Experiments Directed toward the Total Synthesis of Terpenes. 24. On the π Route to Aphidicolin: Synthesis of 18,19-Bisnoraphidicolan-3-one[1]

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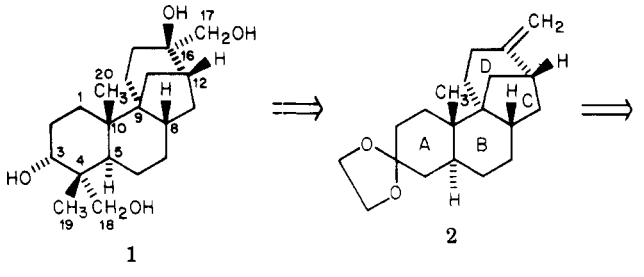
An approach to the synthesis of aphidicolane-type diterpenes is described. The key to the bicyclo[3.2.1] ring construction entails a solvolytic π route from the tricyclic olefin **20**. Construction of the latter system required the development of a spiro ketone synthesis. Use of the hetero-Diels–Alder reaction with the α-methylene ketones **4** and **11** and then Claisen rearrangement of the derived vinyldihydropyrans **5c** and **6c** and **12c** and **13c** accomplished this spiroannelation process. In the latter decahydrobenzosuberan system the seven-membered B ring was contracted to a six-membered ring through photolysis of the α-diazo ketone **16**. In the absence of added sodium methoxide this photolysis leads to the cyclobutanone **18**.

The tetracyclic diterpene aphidicolin (1) was isolated in 1972[3] by Hesp and co-workers from cultures of *Cephalosporium aphidicola* Petch. The structure of this novel tetracyclic diterpenoid tetraol was determined by Hesp[4] through a combination of degradative and spectroscopic methods and through X-ray crystal analysis of the bis(acetonide). Hesp[4] proposed that the parent hydrocarbon be called aphidicolane and be numbered as shown. Since then several related diterpenes have been isolated and their structures determined;[5] the most notable feature of these latter substances is that they are epimeric with aphidicolin (1) at C9 and C12. All of these substances possess interesting physiological characteristics, and the antiviral activity[6] of aphidicolin (1) itself has attracted significant attention. Two syntheses 17-noraphidicolan-16-one have been recorded.[7]

In planning the synthesis of aphidicolin (1) the close similarity between the BCD ring system of this diterpene (see **2**) and the skeleton of the sesquiterpene cedrene suggested that a synthetic plan comparable to one of those previously used for the construction of the latter substance might be applicable here. The most attractive and efficient of these approaches is the π route developed by Lawton[9] and Corey[9] independently. For this to be a viable approach here, it was first necessary to generate the spiro olefin system **3**. Thus the first stages of this work resulted in the development of an efficient procedure for spiroannelation and then the demonstration in this model system that the π route is a suitable method for the construction of the aphidicolane ring system.



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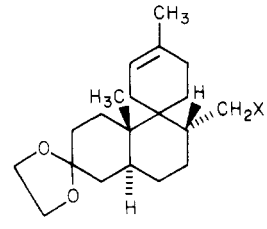

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The spiroannelation scheme chosen for investigation was a combination of the hetero-Diels–Alder and then Claisen rearrangement reactions.[10] With this in mind the logical precursor for the spiro olefin **3** was then the α-methylene ketone **4**, the chemistry of which has been extensively investigated in these laboratories[11] (Scheme I). Condensation of **4** with methyl methacrylate led in 80% yield to a 1:1 mixture of the isomeric dihydropyrans **5a** (37%) and **6a** (43%). After chromatographic separation, each was efficiently converted to the corresponding vinyldihydropyran **5c** (67%) and **6c** (84%) through the aldehydes **5b** and **6b**. On heating in a sealed tube, each of the vinyldihydropyran derivatives readily underwent Claisen rearrangement to the spiro ketones **7** (75%) and **8** (88%) which differ in the location of the double bond. If the π-route plan were to follow the formation of these spiroannelated systems, the structure represented by spiro ketone **7** would lead to the aphidicolane skeleton, while that represented by its isomer **8** would lead to a tetracyclic skeleton isomeric with aphidicolane at C9 and C12 (stemodane skeleton[5]). In this case it was not possible to control the stereochemical outcome of the initial hetero-Diels–Alder reaction so as to favor precursors of the aphidicolane structure only.

While an efficient spiroannelation sequence has been demonstrated (spiro ketone **7** in 18.6% overall yield and

(1) This investigation was supported by Grant No. CA18191, awarded by the National Cancer Institue, DHEW.
(2) Predoctoral Fellow of the National Science Foundation, 1973–1976.
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(10) Büchi, G.; Powell, J. E., Jr. *J. Am. Chem. Soc.* **1970**, *92*, 3126.
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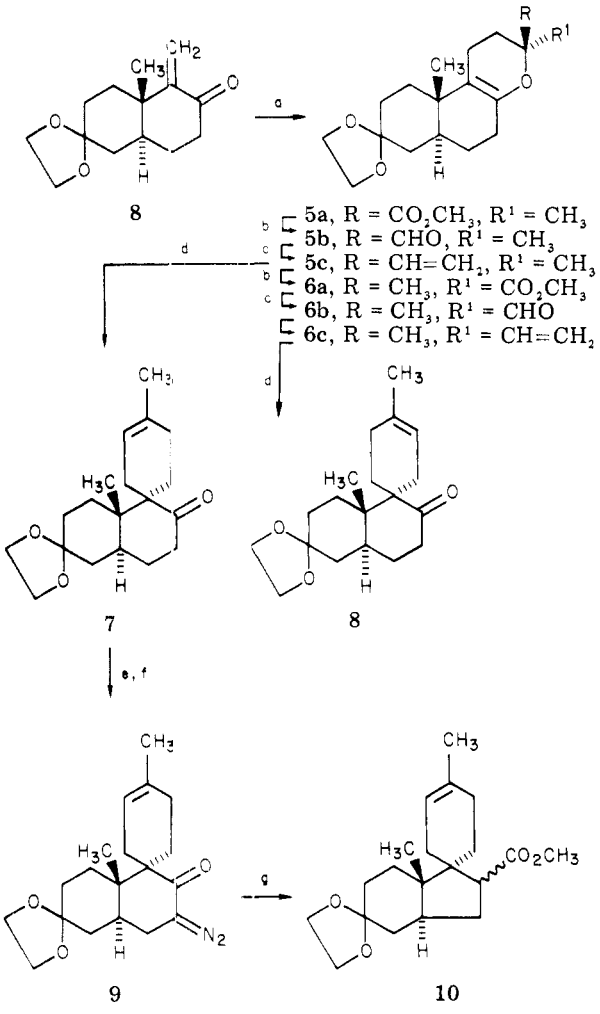
Scheme I. Spiroannelation of the Decalin System[a]



[a] a, $CH_2=C(CH_3)CO_2CH_3$, Δ; b, $(i\text{-Bu})_2AlH$, Et_2O, −78 °C; c, $(C_6H_5)_3PCH_3^+I^-$, Me_2SO; d, Δ, e, *i*-AmONO, KO-*t*-Bu; f, NH_4OH, NaOCl, THF; g, *hν*, CH_3OH-THF.

8 in 32% overall yield), the synthetic program broke down at this point when it was not possible to introduce a functionalized one-carbon unit at the site of the ketone carbonyl. The aphidicolane precursor **7** is particularly hindered and even (methylthio)methyllithium resulted in enolization of the ketone and no addition. As a means to overcome the severe steric hindrance at this position, an *intramolecular* reaction sequence was sought that would result in the incorporation of the necessary functionalized one-carbon unit there. Such a sequence appeared to be the Meinwald–Cava ring contraction procedure[12] in which a cyclic diazo ketone generates the lower homologue carboxylic acid photochemically. This would require the reconstruction of the spiro ketone system **7** with a seven-membered B ring, but the present technology for spiroannelation of the appropriate α-methylene ketone should still suffice.

Before effort was expended to make the B-homo spiro ketone, the Meinwald–Cava sequence[12] in these systems was tested by investigating the reactions with the available spiro ketone **7**. The diazo ketone **9** was easily obtained in 78% overall yield by first oximination and then chloramine oxidation of the resulting oximino ketone. Photolysis of **9** proceeded smoothly and generated the five-membered B-ring spiro ester **10** in 81% yield. Thus contraction of the six-membered ring to its lower homologue was efficiently (63% overall yield) attained, and the preparation of the corresponding seven-membered B-ring spiro ketone **14** became the next objective.

For this synthesis the starting α-methylene ketone **11** (Scheme II) was prepared in the same fashion as used earlier[11] for the lower homologue **4**. While it was not possible to make preparative amounts of the trans-fused 6–7 dicyclic system,[13] the readily available cis-fused isomer served equally well. Pure endocyclic olefin ketal for photooxygenation to the α-methylene ketone **11** also was not available and only 60:40 mixtures of the exocyclic–endocyclic olefins could be obtained.[13] This result proved to be no obstacle when it was found that only the endocyclic olefin underwent photooxygenation, while the exocyclic olefin isomer was recovered unchanged. Iodine isomerization of the recovered exocyclic olefin isomer then reestablished the 60:40 isomeric mixture of olefins, and ultimately a high conversion of this system to the desired α-methylene ketone **11** was possible.

The generation of the spiro ketones **14** and **15** was accomplished by the spiroannelation sequence used earlier. In this decahydrobenzosuberan series, however, the stereochemical outcome of the hetero-Diels–Alder reaction was found to be temperature dependent. Thus, the aphidicolin precursor ester **12a** predominated (2:1 ratio) when the condensation was carried out at 160 °C and the epimeric ester **13a** was the major product at 220 °C. It was therefore possible to obtain predominantly the aphidicolin spiro ketone **14** (45% overall yield), whose conversion to the diazo ketone **16** followed the previous model system after some technical modifications in the reaction conditions. At this point confirmation of the structure assigned this spiro ketone **14** (and hence those of its precursors as well) was sought through single-crystal X-ray analysis. While this analysis, kindly provided by Professor Jon Bordner,[14] confirmed the regio- and stereochemistry of the spiro ketone portion of the molecule, it revealed for the first time that the A/B rings were cis rather than trans fused.

On irradiation of the diazo ketone **16** under the same conditions used above in the model system the only product formed was the cyclobutanone derivative **18**. Apparently, the intermediate ketene **17** is perfectly aligned to undergo a thermal $[_\pi2_s + _\pi2_a]$ cycloaddition with the spirocyclohexene. That this process was a thermal cycloaddition rather than a photochemical cycloaddition was later shown when enolization of the esters **19a** and **19b** (vide infra) under standard "dark" conditions also led in part to the formation of the same cyclobutanone **18**. In this case the steric congestion about the C8 position (aphidicolane numbering) is probably responsible for the ease with which the ester enolates eject methoxide ion and form the less congested, but highly reactive, ketene **17**.

It was, however, possible to trap the intermediate ketene **17** intermolecularly by increasing the nucleophilicity of the trapping agent. When the photolysis was carried out at −70 °C in the presence of excess added sodium methoxide and then the mixture was allowed to warm to 25 °C, a 5:1 mixture of the expected esters **19a** and **19b** was formed in 70% yield. While these esters were readily separable by column chromatography, it was not possible to equilibrate the isomers through base-catalyzed enolization due to the intervention of cyclobutanone **18** formation.

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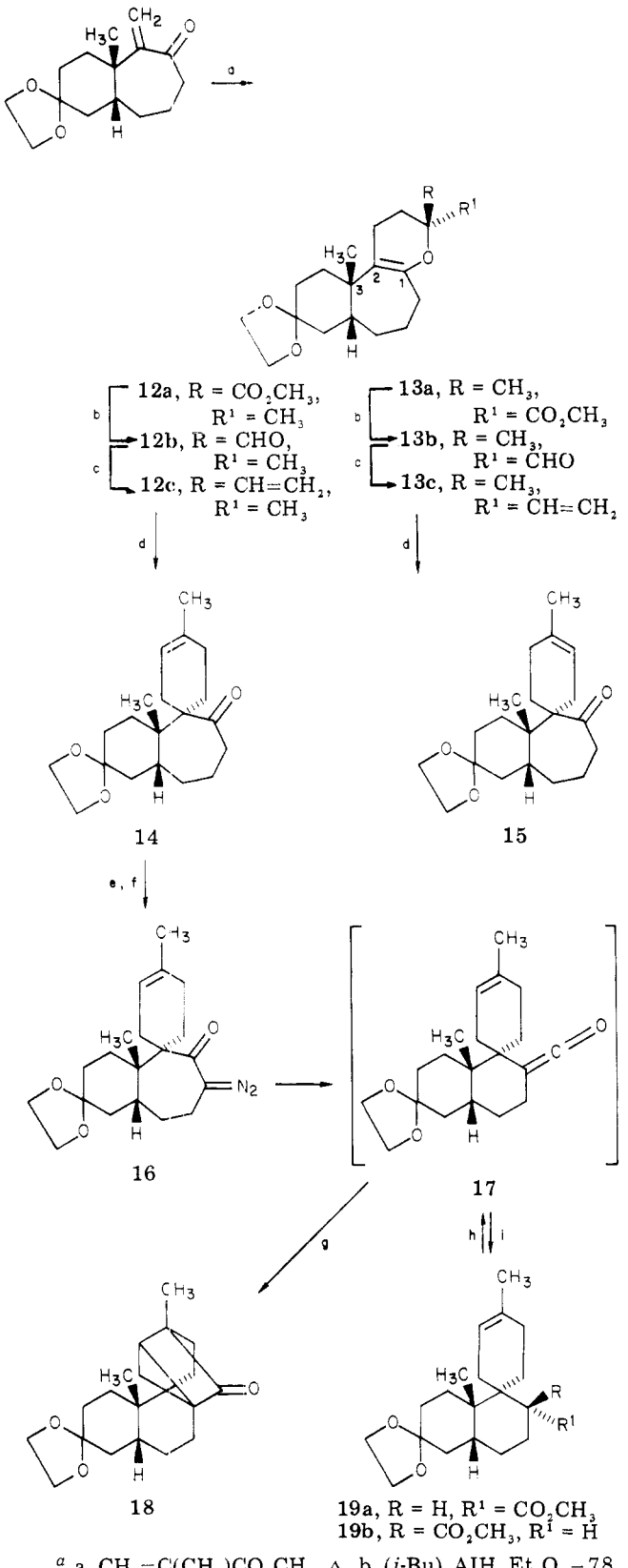
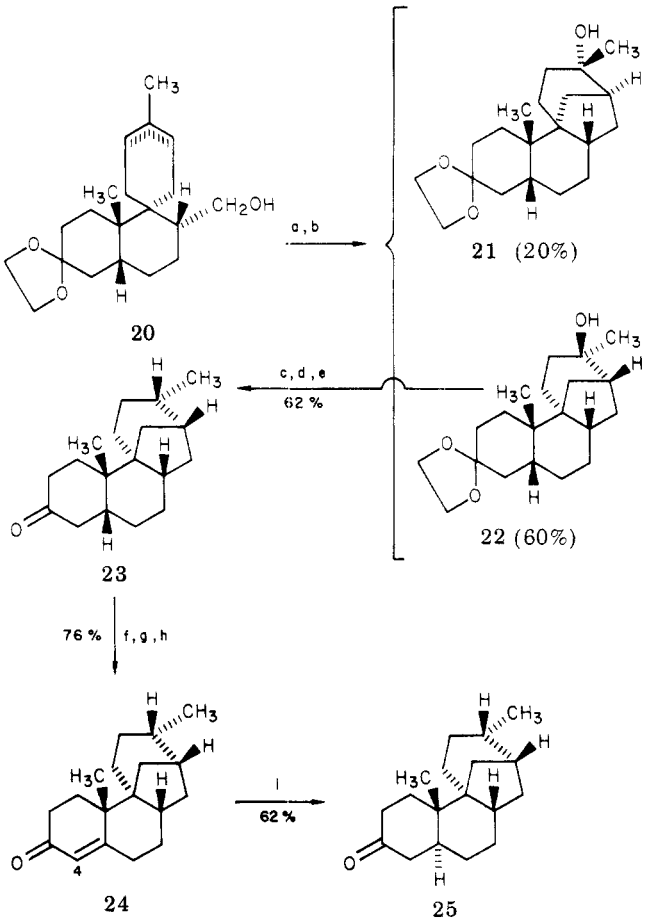
(14) Unpublished results of Professor Jon Bordner, North Carolina State University, Raleigh, NC.

Scheme II. Spiroannelation and Ring Contraction Sequence[a]



[a] a, $CH_2=C(CH_3)CO_2CH_3$, Δ, b, $(i\text{-Bu})_2AlH$, Et_2O, −78 °C; c, $(C_6H_5)_3PCH_3^+ I^-$, NaH, Me_2SO; d, heat in sealed tube; e, *n*-BuLi, *i*-AmONO, THF; f, NH_4OH, NaOH, NaOCl, THF; g, *hν*, THF-CH_3OH, −60 to +25 °C; h, LDA, THF-HMPA, −10 °C; i, *hν*, 10 equiv of $NaOCH_3$, CH_3OH, −70 to +25 °C.

Scheme III. Exploratory Conversion to the Aphidicolin Carbon Skeleton[a]



[a] a, BsCl, Pyr; b, H_2O-dioxane, 50 °C, K_2CO_3; c, $SOCl_2$, Pyr, −15 °C; d, $(CO_2H)_2$, H_2O-CH_3OH; e, H_2, 10% Pd-C, HOAc; f, Ac_2O, $HClO_4$; g, Br_2, CCl_4; h, semicarbazide·HCl, NaOAc; CH_3COCO_2H; i, Li, NH_3.

This synthetic scheme then leads to the desired precursor for an investigation of the π route to the C/D ring formation of aphidicolin—namely, the alcohol **20** formed from the ester **19a** on lithium aluminum hydride reduction (Scheme III). Unfortunately, it was found through ^{13}C NMR spectroscopy and X-ray analysis[14] of **20** that during the sequence of reactions from spiro ketone **14** to alcohol **20** (particularly, during workup of the hydride reduction) the location of the double bond in the cyclohexene ring had been partially scrambled. It seems probable that this unexpected double-bond liability can be avoided in the future by greater attention to experimental detail, but at this juncture the synthetically more important question was the viability of the proposed π route for the ring construction. Utilization of this isomeric mixture of alcohols **20** in the solvolysis reaction would thus be expected to generate predominantly the aphidicolane skeleton together with some of the C9–C12 isomeric tetracyclic ring system. In point of fact, the solvolysis of the brosylates derived from the alcohol mixture **20** in dioxane–water led very efficiently to the isomeric tertiary alcohols **21** and **22** which were separated by column chromatography; the major component was assumed to be **22** from the predominant olefinic alcohol in the alcohol mixture **20**. In a separate experiment a small sample of the rigorously purified alcohol **20** derived for the ester **19a** led exclusively to the aphidicolane solvolysis product **22** which confirms this assignment and the structural uniqueness of the solvolysis. Thus, the π route to the aphidicolane ring system is a

useful approach and ongoing work is addressing the problem of the control of double-bond isomerization in the precursors of the alcohol **20**.

The final basic question to be answered about this scheme for the construction of the aphidicolane skeleton was whether the A/B cis ring fusion could be transformed to the natural A/B trans fusion. Coupled with this operation was the necessity to provide for the introduction of the C4 substituents that ultimately would be required in the aphidicolin (**1**) project itself. At this point the earlier, unexpected foundation of the A/B cis fusion in the benzosuberan precursors of the α-methylene ketone **11** became a distinct advantage, for enone formation from the saturated ketone **23** generated exclusively the C4–C5 α,β-unsaturated ketone **24**. Thus, despite the complex ring structure represented here, the C3 ketone enolizes preferentially toward C4 in agreement with steroidal analogies.[15] Lithium–ammonia reduction of the enone **24** then established the desired A/B trans fusion and 18,19-bisnoraphidicolane (**25**) became available. It is proposed to utilize the intermediate enolate from a similar reduction in the natural series for the introduction of the C4 substituents, and this work is currently under way.

Experimental Section[16]

8,8(7*H*)-(Ethylenedioxy)-3β-(methoxycarbonyl)-3α,10aβ-dimethyl-2,3,5,6,6aα,9,10,10a-octahydro-1*H*-naphtho[2,1-*b*]pyran (5a) and 8,8(7*H*)-(Ethylenedioxy)-3α-(methoxycarbonyl)-3β,10aβ-dimethyl-2,3,5,6,6aα,9,10,10a-octahydro-1*H*-naphtho[2,1-*b*]pyran (6a). A solution of 3.55 g (15.0 mmol) of the methylene ketone **4**[14] in 16.0 mL (15.1 g, 151 mmol) of methyl methacrylate (freshly distilled over CaH_2 and stabilized with 0.5% hydroquinone) in a base-washed and oven-dried tube was degassed under argon, sealed under vacuum, and heated for 22 h at 180 °C. Upon cooling, the viscous liquid was dissolved in 8 mL of chloroform; 100 mL of ether was added, and the solution was heated for 15 min on a steam bath and then filtered. The white precipitate was twice extracted with an additional 75 mL of ether. Removal of the solvents at reduced pressure gave a yellow liquid which on chromatography (medium pressure) on silica gel with 1:1 petroleum ether–ether afforded 1.88 g (37%) of ester **5a** (R_f 0.25) and 2.17 g (43%) of ester **6a** (R_f 0.2). The ester **5a** was a white solid: mp 87.5–90.5 °C; IR ($CHCl_3$) 1730 (C=O), 1680 (C=C) cm^{-1}; ^1H NMR ($CDCl_3$) 0.91 (3, s, C-10a CH_3), 1.41 (3, s, C-3 CH_3), 3.72 (s, 3, methyl ester), 3.92 (s, 4, ketal). One recrystallization from hexane–ether furnished an analytically pure sample, mp 89–92 °C.

Anal. Calcd for $C_{19}H_{28}O_5$: C, 67.83; H, 8.39. Found: C, 67.76; H, 8.43.

The ester **6a** was also a white solid: mp 82–89 °C; IR ($CHCl_3$) 1730 (C=O), 1680 (C=C) cm^{-1}; ^1H NMR ($CDCl_3$) 0.91 (s, 3, C-10a CH_3), 1.48 (s, 3, C-3 CH_3), 3.72 (s, 3, methyl ester), 3.92 (s, 4, ketal). Recrystallization from ether–hexane gave an analytically pure sample, mp 97.5–99 °C.

Anal. Calcd for $C_{19}H_{28}O_5$: C, 67.83; H, 8.39. Found: C, 67.90; H, 8.41.

8,8(7*H*)-(Ethylenedioxy)-3β,10aβ-dimethyl-2,3,5,6,6aα,9,10,10a-octahydro-1*H*-naphtho[2,1-*b*]pyran-3α-carbaldehyde (6b). To a solution of 1.97 g (5.86 mmol) of the ester **6a** in 400 mL of dry ether at −78 °C was added dropwise 22.0 mL (17.8 mmol) of 0.81 M diisobutylaluminum hydride in benzene. After 20 min at −78 °C, the reaction was quenched with 4.2 mL of absolute methanol, and then the solution was allowed to warm to room temperature. After the addition of 400 mL of saturated sodium bicarbonate solution, the organic layer was separated, and the aqueous layer was extracted three times with 300-mL portions of ether. The combined organic layers were washed with 500 mL of saturated sodium bicarbonate solution and 500 mL of brine and then dried (K_2CO_3). After removal of the solvents at reduced pressure, there remained 1.79 g (100%) of the aldehyde **6b** as a white solid. One recrystallization of a sample of this material from hexane gave analytically pure material: mp 108–111 °C; IR ($CHCl_3$) 1735 (C=O), 1674 (C=C) cm^{-1}; ^1H NMR ($CDCl_3$) 0.90 (s, 3, C-10a CH_3), 1.25 (s, 3, C-3 CH_3), 3.83 (s, 4, ketal), 9.5 (s, 1, aldehyde).

Anal. Calcd for $C_{18}H_{26}O_4$: C, 70.56; H, 8.55. Found: C, 70.45; H. 8.70.

8,8(7*H*)-(Ethylenedioxy)-3β,10aβ-dimethyl-3α-vinyl-2,3,5,6,6aα,9,10,10a-octahydro-1*H*-naphtho[2,1-*b*]pyran (6c). To a solution of 1.00 g (23.8 mmol) of 57% sodium hydride in mineral oil (washed two times with pentane) in 250 mL of dry dimethyl sulfoxide was added 8.50 g (23.8 mmol) of methyltriphenylphosphonium bromide. After the resulting solution was stirred for 1 h at room temperature, 1.78 g (5.82 mmol) of the crude aldehyde **6b** was added. The solution was stirred for 26 h and then poured into a mixture of 250 mL of ether and 750 mL of water. The organic layer was separated, and the aqueous layer was extracted three times with 250-mL portions of ether. The combined organic layers were washed with 250 mL of water and 250 mL of brine and then dried (K_2CO_3). After removal of the solvents at reduced pressure, the resulting solid was dissolved in 50 mL of ether and the solution was filtered through 5 g of silica gel to remove most of the triphenylphosphine oxide. Chromatography of the eluent on silica gel with 3:1 petroleum ether–ether afforded 1.48 g (84%) of the α-vinyl derivative **6c** as a white solid (R_f 0.27), mp 95–100 °C. One recrystallization of a sample of this material from methanol gave analytically pure material: mp 97.5–99.5 °C; IR ($CHCl_3$) 1680 (C=C) cm^{-1}; ^1H NMR ($CDCl_3$) 0.95 (s, 3, C-10a CH_3), 1.30 (s, 3, C-3 CH_3), 3.93 (s, 4, ketal), 5.4 (complex multiplet, 3, vinyl H).

Anal. Calcd for $C_{19}H_{28}O_3$: C, 74.96; H, 9.27. Found: C, 74.81; H, 9.21.

8,8(7*H*)-(Ethylenedioxy)-3α,10aβ-dimethyl-3β-vinyl-2,3,5,6,6aα,9,10,10a-octahydro-1*H*-naphtho[2,1-*b*]pyran (5c). To a solution of 2.17 g (6.45 mmol) of ester **5a** in 400 mL of dry ether at −78 °C was added dropwise 24.0 mL (19.4 mmol) of 0.81 M diisobutylaluminum hydride in benzene. After 30 min at −78 °C, the reaction was quenched with 4.6 mL of absolute methanol, and then the solution was allowed to warm to room temperature. After a solution of 400 mL of saturated aqueous sodium bicarbonate was added, the layers were separated, the aqueous layer was extracted three times with 300-mL portions of ether, and the combined organic layers were washed with 500 mL of saturated

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(16) All melting points and boiling points are uncorrected. Infrared (IR) spectra were determined on a Perkin-Elmer 237B grating infrared spectrometer, and nuclear magnetic resonance (NMR) spectra were recorded with a Varian T-60, a Varian A-60, or a Varian EM390 spectrometer. Chemical shifts are reported as δ values in parts per million relative to tetramethylsilane (δ_{Me_4Si} 0.0) as an internal standard. Gas–liquid phase chromatographic (VPC) analyses were determined on a Hewlett-Packard 5750 gas chromatograph using helium carrier gas at a flow rate of 60 mL/min. All analytical VPC was conducted on a 5 ft × 0.125 in. column packed with 4% SE-30 on 60–80 mesh Chromosorb WAS DMCS. Preparative layer chromatography (PTLC) was carried out on precoated PLC plates with a 20 × 20 × 2 mm layer of silica gel 60F-254 on glass plates manufactured by E. Merck. Alumina used for chromatography refers to the grade I, neutral variety manufactured by M. Woelm made up to grade II or III as indicated by addition of 3% or 6% water prior to use. Silica gel columns used the 0.05–0.2-mm silica gel manufactured "for column chromatography" by E. Merck. Preparative medium-pressure column chromatography was performed by using $^1/_2$ × 20 in. or 2 × 20 in. glass columns with fittings supplied by Chromatronix, Inc., and an instrument minipump supplied by Milton Roy Co. The columns were packed with silica gel H "for tlc acc. to Stahl" (10–40) manufactured by E. Merck. Ether and petroleum ether were degassed under water aspirator vacuum prior to use. "Dry" solvents were dried immediately prior to use. Ether and tetrahydrofuran were distilled from lithium aluminum hydride, *tert*-butyl alcohol, pyridine, and benzene were distilled from calcium hydride, dichloromethane and iodomethane were distilled from phosphorus pentoxide, and methanol was distilled from magnesium turnings. "Ether" refers to anhydrous diethyl ether which was supplied by Mallinckrodt. "Petroleum ether" refers to the "analyzed reagent" grade hydrocarbon fraction, bp 35–60 °C, which was supplied by J. T. Baker Co., and was not further purified. All water used in the reactions and workups was distilled water. Brine refers to a saturated aqueous solution of sodium chloride. All reaction flasks and syringes were dried for at least 12 h in an oven (at 140 °C) and cooled in a desiccator over anhydrous calcium sulfate prior to use. All reactions (except the photooxygenations and hydrogenations) were run under an atmosphere of argon, and at the beginning of all reactions, the solutions were degassed. Mass spectral analyses were performed by Ms. Beth Irwin, UCLA, Los Angeles, Calif. Microanalyses were performed by Spang Microanalytical Laboratory.

aqueous sodium bicarbonate and 500 mL of brine and then dried (K_2CO_3). Removal of the solvents at reduced pressure gave 2.0 g (100%) of the aldehyde **5b** as a clear, colorless viscous liquid: IR ($CHCl_3$) 1736 (C=O), 1676 (C=C) cm^{-1}; ^1H NMR ($CDCl_3$) 0.88 (s, 3, C-10a CH_3), 1.21 (s, 3, C-3 CH_3), 3.90 (s, 4, ketal), 9.60 (s, 1, CHO). This material was used directly in the following experiment without further purification.

To a solution of 1.08 g (25.7 mmol) of 57% sodium hydride in mineral oil (washed twice with pentane) and 9.20 g (25.7 mmol) of methyltriphenylphosphonium bromide in 175 mL of dry dimethyl sulfoxide was added 1.83 g (5.98 mmol) of the crude aldehyde **5b**. After 26 h at room temperature, the solution was added to 250 mL of ether and 750 mL of water. The organic layer was separated, and the aqueous layer was extracted three times with 250-mL portions of ether. The combined organic layers were washed with 250 mL of water and 250 mL of brine and then dried (K_2CO_3). After removal of the solvents at reduced pressure a solution of the resulting solid in 100 mL of 3:1 petroleum ether–ether was filtered through 10 g of silica gel. Evaporation of the solvents and then recrystallization of the residue afforded 0.87 g (48%) of β-vinyl derivative **5c** as a white solid, mp 62–66 °C. Chromatography of the mother liquors on silica gel with 5:1 petroleum ether–ether afforded an additional 0.34 g of similar material (total yield 1.21 g (67%)): IR ($CHCl_3$) 1670 (C=C) cm^{-1}; ^1H NMR ($CDCl_3$) 0.90 (s, 3, C-10a CH_3), 1.19 (s, 3, C-3 CH_3), 3.82 (s, 4, ketal), 5.5 (complex multiplet, 3, vinyl H).

One recrystallization of a sample of this material from the methanol gave the analytically pure olefin **4**, mp 67–68.5 °C.

Anal. Calcd for $C_{19}H_{28}O_3$: C, 74.96; H, 9.27. Found: C, 74.99; H, 9.19.

6′,6′(5′*H*)-(Ethylenedioxy)-4,8′aβ-dimethyl-3′,4′,4′aα,7′,8′,8′a-hexahydrospiro[cyclohex-3α-ene-1,1′-naphthalen]-2′(1′*H*)-one (8). A base-washed and oven-dried tube containing 1.44 g (4.73 mmol) of olefin **6c** was sealed under vacuum and heated for 1 h and 5 min at 170 °C. The tube was cooled and opened, and then a solution of the contents in 120 mL of ether was filtered through 10 g of silica gel to give (after crystallization from ether) 1.11 g (77%) of a white solid, mp 102–104 °C. Chromatography of the mother liquors on silica gel with 1.5:1 petroleum ether–ether afforded an additional 0.15 g of similar material (total yield 1.26 g (88%)): IR ($CHCl_3$) 1700 (C=O) cm^{-1}; ^1H NMR ($CDCl_3$) 0.79 (s, 3, C-8′a CH_3), 3.92 (s, 4, ketal), 5.25 (s, 1, $w_{1/2}$ = 8 Hz, vinyl H).

An analytical sample of this ketone **8** was prepared by crystallization from hexane and ether, mp 117–118.4 °C.

Anal. Calcd for $C_{19}H_{28}O_3$: C, 74.96; H, 9.27. Found: C, 74.97; H, 9.18.

6′,6′(5′*H*)-(Ethylenedioxy)-4,8′aβ-dimethyl-3′,4′,4′aα,7′,8′,8′a-hexahydrospiro[cyclohex-3β-ene-1,1′-naphthalen]-2′(1′*H*)-one (7). A base-washed and oven-dried tube containing 30 mg (0.098 mmol) of the olefin **5c** was sealed under vacuum and heated at 200–218 °C for 1 h. The tube was cooled and opened, and then the contents were chromatographed on silica gel with 3:1 benzene–ethyl acetate. In this manner there was obtained 22.6 mg (75%) of the ketone **7** as a solid: mp 95–97 °C; IR ($CHCl_3$) 1705 (C=O) cm^{-1}; ^1H NMR ($CDCl_3$) 0.71 (s, 3, C-8′a CH_3), 3.92 (s, 3, ketal), 5.40 (s, 1, $w_{1/2}$ = 8 Hz).

Anal. Calcd for $C_{19}H_{28}O_3$: C, 74.96; H, 9.27. Found: C, 75.01; H, 9.26.

A sample of 46 mg (0.151 mmol) of olefin **5c** heated at 176–180 °C for 2 h gave after chromatography on silica gel (8:1 benzene–ethyl acetate) 9.4 mg (20%) of ketone **7** and 32.4 mg (70%) of starting material **5c**.

5′,5′(4′*H*)-(Ethylenedioxy)-2′-(methoxycarbonyl)-4,7′aβ-dimethyl-2′,3′,3′aα,6′,7′,7′a-hexahydrospiro[cyclohex-3β-ene-1,1′-indene] (10). To a solution of 177 mg (0.581 mmol) of ketone **7** and 2.80 mL (1.23 mmol) of 0.44 M potassium *tert*-butoxide in *tert*-butyl alcohol in 4.0 mL of dry *tert*-butyl alcohol was added 0.80 mL (70 mg, 5.95 mmol) of isoamyl nitrite. After 19 h at 25 °C, the reaction was neutralized with 2% aqueous sulfuric acid, and 25 mL of water was added. The aqueous solution was extracted four times with 25-mL portions of ether, and then the combined ethereal extracts were washed with brine and then dried (Na_2SO_4). After removal of the solvents at reduced pressure, chromatography of the residue on silica gel with 1:1 petroleum ether–ether afforded 155 mg (80%) of the oximino ketone (R_f 0.08) as a white solid: mp 230–233 °C dec; IR ($CHCl_3$) 3550 and 3260 (OH), 1708 (C=O), 1609 (C=N) cm^{-1}; ^1H NMR ($CDCl_3$) 0.85 (s, 3, C-8′a CH_3), 3.92 (s, 4, ketal), 5.40 (s, 1, $w_{1/2}$ = 10 Hz, vinyl). This material was used directly in the following experiment.

To a solution of 149 mg (0.445 mmol) of the oximino ketone, 2.25 mL (9 mmol) of 4 N aqueous sodium hydroxide, and 0.75 mL (12 mmol) of 15 M ammonium hydroxide in 23 mL of tetrahydrofuran at 10 °C was added 1.90 mL (1.35 mmol) of 5.25% sodium hypochlorite (Clorox) over a 5-min period. The reaction mixture was stirred for 1 h at 10 °C and then for 5 h at room temperature before the addition of 200 mL of water and 200 mL of dichloromethane. The combined organic layers were washed once with 200 mL of brine and dried ($MgSO_4$), and then the solvents were removed at reduced pressure. Chromatography of the residue on silica gel with 1:1 petroleum ether–ether afforded 144 mg (97%) of diazo ketone **9** (R_f 0.18) as a yellow-orange solid: mp 104–108 °C; IR ($CHCl_3$) 2070 (N_2), 1702 (C=O), 1620 (C=N) cm^{-1}; ^1H NMR ($CDCl_3$) 0.91 (s, 3, C-8′a CH_3), 3.96 (s, 4 ketal), 5.40 (s, 1, $w_{1/2}$ = 10 Hz, vinyl). This material was again used directly in the following experiment without further purification.

A solution of 81 mg (0.245 mmol) of the above diazo ketone **9** and 177 mg of sodium bicarbonate in 30 mL of dry methanol and 30 mL of dry tetrahydrofuran was photolyzed under nitrogen for 1 h at room temperature (water bath) with a Hanovia medium-pressure mercury vapor lamp and a Pyrex filter. After 250 mL of water was added, the solution was extracted three times with 250-mL portions of dichloromethane. The combined aqueous layers were washed with 250 mL of brine and dried (K_2CO_3), and then the solvents were removed at reduced pressure. Chromatography of the residue on silica gel with 3:1 petroleum ether–ether afforded a total of 66 mg (81%) of the esters (**10**).

Ester **10a** (36 mg, 44%) was a yellow oil (R_f 0.17): IR ($CHCl_3$) 1720 (C=O) cm^{-1}; ^1H NMR ($CDCl_3$) 0.82 (s, 3, C-7′a CH_3), 3.61 (s, 3, OCH_3), 3.84 (s, 4, ketal), 5.43 (s, 1, $w_{1/2}$ = 8 Hz, vinyl H); mass-measured molecular ion calcd for $C_{20}H_{30}O_4$, 334.214396; found, 334.2143 ± 0.0003.

Ester **10b** (30 mg, 37%) was a white solid (R_f 0.25): mp 104–108 °C; IR ($CHCl_3$) 1718 (C=O) cm^{-1}; ^1H NMR ($CDCl_3$) 0.91 (s, 3, C-7′a CH_3), 3.53 (s, 3, OCH_3), 3.93 (s, 4, ketal), 5.27 (s, 1, $w_{1/2}$ = 8 Hz, vinyl).

An analytical sample of ester **10b** was prepared by one recrystallization from hexane, mp 108–110 °C.

Anal. Calcd for $C_{20}H_{30}O_4$: C, 71.82; H, 9.04. Found: C, 71.91; H, 9.01.

4aβ,5-Dimethyl-3,4,4a,7,8,9aβ-hexahydro-9*H*-benzocyclohepten-2(1*H*)-ones. To 36 g (0.171 mol) of the corresponding ketone alcohol heated at 130–140 °C was added 450 mg of resublimed iodine in 75-mg batches every 10 min. After 1 h the reaction mixture was cooled, 500 mL of ether was added, and the solution was washed twice with 250-mL portions of 10% aqueous sodium thiosulfate, once with saturated aqueous sodium bicarbonate, and once with brine. The aqueous layers were extracted with an additional 300 mL of ether, and the combined ether layers were then dried over anhydrous magnesium sulfate. Removal of the solvents at reduced pressure gave 33% (100%) of a 57:43 mixture (VPC at 190 °C, **11** eluted first) of the ketone olefins **8** and **15**. This mixture was not normally further purified but used directly in the following ketalization reaction.

Chromatography of 964 mg of this mixture on silica gel with 7:3 petroleum ether–ether gave 203 g (21%) of endocyclic olefin ketone (R_f 0.33) and 308 mg (32%) of its exocyclic isomer (R_f 0.29). An analytically pure sample of the endocyclic olefin ketone was then prepared by bulb-to-bulb distillation at 75–80 °C (0.05 mm) which gave the olefin ketone as a clear colorless liquid: IR ($CHCl_3$) 1700 (C=O) cm^{-1}; NMR ($CDCl_3$) 1.19 (s, 3, C-4a CH_3), 5.8 (m, 1, vinyl).

Anal. Calcd for $C_{13}H_{20}O$: C, 81.20; H, 10.48. Found: C, 81.26; H, 10.49.

2,2(1*H*)-(Ethylenedioxy)-4aβ,5-dimethyl-3,4,4a,7,8,9aβ-hexahydro-9*H*-benzocycloheptene. A solution of 149 mg (0.776 mmol) of pure endocyclic olefin ketone, 3.1 mg of *p*-toluenesulfonic acid monohydrate, and 0.28 mL (310 mg, 5.0 mmol) of ethylene glycol in 10 mL of dry benzene was heated at reflux for 3 h under a Dean–Stark water trap. After 50 mL of ether was added, the solution was washed twice with 50-mL portions of saturated aqueous sodium bicarbonate and then twice with 50-mL portions

of brine. The aqueous layers were extracted with an additional 100 mL of ether, and the combined organic layers were dried over anhydrous potassium carbonate. Removal of the solvents at reduced pressure gave 183 mg (100%) of the derived ketal, which was normally used without further purification.

Analytically pure material as a clear, colorless liquid could be prepared by chromatography of a portion of this material on silica gel with 9:1 petroleum ether–ether (R_f 0.25) and then bulb-to-bulb distillation of the resultant sample at 85–90 °C (0.05 mm): IR ($CHCl_3$) 1440, 1360, 1255, 1085, 1070 cm^{-1}; ^1H NMR ($CDCl_3$) 1.09 (s, 3, C-4a CH_3), 3.90 (s, 4, ketal), 5.47 (m, 1, vinyl).

Anal. Calcd for $C_{15}H_{24}O_2$: C, 76.23; H, 10.24. Found: C, 76.21; H, 10.29.

2,2(1*H*)-(Ethylenedioxy)-4aβ-methyl-5-methylene-3,4,4a,5,6,7,8,9aβ-octahydro-9*H*-benzocycloheptene. A solution of 256 mg (1.33 mmol) of exocyclic olefin ketone, 0.5 mL (8.90 mmol) of ethylene glycol, and 5 mg (0.03 mmol) of *p*-toluenesulfonic acid monohydrate in 25 mL of dry benzene was heated to reflux under an argon atmosphere. A Dean–Stark trap packed with activated 4-Å sieves and filled with 10 mL of dry benzene was used to assist in the azeotropic removal of water. The reaction mixture was maintained at reflux temperature with stirring for 5 h, allowed to cool to room temperature, and then diluted with 50 mL of ethyl ether. The solution was washed with saturated aqueous sodium bicarbonate solution (2 × 30 mL) and saturated aqueous brine solution (1 × 25 mL). All aqueous washings were pooled and then extracted with ethyl ether (1 × 40 mL). The organic layers were combined, dried over anhydrous potassium carbonate, and concentrated under reduced pressure. Evaporative distillation of the liquid residue afforded 235 mg (75%) of the exocyclic olefin ketal as a colorless oil: bp 100–115 °C (0.05 mm); IR ($CHCl_3$) 1622, 1092, 903 cm^{-1}; ^1H NMR ($CDCl_3$) 1.09 (s, 3 H, C-4a CH_3), 3.89 (s, 4 H, OCH_2CH_2O), 4.76 (br s, 2 H, $H_2C{=}C$).

Anal. Calcd for $C_{15}H_{24}O_2$: C, 76.23; H, 10.24. Found: C, 76.13; H, 10.26.

2,2(1*H*)-(Ethylenedioxy)-4aβ-methyl-5-methylene-3,4,4a,7,8,9aβ-hexahydro-9*H*-benzocyclohepten-6(5*H*)-one (11). A solution of 183 mg (0.775 mmol) of endocyclic olefin ketal (90% pure by VPC at 180 °C), 3.1 mg of hematoporphyrin dihydrochloride, 7.5 mL of pyridine, and 8.5 mL of ethyl acetate was irradiated for 2 h with a 450-W Hanovia medium-pressure mercury vapor lamp in a Pyrex jacket cooled to 10 °C while oxygen was bubbled through the solution. The solution was added to 5.5 mL of acetic anhydride, and the mixture was stirred for 2 h at room temperature before being carefully added to 50 mL of cold 15% aqueous sodium carbonate solution. This aqueous mixture was extracted three times with 50-mL portions of ether, and the combined ethereal layers were washed three times with 50-mL portions of saturated aqueous sodium bicarbonate and then dried over anhydrous potassium carbonate. Removal of the solvents at reduced pressure and then chromatography of the residue on Florisil with 1:1 petroleum ether–ether gave 161 mg (83%) of the α-methylene ketone 11 (R_f 0.21) as a clear colorless liquid.

Analytically pure material was obtained by distillation at 110–120 °C (0.05 mm); IR ($CHCl_3$) 1675 (C=O), 1595 (C=C) cm^{-1}; ^1H NMR ($CDCl_3$) 1.22 (s, 3, C-4a CH_3), 3.82 (s, 4, ketal), 5.23 (s, 1, vinyl), 5.65 (s, 1, vinyl).

Anal. Calcd for $C_{15}H_{22}O_3$: C, 71.97; H, 8.86. Found: C, 71.96; H, 8.80.

Preparation of the Exocyclic–Endocyclic Olefin Ketal Mixture from the Exocyclic–Endocyclic Olefin Ketone Mixture. A solution of 33 g (0.17 mol) of a crude mixture of exocyclic–endocyclic olefin ketones (43% endocyclic olefin and 57% exocyclic olefin by VPC at 190 °C), 0.6 g (3 mmol) of *p*-toluenesulfonic acid monohydrate, 60 mL of ethylene glycol, and 600 mL of benzene was heated at reflux under a Dean–Stark water trap. After 3.5 h, 3.0 mL of water had collected, and the reaction was cooled and washed twice with 300-mL portions of saturated aqueous sodium bicarbonate and twice with 250-mL portions of brine. The aqueous layers were extracted with an additional 400 mL of ether, and the combined organic layers were then dried over anhydrous potassium carbonate. After removal of the solvents at reduced pressure and then distillation of the residue at 100–110 °C (0.05 mm) in a base-washed short-path distillation apparatus, there was obtained 34 g (85%) of a mixture of the exocyclic–endocyclic olefin ketals (43% endocyclic olefin **17** and 57% exocyclic olefin **16** by VPC at 80 °C).

Preparation of Methylene Ketone 11 from the Exocyclic–Endocyclic Olefin Mixture. A solution of 1.06 g (4.49 mmol) of a mixture of endocyclic olefin ketal (43%) and exocyclic olefin ketal (57%), 20 mg of hematoporphyrin dihydrochloride, 9.0 mL of pyridine, and 10 mL of ethyl acetate was irradiated with a Hanovia 450-W medium-pressure mercury vapor lamp in a Pyrex jacket cooled to 10 °C while oxygen was bubbled continuously through the solution. After 1 h 45 mL of oxygen had been absorbed (45% of theoretical), and then the solution was added to 7.0 mL of acetic anhydride. After this mixture was stirred for 2 h at room temperature, the solution was added carefully to 50 mL of cold 15% aqueous sodium carbonate, and the resultant solution was then extracted three times with 50-mL portions of ether. The combined ether extracts were washed three times with 50-mL portions of saturated aqueous sodium bicarbonate and then dried over anhydrous potassium carbonate. Removal of the solvents at reduced pressure with the aid of a cyclohexane azeotrope to remove pyridine and then chromatography of the residue on Florisil with 1:1 petroleum ether–ether, there was obtained 550 mg (91% recovery) of exocyclic olefin ketal (eluted with the second column volume of solvent and 95% pure by VPC at 180 °C) and 392 mg (81% based on endocyclic ketal olefin present) of methylene ketone **11** (eluted beginning with the fourth column volume of solvent and 96% pure by TLC).

Equilibration of Exocyclic Olefin Ketal with Iodine. To 21.5 g (91.1 mmol) of exocyclic olefin ketal heated at 135–140 °C was added 240 mg of resublimed iodine in batches of 40 mg every 10 min. After 1 h the reaction was cooled, and 400 mL of ether was added. The solution was washed twice with 200-mL portions of 10% sodium thiosulfate, once with 250 mL of saturated aqueous sodium bicarbonate, and once with 250 mL of brine. The aqueous extracts were extracted with an additional 300 mL of ether, and the combined ether extracts were then dried over anhydrous potassium carbonate. Removal of the solvents at reduced pressure gave 20.8 g (97%) of a black liquid which, by VPC (at 190 °C), consisted of 45% endocyclic olefin ketal and 55% exocyclic olefin ketal. This mixture was used without further purification in subsequent photooxygenation experiments.

9,9(8*H*)-(Ethylenedioxy)-3β-(methoxycarbonyl)-3α,11aβ-dimethyl-1,2,3,5,6,7,7aβ,10,11,11a-decahydrobenzo[3,4]cyclohepta[1,2-*b*]pyran (12a) and 9,9(8*H*)-(Ethylenedioxy)-3α-(methoxycarbonyl)-3β,11aβ-dimethyl-1,2,3,5,6,7,7aβ,10,11,11a-decahydrobenzo[3,4]cyclohepta[1,2-*b*]pyran (13a). A solution of 3.02 g (12.1 mmol) of the methylene ketone 11 in 11 mL (10 g, 100 mmol) of methyl methacrylate in a base-washed tube was degassed and sealed under vacuum. After being heated for 25 h at 170 °C, the tube was cooled and its contents (a viscous yellow oil) dissolved in 50 mL of chloroform. The addition of 500 mL of ether caused the precipitation of a white polymer which was digested for 10 min on a steam bath and then removed by filtration. The solvents were removed at reduced pressure, and the residue was filtered through 200 g of silica gel with 1 L of ether. Rechromatography of the eluent on silica gel with 2:1 petroleum ether–ether afforded 3.40 g (80%) of a 1:1 mixture (by VPC at 250 °C) of esters **12a** and **13a**.

These esters could be efficiently separated by medium-pressure liquid chromatography with 2:1 petroleum ether–ether but there were always mixed fractions. For example, 1.21 g of a 3:2 mixture of esters **12a** and **13a** gave 436 mg (36%) of ester **12a** (R_f 0.25) as a clear colorless liquid, 70 mg (6%) of mixed fractions, and 630 mg (52%) of ester **13a** (R_f 0.20) as a white solid, mp 65–67 °C.

An analytically pure sample of the ester **12a** was prepared by bulb-to-bulb distillation at 135–140 °C (0.01 mm): IR ($CHCl_3$) 1730 (C=O), 1642 (C=C) cm^{-1}; ^1H NMR ($CDCl_3$) 1.02 (s, 3, C-11a CH_3), 1.41 (s, 3, C-3 CH_3), 3.70 (s, 3, OCH_3), 3.92 (s, 4, ketal).

Anal. Calcd for $C_{20}H_{30}O_5$: C, 68.55; H, 8.63. Found: C, 68.56; H, 8.79.

An analytically pure sample of the ester **13a** was obtained after one recrystallization of a portion from hexane–ether as a white solid: mp 67–69 °C; IR ($CHCl_3$) 1725 (C=O), 1649 (C=C) cm^{-1}; ^1H NMR ($CDCl_3$) 1.09 (s, 3, C-11a CH_3), 1.48 (s, 3, C-3 CH_3), 3.78 (s, 3, OCH_3), 3.92 (s, 4, ketal).

Anal. Calcd for $C_{20}H_{30}O_5$: C, 68.55; H, 8.63. Found: C, 68.56; H, 8.67.

A sample of 623 mg (2.49 mmol) of methylene ketone **11** and 3.0 mL (27 mmol) of methyl methacrylate heated for 25 h at 154–160 °C gave 750 mg (86%) of a 2:1 mixture (by VPC at 250 °C) of the esters **12a** and **13a**.

A sample of 167 mg (0.67 mmol) of methylene ketone **11** and 1.4 mL (13 mmol) of methyl methacrylate heated 13.5 h at 220–225 °C gave 200 mg (85%) of a 1:2 mixture (by VPC at 260 °C) of the esters **12a** and **13a**.

9,9(8*H*)-(Ethylenedioxy)-3α,11aβ-dimethyl-1,2,3,5,6,7,7aβ,10,11,11a-decahydrobenzo[3,4]cyclohepta[1,2-*b*]pyran-3β-carbaldehyde (12b). To a solution of 7.4 g (21 mmol) of ester **17a** in 500 mL of dry ether at −78 °C was added dropwise 65 mL (63 mmol) of 0.98 M diisobutylaluminum hydride in hexane. The solution was stirred for 35 min at −78 °C, quenched with 26 mL of methanol, and allowed to warm to room temperature. After 1 h, 1 L of saturated aqueous sodium bicarbonate was added, and the solution was extracted three times with 1-L portions of ether. The combined ethereal extracts were washed with 1 L of saturated aqueous sodium bicarbonate and brine and then dried (K_2CO_3). Removal of the solvents at reduced pressure gave 6.7 g of the aldehyde **12b** as a pale yellow oil which was generally used in the following experiment without further purification.

Distillation of a sample of this aldehyde at 138–140 °C (0.005 mm) gave an analytically pure material as a pale yellow liquid: IR ($CHCl_3$) 1735 (C=O), 1638 (C=C) cm^{-1}; ^1H NMR ($CDCl_3$) 1.07 (s, 3, C-11a CH_3), 1.21 (s, 3, C-3 CH_3), 3.97 (s, 4, ketal), 9.53 (s, 1, CHO).

Anal. Calcd for $C_{19}H_{28}O_4$: C, 71.22; H, 8.81. Found: C, 71.29; H, 8.94.

9,9(8*H*)-(Ethylenedioxy)-3β,11aβ-dimethyl-1,2,3,5,6,7,7aβ,10,11,11a-decahydrobenzo[3,4]cyclohepta[1,3-*b*]pyran-3α-carbaldehyde (13b). In a completely analogous manner to the formation of the aldehyde **12b**, 5.7 g (16 mmol) of ester **13a** in 500 mL of ether was treated with 50 mL (50 mmol) of 0.98 M diisobutylaluminum hydride in hexane. The reaction quenched with 20 mL of methanol, and then workup of the mixture as before gave 5.1 g of the aldehyde **13b** as a white solid (mp 120–125 °C) which was generally used without further purification.

One recrystallization of a portion of this aldehyde from hexane–ether gave an analytically pure sample: mp 133–135 °C; IR ($CHCl_3$) 1735 (C=O), 1640 (C=C) cm^{-1}; ^1H NMR ($CDCl_3$) 1.10 (s, 3, C-11a CH_3), 1.24 (s, 3, C-3 CH_3), 3.81 (s, 4, ketal), 9.53 (s, 1, CHO).

9,9(8*H*)-(Ethylenedioxy)-3α,11aβ-dimethyl-3β-vinyl-1,2,3,5,6,7,7aβ,10,11,11a-decahydrobenzo[3,4]cyclohepta[1,2-*b*]pyran (12c). To a solution of 3.5 g (84 mmol) of 57% sodium hydride in mineral oil (washed twice with pentane), 30 g (84 mmol) of methyltriphenylphosphonium bromide, and 300 mL of dry dimethyl sulfoxide was added to a solution of 6.65 g (21 mmol) of the β-aldehyde **12b** in 300 mL of dry dimethyl sulfoxide. The solution was stirred for 24 h at room temperature, added to 2 L of ice–water, and then extracted three times with 600-mL portions of ether. The combined ethereal extracts were washed with 500 mL of water and 500 mL of brine and then dried (K_2CO_3). The solvents were removed at reduced pressure, and a solution of the residue in 500 mL of 2:1 petroleum ether–ether was filtered through 100 g of silica gel to remove the triphenylphosphine oxide. Crystallization of the residue after evaporation of the solvents from ether and petroleum ether afforded 4.3 g (65%) of the olefin **12c** as a white solid, mp 46–48 °C. An additional 1.3 g (total yield 5.6 g (85%)) of the olefin, mp 46–58 °C, was obtained by chromatography of the mother liquors on silica gel with 5:1 petroleum ether–ether.

One recrystallization of a portion of this olefin **12c** from hexane and ether furnished an analytically pure sample: mp 47–48.5 °C; IR ($CHCl_3$) 1640 (C=C) cm^{-1}; ^1H NMR ($CDCl_3$) 1.06 (s, 3, C-11a CH_3), 1.21 (s, 3, C-3 CH_3), 3.90 (s, 4, ketal), 5.42 (m, 3, vinyl).

Anal. Calcd for $C_{20}H_{36}O_3$: C, 75.43; H, 9.50. Found: C, 75.43; H, 9.43.

9,9(8*H*)-(Ethylenedioxy)-3β,11aβ-dimethyl-3α-vinyl-1,2,3,5,6,7,7aβ,10,11,11a-decahydrobenzo[3,4]cyclohepta[1,2-*b*]pyran (13c). In a completely analogous manner, a total yield of 4.6 g (91%) of the olefin **13c**, mp 76–79 °C, was obtained from 5.1 g (16 mmol) of α-aldehyde **13b** with 2.7 g (64 mmol) of 57% sodium hydride and 23 g (64 mmol) of methyltriphenylphosphonium bromide in 600 mL of dry dimethyl sulfoxide.

One recrystallization of a portion of the olefin **13c** from hexane–ether furnished an analytically pure sample: mp 80.5–82 °C; IR ($CHCl_3$) 1640 (C=C) cm^{-1}; ^1H NMR ($CDCl_3$) 1.09 (s, 3, C-11a CH_3), 1.23 (s, 3, C-3 CH_3), 3.86 (s, 4, ketal), 5.39 (m, 3, vinyl).

Anal. Calcd for $C_{20}H_{30}O_3$: C, 75.43; H, 9.50. Found: C, 75.48; H, 9.53.

2,2(1*H*)-(Ethylenedioxy)-4′,4aβ-dimethyl-3,4,4a,8,9,9aβ-hexahydrospiro[5*H*-benzocycloheptene-5,1′-cyclohex-3β-en]-6(7*H*)-one (14). A base-washed and oven-dried tube containing 5.1 g (16 mmol) of the olefin **12c** was sealed under vacuum and heated at 225–234 °C. After 1 h the tube was cooled and opened, and its contents crystallized from ether. In this fashion there was obtained 5.0 g (98%) of ketone **14** (R_f 0.24 with 2:1 petroleum ether–ether) as a white solid, mp 120–126 °C.

One recrystallization of a portion of this material from hexane–ether furnished an analytically pure sample of the ketone **14**: mp 131–133 °C; IR ($CHCl_3$) 1683 (C=O) cm^{-1}; ^1H NMR ($CDCl_3$) 1.10 (s, 3, C-4a CH_3), 3.87 (d, 4, J = 1 Hz, ketal), 5.4 (m, 1, vinyl); ^{13}C NMR ($CDCl_3$) 58.0 and 58.5 (ketal), 102.9 (C-2), 114.7 (C-3′), 128.9 (C-4′), 209.1 (C-6) ppm.

Anal. Calcd for $C_{20}H_{30}O_3$: C, 75.43; H, 9.50. Found: C, 75.41; H, 9.45.

A sample of the ketone **14** was submitted for X-ray analysis[14] to Professor Jon Bordner of North Carolina State University, Raleigh, NC.

2,2(1*H*)-(Ethylenedioxy)-4′,4aβ-dimethyl-3,4,4a,8,9,9aβ-hexahydrospiro[5*H*-benzocycloheptene-5,1′-cyclohex-3α-en]-6(7*H*)-one (15). A base-washed and oven-dried tube containing 75 mg (0.24 mmol) of olefin **13c** was sealed under vacuum and heated at 182–188 °C. After 1 h the tube was cooled and opened, and its contents were chromatographed on silica gel with 2:1 petroleum ether–ether. There resulted 7 mg (9%) of starting olefin **13c** (R_f 0.43) and 56 mg (75%) of ketone **15** (R_f 0.23), mp 78–80 °C.

Crystallization of a portion of this material from hexane–ether afforded an analytically pure sample of the ketone **15** as a white solid: mp 81.5–83.5 °C; IR ($CHCl_3$) 1705 (C=O) cm^{-1}; ^1H NMR ($CDCl_3$) 0.94 (s, 3, C-4a CH_3), 3.93 (s, 4, ketal), 5.4 (m, 1, vinyl); ^{13}C NMR ($CDCl_3$) 58.6 (ketal), 103.6 (C-2), 117.2 (C-3′), 133.7 (C-4′), 211.0 (C-6) ppm.

Anal. Calcd for $C_{20}H_{30}O_3$: C, 75.43; H, 9.50. Found: C, 75.34; H, 9.42.

Formation of Oximino Ketone from Ketone 14. To a solution of 4.42 g (13.9 mmol) of ketone **14** in 250 mL of dry tetrahydrofuran at 0–5 °C was added dropwise with stirring 5.8 mL (13.9 mmol) of a 2.40 M *n*-butyllithium in hexane solution. After the solution was stirred for 10 min at 0 °C, 1.80 mL (1.62 g, 13.8 mmol) of freshly distilled isoamyl nitrate was added, and the solution was stirred for an additional 10 min at 0 °C and then 3.5 h at room temperature. The solution was made acidic (litmus paper) by the addition of 2% sulfuric acid, diluted with 800 mL of water, and then extracted four times with 800-mL portions of ether. The ethereal extracts were washed with 400 mL of brine and then dried ($MgSO_4$).

After removal of the solvents at reduced pressure, crystallization of the residue from ether gave 2.0 g (42%) of the corresponding oximino ketone as a white solid. Chromatography of the mother liquors on silica gel with 1:1 petroleum ether–ether afforded 2.0 g (45%) of starting ketone **14** (R_f 0.36) and 0.4 g (8%) of the oximino ketone (R_f 0.14). Thus, the total yield of the oximino ketone, mp 225–230 °C dec, was 2.4 g (50%).

One crystallization of a portion of this material from chloroform–ether afforded an analytically pure sample of the oximino ketone as a white solid: mp 238–240 °C dec; IR ($CHCl_3$) 3555 and 3270 (OH), 1688 (C=O) cm^{-1}; ^1H NMR ($CDCl_3$) 1.05 (s, 3, C-4a CH_3), 3.86 (s, 4, ketal), 5.28 (m, 1, vinyl).

Anal. Calcd for $C_{20}H_{29}O_4N$: C, 69.14; H, 8.41; N, 4.03. Found: C, 69.19; H, 8.36; N, 4.04.

6′,6′(5′*H*)-(Ethylenedioxy)-2′α-(methoxycarbonyl)-4,8′aβ-dimethyl-1′,2′,3′,4′,4′aβ,7′,8′,8′a-octahydrospiro[cyclohex-3β-ene-1,1′-naphthalene] (19a) and 6′,6′(5′*H*)-(Ethylenedioxy)-2′β-(methoxycarbonyl)-4,8′aβ-dimethyl-1′,2′,3′,4′,4′aβ,7′,8′,8′a-octahydrospiro[cyclohex-3β-ene-1,1′-naphthalene] (19b). A. Preparation of Diazo Ketone 16. To a solution of 3.24 g (9.34 mmol) of the above oximino ketone, 47

mL (190 mmol) of 4 N aqueous sodium hydroxide, and 15.0 mL (225 mmol) of 15 M aqueous ammonium hydroxide in 400 mL of tetrahydrofuran at 10 °C was added 39 mL (27.5 mmol) of a 5.25% aqueous sodium hypochlorite (Clorox) solution over a 5-min period. The reaction was stirred for 1 h at 10 °C and then 4 h at room temperature before the addition of 1 L of water. This aqueous solution was extracted three times with 1-L portions of ether, and then the combined ethereal extracts were washed with 600 mL of brine and dried (K_2CO_3). Removal of the solvents at reduced pressure gave 3.3 g (100%) of the diazo ketone **16** as a yellow foam (R_f 0.26 with 1:1 petroleum ether–ether) which was used without further purification: IR ($CHCl_3$) 2070 (N_2), 1682 (C=O), 1612 (C=N) cm^{-1}.

B. Preparation of Esters 19a and 19b. A solution of 3.30 g (9.60 mmol) of the diazo ketone **16** and 175 mL (96 mmol) of a 0.55 M sodium methoxide in methanol solution in 420 mL of dry methanol at −70 to −80 °C under an argon atmosphere was irradiated for 1 h with a Hanovia 450-W medium-pressure mercury vapor lamp in a Pyrex jacket. After 1 h, the lamp was shut off, and the solution was stirred for an additional hour at −75 °C. The cooling bath was then removed, and the solution was allowed to warm to room temperature for 1 h. This mixture was treated with 2.25 L of water, and the resulting aqueous solution was extracted with three 2.4-L portions of dichloromethane. The combined organic extracts were washed with 1.2 L of brine and then dried ($MgSO_4$). The solvents were removed at reduced pressure, and then chromatography of the residue on silica gel with 2:1 petroleum ether–ether gave 380 mg (11%) of the ester **19b** (R_f 0.34) as a white solid, mp 105–108 °C, and 1.96 g (59%) of the ester **19a** (R_f 0.29) as a white solid, mp 76–79 °C.

One recrystallization of a portion of the ester **19a** from hexane–ether gave an analytically pure sample that melted at 88–90 °C: IR ($CHCl_3$) 1713 (C=O) cm^{-1}; ^1H NMR ($CDCl_3$) 1.02 (s, 3, C-8′a CH_3), 3.63 (s, 3, OCH_3), 3.87 (t, 4, J = 3 Hz, ketal), 5.25 (s, 1, $w_{1/2}$ = 10 Hz, vinyl).

Anal. Calcd for $C_{21}H_{32}O_4$: C, 72.38; H, 9.26. Found: C, 72.34; H, 9.18.

One recrystallization of a portion of the ester **19b** from hexane–ether gave an analytically pure sample: mp 110–112 °C; IR ($CHCl_3$) 1726 (C=O) cm^{-1}; ^1H NMR ($CDCl_3$) 0.95 (s, 3, C-8′a CH_3), 3.58 (s, 3, OCH_3), 3.86 (t, 4, J = 2 Hz, ketal), 5.37 (s, 1, $w_{1/2}$ = 10 Hz, vinyl).

Anal. Calcd for $C_{21}H_{32}O_4$: C, 72.38; H, 9.26. Found: C, 72.46; H, 9.32.

Photolysis of Diazo Ketone 16 in Methanol at Room Temperature (Preparation of Cyclobutanone 18). A solution of 60 mg (0.17 mmol) of the diazo ketone **16** and 130 mg (1.6 mmol) of anhydrous sodium bicarbonate in 8.0 mL of dry methanol and 8.0 mL of dry tetrahydrofuran at room temperature (or −55 °C) was irradiated with a Hanovia 450-W medium-pressure mercury vapor lamp in a Pyrex jacket under an argon atmosphere. After 1 h the solution was added to 50 mL of water, and the aqueous mixture was extracted three times with 50-mL portions of dichloromethane. The combined organic extracts were washed with 50 mL of brine and then dried (K_2CO_3). Removal of the solvents at reduced pressure gave 110 mg of material that consisted of 80% of a single component (cyclobutanone **18**) by VPC at 240 °C. TLC (1:1 petroleum ether–ether) showed no evidence for any ester formation.

Chromatography on silica gel with 55:45 petroleum ether–ether, followed by crystallization from ether–hexane gave an analytically pure sample of the cyclobutanone **18** (R_f 0.28) as a white solid: mp 104–108 °C; IR ($CHCl_3$) 1755 (C=O) cm^{-1}; ^1H NMR ($CDCl_3$) 0.95 (s, 3, CH_3), 1.04 (s, 3, CH_3), 3.92 (s, 4, ketal).

Anal. Calcd for $C_{20}H_{28}O_3$: C, 75.91; H, 8.92. Found: C, 75.94; H, 8.78.

Attempted Ester Equilibration with Lithium Diisopropylamide. To a cold (−78 °C) solution of lithium diisopropylamide prepared from 0.30 mL (0.72 mmol) of a 2.40 M hexane solution of *n*-butyllithium and 0.10 mL (0.71 mmol) of dry diisopropylamine in 5.0 mL of dry tetrahydrofuran was added 18 mg (0.052 mmol) of ester **19b** and 0.50 mL of dry hexamethylphosphoramide. The solution was allowed to warm to −30 °C over a 15-min period and then was stirred at −20 to −10 °C for an additional 15 min before 4 mL of water and 100 mL of pentane were added. The solution was then washed three times with 12-mL portions of water and once with 25 mL of brine and then dried (K_2CO_3). Removal of the solvents at reduced pressure gave 18 mg which consisted of 75% starting ester **19b** and 25% cyclobutanone **18** by VPC at 240 °C.

Under identical conditions, 2.7 mg (0.01 mmol) of ester **19a** gave material that consisted of 75% starting ester **19a** and 25% cyclobutanone **18** by VPC at 240 °C.

6′,6′(5′*H*)-(Ethylenedioxy)-2′α-(hydroxymethyl)-4,8′aβ-dimethyl-1′,2′,3′,4′,4′aβ,-7′,8′,8′a-octahydrospiro[cyclohex-3β-ene-1,1′-naphthalene] (20). A solution of 1.36 g (3.91 mmol) of ester **19a** (75% ester **19a** and 25% 4α-olefin isomer by ^{13}C NMR) and 0.98 g (26 mmol) of lithium aluminum hydride in 0.10 mL of dry pyridine and 140 mL of dry ether was heated at reflux for 3 h, cooled to 0 °C, and quenched with 1.0 mL of water, 1.0 mL of 15% aqueous sodium hydroxide, and then 3.0 mL of water. The solution was then filtered through anhydrous magnesium sulfate, and after removal of the solvents from the filtrate at reduced pressure there remained 1.21 g (97%) of alcohol **20** (contaminated with about 33% of the 4α-olefin isomer (R_f 0.35 with 100% ether)) as a white solid, mp 168–172 °C.

Recrystallization from ether gave an analytically pure sample of alcohol **20** (R_f 0.32 with 100% ether) as a white solid: mp 170–172 °C; IR ($CHCl_3$) 3601 (OH) cm^{-1}; ^1H NMR ($CDCl_3$) 0.96 (s, 3, C-8′a CH_3), 3.72 (s, 1. $w_{1/2}$ = 5 Hz, alcohol), 3.83 (s, 4, $w_{1/2}$ = 3 Hz, ketal), 5.3 (s, 1, $w_{1/2}$ = 10 Hz, vinyl).

Anal. Calcd for $C_{20}H_{32}O_3$: C, 74.96; H, 10.06. Found: C, 74.94; H, 10.04.

A sample of alcohol **20** was submitted for X-ray analysis[14] to Professor Jon Bordner of North Carolina State University, Raleigh, NC.

In a similar reduction with 38 mg (0.11 mmol) of ester **19a** (90% pure by ^{13}C NMR), 13 mg (0.34 mmol) of lithium aluminum hydride, 1 mL of dry pyridine, and 4 mL of dry ether, 35 mg of alcohol **20** (83–86% pure by ^1H NMR and TLC in 100% ether) was obtained.

3,3-(Ethylenedioxy)-16β-hydroxy-5-epi-18,19-bisnoraphidicolane (22) and 3,3-(Ethylenedioxy)-13α-hydroxy-5-epi-18,19-bisnorstemodane (21). A. Preparation of Brosylates. To a solution of 0.76 g (2.38 mmol) of a 67:33 mixture of the alcohols **20** in 107 mL of dry pyridine at 0 °C was added all at once 1.21 g (4.73 mmol) of *p*-bromobenzenesulfonyl chloride. The solution was stirred for 5 min at 0 °C, and then the flask was stoppered and stored at 5–6 °C for 51.5 h. The solution was then poured onto 250 mL of ice and 750 mL of water, and this aqueous mixture was extracted four times with 400-mL portions of ether. The combined ethereal extracts were washed with 400 mL of brine and then dried (K_2CO_3). Removal of the solvents at reduced pressure with the aid of a cyclohexane azeotrope to remove the pyridine gave 1.23 g (96%) of the mixture of the corresponding brosylates (R_f 0.33 with 1:1 petroleum ether–ether) as a white solid: mp 103–106 °C dec; IR ($CHCl_3$) 1580 (Ar), 1358, 1256, 1183 (S=O) cm^{-1}; ^1H NMR ($CDCl_3$) 0.92 (s, 3, C-8′a CH_3), 3.88 (t, 4, J = 3 Hz, ketal), 5.24 (s, 1, $w_{1/2}$ = 9 Hz, vinyl), 7.75 (d, 4, J = 1.5 Hz, aromatic). This mixture was used without further purification.

B. Solvolysis of Brosylate Mixture. A solution of 400 mg (0.74 mmol) of a 65:35 mixture of the above brosylates and 210 mg (1.5 mmol) of anhydrous potassium carbonate in 20 mL of water and 40 mL of dioxane was heated for 5 h at 48–52 °C, cooled, and then added to 400 mL of saturated aqueous sodium bicarbonate. This aqueous solution was extracted twice with 400-mL portions of ether, and the ethereal extracts were washed with 200 mL of brine and then dried (K_2CO_3). The solvents were removed at reduced pressure with the aid of a cyclohexane azeotrope to remove the dioxane, and then chromatography of the residue on silica gel with 95:5 ether–petroleum ether gave 142 mg (60%) of alcohol **22** (R_f 0.3) as a white foam (solid at 0 °C) and 47 mg (20%) of alcohol **21** (R_f 0.2) as a white solid, mp 131–134 °C.

One recrystallization from hexane–ether gave an analytically pure sample of the alcohol **21** as a white solid: mp 140–141 °C; IR ($CHCl_3$) 3600 and 3450 (OH) cm^{-1}; ^1H NMR ($CDCl_3$) 0.97 (s, 3, C-20 CH_3), 1.09 (s, 3, C-17 CH_3), 3.81 (s, 4, ketal).

Anal. Calcd for $C_{20}H_{32}O_3$: C, 74.96; H, 10.06. Found: C, 75.09; H, 10.14.

An analytically pure sample of the alcohol **22** was prepared by bulb-to-bulb distillation at 146–148 °C (0.002 mm) as a clear, colorless liquid: IR ($CHCl_3$) 3600 and 3480 (OH) cm^{-1}; ^1H NMR

($CDCl_3$) 0.97 (s, 3, C-20 CH_3), 1.08 (s, 3, C-17 CH_3), 3.80 (s, 4, ketal).

Anal. Calcd for $C_{20}H_{32}O_3$: C, 74.96; H, 10.06. Found: C, 74.90; H, 10.88.

In a separate experiment a solution of 2 mg (0.004 mmol) of the brosylate (85–90% pure on TLC in ether) of the alcohol derived from the ester **19a** in 2 mL of dioxane and 1 mL of water containing 1 mg of potassium carbonate was heated at 50 °C for 5 h. A similar workup to that described above gave 1 mg of the alcohol **22** that was 90% pure by TLC and VPC at 220 °C.

5-Epi-18,19-bisnoraphidicolan-3-one (23). A solution of 55.7 mg (0.174 mmol) of alcohol **22** and 0.08 mL (1.1 mmol) of thionyl chloride in 4.0 mL of dry pyridine was stirred at −15 to −10 °C for 30 min and then added to 25 mL of ice and 25 mL of water. This aqueous solution was extracted twice with 50-mL portions of ether, and then the ether extracts were washed with 50 mL of saturated aqueous sodium bicarbonate, 50 mL of water, and 50 mL of brine and then dried (K_2CO_3). Removal of the solvents at reduced pressure gave 53 mg of a 3:1 mixture (by VPC at 250 °C, endocyclic olefin eluted first) of the corresponding endocyclic olefin (the major isomer) and exocyclic olefin.

This mixture was hydrolyzed by stirring with 87 mg (0.7 mmol) of oxalic acid dihydrate and 0.4 mL of water in 5.5 mL of absolute methanol for 5 h at room temperature. The solution was quenched with 73 mg (0.7 mmol) of anhydrous sodium carbonate and added to 50 mL of water, and the whole was extracted four times with 50-mL portions of ether. The combined ethereal extracts were washed with 50 mL of brine and then dried ($MgSO_4$). Removal of the solvents at reduced pressure gave 45 mg of the corresponding ketone mixture.

Hydrogenation of this ketone mixture was accomplished by stirring a solution of the material in 15 mL of glacial acetic acid containing 20 mg of 10% palladium on charcoal at room temperature for 1 h under an atmosphere of hydrogen. After filtration of the solution through Celite, 100 mL of water was added and the aqueous mixture was extracted three times with 100-mL portions of ether. The combined ether extracts were washed three times with 100-mL portions of saturated aqueous sodium bicarbonate and once with 100 mL of brine and then dried ($MgSO_4$).

Removal of the solvents at reduced pressure and chromatography of the residue on silica gel with 7:1 hexane–ethyl acetate gave 5 mg (11%) of the starting ketone olefin mixture (R_f 0.17) and 28 mg (62%) of the ketone **23** (R_f 0.22) as a colorless liquid.

Bulb-to-bulb distillation at 108–110 °C (0.005 mm) gave an analytically pure sample of the ketone **23** as a colorless liquid: IR ($CHCl_3$) 1720 (C=O) cm^{-1}; ^1H NMR ($CDCl_3$) 0.75 (d, 3, J = 5.3 Hz, C-17 CH_3), 0.89 (s, 3, C-20 CH_3).

Anal. Calcd for $C_{18}H_{28}O$: C, 83.02; H, 10.84. Found: C, 83.20; H, 10.88.

18,19-Bisnoraphidicolan-4-en-3-one (24). A solution 1 M in acetic anhydride and 10^{-2} M in perchloric acid was prepared by adding 4.8 mL (51 mmol) of acetic anhydride and 0.06 mL (0.6 mmol) of 60% aqueous perchloric acid to 40 mL of ethyl acetate and diluting the whole to 50 mL with additional ethyl acetate. A total of 3.0 mL of this solution was added all at once to 28 mg (0.108 mmol) of the ketone **23**. The resulting solution was stirred for 5 min at room temperature and added to 50 mL of ethyl acetate, and the resulting mixture washed with 50 mL of saturated aqueous sodium bicarbonate and 50 mL of brine and then dried (Na_2SO_4). Removal of the solvents at reduced pressure afforded 32 mg of the enol acetate (R_f 0.45 with 7:1 hexane–ethyl acetate).

A solution of 32 mg (0.106 mmol) of the above crude enol acetate, 0.03 mL of distilled epichlorohydrin, and 3 mL of carbon tetrachloride at 0 °C was treated dropwise with 1.0 mL (0.12 mmol) of a 0.12 M carbon tetrachloride solution of bromine. The resulting solution was stirred for 10 min at 0 °C, and then the solvents were removed at reduced pressure. The residual bromo ketone mixture (36 mg, R_f 0.3 and 0.25 with hexane–ethyl acetate) was not further purified but used directly.

A solution of 36 mg (0.106 mmol) of the above crude bromo ketone mixture, 35 mg (0.31 mmol) of semicarbazide hydrochloride, and 35 mg (0.43 mmol) of anhydrous sodium acetate in 9.3 mL of glacial acetic acid was heated at 68–72 °C. After 2 h the solution was treated with 0.5 mL of pyruvic acid in 1.0 mL of water. This mixture was heated for 2 h at 70 °C, cooled, and added to 100 mL of ether. The ethereal solution was separated and washed six times with 100-mL portions of 5% aqueous sodium hydroxide and twice with 50-mL portions of brine and then dried ($MgSO_4$).

Removal of the solvents at reduced pressure and chromatography of the residue on silica gel with 3:1 hexane–ethyl acetate gave 21 mg (77%) of the unsaturated ketone **24** as a pale yellow liquid (R_f 0.27).

An analytically pure sample of the enone **24** was prepared by bulb-to-bulb distillation at 98–102 °C (0.002 mm) as a clear, colorless liquid: IR ($CHCl_3$) 1673 (C=O), 1618 (C=C) cm^{-1}; ^1H NMR ($CDCl_3$) 0.75 (d, 3, J = 5.5 Hz, C-17 CH_3), 1.22 (s, 3, C-20 CH_3), 5.6 (s, 1, $w_{1/2}$ = 4 Hz. vinyl).

Anal. Calcd for $C_{18}H_{26}O$: C, 83.67; H, 10.14. Found: C, 83.49; H, 9.97.

18,19-Bisnoraphidicolan-3-one (25). To a solution of 15 mg (2.4 mmol) of lithium wire and 2.0 mL of dry ether in 30 mL of dry ammonia was added 16 mg (0.062 mmol) of the unsaturated ketone **24** in 3.0 mL of ether over a 10-min period. The solution was stirred for an additional 20 min and then quenched with sodium benzoate (until the blue color disappeared) and 128 mg (2.4 mmol) of ammonium chloride. The ammonia was allowed to evaporate, and the resulting solution was added to 75 mL of ether. The ethereal extract was washed with 50 mL of water, twice with 40-mL portions of saturated aqueous sodium bicarbonate, and twice with 35-mL portions of brine. The aqueous layers were extracted with an additional 50 mL of ether, and the combined organic extracts were then dried ($MgSO_4$).

After removal of the solvents at reduced pressure, chromatography of the residue on silica gel with 7:1 hexane–ethyl acetate gave 4 mg (25%) of starting unsaturated ketone **24** (R_f 0.11) and 10 mg (62%) of the saturated ketone **25** (R_f 0.25) as a white solid, mp 104–108 °C.

One recrystallization of this material from hexane–ether gave an analytically pure sample of ketone **25** as a white solid: mp 116–118 °C; IR ($CHCl_3$) 1710 (C=O) cm^{-1}; ^1H NMR ($CDCl_3$) 0.75 (d, 3, J = 5.5 Hz, C-17 CH_3) 1.08 (s, 3, C-20 CH_3).

Anal. Calcd for $C_{18}H_{28}O$: C, 83.02; H, 10.84. Found: C, 82.96; H, 10.85.

Registry No. **4**, 35890-72-3; **5a**, 61570-25-0; **5b**, 71749-23-0; **5c**, 71749-24-1; **6a**, 61616-09-9; **6b**, 71829-75-9; **6c**, 71829-76-0; **7**, 71749-25-2; **7** oximino ketone, 71749-26-3; **8**, 71772-98-0; **9**, 71749-27-4; **10a**, 71749-28-5; **10b**, 71772-99-1; **11**, 71749-29-6; **12a**, 71749-30-9; **12b**, 71749-40-1; **12c**, 71749-41-2; **13a**, 71773-04-1; **13b**, 71773-05-2; **13c**, 71773-06-3; **14**, 71749-42-3; **14** oximino ketone, 71749-43-4; **15**, 71773-07-4; **16**, 71749-44-5; **18**, 71749-45-6; **19a**, 71749-46-7; **19a** 4α-olefin isomer, 71773-08-5; **19b**, 71773-09-6; **20**, 71749-47-8; **20** 4α-olefin isomer, 71773-10-9; **20** brosylate, 71749-48-9; **20** 4α-olefin isomer brosylate, 71773-11-0; **21**, 71749-49-0; **22**, 71773-12-1; **22** endocyclic olefin, 71749-50-3; **22** exocyclic olefin, 71749-51-4; **23**, 71749-52-5; **23** endocyclic olefin, 71749-53-6; **23** exocyclic olefin, 71749-54-7; **23** enol acetate, 71749-55-8; **23** bromo ketone isomer 1, 71749-56-9; **23** bromo ketone isomer 2, 71773-14-3; **24**, 71749-57-0; **25**, 71773-13-2; 4aβ,5-dimethyl-3,4,4a,7,8,9aβ-hexahydro-9*H*-benzocyclohepten-2(1*H*)-one, 71749-58-1; 4aβ-methyl-5-methylene-3,4,4a,5,6,7,8,9aβ-octahydro-9*H*-benzocyclohepten-2(1*H*)-one, 71735-04-1; 2,2(1*H*)-(ethylenedioxy)-4aβ,5-dimethyl-3,4,4a,7,8,9aβ-hexahydro-9*H*-benzocycloheptene, 71785-26-7; 2,2(1*H*)-(ethylenedioxy)-4aβ-methyl-5-methylene-3,4,4a,5,6,7,8,9aβ-octahydro-9*H*-benzocycloheptene, 71735-05-2; methyl methacrylate, 96-33-3.