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.

(34) E. LeGoff, *J. Org. Chem.*, **29**, 2048 (1964).
(35) R. Ratcliffe and R. Rodehorst, *J. Org. Chem.*, **35**, 4000 (1970).
(36) J. M. Denis, G. Girard, and J.-M. Conia, *Synthesis*, 549 (1972).

Experiments Directed toward the Total Synthesis of Terpenes. XXI. An Alternate Total Synthesis of *dl*-Alnusenone *via* Polyene Cyclization[1]

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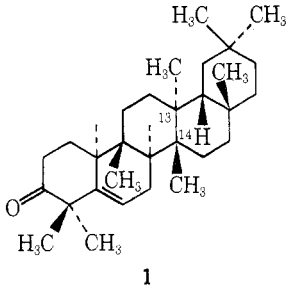
Using the aldehyde **2** as a model for the alnusenone (**1**) precursor **15**, a method based on acid-catalyzed polyene cyclization procedures was developed for the synthesis and cyclization of the 3-methyl-2-cyclopentenol **5** that gave the tricyclics **6**, **7**, and **8**. Oxidative ring enlargement of the alcohol **8** led to the tricyclic enone **11**, a model of the C, D, and E rings of the key pentacyclic alnusenone intermediate **19**. The structure of this enone **11** was proven by its independent synthesis from the ketonitrile **13** of known structure and stereochemistry. Application of the methods developed in this model study to the aldehyde **15** leads through the 3-methyl-2-cyclopentenone **16** to both the ortho- (**18**) and para- (**17**) substituted pentacyclic olefins. Conversion of the latter to the enone **19** by the oxidative ring enlargement procedure completes the second total synthesis of *dl*-alnusenone (**1**), by virtue of the use of this enone **19** in an earlier study. Confirmation of the structure and stereochemistry of the ortho-substituted pentacyclic olefin **18** was obtained by the formation of the hydrocarbon **20** from demethoxylation of both olefinic isomers **17** and **18**.

In earlier work[4] on the total synthesis of the pentacyclic triterpenes of the alnusenone (**1**) class, it became apparent that, in addition to the obvious logistic problems, the synthetic difficulties that attended the introduction of the two trans-disposed angular methyl groups at C-13 and C-14 were not trivial. Several approaches[5] aimed specifically at



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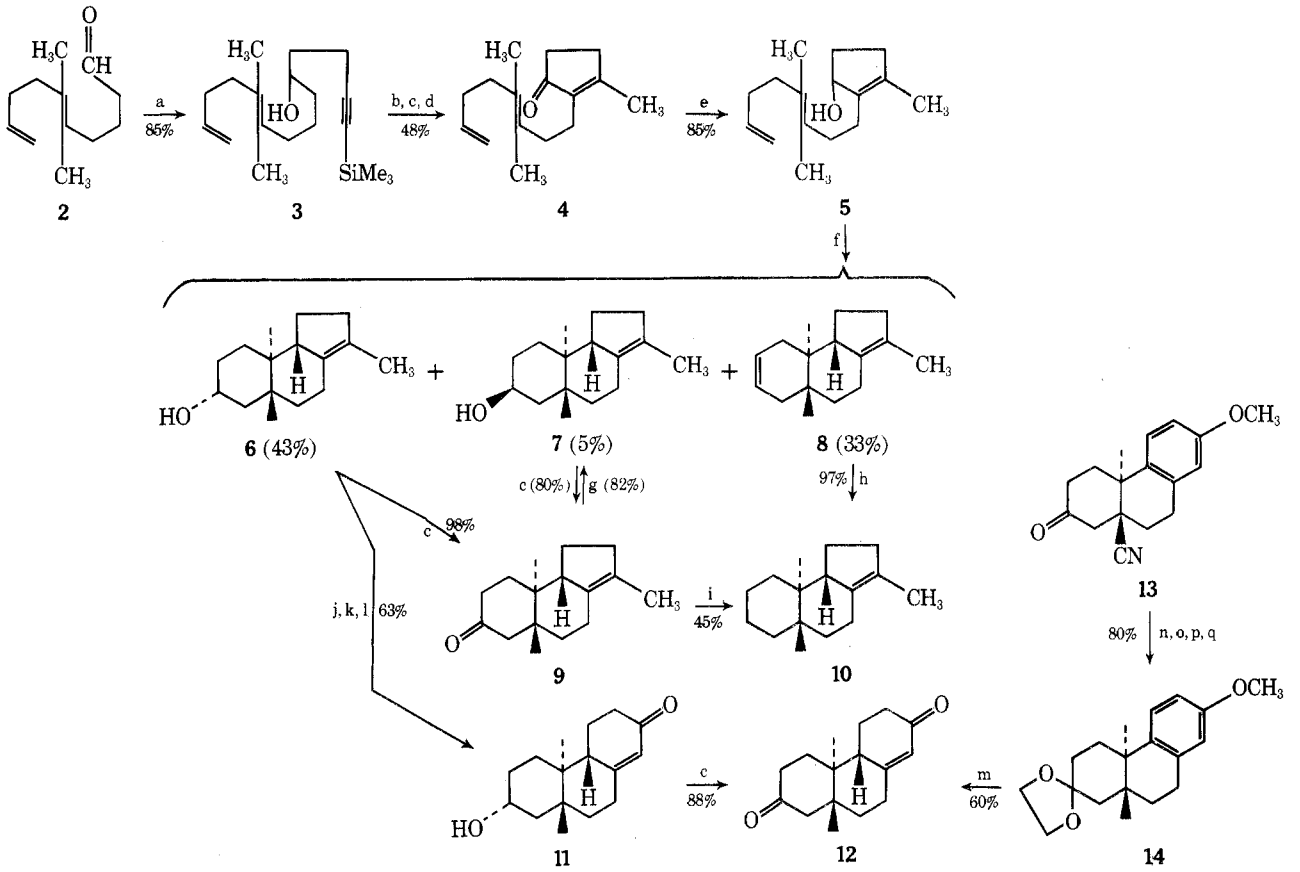
accomplishing this task were investigated, and a particularly efficient scheme[6] was developed through the use of the Nagata procedure[7] for the conjugate hydrocyanation of enones. Another approach that was demonstrated[5a] to be of value for this situation was the acid-catalyzed cyclization of polyolefinic substrates[8] that incorporated a tetrasubstituted double bond. Thus, from a two-stage, acid-catalyzed cyclization of the aldehyde **15**,[9] it was possible to prepare the corresponding tetracyclic, A ring aromatic ketone. While this ketone was used in the total synthesis of the tetracyclic triterpene shionone[10] and has potential as an intermediate in schemes for the synthesis of pentacyclic triterpenes, the low overall yield of the two-stage, acid-catalyzed cyclization and the desire to incorporate the rudiments of the E ring in the polyolefinic substrate prompted a further investigation of other related systems.

The aim of this phase of the work was threefold. First, systems were sought that could be prepared from the aldehyde **15**, such that the efficient synthesis[9] of this material could form the backbone of the approach. Secondly, on the assumption that the low yields experienced from the cyclization of the aldehyde **15** were in part the result of the utilization of the labile aldehyde function to initiate the cyclization process, a less sensitive, yet still effective, source of cationic character in this position was sought. Finally, in view of the potential difficulties associated with the selective reduction of the two dissimilar A and E aromatic rings in the intermediates from the conjugate hydrocyanation route,[6] systems were sought that would result directly in the formation of a nonaromatic E ring after the cyclization process. From a synthetic design standpoint, the polyolefinic cyclization approach[8] offers a particularly elegant solution to the latter situation.

From the extensive work of Johnson and coworkers,[11] the systems that appear to meet the above criteria are the cyclic allylic alcohols. Such systems offer the advantage of lower sensitivity to the acidic conditions than the aldehydes, and the potential for the incorporation of larger carbon residues at the cationic site. Particularly suited to the present situation is the 3-methyl-2-cyclopentenol unit, as Johnson has shown[11c] that this system is an excellent precursor of a fused 2-cyclohexenone ring system after cyclization and then oxidative ring enlargement. The present report describes the results of an investigation into the synthesis and subsequent cyclization of such a system that leads ultimately to the construction of the pentacyclic enone **19**, an intermediate previously converted to *dl*-alnusenone (**1**) in earlier work.[6]

Before utilization of the aldehyde **15** for any studies, a model system was investigated to develop means for the conversion of the aldehyde function to the 3-methyl-2-cyclopentenol system and to study the compatibility of the central, tetrasubstituted double bond in this type of cationic cyclization. The starting material for this work was the aldehyde **2** (Chart I), prepared previously[5a] for the initial polyene cyclization studies with a tetrasubstituted double bond. After some experimentation with other schemes, the utility of 4-trimethylsilylhomopropargylmagnesium chloride as a masked 2-butanone synthon evolved, and the scheme outlined in Chart I for the construction of the desired cyclopentenol **5** was developed. The carbonyl addition of this fragment went in excellent yield, and after hydration with concomitant desilylation, oxidation of the result-

Chart I
Synthesis and Cyclization of the Model 3-Methyl-2-cyclopentenol 5[a]



[a] a, $(CH_3)_3SiC{\equiv}CCH_2CH_2MgCl$, Et_2O; b, $HgSO_4$, aq H_2SO_4, THF; c, 8 *N* H_2CrO_4, acetone; d, 2% aq NaOH, EtOH; e, $LiAlH_4$, Et_2O; f, HCO_2H, 9°; g, $LiAl(O\text{-}t\text{-}Bu)_3H$, THF; h, $(Ph_3P)_3RhCl$, C_6H_6, H_2; i, N_2H. $2HCl,N_2H_4 \cdot H_2O$, KOH, DEG; j, OsO_4, dioxane, H_2S, CH_2Cl_2; k, $Pb(OAc)_4$, THF; l, 2.5% aq KOH; m, Li, NH_3, *t*-BuOH, 5 *N* aq HCl, C_6H_6–EtOH; n, $(CH_2OH)_2$, *p*-TsOH,C_6H_6; o, $(i\text{-}Bu)_2AlH$, C_6H_6; p, NaOAc, aq HOAc; q, $N_2H_4EG \cdot H_2O$, KOH, DEG.

ing hydroxy ketone led to the corresponding dione. While intramolecular aldol condensation of this dione could lead to two different cyclopentenone derivatives, only the enone **4** related to methylene condensation was observed. Reduction of the enone **4** with lithium aluminun hydride completed a successful route for the transformation of the aldehyde function to the desired 3-methyl-2-cyclopentenol system **5**.

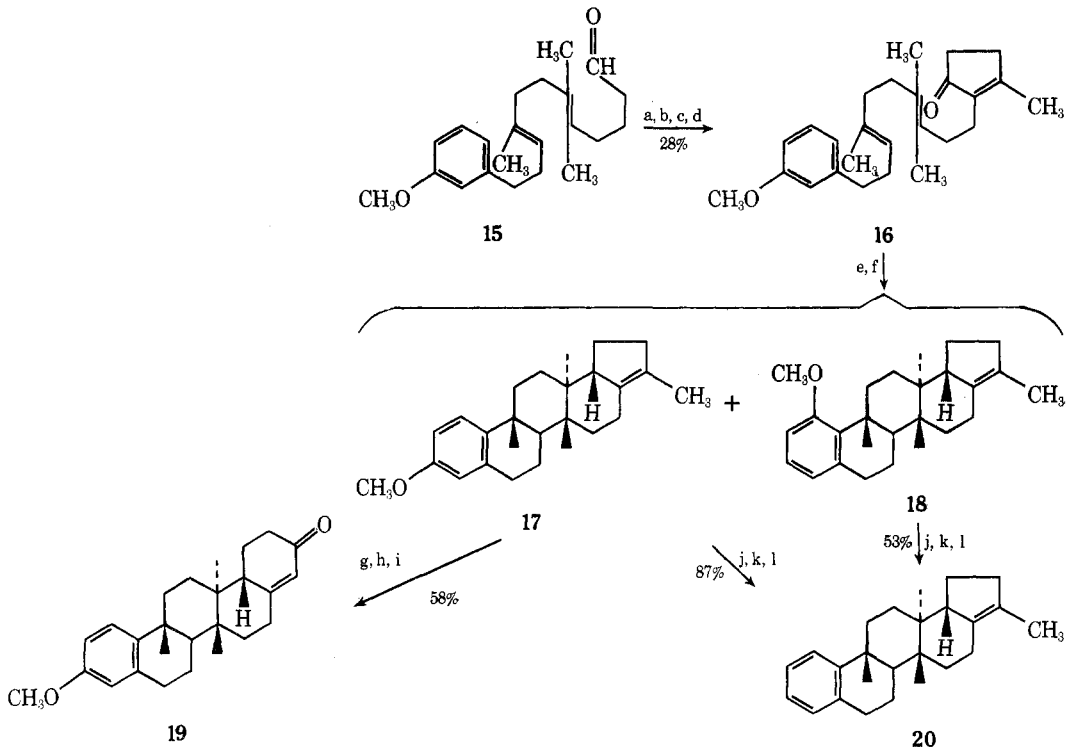
Cyclization of this alcohol **5** in formic acid at 9° resulted in the formation of tricyclic material in high (81%) yield. Separation of the product mixture by silica gel chromatography afforded the alcohols **6** and **7** and the hydrocarbon **8**. The efficiency of this cyclization was quite encouraging in spite of the formation of these three individual products. The observed mixture of products from this cyclization was a result of the mode in which the final tricyclic cation was quenched, and in the triterpene synthesis, an internal nucleophile (the anisole ring) would be present to carry such a tricyclic cation on to the desired pentacyclic stage.

The correlation of the three products isolated from the formic acid cyclization of the alcohol **5** was accomplished as shown in Chart I, and the major alcoholic product **6** was transformed into the enone **11** by oxidative ring enlargement.[11c] Not only did this process substantiate the utility of this scheme[11] for the formation of the C, D, and E rings of the alnusenone (**1**) molecule, but it also provided material which was readily amenable to correlation with compounds of known[6] structure and stereochemistry (Chart I). With these results in hand the construction of material suitable for the formation of the corresponding pentacyclic analogs was pursued.

Conversion of the aldehyde **15** to the required cyclopentenone **16** (Chart II) was accomplished in good overall yield by the procedures developed in the model series. After reduction of this enone **16** with lithium aluminum hydride, cyclization of the resulting cyclopentonol under the same conditions used in the model series led to an inseparable mixture of products. After some experimentation, it was found that stannic chloride in dichloromethane[11a] at −78° provided the most readily separable mixture of products, although simple silica gel chromatography of the cyclopentenol also led to cyclized material. From a combination of these procedures, it was possible to isolate the olefins **17** and **18**, as pure compounds, albeit in low yield. The lack of correlation between the cyclization results realized in the model series (Chart I) and those observed in this case, as well as the formation[12] of *both* the para and ortho isomers **17** and **18**, seems to be a function of the incorporation of the anisole ring in the system as a trap for the tricyclic cation. A similar result was observed[9] in the cyclization experiments performed on the aldehyde **15**. Unfortunately, the system **16** required for this synthesis does not adequately test this point, as the sensitivity of the tetrasubstituted double bond to protonation under harsher acidic conditions (trifluoroacetic acid with or without dichloromethane as a diluent) and the insolubility of the substrate 3-methyl-2-cyclopentenol in certain media (formic acid) limit severely the range of experimentation.

Despite the unsatisfying yields observed in this cyclization, sufficient quantities of each pentacyclic isomer **17** and **18** were obtained to allow further investigations. Oxidative ring enlargement[11c] of the major isomer **17** resulted in the

Chart II
Pentacyclic Olefin Synthesis by Polyene Cyclization[a]



[a] a, $(CH_3)_3SiC{\equiv}CCH_2CH_2MgCl$, Et_2O; b, $HgSO_4$, aq H_2SO_4, THF; c, 8 *N* H_2CrO_4, acetone; d, 2% aq NaOH, EtOH; e, $LiAlH_4$, Et_2O; f, $SnCl_4$, CH_2Cl_2, −78° or silica gel chromatography; g, OsO_4, dioxane, H_2S, CH_2Cl_2; h, $Pb(OAc)_4$, THF; i, 10% aq NaOH, CH_3OH; j, $LiPPh_2$, TMEDA, THF; k, $ClPO(NMe_2)_2$, HMPA, Et_3N, THF; l, $LiNH_3$, THF, EtOH.

formation of the target enone **19**[6] and thus completed an alternate total synthesis of alnusenone (**1**). This transformation also served to confirm the structure and stereochemistry assigned to the pentacyclic olefin **17** from the polyene cyclization. Finally, in order to provide similar confirmation of the structural assignment made for the minor pentacyclic olefin **18**, samples of both isomers **17** and **18** were demethoxylated[13] through reductive removal of the intermediate phosphorodiamidate.[14] In both cases the same pentacyclic hydrocarbon **20** resulted from these experiments, and the identity of the two samples established beyond reasonable doubt the structure assigned the minor pentacyclic isomer **18**.

This work, then, establishes another route, albeit less efficient owing to the problem of the acid-catalyzed cyclization stage,[15] for the synthesis of pentacyclic intermediates suitable for conversion to the alnusenone class of triterpenes. Not to be overlooked in this connection is the efficiency of the polyene cyclization scheme for the synthesis of the *tricyclic* systems **6**, **7**, and **8**, used here as model compounds, but potentially interesting intermediates themselves.

Experimental Section[16]

1-Trimethylsilyl-4-chloro-1-butyne. To a solution of ethylmagnesium bromide prepared from 36.6 g (1.5 g-atoms) of magnesium and 114 ml (1.5 mol) of ethyl bromide in 300 ml of dry tetrahydrofuran under a nitrogen atmosphere was added with stirring over a 0.5-hr period a solution of 42 g (0.6 mol) of 4-hydroxy-1-butyne in 360 ml of dry tetrahydrofuran, and after stirring for 20 min the mixture was treated with 190 ml (1.5 mol) of trimethylchlorosilane in 400 ml of dry tetrahydrofuran. After stirring for an additional 1.5 hr the reaction mixture was hydrolyzed with an aqueous (500 ml) solution of 132 g of ammonium chloride, and then the organic phase was decanted from the resulting thick, white aqueous suspension. The organic extract was concentrated to 400 ml and then stirred overnight at room temperature with a solution of 132 g of ammonium chloride in 500 ml of water. The residue obtained after ether extraction[17] was dissolved in 140 ml of freshly distilled thionyl chloride containing 10 ml of dry pyridine, and the mixture was refluxed under a nitrogen atmosphere for 7 hr. After cooling, the reaction mixture was poured into ice and water, and the product was isolated by ether extraction,[17] including an acid wash. Distillation of the dark brown residue through a 1.5-ft spinning band column afforded 40 g (42%) of 1-trimethylsilyl-4-chloro-1-butyne, bp 74° (30 mm), as a clear, colorless liquid. Redistillation of a portion of this material in the same apparatus afforded the analytical sample which boiled at 72° (28 mm) and consisted of a single volatile component on GLC (100°): ir (neat) 2190 (C≡C), 850, and 760 cm^{-1}; NMR ($CDCl_3$) δ 0.16 [s, 9, $Si(CH_3)_3$], 2.66 (t, 2, J = 7 Hz, $C{\equiv}CCH_2$), and 3.63 (t, 2, J = 7 Hz, $-CH_2Cl$).

Anal. Calcd for $C_7H_{13}SiCl$: C, 52.35; H, 8.10. Found: 52.16; H, 8.30.

1-Trimethylsilyl-9,10-dimethyl-(*E*)-9,13-tetradecadien-1-yn-5-ol (3). A nitrogen-protected solution of the Grignard reagent prepared from 8.3 g (0.052 mol) of 1-trimethylsilyl-4-chloro-1-butyne and 2 g (0.082 g-atom) of magnesium in 25 ml of dry ether was separated from excess magnesium by syringe, and after the solution was cooled to −5°, a solution of 4.0 g (0.022 mol) of the aldehyde **2** in 20 ml of dry ether was added over a 1-hr period under a nitrogen atmosphere. The reaction mixture was then quenched with 80 ml of a 10% aqueous ammonium chloride solution, and the product was isolated by ether extraction.[17] Chromatography of the crude product (9.06 g) on 400 g of silica gel afforded 4.9 g (85%) of the alcohol **3** as a mobile, colorless liquid which was eluted with 3 l. of 20% ether–petroleum ether and represented 93% of the volatile components on GLC (215°). The analytical sample was prepared by evaporative distillation of a portion of this material at 120° and 0.1 mm: ir (neat) 3600–3150 (OH), 2190 (C≡C), and 1645 cm^{-1} (C=CH_2); NMR ($CDCl_3$) δ 0.1 [s, 9, $Si(CH_3)_3$], 1.64 (s, 2 × 3, $CH_3C{=}C{-}CH_3$), 3.50–4.00 (m, 1, CHO), 4.76–5.23 (m, 2, C=CH_2), and 5.50–5.90 (m, 1, CH=C).

Anal. Calcd for $C_{19}H_{34}SiO$: C, 74.44; H, 11.18; Si, 9.16. Found: C? 74.33; H, 11.01; Si, 9.05.

9,10-Dimethyl-(*E*)-9,13-tetradecadiene-2,5-dione. To a solution of 5.9 g (0.019 mol) of the alcohol **3** in 400 ml of tetrahydrofuran and 160 ml of water under a nitrogen atmosphere was added 40

ml of a saturated solution of mercuric sulfate in 1% aqueous sulfuric acid. After stirring for 4 hr at room temperature, the cloudy mixture was saturated with salt, and the product was isolated by ether extraction.[17] This crude material (4.65 g of a colorless oil) was dissolved in 60 ml of dry acetone, and the solution was cooled to 0° and then treated with 4.6 ml of a 2.7 *M* aqueous chromic acid solution.[18] After stirring for 5 min the reaction mixture was quenched with a few drops of isopropyl alcohol and diluted with water, and then the product was isolated by ether extraction,[17] including a base wash. On chromatography of the crude product (4.2 g of colorless oil) on 300 g of silica gel, 2.45 g (54%) of the corresponding diketone was eluted with 2 l. of 30% ether–petroleum ether. This material consisted of 93% of a single volatile component on GLC (210°). The analytical sample was obtained by evaporative distillation of a portion of this material at 110° (0.1 mm): ir (neat) 1720 and 1715 (C=O), 1645 (C=C), and 910 cm^{-1} (C=CH_2); NMR ($CDCl_3$) δ 1.63 (s, 2 × 3, CH_3C=CCH_3), 2.66 (s, 4, $COCH_2CH_2CO$), 4.76–5.23 (m, 2, C=CH_2), and 5.50–5.90 (m, 1, CH=C).

Anal. Calcd for $C_{16}H_{26}O_2$: C, 76.75; H, 10.47. Found: C, 76.85; H, 10.51.

2-(3′,4′-Dimethyl-(*E*)-3′,7′-octadienyl)-3-methyl-2-cyclopentenone. A solution of 2.45 g (9.8 mmol) of the above diketone in 300 ml of ethanol and 70 ml of a 2% aqueous sodium hydroxide solution was refluxed under a nitrogen atmosphere for 4 hr. After a solution of 2.8 ml of concentrated hydrochloric acid in 100 ml of water was added, most of the ethanol was removed at the rotary evaporator, and then the product was isolated by ether extraction,[17] including a base wash. On chromatography of the crude material (2.25 g of colorless oil) on 150 g of silica gel, 2.01 g (88%) of the cyclopentenone as a colorless oil was eluted with 2 l. of 30% ether–petroleum ether. This material consisted of >97% of a single volatile component on GLC (180°), and the analytical sample was prepared by evaporative distillation of a portion of this product at 110° (0.5 mm): ir (neat) 1705 (conjugated C=O), 1650 (conjugated C=C), and 910 cm^{-1} (C=CH_2); NMR ($CDCl_3$) δ 1.62, 1.66 (2 s, 3 each, CH_3C=C–CH_3), 2.2 (s, 3, C_3CH_3), 4.76–5.23 (m, 2, C=CH_2), and 5.50–5.90 (m, 1, CH=C).

Anal. Calcd for $C_{16}H_{24}O$: C, 82.70; H, 10.41. Found: C, 82.65; H, 10.41.

2-(3′,4′-Dimethyl-(*E*)-3′,7′-octadienyl)-1-methylcyclopenten-3-ol (5). To a solution of 118 mg (0.51 mmol) of the above cyclopentenone in 10 ml of dry ether cooled to 0° was added 20 mg (0.53 mmol) of lithium aluminum hydride, and then the mixture was stirred at 0° for 1 hr. After the addition of 0.08 ml of water and then magnesium sulfate, the heterogeneous mixture was stirred at room temperature for 1 hr and then filtered. After evaporation of the ether at reduced pressure and then preparative TLC (50% ether–petroleum ether) of the residue, there was obtained 98 mg (85%) of the cyclopentenol **5** (R_f 0.4–0.5) as a colorless liquid. The analytical sample was obtained by evaporative distillation of this material at 90–100° and 0.5 mm: ir (neat) 3600 (OH), 1645 (C=C), and 910 cm^{-1} (C=CH_2); NMR ($CDCl_3$) δ 1.66 (s, 2 × 3, CH_3C=CCH_3), 2.10 (s, 3, C-1 CH_3), 4.75 (m, 1, C-1 H), 4.8–5.1 (m, 2, C=CH_2), and 5.5–6.1 (m, 1, CH=C).

Anal. Calcd for $C_{16}H_{26}O$: C, 81.99; H, 11.18. Found: C, 82.09; H, 11.11.

Cyclization of 2-(3′,4′-Dimethyl-(*E*)-3′,7′-octadienyl)-1-methylcyclopenten-3-ol (5). To 500 mg (2.14 mmol) of the cyclopentenol **5**, precooled in an ice bath, was added under a nitrogen atmosphere 50 ml of dry formic acid, precooled to 9°. After the cloudy reaction mixture had stirred in the ice bath for 4 min, it was poured into a mixture of 200 g of ice and 400 ml of water that contained 70 g of sodium hydroxide. After isolation by ether extraction,[17] the crude product (510 mg) was reduced with 55 mg (1.45 mmol) of lithium aluminum hydride in 50 ml of dry ether. After stirring for 1 hr at room temperature, this mixture was treated with 0.2 ml of water and then solid magnesium sulfate, and the resulting suspension was stirred for an additional 1 hr. After filtration and then removal of the solvent at reduced pressure, the semicrystalline residue (490 mg) was chromatographed on 55 g of silica gel. Elution with 100 ml of 20% ether–petroleum ether afforded 185 mg of a hydrocarbon mixture which consisted of 85% of a major volatile component on GLC (170°). Rechromatography of this material on 30 g of alumina impregnated with 10% silver nitrate gave 152 mg (33%) of the diene **8**, as a colorless oil which was eluted with 30 ml of 50% benzene–ether and consisted of a single volatile component by GLC (175°). The analytical sample was obtained by evaporative distillation of a portion of this material at 80° and 0.5 mm: ir (neat) 1650 cm^{-1} (C=C); NMR ($CDCl_3$) δ 0.66 and 1.00 (2 s, 3 each, C-5a and C-9a CH_3), 1.63 (s, 3, C-3 CH_3), and 5.63 (s, 2, CH=CH).

Anal. Calcd for $C_{16}H_{24}$: C, 88.82; H, 11.18. Found: C, 88.64; H, 11.21.

Continued elution of the silica gel column with 200 ml of 40% ether–petroleum ether afforded a mixture of alcohols shown by comparison NMR spectra (vide infra) to contain ~50% (5%) of the axial tricyclic alcohol **7** which after two crystallizations from hexane at −20° and then sublimation at 70° and 0.2 mm gave 15 mg of the crystalline alcohol **7**, mp 74–78°. This material, which consisted of 85% of a major component on GLC (175°), was not further purified, as comparison ir and NMR spectra with the authentic alcohol **7** were identical.

Continued elution of the column with 300 ml of 50% ether–petroleum ether afforded 217 mg (43%) of the equatorial alcohol **6**, mp 125–127°. The analytical sample, obtained after crystallization of a portion of this material from hexane, melted at 124–126°: ir ($CHCl_3$) 3610 cm^{-1} (OH); NMR ($CDCl_3$) δ 0.77 and 1.07 (2 s, 3 each, C-5a and C-9a CH_3), 1.63 (br s, 3, C-3 CH_3), and 3.83 (br m, 1, C-7 H).

Anal. Calcd for $C_{16}H_{26}O$: C, 81.99; H, 11.18. Found: C, 81.99; H, 11.21.

3,5aβ,9aα-Trimethyl-2,4,5,5a,8,9,9a,9bβ-octahydro-7(6*H*)-1*H*-benz[*e*]indenone (9). A. From the Alcohol 6. To a solution of 300 mg (1.28 mmol) of the tricyclic alcohol **6** in 12 ml of dry acetone was added at room temperature 0.3 ml of 2.7 *M* aqueous chromic acid solution,[18] and the mixture was stirred for 5 min. After dilution with water and isolation of the product by ether extraction,[17] including a base wash, chromatography of the crude material on 10 g of silica gel with 1 ether–petroleum ether afforded 300 mg (98%) of the ketone **9**, mp 54–56°, which consisted of a single volatile component on GLC (170°). The analytical sample was obtained by sublimation of a portion of this material at 40° and 0.1 mm: ir ($CHCl_3$) 1700 cm^{-1} (C=O); NMR ($CDCl_3$) δ 0.97 and 1.03 (2 s, 3 each, C-5a and C-9a CH_3) and 1.62 (br s, 3, C-3 CH_3).

Anal. Calcd for $C_{16}H_{24}O$: C, 82.70; H, 10.41. Found: C, 82.59; H, 10.42.

B. From the Alcohol 7. In a manner similar to that described above, 15 mg of 85% pure alcohol **7** from the cyclization reaction was oxidized with 0.1 ml of 2.672 *M* aqueous chromic acid solution[18] in 5 ml of dry acetone. After isolation of the product by ether extraction[17] and filtration of the crude material through 5 g of silica gel with 10% ether–petroleum ether, there was isolated 10 mg (80%) of the ketone **9**, mp 54–56°, alone or in admixture with a sample of the material prepared above.

7β-Hydroxy-3,5aβ,9aα-trimethyl-2,4,5,5a,6,7α,8,9,9a,9bβ-decahydro-1*H*-benz[*e*]indene (7). To a solution of 58 mg (0.25 mmol) of the ketone **9** in 8 ml of dry tetrahydrofuran was added 167 mg (1.55 mmol) of lithium tri-*tert*-butoxyaluminum hydride, and then the reaction mixture was stirred at room temperature for 2 hr. After the reaction was quenched with 0.2 ml of 2 *N* aqueous hydrochloric acid and then dried over 1 g of magnesium sulfate, filtration and then removal of the solvent at reduced pressure afforded 58 mg of semicrystalline residue. On purification of this material by preparative TLC (50% ether–petroleum ether) 48 mg (82%) of the alcohol **7**, mp 78–80°, was obtained at R_f 0.4. The analytical sample, prepared by sublimation of this material at 70° and 0.1 mm, also melted at 78–80° with softening at 55°: ir ($CHCl_3$) 3610 cm^{-1} (OH); NMR ($CDCl_3$) δ 0.71 and 1.27 (2 s, 3 each, C-5a and C-9a CH_3), 1.62 (br s, 3, C-3 CH_3), and 4.10 (br s, 1, C-7 H).

Anal. Calcd for $C_{16}H_{26}O$: C, 81.99; H, 11.18. Found: C, 81.95; H, 11.02.

The solution ir and NMR of this material were identical with those of the minor alcohol obtained above on cyclization of the cyclopentenol **5** and distinctly different from the spectra of the major alcohol **6** from this cyclization.

3,5aβ,9aα-Trimethyl-2,4,5,5a,6,7,8,9,9a,9bβ-decahydro-1*H*-benz[*e*]indene (10). A. By Reduction of the Ketone 9. To a solution of 100 mg (0.43 mmol) of the ketone **9** in 5 ml of diethylene glycol under a nitrogen atmospehre was added 0.5 ml of 100% hydrazine hydrate and 0.166 g of hydrazine dihydrochloride. The reaction mixture was heated at 110° for 21 hr, and then 0.85 g of potassium hydroxide was added. The temperature was raised to 165°, and a stream of nitrogen was passed over the solution for 1.5 hr to remove volatile material. The temperature was maintained at 165° for 3.5 hr; then the mixture was cooled and poured into water, and the product was isolated by ether extraction.[17] Filtration of the residue through 5 g of silica gel in 2% ether–petroleum ether afforded 47 mg of a colorless oil which gave 41 mg (45%) of analytically pure olefin **10** on evaporative distillation at 80–90° and 0.3

mm: ir ($CHCl_3$) 1375, 1155, 1055, and 912 cm^{-1}; NMR ($CDCl_3$) δ 0.73 and 1.07 (2 s, 3 each, C-5a and C-9a CH_3), and 1.60 (br s, 3, C-3 CH_3).

Anal. Calcd for $C_{16}H_{26}$: C, 88.00; H, 12.00. Found: C, 88.02; H, 12.14.

B. By Hydrogenation of the Diene 8. A solution of 70 mg (0.32 mmol) of the diene **8** and 20 mg of tris(triphenylphosphine)-rhodium chloride[19] in 4 ml of benzene was stirred at room temperature under a hydrogen atmosphere for 20 hr. After filtration of the reaction mixture through 5 g of Florisil with ether eluent, there was obtained 68 mg (97%) of the olefin **10** as a colorless oil. The solution ir and NMR spectra of this material were identical with those reported above for the olefin **10** obtained from reduction of the ketone **9**.

4bα,8aβ-Dimethyl-7α-hydroxy-4,4aβ,4b,5,6,7β,8,8a,9,10-decahydro-2(3*H*)-phenanthrenone (11). A solution of 170 mg (0.73 mmol) of the alcohol **6** and 400 mg (1.57 mmol) of osmium tetroxide in 40 ml of dry dioxane was allowed to stand at room temperature under a nitrogen atmosphere for 3 days. After 5 ml of pyridine was added, the black reaction mixture was allowed to stand for an additional 3 days, and then the solvent was removed at reduced pressure. The black residue was dissolved in 40 ml of dry dichloromethane, and a stream of hydrogen sulfide was bubbled through the black solution for 20 min. The resulting black precipitate was removed by filtration, and the crystalline residue obtained after removal of the solvent from the filtrate at reduced pressure was dissolved in 40 ml of dry tetrahydrofuran. This solution was cooled to 0° and then treated with 1 g (2.26 mmol) of lead tetraacetate. After this mixture had stirred at 0° for 15 min, 1 ml of ethylene glycol was added, and the resulting brown precipitate was removed by filtration. The filtrate was diluted with water, and the product was isolated by ether extraction.[17] The resulting residue (170 mg of a colorless oil) was then heated at 65° with 40 ml of a 2.5% aqueous potassium hydroxide solution under a nitrogen atmosphere for 14 hr. After neutralization with 2*N* aqueous hydrochloric acid and isolation of the product by ether extraction,[17] purification of the residue (140 mg of colorless oil) by preparative TLC (5% methanol–ether) gave 118 mg (63%) of the enone **11**, mp 144–146°, at R_f 1.5–2.0. This material was not further purified for combustion analysis: ir ($CHCl_3$) 3610 (OH), 1660 (conjugated C=O) and 1615 cm^{-1} (conjugated C=C); NMR ($CDCl_3$) δ 0.91 and 1.15 (2 s, 3 each, C-4b and C-8a CH_3), 4.00 (m, 1, C-7 H), and 5.98 (s, 1, C-1 H).

Anal. Calcd for $C_{16}H_{24}O_2$: C, 77.34; H, 9.74. Found: C, 77.24; H, 9.71.

4bα,8aβ-Dimethyl-4,4aβ,4b,5,6,8a,9,10-octahydro-2(3*H*),7-(8*H*)-phenanthrenedione (12). A. By Reduction of the Aromatic Ketal 14. To a solution of 650 mg (0.093 g-atom) of lithium in 210 ml of dry liquid ammonia was added with stirring over a 10-min period a solution of 1.080 g (3.58 mmol) of the aromatic ketal **14** in 68 ml of dry tetrahydrofuran. After 10 min 63 ml of *tert*-butyl alcohol was added dropwise, and the reaction mixture was stirred for an additional 1 hr. During this period two 210-mg (0.03 g-atom) batches of lithium were added after 10 min and again after 35 min when the blue color discharged. Finally, the blue color was discharged by the addition of 3 ml of methanol; the ammonia was removed in a stream of nitrogen, and after the addition of 100 ml of water, the product was isolated by ether extraction.[17] A solution of the crude residue in 26 ml of benzene and 130 ml of ethanol was stirred and heated at reflux for 30 min with 70 ml of 5 *N* aqueous hydrochloric acid. Isolation of the product by ether extraction[17] including a base wash afforded 840 mg of a crystalline residue which after repeated washing with ether gave 518 mg (60%) of the enedione **12**, mp 187–192°. The analytical sample, obtained after two crystallizations of a portion of this material from dichloromethane–hexane, melted at 190–193°: ir ($CHCl_3$) 1710 (C=O), 1660 (conjugated C=O), and 1615 cm^{-1} (conjugated C=C); NMR ($CDCl_3$) δ 1.13 (s, 2 × 3, C-4b and C-8a CH_3) and 6.00 (br s, 1, C-1 H).

Anal. Calcd for $C_{16}H_{22}O_2$: C, 78.01; H, 9.00. Found: C, 77.82; H, 8.92.

B. By Oxidation of Keto Alcohol 11. To a solution of 54 mg (0.22 mmol) of the keto alcohol **11** in 3 ml of dry acetone at 0° was added 0.055 ml of 2.7 *M* aqueous chromic acid solution.[18] The mixture was stirred for 2 min and then quenched with a few drops of isopropyl alcohol. After dilution with water and isolation of the product by ether extraction,[17] including a base wash, there resulted 51 mg (95%) of the enedione **12**, mp 181–189°. After two crystallizations of this material from dichloromethane–hexane there was obtained 48 mg (88%) that melted at 190–193° alone or in admixture with the authentic material prepared above. The ir and NMR spectra of the two samples were also identical.

10aβ-Cyano-2,2-ethylenedioxy-7-methoxy-4aα-methyl-1,2,-3,4,4a,9,10,10a-octahydrophenanthrene. In a flask fitted with a Dean-Stark water separator was placed 2.30 g (8.65 mmol) of trans cyano ketone **13**, 10 ml of ethylene glycol, 150 mg of *p*-toluenesulfonic acid monohydrate, and 200 ml of dry benzene. The mixture was stirred vigorously at reflux overnight in an atmosphere of argon. After the mixture was cooled, it was poured into 500 ml of water and the ketal [2.63 g (98%), mp 161–162°] was isolated by ether extraction, including a base wash. The analytical sample, prepared by one crystallization of a portion of this material from methanol, also melted at 161–162°: ir ($CHCl_3$) 2250 (C≡N), 1610, 1580, 1500 (ArH), and 1250 cm^{-1} ($ArOCH_3$); NMR ($CDCl_3$) δ 1.20 (s, 3, C-4a CH_3), 3.77 (s, 3, $ArOCH_3$), 4.3–6.2 (m, 4, OCH_2CH_2O), and 7.3–6.5 (m, 3, ArH).

Anal. Calcd for $C_{19}H_{23}NO_3$: C, 72.82; H, 7.40; N, 4.47. Found: C, 72.92; H, 7.38; N, 4.36.

4aα,10aβ-Dimethyl-2,2-ethylenedioxy-7-methoxy-1,2,3,4,-4a,9,10,10a-octahydrophenanthrene (14). In a dry flask was placed 9.42 g (0.030 mol) of the above cyano ketal, 450 ml of dry benzene, and 24 ml (0.036 mol) of a 1.5 *M* benzene solution of diisobutylaluminum hydride in an atmosphere of argon. The resulting solution was stirred at room temperature for 2 hr and then poured into 1 l. of a well-stirred, ice-cold, aqueous 5% sodium hydroxide solution. Isolation of the product by ether extraction, including a base wash, gave 9.49 g (100%) of a white foam, the solution ($CHCl_3$) infrared spectrum of which showed imine absorption at 1630 cm^{-1}, but no nitrile absorption at 2250 cm^{-1}.

A solution of this crude imine in 270 ml of tetrahydrofuran and 270 ml of methanol was heated to reflux in an atmosphere of argon, and then a solution of 4.2 g (0.051 mol) of anhydrous sodium acetate and 11.5 ml (12 g, 0.20 mol) of glacial acetic acid in 34 ml of water was added. After the resulting solution was heated at reflux for 10 min, the mixture was cooled to 40°, concentrated to approximately 150 ml at reduced pressure, and then poured into 1 l. of a well-stirred, ice-cold 5% aqueous sodium carbonate solution. Isolation of the crude product by ether extraction afforded 9.48 g (100%) of a white, crystalline solid, mp 117–120°, the solution ($CHCl_3$) infrared spectrum of which showed aldehyde absorption at 1710 cm^{-1}. Similar material from another experiment was crystallized twice from ether–hexane for combustion analysis, and this sample melted at 117–120° also: ir ($CHCl_3$) 2770 (CHO), 1710 (C=O), 1610, 1575, 1495 (ArH), and 1245 cm^{-1} ($ArOCH_3$); NMR ($CDCl_3$) δ 1.20 (s, 3, C-4a CH_3), 4.1–3.5 (m, 4, OCH_2CH_2O), 3.75 (s, 3, $ArOCH_3$), 7.3–6.5 (m, 3, ArH), and 9.45 (s, 1, CHO).

Anal. Calcd for $C_{19}H_{24}O_4$: C, 72.13; H, 7.65. Found: C, 72.05; H, 7.60.

The crude aldehyde, 72 ml (72 g, 1.44 mol) of 99% hydrazine hydrate, and 500 ml of diethylene glycol were heated at 140–145° (internal) for 23 hr in an atmosphere of argon. After the solution was cooled to approximately 110° (internal), 81 g of 85% potassium hydroxide was added. The reaction mixture was then stirred at 170–175° (internal) in a stream of argon for 2 hr, and finally at 165–170° (internal) for 3 hr under an atmosphere of argon. The pale yellow solution was cooled, poured into 2 l. of water and the product was isolated by extraction with 3:1 ether–dichloromethane. The residue amounted to 8.00 g (88%) of a crystalline solid which consisted of 99% of a single volatile component on GLC (225°). One crystallization of this material from ether–hexane afforded 7.45 g (82%) of the ketal **14** as white crystals, mp 111.5–112.5°, which was sufficiently pure for analytical purposes: ir ($CHCl_3$) 1605, 1575, 1495 (ArH), 1240 ($ArOCH_3$), 1150, and 1145 cm^{-1} (C–O–C); NMR ($CDCl_3$) δ 0.93 (s, 3, C-10a CH_3), 1.13 (s, 3, C-4a CH_3), 3.57 (s, 3, $ArOCH_3$), 4.1–3.5 (m, 4, OCH_2CH_2O), and 7.5–6.5 (m, 3, ArH).

Anal. Calcd for $C_{19}H_{26}O_3$: C, 75.46; H, 8.67. Found: C, 75.46; H, 8.76.

1-Trimethylsilyl-9,10,13-trimethyl-16-(*m*-methoxyphenyl)-(*E,E*)-9,13-hexadecadien-1-yn-5-ol. In a manner similar to that described for the preparation of the alcohol **3** a solution of the Grignard reagent from 2.43 g (0.1 g-atom) of magnesium and 10.75 g (67.2 mmol) of 1-trimethylsilyl-4-chloro-1-butyne in 45 ml of dry ether was cooled to −15° and added over a 1-hr period under an argon atmosphere to a cooled (−15°) solution of 7.355 g (22.4 mmol) of the aldehyde **15**[9] in 20 ml of dry ether. After stirring at room temperature for an additional 1 hr, the reaction mixture was worked up as described above, and the crude product (11.94 g) was purified on 410 g of silica gel in a medium-pressure chromatography apparatus[16] using 20% ether–petroleum ether as eluent. Elu-

tion with 2.5 l. of solvent afforded 7.084 g (70%) of the desired alcohol as an oil in the fractions from 1–2 l. The analytical sample was obtained by evaporative distillation of a portion of this material at 190° and 0.01 mm: ir ($CHCl_3$) 3650–3500 (OH), 2180 (C≡C), and 16i0, 1605 cm^{-1} (C=C); NMR ($CDCl_3$) δ 0.15 [s, 9, $Si(CH_3)_3$], 1.61 (br s, 3, C-13 CH_3), 1.63 (s, 2 × 3, C-9 and C-10 CH_3), 3.80 (m, 1, C-5 H), 3.82 (s, 3, $ArOCH_3$), 5.20 (br t, 1, C-14 H), and 6.5–7.3 (m, 4, ArH).

Anal. Calcd for $C_{29}H_{46}O_2Si$: C, 76.59; H, 10.20. Found: C, 76.35; H, 10.00.

9,10,13-Trimethyl-16-(*m*-methoxyphenyl)-(*E,E*)-9,13-hexadecadiene-2,5-dione. In a manner similar to that described above for the formation of the model dione a solution of 6.98 g (15.37 mmol) of the above silyl alcohol in 320 ml of tetrahydrofuran and 130 ml of water was treated with 32 ml of a saturated solution of mercuric sulfate in 1% aqueous sulfuric acid. After stirring at room temperature for 1.5 hr, the mixture was saturated with sodium chloride, and the product was isolated by ether extraction,[17] including a base wash.

A solution of the crude product (6.85 g) from the above hydrolysis in 60 ml of dry acetone was treated with 4.5 ml of 8 *N* aqueous chromic acid solution,[18] and the mixture was stirred at 0° for 20 min. After dilution of the mixture with water and isolation of the product by ether extraction,[17] including a base wash, the crude diketone (5.374 g) was purified by medium-pressure chromatography[16] on 410 g of silica gel. Elution with 1.4 l. of 40% ether–petroleum ether afforded 3.083 g (50%) of the diketone as an oil in the fractions from 750–1100 ml. The analytical sample was prepared by evaporative distillation of a portion of this material at 160–165° and 0.001 mm: ir (CCl_4) 1720 and 1715 (C=O) and 1640, 1620 cm^{-1} (C=C); NMR (CCl_4) δ 1.58 (br s, 3, C-13 CH_3), 1.60 (s, 2 × 3, C-9 and C-10 CH_3), 2.07 (s, 3, C-1 CH_3), 3.88 (s, 3, $ArOCH_3$), 5.02 (br t, 1, C-14 H), and 6.4–7.2 (m, 4, ArH).

Anal. Calcd for $C_{26}H_{38}O_3$: C, 78.35; H, 9.61. Found: C, 78.35; H, 9.59.

2-(3′,4′,7′-Trimethyl-10′-(*m*-methoxyphenyl)-(*E,E*)-3′,7′-decadienyl)-3-methyl-2-cyclopentenone (16). In a manner similar to that described above for the formation of the cyclopentenone 4 a solution of 2.93 g (7.36 mmol) of the above diketone in 225 ml of ethanol and 53 ml of aqueous sodium hydroxide solution was heated at reflux under an argon atmosphere for 4 hr. After the reaction was cooled and neutralized with 10% aqueous hydrochloric acid, most of the ethanol was removed at reduced pressure, and then the product was isolated by ether extraction.[17] The crude product (2.793 g) was purified by medium-pressure chromatography[16] on 200 g of silica gel, and elution with 750 ml of 40% ether–petroleum ether afforded 2.236 g (80%) of the cyclopentenone **16** as an oil in the fractions from 300–600 ml. The analytical sample was prepared by evaporative distillation of a portion of this material at 145° and 0.003 mm: ir (CCl_4) 1705 (C=O) and 1650 cm^{-1} (C=C); NMR (CCl_4) δ 1.5–1.7 (m, 9, C-3′, C-4′, and C-7′ CH_3), 2.00 (s, 3, C-3 CH_3), 3.75 (s, 3, $ArOCH_3$), 5.16 (br t, 1, C-8′ H), and 6.5–7.35 (m, 4, ArH).

Anal. Calcd for $C_{26}H_{36}O_2$: C, 82.06; H, 9.53. Found: C, 81.83; H, 9.24.

2-(3′,4′,7′-Trimethyl-10′-(*m*-methoxyphenyl)-(*E,E*)-3′,7′-decadienyl)-1-methylcyclopenten-3-ol. Reduction of 668 mg (1.76 mmol) of the cyclopentenone **16** was accomplished in a manner similar to that described above for the formation of the alcohol **5** with 100 mg (2.63 mmol) of lithium aluminum hydride in 30 ml of dry ether. After a similar work-up there resulted 661 mg of a colorless oil that on purification by preparative TLC (33% ether–petroleum ether) afforded 595 mg (90%) of the desired cyclopentenol (R_f 0.21) as an oil, 90% of which consisted of a single volatile component on GLC (280°). This material was not further purified but used directly in the cyclization experiments described below: ir (CCl_4) 3600, 3500 cm^{-1} (OH); NMR (CCl_4) δ 1.60 (br s, 3, C-1 CH_3), 1.65 (s, 3 × 3, C-3′, C-4′, and C-7′ CH_3), 3.73 (s, 3, $ArOCH_3$), 4.7 (br m, 1, C-3 H), 5.17 (br t, 1, C-8′ H), and 6.5–7.3 (m, 4, ArH).

Cyclization of 2-(3′,4′,7′-Trimethyl-10′-(*m*-methoxyphenyl)-(*E,E*)-3′,7′-decadienyl-1-methylcyclopenten-3-ol. A. With Stannic Chloride in Dichloromethane. A solution of 38.2 mg (0.1 mmol) of the above cyclopentenol in 3 ml of dry dichloromethane was cooled to −78°, and then 1.2 ml of a 0.1 *M* dichloromethane solution of stannic chloride was added. After 5 min 3 ml of a 20% aqueous potassium carbonate solution and then 5 ml of ether were added, and the mixture was poured into 50 ml of water. Analysis by GLC (280°) of the crude product (40 mg) isolated by ether extraction[17] showed a mixture that consisted of three major components (D, E, and F) with retention times of 4.0, 5.05, and 6.1 min, respectively, and in a ratio of 1:3:12. In addition there were several unresolvable peaks from 2.8–4.4 min.

This crude product was combined with 309 mg of identical material obtained from the cyclization of 264 mg of the cyclopentenol under identical conditions, and this mixture was chromatographed on 45 g of silica gel impregnated with 10% silver nitrate. Elution was accomplished with 50% ether–petroleum ether; 10-ml fractions were collected and the residues were analyzed by GLC (280°).

Fraction	Wt, mg	Composition
14, 15	18	E (90%)
16	3	E:F (1:3)
17–22	157	D:E:F (5:4:90)
23	3	D:F (1:1)
24–28	23	D + others (1:1)
29–45	17	Eleven side products

Trituration of the material from fractions 17–22 with petroleum ether at −78° afforded 96 mg (33%; estimated by GLC 108 mg, 3) of the olefin **17** (component F), mp 149–151°, 96% of which was a single volatile component on GLC (280°). The analytical sample, prepared by crystallization of this material from ether–hexane, melted at 150–151.5°: ir ($CHCl_3$) 1610 cm^{-1} (1,2,4-trisubstituted aromatic); NMR ($CDCl_3$) 0.72, 1.03, 1.21 (3 s, 3 each, C-5a, C-11b, and C-13a CH_3), 1.61 (s, 3, C-3 CH_3), 3.76 (s, 3, $ArOCH_3$), 6.60 (d, 1, $J_{8,10}$ = 2 Hz, C-8 H), 6.70 (d of d, 1, $J_{8,10}$ = 2, $J_{10,11}$ = 8 Hz, C-10 H), and 7.20 (d, 1, $J_{10,11}$ = 8 Hz, C-11 H).

Anal. Calcd for $C_{26}H_{36}O$: C, 85.66; H, 9.95. Found: C, 85.65; H, 9.99.

Components D and E from this experiment could not be further purified but were obtained in part B.

B. With Silica Gel. On attempted purification of 1.36 g (3.56 mmol) of the above cyclopentenol by chromatography on 95 g of silica gel, 890 mg (69%) of cyclized material, the major components of which were D, E, and F (**17**) in a ratio of 13:3:4 by GLC (280°), was obtained on elution with 300 ml of 30% ether–petroleum ether. After rechromatography of this material on 40 g of silica gel impregnated with 2% silver nitrate and then preparative TLC (petroleum ether) of the residues from the major fractions, both components D and E were obtained pure.

Component D, isolated in 14% yield (184 mg) as a colorless oil, was shown to be 6-(2′-*m*-methoxyphenylethyl)-3,5aβ,7,9aα-tetramethyl-2,4,5,5a,6α,9,9a,9bβ-octahydro-1*H*-benz[*e*]indene and was evaporatively distilled for analysis at 110° and 0.075 mm: ir ($CHCl_3$) 1605, 1585 cm^{-1} (C=C, Ar); NMR ($CDCl_3$) δ 0.62, 0.85 (2 s, 3 each, C-5a and C-9a CH_3), 1.60 1.80 (2 br s, 3 each, C-3 and C-7 CH_3), 3.75 (s, 3, $ArOCH_3$), 5.36 (m, 1, C-8 H), and 6.48–7.35 (m, 4, ArH).

Anal. Calcd for $C_{26}H_{36}O$: C, 85.66; H, 9.95. Found: C, 85.76; H, 10.01.

Component E, isolated in 3% yield (45 mg), was crystallized from ether–hexane and shown to be the isomeric pentacyclic ether **18**: mp 157.5–161°; ir ($CHCl_3$) 1575 cm^{-1} (C=C, Ar); NMR ($CDCl_3$) δ 0.72, 1.01, 1.33 (3 s, 3 each, C-5a, C-11b, and C-13a CH_3), 1.60 (br s, 3, C-3 CH_3), 3.75 (s, 3, $ArOCH_3$), 6.67 (d of d, 1, $J_{9,10}$ = 8, $J_{8,10}$ = 1.5 Hz, C-10 H), 6.73 (s, 1, C-8 H), and 7.05 (d of d, 1, $J_{8,9}$ = 7, $J_{9,10}$ = 8 Hz, C-9 H).

Anal. Calcd for $C_{26}H_{36}O$: C, 85.66; H, 9.95. Found: C, 85.57; H, 9.97.

3,5aβ,11bβ,13aα-Tetramethyl-2,4,5,5a,5bα,6,7,11b,12,13,13a,-13bβ-dodecahydro-1*H*-cyclopenta[*a*]chrysene (20). To a solution of 0.6 mmol of lithium diphenylphosphide[20] [prepared from 111.6 mg (0.6 mmol) of a 2.2 *M* hexane solution of *n*-butyllithium in 1 ml of dry tetrahydrofuran under an argon atmosphere] was added 80 μl of *N,N,N′,N′*-tetramethylethylenediamine and 36.4 mg (0.1 mmol) of the olefin **17**, and then the mixture was refluxed for 19 hr. After the addition of 1 ml of water and then isolation of the product by ether extraction,[17] including both an acid and base wash, purification of the crude product (110 mg) by preparative TLC (20% ether–petroleum ether) afforded 32 mg (9) of the corresponding phenolic olefin (R_f 0.25), mp 188–191° dec. The analytical sample, prepared by crystallization of this material from ether–hexane, also melted at 188–191°: ir ($CHCl_3$) 3600 cm^{-1} (OH); NMR ($CDCl_3$) δ 0.70, 1.01, 1.20 (3 s, 3 each, C-5a, C-11b, and C-13a CH_3), 1.61 (br s, 3, C-3 CH_3), 4.58 (br s, 1, C-9 OH), and 6.43–7.43 (m, 3, ArH).

Anal. Calcd for $C_{25}H_{34}O$: C, 85.66; H, 9.78. Found: C, 85.57; H, 9.74.

To a solution of 17.5 mg (0.05 mmol) of the 9-hydroxy olefin

above and a few crystals of 1,10-phenanthroline in 1 ml of dry tetrahydrofuran was added enough ethereal methyllithium to impart a brown color to the solution. This mixture was treated sequentially with 35 μl of triethylamine, 35 μl of hexamethylphosphoramide, and 50 μl of the *N,N,N',N'*-tetramethyldiamidophosphorochloridate,[20] and after stirring at room temperature for 17 hr, the mixture was poured into 15 ml of water. Isolation of the product by ether extraction,[17] including an acid wash, afforded 24 mg (99%) of white crystals of the corresponding phosphorodiamidate as the only volatile component by GLC (300°): ir ($CHCl_3$) 1610 cm^{-1} (C=C); NMR ($CDCl_3$) δ 0.70, 1.03, 1.20 (3 s, 3 each, C-5a, C-11b, and C-13a CH_3), 1.61 (br s, 3, C-3 CH_3), 2.58 (d, 12, J = 12 Hz, NCH_3), and 6.80–7.33 (m, 3, ArH).

This crude phosphorodiamidate was dissolved in 15 ml of ammonia and 2 ml of dry tetrahydrofuran, and ca. 3 mg of lithium was added. The blue solution was stirred for 15 min at reflux, and then 0.5 ml of ethanol was added. The ammonia was evaporated under a stream of dry nitrogen, and the residue was dissolved in 20 ml of water and extracted with 3 × 15 ml of ether. The combined ethereal extracts were washed with 2 × 15 ml of water and dried ($MgSO_4$). Evaporation of the solvent at reduced pressure afforded 21 mg of an oil which contained one volatile component by GLC (300°), and on preparative TLC (benzene) afforded 16 mg (96%) of the pentacyclic hydrocarbon **20**. Crystallization of this material from methanol and then bulb-to-bulb distillation (167° at 0.0015 mm) gave analytically pure material: mp 99–101.5°; NMR ($CDCl_3$) δ 0.70, 1.03, 1.23 (3 s, 3 each, C-5a, C-11b, and C-13a CH_3), 1.61 (br s, 3, C-3 CH_3, ArH); ir ($CHCl_3$) 3060 (ArH) and 1490, 1455, 1445, and 1385 cm^{-1}.

Anal. Calcd for $C_{25}H_{34}$: C, 89.76; H, 10.24. Found: C, 89.85; H, 10.19.

B. From the 11-Methoxy Olefin 18. Demethylation of 36.4 mg (0.1 mmol) of the 11-methoxy olefin was accomplished in 71% (25 mg) yield in the same manner as that described above for the 9-methoxy olefin **17** except that 0.3 mmol of lithium diphenylphosphide[20] [prepared from 56 mg (0.30 mmol) of diphenylphosphine and 150 μl (0.33 mol) of a 2.2 *M* hexane solution of *n*-butyllithium], 40 μl of *N,N,N',N'*-tetramethylethylenediamine, and 200 μl of dry tetrahydrofuran were used. This material, which was not further purified for combustion analysis but used directly in subsequent experiments, melted at 192–196° dec: ir ($CHCl_3$) 3590 (OH) and 1580 cm^{-1} (Ar); NMR ($CDCl_3$) δ 0.71, 1.01, 1.36 (3 s, 3 each, C-5a, C-11b, and C-13a CH_3), 1.60 (br s, 3, C-3 CH_3), and 6.35–7.53 (m, 3, ArH); TLC (benzene) R_f 0.6.

The phosphorodiamidate [26 mg crude, >99% single volatile component on GLC (300°)] was prepared from 14 mg (0.04 mmol) of the above phenol as described above in part A with 40 μl of *N,N,N',N'*-tetramethyldiamidophosphorochloridate,[21] 30 μl of triethylamine, and 30 μl of hexamethylphosphoramide in 1 ml of dry tetrahydrofuran: ir ($CHCl_3$) 3150 cm^{-1} (ArH); nmr ($CDCl_3$) δ 0.73, 1.03, 1.40 (3 s, 3 each, C-5a, C-11b, and C-13a CH_3), 1.60 (br s, 3, C-3 CH_3), 2.73 (d, 12, J = 13 Hz, NCH_3), and 6.70–7.36 (m, 3, ArH).

On reduction of this material by the same procedure as described in part A in 15 ml of dry ammonia and 2 ml of dry tetrahydrofuran with ca. 3 mg of lithium and 0.5 ml of ethanol, 10 mg (74%) of the hydrocarbon **20**, mp 97.5–99.5°, was obtained after preparative TLC (benzene, R_f 0.7) and then crystallization (methanol) of the crude product. The melting point of a mixture of this material and that, mp 99–101.5°, prepared from the 9-methoxy olefin **17** was 98.5–101.5° and quantitative peak enhancement of GLC[17] (300°) indicate only one volatile component.

1-(3-Oxobutyl)-8-methoxy-4aβ,10bβ,12aα-trimethyl-3,4,-4a,4bα,5,6,10b,11,12,12a-decahydro-2(1*H*)-chrysenone. The methoxy olefin **17** (52.4 mg, 0.144 mmol) was hydroxylated and then cleaved with 119.7 mg (0.432 mmol) of osmium tetroxide in 12 ml of dry dioxane and 0.75 ml of dry pyridine (62 hr at room temperature; osmate ester cleaved with hydrogen sulfide in 12 ml of dichloromethane), followed by treatment with 1.0 g of lead tetraacetate in 12 ml of dry tetrahydrofuran. On purification of the crude product (60 mg) by preparative TLC (40% ether–chloroform), 49 mg (88%) of the desired diketone, mp 148–150.5°, was obtained. An analytical sample, obtained after crystallization of this material from ether–hexane, was a polymorph of the original material (identical solution ir and NMR) and melted at 134–135°: ir ($CHCl_3$) 1710 cm^{-1} (C=O); NMR ($CDCl_3$) δ 0.80 (s, 3, C-4a CH_3), 1.25 (s, 2 × 3, C-10b and C-12a CH_3), 2.15 (s, 3, CH_3CO), 3.80 (s, 3, $ArOCH_3$), and 6.53–7.38 (m, 3, ArH).

Anal. Calcd for $C_{26}H_{36}O_3$: C, 78.75; H, 9.15. Found: C, 78.68; H, 9.14.

10-Methoxy-6aβ,12bβ,14aα-trimethyl,1,5,6,6a,6bα,7,8,12b,-13,14,14a,14bβ-dodecahydro-3(2*H*)-picenone (19). A solution of 19 mg (0.048 mmol) of the diketone above in 10 ml of methanol and 1 ml of 10% aqueous sodium hydroxide solution was heated at reflux for 10 hr, and then the product was isolated by benzene extraction.[17] After preparative TLC (9:2 chloroform–ether) of the crude product (22 mg) and then crystallization (hexane–dichloromethane) of the material in the band at R_f 0.45, there was obtained 12 g (66%) of the enone **19**, mp 196–198.5°. Recrystallization of this material from the same solvent mixture afforded material which melted at 197–199°, and on admixture with authentic enone,[6] mp 197–200.5°, the mix melted at 196–198.5°. The ir and NMR spectra of this material were identical with those recorded[6] previously, and the mobility of samples from the two different sequences on TLC (9:2 chloroform–ether) and GLC (300°) were indistinguishable.

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Registry No.—**1**, 50676-11-4; **2**, 29023-69-6; **3**, 54181-98-5; **4**, 54191-90-1; **5**, 54181-99-6; **6**, 54182-00-2; **7**, 54182-01-3; **8**, 54182-02-4; **9**, 54182-03-5; **10**, 54182-04-6; **11**, 54182-05-7; **12**, 54182-06-8; **13**, 54191-89-8; **14**, 54182-07-9; **15**, 53311-19-6; **16**, 54182-09-1; **17**, 54182-10-4; **17** OH analog, 54182-11-5; **17** OH analog *N,N,N',N'*-tetramethylphosphorodiamidate, 54182-12-6; **18**, 54191-68-3; **18** OH analog, 54182-13-7; **18** OH analog *N,N,N',N'*-tetramethylphosphorodiamidate, 54182-14-8; **19**, 30454-41-2; **20**, 54182-15-9; 1-trimethylsilyl-4-chloro-1-butyne, 54182-16-0; 4-hydroxy-1-butyne, 927-74-2; trimethylchlorosilane, 75-77-4; 9,10-dimethyl-(*E*)-9,13-tetradecadiene-2,5-dione, 54182-17-1; 10aβ-cyano-2,2-ethylenedioxy-7-methoxy-4aα-methyl-1,2,3,4,4a,9,10,10a-octahydrophenanthrene, 54182-18-2; 10aβ-formyl-2,2-ethylendioxy-7-methoxy-4aα-methyl-1,2,3,4,4a,9,10,10a-octahydrophenanthrene, 54182-19-3; 1-trimethylsilyl-9,10,13-trimethyl-16-(*m*-methoxyphenyl)-(*E,E*)-9,13-hexadecadien-1-yn-5-ol, 54182-20-6; 9,10,13-trimethyl-16-(*m*-methoxyphenyl)-(*E,E*)-9,13-hexadecadiene-2,5-dione, 54182-21-7; 2-(3′,4′,7′-trimethyl-10′-(*m*-methoxyphenyl)-(*E,E*)-3′,7′-decadienyl)-1-methylcyclopenten-3-ol, 54182-22-8; 6-(2′-*m*-methoxyphenylethyl)-3,5aβ,7,9aα-tetramethyl-2,4,5,5a,6α,-9,9a,9bβ-octahydro-1*H*-benz[*e*]indene, 54182-23-9; *N,N,N',N'*-tetramethyldiamidophosphorochloridate, 1605-65-8; diketone (mp 148–150.5°), 54182-24-0.

References and Notes

(1) The structural formulas containing one or more asymmetric carbon atoms depict one enantiomer, but refer to racemic compounds unless otherwise designated. In the text, the (±) prefix will be omitted, and intermediates are assumed to be racemic. The tricyclic compounds will be described by the 1*H*-benz[*e*]indene or phenanthrene nomenclature, and each racemate is arbitrarily represented by that enantiomer that has the C-9a or C-4b methyl group, respectively, in the α configuration. The pentacyclic compounds will be described by the 1*H*-cyclopenta-[*a*]chrysene or picene nomenclature, and each racemate is arbitrarily represented by that enantiomer that has the C-13a or C-14a methyl group, respectively, in the α configuration.
(2) On study leave from the Centre National de la Recherche Scientifique, France.
(3) Trainee of the National Institute of General Medical Sciences, National Institutes of Health.
(4) R. E. Ireland, D. A. Evans, D. Glover, G. M. Rubottom, and H. Young, *J. Org. Chem.*, **34**, 3717 (1969).
(5) (a) R. E. Ireland, M. I. Dawson, J. Bordner, and R. E. Dickerson, *J. Am. Chem. Soc.*, **92**, 2568 (1970); (b) R. E. Ireland, D. R. Marshall, and J. W. Tilley, ibid., **92**, 4754 (1970).
(6) R. E. Ireland, M. I. Dawson, S. C. Welch, A. Hagenbach, J. Bordner, and B. Trus, *J. Am. Chem. Soc.*, **95**, 7829 (1973).
(7) W. Nagata, M. Yoshioka, and S. Hiral, *J. Am. Chem. Soc.*, **94**, 4635 (1972).
(8) W. S. Johnson, *Acc. Chem. Res.*, **1**, 1 (1968); E. E. van Tamelen, ibid., **1**, 111 (1968); P. A. Bartlett, J. I. Brauman, W. S. Johnson, and R. A. Volkmann, *J. Am. Chem. Soc.*, **95**, 7502 (1973); E. E. van Tamelen, M. P. Seiler, and W. Wierenga, ibid., **94**, 8229 (1972).
(9) R. E. Ireland, M. I. Dawson, C. J. Kowalski, C. A. Lipinski, D. R. Marshall, J. W. Tilley, J. Bordner, and B. Trus, *J. Org. Chem.*, **40**, 973 (1975).
(10) R. E. Ireland, C. J. Kowalski, J. W. Tilley, and D. M. Walba, *J. Org. Chem.*, **40**, 990 (1975).
(11) (a) R. L. Carney and W. S. Johnson, *J. Am. Chem. Soc.*, **96**, 2549 (1974); (b) D. R. Morton, M. B. Gravestock, R. J. Parry, and W. S. Johnson, ibid., **95**, 4417 (1973); (c) W. S. Johnson, M. B. Gravestock, and B. E. McCarry, ibid., **93**, 4332 (1971).
(12) P. A. Bartlett, J. I. Brauman, W. S. Johnson, and R. A. Volkmann, *J. Am. Chem. Soc.*, **95**, 7502 (1973).

(13) G. W. Kenner and N. R. Williams, *J. Chem. Soc.*, 522 (1955).
(14) R. E. Ireland, D. C. Muchmore, and U. Hengartner, *J. Am. Chem. Soc.*, **94**, 5098 (1972).
(15) Since completion of this work the results of the work of Johnson and coworkers[12] became available. This evidence suggests the possibility that the yield of the isomer **17** in the cyclization stage of the present scheme could be improved.
(16) 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 -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, dioxane, 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, diodomethane, and methyl iodide were distilled from phosphorus pentoxide; ammonia was distilled from the tank and then from a blue lithium or sodium solution; acetone was analytical reagent grade distilled from potassium permanganate; formic acid was distilled from boric anhydride. "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.
(17) 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.
(18) 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, fiJ. Org. Chem., **21**, 1547 (1956).
(19) J. F. Young, J. A. Osborn, F. H. Jardine, and G. Wilkinson, *Chem. Commun.*, 131 (1965).
(20) F. G. Mann and M. J. Pragnell, *Chem. Ind. (London)*, 1386 (1964).
(21) E. Crunden and F. Hudson, *J. Chem. Soc.*, 3591 (1962); H. G. Cook, J. D. Ilett, B. C. Saunders, G. J. Stacey, H. G. Watson, I. G. Wilding, and S. J. Woodcock, ibid., 2921 (1949).

Experiments Directed toward the Total Synthesis of Terpenes. XXII. A Polyene Cyclization Approach to Tetradecahydropicene Derivatives for Pentacyclic Triterpene Synthesis[1]

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The syntheses of two trienols through the ketones **8** and **9** are described, and the results of the stannic chloride catalyzed cyclizations of these materials is presented. The product variation as a result of solvent changes in the cyclization of the trienol from the ketone **8** revealed the formation of significant amounts of solvent-trapped products. The synthesis of the trienol from the ketone **25** follows the same pattern as the above models, but the yield of the olefin **26** in the stannic chloride cyclization is significantly lower than in the model series. Attempts to convert the olefin **26** to a known intermediate in a previous alnusenone (**1**) total synthesis were unsuccessful. The X-ray structural analysis of the ketone **27** is presented.

In the preceding paper[4] in this series the results of a program designed to construct intermediates for the total synthesis of alnusenone (**1**) via the acid-catalyzed cyclization of the 3-methyl-2-cyclopentenol A were discussed. At the inception of this synthetic scheme two possible cyclic allylic alcohol systems were considered useful candidates for the initiation of the cyclization step.[5] In addition to the 3-methyl-2-cyclopentenol system A, the 4-methyl-2-cyclohexenol system B has significant potential. In principle cyclization of this molecule will establish a pentacyclic intermediate in which the E ring is already six-membered and bears the desired C-17[1] methyl group at a cis D/E ring fusion. Addition of the *gem*-dimethyl grouping at C-20[1] through the agency of the C-19–C-20[1] double bond that results from cyclization would then complete the construction of the triterpenoid E ring. The advantages of this concept are apparent, for it avoids not only the selective lithium–ammonia reduction of the A,E-diaromatic pentacyclic intermediate used in the initial approach[6] but also the necessity for the subsequent incorporation of the C-17[1] angular methyl group that is inherent in both preceding syntheses.[4,6] While these two operations did not pose significant problems in fact, the advantages of this proposed scheme were great enough to warrant a concurrent investigation. The results of both a model study and the cyclization of the alcohol B are presented here.

Of initial concern in this work was the development of procedures for the conversion of the dienol **24** (Chart III) to the desired cyclization substrate B. The efficient synthesis already described[7] for the dienol **24** dictated its use in the synthesis of both allylic alcohols A[4] and B, but different subsequent schemes were required in each case. In addition a model series designed to test the efficiency of the cyclization step was deemed advisable. Even though this stage of the scheme is based on the principles that have been developed in the Johnson laboratories,[5,8] the presently proposed