Hydrogenation of Compound 4a. A solution of **4a** (0.5 g) in methanol (20 ml) was hydrogenated over PtO_2 (50 mg) for 8 hr at room temperature. The catalyst was separated by filtration and the solvent was removed under reduced pressure. The residue was recrystallized from chloroform–*n*-hexane to give colorless prisms in quantitative yield: mp 239–241°; ir (KBr) 1675 cm^{-1} (C=O).

Anal. Calcd for $C_{12}H_{16}O_2$: C, 74.97; H, 8.39. Found: C, 75.03; H, 8.45.

Cycloaddition of Methyl Coumalate (2b) with Cycloheptatriene. A solution of methyl coumalate (**2b**) (5.6 g, 0.036 mol) and cycloheptatriene (6.6 g, 0.072 mol) in xylene (30 ml) was heated at 170° at various reaction times. The reaction mixture was evaporated under reduced pressure and analyzed by preparative glpc. The results are listed in Table I.

Pyrolysis of Adduct 5a. In the reaction flask connected with a trap immersed into Dry Ice–acetone, adduct **5a** (0.1 g) was heated under reduced pressure (1 mm) at 230° for 2 hr. The volatile material was collected on a cold finger at −30°, in which cycloheptatriene was detected by glpc inspection and much polymeric material remained in the pot.

Cycloaddition of 4,6-Dimethylcoumalic Acid (9) with Cycloheptatriene. A solution of 9 (5 g, 0.03 mol) and cycloheptatriene (5.4 g, 0.06 mol) in xylene (30 ml) was heated in a sealed tube at 200° for 2 days. Then the mixture was evaporated under reduced pressure and purified by silica gel chromatography using benzene to give **11** in 16% yield: mp 235–237° (in a sealed tube); ir (KBr) 1665 (C=O), 1623 (C=C) cm^{-1}; nmr ($CDCl_3$) τ −1.50 (br s, 1 H), 4.05 (m, 3 H), 4.75 (m, 1 H), 7.50–7.80 (m, 4 H), 8.65 (s, 4 H), 9.10 (s, 3 H, CH_3); Raman 1645, 1630 (C=C) cm^{-1}.

Anal. Calcd for $C_{14}H_{16}O_2$: C, 77.75; H, 7.46. Found: C, 77.82; H, 7.46.

Cycloaddition of Ethyl 4,6-Dimethylcoumalate (10) with Cycloheptatriene. A solution of ethyl 4,6-dimethylcoumalate (**10**) (4.9 g, 0.025 mol) and cycloheptatriene (4.6 g, 0.05 mol) in xylene (25 ml) was heated in a sealed tube at 200° for 2 days. The solvent was removed under reduced pressure and the residue was purified by silica gel chromatography using benzene to give **12** as a colorless oil in 25% yield.

A mixture of **12** (900 mg), 20% aqueous KOH (15 ml), and 20% methanolic KOH (15 ml) was refluxed for 20 hr. The solvent was removed under reduced pressure and then the residue was added with water (10 ml) and with 10% HCl (10 ml). Then pale yellow precipitate was filtered and recrystallized from chloroform to give colorless needles (**11**) in 40% yield, mp 235° (in a sealed tube), which was identified by mixture melting points with an authentic sample (**11**).

Hydrogenation of 11. A solution of **11** (108 mg, 0.5 mmol) in 20 ml of methanol was hydrogenated over 5% Pd-C (50 mg) for 0.5 hr at room temperature. The catalyst was then separated by filtration and solvent was removed under reduced pressure. The residue was recrystallized from chloroform–*n*-hexane to give colorless needles (**13**) in quantitative yield: mp 272–274° (in a sealed tube); ir (KBr) 1660 (C=O) cm^{-1}; nmr ($CDCl_3$) τ 0.00 (br s, 1 H), 8.70 (s, 3 H, CH_3), 8.83 (s, 3 H, CH_3), 7.50–9.00 (m, 13 H).

Anal. Calcd for $C_{14}H_{20}O_2$: C, 76.32; H, 9.15. Found: C, 76.61; H, 9.01.

Preparation of Compound 14. A mixture of **12** (2 mmol) and lithium aluminum hydride (4 mmol) in dry ether (20 ml) was stirred for 1 day. After addition of water, the solution was extracted with ether and the solvent was evaporated to dryness. The crude compound was used in the following reaction without further purification. A solution of the crude compound and *p*-bromobenzoyl chloride (2 mmol) and a drop of dry pyridine was stirred for 1 day at room temperature. The solvent was removed under reduced pressure and the residue was purified by silica gel chromatography using *n*-hexane to give *p*-bromobenzoate (**14**) in 50% yield: colorless prisms; mp 60–61° (from *n*-hexane); ir (KBr) 1705 (C=O), 1620 (C=C) cm^{-1}; nmr ($CDCl_3$) τ 2.25 (d, 2 H, J = 9.0 Hz), 2.55 (d, 2 H, J = 9.0 Hz), 4.25 (m, 3 H), 4.75 (m, 1 H), 5.60 (s, 3 H), 7.70 (m, 3 H), 8.52 (dd, 1 H, J = 6.0 and 3.0 Hz), 8.76 (s, 4 H), 9.20 (s, 3 H).

Anal. Calcd for $C_{21}H_{21}O_2Br$: C, 65.46; H, 5.49. Found: C 65.44; H, 5.51.

Cyclization of 4-(*trans*-3,7-Octadienyl)-3-methyl-2-cyclohexen-1-ol and 4-(*trans,trans*-7-Methyl-3,7,11-dodecatrienyl)-3-methyl-2-cyclohexen-1-ol[1]

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Abstract: The trienol **3** has been synthesized from the substituted acetylene **9** (prepared as outlined in Scheme I) according to Scheme II, *i.e.*, **9** → **10** → **11a** → **3**. Similarly, the tetraenol **4** has been synthesized as depicted in Scheme III. Cyclization of trienol **3** with formic acid, followed by cleavage of the resulting formate esters, gave the tricyclic alcohol **14** as the major product, along with some of the epimer **15**. The cis,anti,trans configuration was established by reductive conversion to the hydrocarbon **18** which was compared with authentic material produced by reduction of the known diketone **26** *via* the bisthioketal **27**. Cyclization of the tetraenol **4** with formic acid (1 min) led to the tetracyclic substance **19** along with tricyclic material **23**. The latter material on further treatment with formic acid (20 min) was converted mainly into the C/D cis tetracyclic substance **22**. The structures and configurations of these tetracyclic products were proved by comparison of their derivatives with authentic materials produced by partial synthesis from natural steroids.

In 1966 the use of nonenzymatic cyclizations of allylic alcohol functionalized polyenes was extended to the stereospecific production of tricyclic systems, as exemplified by the synthesis of fichtelite.[2] This achievement, as well as a significant improvement in the ease and stereoselectivity of introducing trans trisubstituted olefinic bonds into cyclization substrates,[3] led imme-

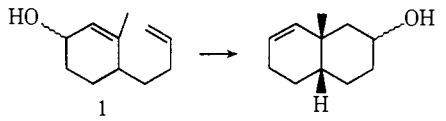
(1) This represents part of a general study of nonenzymic biogenetic like olefinic cyclizations. For the previous paper of this series, see D. R. Morton and W. S. Johnson, *J. Amer. Chem. Soc.*, **96**, in press.

(2) W. S. Johnson, N. P. Jensen, and J. Hooz, *J. Amer. Chem. Soc.*, **88**, 3859 (1966); W. S. Johnson, N. P. Jensen, J. Hooz, and E. J. Leopold, *ibid.*, **90**, 5872 (1968).

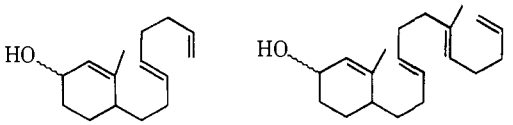
(3) S. F. Brady, M. A. Ilton, and W. S. Johnson, *J. Amer. Chem. Soc.*, **90**, 2882 (1968).

diately to attempts to apply the general method to the stereospecific formation of tetracyclic products. In this and the following two papers are reported the synthesis and cyclization of several allylic alcohol substrates which were designed to lead to tri- and tetracyclic products.[4]

Since it had been shown[5] that mild formic acid treatment of 4-(3-butenyl)-3-methyl-2-cyclohexen-1-ol (**1**) gave, after cleavage of the formate esters, *cis*-9-methyl-Δ^7-2-octalol (**2**) in essentially quantitative yield, monocyclic alcohols **3** and **4** were chosen for the initial studies which constitute the subject of the present paper.



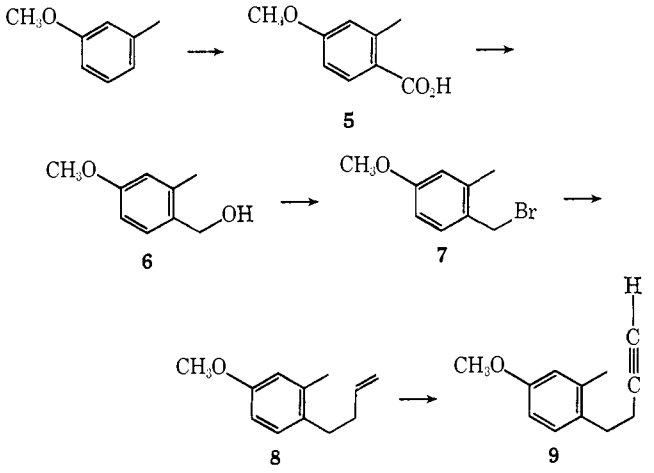
1 2



3 4

The substrates **3** and **4** were both synthesized from the butynylmethylanisole **9** which was prepared by Scheme I.[6] The key steps in the process involved the coupling

Scheme I

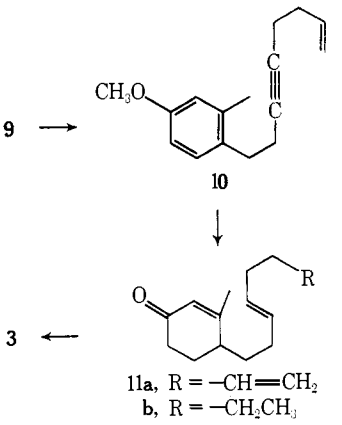


5 6 7 8 9

of the bromide **7** with allylmagnesium chloride to give the known[5] (by a different route) butenyl compound **8** which was in turn brominated and dehydrobrominated to yield **9**.

For the synthesis of trienol **3** (see Scheme II), the lithium salt of the alkyne **9** was treated in refluxing dioxane with the *p*-toluenesulfonate ester of 3-butenol[7] to give the alkylation product **10** in 85% yield. Treatment of the substance **10** with lithium in liquid ammonia effected concomitant reduction of the triple bond to a trans double bond[8] and of the aromatic ring to the dihydroanisole (Birch reduction). Acid hydrolysis of the resulting enol ether, followed by treatment with sodium ethoxide in ethanol, gave the conjugated cyclohexenone **11a** in 42% yield from **10**. This substance was contaminated with approximately 15% ketone **11b**, resulting from reduction of the terminal vinyl group.[8,9] Reduction with lithium aluminum hydride in ether at 0° gave the allylic alcohol **3** contaminated with some of the dihydro compound (see above). This product was used for the cyclization studies.

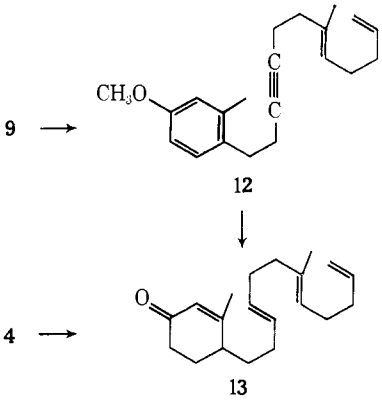
Scheme II



10 11a, R = $-CH=CH_2$ b, R = $-CH_2CH_3$

The tetraenol **4** was prepared in a similar manner as outlined in Scheme III. In this case the lithium salt of the alkyne **9** was alkylated with the *p*-toluenesulfonate ester of *trans*-3-methyl-3,7-octadienol[3] giving **12** in 69% yield. The ketone **13**, obtained in 48% yield, contained 10–15% of terminal dihydro impurity as determined by nmr. The substrate **4** also must have been contaminated with terminal dihydro impurity which, on cyclization (see below), presumably ended up in the fraction called hydrocarbon A.

Scheme III



12 13

Cyclization Studies

Treatment of the trienol **3** with anhydrous formic acid at room temperature for 5–6 min, followed by

(4) Subsequent to completion of the work described here, cyclizations of other allylic alcohol systems to give tricyclic and tetracyclic systems have been disclosed in preliminary reports: W. S. Johnson, M. F. Semmelhack, M. U. S. Sultanbawa, and L. A. Dolak, *J. Amer. Chem. Soc.*, **90**, 2994 (1968); W. S. Johnson and T. K. Schaaf, *Chem. Commun.*, 611 (1969); W. S. Johnson, T. Li, C. A. Harbert, W. R. Bartlett, T. R. Herrin, B. Staskun, and D. H. Rich, *J. Amer. Chem. Soc.*, **92**, 4461 (1970); for earlier examples of allylic alcohol promoted cyclizations see W. S. Johnson, *Accounts Chem. Res.*, 1, 1 (1968).

(5) W. S. Johnson, P. J. Neustaedter, and K. K. Schmiegel, *J. Amer. Chem. Soc.*, **87**, 5148 (1965).

(6) A new route to 4-alkenyl-3-methyl-2-cyclohexenones has recently been reported: K. E. Harding and K. A. Parker, *Tetrahedron Lett.*, 1633 (1971).

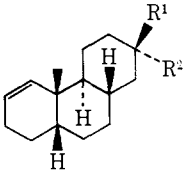
(7) K. L. Servis and J. D. Roberts, *J. Amer. Chem. Soc.*, **86**, 3773 (1964).

(8) H. Smith in "Chemistry in Non-Aqueous Ionizing Solvents," Vol. 1, Part 2, G. Jander, H. Spandau, and C. C. Addision, Ed., Interscience, New York, N. Y., 1963.

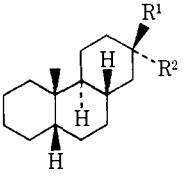
(9) *Cf.* (a) W. S. Johnson, W. H. Lunn, and K. Fitzi, *J. Amer. Chem. Soc.*, **86**, 1972 (1964); (b) H. Greenfield, R. A. Friedel, and M. Orchin, *ibid.*, **76**, 1258 (1954); (c) B. W. Roberts, Ph.D. Thesis, Stanford University, 1963; (d) A. P. Krapcho and M. E. Nadel, *J. Amer. Chem. Soc.*, **86**, 1096 (1964).

cleavage of the formate esters with lithium aluminum hydride, gave a mixture of products. Gas chromatography showed several peaks, but the two with the longest retention times, present in relative amounts of 1 to 9, accounted for 62% of the total peak area. By means of column chromatography and recrystallization, the major product, mp 78.5–79.5°, was isolated in 46% yield (55% taking into account the degree of purity of the substrate). The spectral data for this compound were compatible with structure **14**. The nmr spectrum showed absorption for the proton on the carbon bearing the hydroxyl group as a broad multiplet centered at δ 3.33 ppm. The width at half-height was 20 Hz, indicating the axial nature of the proton.[10] A sample of the minor, longer retention time product was also isolated from the chromatography and it was assigned structure **15** because oxidation of this alcohol and of alcohol **14** with Jones reagent gave the same ketone.

The ring stereochemistry and gross structure of alcohol **14** were confirmed as follows. Hydrogenation of alcohol **14** gave the saturated alcohol **16**, mp 102–104°, which was oxidized with Jones reagent to the ketone **17**, mp 54–56°. Wolff–Kishner reduction gave the tricyclic hydrocarbon **18** which was identical with authentic material prepared from compounds of known stereochemistry (see below).



14, $R^1 = H; R^2 = OH$
15, $R^1 = OH; R^2 = H$

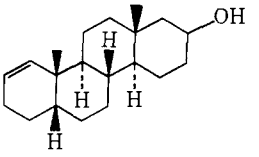


16, $R^1 = H; R^2 = OH$
17, $R^1, R^2 = O$
18, $R^1 = R^2 = H$

The cyclization products from the tetraenol **4** were found to vary considerably with changes in cyclization conditions. Treatment with anhydrous formic acid for 1 min at room temperature gave a product which was separated by column chromatography into a hydrocarbon fraction (50% yield) and an alcoholic fraction (48% yield). Thin layer chromatography of the alcoholic fraction indicated a major product (alcohol A) which was isolated as a crystalline solid, mp 158–159°, in 16% yield. When the cyclization was conducted for a period of 20 min, thin layer chromatography of the alcoholic fraction showed two major spots. A crystalline sample of the second alcohol (alcohol B, mp 122.5–124°) was obtained by thin layer chromatography, sublimation, and recrystallization.

Both alcohol A and alcohol B appear to be tetracyclic. Oxidation of a mixture of the two alcohols gave a mixture of two ketones. In the nmr spectrum of each alcohol the broad width at half-height of the signal for the proton on the carbon bearing the hydroxyl group indicated that the hydroxyl group was equatorial.[10]

Alcohol A was shown to have the structure **19** with cis,anti,trans,anti,trans ring stereochemistry by conversion (hydrogenation and oxidation) to the corresponding saturated ketone **20** which was compared with authentic optically active ketone *d*-**20**. Alcohol B was shown to have structure **21** by hydrogenation to alcohol **22**



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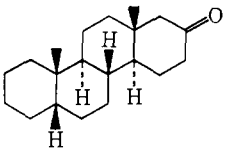

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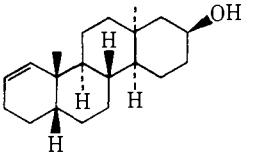

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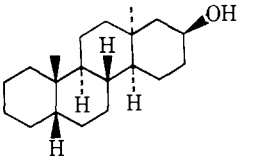

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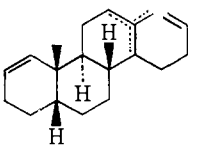
which was compared with authentic optically active material. The authentic comparison compounds were prepared from natural steroids as described at the end of the Discussion.

The hydrocarbon fraction obtained from cyclization of tetraenol **4** showed two major peaks on gas chromatography. The component with the lower retention time (hydrocarbon A) was isolated by preparative gas chromatography in 97% purity. The component with the higher retention time (hydrocarbon B) was isolated in 83% purity.

The nmr spectrum of hydrocarbon A exhibited sharp absorption at δ 0.97 (angular methyl) and 1.60 ppm (vinyl methyl). There was also absorption at 4.8–5.15 characteristic of the terminal vinyl group. This evidence suggested that hydrocarbon A was mainly the tricyclic substance **23** (presumed to be a mixture of double bond isomers). A bicyclic structure is not ruled out, however.

The nmr spectrum of hydrocarbon B exhibited absorption at δ 0.80 and 1.0 ppm for two angular methyl groups. No absorption characteristic of a terminal vinyl double bond was observable. This material was hydrogenated to give saturated hydrocarbon. Analysis by gas chromatography showed the retention time of the major component of this hydrogenation product to be identical with that of authentic 5β-*D*-Homoandrostane (*d*-**25**) (see below for preparation). The nmr absorption of the angular methyls in the hydrogenated product and in the authentic hydrocarbon were identical (δ 0.79 and 0.89 ppm). On this basis hydrocarbon B was assigned the structure **24**.



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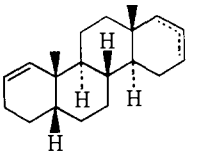

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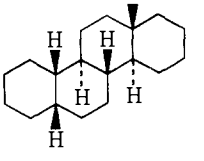

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It could be shown that during the 20-min cyclization with formic acid, a portion of the tetracyclic alcohols was formed by cyclization of the tricyclic olefin **23**. Thus a hydrocarbon sample, 79% A and 16% B by vpc,

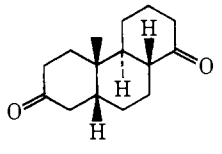
(10) (a) J. I. Musher, *J. Amer. Chem. Soc.*, **83**, 1146 (1961); (b) R. U. Lemieux, R. K. Kullnig, H. J. Bernstein, and W. G. Schneider, *ibid.*, **80**, 6098 (1958); (c) A. Hassner and C. Heathcock, *J. Org. Chem.*, **29**, 1350 (1964).

was shaken with formic acid at room temperature for 20 min. The formate esters were cleaved and the resulting alcoholic fraction oxidized with Jones reagent. Gas chromatographic analysis showed two major peaks in a ratio of 85 to 15, with retention times corresponding to those of the ketones obtained by oxidation of alcohols **21** and **19**, respectively. In contrast a 1-min cyclization of **4** followed by oxidation as above gave a ketone ratio of 15 to 85. When alcohol **19** was isolated from a 1-min cyclization of tetraenol **4** in *deuterioformic acid*, the mass spectrum was essentially identical with that of a sample of alcohol **19** isolated from cyclization in protioformic acid. In particular, there was *no significant incorporation of deuterium in the tetracyclic product*, proving that this cyclization proceeds without the intermediacy of any partially cyclized olefins, and in this sense it resembles the enzymatic cyclization of squalene.[11] Consistent with the aforementioned results, when alcohol **19** was isolated from a 20-min cyclization in deuterioformic acid, the mass spectrum indicated that there had been about 12% incorporation of one deuterium. A sample of alcohol **21** was also isolated from the 20-min cyclization, and the mass spectrum indicated extensive incorporation of one deuterium. It may be concluded, therefore, that most (probably all) of alcohol **21** is formed by acid-catalyzed cyclization of tricyclic olefin **23**. Protonation of **23** on the α side at C-14 with concomitant (concerted) nucleophilic attack by the vinyl group on the β side at C-13 would rationalize the stereochemical course of the reaction.

A cyclization of alcohol **4** with trifluoroacetic acid in pentane at $< -15°$ gave cyclic product in which the ratio of alcohol **19** to **21** was approximately 20 to 1. The yield of alcohol **19** was estimated to be 19% by quantitative gas chromatographic experiments.

Preparation of Comparison Compounds

Authentic *cis,anti,trans*-4a-methylperhydrophenanthrene (**18**) was prepared as follows. Diketone **26**, a compound of established structure and configuration,[12] was converted to the crystalline bis(ethylene thioketal) **27** in 81% yield. Desulfurization with W-2 Raney



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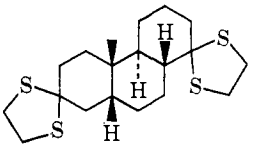

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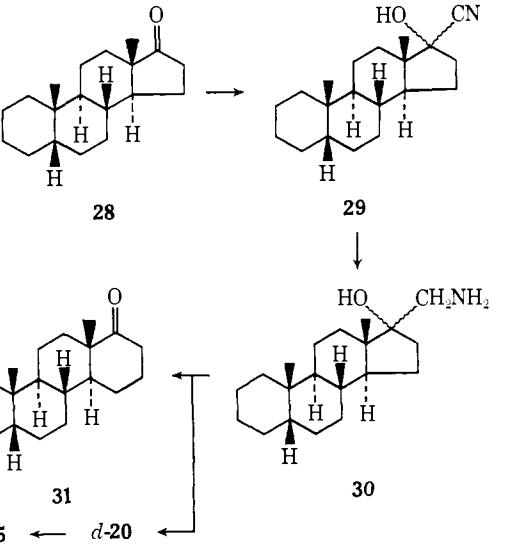
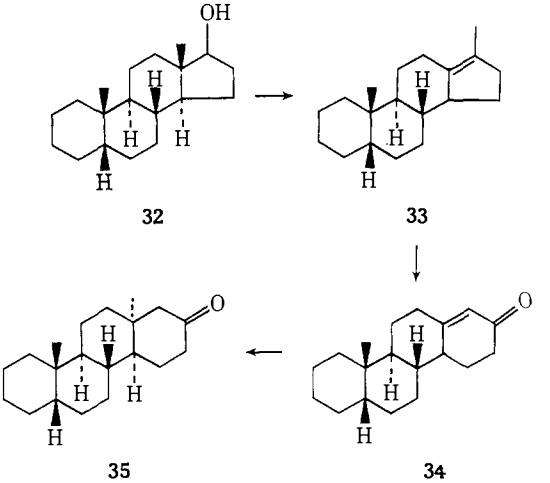
nickel in boiling ethanol gave a single, pure hydrocarbon in 56% yield.

The tetracyclic comparison compounds were prepared as described below. 5β-Androstan-17-one (**28**)[13] was converted, by treatment with potassium cyanide in acetic acid,[14] into the cyanohydrin **29**, which was hydrogenated over reduced platinum oxide to give the corresponding amino alcohol **30**.[15] Dem'janov re-



arrangement with nitrous acid[15] gave a mixture of 5β-*D*-homoandrostan-17a-one (**31**) and 5β-*D*-homoandrostan-17-one (*d*-**20**). The two isomers were separated by column chromatography and differentiated by nmr (see Experimental Section). Hydrocarbon *d*-**25** was prepared by Wolff–Kishner reduction of ketone *d*-**20**.

The alcohol *d*-**22** was prepared as follows. 5β-Androstan-17β-ol (**32**)[13] was distilled from boric acid according to a procedure of Johns[16] to produce the rearranged olefin **33** as the major product. Ozonolysis of this olefin gave an oily diketone which, on treatment with methanolic potassium hydroxide, underwent cyclization to give the unsaturated ketone **34**. Conjugate addition of methylmagnesium iodide in the presence of cupric acetate produced the ketone **35**.



The C–D cis ring fusion was expected by analogy to other systems;[17] moreover, the ketone **35** was distinctly different from the C–D trans ketone *d*-**20**. Ketone **35**

(11) T. T. Tchen and K. Bloch, *J. Amer. Chem. Soc.*, **78**, 1516 (1956); *J. Biol. Chem.*, **226**, 931 (1957).

(12) We thank Professor A. L. Wilds, University of Wisconsin, for supplying us with a specimen of this ketone which was prepared in his laboratory by R. Daniels and J. S. Jellinek *via* lithium-in-ammonia reduction of the unsaturated ketone described by A. L. Wilds, J. W. Ralls, W. C. Wildman, and K. E. McCaleb, *J. Amer. Chem. Soc.*, 72, 5794 (1950); see also J. S. Jellinek, Ph.D. Thesis, University of Wisconsin, 1955. The mp of this ketone and its 2,4-dinitrophenylhydrazone corresponded to those of the Cornforth–Robinson isomer B of known stereochemistry: J. Cornforth and R. Robinson, *J. Chem. Soc.*, 1855 (1949).

(13) L. Tökés, R. T. LaLonde, and C. Djerassi, *J. Org. Chem.*, **32**, 1012 (1967).

(14) L. Tökés, R. T. LaLonde, and C. Djerassi, *J. Org. Chem.*, **32**, 1020 (1967).

(15) *Cf.* M. W. Goldberg and E. Wydler, *Helv. Chim. Acta*, **26**, 1142 (1943).

(16) W. F. Johns and G. P. Mueller, *J. Org. Chem.*, **28**, 1854 (1963).

(17) J. A. Marshall, W. I. Fanta, and H. Roebke, *J. Org. Chem.*, **31**, 1016 (1966).

was reduced with aluminum isopropoxide to give a mixture of epimeric alcohols. The pure equatorial isomer *d*-**22** (recognized by the width at half-height of the nmr signal of the proton on the carbon bearing the hydroxyl group) was isolated by preparative thin layer chromatography.

Experimental Section[18]

The prefix "*dl*" has been omitted from the names of most of the racemic compounds described in this section. Microanalyses and microhydrogenations were performed by E. H. Meier and J. Consul, Department of Chemistry, Stanford University. Melting points were determined on a Kofler hot-stage microscope.

Vapor phase chromatographic (vpc) analyses were performed on an Aerograph Model 600-C instrument. Preparative vapor phase chromatographic separations were performed on a Varian-Aerograph Model A-710 using a 20-ft × 0.375-in. column packed with 20% SE-30 on 60–80 mesh Chromosorb W.

Infrared spectra were obtained using Perkin–Elmer spectrophotometers, Models 137B and 421. Mass spectra were obtained on an Atlas CH-4 or an A.E.I. MS-9 spectrometer using a direct inlet system or on a CEC Model 21-103C using a heated inlet system.

Nuclear magnetic resonance (nmr) spectra were determined under the supervision of Dr. L. J. Durham on Varian Associates Model A-60 or HA-100 spectrometers. Carbon tetrachloride was used as solvent unless otherwise stated and tetramethylsilane (TMS) was employed as the internal reference. Chemical shifts are reported as δ values in ppm relative to TMS (δ_{TMS} 0.0 ppm).

Silica gel G and GF_{254} (E. Merck) were used for thin layer chromatography (tlc). Column chromatography was performed on acid-washed alumina (Merck and Co., Inc.) unless otherwise noted. The order of solvents used for elution was pentane (or petroleum ether), pentane–ether mixtures, and finally ether.

4-Methoxy-2-methylbenzoic Acid (5). A mixture of 2-methoxy-4-methylbenzaldehyde and 4-methoxy-2-methylbenzaldehyde was prepared using a previously described procedure.[19] Distillation of the crude product through a 24-in. spinning band column gave a 59% yield of product, bp 73–74° (0.33 mm), which showed two partially resolved peaks on vpc.

The aldehyde mixture was oxidized using a modification of a previously reported procedure.[20] Thus, 162.5 g (1.08 mol) of the aldehyde mixture and 3.75 l. of water were stirred vigorously in a 12-l. flask and heated to 45°. A solution of 244 g (1.54 mol) of potassium permanganate in 4.5 l. of water was added at a rate sufficient to maintain a reaction temperature of approximately 45°. After all of the permanganate had been reduced, a small amount of 10% aqueous sodium hydroxide was added. The reaction mixture was filtered through Celite and the filter cake was washed well with water. The combined filtrate and washings were extracted with 1 l. of ether. Acidification of the aqueous solution with concentrated hydrochloric acid yielded a white precipitate which was collected by filtration and air-dried. Recrystallization from benzene gave 4-methoxy-2-methylbenzoic acid (**5**) as colorless needles: 51.6 g, mp 176–177.5°, 6.45 g, mp 174–178° (lit.[21] mp 174.5–175°). The total yield was 32%.[22]

4-Methoxy-2-methylbenzyl Alcohol (6). A suspension of 8.8 g (0.232 mol) of lithium aluminum hydride in 250 ml of anhydrous ether was cooled in an ice bath, and a solution of 38.35 g (0.230 mol) of acid **5**, mp 175–177°, in 500 ml of tetrahydrofuran was added over a 4-hr period. The mixture was stirred at room temperature for 3 hr and then cooled in an ice bath while 25 ml of water was added. The mixture was stirred overnight at room temperature, anhydrous magnesium sulfate was added, and stirring was continued for 3 hr. The salts were removed by filtration and washed well with hot tetrahydrofuran and ether. Solvent was removed at reduced pressure and the product distilled to give 33.22 g (95% yield) of 4-methoxy-2-methylbenzyl alcohol,[23] bp 95° (0.30 mm), which showed one major peak on vpc (93% of total peak area). In another preparation the product solidified on standing at 0° overnight. Recrystallization from pentane–ether gave fine colorless needles; mp 28–29°.

3-Methyl-4-(3-butenyl)anisole (8).[5] Phosphorus tribromide (31 ml, 320 mmol) was added to a stirred solution of 40.95 g (269 mmol) of distilled alcohol **6** and 25 drops of pyridine in 650 ml of benzene. The mixture was stirred at 50–60° for 45 min, cooled, and washed with water and saturated sodium bicarbonate. After the solution had been dried over anhydrous sodium sulfate, it was concentrated. Attempts to distill the residue (short-path) at 0.50 mm or 2 μ led only to darkening of the product and gas evolution. The darkened product was dissolved in ether, washed with water and saturated sodium bicarbonate, dried over anhydrous magnesium sulfate, and concentrated to give 43.6 g (81% yield) of nearly colorless bromide **7**. This was dissolved in 200 ml of dry tetrahydrofuran and added dropwise over a 30-min period to a stirred, filtered solution of allylmagnesium chloride (prepared from 61 g, 0.796 mol, of allyl chloride and 3.25 g-atoms of magnesium in 800 ml of tetrahydrofuran). After the reaction mixture had refluxed for 30 min, 150 ml of saturated ammonium chloride solution and anhydrous magnesium sulfate were added, and the mixture was stirred for several hours. The salts were removed by filtration and washed well with tetrahydrofuran and ether. The combined filtrate and washings were concentrated and the residue was distilled (short-path) at 93–95° (1 mm) to give a total of 20.5 g (43% yield) of 3-methyl-4-(3-butenyl)anisole, which was homogeneous by vpc.

In a small scale preparation (1.38 g of alcohol **6**), the bromide **7** was successfully distilled, and the olefin **8** was obtained in 75% yield.

3-Methyl-4-(3-butynyl)anisole (9). A solution of the olefin **8** (10.0 g, 56.7 mmol) in 250 ml of carbon tetrachloride was cooled below −5°. A solution of bromine (3.2 ml, 9.37 g, 58.6 mmol) in 50 ml of carbon tetrachloride was added dropwise. The mixture was stirred for several minutes, and excess bromine and solvent were evaporated. The residue was passed through 200 g of alumina with 400 ml of 10% ether–pentane to give 18.0 g (95% yield) of crude 3-methyl-4-(3,4-dibromobutyl)anisole.

A stirred sodium amide solution prepared from 8.51 g of sodium and 150 ml of liquid ammonia was cooled to −78°, and a solution of 20.0 g (59.5 mmol) of crude 3-methyl-4-(3,4-dibromobutyl)-anisole in 50 ml of anhydrous ether was added. The cooling bath was removed, and stirring was continued for 3 hr. Solid ammonium chloride and ether were added, and the ammonia was allowed to evaporate. Water was added and the product, which was isolated by ether extraction including an acid and base wash,[18] amounted to 9.52 g of a brown oil which was washed through 200 g of alumina with 500 ml of 10% ether–pentane to give a colorless oil. Short-path distillation at 80° (0.09 mm) gave 8.41 g (75% yield from olefin **8**) of 3-methyl-4-(3-butynyl)anisole: λ_{max}^{film} 3.04 and 4.75 μ (−C≡CH).

Anal. Calcd for $C_{12}H_{14}O$: C, 82.72; H, 8.10. Found: C, 82.7; H, 8.05.

3-Butenyl *p*-Toluenesulfonate. An ice-cold solution of 40.9 g (214 mmol) of *p*-toluenesulfonyl chloride in 70 ml of pyridine was added, with stirring, to an ice-cold solution of 10.2 g (141 mmol) of 3-butenol[7,24] in 50 ml of pyridine. The reaction mixture was stored at 3° for 17 hr; then 10 ml of ice-cold water was added slowly. The mixture was diluted further with water and the product isolated by ether extraction including an acid and base wash.[18] Filtration through 300 g of alumina with 1350 ml of 10% ether–pentane gave 27.3 g (85% yield) of colorless 3-butenyl *p*-toluenesulfonate.

(18) 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 "base wash" or "acid wash" indicates 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.

(19) N. P. Buu-Hoi, G. Lejeune, and M. Sy, *C. R. Acad. Sci.*, **240**, 2241 (1955); N. P. Buu-Hoi, N. D. Xuong, M. Sy, G. Lejeune, and N. B. Tein, *Bull. Soc. Chim. Fr.*, 1594 (1955). These authors report the isolation of only 4-methoxy-2-methylbenzaldehyde from this reaction.

(20) R. L. Schriner and E. C. Kleiderer, "Organic Syntheses," Collect. Vol. II, Wiley, New York, N. Y., 1954, p 538.

(21) C. Schall, *Chem. Ber.*, **12**, 816 (1879); W. S. Johnson, S. Shulman, K. L. Williamson, and R. Pappo, *J. Org. Chem.*, **27**, 2015 (1960).

(22) An improved procedure for preparation of acid **5** has been developed in these laboratories: R. C. Ronald, Ph.D. Thesis, Stanford University, 1970.

(23) R. Quelet and J. Allard, *C. R. Acad. Sci.*, **204**, 130 (1937); R. Quelet, J. Allard, J. Ducasse, and Y. Germain, *Bull. Soc. Chim. Fr.*, **4**, 1092 (1937).

(24) Prepared in the present work by reaction of allylmagnesium chloride in tetrahydrofuran with paraformaldehyde: R. B. Kinnel, B. B. Malloy, D. W. Graham, and K. E. Harding, *Org. Prep. Proced. Int.*, **4**, 27 (1972).

8-(4-Methoxy-2-methylphenyl)-1-octen-5-yne (10). To a solution of 995 mg (5.72 mmol) of 3-methyl-4-(3-butynyl)anisole (9) in 30 ml of dioxane was added 3.6 ml of 1.6 *M* *n*-butyllithium; then a solution of 1.30 g (5.72 mmol) of 3-butenyl *p*-toluenesulfonate in 1 ml of dioxane was added. The solution was distilled until the head temperature reached 100°, and the reaction mixture was allowed to reflux for 41.5 hr. The mixture was cooled to room temperature; an additional 1.8 ml of *n*-butyllithium and 654 mg of 3-butenyl *p*-toluenesulfonate were added, and the solvent was distilled as above. After the mixture had refluxed for 35 hr, the addition of reagents (0.9 ml and 330 mg) was repeated, and refluxing was resumed for another 36 hr. The cooled reaction mixture was diluted with 135 ml of water and 15 ml of brine, and the product, which was isolated by extraction with ether,[18] amounted to 2.02 g of a light-yellow oil. This oil was washed through 80 g of alumina with 960 ml of petroleum ether to give 1.28 g of colorless oil, which was dissolved in 95% ethanol and treated with excess aqueous silver nitrate. The precipitate was separated by filtration, the filtrate was diluted with water, and the product was isolated by ether extraction.[18] Short-path distillation at 100° (3 μ) gave 1.11 g (85% yield) of 8-(4-methoxy-2-methylphenyl)-1-octen-5-yne: n^{25}D 1.5280; nmr 2.1–2.9 (m, 11 H, Ar–CH_3 and methylene groups), 3.67 (s, 3 H, OCH_3), 4.75–5.75 (m, 3 H, vinylic), and 6.3–7.15 ppm (m, 3 H, aromatic). Analysis by vpc showed the product to be greater than 99% pure.

Anal. Calcd for $C_{16}H_{20}O$: C, 84.16; H, 8.83. Found: C, 83.9; H, 8.8.

3-Methyl-4-(*trans*-3,7-octadienyl)-2-cyclohexenone (11a). The procedure used for the reduction of 3-methyl-4-(3-butenyl)anisole[5] was modified. A solution of 1.00 g (4.37 mmol) of 8-(4-methoxy-2-methylphenyl)-1-octen-5-yne (n^{25}D 1.5280), in 14 ml of dimethoxyethane and 27 ml of liquid ammonia (distilled from lithium), was cooled to −78°; then 65 mg (9.4 mmol) of lithium wire was added to the vigorously stirred mixture which became deep blue within 2 min. After additional lithium wire (195 mg, 28.1 mmol) had been added, 920 μl of absolute ethanol was added dropwise from a syringe over a period of 4–5 min. Solid ammonium chloride was added and the ammonia was evaporated. The residue was diluted with water, and the crude product, which was isolated by ether extraction,[18] was dissolved in 175 ml of methanol and 20 ml of water. Two drops of concentrated hydrochloric acid was added, and the mixture was stirred at room temperature for 1 hr. Then saturated bicarbonate solution and dilute brine solutions were added, and the product was isolated by ether extraction[18] to afford 0.963 g of oil: λ_{max}^{film} 5.82 (C=O), 10.3 (*trans*-RCH=CHR′), and 11 μ (RCH=CH_2).

A solution of 884 mg of this product in 85 ml of absolute ethanol was added to a solution of sodium ethoxide (from 148 mg of sodium) in 40 ml of ethanol. The mixture was stirred under nitrogen at 50° for 10 min, acidified with 0.5 ml of glacial acetic acid, and poured into dilute sodium bicarbonate solution. Brine was added and the product was isolated by ether extraction[18] giving 839 mg of oil, which was chromatographed on 100 g of alumina. Elution with 200 ml of 10% ether–pentane gave 228 mg (23% yield) of material which appeared to be 3-methyl-4-(*trans*-3,7-octadienyl)-anisole. The fractions eluted with 320 ml of 15% ether–pentane afforded 99.5 mg of ketonic material: λ_{max}^{film} 5.84 and 5.99 μ (C=O and C=CC=O). Further elution with 215 ml of 15% ether–pentane and 360 ml of 20% ether–pentane gave material with carbonyl absorption only at 5.99 μ. Short-path distillation of this material gave 386 mg (42% yield from anisole **10**) of colorless oil: λ_{max}^{film} 5.99 (C=CC=O), 6.1 and 6.15 (C=C), 10.3 (*trans*-RCH=CHR′), and 11 μ (RCH=CH_2). Analysis by vpc showed two components in relative amounts of 15 and 85%. The nmr spectrum exhibited singlet absorption at 1.94 ppm for the methyl group and a complex set of multiplets at 4.75–6.1 ppm for the vinyl protons.

Analysis of intermediate chromatographic fractions by vpc showed one major component with the same retention time as the 15% impurity in the "purified" ketone. A 67-mg sample of such material was again treated with sodium ethoxide. The resulting product showed no significant change by vpc analysis. The infrared spectrum of this material showed strong bands at 6.0 and 6.19 (C=C-C=O) and at 10.3 μ (*trans*-RCH=CHR′). The characteristic absorptions at 11 μ for the terminal vinyl double bond (RCH=CH_2) were not observable. This material is therefore regarded as 3-methyl-4-(*trans*-3-octenyl)-2-cyclohexenone (**11b**).

3-Methyl-4-(*trans*-3,7-octadienyl)-2-cyclohexenol (3). A solution of 360 mg (1.64 mmol) of the trienone **11a** (85% pure) in 10 ml of anhydrous ether was added dropwise, with stirring, to an ice-cold suspension of lithium aluminum hydride (220 mg, 5.8 mmol) in 20 ml of anhydrous ether. After the mixture had been stirred at 0° for 1 hr, 0.6 ml of water was added slowly, and stirring was continued for another hour while the mixture was allowed to warm to room temperature. Anhydrous magnesium sulfate was added and the mixture was stirred for 2 hr. The salts were removed by filtration; the filtrate and washings were combined and concentrated to give 350 mg (97% yield) of colorless oil: λ_{max}^{film} 3.0 (OH) and 6.04, 6.11, 10.1, 10.3, and 11 μ (C=C); nmr 1.67 (broad s, 3 H, C=CCH_3), 2.27 (s, 1 H, OH), 4.02 (broad m, 1 H, >CHO–), and 4.75–6.1 ppm (m, 5 H, vinylic).

***trans*-6-Methyl-12-(4-methoxy-2-methylphenyl)-1,5-dodecadien-9-yne (12).** Lithium amide was prepared from 135.5 mg (19.5 mmol) of lithium wire and a small amount of ferric nitrate in 100 ml of liquid ammonia; then 3.06 g (17.55 mmol) of 3-methyl-4-(3-butynyl)anisole (9) was added in a small amount of ether. The mixture was stirred for 30 min, the ammonia was allowed to evaporate, 150 ml of dioxane was added, the ether was removed at reduced pressure, then 4.69 g (15.9 mmol) of *trans*-3-methyl-3,7-octadienyl *p*-toluenesulfonate[3] was added. The mixture was stirred at reflux for 83 hr, cooled to room temperature and poured into a mixture of 50 ml of water and 450 ml of brine, and the product was isolated by ether extraction.[18] Chromatography on 100 g of alumina gave, on elution with 500 ml of pentane and 500 ml of 10% ether–pentane, 4.41 g of colorless oil. This oil was dissolved in 75 ml of 95% ethanol and treated with an excess of saturated aqueous silver nitrate solution. The precipitate was removed by filtration, the filtrate was diluted with water, and the product was isolated by extraction with ether.[18] Short-path distillation at 120° (1 mm) gave 3.23 g (69% yield based on the sulfonate ester) of *trans*-6-methyl-12-(4-methoxy-2-methylphenyl)-1,5-dodecadien-9-yne: n^{25}D 1.5265; λ_{max}^{film} 6.1, 10.0, and 10.98 (RCH=CH_2) and 6.0 μ (RCH=CMeR′); nmr 1.60 (s, 3 H, C=CCH_3), 3.68 (s, 3 H, OCH_3), and 4.75–6.1 ppm (m, 4 H, vinylic protons).

Anal. Calcd for $C_{21}H_{28}O$: C, 85.08; H, 9.52. Found: C, 85.1; H, 9.4.

3-Methyl-4-(*trans,trans*-7-methyl-3,7,11-dodecatrienyl)anisole. To a solution of 3.59 g (12.1 mmol) of the anisole **12** in 80 ml of tetrahydrofuran and 160 ml of liquid ammonia was added 252 mg (36.4 mmol) of lithium wire. The solution became blue within 2 min. It was stirred for 8 min more and then cooled to −78°. 2-Butyne (0.6 ml) followed by excess ammonium chloride was added in order to consume excess lithium, and the ammonia was allowed to evaporate overnight. The mixture was diluted with water and the product, which was isolated by extraction with ether,[18] was washed through 20 g of alumina with 250 ml of pentane to give 3.41 g (95% yield) of 3-methyl-4-(*trans,trans*-7-methyl-3,7,11-dodecatrienyl)anisole: λ_{max}^{film} 6.00 (RCH=CMeR′), 6.1, 10.1, 10.35, and 11 μ (*trans*-RCH=CHR′ and RCH=CH_2); nmr 1.58 (s, 3 H, vinyl methyl), 3.70 (s, 3 H, OCH_3), 4.8–5.25 (m, 3 H, vinyl protons at C-8 and C-12), 5.44 (m, 2 H, vinyl protons at C-3 and C-4), 5.4–6.1 (m, 1 H, C-11 vinyl proton), and 6.45–7.1 ppm (m, 3 H, aromatic protons). Analysis by vpc showed one major peak with only traces of other peaks.

Anal. Calcd for $C_{21}H_{30}O$: C, 84.51; H, 10.13. Found: C, 84.7; H, 10.1.

3-Methyl-4-(*trans,trans*-7-methyl-3,7,11-dodecatrienyl)-2-cyclohexenone (13). A solution of 990 mg (3.3 mmol) of 3-methyl-4-(*trans,trans*-7-methyl-3,7,11-dodecatrienyl)anisole in 25 ml of tetrahydrofuran and 25 ml of liquid ammonia was cooled to −78°. Lithium wire (115 mg, 16.6 mmol) was added to the vigorously stirred solution. An additional, equal amount of lithium was added after blue color had persisted for 5 min. Stirring was continued for another 5 min; then 970 μl (16.6 mmol) of absolute ethanol was added over a 4-min period. The mixture was stirred for 1 min, and excess ammonium chloride was added. After about 15 min the blue color had disappeared completely. The ammonia was allowed to evaporate, the residue was diluted with water, and the product was isolated by ether extraction.[18] This material was dissolved in 120 ml of 95% ethanol and treated, under nitrogen, with 3 ml of 10% hydrochloric acid for 15 min. The mixture was diluted with sodium bicarbonate solution and water, and the product, which was isolated by extraction with ether,[18] was added to a solution of sodium ethoxide (from 70 mg of sodium) in 50 ml of absolute ethanol. After standing at 45° for 10 min the mixture was diluted with water and made slightly acidic with glacial acetic acid, and the product was isolated by extraction with ether, including a base wash,[18] giving 933 mg of light-yellow oil.

This oil was submitted to dry-column chromatography[25] on a

(25) B. Loev and K. M. Snader, *Chem. Ind. (London)*, 15 (1965).

25 × 0.75 in. column using 25% ether–pentane as eluent. An uv-absorbing band with high R_f afforded 83.7 mg (8% yield) of recovered starting material. The main uv-absorbing band was divided into two fractions. The upper three-fourths of this band gave 388.5 mg of material with no ir absorption in the saturated carbonyl region in its infrared spectrum. The lower one-fourth of this band gave 65 mg of material, which was submitted to preparative tlc, affording 51.2 mg of material which was combined with the main fraction described above. An additional 94 mg of material was obtained from the zone of the column between the two bands, and this portion also was submitted to preparative tlc to give another 65.1 mg of material to be combined with the main fraction. The combined fractions were distilled (short-path) at 135° (7 μ) to give 490 mg (51% yield) of 3-methyl-4-(*trans,trans*-7-methyl-3,7,11-dodecatrienyl)-2-cyclohexenone: λ_{max}^{film} 5.98 and 6.16 (C=C-C=O) and 6.11, 10.35, and 11 μ (*trans*-RCH=CHR′ and RCH=CH_2); nmr 1.59 (s, 3 H, C=CCH_3), and 4.75–6.1 ppm (m, vinyl protons). Comparison of the integration value for the vinyl protons with the integration value for all upfield protons indicated that some reduction of the terminal double bond had occurred. The mole per cent of the dihydro compound in the sample was thus estimated to be 15%.

Another preparation gave a product the nmr spectrum of which indicated about 10–11% of dihydro impurity. This sample, λ_{max}^{film} 239 mμ (ε 12,100), was used for combustion analysis.

Anal. Calcd for 90% $C_{20}H_{30}O$ and 10% $C_{20}H_{32}O$: C, 83.80; H, 10.62. Found: C, 83.7; H, 10.4.

3-Methyl-4-(*trans,trans*-7-methyl-3,7,11-dodecatrienyl)-2-cyclohexenol (4). A suspension of 94.3 mg (2.48 mmol) of lithium aluminum hydride in 10 ml of ether was cooled in an ice bath and a solution of 171.5 mg (0.598 mmol) of the cyclohexenone **13** (containing approximately 10% of dihydro impurity) in 1 ml of ether was added over a period of a few minutes. The mixture was then stirred for 15 min and hydrolyzed at 0° as described above for the preparation of the trienol **6**. Short-path distillation of the product at 115° (1 μ) gave 167 mg (97% yield) of 3-methyl-4-(*trans,trans*-7-methyl-3,7,11-dodecatrienyl)-2-cyclohexenol: λ_{max}^{film} 3.0 (OH), 6.02, 6.06, and 6.11 (C=C), 10.1 and 11 (RCH=CH_2), and 10.4 μ (*trans*-RCH=CHR′); nmr 1.59 (s, C=CCH_3), 1.68 (s, C=CCH_3 in ring), 4.03 (m, >CHO–), and 4.75–6.1 ppm (m, vinyl protons).

Anal. Calcd for $C_{20}H_{32}O$: C, 83.27; H, 11.18. Found: C, 83.2; H, 11.2.

Cyclization of 3-Methyl-4-(*trans*-3,7-octadienyl)-2-cyclohexenol (3). A. Isolation of Major Tricyclic Product. A 194-mg sample (0.88 mmol) of trienol **3** (containing approximately 15% of the dihydro product) was added to 45 ml of anhydrous formic acid.[26] The cloudy mixture was swirled for 5.5 min at room temperature and poured into water and brine, and the product was isolated by extraction with pentane (including a base wash).[18] This material was dissolved in 100 ml of ether, and 205 mg of lithium aluminum hydride was added. The mixture was heated at reflux for 20 min and cooled. Hydrolysis with 0.5 ml of water as described above for the alcohol **6** gave 188 mg of colorless oil. The infrared spectrum of this product showed little absorption at 10.1, 10.3, and 11 μ (*trans*-RCH=CHR′ and RCH=CH_2).

Analysis by vpc at 220° showed at least 12 components. However, only two peaks had relatively long retention times. These two peaks which accounted for approximately 62% of the total peak area were present in relative amounts of about 10 (retention time 16 min) and 90% (retention time 18.5 min).

The crude products from several such experiments on a total of 328 mg of cyclization substrate were combined. After collection of some solid product by crystallization from pentane, the mother liquors were chromatographed on 10 g of alumina. Elution with pentane gave 67 mg (22%) of a hydrocarbon fraction which was shown by vpc analysis to consist of five components with retention times of 1.5 to 4 min. The infrared spectrum of this fraction exhibited a small amount of absorption at 10.3 (*trans*-RCH=CHR′) and 11 μ (RCH=CH_2). Further elution of the column with ether gave an alcoholic fraction which on vapor phase chromatography showed five peaks with retention times of 4.5 to 8.5 min and two peaks with retention times of 16 and 18.5 min.

Recrystallization of the alcoholic fractions from pentane afforded 130 mg (46% yield, 55% taking into account 15% dihydro impurity in starting material) of a pure **tricyclic alcohol 14** as colorless needles: mp 78.5–79.5°; λ_{max}^{KBr} 3.1 (OH), 9.44, 9.67, and 14.1 μ; nmr 0.90 (s, angular methyl), 3.14 (–OH, removed upon D_2O exchange), 3.33 (m, $W_{h/2}$ = 20 Hz, axial proton on a carbon bearing an oxygen), and 5.43 ppm (s, vinyl protons).

Anal. Calcd for $C_{15}H_{24}O$: C, 81.76; H, 10.98. Found: C, 81.8; H, 11.0.

B. Identification of Minor Tricyclic Product (15). A 7.2-mg sample of the minor alcoholic product (vpc retention time 16 min) was also obtained from the chromatography. This material was oxidized at 0° with Jones reagent[27] to give 5.8 mg of a ketonic product. A 5.1-mg sample of the major tricyclic alcohol, mp 78.5–79.5°, was oxidized in the same manner to give 3.7 mg of a ketonic product. The infrared spectra of the two ketonic products were identical. Analysis by vpc showed that both samples contained only one major component with identical retention times, and a mixture injection gave one sharp peak.

The ketonic product derived from the major tricyclic alcohol, mp 78.5–79.5°, was dissolved in about 1 ml of anhydrous ether and treated with excess lithium aluminum hydride. Analysis by vpc of the product showed two major components having retention times which were identical with those observed for the two alcohols used in the above oxidation experiments.

C. Conversion of Tricyclic Alcohol 14 to 4a-Methyl-*cis,anti,trans*-perhydrophenanthrene (18). A quantitative hydrogenation was performed by M. E. Meier using a microhydrogenation apparatus. Thus, 28.62 mg (0.13 mmol) of the alcohol **14**, mp 78.5–79.5°, was hydrogenated in ethanol at room temperature and atmospheric pressure over reduced platinum oxide. The hydrogenation was complete within 30 min with an uptake of 2.99 ml (corrected to STP) or 1.03 equiv. The catalyst was removed by filtration and washed with ethanol. Solvent was evaporated from the filtrate to give 28.7 mg of crude crystalline product. A comparable sample was recrystallized three times from pentane to give a sample of **2α-hydroxy-4b-methyl-*trans,anti,cis*-perhydrophenanthrene (16)** as colorless needles: mp 102–104°; λ_{max}^{KBr} 3.09 (OH), 9.5, 9.65, and 9.85 μ; nmr 0.834 (s, angular methyl) and 3.34 ppm (m, $W_{h/2}$ = 20 Hz, axial proton on carbon bearing oxygen).

Anal. Calcd for $C_{15}H_{26}O$: C, 81.02; H, 11.79. Found: C, 80.8; H, 11.8.

A 21.4-mg sample (0.096 mmol) of the crude alcohol **16** was oxidized with 0.2 ml of Jones reagent[27] at 0°. The product, which was isolated by extraction with ether,[18] was washed through 1 g of alumina with 10 ml of pentane and 10 ml of 10% ether–pentane; then it was distilled (short-path) at 125° (1.5 μ) to give 20.3 mg (95% yield) of **4b-methyl-*trans,anti,cis*-perhydrophenanthren-2-one (17)** as a colorless oil: λ_{max}^{film} 5.95 μ (C=O); nmr 0.838 ppm (s, angular methyl).

Anal. Calcd for $C_{15}H_{24}O$: C, 81.76; H, 10.98. Found: C, 81.5; H, 11.0.

Analysis by vpc of this ketone showed only one peak. A portion of the product was induced to crystallize from pentane, mp 54–56°.

A solution of 10.6 mg (48.1 μmol) of liquid ketone **17** in 1 ml of pentane was added to 3 ml of diethylene glycol in which 40 mg of sodium had been dissolved. The pentane was evaporated at reduced pressure, 50 μl of anhydrous hydrazine was added, and the mixture was heated at 130° for 1 hr and at 200–205° for 2 hr. After cooling and dilution with water, the product was isolated by extraction with ether using an acid wash.[18] This material was washed through 1 g of alumina with 10 ml of pentane and distilled (short-path) at 110° (1.5 mm) to give 6.86 mg (69% yield) of **4a-methyl-*cis,anti,trans*-perhydrophenanthrene (18)** as a colorless oil.

Anal. Calcd for $C_{15}H_{26}$: C, 87.30; H, 12.70. Found: C, 87.3; H, 12.9.

Analysis of this product by vpc showed a single peak and coinjection with authentic hydrocarbon **18** gave a sharp peak. The infrared and mass spectra were essentially identical with those of the authentic material (see below).

Cyclization of 3-Methyl-4-(*trans,trans*-7-methyl-3,7,11-dodecatrienyl)-2-cyclohexenol (4). A. With Formic Acid for 1 Min (Isolation of Alcohol A). A 94.3-mg sample (0.326 mmol) of the tetraenol **4** was shaken with 15 ml of anhydrous formic acid[26] for 1 min. The mixture was poured into water and extracted with ether. The combined extracts were washed with water, sodium bicarbonate solution, and brine and dried over anhydrous sodium sulfate. Most of the solvent was evaporated and the residual solution was treated with excess lithium aluminum hydride in ether. Water was added and the product was isolated by ether extraction[18] to give

(26) H. I. Schlesinger and A. W. Martin, *J. Amer. Chem. Soc.*, **36**, 1589 (1914).

(27) K. Bowden, I. M. Heilbron, E. R. H. Jones, and B. C. L. Weedon, *J. Chem. Soc., London*, 39 (1946).

89.7 mg of semicrystalline material, which was chromatographed on 5 g of alumina. Elution with 50 ml of pentane gave 44.6 mg (50% yield) of a hydrocarbon fraction. Further elution with ether gave 45.7 mg (48% yield) of an alcoholic fraction.

The alcoholic fraction was submitted to preparative tlc (7 hr). A 19.7-mg sample (21% yield) of crystalline solid (R_f 0.23, 1:1 ether–pentane) and a 4.0-mg sample of orange crystals (R_f 0.26) were recovered. The major component was sublimed at 2 μ and recrystallized once from petroleum ether and again from acetonitrile to give 15.0 mg (16% yield, uncorrected for purity of substrate) of alcohol A [*dl*-**5β-*D*-homoandrost-1-en-17α-ol (19)**]: mp 158–159°; λ_{max}^{film} 2.95 (OH), 9.31, 9.42, 9.55, 9.86, and 14.1 μ; nmr 0.82 (s, C-18 methyl), 0.99 (s, C-19 methyl), 3.8 (m, $W_{h/2}$ = 20 Hz, axial hydrogen on carbon bearing oxygen), and 5.58 ppm (s, vinyl protons). The combustion analysis of comparable material is reported below.

B. With Formic Acid for 20 Min (Isolation of Alcohol B). A 96-mg sample of the tetraenol **4** was shaken with 15 ml of anhydrous formic acid for 20 min. The reaction mixture was processed just as described above (part A) to give 95 mg of crude product after cleavage of the formate esters. This material was combined with that from the similar cyclization of a 52-mg sample, and purified, as described above, to give 13 mg of a semicrystalline alcohol (R_f 0.26, 1:1 ether–pentane), which was sublimed at 110° (1 μ) and then was recrystallized from acetonitrile to give colorless needles: mp 122.5–124°; λ_{max}^{film} 3.0 (OH), 9.65 and 14.1 μ; nmr 0.94 (s, C-18 methyl), 0.99 (s, C-19 methyl), 3.9 (m, $W_{h/2} \cong 20$ Hz, axial proton on carbon bearing oxygen), and 5.6 ppm (s, vinyl protons). The mass spectrum (MS-9) of this sample exhibited a parent ion at *m/e* 288, M^+. This substance was shown (see below) to be *dl*-**5β,13α-*D*-homoandrost-1-en-17β-ol (21)**.

Two fractions of alcohol A (**19**) were also obtained: 16 mg, mp 156–158° (recrystallized from petroleum ether), and 3.5 mg, mp 158–159° (recrystallized from acetonitrile).

Anal. Calcd for $C_{20}H_{32}O$: C, 83.27; H, 11.18. Found: C, 83.5; H, 11.3.

An 8-mg sample of a mixture of alcohols A and B was dissolved in 1 ml of acetone and oxidized with Jones reagent.[27] The crude product was washed through 1 g of alumina with 20% ether–pentane to give 5.6 mg of colorless oil. Analysis by vpc showed two peaks of comparable area and the nmr spectrum exhibited sharp absorptions for the angular methyls at 0.78, 0.90, and 1.00 ppm.

C. Conversion of Alcohol A to *dl*-5β-*D*-Homoandrostan-17-one (20). A 14.2-mg sample (0.049 mmol) of tetracyclic alcohol A, mp 158–159°, was submitted to oxidation with Jones reagent.[27] The product, 14.7 mg of crude crystalline material, was washed through 1 g of alumina with 10 ml of 20% ether–pentane to give 11.4 mg of colorless crystals. Recrystallization from petroleum ether gave 8.6 mg of *dl*-**5β-*D*-homoandrost-1-en-17-one** as colorless prisms: mp 110.5–111.5°; λ_{max}^{film} 5.85 μ (C=O); nmr: 0.79 (s, C-18 methyl), 1.00 (s, C-19 methyl), and 5.62 ppm (s, vinyl protons).

Anal. Calcd for $C_{20}H_{30}O$: C, 83.86; H, 10.56. Found: C, 83.6; H, 10.4.

A 3.75-mg sample of this unsaturated ketone was hydrogenated in ethanol over 5 mg of 5% Pd/C at room temperature and atmospheric pressure. The catalyst was removed by filtration and washed with ethanol. The residue obtained after evaporation of the solvent was washed through 1 g of alumina with 4 ml of 20% ether–pentane and sublimed at 75° (2 μ) to give 3.45 mg of colorless crystals. Recrystallization from pentane gave material, mp 105.5–108°. The solution (CCl_4) spectrum and mass spectrum (MS-9) of this material were identical in all respects with the corresponding spectra of authentic 5β-*D*-homoandrostan-17-one (see below).

D. Hydrogenation of Alcohol B. The hydrogenation was performed by Mr. E. Meier using a microhydrogenation apparatus. Thus, 0.699 mg of alcohol B (mp 119–121°) was hydrogenated in ethanol at room temperature and atmospheric pressure over 1 mg of prereduced platinum oxide. The catalyst was removed by filtration and washed with ethanol. The crystalline residue obtained on evaporation of the filtrate was recrystallized twice from acetonitrile, to give colorless crystals of *dl*-**5β,13α-*D*-homoandrostan-17β-ol (22)**, mp 138–140°. The mass spectrum (MS-9) of this sample was identical with that of authentic alcohol *d*-**22** (see below). The mother liquors were combined and evaporated, and the residue was recrystallized from acetonitrile to give colorless crystals, mp 135–139°. The nmr spectrum (HA-100, $CDCl_3$) showed two singlet absorptions at 0.89 and 0.97 ppm and was essentially identical with that of authentic alcohol *d*-**22**. The solution ir spectrum contained all the bands in the spectrum of alcohol *d*-**22** and additional ones at 5.8 and 9 μ. The behavior of this product on tlc was identical with that of the authentic alcohol *d*-**22** using 2:1 cyclohexane–ethyl acetate (R_f 0.41) and 9:1 cyclohexane–ethyl acetate (continuous elution for 2 hr).

E. Cyclization in Formic Acid with Lithium Perchlorate. Isolation of Hydrocarbons. A 50.5-mg sample of the tetraenol **4** was added to a solution of 5.1 g (0.048 mmol) of anhydrous lithium perchlorate in 10 ml of anhydrous formic acid, and the mixture was shaken for 1 min and poured into water. The product, which was isolated by extraction with ether using a base wash,[18] was chromatographed on 5 g of alumina. Elution with 50 ml of pentane gave 25.3 mg of colorless oil. Further elution with 50 ml of ether gave 23.0 mg of colorless semicrystalline formates.

Vapor phase chromatography of the hydrocarbon fraction showed two major peaks with relative peak areas of 47 (hydrocarbon A, lower retention time) and 53% (hydrocarbon B). Hydrocarbon A, collected by preparative vpc, was distilled (short-path) at 110° (1 μ) to give a colorless oil. The nmr spectrum (HA-100 used in conjunction with a Varian Associates C-1024 time averaging computer) of this material showed absorption as a sharp singlet at 0.97 ppm (angular methyl), as a broad singlet at 1.60 ($C{=}CCH_3$), as a set of three multiplets at 4.8–5.15 ($C{=}CH_2$), and as a broadened singlet at 5.59 apparently overlapping a very broad multiplet at 5.4–5.9 ppm.

The higher retention time component, also collected by preparative vpc, was distilled at 115° (1 μ) to give a colorless oil. Analytical vpc showed two peaks, hydrocarbon B (83%) and an impurity (17%) with a slightly higher retention time. The nmr spectrum of this fraction exhibited two sharp singlet absorptions at 0.80 and at 1.0 ppm. Hydrogenation over reduced platinum oxide in ethanol gave a saturated hydrocarbon. Analysis by vpc showed one major peak with a retention time identical with that of authentic 5β-*D*-homoandrostane (*d*-**25**), prepared as described below. The nmr spectrum (HA-100) of the hydrogenated sample exhibited two singlet absorptions at 0.79 and 0.89 ppm. These values were identical with those found for authentic 5β-*D*-homoandrostane.

The saturated hydrocarbon was distilled at 160° (12 μ) to give a colorless semicrystalline solid. The solution (CS_2) infrared spectrum of this sample contained all of the major absorptions found in the spectrum of authentic 5β-*D*-homoandrostane as well as a few others.

F. Treatment of Tricyclic Hydrocarbon with Formic Acid. A mixture of hydrocarbons (79% hydrocarbon A and 16% hydrocarbon B by vpc) obtained from 1- and 4-min cyclizations (~6 mg) was shaken with 1 ml of anhydrous formic acid under nitrogen for 20 min. The product was isolated and treated with 13 mg of lithium aluminum hydride as described above (part A) to give 6 mg of slightly orange oil: λ_{max}^{film} 2.95 (OH), 6.1, 10.1, and 11 μ ($RCH{=}CH_2$). Thin layer chromtography (1:1 ether–pentane) showed strong spots at R_f 0.79 and 0.26 and a weak spot at R_f 0.23. Chromatography of this material on 0.5 g of alumina gave a 3.8-mg hydrocarbon fraction (eluted with pentane) and a 2.4-mg alcoholic fraction (eluted with ether). The alcoholic fraction was treated with Jones reagent[27] in acetone at 0° and the crude product was washed through 0.5 g of alumina with 8 ml of 20% ether–pentane to give a colorless oil. Analysis by vpc showed two major peaks with retention times corresponding to the ketones derived from alcohol **19** (~15% of the relative peak area) and from alcohol **21** (~85%).

G. Deuterioformic Acid Cyclizations. A 5.2-mg sample of tetraenol **4** was shaken with 0.3 ml of deuterioformic acid (94% *d*) for 1 min at room temperature. The product was isolated and treated with lithium aluminum hydride as described above (part A). Chromatography on 0.5 g of alumina afforded 1.2 mg of colorless oil, eluted with pentane, and an orange, semicrystalline solid, eluted with ether. The latter fraction was purified by preparative tlc (1:5 ether–pentane). Recrystallization from petroleum ether of the product with lowest R_f gave alcohol **19** as colorless needles, mp 155–157°.

The mass spectrum (MS-9) of this product was identical with that of the alcohol produced from cyclization of tetraenol **4** in protioformic acid as described above (part A). In particular, the relative intensities of the peaks at *m/e* 288 (parent peak), 289, and 290 were identical within experimental error. In a similar experiment 9.8 mg of tetraenol **4** was shaken with 2 ml of deuterioformic acid for 20 min. A higher R_f band from the tlc plate afforded an orange oil which was sublimed at 125° (2 μ) to give 1.28 mg of crystalline material. Recrystallization from petroleum ether and then from acetonitrile gave 0.48 mg of alcohol **21** as colorless needles, mp 121–124°. The mass spectrum of this material indicated that a large

proportion of it contained one deuterium atom. The following relative intensities were found: *m/e* 288, 1.68; *m/e* 289, 4.08; *m/e* 290, 1.00; *m/e* 291, 0.14. If the values for the ions with a mass greater than the parent ion (*m/e* 288) are adjusted for the contributions expected from natural isotopic abundances, the value for *m/e* 289 becomes 3.62 and the value for *m/e* 290 becomes 0.16. These values indicate that about 68% of the material, mp 121–124°, had incorporated one deuterium atom during the cyclization and that 3% had incorporated two deuterium atoms.

The mass spectrum of alcohol **19**, mp 157.5–159°, also isolated from the 20-min cyclization, indicated that some deuterium incorporation had taken place. The following relative intensities were found: *m/e* 288, 2.785; *m/e* 289, 1.00; *m/e* 290, 0.17. Correction for natural isotopic abundances leads to the conclusion that about 12% of the alcohol had incorporated one deuterium.

H. Small-Scale Cyclization with Trifluoroacetic Acid in Pentane. A 5.05-mg sample of tetraenol **4** was added to a mixture of 50 ml of dry pentane and 3 ml of trifluoroacetic acid at −40°. The temperature of the reaction mixture was allowed to rise to −15° over a period of 3 hr, then 10% sodium hydroxide and ice were added. The product was isolated and treated with lithium aluminum hydride as described above, and the alcoholic product was oxidized with Jones reagent.[27] Chromatography on 1 g of alumina gave, on elution with 10 ml of 50% ether–pentane, the ketonic fraction. The yield of ketone **20** as determined by vpc using *n*-docosane as an internal standard was approximately 19%. The ratio of this ketone to that derived from alcohol **21** was ~20:1.

I. Small-Scale Cyclization with Formic Acid. A 5.69-mg sample of tetraenol **4** was added to 1 ml of anhydrous formic acid. The mixture was shaken at room temperature for 1 min and then processed as described above. Analysis of the ketonic mixture by vpc as above indicated that the yield of alcohol **19** was 22% and that the ratio of **19** to **21** was 85:15.

4a-Methylperhydrophenanthrene (18). A sample of 4b-methylperhydrophenanthrene-1,7-dione (**26**), mp 106.5–110.6°,[12] was converted to the bis(ethylene thioketal) according to the procedure of Fieser.[28] The product was recrystallized from ethanol to give three crops of white crystals: 11 mg, mp 140–143°; 2 mg, mp 139–142°; and 3 mg, mp 136–142° (81% yield).

A 16-mg sample of the combined product was dissolved in 4 ml of ethanol. The solution was flushed several times with nitrogen and a slurry of W-2 Raney nickel[29] in ethanol (stored under ethanol at 0°) was added. The mixture was allowed to reflux vigorously for 20 hr, cooled, and filtered through Celite. The catalyst was washed well with hot ethanol. The combined filtrate and washings were poured into water and the product was isolated by extracting with pentane.[18] Chromatography over 1 g of alumina, using 10 ml of pentane for elution, afforded 4.8 mg (56% yield) of a colorless oil which was distilled (short-path) at 110° (0.4 mm). Analysis by vpc showed a single peak. The mass spectrum (CEC) showed a molecular ion at *m/e* 206 (calcd mol wt for $C_{15}H_{26}$, 206.4).

5β-Androstane-17-cyanohydrin (29). A 5.45-g sample of 5-androstan-17-one[13] was converted to its cyanohydrin by the procedure already described for the 5α isomer.[14] Recrystallization from pentane gave 4.92 g (82%) of product: mp 102–110°; $\lambda_{max}^{CCl_4}$ 2.90 (OH) and 4.46 μ (C≡N).

Anal. Calcd for $C_{20}H_{31}NO$: C, 79.67; H, 10.37. Found: C, 79.8; H, 10.4.

5β-*D*-Homoandrostan-17-one (*d*-20). The procedure for the preparation of the 5α isomer[15] was used. Thus 1.00 g of the aforementioned cyanohydrin **29** gave 990 mg of a yellow crystalline solid. Chromatography on 50 g of activity 2.5 Woelm neutral alumina (pentane eluent) gave 594 mg of **5β-*D*-homoandrostan-17a-one**: $\lambda_{max}^{CCl_4}$ 5.80 μ (C=O); nmr: 2.15 (s, 2 H, $-CH_2C(=O)-$), 1.02 (s, CH_3C), and 0.94 ppm (s, CH_3C).

Anal. Calcd for $C_{20}H_{32}O$: C, 83.27; H, 11.18. Found: C, 83.0; H, 11.1.

Further elution with 4:1 pentane–methylene chloride gave 76 mg of crystalline 5β-*D*-homoandrostan-17-one (*d*-**20**); $\lambda_{max}^{CCl_4}$ 5.80 μ (C=O); nmr 2.15 (s, 4 H, $-CH_2COCH_2-$), 0.92 (s, CH_3C), and 0.78 ppm (s, CH_3C).

Anal. Calcd for $C_{20}H_{32}O$: C, 83.27; H, 11.18. Found: C, 83.4; H, 11.2.

5β-*D*-Homoandrostane (*d*-25). A modification of the Huang-Minlon method was used. Thus a solution of 5.5 mg (0.19 mmol) of 5β-*D*-homoandrostan-17-one, mp 145–146.5°, in pentane was added to 1 ml of diethylene glycol in which 10.5 mg of sodium metal had been dissolved. The pentane was removed at reduced pressure, 15 μl of anhydrous hydrazine was added, and the mixture was heated under nitrogen at 135° for 1 hr. The temperature was then raised to 200–205° for 2 hr, cooled, and poured into water, and the product was isolated by extraction with pentane using a base wash.[18] Chromatography on 1 g of alumina (pentane elution) gave 3.63 mg of semicrystalline material. Tritturation with pentane gave 2.5 mg of amorphous white solid which showed a single peak on vpc. Recrystallization from pentane gave colorless microprisms: mp 115–116°; nmr (100 MHz) 0.79 (s, CH_3C) and 0.896 ppm (s, CH_3C); *m/e* 274 (calcd for $C_{20}H_{34}$, 274.49).

17-Methyl-18-nor-5β-androst-13(17)-ene (33). The method for producing the 5α isomer[16] was used. Thus 86.4 mg of 5β-androstan-17β-ol,[13] mp 130–131.5° (*Anal.* Calcd for $C_{18}H_{32}O$: C, 82.54; H, 11.66. Found: C, 82.4; H, 11.8), on dehydration with 47.2 mg of boric acid at 360° for 6 min gave a product which, after chromatography on 10 g of Florisil, amounted to 58.5 mg (72%) of a colorless oil (pentane elution) and 14.6 mg of the starting material (methylene chloride elution). Analysis by vpc showed 5 peaks, the major one amounting to 75% of total peak area. The nmr spectrum showed a sharp singlet at 0.84 ppm and a broad singlet at 1.58 ppm.

A portion of the hydrocarbon product from another experiment was induced to crystallize. Two recrystallizations from ether–methanol gave a single compound, mp 71–72°.

Anal. Calcd for $C_{19}H_{30}$: C, 88.30; H, 11.70. Found: C, 88.2; H, 11.6.

18-Nor-*D*-homo-5β-androst-13(17a)-en-17-one (34). A solution of 103.1 mg of the aforementioned olefin **33**, mp 60–67°, in 5 ml of methylene chloride and 0.1 ml of methanol, was treated at −78° with excess ozone followed by zinc dust (130 mg) and acetic acid (0.13 ml). The mixture was stirred at 0° for 20 min and then filtered through Filter Cel (methylene chloride rinse). The filtrate was washed twice with saturated sodium bicarbonate, dried over magnesium sulfate, and concentrated. The residue was chromatographed on Florisil to give, on elution with 60% methylene chloride in pentane, 87.4 mg (75% yield) of colorless oil: $\lambda_{max}^{CHCl_3}$ 5.86 μ; nmr 0.88 (s, CH_3C) and 2.08 ppm (s, $CH_3C{=}O$). Short-path distillation gave an analytical sample of the *D*-seco diketone.

Anal. Calcd for $C_{19}H_{30}O_2$: C, 78.57; H, 10.41. Found: C, 78.3; H, 10.4.

A mixture of 36.6 mg of the above diketone, 1.4 ml of methanol, and 0.2 ml of 15% potassium hydroxide was heated at 85° under a nitrogen atmosphere for 55 min. Water (0.4 ml) was added and the solution was cooled in an ice bath. The crystals which formed were collected and dried in a vacuum desiccator (32.6 mg, mp 113–115°). Recrystallization from hexane produced 25.5 mg (74% yield) of ketone **34** as colorless crystals: mp 117–119°; $\lambda_{max}^{CHCl_3}$ 6.0 and 6.08 μ (C=CC=O); nmr ($CDCl_3$) 0.88 (s, CH_3C-) and 5.82 ppm (m, C=CHC=O). Repeated recrystallizations (hexane) of comparable material from another similar experiment gave a product, mp 116–118°.

Anal. Calcd for $C_{19}H_{28}O$: C, 83.77; H, 10.36. Found: C, 83.5; H, 10.4.

5β,13α-*D*-Homoandrostan-17-one (35). A 0.48-ml sample of methylmagnesium iodide solution (from 104 mg of magnesium, 650 mg of methyl iodide, and 3.5 ml of ether) was cooled to −10°. A solution of 44 mg (0.162 mmol) of the unsaturated ketone **34**, mp 117–119°, and 8.1 mg of cupric acetate monohydrate (0.041 mmol) dissolved in 1.5 ml of dry tetrahydrofuran was added dropwise over a 15-min period. The mixture was kept at −10° for 15 min, warmed to room temperature over 2 hr, then heated at reflux for 15 min. Excess ammonium chloride was added and the product was isolated by ether extraction.[18] Recrystallization from methanol gave 22.5 mg of colorless crystals, mp 116–119°. The mother liquors were chromatographed on Florisil yielding 13.8 mg of crystalline material on elution with 30% methylene chloride in pentane. Recrystallization from methanol produced 10 mg of colorless crystals, mp 117–120°. Thus the total yield of ketone **35** was 32.5 mg (70%): $\lambda_{max}^{CHCl_3}$ 5.88 μ (C=O); nmr ($CDCl_3$) 0.94 ppm (s, CH_3C). A comparable sample from another similar experiment was repeatedly recrystallized from methanol, giving colorless crystals, mp 118–120°.

Anal. Calcd for $C_{20}H_{32}O$: C, 83.27; H, 11.18. Found: C, 82.9; H, 11.1.

5β,13α-*D*-Homoandrostan-17β-ol (*d*-22). A. Reduction with Sodium Borohydride. A mixture of 5.9 mg of ketone **35**, 48 mg of sodium borohydride, and 3 ml of isopropyl alcohol (distilled from

(28) L. F. Fieser, *J. Amer. Chem. Soc.*, **76**, 1945 (1954).

(29) R. Mozingo, "Organic Syntheses," Collect. Vol. III, Wiley, New York, N. Y., 1955, p 181.

calcium hydride) was heated at reflux for 2 hr. Water was added and the product, which was isolated by ether extraction,[18] was crystallized from pentane to give colorless crystals, mp 122–142°. This material showed two major spots on tlc (R_f 0.21, 0.25, 4:1 cyclohexane–ethyl acetate) but no spot corresponding to the ketone (R_f 0.4).

B. By Reduction with Aluminum Isopropoxide. A solution of 202 mg of purified (dissolved in hot benzene, filtered, and concentrated) aluminum isopropoxide, 15 mg of ketone **35**, and 2 ml of isopropyl alcohol (distilled from calcium hydride) was heated at reflux under nitrogen for 3 hr. An additional 2 ml of alcohol was added, and 2 ml of solvent was distilled. The solution was heated at reflux for another 30 min and cooled. Dilute hydrochloric acid was added and the product was isolated by ether extraction.[18] Repeated recrystallization of the residue from pentane afforded colorless crystals, mp 184–186°, which showed two spots on tlc corresponding to the two major spots produced by the product from the sodium borohydride reaction.

The two mixtures of alcohols were combined and chromatographed on Florisil yielding 24.3 mg of colorless crystals which produced two major spots on tlc. A portion of the material was submitted to preparative thin layer chromatography (10% ethyl acetate in cyclohexane, continuous elution for 2.5 hr). The faster moving band yielded 5.3 mg of colorless crystals: mp 188–189°; $\lambda_{max}^{CHCl_3}$ 2.95 μ (OH); nmr ($CDCl_3$) 0.88 (s, CH_3C), 1.18 (s, CH_3C), and 4.15 ppm (m, $W_{h/2}$ = 10 Hz, equatorial proton on carbon bearing oxygen); mass spectrum, *m/e* 290 (calcd $C_{20}H_{34}O$, 290).

The slower moving band yielded 4.9 mg of alcohol *d*-**22** as colorless crystals, mp 148–150°, which appeared to be homogeneous by tlc. Recrystallization from pentane produced pure material: mp 149.5–150°; $\lambda_{max}^{CHCl_3}$ 2.95 μ (OH); nmr [HA-100, $CDCl_3$) 0.89 (s, CH_3C), 0.97 (s, CH_3C), and 3.9 ppm (m, $W_{h/2}$ = 20 Hz, axial hydrogen on carbon bearing oygen); mass spectrum, *m/e* 290 (calcd for $C_{20}H_{34}O$, 290).

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Cyclization of 1-Methyl-6-(*trans,trans*-7,11-dimethyl-3,7,11-dodecatrienyl)-2-cyclohexen-1-ol[1]

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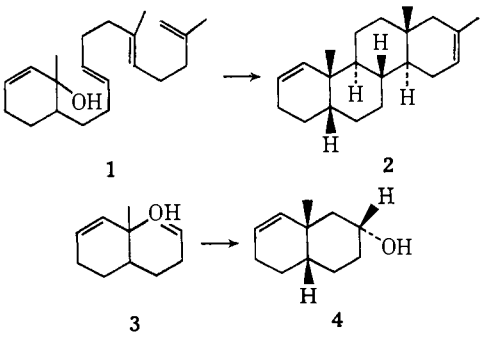
Abstract: The tetraenol **1** has been synthesized by addition of methyllithium to the α,β-unsaturated ketone **14**, derived in turn from the β,γ-isomer **13**, which has been produced by two different convergent pathways. Scheme I involved alkylation of *tert*-butyl acetoacetate with 4-iodo-1-butyne to give **7** which, on Michael addition of acrolein, was converted into **8**. This substance, on treatment with acetic and hydrochloric acid, underwent ester cleavage, decarboxylation, and cyclization affording the acetylenic ketone **9**, which was ketalized (to give **10**) and then, as its lithium salt, alkylated with the previously known bromodiene **6**. The product **11**, on reduction with lithium in ammonia (to give **12**), followed by acid hydrolysis, afforded the tetraenone **13**. Alternatively, the butynylanisole **17**, prepared by coupling of *o*-methoxybenzyl bromide with propargylmagnesium bromide, was alkylated with the bromodiene **6** to give **18**. Birch reduction of **18**, followed by hydrolysis with oxalic acid, also afforded the tetraenone **13**. Treatment of the tetraenol **1** with stannic chloride in nitroethane at −78° proceeded stereoselectively to give the tetracyclic diene **2** in 60% yield. The structure and configuration (cis,anti,trans,anti,trans) of this product were proved by hydrogenation to give two crystalline epimeric saturated hydrocarbons *dl*-**20a** and *dl*-**20b** which were separated and compared with authentic *d*-**20a** and *d*-**20b** prepared as follows. Methyllithium was added to the previously known 5β-*D*-homoandrostan-17-one, and the resulting carbinol dehydrated, then hydrogenated to give the mixture of *d*-**20a** and *d*-**20b** which was separated into its components. Cyclization of **1** with trifluoroacetic acid in dichloromethane also gave **2** in 20% yield. When deuteriotrifluoroacetic acid was used as the catalyst, no deuterium was incorporated in the product **1**, thus showing that the mechanism of this cyclization does not involve deprotonation and reprotonation of carbonium ion intermediates.

As part of a continuing program to investigate stereospecific, nonenzymic cyclizations of polyolefins,[2] we wish to report the synthesis of monocyclic tetraenol **1** and its efficient transformation into the tetracyclic diene **2** under mild, acidic conditions.

As a cyclization substrate the tetraenol **1** incorporates two structural features of particular significance: the tertiary allylic cyclohexenol system which promised to be more readily available than the previously used isomeric system,[3,4] and the terminal isopropenyl group.



In comparison with the less nucleophilic vinyl group employed in several previous studies,[1] the terminal isopropenyl group was expected to enhance formation of the final ring without deprotonation or nucleophilic

(1) This represents part of a general study of nonenzymic, biogenetic like olefinic cyclizations. For the previous paper of this series, see K. E. Harding, E. J. Leopold, A. M. Hudrlik, and W. S. Johnson, *J. Amer. Chem. Soc.*, **96**, 2540 (1974).
(2) W. S. Johnson, *Accounts Chem. Res.*, 1, 1 (1968).
(3) W. S. Johnson, P. J. Neustaedter, and K. K. Schmiegel, *J. Amer. Chem. Soc.*, **87**, 5148 (1965).
(4) W. S. Johnson and K. E. Harding, *J. Org. Chem.*, **32**, 478 (1967).