A Stereoselective Total Synthesis of the Guaiazulenic Sesquiterpenoids α-Bulnesene and Bulnesol[1]

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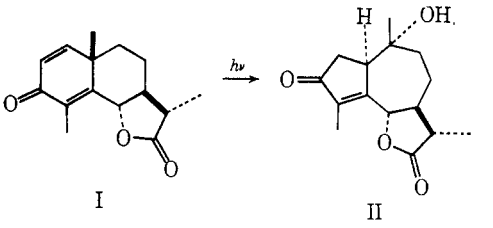
Abstract: (±)-α-Bulnesene (**39**) and (±)-bulnesol (**40**) have been synthesized in 17 stage routes from the unsaturated keto alcohol **1**. The key step involves solvolytic rearrangement of a decalyl tosylate to a hydroazulene, *i.e.*, **38** → **39** and **43** → **40**. The relative stereochemistry of keto ether **30**, an intermediate in the synthesis of both sesquiterpenes, has been determined by correlation with dihydroeudesmol (**23**). The syntheses illustrate a general route to guaiazulenes which involves: (a) construction of a hydronaphthalene precurser, (b) establishment of relative stereochemistry, and (c) solvolytic rearrangement to a guaiazulene.

In recent years, an extraordinary amount of effort has been directed toward the synthesis of sesquiterpenes. A major portion of this activity has occurred in the decalinic area. There are two primary reasons for the synthetic success which has resulted in this group of compounds. Several reliable methods now exist for elaboration of the hydronaphthalene skeleton (Robinson annelation, Diels–Alder reaction, Birch reduction of naphthalenes, π-cyclization routes). The second factor contributing to this success is the highly developed understanding of stereochemistry and conformational analysis in cyclohexane systems. Stereospecific syntheses may be designed rather easily, in which asymmetry is established either kinetically or thermodynamically.

In contrast to this situation, the hydroazulenic sesquiterpenes present synthetic challenges which are much less amenable to present methodology. Efficient methods for elaboration of the hydroazulene skeleton are not generally available, and conformational analysis in this system is still in an infant stage.[4] We have explored an approach to hydroazulene synthesis in which both of these problems may be overcome by proceeding through decalinic intermediates.[5] Thus, one may utilize one of the available methods to generate a hydronaphthalene intermediate, make use of conformational principles to establish relative stereochemistry, and then cause the hydronaphthalene skeleton to rearrange to the desired hydroazulene system.

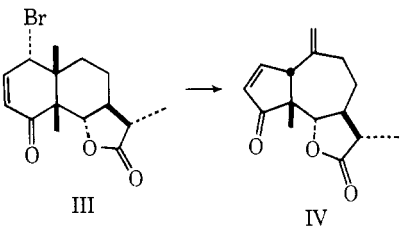
The basic approach has been recognized by others; indeed, the various guaiazulene syntheses which begin with santonin, in which a considerable amount of relative stereochemistry is already fixed, are examples of this approach. In these cases, the hydronaphthalene to hydroazulene rearrangement is usually accomplished by the well known photoconversion of santonin (I) to isophotosantonic lactone (II). Examples of this route to guaiazulenes are the syntheses of achillin,[6]



I II

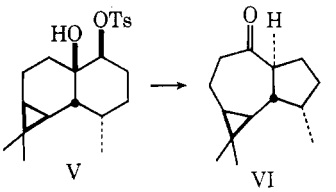
desacetoxymatricarin,[7] α-bulnesene,[8] geigerin,[9] and arboresin.[10]

Hendrickson has reported an application of the decalinic route to the synthesis of the unnatural pseudoguaianolide IV.[11] The rearrangement was accomplished by solvolysis of bromide III, derived ultimately from santonin.



III IV

Büchi has applied the decalinic route in the synthesis of aromadendrene.[12] In this case, skeletal reorganization was brought about by pinacol rearrangement of hydroxy tosylate (V), yielding (−)-apoaromadendrene (VI).



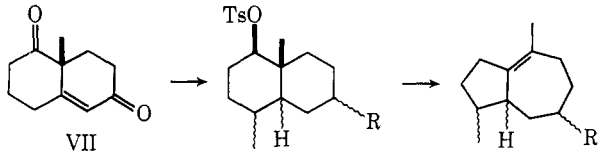
V VI

An alternative solution to the problem has been offered by Marshall and Partridge.[13] The Marshall–

(1) Presented in preliminary form at a joint meeting of the American Chemical Society and the Canadian Institute of Chemistry, Toronto, Canada, May 26, 1970.
(2) Fellow of the Alfred P. Sloan Foundation, 1967–1969.
(3) National Institutes of Health Predoctoral Fellow, 1967–1970.
(4) For the most definitive treatment of the subject, see J. B. Hendrickson, *Tetrahedron*, **19**, 1387 (1963).
(5) (a) C. H. Heathcock and R. Ratcliffe, *Chem. Commun.*, 994 (1968); (b) C. H. Heathcock, R. Ratcliffe, and C. Quinn, 158th National Meeting of the American Chemical Society, New York, N. Y., Sept 1969.
(6) J. N. Marx and E. H. White, *Tetrahedron*, **25**, 2117 (1969).
(7) E. H. White, S. Equchi, and J. N. Marx, *ibid.*, **25**, 2009 (1969).
(8) E. Piers and K. F. Cheng, *Chem. Commun.*, 562 (1969).
(9) D. H. R. Barton, J. T. Pinkey, and R. J. Wells, *J. Chem. Soc.*, 2518 (1964).
(10) M. Suchy, V. Herout, and F. Sorm, *Collect. Czech. Chem. Commun.*, **29**, 1829 (1964).
(11) J. B. Hendrickson, C. Ganter, D. Dorman, and H. Link, *Tetrahedron Lett.*, 2235 (1968).
(12) G. Büchi, W. Hofheinz, and J. V. Paukstelis, *J. Amer. Chem. Soc.*, **91**, 6473 (1969).
(13) J. A. Marshall and J. J. Partridge, *Tetrahedron*, **25**, 2159 (1969).

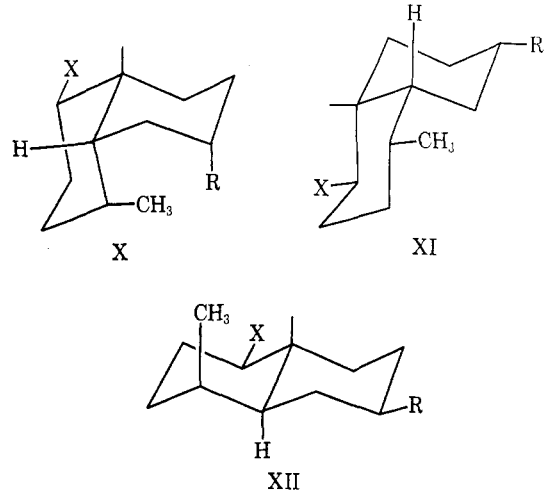
Partridge method, which proceeds through bicyclo-[4.3.1]decane intermediates, and which has been applied to the synthesis of bulnesol, suffers from the difficulty in obtaining the requisite bicyclic precursors and from the limited stereochemical control which may be exerted in this system.

In our own approach to the problem, we envisioned the stereospecific conversion of the well-known Wieland–Miescher diketone (VII)[14] into a decalyl tosylate of type VIII, which might solvolyze with concomitant skeletal reorganization, thus yielding a guaiazulene (IX). Model studies convinced us that such rearrangements can be made to occur either in the *trans*-[5a] or *cis*-decalin[5b] series.[15] When one considers



VII VIII IX

the known stereochemistry of the Wagner–Meerwein rearrangement (*i.e.*, rearrangement is most facile when the leaving group and migrating group are antiperiplanar),[16] along with the relative stereochemistry of the three asymmetric centers in bulnesol (**40**)[17] and α-bulnesene (**39**),[18] three candidates for rearrangement emerge (X–XII). Compound X, in which the leaving group and angular methyl group are trans, must



X XI XII

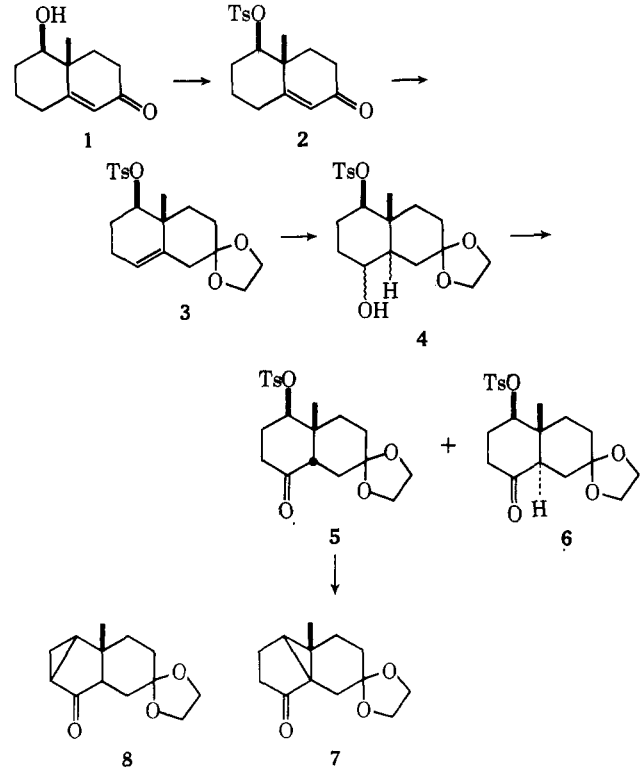
X = leaving group; R = three-carbon side chain

solvolyze in the "steroid conformation" in order to achieve the requisite antiperiplanar geometry. Severe nonbonded interactions in this conformation would obviously cause it to be unpopulated relative to the alternate nonsteroid conformation. Both XI and XII can reasonably be expected to solvolyze with rearrangement to guaiazulenes of the proper stereochemistry. The rigid nature of the *trans*-decalin skeleton in XII requires the proper geometry for rearrangement. Compound XI, which has an alternate chair–chair conformation available, is expected to exist in the illustrated nonsteroid conformation, which has three equatorial substituents.

At the outset, we decided to focus our attention on the *trans*-decalin series, as typified by compound XII, since this series appeared more amenable to stereospecific synthesis. Yoshikoshi has recently reported an application of the method, in the *cis*-decalin series XI, to the synthesis of bulnesol.[19]

Unsaturated keto alcohol **1**, prepared from the Wieland–Miescher diketone by the method of Boyce and Whitehurst,[20] was converted into tosylate **2**.[21] Ketalization proceeded normally, with concomitant double bond isomerization, to yield compound **3**. Compound **3** underwent hydroboration, yielding a mixture of diastereomeric secondary alcohols **4**, which was oxidized to a mixture of decalones **5** and **6**.

We had anticipated on the basis of analogy that compound **3** would add diborane predominately from the side of the molecule cis to the angular methyl group.[22] In accordance with expectation, *cis*-decalone **5**, which could be obtained in a pure state by fractional crystallization of the mixture, was the predominant product (**5**:**6** = 3:1). Attempted base-catalyzed epimerization of **5** to **6** led only to intramolecular alkylation, yielding the tricyclic compound **7**. The



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

(15) A full account of our model studies in this area will be communicated separately.

(16) D. N. Kirk and M. P. Hartshorn in "Reaction Mechanisms in Organic Chemistry," Vol. 7, C. Eaborn and N. B. Chapman, Ed., Elsevier, Amsterdam, 1968, pp 228–230.

(17) (a) H. Minato, *Tetrahedron*, **18**, 365 (1962); (b) L. Dolejs, A. Mironov, and F. Sorm, *Tetrahedron Lett.*, **No. 11**, 18 (1960); (c) L. Dolejs, A. Mironov, and F. Sorm, *Collect. Czech. Chem. Commun.*, **26**, 1015 (1961).

(18) R. B. Bates and R. C. Slagel, *J. Amer. Chem. Soc.*, **84**, 1307 (1962), and references therein.

(19) M. Kato, H. Kosugi, and A. Yoshikoshi, *Chem. Commun.*, 185 (1970).

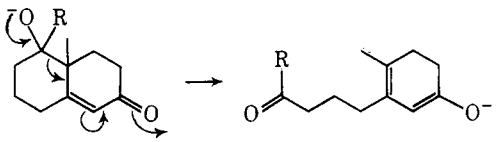
(20) C. B. C. Boyce and J. S. Whitehurst, *J. Chem. Soc.*, 2680 (1960).

(21) C. H. Heathcock, R. A. Badger, and J. W. Patterson, Jr., *J. Amer. Chem. Soc.*, **89**, 4133 (1967).

(22) J. A. Marshall, M. T. Pike, and R. D. Carroll, *J. Org. Chem.*, **31**, 2933 (1966).

tricyclic nature of compound **7** was suggested by elemental analysis, which indicated the loss of *p*-toluenesulfonic acid, and the absence of olefinic absorption in its ir and pmr spectra. The carbonyl absorption of **7** (ν_{max} 1704 cm^{-1}) is consistent with a bicyclo[3.1.0]-hexan-2-one moiety, as is the observed uv absorption [λ_{max} 217 nm (ϵ 4400)]. The latter datum excludes the alternate formulation **8**, since its predicted uv absorption maximum is 190 nm.[23,24]

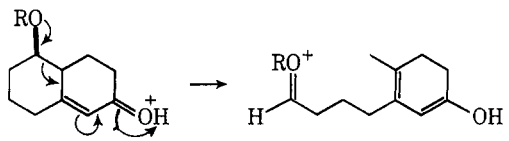
Since the *p*-toluenesulfonate grouping is clearly incompatible with basic media, and we recognized the necessity of such conditions in introducing the secondary methyl group, we decided to delay its introduction until a later stage. It therefore becomes necessary to block the secondary hydroxyl function temporarily. An ideal blocking group would be benzyl, which could be removed later by catalytic hydrogenolysis. However, direct benzylation is ruled out by the known propensity of such systems to undergo vinylogous retrograde aldol reactions (*i.e.*, XIII → XIV).[25] Indeed, in several attempts to accomplish



XIII XIV

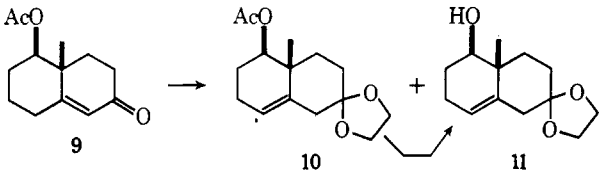
base-catalyzed benzylation of **1**, we obtained only polymeric products apparently derived from polymerization of the fragmented keto aldehyde.[26]

The complication could, in theory, be avoided by reversing the order of the benzylation and ketalization steps. However, it is well known that compound **1** cannot be ketalized because of the intrusion of the acid-catalyzed equivalent of the aforementioned retrograde aldol reaction.[28] A possible solution to this apparent dilemma is suggested by a consideration of the initial product of the acid-catalyzed retrograde aldol reaction XV. If R is changed from H to acetyl, then XV should be destabilized by the inductive effect of the carbonyl group. Therefore, simple acetylation of **1** might allow it to be ketalized without fragmentation. Acetate **9** was prepared in quantitative yield by acetylation of **1** with acetic anhydride in pyridine. Ketalization of acetate **9** under carefully controlled conditions (tenfold excess of ethylene glycol in benzene, 1 mol % 2-naphthalenesulfonic acid) gave a mixture



XV

of ketal acetate **10**, ketal alcohol **11**, and unreacted keto acetate **9**. Direct crystallization yielded the desired ketal **10** in 68% yield. The acetyl protecting group was then removed by $LiAlH_4$ reduction, which afforded **11** in 90–95% yield. The overall yield for the conversion of **9** to **11** was raised to 76% by recycling the mother liquors from the initial crystallization, reducing the crude product with $LiAlH_4$, and crystallizing compound **11** (see Experimental Section). The fact that no rearranged products are formed in the reaction

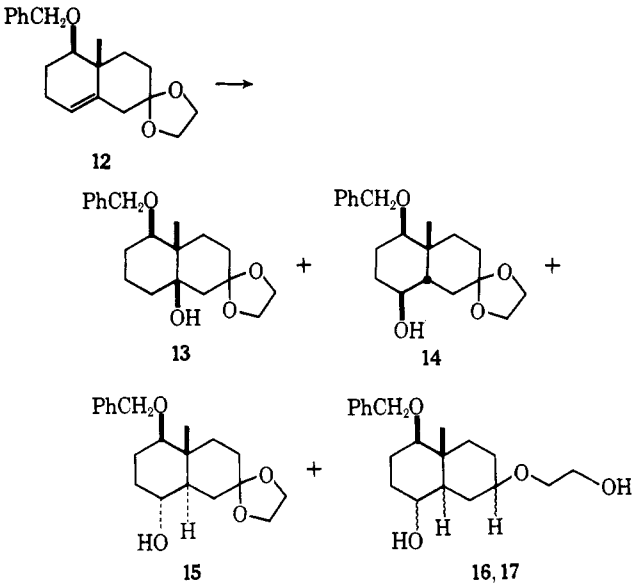


9 10 11

indicates that **11** must arise by acid-catalyzed transesterification *after* ketalization has occurred.

At this point, we could easily introduce the necessary benzyl protecting group without incident. The anion of compound **11** reacted with benzyl bromide in benzene–5% dimethyl sulfoxide to give benzyl ether **12** in 80% yield.

Reaction of **12** with excess diborane in tetrahydrofuran gave a complex mixture which was separated into five components by preparative tlc. Consideration of the ir, pmr, and mass spectra revealed that the five products were alcohols **13–17**, formed in an isolated ratio of 5:30:22:16:27, respectively. The hydrogenolysis reaction leading to ring-opened products **16** and **17** has been encountered previously by others.[22,29] The reaction was improved dramatically by using a smaller amount of diborane. Under these conditions, secondary alcohols **14** and **15** were obtained in a total yield of 96%. As expected (*vide supra*), the cis isomer **14** predominated in a ratio of 2:1. No ring-opened products, **16** or **17**, and only traces of tertiary alcohol **13** were produced under these conditions.



12 13 14 15 16,17

The mixture of **14** and **15** was oxidized with bispyridinechromium(VI) oxide in methylene chloride[30]

(23) W. G. Dauben and G. H. Berezin, *J. Amer. Chem. Soc.*, **89**, 3449 (1967).

(24) Although further studies on **7** have not been carried out, it does represent a potential hydroazulene precursor if one considers electrophilic cleavage of the internal bicycloheptane bond.

(25) S. Swaminathan, J. P. John, and S. Ramachandran, *Tetrahedron Lett.*, 729 (1962).

(26) Our results are clearly incompatible with the report by Minato and Nagasaki that **1** reacts with benzyl chloride and sodium hydride in benzene to give the desired benzyl ether in 86% yield.[27] Replication of the experimental conditions reported by these workers led only to intractable material.

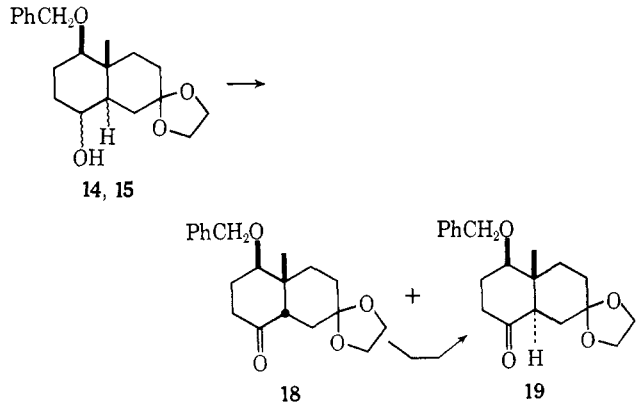
(27) H. Minato and T. Nagasaki, *J. Chem. Soc. C*, 621 (1968).

(28) M. Los and A. D. Mighell, *Tetrahedron*, **21**, 2297 (1965).

(29) M. Nussim, T. Mazur, and F. Sondheimer, *J. Org. Chem.*, **29**, 1120 (1964).

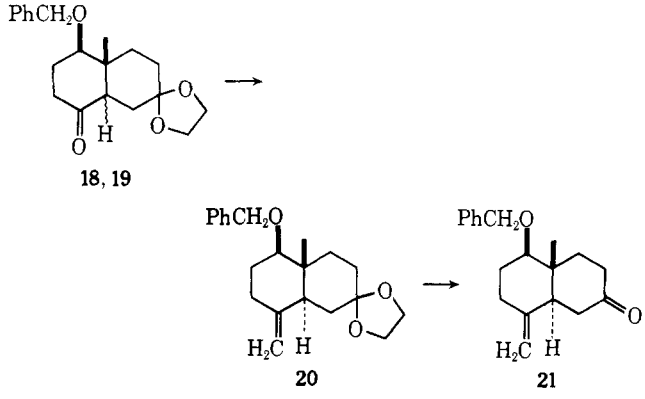
(30) R. Ratcliffe and R. Rodehorst, *ibid.*, **35**, 4000 (1970).

to obtain a 2:1 mixture of decalones **18** and **19** in 94% yield. Treatment of the mixture with methanolic sodium methoxide caused epimerization to occur at the angle, leading to a pure crystalline decalone **19**. This homogenization confirmed our assumption that hydroboration had occurred predominately cis to the angular methyl group and also provided a pure intermediate for further elaboration.



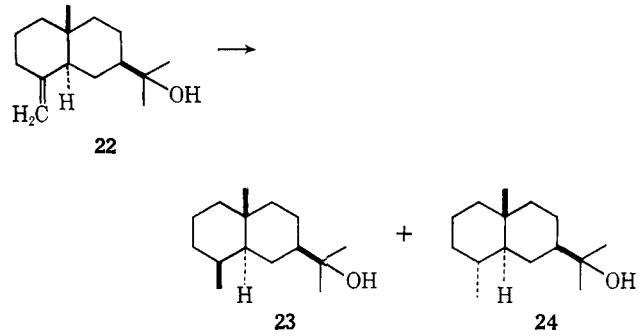
14, 15 **18** **19**

Compound **19** reacted readily with methylenetriphenylphosphorane in dimethyl sulfoxide,[31] affording the crystalline methylenedecalin **20** in 84% yield. Alternatively, the 2:1 mixture of **18** and **19** could be used directly, without prior homogenization. From such a reaction, compound **20** was obtained in 87% yield. No trace of cis-fused methylene decalin could be detected in the reaction product. This observation of prior epimerization in the Wittig reaction is but another in a growing list of such occurrences.[22,32,33] The ethylenedioxy group, having served its intended function, was now removed by hydrolysis (aqueous acetic acid), giving the crystalline methylene decalone **21** in 93% yield.



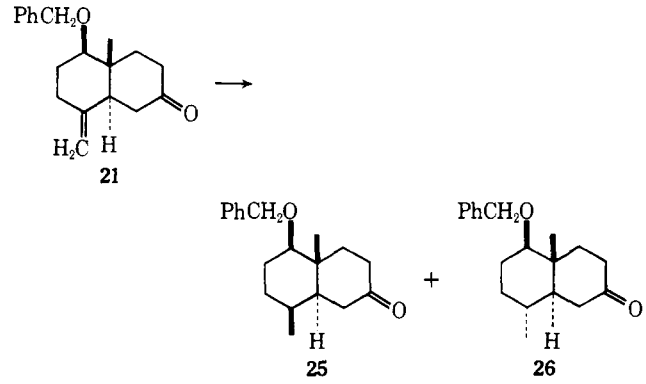
18, 19 **20** **21**

At this point we had intended to introduce the proper relative stereochemistry at two of the eventual asymmetric centers in bulnesol and α-bulnesene by catalytic hydrogenation of the exocyclic methylene linkage. The crystalline dihydroeudesmol **23**, obtained as the major product in the hydrogenation of β-eudesmol (**22**) over platinum,[34] was assumed by Barton to have an axial methyl group on the ground that hydrogen should be added to the less hindered α face of the molecule.[35] Subsequent correlations have provided unambiguous verification of this assumption.[36] We repeated this hydrogenation, using (±)-eudesmol,[37] in order to provide a pure sample of (±)-dihydroeudesmol for later comparison. We found that isomers **23** and **24** are produced in a ratio of 80:20.



22 **23** **24**

When methylenedecalone **21** was reduced over rhodium/alumina in hexane,[38] isomers **25** and **26** were produced in a ratio of 7:1. The major isomer **25** was obtained by fractional crystallization in 76% yield.

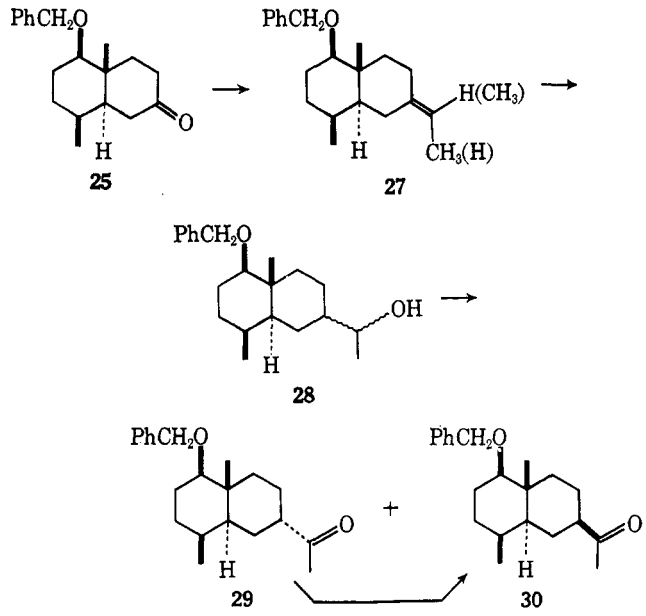


21 **25** **26**

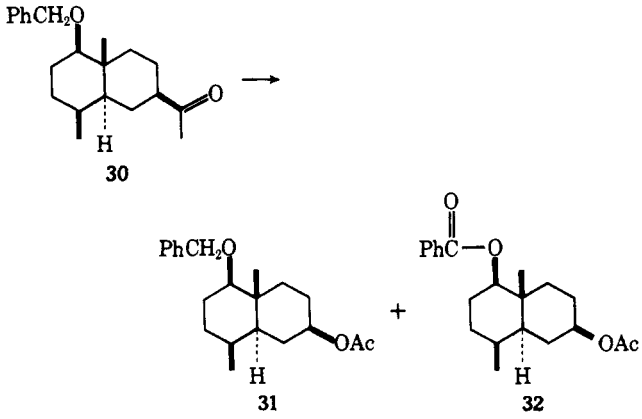
With the proper relative stereochemistry now established at these two centers, we turned our attention to the three-carbon side chain, which must replace the carbonyl group in **25**. Since this group is cis to the secondary methyl group in bulnesol and α-bulnesene, which corresponds to an equatorial disposition in a *trans*-decalin precursor, the relative stereochemistry can again be established thermodynamically. Compound **25** reacted smoothly with ethylidinetriphenylphosphorane in dimethyl sulfoxide,[31] giving a mixture of olefins **27** in 94% yield. Hydroboration of **27** gave a mixture of diastereomeric alcohols **28**, which was oxidized by bispyridinechromium(VI) oxide[30] to a mixture of methyl ketones **29** and **30** (overall yield for the two steps, 99%). Upon treatment with HCl in methanol, the mixture was equilibrated, affording the pure stereoisomer **30** as a viscous oil.

At this juncture, the complete relative stereochemistry of bulnesol and α-bulnesene has been established. Because of the fact that compound **30** could not be induced to crystallize, we sought independent veri-

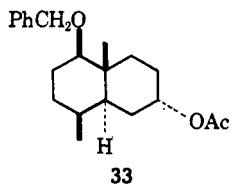
(31) R. Greenwald, M. Chaykovsky, and E. J. Corey, *J. Org. Chem.*, **28**, 1128 (1963).
(32) M. D. Soffer and L. A. Burk, *Tetrahedron Lett.*, 211 (1970).
(33) *cis*-1,4-Dioxodecalin has also been found to undergo epimerization when subjected to the Wittig reaction in dimethyl sulfoxide: C. H. Heathcock, unpublished results.
(34) F. J. McQuillin and J. D. Parrack, *J. Chem. Soc.*, 2973 (1956).
(35) D. H. R. Barton, *Chem. Ind. (London)*, 644 (1953).
(36) W. Cocker and T. B. H. McMurry, *Tetrahedron*, **8**, 181 (1952); see p 187.
(37) C. H. Heathcock and T. R. Kelly, *ibid.*, **24**, 1801 (1968).
(38) These conditions were chosen in order to maximize the stereoselectivity and minimize hydrogenolysis of the benzyl group. Reduction ceased after 1 mol of hydrogen had been absorbed. Other conditions were found to be less stereoselective (see Experimental Section).



fication of its homogeneity. Baeyer–Villiger oxidation of compound **30** (excess *m*-chloroperbenzoic acid in methylene chloride at reflux for 178 hr) gave a mixture of acetate **31** and diester **32** in an isolated ratio of 4:1.[39] The pmr spectrum of compound **31**, isolated by preparative tlc, was fully consistent with the assigned structure, and contained three-proton singlets at τ 9.02 (angular methyl) and 8.08 (acetoxy methyl). When the mixture of **29** and **30** was oxidized under the same conditions, similar results were obtained. In this case, the acetate fraction, again isolated by preparative tlc, showed three-proton singlets in the pmr at τ 9.02

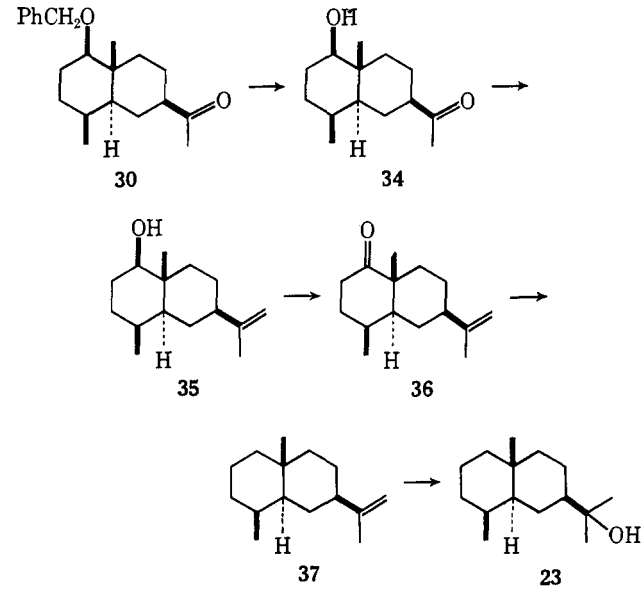


(angular methyl), 8.08, and 8.12 (acetoxy methyls of the two isomeric acetates). Integration of the peaks at τ 8.08 and 8.12, assignable to isomers **31** and **33**, respectively, showed that these compounds were present in a ratio of 2:3.

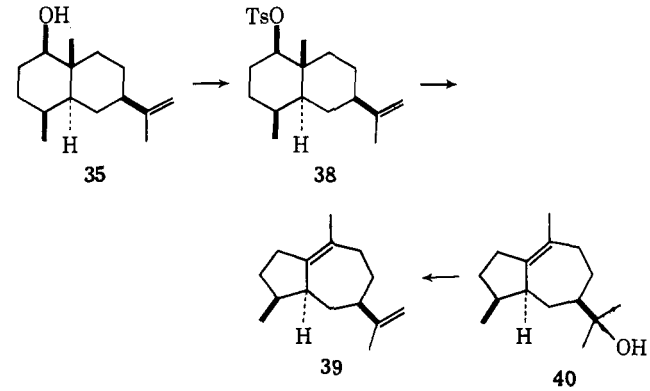


(39) The oxidation of a benzyl ether to a benzoate ester by peracid is apparently unprecedented, but is not surprising. Under milder conditions (1 mol equiv of peracid in methylene chloride at reflux for 67 hr), compound **31** and unreacted **30** were obtained in a ratio of 9:1.

In order to confirm the relative stereochemistry indicated for compound **30**, it was correlated with (±)-dihydroeudesmol (*vide supra*).[40] Catalytic hydrogenolysis of compound **30** (palladized carbon in aqueous ethanol) gave the crystalline keto alcohol **34** in 95% yield. This material reacted with methylenetriphenylphosphorane in dimethyl sulfoxide[31] to yield unsaturated alcohol **35**, which was oxidized [bispyridinechromium(VI) oxide in methylene chloride] to ketone **36**. Wolff–Kishner reduction of **36** afforded olefin **37**. Oxymercuration–demercuration[41] of this substance gave crystalline (±)-dihydroeudesmol (**23**), which was identical spectrally and chromatographically with the major product from the hydrogenation of (±)-eudesmol.



The crystalline unsaturated alcohol **35**, used in the above correlation, served admirably as an intermediate for the synthesis of α-bulnesene. Tosylation (*p*-toluenesulfonyl chloride in pyridine) gave **38**, which was solvolyzed in buffered acetic acid at 80° for 8 hr. The hydrocarbon product, obtained in 86% yield, was composed of three compounds in a ratio of 88:4:8. The major product, isolated by preparative glpc, was



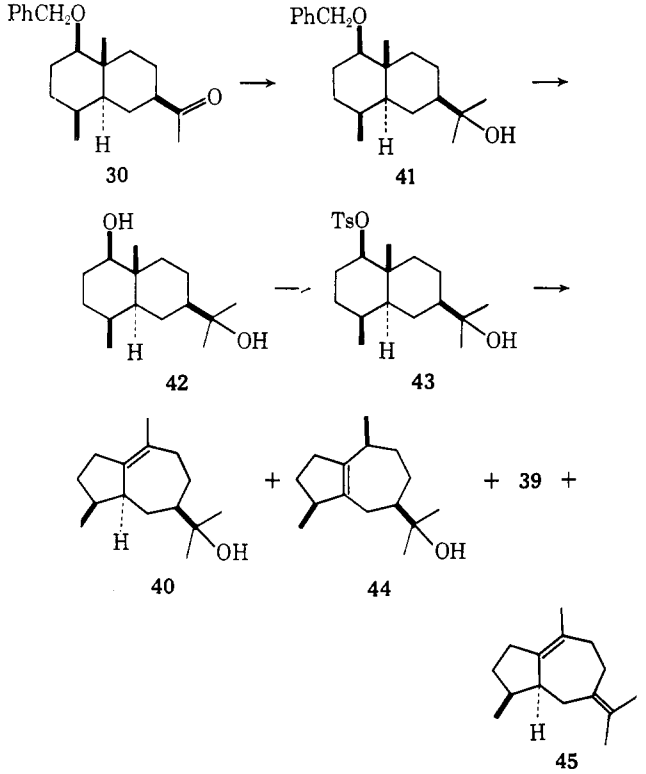
(40) This correlation was actually conceived and executed after we had completed the total synthesis of (±)-bulnesol. The correlation was deemed necessary in order to remove any stereochemical ambiguity in our synthetic product, and was prompted by the discrepancy between our physical properties for (±)-bulnesol and those reported for this compound by Marshall[13] and Yoshikoshi[19] (see Experimental Section).

(41) H. C. Brown and P. Geohagen, *J. Amer. Chem. Soc.*, **89**, 1522 (1967).

identical by ir, nmr, and chromatographic mobility with a sample of α-bulnesene (**39**), prepared by phosphorus oxychloride–pyridine dehydration of natural bulnesol **40**.[42] The minor products were not identified.

For the synthesis of (±)-bulnesol, we utilized the keto ether **30**. This compound reacted with methyllithium, affording alcohol **41**, which was debenzylated by reduction over palladized carbon to yield the crystalline diol **42**. Compound **42** gave tosylate **43**, when treated with *p*-toluenesulfonyl chloride in pyridine. When tosylate **43** was solvolyzed in buffered acetic acid at 80° for 4 hr, a mixture of products was obtained in high yield. The major product, comprising 87% of the mixture, which was obtained in a pure state by crystallization of the mixture, was shown to be (±)-bulnesol (**40**) by comparison of its ir and pmr spectra and its chromatographic mobility with the natural substance.[42]

Three of the five by-products were identified by coinjection experiments as (±)-guaiol (**44**),[17a] (±)-α-bulnesene (**39**), and (±)-β-bulnesene (**45**).[18] These substances were present in the crude mixture to the extent of 5, 2, and 2%, respectively. Two additional by-products, comprising a total of 4% of the mixture, were not identified.



The syntheses outlined here for the sesquiterpenes bulnesol and α-bulnesene demonstrate the efficacy of the decalinic route to totally synthetic guaiazulenes. Although lengthy, the syntheses are highly stereoselective and are remarkably efficient. The overall yield for the production of pure bulnesol from keto alcohol **1** (17 stages) was 19%. α-Bulnesene, also requiring 17 stages, was produced in 16% yield.

Experimental Section

Melting points (Pyrex capillary) are uncorrected. Infrared spectra (ir) were recorded on Perkin-Elmer 137 and 237 spectrophotometers. Proton magnetic resonance spectra (pmr) were obtained on Varian A-60 and T-60 spectrometers. Line positions are given in the Tiers τ scale, with internal tetramethylsilane as standard; the multiplicity, peak areas, coupling constants, and proton assignments are given in parentheses. Consolidated 21-103c and Varian M-66 mass spectrometers provided the mass spectra. High-resolution molecular weight determinations were obtained on a Consolidated 21-110 spectrometer.

Gas–liquid partition chromatography (glpc) analyses were performed on Aerograph Models 90-P and 600-D instruments. Silica gel G was used for thin-layer chromatography (tlc) and silica gel PF_{254} for preparative tlc. Unless otherwise stated, the supports for column chromatography were Mallinckrodt 100–200 mesh SilicAR CC-7 and Woelm neutral alumina. Elemental analyses were performed by the Microanalytical Laboratory, operated by the Department of Chemistry, University of California, Berkeley, Calif.

4aβ-Methyl-5β-*p*-toluenesulfonyloxy-3,4,4a,5,6,7-hexahydronaphthalen-2(1*H*)-one Ethylene Ketal (3). A mixture of 15.899 g (47.6 mmol) of enone tosylate **2**, 400 mg of 2-naphthalenesulfonic acid, 20 ml of freshly distilled ethylene glycol, and 200 ml of dry benzene was heated at reflux for 14 hr in an apparatus equipped with a water separator (Soxhlet extractor containing calcium hydride). After having been cooled, the mixture was added to 200 ml of 5% aqueous potassium bicarbonate and extracted with ether. The combined extracts were washed with water and saturated brine, dried over magnesium sulfate, and evaporated to afford 17.1 g of an orange gum. Two crystallizations of this material from ethyl acetate–pentane gave 9.674 g (54% yield) of ketal tosylate **3** as fine, white needles: ir ($CHCl_3$) 1595, 1490, 1174, 1096, 932, 861, 659 cm^{-1}; pmr ($CDCl_3$) τ 8.88 (s, 3, angular Me), 7.55 (s, 3, aryl Me), 6.08 (s, 4, ketal Hs), 5.48 (broad m, 1, C-5 H), 4.72 (broad s, 1, olefinic H), 2.44 (A_2B_2 with τ_A 2.21 and τ_B 2.66, 4, J_{AB} = 8 Hz, aryl Hs).

Anal. Calcd for $C_{20}H_{26}O_5S$: C, 63.47; H, 6.92; S, 8.47. Found: C, 63.66; H, 7.03; S, 8.23.

8β-Hydroxy-4aβ-methyl-5β-*p*-toluenesulfonyloxy-3,4,4a,5,6,7,8,-8aβ-octahydronaphthalen-2(1*H*)-one Ethylene Ketal and 8β-Hydroxy-4aβ-methyl-5β-*p*-toluenesulfonyloxy-3,4,4a,5,6,7,8-8aα-octahydronaphthalen-2(1*H*)-one Ethylene Ketal (4). Diborane, 100 ml of a 1 *M* BH_3 in tetrahydrofuran solution, was added dropwise over a 25-min period to a stirring solution of 4.517 g (11.9 mmol) of crystalline tosylate **3** in 50 ml of tetrahydrofuran at 0° and under a nitrogen atmosphere. The solution was stirred an additional 1.5 hr at 0° and 2 hr at room temperature. After cooling the solution in an ice bath, 10 ml of methanol was carefully added, followed by 10 ml of 2 *N* sodium hydroxide solution and 30 ml of 30% aqueous hydrogen peroxide. The mixture was stirred for 1 hr at room temperature and then poured into ice–water and extracted with chloroform. The combined extracts were washed with dilute aqueous sodium sulfite solution, water, and saturated brine, and dried over magnesium sulfate. Evaporation of the solvent left 4.672 g (99% yield) of a 3:1 mixture of isomeric hydroxy tosylates as a white solid: ir ($CHCl_3$) 3430, 1597, 1174, 1096, 901, 867, 813 cm^{-1}; pmr ($CDCl_3$) τ 9.10 (s, 0.75, angular Me for minor isomer), 8.95 (s, 2.25, angular Me for major isomer), 7.55 (s, 3, aryl Me), 6.55–5.34 (m, 2, C-5 and C-8 Hs), 6.08 (s, 4, ketal Hs), 2.43 (A_2B_2 with τ_A 2.22 and τ_B 2.65, 4, J_{AB} = 8 Hz, aryl Hs).

4aβ-Methyl-4β-*p*-toluenesulfonyloxy-3,4,4a,5,6,8aβ-hexahydronaphthalen-1(2*H*),7(8*H*)-dione 7-Ethylene Ketal (5). A solution of 4.61 g (11.6 mmol) of isomeric hydroxy tosylates **4** in 25 ml of pyridine was added to an ice-cold dispersion of 2.90 g (29.0 mmol) of chromium trioxide in 50 ml of pyridine. The mixture was kept at room temperature overnight, poured into ice–water, and extracted with ether. The combined extracts were washed thoroughly with water and saturated salt solution, dried over magnesium sulfate, and evaporated to afford 4.52 g of crude keto tosylate mixture (**5** and **6**) as a yellow glass. The crude product crystallized from ethyl acetate–pentane to give 1.90 g of tosylate **5** as a white powder: mp 136–137°; ir ($CHCl_3$) 1707, 1597, 1167, 1089, 935, 909, 840, 807 cm^{-1}; pmr ($CDCl_3$) τ 9.05 (s, 3, angular Me), 7.55 (s, 3, aryl Me), 6.10 (s, 4, ketal Hs), 4.87 (broad m, 1, C-4 H), 2.40 (A_2B_2 with τ_A 2.18 and τ_B 2.61, 4, J_{AB} = 8 Hz, aryl Hs).

Anal. Calcd for $C_{20}H_{26}O_6S$: C, 60.89; H, 6.64; S, 8.13. Found: C, 60.94; H, 6.85; S, 8.06.

6-Methyltricyclo[4.4.0.0^{1,5}]decane-2,9-dione 9-Ethylene Ketal (7). A solution of 591.6 mg (1.5 mmol) of crystalline keto tosylate **5** in 25 ml of 0.25 *N* sodium methoxide in methanol was stirred at room temperature and under nitrogen for 27 hr. Methanol was removed at reduced pressure and the residue dissolved in wet ether.

(42) We thank Drs. H. Minato and H. Ishii of Shionogi and Co., Ltd., in Osaka, Japan, for samples of natural bulnesol and guaiol.

The solution was washed with water and saturated brine, dried over magnesium sulfate, and evaporated to give 262.7 mg of crude tricyclic ketone **7** as an orange oil (79% yield). The crude material solidified on standing. Three recrystallizations from ether gave the analytical sample: mp 52–53°; uv (95% EtOH)[43] 217 (ε 4400) mμ; ir ($CHCl_3$) 1704, 1266, 1091, 1017, 944, 859 cm^{-1}; pmr (CCl_4) τ 8.92 (s, 3, angular Me), 6.16 (m, 4, ketal Hs).

Anal. Calcd for $C_{13}H_{18}O_3$: C, 70.24; H, 8.16. Found: C, 70.14; H, 7.99.

5β-Acetoxy-4aβ-methyl-4,4a,5,6,7,8-hexahydronaphthalen-2(3*H*)-one (9). A solution of 100.0 g (0.56 mol) of hydroxy enone **1**[27] in 400 ml of anhydrous pyridine was treated with 210 ml (2.22 mol) of acetic anhydride. After 27 hr at room temperature, the solution was poured into ice–water and extracted with methylene chloride. The organic extracts were washed with cold 10% aqueous sulfuric acid, saturated sodium bicarbonate solution, water, and saturated brine. The solution was dried (magnesium sulfate) and evaporated to give 122.9 g (99.7% yield) of acetate **9** as an off-white solid. A small portion of the product was recrystallized from ether–petroleum ether to give the analytical sample: mp 89–91°; ir (CCl_4) 1745, 1735, 1680, 1235, 1034, 1007, 935, 864 cm^{-1}; pmr (CCl_4) τ 8.75 (s, 3, angular Me), 7.98 (s, 3, acetoxy Me), 5.42 (broad m, 1, C-5 H), 4.32 (d, 1, J = 1 Hz, olefinic H).

Anal. Calcd for $C_{13}H_{18}O_3$: C, 70.34; H, 8.16. Found: C, 70.17; H, 8.03.

5β-Acetoxy-4aβ-methyl-3,4,4a,5,6,7-hexahydronaphthalen-2(1*H*)-one Ethylene Ketal (10). In a 2-l. three-necked, round-bottomed flask fitted with a magnetic stirrer and two large Soxhlet extractors containing 4A molecular sieves was placed 44.460 g (0.2 mol) of enone acetate **9**, 124.2 g (2 mol) of freshly distilled ethylene glycol, 0.416 g (0.002 mol) of 2-naphthalenesulfonic acid, and 1000 ml of dry benzene. The mixture was stirred and refluxed for 24 hr, cooled in an ice bath, and washed with 5% aqueous sodium bicarbonate, water, and saturated brine. The benzene solution was dried over magnesium sulfate and evaporated to give 53.1 g of a white solid. A pmr spectrum of the crude product revealed the presence of the desired ketal acetate **10**, ketal alcohol **11**, and enone **9**, in a ratio of approximately 7:2:1.

The procedure was repeated with two 44.46-g portions and one 33.63-g portion (reactants appropriately scaled down) of enone **9** to give an additional 143.7 g of crude, white solid. The combined product from the four operations, 196.8 g, was recrystallized from methanol to afford 136.4 g of ketal acetate **10** as a white powder melting at 105–106° (68% yield). Two recrystallizations from methanol gave the analytical sample as fine, white needles: mp 108–109°; ir (CCl_4) 1742 (shoulder), 1732, 1239, 1104, 1028, 1019, 989, 848 cm^{-1}; pmr (CCl_4) τ 8.88 (3, s, angular Me), 8.03 (s, 3, acetoxy Me), 6.16 (s, 4, ketal Hs), 5.32 (d of d, 1, J = 6 and 9 Hz, C-5 H), 4.78 (broad s, 1, olefinic H).

Anal. Calcd for $C_{15}H_{22}O_4$: C, 67.65; H, 8.33. Found: C, 67.56; H, 8.30.

The filtrate from the combined recrystallization was evaporated. The residue was dissolved in ether and the solution dried over magnesium sulfate and evaporated to give 53.9 g of an orange oil. A mixture of the crude oil, 60.0 g of ethylene glycol, 200 mg of 2-naphthalenesulfonic acid, and 500 ml of benzene was stirred and refluxed under a water separator (Soxhlet extractor containing molecular sieves) for 24 hr. After having been cooled to room temperature, the two-phase mixture was separated. The benzene layer was washed with 5% aqueous sodium bicarbonate, water, and saturated brine, and dried over magnesium sulfate. Evaporation of the solvent left 52.6 g of a mixture of ketal acetate **10** and ketal alcohol **11** as an orange solid. This material, without further purification, was reduced with lithium aluminum hydride to compound **11** (*vide infra*).

5β-Hydroxy-4aβ-methyl-3,4,4a,5,6,7-hexahydronaphthalen-2(1*H*)-one Ethylene Ketal (11). a. A solution of 95.0 g (0.357 mol) of ketal acetate **10** in 2000 ml of anhydrous ether was added dropwise over a 40-min period to a stirring suspension of 13.54 g (0.357 mol) of lithium aluminum hydride and 1000 ml of ether. The mixture was stirred an additional 2.25 hr at room temperature under a nitrogen atmosphere. Excess hydride reagent was destroyed by the careful, dropwise addition of 27 ml of water and 22 ml of 10% aqueous sodium hydroxide. The mixture was filtered, and the filtrate was washed with water and saturated salt solution and dried over magnesium sulfate. Evaporation of the solvent left 72.1 g of alcohol **11** as white crystals (90% yield). Two recrystallizations from ether gave the analytical sample: mp 84–85°; ir (CCl_4) 3600, 3470, 1100, 1014, 983, 943, 845 cm^{-1}; pmr (CCl_4) τ 8.97 (s, 3, angular Me), 7.72 (s, 1, OH), 6.53 (m, 1, C-5 H), 6.15 (s, 4, ketal Hs), 4.83 (broad s, 1, olefinic H).

Anal. Calcd for $C_{13}H_{20}O_3$: C, 69.61; H, 8.99. Found: C, 69.73; H, 9.11.

Repetition of the reductive acetate cleavage on two additional samples of ketal acetate **10**, with destruction of excess hydride using water only, gave alcohol **11** in yields of 94 and 95%.

b. A solution of 52.6 g of a crude mixture of ketal acetate **10** and ketal alcohol **11** (*vide supra*) in 700 ml of anhydrous ether was added dropwise over a 40-min period to a stirring suspension of 5.00 g of lithium aluminum hydride in 600 ml of ether. After stirring the mixture an additional 2 hr at room temperature under a nitrogen atmosphere, excess lithium aluminum hydride was destroyed by the careful addition of 50 ml of water. The resulting precipitate was filtered, and the filtrate was washed with water and saturated brine and dried over magnesium sulfate. Evaporation of the solvent left 37.1 g of a yellow oil which crystallized from ether–petroleum ether to afford 20.45 g of ketal alcohol **11**.

5β-Benzyloxy-4aβ-methyl-3,4,4a,5,6,7-hexahydronaphthalen-2(1*H*)-one Ethylene Ketal (12). A 5-l., three-necked, round-bottomed flask fitted with a mechanical stirrer, pressure-equalizing dropping funnel, reflux condenser, and nitrogen inlet was flame dried under a stream of dry nitrogen. Sodium hydride, 24.50 g (0.579 mol, as a 56.8% dispersion in mineral oil), was added to the apparatus and the mineral oil removed by two washings with 50 ml of benzene. A solution of 108.1 g (0.482 mol) of ketal alcohol **11** in 1500 ml of anhydrous benzene and 75 ml of dry dimethyl sulfoxide was added. The mixture was stirred and heated at reflux for 2 hr and a further 1 hr with gradual cooling to room temperature. A solution of 99.0 g (0.579 mol) of benzyl bromide in 750 ml of benzene was added dropwise over 10 min to the stirring mixture at room temperature. The mixture was then stirred and heated at reflux for 1 hr followed by an additional 16 hr of stirring at room temperature. The precipitated sodium bromide was dissolved by the addition of 200 ml of water; the phases were separated, and the aqueous phase extracted with benzene. The combined organic solutions were washed with dilute aqueous ammonia, water, and saturated brine, and dried over magnesium sulfate. Evaporation of the solvent at reduced pressure left 156.6 g of a yellow oil which solidified. Recrystallization of the crude product from ether gave 99.0 g of benzyl ether **12** as a white powder.

The mother liquors were dried and evaporated to afford 55.9 g of an orange oil whose pmr spectrum indicated a 37:13:50 molar ratio of ketal alcohol **11**, benzyl ether **12**, and benzyl bromide, respectively. The oil was dissolved in 500 ml of tetrahydrofuran and added to 4.9 g (0.115 mol, as a 56.8% dispersion in mineral oil) of sodium hydride. The mixture was stirred and heated at reflux for 14 hr and then cooled in an ice bath and diluted with 50 ml of water to dissolve the sodium bromide. The mixture was further diluted with ether. The organic phase was separated, washed with dilute aqueous ammonia, water, and saturated brine, and dried over magnesium sulfate. Evaporation of the solvent left 49.6 g of an orange oil which crystallized from ether to give an additional 22.8 g of crystalline benzyl ether **12**. The total yield of benzyl ether obtained in the two steps was 121.8 g (81% of the theoretical).

The analytical sample was obtained by two recrystallizations from ether: mp 94–95°; ir (CCl_4) 3055, 3015, 1495, 1100, 1024, 981, 940, 845 cm^{-1}; pmr ($CDCl_3$) τ 8.83 (s, 3, angular Me), 6.72 (d of d, 1, J = 4 and 11 Hz, C-5 H), 6.05 (s, 4, ketal Hs), 5.43 (AB q with τ_A 5.32 and τ_B 5.55, 2, J_{AB} = 12 Hz, benzyl CH_2), 4.72 (broad s, 1, olefinic H), 2.66 (s, 5, aryl Hs).

Anal. Calcd for $C_{20}H_{26}O_3$: C, 76.40; H, 8.33. Found: C, 76.17; H, 8.17.

5β-Benzyloxy-8β-hydroxy-4aβ-methyl-3,4,4a,5,6,7,8,8aβ-octahydronaphthalen-2(1*H*)-one Ethylene Ketal (14) and 5β-Benzyloxy-8α-hydroxy-4aβ-methyl-3,4,4a,5,6,7,8,8aα-octahydronaphthalen-2(1*H*)-one Ethylene Ketal (15). a. A solution of diborane (0.752 mol) in tetrahydrofuran was prepared under a dry nitrogen atmosphere at 0–5° by the addition of 213.6 g (1.504 mol) of freshly distilled boron trifluoride ether complex to a stirring suspension of 47.0 g (1.242 mol) of sodium borohydride in 250 ml of tetrahydrofuran. After stirring the mixture for 10 min, a solution of 118.2 g (0.376 mol) of ketal olefin **12** in 1300 ml of tetrahydrofuran was added. The mixture was stirred for 14 hr at 0° and then allowed to warm to room temperature over a 1-hr period. To the mixture

(43) The uv spectrum was measured on a Beckman DK-2A "Ratio Recording" spectrophotometer.

were added cautiously 600 ml of 3 *N* sodium hydroxide solution and 600 ml of 30% aqueous hydrogen peroxide, with stirring in an ice bath. The mixture was heated at reflux for 1 hr, cooled, and diluted with 1.5 l. of ether. The organic phase was separated and washed with dilute aqueous sodium sulfite solution (caution, exothermic). The combined aqueous solutions were extracted with ether; the ether extracts were combined and added to the original organic phase. The combined organic solution was washed with water and saturated salt solution, dried over magnesium sulfate, and evaporated at reduced pressure to yield 123.7 g of a cloudy oil. The pmr spectrum of the crude product indicated considerable loss of the ketal function.

A 140-mg sample of crude product was applied to a preparative tlc plate (20 cm × 20 cm × 2 mm). The plate was developed twice with 1:1 benzene–ethyl acetate. Visualization by uv light revealed the presence of 5 distinct bands: A (R_f 0.80), B (0.59), C (0.47), D (0.25), and E (0.16). The bands were scraped off the plate individually and extracted with hot ethyl acetate. Evaporation of the solvent gave the pure compounds, which were characterized by their ir and pmr spectra, and high-resolution mass spectrum molecular weights.

Band A afforded 5.3 mg of tertiary alcohol **13** as an oil: ir (CCl_4) 3500, 1089, 1053, 949, 848 cm^{-1}; pmr ($CDCl_3$) τ 8.97 (s, 3, angular Me), 6.64 (broad m, 1, $PhCH_2OCH$), 6.03 (s, 4, ketal Hs), 5.46 (AB q with τ_A 5.33 and τ_B 5.60, 2, J_{AB} = 12 Hz, benzyl CH_2), 2.65 (s, 5, aryl Hs). Calcd for $C_{20}H_{28}O_4$: mol wt 332.1987. Found: 332.1982 (high-resolution mass spectrum).

Band B afforded 31.6 mg of *cis*-alcohol **14** as an oil: ir ($CHCl_3$) 3600, 3340, 1085, 1055, 1017, 938 cm^{-1}; pmr ($CDCl_3$) τ 8.82 (s, 3, angular Me), 6.80 (broad m, 1, $W_{h/2}$ = 10 Hz, C-5H), 6.06 (s, 4, ketal Hs), 6.06 (m, 1, C-8 H), 5.48 (AB q with τ_A 5.36 and τ_B 5.60, 2, J_{AB} = 12 Hz, benzyl CH_2), 2.63 (s, 5, aryl Hs). Calcd for $C_{20}H_{28}O_4$: mol wt 332.1987. Found: 332.1989 (high-resolution mass spectrum).

Band C yielded 22.5 mg of *trans*-alcohol **15** as an oil: ir ($CHCl_3$) 3585, 3425, 1095, 1045, 949, 899 cm^{-1}; pmr ($CDCl_3$) τ 9.07 (s, 3, angular Me), 7.1–6.5 (broad m, 2, C-5 and C-8 Hs), 6.03 (s, 4, ketal Hs), 5.46 (AB q with τ_A 5.36 and τ_B 5.56, 2, J_{AB} = 12 Hz, benzyl CH_2), 2.66 (s, 5, aryl Hs). Calcd for $C_{20}H_{28}O_4$: mol wt 332.1987. Found: 332.1999 (high-resolution mass spectrum).

Band D yielded 17.2 mg of diol **16** as an oil: ir ($CHCl_3$) 3400 cm^{-1}; pmr ($CDCl_3$) τ 8.85 (s, 3, angular Me), 6.36 (broad m, 4, $W_{h/2}$ = 7 Hz, OCH_2CH_2OH), 5.48 (AB q with τ_A 5.36 and τ_B 5.60, 2, J_{AB} = 12 Hz, benzyl CH_2), 2.66 (s, 5, aryl Hs). Calcd for $C_{20}H_{30}O_4$: mol wt 334.2144. Found: 334.2146 (high-resolution mass spectrum).

Band E afforded 27.7 mg of oily diol **17**: ir ($CHCl_3$) 3410 cm^{-1}; pmr ($CDCl_3$) τ 8.82 (s, 3, angular Me), 6.97 (m, 1, $W_{h/2}$ = 6 Hz), 6.36 (broad m, 4, $W_{h/2}$ = 7 Hz, OCH_2CH_2OH), 5.52 (AB q with τ_A 5.40 and τ_B 5.63, 2, J_{AB} = 12 Hz, benzyl CH_2), 2.66 (s, 5, aryl Hs). Calcd for $C_{20}H_{30}O_4$: mol wt 334.2144. Found: 334.2146 (high-resolution mass spectrum).

The crude reaction mixture, 111.4 g, was chromatographed on 2 kg of SilicAR using ether as eluent. The progress of the separation was followed by tlc analysis. Combination of many intermediate fractions and evaporation of the solvent gave 49.37 g of a 7:3 mixture of isomeric ketal alcohols **14** and **15** contaminated with *ca.* 10% tertiary alcohol **13**. This material was used subsequently without further purification.

b. Diborane, 6.4 ml of a 1 *M* BH_3 in tetrahydrofuran solution, was added to a stirring, ice-cold solution of 2.000 g (6.35 mmol) of ketal olefin **12** in 20 ml of tetrahydrofuran. The cooling bath was removed and the solution stirred under a nitrogen atmosphere at room temperature for 6 hr. The reaction flask was cooled in an ice bath and excess diborane was destroyed by the careful addition of 0.2 ml of water, followed immediately by 2.5 ml of 3 *N* sodium hydroxide solution and 2.5 ml of 30% aqueous hydrogen peroxide. After having been stirred for 3.25 hr at room temperature, the mixture was diluted with ether and washed with saturated brine. The ethereal solution was dried over magnesium sulfate and evaporated to give 2.021 g of a viscous, clear oil (96% yield). The pmr spectrum of the crude product showed a 2:1 ratio of *cis*-ketal alcohol **14** to *trans*-ketal alcohol **15**, based on peak areas of the corresponding angular methyl resonances. Preparative tlc, as described in part a, led to the isolation of a 2:1 ratio of isomers **14** and **15** and trace amounts of tertiary alcohol **13**. There was no evidence for reductive ketal cleavage.

4β-Benzyloxy-4aβ-methyl-3,4,4a,5,6,8aβ-hexahydronaphthalen-1(2*H*),7(8*H*)-dione 7-Ethylene Ketal (18) and 4β-Benzyloxy-4aβ-methyl-3,4,4a,5,6,8aα-hexahydronaphthalen-1(2*H*),7(8*H*)-dione 7-Ethylene Ketal (19). Chromium trioxide, 82.20 g (0.822 mol, dried in a vacuum desiccator over phosphorus pentoxide), was added to a stirring solution of 130.04 g (1.644 mol) of anhydrous pyridine in 2000 ml of anhydrous methylene chloride cooled in an ice bath. The deep red suspension was stirred for 15 min at 0° and 45 min at room temperature. A solution of 45.615 g (0.137 mol) of a 7:3 mixture of isomeric alcohols **14** and **15** in 200 ml of methylene chloride was added, all at once, to the suspension. A black, tarry deposit was formed immediately. After stirring the mixture for 15 min at room temperature, the methylene chloride solution was decanted from the tarry precipitate which was triturated with four 500-ml portions of ether. The combined organic phases were washed with 5% aqueous sodium hydroxide, water, ice-cold 5% aqueous hydrochloric acid, 5% aqueous sodium bicarbonate, and saturated sodium chloride solution. The solution was dried over magnesium sulfate and evaporated to give 42.633 g of isomeric ketones **18** and **19** as a viscous yellow oil (94% yield). The ratio of *cis*-ketone **18** to *trans*-ketone **19** was determined to be 7:3 by comparison of the peak areas of the angular methyl resonances at τ 9.03 (ketone **18**) and τ 9.17 (ketone **19**) in the pmr spectrum.

A similar oxidation of a 2:1 mixture of alcohols **14** and **15**, contaminated with a trace of tertiary alcohol **13**, gave a 2:1 mixture of ketones **18** and **19** in 94% yield.

4β-Benzyloxy-4aβ-methyl-3,4,4a,5,6,8aα-hexahydronaphthalen-1(2*H*),7(8*H*)-dione 7-Ethylene Ketal (19). A helium-purged solution of 45.315 g (0.137 mol) of a 7:3 mixture of isomeric ketones **18** and **19** in 600 ml of methanol was treated with 200 ml of a 3% methanolic sodium methoxide solution. The resulting solution was stirred for 1 hr under a helium atmosphere. Evaporation of the methanol at reduced pressure left an orange, semisolid residue which was dissolved in 1 l. of ether. The ethereal solution was washed with water and saturated brine, dried over magnesium sulfate, and evaporated. Crystallization of the residue, 44.29 g of a yellow oil, from ether at −10° gave 28.64 g of ketone **19** as white crystals having mp 87–89°.

Evaporation of the mother liquors left 15.45 g of a yellow oil. This material was dissolved in 200 ml of methanol; the solution was purged with helium, treated with 70 ml of 3% methanolic sodium methoxide, and stirred for 1 hr at room temperature under helium. Work-up gave 14.46 g of a yellow oil which partially crystallized from ether at −10° to afford an additional 3.90 g of ketone **19**. The total yield of crystalline *trans* ketone **19** was 32.54 g (72% of the theoretical). The analytical sample was obtained by recrystallization from ether: mp 88–89°; ir (CCl_4) 1716, 1495, 1199, 1095, 1024, 887, 858, 742 cm^{-1}; pmr (CCl_4) τ 9.17 (s, 3, angular Me), 6.53 (d of d, 1, J = 5 and 10 Hz, C-4 H), 6.18 (s, 4, ketal Hs), 5.46 (AB q with τ_A 5.39 and τ_B 5.54, 2, J_{AB} = 11 Hz, benzyl CH_2), 2.73 (s, 5, aryl Hs).

Anal. Calcd for $C_{20}H_{26}O_4$: C, 72.70; H, 7.93. Found: C, 72.46; H, 7.97.

5β-Benzyloxy-4aβ-methyl-8-methylene-3,4,4a,5,6,7,8,8aα-octahydronaphthalen-2(1*H*)-one Ethylene Ketal (20). a. Sodium hydride, 7.63 g (180.2 mmol, as a 56.8% dispersion in mineral oil), in a 1-l., three-necked, round-bottomed flask fitted with a condenser, mechanical stirrer, and nitrogen inlet was washed with two 50-ml portions of dry pentane under a stream of nitrogen. The flask was stoppered with a serum cap and 90 ml of dimethyl sulfoxide was added *via* syringe. The mixture was heated at 73–75° for 60 min, during which time hydrogen evolution ceased. The resulting solution of methylsulfinyl carbanion[31] was cooled in an ice bath and 61.20 g (171.6 mmol) of methyltriphenylphosphonium bromide in 175 ml of warm dimethyl sulfoxide was added. After stirring the deep red solution of ylide for 15 min at room temperature, 28.363 g (85.8 mmol) of crystalline ketal ketone **19** in 120 ml of dimethyl sulfoxide was added. The dark red solution was stirred at 53° for 17 hr under a nitrogen atmosphere, then allowed to cool to room temperature, and poured into ice–water. The mixture was thoroughly extracted with pentane. The combined extracts were washed with ice-cold 1:1 dimethyl sulfoxide–water, water, and saturated brine, dried over magnesium sulfate, and evaporated. The residual pale yellow oil, 29.2 g, was filtered through 75 g of activity I alumina, using 1500 ml of pentane for the operation. Evaporation of the solvent left 25.094 g of a clear oil which solidified. The crude product was recrystallized from pentane at −10° to give 23.593 g of olefin **20** as hard, white crystals with mp 65–67° (84% yield). Recrystallization from pentane afforded the analytical sample: mp 65.8–66.2°; ir (CCl_4) 3085, 3020, 1645, 1496, 1099, 1027, 942, 893 cm^{-1}; pmr (CCl_4) τ 9.23 (s, 3, angular Me), 6.86 (d of d, 1, J = 4 and 11 Hz, C-5 H), 6.15 (s, 4, ketal Hs), 5.50 (AB

q with τ_A 5.42 and τ_B 5.58, 2, J_{AB} = 12 Hz, benzyl CH_2), 5.56 (s, 1, olefinic H), 5.27 (s, 1, olefinic H), 2.74 (s, 5, aryl Hs).

Anal. Calcd for $C_{21}H_{28}O_3$: C, 76.79; H, 8.59. Found: C, 76.89; H, 8.76.

b. A solution of 1.550 g (4.69 mmol) of a 2:1 mixture of cis- and trans-fused ketones **18** and **19**, respectively, in 6 ml of dimethyl sulfoxide was added to a slurry of 9.38 mmol of methylenetriphenylphosphorane in 15 ml of dimethyl sulfoxide, prepared as in part **a** above. The resulting dark red solution was stirred for 48.5 hr at room temperature, poured into ice–water, and extracted with pentane. The combined extracts were washed with 1:1 water–dimethyl sulfoxide, water, and saturated brine, and dried. Evaporation of the solvent left 1.344 g of olefin **20** as a pale yellow oil (87% yield). The pmr and ir spectra of this material were identical with those of the analytically pure material. Crystallization from pentane at −10° gave 0.958 g of **20** as white crystals melting at 62–65°.

5β-Benzyloxy-4aβ-methyl-8-methylene-3,4,4a,5,6,7,8,8aα-octahydronaphthalen-2(1*H*)-one (21). A solution of 23.67 g of ketal olefin **20** in 90 ml of glacial acetic acid was diluted with 10 ml of water and heated on a steam bath with occasional swirling for 30 min. The solution was then poured into 2 l. of ice–water and extracted with ether. The combined extracts were washed with 5% aqueous sodium hydroxide, water, and saturated brine, and dried over magnesium sulfate. Evaporation of the solvent left 20.51 g of a white solid, mp 72–75°. The crude product was recrystallized from hexane to give 18.40 g of enone **21** as white needles: mp 74–75.5°; ir (CCl_4) 3085, 3030, 1715, 1645, 1156, 1095, 1053, 1028, 899, 887 cm^{-1}; pmr (CCl_4) τ 9.05 (s, 3, angular Me), 6.88 (d of d, 1, J = 4 and 11 Hz, C-5 H), 5.50 (AB q with τ_A 5.38 and τ_B 5.62, 2, J_{AB} = 12 Hz, benzyl CH_2), 5.55 (s, 1, olefinic H), 5.20 (s, 1, olefinic H), 2.75 (s, 5, aryl Hs).

Anal. Calcd for $C_{19}H_{24}O_2$: C, 80.24; H, 8.51. Found: C, 80.33; H, 8.45.

A second crop of enone **21** having mp 70–72.5° raised the yield of recrystallized product to 19.00 g (93% yield).

5β-Benzyloxy-4aβ,8aβ-dimethyl-3,4,4a,5,6,7,8,8aα-octahydronaphthalen-2(1*H*)-one (25). a. Rh/Al_2O_3–Hexane Hydrogenation of Keto Olefin 21. A mixture of 100 mg of enone **21** and 20 mg of 5% rhodium/alumina in 7 ml of hexane was hydrogenated at room temperature and atmospheric pressure. Hydrogen uptake ceased after 14 min with 1 equiv of hydrogen absorption. The mixture was filtered and the filtrate evaporated to yield 97 mg of a 7:1 mixture of ketone **25** and its C-8 epimer **26**, respectively, as a clear oil. The composition of the mixture was determined by comparison of the peak areas of the angular methyl resonances at τ 8.87 (ketone **25**) and τ 8.95 (ketone **26**) in the pmr spectrum.

In a preparative run, a mixture of 10.000 g of enone **21** and 1.000 g of 5% rhodium/alumina in 500 ml of hexane was hydrogenated at room temperature and atmospheric pressure. Hydrogen uptake ceased after 50 min and 1 equiv of hydrogen absorption. The catalyst was removed by suction filtration and the filtrate evaporated to afford 10.076 g of a 7:1 mixture of ketones **25** and **26** as a clear oil. Crystallization of the crude product from hexane at −10° gave 7.671 g of ketone **25** as hard, white crystals, mp 58–60° (76% yield). The analytical sample was obtained by recrystallization from hexane: mp 59–60°; ir (CCl_4) 1715, 1497, 1205, 1147, 1111, 1093, 1049, 1026, 995 cm^{-1}; pmr (CCl_4) τ 9.08 (d, 3, J = 6.6 Hz, secondary Me), 8.87 (s, 3, angular Me), 7.10 (broad m, 1, $W_{h/2}$ = 14 Hz, C-5 H), 5.53 (AB q with τ_A 5.40 and τ_B 5.66, 2, J_{AB} = 12 Hz, benzyl CH_2), 2.80 (s, 5, aryl Hs).

Anal. Calcd for $C_{19}H_{26}O_2$: C, 79.68; H, 9.15. Found: C, 79.47; H, 9.31.

b. Rh/Al_2O_3–Ethyl Acetate Hydrogenation of Keto Olefin 21. A mixture of 100 mg of enone **21** and 20 mg of 5% rhodium/alumina in 3 ml of ethyl acetate was hydrogenated at room temperature and atmospheric pressure. Hydrogen absorption ceased after 90 min and the uptake of 1 equiv of hydrogen. The mixture was filtered and the filtrate evaporated to give 98 mg of a 5:1 mixture of epimeric ketones **25** and **26** as a clear oil.

c. Rh/C–Ethyl Acetate Hydrogenation of Keto Olefin 21. A mixture of 100 mg of enone **21** and 20 mg of 5% rhodium/carbon in 3 ml of ethyl acetate was hydrogenated at room temperature and atmospheric pressure. Hydrogenation ceased after 90 min with the uptake of 1 equiv of hydrogen. The mixture was filtered and the filtrate evaporated to afford 100 mg of a 5:1 mixture of ketones **25** and **26** as a clear oil.

d. Pt/C–Hexane Hydrogenation of Keto Olefin 21. A mixture of 100 mg of ketone **21** and 10 mg of 5% platinum/carbon in 8 ml of hexane was hydrogenated at room temperature and atmospheric pressure. Hydrogen uptake ceased at 1-equiv absorption in 50 min. The mixture was filtered and the filtrate evaporated to give 98 mg of a 5:1 mixture of epimeric ketones **25** and **26** as a clear oil.

e. PtO_2–Ethyl Acetate Hydrogenation of Keto Olefin 21. A mixture of 89 mg of ketone **21**, 20 mg of reduced platinum oxide, and 6 ml of ethyl acetate was hydrogenated at room temperature and atmospheric pressure. Absorption of 1 equiv of hydrogen required *ca.* 3 hr; an additional 0.1 equiv of hydrogen was absorbed after 20 hr. The mixture was filtered and the filtrate evaporated to afford 89 mg of a 5:1 mixture of ketones **25** and **26** as a clear oil.

1β-Benzyloxy-4β,8aβ-dimethyl-6-ethylidene-4aα-decahydronaphthalene (27). Sodium hydride, 2.95 g (69.7 mmol, as a 56.8% dispersion in mineral oil), was placed in a 500-ml, three-necked, round-bottomed flask fitted with a magnetic stirrer, condenser, and nitrogen inlet tube. The mineral oil was removed by three 20-ml pentane washes, under a stream of nitrogen. The flask was stoppered with a serum cap, 35 ml of dimethyl sulfoxide was added *via* syringe, and the mixture was heated with stirring at 74° for 60 min, during which time hydrogen evolution ceased. The resulting solution of methylsulfinyl carbanion[31] was cooled in an ice–water bath, and 24.63 g (66.4 mmol) of ethyltriphenylphosphonium bromide in 75 ml of warm dimethyl sulfoxide was added *via* syringe. The red-orange suspension of ylide was stirred at room temperature for 15 min. A solution of 9.525 g (33.2 mmol) of ketone **25** in 50 ml of dimethyl sulfoxide was introduced into the flask by syringe, and the solution stirred for 17 hr at 55° under a nitrogen atmosphere. The red solution was allowed to cool to room temperature and poured onto 200 ml of ice–water, and the heterogenous mixture thoroughly extracted with pentane. The combined extracts were washed with ice-cold 1:1 water–dimethyl sulfoxide, water, and saturated brine solution, dried over magnesium sulfate, and evaporated. The residual light yellow oil, 9.923 g, was filtered through 20 g of activity I alumina, using 100 ml of pentane to elute the product. Evaporation of the solvent left 9.267 g of oily olefin **27** (93.5% yield): ir (neat) 1495, 1095, 1027, 734 cm^{-1}; pmr (CCl_4) τ 9.08 (two doublets, 3, secondary methyls), 8.97 (s, 3, angular Me), 8.47 (d, 3, J = 6 Hz, olefinic Me), 7.20 (broad m, 1, $W_{h/2}$ = 12 Hz, C-1 H), 5.58 (AB q with τ_A 5.47 and τ_B 5.70, 2, J_{AB} = 12 Hz, benzyl CH_2), 4.95 (q, 1, J = 6 Hz, olefinic H), 2.83 (s, 5, aryl Hs).

The analytical sample was secured by filtering 200 mg of crude product through 1 g of activity I alumina, using pentane as solvent.

Anal. Calcd for $C_{21}H_{30}O$: C, 84.51; H, 10.13. Found: C, 84.34; H, 9.93.

1β-Benzyloxy-4β,8aβ-dimethyl-6ξ-(1ξ-hydroxyethyl)-4aα-decahydronaphthalene (28). Diborane, 60 ml of a 1 *M* BH_3 in tetrahydrofuran solution, was added dropwise over 45 min to a stirring, cold (ice bath) solution of 8.754 g (29.4 mmol) of olefin **27** in 40 ml of tetrahydrofuran. The resulting solution was stirred for 7.5 hr, under a dry nitrogen atmosphere, with gradual warming to room temperature. The solution was cooled in an ice bath, and excess diborane destroyed by careful addition of a solution of 3 ml of water in 30 ml of tetrahydrofuran, followed immediately by the rapid addition of 20 ml of 3 *N* sodium hydroxide solution and 20 ml of 30% aqueous hydrogen peroxide. The mixture was stirred overnight at room temperature, diluted with 100 ml of ether, and poured into 150 ml of saturated sodium chloride solution. The aqueous phase was separated and extracted with ether. The extracts were combined with the original ether solution and the combination washed with water and saturated sodium chloride solution, and dried over magnesium sulfate. Evaporation of the solvent at reduced pressure left 9.283 g of isomeric alcohols **28** as a clear oil (100% yield). The analytical sample was obtained by filtering 120 mg of crude product through 1.2 g of activity II alumina, using ether as solvent: ir (neat) 3330, 1490, 1090, 975, 935, 888, 734 cm^{-1}; pmr (CCl_4) τ 9.17, 9.08, 9.02 (secondary and angular methyls), 8.90 (d, J = 6 Hz, RCHOHCH_3, 8.87 (d, J = 6 Hz, RCHOHCH_3), 7.15 (broad m, C-1 H), 6.33 (broad m, RCHOHCH$_3$), 5.56 (overlapping AB quartets, benzyl CH_2), 2.81 (s, aryl Hs).

Anal. Calcd for $C_{21}H_{32}O_2$: C, 79.79; H, 10.19. Found: C, 79.85; H, 10.33.

6α-Acetyl-1β-benzyloxy-4β,8aβ-dimethyl-4aα-decahydronaphthalene (29) and 6β-Acetyl-1β-benzyloxy-4β,8aβ-dimethyl-4aα-decahydronaphthalene (30). To a 1-l., three-necked, round-bottomed flask fitted with a mechanical stirrer and a drying tube containing Drierite was added 25.07 g (317 mmol) of anhydrous pyridine and 400 ml of dry methylene chloride. The solution was stirred in an ice bath and 15.85 g (158.5 mmol) of dry chromium trioxide was added in one portion. The deep brown-orange solution was stirred for 15 min at 0° and 60 min at room temperature. A solution of 8.337 g of isomeric alcohols **28** was added, and the solution

stirred for 15 min at room temperature, during which time a tarry deposit formed on the surface of the flask. The methylene chloride solution was decanted from the deposit, which was triturated with three 200-ml portions of ether. The combined, organic phases were washed with 5% sodium hydroxide solution, and the resulting aqueous phase was extracted with ether. The combined extracts were washed with 5% aqueous hydrochloric acid, 5% aqueous sodium bicarbonate solution, and saturated brine, and dried over magnesium sulfate. Evaporation of the solvent gave 8.190 g of epimeric ketones **29** and **30** as a clear oil (99% yield): ir (neat) 1705, 1493, 736 cm^{-1}; pmr (CCl_4) τ 9.12 (d, 3, J = 6 Hz, secondary Me), 9.03 (s, 3, angular Me), 7.99 (s, 3, acetyl Me), 7.53 (broad s, equatorial C-6 H), 7.15 (broad m, 1, C-1 H), 5.56 (two overlapping AB quartets, benzyl CH_2), 2.78 (s, 5, aryl Hs); mass spectrum, *m/e* 314.

6β-Acetyl-1β-benzyloxy-4β,8aβ-dimethyl-4aα-decahydronaphthalene (30). A solution of 3.612 g (11.48 mmol) of epimeric ketones **29** and **30** in 250 ml of methanol was treated with 4.8 ml (57.5 mmol) of concentrated hydrochloric acid. The solution was refluxed for 2 hr, then cooled, and 4.88 g of sodium bicarbonate was added to neutralize the acid. Evaporation of the methanol left a semisolid residue, which was triturated with several portons of ether. The combined ether extracts were washed with water and saturated sodium chloride solution, and dried over magnesium sulfate. Evaporation of the solvent at reduced pressure left 3.501 g of ketone **30** as a light yellow oil (97% yield). The analytical sample was obtained by filtering 129 mg of crude product through 1.4 g of activity I alumina, using ether as eluent: ir (neat) 1705, 1495, 1205, 1096, 1064, 1027, 736 cm^{-1}; pmr (CCl_4) τ 9.12 (d, 3, $J \sim$ 6 Hz, secondary Me), 9.05 (s, 3, angular Me), 8.00 (s, 3, acetyl Me), 7.15 (broad m, 1, $W_{h/2}$ = 15 Hz, C-1 H), 5.53 (AB q with τ_A 5.42 and τ_B 5.65, 2, J_{AB} = 12 Hz, benzyl CH_2), 2.80 (s, 5, aryl Hs).

Anal. Calcd for $C_{21}H_{30}O_2$: C, 80.21; H, 9.62. Found: C, 79.95; H, 9.44.

6β-Acetoxy-1β-benzyloxy-4β,8aβ-dimethyl-4aα-decahydronaphthalene (31) and 6α-Acetoxy-1β-benzyloxy-4β,8aβ-dimethyl-4aα-decahydronaphthalene (33). a. From Ketone 30. A solution of 220 mg (0.70 mmol) of methyl ketone **30** and 284 mg (1.40 mmol) of 85% *m*-chloroperbenzoic acid in 10 ml of methylene chloride was kept at reflux for 178 hr. After having been cooled, the solution was diluted with ether, washed with 5% sodium hydroxide solution, water, and saturated brine, and dried over magnesium sulfate. Evaporation of the solvent left 211 mg of a clear, viscous oil. A portion of the crude product, 169 mg, was spotted on a preparative tlc plate (20 cm × 20 cm × 2 mm) and developed twice with 20:1 benzene–ethyl acetate. Uv visualization revealed the presence of two bands, which were scraped off and extracted with hot ethyl acetate. Evaporation of the solution of the faster moving component gave 65 mg of **31** as a light yellow oil: ir (neat) 1733, 1495, 1241, 1098, 1053, 1025, 955, 901, 733 cm^{-1}; pmr (CCl_4) τ 9.13 (d, 3, J = 8 Hz, secondary Me), 9.02 (s, 3, angular Me), 8.08 (s, 3, acetoxy Me), 7.16 (broad m, 1, $W_{h/2}$ = 14 Hz, C-1 H), 5.55 (AB q with τ_A 5.42 and τ_B 5.68, 2, J_{AB} = 12 Hz, benzyl CH_2), 5.40 (broad m, 1, C-6 H), 2.80 (s, 5, aryl Hs).

Anal. Calcd for $C_{21}H_{36}O_3$: C, 76.33; H, 9.15. Found: C, 76.14; H, 8.96.

The slower moving band afforded 17 mg of diester **32** as an oil. The structure of **32** follows from its spectral data: ir (neat) 1733, 1715, 1266, 1238, 1111, 1022, 986, 906, 790, 763, 712 cm^{-1}; pmr (CCl_4) τ 9.03 (d, 3, J = 6.4 Hz, secondary Me), 8.82 (s, 3, angular Me), 8.05 (s, 3, acetoxy Me), 5.35 (broad m, 2, $W_{h/2}$ = 14 Hz, C-1 H and C-6 H), 2.67 (m, 3, aryl Hs), 2.05 (m, 2, aryl Hs).

In another experiment, ketone A and 10% excess *m*-chloroperbenzoic acid in methylene chloride were refluxed for 67 hr. Work-up afforded an oil consisting of a 9:1 mixture of acetate **31** and starting material **30**.

b. From a Mixture of Ketones 29 and 30. A solution of 220 mg (0.70 mmol) of epimeric ketones **29** and **30** and 284 mg (1.40 mmol) of 85% *m*-chloroperbenzoic acid in 10 ml of methylene chloride was refluxed for 178 hr. The solution was cooled, diluted with ether, washed with 5% aqueous sodium hydroxide solution, water, and saturated brine, and dried over magnesium sulfate. Evaporation of the solvent left 217 mg of a clear, viscous oil. A 132-mg sample of the crude product was spotted on a preparative tlc plate (20 cm × 20 cm × 2 mm) and developed twice with 20:1 benzene–ethyl acetate. Uv visualization indicated two distinct bands, which were scraped off and extracted with hot ethyl acetate.

The band of larger R_f gave 40 mg of a 2:3 mixture of epimeric acetates **31** and **33**, respectively. The infrared spectrum of the mixture was nearly superimposable on that of pure compound **31**, with new bands appearing at 786 and 751 cm^{-1}. In addition to the resonances attributable to **31**, the pmr spectrum of the mixture showed new signals at τ 8.12 (s, acetoxy Me) and 5.03 (broad s, $W_{h/2}$ = 7 Hz, C-6 H) for compound **33**. The composition of the mixture was determined by analysis of the integrated peak areas from τ 4.8 to 6 and by the relative intensities of the acetoxy methyl singlets.

The slower moving tlc band yielded 9 mg of a mixture of epimeric diesters.

6β-Acetyl-4β,8aβ-dimethyl-4aα-decahydronaphth-1β-ol (34). A mixture of 2.421 g of benzyl ether **30** and 0.50 g of preequilibrated 10% palladium/carbon in 40 ml of 95% ethanol was hydrogenated at room temperature and atmospheric pressure. Hydrogen absorption ceased after the uptake of 1 equiv of hydrogen. The mixture was filtered, and the filtrate evaporated at reduced pressure to afford 1.643 g of oily ketol **34** (95% yield), which solidified to a white solid, mp 67–75°, on standing in a refrigerator. Recrystallization from ether gave the analytical sample: mp 84–85°; ir (CCl_4) 3600, 3485, 1709, 1080, 1010 cm^{-1}; pmr (CCl_4) τ 9.12 (s, 3, angular Me), 9.10 (d, 3, J = 6.5 Hz, secondary Me), 7.93 (s, 3, acetyl Me), 7.78 (broad s, 1, OH), 6.90 (diffuse m, 1, $W_{h/2}$ = 13 Hz, C-1 H).

Anal. Calcd for $C_{14}H_{24}O_2$: C, 74.94; H, 10.78. Found: C, 74.76; H, 10.56.

4β,8aβ-Dimethyl-6β-isopropenyl-4aα-decahydronaphth-1β-ol (35). Sodium hydride, 861 mg (20.36 mmol, as a 56.8% dispersion in mineral oil), was placed in a 100-ml, three-necked, round-bottomed flask fitted with a magnetic stirrer, condenser, and nitrogen inlet tube, and washed under a stream of nitrogen with three 5-ml portions of pentane. The flask was sealed with a serum cap, 10 ml of dimethyl sulfoxide was added *via* syringe, and the mixture was heated at 79° for 35 min, during which time hydrogen evolution ceased. The resulting solution of methylsulfinyl carbanion[31] was cooled in an ice bath, and 6.93 g (19.39 mmol) of methyltriphenylphosphonium bromide in 20 ml of warm dimethyl sulfoxide was added by syringe. The yellow slurry of ylide was stirred for 10 min at room temperature, followed by the addition of 1.450 g (6.47 mmol) of ketol **34** in 10 ml of dimethyl sulfoxide. After stirring the orange-brown solution for 5 hr at 50–54°, it was poured onto ice–water and throughly extracted with pentane. The combined extracts were washed with 1:1 dimethyl sulfoxide–water, water, and saturated brine solution, dried over magnesium sulfate, and evaporated. The residual yellow oil, 1.606 g, was filtered through 4.0 g of activity I alumina using 100 ml of pentane as eluent. Evaporation of the pentane at reduced pressure gave 1.332 g of a white solid, mp 56–64°. Sublimation of this material [bath temperature 55° (0.08 Torr)] afforded 1.078 g of **35**, mp 66–69° (75% yield). Resublimation of a small sample gave the analytical sample: mp 67–70°; ir (CCl_4) 3620, 3450, 3080, 1645, 1075, 1003, 887 cm^{-1}; pmr (CCl_4) τ 9.13 (s, 3, angular Me), 9.13 (d, 3, J = 7.2 Hz, secondary Me), 8.28 (s, 3, olefinic Me), 7.62 (broad s, 1, OH), 6.90 (broad m, 1, $W_{h/2}$ = 14 Hz, C-1 H), 5.36 (broad s, 2, $W_{h/2}$ = 4 Hz, olefinic Hs).

Anal. Calcd for $C_{15}H_{26}O$: C, 81.02; H, 11.79. Found: C, 81.05; H, 11.64.

4β,8aβ-Dimethyl-6β-isopropenyl-3,4,4aα,5,6,7,8,8a-octahydronaphthalen-1(2*H*)-one (36). Chromium trioxide, 828 mg (8.28 mmol), was added in one portion to a stirring solution of 1.310 g (16.56 mmol) of anhydrous pyridine in 20 ml of dry methylene chloride. The flask was stoppered with a drying tube containing Drierite, and the solution stirred for 15 min at room temperature. At the end of this period, 306 mg (1.38 mmol) of alcohol **35** in 3 ml of methylene chloride was added all at once. The deep burgundy solution immediately gave a tarry black deposit. After stirring for 15 min at room temperature, the methylene chloride solution was decanted and the tarry deposit washed with 30 ml of ether. The combined organics were washed with 5% aqueous sodium hydroxide solution, water, and saturated brine, and dried over magnesium sulfate. Evaporation of the solvent at water aspirator pressure and removal of residual pyridine at high vacuum afforded 290 mg of yellow liquid **36** (95% yield): ir (neat) 3077, 1709, 1642, 1241, 1125, 883 cm^{-1}; pmr (CCl_4) τ 8.93 (d, 3, $J \sim$ 7 Hz, secondary Me), 8.88 (s, 3, angular Me), 8.30 (t, 3, $J \sim$ 1 Hz, olefinic Me), 5.35 (broad s, 2, $W_{h/2} \sim$ 4 Hz, olefinic Hs).

The analytical sample was obtained by filtering a small sample of the crude product through activity I alumina, using ether as eluent.

Anal. Calcd for $C_{15}H_{24}O$: C, 81.76; H, 10.98. Found: C, 81.57; H, 10.94.

1β,4aβ-Dimethyl-7β-isopropenyl-8aα-decahydronaphthalene (37). A solution of 239 mg (1.08 mmol) of decalone **36** and 1.8 ml of 85% aqueous hydrazine hydrate in 7 ml of freshly distilled diethylene glycol was heated under a dry nitrogen atmosphere for 2.5 hr at 120° (oil bath). After having been cooled, 0.9 g of potassium hydroxide pellets was added to the solution and the condenser replaced by a Hickmann distillation head. The temperature of the oil bath was raised to 210° over a 1-hr period, and water removed under a slow stream of nitrogen. The reaction mixture was heated an additional 2.5 hr at 210°. After cooling to room temperature, the reaction mixture and water distillate were poured into ice–water and extracted with pentane. The combined extracts were washed with water and saturated brine, and dried over magnesium sulfate. Evaporation of the solvent left 154 mg of a clear liquid (69% yield). Glpc analysis (5 ft × 1/4 in. 20% Carbowax 20 M on 60–80 Chromosorb W) indicated the desired hydrocarbon **37** (96.5%, retention time 10.8 min) was contaminated by two faster moving, minor products (1.5 and 2%, respectively). The analytical sample was obtained by preparative glpc on the above described column: ir (neat) 3086, 1645, 1170, 885 cm^{-1}; pmr (CCl_4) τ 9.10 (d, 3, J = 6.6 Hz, secondary Me), 9.07 (s, 3, angular Me), 8.29 (t, 3, J = 1 Hz, olefinic Me), 5.35 (broad s, 2, $W_{h/2}$ = 4 Hz, olefinic Hs).

Anal. Calcd for $C_{15}H_{26}$: C, 87.30; H, 12.70. Found: C, 87.44; H, 12.71.

1β,4aβ-Dimethyl-7β-(2-hydroxy-2-propyl)-8aα-decahydronaphthalene [(±)-Dihydroeudesmol] (23) and 1α,4aβ-Dimethyl-7β-(2-hydroxy-2-propyl)-8aα-decahydronaphthalene [(±)-Epidihydroeudesmol] (24). a. By Oxymercuration–Demercuration[41] of Olefin 37. A solution of 92.1 mg (0.446 mmol) of olefin **37** in 50 μl of tetrahydrofuran was added to a stirring suspension of 143 mg (0.448 mmol) of mercuric acetate, 0.45 ml of water, and 0.45 ml of tetrahydrofuran. The yellow color dissipated in 3.5 min. The reaction mixture was stirred for 40 min at room temperature, then 0.45 ml of 3 *N* aqueous sodium hydroxide solution was added, followed immediately by 0.45 ml of a 0.5 *M* sodium borohydride in 3 *N* sodium hydroxide solution. The gray mixture was stirred until it clarified and mercury settled out. Sodium chloride was added and the upper tetrahydrofuran layer separated. The aqueous phase was extracted with ether, the ether extracts were added to the tetrahydrofuran phase, and the combination was washed with water and saturated brine and dried over magnesium sulfate. Evaporation of the solvent left 98.7 mg of a clear oil (99% yield). Glpc analysis (3 ft × 1/4 in. 10% Carbowax 20M on 60–80 AW-DMCS Chromosorb P at 196°) indicated a single dihydroeudesmol, **23**. Preparative glpc on the above column afforded the analytical sample, which solidified on standing: mp 56–57° (micro-hot stage); ir (CCl_4) 3579, 3460, 1170, 1091, 916, 906 cm^{-1}; pmr (CCl_4) τ 9.12 (s, 3, angular Me), 9.12 (d, 3, J = 6.8 Hz, secondary Me), 8.88 (s, 6, *i*-Pr methyls).

Anal. Calcd for $C_{15}H_{28}O$: C, 80.29; H, 12.58. Found: C, 80.50; H, 12.86.

b. From (±)-Eudesmol (22). A mixture of 37.2 mg of (±)-β-eudesmol[37] and 4 mg of prereduced platinum oxide in 0.5 ml of methanol was hydrogenated at room temperature and atmospheric pressure. Upon cessation of hydrogen uptake, the mixture was filtered and the filtrate evaporated at reduced pressure to afford 34.7 mg of clear oil. Glpc analysis of the product (3 ft × 1/4 in. 10% Carbowax 20M on 60–80 AW-DMCS Chromosorb P at 196°) revealed the pressure of two components: 80% **23** (retention time 8.4 min) and 20% **24** (6.6 min). Preparative glpc on the above column afforded homogeneous samples of **23** and **24**.

Dihydroeudesmol **23** prepared in part **a** was identical by solution ir, pmr, and glpc retention time with the major hydrogenation product. Compound **24** has the following spectral characteristics: ir (CCl_4) 3600, 3460, 1133, 1093, 907, 847 cm^{-1}; pmr (CCl_4) τ 9.20 (s, 3, angular Me), 9.18 (d, 3, J = 5 Hz, secondary Me), 8.88 (s, 6, *i*-Pr methyls).

4β,8aβ-Dimethyl-6β-isopropenyl-4aα-decahydronaphth-1β-ol *p*-Toluenesulfonate (38). *p*-Toluenesulfonyl chloride, 713 mg (3.74 mmol), was added to a solution of 695 mg (3.12 mmol) of decalol **35** in 4 ml of pyridine. The mixture was swirled to make homogeneous, kept at room temperature for 43 hr, poured onto ice, and extracted with ether. The extracts were washed with ice-cold 10% hydrochloric acid, 5% aqueous sodium bicarbonate solution, and saturated brine, and dried over $MgSO_4$. Evaporation of the solvent at reduced pressure afforded 1.175 g of tosylate **38** as a clear oil (100% yield): ir (neat) 3050, 1640, 1590, 1350, 1182, 1172, 1093, 923, 885, 868, 843, 814 cm^{-1}; pmr ($CDCl_3$) τ 9.17 (d, 3, J = 7.4 Hz, secondary Me), 9.05 (s, 3, angular Me), 8.30 (broad s, 3, olefinic Me), 7.56 (s, 3, aryl Me), 5.77 (m, 1, C-1 H), 5.32 (broad s, 2, olefinic Hs), 2.45 (A_2B_2 with τ_A 2.22 and τ_B 2.68, 4, J_{AB} = 8 Hz, aryl Hs).

The crude tosylate contained entrapped ether which could not be removed by evaporation at high vacuum. This material was used in subsequent reactions without further purification.

1β,4-Dimethyl-7β-isopropenyl-1,2,3,5,6,7,8,8aα-octahydroazulene [α-Bulnesene] (39) and 1β,4-Dimethyl-7-isopropylidene-1,2,3,5,6,7,8,-8aα-octahydroazulene [β-Bulnesene] (45). a. From Tosylate 38. A solution of 1.127 g (2.99 mmol) of crude tosylate **38** in 12.0 ml of a 0.5 *N* potassium acetate in acetic acid solution was heated at 80 ± 1° for 8 hr. The cooled solution was added to 70 ml of ice-cold 3 *N* sodium hydroxide solution and extracted with ether. The combined extracts were washed with water and saturated brine, dried over magnesium sulfate, and evaporated to afford 525 mg of a yellow liquid (86% yield). Pmr examination of the crude product indicated only trace amounts of unreacted tosylate (<2%). Glpc analysis (5 ft × 1/8 in. 20% Carbowax 20M on 60–80 Chromosorb W at 206°) revealed the presence of three components: 87.9% **39** (retention time 5.4 min), 3.7% (4.5 min), and 8.4% (3.6 min). Pure, racemic α-bulnesene was obtained by preparative glpc (5 ft × 1/4 in. 20% Carbowax 20M on 60–80 Chromosorb W at 198°): ir (CCl_4) 3070, 1642, 1640 (shoulder), 1088, 887 cm^{-1}; pmr (CCl_4) τ 9.10 (d, 3, J = 6.7 Hz, secondary Me), 8.32 (splintered s, 6, $W_{h/2}$ = 5.5 Hz, olefinic methyls), 5.40 (broad s, 3, $W_{h/2}$ = 3.5 Hz, olefinic Hs).

Anal. Calcd for $C_{15}H_{24}$: C, 88.16; H, 11.84. Found: C, 87.97; H, 11.71.

b. From Racemic Bulnesol (40). A solution of 46.8 mg (0.21 mmol, mp 91–92.5°) of (±)-bulnesol (*vide infra*) in 0.4 ml of pyridine was treated with 80 μl of freshly distilled phosphorus oxychloride. The solution was swirled to make homogeneous, kept in an oil bath maintained at 80° for 5 min, and allowed to stand an additional 15 min at room temperature. The reaction mixture was added to ice and extracted with ether. The combined extracts were washed with ice-cold 10% hydrochloric acid, 5% aqueous sodium bicarbonate, and saturated brine solution. Evaporation of the solvent from the magnesium sulfate dried solution left 37.0 mg of a clear liquid (86% yield). Glpc analysis indicated a mixture of 73% (±)-α-bulnesene (**39**) and 25% (±)-β-bulnesene (**45**) contaminated by 2% of an unknown component.

c. From Natural Bulnesol (40).[42] A solution of 27.4 mg (0.123 mmol) of natural bulnesol in 0.2 ml of pyridine was treated with 50 μl of phosphorus oxychloride. The solution was swirled to make homogeneous and heated in an oil bath maintained at 80° for 5 min. After standing an additional 15 min at room temperature, the reaction mixture was added to ice and extracted with ether. The extracts were washed with ice-cold 10% hydrochloric acid, 5% aqueous sodium bicarbonate solution, and saturated brine solution, and dried over magnesium sulfate. Evaporation of the solvent afforded 18.2 mg of a yellow liquid (72.5% yield). Glpc analysis (5 ft × 1/8 in. 20% Carbowax 20M on 60–80 Chromosorb W at 206°) indicated the presence of 65% α-bulnesene (**39**, retention time 5.4 min) and 29% β-bulnesene (**45**, 7.0 min) contaminated with 5% of several minor constituents. Pure samples of the dienes were obtained by preparative glpc (5 ft × 1/4 in. 20% Carbowax 20M on 60–80 Chromosorb W at 195°).

The synthetic racemic α-bulnesene obtained in part a exhibited identical ir and nmr spectra with those of natural bulnesene. The two substances also exhibited identical glpc retention times. The structure of β-bulnesene follows from its mode of formation and spectral data: ir (CCl_4) hydrocarbon absorption; pmr (CCl_4) τ 9.13 (d, 3, J = 7.5 Hz, secondary Me), 8.37 (broad s, 9, $W_{h/2}$ = 4.5 Hz, olefinic methyls).

1β-Benzyloxy-4β,8aβ-dimethyl-6β-(2-hydroxy-2-propyl)-4aα-decahydronaphthalene (41). A solution of 3.153 g (10.0 mmol) of ketone **30** in 30 ml of ether was added dropwise, over a period of 20 min, to 30 ml of stirring 1.64 *M* methyllithium in ether maintained under a nitrogen atmosphere. Stirring was continued an additional 30 min at room temperature, followed by destruction of the excess lithium reagent by the careful, dropwise addition of saturated, aqueous ammonium chloride solution. The resulting mixture was diluted with ether and water and shaken, and the aqueous phase separated and discarded. The ethereal solution was washed with saturated brine, dried over magnesium sulfate, and evaporated to give 3.251 g of a clear oil. The infrared spectrum of the crude product revealed the presence of 5–10% unreacted ketone. This material was submitted once more to the above procedure to afford 3.250 g of **41** as a clear oil (98% yield). The analytical sample was obtained by filtering 152 mg of product through 1.4 g of activity

II alumina, using ether as eluent: ir (CCl_4) 3610, 3470, 1495, 1095, 1027, 906, 727 cm^{-1}; pmr (CCl_4) τ 9.13 (d, 3, $J \sim 6.5$ Hz, secondary Me), 9.08 (s, 3, angular Me), 7.17 (broad m, 1, $W_{h/2}$ = 15 Hz, C-1 H), 5.57 (AB q with τ_A 5.45 and τ_B 5.68, 2, J_{AB} = 12 Hz, benzyl CH_2), 2.80 (s, 5, aryl Hs).

Anal. Calcd for $C_{22}H_{34}O_2$: C, 79.95; H, 10.37. Found: C, 79.89; H, 10.26.

4β,8aβ-Dimethyl-6β-(2-hydroxy-2-propyl)-4aα-decahydronaphth-1β-ol (42). A mixture of 3.065 g (9.28 mmol) of benzyl ether **41** and 700 mg of preequilibrated 10% palladium/carbon in 55 ml of 95% ethanol was hydrogenated at room temperature and atmospheric pressure. Hydrogen uptake was rapid and ceased after the absorption of 1 equiv of hydrogen. The mixture was filtered, and the filtrate evaporated to yield 2.181 g of solid diol **42** (98% yield). Three recrystallizations from ether at −10° gave the analytical sample as a white powder: mp 125–130° with prior softening; ir ($CHCl_3$) 3605, 3435, 1003, 903 cm^{-1}; pmr ($CDCl_3$) τ 9.12 (s, 3, angular Me), 9.12 (d, 3, J = 6.9 Hz, secondary Me), 8.82 (s, 6, *i*-Pr methyls), 7.87 (broad s, 2, hydroxyls), 6.83 (broad m, 1, $W_{h/2}$ = 13 Hz, C-1 H).

Anal. Calcd for $C_{15}H_{28}O_2$: C, 74.95; H, 11.74. Found: C, 74.72; H, 11.65.

4β,8aβ,Dimethyl-6β-(2-hydroxy-2-propyl)-4aα-decahydronaphth-1β-ol *p*-Toluenesulfonate (43). Crystalline diol **42**, 1.045 g (4.35 mmol), in 5 ml of pyridine was treated with 0.913 g (4.79 mmol) of *p*-toluenesulfonyl chloride. The mixture was swirled to make homogeneous, kept at room temperature for 21 hr, poured onto ice, and extracted with ether. The combined extracts were washed with ice-cold 10% hydrochloric acid, 5% sodium bicarbonate solution, and saturated sodium chloride solution, and dried over magnesium sulfate. Evaporation of the solvent left 1.477 g of a white foam, whose pmr spectrum revealed the presence of some unreacted diol.

The crude product was dissolved in 5 ml of pyridine, treated with 400 mg of *p*-toluenesulfonyl chloride, and kept at room temperature for 20.5 hr. Work-up as described above afforded 1.476 g of ester **43** as a sticky, white foam (86% yield): ir ($CHCl_3$) 3600, 1596, 1186, 1172, 1095, 916, 883, 870, 840, 810 cm^{-1}; pmr ($CDCl_3$) τ 9.15 (d, s, $J \sim 6$ Hz, secondary Me), 9.08 (s, 3, angular Me), 8.83 (s, 6, *i*-Pr methyls), 7.56 (s, 3, aryl Me), 5.80 (broad m, 1, $W_{h/2}$ = 13 Hz, C-1 H), 2.47 (A_2B_2 with τ_A 2.24 and τ_B 2.70, 4, J_{AB} = 8.4 Hz, aryl Hs); mass spectrum, *m/e* 376.

In previous runs, using 588 and 317 mg of diol **42**, a 10% excess of toluenesulfonyl chloride smoothly gave the desired tosylate **43** in yields of 93 and 92%, respectively.

1β,4-Dimethyl-7β-(2-hydroxy-2-propyl)-1,2,3,5,6,7,8,8aα-octahydroazulene [±-Bulnesol] (40). Crude tosylate **43**, 1.384 g (3.51 mmol), was dissolved in 14.0 ml of a 0.5 *N* potassium acetate in glacial acetic acid solution. The solution was heated in an oil bath maintained at 80 ± 1° for 4 hr, cooled in an ice bath, added to 80 ml of ice-cold 3 *N* sodium hydroxide solution, and extracted with ether. The combined extracts were washed with water and saturated sodium chloride solution, dried over magnesium sulfate, and evaporated to afford 840 mg of a light yellow oil. The pmr spectrum of this material indicated *ca.* 5% unreacted tosylate. Glpc analysis of the crude product (5 ft × 1.8 in. 20% Carbowax 20M on 60–80 Chromosorb W at 201°) revealed the presence of six components: 86.8% (±)-bulnesol (**40**, retention time 23.0 min), 3.3% (19.4 min), 5.1% (±)-guaiol (**44**, 15.9 min), 1.7% (±)-β-bulnesene (**45**, 7.3 min), 2.3% (±)-α-bulnesene (**39**, 5.8 min), and 0.8% (3.8 min). Compounds **40**, **44**, **45**, and **39** were identified by coinjection of authentic natural products.

Refrigeration of a solution of the crude product in 2 ml of hexane afforded 455 mg of a white solid [96% (±)-bulnesol (**40**) by glpc]. Chromatography of the mother liquors on 8.0 g of SilicAR and elution with benzene and 20:1 benzene–ethyl acetate yielded 280 mg of a solid whose recrystallization from hexane at −10° gave 120 mg of white crystals [mp 88.5–90.5°, 95% (±)-bulnesol by glpc]. The total yield of isolated, crystalline bulnesol was 575 mg (74% of theoretical).

The analytical sample was obtained by sublimation [54–55° (0.05 Torr)] and recrystallization from hexane at −10°: mp 91–92.5°;[44] ir (CCl_4) 3600, 3435, 1122, 1091, 964, 933, 895 cm^{-1}; pmr (CCl_4) τ 9.10 (d, 3, J = 6.3 Hz, secondary Me), 8.90 (s, 6, *i*-Pr methyls), 8.44 (broad s, 1, OH), 8.38 (broad s, 3, olefinic Me). The ir and pmr spectra of racemic bulnesol were identical with those of the natural isomer.

Anal. Calcd for $C_{15}H_{26}O$: C, 81.02; H, 11.79. Found: C, 80.89; H, 11.61.

A solution of 35.5 mg (0.09 mmol) of tosylate **43** in 1 ml of ether was added to a stirring suspension of 20.5 mg (0.54 mmol) of lithium aluminum hydride in 1 ml of ether. The mixture was stirred for 67.5 hr at room temperature, then excess hydride was destroyed by the careful addition of wet ether. The resulting slurry was treated with several drops of 3 *N* sodium hydroxide solution, stirred 1 hr, and filtered to remove the white precipitate. Drying and evaporation of the solvent left 19 mg of a clear oil whose pmr spectrum indicated predominantly (±)-bulnesol (**40**). Glpc analysis (5 ft × 1/8 in. 20% Carbowax 20M on 60–80 Chromosorb W at 205°) showed the presence of seven components, the major product being (±)-bulnesol (75%).

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(44) The melting point of (±)-bulnesol is given by Marshall[13] as 77–79° and by Yoshikoshi[19] as 78–80°. Marshall's sample, prepared on a much smaller scale than ours, was purified only by sublimation.[13] Yoshikoshi's sample, which was isolated by preparative glpc, was apparently not recrystallized, although full experimental details are lacking.[19]