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Experiments Directed toward the Total Synthesis of Terpenes. XIX. Synthesis of 8-Methoxy-4aβ,10bβ,12aα-trimethyl-3,4,4a,4bα,5,6,10b,11,12,12a-decahydrochrysen-1(2*H*)-one, a Key Intermediate in the Total Synthesis of (±)-Shionone[1]

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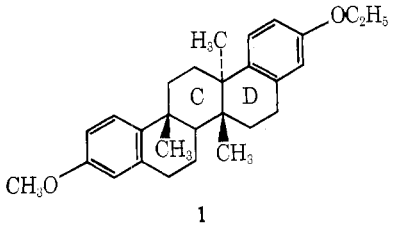
Three approaches to the synthesis of the tetracyclic ketone **3** (title compound), a key intermediate in the total synthesis of *dl*-shionone, are presented. One approach entails the introduction of the C-8a angular methyl group through the protolysis of the methoxycyclopropane grouping in the bicyclic alcohol **22**. The most efficient approach utilizes the triethylaluminum-catalyzed conjugate addition of hydrogen cyanide to introduce the C-4a angular methyl into the bicyclic enone **28**. The final approach reported entails the cationic cyclization of the polyolefinic aldehyde **47** which results in the direct conversion of an acyclic to a tetracyclic system. Confirmation of the structure and stereochemistry of the tetracyclic ketone **3** was obtained through single-crystal X-ray structure analysis.

Previous reports[5] in this series have discussed the planning and experiments that have led to the total synthesis of the pentacyclic triterpene alnusenone (**2**) through the key intermediate pentacyclic diether **1**. Earlier results[6] from



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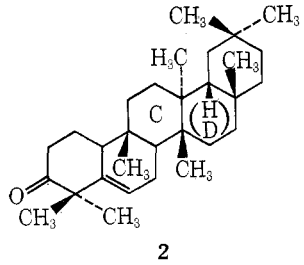

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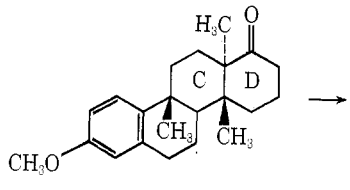
experiments designed to effect the synthesis of the diether **1** showed that the construction of polycyclic systems that contain the trans-fused, diangularly methylated C/D ring system present in alnusenone (**2**) would be a significant synthetic obstacle. As a result, several programs were initiated that were aimed specifically at the development of synthetic procedures for the elaboration of this crucial portion of the molecule. One[5] of these programs (the triethylaluminum-catalyzed conjugate addition of hydrogen cyanide to an appropriate enone) resulted in an efficient means for the synthesis of the diether **1**. The results of the other programs[7] are the subject of this and the following reports. These procedures provide alternate means for the synthesis of the alnusenone class of triterpenes in general and complementary schemes for the construction of trans-fused, diangularly methylated decalin systems in particular.

At the inception of this work two key intermediates for the triterpene syntheses were in mind. In addition to the diether **1**, the tetracyclic ketone **3** was proposed. This substance provides not only the opportunity for elaboration to a pentacyclic structure by the addition of ring E through an annelation procedure, but also the opportunity to develop a total synthesis of the tetracyclic triterpene shionone (**4**).[8] Thus the ketone **3** has functionality appropriately placed in the D ring for the addition of the side chain of shionone (**4**),[8] and the aromatic ring should provide ideal access to



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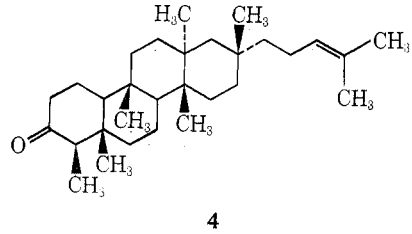

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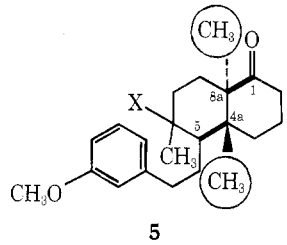
the substitution pattern present in the A ring of the triterpene. An added advantage inherent in the choice of shionone (**4**)[8] as an objective is that methods developed for the elaboration of the A ring in this molecule should also be applicable for the similar transformation of an aromatic ring in the synthesis of the pentacyclic triterpene friedelin.[9] Therefore, the key intermediate tetracyclic ketone **3** serves as a necessary component of the shionone (**4**) synthesis, a potentially useful intermediate in the synthesis of the pentacyclic triterpene series and a model for the investigation of the conversion of an aromatic ring to the shionone–friedelin A ring. As well, the ketone **3** retains the principal synthetic challenge of this series of triterpenes, namely, the trans-fused, diangularly methylated C/D ring system.

Since prior experience[10] in model systems had demonstrated the utility—both stereochemical and practical—of the Friedel–Crafts-type cyclialkylation for the formation of similar tetracyclic ketones, the intermediate objective became the construction of a functional derivative of the ketone **5**. Three approaches were taken to the problem: (1)



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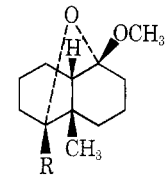
the stereoselective introduction of the C-8a angular methyl group into a dicyclic system that already contained the C-4a methyl group;[7a] (2) the reverse mode that entailed the stereoselective introduction of the C-4a angular methyl group into a dicyclic that already contained the C-8a methyl group;[7b] and (3) the stereoselective formation of the diangularly methylated, dicyclic system through the formation of the C-1 (8a) and C-4a (5) bonds in an acid-catalyzed cyclization of the appropriate polyene.[7c] Each of these approaches successfully led to the desired intermediate ketone **5** and thence to the tetracyclic ketone **3**; the unique features of each approach are discussed below.

1. Stereoselective Introduction of the C-8a Methyl Group. The starting material envisaged for this approach was the methoxyenone **10** (Chart I); this material was prepared in 24% overall yield on large scale from 2-methyldihydroresorcinol and 1,4-dimethoxy-2-butanone[11] through a five-step procedure (see Experimental Section) that involved annelation[12] and then reductive removal[13] of the allylic oxygen function. The location of the functionality in this ketone **10** is ideal for the introduction of both the C-8a methyl group and the β-arylethyl side chain. For the former transformation the protolysis of the derived cyclopropyl ether after a procedure suggested by the work of Wenkert and Berges[12] appeared well suited. In this work an efficient, stereoselective route to the 4a,8a-dimethyl-*cis*-1-decalone system was developed through protolysis of the cyclopropyl ether derived from the corresponding β-methoxyallylic alcohol. The stereochemical control results from the directive effect[14] of the alcohol function in the Simmons–Smith methylenation reaction,[15] and thus the overall stereochemical result is a function of the original configuration of this alcohol.

For the present purposes the desired *trans*-1-decalone series proscribed the use of a similar β-methoxy*allylic* alcohol in the methylenation reaction by virtue of the relative inaccessibility of the required axially oriented alcohol function. The disposition of the functionality in the ketone **10**, however, suggested that the desired outcome might be realized through the methylenation of the corresponding axial *homoallylic* alcohol system and that the latter arrangement might be attainable through condensation and/or reduction reactions of the starting ketone **10**. Two such series were investigated (Chart I).

Condensation of the ketone **10** with dimethyloxosulfonium methylide[16] resulted in equatorial attack by the ylide and the subsequent formation of the α-oxirane **15**, which on reduction with lithium aluminum hydride afforded the α (axial) alcohol **16** (R = H) in 77% overall yield. This alcohol **16** (R = H) was quite labile in contrast to the epimer formed by the direct addition of methyllithium to the ketone **10**, and was not purified sufficiently for combustion analysis. Indeed, the lability of the epimer **16** (R = H) served to prove its stereochemistry, for on standing at room temperature in chloroform solution or on treatment with mild anhydrous acid, the hydroxy enol ether cyclized to form the stable ketal **24** (R = CH_3). The epimeric alcohol was stable to these and even harsher acid conditions.



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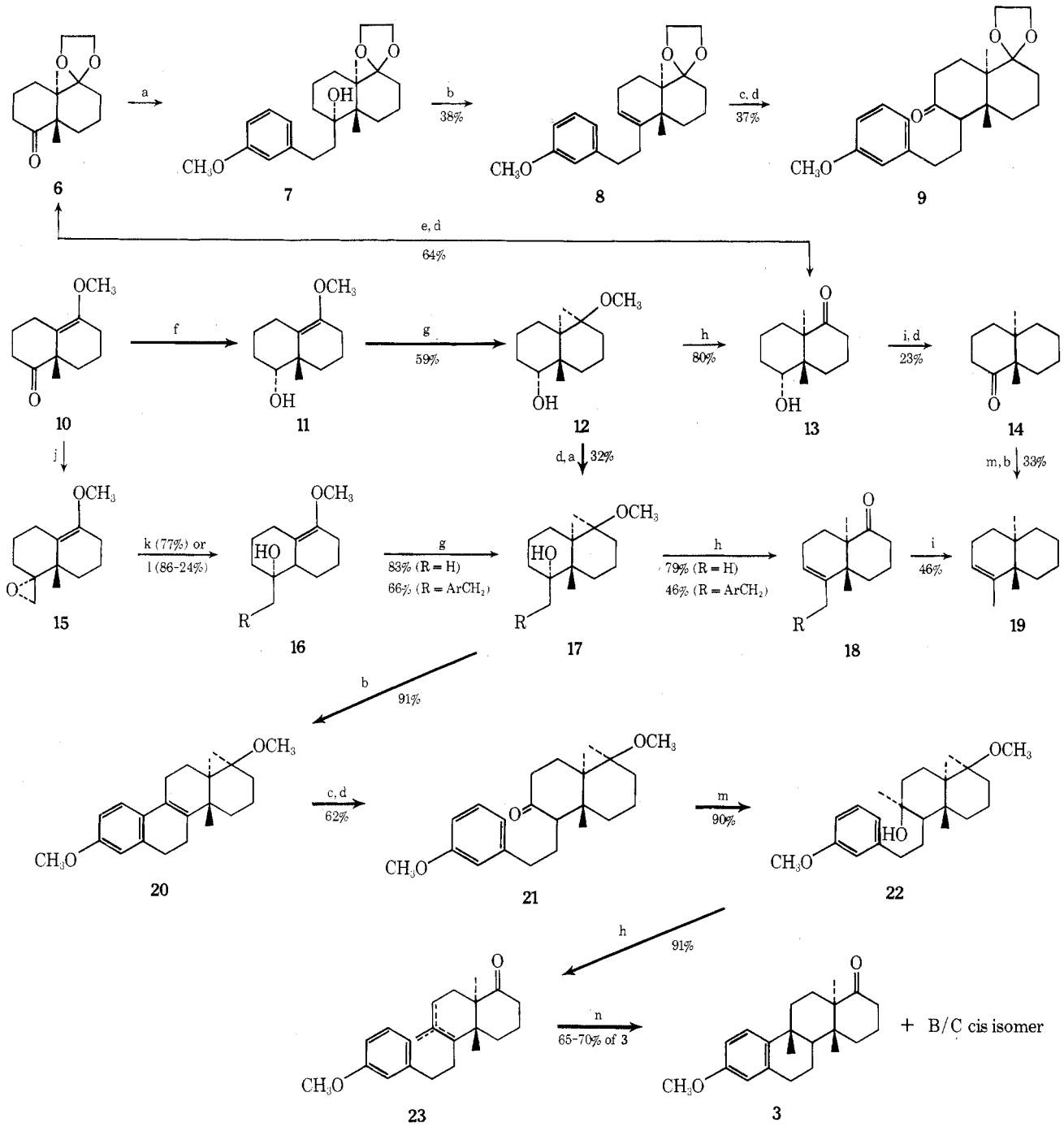
The lower homolog **11** of the axial alcohol **16** (R = H) also became available with the introduction of lithium 9b-boraperhydrophenalyl hydride[17] as a selective reducing agent. Thus, reduction of the ketone **10** with this reagent afforded a quantitative yield of a 70:30 mixture (NMR analysis) of the axial alcohol **11** and its epimeric equatorial isomer in contrast to the results with lithium aluminum hydride or sodium borohydride, which both gave >80% yields of only the equatorial alcohol. Again the axial alcohol **11** was quite labile and was readily converted to the ketal **24** (R = H) on standing in chloroform solution. For this reason both mixtures containing this axial alcohol **16** (R = H) and its higher homolog **16** (R = CH_3) were used in the methylenation reaction without further purification.

Methylenation[15] of both of these alcohol mixtures proceeded smoothly, and the methoxycyclopropane **12** was isolated in 59% overall yield from the ketone **10**, while the higher homolog **17** (R = H) was available in 64% overall yield. In each case the crucial stereochemical question was answered by conversion of these methoxycyclopropane derivatives to the corresponding diangularly methylated dicyclic compounds **14** and **19**. Thus, protolysis[12] of the methoxycyclopropane **12** afforded the keto alcohol **13**, while under similar protolytic conditions the tertiary alcohol in the higher homolog **17** (R = H) suffered dehydration during the cleavage, and the keto olefin **18** (R = H) resulted. Wolff–Kishner reduction and then oxidation of the keto alcohol **13** afforded the decalone **14**, the structure of which was unambiguously established through X-ray single-crystal structural analysis of a derivative (vide infra). Interrelation of this series with the materials prepared from the higher homolog was achieved through the olefin **19**.

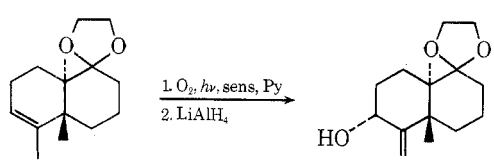
With the preparative and stereochemical success of this sequence for the formation of a trans-fused, diangularly methylated 1-decalone derivative assured, attention was turned to the conversion of these intermediates to the desired tetracyclic ketone **3**. While this objective was ultimately achieved as outlined in Chart I (boldface arrows), this scheme was not possible until several unexpected characteristics of these decalone systems were uncovered.

Chart I
Synthesis of the Tetracyclic Ketone 3 via the Stereoselective Introduction of the C-8a Methyl Group[a]



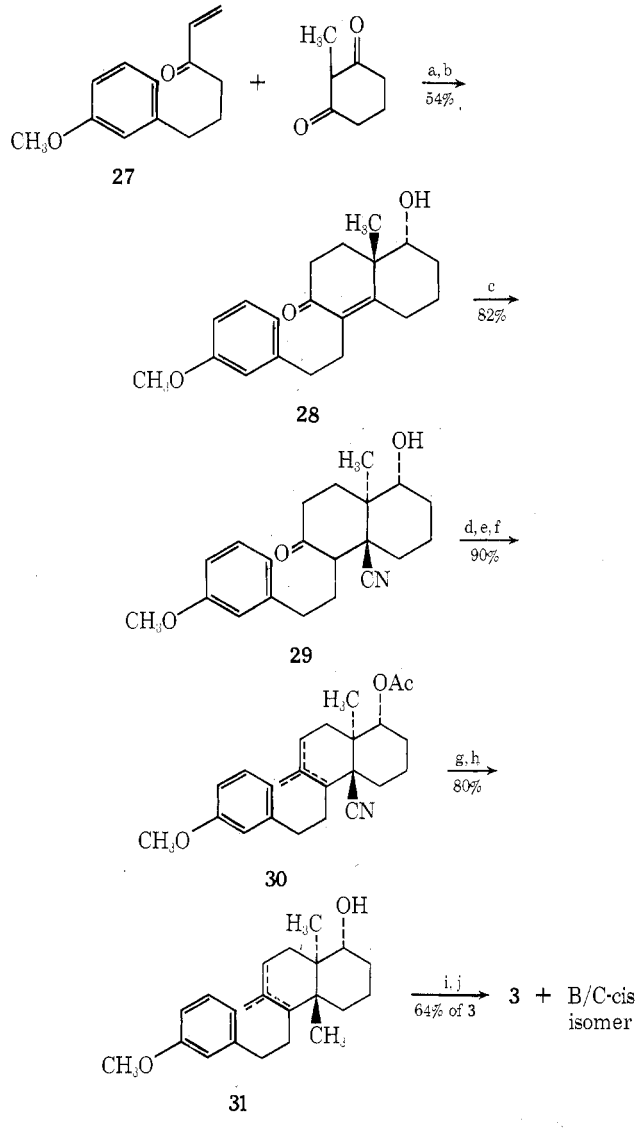
[a] a, *m*-$CH_3OC_6H_4C{\equiv}CLi$, H_3O^+; 10% Pd/Cl, H_2, EtOAc; b, Py, $SOCl_2$, 0°; c, $BH_3 \cdot THF$; OH^-, H_2O_2; d, 8 *N* H_2CrO_4, acetone; e, $(HOCH_2)_2$, H^+, C_6M_6; f, $LiBR_3H$, THF; g, CH_2I_2, Zn(Cu), Et_2O, DME; h, 7% aq CH_3OH–HCl; i, N_2H_4–H_2O, KOH, DEG; j, $(CH_3)_2S^+OCH^-{}_2$, DMSO; k, $LiAlH_4$, Py; l, $(m\text{-}CH_3OC_6H_4CH_2)_2Mg$, dioxane; m, CH_3Li, Et_2O; n, *p*-TsOH, $C_6H_5CH_3$, Δ.

The initial plan entailed the conversion of the ketone **18** (R = H) to the corresponding α-methylene ketone[18] through a series of reactions in which sensitized photooxygenation[19] of the derived ketal **25** was a central feature. A



variety of reaction conditions failed to generate any oxidation product, and only when the reaction was carried out in pyridine with hematophorphyrin[19] as the sensitizer for 132 hr was it possible to realize a meager 32% yield of the intermediate allylic alcohol **26**. The photooxygenation reaction is known[19] to be very sensitive to steric hindrance, and apparently the presence of angular methyl groups on both sides of this rigid olefin **25** sufficiently shields the rather remote double bond from attack by singlet oxygen. The α orientation of the hydroxyl group in the product **26** is proposed on the basis that the C-4a angular methyl group will

Chart II
Synthesis of the Tetracyclic Ketone 3 via the Stereoselective Introduction of the C-4a Methyl Group[a]



[a] a, Et_3N, CH_3OH; $C_6H_5CO_2H$, Et_3N; b, $NaBH_4$, EtOH; c, Et_2AlCN, C_6H_6 or Et_3Al, HCN, THF; d, CH_3MgI, C_6H_6–Et_2O; e, $(CH_3CO)_2O$, Py; f, $SOCl_2$, Py; g, $(i\text{-}Bu)_2AlH$, C_6H_6; h, N_2H_4, $N_2H_4 \cdot 2HCl$, TEG, KOH; i, 8 *N* H_2CrO_4, acetone; j, CF_3CO_2H, reflux.

offer more steric hindrance to the photooxygenation than the more distant C-8a methyl group.

Steric congestion was again shown to be an insurmountable factor in the preparation and reactions of the ketone **9** from the hydroxy ketone **13** (Chart I). Thus, the reaction of lithium (*m*-methoxyphenyl)acetylide with the ketone ketal **6** occurred in poor yield, and significant amounts of starting ketone ketal **6** were recovered. In spite of this it was possible to realize a 38% overall yield of the olefin **8** through dehydration of the saturated alcohol **7**. Again steric hindrance played a significant role, for hydroboration of this olefin **8** went slowly and even under optimized conditions led to only a 38% yield of the desired secondary alcohol. Chromic acid oxidation of this alcohol afforded the ketone **9** in excellent yield, but this ketone proved completely resistant toward the action of methyllithium, methylmagnesium bromide, and dimethylmagnesium. Thus, the steric hindrance toward reactions at C-5 and C-6 offered by the two angular methyl groups and buttressed by the C-1 ketal precluded further investigation of this already low-yield approach.

Inasmuch as the steric problems encountered above seemed to be associated with the tetrahedral substitution at positions 1 and 8a, attention was turned to an approach that avoided tetrahedral character at these positions until the remainder of the ring substitutions had been made. A means for accomplishing this goal became apparent when it was realized through handling experience that the methoxycyclopropane moiety was quite stable to all but relatively vigorous (refluxing 7% aqueous methanolic hydrochloric acid) protolytic conditions.

The first approach investigated stemmed from the α-oxirane **15** and led through the α (axial) alcohol **16** (R = $CH_2C_6H_5OCH_3$-*m*), formed by cleavage of the oxirane with di-*m*-methoxybenzylmagnesium bromide, to the methoxycyclopropane **17** (R = $CH_2C_6H_5OCH_3$-*m*). In one case this approach led to a 57% overall yield of the desired methoxycyclopropane, but these results proved unreproducible. Despite considerable experimentation the cleavage of the oxirane system by the magnesium derivative was very capricious (yields from 24 to 57%) and could not be standardized.

Finally, an acceptable, though far from ideal, route to the methoxycyclopropane **17** (R = $CH_2C_6H_5)OCH_3$-*m*) was realized through the alcohol **12**. Treatment of the ketone, formed in 73% yield by chromic acid oxidation of the alcohol **12**, with lithium *m*-methoxyphenylacetylide and catalytic hydrogenation of the product afforded a 44% overall yield of the α (axial) alcohol **17** (R = $CH_2C_6H_5OCH_3$-*m*), together with a 46% overall yield of the epimeric β (equatorial) alcohol. This unfortunate ratio of alcohol isomers severely reduced the attractiveness of this approach, for while dehydration of the α (axial) isomer **17** (R = $CH_2C_6H_5OCH_3$-*m*) with thionyl chloride–pyridine led to a 91% yield of the desired endocyclic olefin **20**, the same treatment of the β (equatorial) alcohol isomer resulted in a 43% yield of the corresponding exocyclic olefin as the only pure, isolable product.[20]

Despite these lackluster yields the olefin **20** was carried through the remainder of the proposed transformations, which resulted in the generation of the first samples of the tetracyclic ketone **3**. The final acid-catalyzed cyclization of the olefinic ketone **23** behaved as expected from the model series,[10] and while the B/C-trans isomer **3** was the predominant product, the cyclization also produced the B/C-cis isomer. The fact that these latter transformations can be realized at all adds credence to the hypothesis that the methoxycyclopropane moiety in the 1 and 8a positions reduces significantly the steric hindrance toward reaction at C-5 and C-6 over those cases cited earlier where the 1 and 8a positions were tetrahedrally substituted. Unfortunately, the overall yield of this successful approach to the tetracyclic ketone **3** was only 3.3% in 15 steps and further work on more viable approaches was warranted.

2. Stereoselective Introduction of the C-4a Methyl Group. Another sequence[7b] investigated for the preparation of the tetracyclic ketone **3** entailed the introduction of the C-4a angular methyl group through the initial conjugate addition of cyanide[21] to the enone **27** (Chart II). This sequence, which ultimately proved by far the most practical, closely parallels that used in the total synthesis of *dl*-alnusenone,[5] and some of the results reported in that series stemmed from observations made in the present case. Since these two experiences are so similar, only the unique features of the synthesis of the tetracyclic ketone **3** will be mentioned here.

An interesting feature of the present series was that, unlike the results found in the *dl*-alnusenone work,[5] the hy-

drocyanation of the enone **28** led to the same trans-fused cyano ketone **29** no matter whether preformed diethylaluminum cyanide[21c] or the mixture of triethylaluminum–hydrogen cyanide[21c] were used as the reagent. In both the triterpene synthesis and the extensive investigations of this method by its originator,[21b] these two conditions for the Nagata hydrocyanation led to mixtures of isomers that in the first case were considered to reflect thermodynamic control of the reaction, while in the second kinetic control was judged to predominate under the protic conditions. Indeed the protic character inherent in the hydroxy enone **28** may be the answer, and reaction under *both conditions* may reflect the protonation of the initially formed cyano diethylaluminum enolate[21a] by the ever-present hydroxyl group. In accord with this rationalization the hydrocyanation of the acetate or trimethylsilyl ether of the hydroxy enone **28** with diethylaluminum cyanide[21c] led to a mixture of products in which the trans cyano ketone was accompanied by at least one other isomer as judged by the NMR spectrum of the crude product. Unfortunately, after hydrolysis the only pure crystalline material that could be isolated from these mixtures in low yield was the familiar trans isomer **29,** and the hypothesis remains to be conclusively established by isolation of the cis cyano ketone.

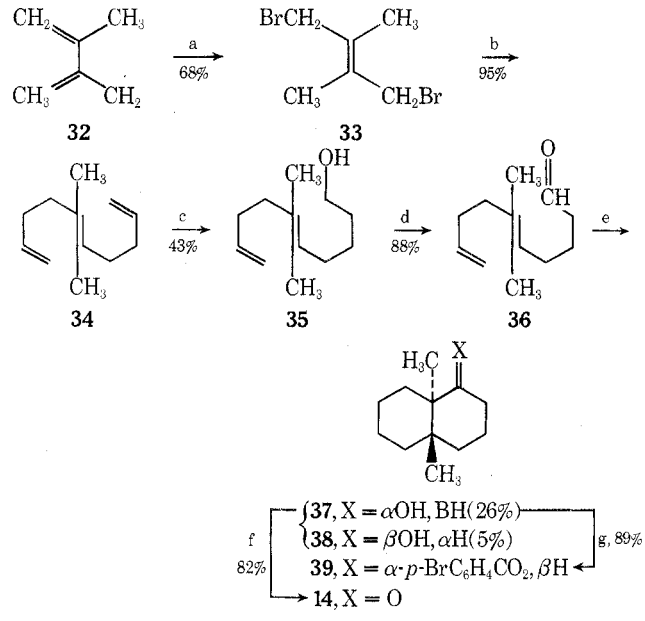
In view of the apparent efficiency of this sequence for the synthesis of the tetracyclic ketone **3,** an effort was made to optimize and streamline the synthesis so as to produce significant quantities of the ketone for further experimentation. This effort resulted in the procedures reported here (see Experimental Section) and the isolations outlined in Chart II. The overall yield of the ketone **3** from 2-methyldihydroresorcinol was 20.4% in ten steps and 10% from the *m*-methoxycinnamic acid used to prepare the vinyl ketone **27.**

Single-crystal X-ray structure analysis established that the structure of the tetracyclic ketone **3** was indeed that inferred from the chemical and spectroscopic data. The ketone **3** crystallized from ether as colorless plates elongated along the *c* axis, and the crystals were shown to belong to the $P_{na}2_1$ space group (Table I). The stereoscopic view (Figure 1) of the molecule shows that the conformations of the B, C, and D rings are half-boat, chair, and flattened chair, and the desired trans fusion between the C and D rings is apparent.

3. Polyene Cyclization Approach. An alternate approach to the synthesis of polycyclic systems with terpenoid stereochemistry and substitution is through the acid-catalyzed cyclization of polyolefinic substrates. The elegant work[22] of Johnson, Corey, and van Tamelen has reduced this biochemically patterned route[23] to laboratory practice for the construction of steroids and certain terpenes. Before these principles could be applied to the synthesis of the tetracyclic ketone **3** it seemed wise to test certain aspects of the approach in model systems.

Consideration of the disposition of the angular methyl groups in the target ketone **3** suggests that cyclization of the aldehyde **46** (Chart IV) or a derivative would lead to an alcohol which could easily be transformed into the desired product. Even at the outset of this work there was ample precedent[24] for the utility of the anisyl ring in the termination of a cationic cyclization process, although in most cases both ortho and para substitution products were observed. Of preliminary concern, therefore, was the lack of prior evidence for the compatibility of a tetrasubstituted double bond with the cationic cyclization process.[25] Two problems were considered, namely, the greater basicity of the tetrasubstituted double bond might interfere in the acidic conditions necessary for cyclization through initial complexation with the catalyst, and the symmetrical substitution of the tetrasubstituted double bond could result[26] in the formation of *either* five- or six-membered rings during the cyclization process. Rather than deferring the answers to these questions until the complex olefinic aldehyde **46** was prepared, it was decided that they could best be determined in the less complex model system[7c] that represented the C/D ring system of the ketone **3.** This approach also provided experience with the stereoselective synthesis of polyolefinic materials that contain such tetrasubstituted double bonds—an ancillary question of no minor concern.

Chart III
Formation of 4aβ,8aα-Dimethyl-1-decalone via Polyene Cyclization[a]



[a] a, Br_2, $HCCl_3$; b, CH_2=$CHCH_2MgBr$, Et_2O–THF; c, Sia_2BH, OH^-, M_2O_2; d, $CrO_3 \cdot 2Py$, CH_2Cl_2; e, 5 equiv $SnCl_4$, CH_3NO_2; Pt, EtOH, H_2; f, 8 *N* H_2CrO_4, acetone; g, *p*-BrC_6H_4COCl, Py.

The desired substrate for this model study was the aldehyde **36,** which was conveniently prepared from 2,3-dimethylbutadiene (**32**) as outlined in Chart III. Indeed this synthetic scheme, and particularly the trans dibromide **33,**[27] served the dual role of providing the compounds for the model series, as well as a viable approach and the key starting material for the ultimate synthesis of the aldehyde **46.** Particularly important were the ease of generating stereochemically homogeneous materials that contained the tetrasubstituted double bond, and the functional symmetry of the initial intermediates that obviated tedious, yield-consuming selective reactions early in the scheme.

The cationic cyclization[22] of the aldehyde and the derived ethylene acetal were investigated in several solvent systems with stannic chloride, boron trifluoride, or trifluoroacetic acid catalysts. The yields of cyclic material were rather low in all systems but appeared best when the aldehyde **36** itself in nitromethane at 0° was treated with 5 equiv of stannic chloride. The initial product mixture from such treatment was subjected to catalytic hydrogenation without purification, and the saturated alcohols **37** and **38** were isolated by a combination of direct crystallization and preparative thin layer chromatography. Oxidation of these alcohols **37** and **38** afforded the same saturated ketone **14,** the infrared spectrum of which confirmed the formation of a six-membered ring ketone. In addition the NMR spectrum of the major alcohol **37** showed resonances at δ 0.96 and 1.0 which were assigned to angular methyl groups in the bicyclic system. Further, Wolff–Kishner reduction of

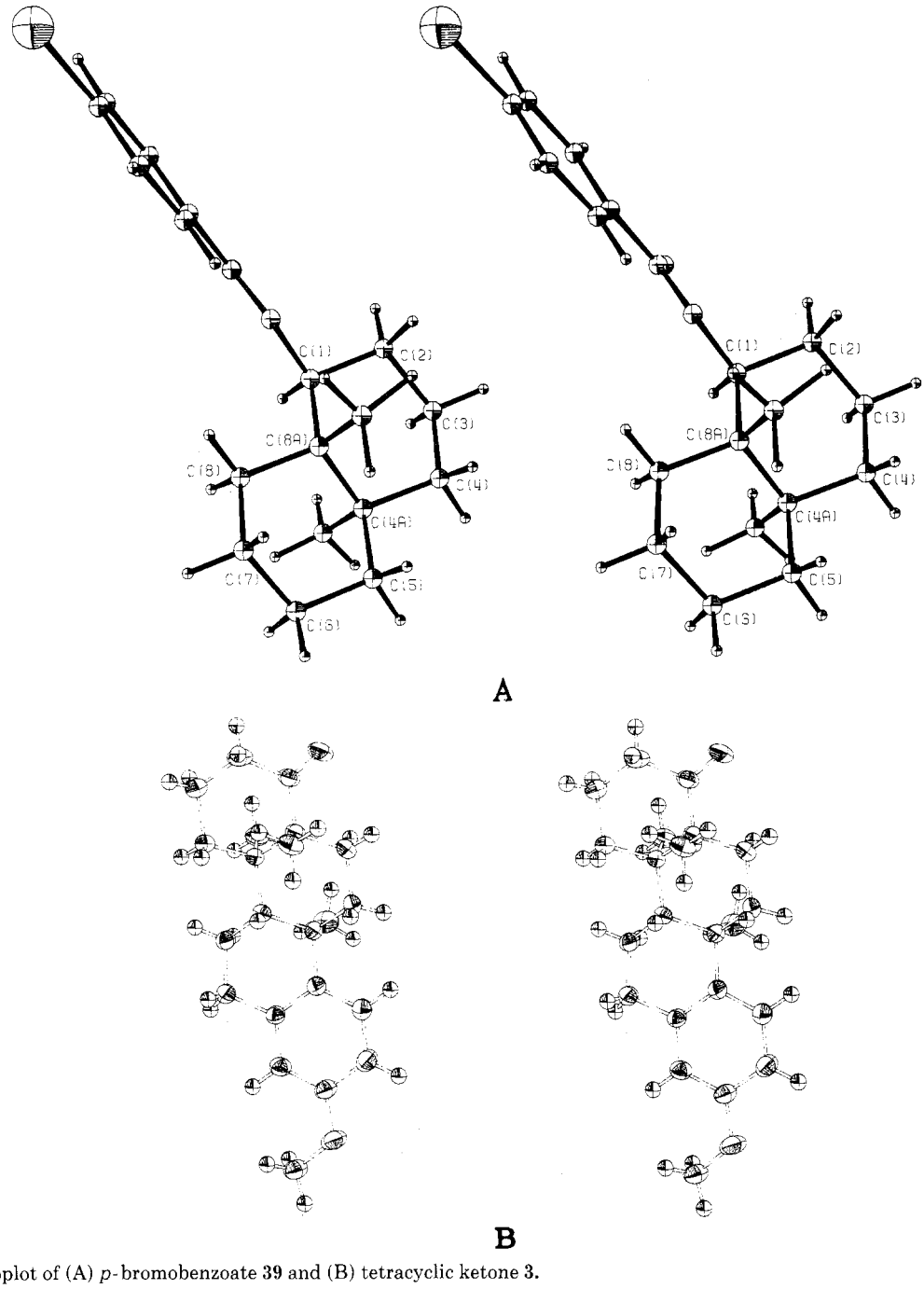


Figure 1. Stereoplot of (A) *p*-bromobenzoate **39** and (B) tetracyclic ketone **3.**

the ketone **14** afforded a hydrocarbon (mp 97–98°) that was *different* from the corresponding 4aβ,8aβ-dimethyldecalin (mp 88–91°) obtained by the similar reduction of the known[28] 4aβ,8aβ-dimethyl-2-decalone. Thus, on the assumption that a decalin system has been formed by this cyclization, it was reasonable to propose the trans-fused, diangularly methylated structures **37** and **38** on the basis of the above evidence. Confirmatory proof that this hypothesis was correct was found in the single-crystal X-ray structure analysis of the *p*-bromobenzoate **39,** prepared from the major alcohol **37.** The stereoplot of the structure that resulted from this analysis (Figure 1) shows the trans-fused decalin system, the equatorial *p*-bromobenzoate, and the chair conformation of each six-membered ring. The dramatic steric congestion at the ring positions adjacent to the fusion experienced in the chemistry described in the first approach above is not obvious from this molecular picture. However, the important questions for the approach at hand have been satisfactorily answered, and a trans-fused, diangularly methylated bicyclic system does result from the cationic cyclization of a system that contains a tetrasubstituted double bond. The low yield (31% total of alcohols **37** and **38**) may be result of several factors, one of which may indeed be the presence of the basic tetrasubstituted double bond.

Despite the discouraging yields in the model series, the investigation was pressed further to the tetracyclic cyclization. For the synthesis of the aldehyde **46** for cyclization to the tetracyclic ketone **3,** it was necessary to modify the scheme used in the model series so as to incorporate differentiatable functionality in the branches (Chart IV). The convenient stereochemical control provided by the dibromide **33** dictated its use as the starting material, and the plan entailed the dienyne **42** as a crucial intermediate. Several attempts to convert the triene **34** to the dienyne **42** by selective additions to one terminal double bond were unsuccessful, and the coupling of the dibromide **33** with 1 equiv of allylmagnesium bromide gave only polymeric materials

and none of the desired monocoupling product. In an attempt to form the enediyne **41** the coupling reaction between the dibromide **33** and propyne derivatives was investigated. Application of the lithio-1-trimethylsilylpropyne coupling procedure[29] afforded less than 5% (GLC analysis) of the expected disilyl derivative **42,** but direct coupling[7d] of the dibromide **33** with propargylmagnesium bromide and then trimethylsilylation of the crude product to derivatize the acetylenic portion in the presence of any allenes formed afforded the desired disilyl enediyne **42** in good yield. In this manner the symmetrical enediyne **41** became readily available after cleavage[30] of the trimethylsilyl groups, and monoreduction[31] of one acetylenic group through protolysis of the derived organoborane provided a viable route to the crucial dienyne **42.** The plan for this molecule entailed the use of the remaining acetylenic unit for the incorporation of the trisubstituted double bond and its appended aromatic substituent while the terminal double bond was used to mask the aldehyde function throughout these operations. These transformations, which were accomplished as outlined in Chart IV, led to the desired aldehyde **46** in good yield. Central to this scheme was the application of the Corey trisubstituted olefin synthesis[32] for the stereoselective generation of the last double bond.

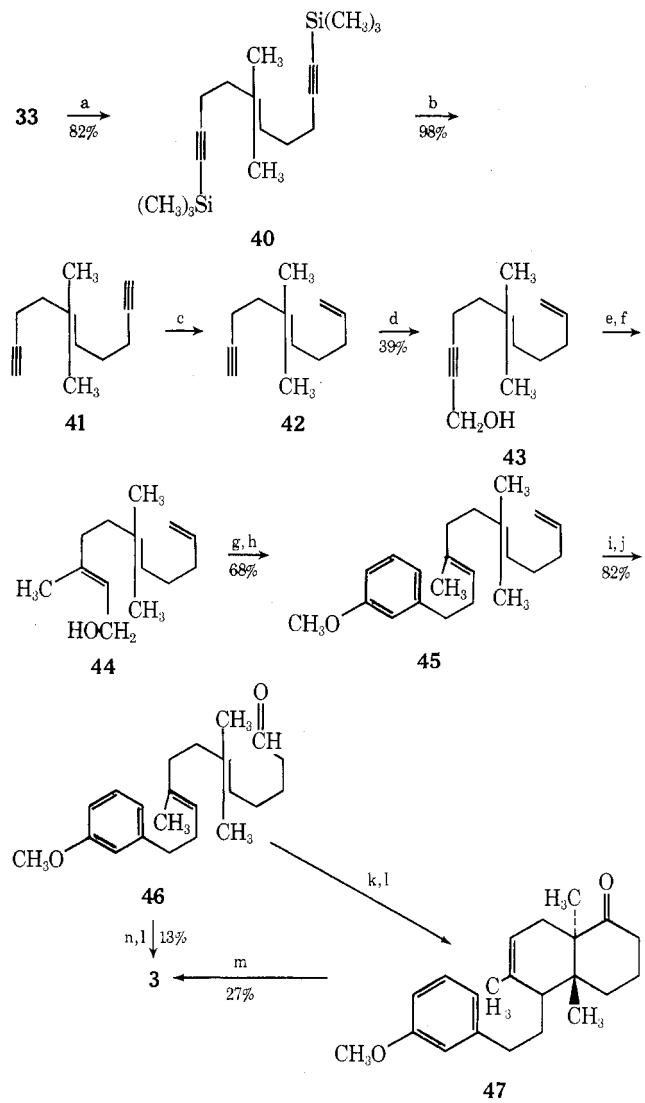
The cationic cyclization of the aldehyde **46** was again investigated under several sets of conditions suggested by the work of Johnson and coworkers.[22] While the corresponding acetal of the aldehyde **46** was investigated as well, again there seemed to be no advantage in using this more stable derivative. None of these cyclizations were clean, and in addition to polymeric material, the product mixture always contained four or more components. Three of these were rigorously identified after preparative thin layer and gas–liquid chromatography of the mixture formed by treatment of the aldehyde **46** with 0.5 equiv of stannic chloride in benzene at 25° for 75 sec and then oxidation to form ketonic products. The nonpolymeric portion of this mixture, obtained in a 58% yield, consisted of 12% of what was judged by NMR and infrared spectroscopy to be a mixture of monocyclic five- and six-membered ring, unsaturated ketones, 44% of the octalinone **47,** 23% of the desired tetracyclic ketone **3,** and 15% of the isomeric 1-methoxytetracyclic ketone that results from cationic attack of the anisyl ring in the poition ortho to the methoxyl group. At best this represents only a 13% yield of the ketone **3** from direct cyclization of the aldehyde **46.** The major product was the octalinone **47** that results from deprotonation of the intermediate cation rather than attack of the aromatic ring. Concurrent work referred to above indicated that strong protonic acid catalyzed cyclization of the octalinone **47** should complete the formation of the ketone **3,** and this proved to be the case. Interestingly, in this latter experiment none of the isomeric ortho-substituted tetracyclic ketone was formed but, as experienced earlier, significant quantities of the epimeric B/C cis-fused tetracyclic ketone were formed. As expected from the extensive work of the Johnson group,[22] none of the latter epimer was observed from the polyolefin cyclization.

Since an efficient method was available for the subsequent conversion of the octalinone **47** to the desired tetracyclic ketone **3,** an effort was made to optimize the formation of this bicyclic derivative at the expense of the tetracyclic substances. Even this ploy met with only limited success, and after considerable experimentation, the best yield of the tetracyclic ketone **3** that could be realized from the aldehyde **46** by a combination of stannic chloride and, after oxidation, *p*-toluenesulfonic acid catalyzed cyclization was 27%.

While in our hands this polyolefin cyclization route is not competitive with the preceding conjugate cyanide addition sequence for the preparative formation of the tetracyclic ketone **3,** these experiments do offer some insight about both the process and this system. The success of the laboratory polyene cyclization scheme for the synthesis[22] of steroids and terpenes from acyclic substrates that bear the squalene-like disposition of methyl substituents is well documented. The polyene used here deviates from this pattern substantially, and yet cyclization to a tetracyclic system does indeed occur in significant amounts. Unfortunately, inherent in these deviations of more normal polyisoprenoids is the introduction of a more labile tetrasubstituted double bond and a less nucleophilic aromatic ring. It seems probable that these components of the substrate coupled with the apparent necessity that the cyclization be initiated from the sensitive aldehyde function account for the relatively low overall yields observed.

In spite of the difficulties encountered in the cyclization of the aldehyde **46,** this polyolefin approach to the synthe-

Chart IV
Synthesis of the Tetracyclic Ketone 3 via Polyene Cyclization[a]



[a] a, CH_2=C=CHMgBr, THF; EtMgBr, THF, $(CH_3)_3SiCl$; b, $AgNO_3$, KCN, aq EtOH; c, Sia_2BH, HOAc; d, EtMgBr, HCHO, THF; e, $LiAlH_4$, $NaOCH_3$, THF; I_2, THF, −78°; f, $LiCu(CH_3)_2$, Et_2O; g, $(C_6H_5)_3P$, CCl_4; h, *m*-$CH_3OC_6H_4CH_2MgCl$, 20% HMPA–THF; i, Sia_2BH, OH^-, H_2O_2; j, $CrO_3 \cdot 2Py$, CH_2Cl_2; k, 0.5 equiv $SnCl_4$, C_6H_6, 25°, 65 sec; l, 8 *N* H_2CrO_4, acetone; m, *p*-TsOH, $CH_3C_6H_5$, Δ; n, 0.5 equiv $SnCl_4$, C_6H_6, 25°, 75 sec.

sis of the tetracyclic ketone **3** was competitive with the more classical approach through protolysis of the methoxycyclopropane **22**. The aldehyde **46** was available in 17% overall yield from the dibromide **33** in ten operations, and this yield, coupled with the 27% observed for the two-stage cationic cyclization, amounts to a 4.5% overall yield of the tetracyclic ketone **3** in 12 steps. The ease and efficiency of the formation of the aldehyde **46** developed in this work prompted a further investigation[33] of its use for the preparation of alternate substrates for related cationic cyclizations to pentacyclic intermediates in the synthesis of the friedelin–alnusenone family of triterpenes.

Experimental Section[34]

5-Methoxy-8aβ-methyl-3,4,8,8a-tetrahydro-1,6(2*H*,7*H*)-naphthalenedione. To a 2-l. flask containing 70.0 g (0.555 mol) of 2-methyldihydroresorcinol was added a solution of 69.2 g (0.522 mol) of 1,4-dimethoxy-2-butanone[11] and 16.0 ml of triethylamine in 100 ml of triethylamine in 100 ml of xylene. The atmosphere was replaced with nitrogen, and the mixture was heated to reflux. After 1.5 hr, 50 ml of solvent was removed by distillation, and 23.6 g of benzoic acid and 23 ml of triethylamine were added. Reflux was continued for 15 hr while the water formed was removed through a Dean-Stark apparatus. Upon cooling, the solution was washed with three 250-ml portions of 5% aqueous potassium hydroxide and dried (Na_2SO_4). After filtration, removal of the solvent at reduced pressure afforded 51.3 g (47%) of a yellow, crystalline solid, mp 66–71°. Extraction of the aqueous washings with chloroform yielded an additional 5.30 g (5%) of the same material (overall yield based on 1,4-dimethoxy-2-butanone, 52%). The analytical sample obtained after two crystallizations of a sample of this material from ether–hexane melted at 78–80°: ir ($CHCl_3$) 1715 (C=O), 1680 (unsaturated C=O), and 1615 cm^{-1} (conjugated C=C); NMR ($CDCl_3$) δ 1.43 (s, 3, C-8a CH_3), 3.67 (s, 3, OCH_3).

Anal. Calcd for $C_{12}H_{16}O_3$: C, 69.21; H, 7.75. Found: C, 69.10; H, 7.81.

5-Methoxy-8aβ-methyl-3,4,6,7,8,8a-hexahydro-1(2*H*)-naphthalenone (10). A solution of 37.70 g (0.181 mol) of the above diketone in 250 ml of ether was added to a stirred solution of 15.70 g (0.413 mol) of lithium aluminum hydride in 2 l. of dry ether over the course of 1 hr. After decomposition of the excess hydride with ethyl acetate and 10% aqueous sodium hydroxide and then filtration of the solids, followed by evaporation of the ether, 35.8 g (95%) of a white, crystalline solid, mp 88–92° (part melt) and 134–140°, was isolated that consisted of a 2:1 mixture of the 6β and 6α alcohol isomers by NMR integration of the C-8a angular methyl resonances. An analytical pure sample of the 6β isomer obtained from another experiment under the same conditions, prepared after two crystallizations of this mixture from ethyl acetate, melted at 147–150°: ir ($CHCl_3$) 3600 (OH) and 1665 cm^{-1} (C=C); NMR ($CDCl_3$) δ 1.22 (s, 3, C-8a CH_3) and 3.70 (s, 3, OCH_3).

Anal. Calcd for $C_{12}H_{20}O_3$: C, 67.89; H, 9.50. Found: C, 67.98; H, 9.59.

A solution of 35.8 g (0.169 mol) of the crude diol above in 600 ml of dry pyridine was treated with 62.5 ml (0.85 mol) of acetic anhydride, and the reaction mixture was stirred at room temperature for 17 hr. After dilution with 500 ml of saturated aqueous sodium bicarbonate, the product was isolated by ether extraction.[35] The residue amounted to 50.1 g (quantitative) of the corresponding diacetates as an oil. Purification by preparative TLC (40% ether–petroleum ether, double elution) and evaporative distillation (100°, 0.025 mm) of a portion of this material afforded an analytically pure sample of a mixture of C-6 isomers: ir ($CHCl_3$) 1725 (C=O) and 1655 cm^{-1} (C=C); nmr ($CDCl_3$) δ 1.08 (s, 1, C-8a CH_3 of 6αa isomer), 1.15 (5, 2, C-8a CH_3 of 6β isomer), 2.03 and 2.05 (pair of s, 6, acetate CH_3), and 3.48 (s, 3, OCH_3).

Anal. Calcd for $C_{16}H_{24}O_5$: C, 64.84; H, 8.16. Found: C, 64.88; H, 8.24.

To a solution of 23.7 g (0.08 mol) of the above diacetate mixture and 60 ml (0.63 mol) of dry *tert*-butyl alcohol in 1 l. of ethylamine was added 5.5 g (0.80 mol) of lithium wire in small pieces over 5 min with rapid stirring. After stirring for 20 min, excess lithium was destroyed with solid ammonium chloride, and the ethylamine was removed by evaporation in a stream of nitrogen. The product was isolated by ether extraction[35] and chromatographed on 920 g of neutral alumina I. Elution with 17 l. of ether afforded 15.78 g (58%) of the methoxyoctalol, mp 83.5–86.5°. The analytical sample, obtained after three crystallizations from ether–hexane, melted at 85.5–865°: ir ($CHCl_3$) 3610 (OH) and 1645 cm^{-1} (C=C); NMR ($CDCl_3$) δ 1.02 (s, 3, C-8a CH_3)and 3.47 (s, 3, OCH_3).

Anal. Calcd for $C_{12}H_{20}O_2$: C, 73.43; H, 10.27. Found: C, 73.50; H, 10.23.

A solution of 6.10 g (31.1 mmol) of the above alcohol in 50 ml of dry dichloromethane was oxidized with 900 ml (0.175 mol) of a 5% solution of chromium trioxide–dipyridine complex[36] in dry dichloromethane, and the product was isolated by suction filtration of the reaction mixture through 375 g of grade II alumina, which was followed by a washing with 1 l. of ether. After evaporation of the solvents at reduced pressure, the residue (5.86 g) was adsorbed on 150 g of grade II alumina, and then 5.02 g (82%) of the ketone **10** as a water-white oil was eluted with 700 ml of 10% ether–petroleum ether. The analytical sample was obtained after evaporative distillation of a sample at 50° and 0.025 mm: ir ($CHCl_3$) 1705 (C=O) and 1670 cm^{-1} (C=C); NMR ($CDCl_3$) δ 1.35 (s, 3, C-8a CH_3) and 3.40 (s, 3, OCH_3).

Anal. Calcd for $C_{12}H_{18}O_2$: C, 74.19; H, 9.34. Found: C, 74.01; H, 9.49.

Spiro-1α-oxiranyl-5-methoxy-8aβ-methyl-1,2,3,4,6,7,8,8a-octahydronaphthalene (15). A solution of dimethyloxosulfonium methylide[16] from 798 mg (19.0 mmol) of 57% sodium hydride dispersion and 4.25 g (19.3 mmol) of dry trimethyloxosulfonium iodide in 40 ml of dry dimethyl sulfoxide was transferred by syringe to a 50-ml flask that contained a solution of 361 mg (1.86 mmol) of ketone **10** in 4 ml of dry dimethyl sulfoxide under a nitrogen atmosphere. The course of the reaction was monitored by GLPC,[35] and after 7 hr at 23° when the peak representing starting material had disappeared, the excess reagent was carefully decomposed with 1.0 ml of water. An additional 15 ml of water was then added, and the product was isolated by ether extraction.[35] The residue, purified by preparative TLC (20% ether–petroleum ether, double elution), afforded 315 mg (81%) of the α-oxirane **15** (R_f 0.7) which crystallized on standing at −10°: ir ($CHCl_3$) 1670 (C=C), 1130 (C–O), and 1055 cm^{-1} (C–O); NMR ($CDCl_3$) δ 1.20 (, 3, C-8a CH_3), 2.33 and 2.70 (2 d, 1 each, J = 5.5 Hz, oxirane CH_2), and 3.42 (s, 3, OCH_3). This material was sensitive to storage and was not purified further for additional analysis but used directly.

1β,8aβ-Dimethyl-5-methoxy-1,2,3,4,6,7,8,8a-octahydro-1α-naphthol (16, RH = H). To a solution of 740 mg (3.55 mmol) of the above oxirane in 25 ml of dry pyridine at 0° (ice bath) was added 440 mg (11.6 mmol) of lithium aluminum hydride. The mixture was stirred 10 min at 0°, then 1 hr at room temperature. The muddy-green solution was diluted with 25 ml of ether; the excess hydride was destroyed by the consecutive addition of 0.45 ml of water, 0.45 ml of 10% aqueous potassium hydroxide solution, and 1.35 ml water, and then the mixture was filtered. The filtrate was washed with water (2 × 20 ml), saturated aqueous copper(II) sulfate (2 × 20 ml), and saturated brine (2 × 20 ml) and then dried ($MgSO_4$). Filtration of this mixture through 30 g of grade II alumina with the aid of 200 ml of 50% ether–petroleum ether and evaporation of the solvents at reduced pressure afforded 690 mg (94%) of the alcohol **16** (R = H) as an oil, which was contaminated with less than 5% of the equatorial alcohol isomer by comparative NMR integration of the C-1 and C-8a methyl groups. This alcohol was quite labile and was used without further purification: ir ($CHCl_3$) 3500 (OH) and 1665 cm^{-1} (C=C); NMR ($CDCl_3$ + 1 drop pyridine) δ 1.11 (s, 3, C-8a CH_3), 1.13 (s, 3, C-1 CH_3), and 3.47 (s, 3, OCH_3).

1α,8β-Dimethyl-5-methoxy-1,2,3,4,6,7,8,8a-octahydro-1β-naphthol. To a solution of 2 ml (4 mmol) of a 2 *M* ethereal solution of methyllithium in 5 ml of dry ether was added dropwise 109 mg (0.52 mmol) of the ketone **10** in 1.0 ml of dry ether under a nitrogen atmosphere. After 1 min the mixture was cooled in an ice bath, and the remaining reagent was decomposed with 0.50 ml of water. Isolation of the product by ether extraction[35] afforded 118 mg of a colorless oil. The analytical sample was prepared by preparative TLC (20% ether–petroleum ether) and evaporative distillation (60°, 0.005 mm) of a sample of this material: ir ($CHCl_3$) 3600 (OH) and 1665 cm^{-1} (C=C); NMR ($CDCl_3$) δ 1.15 (s, 3, C-8a CH_3), 1.20 (s, 3, C-1 CH_3), and 3.45 (s, 3, OCH_3).

Anal. Calcd for $C_{13}H_{22}O_2$: C, 74.24; H, 10.54. Found: C, 74.33; H, 10.51.

1,2,3,4,4aβ,5,6,7,8,8a-Decahydro-1β,8aβ-dimethyl-5β-methoxy-1α-naphthol Ketal (24, R = CH_3). A solution of 79 mg (0.38 mmol) of the alcohol **16** (R = H) in 1 ml of chloroform-*d* was stored in an NMR tube, and after 5 days at 25° the NMR spectrum indicated that the starting alcohol had disappeared and that

a single product was formed. Evaporation of the solvent gave 63 mg (80%) of an oil which afforded 43 mg (55%) of the pure ketal **24** (R = CH_3) after preparative TLC (15% ether–benzene) and evaporative distillation at 55° and 0.05 mm: ir ($CHCl_3$) 1085 cm^{-1} (C–O–C); NMR ($CDCl_3$) δ 0.92 (s, 3, C-8a CH_3) and 3.37 (s, 3, OCH_3).

Anal. Calcd for $C_{13}H_{22}O_2$: C, 74.24; H, 10.54. Found: C, 74.26; H, 10.56.

1,2,3,4,4a,5,6,7,8,8a-Decahydro-1β,8aβ-dimethyl-5α,4a-methano-5β-methoxy-1α-naphthol (17, R = H). To a solution of the Simmons–Smith reagent[15] prepared from 12.8 g (0.183 mol) of zinc–copper couple[37] and 14.7 ml (0.183 mol) of dry diiodomethane in 250 ml of dry ether was added a solution of 4.04 g (0.019 mol) of the alcohol **16** (R = H) in 20 ml of dry ether and 15 ml (0.17 mol) of dry 1,2-dimethoxyethane over a period of 10 min. After 40 min at room temperature the flask was cooled in an ice bath, and the excess reagent was decomposed with 3.0 ml of 10% aqueous ammonium chloride. The product was isolated by ether extraction including a base wash[35] and the residue was chromatographed on 300 g of grade II alumina. Elution with 1200 ml of 50% ether–petroleum ether gave 3.54 g (83%) of crystalline methoxycyclopropane **17** (R = H), mp 58–60°. The analytical sample, obtained by crystallization of a sample from ether–heptane, then from ethanol–water, melted at 60–61.5°: ir ($CHCl_3$) 3600 (OH) and 1075 and 1060 cm^{-1} (C–O–C); NMR ($CDCl_3$) δ 0.52 and 0.82 (2 d, 1 each, J = 5.5 Hz, cyclopropyl CH_2), 1.03 (s, 3, C-8a CH_3), 1.15 (s, 3, C-1 CH_3), and 3.23 (s, 3, OCH_3).

Anal. Calcd for $C_{14}H_{24}O_2$: C, 74.95; H, 10.78. Found: C, 75.01; H, 10.78.

3,4,4a,7,8,8a-Hexahydro-1,4aα,8aβ-trimethyl-5(6*H*)-naphthalenone (18, R = H). A solution of 595 mg (2.65 mmol) of the methoxycyclopropane **17** (R = H) in 20 ml of methanol and 2.0 ml of 37–38% hydrochloric acid was refluxed for 4 hr, cooled, and then neutralized with saturated aqueous sodium bicarbonate. After most of the methanol was removed at reduced pressure, the product was isolated by ether extraction, including a base wash,[35] and then the residual yellow oil (510 mg) was chromatographed on 20 g of grade II alumina. Petroleum ether (150 ml) eluted 376 mg (74%) of the ketone **18** (R = H), mp 67–68°, the analytical sample of which was prepared by crystallization of a portion from ethanol–water and sublimation (50°, 0.025 mm) and melted at 68–69°: ir ($CHCl_3$) 1700 cm^{-1} (C=O); NMR ($CDCl_3$) δ 1.00 (s, 3, C-8a CH_3), 1.22 (s, 3, C-4a CH_3), 1.65 (d, 3, J = 1.5 Hz, C-1 CH_3), and 5.20 (m, 1, vinyl).

3,4,4a,5,6,7,8,8a-Octahydrol-1,4aα,8aβ-trimethylnaphthalene (19). A. From Ketone 18 (R = H). A solution of 141 mg (0.735 mmol) of the ketone **18** (R = H), 500 mg of crushed potassium hydroxide, and 0.40 ml of 85% hydrazine hydrate in 5 ml of diethylene glycol was heated under nitrogen to 100–105° for 30 min and then to 200–205° for 120 min while the volatile products distilled. The apparatus was cooled, and the contents of the pot and receiver were combined and extracted with ether. The ether solution was dried ($MgSO_4$), and the solvent was distilled at atmospheric pressure; sublimation of the crude product at 40° and 0.025 mm afforded 60 mg (46%) of white crystals. The analytical sample, obtained after preparative TLC (petroleum ether) and resublimation (40°, 0.025 mm), melted at 52–55°: ir ($CHCl_3$) 1640 cm^{-1} (weak); NMR ($CDCl_3$) δ 0.90 (s, 3, C-4a CH_3), 1.03 (s, 3, C-8a CH_3), 1.58 (d, 3, J = 1.5 Hz, C-1 CH_3), and 5.03–5.23 (m, 1, vinyl).

Anal. Calcd for $C_{13}H_{22}$: C, 87.56; H, 12.44. Found: C, 87.36; H, 12.48.

B. From Ketone 14. The corresponding tertiary alcohol was prepared from 59 mg (0.33 mmol) of the ketone **14** in 12 ml of ether by the addition of 2 ml of a 2 *M* ethereal solution of methyllithium under a nitrogen atmosphere. The product (59 mg) from this treatment was shown to contain 25% of the ketone **14** and 75% of the desired alcohol by GLC (150°),[35] and this mixture was retreated with methyllithium as above. After preparative TLC (benzene) of the crude product and then evaporative distillation (60–70°, 0.25 mm) of the tertiary alcohol band, the analytical pure alcohol (40 mg) was obtained as crystals that melted at 40–41°: ir ($CHCl_3$) 3600 cm^{-1} (OH); NMR ($CDCl_3$) δ 1.03 (s, 3, C-8a CH_3), 1.08 (s, 3, C-1 CH_3), and 1.30 (s, 3, C-4a CH_3).

Anal. Calcd for $C_{13}H_{24}O$: C, 79.53; H, 12.33. Found: C, 79.41; H, 12.33.

Dehydration of the alcohol (50 mg, 0.25 mmol) in 5 ml of dry pyridine was accomplished at −10° in 45 min with 0.30 ml (4.1 mmol) of thionyl chloride. After dilution of the reaction with water, the product was isolated by ether extraction[35] and then chromatographed on 5 g of grade I alumina. Elution with 15 ml of pentane afforded the olefin **19**, mp 50–54°, as a crystalline solid. The infrared and NMR spectra of this sample were identical with those of the material prepared in part A, and the melting point of a mixture of the material from part A, mp 45–50°, and part B, mp 50–54°, was 45–50°.

5-Methoxy-8aβ-methyl-1,2,3,4,6,7,8,8a-octahydro-15-naphthol (11). To a solution of 448 mg (2.30 mmol) of the ketone **10** in 5 ml of dry tetrahydrofuran was added 4.20 ml (3.20 mmol) of a 0.77 *M* tetrahydrofuran solution of lithium perhydro-9b-boraphenalylhydride[17] at −10° (ice–salt bath) under a nitrogen atmosphere. After 30 min, the excess reagent was destroyed by the careful, dropwise addition of 2.0 ml of 3 *N* aqueous sodium hydroxide, followed by 1.0 ml of 30% hydrogen peroxide. The mixture was poured onto 30 ml of 20% aqueous potassium carbonate, and the product was isolated by ether extraction.[35] There remained a residue of 483 mg of a colorless oil that comparative NMR integration of the angular methyl resonances showed was a 70:30 mixture of the axial alcohol **11** and its equatorial epimer. The axial alcohol was quite labile, and therefore this mixture was used without further purification: ir ($CHCl_3$) 3600 (OH), 1670 cm^{-1} (C=C); NMR (CCl_4) δ 0.95 (s, 0.9, C-8a CH_3, equatorial alcohol), 1.05 (s, 2.1, C-8a CH_3, axial alcohol), 3.40 (s, 0.9, OCH_3, equatorial alcohol), and 3.43 (s, 2.1, OCH_3, axial alcohol).

1,2,3,4,4a,β,5,6,7,8,8a-Decahydro-5β-methoxy-8aβ-methyl-1α-naphthol Ketal (24, R = H). A solution of 154 mg (0.785 mmol) of the above crude mixture of alcohols in 3 ml of chloroform-*d* that contained 1–2 mg of *p*-toluenesulfonic acid was allowed to stand for 12 hr at room temperature. After removal of the solvent, preparative TLC (30% ether–petroleum ether) gave two bands, the first of which (R_f 0.1, 64 mg) was shown to be a mixture of starting alcohols and their hydrolysis products by NMR. The faster moving band (R_f 0.3) contained 43 mg (28% from the ketone **10**) of the pure ketal **24** (R = H). The analytical sample was obtained by evaporative distillation of this sample at 45° and 0.15 mm: ir ($CHCl_3$) 1055 cm^{-1} (C–O–C); NMR ($CDCl_3$) δ 0.97 (s, 3, C-8a CH_3), 3.30 (s, 3, OCH_3), and 3.77–3.90 (m, 1, CH–O–C).

Anal. Calcd for $C_{12}H_{20}O_2$: C, 73.43; H, 10.27. Found: C, 73.54; H, 10.23.

1,2,3,4,4a,5,6,7,8,8a-Decahydro-5α,4a-methano-5β-methoxy-8aβ-methyl-1α-naphthol (12). In a manner similar to that described above for the formation of the methoxycyclopropane **17** (R = H), the Simmons–Smith reagent[15] prepared from 2.10 g (30.0 mmol) of zinc–copper couple[37] and 2.40 ml (30.0 mmol) of diiodomethane in 30 ml of dry ether was added to a solution of 483 mg (2.30 mmol) of the above 70:30 mixture of alcohols in 3.2 ml (30 mmol) of dry 1,2-dimethoxyethane under a nitrogen atmosphere. After 1 hr the reaction was quenched with 1.0 ml of 10% aqueous ammonium chloride, and the product was isolated by ether extraction including a base wash.[35] After preparative TLC (30% ether–petroleum ether) of the crude product, there was obtained 278 mg (59% from the ketone **10**) of the methoxycyclopropane **12**. Rechromatography and then evaporative distillation (120°, 0.65 mm) of a sample gave analytically pure material: ir ($CHCl_3$) 3600 cm^{-1} (OH); NMR ($CDCl_3$) δ 0.38 and 0.78 (2 d, 1 each, J = 5 Hz, cyclopropyl CH_2), 1.11 (s, 3, C-8a CH_3), 3.17 (s, 3, OCH_3), and 3.17–3.37 (m, 1, CHOH).

Anal. Calcd for $C_{13}H_{22}O_2$: C, 74.24; H, 10.54. Found: C, 74.32; H, 10.63.

4aα,8aβ-Dimethyl-1α-hydroxy-1,2,3,4,4a,7,8,8a-octahydro-5(6*H*)-naphthalenone (13). In a manner similar to that described above for the formation of the ketone **18** (R = H), a solution of 114.2 mg (0.545 mmol) of the methoxycyclopropane **12**, 0.5 ml of water, and 2.0 ml of 38–39% hydrochloric acid in 8 ml of methanol was refluxed for 1.5 hr. The product was isolated by ether extraction including a base wash[35] and trituration of the crude crystalline solid with ether afforded 78 mg (80%) of the ketone **13**, mp 125–130°. The analytical sample, obtained after crystallization (ether–heptane) and sublimation (150°, 0.025 mm) of a portion of this material, melted at 158–159°: ir ($CHCl_3$) 3615 (OH) and 1695 cm^{-1} (C=O); NMR ($CDCl_3$) δ 0.83 (s, 3, C-8a CH_3), 1.46 (s, 3, C-4a CH_3), and 3.50–3.65 (m, 1, HCOH).

Anal. Calcd for $C_{12}H_{20}O_2$: C, 73.43; H, 10.27. Found: C, 73.29; H, 10.17.

1,2,3,4,4a,5,6,7,8,8a-Decahydro-4aα,8aβ-dimethyl-1α-naphthol (38). The Huang-Minlon modification[38] of the Wolff–Kischner reduction was carried out on 73 mg (0.38 mmol) of keto alcohol **13** in 1.0 ml of ethanol and 2.5 ml of diethylene glycol with 0.20 ml of 85% hydrazine hydrate and 250 mg of crushed potassium hydroxide. The reaction mixture was heated to 100–105° for 0.5 hr

and then to 200–205° for 2 hr. After cooling, the contents of the pot and the distillate were combined, and the product was isolated by ether extraction.[35] After two successive preparative TLC (30% ether–petroleum ether) of the crude product, 15 mg (23%) of the pure alcohol **38**, mp 70.5–72°, was isolated as white crystals: ir ($CHCl_3$) 3615 (OH) and 1260 cm^{-1} (COH); NMR ($CDCl_3$) δ 0.98 (s, 3, C-8a CH_3), 1.23 (s, 3, C-4a CH_3), and 3.33–3.50 (m, 1, CHOH).

Anal. Calcd for $C_{12}H_{22}O$: C, 79.06; H, 12.16. Found: C, 78.93; H, 12.05.

The infrared and NMR spectra of this material were identical with those of the minor alcohol formed during stannic chloride catalyzed cyclization of the aldehyde **36** (vide infra). Oxidation of this material with 8 *N* chromic acid in acetone[39] afforded the ketone **14**, which on crystallization from heptane and then petroleum ether melted at 108–110° (sealed capillary), alone and in admixture with a sample, mp 108–110° (sealed capillary), obtained by a similar oxidation[39] of the alcohol **37** from cyclization of the aldehyde **36** (vide infra). The infrared and NMR spectra of the two samples of the ketone **40** were indistinguishable.

4aα,8aβ-Dimethyl-5,5-ethylenedioxo-3,4,4a,5,6,7,8,8a-octahydro-1(2*H*)-naphthalenone (6). A solution of 117 mg (0.596 mmol) of the ketone **13** and 2.5 ml of ethylene glycol and 11 mg of *p*-toluenesulfonic acid in 35 ml of benzene was heated at reflux under a Dean-Stark water separator for 7.5 hr. The cooled solution was poured onto 30 ml of water, and the product was isolated by ether extraction, including a base wash.[35] After preparative TLC (50% ether–petroleum ether) of the crude product, there was obtained 66 mg (64%) of the hydroxy ketal, mp 89–91°. The analytical sample, obtained after two crystallizations of a portion of this material from ether–heptane, melted at 92–94°: ir ($CHCl_3$) 3615 cm^{-1} (OH); NMR ($CDCl_3$) δ 1.12 (s, 3, C-8a CH_3), 1.40 (s, 3, C-4a CH_3), 3.37–3.50 (m, 1, CHOH), and 3.67–4.1 (m, 4, $-OCH_2CH_2O-$).

Anal. Calcd for $C_{14}H_{24}O_3$: C, 69.96; H, 10.07. Found: C, 69.99; H, 9.99.

The oxidation of 133 mg (0.554 mmol) of the hydroxy ketal in 20 ml of acetone was carried out with 0.25 ml (1.0 mequiv) of 8 *N* chromic acid.[39] After 1 min, 0.10 ml of isopropyl alcohol was added; the mixture was diluted with 20 ml of saturated aqueous sodium bicarbonate, and isolation of the product by ether extraction[35] gave 32 mg (quantitative) of the ketal **6**, mp 78–82°, as yellow crystals. The analytical sample, prepared by two crystallizations of a portion of this material from ether–hexane and then sublimation at 80° and 0.05 mm, melted at 88–89°: ir ($CHCl_3$) 1695 cm^{-1} (C=O); NMR ($CDCl_3$) δ 1.00 (s, 3, C-4a CH_3), 1.35 (s, 3, C-8a CH_3), and 3.70–4.17 (m, 4, $-OCH_2CH_2O-$).

Anal. Calcd for $C_{14}H_{22}O_3$: C, 70.56; H, 9.30. Found: C, 70.61; H, 9.44.

4aα,8aβ-Dimethyl-5,5-ethylenedioxo-1-(2′-*m*-methoxyphenylethyl)-3,4,4a,5,6,7,8,8a-octahydronaphthalene (8). After lithium *m*-methoxyphenylacetylide was prepared from 931 mg (7.05 mmol) of *m*-methoxyphenylacetylene in 15 ml of dry ether under a nitrogen atmosphere by the addition of 2.0 ml of a 2.5 *M* hexane solution of *n*-butyllithium, a solution of 76 mg (0.32 mmol) of the ketone ketal **6** in 3 ml of dry ether was added, and the mixture was stirred at −78° for 4 hr. The reaction was quenched with 0.5 ml of 10% aqueous ammonium chloride solution followed by 15 ml of water, and the product wa isolated by ether extraction.[35] After preparative TLC (40% ether–petroleum ether) there was obtained 102 mg of an oil which was judged to consist of 50% of the addition product and 50% of the starting ketone by integration of the methoxyl region of the NMR spectrum. This crude mixture was dissolved in 5 ml of ethyl acetate, and the solution was stirred under a hydrogen atmosphere for 1 hr in the presence of 30 mg of 10% palladium on carbon. After removal of the catalyst and evaporation of the solvent at reduced pressure, 78 mg of an inseparable mixture of the tertiary-alcohol **7** and the starting ketone **6** remained.

A solution of 150 mg (0.52 mmol) of this crude reduction product from two experiments in 5 ml of dry pyridine was cooled in an ice bath, and 0.20 ml (2.8 mmol) of thionyl chloride was added. The yellow solution was stirred for 50 min at 0° and then poured into 25 ml of ice and water, and the product was isolated by ether extraction including an acid wash.[35] On preparative TLC (30% ether–petroleum ether) of the residue there were obtained two bands which consisted of 45 mg (28%) of starting ketone **6** (R_f 0.5) and 68 mg (38% based on the ketone **6** used) of the desired olefin **8** (R_f 0.7). The analytical sample of this olefin was obtained after another preparative TLC (30% ether–petroleum ether) and evaporative distillation at 120° and 0.005 mm: ir ($CHCl_3$) 1600, 1585 cm^{-1} (Ph); NMR ($CDCl_3$) δ 1.10 (s, 3, C-4a CH_3), 1.25 (s, 3, C-8a CH_3), 3.78–4.08 (m, 7, $-OCH_2CH_2O-$ and OCH_3), 5.15–5.35 (m, 1, –C=CM–), and 6.62–7.37 (m, 4, ArH).

Anal. Calcd for $C_{23}H_{32}O_3$: C, 77.49; H, 9.05. Found: C, 77.35; H, 9.15.

4aα,8aβ-Dimethyl-5,5-ethylenedioxo-1β-(2′-*m*-methoxyphenylethyl)-1α,4,4a,5,6,7,8,8a-octahydro-2(3*H*)-naphthalenone (9). The hydroboration[40] of 165 mg (0.464 mmol) of the olefin **8** in 4 ml of dry tetrahydrofuran was accomplished through the addition of 3.0 ml (3 mmol) of a 1 *M* tetrahydrofuran solution of borane under a nitrogen atmosphere. The reaction mixture was stirred for 50 min, cooled to 0°, and then treated with 0.20 ml of water, followed by 2.0 ml of 3 *N* aqueous sodium hydroxide and 2.0 ml of 30% hydrogen peroxide. After an additional 45 min, the resultant mixture was diluted with 25 ml of 10% aqueous potassium carbonate, and the product was isolated by ether extraction.[35] The residue amounted to 107 mg of an oil which was fractionated by preparative TLC (40% ether–petroleum ether). The desired alcohol (63 mg, 37%) was obtained in the band with R_f 0.2 as an oil: ir ($CHCl_3$) 3600 (OH) and 1600, 1585 cm^{-1} (ArH); NMR ($CDCl_3$) δ 1.07 (s, 3, C-4a CH_3), 1.42 (s, 3, C-8a CH_3), 3.67–4.07 (m, 8, $-OCH_2CH_2O-$, OCH_3, CHOH), and 6.60–7.37 (m, 4, ArH).

The oxidation of this alcohol (63 mg, 0.168 mmol) in 5 ml of acetone was accomplished with 0.06 ml (0.24 mequiv) of 8 *N* chromic acid solution,[39] and the ketone **9** (62 mg, 37% from the olefin **8**) was isolated by ether extraction[35] after dilution of the oxidation mixture with 20 ml of water. The analytical sample was obtained by preparative TLC (50% ether–petroleum ether) and then flame flash distillation (0.15 mm) of this sample: ir ($CHCl_3$) 1695 (C=O), 1600, 1585 cm^{-1} (Ar); NMR ($CDCl_3$) δ 1.05 (s, 3, C-4a CH_3), 1.23 (s, 3, C-8a CH_3), 3.60–3.97 (m, 7, $-OCH_2CH_2O-$ and OCH_3), and 6.60–7.40 (m, 4, ArH).

Anal. Calcd for $C_{23}H_{32}O_4$: C, 74.16; H, 8.66. Found: C, 74.17; H, 8.79.

4a,5α-Methano-5β-methoxy-8aβ-methyl-3,4,4a,5,6,7,8,8a-octahydro-1(2*H*)-naphthalenone. An ice-cooled solution of 240 mg (1.22 mmol) of the alcohol **12** in 45 ml of acetone was oxidized with 0.40 ml (1.60 mequiv) of 8 *N* chromic acid solution[39] over a period of 3 min. After the addition of 0.20 ml of isopropyl alcohol and 5 ml of saturated aqueous sodium bicarbonate solution, the acetone was removed at reduced pressure; 30 ml of water was added, and the product was isolated by ether extraction.[35] After preparative TLC (30% ether–petroleum ether) of the residue, 174 mg (73%) of the ketone, mp 60.5–2°, was obtained. Crystallization of a portion of this material from hexane and then sublimation at 55° and 0.005 mm provided the analytical sample: mp 61–62°; ir ($CHCl_3$) 3075 (cyclopropyl CH), 1705 (C=O), and 1055 cm^{-1} (C–O–C); NMR ($CDCl_3$) δ 0.38 and 0.60 (2 d, 1 each, J = 5.5 Hz, cyclopropyl CH_2), 1.38 (s, 3, C-8a H_3), and 3.27 (s, 3, OCH_3).

Anal. Calcd for $C_{13}H_{20}O_2$: C, 76.70; H, 9.36. Found: C, 76.64; H, 9.47.

1,2,3,4,4a,5,6,7,8,8a-Decahydro-4a,5α-methano-5β-methoxy-1β-(2′-*m*-methoxyphenylethyl)-8aβ-methyl-1α-naphthol (17, R = CH_2Ar). A. From Grignard Cleavage of Oxirane 15. To a suspension of 313 mg (12.9 mg-atoms) of magnesium shavings in 5 ml of dry ether was added a solution of 1.867 g (11.9 mmol) of *m*-methoxybenzyl chloride in 5 ml of dry ether over the course of 15 min while the mixture refluxed spontaneously. After an additional 30-min reflux, 10 ml of dry tetrahydrofuran was introduced and then 10 ml (11.7 mmol) of dry dioxane.[41] After 2 min, stirring was stopped, and the precipitate was permitted to settle for 10 min. Titration of an aliquot of this solution was *sec*-butyl alcohol in xylene using 1,10-phenanthrolene as indicator[42] showed that the solution was 0.26 *M* in dialkylmagnesium. The supernatant, 13 ml (3.4 mmol), was transferred with a syringe to a flask that contained a solution of 200 mg (0.96 mmol) of the oxirane **15** in 1 ml of dry dioxane under a nitrogen atmosphere. The reaction mixture was refluxed for 65 min, cooled, and quenched with 1 ml of water, and the resulting mixture was poured into 50 ml of water. Isolation of the product by ether extraction[35] gave 411 mg of an oil which was adsorbed on 20 g of alumina. Elution with 60 ml of petroleum ether gave 119 mg of 3,3′-dimethoxybibenzyl, and then 60 ml of 10% ether–petroleum ether gave 74 mg (37%) of recovered starting oxirane **15**. Further elution with 80 ml of ether afforded 181 mg of a mixture which consisted of 65% of the desired alcohol **16** (R = CH_2Ar) by integration of the methoxyl region of the NMR spectrum: ir ($CHCl_3$) 3550–3500 (broad, w, OH), 1665 (C=C), and 1600, 1585 cm^{-1} (Ar); NMR ($CDCl_3$ + 1 drop of pyridine) δ 1.13 (s, 3, C-8a CH_3), 3.50 (s, 3, OCH_3), and 3.82 (s, 3, $ArOCH_3$). The product was extremely labile and was used directly in the methylenation reaction. The yields of the alcohol **16** (R = CH_2Ar) from other

similar experiments were highly variable and ranged from 29 to 86% based on consumed starting material. In one experiment the alcohol **16** (R = CH_2Ar) was obtained free of impurities; in this case the methylenation proceeded well. In other instances poor yields were realized.

To a solution of the Simmons–Smith reagent[15] prepared from 1.168 g (16.7 mmol) of zinc–copper couple[37] in 17 ml of dry ether and 1.30 ml (16.2 mmol) of diiodomethane was added a solution of 520 mg (1.57 mmol) of the alcohol **16** (R = CH_2Ar) (obtained free of impurities from one cleavage experiment) in 1.75 ml (16.7 mmol) of dry 1,2-dimethoxyethane and 5 ml of dry ether under a nitrogen atmosphere. After 50 min at room temperature the excess reagent was destroyed with 0.5 ml of water, and the mixture was poured into 35 ml of saturated aqueous potassium carbonate solution. Isolation of the crude product by ether extraction[35] and then preparative TLC (20% ether–petroleum ether) gave two products. The first band at R_f 0.2 amounted to 352 mg (66%) of the desired methoxycyclopropane **17** (R = CH_2Ar). A portion of this material was further purified by preparative TLC (20% ether–petroleum ether), and the resulting oil was flame flash distilled (0.01 mm) to give the analytical sample: ir ($CHCl_3$) 3600 (OH) and 1600 1585 cm^{-1} (Ar); NMR ($CDCl_3$) δ 0.50 and 0.80 (2 d, 1 each, J = 5 Hz, cyclopropyl CH_2), 1.13 (s, 3, C-8a CH_3), 3.22 (s, 3, OCH_3), 3.77 (s, 3, $ArOCH_3$), and 6.57–7.37 (m, 4, ArH).

Anal. Calcd for $C_{22}H_{30}O_3$: C, 76.70; H, 9.36. Found: C, 76.62; H, 9.22.

The second band at R_f 0.7 amounted to 42 mg (8%) of the ketal **24** (R = CH_2CH_2Ar), which was further purified by preparative TLC (20% ether–petroleum ether) and also flame flash distilled (0.01 mm) to afford the analytical sample: ir ($CHCl_3$) 1600, 1585 (Ar), and 1155, 1085 cm^{-1} (C–O–C); NMR ($CDCl_3$) δ 0.95 (s, 3, C-8a CH_3), 3.37 (s, 3, OCH_3), 3.77 (s, 3, $ArOCH_3$), and 6.53–7.25 (m, 4, ArH).

Anal. Calcd for $C_{21}H_{32}O_3$: C, 76.33; H, 9.15. Found: C, 76.36; H, 9.20.

B. From the Methoxycyclopropyl Ketone. Lithium *m*-methoxyphenylacetylide was prepared in a nitrogen atmosphere from 3.2 g (10 mmol) of *m*-methoxyphenylacetylene in 27 ml of dry ether by the addition of 3.0 ml of 2.5 *M* hexane solution of *n*-butyllithium, and then a solution of 287 mg (1.38 mmol) of the methoxycyclopropyl ketone in 4 ml of dry ether was added. The resulting mixture was stirred at room temperature for 1 hr and then the excess acetylide was decomposed by the addition of 0.5 ml of 10% aqueous ammonium chloride solution. The resulting mixture was poured into 50 ml of water, and the product was isolated by ether extraction.[35] After preparative TLC (50% ether–petroleum ether) there was obtained 455 mg (96%) of a yellow oil.

This crude product was hydrogenated as described above in the formation of the hydroxy ketal **7** by stirring in 10 ml of ethyl acetate with a suspension of 200 mg of 10% palladium on carbon in a hydrogen atmosphere. After filtration of the catalyst and removal of the solvent from the filtrate at reduced pressure, fractionation of the residue by preparative TLC (50% ether–petroleum ether) gave two products. The more polar band at R_f 0.3 contained 204 mg (46%) of the equatorial alcohol, mp 95–98°. Crystallization of a portion of this material from ether–heptane gave the analytically pure sample: mp 100.5–101.5°; ir ($CHCl_3$) 3610 (OH) and 1600, 1585 cm^{-1} (Ar); NMR ($CDCl_3$) δ 0.53 (m, 2, cyclopropyl CH_2), 1.25 (s, 3, C-8a CH_3), 3.23 (s, 3, OCH_3), 3.80 (s, 3, $ArOCH_3$), and 6.57–7.37 (m, 4, ArH).

Anal. Calcd for $C_{22}H_{32}O_3$: C, 76.70; H, 9.36. Found: C, 76.64; H, 9.17.

The less polar band, at R_f 0.4, contained 192 mg (44%) of the desired axial alcohol **17** (R = CH_2Ar), which was identical with that obtained in part A above.

4aα,8aβ-Dimethyl-3,4,4a,7,8,8a-hexahydro-1-(2′-*m*-methoxyphenyethyl)-5(6*H*)-naphthalenone (18, R = CH_2Ar). A solution of 181 mg (0.525 mmol) of the cyclopropyl alcohol **17** (R = CH_2Ar) in 15 ml of methanol containing 1.5 ml of 37–38% hydrochloric acid was refluxed for 4 hr. The solution was poured into 25 ml of saturated aqueous sodium bicarbonate solution, and the product was isolated by ether extraction.[35] Purification of the residue (159 mg) by preparative TLC (20% ether–petroleum ether) gave a band at R_f 0.3 that contained 89 mg (46%) of the ketone **18** (R = CH_2Ar), as a colorless oil that was contaminated with about 20% of the exocyclic olefin by NMR analysis. A portion of this material was further purified by preparative TLC (20% ether–petroleum ether) and then flame flash distillation (0.01 mm) for the analytically pure sample: ir ($CHCl_3$) 1695 (C=O) and 1600, 1585 cm^{-1} (Ar); NMR ($CDCl_3$) δ 1.02 (s, 3, C-8a CH_3), 1.20 (s, 3, C-4a CH_3), 3.80 (s, 3, $ArOCH_3$), 5.22–5.37 (m, 1, –C=CH–), and 6.58–7.42 (m, 4, ArH).

Anal. Calcd for $C_{21}H_{28}O_2$: C, 80.73; H, 9.03. Found: C, 80.65; H, 9.11.

1,2,3,4,4a,5,6,7,8,8a-Decahydro-1-(2′-*m*-methoxyphenylethylidene)-4a,5α-methano-5β-methoxy-8aβ-methylnaphthalene. To a solution of 204 mg (0.594 mmol) of the above equatorial alcohol in 5 ml of dry pyridine at −10° (ice–salt bath) was added 0.25 ml (3.44 mmol) of thionyl chloride. The reaction mixture was stirred in the cold for 45 min and then poured into ice and water, from which the product was isolated by ether extraction.[35] After preparative TLC (20% ether–petroleum ether) of the residue, there was obtained 82 mg (43%) of an olefin that was different from that prepared below from the axial alcohol **17** (R = CH_2Ar). Rechromatography and then flame flash distillation (0.1 mm) gave the analytical sample: ir ($CHCl_3$) 1665 (C=C), 1600, 1585 (Ar), and 1055 cm^{-1} (C–O–C); NMR ($CDCl_3$) δ 0.37 (m, 2, cyclopropyl CH_2), 1.28 (s, 3, C-8a CH_3(= 3/23 (s, 3, OCH_3), 3.77 (s, 3, $ArOCH_3$), 5.00–5.33 (m, 1, –C=CH–), and 6.57–7.33 (m, 4, ArH).

Anal. Calcd for $C_{22}H_{30}O_2$: C, 80.94; H, 9.26. Found: C, 80.82; H, 9.20.

4a,5α-Methano-5β-methoxy-1-(2′-*m*-methoxyphenylethyl)-8aβ-methyl-3,4,4a,5,6,7,8,8a-octahydronaphthalene (20). To a solution of 317 mg (0.92 mmol) of the axial alcohol **17** (R = CH_2Ar) in 7 ml of dry pyridine cooled to −10° was added 0.35 ml (4.5 mmol) of thionyl chloride. After 45 min the reaction mixture was diluted with 300 ml of ether, and the product was isolated by ether extraction.[35] Purification of the residue by preparative TLC (20% ether–petroleum ether) gave 241 mg (91%) of the endocyclic olefin **20** as an oil. Rechromatography of a sample of this material and then flame flash distillation at 0.01 mm gave analytically pure material: ir ($CHCl_3$) 1600, 1585 (Ar), and 1155 cm^{-1} (C–O–C); NMR ($CDCl_3$) δ 0.35 and 0.62 (2 d, 1 each, J = 5 Hz, cyclopropyl CH_2), 1.27 (s, 3, C-8a CH_3), 3.23 (s, 3, OCH_3), 3.77 (s, 3, $ArOCH_3$), 5.30–5.50 (m, 1, –C=CH–), and 6.57–7.37 (m, 4, ArH).

Anal. Calcd for $C_{22}H_{30}O_2$: C, 80.94; H, 9.26. Found: C, 81.17; H, 9.13.

4a,5αa-Methano-5β-methoxy-1β-(2′-*m*-methoxyphenylethyl)-8aβ-methyl-1α,2,3,4,4a,7,8,8a-octahydro-5(6*H*)-naphthalenone (21). The hydroboration of 210 mg (0.645 mmol) of the olefin **20** in 6 ml of dry tetrahydrofuran was carried out under a nitrogen atmosphere by the addition of 2.0 ml of a 1 *M* tetrahydrofuran solution of borane. After 1 hr at 25° the reaction mixture was cooled to 0° and treated successively with 0.5 ml of water, 3 ml of 3 *N* aqueous sodium hydroxide, and 3 ml of 30% hydrogen peroxide. After an additional 45 min, the mixture was poured into 30 ml of 10% aqueous potassium carbonate, and the product was isolated by ether extraction.[35] Purification of the residue by preparative TLC (50% ether–petroleum ether) gave 185 mg (84%) of the secondary alcohol (R_f 0.2), isolated as an oil which crystallized on standing, mp 90–97°. A portion of this material was crystallized from ether–hexane and then further purified by rechromatography to give analytically pure material: mp 100–102° (amorphous solid); ir ($CHCl_3$) 3600 (OH), 1602, 1585 (Ar), and 1155 cm^{-1} (C–O–C); NMR ($CDCl_3$) δ 0.35 and 0.58 (2 d, 1 each, J = 5 Hz, cyclopropyl CH_2), 0.98 (s, 3, C-8a CH_3), 3.20 (s, 3, OCH_3), 3.75 (s, 3, $ArOCH_3$), and 6.57–7.18 (m, 4, ArH).

Anal. Calcd for $C_{22}H_{32}O_3$: C, 76.70; H, 9.36. Found: C, 76.87; H, 9.37.

Oxidation of the above alcohol was accomplished through the addition of 0.15 ml (0.60 mequiv) of 8 *N* chromic acid solution[39] to 164 mg (0.476 mmol) of the alcohol in 15 ml of acetone, followed by the same work-up described above for similar oxidations. Purification of the crude product by preparative TLC (50% ether–petroleum ether) gave 130 mg (74%) of the ketone **21** (R_f 0.3), which formed waxy crystals on standing. Two crystallizations of a portion of this material from ether–heptane gave the analytical sample: mp 108–110°; ir ($CHCl_3$) 1700 (C=O), 1600, 1585 (Ar), and 1155 cm^{-1} (C–O–C); NMR ($CDCl_3$) δ 0.67 (m, 2, cyclopropyl CH_2), 0.90 (s, 3, C-8a CH_3), 3.23 (s, 3, OCH_3), 3.77 (s, 3, $ArOCH_3$), and 6.57–7.27 (m, 4, ArH).

Anal. Calcd for $C_{22}H_{30}O_3$: C, 77.16; H, 8.83. Found: C, 77.23; H, 8.87.

1α,2,3,4,4a,5,6,7,8,8a-Decahydro-2α,8aβ-dimethyl-4a,5α-methano-5β-methoxy-1β-(2′-*m*-methoxyphenylethyl)-2β-naphthol (22). To 1.4 ml (3.3 mmol) of a 2.4 *M* ethereal solution of methyllithium in 10 ml of dry ether at 0° under a nitrogen atmosphere was added a solution of 109 mg (0.318 mmol) of the ketone **21** in 4 ml of dry ether. After 10 min the excess reagent was quenched with 0.5 ml of water and the product was isolated by

ether extraction.[35] Fractionation of the residue by preparative TLC (50% ether–petroleum ether) gave 102 mg (90%) of white crystals, mp 87–101°. Two crystallizations of a portion of this material from ether–hexane gave the analytical sample: mp 106.5–107.5; ir ($CHCl_3$) 3605 (OH), 1600, 1585 (Ar), and 1155 cm^{-1} (C–O–C); NMR ($CDCl_3$) δ 0.30 and 0.63 (2 d, 1 each, J = 5 Hz, cyclopropyl CH_2), 1.40 (s, 6, C-4a and C-8a methyls), 3.25 (s, 3, OCH_3), 3.78 (s, 3, $ArOCH_3$), and 6.57–7.37 (m, 4, ArH).

Anal. Calcd for $C_{23}H_{34}O_3$: C, 77.05; H, 9.56. Found: C, 77.19; H, 9.63.

1α-Hydroxy-5β-(2′-*m*-methoxyphenylethyl)-8aα-methyl-6-oxo-1,2,3,4,4a,5,6,7,8,8a-decahydronaphthalene-4aβ-carbonitrile (29). According to the general procedure of Nagata and coworkers,[21a,c] 140 ml (210 mmol) of a 1.5 *M* benzene solution of diethylaluminum cyanide was added in a slow stream over several minutes to a stirred, ice-cooled solution of 21.9 g (69.8 mmol) of the enone **28** in 230 ml of dry benzene. After stirring for 2.5 hr without cooling, the mixture was poured with vigorous stirring onto 1 l. of 10% aqueous sodium hydroxide solution and 1 kg of ice, and the product was isolated by dichloromethane extraction with a base wash.[35] Crystallization of the resulting gum from ether–hexane afforded 19.04 g (80%) of trans cyanide **29** as white crystals, mp 115–121°. The analytical sample, obtained after two further crystallizations of a portion of this material from ether–hexane, melted at 122–125°; ir ($CHCl_3$) 3615, 3480 (OH), 2225 (C≡N), 1720 (C=O), 1600, 1585, 1490 (aromatic), and 1260, 1150, 1050 cm^{-1} (ArOMe); NMR ($CDCl_3$) δ 1.12 (s, 3, C-8a CH_3), 3.70 (m, 1, C-1 H), 3.80 (s, 3, $ArOCH_3$), and 6.6–7.3 (m, 4, ArH).

Anal. Calcd for $C_{21}H_{27}NO_3$: C, 73.87; H, 7.97; N, 4.10. Found: C, 73.96; H, 7.96; N, 4.06.

The mother liquors from the first crystallization were chromatographed on 1 kg of silica gel. After elution with 4.5 l. of ether, continued elution with 1.5 l. of ether gave 0.610 g of an oil which on crystallization from ether–hexane afforded an additional 0.361 g of crystalline cyanide **29**, mp 119–122°. The total yield of the trans cyano ketone **29** was thus 19.4 g (82%).

1α-Acetoxy-5β-(2′-*m*-methoxyphenylethyl)-6-8aα-dimethyl-1,2,3,4,4a,7,8,8a-octahydronaphthalene-4aβ-carbonitrile (30). A solution of methylmagnesium iodide from 88 ml (200 g, 1.41 mol) of iodomethane and 40.5 g (1.67 mol) of magnesium turnings in 930 ml of dry ether was cooled in an ice bath, and then a solution of 51 g (0.15 mol) of the cyano ketone **29** in 900 ml of benzene was added over a 50-min period. Stirring and cooling were continued for an additional 45 min, and the solution was then carefully treated with 40 ml of saturated aqueous ammonium chloride solution. This mixture was poured onto 2.0 l. of ice and saturated aqueous ammonium chloride solution, and after the product was isolated by dichloromethane extraction,[35] 51.6 g of the crude cyanodiol, mp 170–173°, remained. The analytical sample, obtained after three crystallizations of similar material from another experiment from ether–acetone, melted at 175–178°: ir ($CHCl_3$) 3610, 3460 (OH), 2220 (-C≡N), 1600, 1585, 1485 (aromatic), and 1150, 1040 cm^{-1} ($ArOCH_3$); NMR ($CDCl_3$) δ 0.93 (s, 3, C-8a CH_3), 1.13 (s, 3, C-6 CH_3), 3.80 (s, 3, $ArOCH_3$), 3.82 (m, 1, C-1 H), and 6.6–7.3 (m, 4, ArH).

Anal. Calcd for $C_{22}H_{31}NO_3$: C, 73.92; H, 8.74; N, 3.92. Found: C, 73.82; H, 8.69; N, 3.81.

A solution of 51.6 g of this crude diol in 1 l. of dry pyridine was treated with 385 ml of acetic anhydride and stirred at room temperature for 22 hr. The mixture was diluted with 2.0 l. of ethyl acetate, and then isolation of the product by ether extraction, including a base wash,[35] gave 57 g of solid hydroxy acetate. The analytical sample, obtained after three crystallizations of similar material from another experiment from ethyl acetate–chloroform, melted at 163–165°: ir ($CHCl_3$) 3600 (OH), 2225 (C≡N), 1725 (CH_3C=O), 1600, 1585, 1485 (aromatic), and 1150, 1035 cm^{-1} ($ArOCH_3$); NMR ($CDCl_3$) δ 1.02 (s, 3, C-8a CH_3), 1.12 (s, 3, C-6 CH_3), 2.03 (s, 3, $COCH_3$), 3.80 (s, 3, $ArOCH_3$), 5.1 (m, 1, C-1 H), and 6.7–7.4 (m, 4, ArH).

Anal. Calcd for $C_{24}H_{33}NO_4$: C, 72.15; H, 8.33; N, 3.51. Found: C, 72.22; H, 8.22; N, 3.48.

This crude alcohol (57 g) was dissolved in 1.1 l. of dry pyridine, and the solution was chilled with a ice bath. To this solution 61 ml (102 g, 0.856 mol) of thionyl chloride was then added dropwise with stirring over a 30-min period. The solution was stirred at 0° for an additional 75 min, and then without cooling for 45 min. This mixture was poured into 500 ml of ice and water and then isolation of the product by benzene–ether–ethyl acetate (1:1:1) extraction, including an acid and a base wash,[35] gave 55.6 g of brown oil which on crystallization from ethanol afforded 42.2 g (74%) of cyano olefin mixture **30**, mp 85–105°, as slightly brown crystals. The mother liquors from this crystallization were concentrated and then chromatographed on 2 kg of silica gel, and after 4 l. of 70% ether–petroleum ether eluent was discarded, continued elution with 3 l. of the same solvent system afforded an additional 8.83 g (16.2%) of the cyano olefin mixture **30** as an oil. The combined yield of the cyano olefin mixture **30** from crystallization and chromatography was 51.03 g (90%). The analytical sample, obtained after preparative TLC (50% ether–petroleum ether) and then crystallization from ethanol of a portion of this material, melted over the range 89–108°: ir ($CHCl_3$) 2220 (C≡N(= [735 (acetate C=O), 1600, 1585, 1490 (aromatic), and 1150, 1035 cm^{-1} ($ArOCH_3$); NMR ($CDCl_3$) δ 0.95, 1.08 (two singlets, 3 each, C-8a CH_3, ratio ca. 4:1), 1.62 (s, 3, C-6 CH_3), 2.04 (s, 3, $COCH_3$), 3.80 (s, 3, $ArOCH_3$), 5.0 (m, 1, C-1 H), 5.41 (m, ca. 0.2, C-7 H of Δ^6 olefin component), and 6.7–7.4 (m, 4, ArH). The bulk material obtained above also had the same spectral properties.

Anal. Calcd for $C_{24}H_{31}NO_3$: C, 75.56; H, 8.19; N, 3.67. Found: C, 75.64; H, 8.21; N, 3.66.

5β-(2′-*m*-Methoxyphenylethyl)-4aβ,6,8aα-trimethyl-1,2,3,4,-4a,7,8,8a-octahydronaphth-1α-ol (31). To a stirred solution of 14.0 g (36.7 mmol) of cyano olefin mixture **30** in 560 ml of dry benzene at room temperature was added 92 ml (0.147 mol) of a 1.6 *M* benzene solution of diisobutylaluminum hydride. After stirring for 2.5 hr, the mixture was poured into 1 l. of 10% aqueous potassium hydroxide solution and ice, and on isolation of the crude product by ether extraction[35] there remained 12.9 g of crude hydroxy imine as a white foam: ir ($CHCl_3$) 3620 (OH), 1612 (HC=NH), 1600, 1585, 1485 (aromatic), and 1260, 1150, 1040 cm^{-1} ($ArOCH_3$).

This entire crude product was treated[43] with 60 ml of 99% hydrazine hydrate and 17.6 g of hydrazine dihydrochloride in 540 ml of triethylene glycol. This mixture was heated under an argon atmosphere with stirring for 5 hr at an internal temperature of 135°, and then 116 g of 85% potassium hydroxide pellets was added portionwise. The internal temperature was raised to 155° and for 1.5 hr volatile mixture was allowed to distil in an argon flow. The argon flow was then stopped, and stirring and heating were continued for 5 hr. The mixture was then allowed to cool to room temperature over a 7-hr period, and after the resulting solid white mass was dissolved in 1.4 l. of water, the product was isolated by ether extraction.[35] The residue amounted to 10.2 g of a white solid which on crystallization from ether–hexane gave 9.57 g (80%) of crystalline olefin mixture **31**, mp 92–103°. Two subsequent crystallizations of a portion of this olefin mixture from ether–hexane afforded the analytical sample: mp 98–105°; ir ($CHCl_3$) 3610, 3450 (OH), 1600, 1585, 1485 (aromatic), 1370 (CH_3), and 1150 cm^{-1} ($ArOCH_3$); NMR ($CDCl_3$) δ 0.75, 0.90 (two singlets, 3 each, C-8a CH_3, ratio ca. 1:3), 0.82, 1.00 (two singlets, 3 each, C-4a CH_3, ratio ca. 1:3), 1.61 (s, C-6 CH_3), 37 (m, 1 C-1 H), 3.76 (s, 3, $ArOCH_3$), 5.38 (m, ca. 0.25, C-7 H of Δ^6 olefin component), and 6.6–7.3 (m, 4, ArH).

Anal. Calcd for $C_{22}H_{32}O_2$: C, 80.44; H, 9.82. Found: C, 80.23; H, 9.82.

5β-(2′-*m*-Methoxyphenylethyl)-4aβ,6,8aα-trimethyl-3,4,4a,-7,8,8a-hexahydro-1(2*H*)-naphthalenone (23). A solution of 60.5 mg (0.169 mmol) of the alcohol **22** in 8 ml of methanol and 2.0 ml of 37–38% hydrochloric acid was refluxed under an argon atmosphere for 2 hr. The course of the reaction was followed by TLC (30% ether–petroleum ether); over the 2-hr period the spot for the alcohol **22** (R_f 0.3) was quickly replaced by one (R_f 0.7) corresponding to an intermediate olefin, which in turn was replaced by a spot (R_f 0.6) that represented the ketone **23**. The reaction mixture was diluted to 150 ml with water. The product was isolated by ether extraction, including a base wash.[35] Purification of the residue by preparative TLC (30% ether–petroleum ether) afforded 50 mg (91%) of a colorless oil. This material, which consisted of a 71:29 mixture of Δ^5 and Δ^6 isomeric olefins by comparative integration of the angular methyl region of the NMR spectrum, slowly crystallized on standing and melted over the range 60–87°. The analtyical sample, prepared by crystallization of this material from ether, melted at 68–93°: ir ($CHCl_3$) 1700 (C=O) 1600, 1585, 1485 (aromatic), and 1260, 1150, 1040 cm^{-1} ($ArOCH_3$); NMR ($CDCl_3$) δ 0.68 (s, 0.85, C-8a CH_3, Δ^6 isomer), 0.97 (s, 2.15, C-8a CH_3, Δ^5 isomer), 1.08 (s, 0.85, C-4a CH_3, Δ^6 isomer), 1.17 (s, 2.15, C-4a CH_3, Δ^5 isomer), 1.65 (s, 3, C-6 CH_3), 3.80 (s, 3, OCH_3), and 6.60–7.40 (m, 4, ArH).

Anal. Calcd for $C_{22}H_{30}O_2$: C, 80.94; H, 9.26. Found: C, 81.02; H, 9.38.

8-Methoxy-4aβ,10bβ,12aα-trimethyl-3,4,4a,4bα,5,6,10b,-11,12,12a-decahydro-1(2*H*)-chrysenone (3). A. From Cycliza-

tion of the Keto Olefin 23. A solution of 67 mg (0.20 mmol) of the keto olefin mixture **23** and 100 mg of *p*-toluenesulfonic acid monohydrate in 7 ml of toluene was heated at reflux in an argon atmosphere under a Dean-Stark water separator for 2 hr. After the reaction mixture was cooled the product was isolated by ether extraction, including a base wash.[35] After preparative TLC (30% ether–petroleum ether) of the residue, there was obtained 53 mg (81%) of a white solid that consisted of an 80:20 mixture of the trans-anti-trans ketone **3** and its cis-anti-trans isomer by comparative integration of the angular methyl region in the NMR spectrum. Three crystallizations of this material from ether gave 42 mg (65%) of the ketone **3**, mp 150–152° (vacuum), which was of sufficient purity for analysis: ir ($CHCl_3$) 1700 (C=O), 1605, 1575, 1500 (3,4-disubstituted anisole ring), and 1030 cm^{-1} ($ArOCH_3$); NMR ($CDCl_3$) δ 0.90 (s, 3, C-4a CH_3), 1.19 (s, 3, C-12a CH_3), 1.22 (s, 3, C-10b CH_3), 3.77 (s, 3, OCH_3), and 6.6–7.3 (m, 3, ArH).

Anal. Calcd for $C_{22}H_{30}O_2$: C, 80.94; H, 9.26. Found: C, 80.89; H, 9.34.

A mixture of a sample of this material, mp 150–152° (vacuum), with material obtained from the hydrocyanation route, mp 150–152° (vacuum) as well as with that obtained from the polyene cyclization route, mp 150–152° (vacuum), melted at 150–152° (vacuum). The infrared and NMR spectra of all three samples were also identical.

A sample of the ketone **3** which was crystallized from ether–heptane, twice from ethyl alcohol, and finally from ether formed clear needles, mp 153–154° (vacuum), which were used for single-crystal X-ray structure analysis (vide infra).

B. From the Hydroxy Olefin Mixture 31. A stirred and ice-cooled solution of 12.49 g (38 mmol) of the hydroxy olefin mixture **31** in 850 ml of acetone was treated portionwise over a 5-min period with 19.0 ml (152 mequiv) of 8 *N* chromic acid solution.[39] After stirring for 10 min with cooling, the solution was treated with 12 ml of isopropyl alcohol and poured into 1.8 l. of water. After isolation of the product by ether extraction,[35] there was obtained 12.0 g of ketone **23** as a light brown solid. An 11.5-g portion of the above crude keto olefin **23** was dissolved in 115 ml of trifluoroacetic acid, and the solution was heated at reflux with stirring for 3.5 hr. The black mixture was cooled with an ice bath and the product (12 g) was isolated by ether–benzene (1:1) extraction, including a base wash.[35] Two crystallizations of this material from ethanol afforded 7.6 g (64% from alcohol **31**) of tetracyclic ketone **3**, mp 149–151° (vacuum), as light tan crystals.

The mother liquors from these crystallizations were purified by preparative GLC on a 10 ft × 0.25 in. 20% SE-30 on 60–80 Chromosorb W at 290° with a helium flow of 70 ml/min. The compounds with retention times of 16 and 20 min were collected by passing the effluent gases through glass tubes packed with alumina. The product with retention time of 20 min had a NMR spectrum which was identical with that of the ketone **3** obtained above.

The compound with a retention time of 16 min was freed from SE-30 by preparative TLC (50% ether–petroleum ether) and then crystallized by scratching, mp 125–134° (vacuum). Crystallization from ethanol and then flame flash sublimation at 0.1 mm gave the analytical sample of the cis-anti-trans tetracyclic ketone isomer: mp 136–138° (vacuum); ir ($CHCl_3$) 1700 (C=O) and 1605, 1500 cm^{-1} (aromatic); NMR ($CDCl_3$) δ 0.35 (s, 3, C-4aβ CH_3), 1.17 (s, 3, C-10bα CH_3), 1.30 (s, 3, C-12aα CH_3), 3.75 (s, 3, OCH_3), and 6.50–7.40 (m, 3, ArH).

Anal. Calcd for $C_{22}H_{30}O_2$: C, 0.94; H, 9.26. Found: C, 80.98; H, 9.20.

5,6-Dimethyl-(*E*)-1,5,9-decatriene (34). To 650 ml (0.715 mol) of a 1.1 *M* ethereal solution of allylmagnesium bromide diluted with 450 ml of dry tetrahydrofuran was added at reflux over a 3-hr period 39 g (0.161 mol) of 1,4-dibromo-2,3-dimethyl-(*E*)-2-butene[27] in 100 ml of dry tetrahydrofuran. After stirring for 1 hr at 25°, the reaction mixture was cooled to 0° and then quenched with 20 ml of saturated ammonium chloride solution, and the product was isolated by ether extraction[35] except that the solvent was removed by distillation through a 1-ft Vigreux column at atmospheric pressure. Distillation of the colorless liquid residue through a 2-ft Teflon spinning band column gave 25 g (95%) of the triene **34**, bp 86–87° (15 mm). Gas–liquid chromatography (130°, 7.5 ft × 0.125 in., 5% SE-30 on Diatoport S) of this material showed a single volatile component that amounted to 99% of the effluent at a retention time of 1.3 min. Redistillation of a sample of this material in the same apparatus afforded the analytical sample: bp 100–105° (25 mm); ir (film) 1650 (C=C) and 990, 910 cm^{-1} (–CH=CH_2); NMR ($CDCl_3$) δ 1.65 (s, 6, C-5 and C-6 CH_3), 4.8–5.25 (m, 4, C=CH_2), and 5.6–6.15 (m, 2, –CH=C).

Anal. Calcd for $C_{12}H_{20}$: C, 87.73; H, 12.27. Found: C, 87.56; H, 12.29.

5,6-Dimethyl-(*E*)-5,9-decadienol-1 (35). To a solution of 36.5 g (0.225 mol) of the triene **34** in 200 ml of dry tetrahydrofuran under a nitrogen atmosphere at 0° was added 400 ml (0.292 mol) of 0.77 *M* tetrahydrofuran solution of disiamylborane[31] over a 2-hr period. After stirring for 1 hr, the mixture was treated with 120 ml of 6 *N* sodium hydroxide solution and then 90 ml of 30% hydrogen peroxide. The aqueous layer was saturated with potassium carbonate, and then the organic phase was decanted and dried ($MgSO_4$). After filtration to remove the drying agent, the solvent was removed by distillation through a 1-ft Vigreux column at atmospheric pressure, and the residue was then chromatographed on 1.5 kg of grade III alumina. Elution with 3 l. of 10% ether–petroleum ether gave 8.2 g (22%) of unreacted triene **34**, bp 92–95° (20 mm). Further elution with 6 l. of 75% ether–petroleum ether afforded a mixture of alcohols which was separated by distillation through a 2-ft Teflon spinning band column at reduced pressure. After a forerun of 3-methyl-2-butanol, bp 40–42° (20 mm), there was obtained 17.2 g (43%) of the dienol **35**, bp 94–95% (0.25 mm), the GLC (200°, 6 ft × 0.125 in. 10% SE-30 on Diatoport S) of which showed >99% of a single volatile component with a retention time of 1.5 min. The analytical sample was obtained by evaporative distillation of a portion of this material at 120° and 0.25 mm: ir (film) 3300 (OH), 1640 (C=C), and 980, 905 cm^{-1} (–CH=CH_2); NMR ($CDCl_3$) δ 1.6 (s, 6, C-5 and C-6 CH_3), 3.45–3.8 (m, 2, –CH_2O), 4.8–5.2 (m, 2, C=CH_2), and 5.4–6.15 (m, 1, –CH=C–).

Anal. Calcd for $C_{12}H_{22}O$: C, 79.06; H, 12.06. Found: C, 78.91; H, 12.09.

5,6-Dimethyl-5,9-decadienal (36). A solution of 1.0 g (5.5 mmol) of the alcohol **35** in 60 ml of dry dichloromethane was added to a stirred suspension of 8.6 g (33.1 mmol) of chromic anhydride–dipyridine complex[36] in 60 ml of dry dichloromethane, and the mixture was stirred at room temperature for 15 min. The entire reaction mixture was then filtered though 100 g of Merck acid-washed alumina with the aid of an additional 600 ml of dichloromethane. After the solution was concentrated at reduced pressure, the crude aldehyde, which contained some pyridine, was taken up in 300 ml of ether, and the ethereal solution was washed successively with saturated aqueous copper sulfate (2 × 70 ml), water (50 ml), and saturated brine (50 ml), and then dried ($MgSO_4$). Removal of the solvent at reduced pressure afforded 0.886 g (88%) of the aldehyde **36** as a colorless liquid which was >95% a single volatile component on GLC (200°, 6 ft × 0.125 in., 10% SE-30 on Diatoport S, retention time 1.2 min). The analytical sample was obtained by evaporative distillation of a portion of this material at 70° (0.08 mm): ir (film) 2710 (CHO), 1725 (>C=O), and 1640 cm^{-1} (C=C).

Anal. Calcd for $C_{12}H_{20}O$: C, 79.94; H, 11.18. Found: C, 79.80; H, 11.15.

The **2,4-dinitrophenylhydrazone** of the aldehyde **36** melted at 88–90° after two crystallizations from ethanol.

Anal. Calcd for $C_{18}H_{24}N_4O_4$: C, 59.99; H, 6.71; N, 15.55. Found: C, 60.18; H, 6.78; N, 15.70.

Cyclization of the Aldehyde 36. To a solution of 9.8 g (37.6 mmol) of stannic chloride in 155 ml of nitromethane cooled in an ice bath was added a solution of 1.36 g (7.55 mmol) of the aldehyde **36** in 100 ml of nitromethane. The mixture was stirred for 9 min at the bath temperature and then partitioned between 150 ml of 1 *N* hydrochloric acid and 150 ml of ether. Isolation of the product by ether extraction including an acid wash[35] afforded 1.40 g of brown oil which on evaporative distillation (90–100°, 0.15 mm) gave 1.05 g (77%) of a volatile, yellow oil, the GLC (220°) of which showed in addition to numerous minor volatile components major peaks with retention times of 0.6 (20%), 0.8 (70%), and 1.1 min (3%).

A solution of the above mixture in 25 ml of ethyl alcohol in which was suspended 150 mg of platinum oxide was stirred in a hydrogen atmosphere at room temperature for 24 hr. After removal of the catalyst by filtration and then the solvent at reduced pressure, the residual oil was evaporatively distilled at 90–100° and 0.15 mm. Crystallization of the semisolid distillate (940 mg) from hexane afforded 82 mg (6%), mp 115–117°, of the equatorial alcohol **37**, and an additional 274 mg (20%), mp 115–117°, of the same alcohol **37** was obtained by preparative TLC (30% ether–petroleum ether, R_f 0.3). The analytical sample, obtained after one further crystallization of a portion of this material from hexane, also melted at 115–117°: ir ($CHCl_3$) 3400 cm^{-1} (OH); NMR ($CDCl_3$) δ 0.96 and 1.00 (2 s, 3 each, C-4a and C-8a CH_3) and 3.33–3.83 (m, 1, C-1 H).

Anal. Calcd for $C_{12}H_{22}O$: C, 79.06; H, 12.16. Found: C, 79.16; H, 12.03.

Extraction of the band at R_f 0.4 in the above chromatogram afforded 69 mg (5%) of the axial alcohol **38** as a viscous oil which crystallized on trituration with petroleum ether and melted at 69–71° alone or in admixture with material prepared above from the methoxycyclopropane route (vide supra).

The *p*-bromobenzoate **39**, mp 76–78°, was formed in 89% yield (95 mg) from 53 mg (0.29 mmol) of the equatorial alcohol **37** and 128 mg (0.58 mmol) of *p*-bromobenzoyl chloride in 3 ml of pyridine. After crystallization of this material from petroleum ether, material was obtained which was suitable for single-crystal X-ray structure analysis and melted at 77–78°: NMR ($CDCl_3$) δ 1.12 and 1.16 (2 s, 3 each, C-4a and C-8a CH_3) and 7.73 (m, 4, ArH).

Anal. Calcd for $C_{19}H_{25}BrO_2$: C, 62.47; H, 6.90; Br, 21.88. Found: C, 62.28; H, 6.80; Br, 21.80.

4aβ,8aα-Dimethyl-3,4,4a,5,6,7,8,8a-octahydro-1(2*H*)-naphthalenone (14). A solution of 100 g (0.55 mmol) of the alcohol **37** in 20 ml of acetone was oxidized with 0.25 ml of 8 *N* chromic acid solution,[39] and the product was isolated by ether extraction[35] except that the solvent was removed by distillation through a 1-ft Vigreux column at atmospheric pressure. Evaporative distillation of the pale yellow residue at 95° and 0.5 mm gave 82 mg (82%) of the ketone **14** as a viscous liquid which crystallized on trituration with ether and melted at 101–103°. The analytical sample, obtained after two crystallizations of this material from petroleum ether, melted at 108–110° (sealed capillary): ir (CCl_4) 1710 cm^{-1} (>C=O); NMR ($CDCl_3$) δ 0.90 and 1.23 (2 s, 3 each, C-4a and C-8a CH_3).

Anal. Calcd for $C_{12}H_{20}$: C, 79.94; H, 11.18. Found: C, 80.07; H, 11.23.

4aβ,8aα-Dimethyldecalin. Application of the Huang-Minlon modification[38] of the Wolff–Kishner reduction to 50 mg (0.28 mmol) of the ketone **14** in 3 ml of triethylene glycol with 0.2 ml of 98% hydrazine and 88 mg of potassium hydroxide afforded 22 mg (48%) of 4aβ,8aα-dimethyldecalin, mp 97–98°, after chromatography of the crude product on 2 g of Merck acid-washed alumina (elution with 6 ml of hexane) and then evaporative distillation at 100–120° (30 mm): ir (CCl_4) 1370, 1210, 1160, 1020, 970, 926 cm^{-1}; NMR ($CDCl_3$) δ 1.01 (s, 6, C-4a and C-8a CH_3) and 1.55 (CH_2 envelope).

Anal. Calcd for $C_{12}H_{22}$: C, 86.67; H, 13.33. Found: C, 86.76; H, 13.32.

A similar reduction[38] performed on 248 mg (1.38 mmol) of 4aβ,8aβ-dimethyl-3,4,4a,5,6,7,8,8a-octahydro-2(1*H*)-naphthalenone[28] with 1.46 ml of 97% hydrazine and 785 mg of potassium hydroxide in 10 ml of triethylene glycol afforded 138 mg (60%) of 4aβ,8aβ-dimethyldecalin, mp 88–91°: ir (CCl_4) 1380, 1370, 1180, 1003, and 926 cm^{-1} (all strong); NMR ($CDCl_3$) δ 88 (s, 6, C-4a and C-8a CH_3) and 1.46 (CH_2 envelope).

Anal. Calcd for $C_{12}H_{22}$: C, 86.67; H, 13.33. Found: C, 86.71; H, 13.40.

The melting point of a mixture of this material, mp 88–91°, and the trans isomer prepared above, mp 97–98°, was 55–70°.

5,6-Dimethyl-1,10-bis(trimethylsilyl)-(*E*)-5-decene-1,9-diyne (40). To a solution of propargylmagnesium bromide prepared in 450 ml of dry ether from 143 g (1.2 mol) of propargyl bromide and 28.8 g (1.2 g-atoms) of magnesium turnings was added 72.6 g (0.3 mol) of the dibromide **33**[27] in 100 ml of dry tetrahydrofuran over a 10-min period, while the temperature was maintained between 10 and 15°. After the addition was complete, the mixture was allowed to warm to 25°, and stirring was continued for 2 hr. The mixture was then treated with 120 ml of saturated aqueous ammonium chloride solution, and the product was isolated by ether extraction.[35] A solution of the resulting crude coupling product (ca. 60 g) in 50 ml of dry tetrahydrofuran was added dropwise over 45 min to 400 ml (0.8 mol) of a 2 *M* tetrahydrofuran solution of ethylmagnesium bromide, and then the mixture was refluxed for 1 hr. After cooling to 40°, the gelatinous mixture was treated with a solution of 94 g (0.86 mol) of trimethylchlorosilane in 100 ml of dry tetrahydrofuran and then refluxed for 1 hr. After cooling to room temperature, the reaction mixture was treated with a mixture of 100 ml of saturated aqueous ammonium chloride solution and 10 ml of concentrated ammonium hydroxide, and then the product was isolated by ether extraction.[35] Crystallization of the residue from ethanol gave 75.1 g (82%) of the disilane **40**, mp 65–67°, in two crops of 71.5 and 3.6 g each. The analytical sample, obtained after an additional crystallization of a sample of this material from pentane–ethanol, also melted at 65–67°: ir (film 2170 (C=C) and 835–875 cm^{-1} (CH_3Si); NMR ($CDCl_3$) δ 0.11 (s, 2 × 9, 2 $(CH_3)_3Si$), 1.68 (s, 2 × 3, C-5 and C-6 CH_3), and 2.26 (m, 2 × 4, $-CH_2-$).

Anal. Calcd for $C_{18}H_{32}Si_2$: C, 70.97; H, 10.59; Si, 18.44. Found: C, 70.96; H, 10.51; Si, 18.39.

5,6-Dimethyl-(*E*)-5-decene-1,9-diyne (41). To a solution of 58.7 g (0.192 mol) of disilane **40** in 600 ml of absolute ethanol at 30° was added dropwise over 0.5 hr a solution of 81.5 g (0.480 mol) of silver nitrate in 180 ml of water and 180 ml of 95% ethanol. After stirring for 2 hr, the mixture was treated with a solution of 62.5 g (0.960 mol) of potassium cyanide in 500 ml of water. When the addition was complete, the mixture was stirred until it had cooled to room temperature and then poured into 1 l. of water. The product was isolated from this aqueous mixture by petroleum ether extraction,[35] and then distillation of the residue afforded 30.2 g (98%) of the enediyne **41** as a colorless liquid, bp 85.5–86.0° (4.3 mm). The analytical sample was obtained by evaporative distillation of a portion of this material at 110° (2 mm): ir (neat 3290 (C≡CH) and 2120 cm^{-1} (C≡C); NMR ($CDCl_3$) δ 1.70 (s, 2 × 3, C-5 and C-6 CH_3), 1.93 (m, 2 × 1, C≡CH), and 2.26 (br s, 2 × 4, CH_2).

Anal. Calcd for $C_{12}H_{16}$: C, 89.94; H, 10.06. Found: C, 90.08; H, 10.14.

6,7-Dimethyl-(*E*)-6,10-undecadien-2-ynol (43). A solution of 30.2 g (0.189 mol) of the enediyne **41** in 300 ml of dry tetrahydrofuran was cooled to 0°, and then 190 ml (0.19 mol) of a tetrahydrofuran solution of disiamylborane[31] (prepared from 190 ml of a 1 *M* tetrahydrofuran solution of diborane and excess 2-methyl-2-butene) was added dropwise over 2 hr. The mixture was stirred at room temperature for 4 hr, and then 45 ml of glacial acetic acid was added dropwise over 0.5 hr. The mixture was stirred for an additional 2 hr, and then poured into 1.5 l. of cold water, from which mixture the product was isolated by ether extraction including a base wash[35] except that the solvent was removed by distillation through a 1-ft Vigreux column at atmospheric pressure. The resulting opaque liquid residue was distilled through a 6-in. Vigreux column at 3 mm and the following fractions were obtained.

Fraction	Bp, °C (3 mm)	Wt, g	Composition (GLC, 90°)[35]
A	65–69	12.4 g	**34**:**42** (1:1)
B	69–73	19.0 g	**34**:**42**:**41** (1:5:2)
Residue		22.6 g	**42**:**41** (1:8)

In addition to the expected components, each fraction contained a substantial amount of boronic impurities. Each fraction was subjected to filtration through silica gel (10 g/g product) with petroleum ether. The fractions thus obtained were then subjected to medium-pressure chromatography (petroleum ether). From these purifications, 7.4 g of pure enediyne **41** was recovered, and 13.2 g of a 1:8 mixture of triene **34** and dienyne **42** were obtained.

The latter mixture was dissolved in 50 ml of dry tetrahydrofuran and added dropwise over 0.5 hr to a solution of 200 ml (0.164 mol) of a 0.82 *M* tetrahydrofuran solution of ethylmagnesium bromide. After the mixture was added, the reaction was maintained at reflux for 1 hr, then cooled to 20°, and dry paraformaldehyde was depolymerized at 160–180° and bubbled through the solution for 30 min in a stream of dry nitrogen. A cooling bath was used to keep the temperature between 25° during the formaldehyde addition. After the mixture was cooled to 0°, 75 ml of a saturated aqueous ammonium chloride solution was added, and the product was then isolated by ether extraction.[35] The crude product (16.3 g) was chromatographed on 140 g of silica gel. Elution with 500 ml of petroleum ether afforded 1.3 g of the triene **34**, and continued elution with 1.5 l. of 40% ether–petroleum ether gave 10.7 g (39% based on recovered enediyne **41**) of the alcohol **43** as a colorless liquid which was used in subsequent experiments without further purification. The analytical sample, obtained by distillation and then evaporation distillation of a portion of this material, boiled at 109–110° (0.15 mm): ir (neat) 3700 (OH), 2290, 2230 (C≡C), 1640, 1000, and 910 cm^{-1} (–CH=CH_2); NMR (CCl_4) δ 1.70 (s, 2 × 3, C-6 and C-7 CH_3), 2.11 (d, 4, J = 3 Hz, C-8 and C-9 CH_2), 4.14 (broad s, 2, CH_2OH), 4.83 (d, 1, J = 4 Hz, C-11 H), 5.08 (d of d, 1, J = 9 and 3 Hz, C-11 H), and 5.75 (m, 1, C-10 H).

Anal. Calcd for $C_{13}H_{20}O$: C, 81.20; H, 10.48. Found: C, 81.06; H, 10.39.

6,7-Dimethyl-3-iodo-(*E,E*)-2,6,10-undecatrienol. The procedure of Corey, Katzenellenbogen, and Posner[32] was followed. To a suspension of 30.45 g (0.564 mol) of sodium methoxide in 625 ml of dry tetrahydrofuran was added 137 ml (0.282 mol) of a 2.06 *M* tetrahydrofuran solution of lithium aluminum hydride over a 10-min period. The mixture was stirred at room temperature for 30 min, and then a solution of 27.1 g (0.141 mol) of the propargylic alcohol

43 in 100 ml of dry tetrahydrofuran was added over 20 min. After heating the mixture at reflux for 1.5 hr it was cooled to −5°, and then 26.3 ml (23.6 g, 0.282 mol) of dry ethyl acetate was added to destroy the excess hydride. The resulting mixture was cooled to −78°, and 178 g (0.701 mol) of iodine in 310 ml of dry tetrahydrofuran was added dropwise over a 40-min period. The reaction mixture was quickly warmed to 0° with an ice bath and then allowed to stir at room temperature until the internal temperature reached 25°. The reaction was quenched by the addition of 18 ml of water, followed by 600 ml of ether, and then the product was isolated by ether extraction.[35] The residue amounted to 43.85 g (97%) of the 3-iodo alcohol, which was not further purifie but used in the following experiment. The analytical sample was obtained by evaporative distillation at 85° and 0.12 mm of a sample of similar purity from another experiment: ir (neat) 3700–3650 (OH), 1640, 1000, and 910 cm^{-1} (-CH=CH_2); NMR ($CDCl_3$) 1.68 (s, 2 × 3, C-6 and C-7 CH_3), 4.18 (d, 2, J = 5 Hz, CH_2OH), 4.85 (d, 1, J = 3 Hz, C-11 H), 5.09 (d of d, 1, J = 9 and 3 Hz, C-11 H), 5.7 (m, 1, C-10 H), and 5.80 (t, 1, J = 5 Hz, C-2 H).

Anal. Calcd for $C_{13}H_{21}OI$: C, 48.76; H, 6.61; I, 39.63. Found: C, 48.96; H, 6.57; I, 39.56.

3,6,7-Trimethyl-(*E,E*)-2,6,10-undecadienol (44). A solution of the above crude iodo alcohol (43.85 g, 0.137 mol) in 100 ml of dry hexane was added over a 0.5-hr period at 0° to 1 l. (0.705 mol) of a 0.705 *M* ethereal solution of lithium dimethylcuprate,[44] and the mixture was stirred overnight at 0°. The mixture was then treated with 190 ml of methyl iodide, and after stirring for 0.5 hr at 0°, the reaction was quenched by the addition of 300 ml of saturated aqueous ammonium chloride solution. The product was isolated by ether extraction,[35] and the residue amounted to 28.9 g (98%) of the alcohol **44**, as a clear, colorless oil. Since GLC analysis (190°) indicated that this material consisted of a 95:5 mixture of the desired alcohol **44** and the corresponding C-2-methylated isomer, no further purification was done before use in the following work. An analytical sample was obtained by evaporative distillation at 70° and 0.5 mm of a sample of similar purity for another experiment: ir (neat) 3650–3100 (OH), 1670 (C=C), 1645, 995, and 910 cm^{-1} (-CH=CH_2); NMR ($CDCl_3$) δ 1.65 (s, 2 × 3, C-6 and C-7 CH_3), 1.70 (d, 3, J = 1.5 Hz, C-3 CH_3), 4.11 (d, 2, J = 7 Hz, CH_2OH), 4.81 (d, 1, J = 3 Hz, C-11 H0, 5.05 (d of d, 1, J = 9 and 3 Hz, C-11 H), 5.38 (t, 1, J = 7 Hz, C-2 H), and 5.6 (m, 1, C-10 H).

Anal. Calcd for $C_{14}H_{24}O$: C, 80.71; H, 11.61. Found: C, 80.74; H, 11.50.

12-*m*-Methoxyphenyl-5,6,9-trimethyl-(*E,E*)-1,5,9-dodecatriene (45). The crude allylic alcohol (52.8 g, 0.254 mol) from two experiments as described above in 300 ml of dry carbon tetrachloride was converted into the corresponding allylic chloride by the addition of 79.7 g (0.304 mol) of triphenylphosphine.[45] After a 3-hr reflux, the excess triphenylphosphine was decomposed with 2.5 ml of methanol, and the precipitated triphenylphosphine oxide was removed by filtration. After the solvent was removed at reduced pressure, distillation of the residue afforded 43.5 g (76%) of the allylic chloride, bp 87–92° (0.2 mm), as a pale yellow liquid. This material was not stored but used directly in the coupling reaction:[46] ir (neat) 1662 (C=C) and 1637 cm^{-1} (-CH=CH_2); NMR ($CDCl_3$) δ 1.65 (s, 2 × 3, C-6 and C-7 CH_3), 1.76 (s, 3, C-3 CH_3), 4.07 (d, 2, J = 8 Hz, CH_2OH), 4.81 (d, 1, J = 3 Hz, C-11 H), 5.08 (d of d, 1, J = 9 and 3 Hz, C-11 H), 5.46 (t, 1, J = 8 Hz, C-2 H), and 5.6 (m, 1, C-10 H).

To a solution of 43.5 g (0.192 mol) of the above chloride in 200 ml of dry tetrahydrofuran and 200 ml of dry hexamethylphosphoramide was added over a 4-hr period a solution of *m*-methoxybenzylmagnesium chloride prepared from 134.9 g (0.862 mol) of *m*-methoxybenzyl chloride and 82.8 g (3.45 g-atoms) of magnesium turnings in 800 ml of dry tetrahydrofuran, and the mixture was stirred at room temperature overnight. The reaction mixture was then cooled to 0°; 100 ml of saturated aqueous ammonium chloride solution was carefully added, and the product was isolated by ether extraction.[35] Distillation of the resulting residue (80.5 g) afforded 38.0 g (63%) of the triene **45**, bp 148–152° (0.001 mm), which consisted of >98% of a single volatile component on GLC (210° on the column described;[34] 230°, 6 ft × 0.125 in., 2.5% SE-30 on Chromosorb W AW DMCS, retention time 5.51 min; and 140°, 6 ft × 0.125 in. 10% Carbowax 20M on Diatoport S, retention time 4.98 min). The medium boiling range forerun [25.9 g, bp 131–148° (0.001 mm)] from this distillation was chromatographed on 600 g of silica gel, and elution with 2.5 l. of 4% ether–petroleum ether afforded an additional 15.8 g (26%) of the triene **45** of the same purity as above. The analytical sample was obtained by evaporative distillation of a portion of this material at 125° and 0.01 mm: ir (film) 1640, 995, and 910 (CH=CH_2), and 1615–1585 cm^{-1} (Ar); NMR ($CDCl_3$) δ 1.62 (s, 3, C-9 CH_3), 1.66 (s, 2 × 3, C-5 and C-6 CH_3), 3.83 (s, 3, OCH_3), 4.94 (d, 1, J = 3 Hz, C-1 H), 5.16 (d of d, 1, J = 9 and 3 Hz, C-1 H), 5.27 (t, 1, J = 8 Hz, C-10 H), 5.8 (m, 1, C-2 H) and 7.45–6.70 (m, 4, ArH).

Anal. Calcd for $C_{22}H_{32}O$: C, 84.56; H, 10.32. Found: C, 84.82; H, 10.34.

12-*m*-Methoxyphenyl-5,6,9-trimethyl-(*E,E*)-5,9-dodecadienal (46). A solution of 10.1 g (32.3 mmol) of the triene **45** in 10 ml of dry tetrahydrofuran was cooled to 0°, and 52.9 ml (35.7 mmol) of a 6.76 *M* tetrahydrofuran solution of disiamylboran[31] was added. After stirring for 3 hr at 0°, the mixture was treated with 1 ml of water, followed by 40 ml of 3 *N* aqueous sodium hydroxide solution and then 15 ml of 30% hydrogen peroxide. After the addition was complete, the mixture was heated to 40–45° and maintained at that temperature for 2 hr. The mixture was then poured into 200 ml of water and the product isolated by ether extraction.[35] Chromatography of the residue (10.8 g) on 176 g of Florisil afforded 9.05 g (85%) of the corresponding primary alcohol as a colorless liquid which was eluted with 2 l. of 20% ether–petroleum ether. This material consisted of >98% of a single volatile component on GLC (280°). The analytical sample was obtained by evaporative distillation of a sample of this material at 140–160° and 0.06 mm: ir ($CHCl_3$) 3620 (OH), 1665 (C=C), and 1615–1585 cm^{-1} (Ar); NMR ($CDCl_3$) δ 1.59 (s, 3, C-9 CH_3), 1.63 (s, 2 × 3, C-5 and C-6 CH_3), 3.60 (m, 2, CH_2OH), 3.77 (s, 3, OCH_3), 5.18 (t, 1 J = 6 Hz, C-10 H), and 7.4–7.6 (m, 4, ArH).

Anal. Calcd for $C_{22}H_{34}O_2$: C, 79.95; H, 10.37. Found: C, 79.82; H, 10.40.

To a solution of chromium trioxide–dipyridine complex[36] prepared from 6 g (60 mmol) of chromium trioxide and 9.62 ml (9.48 g, 120 mmol) of dry pyridine in 150 ml of dichloromethane was added a solution of 3.3 g (10 mmol) of the dienol above in 5 ml of dichloromethane. After 40 min the mixture was filtered through a bed of 50 g of Florisil with the aid of ether washes. After concentration of the filtrate at reduced pressure, the concentrate was taken up in 200 ml of ether, and the ethereal solution was washed successively with 5% aqueous sodium hydroxide solution (100 ml), 5% hydrochloric acid (2 × 100 ml), saturated aqueous sodium bicarbonate solution (100 ml), and saturated brine (100 ml) and dried ($MgSO_4$). Removal of the solvent at reduced pressure afforded 3.15 g (90%) of the aldehyde **46** as a clear, colorless liquid which consisted of >97% of one volatile component on GLC analysis (240°, retention time 2.12 min). Material of this purity was used in the cyclization studies described below. An analytical sample was obtained by evaporative distillation of a portion of this material at 150° and 0.05 mm: ir ($CHCl_3$) 2730 (CHO), 1720 (CO), and 1615–1585 cm^{-1} (Ar); NMR ($CDCl_3$) δ 1.57 (s, 3, C-9 CH_3), 1.61 (s, 2 × 3, C-5 and C-6 CH_3), 3.73 (s, 3, OCH_3), 5.15 (t, 1, J = 6 Hz, C-10 H), and 7.3–6.5 (m, 4, ArH).

Anal. Calcd for $C_{22}H_{32}O_2$: C, 80.44; H, 9.82. Found: C, 80.41; H, 9.87.

Cyclization of Aldehyde 46. A solution of 657 mg (2.0 mmol) of the aldehyde **46** in 40 ml of dry benzene was stirred at room temperature under a nitrogen atmosphere and 117.0 μl (0.5 mequiv) of dry stannic chloride was rapidly injected. After exactly 75 sec the reaction mixture was poured into iced 0.05 *N* aqueous sodium hydroxide solution layered with ether in a separatory funnel, and the product was isolated by ether extraction.[35] The resulting residue was oxidized by titration of an acetone solution with 8 *N* chromic acid.[39] The crude product from this treatment amounted to 636 mg, which on preparative TLC (15% ether–petroleum ether) gave 384 mg of clear, colorless oil. The remaining 252 mg consisted of tarry nonvolatile material. GLC examination (240°) of the product showed four clearly resolved peaks at 1.88, 2.43, 3.25, and 4.08 min, which were separated (poor recovery owing to aerosoling) by preparative GLC (20°, 6 ft × 0.25 in. SE-52 on Diatoport S, He flow 60 ml/min).

Three of the main components of this mixture was identified. The peak at 1.88 min (12% of the crude mixture) showed only one unsplit methyl resonance at δ 1.13 in the NMR spectrum and two absorptions at 1710 and 1735 cm^{-1} in the ir spectrum. This suggests monocyclic material consisting of a mixture of the five- and six-membered ketone rings.

5β-(2′-*m*-Methoxyphenylethyl)-4aβ,6,8aα-trimethyl-3,4,4a,-5,8,8a-hexahydro-1(2*H*)-naphthalenone (47) (retention time 2.43 min at 240° on analytical GLC, 44% of the crude mixture) was isolated as a clear, colorless oil which after evaporative distillation

at 100° and 0.1 mm solidified and melted at 58.5–65°: ir (CCl_4) 1708 (C=O) and 1600 cm^{-1} (Ar); NMR (CCl_4) δ 0.70 (s, 3, C-8a CH_3), 1.05 (s, 3, C-4a CH_3), 1.82 (broad d, 3, C-6 CH_3, irradiation at 5.42 results in d, J = 2 Hz), 3.77 (s, 3, OCH_3), 5.42 (m, 1, C-7 H), and 7.3–6.5 (m, 4, ArH).

Anal. Calcd for $C_{22}H_{30}O_2$: C, 80.94; H, 9.26. Found: C, 81.07; H, 9.40.

3,4,4a,4b,5,6,10b,11,12,12a-Decahydro-10-methoxy-4aβ,-10bβ,12aα-trimethyl-1(2*H*)-chrysenone (retention time 3.25 min at 250° on analytical GLC,[35] 15% of the crude mixture) was isolated as an oil which soon solidified. Three crystallizations of this material from ether gave material of 90% purity as determined by GLC (240°) on analytical GLC: ir (CCl_4) 1710 (C=O), 1595, and 1575 cm^{-1} (Ar); NMR (CCl_4) δ 0.90 (s, 3, C-4aβ CH_3), 1.30 and 1.23 (s, 2 × 3, C-10β and C-12aα CH_3), 3.93 (s, 3, OCH_3), and 6.48, 6.52, 6.64, 6.85, 6.95, 6.98, 7.09 (m, 3, ArH). The analytical sample prepared by two crystallizations of this material from aqueous acetone and then sublimation at 100° (0.1 mm) melted at 129–132°.

Anal. Calcd for $C_{22}H_{30}O_2$: C, 80.94; H, 9.26. Found: C, 80.79; H, 9.37.

3,4,4a,4b,5,6,10b,11,12,12a-Decahydro-8-methoxy-4aβ,-10bβ,12aα-trimethyl-1(2*M*)-chrysenone (3) (retention time 4.08 min on analytical GLC at 240°, 23% of the crude mixture) was isolated as an oil which soon crystallized. After two crystallizations from ether, this material melted at 150–152° alone or in admixture with the material prepared above. The spectral comparison (ir and NMR) of the two samples also revealed their identity.

Two-Stage Cyclization of the Aldehyde 46. The yield of the bicyclic ketone **47** was maximized by treatment of 190 mg (0.58 mmol) of the aldehyde **46** in 11.6 ml of dry benzene (0.05 *M* solution) with 33.8 μl of dry stannic chloride for exactly 65 sec. The reaction was run as described above, and after work-up and oxidation, there resulted 174 mg of ketonic material. A solution of this crude material in 10 ml of dry toluene containing 300 mg of *p*-toluenesulfonic acid was heated at reflux for 48 hr, and then the product was isolated by ether extraction.[35] Purification of the residue (167 mg) by preparative TLC (20% ether–petroleum ether) gave 78 mg of an oil which on GLC (240°) consisted of two volatile components at 4.08 (86%) and 3.30 min (12%). An ether solution of this oil deposited needle-shaped crystals which after two crystallizations from ether amounted to 58 mg (27%) of the tetracyclic ketone **3**, mp 150–152°, alone or in admixture with authentic material, mp 150–152°, prepared above. The infrared and NMR spectra of the two samples were also identical.

X-Ray Analysis of Decalyl *p*-Bromobenzoate 39 and Tetracyclic Ketone 3. Suitable crystals of the *p*-bromobenzoate **39** were grown from petroleum ether by slow evaporation. The large, prismatic crystals were surveyed with a precession camera, and the photographs indicated the monoclinic space group $P2_1/c$. The cell dimensions were established by NaCl-calibrated precession photographs. Crystals of the tetracyclic ketone **3** in the form of colorless plates elongated along *C* were prepared from an ether solution by evaporation. The space group $Pna2_1$ and approximate cell constants were obtained from Weissenberg photographs; more accurate cell constants were obtained by a least-squares fit to 20 values measured on a diffractometer. The densit was measured in a zinc chloride solution by flotation. Crystal data are given in Table I.

Intensity data to a resolution of 1 Å (max sin θ/λ = 0.5) were collected on a Datex automated General Electric diffractometer using θ–2θ scanning. A single check reflection (130) was monitored every 30 reflections for the *p*-bromobenzoate **39** and two check reflections were monitored every 40 reflections for the tetracyclic ketone **3**. The crystals showed no sign of decomposition in the course of the data collection.

Each reflection was assigned a variance $\sigma^2(I)$ based on counting statistics plus an empirical term $(0.02s)^2$, where s is the scan count. Values of F_o^2 and $\sigma(F_o^2)$ were derived from the net intensities by application of Lorentz and polarization factors. Any reflection for which the net value of $|F_o|^2$ was less than or equal to zero was assigned an intensity and a weight of zero. The data were scaled by Wilson's[47] method, and values of $|E|$ and $|F|$ calculated.

Determination and Refinement of Structure of *p*-Bromobenzoate 39. The trial structure was derived by the usual Patterson and Fourier techniques in three dimensions. Full-matrix least-squares refinement of coordinates, isotropic temperature factors (bromine anisotropic), and scale factor reduced the R index to 10.6%. A difference Fourier indicated no misplaced or missing Br, C, or O atoms. The difference Fourier was also utilized to locate the hydrogen atoms. The addition of the hydrogen atoms to the structure factor calculation and the application of anisotropic temperature factors and second extinction factor[48] to the refinement reduced the R index to its final value of 0.056.

Table I
Crystal Data

Molecule	Tetracyclic ketone **3**	Decalyl *p*-bromobenzoate **39**
Formula	$C_{22}H_{30}O_2$	$C_{19}H_{25}BrO_2$
Formula weight	326.5	365.4
Approximate crystal size, mm	0.12 × 0.22 × 0.33	0.3 × 0.3 × 0.2
Space group	$Pna2_1$	$P2_1/c$
Systematic absences	$0klk + l = 2n + 1$ $h0l, h = 2n + 1$	$h0l: l$ odd $0k0: k$ odd
a, Å	29.922 (4)	7.075 ± 0.001
b, Å	7.752 (1)	25.062 ± 0.005
c, Å	7.630 (4)	10.312 ± 0.002
β		106.08 ± 0.08°
Z	4	4
F_{000}	712	760
λ	Cu Kα = 1.5418Å	1.5418 Å
D_c	1.225 g cm^{-3}	1.381 g cm^{-3}
D_m	1.23	1.38 g cm^{-3}
μ	6.0 cm^{-1}	35.
V	1770 Å	1757 $Å^3$
Diffractometer background time	30 sec	10 sec
Diffractomer scan rate	2°/min	2°/min
Number of reflections	1970	1831
Nonzero reflections	1834	1721
Final R index[a]	0.048	0.056
Standard deviations in C, O bond lengths	0.005 Å	0.005 Å
Standard deviations in C, O bond angles	0.3°	0.5°

[a] $R = \Sigma||F_o| - |F_c||/\Sigma|F_o|$.

Determination and Refinement of Structure of Tetracyclic Ketone 3. The structure was solved by the symbolic addition method[49,50,51] applied to 73 reflections with $E > 2.0$. Table II lists the origin choice and symbols. There were no $00l$ reflections with high E which could be used to fix the origin. The results which led to the correct solution had the higher consistency (0.69). These 73 phases were tangent refined[48] and expanded to 241 reflections with $E > 1.3$.

Table II
Data from Symbolic Addition

	h	k	l	E	Fixed phases	Assigned phase
Origin	22	2	3	3.532	45°	
	4	1	7	3.314	90°	
	3	2	0	2.049	0°	
From σ_2's	0	2	0	1.819	180°	
Symbol	24	1	3	3.061		135°

An E map based on phases from the tangent refinement showed a continuum of hexagons. The best model gave the best fit to the $h00$ data, though other models fit the E map better. The resulting structure factor calculation based on the best model gave an R of 0.367. A series of difference-map calculations, model adjustments, and structure-factor calculations was begun reducing R to 0.247 for all nonhydrogen atoms. Full-matrix least-squares adjustment of the coordinates and isotropic temperature factors lowered R to 0.163. Difference maps clearly indicated the location of all the hydrogen atoms. Hydrogen atoms were included in subsequent structure-factor calculations in idealized positions 0.95 Å from the neighboring carbon atom. Anisotropic and positional refinement

for all heavy atoms, a scale factor, and a secondary-extinction factor[52] decreased R to 0.048.

We observed that the best model was not exactly the correct solution. In fact, they differ by about 0.6 Å along a. One explanation is the difficult application of direct methods for this data set. The phases with low and high h from the original 73 phases were determined correctly. However, the middle phases ($h \sim 20$) were essentially off by 180°. One reason for this is the poor distribution of high E reflections; there are no $E > 2.0$ with $8 < h < 18$ or $28 < h < 33$.

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Registry No.—**3**, 53311-24-3; **3** cis-anti-trans isomer, 54163-13-2; **6**, 54099-89-7; **8**, 54143-28-1; **9**, 54099-88-6; **10**, 54099-90-0; **11**, 54099-91-1; **11** equatorial alcohol epimer, 54099-92-2; **12**, 54163-14-3; **13**, 54099-93-3; **14**, 54099-94-4; **15**, 54099-95-5; **16** (R = H), 54099-96-6; **16** (R = CH_2Ar), 54099-97-7; **17** (R = H), 54163-15-4; **17** (R = CH_2Ar), 54099-98-8; **17** (R = CH_2Ar) equatorial OH epimer, 54163-16-5; **18** (R = H), 54099-99-9; **18** (R = CH_2Ar), 54100-00-4; **19**, 54100-01-5; **20**, 54100-02-6; **21**, 54100-03-7; **22**, 54100-04-8; Δ^5-**23**, 53311-23-2; Δ^6-**23**, 53311-20-9; **24** (R = CH_3), 54163-17-6; **24** (R = H), 54163-18-7; **24** (R = CH_2CH_2Ar), 54143-29-2; **28**, 54100-05-9; **29**, 54100-06-0; Δ^5-**30**, 53311-22-1; Δ^6-**30**, 54100-07-1; Δ^5-**31**, 54100-08-2; Δ^6-**31**, 54100-09-3; **33**, 6044-73-1; **34**, 52713-77-6; **35**, 54100-10-6; **36**, 29023-69-6; **36** 2,4-DNP, 54100-11-7; **37**, 54100-12-8; **38**, 54100-13-9; **39**, 54100-14-0; **40**, 54100-15-1; **41**, 53311-29-8; **42**, 54100-16-2; **43**, 54100-17-3; **44**, 54100-18-4; **45**, 54100-19-5; **46**, 53311-19-6; **47**, 53311-20-9; methoxy-8aβ-methyl-3,4,8,8a-tetrahydro-1,6(2H,7H)naphthalenedione, 54100-20-8; 2-methyldehydroresorcinol, 1193-55-1; 1,4-dimethoxy-2-butanone, 25680-86-8; 5-methoxy-8aβ-methyl-1,2,3,4,6,7,8,8a-octahydro-1α,6β-naphthalenediol, 54100-21-9; 5-methoxy-8aβ-methyl-1,2,3,-4,6,7,8,8a-octahydro-1α,6α-naphthalenediol, 54100-22-0; 5-methoxy-8aβ-methyl-1,2,3,4,6,7,8,8a-octahydro-1α,6β-naphthalenediol diacetate, 54100-23-1; 5-methoxy-8aβ-methyl-1,2,3,4,6,7,8,8a-octahydro-1α,6α-naphthalenediol diacetate, 54100-24-2; 5-methoxy-8aβ-methyl-1,2,3,4,6,7,8,8a-octahydro-1α-naphthenol, 54099-91-1; 1,2,3,4,4a,5,6,7,8,8a-decahydro-1β,4aα,8aβ-trimethyl-1α-naphthalenol, 54100-25-3; 1,2,3,4,4a,5,6,7,8,8a-decahydro-4aα,8aβ-dimethyl-5,5-ethylenedioxo-1α-naphthenol, 54100-26-4; 1,2,3,4,4a,5,6,7,8,8a-decahydro-4a,8a-dimethyl-5,5-ethylenedioxo-1-(2′-m-methoxyphenylethyl)-2-naphthalenol, 54100-27-5; 4a,5α-methano-5β-methoxy-8aβ-methyl-3,4,4a,5,6,7,8,8a-octahydro-1(2H)-naphthalenone, 54100-28-6; m-methoxybenzyl chloride, 824-98-6; 1,2,3,4,4a,5,6,7,8,8a-decahydro-1-(2-m-methoxyphenylethylidene)-4a,5α-methano-5β-methoxy-8aβ-methylnaphthalene, 54100-29-7; 1,2,3,4,4a,5,6,7,8,8a-decahydro-1-(2′-m-methoxyphenylethyl)-4a,5-methano-5-methoxy-8a-methyl-2-naphthalenol, 54100-30-0; 1,2,3,4,4a,5,6,7,8,8a-decahydro-1,6-dehydroxy-6,8a-dimethyl-5-(2′-m-methoxyphenylethyl)-4a-naphthalenecarbonitrile, 54100-31-1; 1,2,3,4,4a,5,6,7,8,8a-decahydro-1-acetoxy-6-hydroxy-6,8a-dimethyl-5-(2′-m-methoxyphenylethyl)-4a-naphthalenecarbonitrile, 54100-32-2; 5-(2′-m-methoxyphenylethyl)-6,8aα-dimethyl-1α-hydroxy-4aβ-(iminomethyl)-1,2,3,4,4a,-7,8,8a-octahydronaphthalene, 54100-33-3; 5β-(2′-m-methoxyphenylethyl)-6,8aα-dimethyl-1α-hydroxy-4aβ-(iminomethyl)-1,2,3,4,-4a,5,8,8a-octahydronaphthalene, 54100-34-4; 4aβ,8aα-dimethyldecalin, 28831-72-3; 4aβ,8aβ-dimethyl-3,4,4a,5,6,7,8,8a-octahydro-2(1H)-naphthalenone, 54100-35-5; 4aα,8aβ-dimethyldecalin, 13950-38-4; 6,7-dimethyl-3-iodo-(*E*,*E*)-2,6,10-undecatrienol, 54100-36-6; 1-chloro-3,6,7-trimethyl-(*E*,*E*)-2,6,10-undecatriene, 53311-18-5; 12-(m-methoxyphenyl)-5,6,9-trimethyl-(*E*,*E*)-5,9-dodecadienol, 54062-61-2; 3,4,4a,4b,5,6,10b,11,12,12a-decahydro-10-methoxy-4aβ,10bβ,12aα-trimethyl-1(2H)-chrysenone, 54100-37-7.

Supplementary Material Available. Structure factor tables and the final parameters and their standard deviations for the structural analyses of both the p-bromobenzoate **39** and the tetracyclic ketone **3** are listed in Tables III–X, which wil appear following these pages in the microfilm edition of this volume of the journal. Photocopies of the supplementary material from this paper only or microfiche (105 × 148 mm, 24× reduction, negatives) containing all of the supplementary material for the papers in this issue may be obtained from the Journals Department, American Chemical Society, 1155 16th Street, N.W., Washington, D.C. 20036. Remit check or money order for $4.50 for photocopy or $2.50 for microfiche, referring to code number JOC-75-973.

References and Notes

(1) The structural formulas containing one or more asymmetric carbon atoms depict one enantiomer but refer to racemic compounds throughout. In the text the (±) prefix will be omitted and intermediates are to be assumed to be racemic. In this discussion, naphthalene nomenclature and numbering will be used to describe dicyclic compounds, and each racemate is arbitrarily represented by that enantiomer that has the C-8a methyl group in the α configuration. The tetracyclic compounds will be described by the chrysene nomenclature, and each racemate is arbitrarily represented by that enantiomer that has the C-12a methyl group in the α configuration.
(2) National Institutes of Health Trainee, 1969–1973.
(3) Postdoctoral Fellow (GM 39806) of the National Institute of General Medical Sciences, 1968–1970.
(4) National Science Foundation Predoctoral Fellow, 1968–1972.
(5) R. E. Ireland, M. I. Dawson, S. C. Welch, A. Hagenbach, J. Bordner, and B. Trus, *J. Am. Chem. Soc.*, **95**, 7829 (1973).
(6) R. E. Ireland, D. A. Evans, D. Glover, G. M. Rubottom, and H. Young, *J. Org. Chem.*, **34**, 3717 (1969). Direct methylation of suitable 1-decalone derivatives had led to low yields and predominantly cis-fused products in our hands and those of others: J. A. Marshall, G. L. Bundy, and W. I. Fanta, *J. Org. Chem.*, **33**, 3913 (1968); H. W. Whitlock, Jr., and L. E. Overman, *J. Org. Chem.*, **34**, 1962 (1969).
(7) Preliminary reports of portions of this work have been published: (a) R. E. Ireland, D. R. Marshall, and J. W. Tilley, *J. Am. Chem. Soc.*, **92**, 4754 (1970); (b) R. E. Ireland, C. A. Lipinski, C. J. Kowalski, J. W. Tilley, and D. M. Walba, ibid., **96**, 3333 (1974); (c) R. E. Ireland, M. I. Dawson, J. Bordner, and R. E. Dickerson, ibid., **92**, 2568 (1970); (d) R. E. Ireland, M. Dawson, and C. A. Lipinski, *Tetrahedron Lett.*, 2247 (1970).
(8) Y. Tarrahashi, Y. Moriyama, T. Takahashi, F. Patil, and G. Ourisson, *Bull. Soc. Chim. Fr.*, 2374 (1966); T. Takahashi, T. Tsuyuki, T. Hoshimo, and M. Ito, *Tetrahedron Lett.*, 2997 (1967).
(9) E. J. Corey and J. J. Ursprung, *J. Am. Chem. Soc.*, **78**, 5041 (1956); G. Brownlie, F. S. Spring, R. Stevenson, and W. S. Strachan, *J. Chem. Soc.*, 2419 (1956).
(10) R. E. Ireland, S. M. Baldwin, and S. C. Welch, *J. Am. Chem. Soc.*, **94**, 2056 (1972).
(11) G. F. Hennion and F. P. Kupiecki, *J. Org. Chem.*, **18**, 1601 (1953).
(12) E. Wenkert and D. A. Berges, *J. Am. Chem. Soc.*, **89**, 2507 (1967).
(13) J. A. Marshall and G. L. Bundy, *J. Am. Chem. Soc.*, **88**, 4291 (1966).
(14) W. G. Dauben and G. H. Berezin, *J. Am. Chem. Soc.*, **85**, 468 (1963); W. G. Dauben and A. C. Ashcraft, ibid., **85**, 3673 (1963).
(15) H. E. Simmons and R. D. Smith, *J. Am. Chem. Soc.*, **81**, 4256 (1959).
(16) C. E. Cook, R. C. Corky, and M. E. Wall, *J. Org. Chem.*, **33**, 2789 (1968); E. J. Corey and M. Chaykovsky, *J. Am. Chem. Soc.*, **87**, 1353 (1965).
(17) H. C. Brown and W. C. Dickason, *J. Am. Chem. Soc.*, **92**, 709 (1970).
(18) For an example of the comparable utility of this functional group combination, see ref 10.
(19) A. Nickon and J. F. Bagli, *J. Am. Chem. Soc.*, **83**, 1498 (1961).
(20) D. H. R. Barton, A. S. Campos-Neves, and R. C. Cookson, *J. Chem. Soc.*, 3500 (1956).
(21) (a) W. Nagata, M. Yoshioka, and S. Hirai, *J. Am. Chem. Soc.*, **94**, 4635 (1972); W. Nagata, M. Yoshioka, and M. Murakami, ibid., **94**, 4654 (1972); (b) W. Nagata, M. Yoshioka, and T. Terasawa, ibid., **94**, 4672 (1972); (c) W. Nagata and M. Yoshioka, *Org. Syn.*, **52**, 90, 100 (1972).
(22) W. S. Johnson, *Acc. Chem. Res.*, **1**, 1 (1968); for most recent report in this series see K. A. Parker and W. S. Johnson, *J. Am. Chem. Soc.*, **96**, 2556 (1974); E. E. van Tamelen, *Acc. Chem. Res.*, **1**, 111 (1968); for most recent report in this series see E. E. van Tamelen, R. G. Lees, and A. Grieder, *J. Am. Chem. Soc.*, **96**, 2255 (1974). E. J. Corey, W. E. Russey, and P. R. Ortiz de Montellano, ibid., **88**, 4750 (1966).
(23) A. Eschenmoser, L. Ruzicka, O. Jeger, and D. Arigoni, *Helv. Chim. Acta*, **38**, 1890 (1955); G. Stork and A. W. Burgstahler, *J. Am. Chem. Soc.*, **77**, 5068 (1955).
(24) D. J. Goldsmith and C. F. Phillips, *J. Am. Chem. Soc.*, **91**, 5862 (1969); G. Stork and M. Gregson, ibid., **91**, 2373 (1969); for a more recent reference reported since this work was completed, see P. A. Bartlett and W. S. Johnson, ibid., **95**, 7501 (1973).
(25) Since this work was completed, other polyolefinic substrates that contain tetrasubstituted double bonds have been used: E. E. van Tamelen, M. P. Seiler, and W. Wierenga, *J. Am. Chem. Soc.*, **94**, 8229 (1972); D. R. Morton, M. B. Gravestock, R. J. Parry, and W. S. Johnson, Ibid., **95**, 4417 (1973).
(26) See, for examples of five-membered ring formation, W. S. Johnson and J. K. Crandall, *J. Org. Chem.*, **30**, 1785 (1965); W. S. Johnson and R. B. Kinnel, *J. Am. Chem. Soc.*, **88**, 3861 (1966); W. S. Johnson and R. Owyang, ibid., **86**, 5593 (1964); and K. A. Parker and W. S. Johnson, ref 22.
(27) O. J. Sweeting and J. R. Johnson, *J. Am. Chem. Soc.*, **68**, 1057 (1946).
(28) A. J. Birch and R. Robinson, *J. Chem. Soc.*, 501 (1943).
(29) E. J. Corey and H. A. Kirst *Tetrahedron Lett.*, 5041 (1968).
(30) H. M. Schmidt and J. F. Arens, *Recl. Trav. Chim. Pays-Bas*, **86**, 1138 (1967).
(31) H. C. Brown and A. W. Moerikofer, *J. Am. Chem. Soc.*, **85**, 2063 (1963).

(32) E. J. Corey, J. A. Katzenellenbogen, and G. H. Posner, *J. Am. Chem. Soc.*, **89**, 4245 (1967).
(33) R. E. Ireland, P. Bey, K.-F. Cheng, R. J. Czarny, J.-F. Moser, and R. I. Trust, *J. Org. Chem.*, **40**, 1000 (1975).
(34) Melting points labeled (vacuum) were taken in evacuated capillaries on a Hoover capillary melting point apparatus, while all others were determined on a Kofler micro hot stage melting point apparatus. All melting points and boiling points are uncorrected. Infrared (ir) spectra were determined on a Perkin-Elmer 237B grating infrared spectrometer, and nuclear magnetic resonance (NMR) spectra were recorded using either a Varian A-60A or T-60 spectrometer. Chemical shifts are reported as δ values in parts per million relative to TMS (δ_{TMS} 0.0 ppm) as an internal standard.

Gas–liquid phase chromatographic (GLC) analyses were determined on either a Hewlett-Packard 5750 or F & M 810 research chromatograph using helium carrier gas at a flow rate of 60 ml/min. Unless otherwise noted, all analytical GLC was conducted on a 6 ft × 0.125 in. column packed with 4% SE-30 on 60–80 mesh Chromosorb W AW DMCS.

Preparative thin layer chromatography (preparative TLC) was carried out on 20 × 20 × 0.2 cm glass plates coated with silica gel $PF_{254+266}$ (Brinkman Instruments Co.). Analytical thin layer chromatography (TLC) was conducted on 1 × 3 in. microscope slides coated with a 0.5-mm layer of silica gel G or $PF_{254+266}$.

Alumina used for column chromatography refers to the grade I, neutral variety manufactured by M. Woelm, Eschwege, Germany and made up to grade II or III as indicated by the addition of 3% or 6% water prior to use. Silica gel columns used the 0.05–0.2 mm silica gel manufactured "for column chromatography" by E. Merck & Co., Darmstadt, Germany. Preparative medium-pressure column chromatography was performed using 0.5 × 20 in. or 2 × 20 in. glass columns with fittings supplied by Chromatronix, Inc., Berkeley, Calif., and an Instrument minipump supplied by Milton Roy Co., St. Petersburg, Fla. (instrumentation designed by R. H. Mueller, these laboratories, and copies are available on request). The columns were packed with silica gel H "for TLC acc. to Stahl" (10–40 μ) manufactured by E. Merck & Co., Darmstadt, Germany. Solvents were degassed under water aspirator vacuum prior to use.

"Dry" solvents were dried immediately prior to use. Ether, benzene, tetrahydrofuran, and dimethoxyethane were distilled from lithium aluminum hydride; *tert*-butyl alcohol, dimethyl sulfoxide, pyridine, and hexamethylphosphoramide (HMPA) were distilled from calcium hydride; dichloromethane, carbon tetrachloride, diiodomethane, and methyl iodide were distilled from phosphorus pentoxide; ammonia was distilled from the tank and then from a blue lithium or sodium solution. "Petroleum ether" refers to the "Analyzed Reagent" grade hydrocarbon fraction, bp 30–60°, which is supplied by J. T. Baker Co., Phillipsburg, N.J., and was not further purified.

Reactions described as run under nitrogen or argon employed a mercury bubbler arranged so that the system could be alternately evacuated and filled with the inert gas and left under a positive pressure.

Microanalyses were performed by Spang Microanalytical Laboratory, Ann Arbor, Mich.

(35) In cases where products were isolated "by solvent extraction", the procedure generally followed was to extract the aqueous layer with several portions of the indicated solvent; then the organic layers were combined and washed with water, followed by saturated brine. The organic layer was dried over anhydrous sodium or magnesium sulfate, then filtered, and the solvent was evaporated from the filtrate under reduced pressure (water aspirator) using a rotary evaporator. The use of the terms "base wash" or "acid wash" indicate washing the combined organic layers with saturated aqueous sodium bicarbonate solution or with dilute aqueous hydrochloric acid, respectively, prior to the aforementioned washing with water.
(36) J. C. Collins, W. W. Hess, and F. J. Frank, *Tetrahedron Lett.*, 3363 (1968).
(37) E. LeGoff, *J. Org. Chem.*, **29**, 2048 (1964).
(38) The procedure of Huang-Minlon was followed.
(39) K. Bowden, I. M. Heilbron, E. R. H. Jones, and B. C. L. Weedon, *J. Chem. Soc.*, **39** (1946); see also C. Djerassi, R. R. Engle, and A. Bowers, *J. Org. Chem.*, **21**, 1547 (1956).
(40) H. C. Brown and G. Zweifel, *Org. React.*, **13**, 33 (1963).
(41) B. J. Christensen, R. G. Strachan, N. R. Trenner, B. H. Arison, R. Hirschmann, and J. M. Chemerda, *J. Am. Chem. Soc.*, **82**, 3995 (1960).
(42) The method of S. C. Watson and J. F. Eastham, *J. Organomet. Chem.*, **9**, 165 (1967).
(43) W. Nagata and H. Itazaki, *Chem. Ind. (London)*, 1194 (1964).
(44) E. J. Corey and G. H. Posner, *J. Am. Chem. Soc.*, **89**, 3911 (1967).
((45) J. B. Lee and T. J. Nolan, *Tetrahedron*, **23**, 2789 (1967).
(46) The method of G. Stork, P. A. Grieco, and M. Gregson, *Tetrahedron Lett.*, 1393 (1969), was used.
(47) A. J. C. Wilson, *Nature (London)*, **150**, 152 (1942).
(48) A. C. Larson, *Acta Crystallogr.*, **23**, 664 (1967).
(49) W. H. Zachariasen, *Acta Crystallogr.*, **5**, 68 (1952).
(50) J. Karle and I. L. Karle, *Acta Crystallogr.*, **21**, 849 (1966).
(51) Chun-che Tsai, Ph.D. Thesis, Part III, Indiana University, Bloomington, Ind., 1968).
(52) "International Tables for X-Ray Crystallography", Vol. III, Kynoch Press, Birmingham, England, 1962, pp 202–203.

Experiments Directed toward the Total Synthesis of Terpenes. XX. Total Synthesis of (±)-Shionone, a Tetracyclic Triterpene[1]

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The conversion of the tetracyclic ketone **1** to the triterpene shionone (**23**) is explored by two alternative sequences. Both approaches rely on the introduction of the more or less completely formed side chain and then modification of the aromatic A ring. One unsuccessful approach entails incorporation of the intact side chain and then cleavage and recyclization of the enone **18**. Acid-catalyzed recyclization of the A ring results in hydration of the side-chain double bond. This problem was overcome and the synthesis of (±)-shionone achieved through postponement of the introduction of the side-chain unsaturation until the A ring sequence was complete.

In the preceding paper[5] in this series the development of a practical and efficient synthesis of the tetracyclic ketone **1** is described. This material, as well as some of the intermediates used in its synthesis, were envisaged as key intermediates for synthesis of both penta- and tetracyclic triterpenes. In this report the successful conversion of the ketone **1** to the tetracyclic triterpene shionone (**23**)[6] is described.[7] For this synthesis it was necessary to devise two mutually compatible schemes for the remaining operations, namely, the introduction of the side chain in ring D and the modification of the aromatic A ring to that of the natural product. The investigation of the latter problem was undertaken first (Chart I).

A convenient system—the enone **3**—with which to explore means for the A ring conversion was obtained by first transformation of the tetracyclic ketone **1** to the enol phosphorodiamidate (TMPDA) **2**[8] and then Birch reduction to remove the TMPDA as well as reduce the aromatic ring. This two-stage transformation afforded the enone **3** in 70% overall yield; during the course of optimizing this yield, it was observed that if a proton source, such as alcohol, was omitted from the Birch reduction step, the TMPDA grouping was still reductively removed in high yield, but the aromatic ring remained intact. Of course, the corresponding aromatic olefin could be subsequently reduced to the enone **3** under standard Birch reduction conditions, and this two-step reduction sequence primarily serves to demonstrate the functional selectivity possible during the reductive removal[8] of the TMPDA grouping.

The α,β-unsaturated ketone system of the enone **3** offers an ideal substrate for the regioselective introduction of the two remaining methyl groups at C-12a and C-1 through conjugate addition and then α-methylation. The stereochemical situation is, however, somewhat less satisfactory.