to afford 17.42 g of the tosylate, mp 140–143°. The petroleum ether filtrate, on concentration and cooling, gave 1.706 g of unreacted alcohol, mp 75–80°. An analytical specimen of the tosylate, mp 144.5–146°, was prepared by two recrystallizations from ethyl acetate.

Anal. Calcd for $C_{27}H_{34}SO_6$: C, 66.63; H, 7.04. Found: C, 66.58; H, 6.92.

The infrared spectrum shows bands at 3070, 3040, 1600, 1500, 1190, 1180, 940, 695, and 670 cm^{-1}. The nmr spectrum has a five-proton multiplet centered at approximately τ 2.95 (benzyl ring protons), a one-proton doublet at τ 5.12 (J = 9 cps, C_5–H), a two-proton AB system at τ 5.8 and 6.0 (J = 12 cps benzyl CH_2), a four-proton singlet at τ 6.17 (dioxolane methylenes), and a three-proton singlet at τ 9.03 (angular methyl), in addition to the resonances due to the *p*-toluenesulfonate group.

4aβ-Methyl-5β-hydroxy-6α-benzyloxy-3,4,4a,5,6,7,8,8aβ-octahydronaphthalen-2(1H)-one *p*-Toluenesulfonate (36). To a refluxing solution of 10.47 g of the ketal **34** in 100 ml of acetone was added a mixture of 18 ml of water and 2 ml of concentrated sulfuric acid. After 30 min at 65°, the solution was concentrated to 50 ml (reduced pressure) and poured into 100 ml of cold water. The resulting mixture was extracted with ether (100 ml, two 50-ml portions). The ether extracts were washed with water (three 100-ml portions), dried, and evaporated. The product was 9.843 g of clear white oil which crystallized on scratching under cold ethyl acetate. The resulting solid was recrystallized from ethyl acetate–petroleum ether (bp 30–60°) at −20°. The product, large white prisms, melting at 103–105°, weighed 8.055 g (85%). Two recrystallizations from the same solvent system afforded an analytical sample, mp 105–106°.

Anal. Calcd for $C_{25}H_{30}SO_4$: C, 67.84; H, 6.83. Found: C, 67.62; H, 6.70.

The infrared spectrum has bands at 3070, 3040, 1715, 1600, 1500, 1190, 1180, 970, 890, 875, 695, and 672 cm^{-1}. The nmr spectrum has a five-proton multiplet centered at approximately τ 2.9 (benzyl ring protons), a one-proton doublet at τ 5.11 (J = 8 cps, C_5–H), a two-proton AB system at τ 5.70 and 5.95 (J = 12 cps, benzyl methylenes), and a three-proton singlet at τ 8.98 (angular methyl), in addition to the resonances due to the *p*-toluenesulfonate group.

1-Methyl-*anti*-3-benzyloxytricyclo[4.4.0.0^{2,7}]decan-8-one (38). A solution of methylsulfinyl carbanion was prepared by the method of Corey and Chakovsky[10] from 9.45 g of 55% sodium hydride emulsion (washed with hexane) and 230 ml of dimethyl sulfoxide. To this solution, at 75°, under nitrogen, was added a solution of 95 g of keto tosylate **36** in 970 ml of dimethyl sulfoxide. The resulting brown solution was stirred at 75° for 140 min, then poured into 6 l. of ice-cold water. The resulting mixture was extracted with chloroform (1.5 l., two 1-l. portions, and 500 ml). The combined chloroform extracts were washed with water (two 3-l. portions), dried over magnesium sulfate, and evaporated at reduced pressure. The resulting brown oil was dissolved in 150 ml of ether, washed with water (three 50-ml portions) and saturated sodium chloride solution, and dried over magnesium sulfate. The dried ether solution was then decolorized with activated charcoal, filtered, and evaporated to yield 57.80 g of **38** as a colorless oil (96% of the theoretical). The material had an nmr spectrum identical with that of the analytical sample, which was obtained by evaporative distillation of a portion of the above material at 65° (0.1 mm).

Anal. Calcd for $C_{15}H_{22}O_2$: C, 79.96; H, 8.20. Found: C, 79.68; H, 8.00.

The infrared spectrum has bands at 1715, 1500, 1420, 1089, 1066, 1027, 726, and 694 cm^{-1}. The nmr spectrum has a five-proton singlet at τ 2.80 (benzyl ring protons), a two-proton singlet at τ 5.58 (benzyl methylene), a one-proton singlet at τ 7.30 (C_7–H), and a three-proton singlet at τ 9.10 (methyl).

A 2,4-dinitrophenylhydrazone derivative melted at 211–213° after two recrystallizations from 95% ethanol.[15]

Anal. Calcd for $C_{24}H_{26}N_4O_5$: C, 63.99; H, 5.82; N, 12.44. Found: C, 63.86; H, 5.78; N, 12.69.

Compound **38** was also obtained, in 50% yield, from a similar cyclization of the bromobenzyl ether **48** (*vide infra*).

1-Methyl-3-*anti*-acetoxytricyclo[4.4.0.0^{2,7}]decan-8-one (41). A solution of 32.43 g of benzyl ether **38** in 200 ml of glacial acetic acid, 1 *N* in anhydrous hydrogen bromide, was kept at room temperature for 19 hr. The resulting red solution was diluted with 800 ml of ether and washed with ice-cold 4% sodium hydroxide solution (four 1-l. portions). The combined alkaline solutions were extracted with 200 ml of ether. The combined ether extracts were washed with saturated sodium chloride solution, dried over magnesium sulfate, and evaporated. After the removal of the benzyl bromide at 65° (0.3 mm), there was obtained 30.18 g of viscous, brown oil which was chromatographed on 500 g of Woelm neutral alumina, activity II. The column was prepared in hexane, and the eluent was hexane (ten 100-ml fractions) and 1:1 hexane–ether (15 200-ml fractions). Fractions 1–10 contained benzyl bromide, fractions 11–14 contained 1.44 g of yellow oil, and fractions 15–25 contained 15.61 g (57%) of crystalline keto acetate **41**, mp 51–60°. The analytical sample, obtained from a similar run, after two recrystallizations from pentane and sublimation at 65° (0.5 mm), melted at 67–68°.

Anal. Calcd for $C_{13}H_{18}O_3$: C, 70.24; H, 8.16. Found: C, 69.99; H, 7.97.

The infrared spectrum has bands at 1739, 1712, 1245, and 1020 cm^{-1}. The nmr spectrum has a three-proton singlet at τ 8.97 (angular methyl), a three-proton singlet at τ 8.04 (acetate methyl), a one-proton singlet at τ 7.31 (C_7–H), and a one-proton triplet at τ 4.81 (J = 7.5 cps, C_3–H).

Acetolysis of the Methyl Ether 37. A solution of 1.0 g of compound **37** in 20 ml of 1 *N* hydrogen bromide in glacial acetic acid was kept at 45° for 10 hr. The dark solution was concentrated under reduced pressure to a brown oil. The nmr and infrared spectra of this material suggested that it consisted of a mixture of the phenol **39** and the corresponding acetate **40**. The product from a similar run was hydrolyzed with methanolic potassium hydroxide. The resulting crude phenol was purified by peparative vpc (5 ft × 0.25 in. SE-30 at 175°) to afford a sample of pure **39**, mp 88–89° (lit. 87.5–88.5°,[16] 87–88°,[17] 88–89°[18,19]).

The nmr and infrared spectra of **39** are in full accord with its formulation.

4aβ-Methyl-5β-bromo-6α-hydroxy-3,4,4a,5,6,7,8,8aβ-octahydronaphthalen-2(1H)-one Ethylene Ketal (43). To a solution of 6.58 g of the unsaturated ketal **29** in a mixture of 10 ml of tetrahydrofuran and 30 ml of water, at 0°, was added 5.83 g of N-bromosuccinimide. After 10 min, the ice bath was removed, and the slurry was stirred at room temperature for 7 hr. At this time there were two phases present. The mixture was extracted with ether (three 30-ml portions), and the combined ether extracts were dried and evaporated. The crude product was chromatographed on 35 g of Woelm neutral alumina, activity III. The bromohydrin was eluted with 750 ml of benzene. Evaporation of the benzene gave a residue which was recrystallized from pentane–benzene. Two crops of crystalline bromohydrin, weighing 6.81 g (71%) were obtained. After recrystallization from 2:1 pentane–benzene, the material melted at 106.5–108°.

Anal. Calcd for $C_{13}H_{21}BrO_3$: C, 51.35; H, 6.96; Br, 26.28. Found: C, 51.46; H, 6.78; Br, 26.12.

The infrared spectrum (in chloroform) has bands at 3600, 3470, 1370, 1170, 1085, 1035, 940, 870, and 810 cm^{-1}. The nmr spectrum (in chloroform) has three-proton singlets at τ 8.86 (angular methyl) and τ 6.07 (methoxyl) and a one-proton doublet at τ 5.56 (J = 10 cps, C_5–H).

4aβ-Methyl-5β-bromo-6α-hydroxy-3,4,4a,5,6,7,8,8aβ-octahydronaphthalen-2(1H)-one (42). A mixture of 4.72 g of octalone **11**, 4.85 g of N-bromosuccinimide, and 4 ml of water was stirred at room temperature for 3 hr. After dilution of the reaction mixture with 10 ml of water, the aqueous solution was extracted with chloroform (three 10-ml portions). The chloroform extracts were dried and evaporated to yield a crude product. The succinimide was removed by washing the crude product through a short column of 25 g of Woelm neutral alumina, activity III, with 500 ml of benzene. The resulting eluent was concentrated to 5 ml, and 5 ml of pentane was added. A first crop of crystalline bromohydrin, weighing 4.60 g (67%), was obtained in this manner. Additional crops yielded another 1.40 g (20%) of product. After recrystallization from ethyl acetate, the material melted at 127–129°.

The bromohydrin **42** was also obtained by deketalization of ketal **43** using the following procedure. To a solution of 5.8 g of ketal **43** in a mixture of 50 ml of acetone and 8 ml of water was added 2 ml of concentrated sulfuric acid. The resulting solution was kept at 50° for 90 min, then concentrated under vacuum to 10 ml. Water (20 ml) was added, and the mixture was extracted with benzene (two 75-ml portions). The benzene extract was dried and evaporated to afford a crude bromohydrin which was recrystallized from pentane–chloroform. The purified material weighed 3.29 g (67%) and melted at 127–128.5°.

Anal. Calcd for $C_{11}H_{17}BrO_2$: C, 50.59; H, 6.56; Br, 30.60. Found: C, 50.44; H, 6.34; Br, 30.82.

The infrared spectrum (in chloroform) has strong bands at 1721 and 1181 cm^{-1}. The nmr spectrum (in chloroform) has a three-proton singlet at τ 8.82 (methyl) and a one-proton doublet at τ 5.50 (J = 10 cps, C_5–H).

4aβ-Methyl-5β-bromo-6α-formyloxy-3,4,4a,5,6,7,8,8aβ-octahydronaphthalen-2(1H)-one (44). A solution of 2.39 g of bromohydrin **42** in 6 ml of anhydrous formic acid was kept at room temperature for 17 hr. At the end of this period, 20 ml of chloroform was added, and the resulting solution was washed with water, dried over magnesium sulfate, and evaporated. The product was 2.48 g of white solid. After recrystallization from chloroform, the material weighed 1.49 g and melted at 145.5–147°.

Anal. Calcd for $C_{12}H_{17}BrO_3$: C, 49.84; H, 5.93; Br, 27.63. Found: C, 50.14; H, 6.12; Br, 27.58.

The infrared spectrum (in chloroform) has strong bands at 1721 and 1181 cm^{-1}. The nmr spectrum (in chloroform) has a one-proton singlet at τ 2.00 (formate), a broad, one-proton multiplet at τ 4.70 (C_6–H), a one-proton doublet at τ 5.57 (J = 10 cps, C_5–H), and a three-proton singlet at τ 8.87 (methyl).

4aβ-Methyl-5α,6α-oxido-3,4,4a,5,6,7,8,8aβ-octahydronaphthalen-2(1H)-one (45). To a solution of 2.07 g of the bromohydrin **42** in 15 ml of ethanol was added 15 ml of 10% aqueous sodium hydroxide solution. After stirring for 30 min at 70°, the solution was concentrated to 15 ml, and extracted with ether (three 25-ml portions). The ether extracts were dried and evaporated to afford

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1.11 g of a pale yellow oil, whose infrared and nmr spectra were identical with those of the analytically pure material. The product was distilled in a Hickman microstill to afford 850 mg of colorless epoxide, bp 65° (0.2 mm).

Anal. Calcd for $C_{11}H_{16}O_2$: C, 73.30; H, 8.95. Found: C, 73.09; H, 8.79.

The infrared spectrum has bands at 1715, 1255, 1064, 928, and 828 cm^{-1}. The nmr spectrum has a three-proton singlet at τ 8.76 (methyl), a one-proton doublet at τ 7.28 (J = 4.5 cps, C_5–H), and a one-proton multiplet at τ 6.9 (C_6–H).

Reaction of Bromoformate 44 with Strong Bases. It was thought that compound **44** might be capable of transformation into a tricyclic ketoformate. Since the formyloxy group should be susceptible to attack by bases, with the ultimate production of the epoxide **45**, we sought to use a very powerful base in the hope that enolate formation would be rapid and quantitative, and that the derived enolate would then undergo cyclization. However, treatment of **44** with 1.0 equiv of methylsulfinyl carbanion in dimethyl sulfoxide led only to the oxide **45**, identified by its infrared and nmr spectra. Similar results were obtained when **44** was treated with 1.0 equiv of potassium triphenylmethane in dimethoxyethane.

4aβ-Methyl-5β-bromo-6α-methoxy-3,4,4a,5,6,7,8,8aβ-octahydronaphthalen-2(1H)-one (47). To a solution of 9.25 g (56.3 mmoles) of compound **11** in 125 ml of methanol was added 10.05 g (56.5 mmoles) of N-bromosuccinimide. After 2 hr at room temperature, the slurry was diluted with an additional 120 ml of methanol, to complete dissolution of the NBS. After 21 hr, the solvent was removed at reduced pressure. The infrared and nmr spectra of the semisolid product so obtained indicated that the carbonyl group had become partially ketalized. The crude product was dissolved in 120 ml of acetone and treated with a solution of 1 ml of concentrated hydrochloric acid in 11 ml of water. After 16 hr at room temperature and 1 hr at 55°, the solvent was removed at reduced pressure to yield a brown slurry which was added to 50 ml of water and extracted with ether (two 50-ml portions). The ether extract was washed with water (two 50-ml portions), 5% sodium hydroxide (two 50-ml portions), water (50 ml), and saturated sodium chloride (50 ml). The solution was dried and the solvent evaporated to afford 12.89 g of a tan solid, melting at 69–82° (83% of the theoretical). This solid was recrystallized from ether–pentane to yield 7.15 g of white needles, mp 87–89°, and 2.0 g of tan prisms, mp 83–86°. The analytical sample, mp 90–90.5°, was obtained by recrystallization from methanol.

Anal. Calcd for $C_{12}H_{19}BrO_2$: C, 52.40; H, 6.92; Br, 29.00. Found: C, 52.24; H, 6.94; Br, 29.22.

The nmr spectrum has a one-proton doublet at τ 5.69 (J = 9 cps, C_5–H), a three-proton singlet at τ 6.62 (methoxyl), and a three-proton singlet at τ 8.82 (methyl).

The minor isomer produced in this reaction, 4aβ-methyl-5α-bromo-6β-methoxy-3,4,4a,5,6,7,8,8aβ-octahydronaphthalen-2(1H)-one (**46**), was obtained after cyclization of semipure **47** (*vide supra*). From 7.15 g of **47**, mp 87–89°, after distillation of the cyclization product **37**, there remained a semisolid residue. After washing the residue with ether–pentane, there was obtained 150 mg of white crystals, mp 167–168°. Recrystallization from ethyl acetate–pentane raised the melting point to 168.5–169.5°.

Anal. Calcd for $C_{12}H_{19}BrO_2$: C, 52.40; H, 6.92; Br, 29.00. Found: C, 52.39; H, 6.94; Br, 28.92.

The nmr spectrum has a one-proton doublet at τ 6.24 (J = 10 cps, C_5–H), a three-proton singlet at τ 6.63 (methoxyl), and a three-proton singlet at τ 8.58 (methyl).

4aβ-Methyl-5β-bromo-6α-benzyloxy-3,4,4a,5,6,7,8,8aβ-octahydronaphthalen-2(1H)-one (48). To a solution of 15.5 g of octalone **11** in 150 ml of freshly distilled benzyl alcohol was added 16.0 g of N-bromosuccinimide. The solution was stirred at 50–55° for 44 hr under nitrogen. The excess benzyl alcohol was evaporated under reduced pressure (steam bath) to leave a dark brown gum. Spectral analysis of this crude product indicated that partial ketalization had occurred. The material was dissolved in 200 ml of 90% acetic acid, treated with 5 ml of concentrated hydrochloric acid, and kept at room temperature for 18 hr. After removal of the solvent under reduced pressure, the resulting brown oil was chromatographed on 500 g of Woelm neutral alumina, activity I. Elution of the column with mixtures of ether and benzene gave 14.7 g of compound **48** as a pale yellow oil. Although relatively pure (>90%) as judged by its nmr spectrum, this material could not be induced to crystallize.

The infrared spectrum has a prominent carbonyl band at 1715 cm^{-1}. The nmr spectrum has a five-proton singlet at τ 2.78 (aromatic protons), a two-proton singlet at τ 5.43 (benzyl methylene), a one-proton doublet at τ 5.60 (J = 9 cps, C_5–H), and a three-proton singlet τ 8.84 (methyl).

1-Methyl-8-isopropyltricyclo[4.4.0.0^{2,7}]dec-8-en-3-one (51). To a refluxing solution of 17.29 g of keto acetate **41** in 150 ml of absolute ether, under nitrogen, was added 130 ml of 2.38 *M* isopropyllithium in pentane. After stirring the resulting mixture vigorously for 50 min, it was cooled to room temperature, and 100 ml of water was cautiously added. The ether layer was washed with water (three 20-ml portions), and the resulting aqueous phase was extracted with ether (four 20-ml portions). The combined ether extracts were dried and evaporated at reduced pressure. After pumping the residue at 65° (0.3 mm) for 90 min, there was obtained 13.98 g of viscous yellow oil. This material was submitted twice more to the above procedure, using 80 ml of 2.38 isopropyllithium each time to afford 14.85 g of the diol **49** as a viscous yellow oil. The material, which contained a small amount of unreacted ketone as evidenced by its infrared spectrum was not purified further.

To a solution of 14.67 g of the crude diol **49**, in 150 ml of acetone at −5°, was added dropwise 16 ml of Jones reagent.[14] The addition required 20 min. After an additional 20 min at −5°, the green mixture was poured into 500 ml of ether and 200 ml of water The aqueous phase was extracted with more ether (two 50-ml portions), and the combined organic layers were washed with water (three 100-ml portions), dried, and evaporated. There was obtained in this way 12.22 g of ketol **50**, as a viscous brown oil.

To the above ketol, in 90 ml of pyridine, was added 15.13 g of phosphorus oxychloride. The orange solution was heated to 95° and maintained at this temperature for 5 min, then allowed to cool to room temperature. After a total reaction time of 2 hr, the solution was poured into a mixture of 300 g of ice and 300 ml of chloroform. The layers were separated, and the aqueous layer was extracted with chloroform (two 50-ml portions). The combined chloroform extracts were washed with cold, 10% hydrochloric acid (three 500-ml portions), cold 5% sodium hydroxide (250 ml), and saturated sodium chloride solution (200 ml), dried, and evaporated. The residue, 9.90 g of brown oil, was distilled from an oil-jacketed flask (0.5 mm) with a bath temperature of 130–150° to afford 4.15 g of semipure **51** as a pale yellow oil. Gas chromatography of this material revealed that it was approximately 75% pure, with the major contaminant being a compound which appeared to be the exocyclic double-bond isomer of **51**. Final purification of **51** was effected by preparative vpc on a 10 ft × 3/8 in. Carbowax 20 M column at 208°, with a helium flow rate of 200 cc/min.

Anal. Calcd for $C_{14}H_{20}O$: C, 82.30; H, 9.87. Found: C, 82.13; H, 10.03; mol wt (mass spectral), 204.

The infrared spectrum has bands at 1718, 1420, 1387, and 1202 cm^{-1}. The nmr spectrum has a one-proton broad multiplet at τ 4.70 (C_9-olefinic proton), a three-proton singlet at τ 9.08 (C_1-methyl), and a six-proton doublet at τ 9.02 (J = 6.5 cps, isopropyl methyls).

The 2,4-dinitrophenylhydrazone of **51** melted at 182–184° after three recrystallizations from methanol.[15]

Anal. Calcd for $C_{20}H_{24}N_4O_4$: C, 62.49; H, 6.29; N, 14.57. Found: C, 62.79; H, 6.09; N, 14.35.

1-Methyl-8-*syn*-isopropyltricyclo[4.4.0.0^{2,7}]decan-3-one (55) and 1-Methyl-8-*anti*-isopropyltricyclo[4.4.0.0^{2,7}]decan-3-one (56). A mixture of 314 mg of enone **51** and 100 mg of 5% palladium on carbon in 10 ml of ethyl acetate was hydrogenated for 12 hr at atmospheric pressure. A total of 37.6 ml of hydrogen was taken up (1.0 molar equiv). The catalyst was removed by filtration and the solvent was evaporated to afford 319 mg of clear liquid, which was seen by its gas chromatogram (10 ft × 0.25 in. DEGS on Chromosorb at 180°) to consist of a mixture of saturated ketones **55** and **56** in a ratio of 7:3. The product was fractionated by preparative vpc (15 injections of 20 μl each on the aforementioned column) to afford 152 mg of pure **55** and 44 mg of pure **56**.

Anal. Calcd for $C_{14}H_{22}O$: C, 81.50; H, 10.75. Found (compound **55**, major isomer): C, 81.28; H, 10.56. Found (compound **56**, minor isomer): C, 81.27; H, 10.64.

The infrared spectra of the two isomeric ketones are identical from 2.5 to 7.8 μ and from 11.5 to 16 μ. However, the spectra differ substantially in the fingerprint region. Compound **55** (major isomer) has infrared bands in this region at 1238, 1208, 1200, 1167, 1089, and 907 cm^{-1}. Compound **56** (minor isomer) has infrared bands in this region at 1255, 1232, 1208, 1176, 1099, 934, and 919 cm^{-1}. Both isomers have bands at 1721, 1416, 1389, 1385, 1372, and 1328 cm^{-1}. The nmr spectra of **55** and **56** are strikingly different. Both have a six-proton doublet with J = 6 cps at τ 9.10 (isopropyl) and a three-proton singlet at τ 9.18 (methyl). In the spectrum of **55**, the C_2–H appears as a doublet at τ 7.43 with J = 5.5 cps (due to cross-ring coupling with C_6–H). In the spectrum of **56**,

this resonance is not discernable, since it shifted upfield and is obscured by the signals due to the protons at C_4, C_7, and C_6.

The 2,4-dinitrophenylhydrazone derivatives of **55** and **56** were prepared in the standard manner,[15] and recrystallized three times from methanol.

Anal. Calcd for $C_{20}H_{26}N_4O_4$: C, 62.16; H, 6.78; N, 14.50. Found (**55**, mp 187–188°): C, 61.83; H, 6.97; N, 14.66. Found (**56**, mp 214–215°): C, 62.16; H, 6.82; N, 14.70.

When compound **51** was hydrogenated in methanol, the ratio of **55** to **56** was 7:3. When hexane was used as the solvent, the ratio was 43:57.

The conversion of **51** to **55** and **56** was also carried out as follows. To a solution of 45 mg of **51** in 2.0 ml of ethanol was added 50 mg of sodium borohydride. After 2.5 hr at room temperature, the solution was poured into 10 ml of water and extracted with ether (two 10-ml portions). The ether extracts were washed with water, dried, and evaporated, to yield 40 mg of crude alcohol. This alcohol was dissolved in 2.0 ml of hexane, and 20 ml of 5% palladium on carbon was added. After hydrogenating the mixture at atmospheric pressure for 20 hr, the catalyst was removed, and the solvent was evaporated. The residue was dissolved in 4 ml of acetone, and 0.2 ml of Jones reagent[14] was added. After 10 min, the reaction was worked up in the normal manner to afford 30 mg of a mixture of **55** and **56**. The composition of this mixture was 9% **55** and 91% **56**.

1,3-*anti*-Dimethyl-8-isopropyltricyclo[4.4.0.0^{2,7}]dec-8-en-3-*syn*-ol (52). To a solution of 140 mg of 1-methyl-8-isopropyltricyclo-[4.4.0.0^{2,7}]dec-8-en-3-one (**51**), in 5 ml of ether, was added 5.0 ml of 1.6 *M* methyllithium in ether. The solution was kept at room temperature for 40 min, then quenched by the addition of 10 ml of water. The aqueous layer was separated and extracted with 10 ml of ether. After washing the combined ether extracts with 10 ml of saturated sodium chloride solution, they were dried and evaporated to afford 139 mg of cloudy oil, which still contained unreacted ketone, as judged by its infrared spectrum. The above procedure was repeated to yield 135 mg of nearly pure **52**. This material was chromatographed on 12 g of Merck alumina, taking 20-ml fractions. Fraction 10, eluted with 1:1 hexane–ether, contained 105 mg of pure product, which was distilled at 150° (0.3 mm) to afford 73 mg of a water-white, viscous liquid.

Anal. Calcd for $C_{15}H_{24}O$: C, 81.76; H, 10.98. Found: C, 81.69; H, 10.81.

The infrared spectrum has prominent bands at 3636, 3497, 1111, 1020, 980, 939, 929, 899, and 877 cm^{-1}. The nmr spectrum has a six-proton doublet at τ 9.03 (J = 6.5 cps, isopropyl methyls), three-proton singlets at τ 8.86 and 8.78 (methyls), and a one-proton multiplet at τ 4.83 (C_9–H).

1,3-*anti*-Dimethyl-8-*syn*- and -*anti*-isopropyltricyclo[4.4.0.0^{2,7}]decan-3-*syn*-ol (53 and 54). A mixture of 58 mg of alcohol **52** and 50 mg of 5% palladium on carbon in 3 ml of ethyl acetate was hydrogenated at atmospheric pressure for 48 hr. The catalyst was removed by filtration, and the solvent was evaporated to obtain 44 mg of the stereoisomeric mixture as a clear oil. The material was distilled at 150° (0.3 mm) to obtain 38.4 mg of analytically pure material.

Anal. Calcd for $C_{15}H_{26}O$: C, 81.02; H, 11.79. Found: C, 80.86; H, 11.96.

The pure 8-*syn* isomer **53** was prepared in the following manner. To a solution of 150 mg of 1-methyl-8-*syn*-isopropyltricyclo-[4.4.0.0^{2,7}]decan-3-one (**55**) in 5 ml of ether was added 5 ml of 1.6 *M* methyllithium in ether. After 1 hr at room temperature, the reaction was worked up by addition of water to yield 161 mg of oily alcohol, containing 5–10% unreacted ketone. The alkylation procedure was repeated to afford 147 mg of crystalline alcohol, melting at 62–75°. A single recrystallization from pentane at −20° gave analytically pure material, mp 85–85.5°.

Anal. Calcd for $C_{15}H_{26}O$: C, 81.02; H, 11.79. Found: C, 80.84; H, 11.59.

The infrared spectrum of **53** has bands at 3600, 3450, 1389, 1377, 1220, 1106, 1010, 977, 942, 909, and 896 cm^{-1}. The nmr spectrum has a six-proton doublet at τ 9.15 (J = 6 cps, isopropyl) and three-proton singlets at τ 8.97 and 8.80 (methyls).

The pure 8-*anti* isomer **54** was prepared in a strictly analogous manner from 43 mg of 1-methyl-8-*anti*-isopropyltricyclo[4.4.0.0^{2,7}]-decan-3-one (**56**). However, this product could not be induced to crystallize and, due to the paucity of material available to us (39.0 mg), it was not further purified, but was used directly for conversion into (±)-copaene.

(±)-Copaene (1) and (±)-Ylangene (2). To a solution of 340 mg of a 1:1 mixture of alcohols **53** and **54** in 5 ml of anhydrous pyridine, was added 1.25 ml of phosphorus oxychloride. The solution was heated to 100° and kept at this temperature for 5 min, then allowed to cool to room temperature. After a total reaction time of 45 min, the mixture was poured into a slurry of 30 g of ice in 30 ml of chloroform. The aqueous phase was extracted with 25 ml of chloroform, and the combined chloroform layers were washed with 50 ml of 10% hydrochloric acid, then dried. Evaporation of the solvent gave 330 mg of brown oil. This material was seen by vpc to consist of approximately 50% of the desired product, along with numerous impurities. Preliminary purification was effected by preparative vpc (10 ft × 3/8 in. Carbowax 20 M at 175°, helium flow rate 200 cc/mm). There was obtained 80 mg of a clear liquid. High-resolution gas chromatographic analysis, using a 1000 ft × 0.03 in. open tubular column,[20] coated with SF-96(50) methyl silicone oil at 150°, showed that the mixture consisted of a 1:1 mixture of (±)-ylangene and (±)-copaene (relative retention times of 1.00 and 1.02). The mixture was further purified by trapping from a 100 ft × 0.25 in. 1% Carbowax 30 M column at 178°. Final purification was accomplished using the aforementioned 1000 ft × 0.03 in. tubular column.[21] The (±)-copaene so obtained was identified by comparison of its infrared spectrum[22] with samples of (−)-copaene from copaiba oil,[23] ylang-ylang oil,[23] and a chloranthus oil of Chinese origin.[4a,24] The (±)-ylangene was identified by comparison of its infrared spectrum with a sample of (+)-ylangene from *Schizandra chinensis* (Turcz.) Baill.[25]

Both (±)-copaene and (±)-ylangene gave nmr and mass spectra which were identical with the corresponding spectra of their natural counterparts.

(±)-Copaene and (±)-ylangene were also obtained by a similar dehydration of the pure alcohols **54** and **53**, respectively.

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(20) R. Teranishi and T. R. Mon, *Anal. Chem.*, **36**, 1490 (1964).

(21) We gratefully acknowledge the assistance of Dr. Roy Teranishi of the Western Regional Laboratories of the USDA in Albany, Calif., for accomplishing the separation of (±)-copaene and (±)-ylangene.

(22) Infrared spectra for (±)-copaene, (±)-ylangene, and their natural counterparts were measured on a Cary Model 90 infrared spectrometer by Dr. J. R. Scherer of the Western Regional Laboratories of the USDA in Albany, Calif. We thank Dr. Scherer for his assistance.

(23) Obtained from Fritsche Bros., New York, N. Y.

(24) We thank Professor Büchi and Professor de Mayo for this sample.

(25) O. Motl, V. G. Bucharov, V. Herout, and F. Sorm, *Chem. Ind.* (London), 1759 (1963). We thank Dr. Herout for this sample.