Oxidation of 13 with TTFA. To a standard solution of 20 mL of trifluoroacetic acid (TFA) containing 1.4 mmol of $Tl(TFA)_3$ was added 1.0 g (3.2 mmol) of **13** at 0 °C, and the resulting deep red mixture was stirred at room temperature for 2.5 h. The reaction mixture was poured into ice water and extracted with CH_2Cl_2, and the CH_2Cl_2 extracts were washed with water and dried over Na_2SO_4. Concentration of the solution gave the yellow paste that on column chromtography (silica gel 300 mesh) afforded crude quinone **24**. Recrystallization from ethanol gave 300 mg (35%) of **24**: bright yellow prisms (ethanol); mp 196-205 °C; IR (KBr) 1670, 1655, 1435, 1280, 1235, 920 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.1-3.85 (8 H, m), 6.20 (1 H, m), 6.34 (1 H, m), 6.46 (1 H, m), 6.49 (1 H, m); ^{13}C NMR ($CDCl_3$) δ 26.85, 28.17, 29.19, 31.29, 131.08, 132.74, 133.86, 135.91, 149.65, 149.90, 151.70, 152.43, 185.51, 186.20, 187.91, 189.60; mass spectrum, *m/e* 268 (M^+); UV ($CHCl_3$) λ_{max} 251 nm (log ε 4.35).

Anal. Calcd for $C_{16}H_{12}O_4$: C, 71.63; H, 4.51. Found: C, 71.93; H, 4.49.

Reduction of [2.2]Metaparacyclophanequinone (24). Method A: AcOH-Zn Reduction. To a solution of 100 mg (0.37 mmol) of [2.2]-metaparaquinonophane (**24**) in 40 mL of acetic acid was added 1.0 g of zinc powder. Addition of zinc powder to the mixture produced a reddish brown to dark wine-red color immediately. The reaction mixture was stirred at room temperature for a few minutes. After the reaction miture became colorless, zinc powder was removed by filtration and the solvent of the filtrate was distilled away in vacuo to leave a very pale violet solid containing $(AcO)_2Zn$, which dissolve in water. The aqueous solution was allowed to stand for some time in contact with air. The solution turned reddish violet rapidly. It was extracted with ether several times, dried over Na_2SO_4, and concentrated in vacuo to leave 100 mg of dark violet solid. Reprecipitation with ether-hexane and washing with CH_2Cl_2 gave 32 mg (32%) of purplish black solid **25**.

Method B: Hydrogenation (PtO_2/H_2). Hydrogen gas was bubbled into the stirred mixture of 30 mg (0.11 mmol) of **24** and 10 mg of PtO_2 (Adams' catalyst) in 25 mL of ethanol at room temperature. The reaction mixture turned reddish brown from yellow quickly, and the brown color disappeared gradually. After the solution turned colorless, the catalyst was removed by filtration and the filtrate, which turned dark violet gradually, was concentrated in vacuo to leave a dark violet solid and was worked up described above; the yield was 17 mg (56%) of **25**: purplish black solid; mp 184 °C; IR (KBr) 3440, 3360, 2950, 1635, 1615, 1420, 1290, 1200, 1140, 900, 870 cm^{-1}; NMR (Me_2SO-d_6) δ 2.0-3.3 (8 H, m), 5.95 (1 H, s), 6.18 (1 H, d, *J* = 2.5 Hz), 6.28 (1 H, s), 6.32 (1 H, d, *J* = 2.5 Hz), 8.60 (1 H, s, exchanged with D_2O); mass spectrum, *m/e* 270 (M^+); UV (THF) λ_{max} 490 (log ε 2.83), 355 (log ε 2.92), 315 (log ε 3.50), 245 nm (log ε 4.00).

Anal. Calcd for $C_{16}H_{14}O_4 + {}^1/_4H_2O$: C, 69.94; H, 5.32. Found: C, 69.88; H, 5.33.

Acetylation of 26. To a solution of 30 mg (0.11 mmol) of [2.2]-metaparaquinonophane (**24**) in 10 mL of acetic acid was added 0.5 g (7.7 mmol) of zinc powder. The reaction mixture was stirred at room temperature for a few minutes. After the bright yellow solution turned colorless, 10 mL of acetic anhydride and 8 drops of concentrated HCl were added to the reaction miture. The reaction mixture was stirred at 80 °C for 10 min, filtered, and poured into 100 mL of water. After the aqueous solution was stirred at room temperature for 1.5 h, it was extracted with CH_2Cl_2, washed with water, dried over Na_2SO_4, and concentrated in vacuo to leave 50 mg (100%) of crude **27**. Recrystallization from hexane-benzene (5:1) gave 30 mg (61%) of **27**: colorless prisms (hexane-benzene); mp 176-181 °C; IR (KBr) 2940, 1750, 1585, 1490, 1450, 1435, 1365, 1210, 1170, 1160, 1120, 1010, 955, 910, 800 cm^{-1}; NMR ($CDCl_3$) δ 1.25 (3 H, s), 2.13 (3 H, s), 2.26 (3 H, s), 2.32 (3 H, s), 2.0-3.15 (8 H, m), 6.06 (1 H, s), 6.59 (1 H, d, *J* = 3 Hz), 6.65 (1 H, d, *J* = 3 Hz), 6.91 (1 H, d); mass spectrum, *m/e* 440 (M^+).

Anal. Calcd for $C_{24}H_{24}O_8$: C, 65.45; H, 5.49. Found: C, 65.33; H, 5.54.

Registry No. **7**, 62224-04-8; **8**, 50874-28-7; **9**, 87207-25-8; **10**, 87207-26-9; **11**, 87207-27-0; **12**, 87207-28-1; **13**, 87207-29-2; **22**, 87207-30-5; **23**, 87207-31-6; **24**, 72652-39-2; **25**, 87207-32-7; **26**, 87207-33-8; **27**, 87207-34-9.

Termination of Biomimetic Cyclizations by the Allylsilane Function. Formation of the Steroid Nucleus in One Step from an Acyclic Polyenic Chain

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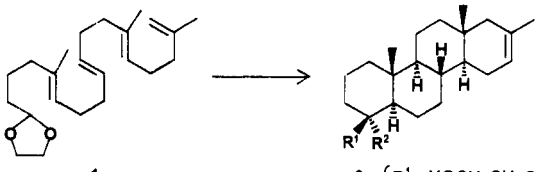
Contribution from the Department of Chemistry, Stanford University, Stanford, California 94305. *Received April 11, 1983*

Abstract: The aim of this project was to modify the cyclization substrate **1**, which is known to undergo ring closure to give **2a** and **2b**, in such a way that a five- instead of six-membered ring D is formed, thus resulting in the construction of the complete steroid nucleus. The substrate **5** was first prepared as shown in Scheme I, but it gave a very complicated mixture of cyclization products. However, the substrate **18**, which was obtained as depicted in Scheme II, afforded the tetracyclic products **24** and **25** in >34% yield. The steroidal constitution of the nucleus of these products was established by their transformation into the known 17α- and 17β-vinylandrostenones **36**, which are convertible into progesterone.

The stannic chloride catalyzed cyclization of the tetraenic acetal **1** has been shown[1] to proceed highly regio- as well as stereoselectively to give, as the only detectable tetracyclic material, two readily separated crystalline products which proved to be the D-homosteroidal substances **2a** and **2b**, differing only in that they were epimeric at C-4 (steroid numbering). Up until now this case has represented the closest nonenzymatic analogy to the biological process for the production of tetracyclic triterpenoids from squalene. Thus in the one-step conversion **1** → **2**, four rings and seven chiral centers are formed in predominantly one stereochemical sense from an acyclic polyene chain—a process which



1

2a (R^1 = $HOCH_2CH_2O$-, R^2 = H)

2b (R^1 = H, R^2 = $HOCH_2CH_2O$-)

in this respect is comparable in complexity to the biological conversion of squalene into lanosterol.

It has been our aim, for some time, to modify the substrate **1** so that cyclization would give a tetracyclic product with a five-membered ring D, thus yielding the complete steroid nucleus. By

(1) Johnson, W. S.; Wiedhaup, K.; Brady, S. F.; Olson, G. L. *J. Am. Chem. Soc.* **1968**, *90*, 5277-5279; **1974**, *96*, 3979-3984.

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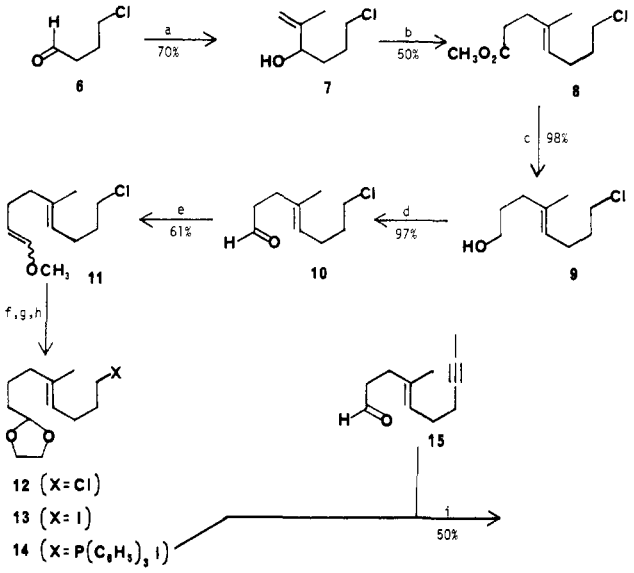
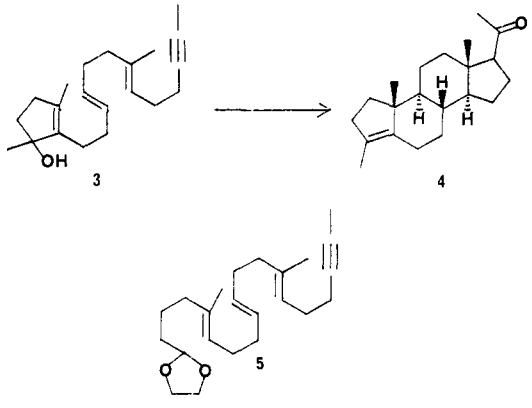
Scheme I



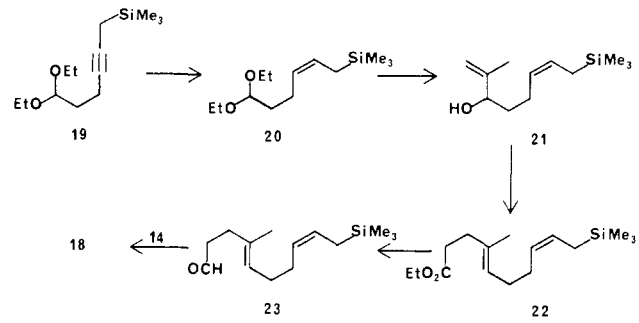
[a] 6[4] treated with excess $CH_2=C(CH_3)MgBr$ in THF gave 7.[5a,6a] [b] Orthoester Claisen reaction[7] gave 8.[5a,6a,b] [c] Excess $Na(CH_3OCH_2CH_2O)_2AlH_2$, C_6H_6, and THF gave 9.[6a,b] [d] Collins oxidation[8] gave 10.[6a,b] [e] $CH_3OCH_2(C_6H_5)_3PCl$ (32 mmol), THF, C_6H_5Li (32 mol) in C_6H_6, and 10 (29 mmol) at −78 °C, 20 min, then 25 °C, 16 h, gave 11.[5b,6b] [f] Excess $HO(CH_2)_2OH$ and trace p-$CH_3C_6H_4SO_3H$, 24 h, 25 °C, gave 12.[6a,b] [g] Excess NaI, acetone, and trace Hünigs base, reflux, 12 h, gave 13[5c,6a,b] (75% yield from 11). [h] $(C_6H_5)_3P$, CH_3CN, and trace Hünigs base, 75 °C, 15 h, wash with hexane, gave 14[6a] (80% yield). [i] Wittig-Schlosser condensation[3] gave 5,[5c,6a] 96% trans at pro-C-8,9 bond by GC.

analogy to previous findings, e.g., the trifluoroacetic acid catalyzed cyclization **3** → **4**,[2] the substrate **5** was considered a likely can-



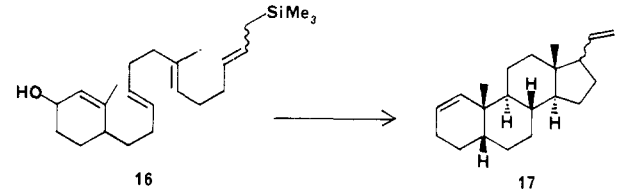
didate for realizing this goal; hence it was synthesized by the approach summarized in Scheme I involving, as a convergent step, the Wittig–Schlosser condensation[3] of the known[2] aldehyde **15**

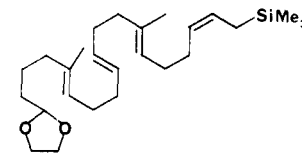
Scheme II



with the phosphorane derived from the phosphonium salt **14**. Unfortunately, acetal-initiated cyclizations of any complexity, e.g., **1** → **2**, do not proceed to completion with protic acids which, however, are the preferred catalysts for processes terminated by the methylacetylenic function. Thus when **5** was treated with stannic chloride in pentane, the resulting tetracyclic material proved to be a very complex mixture, probably containing various bridgehead configurations as well as five- and six-membered D-ring vinyl chlorides.[9a] Similarly, in the case of the BF_3-catalyzed cyclization of a close analogue of **5** (epoxide instead of acetal initiator), the selectively for formation of the "natural" tetracycle was disappointingly low (ca. 2% yield).[9b]

Considering the recent success in effecting Lewis acid catalyzed termination of a polyene cyclization by the Fleming allylic silane function so as to give a five-membered D ring, e.g., **16** → **17**,[10]





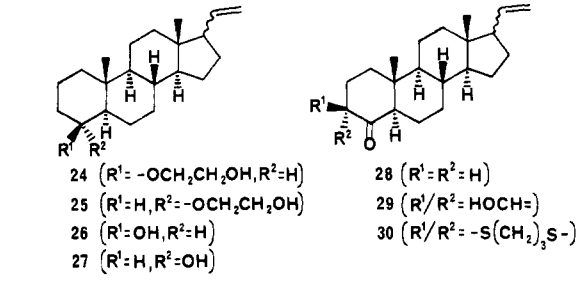
we were prompted to investigate the cyclization of the acetal **18**. The present paper includes an account of such a study which has resulted in the realization of the remarkably selective, one-step production of the complete steroid nucleus by the nonenzymatic cyclization of an acyclic polyene chain.

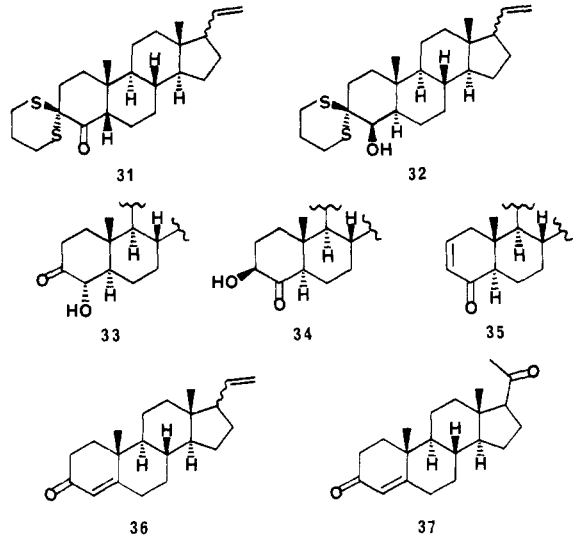
The synthesis of substrate **18**, was performed by a convergent scheme involving the Wittig–Schlosser condensation of the phosphorane, derived from the phosphonium salt **14**, with the aldehyde **23**. This aldehyde which has been previously described[10] as a mixture of *E* and *Z* allylic silane isomers, was produced (as the *Z* isomer) by an alternative method shown in Scheme II. The steps **19** → **20** → **21** were developed by Livinghouse.[11] Thus selective hydrogenation of the known[12] acetal **19** over P-2 nickel poisoned with ethylenediamine[13] gave the acetal **20**[5b,6a,b] in 91%

(2) Gravestock, M. B.; Johnson, W. S.; McCarry, B. E.; Parry, R. J.; Ratcliffe, B. E. *J. Am. Chem. Soc.* **1978**, *100*, 4274–4282.
(3) The procedure was similar to that described in ref 2.
(4) Pleshakov, M. G.; Vasil'ev, A. E.; Sarycheva, I. K.; Preobrazhenskii, N. A. *J. Gen. Chem. USSR* **1961**, *31*, 1433–1435. van der Gen, A.; Wiedhaup, K.; Swoboda, J. J.; Dunathan, H. C.; Johnson, W. S. *J. Am. Chem. Soc.* **1973**, *95*, 2656–2663.
(5) The product was purified by (a) distillation through a short Vigreux column, (b) short-path distillation, (c) chromatography on Florisil, (d) chromatography on silica gel, (e) preparative TLC.
(6) (a) The ^1H NMR and IR spectra were consistent with the assigned structure. (b) A satisfactory combustion analysis was obtained for an appropriately purified specimen of this compound. (c) The mass spectrum exhibited the correct molecular ion peak.
(7) Johnson, W. S.; Werthemann, L.; Bartlett, W. R.; Brocksom, T. J.; Li, T.-t.; Faulkner, D. J.; Petersen, M. R. *J. Am. Chem. Soc.* **1970**, *92*, 741–743.
(8) Ratcliffe, R.; Rodehorst, R. *J. Org. Chem.* **1970**, *35*, 4000–4003.
(9) (a) Johnson, W. S.; Ward, C. E.; Boots, S. G.; Gravestock, M. B.; Markezich, R. L.; McCarry, B. E.; Okorie, D. A.; Parry, R. J. *J. Am. Chem. Soc.* **1981**, *103*, 88–98. (b) van Tamelen, E. E.; Leiden, T. M. *Ibid.* **1982**, *104*, 2061–2062.
(10) Hughes, L. R.; Schmid, R.; Johnson, W. S. *Bioorg. Chem.* **1979**, *8*, 513–518.
(11) Livinghouse, T. NIH Postdoctoral Fellow, Stanford University, 1979–80.
(12) Schmid, R.; Huesmann, P. L.; Johnson, W. S. *J. Am. Chem. Soc.* **1980**, *102*, 5122–5123.
(13) Brown, C. A.; Ahuja, V. K. *J. Chem. Soc., Chem. Commun.* **1973**, 553–554.

yield; then the crude aldehyde, obtained on acid hydrolysis, was treated with excess isopropenylmagnesium bromide, giving **21**[5b,6a,b] in 86% yield. The alcohol **21** was then submitted to the ortho-acetate Claisen reaction[7] to give **22**[5a,6a] in 90% yield. Reduction of the ester **22** with lithium aluminum hydride afforded the corresponding alcohol[5d,6a] (76.5% yield) which on oxidation with pyridinium chlorochromate[14] gave the aldehyde **23**[5c,6a] in 91% yield. Finally condensation of **23** with **14** (see above) gave the substrate **18**[5d,6a,b] in 57% yield (94% pure by GC). The trans/cis ratio about the pro-C-8,9 double bond was estimated by GC to be ca. 96:4.

Treatment of the acetal **18** with 0.2 M stannic chloride in pentane at 0 °C for 15 min, then at 15 °C for 5 min,[15] afforded as the principal products two pairs of isomers, which proved (see below) to be **24** and **25** as mixtures of their 17α and 17β epimers. Analytical GC showed **24** (as a 2:3 mixture of 17 epimers) and **25** (as a 1:1 mixture of 17 epimers) in the ratio 2:1. Chromatography[5d] gave **24**[6a,c] in 23% yield. The ^{1}H NMR singlet for the C-19 methyl group appeared at δ 0.98 ppm, indicating that the side chain at C-4 was β (axial).[15] The absorption for the C-18 methyl group appeared as two singlets at δ 0.58 and 0.78 ppm, as observed in a similar case.[15] Further development of the chromatogram gave **25**[6a,c] in 11% yield. The ^{1}H NMR singlet for the C-19 methyl appeared at 0.79 ppm indicating that the side chain at C-4 was α (equatorial).[15] The hydroxyethoxy side chain was removed by tosylation followed by treatment with zinc and sodium iodide[15] to give **26**[5e,6a,c] (63% yield from **24**) and **27**[5e,6a,c] (81% yield from **25**), showing absorption in the ^{1}H NMR at δ 1.04 and 0.79 ppm, respectively, for the C-19 methyl[15] and at δ 3.8 (narrow multiplet) and 3.4 ppm, respectively (broad multiplet), for the C-4 proton.[15] The epimeric relationship of **26** and **27** at





C-4 was proved by their oxidation[15] (83–89% yield) to the same ketone **28** (C-17 epimeric mixture).[5e,6a,c] At this stage it was possible to separate by chromatography,[5c] or better by HPLC, the C-17 epimers, one of which, corresponding to the longer retention time isomer on GC, was obtained pure, mp 124–125 °C.[5c,6a] The ^{1}H NMR signal for the C-18 methyl of this isomer appeared at δ 0.57 ppm, suggesting that it was the 17β epimer of **28**.[16]

In order to prove the steroidal nature of the tetracyclic nucleus, the ketone **28** (as the C-17 epimeric mixture) was submitted to a number of transformations (see below) that resulted in its conversion into products of known constitution. Thus condensation of **28** with ethyl formate (to give **29**)[17] followed by treatment with 1,3-propanedithiol di-*p*-toluenesulfonate[18] gave a mixture of two thioketal ketones, separable by TLC: the expected 5α compound **30**[6a,c] and the 5β (A/B cis) isomer **31**[6ac] in ratio of 5:4 by GC. This ratio was changed to 7:3 by heating the mixture with 0.5% potassium carbonate in 90% ethanol. The convertibility of the latter into the former isomer (see above), along with the ^{1}H NMR signals for the C-19 methyl group at δ 0.76 and 1.06 ppm, respectively,[19] is consistent with the configurational assignments.

Reduction of ketone **30** with sodium borohydride afforded the hydroxy thioketal **32**[5e,6a,c] in 90% yield. The expected[20] β(axial) configuration of the hydroxyl group was confirmed by the appearance of the C-19 methyl signal in the ^{1}H NMR at δ 1.02 ppm, the downfield shift being due to the 1,3-diaxial interaction with the hydroxyl group.[15] Dethioketalization of **32** under mild conditions (MeI, CH_3CN, H_2O, $CaCO_3$)[21] unfortunately was accompanied by prototropic shifts (via enol forms), giving a mixture of hydroxy ketones which, by the ^{1}H NMR spectrum, appeared to be **33** and **34** in a ratio of about 2:1. Tosylation of this mixture, followed by treatment with lithium carbonate and lithium bromide in DMF,[22] gave a mixture of two unsaturated ketones **35**[5e,6a,c] and **36**[5e,6a,c] which were readily separated by TLC in a ratio of about 2:1. The structural assignment of **35** is tentative, being based primarily on the ^{1}H NMR spectrum which showed, in particular, a pair of multiplet signals for one proton (C-2) at δ 6.73 ppm and for one proton (C-3) at 5.94 ppm. The 17α[23] and 17β[24] forms of **36** are known in their natural enantiomeric forms. A specimen of the former was given to us by Hoffmann-La Roche Inc., and we prepared the latter by Oppenauer oxidation of 3β-hydroxypregna-5,20-diene.[23] Using these authentic specimens the identity of our totally synthetic racemic mixture was established beyond doubt by ^{1}H NMR, GC (coinjection experiments on a 14-m SE-54 capillary column) and HPLC (ODS-2 95% MeOH). The mixture of C-17 epimers of totally synthetic **36** was separated by HPLC giving a sample of 96% pure (by GC) 17β-**36**, mp 121–123 °C. The fraction of 17α-**36** (95% pure by GC) was used for the conversion to racemic progesterone **37** (see below).

The Wacker reaction[25] was first studied with the naturally derived forms of **36**. Thus 17β-**36** was converted into progesterone, but the yield was poor (22%); 17α-**36**, however, was transformed into 17α-progesterone in fair (70%) yield. The identity of the products was established by comparison (^{1}H NMR and GC) with authentic specimens. Because of the more favorable yield in the 17α series, the aforementioned totally synthetic specimen of racemic 17α-**36** was submitted to the Wacker reaction.[25] The product was racemic 17α-progesterone, which on isomerization (K_2CO_3, 90% EtOH, reflux 16 h) was partially equilibrated, giving a mixture of racemic progesterone and the 17α epimer in a ratio of 61:39. The identity of these racemic products was established by comparison (GC coinjection and HPLC experiments) with authentic materials. These experiments provided confirmation of the constitution of the products resulting from the cyclization

(14) Corey, E. J.; Suggs, J. W. *Tetrahedron Lett.* **1975**, 2647–2650.
(15) Cf. ref 1.
(16) See footnote 11 of ref 10.
(17) Cf. Corey, E. J.; Cane, D. E. *J. Org. Chem.* **1971**, *36*, 3070.
(18) Cf. Woodward, R. B.; Patchett, A. A.; Barton, D. H. R.; Ives, D. A.; Kelley, R. B. *J. Chem. Soc.* **1957**, 1131–1144.
(19) Bhacca, N. S.; Williams, D. H. "Application of NMR Spectroscopy in Organic Chemistry"; Holden-Day: San Francisco, 1964; pp 19–20.
(20) Barton, D. H. R. *J. Chem. Soc.* **1953**, 1027–1040.
(21) Cf. Johnson, W. S.; McCarry, B. E.; Markezich, R. L.; Boots, S. G. *J. Am. Chem. Soc.* **1980**, *102*, 352–359.
(22) Furlenmeier, A.; Fürst, A.; Langemann, A.; Waldvogel, G.; Kerb, U.; Hocks, P.; Wiechert. R. *Helv. Chim. Acta* **1966**, *49*, 1591–1601.
(23) Krubiner, A. M.; Gottfried, N.; Oliveto, E. P. *J. Org. Chem.* **1969**, *34*, 3502–3505.
(24) Krieger, B.; Kaspar, E. *Chem. Ber.* **1967**, *100*, 1169–1178.
(25) Cf. Tsuji, J.; Shimizu, I.; Yamamoto, K. *Tetrahedron Lett.* **1976**, 2975–2976.

of **18**, which was therefore unequivocally shown to proceed highly regio- as well as diastereoselectively to form the complete steroid nucleus.

Acknowledgment. We are indebted to the National Institutes of Health, the National Science Foundation, and to the donors of the Petroleum Research Fund, administered by the American Chemical Society, for support of this research. We also wish to thank Drs. N. Cohen and G. Saucy of Hoffmann-La Roche Inc. for arranging for us to receive a generous specimen of the 17α form of substance **36**.

Registry No. (*E,E,E*)-**5**, 87305-79-1; **6**, 6139-84-0; (±)-**7**, 87305-80-4; (*E*)-**8**, 87318-47-6; (*E*)-**9**, 87305-81-5; (*E*)-**10**, 87305-82-6; (*x,E*)-**11**, 87305-83-7; (*E*)-**12**, 87318-48-7; (*E*)-**13**, 87318-49-8; (*E*)-**14**, 87305-84-8; (*E*)-**15**, 41143-17-3; (*E,E,Z,E*)-**18**, 87305-85-9; **19**, 74377-87-0; (*Z*)-**20**, 87305-86-0; (±)-(*Z*)-**21**, 87305-87-1; (*Z,E*)-**22**, 87305-88-2; (*Z,E*)-**23**, 87305-89-3; (±)-**24**(17α), 87305-90-6; (±)-**24**(17β), 87334-72-3; (±)-**25**(17α), 87305-91-7; (±)-**25**(17β), 87334-73-4; (±)-**26**(17α), 87305-92-8; (±)-**26**(17β), 87334-74-5; (±)-**27**(17α), 87305-93-9; (±)-**27**(17β), 87334-75-6; (±)-**28**(17α), 87305-94-0; (±)-**28**(17β), 87334-76-7; (±)-**29**(17α), 87305-95-1; (±)-**29**(17β), 87334-77-8; (±)-**30**(17α), 87305-96-2; (±)-**30**(17β), 87334-78-9; (±)-**31**(17α), 87305-97-3; (±)-**31**(17β), 87334-79-0; (±)-**32**(17α), 87305-98-4; (±)-**32**(17β), 87334-80-3; (±)-**33**(17α), 87305-99-5; (±)-**33**(17β), 87334-81-4; (±)-**34**(17α), 87306-00-1; (±)-**34**(17β), 87334-82-5; (±)-**35**(17α), 87306-01-2; (±)-**35**(17β), 87334-83-6; (±)-**36**(17α), 87334-84-7; (±)-**36**(17β), 87334-85-8; CH_2=$C(CH_3)Br$, 557-93-7; $CH_3OCH_2(C_6H_5)_3PCl$, 4009-98-7; 1,3-propanedithiol di-*p*-toluenesulfonate, 3866-79-3; progesterone, 57-83-0; 17α-progesterone, 2000-66-0; (±)-17α-progesterone, 73889-98-2; (±)-progesterone, 14546-13-5.

Supplementary Material Available: IR, NMR, mass spectral, and analytical data (6 pages). Ordering information is given on any current masthead page.

Discrimination between Exo- and Endo-3,2-Methyl Shifts in Substituted 2-Norbornyl Cations on the (+)-Camphenilone Route to (−)-Albene

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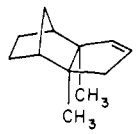
Abstract: One key step in the synthetic route leading from (+)-camphenilone to (−)-albene, a chloro olefin annelation reaction, occurs with concomitant diminution of optical purity. An investigation of this reaction with a $^{13}C,^{2}H_2$-labeled version of the chloro olefin accords with a recent reassignment of the absolute stereochemistry of (−)-albene as (1*S*,2*S*,6*S*,7*R*)-2-*endo*,6-*endo*-dimethyltricyclo[5.2.1.$0^{2,6}$]dec-3-ene and demonstrates that neither enantiomer of the rearrangement product depends on an endo-3,2-methyl shift in a substituted 2-norbornyl cationic intermediate.

(−)-Albene, a tricyclic olefin first isolated in 1962 from *Petasites albus*,[1] is now known to be the 1*S*,2*S*,6*S*,7*R* enantiomer of 2-*endo*,6-*endo*-dimethyltricyclo[5.2.1.$0^{2,6}$]dec-3-ene (**1**).[2]



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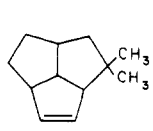
Accurate structural, stereochemical, and absolute configurational assignments for this natural product have not been secured without difficulty. The first tentative structural proposal advanced in 1964,[3] the dimethyltetrahydrotriquinacene formulation **2**, was



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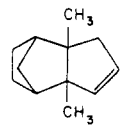

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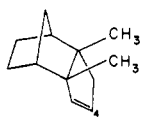

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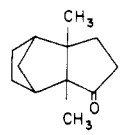

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abandoned in 1972 as additional evidence, including a chemical correlation between (−)-albene and (+)-camphene, was interpreted in terms of the correct structure (**3**) but the wrong stereochemistry (**4**).[4] Structure **4** was supported in 1973 through independent work providing a synthesis of a degradation product, albanone (**5**; 2,6-dimethyltricyclo[5.2.1.$0^{2,6}$]decan-3-one), from camphenilone.[5] The correct stereochemistry but the wrong absolute configuration were assigned in 1978 in work that included an X-ray crystallographic structure determination[6] for the 4-phenylthio derivative of (±)-isoalbene ((±)-**4**), careful ^{13}C NMR comparisons between albene and isoalbene,[7] and a total synthesis of (−)-albene from (+)-camphenilone.[8,9]

The correct structural and absolute stereochemical representation of (−)-albene has thus been notably elusive in spite of extensive efforts employing a variety of degradative and synthetic studies relating this comparatively small molecule to natural products of known stereochemistry and absolute configuration. Part of that chemistry, then, must be imperfectly understood and formulated according to invalid mechanistic assumptions.

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