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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.

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

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Received October 18, 1974

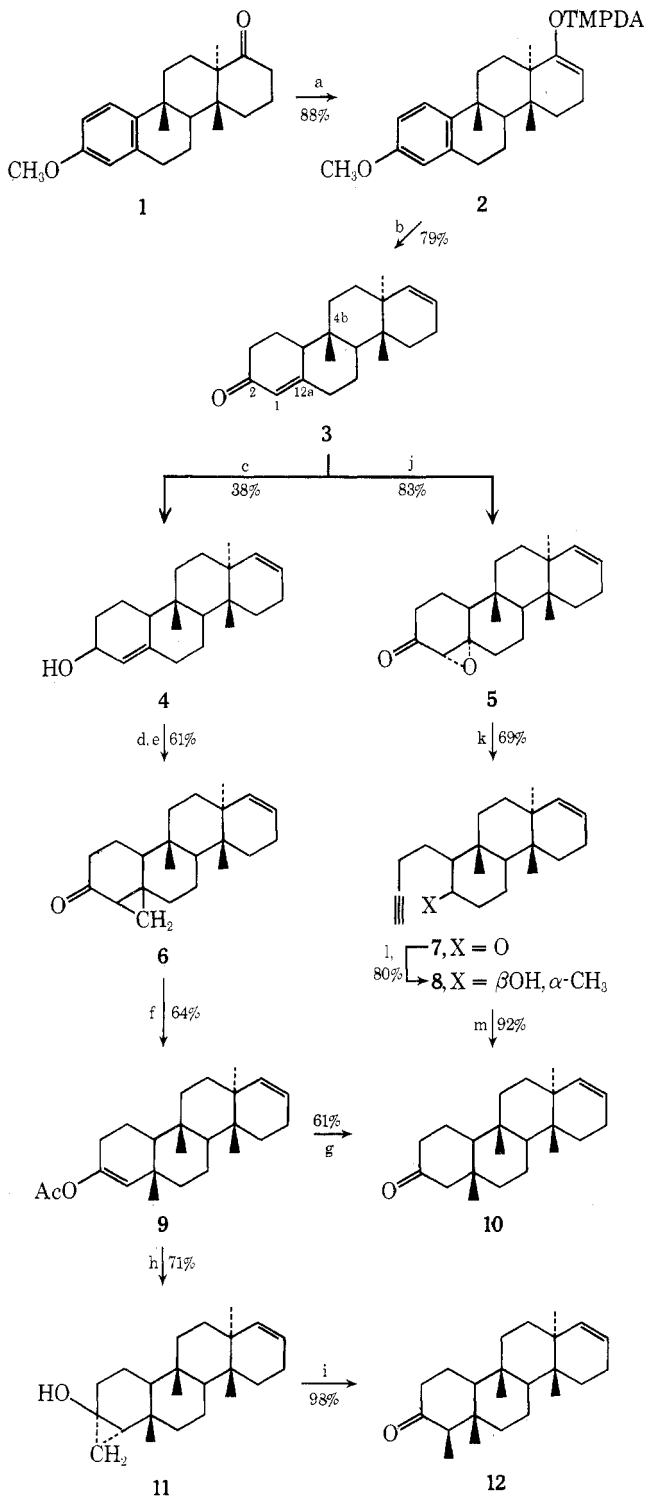
The conversion of the tetracyclic ketone **1** to the triterpene shionone (**23**) is explored by two alternative sequences. Both approaches rely on the introduction of the more or less completely formed side chain and then modification of the aromatic A ring. One unsuccessful approach entails incorporation 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.

Chart I
Ring A Modification of Tetracyclic Ketone 1[a]



[a] a, LiN[CH(CH3)2]2, THF; ClPO[N(CH3)2]2; b, Li, NH3, THF, t-BuOH; 5 *N* HCl, ETOH; c, LiR3BH, THF; d, Zn–Cu, CH2I2, Et2O; e, CrO3 · 2Py, CH2Cl2; f, Li, NH3, THF; Ac2O; g, KOH, EtOH; h, CH3Li, DME; Zn–Cu, CH2I2, Et2O; i, HCl, H2O, EtOH; j, H2O2, aq NaOH, CH3OH; k, *p*-TsNHNH2, HOAc, CH2Cl2; l, CH3Li, Et2O; m, CF3CO2H–(CF3CO)2O, CH3COCH3, CH3OH, aq HCl.

The C-4bβ angular methyl group severely shields the C-12a carbon from attack by a reagent from the desired β face of the molecule. Thus, while conjugate addition of a methyl group per se [LiCu(CH3)2] to this enone system would be expected to lead to a cis-fused product, even a reagent known to produce trans-fused rings systems in other molecules[9] (AlEt3–HCN[10]) gave no reaction or predominantly a low yield of cis-fused product here.[11] To overcome this stereochemical situation a method was sought that relied on the *intra*molecular orientation of carbon–carbon bond formation at C-12a, and two such schemes were investigated.

One method relies on the orientation[12] of the Simmons–Smith methylenation reaction[13] by the alcohol function in an allylic alcohol system, and here requires the generation of a C-2β (axial) hydroxyl group. The formation of the desired allylic alcohol **4** proved itself to be a thorny problem, for standard hydride reductions ($LiAlH_4$, $NaBH_4$) produced little, if any, of the β (axial) alcohol. The only satisfactory method for reduction of this enone system was through the use of lithium perhydro-9b-boraphenalylhydride recently developed by Brown and Dickason[14] and utilized effectively in an earlier stage[5] in the synthesis. Unfortunately, probably owing to the flat, unhindered character of the enone system, the yield of the desired β (axial) alcohol **4** was not as high as the yields experienced elsewhere when saturated ketones were reduced.[14] It was possible, however, after a rather tedious and inefficient chromatographic sequence, to realize a fair yield of the desired allylic alcohol **4** and pursue the sequence further, as shown in Chart I.

These remaining stages resulted in quite satisfactory yields of the respective intermediate products. A useful consequence, of course, of the methylenation process for the formation of the C-12a bond in the β (axial) orientation is that lithium–ammonia reduction[15] of the cyclopropyl ketone **6** generates the enolate anion necessary for the introduction of the C-1 methyl group by methylation. In spite of the fact that this methylation would be expected to take place through the unhindered, α (axial) approach to the tetracyclic enolate, direct methylation[16] of the enolate generated during reduction of the cyclopropyl ketone **6** or methylation[17] of the enolate regenerated in dimethoxyethane from the intermediate enol acetate **9** were singularly unsuccessful. The desired monomethylated ketone in low yield was always accompanied by unmethylated material in much higher yield. While the reasons for this behavior are unclear, a convenient solution to the problem was found in the Simmons–Smith methylenation[13] of this same enolate—a procedure suggested by the work of Whitlock and Overman.[18] While it was possible to achieve the desired end result by removal of the ammonia and then addition of the Simmons–Smith reagent directly to the enolate formed from reduction of the cyclopropyl ketone **6**, a cleaner product was obtained in more reproducible yields if this enolate was regenerated in dimethoxyethane with methyllithium from the initially trapped enol acetate **9**. Contrary to the results reported by Whitlock and Overman,[18] there is no question but that the expected cyclopropyl alcohol is the primary product of this process. By rapid and careful chromatography of the crude product, it is possible to remove all the iodide–iodine formed and isolate the cyclopropyl alcohol **11** in good yield. This material is quite labile to traces of iodide ion in hydroxylic solvents and is rapidly cleaved to the corresponding methylated ketone. This lability and the failure to remove these by-products probably accounts for the fact that Whitlock and Overman[18] did not observe the formation of a cyclopropyl alcohol in their investigations. For preparative purposes a more convenient means of cyclopropyl alcohol cleavage is the use of mineral acid, which not only provides for the cleavage but also isomerizes the initially α (axial) methyl group.

The overall yield of the ketone **12** from the enone **3** by this sequence is only 10.3%, and the route suffers primarily

from the only fair yield of the allylic alcohol **4** and the tedious procedure necessary to achieve even that result. As a consequence of this experience another sequence was investigated in which the stereochemical outcome of the formation of a carbon–carbon bond at C-12a is controlled *in a desirable fashion* by the C-4bβ methyl group. For this result to pertain it is necessary to plan for the formation of the C-1–C-12a ring bond which is α (equatorial) to the B ring. Such a plan implies the prior introduction of the potential C-12a methyl group, as well as the cleavage and reformation of the C-1–C-12a bond which already exists in the enone **3**. A sequence which involved just such a process is outlined in Chart I, and in spite of what at first sight seems inefficiency owing to the necessity of ring cleavage, this route is significantly more efficient than that just described.

Utilization of the sequence developed by Eschenmoser and coworkers[19] provided an excellent means for cleavage of the A ring of the enone **3** without the loss of any carbon atoms. Owing to the diversity of the functionality that results from the Eschenmoser cleavage, it was now possible to incorporate the potential C-12a angular methyl group through the direct addition of methyllithium to the acetylenic ketone **7** without the necessity of incorporating blocking groups in the sequence. With the acetylenic alcohol **8** in hand the stage was set for the re-formation of the C-1–C-12a ring bond through cyclization. The pioneering work of Peterson[20] and the extensive work of Johnson and Lansbury and their coworkers[21] provided the basis for the selection of the reaction conditions. Confidence that the stereochemistry of the molecule that would result from this cyclization would be that with the C-12a methyl group in the desired β (axial) orientation stemmed from the extensive previous experience[22] in these laboratories that demonstrated the stereochemical control provided by the axial C-4bβ methyl group during similar cationic ring closures. It was nevertheless gratifying to find that cyclization of the acetylenic alcohol **8** in trifluoroacetic acid led to an enol trifluoroacetate in excellent yield and that hydrolysis of this intermediate provided the same saturated ketone **10** that was obtained on saponification of the corresponding enol acetate **9** from the previously described route. The convergence of these two routes at this point serves to confirm the β (axial) orientation of the C-12a methyl group, for the β (quasi-axial) assignment of the configuration of the C-2 hydroxyl group in the allylic alcohol **4**—and hence the orientation of the Simmons–Smith methylenation reaction—rests on firm ground. In view of the ease with which the enol trifluoroacetate could be isolated from this cyclization and the already proven utility of the enol acetate **9** for the incorporation of the remaining methyl group at C-1, the present route seemed well suited to the construction of the shionone A ring, and attention was turned to the introduction of the side chain in ring D.

Since the general plan for the total synthesis of shionone (**23**) entailed the incorporation of the ring D side chain and then modification of the aromatic A ring by the process discussed above, the tetracyclic ketone **1** again became the starting point. While the ketone functionality in the D ring of this material would obviously serve to introduce the two required alkyl groups in the adjacent α position, the efficiency and stereochemical outcome of these alkylation reactions were circumspect. In addition such a plan incorporates the potential difficulties that would be associated with the ultimate necessary removal of what would then be a very hindered ketone function. In order to circumvent these anticipated chemical problems, as well as have a sound basis for the stereochemical results, means were sought to remove the existing ring D ketone and at the same time introduce activating functionality external to the ring system. This plan was effectively accomplished (Chart II) by a two-step process that led from the tetracyclic ketone **1** through the chloro aldehyde **13** from the Vilsmeier reaction[23] and then by lithium–ammonia reduction–methylation[16] to the aldehyde **14**. The yields in this process were quite satisfactory, and the efficiency of the structural changes that attend the reduction–methylation step is noteworthy. The stereochemical outcome of the methylation of the enolate from the lithium–ammonia reduction of the chloro aldehyde **13** is well precedented[24] in similar systems, but the preparative use of α,β-unsaturated aldehydes in such reductions to generate useful aldehyde enolates appears[25] to be novel. As might be expected, the conditions for the reduction stage had to be carefully controlled (see Experimental Section) in order to prevent dimerization and overreduction.

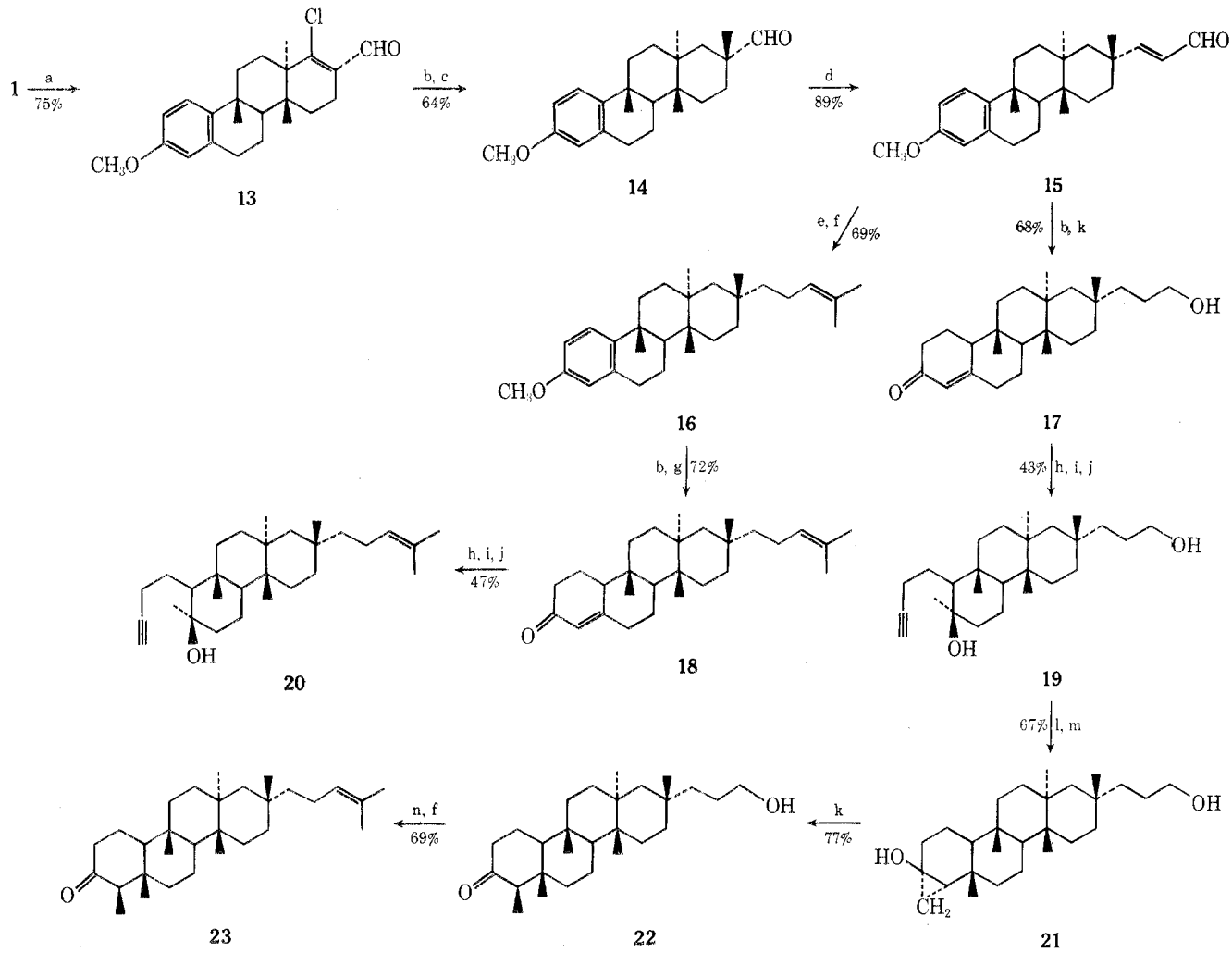
With an eye toward the rapid completion of the side chain, the aldehyde **14** was quantitatively reduced to the corresponding primary alcohol with lithium aluminum hydride and efforts were made to convert this alcohol to the iodide preparative to a coupling reaction[26] with π-(1,1-dimethylallyl)–nickel bromide complex. Unfortunately, both the neopentyl character and the severe steric congestion about this axial hydroxymethyl grouping thwarted all attempts to prepare the iodide or other halides. Reactions of the alcohol with triphenyl phosphite–methyl iodide,[27] triphenylphosphine, carbon tetrabromide, and carbon tetrachloride,[28] and thionyl chloride–quinoline led either to recovered alcohol after no reaction or a plethora of products that resulted from the intervention of cationic species that led to backbone rearrangements.

To overcome these difficulties an alternate scheme was developed for the addition of the remainder of the side chain through the use of two successive Wittig-type condensations. The aldehyde **14** was first converted to the unsaturated aldehyde **15** by the efficient formylolefination procedure of Nagata and Hayase,[29] and after reduction[30] of the unsaturated aldehyde **15** with triethylsilane in the presence of tris(triphenylphosphine)rhodium chloride, the process was completed in 30% overall yield from the tetracyclic ketone **1** by the condensation of the saturated aldehyde with isopropylidenephosphorane.

With the aromatic olefin **16** thus in hand, modification of the A ring by the method developed above was projected to complete the synthesis. Indeed this process proceeded well (Chart II) up to the stage of final reformation of the A ring from the acetylenic alcohol **20**. This approach irreversibly broke down at this point, for the acidic conditions necessary to effect the cyclization invariably resulted in acid-catalyzed hydration of the side-chain trisubstituted double bond. When modifications were made in the reaction conditions in order to avoid this addition reaction by reducing the acidity, lowering the temperature, and/or changing the acid catalyst, it was found that the sequence of events involved initial rapid addition to the side-chain double bond. In experiments where the conditions were vigorous enough, cyclization of the acetylenic alcohol was a subsequent step. Indeed, it was possible to hydrate the side-chain double bond without affecting the acetylenic alcohol system. The lability of this side-chain unsaturation was a surprise, particularly when the model system used to explore this sequence—the acetylenic alcohol **8**—was specifically chosen with this side chain in mind and itself contains an isolated (albeit disubstituted) double bond.

The solution to this last problem dictated a change in methodology for either the A ring modifications or the

Chart II
Conversion of Tetracyclic Ketone 1 to (±)-Shionone (23)[a]



[a] a, $POCl_3$, DMF; b, Li, NH_3, THF, *t*-BuOH; c, $NaO_2CC_6H_5$, CH_3I; d, NaH, $(EtO)_2POCH_2CH{=}NC_6H_{11}$, THF, aq $(CO_2H)_2$, C_6H_6; e, Et_3SiH, $[(C_6H_5)_3P]_3RhCl$, C_6H_6, CH_3COCH_3, aq HCl; f, $(C_6H_5)_3PCH(CH_3)_2{}^+I^-$, C_6H_5Li, THF; g, $(CO_2H)_2$, aq EtOH, NaOH, aq EtOH; h, H_2O_2, aq NaOH, CH_3OH–CH_2Cl_2; i, *p*-TsNHNH$_2$, HOAc–CH_2Cl_2; j, CH_3Li, THF; k, aq HCl, EtOH; l, CF_3CO_2H–$(CF_3CO)_2O$; m, $LiN[CH(CH_3)_2]$, THF, Zn–Ag, CH_2I_2, Et_2O; n, $CrO_3 \cdot 2Py$, CH_2Cl_2.

side-chain construction. Rather than tamper with the more intricate procedures in the former process, a reshuffling of the steps in the side-chain construction seemed advisable. Since the offending functionality in the side chain was the double bond that resulted from the last stage in the process, this reaction was deferred until the completion of the A ring. Thus, complete reduction of the unsaturated aldehyde **15** led in good yield to the hydroxyenone **17**, which could be carried through the A ring synthesis without major incident (Chart II). The result of the trifluoroacetic acid catalyzed cyclization of the acetylenic alcohol **19** was the expected bis trifluoroacetate, but this posed no significant experimental problem in the subsequent stages that completed the shionone (**23**) synthesis.

A noteworthy point did come to light when the bis trifluoroacetate was used to generate the enolate in ring A. Under the conditions used earlier for the generation and methylenation of the enolate from the enol acetate **9**, none of the expected cyclopropyl alcohol was observed, and the product was the C-1 demethyl keto alcohol. Model studies showed that this was not the result of hydrolysis or protonation of the enolate by traces of moisture, nor was it the result of the failure of the methylenation reaction. Reasoning that the enolate generated by methyllithium addition[17] was being rapidly protonated by the initially formed 1,1,1-trifluoroacetone, an aminolysis reaction was substituted for the Grignard reaction with salutory results. The enol trifluoroacetate was readily cleaved by lithium diisopropylamide, and the resulting enolate behaved as expected in the methylenation reaction. This observation should render enol trifluoroacetates generally useful for the formation of ketone enolates, and coupled with the addition of trifluoroacetic acid to acetylenes, the overall process is an interesting ketone synthesis.

Experimental Section[31]

8-Methoxy-4aβ,10bβ,12aα-trimethyl-3,4,4a,4bα,5,6,10b,-11,12,12a-decahydrochrysen-1-yl Tetramethylphosphorodiamidate (2). To a solution of lithium diisopropylamide prepared from 8 ml (57 mmol) of diisopropylamine and 13 ml of a 2.84 *M* hexane solution of *n*-butyllithium in 150 ml of dry ether under an argon atmosphere was added over a 10-min period a solution of 2.27 g (7 mmol) of the ketone **1** in 20 ml of dry tetrahydrofuran and 8 ml of *N,N,N',N'*-tetramethylethylenediamine. The mixture was then cooled in an ice bath, and 15 ml (81 mmol) of tetramethyldiamidophosphorochloridate[32] was added dropwise. After the resulting yellow solution was allowed to warm to room temperature and then stirred for 1.5 hr, the mixture was poured into ice and 400 ml of 10% aqueous hydrochloric acid, and the product was isolated by ether extraction[33] including a base wash. On chromatography of

the crude product on 200 g of silica gel, 2.81 g (88%) of the phosphorodiamidate **2**, mp 108–111° (vacuum), was eluted with 1800 ml of 10% acetone–ethyl acetate after an initial wash with 800 ml of ethyl acetate and then 600 ml of 5% acetone–ethyl acetate. The analytical sample, obtained after cystallization of a portion of this material from ether–heptane, also melted at 108–111° (vacuum): ir ($CHCl_3$) 1670 (C=C), 1605, 1500 (Ar), 1305 (P–N), and 980 cm^{-1} (P–O–C); NMR ($CDCl_3$) δ 1.02 (s, 3, C-4a CH_3), 1.22 (s, 2 × 3, C-10b and C-12a CH_3), 2.70 (d, 12, J = 10 Hz, NCH_3), 3.75 (s, 3, OCH_3), and 5.20 (m, 1, C=CH).

Anal. Calcd for $C_{26}H_{41}O_3N_2P$: C, 67.80; H, 8.97; N, 6.08; P, 6.73. Found: C, 67.96; H, 8.86; N, 6.16; P, 6.64.

8-Methoxy-4aβ,10bβ,12aα-trimethyl-3,4,4a,4bα,5,6,10b,-11,12,12a-decahydrochrysene. To a solution of 37 mg (5.3 mg-atoms) of lithium in 50 ml of dry ammonia and 10 ml of dry tetrahydrofuran under an argon atmosphere was added a solution of 210 mg (0.45 mmol) of the phosphorodiamidate **2** in 6 ml of dry tetrahydrofuran. After 1.5 hr the blue color faded, and an additional 37 mg (5.3 mg-atoms) of lithium was added. After stirring for 3.5 hr longer, the reaction mixture was treated with 400 mg of sodium benzoate and then 200 mg of solid ammonium chloride. After the ammonia was evaporated in a stream of argon, the residue was dissolved in 50 ml of water, and the product was isolated by ether extraction[33] including an acid and base wash. On preparative TLC (30% ether–petroleum ether) of the crude product there was obtained 115 mg (82%) of the tetracyclic olefin (R_f 0.7) as a colorless oil. The analytical sample was obtained after further preparative TLC (30% ether–petroleum ether) and then evaporative distillation (120°, 0.01 mm) of a portion of this material: ir ($CHCl_3$) 1605 and 1500 cm^{-1} (Ar); NMR ($CDCl_3$) δ 0.82 (s, 3, C-4a CH_3), 1.00 (s, 3, C-12a CH_3), 1.22 (s, 3, C-10b CH_3), 3.77 (s, 3, $ArOCH_3$), 5.52 (m, 2, CH=CH), and 6.50–7.17 (m, 3, ArH).

Anal. Calcd for $C_{22}H_{30}O$: C, 85.11; H, 9.74. Found: C, 84.96; H, 9.64.

4bβ,6aα,10aβ-Trimethyl-4,4aα,4b,5,6,6a,9,10,10a,10bα,11,12-dodecahydro-2(3*H*)-chrysenone (3). A. From the Phosphorodiamidate 2. A solution of 370 mg (53 mmol) of lithium wire in 550 ml of dry ammonia and 140 ml of dry tetrahydrofuran was stirred for 30 min, and then a solution of 1.53 g (3.32 mmol) of the phosphorodiamidate **2** in 30 ml of dry tetrahydrofuran was injected all at once with a syringe. After 5 hr an additional 960 mg (139 mmol) of lithium and 85 ml of dry *tert*-butyl alcohol were added. After the reaction had stirred for an additional 2 hr, the excess lithium was decomposed with 20 ml of methanol, and the ammonia was allowed to evaporate overnight. The gray residue was treated with 500 ml of water, and the product was isolated by ether extraction.[33] A solution of the resulting residue in 200 ml of ethanol and 130 ml of 5 N aqueous hydrochloric acid was heated at 65–70° for 40 min in an argon atmosphere. The cooled reaction mixture was then poured into 500 ml of water, and the product was isolated by ether extraction,[33] including a base wash. On chromatography of the dark yellow, oily residue on 100 g of silica gel there was obtained 782 mg (79%) of the enone **3**, mp 88–92°, by elution with 600 ml of 50% ether–petroleum ether. Crystallization (ethanol–water) and then sublimation (120°, 0.01 mm) of a portion of this material gave the analytical sample: mp 94–97°; ir ($CHCl_3$) 1665 (C=O) and 1620 cm^{-1} (C=C); NMR ($CDCl_3$), δ 0.87 (s, 2 × 3, C-4b and C-10a CH_3), 1.07 (s, 3, C-6a CH_3), 5.47 (m, 2, CH=CH), and 5.92 (s, 1, O=C–CH=C).

Anal. Calcd for $C_{21}H_{30}O$: C, 84.54; H, 10.13. Found: C, 84.51; H, 10.22.

B. From Tetracyclic Olefin. A stirred solution of 182 mg (0.58 mmol) of the above olefin in 60 ml of dry ammonia, 20 ml of dry tetrahydrofuran, and 10 ml of dry *tert*-butyl alcohol under an argon atmosphere was treated with 111 mg (16 mg-atoms) of lithium. After 2 hr the excess lithium was decomposed with 3 ml of methanol, and the ammonia was evaporated in a stream of argon. The gray residue was dissolved in 150 ml of water, and the product was isolated by ether extraction.[33] A solution of the crude product in 30 ml of ethanol and 20 ml of 5 N aqueous hydrochloric acid was heated at 65–70° for 40 min under an argon atmosphere, and after dilution of the cooled reaction mixture with 100 ml of water, the product was isolated by ether extraction,[33] including a base wash. The crude product was chromatographed on 22 g of silica gel, and elution with 175 ml of 50% ether–petroleum ether afforded 153 mg (78%) of the enone **3**, mp 91–94°, that was identical (mixture melting point, ir, NMR) with the material prepared above in part A.

2β-Hydroxy-4bβ,6aα,10aβ-trimethyl-2α,3,4,4aα,4b,5,6,6a,9,-10,10a,10bα,11,12-tetradecahydrochrysene (4). Following the general procedure of Brown and Dickason,[14] an ice-cold solution of 781 mg (2.62 mmol) of the enone **3** in 15 ml of dry tetrahydrofuran under an argon atmosphere was treated with 6.0 ml (5.1 mmol) of a 0.85 M tetrahydrofuran solution of the trialkylborohydride. After 30 min the organoborane was decomposed by the sequential addition of 1.0 ml of 3 N aqueous sodium hydroxide solution and 2.0 ml of 30% hydrogen peroxide. The reaction mixture was immediately poured into 50 ml of saturated aqueous sodium carbonate solution and the product isolated by ether–benzene (4:1) extraction. The crude product was chromatographed on 100 g of Florisil which was eluted with 59% ether–petroleum ether. The first 300 ml eluted 75 mg of a mixture of nonpolar products that was discarded. The next 200 ml afforded 183 mg (23%) of the axial alcohol **4**, mp 130–133°. Further elution with 400 ml of the same solvent gave 316 mg of a mixture of the two alcohols which on further separation by preparative TLC (10% ether–chloroform) gave 188 mg (24%) of the equatorial alcohol (R_f 0.4) and 114 mg (15%) of the axial alcohol **4** (R_f 0.5). Finally, washing the column with 500 ml of ether gave 206 mg (26%) of the equatorial alcohol, mp 119–120° (vacuum). The total yield of axial alcohol **4** was 296 mg (38%) and that of the equatorial alcohol was 394 mg (50%).

The analytical sample of the axial alcohol **4**, prepared by crystallization of a portion of similar material from another reduction experiment from ethyl acetate–heptane and then ethanol–water, melted at 131–134° (vacuum): ir 3600, 3450 (OH), and 1650 cm^{-1} (C=C); NMR ($CDCl_3$) δ 0.85 (s, 2 × 3, C-4b and C-10a CH_3), and 1.05 (s, 3, C-6a CH_3), 4.00–4.20 (m, 1, CHO), 5.48 (m, 2, CH=CH), and 5.50–5.77 (m, 1, OCCH=C).

Anal. Calcd for $C_{21}H_{32}O$: C, 83.94; H, 10.73. Found: C, 83.87; H, 10.78.

The analytical sample of the equatorial alcohol was prepared in the same fashion and melted at 114–116° (vacuum): ir ($CHCl_3$) 3605, 3450 (OH), and 1655 cm^{-1} (C=C); NMR ($CDCl_3$) δ 0.77, 0.82, and 1.05 (s, 3 each, C-4b, C-6a, and C-10a CH_3), 3.95–4.30 (m, 1, CHO), and 5.37–5.53 (m, 3, CH=C).

Anal. Calcd for $C_{21}H_{32}O$: C, 83.94; H, 10.73. Found: C, 83.93; H, 10.87.

1β,12aβ-Methano-4bβ,6aα,10aβ-trimethyl-1α,4,4aα,4b,5,6,-6a,9,10,10a,10bα,11,12,12a-tetradecahydro-2(3*H*)-chrysenone (6). To a suspension of 4.0 g (57 mmol) of zinc–copper couple[34] in 4.6 ml (57 mmol) of diiodomethane and 60 ml of dry ether was added a solution of 638 mg (2.21 mmol) of the axial alcohol **4** in 10 ml of dry ether, and the resulting mixture was heated at reflux under an argon atmosphere for 4 hr. After cooling, the reaction mixture was poured into 100 ml of saturated aqueous sodium carbonate, and the product was isolated by ether–benzene (4:1) extraction.[33] On chromatography of the product on 250 g of grade III alumina, elution with 600 ml of 3% methanol–ether gave 512 mg (80%) of the corresponding cyclopropyl alcohol, mp 135–139° (vacuum): ir ($CHCl_3$) 3600, 3450 cm^{-1} (OH); NMR ($CDCl_3$) δ 0.85, 0.95, 1.05 (3 s, 3 each, C-4b, C-6a, and C-10a CH_3), 4.07–4.43 (m, 1, CHO), and 5.47 (s, 2–CH=CH–)

After the procedure of Radcliffe and Rodehorst,[35] a solution of 512 mg (1.69 mmol) of the above cyclopropyl alcohol in 8 ml of dry dichloromethane was added under an argon atmosphere to a solution of 1.62 ml (20 mmol) of dry pyridine and 1.00 g (10 mmol) of anhydrous chromium trioxide in 50 ml of dry dichloromethane, and the red solution was stirred for 10 min. The dark mixture was then filtered through a pad of grade III alumina with the aid of 200 ml of ether. Evaporation of the solvents from the filtrate at reduced pressure afforded 490 mg (77%, 61% overall) of the ketone **6**, mp 149–152° (vacuum). The analytical sample, prepared from a portion of this material by preparative TLC (50% ether–petroleum ether) and then crystallization from ether–hexane, melted at 150–153° (vacuum): ir ($CHCl_3$) 1670 cm^{-1} (C=O); NMR ($CDCl_3$) δ 0.90, 1.02, 107 (3 s, 3 each, C-4b, C-6a, and C-10a CH_3), and 5.47 (s, 2, CH=CH).

Anal. Calcd for $C_{22}H_{32}O$: C, 84.56; H, 10.32. Found: C, 84.49; H, 10.39.

2-Acetoxy-4bβ,6aα,10aβ,12aβ-tetramethyl-3,4,4aα,4b,5,6,6a,-9,10,10a,10bα,11,12,12a-tetradecahydrochrysene (9). To an argon-protected solution of 18 mg (2.6 mg-atoms) of lithium in 60 ml of dry ammonia and 20 ml of dry tetrahydrofuran was added a solution of 203 mg (0.65 mmol) of the cyclopropyl ketone **6** in 5 ml of dry tetrahydrofuran. After stirring for 1.5 hr, the blue color faded; an additional 18 mg (2.6 mg-atoms) of lithium was then added, and the mixture was stirred for 2.5 hr. Most of the ammonia was then removed by evaporation in a stream of argon through a mercury bubbler, and the resulting gray suspension was treated

with 5 ml (53 mmol) of dry acetic anhydride at room temperature. After stirring for 6 hr, the reaction mixture was poured into a mixture of ice and 70 ml of 10% aqueous potassium hydroxide solution, and the product was isolated by ether–benzene (1:1) extraction.[33] On chromatography of the crude product (285 mg) on 30 g of silica gel, elution with 150 ml of 20% ether–petroleum ether gave 146 mg (64%) of the enol acetate **9**, mp 119–121° (vacuum). The analytical sample, prepared from a portion of this material by preparative TLC (20% ether–petroleum ether) and crystallization from ether–hexane, melted at 121–123° (vacuum): ir ($CHCl_3$) 1755 (C=O), 1690 (C=C), and 1220 cm^{-1} (C–O–C); NMR (CCl_4) δ 0.78, 0.88 (2 s, 3 each, C-4b, and C-10b CH_3), 1.02 (s, 2 × 3, C-6a and C-12a CH_3), 2.00 (s, 3, CH_3CO), 4.97 (s, 1, C-1 H), and 5.40 (s, 2, CH=CH).

Anal. Calcd for $C_{24}H_{36}O_2$: C, 80.85; H, 10.18. Found: C, 81.05; H, 10.23.

Further elution of the column with 25 ml of the same solvent mixture gave 37 mg of a mixture that consisted of approximately equal parts of the enol acetate **9** and the Δ^2-enol acetate of the starting ketone **6** (**2-acetoxy-1β,12aβ-methano-4bβ,6aα,10aβ-trimethyl-1,4,4aα,4b,5,6,6a,9,10,10a,10bα,11,12,12a-tetradecahydrochrysene**) on the basis of the comparative integration of the acetyl methyl signals at δ 2.00 and 2.03 in the NMR spectrum. An analytically pure sample of the latter Δ^2-enol acetate was obtained from another similar experiment after preparative TLC (20% ether–petroleum ether) and then crystallization of the material with R_f 0.4 from hexane and melted at 110–112° (vacuum): ir (CCl_4) 1755 (C=O), 1685 (C=C), and 1220 cm^{-1} (C–O–C); NMR (CCl_4) δ 0.85, 0.98, and 1.03 (3 s, 3 each, C-4b, C-6a, and C-10a CH_3), 2.03 (s, 3, CH_3CO), 4.80–5.05 (m, 1, C-3 H), and 5.40 (s, 2, CH=CH).

Anal. Calcd for $C_{24}H_{34}O_2$: C, 81.31; H, 9.67. Found: C, 81.46; H, 9.75.

Saponification of this Δ^2-enol acetate in aqueous, alcoholic potassium hydroxide solution afforded a 70% yield of the cyclopropyl ketone **6**, mp 123–126°, alone or in admixture with authentic material of the same melting range.

Finally, continued elution of the column with 100 ml of the same solvent mixture afforded 10 mg (5%) of the ketone **10**, mp 150–158°. Further purification of this material by preparative TLC (40% ether–petroleum ether) and then crystallization from hexane–dichloromethane gave material that melted at 172–176°, alone or in admixture with authentic ketone **10**, mp 172–176°, prepared below by hydrolysis of the enol acetate **9**.

4bβ,6aα,10aβ,12aβ-Tetramethyl-3,4,4aα,4b,5,6,6a,9,10,10a,-10bα,11,12,12a-tetradecahydro-2(1*H*)-chrysenone (10). A. From Enol Acetate 9. A solution of 90 mg (0.25 mmol) of the enol acetate **9** and 180 mg (2.7 mmol) of potassium hydroxide in 5 ml of ethanol was stirred at room temperature for 14 hr under argon atmosphere. The mixture was then diluted with water, and the product was isolated by ether–benzene (1:1) extraction.[33] Purification of the crude product by preparative TLC (40% ether–petroleum), then crystallization from hexane–dichloromethane, and finally sublimation at 160–170° and 0.025 mm gave 46 mg (61%) of analytically pure ketone **10**: mp 172–176° (vacuum); ir ($CHCl_3$) 1705 cm^{-1} (C=O); NMR ($CDCl_3$) δ 0.82 (s, 3), 0.90 (s, 6), and 1.06 (s, 3) (C-4b, C-6a, C-10a, and C-12a CH_3), and 5.48 (s, 2, CH=CH).

Anal. Calcd for $C_{22}H_{34}O$: C, 84.02; H, 10.90. Found: C, 83.90; H, 10.99.

B. From Acetylenic Alcohol 8. A mixture of 2.0 ml of trifluoroacetic acid and 0.6 ml of trifluoroacetic anhydride was cooled in a −18° bath; 1.6 ml of this cold solution was then added to 16.0 mg (0.051 mmol) of the acetylenic alcohol **8** at −18°, and the mixture was stirred at this temperature for 20 min. The pressure in the system was then reduced with a vacuum pump, and the cooling bath was then removed to facilitate evaporation of the solvents. Most of the liquid was gone within 5 min, but the residual oil was dried at room temperature for 20 min at ca. 0.05 mm pressure. This oil was handled so as to avoid prolonged contact with moist air and appeared to be the desired enol trifluoroacetate: ir ($CHCl_3$) 1790 (CF_3CO), 1695 (–OC=C–), 1385 (CH_3), and 1220, 1170, 1140 cm^{-1} (C–O–C and CF_3); no remaining 3300 cm^{-1} (–C≡CH); NMR ($CDCl_3$) δ 0.81, 0.90, 1.04 (3 s, 3, 3, and 6, respectively, C-4a, C-6a, C-10a, and C-12a CH_3), 5.28 (m, 1, CF_3CO_2C=CH), and 5.44 (s, 2, HC=CH); analysis by GLC (250°) showed only one peak at retention time 1.2 min.

A solution of this crude enol trifluoroacetate in 1 ml of acetone and 1 ml of methanol was treated with 5 drops of water and 5 drops of 10% aqueous hydrochloric acid and then stirred at room temperature for 75 min. After neutralization of this solution with solid sodium bicarbonate, the product was isolated by ether extraction.[33] Purification of the crude product (17.5 mg) by preparative TLC (40% ether–petroleum ether) afforded 14.7 mg (92%) of the tetracyclic ketone **10** as a white solid, mp 166–172° (vacuum); the ir and NMR spectra of this material were identical with those of purified ketone **10** prepared in part A above. Crystallization of this solid from dichloromethane–hexane afforded white crystals, mp 170–174° (vacuum), alone or in admixture with material prepared above, mp 172–176° (vacuum), in part A.

2β-Hydroxy-1α,2α-methano-4bβ,6aα,10aβ,12aβ-tetramethyl-1β,2,3,4,4aα,4b,5,6,6a,9,10,10a,10bα,11,12,12a-hexadecahydrochrysene (11). A solution of 153 mg (0.43 mmol) of the enol acetate **9** in 5 ml of dry dimethoxyethane was added to an argon-protected solution of methyllithium (0.7 ml, 1.2 mmol), and the mixture was stirred at room temperature for 30 min. To this solution was added by syringe the supernatant solution from the preparation of the Simmons–Smith reagent from 1.20 g (17 mmol) of zinc–copper couple[34] and 1.40 ml (1.20 mmol) of diiodomethane in 17 ml of dry ether. After stirring in an ice bath for 1 hr, the reaction mixture was poured into 50 ml of saturated aqueous sodium carbonate solution, and the product was isolated by ether–benzene (1:1) extraction[33] including a base and 10% aqueous sodium thiosulfate solution wash. On chromatography of the crude material on 70 g of grade III alumina, elution with 200 ml of ether gave 100 mg (71%) of the cyclopropyl alcohol **11**, mp 161–165° (vacuum). The analytical sample, obtained after crystallization of a portion of this material from dichloromethane–hexane, melted at 166–168° (vacuum): ir ($CHCl_3$) 3600, 3450 (OH), and 1180 cm^{-1} (C–O–C); NMR ($CDCl_3$) δ 0.80, 0.87, 1.02, and 1.15 (4 s, 3 each, C-4b, C-6a, C-10a, and C-12a CH_3), and 5.42 (s, 2, CH=CH).

Anal. Calcd for $C_{23}H_{36}O$: C, 84.09; H, 11.04. Found: C, 83.85; H, 11.13.

1β,4bβ,6aα,10aβ,12aβ-Pentamethyl-3,4,4aα,4b,5,6,6a,9,10,-10a,10bα,11,12,12a-tetradecahydro-2(1*H*)-chrysenone (12). A solution of 161 mg (0.49 mmol) of the cyclopropyl alcohol **11** and 1 ml of concentrated hydrochloric acid in 12 ml of ethanol was heated under reflux in an argon atmosphere for 1 hr. After cooling, the solution was diluted with 50 ml of water, and the product was isolated by ether extraction,[33] including a base wash. The resulting material amounted to 157 mg (98%) of the ketone **12**, mp 169–176° (vacuum), from which the analytical sample, mp 178–182° (vacuum), was prepared by preparative TLC (40% ether–petroleum ether) and then sublimation at 150–155° and 0.7 mm: ir ($CHCl_3$) 1705 cm^{-1} (C=O); NMR ($CDCl_3$) δ 0.73 (s, 3), 0.83 (s, 4.5), 0.95, (s, 4.5), and 1.05 (s, 3) (C-1, C-4b, C-6a, C-10a, and C-12a CH_3), and 5.47 (s, 2, CH=CH).

Anal. Calcd for $C_{23}H_{36}O$: C, 84.09; H, 11.04. Found: C, 84.16; H, 11.16.

1α,12aα-Epoxy-4bβ,6aα,10aβ-trimethyl-3,4,4aα,4b,5,6,6a,9,-10,10a,10bα,11,12,12a-tetradecahydro-2(1*H*)-chrysenone (5). To a stirred solution of 125 mg (0.42 mmol) of the enone **3** in 10 ml of methanol at room temperature was added 1 ml (*ca.* 300 mg, 16 mmol) of 30% aqueous hydrogen peroxide solution and 0.5 ml of 10% aqueous sodium hydroxide solution, and the mixture was stirred at room temperature for 1 hr. The solution was then diluted with ether and water, and the product was isolated by ether extraction.[33] Purification of the resulting semicrystalline solid (126 mg) by preparative TLC (30% ether–petroleum ether) afforded 109 mg (83%) of the epoxy ketone **5** (R_f 0.45), mp 98–100° (vacuum). The analytical sample, mp 102.5–103.5° (vacuum), was obtained after two crystallizations of this material from methanol–dichloromethane: ir ($CHCl_3$) 1700 (C=O), 1450 (CH_2), and 1385 cm^{-1} (CH_3); NMR ($CDCl_3$) δ 0.82, 0.87, and 1.05 (3 s, 3 each, C-4b, C-6a, and C-10a CH_3), 3.16 (s, 1, C-1 H), and 5.49 (s, 2, CH=CH).

Anal. Calcd for $C_{21}H_{30}O_2$: C, 80.21; H, 9.62. Found: C, 80.44; H, 9.69.

1β-(3′-Butynyl)-4bβ,8aα,10aβ-trimethyl-3,4,4aα,4b,5,6,8a,9,-10,10a-decahydrophenanthren-2(1*H*)-one (7). A slight modification of the general procedure of Eschenmoser and coworkers[19] was employed. To a dry mixture of 77.0 mg (0.244 mmol) of the epoxy ketone **5** and 48.8 mg (0.261 mmol) of *p*-toluenesulfonylhydrazine at −20° was added with stirring and swirling 1.5 ml of −20° acetic acid–dichloromethane (1:1). After stirring for 5 min at −20°, the solution was stored at −20° for 15 hr. The mixture was then stirred at room temperature for an additional 4 hr (during which time it turned red) and then the product was isolated by ether extraction,[33] including a base wash. Purification of the crude product (81 mg) by preparative TLC (30% ether–petroleum ether)

afforded 50.5 mg (69%) of the acetylenic ketone **7** as a yellow oil (R_f 0.48) which was suitable for analysis: ir ($CHCl_3$) 3300 (–C≡CH), 2120 (–C≡C–), 1700 (C=O), and 1390 cm^{-1} (CH_3); NMR ($CDCl_3$) δ 0.77, 0.85, 1.13 (3 s, 3 each, C-4b, C-8a, and C-10a CH_3), and 5.49 (s, 2, HC=CH).

Anal. Calcd for $C_{21}H_{30}O$: C, 84.51; H, 10.13. Found: C, 84.25; H, 10.02.

1β-(3′-Butynyl)-2α,4bβ,8aα,10aβ-tetramethyl-1,2,3,4,4aα,4b,-5,6,8a,9,10,10a-dodecahydro-2β-phenanthrol (8). To a stirred and ice-cooled mixture of 0.36 ml (0.68 mmol) of 1.9 *M* ethereal methyllithium solution and 2.0 ml of dry ether was added over a 2-min period a solution of 19.0 mg (0.064 mmol) of the acetylenic ketone **7** in 1.2 ml of dry ether. After stirring for 10 min longer at 0°, and for 5 min without cooling, the reaction mixture was cautiously quenched with 0.5 ml of water and then the product was isolated by ether extraction.[33] Purification of the crude product (18.8 mg) by preparative TLC (50% ether–petroleum ether) afforded 16.0 mg (80%) of the alcohol **8** as a white solid, mp 84–88° (vacuum). The analytical sample, obtained after two crystallizations of a portion of this material from ether–hexane, melted at 91.0–92.5° (vacuum): ir ($CHCl_3$) 3600 (OH), 3300 (–C≡CH), 2115 (–C≡C–), and 1385, 1370 cm^{-1} (CH_3); NMR ($CDCl_3$) δ 0.81, 1.00, 1.03, 1.17 (4 s, 3 each, C-2, C-4b, C-8a, and C-10a CH_3), and 5.45 (s, 2, HC=CH).

Anal. Calcd for $C_{22}H_{34}O$: C, 84.02; H, 10.90. Found: C, 84.01; H, 11.04.

1-Chloro-2-formyl-8-methoxy-4aβ,10bβ,12aα-trimethyl-3,-4,4a,4bα,5,6,10b,11,12,12a-decahydrochrysene (13). Following a modification of the procedure of Moersch and Neuklis,[23] ice-cooled phosphoryl chloride (12 ml, 20.1 g, 0.131 mmol) was stirred and treated over a 1-min period with 13.6 ml (12.8 g, 0.176 mmol) of dimethylformamide. After stirring for 30 min without cooling, the viscous solution of reagent was added at room temperature to a stirred solution of 1.158 g (3.54 mmol) of the tetracyclic ketone **1** in 24 ml of dimethylformamide. The stirred reaction mixture was then heated with a preheated, 60° oil bath for 6 hr so that the internal temperature rose to a constant 55–56°. After cooling with an ice bath, the solution was poured onto 350 g of ice and 40 ml of 40% aqueous sodium hydroxide solution, and the product was isolated by dichloromethane extraction.[33] The crude residue (1.310 g) was chromatographed on 200 g of silica gel in a medium-pressure column with dichloromethane. After the first 400 ml of eluent was discarded, evaporation of the next 600 ml of eluent at reduced pressure provided 854 mg (65%) of the chloroaldehyde **13** as a white solid, mp 196–198° (vacuum). The analytical sample, obtained after crystallization of a portion of this material from acetone–dichloromethane–water, melted at 198.5–199° (vacuum): ir ($CHCl_3$) 2750 (–CHO), 1665 (C=C–CHO) 1605, 1575, 1500 (ArH), 1385 (CH_3), and 1150, 1040 cm^{-1} ($ArOCH_3$); NMR ($CDCl_3$) δ 0.92, 1.21 (2 s, 3 and 6, C-4a, C-10b, and C-12a CH_3), 3.77 (s, 3, $ArOCH_3$), 6.6–7.3 (m, 3, ArH), and 10.30 (s, 1, CHO).

Anal. Calcd for $C_{23}H_{29}O_2Cl$: C, 74.08; H, 7.84; Cl, 9.51. Found: C, 74.12; H, 7.96; Cl, 9.49.

No material was eluted from the column by additional 350 ml of dichloromethane, but evaporation of the following 600 ml of eluent afforded 154 mg (13%) of starting ketone as a white solid; ir and NMR spectra are the same as those of a purified sample of ketone **1**.

Further elution with 500 ml of 5% methanol–ether gave 147 mg of a white solid, which on crystallization from acetone–dichloromethane–water afforded **2,9-bisformyl-1-chloro-8-methoxy-4aβ,10bβ,12aα-trimethyl-3,4,4a,4bα,5,6,10b,11,12,12a-decahydrochrysene:** mp 265–266° dec (vacuum); ir ($CHCl_3$) 2770 (CHO), 1670 (C=O), 1605, 1570, 1495 (ArH), and 1150, 1055 cm^{-1} ($ArOCH_3$); NMR ($CDCl_3$) δ 0.92, 1.21 (2 s, 3 and 6, C-4a, C-10b, and C-12a CH_3), 3.90 (s, 3, $ArOCH_3$), 6.70 (s, 1, C-7 H), 7.80 (s, 1, C-10 H), 10.30 (s, 1, C-2 CHO), and 10.50 (s, 1, C-9 CHO).

Anal. Calcd for $C_{24}H_{29}O_3Cl$: C, 71.90; H, 7.29; Cl, 8.84. Found: C, 71.82; H, 7.24; Cl, 8.90.

The yield of the desired chloro aldehyde **13** based upon recovered starting material was 75%. In a similar experiment, in which the reaction mixture was heated with a 69° bath for 4.5 hr, the yield of purified aldehyde **13** (without recovery of starting material) was 71%.

2α-Formyl-8-methoxy-2β,4aβ,10bβ,12aα-tetramethyl-1,2,3,4,-4a,4bα,5,6,10b,11,12,12a-dodecahydrochrysene (14). To an argon-protected solution of 260 mg (38 mg-atoms) of lithium in 120 ml of dry ammonia and 50 ml of dry tetrahydrofuran was slowly added over a 50-min period with vigorous stirring a solution of 253 mg (0.68 mmol) of the chloro aldehyde **13** and 128 μl (100 mg, 1.36 mmol) of dry *tert*-butyl alcohol in 60 ml of dry tetrahydrofuran. After stirring for an additional 15 min the blue color of the reaction mixture was discharged by the portionwise addition of dry, powdered sodium benzoate, and the ammonia was evaporated through a mercury bubbler by heating the mixture with a hot air gun. After the addition of 40 ml of dry tetrahydrofuran, the reaction mixture was stirred with ice cooling and treated with 5 ml (11.4 g, 80 mmol) of iodomethane. After stirring without cooling for 2 hr, the resulting white suspension was diluted with 200 ml of ether and the product was isolated by ether extraction,[33] including both an acid and a base wash. Purification of the crude product (281 mg) by preparative TLC (15% ether–petroleum ether, double development) afforded 154 mg (64%) of the aldehyde **14** (R_f 0.45): mp 111–116° dec (vacuum); ir ($CHCl_3$) 2805, 2705 (CHO), 1720 (C=O), 1605, 1575, 1500 (ArH), 1385 (CH_3), and 1245, 1040 cm^{-1} ($ArOCH_3$); NMR ($CDCl_3$) δ 0.76 (s, 3, C-12a CH_3), 0.93, 1.00 (2 s, 3 each, C-2 and C-4a CH_3), 1.21 (s, 3, C-10b CH_3), 3.76 (s, 3, $ArOCH_3$), 6.6–7.3 (m, 3, ArH), and 9.45 (s, 1, CHO). The same spectral properties were observed for the analytical sample which was prepared by crystallization of a portion of this material from ether–hexane and also melted over the range 111–116° dec (vacuum).

Anal. Calcd for $C_{24}H_{34}O_2$: C, 81.31; H, 9.67. Found: C, 81.43; H, 9.67.

Reduction of 143 mg (0.403 mmol) of this aldehyde **14** in 10 ml of dry tetrahydrofuran with 110 mg (2.9 mmol) of lithium aluminum hydride afforded 139 mg (97%) of the corresponding primary alcohol as a white foam: ir ($CHCl_3$) 3625, 3470 (OH), 1608, 1575, 1495 (ArH), and 1385 cm^{-1} (CH_3); NMR ($CDCl_3$) δ 0.97, 1.00 (2 s, 6 and 3, C-2, C-4a, and C-12a CH_3), 1.21 (s, 3, C-10b CH_3), 3.43, 3.55 (2 s, 1 each, $-CH_2O-$), 3.67 (s, 3, $ArOCH_3$), and 6.6–7.3 (m, 3, ArH). The same spectral properties were observed for the analytical sample which was prepared by crystallization of a portion of this material from methanol and melted at 123.5–125.5° (vacuum).

Anal. Calcd for $C_{24}H_{36}O_2$: C, 80.85; H, 10.18. Found: C, 80.73; H, 10.25.

Attempts to convert this primary alcohol to the corresponding primary halide with triphenyl phosphite–iodomethane,[27] thionyl chloride–quinoline, and triphenylphosphine–carbon tetrachloride[28] led either to no observable reaction or a mixture of numerous products, judged to be the result of deep-seated rearrangements by the ir and NMR spectra.

8-Methoxy-2β,4aβ,10bβ,12aα-tetramethyl-2α-(3′-oxo-1′-propenyl)-1,2,3,4,4a,4bα,5,6,10b,11,12,12a-dodecahydrochrysene (15). Following an adaptation of the general procedure of Nagata and Hayase,[29] a stirred suspension of 880 mg (21 mmol) of 57% sodium hydride–mineral oil dispersion in 13.5 ml of dry tetrahydrofuran was cooled with an ice bath and treated over a 5-min period with a solution of 5.46 g (21 mmol) of diethyl 2-(cyclohexylimino)ethylphosphonate in 25 ml of dry tetrahydrofuran. After 15 min, a solution of 1.100 g (3.10 mmol) of the aldehyde **14** in 20 ml of dry tetrahydrofuran was then added over a 1-min period. This stirred mixture was heated with a preheated 60° oil bath for 80 min, cooled with an ice bath, and then poured onto 150 ml of ice and water. After isolation of the crude product by ether extraction[33] there was obtained 6.3 g of a yellow-brown oil that contained the corresponding aldimine.

Hydrolysis of the aldimine was accomplished by treatment of this crude product in 150 ml of benzene with 500 ml of 1% aqueous oxalic acid solution. This two-phase system was stirred at room temperature for 19 hr. The organic layer was separated and the aqueous layer was then extracted with three 200-ml portions of ether. The combined organic phases were washed with 2% aqueous hydrochloric acid (200 ml), 2% aqueous sodium hydroxide solution (two 200-ml portions), and saturated brine (200 ml), and then dried ($MgSO_4$). After removal of the drying agent and evaporation of the solvent at reduced pressure, 1.64 g of a yellow oil was obtained. Purification of this oil on 200 g of silica gel in a medium-pressure column was accomplished by elution with 40% ether–petroleum ether. When the second 200 ml of eluent from the column was evaporated at reduced pressure, there was obtained 1.066 g (89%) of unsaturated aldehyde **15** as a white solid. Crystallization of a portion of this material from ether–petroleum ether afforded analytically pure material that melted at 131–133° (vacuum): ir ($CHCl_3$) 2735 (CHO), 1675 (C=O), 1625 (C=C), 1605, 1575, 1495 (ArH), 1385 (CH_3), and 1035 cm^{-1} ($ArOCH_3$); NMR ($CDCl_3$) δ 0.87, 1.04 (2 s, 3 and 6, C-2, C-4a, and C-12a CH_3), 1.21 (s, 3, C-10b CH_3), 3.76 (s, 3, $ArOCH_3$), 6.05 (dd, 1, J = 16 and 7.5 Hz, C-2′ C=CH, 6.6–7.3 (m, 4, ArH and C-1′ C=CH), and 9.52 (d, 1, J = 8 Hz, CHO).

Anal. Calcd for $C_{26}H_{36}O_2$: C, 82.06; H, 9.53. Found: C, 82.07; H, 11.41.

8-Methoxy-2β,4aβ,10bβ,12aα-tetramethyl-2α-(3′-oxopropyl)-1,2,3,4,4a,4bα,5,6,10b,11,12,12a-dodecahydrochrysene. After the procedure of Nagai and coworkers,[30] a solution of 135 mg (0.355 mmol) of the unsaturated aldehyde **15** and 1.25 ml of triethylsilane in 1 ml of benzene was treated with 4.5 mg (4.9 μmol) of tris(triphenylphosphine) rhodium chloride, and the mixture was heated at 50° for 1.25 hr. While heating was continued for an additional 1.50 hr, two 2-mg (2.2 μmol) portions of the rhodium catalyst were added at 0.5-hr intervals. After dilution with 25 ml of ether and then fitration, evaporation of the solvents from the filtrate at reduced pressure afforded a yellow oil that contained the corresponding silyl enol ether.

A solution of this oil in 5 ml of acetone was treated with 0.5 ml of 5% aqueous hydrochloric acid, and the mixture was stirred at room temperature for 20 min. Isolation of the product by ether extraction,[33] including a base wash, afforded 200 mg of a yellow, semicrystalline solid which on purification by preparative TLC (35% ether–petroleum ether) gave 113 mg (83%) of the saturated aldehyde (R_f 0.42) as a white, amorphous solid: ir ($CHCl_3$) 2735 (CHO), 1720 (C=O), 1605, 1575, 1495 (ArH), 1380 (CH_3), and 1035 cm^{-1} ($ArOCH_3$); NMR ($CDCl_3$) δ 0.90, 1.00, 1.05 (3 s, 3 each, C-2, C-4a, and C-12a CH_3), 1.22 (s, 3, C-10b CH_3), 3.77 (s, 3, $ArOCH_3$), 6.6–7.3 (m, 3, $ArOCH_3$), and 9.80 (m, 1, CHO). This material was not further purified but used directly in the following experiment.

8-Methoxy-2β,4aβ,10bβ,12aα-tetramethyl-2α-(4′-methyl-3′-pentenyl)-1,2,3,4,4a,4bα,5,6,10b,11,12,12a-dodecahydrochrysene (16). A stirred suspension of 4.62 g (10.7 mmol) of isopropyltriphenylphosphonium iodide in 30 ml of dry tetrahydrofuran at room temperature was treated dropwise over a 3-min period with 4.03 ml (8.55 mmol) of a 2.12 *M* solution of phenyllithium in 30% ether–benzene. The red suspension was stirred for 2.25 hr, and then a solution of 819 mg (2.14 mmol) of the above saturated aldehyde in 13 ml of dry tetrahydrofuran was added over a 5-min period. After stirring at room temperature for 50 min longer the product was isolated by ether extraction,[33] including a 10% hydrogen peroxide wash and a 10% sodium thiosulfate wash. After removal of the desiccant and evaporation of the solvent at reduced pressure, a semisolid mixture was obtained. This material was filtered through a glass wool plug with the aid of 100 ml of petroleum ether to remove most of the relatively insoluble triphenylphosphine oxide. Concentration of the filtrate at reduced pressure afforded 1.2 g of a yellow oil which was purified by chromatography on 120 g of silica gel with 4% ether–petroleum ether. After the first 150 ml of eluent was discarded, the next 25 ml contained 101 mg of a mixture which on preparative TLC (4% ether–petroleum ether) afforded 69 mg (8%) of the olefin **16** which was combined with the bulk of the product obtained later. Concentration of the following 250 ml at reduced pressure afforded 651 mg (75%) of the olefin **16** as a white solid: ir ($CHCl_3$) 1605, 1575, 1495 (ArH), 1385 (CH_3), and 1035 cm^{-1} ($ArOCH_3$); NMR ($CDCl_3$) δ 0.92, 0.98, 1.05 (3, s, 3 each, C-2, C-4a, and C-12a CH_3), 1.21 (s, 3, C-10b CH_3), 1.59, 1.66 [2 s, $C{=}C(CH_3)_2$], 3.76 (s, 3, $ArOCH_3$), 4.85–5.35 (m, 1, C=CH), and 6.6–7.3 (m, 3, ArH). The combined yield of the olefin **16** was thus 720 mg (83%). Crystallization of a portion of this material from methanol with a trace of methylene chloride afforded the analytical sample as fluffy, white crystals, mp 78–80° (vacuum), and with the same ir and NMR spectra as those recorded above.

Anal. Calcd for $C_{29}H_{44}O$: C, 85.23; H, 10.85. Found: C, 85.06; H, 10.66.

4bβ,6aα,8β,10aβ-Tetramethyl-8α-(4′-methyl-3′-pentenyl)-4,4aα,4b,5,6,6a,7,8,9,10,10a,10bα,11,12-tetradecahydro-2(3*H*)-chysenone (18). To a solution of 50 mg (0.127 mmol) of the olefin **16** and 2.1 ml (1.66 g, 22.5 mmol) of dry *tert*-butyl alcohol in 5 ml of dry tetrahydrofuran and 15 ml of dry ammonia under an argon atmosphere was added with stirring 24 mg (3.5 g-atoms) of lithium, and the mixture was allowed to reflux for 2 hr. The excess lithium was then quenched with 0.6 ml of methanol, and after evaporation of the ammonia, the crude product (56 mg) was isolated by ether extraction.[33]

To a stirred solution of this crude dihydroaromatic system in 1 ml of dichloromethane at room temperature was added sequentially 2 ml of ethanol, 0.5 ml of water, and 50 mg of oxalic acid. After stirring for 2 hr, the reaction mixture was diluted with 100 ml of ether, and the product (50 mg) was isolated by ether extraction,[33] including a base wash.

Conjugation of the double bond of this β,γ-unsaturated ketone [ir ($CHCl_3$) 1710 cm^{-1} (C=O)] was effected by stirring at room temperature a solution of the crude material with 1 ml of ethanol, 0.15 ml of water, and 0.30 ml of 10% aqueous sodium hydroxide in 5 ml of dichloromethane. After isolation of the crude product (50 mg) by ether extraction[33] and purification of that material by preparative TLC (40% ether–petroleum ether), there was obtained 35 mg (72%) of the desired enone **18** as a pale yellow solid: ir ($CHCl_3$) 1655 (C=O), 1615 (C=C), and 1390, 1375 cm^{-1} (CH_3); NMR ($CDCl_3$) δ 0.88, 0.90, 0.93, 1.15 (4 s, 3 each, C-4b, C-6a, C-8, and C-10a CH_3), 1.61, 1.67 [2 s, 3 each, $C{=}C(CH_3)_2$], 5.08 (m, 1, $RCH{=}CR_2'$), and 5.87 (br s, 1, O=C-CH=C); analysis by GLC (300°)[31] indicated the presence of a single volatile component to the extent of >99% with retention time of 3.8 min. This material was used directly in subsequent experiments without further purification.

1,12a-Epoxy-4bβ,6aα,8β,10aβ-tetramethyl-8α-(4′-methyl-3′-pentenyl)-1,4,4aα,4b,5,6,6a,7,8,9,10,10a,10bα,11,12,12a-hexadecahydro-2(3*H*)-chrysenone. To a stirred solution of 392 mg (1.0 mmol) of the enone **18** in 9 ml of dichloromethane at room temperature was added sequentially 20 ml of methanol, 5.3 ml of 30% aqueous hydrogen peroxide solution, and 1.2 ml of 10% aqueous sodium hydroxide solution. After stirring in a closed flask for 21 hr, the crude product was isolated by ether extraction[33] and on crystallization from methanol–dichloromethane afforded 310 mg (76%) of the epoxy ketone: mp 103.5–105.5° dec (vacuum); ir ($CHCl_3$) 1700 (C=O) and 1375 cm^{-1} (CH_3); NMR ($CDCl_3$) δ 0.90, 1.12 (2 s, 9 and 3, C-4b, C-6a, C-8, and C-10a CH_3), 1.59, 1.67, [2 s, 3 each, $C{=}C(CH_3)_2$], 3.11 (s, 1, epoxy H), and 5.07 (m, 1, C=CH). The analytical sample, obtained after two further crystallizations of a portion of this material from methanol–dichloromethane, had the same spectal properties and melted at 107–108.5° (vacuum).

Anal. Calcd for $C_{28}H_{44}O_2$: C, 81.50; H, 10.75. Found: C, 81.49; H, 10.73.

1β-(3′-Butynyl)-4bβ,7β,8aα,10aβ-tetramethyl-7α-(4′-methyl-3′-pentenyl)-3,4,4aα,4b,5,6,7,8,8a,9,10,10a-dodecahydro-2(1*H*)-phenanthrenone. According to the procedure described above for the cleavage[19] of the epoxy ketone **5**, a solution of 51 mg (0.124 mmol) of the epoxy ketone above and 24.5 mg (0.131 mmol) of *p*-toluenesulfonylhydrazine in 2.5 ml of 1:2 acetic acid–dichloromethane was stored for 30 hr at −20° and then stirred for 13 hr at room temperature. After isolation of the product by ether extraction,[33] including a base wash, and then purification of the residue by preparative TLC (15% ether–petroleum ether), 31 mg (63%) of the acetylenic ketone (R_f 0.32) was obtained as a white solid: ir ($CHCl_3$) 3300 (C≡CH), 2120 (C≡C), 1700 (C=O), and 1390, 1380 cm^{-1} (CH_3); NMR ($CDCl_3$) δ 0.76 (s, 3), 0.91 (s, 6), 1.21 (s, 3) (C-4b, C-7, C-8a, and C-10a CH_3), 1.62 and 1.68 [2 br s, 3 each, $C{=}C(CH_3)_2$], and 5.1 (m, 1, RCH=C). The analytical sample, obtained after two crystallizations of this material from methanol, had the same spectral properties and melted at 90.5–91.5° (vacuum).

Anal. Calcd for $C_{28}H_{44}O$: C, 84.79; H, 11.18. Found: C, 84.72; H, 11.21.

1β-(3′-Butynyl)-2α,4bβ,7β,8aα,10aβ-pentamethyl-7α-(4′-methyl-3′-pentenyl)-1,2,3,4,4aα,4b,5,6,7,8,8a,9,10,10a-tetradecahydro-2β-phenanthrol (20). To a stirred and ice-cooled solution of 1.1 ml (1.81 mmol) of 1.65 *M* ethereal methyllithium in 2.2 ml of dry tetrahydrofuran was added over a 7-min period a solution of 55 mg (0.139 mmol) of the acetylenic ketone above in 4.5 ml of dry tetrahydrofuran, and the mixture was allowed to stir at room temperature for an additional 25 min. After the reaction was quenched with 1 ml of water, the product was isolated by ether extraction[33] and amounted to 56 mg (99%) of a white foam: ir ($CHCl_3$) 3600 (OH), 3300 (C≡CH), 2115 (C≡C), and 1385, 1375 cm^{-1} (CH_3); NMR ($CDCl_3$) δ 0.89 (s, 6), 0.97, 1.06, 1.13 (3 s, 3 each) (C-2, C-4b, C-7, C-8a, and C-10a CH_3), 1.62 and 1.68 [2 br s, 3 each, $C{=}C(CH_3)_2$], and 5.1 (m, 1, RCH=C); analytical TLC (50% ether–petroleum ether) showed a one-component system with R_f 0.50. This material was not further purified but used directly in numerous acid-catalyzed cyclization reactions, all of which resulted in hydration of the terminal double bond with or without cyclization of the acetylenic side chain.

8α-(3′-Hydroxypropyl)-4,4aα,4b,5,6,6a,7,8,9,10,10a,10bα,11,-12-tetradecahydro-4bβ,6aα,8β,10aβ-tetramethyl-2(3*H*)-chrysenone (17). To a solution of 19 ml of dry dimethoxyethane and 2.33 ml of ethanol in 65 ml of dry ammonia containing 56 mg (8 mg-atoms) of lithium was added dropwise with stirring a solution of 76 mg (0.2 mmol) of the aldehyde **15** in 19 ml of dry dimethoxyethane and 2.3 ml of ethanol. The blue color of the solution was maintained over a 2-hr period by the portionwise addition of 497 mg (71 mg-atoms) of lithium, and then the excess lithium was destroyed by the addition of 3 ml of methanol. After evaporation of

the ammonia in a stream of argon and then treatment of the residue with 150 ml of 5% aqueous hydrochloric acid, the product was isolated by ether extraction,[33] including a base wash. The residual, light yellow oil was dissolved in a mixture of 9 ml of ethanol and 6 ml of 5 *N* aqueous hydrochloric acid, and the resulting solution was refluxed under an argon atmosphere for 1 hr. After dilution of the solution with 50 ml of water, the product was isolated by ether extraction,[33] including a base wash, and then purified by preparative TLC (ether). The resulting clear, colorless oil amounted to 51 mg (68%) of the hydroxyenone **17**. Crystallization of a portion of this oil from *n*-hexane–dichloromethane afforded analytically pure material: mp 144–146.5° (vacuum); ir ($CHCl_3$) 3610, 3400 (OH), 1655 (C=O), and 1610 cm^{-1} (C=C); NMR ($CDCl_3$) δ 0.90 (s, 6) 0.95, 1.15 (2 s, 3 each) (C-4b, C-6a, C-8, and C-10a CH_3), and 3.62 (t, 2, J = 6 Hz, $-CH_2OH$).

Anal. Calcd for $C_{25}H_{40}O_2$: C, 80.59; H, 10.82. Found: C, 80.86; H, 10.80.

1,12a-Epoxy-1,4,4aα,4b,5,6,6a,7,8,9,10,10a,10bα,11,12,12a-hexadecahydro-8α-(3′-hydroxypropyl)-4bβ,6aα,8β,10aβ-tetramethyl-2(3*H*)-chrysenone. To a stirred solution of 52 mg (0.15 mmol) of the hydroxyenone **17** in 3.6 ml of dichloromethane were added 5.4 ml of methanol, 0.9 ml of 30% aqueous hydrogen peroxide, and 0.44 ml of 10% aqueous sodium hydroxide solution. After stirring under argon for 8 hr, the reaction mixture was poured into 50 ml of brine, and the product was isolated by ether extraction.[33] Purification by medium-pressure chromatography (ether) afforded 34 mg (64%) of the epoxy ketone and 13 mg (25%) of recovered hydroxyenone **17**. Crystallization of a portion of the epoxy ketone from ether afforded analytically pure material: mp 165–166° (vacuum); ir ($CHCl_3$) 3620 (OH) and 1700 cm^{-1} (C=O); NMR ($CDCl_3$) δ 0.88 (s, 9), 1.10 (s, 3) (C-4b, C-6a, C-8, and C-10a CH_3), 3.13 (s, 1, epoxy H), and 3.62 (t, 2, J = 6 Hz, CH_2OH).

Anal. Calcd for $C_{25}H_{40}O_3$: C, 77.27; H, 10.38. Found: C, 77.33; H, 10.44.

1β-(3′-Butynyl)-3,4,4aα,4b,5,6,7,8,8a,9,10,10a-dodecahydro-7α-(3′-hydroxypropyl)-4bβ,7β,8aα,10aβ-tetramethyl-2(1*H*)-phenanthrone. To a dry mixture of 112 mg (0.29 mmol) of the epoxy ketone above and 59 mg (0.32 mmol) of *p*-toluenesulfonylhydrazine cooled to −20° under an argon atmosphere was added 4 ml of a −20° solution of 1:2 glacial acetic acid–dichloromethane which had been previously degassed by alternate evacuation and ebullition with argon. After 25 hr at −15 to −25°, followed by 12 hr at room temperature, the reaction mixture was poured into 100 ml of water, and the product was isolated by ether extraction,[33] including a base wash. Purification by chromatography on Florisil (1:1 chloroform–ether) gave 82 mg (77%) of the acetylenic ketone as a slightly yellow oil that was a single-component system by tlc (1:1 chloroform–ether, R_f 0.39): ir ($CHCl_3$) 3610 (OH), 3300 (C≡CH), 2120 (C≡C), and 1700 cm^{-1} (C=O); NMR ($CDCl_3$) δ 0.77 (s, 3), 0.90 (s, 6), 1.18 (s, 3) (C-4b, C-7, C-8a, and C-10a CH_3), and 3.60 (t, 2, J = 6 Hz, CH_2OH). A portion of this oil was crystallized from ethanol–water, mp 99.5–101° (vacuum). However, the resulting solid did not give a satisfactory combustion analysis. Satisfactory results were obtained from a sample prepared by flash distillation of a portion of the original oil at 10^{-4} mm.

Anal. Calcd for $C_{25}H_{40}O_2$: C, 80.59; H, 10.82. Found: C, 80.60; H, 10.85.

1β-(3′-Butynyl)-7α-(3′-hydroxypropyl)-2α,4bβ,7β,8aα,10aβ-pentamethyl-1,2,3,4,4aα,4b,5,6,7,8,8a,9,10,10a-tetradecahydro-2β-phenanthrol (19). To a stirred and ice-cooled mixture of 4.8 ml (8.5 mmol) of 1.7 *M* ethereal methyllithium solution and 7.5 ml of dry tetrahydrofuran under an argon atmosphere was added dropwise a solution of 82 mg (0.22 mmol) of the acetylenic ketone above in 8 ml of tetrahydrofuran. After 10 min of stirring without cooling the excess methyllithium was destroyed with water, and the solution was diluted with 100 ml of brine. Isolation of the product by ether extraction,[33] followed by purification by chromatography on Florisil (10% ether–chloroform), afforded 75 mg (88%) of acetylenic alcohol **19** as a white, crystalline solid. Crystallization of a portion of this material from *n*-hexane–ether afforded analytically pure material that melted at 153–155° (vacuum): ir ($CHCl_3$) 3610 (OH), 3300 (C≡CH), and 2120 cm^{-1} (C≡C); NMR ($CDCl_3$) δ 0.88 (s, 6), 1.0, 1.07, 1.15 (3 s, 3 each) (C-2, C-4b, C-7, C-8a, and C-10a CH_3), and 3.62 (t, 2, J = 6 Hz, CH_2OH).

Anal. Calcd for $C_{26}H_{44}O_2$: C, 80.35; H, 11.41. Found: C, 80.32; H, 11.41.

8α-(3′-Hydroxypropyl)-1α,2α-methano-1,2,3,4,4aα,4b,5,6,-6a,7,8,9,10,10a,10bα,11,12,12a-octadecahydro-4bβ,6aα,8β,10a-β,12aβ-pentamethyl-2β-chrysenol (21). A. Preparation of the Enol Bis Trifluoroacetate. To 85 mg (0.22 mmol) of the acetylenic diol **19** cooled to −25° under an argon atmosphere was added 14.5 ml of a −25° solution of 30% trifluoroacetic anhydride in trifluoroacetic acid. After 45 min of stirring at −25°, the solvents were removed at reduced pressure (~1 mm), and the dark residue was taken up in ether and washed with water and saturated aqueous sodium bicarbonate solution. The resulting oil, which amounted to 136 mg, was used directly in the next experiment: ir ($CHCl_3$) 1780 cm^{-1} (C=O); NMR ($CDCl_3$) δ 0.87 (s, 9), 1.0, 1.03 (2 s, 3 each) (C-4b, C-6a, C-8, C-10a, and C-12a CH_3), 4.33 (t, 2, J = 6 Hz, CH_2–OTFA), and 5.30 (s, 1, C-1 H).

B. Cleavage of the Trifluoroacetate and Methylenation. To a stirred solution of lithium diisopropylamide prepared from 5.1 ml (10.9 mmol) of 2.13 *M* hexane solution of *n*-butyllithium and 1.82 ml (12.0 mmol) of diisopropylamine in 12 ml of dry tetrahydrofuran at 0° under an argon atmosphere was added a solution of 136 mg of the crude bis trifluoroacetate from above in 5 ml of dry tetrahydrofuran. To the cloudy, red-brown solution which resulted after 15 min of stirring were added all at once 43.6 ml (43.6 mmol) of the Simmons–Smith reagent prepared from the zinc–silver couple[36] [4.9 g (75 mmol) of granular zinc, 38 mg of silver acetate, and 38 ml of glacial acetic acid] and 5.78 ml (72 mmol) of diiodomethane in 66 ml of dry ether in the presence of a few strands of silver wool after the procedure of Conia.[36]

After stirring at room temperature for 50 min, the solution was diluted with 200 ml of ice cold, saturated sodium carbonate solution and 30 ml of 40% aqueous ammonium sulfate solution. Isolation of the product by ether extraction[33] including saturated aqueous sodium carbonate and 10% aqueous sodium thiosulfate solution washes afforded a dark red oil which was immediately chromatographed on 130 g of Florisil. Elution with 300 ml of petroleum ether removed diiodomethane, and continued elution with 250 ml of 1:1 ether–petroleum ether and then 350 ml of ether afforded 59 mg (67%) of the cyclopropanol **21** as a yellow, crystalline solid. Crystallization of this material from $CHCl_3$ or hexane–dichloromethane gave colorless crystals, mp ~200° dec (vacuum): ir ($CHCl_3$) 3580 cm^{-1} (OH); NMR (DMSO-d_6) δ 0.449 (m, 2, cyclopropyl CH_2), 0.915 (s, 9), 1.12, 1.17 (2 s, 3 each) (C-4b, C-6a, C-8, C-10a, and C-12a CH_3), and 4.16 (t, 2, J = 6 Hz, CH_2OH); high-resolution, mass measured molecular ion 402.3497 ± 0.0008 (calcd for $C_{27}H_{46}O_2$, 402.34976).

1,4,4aα,4b,5,6,6a,7,8,9,10,10a,10bα,11,12,12a-Hexadecahydro-1β,4bβ,6aα,8β,10aβ,12aβ-hexamethyl-8α-(3′-hydroxypropyl)-2(3*H*)-chrysenone (22). To a solution of 54 mg (0.13 mmol) of the cyclopropanol **21** in 25 ml of ethanol was added 30 drops of concentrated hydrochloric acid solution, and the mixture was refluxed in an argon atmosphere for 40 min. After dilution of the solution with 175 ml of water, the product was isolated by ether extraction,[33] including base wash, and then purified by chromatography on 20 g of Florisil. Elution with 120 ml of ether gave 41 mg (77%) of tetracyclic hydroxy ketone **22**. Crystallization of a portion of this material from *n*-hexane afforded analytically pure material: mp 158–160° (vacuum); ir ($CHCl_3$) 3610 (OH) and 1700 cm^{-1} (C=O); NMR ($CDCl_3$) δ 0.72 (s, 3, C-12a CH_3), 0.80, 0.90, 0.93, 1.13 (s, 15, C-1, C-4b, C-6a, C-8, and C-10a CH_3), and 3.62 (t, 2, J = 7 Hz, CH_2OH).

Anal. Calcd for $C_{27}H_{46}O_2$: C, 80.54; H, 11.51. Found: C, 80.43; H, 11.43.

1,4,4aα,4b,5,6,6a,7,8,9,10,10a,10bα,11,12,12a-Hexadecahydro-1β,4bβ,6aα,8β,10aβ,12aβ-hexamethyl-8α-(3′-oxopropyl)-2(3*H*)-chrysenone. To a suspension of 300 mg (3 mmol) of chromic anhydride in 15 ml of dry dichloromethane under an argon atmosphere was added dropwise 0.48 ml (6 mmol) of pyridine. After 20 min of stirring at room temperature, 2.39 ml (0.48 mmol) of this deep burgundy solution was added to 19 mg (0.048 mmol) of the hydroxy ketone **22**, and the mixture was stirred for 10 min. The red and black mixture was then filtered with the aid of suction through alumina (III), and the alumina was washed with 150 ml of dichloromethane. Removal of the solvent at reduced pressure afforded 16 mg (84%) of the keto aldehyde as a slightly yellow crystalline solid. Crystallization of a portion of this material from *n*-hexane afforded analytically pure material as colorless crystals: mp 177–179° (vacuum); ir ($CHCl_3$) 2775 (CHO), 1720 (C=O), and 1700 cm^{-1} (C=O); NMR ($CDCl_3$) δ 0.71 (s, 3, C-12a CH_3), 0.88, 0.89, 0.92, 1.11 (4 s, 3 each, C-4b, C-6a, C-8, and C-10a CH_3), 0.88 (d, 3, J = 7 Hz, C-1 CH_3), and 9.8 (s, 1, CHO).

Anal. Calcd for $C_{27}H_{44}O_2$: C, 80.94; H, 11.07. Found: C, 80.93; H, 11.11.

(±)-Shionone. To a solution of 62 mg (1.3 mmol) of triphenylisopropylphosphonium iodide in 4.5 ml of dry tetrahydrofuran under an argon atmosphere was added dropwise 0.50 ml (1 mmol)

of a 2 *M* *n*-hexane–phenyllithium solution. After stirring for 2 hr at room temperature, 3.7 ml (0.74 mmol) of this reagent was added to a solution of 19.6 mg (0.049 mmol) of the above keto aldehyde in 2 ml of dry tetrahydrofuran. After stirring for 20 min at room temperature the product was isolated by ether extraction,[33] including a 10% aqueous hydrogen peroxide wash, and purified by chromatography on 20 g of silica gel. Elution with 100 ml of 10% ether–petroleum ether afforded 17 mg (82%) of (±)-shionone. Analytically pure material was obtained upon crystallization from methanol as small needles: mp 161.5–163° (vacuum); ir ($CHCl_3$) 1700 cm^{-1} (C=O); NMR ($CDCl_3$) δ 0.71 (s, 3, C-12a CH_3), 0.88, 0.90, 0.92, 1.13 (4 s, 3 each, C-4b, C-6a, C-8, and C-10a CH_3), 0.88 (d, 3, J = 7 Hz, C-1 CH_3), 1.61, 1.69 [2 s, 3 each, C=C(CH_3)$_2$], and 5.10 (t, 1, J = 8 Hz, RCH=CR_2).

Anal. Calcd for $C_{30}H_{50}O$: C, 84.44; H, 11.81. Found: C, 84.38; H, 11.90.

The ir, NMR, GLC, and TLC of this material were identical with those found for an authentic sample of natural shionone provided by Professor G. Ourisson.

Registry No.—**1**, 53311-24-3; **2**, 54141-74-1; **3**, 54036-92-9; **4** axial alcohol, 54036-93-0; **4** equatorial alcohol, 54036-94-1; **5**, 54036-95-2; **6**, 54036-96-3; **7**, 54036-97-4; **8**, 54036-98-5; **9**, 54036-99-6; **10**, 54037-00-2; **11**, 54037-01-3; **12**, 54037-02-4; **13**, 54062-79-2; **14**, 53311-25-4; **15**, 54037-03-5; **16**, 54054-05-6; **17**, 53311-26-5; **18**, 54054-06-7; **19**, 54037-04-6; **20**, 54054-07-8; **21**, 54082-41-6; **22**, 54037-05-7; **23**, 53402-15-6; tetramethyldiamidophosphorochloridate, 1605-65-8; 8-methoxy-4aβ,10bβ,12aα-trimethyl-3,4,4a,4bα,5,6,10b,11,12,12a-decahydrochrysene, 54141-75-2; 1β,12aβ-methano-4bβ,6aα,10aβ-trimethyl-1α,2,3,4,4aα,4b,5,6,6a,-9,10,10a,10bα,11,12,12a-hexadecahydro-2β-chrysenol, 54037-06-8; 2-acetoxy-1β,12aβ-methano-4bβ,6aα,10aβ-trimethyl-1,4,4aα,4b,5,-6,6a,9,10,10a,10bα,11,12,12a-tetradecahydrochrysene, 54062-80-5; 2-trifluoroacetoxy-4bβ,6aα,10aβ,12aβ-tetramethyl-3,4,4aα,4b,-5,6,6a,9,10,10a,10bα,11,12,12a-tetradecahydrochrysene, 54037-07-9; 2,9-bisformyl-1-chloro-8-methoxy-4aβ,10bβ,12aα-trimethyl-3,4,4a,4bα,5,6,10b,11,12,12a-decahydrochrysene, 54037-08-0; 8-methoxy-2β,4aβ,10bβ,12aα-tetramethyl-1,2,3,4,4a,4bα,5,6,10b,11,-12,12a-dodecahydrochrysen-2α-methanol, 54037-09-1; 8-methoxy-2β,4aβ,10bβ,12aα-tetramethyl-2α-(3′-oxopropyl)-1,2,3,4,4a,4bα,5,-6,10b,11,12,12a-dodecahydrochrysene, 54037-10-4; 1,12a-epoxy-4bβ,6aα,8β,10aβ-tetramethyl-8α-(4′-methyl-3′-pentenyl)-1,4,4aα,4b,5,6,6a,7,8,9,10,10a,10bα,11,12,12a-hexadecahydro-2(3*H*)-chrysenone, 54054-08-9; 1β-(3-butynyl)-4bβ,7β,8aα,10aβ-tetramethyl-7α-(4′-methyl-3′-pentenyl)-3,4,4aα,4b,5,6,7,8,8a,9,-10,10a-dodecahydro-2(1*H*)-phenanthrone, 54054-09-0; 1,12a-epoxy-1,4,4aα,4b,5,6,6a,7,8,9,10,10a,10bα,11,12,12a-hexadecahydro-8α-(3′-hydroxypropyl)-4bβ,6aα,8β,10aβ-tetramethyl-2(3*H*)-chrysenone, 54037-11-5; 1β-(3′-butynyl)-3,4,4aα,4b,5,6,7,8,8a,-9,10,10a-dodecahydro-7α-(3′-hydroxypropyl)-4bβ,7β,8aα,10aβ-tetramethyl-2(1*H*)-phenanthrone, 53311-27-6; 2-trifluoroacetoxy-8α-(3′-trifluoroacetoxypropyl)-4bβ,6aα,8β,10aβ,12aβ-pentamethyl-3,4,4aα,4b,5,6,6a,7,8,9,10,10a,10bα,11,12,12a-hexadecahydrochrysene, 54037-12-6; 1,4,4aα,4b,5,6,6a,7,8,9,10,10a,10bα,11,12,12a-hexadecahydro-1β,4bβ,6aα,8β,10aβ,12aβ-hexamethyl-8α-(3′-oxopropyl)-2(3*H*)-chrysenone, 54037-13-7.

Acknowledgment. Grateful acknowledgment is made for the support of this work by grants from the National Science Foundation and the Hoffmann-La Roche Foundation. The authors thank Professor G. Ourisso (University of Strasbourg) for a generous sample of shionone used for comparison purposes.

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 to be assumed to be racemic. The tetracyclic compounds will be described by the chrysene nomenclature and each racemate is arbitrarily represented by that enantiomer that has the C-6a (C-12a) methyl group in the α configuration.
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(3) National Science Foundation Predoctoral Fellow, 1968–1972.
(4) National Defense Education Act Trainee, 1971–1974.
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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 ½ × 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 and 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, trimethyl 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. "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.
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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.

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

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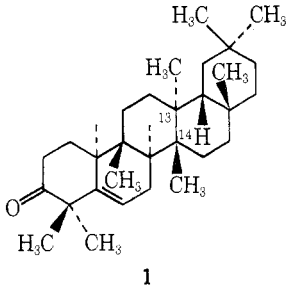
Received October 18, 1974

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-