NMR spectra and TLC behavior of which were identical with those of the sample prepared above.

(±)-4β-[3-(Ethoxycarbonyl)-2-oxopropyl]-3α-((1R*)-1-hydroxyethyl)azetidin-2-one (16). To a stirred and ice-cooled solution of the above ketal (**15**) (11.5 mg, 0.04 mmol) in 2 mL of methylene chloride was added 60% perchloric acid (1 drop). The resulting mixture was stirred for 0.5 h at 0 °C and then for 1 h at room temperature. After neutralization with 10% aqueous ammonium hydroxide solution followed by washing with water and drying (Na_2SO_4), the solvent was evaporated off to give a colorless syrup which was subjected to chromatography on silica gel. Elution with benzene–methanol (49:1) afforded the β-keto ester (**16**) (8.3 mg, 85.2%) as a syrup: exact mass for M^+ peak, calcd *m/e* 243.1107, found 243.1120; IR ($CHCl_3$) 3425 (NH), 1755, 1710 cm^{-1} (C=O); NMR ($CDCl_3$) δ 1.29 (t, 3 H, *J* = 7 Hz, CH_2**Me**), 1.33 (d, 3 H, *J* = 6.5 Hz, CH**Me**), 2.85 (dd, 1 H, *J* = 2, 7 Hz, 3 H), 2.90 (dd, 1 H, *J* = 8.3, 18.5 Hz, 4-CH**H**), 3.10 (dd, 1 H, *J* = 5.7, 18.5 Hz, 4 CH**H**), 3.48 (s, 2 H, $COCH_2CO_2$), 3.84–4.32 (m, 4 H, CHOH, 4 H, CH_2Me), 6.14 (br s, 1 H, NH).

(±)-Ethyl 6α-((1R*)-1-Hydroxyethyl)-3,7-dioxo-1-azabicyclo[3.2.0]heptane-2-carboxylate (18). To an ice-cooled solution of the above β-keto ester (**16**) (24.3 mg, 0.1 mmol) and *p*-toluenesulfonyl azide (21.7 mg, 0.11 mmol) in 2 mL of dry acetonitrile was added a solution of triethylamine (40 mg, 0.4 mmol) in 2 mL of dry acetonitrile under nitrogen. After the resulting mixture was stirred at 0 °C for 30 min, evaporation of the solvent gave a residue which was subjected to chromatography on silica gel. Elution with benzene–acetone (9:1) afforded the diazo compound (**17**) (24 mg, 86%) as a syrup: IR ($CHCl_3$) 3420 (NH), 2140 (diazo), 1758, 1710 cm^{-1} (C=O); NMR ($CDCl_3$) δ 1.32 (d, 3 H, *J* = 6.5 Hz, CH**Me**), 1.34 (t, 3 H, *J* = 7 Hz, CH_2**Me**), 2.89 (ddd, 1 H, *J* = 0.8, 2, 7 Hz, 3 H), 3.16 (dd, 1 H, *J* = 7, 18.5 Hz, 4 CH**H**), 3.34 (dd, 1 H, *J* = 6, 18.5 Hz, 4 CH**H**), 3.97 (ddd, 1 H, *J* = 2, 6, 7 Hz, 4 H), 6.06 (br s, 1 H, NH).

A mixture of the above diazo compound (**17**) (24 mg, 0.086 mmol) and a catalytic amount of rhodium(II) acetate in 3 mL of dry benzene was heated for 1 h at 80 °C under nitrogen. After cooling to room temperature followed by filtration, evaporation of the solvent gave the 3-oxocarbapenam (**18**) (20 mg, 92.6%) as a syrup: exact mass for M^+ peak, calcd *m/e* 241.0949, found 241.0937; IR ($CHCl_3$) 1760, 1735 cm^{-1} (C=O); NMR ($CDCl_3$) δ 1.31 (t, 3 H, *J* = 7 Hz, CH_2**Me**), 1.35 (d, 3 H, *J* = 6.5 Hz, CH**Me**), 2.42 (dd, 1 H, *J* = 8, 19 Hz, 4 H), 2.93 (dd, 1 H, *J* = 6.4, 19 Hz, 4 H), 3.18 (dd, 1 H, *J* = 2, 7 Hz, 6 H), 4.67 (s, 1 H, 2 H).

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Registry No. 9, 32296-89-2; **10**, 32367-46-7; **11**, 32296-85-8; **12**, 81477-53-4; **13**, 81477-54-5; **14**, 81477-55-6; **15**, 81477-56-7; **16**, 81477-57-8; **17**, 81477-58-9; **18**, 81477-59-0; benzylhydroxylamine, 622-30-0; benzyl crotonate, 65416-24-2.

Studies on the Syntheses of Heterocyclic and Natural Compounds. 950. Asymmetric Total Synthesis of (+)-Chenodeoxycholic Acid. Stereoselectivity of Intramolecular Cycloaddition of Olefinic *o*-Quinodimethanes†

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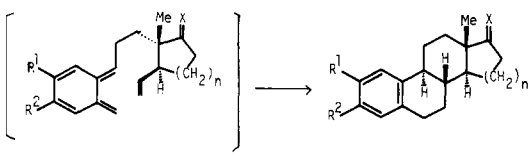
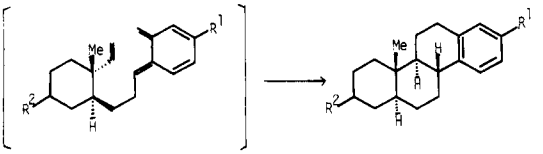
The first asymmetric total synthesis of (+)-chenodeoxycholic acid (**4**) is described. The key step is an intramolecular cycloaddition of the *o*-quinodimethane (**2**), generated in situ from the thermolysis of optically active 4α-acetoxy-1α-ethenyl-2-[2-(4-methoxybenzocyclobutenyl)-2-oxoethyl]-1β-methylcyclohexane (**1**), which gave stereoselectively 3α-acetoxy-17-methoxy-7-oxo-*D*-homo-18-nor-5β-androsta-13,15,17-triene (**3**). The stereoselectivity of this cycloaddition is also discussed.

The versatility of *o*-quinodimethanes in the synthesis of polycyclic ring systems[1] has resulted in a recent focusing of attention on novel methods of generation of such systems.[1,2] The stereochemical course of the synthesis of polycyclic ring system via cycloaddition of olefins and acetylenes to *o*-quinodimethanes has been well studied. Such reactions have been found to proceed with high stereoselectivity, and the stereoselective synthesis of A-ring aromatic steroids, for example, therefore was made possible (eq 1). In connection with our interest in the synthesis of pregnane-type steroids,[3] we have also achieved the stereoselective synthesis of D-ring aromatic steroids (eq 2). The observed stereoselectivity in these syntheses



(1)



(2)

results from the trans relationship of the olefin and

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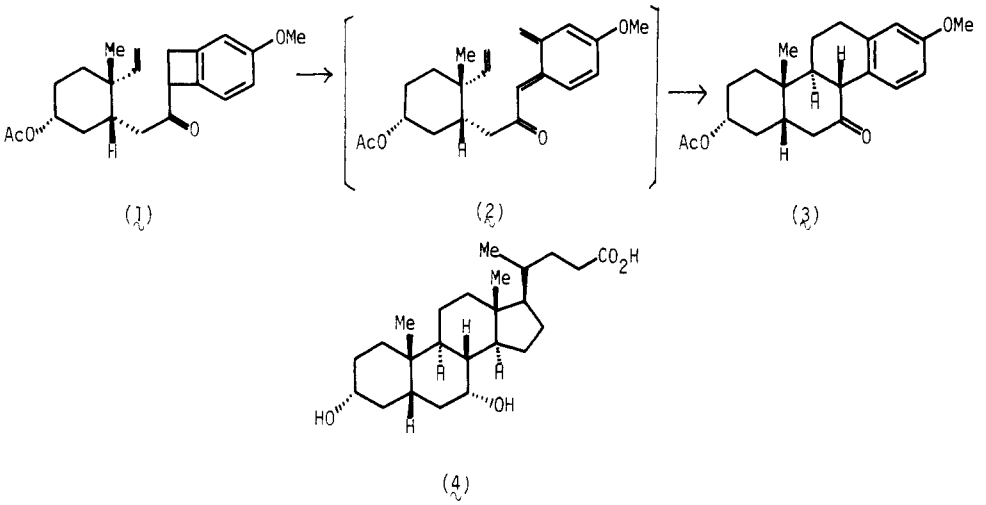
Scheme I



(1) (2) (3) (4)

(benzocyclobutenyl)ethyl moieties on the cyclopentane and cyclohexane rings. To date, there have been no reported examples on the cycloaddition of *o*-quinodimethanes in which these groups, on either a cyclopentane or a cyclohexane ring, have a cis relationship. This method, therefore, has been limited in its application to steroid synthesis, and the important class of 5β-pregnane-type steroids remains inaccessible by such cycloaddition reaction. Herein we report the first example of cycloaddition of an olefinic *o*-quinodimethane (**2**) generated in situ by thermolysis of the olefinic benzocyclobutene (**1**) in which the olefin and (benzocyclobutenyl)ethyl groups on the cyclohexane ring are oriented in a cis relationship, to give the cis-anti-trans fused D-ring aromatic steroid **3** in a stereoselective manner with full experimental details (Scheme I). Thereby, we have succeeded in the first asymmetric total synthesis of (+)-chenodeoxycholic acid which was attracted much attention because of the clinical importance for treatment of gallstones. In fact, studies around the world, including countries where chenodeoxycholic acid (**4**) is now available for general medical use, have shown that about 60% of patients treated with chenodeoxycholic acid (**4**) have stone dissolution.[4]

Preparation of Optically Active Olefinic Benzocyclobutenes. Firstly, the key intermediate **21** for the generation of olefinic benzocyclobutenes required for the studies of cycloaddition reaction of *o*-quinodimethanes was prepared from readily available (8a*S*)-1,1-(1,2-ethylenedioxy)-1,2,3,4,6,7,8,8a-octahydro-8a-methyl-6-oxonaphthalene[3b] (**5**) by the route shown in Scheme II. The *cis*-decalone **9** ($[\alpha]_D$ −16.6°), prepared from **5** via ketal ketone **6**, ketal alcohol **7**, and ketal acetate **8** was converted into *cis*-octalone **11** ($[\alpha]_D$ +22.4°). The *cis*-octalone **11** was then reacted with 1-cyano-4-methoxybenzocyclobutene[5] under basic conditions followed by basic hydrolysis to give the Michael adduct **12** as an unseparable stereoisomeric mixture which on ketalization afforded the cyanobenzocyclobutene **13** [*m/e* 383 (M^+)]. The benzocyclobutene **15** [*m/e* 314 (M^+)], obtained from **13** by reductive decyanation[6] and deprotection of ketal **14**, was converted into epoxide **19** [*m/e* 328 (M^+)] through bromide **16**, enone **17**, and epoxide **18**. Reduction of epoxide **19** followed by selective mesylation of the resulting diol **20** furnished hydroxymesylate **21** [*m/e* 494 (M^+)] as an unseparable stereoisomeric mixture.

Table I. Thermolysis of Olefinic Benzocyclobutenes[a]

entry	compd	rctn time, h	products (% yield)
1	**22**	1	**32** (92.1)
2	**23**	1	**32** (94.2)
3	**24**	6	**24**
4	**1**	0.75	**3** (42.7)
			28 (20.4)
5	**27**	4	**33** (65.2)
6	**25**	0.5	**30** (46.1)

[a] All the reactions were carried out in boiling *o*-dichlorobenzene in a current of nitrogen.

Fragmentation of **21** was effected by using sodium hydride in boiling anhydrous tetrahydrofuran to give the olefinic benzocyclobutene **22** [*m/e* 386 (M^+)], which on hydrolysis followed by acetylation of the resulting alcohol **23** [*m/e* 314 (M^+)] yielded the acetate **1** [*m/e* 356 (M^+)]. Ketal acetate **24** [*m/e* 400 (M^+)] was obtained by ketalization of **1** in a usual manner. Jones oxidation of **23** afforded diketone **25** [*m/e* 312 (M^+)]. The bis(benzyloxy) derivative **27** [*m/e* 496 (M^+)] was also prepared from **23** by reduction followed by benzylation of the resulting diol **26**. Although the stereochemistry at the hydroxy-bearing carbon on the two-carbon bridge in diol **26** could not be determined at this stage, the stereochemical assignments at this center has been made unambiguously via the corresponding cycloadduct (**33**), which will be discussed in next section.

Thermolysis of Olefinic Benzocyclobutenes. At first, the thermolysis of pyranyl ether **22** (Table I, entry 1) and hydroxy compound **23** (entry 2) was carried out and the product thus obtained was found to be intramolecular hemiacetal **32** in which an absorption at 1700 cm^{-1} due to carbonyl group observed in the IR spectra of **22** and **23** could not be detected. Actually, hydroxy compound **23** could be recovered by treating the hemiacetal **32** with *p*-toluenesulfonic acid in dichloromethane. Once hemiacetal **32** was formed, the benzocyclobutenyl group was stabilized for thermolysis. This was found to be the case, for the thermolysis of ketal acetate **24** and **24** was recovered unchanged even after prolonged heating (entry 3). Then ketonic acetate **1** was subjected to the thermolysis, and the

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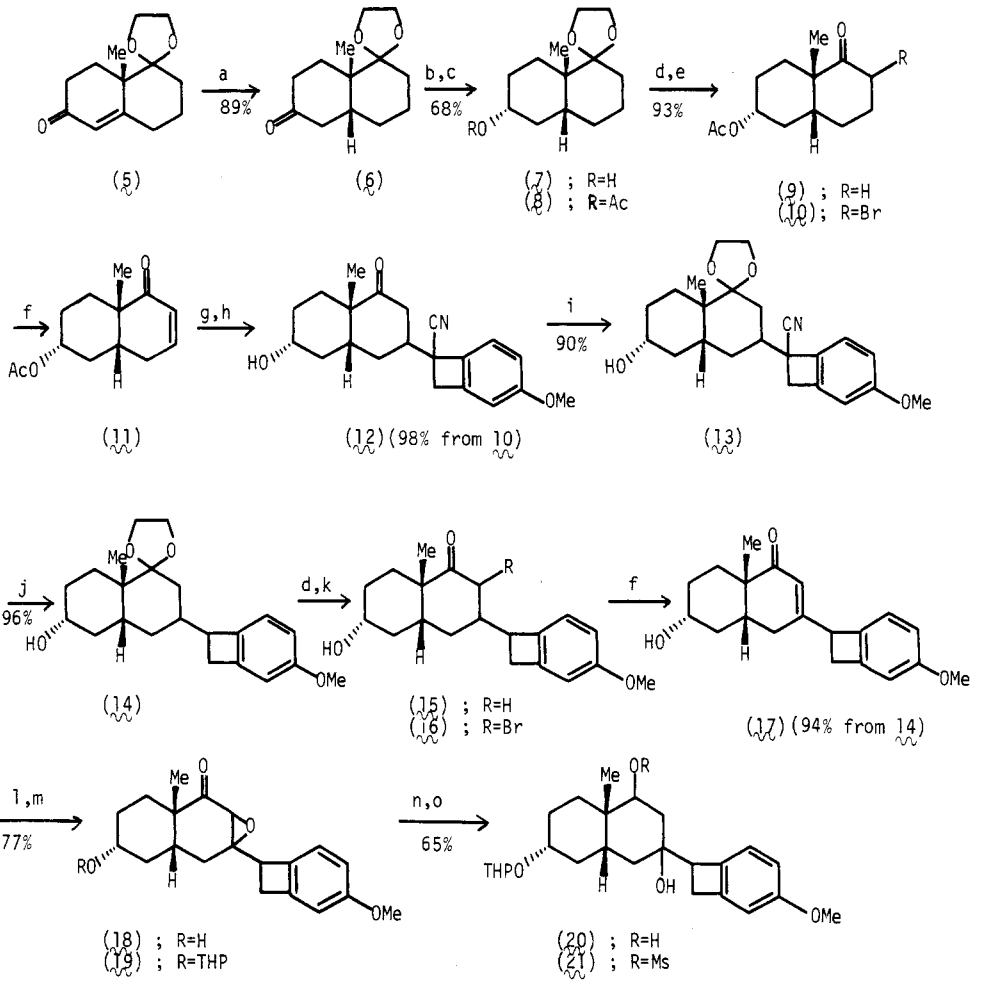
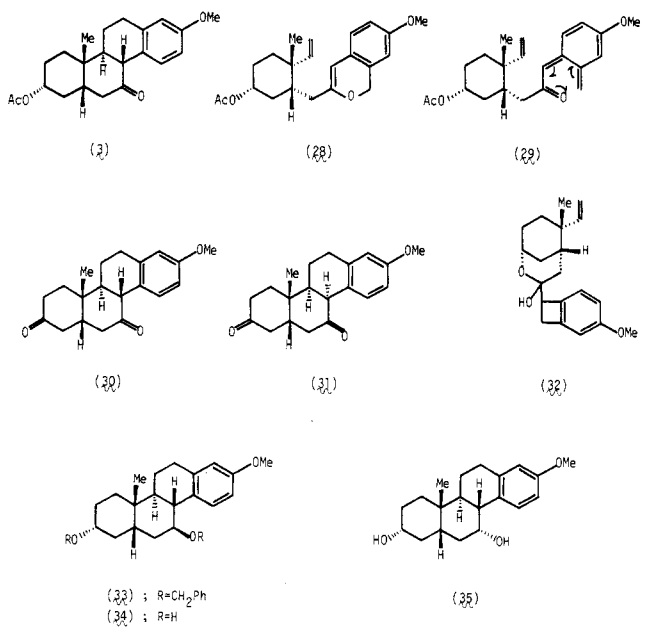
Scheme II[a]



(5) (6) (7) ; R=H (8) ; R=Ac (9) ; R=H (10) ; R=Br (11) (12) (98% from 10) (13) (14) (15) ; R=H (16) ; R=Br (17) (94% from 14) (18) ; R=H (19) ; R=THP (20) ; R=H (21) ; R=Ms

[a] Reagents: (a) H_2, Pd-C, EtOH, room temperature; (b) $NaBH_4$, MeOH, 0 °C; (c) Ac_2O, pyridine, room temperature; (d) 10% HCl, acetone, room temperature; (e) Br_2, $CHCl_3$, room temperature; (f) LiBr, Li_2CO_3, DMF, 125 °C; (g) 1-cyano-4-methoxybenzocyclobutene, $NaNH_2$, liquid NH_3, −78 °C; (h) 5% NaOH, MeOH, room temperature; (i) $HO(CH_2)_2OH$, *p*-TsOH, C_6H_6, reflux; (j) Na, liquid NH_3, −78 °C; (k) pyridinium hydrobromide perbromide, $CHCl_3$, room temperature; (l) 30% H_2O_2, 10% NaOH, MeOH, room temperature; (m) 3,4-dihydro-α-pyran, *p*-TsOH, CH_2Cl_2, room temperature; (n) $LiAlH_4$, THF, room temperature; (o) MsCl, pyridine, room temperature.

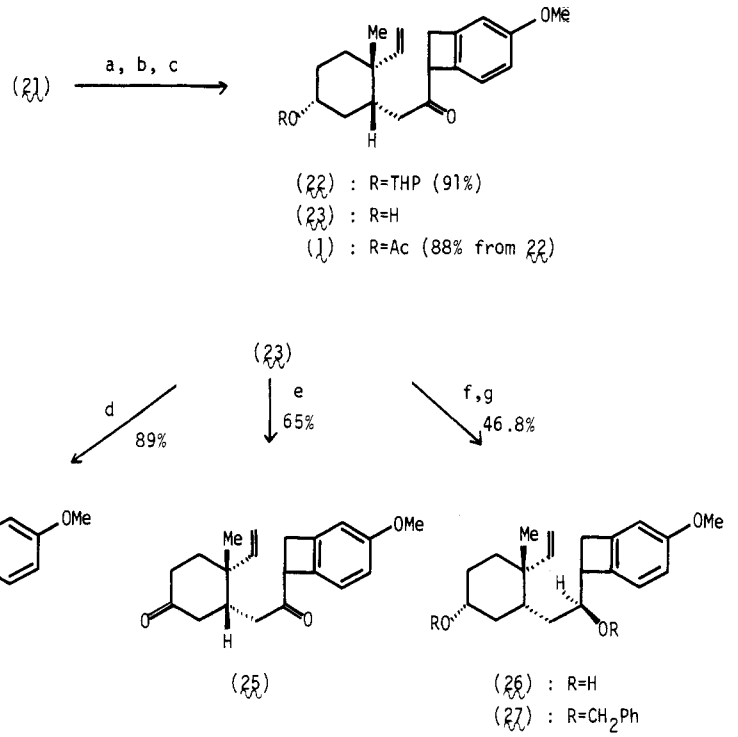


(3) (28) (29) (30) (31) (32) (33) ; R=CH_2Ph (34) ; R=H (35)

Figure 1.

products obtained by careful workup were found to be benzopyran **28** and natural cis-anti-trans D-homo-steroid **3** (entry 4). The formation of benzopyran **28** could be explained by the electrocyclic reaction of inward opened *o*-quinodimethane **29**. The stereoselectivity in the formation of **3** could be well realized by postulating sterically favored outward opened *o*-quinodimethane **2**. The intermediate **2** has a choice of two exo (**2A** and **2B**) and two endo (**2C** and **2D**) transition states potentially yielding four isomeric D-homo steroids (**3**, **36**–**38**). If one examines molecular models depicting the four transition states (**2A**–**2D**), one concludes that **2A** (addition of the vinyl group from the α face) should be preferred over **2B**–**2D**. The reason for this preference may be found in steric consideration. The exo addition as in **2A** proceeds via a chairlike transition state to lead to the natural cis-anti-trans isomer **3**, whereas other transition states suffer from steric interferences, i.e., cyclohexane protons–*o*-quinodimethane protons for **2B** leading to unnatural cis-syn-trans isomer **36** containing all chair conformation after equilibration of initially formed boat conformation, methyl protons–aromatic ring for endo transition-state **2C** to unnatural cis-anti-cis isomer **37**, and cyclohexane protons–aromatic ring for endo transition-state **2D** to unnatural cis-syn-cis isomer **38**. This analysis leads one to the conclusion that **3** should be the predominant product arising from intramolecular *o*-quinodimethane cycloaddition. On thermolysis of dibenzyl ether **27** (entry 5), natural cis-

Scheme III[a]



[a] Reagents: (a) NaH, THF, reflux; (b) *p*-TsOH, CH_2Cl_2, room temperature; (c) Ac_2O, pyridine, room temperature; (d) $HO(CH_2)_2OH$, *p*-TsOH, C_6H_6, reflux; (e) Jones reagent, 0 °C; (f) $LiAlH_4$, THF, room temperature; (g) $PhCH_2Br$, NaH, THF, reflux.

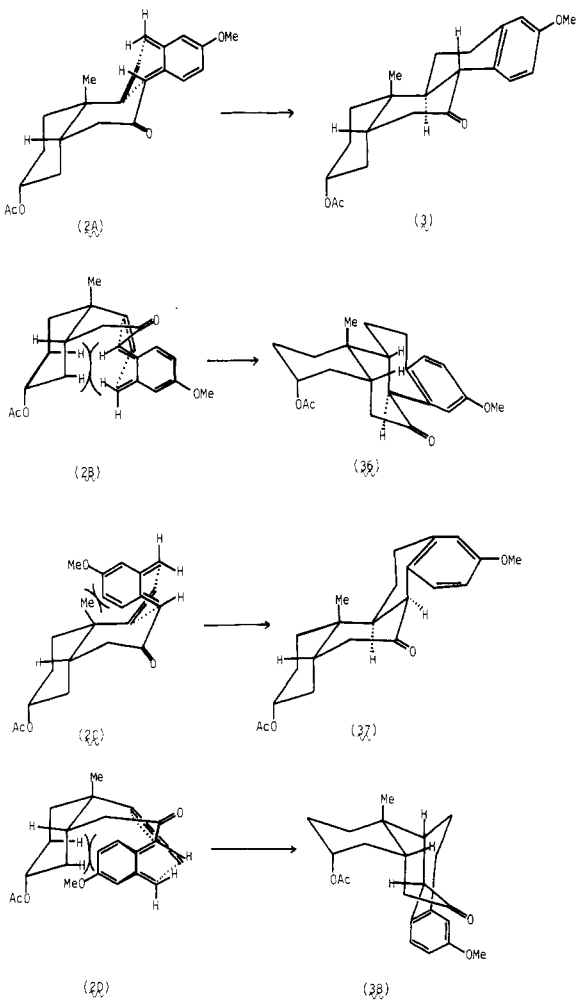


Figure 2.

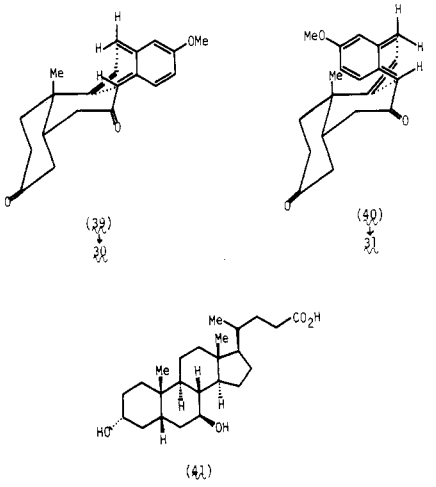
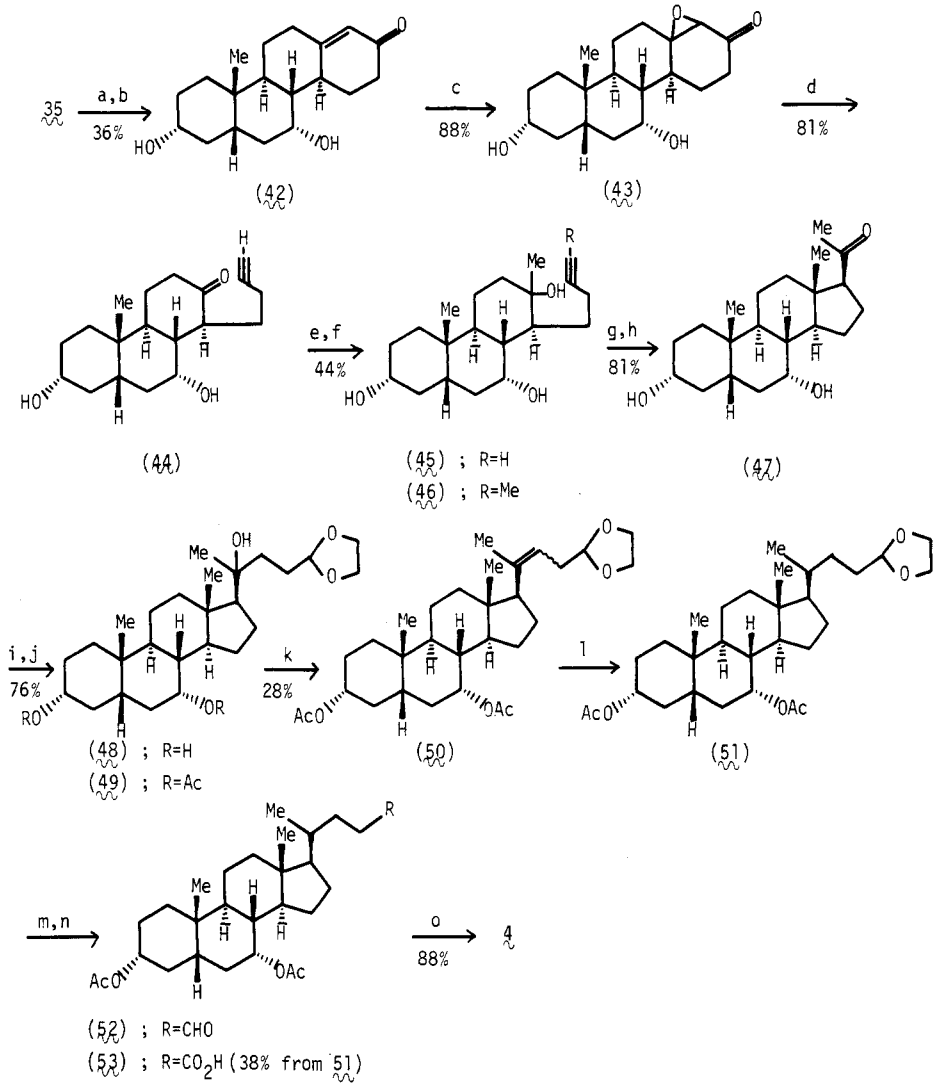


Figure 3.

anti-trans isomer **33** was obtained as a sole product, the formation of which can be recognized by inspection of a molecular model analogous to that of **2**. In the case of diketone **25** (entry 6), serious steric interferences between acetoxy and (benzocyclobutenyl)ethyl groups for **1** and benzyloxy and (benzocyclobutenyl)ethyl groups for **27** in its diaxial arrangements are released, and the conformation of cyclohexane ring of **25** becomes more flexible than that of **1** and **27** especially in the thermolytic condition. As a result, the transition-states **39** and **40** in the thermolysis of **25** may be possible as the most preferred transition states reflecting the product ratio about 4:3 (**30**–**31**).

The structures of the thermolytic products were deduced as follows at this stage although the whole structures including stereochemistry of all chiral centers were determined unambiguously at a later stage. Acetoxy ketone **3** [*m/e* 356 (M^+); $[\alpha]_D$ −49.6°] was reduced with lithium aluminum hydride in anhydrous tetrahydrofuran to give

Scheme IV[a]

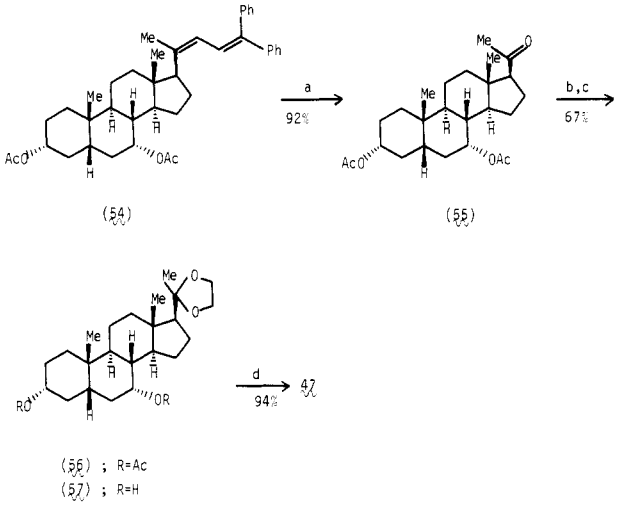


[a] Reagents: (a) Li, liquid NH_3, *t*-BuOH, −78 °C; (b) 10% HCl, MeOH, reflux; (c) 30% H_2O_2, 10% NaOH, MeOH, 0 °C; (d) *p*-$TsNHNH_2$, AcOH, CH_2Cl_2, 15 h at −18 °C then 4 h at room temperature; (e) MeLi, THF, 0 °C; (f) MeI, $LiNH_2$, liquid NH_3, THF, −33 °C; (g) CF_3CO_2H, $(CF_3CO)_2O$, room temperature; (h) 10% KOH, MeOH, room temperature; (i) [3,3-(ethylenedioxy)propyl]magnesium bromide, THF, room temperature; (j) Ac_2O, dimethylaminopyridine, pyridine, room temperature; (k) $POCl_3$, pyridine, room temperature; (l) H_2, Pt, MeOH, room temperature; (m) 10% HCl, acetone, room temperature; (n) Jones reagent, acetone, 0 °C; (o) 10% NaOH, MeOH, reflux.

diol **35** [*m/e* 316 (M^+); $[\alpha]_D$ −42.5°], whose NMR ($CDCl_3$) spectrum showed the methine proton of C-7 at 4.2–4.6 ppm as a multiplet and showed the proton to be arranged in equatorial form as a result of the deshielding effect of the aromatic ring. Diketone **30** [*m/e* 312 (M^+); $[\alpha]_D$ −50.5°] was also reduced with lithium aluminum hydride to give the diol which was identical with authentic diol **35**, showing **30** to be in cis-anti-trans arrangement in a carbocyclic framework. The other diketone **31** [*m/e* 312 (M^+); $[\alpha]_D$ −11.3°] was treated with potassium carbonate in acetone–methanol–water (1:1:1), yielding the thermodynamically more stable **30**, suggesting **31** to be cis-anti-cis fused compounds. Dibenzyl ether **33** [*m/e* 496 (M^+); $[\alpha]_D$ +31.9°] was hydrogenolized on Pd–C under an atmosphere of hydrogen to afford the diol **34** [*m/e* 316 (M^+); $[\alpha]_D$ −17.3°], which was not identical with **35**, and the deshielded methine proton observed in **35** could not be detected in its NMR ($CDCl_3$) spectrum. On the other hand, the product obtained by Jones oxidation of **34** was found to be identical with the diketone **30**. As a result, bis(benzyloxy) compound **33** could be the C-7 isomer of the dibenzyl ether derivative of **35**, showing that stereoselective reduction of **23** was achieved in the stage for preparing diol **26**. It is noteworthy that the stereoselective formation of **33** and **34** could be important for the direct synthesis of ursodeoxycholic acid (**41**) by following the same reaction sequences leading to chenodeoxycholic acid (**4**) from diol **35**, which is described in the next section.

Synthesis of (+)-Chenodeoxycholic Acid (4). With cis-anti-trans D-homo-steroid **35** in hand, conversion to chenodeoxycholic acid (**4**) requires D-ring manipulation and introduction of substituents stereoselectively (Scheme IV). The enone **42** ($[\alpha]_D$ −45.0°), prepared from **35**, was converted into acetylenic ketone **44** ($[\alpha]_D$ −4.0°) via the epoxy ketone **43** [*m/e* 320 (M^+)] by the epoxidation and Eschenmoser ring-opening reaction. Then acetylenic alcohol **46** was obtained by the reaction of **44** with methyllithium followed by methylation of the resulting alcohol **45** with methyl iodide under basic conditions. Acid-catalyzed ring closure of **46** was carried out in a stereoselective manner to give the pregnane-type steroid **47** $[\alpha]_D$ +41.3°) after the hydrolysis of the initial product, enol trifluoroacetate. At this stage, in order to confirm the structure including the stereochemistry of all the chiral

Scheme V[a]



[a] Reagents: (a) O_3, AcOEt, −78 °C, then Me_2S; (b) $HO(CH_2)_2OH$, *p*-TsOH, C_6H_6, reflux; (c) $LiAlH_4$, THF, room temperature; (d) 5% HCl, MeOH, room temperature.

centers, we carried out an alternative synthesis of **47** starting from **54**[7] (Scheme V). Diacetoxy ketal **56** [*m/e* 462 (M^+)], prepared by ozonolysis of **54** followed by ketalization of the resulting ketone **55**, was converted into **47** [*m/e* 334 (M^+); $[\alpha]_D$ +44.3°] by treatment with lithium aluminum hydride and the resulting diol **57** with hydrochloric acid. The synthetic substance was identical with an authentic sample thus obtained by spectral (IR, NMR, mass) comparison. The optical purity of synthetic substance was calculated above.

The 20(22)-dehydro compound **50** [*m/e* 502 (M^+)], derived from **47** via triol **48** and diacetate **49** by Grignard reaction with [3,3-(ethylenedioxy)propyl]magnesium bromide prepared from the corresponding bromide[8] followed by dehydration, was converted into (+)-chenodeoxycholic acid (**4**) via the acetal **51**, the aldehyde **52**, and the diacetoxy acid **53**. The synthetic substance was found to be identical with natural (+)-chenodeoxycholic acid in all aspects, including IR ($CHCl_3$), NMR ($CDCl_3$), mass spectra, optical rotation, and mixture melting point.

Thus we could accomplish the first total synthesis of (+)-chenodeoxycholic acid (**4**). Since (+)-chenodeoxycholic acid (**4**) has been correlated[9] with ursodeoxycholic acid (**41**), this work also constitutes the formal total synthesis of ursodeoxycholic acid, which has also been shown to have almost the same activity as chenodeoxycholic acid for treatment of gallstones.[10] This synthetic methodology could be applied for the synthesis of a wide range of cis-anti-trans fused steroidal compounds.

Experimental Section

General Methods. All melting points are uncorrected. Infrared (IR) spectra were recorded on a Hitachi EPI-3 spectrophotometer. Nuclear magnetic resonance (NMR) spectra were measured on a JEOL JNM-PMX-60 spectrometer. Chemical shifts are reported as δ values relative to internal tetramethylsilane (Me_4Si). Mass spectra were taken on a Hitachi M-52G spectrometer. All optical rotations were measured in chloroform solution on a JASCO PIP-SL polarimeter using a 1-dm cell.

(+)-(4a*R*,8a*S*)-1,2,3,4,4aβ,5,6,7,8,8a-Decahydro-1,1-(1,2-ethylenedioxy)-8aβ-methyl-6-oxonaphthalene (6). A mixture of 62 g (0.28 mol) of **5** and 5 g of 10 % palladium on carbon in 250 mL of 95% ethanol was stirred under an atmosphere of hydrogen at room temperature. Hydrogenation was carried out smoothly at atmospheric pressure and was completed within 6 h. The solution was then filtered to remove the catalyst and the catalyst was washed with 95% ethanol. The filtrate and washing were combined and evaporated to yield a crude product which was chromatographed on 300 g of silica gel, using hexane–ethyl acetate (4:1) as eluant, to give 55 g (89%) of the keto ketal **6** as a colorless oil: IR ($CHCl_3$) 1700 cm^{-1}; NMR ($CDCl_3$) δ 1.18 (3 H, s, CH_3), 3.96 (4 H, s, OCH_2CH_2O); MS *m/e* 224 (M^+); $[\alpha]_D^{20}$ +14.0° (*c* 0.2). Anal. Calcd for $C_{13}H_{20}O_3$: C, 69.61; H, 8.99. Found: C, 69.40; H, 9.91.

(+)-(4a*R*,6*R*,8a*S*)-1,2,3,4,4aβ,5,6,7,8,8a-Decahydro-1,1-(1,2-ethylenedioxy)-6-hydroxy-8aβ-methylnaphthalene (7). To a stirred solution of 55 g (0.246 mol) of keto ketal **6** in 500 mL of methanol at 0 °C was added 8 g (0.21 mol) of sodium borohydride in small portions and the stirring was continued for 1 h at 0 °C. After methanol had been removed by evaporation, 500 mL of water was added and the mixture was extracted 3 times with 300-mL portions of benzene. This benzene extract was washed with saturated sodium chloride solution and dried over anhydrous sodium sulfate. Removal of the solvent afforded a crude product which was chromatographed on 300 g of silica gel, using hexane–ethyl acetate (9:1) as eluant, to give 44 g (79%) of alcohol **7** as a colorless oil: IR ($CHCl_3$) 3600 (OH) cm^{-1}; NMR ($CDCl_3$) δ 1.00 (3 H, s, CH_3), 3.90 (4 H, s, OCH_2CH_2O), 3.56–4.10 (1 H, m, CHOH); MS *m/e* 226 (M^+); $[\alpha]_D^{20}$ +2.2° (*c* 0.278). Anal. Calcd for $C_{13}H_{22}O_3$: C, 68.99; H, 9.80. Found: C, 69.03; H, 10.05.

(+)-(4a*R*,6*R*,8a*S*)-6α-Acetoxy-1,2,3,4,4aβ,5,6,7,8,8a-decahydro-1,1-(1,2-ethylenedioxy)-8aβ-methylnaphthalene (8). To a solution of 44 g (0.195 mol) of alcohol **7** in 200 mL of pyridine was added 35 g (0.343 mol) of acetic anhydride at room temperature under nitrogen, and the mixture was stirred for 16 h. The reaction mixture was poured into 400 mL of water and extracted 3 times with 300-mL portions of benzene. This benzene extract was washed with saturated potassium bisulfate solution, saturated sodium bicarbonate solution, and saturated sodium chloride solution and dried over anhydrous sodium sulfate. Removal of the solvent afforded a crude product which was chromatographed on 300 g of silica gel, using benzene as eluant, to give 45 g (85%) of acetate **8** as a colorless oil: IR ($CHCl_3$) 1720 cm^{-1}; NMR ($CDCl_3$) δ 1.01 (3 H, s, CH_3), 2.02 (3 H, s, CH_3), 3.96 (4 H, s, OCH_2CH_2O), 4.58–5.13 (1 H, m, CHOAc); MS *m/e* 268 (M^+); $[\alpha]_D^{20}$ +16.3° (*c* 0.258). Anal. Calcd for $C_{15}H_{24}O_4$: C, 67.13; H, 9.02. Found: C, 67.39; H, 9.27.

(−)-(4a*R*,6*R*,8a*S*)-6α-Acetoxy-1,2,3,4,4aβ,5,6,7,8a-decahydro-8aβ-methyl-1-oxonaphthalene (9). To a solution of 45 g (0.168 mol) of ketal **8** in 500 mL of acetone was added 5 mL of 5% aqueous hydrochloric acid solution, and the reaction mixture was stirred for 16 h at room temperature. The solvent was removed by evaporation, and the residue was diluted with 300 mL of water and extracted 3 times with 400-mL portions of benzene. The combined benzene extract was washed with saturated sodium bicarbonate solution and saturated sodium chloride solution and dried over anhydrous sodium sulfate. Removal of the solvent afforded a crude product which was chromatographed on 300 g of silica gel, using benzene as eluant, to give 36 g (96%) of ketone **9** as a colorless oil: IR ($CHCl_3$) 1720, 1700 (C=O) cm^{-1}; NMR ($CDCl_3$) δ 1.21 (3 H, s, CH_3), 1.99 (3 H, s, CH_3), 4.50–5.06 (1 H, m, CHOAc); MS *m/e* 224 (M^+); $[\alpha]_D^{20}$ −16.6° (*c* 0.228). Anal. Calcd for $C_{13}H_{20}O_3$: C, 69.61; H, 8.99. Found: C, 69.16; H, 9.26.

(+)-(4a*R*,6*R*,8a*S*)-6α-Acetoxy-1,4,4aβ,5,6,7,8,8a-octahydro-8aβ-methyl-1-oxonaphthalene (11). To a stirred solution of 10 g (44.6 mmol) of the acetate **9** in 200 mL of chloroform at 0 °C under nitrogen was added dropwise a solution of 7.3 g (45.6 mmol) of bromine in 50 mL of chloroform. When stirring had been continued for 2 h at 0 °C, 300 mL of water was poured into the above reaction mixture. The organic layer was separated and washed with saturated sodium bicarbonate solution and saturated sodium chloride solution and then dried over anhydrous sodium sulfate. After evaporation of the solvent, the residue was used for the next reaction without purification. A mixture of 14.5 g of the crude bromide **10**, 7.5 g (86.2 mmol) of lithium bromide, and 6.3 g (94.0 mmol) of lithum carbonate in 70 mL of anhydrous dimethylformamide was stirred for 3.5 h at 125–130 °C under an

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atmosphere of nitrogen. After cooling, the reaction mixture was diluted with 300 mL of water and extracted 3 times with 300-mL portions of benzene. The combined organic layer was washed with saturated sodium chloride solution and dried over anhydrous sodium sulfate. Removal of the solvent afforded a crude product which was chromatographed on 300 g of silica gel, using benzene as eluant, to give 9.59 g (97%) of enone **11** as a colorless oil: IR ($CHCl_3$) 1663, 1720 (C=O) cm^{-1}; NMR ($CDCl_3$) δ 1.13 (3 H, s, CH_3), 1.98 (3 H, s, CH_3), 4.50–5.13 (1 H, m, CHOAc), 5.95 (1 H, dd, J = 3, 10 Hz, olefinic H), 6.68–7.05 (1 H, m, olefinic H); MS m/e 222 (M^+); $[\alpha]^{20}_D$ +22.4° (c 0.268). Anal. Calcd for $C_{13}H_{18}O_3$: C, 70.24; H, 8.16. Found: C, 70.05; H, 8.30.

3-[2-(1-Cyano-4-methoxybenzocyclobutenyl)]-1,2,3,4,4aβ,5,6,7,8,8a-decahydro-6α-hydroxy-8aβ-methyl-1-oxonaphthalene (12). To a stirred solution of sodium amide [from 2.3 g (0.1 mol) of sodium] and 8 g (51.3 mmol) of 1-cyano-4-methoxybenzocyclobutene in 1 L of liquid ammonia and 100 mL of anhydrous tetrahydrofuran was added 9.6 g (43.2 mmol) of enone **11** in 100 mL of anhydrous tetrahydrofuran at −78 °C. After being stirred for 2 h at −78 °C, the reaction mixture was treated with an excess of solid ammonium chloride and the solvent was evaporated. The reddish residue was diluted with 200 mL of saturated aqueous ammonium chloride solution, and the resulting mixture was extracted 3 times with 200-mL portions of benzene. This benzene extract was washed with sodium chloride solution and dried over anhydrous sodium sulfate. Removal of the solvent afforded a reddish gum, which was used in the next reaction without purification.

To a solution of crude adducts in 200 mL of methanol was added 5% aqueous potassium hydroxide solution and the reaction mixture was stirred for 2 h at room temperature. Removal of the solvent afforded a crude product, which was extracted 3 times with 200 mL portions of benzene. The benzene layer was washed with saturated sodium chloride solution and dried over anhydrous sodium sulfate. Evaporation of the solvent afforded a crude gum which was chromatographed on 250 g of silica gel, using benzene-ethyl acetate (10:1) as eluant, to give 14.4 g (98%) of ketone **12** as a colorless oil: IR ($CHCl_3$) 3600 (OH), 2230 (CN), 1700 (C=O) cm^{-1}; NMR ($CDCl_3$) δ 1.13, 1.25 (each s, CH_3), 3.26 (1 H, d, J = 15 Hz, 2-H), 3.68 (1 H, d, J = 15 Hz, 2-H), 3.81 (3 H, s, CH_3), 3.85–4.30 (1 H, br s, CHOH), 6.80–7.45 (3 H, m, ArH); MS m/e 339 (M^+). Anal. Calcd for $C_{21}H_{25}O_3N$: C, 74.31; H, 7.42; N, 4.13. Found: C, 74.02; H, 7.52; N, 3.86.

1,1-(1,2-Ethylenedioxy)-3-[2-(1-cyano-4-methoxybenzocyclobutenyl)]-1,2,3,4,4aβ,5,6,7,8,8a-decahydro-6α-hydroxy-8aβ-methylnaphthalene (13). To a solution of 12.5 g (36.9 mmol) of keto alcohol **12** in 200 mL of benzene were added a catalytic amount of p-toluenesulfonic acid and 20 g (365 mmol) of ethylene glycol. The mixture was refluxed in a flask fitted with a Dean–Stark trap. Water was removed after 3 h, and the reaction mixture was cooled. The benzene layer was washed with saturated sodium carbonate solution and saturated sodium chloride solution and dried over anhydrous sodium sulfate. Removal of the solvent afforded a crude gum which was chromatographed on 200 g of silica gel, using benzene–ethyl acetate (10:1) as eluant, to give 12.7 g (90%) of ketal **13** as a colorless oil: IR ($CHCl_3$) 3610 (OH), 2235 (CN) cm^{-1}; NMR ($CDCl_3$) δ 0.93, 1.03 (each s, CH_3), 3.21 (1 H, d, J = 14 Hz, C_2-H), 3.58 (1 H, s, J = 14 Hz, C_2-H), 3.75 (3 H, s, CH_3), 3.92 (4 H, s, OCH_2CH_2O), 6.74–7.40 (3 H, m, ArH); MS m/e 383 (M^+). Anal. Calcd for $C_{23}H_{29}O_4N$: C, 72.03; H, 7.62; N, 3.65. Found: C, 71.98; H, 7.48; N, 3.31.

1,1-(1,2-Ethylenedioxy)-1,2,3,4,4aβ,5,6,7,8,8a-decahydro-6α-hydroxy-3-[2-(4-methoxybenzocyclobutenyl)]-8aβ-methylnaphthalene (14). To a solution of 1.5 g (65.2 mmol) of sodium in 1 L of liquid ammonia was added a solution of 10.4 g (27.2 mmol) of the ketal **13** in 200 mL of anhydrous tetrahydrofuran and 20 mL of absolute ethanol at −78 °C. The reaction mixture was stirred for 2 h at −78 °C. After addition of ethanol followed by evaporation of the solvent, 300 mL of water was added, and the resulting mixture was extracted 3 times with 300-mL portions of benzene. This benzene extract was washed with saturated sodium chloride solution and dried over anhydrous sodium sulfate. Removal of the solvent afforded a crude product which was chromatographed on 200 g of silica gel, using benzene–ethyl acetate (10:1) as eluant, to give 9.3 g (96%) of ketal **14** as a colorless oil: IR ($CHCl_3$) 3610 (OH) cm^{-1}; NMR ($CDCl_3$) δ 0.95, 0.97 (each s, CH_3), 3.76 (3 H, s, CH_3), 3.93 (4 H, s OCH_2CH_2O), 6.65–7.30 (3 H, m, ArH); MS m/e 358 (M^+). Anal. Calcd for $C_{22}H_{30}O_4$: C, 73.71; H, 8.44. Found: C, 73.79; H, 8.43.

1,2,3,4,4aβ,5,6,7,8,8a-Decahydro-6α-hydroxy-3-[2-(4-methoxybenzocyclobutenyl)]-8aβ-methyl-1-oxonaphthalene (15). To a solution of 9.3 g (26.0 mmol) of ketal **14** in 200 mL of acetone was added 3 mL of 5% aqueous hydrochloric acid solution, and the reaction mixture was stirred for 16 h at room temperature. The solvent was removed by evaporation and the residue was diluted with 200 mL of water and extracted 3 times with 300-mL portions of benzene. The combined benzene extract was washed with saturated sodium bicarbonate solution and saturated sodium chloride solution and dried over anhydrous sodium sulfate. Removal of the solvent afforded a crude product which was chromatographed on 200 g of silica gel, using benzene–ethyl acetate (10:1) as eluant, to give 8.03 g (99%) of keto alcohol **15** as a colorless oil: IR ($CHCl_3$) 3610 (OH), 1700 (C=O) cm^{-1}; NMR ($CDCl_3$) δ 1.14, 1.20 (each s, CH_3), 3.83 (3 H, s, CH_3), 6.72–7.30 (3 H, m, ArH); MS m/e 314 (M^+). Anal. Calcd for $C_{20}H_{26}O_3$: C, 76.40; H, 8.34. Found: C, 76.16; H, 8.30.

1,4,4aβ,5,6,7,8,8a-Octahydro-6α-hydroxy-3-[2-(4-methoxybenzocyclobutenyl)]-8aβ-methyl-1-oxonaphthalene (17). To a stirred solution of 13.5 g (43.0 mmol) of ketone **15** in 1 L of chloroform was added 20 g (62.5 mmol) of pyridinium hydrobromide perbromide at room temperature. After the mixture was stirred for 1 h, 500 mL of water was added. The organic layer was washed with saturated sodium bicarbonate solution and saturated sodium chloride solution and dried over anhydrous sodium sulfate. Removal of the solvent afforded 16.8 g of crude bromide **16**, which was used in the next reaction without purification. A mixture of 16.8 g of the crude bromide **16**, 7 g (80.5 mmol) of lithium bromide, and 5 g (67.6 mmol) of lithium carbonate in 150 mL of anhydrous dimethylformamide was stirred for 14 h at 45 °C under an atmosphere of nitrogen. After cooling, the reaction mixture was diluted with 400 mL of water and extracted 3 times with 300-mL portions of benzene. The combined benzene layer was washed with saturated sodium chloride solution and dried over anhydrous sodium sulfate. Evaporation of the solvent afforded a crude product which was chromatographed on 200 g of silica gel, using chloroform as eluant, to give 12.8 g (96%) of enone **17** as a colorless oil: IR ($CHCl_3$) 3610 (OH), 1660 (C=O) cm^{-1}; NMR ($CDCl_3$) δ 1.04, 1.07 (each s, CH_3), 3.29 (3 H, s, CH_3), 3.95–4.30 (1 H, br s, CHAr), 5.76–6.00 (1 H, br s, C_2-H), 6.60–7.20 (3 H, m, ArH); MS m/e 312 (M^+). Anal. Calcd for $C_{20}H_{24}O_3$: C, 76.89; H, 7.74. Found: C, 76.31; H, 7.40.

2,3-Epoxy-1,2,3,4,4aβ,5,6,7,8,8a-decahydro-6α-hydroxy-3-[2-(4-methoxybenzocyclobutenyl)]-8aβ-methyl-1-oxonaphthalene (18). To a solution of 10.8 g (34.6 mmol) of enone **17** in 30 mL of methanol were added 5 mL of 30% hydrogen peroxide and 5 mL of 10% aqueous sodium hydroxide solution at 0 °C. The reaction mixture was stirred for 6 h at room temperature and diluted with 200 mL of water. After extraction 3 times with 300-mL portions of chloroform, the combined organic extract was washed with saturated sodium chloride solution and dried over anhydrous sodium sulfate. Removal of the solvent gave a crude product which was chromatographed on 200 g of silica gel, using chloroform as eluant, to give 8.5 g (77%) of epoxide **18** as a colorless oil: IR ($CHCl_3$) 3610 (OH), 1700 (C=O) cm^{-1}; NMR ($CDCl_3$) δ 1.00, 1.20 (each s, CH_3), 3.76 (3 H, s, CH_3), 6.60–7.25 (3 H, m, ArH); MS m/e 328 (M^+). Anal. Calcd for $C_{20}H_{24}O_4$: 73.14; H, 7.37. Found: C, 72.88; H, 7.31.

2,3-Epoxy-1,2,3,4,4aβ,5,6,7,8,8a-decahydro-3-[2-(4-methoxybenzocyclobutenyl)]-8aβ-methyl-1-oxo-6α-[(tetrahydropyranyl)oxy]naphthalene (19). To a stirred solution of 8.5 g (25.9 mmol) of epoxy ketone **18** in 200 mL of dichloromethane were added a catalytic amount of p-toluenesulfonic acid and 3 g (35.7 mmol) of dihydropyran under nitrogen. After the mixture was stirred for 4 h at room temperature, 100 mL of water was added to the reaction mixture and the organic layer was then washed with saturated sodium bicarbonate solution and saturated sodium chloride solution and dried over anhydrous sodium sulfate. Evaporation of the solvent afforded a crude gum which was chromatographed on 150 g of silica gel, using benzene as eluant, to give 10.64 g (100%) of pyranyl ether **19** as a colorless oil: IR ($CHCl_3$) 1700 cm^{-1}; NMR ($CDCl_3$) δ 1.03, 1.22 (each s, CH_3), 3.73 (3 H, s, CH_3), 4.35–4.82 (1 H, br s, OC(H)O), 6.55–7.10 (3 H, m,

ArH); MS m/e 412 (M^+). Anal. Calcd for $C_{25}H_{32}O_5$: C, 72.79; H, 7.82. Found: C, 72.66; H, 7.97.

1,2,3,4,4aβ,5,6,7,8,8a-Decahydro-1,3-dihydroxy-8β-methyl-3-[2-(4-methoxybenzocyclobutenyl)]-6α-[(tetrahydropyranyl)oxy]naphthalene (20). To a suspension of 1.2 g (31.6 mmol) of lithium aluminum hydride in 250 mL of anhydrous tetrahydrofuran was added 10.6 g (25.7 mmol) of epoxy ketone **19** in 50 mL of anhydrous tetrahydrofuran and the resulting solution was stirred for 15 h at room temperature. After quenching the reaction mixture with 10% aqueous sodium hydroxide solution, the inorganic substance was filtered off. After evaporation of the solvent, the residue was extracted with chloroform. The organic layer was washed with saturated sodium chloride solution and dried over anhydrous sodium sulfate. Removal of the solvent gave a yellow oil which was chromatographed on 200 g of silica gel, using chloroform as eluant, to give 8.23 g (77%) of diol **20** as a colorless oil: IR ($CHCl_3$) 3600 (OH) cm^{-1}; NMR ($CDCl_3$) δ 0.98, 1.13, 1.24 (each s, CH_3), 3.75 (3 H, s, CH_3), 4.35–4.83 (1 H, br s, –OC(H)O), 6.50–7.15 (3 H, m, ArH); MS m/e 416 (M^+). Anal. Calcd for $C_{25}H_{36}O_5$: C, 72.08; H, 8.71. Found: C, 72.31; H, 8.93.

1,2,3,4,4aβ,5,6,7,8,8a-Decahydro-3-hydroxy-3-[2-(4-methoxybenzocyclobutenyl)]-8aβ-methyl-1-[(methylsulfonyl)oxy]-6α-[(tetrahydropyranyl)oxy]naphthalene (21). To a solution of 3.23 g (19.8 mmol) of diol **20** in 80 mL of pyridine were added 2.7 g (23.6 mmol) of methanesulfonyl chloride and a catalytic amount of 4-(dimethylamino)pyridine was stirred for 16 h at room temperature under nitrogen. The reaction mixture was diluted with 300 mL of water and extracted 3 times with 300-mL portions of benzene. The benzene extract was washed with saturated potassium bisulfate solution, saturated sodium bicarbonate solution, and saturated sodium chloride solution and dried over anhydrous sodium sulfate. Evaporation of the solvent afforded a crude product which was chromatographed on 150 g of silica gel, using chloroform as eluant, to give 8.28 g (85%) of mesylate **21** as a colorless oil: IR ($CHCl_3$) 3600 (OH) cm^{-1}; NMR ($CDCl_3$) δ 1.13, 1.16, 1.22 (each s, CH_3), 3.00 (3 H, s, CH_3), 3.74 (3 H, s, CH_3), 4.30–5.05 (2 H, m CHOMs, OC(H)O), 6.60–7.20 (3 H, m, ArH); MS m/e 494 (M^+). Anal. Calcd for $C_{26}H_{38}O_7S$: C, 63.14; H, 7.75. Found: C, 63.04; H, 7.81.

1α-Ethenyl-2α-[2-(4-methoxybenzocyclobutenyl)-2-oxoethyl]-1β-methyl-4α-[(tetrahydropyranyl)oxy]cyclohexane (22). To a stirred solution of 160 mg (11.1 mmol) of 60% sodium hydride in 5 mL of anhydrous tetrahydrofuran was added 500 mg (1.01 mmol) of mesylate **21** in 5 mL of anhydrous tetrahydrofuran and the resulting mixture was refluxed for 14 h under an atmosphere of nitrogen. Water (50 mL) was added to the reaction mixture and extracted 3 times with 50-mL portions of benzene. The benzene extract was washed with saturated sodium chloride solution and dried over anhydrous sodium sulfate. Evaporation of the solvent gave a crude product which was chromatographed on 10 g of silica gel, using chloroform as eluant, to give 352 mg (91%) of olefin **22** as a colorless oil: IR ($CHCl_3$) 1700 cm^{-1} (C=O); NMR ($CDCl_3$) δ 0.94, 0.97 (each s, CH_3), 3.71 (3 H, s, CH_3), 4.08–4.35 (1 H, m, CHAr), 4.53–4.80 (1 H, br s, OC(H)O), 4.80–6.35 (3 H, m, olefinic protons), 6.63–7.15 (3 H, m, ArH); MS m/e 386 (M^+). Anal. Calcd for $C_{25}H_{34}O_4$: C, 75.34; H; 8.60. Found: C, 75.12; H, 8.20.

1α-Ethenyl-4α-hydroxy-2α-[2-(4-methoxybenzocyclobutenyl)-2-oxoethyl]-1β-methylcyclohexane (23). A mixture of 262 mg (0.69 mmol) of pyranyl ether **22** in 10 mL of dichloromethane and a catalytic amount of *p*-toluenesulfonic acid was stirred for 1 h at room temperature. The dichloromethane layer was washed with saturated sodium bicarbonate solution and saturated sodium chloride solution and dried over anhydrous sodium sulfate. Evaporation of the solvent afforded a gum which was chromatographed on 5 g of silica gel, using chloroform as eluant, to give 205 mg (97%) of the alcohol **23** as a colorless oil: IR ($CHCl_3$) 3600 (OH), 1700 (C=O) cm^{-1}; NMR ($CDCl_3$) δ 0.95, 0.97 (each s, CH_3), 3.73 (3 H, s, CH_3), 4.06–4.40 (1 H, br s, CHAr), 4.80–6.30 (3 H, m, olefinic protons), 6.75–7.10 (3 H, m, ArH); MS m/e 314 (M^+). Anal. Calcd for $C_{20}H_{26}O_3$: C, 76.40; H, 8.34. Found: C, 76.17; H, 8.63.

4α-Acetoxy-1α-ethenyl-2α-[2-(4-methoxybenzocyclobutenyl)-2-oxoethyl]-1β-methylcyclohexane (1). To a solution of 210 mg (0.67 mmol) of alcohol **23** in 5 mL of pyridine was added 200 mg (1.96 mmol) of acetic anhydride and the mixture was stirred for 14 h at room temperature. The reaction mixture was diluted with 50 mL of water and extracted 3 times with 50-mL portions of chloroform. The organic layer was washed with saturated potassium bisulfate solution and saturated sodium chloride solution and dried over anhydrous sodium sulfate. Removal of the solvent afforded a crude product which was chromatographed on 5 g of silica gel, using chloroform as eluant, to give 217 mL (91%) of the acetate 1 as a colorless oil: IR ($CHCl_3$) 1720, 1700 (C=O) cm^{-1}; NMR ($CDCl_3$) δ 0.96, 1.00 (each s, CH_3), 1.99 (3 H, s, CH_3), 3.75 (3 H, s, CH_3), 4.10–4.35 (1 H, br s, CHAr), 4.38–5.00 (1 H, m, CHOAc), 4.83–6.32 (3 H, m, olefinic protons), 6.60–7.16 (3 H, m, ArH); MS m/e 356 (M^+). Anal. Calcd for $C_{22}H_{28}O_4$: C, 74.13; H, 7.92. Found: C, 73.64; H, 7.54.

4α-Acetoxy-1α-ethenyl-2α-[2,2-(1,2-ethylenedioxy)-2-(4-methoxybenzocyclobutenyl)ethyl]-1β-methylcyclohexane (24). To a solution of 100 mg (0.28 mmol) of keto acetate 1 in 20 mL of benzene were added a catalytic amount of *p*-toluenesulfonic acid and 200 mg (3.2 mmol) of ethylene glycol. The reaction mixture was refluxed in a flask fitted with a Dean–Stark trap. After 4 h, the reaction mixture was cooled. The benzene layer was washed with saturated sodium bicarbonate solution and saturated sodium chloride solution and dried over anhydrous sodium sulfate. Removal of the solvent afforded a crude product which was chromatographed on 5 g of silica gel, using chloroform as eluant, to give 100 mg (89%) of ketal **24** as a colorless oil: IR ($CHCl_3$) 1720 (C=O) cm^{-1}; NMR ($CDCl_3$) δ 0.99 (3 H, s, CH_3), 1.95 (3 H, s, CH_3), 3.00 (2 H, d, J = 4 Hz, CH_2Ar), 3.66 (3 H, s, OCH_3), 4.30–5.00 (1 H, m, CHOAc), 4.70–6.25 (3 H, m, olefinic protons), 6.50–7.00 (3 H, m, ArH); MS m/e 400 (M^+).

1α-Ethenyl-2α-[2-(4-methoxybenzocyclobutenyl)-2-oxoethyl]-1β-methyl-3-oxocyclohexane (25). To a solution of 200 mg (0.637 mmol) of keto alcohol **23** in 5 mL of acetone was added 5 drops of an 8 N solution of chromic acid (prepared from 26.72 g of chromium trioxide, 23 mL of concentrated sulfuric acid, and enough water to make the total volume of 100 mL as a solution) at 0 °C and stirring was continued for 1 h at the same temperature. The reaction mixture was diluted with 20 mL of water and extracted 3 times with 50-mL portions of ethyl acetate. The organic layer was washed with saturated sodium chloride solution and dried over anhydrous sodium sulfate. Removal of the solvent afforded a crude product which was chromatographed on 4 g of silica gel, using chloroform as eluant, to give 130 mg (65%) of diketone **25** as a colorless oil: IR ($CHCl_3$) 1700 (C=O) cm^{-1}; NMR ($CDCl_3$) δ 1.34, 1.35 (each s, CH_3), 3.73 (3 H, s, OCH_3), 4.16 (1 H, distorted t, CHPh), 4.80–6.30 (3 H, m, olefinic protons), 6.50–7.10 (3 H, m, ArH); MS m/e 312 (M^+). Anal. Calcd for $C_{20}H_{24}O_3$: C, 76.89; H, 7.74. Found: C, 76.78; H, 7.74.

1α-Ethenyl-4α-hydroxy-2α-[2-(4-methoxybenzocyclobutenyl)-2-hydroxyethyl]-1β-methylcyclohexane (26). To a suspension of 100 mg (2.56 mmol) of lithium aluminum hydride in 20 mL of anhydrous tetrahydrofuran was added a solution of 325 mg (1.04 mmol) of keto alcohol **23** in 5 mL of anhydrous tetrahydrofuran with stirring and the reaction mixture was then stirred for 5 h at room temperature. After addition of 10% aqueous sodium hydroxide solution and filtration of the inorganic material, followed by evaporation of tetrahydrofuran, the aqueous layer was extracted 3 times with 50-mL portions of ethyl acetate. The organic layer was combined, washed with saturated sodium chloride solution, and dried over anhydrous sodium sulfate. Removal of the solvent afforded a crude product which was chromatographed on 10 g of silica gel, using chloroform as eluant, to give 190 mg (58%) of diol **26** as a colorless oil: IR ($CHCl_3$) 3580 (OH) cm^{-1}; NMR ($CDCl_3$) δ 0.96, 1.03 (each s, CH_3), 3.72 (3 H, s, OCH_3), 4.75–6.35 (3 H, m, olefinic protons), 6.53–7.10 (3 H, m, ArH); MS m/e 316 (M^+). Anal. Calcd for $C_{20}H_{28}O_3$: C, 75.91; H, 8.92. Found: C, 75.62; H, 8.79.

4α-(Benzyloxy)-1α-ethenyl-2α-[2-(4-methoxybenzocyclobutenyl)-2-(benzyloxy)ethyl]-1β-methylcyclohexane (27). To a solution of 170 mg (0.538 mmol) of diol **26** in 30 mL of anhydrous tetrahydrofuran were added 100 mg (2.5 mmol) of sodium hydride (60% in oil) and 200 mg (1.17 mmol) of benzyl bromide in 5 mL of anhydrous tetrahydrofuran. The mixture was refluxed for 16 h with stirring. The reaction mixture was poured into water and extracted 3 times with 50-mL portions of chloroform. This chloroform layer was washed with saturated sodium chloride solution and dried over anhydrous sodium sulfate. Evaporation

of the solvent gave a crude gum which was chromatographed on 5 g of silica gel, using benzene as eluant, to give 215 mg (81%) of dibenzyl ether **27** as a colorless oil: NMR ($CDCl_3$) δ 0.94, 1.00 (each s, CH_3), 3.72 (3 H, s, OCH_3), 4.46 (4 H, s, 2 CH_2Ph), 4.75–6.30 (3 H, m, olefinic protons), 6.50–7.10 (3 H, m, ArH), 7.20 (10 H, s, ArH); MS m/e 496 (M^+). Anal. Calcd for $C_{34}H_{40}O_3$: C, 82.22; H, 8.12. Found: C, 81.98; H, 8.25.

2α-Ethenyl-7-hydroxy-7-(4-methoxybenzocyclobutenyl)-2β-methyl-6-oxobicyclo[3.2.1]octane (32). (a). Thermolysis of 22. A solution of 100 mg (0.259 mmol) of pyranyl ether **22** in 20 mL of *o*-dichlorobenzene was refluxed for 1 h under an atmosphere of nitrogen. After evaporation of the solvent, the residue was chromatographed on 5 g of silica gel, using benzene as eluant, to give 75 mg (92%) of hemiacetal **32** as a colorless oil: IR ($CHCl_3$) 3600 (OH) cm^{-1}; NMR ($CDCl_3$) δ 1.11 (3 H, s, CH_3), 3.72 (3 H, s, OCH_3), 2.96–3.30 (2 H, m, CH_2Ar), 4.10–4.28 (1 H, br s, CHAr), 4.45–6.02 (3 H, m, olefinic protons), 6.50–6.97 (3 H, m, ArH); MS m/e 314 (M^+).

b. Thermolysis of 23. A solution of 100 mg (0.318 mmol) of keto alcohol **23** in 20 mL of *o*-dichlorobenzene was refluxed for 1 h under an atmosphere of nitrogen. After evaporation of the solvent, the residue was chromatographed on 5 g of silica gel, using benzene as eluant, to give 94 mg (94%) of hemiacetal **32** as a colorless oil, whose IR ($CHCl_3$) and NMR ($CDCl_3$) spectra were identical with those of the sample obtained above.

Thermolysis of 1. A solution of 525 mg (1.47 mmol) of olefinic ketone **1** in 100 mL of *o*-dichlorobenzene was refluxed for 45 min under an atmosphere of nitrogen. After evaporation of the solvent, the residue was chromatographed on 20 g of silica gel, using chloroform as eluant, to give 107 mg (20%) of (−)-4α-acetoxy-1-ethenyl-2-(7-methoxy-Δ^3-isochromenyl)-1β-methylcyclohexane (**28**) as a colorless oil: IR ($CHCl_3$) 1720 (C=O) cm^{-1}; NMR ($CDCl_3$) δ 1.10 (3 H, s, CH_3), 1.98 (3 H, s, CH_3), 3.75 (3 H, s, CH_3), 4.35–4.95 (1 H, m, CHOAc), 4.80–6.32 (4 H, m, olefinic protons), 6.45–7.10 (3 H, m, ArH); MS m/e 356 (M^+); $[\alpha]^{20}_D$ −12.5° (c 0.2).

Further elution with chloroform gave 244 mg (43%) of (−)-3α-acetoxy-17-methoxy-*D*-homo-18-nor-7-oxo-5β-androsta-13,15,17-triene (**3**) as colorless needles (methanol): mp 179–181 °C; IR ($CDCl_3$) 1720, 1700 (C=O) cm^{-1}; NMR ($CDCl_3$) δ 1.23 (3 H, s, CH_3), 1.96 (3 H, s, CH_3), 3.75 (3 H, s, CH_3), 4.40–5.0 (1 H, m, CHOAc), 6.50–7.20 (3 H, m, ArH); MS m/e 356 (M^+); $[\alpha]^{20}_D$ −49.6° (c 0.23). Anal. Calcd for $C_{22}H_{28}O_4$: C, 74.13; H, 7.92. Found: C, 74.00; H, 7.78.

(−)-3α,7α-Dihydroxy-17-methoxy-*D*-homo-18-nor-5β-androsta-13,15,17-triene (35). To a suspension of 50 mg (1.28 mmol) of lithium aluminum hydride in 10 mL of anhydrous tetrahydrofuran was added a solution of 93 mg (0.26 mmol) of acetate **3** in 5 mL of anhydrous tetrahydrofuran with stirring and the reaction mixture was then stirred for 3 h at room temperature. After addition of 10% aqueous sodium hydroxide solution and filtration of the inorganic material, followed by evaporation of tetrahydrofuran, the aqueous layer was extracted 3 times with 40-mL portions of ethyl acetate. The organic layer was combined, washed with saturated sodium chloride solution, and dried over anhydrous sodium sulfate. Removal of the solvent afforded a crude product which was chromatographed on 5 g of silica gel, using chloroform–ethyl acetate (2:1) as eluant, to give 80 mg (97%) of diol **35** as a colorless oil: IR ($CHCl_3$) 3600 cm^{-1} (OH); NMR ($CDCl_3$) δ 0.89 (3 H, s, CH_3), 3.10–3.60 (1 H, m, C_3-H), 3.73 (3 H, s, CH_3), 4.20–4.60 (1 H, br s, C_7-H), 6.57–7.25 (3 H, m, ArH); MS m/e 316 (M^+); $[\alpha]^{20}_D$ −42.5° (c 0.32). Anal. Calcd for $C_{20}H_{28}O_3$: C, 75.91; H, 8.92. Found: C, 75.67; H, 8.48.

Thermolysis of 25 and Separation of Products 30 and 31. A solution of 155 mg (0.497 mmol) of olefinic diketone **25** in 30 mL of *o*-dichlorobenzene was refluxed for 30 min under an atmosphere of nitrogen. After evaporation of the solvent, the residue was chromatographed on 5 g of silica gel, using chloroform as eluant, to give 115 mg (74%) of a mixture of **30** and **31** as a colorless oil: IR ($CHCl_3$) 1700 (C=O) cm^{-1}; NMR ($CDCl_3$) δ 1.32, 1.40 (each s, CH_3), 3.72 (3 H, s, OCH_3), 6.46–7.20 (3 H, m, ArH); MS m/e 312 (M^+). To a suspension of 50 mg (1.28 mmol) of lithium aluminum hydride in 20 mL of anhydrous tetrahydrofuran was added a solution of 100 mg (0.32 mmol) of the above mixture in 5 mL of anhydrous tetrahydrofuran with stirring and the reaction mixture was then stirred for 5 h at room temperature. After addition of 10% aqueous sodium hydroxide solution and filtration of the inorganic material, followed by evaporation of tetrahydrofuran, the aqueous layer was extracted 3 times with 50-mL portions of ethyl acetate. The organic layer was combined, washed with saturated sodium chloride solution, and dried over anhydrous sodium sulfate. Removal of the solvent afforded a crude product which was chromatographed on 5 g of silica gel, using chloroform as eluant, to give 32 mg (32%) of 3α,7α-dihydroxy-17-methoxy-*D*-homo-18-nor-5β,8α-androsta-13,15,17-triene as a colorless oil: IR ($CHCl_3$) 3580 cm^{-1} (OH); NMR ($CDCl_3$) δ 1.05 (3 H, s, CH_3), 3.75 (3 H, s, OCH_3), 3.85–4.25 (2 H, m, C_3-H, C_7-H), 6.50–7.20 (3 H, m, ArH); MS m/e 316 (M^+). Further elution with chloroform gave 55 mg (54%) of **35** as a colorless oil, whose IR ($CHCl_3$) and NMR ($CDCl_3$) spectra were identical with those of **35** obtained above.

To a solution of 30 mg (0.096 mmol) of 3α,7α-dihydroxy-17-methoxy-*D*-homo-18-nor-5β,8α-androsta-13,15,17-triene in 3 mL of acetone was added 3 drops of an 8 N solution of chromic acid (prepared from 26.72 g of chromium trioxide, 23 mL of concentrated sulfuric acid, and enough water to make the total volume of 100 mL as a solution) at 0 °C and stirring was continued for 10 min at the same temperature. The reaction mixture was diluted with 20 mL of water and extracted with ethyl acetate. The ethyl acetate layer was washed with saturated sodium chloride solution and dried over anhydrous sodium sulfate. Removal of the solvent gave a crude gum which was chromatographed on 2 g of silica gel, using chloroform as eluant, to give 24 mg (79%) of diketone **31** as a colorless oil: IR ($CDCl_3$) 1700 (C=O) cm^{-1}; NMR ($CDCl_3$) δ 1.40 (3 H, s, CH_3), 3.72 (3 H, s, OCH_3), 6.50–7.20 (3 H, m, ArH); MS m/e 312 (M^+); $[\alpha]^{20}_D$ −11.3° (c 0.124). Anal. Calcd for $C_{20}H_{24}O_3$: C, 76.89; H, 7.74. Found: C, 76.40; C, 7.61. To a solution of 55 mg (0.174 mmol) of diol **35** in 3 mL of acetone was added 3 drops of an 8 N solution of chromic acid at 0 °C and stirring was continued for 10 min at the same temperature. The reaction mixture was treated by the same procedure as above to give 48 mg (89%) of dione **30** as a colorless oil: IR ($CHCl_3$) 1700 (C=O) cm^{-1}; NMR ($CDCl_3$) δ 1.32 (3 H, s, CH_3), 3.72 (3 H, s, OCH_3), 6.50–7.20 (3 H, m, ArH); MS m/e 312 (M^+); $[\alpha]^{20}_D$ −50.5° (c 0.404). Anal. Calcd for $C_{20}H_{24}O_3$: C, 76.89; H, 7.74. Found: C, 76.65; H, 7.69.

Epimerization of Diketone 31. To a solution of 24 mg (0.077 mmol) of diketone **31** in 1 mL of acetone, 1 mL of methanol, and 1 mL of water was added 5 mg of potassium carbonate and the mixture then was stirred for 3 h. The reaction mixture was diluted with 30 mL of water and extracted 3 times with 40-mL portions of chloroform. This chloroform layer was washed with saturated sodium chloride solution and dried over anhydrous sodium sulfate. Removal of the solvent afforded a crude product which was chromatographed on 1 g of silica gel, using chloroform as eluant, to give 8 mg (33%) of diketone **30** as a colorless oil, whose IR ($CHCl_3$) and NMR ($CDCl_3$) spectra were identical with those of **30** obtained above.

3α,7β-Bis(benzyloxy)-17-methoxy-*D*-homo-18-nor-5β-androsta-13,15,17-triene (33). A solution of 210 mg (0.423 mmol) of dibenzyl ether **27** in 50 mL of *o*-dichlorobenzene was refluxed for 4 h under an atmosphere of nitrogen. After evaporation of the solvent the residue was chromatographed on 10 g of silica gel, using chloroform as eluant, to give 137 mg (65%) of dibenzyl ether **33** as a colorless oil: NMR ($CDCl_3$) δ 0.97 (3 H, s, CH_3), 3.70 (3 H, s, OCH_3), 4.46 (4 H, s, 2 CH_2Ph2), 6.40–7.00 (3 H, m, ArH), 7.20 (10 H, s, ArH); MS m/e 496 (M^+); $[\alpha]^{20}_D$ +31.9° (c 0.226). Anal. Calcd for $C_{34}H_{40}O_3$: C, 82.22; H, 8.12. Found: C, 81.83; H, 8.20.

3α,7β-Dihydroxy-17-methoxy-*D*-homo-18-nor-5β-androsta-13,15,17-triene (34). A mixture of 100 mg (0.20 mmol) of dibenzyl ether **33** and 10 mg of 20% palladium–carbon in 10 mL of acetic acid was stirred under an atmosphere of hydrogen at room temperature. Hydrogenation was carried out smoothly at 3 atm of hydrogen and was completed within 16 h. The solution was then filtered free of catalyst and the catalyst was washed with ethyl acetate. The filtrates were combined and evaporated to yield the crude product which was chromatographed on 5 g of silica gel, using chloroform as eluant, to give 48 mg (75%) of diol **34** as a colorless oil: IR ($CHCl_3$) 3570 (OH) cm^{-1}; NMR ($CDCl_3$) δ 0.97 (3 H, s, CH_3), 3.72 (3 H, s, OCH_3), 6.45–7.15 (3 H, m, ArH); MS m/e 316 (M^+); $[\alpha]^{20}_D$ −17.3° (c 0.242). Anal. Calcd for $C_{20}H_{28}O_3$: C, 75.91; H, 8.92. Found: C, 75.73; H, 8.82.

17-Methoxy-3,7-dioxo-*D*-homo-18-nor-5β-androsta-13,15,17-triene (30). To a solution of 48 mg (0.152 mmol) of diol **34** in 3 mL of acetone was added 3 drops of an 8 N solution of chromic acid (prepared from 26.72 g of chromium trioxide, 23 mL of concentrated sulfuric acid, and enough water to make the total volume of 100 mL as a solution) at 0 °C and stirring was continued for 10 min at the same temperature. The reaction mixture was diluted with 20 mL of water and extracted with chloroform. The organic layer was washed with saturated sodium chloride solution and dried over anhydrous sodium sulfate. Evaporation of the solvent afforded a crude product which was chromatographed on 2 g of silica gel, using chloroform as eluant, to give 34 mg (72%) of diketone **30** as a colorless oil, which was identical with the compound **30** obtained above by IR ($CHCl_3$) and NMR ($CDCl_3$) spectral comparison.

(−)-3α,7α-Dihydroxy-*D*-homo-18-nor-5β-androst-13(17a)-en-17-one (42). To a stirred solution of 100 mg (14.3 mmol) of lithium in 100 mL of liquid ammonia, 50 mL of anhydrous *tert*-butyl alcohol, and 50 mL of anhydrous tetrahydrofuran at −78 °C was added 850 mg (2.69 mmol) of diol **35** in 10 mL of anhydrous tetrahydrofuran. Stirring was continued for 4 h at −78 °C. After addition of an excess of ethanol, followed by evaporation of the solvent, 50 mL of water was added and the resulting mixture was extracted 3 times with 50-mL portions of ethyl acetate. The organic layer was washed with saturated sodium chloride solution and dried over anhydrous sodium sulfate. After removal of the solvent, the residue was dissolved in 20 mL of methanol. The resulting solution was treated with 0.5 mL of 10% aqueous hydrochloric acid solution and refluxed for 1 h. After evaporation of the solvent, 50 mL of water was added and the resulting mixture was extracted with chloroform. The organic layer was washed with saturated sodium bicarbonate solution and saturated sodium chloride solution and dried over anhydrous sodium sulfate. Evaporation of the solvent afforded a crude product which was chromatographed on 20 g of silica gel, using chloroform–ethyl acetate (4:1) as eluant, to give 295 mg (36%) of enone **42** as colorless needles (ethyl acetate): mp 228–230 °C; IR ($CHCl_3$) 3600 (OH), 1660 (C=O) cm^{-1}; NMR ($CDCl_3$) δ 0.84 (3 H, s, CH_3), 3.25–3.90 (1 H, m, C_3-H), 3.98–4.30 (1 H, br s, C_7-H), 5.80–5.93 (1 H, br s, olefinic proton); MS *m/e* 304 (M^+); $[\alpha]^{20}_D$ −45.0° (*c* 0.2). Anal. Calcd for $C_{19}H_{28}O_3$: C, 74.96; H, 9.27. Found: 74.86; H, 8.86.

(−)-13,17a-Epoxy-3α,7α-dihydroxy-*D*-homo-18-nor-5β-androstan-17-one (43). To a solution of 295 mg (0.97 mmol) of the enone **42** in 10 mL of methanol was added 0.5 mL of 30% aqueous hydrogen peroxide solution and 0.5 mL of 10% aqueous sodium hydroxide solution with stirring at 0 °C. After the mixture was stirred for 30 min at 0 °C, 50 mL of water was added and the resulting mixture was extracted with chloroform. The chloroform layer was washed with saturated sodium chloride solution and dried over anhydrous sodium sulfate. Evaporation of solvent gave a crude product which was chromatographed on 5 g of silica gel, using chloroform–ethyl acetate (4:1) as eluant, to give 273 mg (88%) of epoxy ketone **43** as colorless needles (methanol): mp 258–261 °C; IR ($CHCl_3$) 3600 (OH), 1700 (C=O) cm^{-1}; NMR ($CDCl_3$) δ 0.70 (3 H, s, CH_3), 3.04 (1 H, s, epoxy H), 3.05–3.85 (1 H, br s, $C_{3\beta}$-H), 3.8–4.30 (1 H, br s, $C_{7\beta}$-H); MS *m/e* 320 (M^+); $[\alpha]^{20}_D$ −69.2° (*c* 0.266). Anal. Calcd for $C_{19}H_{28}O_4$: C, 71.22; H, 8.81. Found: C, 71.26; H, 8.44.

(−)-1-(3-Butynyl)-3,4,4aα,4b,5,6,7,8,8a,9,10,10aβ-dodecahydro-7α,10α-dihydroxy-4bβ-methylphenanthren-2(1*H*)-one (44). A mixture of 244 mg (0.76 mmol) of epoxy ketone **43** and 142 mg (0.76 mmol) of *p*-toluenesulfonylhydrazine in 7 mL of acetic acid and 7 mL of dichloromethane was stirred for 10 min at −18 °C and then allowed to stand at −20 °C for 15 h. After being stirred for 4 h at room temperature, the reaction mixture was diluted with 20 mL of water and extracted 3 times with dichloromethane. This extract was washed with saturated sodium bicarbonate solution and saturated sodium chloride solution and dried over anhydrous sodium sulfate. Removal of the solvent afforded a yellow gum which was chromatographed on 5 g of silica gel, using chlorform–ethyl acetate (9:1) as eluant, to give 187 mg (81%) of acetylenic ketone **44** as a colorless oil: IR ($CHCl_3$) 3600 (OH), 3310 (C≡CH), 1700 (C=O) cm^{-1}; NMR ($CDCl_3$) δ 0.83 (3 H, s, CH_3), 3.20–3.80 (1 H, m, $C_{3\beta}$-H), 4.00–4.20 (1 H, br s, $C_{7\beta}$-H); MS *m/e* 286 (M^+ − 18); $[\alpha]^{20}_D$ −4.0° (*c* 0.2). Anal. Calcd for $C_{19}H_{28}O_3$: C, 74.96; H, 9.27. Found: C, 74.72; H, 9.18.

1-(3-Butynyl)-7α,10α-dihydroxy-2,4bβ-dimethyl-1,2,3,4,4aα,4b,5,6,7,8,8a,9,10,10aβ-tetradecahydro-2-phenanthrenol (45). To a solution of 185 mg (0.61 mmol) of acetylenic ketone **44** in 5 mL of anhydrous tetrahydrofuran was added 3 mL of 1.5 M ethereal solution of methyl lithium at 0 °C and the mixture was stirred for 30 min at 0 °C and then for 10 min at room temperature. The reaction mixture was treated with 40 mL of water and extracted with ether. The ethereal layer was washed with saturated sodium chloride solution and dried over anhydrous sodium sulfate. Evaporation of the solvent gave a crude product which was chromatographed on 5 g of silica gel, using chloroform–ethyl acetate (4:1) as eluant, to give 104 mg (55%) of triol **45** as a colorless oil: IR ($CHCl_3$) 3600 (OH), 3310 (C≡CH) cm^{-1}; NMR ($CDCl_3$) δ 0.87 (3 H, s, CH_3), 1.24 (3 H, s, CH_3), 3.15–3.80 (1 H, m, $C_{3\beta}$-H), 4.00–4.22 (1 H, br s, $C_{7\beta}$-H); MS *m/e* 302 (M^+ − 18). Anal. Calcd for $C_{20}H_{30}O_2$: 302.2257 (M^+ − 18). Found: 302.2259.

1,2,3,4,4aα,4b,5,6,7,8,8a,9,10,10aβ-Tetradecahydro-7α,10α-dihydroxy-2,4bβ-dimethyl-1-(3-pentynyl)-2-phenanthrenol (46). To a solution of lithium amide [prepared from 200 mg (28.6 mmol) of lithium and an excess of liquid ammonia] in 50 mL of liquid ammonia was added 101 mg (0.32 mmol) of triol **45** in 10 mL of anhydrous tetrahydrofuran under an atmosphere of nitrogen at −33 °C. After the mixture was stirred for 30 min, 0.7 mL (11.2 mmol) of methyl iodide was added and stirring was continued for 1 h. The reaction mixture was treated with the excess ammonium chloride and the solvent was evaporated. The reddish residue was diluted with saturated aqueous ammonium chloride solution and the resulting mixture was extracted 3 times with 40-mL portions of ethyl acetate. This extract was washed with saturated sodium chloride solution and dried over anhydrous sodium sulfate. Removal of the solvent afforded a crude product which was chromatographed on 3 g of silica gel, using chloroform–ethyl acetate (9:1) as eluant, to give 83.7 mg (79%) of triol **46** as a colorless oil: IR ($CHCl_3$) 3600 (OH) cm^{-1}; NMR ($CDCl_3$) δ 0.88 (3 H, s, CH_3), 1.23 (3 H, s, CH_3), 1.78 (3 H, t, J = 2 Hz, CH_3), 3.10–3.75 (1 H, m, $C_{3\beta}$-H), 3.98–4.20 (1 H, br s, $C_{7\beta}$-H); MS *m/e* 334 (M^+). Anal. Calcd for $C_{21}H_{34}O_3$: 334.24745 (M^+). Found: 334.2471.

(+)-3α,7α-Dihydroxy-5β-pregnan-20-one (47). To a mixture of 1.5 mL of trifluoroacetic acid and 0.75 mL of trifluoroacetic anhydride was added 34 mg (0.10 mmol) of acetylenic alcohol **46** and the resulting mixture was stirred for 1.5 h at room temperature. After evaporation of the solvent, the residue was dissolved in 10 mL of methanol and the resulting solution was treated with 0.5 mL of 10% methanolic potassium hydroxide solution and then stirred for 4 h at room temperature. Removal of the solvent afforded the residue, which was extracted 3 times with 50-mL portions of ethyl acetate. This extract was washed with saturated sodium chloride solution and dried over anhydrous sodium sulfate. Evaporation of the solvent gave a crude product which was chromatographed on 2 g of silica gel, using chloroform–ethyl acetate (9:1) as eluant, to give 27.4 mg (81%) of diol **47** as colorless prisms (acetone): mp 213–215 °C: IR ($CHCl_3$) 3580 (OH), 1685 (C=O) cm^{-1}; NMR ($CDCl_3$) δ 0.61 (3 H, s, CH_3), 0.90 (3 H, s, CH_3), 2.11 (3 H, s, CH_3), 3.15–3.75 (1 H, m, $C_{3\beta}$-H), 3.80–3.95 (1 H, br s, $C_{7\beta}$-H); MS *m/e* 334 (M^+); $[\alpha]^{20}_D$ +41.3° (*c* 0.17). Anal. Calcd for $C_{21}H_{34}O_3$: C, 75.40; H, 10.25. Found: C, 74.95; H, 10.28.

(+)-3α,7α-Diacetoxy-5β-pregnan-20-one (55). A solution of 700 mg (1.18 mmol) of diene **54** dissolved in 10 mL of ethyl acetate was cooled to −78 °C and oxidized by bubbling ozone through the above solution until it became deep blue. This solution was left at −78 °C for 1 h and then an excess of methyl sulfide was added, and the mixture was warmed to room temperature. The organic layer was washed with saturated sodium chloride solution and dried over anhydrous sodium sulfate. Evaporation of the solvent afforded a crude product which was chromatographed on 5 g of silica gel, using benzene–ethyl acetate (9:1) as eluant, to give 450 mg (92%) of diacetate **55** as a colorless oil: IR ($CHCl_3$) 1720 (C=O), 1685 (C=O) cm^{-1}; NMR ($CDCl_3$) δ 0.60 (3 H, s, CH_3), 0.93 (3 H, s, CH_3), 2.00 (3 H, s, CH_3), 2.04 (3 H, s, CH_3), 2.10 (3 H, s, CH_3), 4.25–5.03 (2 H, m, $C_{3\beta}$-H, $C_{7\beta}$-H); MS *m/e* 418 (M^+); $[\alpha]^{20}_D$ +81.8° (*c* 0.21). Anal. Calcd for $C_{25}H_{38}O_5$: C, 71.14; H, 9.15. Found: C, 71.26; H, 9.57.

(+)-3α,7α-Diacetoxy-20,20-(1,2-ethylenedioxy)-5β-pregnane (56). To a solution of 430 mg (1.02 mmol) of ketone **55** in 40 mL of benzene was added a catalytic amount of *p*-toluenesulfonic acid and 1 g (16.3 mmol) of ethylene glycol. The reaction mixture was refluxed in a flask fitted with a Dean–Stark trap. After 4 h the reaction mixture was cooled. The benzene layer was separated and washed with saturated sodium bicarbonate solution and saturated sodium chloride solution and dried over anhydrous sodium sulfate. Removal of the solvent afforded a crude product which was chromatographed on 10 g of silica gel, using benzene–ethyl acetate (20:1) as eluant, to give 405 mg (85%) of ketal **56** as a colorless oil: IR ($CHCl_3$) 1720 (C=O) cm^{-1}; NMR ($CDCl_3$) δ 0.74 (3 H, s, CH_3), 0.94 (3 H, s, CH_3), 1.24 (3 H, s, CH_3), 2.00 (3 H, s, CH_3), 2.03 (3 H, s, CH_3), 3.80–4.00 (4 H, br s, OCH_2CH_2O), 4.25–5.00 (2 H, m, $C_{3\beta}$-H, $C_{7\beta}$-H); MS *m/e* 462 (M^+); $[\alpha]^{20}_D$ +12.4° (*c* 0.31). Anal. Calcd for $C_{27}H_{42}O_6$: C, 70.10; H, 9.15. Found: C, 70.58; H, 9.08.

(+)-20,20-(1,2-Ethylenedioxy)-5β-pregnane-3α,7α-diol (57). To a suspension of 100 mg (2.63 mmol) of lithium aluminum hydride in 50 mL of anhydrous tetrahydrofuran was added 405 mg (0.88 mmol) of diacetate **56** in 5 mL of anhydrous tetrahydrofuran and the resulting solution was stirred for 1.5 h at room temperature. After the reaction mixture was quenched with 10% aqueous sodium hydroxide solution, the inorganic substance was filtered. After evaporation of the solvent the residue was extracted 3 times with 50-mL portions of chloroform. The organic layer was washed with saturated sodium chloride solution and dried over anhydrous sodium sulfate. Removal of solvent gave a crude gum which was chromatographed on 10 g of silica gel, using chloroform–ethyl acetate (9:1) as eluant, to give 260 mg (79%) of diol **57** as a colorless oil: IR ($CHCl_3$) 3600 (OH) cm^{-1}; NMR ($CDCl_3$) δ 0.74 (3 H, s, CH_3), 0.90 (3 H, s, CH_3), 1.28 (3 H, s, CH_3), 3.15–3.75 (1 H, m, $C_{3\beta}$-H), 3.70–4.10 (5 H, br s, $C_{7\beta}$-H, OCH_2CH_2O); MS *m/e* 378 (M^+); $[\alpha]^{20}_D$ +7.10 (*c* 0.226). Anal. Calcd for $C_{23}H_{38}O_4$: C, 72.97; H, 10.12. Found: C, 73.37; H, 10.28.

(+)-3α,7α-Dihydroxy-5β-pregnan-20-one (47). To a stirred solution of 245 mg (0.65 mmol) of ketal **57** in 3 mL of methanol was added 5 drops of 5% aqueous hydrochloric acid solution. After the mixture was stirred for 4 h, evaporation of the solvent afforded a residue, which was extracted 3 times with 40-mL portions of chloroform. This chloroform layer was washed with saturated sodium bicarbonate solution and saturated sodium chloride solution and dried over anhydrous sodium sulfate. Evaporation of the solvent afforded a crude product which was chromatographed on 5 g of silica gel, using chloroform–ethyl acetate (9:1) as eluant, to give 203 mg (94%) of diol **47** as colorless needles (acetone): mp 213–215 °C; $[\alpha]^{20}_D$ +44.3° (*c* 0.252), which was identical with **47** obtained above by IR ($CHCl_3$) and NMR ($CDCl_3$) spectral comparison.

24,24-(Ethylenedioxy)-5β-cholane-3α,7α,20-triol (48). To a solution of 51 mg (0.15 mmol) of diol **47** in 3 mL of anhydrous tetrahydrofuran was added a solution of a Grignard reagent [prepared from 56 mg (2.3 mmol) of magnesium and 417 mg (2.3 mmol) of bromo acetal **7** in 8 mL of anhydrous tetrahydrofuran]. After the mixture was stirred for 1.5 h at room temperature under an atmosphere of nitrogen, 50 mL of water was added and the resulting mixture was extracted 3 times with 50-mL portions of ethyl acetate. This organic layer was washed with saturated sodium chloride solution and dried over anhydrous sodium sulfate. Evaporation of the solvent afforded a crude product which was chromatographed on 2 g of silica gel, using chloroform–ethyl acetate (1:1) as eluant, to give 65 mg (98%) of **48** as a colorless oil: IR ($CHCl_3$) 3600 (OH) cm^{-1}; NMR ($CDCl_3$) δ 0.83 (3 H, s, CH_3), 0.89 (3 H, s, CH_3), 1.25 (3 H, s, CH_3), 3.20–4.20 (6 H, m, OCH_2CH_2O, $C_{3\beta}$-H, $C_{7\beta}$-H), 4.70–4.96 (1 H, br s, HCO_2); MS *m/e* 418 (M^+ – 18). Anal. Calcd for $C_{26}H_{44}O_5$: C, 71.52; H, 10.16. Found: C, 70.94; H, 9.91.

3α,7α-Diacetoxy-24,24-(1,2-ethylenedioxy)-20-hydroxy-5β-cholane (49). To a solution of 65 mg (0.15 mmol) of diol **48** in 5 mL of pyridine were added 0.5 g (4.9 mmol) of acetic anhydride and a catalytic amount of 4-(dimethylamino)pyridine at room temperature under nitrogen and the mixture was stirred for 8 h. The reaction mixture was poured into 30 mL of water and extracted 3 times with 40-mL portions of ethyl acetate. This ethyl acetate extract was washed with saturated potassium bisulfate solution, saturated sodium bicarbonate solution, and saturated sodium chloride solution and dried over anhydrous sodium sulfate. Evaporation of the solvent afforded a crude product which was chromatographed on 2 g of silica gel, using chloroform as eluant, to give 61 mg (78%) of diacetate **49** as a colorless oil: IR ($CHCl_3$) 3600 (OH), 1720 (C=O) cm^{-1}; NMR ($CDCl_3$) δ 0.82 (3 H, s, CH_3), 0.93 (3 H, s, CH_3), 1.23 (3 H, s, CH_3), 2.00 (3 H, s, CH_3), 2.03 (3 H, s, CH_3), 3.70–4.00 (4 H, br s, OCH_2CH_2O), 4.30–4.95 (3 H, m, $C_{3\beta}$-H, $C_{7\beta}$-H, CHO_2); MS *m/e* 502 (M^+ – 18). Anal. Calcd for $C_{30}H_{48}O_7$: 459.3073 (M^+ – 61). Found: 459.3069.

3α,7α-Diacetoxy-24,24-(1,2-ethylenedioxy)-5β-cholan-21-ene (50). A mixture of 59 mg (0.11 mmol) of alcohol **49** in 1.5 mL of pyridine and 0.5 mL of phosphoryl chloride was stirred for 14 h at room temperature under an atmosphere of nitrogen. The reaction mixture was poured into 20 mL of water and extracted 3 times with 40-mL portions of ethyl acetate. This organic layer was washed with saturated potassium bisulfate solution, saturated sodium bicarbonate solution, and saturated sodium chloride solution and dried over anhydrous sodium sulfate. Removal of the solvent afforded a crude product which was chromatographed on 5 g of silica gel, using chloroform as eluant, to give 16 mg (28%) of monoene **50** as a colorless oil: IR ($CHCl_3$) 1720 (C=O) cm^{-1}; NMR ($CDCl_3$) δ 0.53, 0.55 (each s, CH_3), 0.92 (3 H, s, CH_3), 1.65 (3 H, s, CH_3), 1.99 (6 H, s, 2 CH_3), 3.70–4.03 (4 H, br s, OCH_2CH_2O), 4.30–5.25 (4 H, m, CHO_2, olefinic protons, $C_{3\beta}$-H, $C_{7\beta}$-H); MS *m/e* 502 (M^+). Anal. Calcd for $C_{30}H_{46}O_6$: 502.3327 (M^+). Found: 502.3324.

(–)-3α,7α-Diacetoxy-5β-cholanoic Acid (53). A mixture of 16 mg (0.03 mmol) of monoene **50** and 3 mg of platinum oxide in 3 mL of methanol was stirred under an atmosphere of hydrogen at room temperature. Hydrogenation proceeded smoothly at atmospheric pressure and was completed within 3 h. The solution was then filtered to remove the catalyst, which was washed with methanol. The filtrate and washing were combined and evaporated to yield crude ketal **51**, which was used in the next reaction without purification: IR ($CHCl_3$) 1720 (C=O) cm^{-1}; NMR ($CDCl_3$) δ 0.65 (3 H, s, CH_3), 0.93 (6 H, br s, 2 CH_3), 2.01 (6 H, s, 2 CH_3), 3.70–4.00 (4 H, br s, OCH_2CH_2O), 4.30–5.05 (3 H, m, CHO_2, $C_{3\beta}$-H, $C_{7\beta}$-H); MS *m/e* 504 (M^+).

To a solution of crude ketal **51** in 3 mL of acetone was added 3 drops of 10% aqueous hydrochloric acid solution and the reaction mixture was stirred for 1 h at room temperature. The solvent was removed by evaporation and the residue was diluted with 20 mL of water and extracted 3 times with 40-mL portions of ethyl acetate. This organic layer was washed with saturated sodium bicarbonate solution and saturated sodium chloride solution and dried over anhydrous sodium sulfate. Removal of the solvent afforded the crude aldehyde **52**, which was used in the next reaction without purification: IR ($CHCl_3$) 1720 (C=O) cm^{-1}; NMR ($CDCl_3$) δ 0.67 (3 H, s, CH_3), 0.93 (6 H, br s, 2 CH_3), 2.03 (3 H, s, CH_3), 2.06 (3 H, s, CH_3), 4.30–5.00 (2 H, m, $C_{3\beta}$-H, $C_{7\beta}$-H), 9.60–9.80 (1 H, br s, CHO); MS *m/e* 460 (M^+).

To a solution of the above crude aldehyde **52** in 3 mL of acetone was added 1 drop of an 8 N solution of chromic acid (prepared from 26.72 g of chromium trioxide, 23 mL of concentrated sulfuric acid, and enough water to make the total volume of 100 mL as a solution) at 0 °C and stirring was continued for 5 min at the same temperature. The reaction mixture was diluted with 20 mL of water and extracted 3 times with 40-mL portions of ethyl acetate. The combined organic layer was washed with saturated sodium chloride solution and dried over anhydrous sodium sulfate. Removal of the solvent afforded the crude product which was chromatographed on 2 g of silica gel, using chloroform as eluant, to give 5.5 mg (38%) of carboxylic acid **53** as colorless needles (ethyl acetate–hexane): mp 206–208 °C; IR ($CHCl_3$) 1720 (C=O) cm^{-1}; NMR ($CDCl_3$) δ 0.67 (3 H, s, CH_3), 0.93 (6 H, br s, 2 CH_3), 2.01 (3 H, s, CH_3), 4.30–4.95 (2 H, m, $C_{3\beta}$-H, $C_{7\beta}$-H), 8.50–9.50 (1 H, m, CO_2H); MS *m/e* 476 (M^+); $[\alpha]^{20}_D$ –6.2° (*c* 0.128). Anal. Calcd for $C_{28}H_{44}O_6$: C, 70.55; H, 9.31. Found: C, 70.34; H, 9.25.

(+)-Chenodeoxycholic Acid (4). A mixture of 105 mg (0.22 mmol) of diacetate **53** in 20 mL of methanol and 1 mL of 10% aqueous sodium hydroxide solution was refluxed for 48 h. After evaporation of the solvent, the residue was treated with 2 mL of 10% aqueous hydrochloric acid solution and extracted 3 times with 40-mL portions of chloroform. This chloroform layer was washed with saturated sodium chloride solution and dried over anhydrous sodium sulfate. Evaporation of the solvent afforded

a crude product which was chromatographed on 5 g of silica gel, using chloroform–ethyl acetate (3:2) as eluant, to give 76 mg (88%) of chenodeoxycholic acid (4) as colorless needles (ethyl acetate–hexane), which was identified by comparison with an authentic sample, obtained by purification of commercially available (+)-chenodeoxycholic acid, of its IR ($CHCl_3$), NMR ($CDCl_3$), and mass spectra, including optical rotation and mixture melting point test. 4: mp 143–145 °C; IR ($CHCl_3$) 1705 (C=O) cm^{-1}; NMR ($CDCl_3$) δ 0.66 (3 H, s, CH_3), 0.92 (3 H, s, CH_3), 0.94 (3 H, d, J = 4 Hz, CH_3), 3.20–3.75 (1 H, m, $C_{3\beta}$-H), 3.75–4.00 (1 H, br s, $C_{7\beta}$-H); MS m/e 392 (M^+); $[\alpha]^{20}_D$ +11.2° (c 0.142, EtOH).

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Reductive Condensation of Methyl Arylglyoxylates. Direct Synthesis of 2,3-Bis(carbomethoxy)stilbene Oxides and Related Systems

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A number of aryl-substituted 2,3-bis(carbomethoxy)stilbene oxides have been prepared by reductive condensation of the corresponding methyl phenylglyoxylates induced with hexamethylphosphorous triamide. The stereochemical assignments to the parent isomeric phenylglycidates provided an unexpected challenge. The earlier literature in this area has been reviewed and previous structural conclusions have been reconciled. These oxiranes have been prepared in order to employ in our continuing direct, energy and electron transfer photochemical studies of such substrates. The related epoxydiphenylsuccinic anhydride and imide show particularly interesting photochemical properties.

In an expansion of our continuing research on the photochemistry of small-ring heterocyclic compounds, we became interested in preparing substituted 2,3-bis(carbomethoxy)stilbene oxides for use as potential carbene[3] and carbonyl ylide[4] precursors. From our previous observations it was apparent that stilbene oxides of this type should be photolabile, exhibit photochromic properties, and fragment to carbenes.[3,4] For example, *trans*-2,3-dicyanostilbene oxide undergoes photocleavage to phenylcyanocarbene and benzoyl cyanide.[3a,d,f,g] Huisgen[5] was the first to report that the isomeric pair of 2,3-dicyanostilbene oxides undergo *thermal* additions to a variety of dipolarophiles. We anticipated that these synthetically useful reactions which proceed by way of carbonyl ylides might be extended to the title esters and that such [2 + 3 → 5] cycloadditions perhaps could be induced thermally and/or photochemically.[6]

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