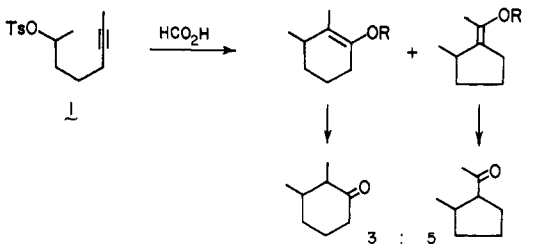
Acetylenic Bond Participation in Biomimetic Polyene Cyclizations.[1] Preliminary Model Studies[2]

Michael B. Gravestock, William S. Johnson,* Robert F. Myers,[3] Thomas A. Bryson,[3] D. Howard Miles,[3] and Bruce E. Ratcliffe

Contribution from the Department of Chemistry, Stanford University, Stanford, California 94305. *Received November 15, 1977*

Abstract: The aim of this study was to examine the possibility that acetylenic bonds might participate in biomimetic polyene cyclizations. The model substrate **4a** was synthesized from the bromodienyne **5a** by the sequence outlined in Scheme I. On treatment with trifluoroacetic acid in methylene chloride at −70 °C, trienynol **4a** underwent cyclization to afford the trans-fused hydrindan **9a** in 68% yield. The structure of **9a** was deduced on the basis of its spectral properties and its oxidative degradation to the hydrindandione **10**, an authentic specimen of which was synthesized by the route depicted in Scheme II. The results of the cyclization of **4a** prompted an examination of the behavior of the homologue **4b**, synthesized in an analogous fashion from bromodienyne **5b** (prepared according to Scheme III). Treatment of **4b** under the aforementioned cyclization conditions resulted in a 60% yield of hydrindan **9b**. Thus the acetylenic bond of the model substrates **4a** and **4b** participates in biomimetic cyclization so as to form a five-membered ring, in preference to the alternative six-membered ring, thereby generating the trans-fused hydrindan ring system.

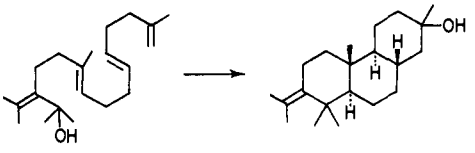
Acetylenic bond participation in the solvolysis of sulfonate esters with concomitant ring formation has been well documented.[4] For example, formolysis of the acetylenic *p*-toluenesulfonate **1** gave products of both five- and six-membered



1

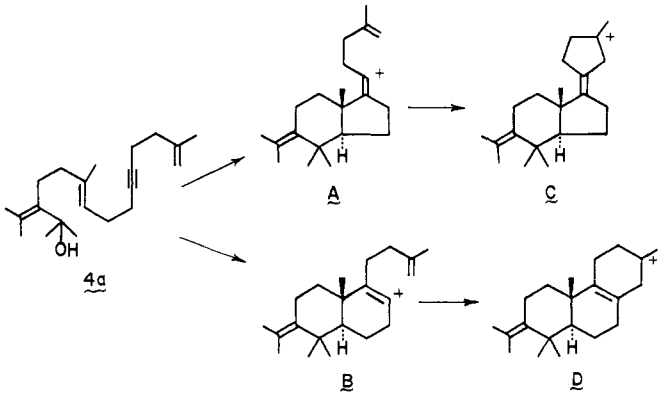
ring closure[5] as depicted in the accompanying flow sheet. These results prompted us to investigate the possibility that acetylenic bonds might also participate in biomimetic polyene cyclizations.[6] The present paper constitutes a detailed account of our preliminary studies probing this question.

Based on the facile acid-catalyzed cyclization of the tetraenol **2**,[7] which gave good yields of tricyclic material **3**



2 3

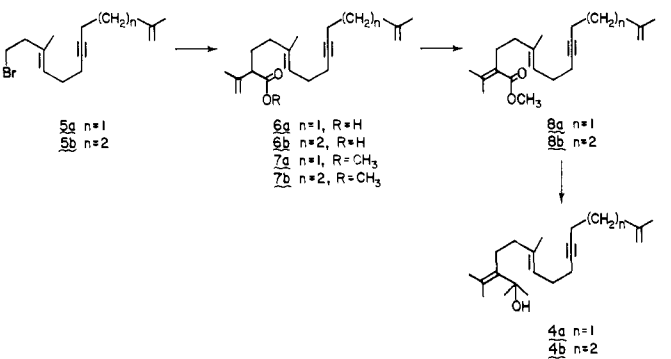
having the rings fused exclusively in the "natural" trans,anti,trans configuration, we decided to examine the cyclization of the trienynol **4a** which has an acetylenic bond where **2** has the disubstituted ethylenic bond. On the basis of the results of the cyclization of substance **1**, it was not obvious, a priori, whether there would be a preference for five- or six-membered ring formation via the vinyl cations A or B, respectively. If cyclization were to continue further, cation A, having the trans-fused hydrindan system, might lead to cation C. Cation B, on the other hand, might lead to cation D, having the lanosterol type A/B/C ring system with an olefinic bond at the 8,9 position.



Synthesis and Cyclization of the Trienynol 4a. The construction of the cyclization substrate was designed in analogy to the route employed in the preparation of tetraenol **2**[7] (see Scheme I). Thus the dianion formed by treatment of lithium 3-methyl-2-butenoate[8] with lithium diisopropylamide was alkylated with the known bromodienyne **5a**,[7,9] and the resulting crude acid **6a** was esterified with ethereal diazomethane to afford the β,γ-unsaturated ester **7a**. Equilibration with potassium *tert*-butoxide in *tert*-butyl alcohol resulted in an 87% yield (from bromide **5a**) of a 7:93 mixture of the β,γ- and the desired α,β-unsaturated esters **7a** and **8a**, respectively. Three successive treatments with methyllithium gave a quantitative yield of a mixture of the trienynol **4a** and 9% of the corresponding homoallylic alcohol derived from the β,γ-unsaturated ester **7a**. This mixture was employed in the cyclization studies without further purification.

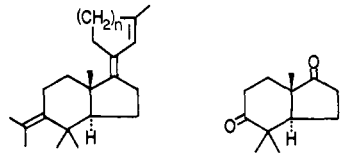
Treatment of a methylene chloride solution of the trienynol **4a** at −70 °C with trifluoroacetic acid for 5 min, conditions which were successfully employed in the cyclization of tetraenol **2**,[7] resulted in the formation of a single major component in 68% yield as estimated by VPC. This material was isolated by preparative TLC on silica gel in 90–95% VPC pu-

Scheme I



0002-7863/78/1500-4268$01.00/0

rity and was tentatively identified as the tricyclic substance **9a** based on the following evidence. The mass spectrum exhibited a parent peak at *m/e* 284 (M^+), and the UV spectrum displayed a maximum at 245 nm (ϵ 10 000) consistent with the conjugated dienic chromophore shown in **9a.**[10] The NMR spectrum showed absorptions for the three methyl groups attached to quaternary carbon atoms as singlets at δ 0.96, 1.12, and 1.37 ppm, and for the isopropylidene methyl groups as singlets at 1.68 and 1.78 ppm. In addition there was a broad singlet for the vinyl methyl group on the cyclopentene ring at 2.17 ppm ($W_{h/2}$ = 4 Hz) and a broad "singlet" for the vinyl proton at 5.58 ppm ($W_{h/2}$ = 5 Hz). There was a notable absence of absorptions for a terminal methylene group in the IR spectrum. Conclusive evidence for the trans hydrindan skeleton of **9a** was obtained by oxidative degradation with excess ru-



9a n=1
9b n=2

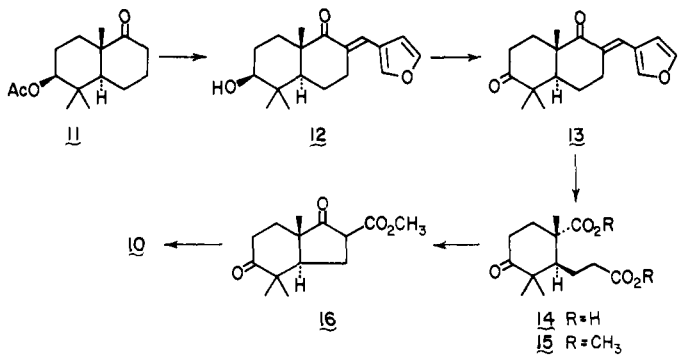
10

thenium tetroxide[11] in carbon tetrachloride, which yielded the crystalline hydrindandione **10,** mp 57–59 °C, indistinguishable from an authentic specimen of **10** (see below) by IR, NMR, VPC, TLC, and mixture melting point (58.0–59.5 °C). It should be noted that the geometrical configuration about the exocyclic olefinic bond at C-1 of the hydrindan system has not been established; however, evidence from studies of similar systems[12] suggest that trans addition to the carbon–carbon triple bond is favored, and this consequence would lead to the configuration shown in formula **9a.**

Synthesis of the Comparison Compound 10. The authentic dione **10** was synthesized by the route shown in Scheme II. Thus treatment of 5,5,9β-trimethyl-6β-acetoxy-*trans*-1-decalone (**11**)[13] with furfuraldehyde in aqueous methanolic sodium hydroxide[14] afforded the hydroxy furfurylidene ketone **12,** mp 136–137 °C, which, upon oxidation with Collins reagent,[15] gave the crystalline diketone **13,** mp 102.0–103.5 °C. A previously reported sequence for ring contraction[14] was applied to the dione **13.** Thus ozonolysis in ethyl acetate at −70 °C followed by treatment with hydrogen peroxide in acetic acid gave the diacid **14,** mp 134–137 °C. The corresponding keto diester **15,** prepared by methylation of **14** with excess diazomethane, was then submitted to a Dieckmann cyclization with potassium *tert*-butoxide in benzene. The resulting β-keto ester **16** was decarbomethoxylated by heating in a mixture of aqueous hydrochloric acid and acetic acid to afford, after careful purification, the crystalline hydrindandione **10,** mp 58.0–59.5 °C.

Synthesis and Cyclization of the Homologous Trienynol 4b. The results of the cyclization of the trienynol **4a** prompted us to examine the behavior of the next higher homologue **4b** to

Scheme II



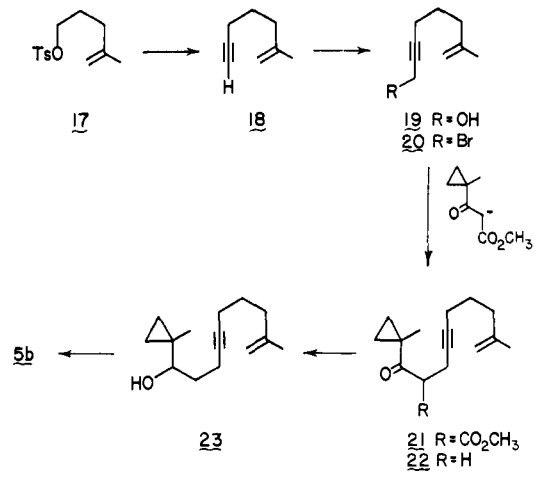
11 12 13

14 R=H
15 R=CH_3

16

10

Scheme III



17 18 19 R=OH
20 R=Br

21 R=CO_2CH_3
22 R=H

23

5b

see if the inclusion of an additional methylene unit would alter the preference for five-membered ring formation. The synthesis of **4b** from the bromodienyne **5b** was achieved using the same route as for the lower homologue **4a** (see Scheme I). The bromide **5b** was constructed as shown in Scheme III. Thus ethynylation of the tosylate **17,**[16] prepared from 4-methyl-4-penten-1-ol,[17] with lithium acetylide ethylenediamine complex in dimethyl sulfoxide afforded 6-methyl-6-hepten-1-yne (**18**) in 69% yield after distillation. This substance was converted to the corresponding Grignard reagent and treated with paraformaldehyde to give a 67% yield of alcohol **19.** Reaction of **19** with triphenyl phosphite dibromide[18] yielded the bromide **20,** which was alkylated with the sodium enolate of 1-methylcyclopropyl carbomethoxymethylene ketone[19] in acetonitrile. The resulting keto ester **21** was decarbomethoxylated by heating with barium hydroxide in aqueous ethanol giving the cyclopropyl ketone **22** in 53% yield from alcohol **19.** Reduction of **22** with lithium aluminum hydride afforded the cyclopropylcarbinol **23** in 97% yield. Stereoselective rearrangement of alcohol **23** to the desired trans bromodienyne **5b** was effected by the modified Julia olefin synthesis.[20] Thus treatment of an ethereal solution of **23** with lithium bromide and *s*-collidine, followed by phosphorus tribromide at −78 °C, gave a mixture of bromides which was directly isomerized with zinc bromide in ether at 0 °C to afford the crude bromodienyne **5b** in 93% yield.

Alkylation of lithium 3-methyl-2-butenoate[8] with bromide **5b** gave the acid **6b** which was directly esterified to the β,γ-unsaturated ester **7b.** The crude ester was equilibrated with potassium *tert*-butoxide to afford the α,β-unsaturated ester **8b** in 30% overall yield from bromide **5b.** Three successive treatments with methyllithium gave the desired trienynol **4b** contaminated with 10% of the corresponding β,γ-unsaturated alcohol and 10% of the tetraenyne resulting from dehydration of **4b.** This crude material was used directly in the cyclization studies described below.

The crude trienynol **4b** was submitted to the cyclization conditions described above for the lower homologue **4a** to give a product consisting of one major component in 60% yield as shown by VPC. Chromatography on Florisil afforded a fraction (80% pure by VPC) which evidently contained the hydrindan derivative **9b.** The spectral properties of this material were quite similar to those of the lower homologue **9a.** The NMR spectrum exhibited singlets for three methyl groups attached to quaternary carbon atoms at δ 1.00, 1.12, and 1.40 ppm, and a broad "singlet" at 5.65 ppm for the vinyl proton of the cyclohexene ring. The mass spectrum displayed a molecular ion at *m/e* 298 (M^+), and the UV showed an absorption maximum at 244 nm (ϵ 18 000). Oxidative degradation with ruthenium tetroxide[11] gave the hydrindandione **10,** mp

57.5–59.5 °C, indistinguishable from authentic **10** by mixture melting point (57.5–60.0 °C), TLC, and VPC.

Conclusion

The acetylenic bond participates in the cyclization of the model substrates **4a** and **4b** resulting in preferential[21] formation of a five-membered ring generating the trans hydrindan fused ring system. This discovery has prompted us to examine the possibility that an appropriately positioned acetylenic bond can be used to direct formation of the five-membered D ring of steroids. To this end, the synthesis and cyclization of substrates with a methylacetylenic terminating group have been studied extensively, and the application to the synthesis of *dl*-progesterone is presented in detail in the accompanying paper.[22]

Experimental Section[23]

General Considerations. Microanalyses were performed by E. H. Meier and J. Consul, Department of Chemistry, Stanford University. Melting points were determined on a Kofler hot-stage microscope and are corrected. NMR spectra were determined under the supervision of Dr. L. J. Durham on a Varian Associates T-60 NMR spectrometer using deuteriochloroform as the solvent. Chemical shifts are reported as δ values in parts per million relative to tetramethylsilane = 0. Low-resolution mass spectra were determined on an AEI MS-9 spectrometer with heated inlet at 70 eV. Infrared (IR) spectra were recorded on a Perkin-Elmer Model 137 spectrometer and ultraviolet (UV) spectra were recorded on a Cary Model 14 spectrometer using 1-cm quartz cells. Vapor phase chromatographic (VPC) analyses were performed on a Hewlett-Packard HP 402 chromatograph equipped with a 6 ft × 6 mm glass column packed with 10% Carbowax M on 60/80 Chromosorb W and a 4 ft × 6 mm glass column packed with 3.8% SE-30 on 80/100 Diatoport S using helium as the carrier gas. Disk chart integrations are uncorrected for the flame-ionization detector response. Thin layer chromatography (TLC) was carried out using silica gel GF_{254} (E. Merck A.G.) for both analytical (0.25 mm thick) and preparative (1.5 mm thick) plates. "Evaporative distillation" refers to bulb-to-bulb short-path distillation in which the bulb was heated in a hot-air oven (Buchi Kügelrohrofen). The cited temperatures for these distillations pertain to the oven temperature and are thus not true boiling points.

Methyl 2-Isopropylidene-5,13-dimethyltetradeca-*trans*-5,13-dien-9-ynoate (8a). A solution of lithium diisopropylamide was prepared by adding 8.0 mL (20 mmol) of a 2.50 M solution of *n*-butyllithium in hexane to a cold (0 °C) solution of 2.02 g (20 mmol) of diisopropylamine (dried over potassium hydroxide pellets) in 5 mL of dry THF under nitrogen. After stirring for 5 min at 0 °C, the above solution was added via syringe over a period of 3 min to a cold (0 °C) slurry of 2.12 g (20 mmol) of lithium 3-methyl-2-butenoate[8] in 15 mL of THF. The mixture was stirred under nitrogen for 15 min at 0 °C, cooled to −70 °C, and a solution of 1.44 g (ca. 5 mmol) of bromide **5a**[7,9] (94% pure by VPC) in 10 mL of THF was added via syringe over a 3-min period. The resulting mixture was allowed to warm slowly to room temperature while stirring for 20 h. The mixture was poured into 100 mL of 5% aqueous sodium hydroxide and extracted with 1:1 ether–pentane (3 × 50 mL). The combined organic extracts were washed with 20 mL of water; then the combined aqueous layers were cooled to 0 °C, acidified to pH 1.0 with 10% hydrochloric acid, and extracted with benzene. The combined organic extracts[23] afforded 1.67 g of crude acid **6a** as a pale yellow oil. Esterification with excess ethereal diazomethane gave 1.55 g of yellow oil consisting of 88% of the β,γ-unsaturated ester **7a**, 0.5% of α,β-unsaturated ester **8a**, 1.5% of an unidentified impurity, and 10% of methyl 3-methyl-2-butenoate as shown by VPC (SE-30).

To a solution of 3.56 g (11.7 mmol) of the crude β,γ-unsaturated ester **7a** (85–88% pure), prepared as described above, in 25 mL of dry *tert*-butyl alcohol under nitrogen, was added via syringe 10 mL of a 5% solution of potassium *tert*-butoxide in *tert*-butyl alcohol. The resulting dark cherry-red mixture was stirred at 23 °C for 6 h, poured into a mixture of brine and dilute hydrochloric acid, and extracted with pentane[23] to give 3.45 g (95% weight recovery) of orange oil containing a 93:7 mixture of α,β- and β,γ-unsaturated esters **8a** and **7a** by VPC. The crude product was evaporatively distilled at 170 °C (0.02 mm) to give 2.70 g (87% yield) of a 93:7 mixture of **8a** and **7a** as a pale yellow oil.

An analytical sample was obtained by preparative TLC on Florisil: IR λ_{max} (film) 3.40, 5.80, 6.02, 8.20, 8.47, and 11.21 μ; NMR 1.58 (s, 3 H, C-14 vinyl CH_3), 1.62 (s, 3 H, C-6 vinyl CH_3), 1.77 (s, 3 H, C-2 vinyl CH_3), 1.90 (s, 3 H, C-2 vinyl CH_3), 1.8–2.45 (m, 12 H, allylic and propargylic CH_2's), 3.65 (s, 3 H, CO_2CH_3), 4.70 (br s, 2 H, C-15 vinyl protons), and 5.15 ppm (unresolved t, J = 6 Hz, 1 H, C-7 vinyl proton); UV λ_{max} (MeOH) 222 nm (ϵ 3000); TLC R_f 0.32 (9:1 hexane–ethyl acetate). The mass spectrum exhibited a molecular ion at *m/e* 302, and major peaks at *m/e* 287 (M − 15) and 243 (M − 59).

Anal. Calcd for $C_{20}H_{30}O_2$: C, 79.42; H, 10.00. Found: C, 79.11; H, 9.92.

3-Isopropylidene-2,6,14-trimethylpentadeca-*trans*-6,14-dien-10-yn-2-ol (4a). To a solution of 302 mg (1 mmol) of the above distilled ester **8a** and a few crystals of 1,10-phenanthroline in 10 mL of dry ether was added 4.0 mL (5 mmol) of a 1.25 M solution of methyllithium in ether. The dark brown mixture was stirred at 23 °C under nitrogen for 5 min, and saturated aqueous ammonium chloride was added until a lime green color persisted. The above process, i.e., addition of methyllithium followed by ammonium chloride, was repeated twice more; then the resulting mixture was poured into saturated ammonium chloride and extracted with ether[23] to afford 319 mg (quantitative yield) of crude alcohol **4a** as a lemon yellow oil which consisted of 91% **4a** and 9% of the corresponding homoallylic alcohol by VPC (SE-30, 170 °C): IR λ_{max} (film) 2.78–3.23 (OH), 3.44, 8.93, and 11.22 μ (C=CH_2); NMR 1.30 (s, 6 H, carbinol CH_3's), 1.58 (s, 3 H, C-14 vinyl CH_3), 1.63 (s, 3 H, C-6 vinyl CH_3), 1.70 (s, 3 H, isopropylidene CH_3), 1.80 (s, 3 H, isopropylidene CH_3), 1.60–2.50 (m, 12 H, allylic and propargylic CH_2's), 4.80 (br s, 2 H, C-15 vinyl protons), and 5.21 ppm (unresolved t, J = 6.0 Hz, 1 H, C-7 vinyl proton); TLC R_f 0.33 (4:1 hexane–ethyl acetate).

This product was exceedingly susceptible to dehydration and could not be further purified without decomposition. Therefore, an analytical sample was not obtained, and the crude product was used directly in the cyclization experiment described below.

Cyclization of Alcohol 4a. 5-Isopropylidene-1-(3-methylcyclopent-2-enylidine)-4,4,8β-trimethyl-9α-hydrindan (9a). A solution of 302 mg (1 mmol) of the crude alcohol **4a** in 160 mL of dry methylene chloride (distilled from phosphorus pentoxide) was cooled to −70 °C under nitrogen, and 3.0 mL (41 mmol) of trifluoroacetic acid was added via syringe. The mixture was stirred at −70 °C for 5 min and poured into 300 mL of saturated aqueous sodium bicarbonate with rapid stirring. Extraction with ether[23] afforded 320 mg of yellow oil which, upon VPC (SE-30, 200 °C) analysis, was comprised of five components of retention times 5.2 (9% of the β,γ-unsaturated alcohol), 5.7 (62%), 7.0 (12%), 7.6 (4%), and 8.4 min (13%).

The major component, hydrindan **9a**, was isolated in 90–95% (VPC) purity by preparative TLC (R_f 0.73, 4:1 pentane–ethyl acetate) and proved to be quite sensitive to heat and light: IR λ_{max} ($CHCl_3$) 3.42, 6.10, 6.90, and 7.30 μ; NMR 0.96 (s, 3 H, C-4 CH_3), 1.12 (s, 3 H, C-4 CH_3), 1.37 (s, 3 H, C-8 CH_3), 1.68 (s, 3 H, isopropylidene CH_3), 1.78 (s, 3 H, isopropylidene CH_3), 0.85–1.9 (methylene envelope, 9 H), 2.17 (br s, $W_{h/2}$ = 4 Hz, 3 H, C-3 vinyl CH_3 of cyclopentene), 2.0–2.5 (m, 4 H, cyclopentene CH_2's), and 5.58 ppm (br s, $W_{h/2}$ = 5 Hz, 1 H, C-2 vinyl proton of cyclopentene); UV λ_{max} (MeOH) 245 nm (ϵ 10 000). The mass spectrum exhibited a molecular ion at *m/e* 284.

A satisfactory combustion analysis could not be obtained for this substance owing to its considerable sensitivity to heat and light.

Oxidative Degradation of Hydrindan 9a. To a solution of 120 mg of the aforementioned crude cyclization product in 30 mL of carbon tetrachloride (spectroquality) was added 10 mL of a solution of ruthenium tetroxide in carbon tetrachloride (prepared according to a published procedure[11]), resulting in an instantaneous precipitation of black ruthenium dioxide. The mixture was stirred for 1 h and the excess oxidant was destroyed by titration with isopropyl alcohol; then the mixture was diluted with chloroform and washed with 5% aqueous sodium hydroxide[23] to give 40 mg of colorless oil. This material was evaporatively distilled at 80–110 °C (0.1 mm) to afford 30 mg of colorless oil. Two recrystallizations from hexane yielded 5 mg of the hydrindandione **10** as colorless plates, mp 57–59 °C, which was indistinguishable from authentic dione **10** (see below) by IR, NMR, VPC, TLC, and mixture melting point (58.0–59.5 °C).

2-Furfurylidene-5,5,9β-trimethyl-6β-hydroxy-*trans*-1-decalone (12). An adaptation of a published procedure[14] was employed. To a solution of 7.445 g (29.6 mmol of **5,5,9β-trimethyl-6β-acetoxy-*trans*-1-decalone (11),**[13] mp 95.5–97.0 °C, in 60 mL of methanol was added 35 mL of furfuraldehyde [distilled twice from sodium carbonate, then fractionally distilled, bp 42 °C (12 mm)] followed by 100 mL of 36.5% aqueous sodium hydroxide. The resulting mixture was stirred in the dark under nitrogen for 4 h, then concentrated to 50% of its original volume at reduced pressure. The resulting precipitate was filtered and recrystallized from ether to afford 4.179 g (49% yield) of the hydroxy furfurylidene ketone **12:** mp 136–137 °C; IR λ_{max} (KBr) 5.97 and 6.15 μ; NMR 0.90 (s, 3 H, CH_3), 1.06 (s, 3 H, CH_3), 1.10 (s, 3 H, CH_3), 1.15–3.70 (m, 11 H), 6.50 (m, 2 H, vinyl protons), 7.25 (m, 1 H, vinyl proton), and 7.50 ppm (m, 1 H, vinyl proton). The mass spectrum exhibited a molecular ion at *m/e* 288.

Anal. Calcd for $C_{18}H_{24}O_3$: C, 74.97; H, 8.29. Found: C, 75.19; H, 8.32.

2-Furfurylidene-5,5,9β-trimethyl-6-oxo-*trans*-1-decalone (13). Collins reagent[15] (100 mmol) was prepared in situ by adding 10.00 g (100 mmol) of chromium trioxide to a solution of 15.80 g (200 mmol) of dry pyridine in 100 mL of dry methylene chloride. A solution of 2.66 g (9.23 mmol) of the furfurylidene keto alcohol **12,** mp 136–137 °C, in 100 mL of dry methylene chloride was added to the solution of Collins reagent, and the resulting mixture was stirred for 10 min at room temperature under nitrogen. The mixture was filtered through 25 g of neutral alumina (Woelm, activity III) followed by further elution with 500 mL of methylene chloride. The solvent was removed at reduced pressure, and the residue was dissolved in 100 mL of ether, washed with saturated aqueous copper sulfate, and dried over anhydrous sodium sulfate. Removal of the solvent at the rotary evaporator followed by recrystallization from ether gave 2.54 g (96% yield) of the furfurylidene dione **13** as colorless rhomboids: mp 102.0–103.5 °C; IR λ_{max} ($CHCl_3$) 5.85 (C=O) and 5.97 μ (conjugated C=O); NMR 0.91 (s, 3 H, CH_3), 1.06 (s, 3 H, CH_3), 1.09 (s, 3 H, CH_3), 1.15–3.70 (m, 9 H), 6.50 (m, 2 H, vinyl protons), 7.25 (m, 1 H, vinyl proton), and 7.50 ppm (m, 1 H, vinyl proton).

Anal. Calcd for $C_{18}H_{22}O_3$: C, 75.49; H, 7.74. Found: C, 75.35; H, 7.63.

4,4,8β-Trimethyl-9α-hydrindan-1,5-dione (10). An adaptation of a published procedure was employed.[14] Ozone was bubbled through a solution of 1.83 g (6.39 mmol) of the dione **13,** mp 102.0–103.5 °C, in 40 mL of ethyl acetate at −70 °C. After 15 min a blue-violet color persisted and ozone treatment was continued for an additional 5 min. The solvent was removed at the rotary evaporator and the residue was dissolved in 40 mL of glacial acetic acid; then 2 mL of water, 1 drop of concentrated hydrochloric acid, and 0.5 mL of 30% hydrogen peroxide were added. The resulting mixture was stirred at room temperature for 17 h; then the solvent was removed at reduced pressure and the residue was dissolved in 200 mL of ether. The ethereal solution was extracted with 10% aqueous potassium bicarbonate solution (3 × 60 mL); then the basic extracts were acidified with concentrated hydrochloric acid and extracted with methylene chloride[23] to afford 0.60 g (37% yield) of the diacid **14** as a colorless, crystalline solid: mp 134–137 °C; IR λ_{max} (CH_2Cl_2) 5.80–5.90 μ (C=O).

A chloroform solution of 1.008 g (3.93 mmol) of the diacid **14,** prepared as described above, was treated with excess diazomethane. The solvent was removed at the rotary evaporator and the residue was evaporatively distilled at 155 °C (0.017 mm) to afford 0.815 g (73% yield) of the keto diester **15** which was 80% pure by VPC: IR λ_{max} ($CHCl_3$) 5.80–5.85 μ (C=O); NMR 1.10 (s, 6 H, *gem*-dimethyl), 1.32 (s, 3 H, CH_3), 1.47–2.85 (m, 9 H), and 3.63 ppm (s, 6 H, CO_2CH_3).

A solution of 6.00 g (153.4 mmol) of potassium in 150 mL of dry *tert*-butyl alcohol (freshly distilled from calcium hydride) was concentrated to dryness at reduced pressure (5 mm). Dry benzene (about 75 mL, distilled from calcium hydride) was added, then removed by distillation at atmospheric pressure, and this process was repeated to ensure removal of *tert*-butyl alcohol. A solution of 0.595 (2.27 mmol) of the aforementioned diester **15** in 100 mL of dry benzene was added to the potassium *tert*-butoxide with stirring under nitrogen. The resulting mixture was heated at reflux for 4 h, then stirred at room temperature for 8 h. The mixture was poured into water, acidified with dilute sulfuric acid, and extracted[23] with benzene (2 × 200 mL) and methylene chloride (100 mL) to afford a yellow solid which gave a positive ferric chloride test. This material was dissolved in 65 mL of glacial acetic acid, then 22.5 mL of concentrated hydrochloric acid and 5 mL of water were added and the solution was heated at reflux for 1 h under nitrogen. The solvent was removed at room temperature (rotary evaporator), and 25 mL of water was added to the residue. Extraction with ether[23] gave 1.00 g of thick oil which was evaporatively distilled at 120 °C (0.012 mm) three times, then chromatographed on 20 g of Florisil (1:1 benzene–methylene chloride) to afford 0.176 g (40% yield) of hydrindandione **10** as a semicrystalline solid.

An analytical sample was obtained after three recrystallizations from hexane as colorless plates: mp 58.0–59.5 °C; IR λ_{max} ($CHCl_3$) 5.75 (five-membered ring C=O) and 5.85 μ (six-membered ring C=O); NMR 1.12 (s, 3 H, C-8 CH_3), 1.20 (s, 6 H, C-4 CH_3's), and 1.67–2.91 ppm (m, 9 H); TLC R_f 0.51 (1:1 hexane–ethyl acetate).

Anal. Calcd for $C_{12}H_{18}O_2$: C, 74.19; H, 9.34. Found: C, 73.96; H, 9.21.

6-Methyl-6-hepten-1-yne (18). A solution of 56.0 g (0.61 mol) of lithium acetylide ethylenediamine complex in 200 mL of dry dimethyl sulfoxide was cooled to 5 °C and 120 g (0.47 mol) of crude **4-methyl-4-penten-1-yl *p*-toluenesulfonate (17)**[16] (prepared from 4-methyl-4-penten-1-ol[17]) in 150 mL of dry dimethyl sulfoxide was added over a period of 20 min with external cooling to maintain the temperature below 10 °C. The resulting dark brown solution was stirred at 23 °C for 1.5 h, then cooled to 0 °C, and 150 mL of 5% aqueous hydrochloric acid was added dropwise. The acidic mixture was poured into 250 mL of water overlaid with 250 mL of ether. The aqueous phase was extracted with ether (4 × 250 mL), and the combined ether extracts were washed with water (4 × 250 mL) and saturated brine (200 mL), then dried over anhydrous magnesium sulfate and filtered. The ether was removed by distillation at atmospheric pressure through a 25-cm Podbelniak column, and the residue was distilled to afford 35.2 g (69% yield) of **18** as a clear, colorless liquid, bp 121–125 °C, which was 96% pure by VPC (Carbowax): IR λ_{max} (film) 3.00 and 4.71 (C≡CH), 6.05 and 11.20 μ (C=CH_2); NMR 1.5–1.9 (m, 2 H, C-4 CH_2), 1.70 (s, 3 H, C-6 CH_3), 1.93 (t, J = 2 Hz, 1 H, acetylenic proton), 2.0–2.2 (m, 4 H, C-3 and C-5 CH_2's), and 4.70 ppm (br s, 2 H, C-7 vinyl protons).

An analytical sample was obtained by evaporative distillation at 125 °C, n^{21}_D 1.4356. The mass spectrum exhibited a molecular ion at *m/e* 108, a base peak at *m/e* 93, and a major peak at *m/e* 41.

Anal. Calcd for C_8H_{12}: C, 88.82; H, 11.18. Found: C, 88.36; H, 10.98.

7-Methyl-7-octen-2-yn-1-ol (19). A solution of 34.6 g (0.32 mol) of acetylene **18** (bp 121–125 °C) in 600 mL of dry THF was heated at reflux under nitrogen, and an excess of ethylmagnesium bromide (prepared from 0.67 mol of ethyl bromide and 0.75 mol of magnesium) in 150 mL of THF was added over a period of 1 h. The resulting solution was heated at reflux for an additional 1.5 h; then a slurry of 36 g (1.2 mol) of paraformaldehyde (dried over phosphorus pentoxide at 0.1 mm) in 150 mL of dry THF was added over a period of 1 h. Heating at reflux was continued for 2 h followed by stirring at 23 °C for 17 h. A saturated solution of aqueous ammonium chloride (250 mL) was added to the reaction mixture followed 10 min later by ca. 100 g of sodium sulfate. The organic layer was decanted and the solid residue was dissolved in a minimal amount of water and extracted with pentane[23] to afford 44.8 g of orange liquid. Distillation of this material gave 31.9 g (67% yield) of alcohol **19,** bp 93–94 °C (1.5 mm), which was 90% pure by VPC (Carbowax).

A 0.50-g sample of the distilled alcohol **19** was chromatographed on 75 g of silica gel (4:1 hexane–ether) to give 0.37 g of **19** which appeared to be pure by VPC (Carbowax, 200 °C): IR λ_{max} (film) 3.0 (OH), 4.38 and 4.49 (C≡C), 6.05 and 11.20 μ (C=CH_2); NMR 1.5–1.9 (m, 2 H, C-5 CH_2), 1.70 (s, 3 H, C-7 CH_3), 1.9–2.2 (m, 4 H, C-4 and C-6 CH_2's), 2.6 (br s, 1 H, OH), 4.24 (t, J = 2 Hz, 2 H, C-1 CH_2), and 4.70 ppm (br s, 2 H, C-8 vinyl protons).

An analytical sample was prepared by evaporative distillation at 95 °C (1.5 mm) of the chromatographed material, n^{21}_D 1.4748. The mass spectrum exhibited a molecular ion at *m/e* 138 and a base peak at *m/e* 41.

Anal. Calcd for $C_9H_{14}O$: C, 78.21; H, 10.21. Found: C, 77.72; H, 10.23.

1-Methylcyclopropyl 1-Carbomethoxy-8-methyl-8-nonen-3-ynyl Ketone (21). The acetylenic bromide **20** was prepared by employing an adaptation of a published procedure.[18] A solution of bromine in methylene chloride was slowly added to a stirred solution of 46.5 g (0.15 mol) of triphenyl phosphite in 180 mL of dry methylene chloride and 180 mL of dry ether under nitrogen until a yellow color persisted.

The resulting solution of triphenyl phosphite dibromide was cooled to −78 °C, 15 mL of dry pyridine was added, and 22.2 g (0.147 mol) of the distilled alcohol **19** in 150 mL of dry ether was added over a period of 1 h. The mixture was stirred at −78 °C for 1 h and at 0 °C for 2 h, then poured into 250 mL of water overlaid with 250 mL of pentane. Extraction with pentane using an acid wash[23] yielded 75 g of crude bromide **20** as a colorless liquid which was used immediately in the alkylation step below.

A solution of the crude bromide (0.147 mol maximum) in 100 mL of dry acetonitrile was added dropwise to a warm (55 °C) solution of 60 g (0.40 mol) of sodium iodide and 40 g (0.22 mol) of the sodium enolate of 1-methylcyclopropyl carbomethoxymethylene ketone[19] in 300 mL of dry acetonitrile under nitrogen. The resulting mixture was stirred at 55 °C for 17 h and poured into a mixture of 100 mL of water, 100 mL of saturated brine, and 100 mL of 10% aqueous hydrochloric acid overlaid with 250 mL of ether. Ether extraction using an acid wash[23] afforded 114 g of crude keto ester **21** as a dark red liquid which was decarbomethoxylated without purification.

Chromatography of a 1.0-g sample of the crude keto ester, prepared by the procedure described above, on 150 g of silica gel (4:1 hexane–ether) gave 0.75 g of **21** which was pure by TLC (R_f 0.61, 1:1 hexane–ether): IR λ_{max} (film) 5.71 (ester C=O), 5.91 (C=O), 6.05 and 11.20 μ (C=CH_2); NMR 0.7–1.0 (m, 2 H, cyclopropyl protons), 1.3–1.6 (m, 2 H, cyclopropyl protons), 1.50 (s, 3 H, cyclopropyl CH_3), 1.75 (s, 3 H, C-8 vinyl CH_3), 1.9–2.3 (m, 4 H, C-5 and C-7 CH_2's), 2.6–2.9 (m, 2 H, C-2 CH_2), 3.65 (s, 3 H, CO_2CH_3), 3.85 (t, J = 7 Hz, 1 H, C-1 CH), and 4.70 ppm (br s, 2 H, C-9 vinyl protons).

An analytical specimen was prepared by evaporative distillation at 120 °C (0.09 mm) of the chromatographed keto ester, n^{21}_D 1.4816. The mass spectrum exhibited a molecular ion at *m/e* 276, a base peak at *m/e* 83, and major peaks at *m/e* 55 and 41.

Anal. Calcd for $C_{17}H_{24}O_3$: C, 73.88; H, 8.75. Found: C, 74.14; H, 8.80.

1-Methylcyclopropyl 8-Methyl-8-nonen-3-ynyl Ketone (22). A mixture of 76 g (0.24 mol) of barium hydroxide octahydrate, 114 g of the aforementioned crude keto ester **21,** 500 mL of water, and 100 mL of ethanol was heated at reflux under nitrogen for 17 h. The mixture was cooled, poured into 300 mL of benzene, and acidified to pH 1 with 10% aqueous hydrochloric acid. Saturated brine (100 mL) was added and the aqueous phase was extracted with benzene using a wash with 5% aqueous sodium hydroxide[23] to yield 28.6 g of crude ketone **22** as an orange liquid. This product was distilled to afford 17.5 g (53% yield from alcohol **19**) of **22,** bp 100–105 °C (0.06 mm), which was 96% pure by VPC (SE-30): IR λ_{max} (film) 5.91 (C=O), 6.05 and 11.20 μ (C=CH_2); NMR 0.6–0.9 (m, 2 H, cyclopropyl protons), 1.20–1.40 (m, 2 H, cyclopropyl protons), 1.40 (s, 3 H, cyclopropyl CH_3), 1.75 (s with a br base, 5 H, C-8 CH_3 and C-6 CH_2), 1.90–2.35 (m, 4 H, C-5 and C-7 CH_2's), 2.35–2.70 (m, 4 H, C-1 and C-2 CH_2's), and 4.70 ppm (br s, 2 H, C-9 vinyl protons).

An analytical sample was prepared by evaporative distillation at 105 °C (0.009 mm): TLC R_f 0.55 (4:1 hexane–ether); n^{21}_D 1.4833. The mass spectrum exhibited a molecular ion at *m/e* 218, a base peak at *m/e* 55, and major peaks at *m/e* 83 and 41.

Anal. Calcd for $C_{15}H_{22}O$: C, 82.52; H, 10.16. Found: C, 82.85; H, 10.20.

1-Methylcyclopropyl-8-methyl-8-nonen-3-ynylcarbinol (23). A solution of 17.5 g (78 mmol) of ketone **22,** bp 100–105 °C (0.06 mm), was added over a period of 45 min to a cold (0 °C), rapidly stirred slurry of 3.22 g (85 mmol) of lithium aluminum hydride in 250 mL of dry ether under nitrogen. The resulting mixture was stirred at 0 °C for 1 h; then 2 mL of water followed by 7 mL of 15% aqueous sodium hydroxide was carefully added. The ether was decanted and the solid residue was washed with ether. The combined ethereal solutions were dried over anhydrous sodium sulfate and evaporated at reduced pressure to afford 19.88 g of crude carbinol **23** as a light yellow liquid. Short-path distillation at 110 °C (0.04 mm) gave 16.65 g (97% yield) of **23** which was pure by VPC (SE-30): IR λ_{max} (film) 2.95 (OH), 6.05 and 11.20 μ (C=CH_2); NMR 0.3–0.5 (m, 4 H, cyclopropyl CH_2's), 1.05 (s, 3 H, cyclopropyl CH_3), 1.4–1.9 (m, 3 H, C-6 CH_2 and OH), 1.70 (s, 3 H, C-8 CH_3), 1.9–2.4 (m, 8 H, C-1, C-2, C-5, and C-7 CH_2's), 3.0 (t, J = 5 Hz, 1 H, C*H*OH), and 4.70 ppm (br s, 2 H, C-9 vinyl protons).

An analytical sample was obtained by evaporative distillation at 110 °C (0.04 mm), n^{21}_D 1.4829. The mass spectrum exhibited a molecular ion at *m/e* 220, a base peak at *m/e* 95, and major peaks at *m/e* 55 and 41.

Anal. Calcd for $C_{15}H_{24}O$: C, 81.76; H, 10.98. Found: C, 81.33; H, 10.84.

1-Bromo-3,12-dimethyltrideca-*trans*-3,12-dien-7-yne (5b). An adaptation of a reported procedure[20] was employed. A solution of 2.85 g (10.5 mmol) of phosphorus tribromide in 50 mL of dry ether was added to a cold (−78 °C), rapidly stirred mixture of 0.937 g (10.8 mmol) of lithium bromide, 4.55 g (37.0 mmol) of *s*-collidine, 2.20 g (10.0 mmol) of the aforementioned cyclopropylcarbinol **23,** and 50 mL of dry ether. The resulting mixture was allowed to warm slowly to room temperature and was stirred for 20 h; then 3 mL of *s*-collidine was added and the mixture was cooled to 0 °C. Water (10 mL) was added dropwise and the mixture was poured into 100 mL of 50% brine overlaid with 50 mL of hexane. Hexane extraction using a cold (0 °C) acid wash and a base wash[23] gave 2.26 g (80% weight recovery) of pale yellow liquid which was used directly in the rearrangement reaction described below.

A solution of the product described directly above in 50 mL of dry ether was added to a cold (0 °C) solution of 11.25 g (50 mmol) of dry zinc bromide in 50 mL of dry ether under nitrogen. The mixture was stirred at 0 °C for 3.5 h, then poured into 40 mL of 50% brine overlaid with 40 mL of pentane. Extraction with pentane[23] gave 2.64 g (93% yield from cyclopropylcarbinol **23**) of bromide **5b** as a pale yellow liquid which was 85% pure by VPC (SE-30). This material was used directly in the alkylation described below.

Partial distillation of a 1.43-g sample of the crude bromide **5b,** prepared as described above, gave a pot residue which contained the desired bromide **5b** as the only volatile component. The pot residue was evaporatively distilled at 99 °C (0.015 mm) to afford 0.15 g of **5b** as a clear, colorless liquid which was 97% pure by VPC: IR λ_{max} (film) 6.05 and 11.20 μ (C=CH_2); NMR 1.4–1.9 (m, 2 H, C-10 CH_2), 1.65 (s, 3 H, C-3 CH_3), 1.75 (s, 3 H, C-12 CH_3), 2.0–2.3 (m, 8 H, C-5, C-6, C-9, and C-11 CH_2's), 2.55 (t, J = 8 Hz, 2 H, C-2 CH_2), 3.45 (t, J = 8 Hz, 2 H, C-1 CH_2), 4.70 (br s, 2 H, C-13 vinyl protons), and 5.30 ppm (m, 1 H, C-4 vinyl proton).

An analytical sample was obtained by a second evaporative distillation at 99 °C (0.015 mm), n^{21}_D 1.5024. The mass spectrum exhibited a molecular ion at *m/e* 282, a base peak at *m/e* 41, and major peaks at *m/e* 284 ($M^+ + 2$) and 202 (−HBr).

Anal. Calcd for $C_{15}H_{23}Br$: C, 63.62; H, 8.12. Found: C, 64.35; H, 8.24.

Methyl 2-Isopropylidene-5,14-dimethylpentadeca-*trans*-5,14-dien-9-ynoate (8b). A solution of lithium diisopropylamide was prepared by adding 17.5 mL (40 mmol) of a 2.28 M solution of *n*-butyllithium in hexane to a cold (0 °C) solution of 4.55 g (45 mmol) of diisopropylamine in 15 mL of dry THF with rapid stirring. After stirring at 0 °C for 7 min, this solution was added via syringe to a cold (0 °C) slurry of 4.80 g (45 mmol) of lithium 3-methyl-2-butenoate[8] in 50 mL of dry THF under nitrogen. The mixture was stirred for 30 min at 0 °C and cooled to −78 °C, and a solution of 2.64 g (8 mmol) of the crude bromide **5b** in 20 mL of dry THF was added via syringe over a period of 10 min. The resulting mixture was allowed to warm slowly to room temperature and was stirred for 17 h. The mixture was poured into 100 mL of 10% aqueous sodium hydroxide solution and extracted with 1:1 ether–hexane (3 × 100 mL). The combined organic extracts were washed with 100 mL of water. The combined aqueous layers were cooled to 0 °C, acidified with 10% aqueous hydrochloric acid, and extracted with benzene (3 × 100 mL) and ether (100 mL). The combined organic extracts[23] gave 3.96 g of crude acid **6b** as a yellow liquid: NMR 4.7 (m, 2 H, terminal C=CH_2), 4.95 (m, 2 H, C=CH_2, β,γ to CO_2H), 5.2 (m, 1 H, R_2C=CHR), and 11.8 ppm (br s, 1 H, CO_2H). This material was esterified with excess ethereal diazomethane to yield 3.60 g of crude ester **7b.** Chromatography on 360 g of silica gel (4:1 hexane–ether) afforded 1.03 g (41% yield from **5b**) of β,γ-unsaturated ester **7b** as a pale yellow liquid which was 85% pure by VPC (SE-30): IR λ_{max} (film) 5.75 (C=O), 6.05 and 11.20 μ (C=CH_2); NMR 1.4–2.4 (br m, 23 H), 3.0 (m, 1 H at C-3), 3.65 (s, 3 H, CO_2CH_3), 4.70 (br s, 2 H, C-16 vinyl protons), 4.85 (br s, 2 H, C-1 vinyl protons), and 5.10 ppm (br s, 1 H, C-7 vinyl proton).

A solution of potassium *tert*-butoxide, prepared by dissolving 65 mg (1.66 mmol) of potassium in 5 mL of dry *tert*-butyl alcohol under nitrogen, was added to a solution of 1.03 g (2.7 mmol) of the chromatographed β,γ-unsaturated ester **7b** in 15 mL of dry *tert*-butyl alcohol, and the resulting yellow-orange mixture was stirred under nitrogen for 20 h. The mixture was poured into 20 mL of 10% aqueous hydrochloric acid and 20 mL of saturated brine overlaid with 50 mL of hexane. Extraction with hexane using a base wash[23] afforded 0.80

g (30% yield from bromide **5b**) of crude α,β-unsaturated ester **8b** as a pale yellow liquid. The basic washings were acidified to pH 1 with 10% aqueous hydrochloric acid and extracted with hexane[23] to yield 0.20 g of crude β,γ-unsaturated acid **7b**.

A 345-mg sample of the crude α,β-unsaturated ester **8b** was purified by preparative TLC (4:1 hexane–ether) followed by evaporative distillation at 132 °C (0.01 mm) to yield 300 mg of pale yellow liquid consisting of 7% of β,γ-unsaturated ester **7b**, 84% of the desired ester **8b**, and 9% of an unidentified component as shown by VPC (SE-30): $n^{21}D$ 1.4919; IR λ_{max} (film) 5.81 (α,β-unsaturated CO_2Me), 6.05 and 11.20 μ ($C{=}CH_2$); NMR 1.65 (br s, 3 H, vinyl CH_3), 1.75 (br s, 3 H, vinyl CH_3), 1.80 (s, 3 H, isopropylidene CH_3), 2.00 (s, 3 H, isopropylidene CH_3), 3.70 (s, 3 H, CO_2CH_3), 4.70 (br s, 2 H, C-16 vinyl protons), and 5.10 ppm (m, 1 H, C-7 vinyl proton); UV λ_{max} (MeOH) shoulder 224 nm ($\epsilon \sim 8000$). The mass spectrum exhibited a molecular ion at *m/e* 316, a base peak at *m/e* 95, and major peaks at *m/e* 137, 67, and 41.

Anal. Calcd for $C_{21}H_{32}O_2$: C, 79.70; H, 10.19. Found: C, 79.27; H, 10.14.

3-Isopropylidene-2,6,15-trimethylhexadeca-*trans*-6,15-dien-10-yn-2-ol (4b). A solution of 101 mg (0.32 mmol) of the aforementioned purified ester **8b** and a few milligrams of 1,10-phenanthroline in 10 mL of dry ether was cooled to 0 °C and 1.0 mL (2.5 mmol) of a 2.5 M solution of methyllithium in ether was added via syringe. The mixture was stirred for 15 min under nitrogen; then the excess methyllithium was decomposed by the careful addition of methanol until a green color persisted. The above procedure, i.e., addition of methyllithium followed by decomposition with methanol, was repeated twice more using 0.5 mL (1.25 mmol) of the methyllithium solution each time. The resulting mixture was poured into 10 mL of saturated aqueous ammonium chloride and extracted with ether[23] to afford 163 mg of crude alcohol **4b** as a yellow liquid consisting of 10% of the dehydrated tetraenyne, 10% of the homoallylic alcohol, and 80% of the desired alcohol **4b** as shown by VPC (SE-30, 200 °C): IR λ_{max} (film) 3.10 (OH), 6.05 and 11.20 μ ($C{=}CH_2$); NMR 1.2–2.6 (complex m, 33 H), 4.70 (br s, 2 H, C-16 vinyl protons), and 5.10 ppm (m, 1 H, C-7 vinyl proton).

As in the case of the lower homologue **4a**, this substance was exceedingly susceptible to dehydration and could not be further purified without decomposition. Therefore, an analytical sample was not obtained, and the crude product was used directly in the cyclization experiment described below.

Cyclization of Alcohol 4b. 5-Isopropylidene-1-(3-methylcyclohex-2-enylidene)-4,4,8β-trimethyl-9α-hydrindan (9b). A solution of 163 mg (0.32 mmol) of the crude alcohol **4b** in 100 mL of dry methylene chloride was cooled to −78 °C under nitrogen and 1.0 mL of trifluoroacetic acid was added. The mixture was stirred for 5 min at −78 °C and then poured into 100 mL of saturated aqueous sodium bicarbonate. Extraction with ether using a base wash[23] yielded 122.3 mg of orange liquid which was shown to consist of one major component (60%) by VPC (SE-30, 200 °C). Chromatography of the crude cyclization product on 5 g of Florisil (pentane) afforded 44.4 mg of hydrindan **9b** which was 80% pure by VPC (SE-30, 200 °C): NMR 1.00 (s, 3 H, C-4 CH_3), 1.12 (s, 3 H, C-4 CH_3), 1.40 (s, 3 H, C-8 CH_3), 0.80–2.8 (methylene envelope, 23 H), and 5.65 ppm (br s, 1 H, C-2 vinyl proton of cyclohexene); UV λ_{max} (MeOH) 244 nm (ϵ 18 000); TLC R_f 0.60 (hexane). The mass spectrum exhibited a molecular ion at *m/e* 298, a base peak at *m/e* 95, and major peaks at *m/e* 283 (M − 15), 201, and 135.

As in the case of the lower homologue **9a**, this material was exceedingly heat- and light-sensitive. Therefore, a satisfactory combustion analysis could not be obtained.

Oxidative Degradation of Hydindan 9b. A solution of 118.3 mg of chromatographed cyclization product **9b**, prepared as described above, in 30 mL of carbon tetrachloride was cooled to 0 °C and 30 mL of a solution of ruthenium tetroxide in carbon tetrachloride (prepared according to a published procedure[11]) was added. The mixture was stirred at 0 °C for 1 h, and 5 mL of isopropyl alcohol was added to destroy excess oxidant. The resulting mixture was stirred for 15 min at 0 °C and poured into 50 mL of water. Ether extraction using a wash with 5% aqueous sodium hydroxide[23] afforded 37 mg of yellow liquid. Chromatography on 15 g of Florisil (2:1 ether–hexane) gave 2 mg (3% yield) of colorless oil which, after two recrystallizations from hexane, yielded colorless crystals, mp 57.5–59.5 °C. This material was indistinguishable from authentic hydrindandione **10** by mixture melting point (57.5–60.0 °C), TLC R_f 0.18 (1:1 hexane–ether), and VPC (SE-30, 150 °C).

Acknowledgment. We are indebted to the National Institutes of Health and the National Science Foundation for support of this research.

References and Notes

(1) For a recent paper in the series on biomimetic polyene cyclizations, see W. S. Johnson, R. S. Brinkmeyer, V. M. Kapoor, and T. Yarnell, *J. Am. Chem. Soc.*, **99**, 8341 (1977).
(2) A preliminary account of the present work has appeared: W. S. Johnson, M. B. Gravestock, R. J. Parry, R. F. Myers, T. A. Bryson, and D. H. Miles, *J. Am. Chem. Soc.*, **93**, 4330 (1971).
(3) NIH Postdoctoral Fellow.
(4) M. Hanack, *Acc. Chem. Res.*, **3**, 209 (1970); P. J. Stang, *Prog. Phys. Org. Chem.*, **10**, 205 (1973); and references cited therein.
(5) P. E. Peterson and R. J. Kamat, *J. Am. Chem. Soc.*, **91**, 4521 (1969).
(6) For a recent review of biomimetic polyene cyclizations, see W. S. Johnson, *Bioorg. Chem.*, **5**, 51 (1976).
(7) W. S. Johnson and T. K. Schaaf, *Chem. Commun.*, 611 (1969).
(8) W. S. Johnson and L. A. Bunes, *J. Am. Chem. Soc.*, **98**, 5597 (1976).
(9) For experimental details of the preparation of bromodienyne **5a**, see T. K. Schaaf, Ph.D. Thesis, Stanford University, 1969.
(10) Calcd: 244 nm. Cf. A. I. Scott, "Ultraviolet Spectra of Natural Products", Pergamon Press, Oxford, 1964, pp 45–52.
(11) H. Nakata, *Tetrahedron*, **19**, 1959 (1963).
(12) P. J. Stang, *Prog. Phys. Org. Chem.*, **10**, 205 (1973), and references cited therein.. Also see ref 6, p 82, for another example.
(13) F. Sondheimer and D. Elad, *J. Am. Chem. Soc.*, **80**, 1967 (1958).
(14) W. S. Johnson, B. Bannister, and R. Pappo, *J. Am. Chem. Soc.*, **78**, 6331 (1956).
(15) J. C. Collins, W. W. Hess, and F. J. Frank, *Tetrahedron Lett.*, 3363 (1968).
(16) M. F. Ansell and D. A. Thomas, *J. Chem. Soc.*, 539 (1961).
(17) M. F. Ansell and D. A. Thomas, *J. Chem. Soc.*, 1163 (1958).
(18) D. K. Black, S. R. Landor, A. N. Patel, and P. F. Whiter, *Tetrahedron Lett.*, 483 (1963); *J. Chem. Soc. C*, 2260 (1967).
(19) Prepared using an adaptation of a published procedure: S. J. Rhoads, J. C. Gilbert, A. W. Decora, T. R. Garland, R. J. Spangler, and M. W. Urbigkit, *Tetrahedron*, **19**, 1625 (1963).
(20) S. F. Brady, M. A. Ilton, and W. S. Johnson, *J. Am. Chem. Soc.*, **90**, 2882 (1968).
(21) Some of the by-products might possibly result from a competing six-membered ring closure via cation B; however this process probably plays a very minor role as suggested by the high yields of hydrindan ring system formation observed in some related cases (see ref 22).
(22) M. B. Gravestock, W. S. Johnson, B. E. McCarry, R. J. Parry, and B. E. Ratcliffe, *J. Am. Chem. Soc.*, following paper in this issue.
(23) 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 sulfate or magnesium sulfate and filtered, and the solvent was evaporated under reduced pressure (water aspirator) using a rotary evaporator. The use of the term "wash" indicates washing the combined organic layers with saturated aqueous sodium bicarbonate solution ("base wash"), with dilute aqueous hydrochloric acid ("acid wash"), or with the indicated solution prior to the aforementioned washing with water.