74-4; *cis*-**3b**, 68889-59-8; *trans*-**3b**, 68813-37-6; **4a**, 106-26-3; **4b**, 141-27-5; **5a**, 68813-50-3; **5b**, 68813-51-4; *cis*-**6**, 68813-35-4; *trans*-**6**, 68813-36-5; *cis*-**7**, 68813-38-7; *trans*-**7**, 68813-39-8; *cis*-**9**, 68813-41-2; *trans*-**9**, 68813-42-3; *cis*-**10**, 68813-44-5; *trans*-**10**, 68813-45-6; **11**, 2438-12-2; **12**, 19651-06-0; **13a**, 3790-68-9; **13b**, 4380-32-9; *cis*-**14a**, 68852-76-6; *cis*-**14b**, 68813-40-1; *trans*-**14b**, 68852-75-5; *cis*-**15a**, 68852-78-8; *trans*-**15a**, 68852-79-9; *cis*-**15b**, 68813-43-4; *trans*-**15**, 68852-77-7; *cis*-**16a**, 68852-81-3; *trans*-**16a**, 68852-82-4; *cis*-**16b**, 68813-46-7; *trans*-**16b**, 68852-80-2; **17a**, 68813-52-5; **17b**, 68852-83-5; **18**, 106-25-2; **19**, 3879-26-3; (2*Z*,6*Z*)-**20**, 4176-78-7; (2*Z*,6*E*)-**20**, 4176-77-6; (2*E*,6*Z*)-**20**, 4176-79-8; (2*E*,6*E*)-**20**, 3675-00-1; (6*E*)-farnesol, 3790-71-4; (6*Z*)-farnesol 16106-95-9; neryl chloride, 20536-36-1; geranial, 106-24-1; (−)-α-bisabolol, 23089-26-1.

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Total Synthesis of an Estrajervatetraene[1]

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The benzdecalone **2a** was converted to the benzindanone **7a** by peroxide cleavage of the furfurylidene derivative **3** and subsequent base-catalyzed cyclization of the corresponding diester **5b**. Michael addition of the keto ester **7a** to methyl vinyl ketone followed by anhydrous lithium iodide–collidine cyclization of the adduct **8b** gave the desired etiojervane **9b** in good yield.

The veratrum alkaloids have long been recognized as potent vasoactive agents.[2] More recently we have described simpler (C_{19}) analogues which contain the same jervane skeleton found in the veratrum alkaloids and which possess similar stereochemistry.[3] These derivatives have shown significant antimineralocorticoid activity.[3,4] Because of this pharmacological activity, it became important to explore alternate synthetic routes in this series in ways which would allow preparation of compounds not readily obtained from natural sources. One such route involves the total synthesis of the etiojervane **9**.

Since the inception of this work, a great deal of effort has been expended in the partial and total syntheses of various etio- and pregnajervanes.[5] However none of these efforts readily provided etiojervanes possessing a cis C/D ring juncture, a feature important to the antimineralocorticoid activity of these compounds.[6]

The initial strategy to obtain a C/D *cis*-estrajervatriene was to find a route which would lead by relatively certain steps to the estrajervatetraene **9**. Simpler, more efficient or more elegant routes would be developed as the need arose. Accordingly an AB → C → D sequence was chosen in which a benzindanone of fixed stereochemistry (B/C trans) would be prepared at an early stage.

The desired benzindanone **4a** was unknown, but work by Juday[7] indicated that a direct reduction of a C ring unsaturated benzindanone would be unlikely to give the desired trans isomer. To circumvent this problem, the corresponding phenanthrone **1** was chosen as a starting material since the B/C *trans*-phenanthrones could be prepared from it by a known route.[8] Direct reduction of the unsaturated ketone **1** with lithium–ammonia gave a 2:3 mixture of *trans*-/*cis*-ketones; moreover, separation of the desired isomer from the mixture was difficult. Catalytic reduction of ketone **1** was remarkably slow, leading to mixtures containing extensive amounts of material containing hydroxyl group absorption but no ketone.

Potassium–ammonia reduction of the ethylenedioxy ketal of **1** afforded a 4:1 ratio of *trans*-/*cis*-ketones which were readily separated by fractional crystallization. Hydrolysis gave the known *trans*-ketone **2a**.[8]

Conversion of the benzdecalone **2a** to the benzindanone **4a** was accomplished by well-established methodology.[9] The furfurylidene ketone **3** was prepared in 87% yield by treatment of the ketone **2a** with furfural in methanolic base. Cleavage of the ketone with basic peroxide provided a crystalline diacid **5a** in 68% yield.

Cyclization of the diacid **5a** to the desired ketone (**4a**) was

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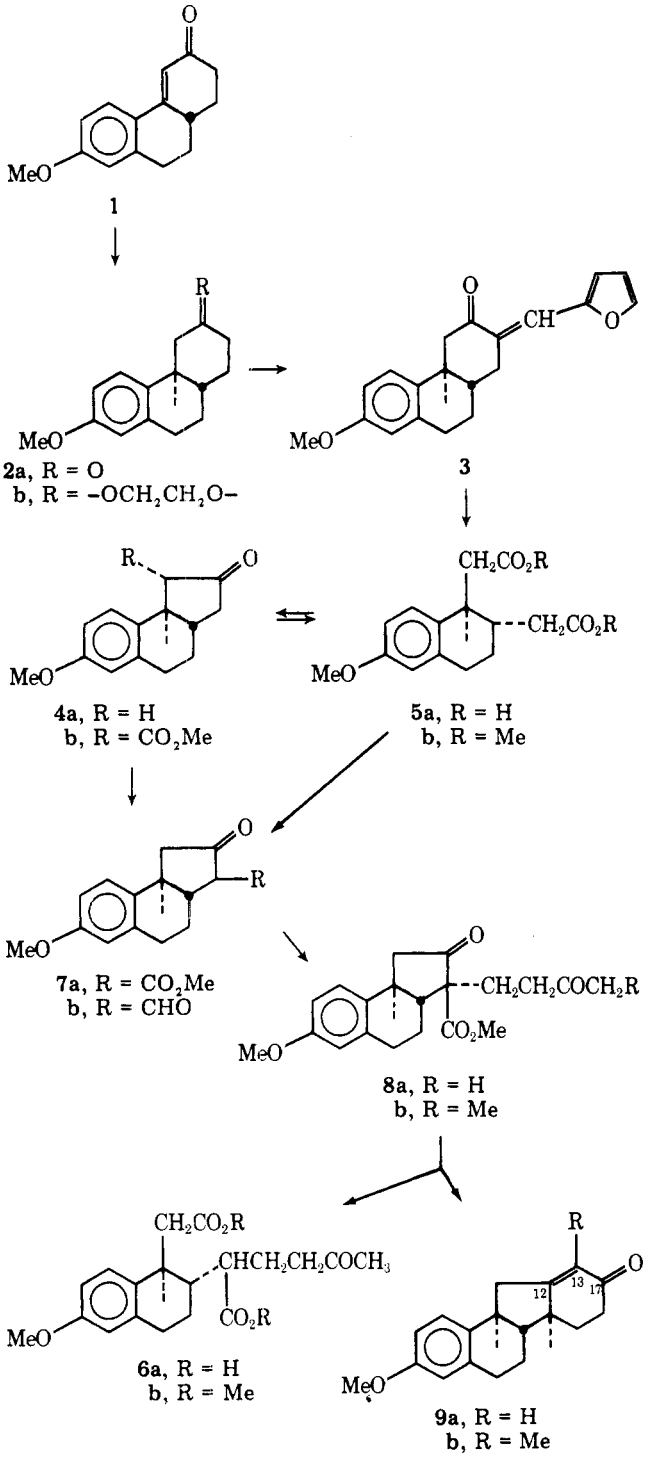

feasible in several ways. The simplest method involved pyrolysis of the corresponding anhydride (generated in situ), yielding the ketone **4a** in 65% yield.[10] Alternatively, the diacid could be distilled from lead carbonate following classical experiments.[11]

Attempts to alkylate ketone **4a** directly with methyl vinyl ketone and several different bases failed, leading to the formation of intractable materials or the return of starting material. Attempted formation of an enamine using titanium amines[12] gave, after isolation, only starting materials. When the enamine reaction mixture was treated directly with methyl vinyl ketone, intractable mixtures were again obtained.

Formylation of the ketone **4a** was possible by use of ethyl formate in benzene with sodium hydride as a catalyst. The product was very difficult to purify by crystallization. Use of the impure material for Michael addition under several conditions provided mixtures containing the desired intermediates, but in yields too low to compete with the methods described below.

The direct cyclization of the diester **5b** was also investigated. The diester was obtained in quantitative yield from the diacid by allowing the diacid to stand in methanolic acid for several days. Use of potassium *tert*-butoxide afforded a mixture of two cyclized keto esters, **4b** and **7a**, in a 2:1 ratio. The structure of **4b**, including its stereochemistry, was suggested by its NMR spectra; also, as evidenced by a negative ferric chloride test, it was not readily enolizable. The alternate ester **7a** had an NMR spectrum consistent with the assigned structure and gave a positive ferric chloride test. Further corroboration of the structure was afforded by acid-catalyzed hydrolysis–decarboxylation to give the ketone **4a** in good yield. Final proof of the gross structures of these compounds did not come, however, until completion of the synthetic sequence.[13]

The relatively low yield of the desired keto ester **7a** from the butoxide-catalyzed cyclization led to the use of sodium methoxide; this procedure afforded the desired tricycle in 82% yield by direct crystallization. The second isomer, **4b**, was present in less than 5% overall yield. The cause for this marked difference in isomer ratios can be explained by a number of hypotheses, but these were not subjected to experimental verification.

The undesired keto ester **4b** was readily converted back to the starting diester **5b** in alkaline methanol. The ease of this transformation was noted when a mixture of keto ester **4b** and **7a** was used in subsequent Michael additions; the ketone **4b** impurity simply reverted to the diester **5b**, whereas the desired isomer underwent the addition reaction. The failure of **4b** or **7a** to isomerize with vigorous potassium butoxide treatment showed that these compounds were not stereoisomers.

Michael addition of methyl vinyl ketone to the keto ester **7a** smoothly afforded a noncrystalline adduct which showed the desired acetyl group in the NMR. Cyclization and decarboxylation of the adduct was effected initially by an acetic-hydrochloric acid mixture, yielding the desired tetracyclic ketone **9a** in 35% yield. The structure of this compound was clear from its UV and NMR spectra.

Alternatively, lithium iodide–collidine[14] was used. This reaction provided 32% of the desired ketone **9a** by direct crystallization, but also provided large amounts (up to a third) of acidic byproducts. One of these materials crystallized readily and was given the tentative structure **6a**, a product which would result from a reverse Claisen cleavage of the C ring. Treatment of this diacid with diazomethane in ether gave a product with three methoxyl groups and an acetyl group, again supporting the assigned structure.

Although the tetracyclic ketone **9a** itself was of interest from a pharmacological point of view, a comparison with the materials obtained from natural sources[13] necessitated synthesis of the 13-methylated derivative **9b** as well. This compound was readily obtained by use of ethyl vinyl ketone, giving in this case the crystalline adduct **8b** in high yield.

Cyclization of the adduct **8b** was accomplished by a modified procedure using anhydrous lithium iodide in collidine. This change essentially eliminated the acidic byproducts seen with the earlier procedure and gave the desired unsaturated ketone **9b** in good yield. The structure of this material was again clear from the UV and NMR spectra.

Experimental Section

General Procedures. Melting points were determined on a Fisher-Johns melting point apparatus and are uncorrected. Unless otherwise specified, NMR spectra were determined in deuteriochloroform on a Varian A-60 spectrometer with Me_4Si as an internal standard; IR spectra were determined in $CHCl_3$ and UV spectra in MeOH. Chromatographies were run on silica gel.

The standard isolation procedure for each reaction consisted of diluting the reaction mixture with water and extracting the product with an immiscible solvent; the organic solution was washed with water, dilute aqueous $NaHCO_3$, and again with water, dried over anhydrous $MgSO_4$, and concentrated to dryness under reduced pressure.

***trans*-1,4,4a,9,10,10a-Hexahydro-7-methoxy-3(2*H*)-phenanthrenone (2a). (a) From the Ketal 2b.** The ketal (**2b**) and its B/C cis isomer were obtained by the potassium–ammonia reduction of the 4a(10a)-unsaturated ketal as described by Fahrenholtz et al.[8] The isomers were present in a 4:1 ratio as determined from the distinctive dioxolane absorption of the two materials (*trans*-ketal, δ 4.03; *cis*-ketal, δ 3.96). Separation was possible by recrystallization from Et_2O and then from MeOH. Hydrolysis to the pure ketone **2b** followed the literature method.[8]

(b) By Lithium–Ammonia Reduction of the Unsaturated Ketone 1. A 10-g amount of the unsaturated ketone **1** in 100 mL of Et_2O was added to 0.5 L of NH_3 containing 1 g of Li. After 5 min, 20 g of NH_4Cl was added portionwise. The NH_3 was distilled, and the reaction mixture was diluted with water. The crude product was isolated by benzene extraction in the standard way and was seen to consist of a mixture of B/C *trans*-/*cis*-ketones in approximately a 2:3 ratio (analysis by TLC). Fractional crystallization (from MeOH) or chromatography did not readily afford a separation of either pure ketone.

(c) By Catalytic Reduction of the Unsaturated Ketone 1. A 50-mg amount of 5% Pd/C catalyst and 0.36 g of the unsaturated ketone **1** in 100 mL of EtOH were stirred in an atmosphere of H_2. A second portion of catalyst was added after 20 h. The total uptake of H_2 was 0.7 mol equiv. The catalyst was filtered and the product analyzed by chromatography and spectroscopy. The predominant product was an amorphous material containing hydroxyl but lacking ketone absorption.

***trans*-2-(2-Furfuranylmethylidine)-1,4,4a,9,10,10a-hexahydro-7-methoxy-3(2*H*)-phenanthrenone (3).** A mixture of 66.0 g of the ketone **2a** in 9.3 L of MeOH at 5 °C under an atmosphere of N_2 was treated with 93 mL of 10% aqueous KOH followed by 178 g of redistilled furfural. After 18 h, the solution was diluted with water and the precipitate filtered. The first crop was 78.8 g (89%) of the furfurylidene ketone **3**, mp 161–165 °C. Further recrystallization from acetone–hexane gave the pure compound: mp 163–165 °C; IR 5.97 μm; UV 328 nm (ϵ 25 400); NMR δ 3.80 (OMe).

Anal. Calcd for $C_{20}H_{20}O_3$: C, 77.90; H, 6.54. Found: C, 77.55; H, 6.64.

The isomeric B/C cis derivative could readily be detected as an impurity in the mother liquor by its distinctive methoxy absorption at δ 3.77.

***trans*-1,2,3,4-Tetrahydro-6-methoxy-1,2-napthalenediacetic Acid (5a).** To a vigorously stirred mixture of 28.5 g of the furfurylidene ketone **3** in 2.8 L of MeOH in a Morton (creased) flask was slowly added a solution (premixed with cooling at 25–30 °C) of 158 g of NaOH in 833 mL of 30% aqueous H_2O_2. The temperature was held at 50–55 °C by means of a cooling bath and the slow addition of the reagent; after the addition was complete, the solution was heated to maintain the 55 °C temperature for 18 h. The MeOH was then distilled under reduced pressure. The solution was acidified with aqueous HCl and the product extracted with Et_2O, using water and excess aqueous $FeSO_4$ washes. The oil remaining after distillation of the ether was crystallized from benzene to give 19.5 g (76%) of diacid **5a**, mp 112–115 °C. Recrystallization from methylene chloride–hexane gave the pure material: mp 120–122 °C; IR 5.83, 6.20 μm.

Anal. Calcd for $C_{15}H_{18}O_5$: C, 64.73; H, 6.52. Found: C, 64.70; H, 6.50.

***trans*-1,3,3a,4,5,9b-Hexahydro-7-methoxy-2*H*-benz[*e*]inden-2-one (4a).** A solution of 31.2 g of the diacid **5a** in 60 mL of Ac_2O was distilled slowly over a 1-h period. The residue was then sublimed at 250–280 °C/0.1 mm. The crystalline sublimate was recrystallized (Darco) from acetone–hexane to yield 8.5 g of ketone **4a**, mp 118–122 °C, and 6.1 g, mp 126–127 °C. Recrystallization of the latter material gave the analytically pure material: mp 126–127 °C; IR 5.72 μm.

Anal. Calcd for $C_{14}H_{16}O_2$: C, 77.75; H, 7.46. Found: C, 77.59; H, 7.29.

An additional 1.3 g of pure ketone **4a** was obtained by chromatography of the mother liquors to bring the yield of product to 65%.

Sublimation of the diacid **5a** from $PbCO_3$ also gave a good yield of ketone **4a**. The diacid, in the absence of any reagent, sublimed with relatively little change at 250 °C/0.1 mm.

Alternatively, the ketone **4a** could be obtained by AcOH–concentrated HCl hydrolysis–decarboxylation of keto ester **7a**.

Direct Alkylation of the Ketone 4a. Initial attempts to alkylate the ketone **4a** involved the use of the bases Et_2NH, Triton B, and $LiNH_2$, in each case followed by addition of methyl vinyl ketone. None of these attempts yielded a tractable adduct. Subsequent experiments attempted formation of the enamine using pyrrolidine–acid or a variety of aminotitanium derivatives.[12] Failure to isolate a distinct enamine led to treatment of crude "enamine" mixtures directly with methyl vinyl ketone. No useful products were obtained.

Formylation of Ketone 4a. The ketone **4a** (3.8 g) in 300 mL of benzene and 4 mL of ethyl formate was treated with 4 g of NaH (52% dispersion in mineral oil). The mixture was stirred at room temperature for 20 h and then diluted by dropwise addition of 15 mL of MeOH in 30 mL of Et_2O. (An IR spectrum of the Et_2O extract showed it to contain largely unreacted starting material.) The aqueous washes were acidified with HCl and extracted with CH_2Cl_2 to yield 1.7 g of the amorphous formyl derivative **7b:** IR 5.70, 5.81, 5.92 μm; UV 308 nm (ϵ 17 700; in 0.1 N KOH–MeOH). Attempts to crystallize this material or purify it by chromatography were unsuccessful.

Alkylation of the crude formyl derivative **7b** with methyl vinyl ketone led to a mixture of amorphous products in a yield too low to compete with the alternate synthetic pathway developed concurrently (see below).

Dimethyl *trans*-1,2,3,4-Tetrahydro-6-methoxy-1,2-naphthalenediacetic Acid (5b). A solution of 29.6 g of the diacid **5a** in 0.5 L of MeOH containing 0.5 g of *p*-toluenesulfonic acid was allowed to stand at room temperature for 5 days. Excess pyridine was then added, and the solution was distilled to a small volume under reduced pressure. Water was added, and the product was isolated by CH_2Cl_2 extraction, yielding 31 g of a mobile oil: IR 5.78 μm; NMR δ 3.65 (OMe), 3.67 (OMe), and 3.75 (OMe).

Alternatively, the diester could be prepared from the diacid **5a** by treating **5a** with excess ethereal diazomethane for 0.5 h at room temperature.

Methyl 1,3,3aβ,4,5,9bα-Hexahydro-7-methoxy-2-oxo-1*H*-benz[*e*]indene-3β-carboxylate (7a). A solution of 30 g of the diester **5b** in 0.5 L of glyme (freshly redistilled from $LiAlH_4$) and 15 g of NaOMe was heated at reflux in an atmosphere of N_2 for 45 min. The heterogeneous mixture was cooled and poured on ice. The resulting crystal mass was collected on a filter and washed well with water to give 21.9 g (82%) of the keto ester **7a**, mp 102–103 °C. Recrystallization from CH_2Cl_2–hexane gave a pure sample: mp 105–106 °C; IR 5.68, 5.77 μm; NMR δ 3.78 (OMe). The compound gave a typical coloration with ethanolic $FeCl_3$.

Anal. Calcd for $C_{16}H_{18}O_4$: C, 70.05; H, 6.61. Found: C, 70.10; H, 6.75.

Chromatography of the material extracted from the acidified aqueous portions of the mother liquors gave the diacid **5a** plus a mixture of keto esters **4b** (see the following experiment) and **7a**. A TLC analysis of this mixture showed the amount of **4b** to consist of ~5% of the total cyclized material obtained.

Keto ester **7a** was stable to $KOCMe_3$ in refluxing benzene for 5 h.

Methyl 1,3,3aβ,4,5,9bα-Hexahydro-7-methoxy-2-oxo-1*H*-benz[*e*]indene-1α-carboxylate (4b). A solution of 9.3 g of the diester **5b** in 450 mL of benzene was treated with 12 g of $KOCMe_3$. The solution was stirred at reflux under an atmosphere of N_2 for 3 h and was then poured on iced aqueous HCl. The product was extracted with benzene in the standard way. The amorphous product was chromatographed and found to consist of a 2:1 mixture of cyclized keto esters **4b/7a**. Fractions containing the first isomer were eluted with 2% ethyl acetate–benzene and afforded crude material, recrystallized to give 2.7 g of the keto ester **4b**, mp 99–100 °C. Recrystallization of this material from CH_2Cl_2–hexane gave the pure isomer: mp 101–102 °C; IR 5.69, 5.76 μm; NMR δ 3.77 (OMe), 3.85 (CO_2Me). This compound gave no coloration when treated with ethanolic $FeCl_3$.

Anal. Calcd for $C_{16}H_{18}O_4$: C, 70.05; H, 6.61. Found: C, 70.36; H, 6.75.

Later fractions from the chromatograph were combined and recrystallized from CH_2Cl_2–hexane to yield 0.38 g of the pure keto ester **7a**, mp 105–106 °C, identical with the material obtained in the preceding experiment.

The keto ester **4b**, after boiling in refluxing benzene containing $KOCMe_3$ for 5 h, gave back principally unchanged starting material.

Methanolysis of the Keto Ester 4b. A slurry of 42 mg of the keto ester **4b** and 0.5 g of NaOMe in 5 mL of MeOH was stirred at 25 °C for 1 h. The resulting solution was poured into iced AcOH. The product was extracted with CH_2Cl_2 in the usual way and gave 28 mg of the diester **5b**, identical in the NMR and IR with previously obtained material.

A similar reaction occurred at room temperature in MeOH con-

taining Et_3N.

Methyl 1,3,3aβ,4,5,9bα-Hexahydro-7-methoxy-2-oxo-3α-(3-oxobutyl)-1*H*-benz[*e*]indene-3-carboxylate (8a). A mixture of 21.8 g of the keto ester **7a** in 1 L of MeOH containing 30 mL of methyl vinyl ketone and 5 mL of Et_3N was stirred at room temperature overnight. Water was added to the reaction mixture, and the product was extracted with CH_2Cl_2 in the usual way. The product was dried at 100 °C/10 mm to remove any residual 4-methoxy-2-butanone. The resulting dark oil (29.5 g) was used directly in the following experiment. Alternatively, chromatographic purification could be used to isolate the oily adduct (eluted with 3% EtOAc–benzene): IR 5.72 (broad absorption), 5.78, 5.82 μm; NMR δ 3.72 (OMe), 3.80 (OMe).

3-Methoxyestrajerva-1,3,5(10),12-tetraen-17-one (9a). Lithium iodide trihydrate (7 g) was added to a solution of 3.8 g of the adduct **8a** in 90 mL of redistilled collidine. The solution was boiled under nitrogen for 1 h. The solution was then cooled and poured onto excess iced aqueous HCl. The product was isolated by CH_2Cl_2 extraction, and the resulting material (1.8 g) was crystallized from ether (Darco) to yield 0.95 g (32%) of the tetracyclic ketone **9a**, mp 125–128 °C. Recrystallization did not improve the melting point. The pure material exhibited the following: IR 6.01 μm; UV 234 nm (ε 23 000); NMR 3.77 (OMe), 6.02 (C=CH).

Anal. Calcd for $C_{18}H_{20}O_2$: C, 80.56; H, 7.51. Found: C, 80.41; H, 7.55.

Additional product was obtainable from the mother liquors by chromatography.

The aqueous washes upon acidification were extracted with CH_2Cl_2, and the resulting product (0.95 g) was crystallized from ether to yield 60 mg of the diacid **6a**, mp 156–161 °C. Recrystallization from ether afforded the pure material: mp 162–163 °C; IR 5.82 μm; NMR δ 2.00 ($COCH_3$).

Anal. Calcd for $C_{19}H_{24}O_6$: C, 65.50; H, 6.94. Found: C, 65.63; H, 6.85.

The diacid **6a** was further characterized by treatment with ethereal diazomethane to yield the corresponding diester **6b**, which was crystallized and recrystallized from hexane to give the pure compound: mp 56–59 °C; IR 5.75–5.78 μm; NMR δ 2.12 ($COCH_3$), 3.72 (OMe, CO_2Me), 3.72 (CO_2Me).

Anal. Calcd for $C_{21}H_{28}O_6$: C, 67.00; H, 7.50. Found: C, 67.11; H, 7.27.

Acid-Catalyzed Cyclization. The Michael adduct **8a** (0.80 g) was boiled for 29 h in a solution of 30 mL of AcOH and 10 mL of concentrated HCl. The solution was cooled, diluted with water, and extracted with benzene in the usual way. The semicrystalline neutral product (0.54 g) was recrystallized from aqueous MeOH to give 165 mg of the pure unsaturated ketone **9a**, mp 125–128 °C. Another 70 mg of the desired product was obtained after chromatography of the mother liquors (total yield 35%).

Methyl 1,3,3aβ,4,5,9bα-Hexahydro-7-methoxy-2-oxo-3α-(3-oxopentyl)-1*H*-benz[*e*]indene-3-carboxylate (8b). Ethyl vinyl ketone (25 mL) was added dropwise to a solution of 20 g of the keto ester **7a** and 4.2 mL of Et_3N in 830 mL of MeOH with stirring. After 4 days, excess dilute HCl was added and the product was isolated by CH_2Cl_2 extraction. The crude product crystallized to yield 1.0 g of starting material. Three further crops of crystals (total, 1.5 g) from ether were the desired adduct **8b**. Recrystallization of the adduct gave the pure material, mp 91–95 °C.

Anal. Calcd for $C_{21}H_{26}O_5$: C, 70.37; H, 7.31. Found: C, 70.43; H, 7.38.

Chromatography of the mother liquors afforded an additional 2.5 g of the starting keto ester **7a** and 5.0 g of the desired adduct **8b**.

3-Methoxy-13-methylestrajerva-1,3,5(10),12-tetraen-17-one (9b). A solution of 3.6 g of the adduct **8b** in 50 mL of collidine was added dropwise to a boiling solution of 13.6 g of anhydrous LiI in 200 mL of anhydrous collidine over a 20-min period. After an additional hour at reflux, the solution was cooled and poured into excess aqueous iced hydrochloric acid. The product was filtered and washed with water. It was then dried, yielding 1.6 g (57%) of the unsaturated ketone **9b**. Recrystallization from ether afforded the pure material, mp 137–138 °C.

Anal. Calcd for $C_{19}H_{22}O_2$: C, 80.81; H, 7.85. Found: C, 80.56; H, 7.68.

Chromatography of the mother liquors afforded the tricyclic ketone **4a** as well as additional **9b**.

A similar reaction using lithium iodide trihydrate yielded lower amounts of the desired tetracycle **9b**.

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Registry No.—**1**, 65817-04-1; **2a**, 68875-94-5; *trans*-**2b**, 68875-95-6; *cis*-**2b**, 68876-08-4; **3**, 68875-96-7; **4a**, 68875-97-8; **4b**, 68875-98-9; **5a**, 68875-99-0; **5b**, 68876-00-6; **6a**, 68876-01-7; **6b**, 68876-02-8; **7a**, 68876-03-9; **7b**, 68890-13-1; **8a**, 68876-04-0; **8b**, 68876-05-1; **9a**, 68876-06-2; **9b**, 68876-07-3; furfural, 98-01-1; ethyl formate, 109-94-4; methyl vinyl ketone, 78-94-4.

References and Notes

(1) The nomenclature of these compounds is derived from the suggestions made by R. C. Ebersole and F. C. Chang, *J. Org. Chem.*, **38**, 2579 (1973). All compounds in this paper are racemic; the structures in the flowchart depict only the *d* form.
(2) See, e.g., A. H. Briggs and W. C. Holland, in J. R. DiPalma, Ed., "Drill's Pharmacology in Medicine", 4th ed., McGraw-Hill, New York, N.Y., 1971, Chapter 41, p 855.
(3) See W. F. Johns and L. M. Hofmann, *J. Med. Chem*, **16**, 568 (1973), and preceding papers.
(4) G. A. Porter and J. Kimsey, *J. Steroid Biochem.*, **3**, 201 (1972).
(5) For an excellent review of this work, see, inter alia, T. Masamune, in W. Johns, Ed., "International Review of Science, Vol. 8, Steroids", Butterworths, Boston, Mass., 1976, Chapter 9, p 250. See also A. Murai, T. Nishimura, and T. Masamune, *Bull. Chem. Soc. Jpn.*, **49**, 1602, 1612 (1976). Note the recent work of J. P. Kutney et al., *Can. J. Chem.*, **53**, 1775 (1975), which generates an unsaturated D ring which is potentially convertible to the C/D cis compounds.
(6) The inactivity of the C/D *trans*-etiojervanes in the antimineralocorticoid assays was noted by Dr. L. M. Hofmann of these laboratories, personal communication.
(7) R. E. Juday, B. Bukwa, K. Kaiser, and G. Webb, *J. Med. Chem.*, **13**, 314 (1970).
(8) K. E. Fahrenholtz, A. Capomaggi, M. Lurie, M. W. Goldberg, and R. W. Kierstead, *J. Med. Chem.*, **9**, 304 (1966).
(9) See, inter alia, W. S. Johnson, B. Bannister, and R. Pappo, *J. Am. Chem. Soc.*, **78**, 6331 (1956).
(10) See, e.g., H. P. Sigg and Ch. Tamm, *Helv. Chim. Acta*, **43**, 1402 (1960).
(11) W. S. Johnson, D. K. Banerjee, W. P. Schneider, C. D. Gutsche, W. E. Shelberg, and L. J. Chinn, *J. Am. Chem. Soc.*, **74**, 2832 (1952); G. Anner and K. Miescher, *Helv. Chim. Acta*, **31**, 2173 (1948).
(12) W. A. White and H. Weingarten, *J. Org. Chem.*, **32**, 213 (1967).
(13) See a forthcoming communication from these laboratories by W. F. Johns and K. W. Salamon.
(14) See, inter alia, W. L. Meyer and A. S. Levinson, *J. Org. Chem.*, **28**, 2184 (1963).