Total Synthesis of 13 β -Allylgonanes. II¹⁾KOUICHI YOSHIOKA, GIICHI GOTO, KENTARO HIRAGA,
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In order to protect selectively the double bond of the allyl group at C-13 in 3-methoxy-13-allyl-8,14-secogona-1,3,5(10),9-tetraene-14,17-dione (I), the authors established the synthesizing route via 9 α ,14 α -epoxy-3-methoxy-13 β -allyl-8,14-secogona-1,3,5(10)-trien-17-one (IV), which was converted into the diol (VI) or the dibromide (XXVI).

Reaction of VI with acetic anhydride and *p*-toluenesulfonic acid gave the gonapentaene triacetate (X), but treatment of VI with hydrochloric acid in methanol yielded a novel steroid (VIII).

In the preceding paper,¹⁾ we reported the synthesis of *dl*-17 α -ethynyl-17 β -hydroxy-13 β -allylgon-4-en-3-one via *dl*-17 β ,2'-epoxy-3-methoxy-13 β -propylgon-1,3,5(10),8,14-pentaene. Formation of the 17 β ,2'-epoxy group protected the allyl group from reducing agents used in the sequence of reactions. This paper describes an alternative synthesis of 13 β -allylgonanes.

Treatment of I with sodium borohydride in tetrahydrofuran and methanol at temperatures of -20° to -30° gave two products. NMR spectral evidence indicated that they were II and III, formed in a ratio of 2:1; δ 3.68 (2/3 $\times$ 3H, singlet, OCH₃), 4.15 (2/3 $\times$ 1H, quartet_{ABX}, J_{AX} =6 Hz, J_{BX} =9 Hz, 14 β H), 3.74 (1/3 $\times$ 3H, singlet, OCH₃), 4.20 (1/3 $\times$ 1H, triplet, J =6 Hz, 14 α H). The yield of the desired II was slightly low compared to the corresponding ketol of the 13-methyl series (77.5%),³⁾ this was due to the difference in bulkiness between the two substituents at C-13.

Treatment of the ketol mixture (II and III) with *p*-toluenesulfonic acid in benzene gave two crystalline products: the 9 α ,14 α -epoxide (IV), $\lambda_{\max}$ nm (ϵ): 277 (1680), 283 (1640), $\nu_{\max}$ cm⁻¹: 1740 (C=O), δ 3.95 (1H, triplet, J =2 Hz, C₁₄-H), 4.9-5.9 (3H, multiplet, CH₂=CH), and the 9 β ,14 α -epoxide (V), δ 3.95 (1H, triplet, J =2 Hz, C₁₄-H). With thin-layer chromatography (TLC), V was easily isomerized in acidic solution into the thermodynamically more stable⁴⁾ IV. These two isomers (IV and V) were formed at a ratio of 1:1 after 1 hour but the ratio became 60:1 after 2 hours. III suffered no reaction.

The 9,14-epoxidation effectively protected the C-9 double bond and provided a convenient intermediate (IV) for selective modification of the angular allyl group. Treatment of IV with osmium tetroxide gave the diol (VI), and treatment with bromine gave the dibromide (XXVI) in good yield.

Attempts to prepare a gonapentaene derivative by treatment of VI with hydrochloric acid in methanol gave only the 14 β ,2'-epoxide (VIII), $\lambda_{\max}$ nm (ϵ): 274 (13300), $\nu_{\max}$ cm⁻¹: 3400-3500 (OH), δ 3.3-3.7 (2H, multiplet, CH₂-O), 4.15-4.40 (1H, multiplet, CH-O). In this case, when the reaction time was short, the acetal (VII) was isolated as an intermediate. VII was easily converted into VIII under these reaction conditions. The nuclear magnetic

1) Part I: K. Yoshioka, T. Asako, G. Goto, K. Hiraga, and T. Miki, *Chem. Pharm. Bull.* (Tokyo), **21**, 2195 (1973).

2) Location: Juso-Nishino-cho, Higashiyodogawa-ku, Osaka.

3) T. Miki and K. Hiraga, *J. Patent* 14781 (1970) [*C.A.*, **73**, 45688 (1970)].

4) T. Asako, K. Hiraga, and T. Miki, *Chem. Commun.*, **1969**, 1011; T. Asako, K. Hiraga, and T. Miki, *Chem. Pharm. Bull.* (Tokyo), **21**, 703 (1973).

resonance (NMR) spectrum of VII had two singlets for O-methyl protons at C-17, indicating that VII was a mixture of two stereoisomers at C-2' in the angular substituent.

Attempts to convert the diacetate (IX) into the gonapentaene (X) by treatment with *p*-toluenesulfonic acid, anhydrous phosphoric acid or acetic acid, resulted in recovery of the starting material. On the other hand, treatment with conc. hydrochloric acid or perchloric acid gave VIII. Finally, X was obtained by treatment of IX with a large excess of *p*-toluenesulfonic acid in acetic anhydride. The ultraviolet (UV) spectrum of X was characteristic of a gonapentaene system, $\lambda_{\max}$ nm (ϵ): 310 (20400). When VI or VIII was treated under the same conditions, the desired X was also obtained in high yield.

In these reactions, the 15-acetyl compound (XI) was isolated as a by-product, $\lambda_{\max}$ nm (ϵ): 350 (17900), δ 2.28 (3H, singlet, COCH₃). Reduction of XI with sodium borohydride yielded XII, $\lambda_{\max}$ nm: 316. Since prolonged treatment of VI increased the yield of XI, this reaction was a good route for introduction of an acetyl group at the C-15 position of the steroidal skeleton.

Chart 1

Selective catalytic hydrogenation of X in the presence of a large amount of Raney nickel or platinum oxide yielded the gonatetraene (XIII), $\lambda_{\max}$ nm 275. The C/D ring junction was assumed to be *trans*, because hydrogen would have attacked from the less hindered α side of X.

Complete catalytic hydrogenation of X or XIII over Raney nickel or platinum oxide gave the 8-isogonatriene (XIV) in high yield, $\lambda_{\max}$ nm 277, 286. These products (X, XIII and XIV) were oily substances, shown to be a mixture of two components by NMR spectra, which indicated the presence of stereoisomers at C-2'. The product (XIV) was separated into two crystalline components (XIVa and XIVb) by careful column chromatography on silica gel. Selective hydrolysis of XIVa and XIVb with 1% potassium hydroxide-methanol to the diols (XVa and XVb), followed by oxidation with periodic acid, yielded the identical 18-aldehyde (XVI) from both diols.

Chart 2

Controlled hydrolysis of XIII with 1% potassium hydroxide-methanol yielded the diol acetate (XVII) as a major product. Treatment of XVII with methanesulfonyl chloride in pyridine gave the dimesylate (XVIII) in quantitative yield, which then was converted by treatment with sodium iodide and zinc powder in dimethyl formamide⁵⁾ to the 13 β -

allyl compound (XIX) in 80% yield. This structure was confirmed by NMR spectrum; the terminal olefinic protons gave a multiplet at δ 4.70–5.40 and the other olefinic proton a multiplet at δ 5.53–6.35. Hydrolysis of XIX gave the 17 α -hydroxy compound (XX) in high yield (98%), $\nu_{\max}$ cm⁻¹: 3400 (OH).

Chart 3

XX, treated with potassium in liq. ammonia and tetrahydrofuran, gave the gonatriene (XXI) in 81% yield, $\lambda_{\max}$ nm: 278, 285. Birch reduction of XXI with lithium in liq. ammonia, ethanol and tetrahydrofuran followed by acid treatment gave the 4-en-3-one compound (XXIII) in 30% yield, $\nu_{\max}$ cm⁻¹: 1660, 1620 (C=C-C=O), 3050, 1635, 910 (allyl). These reaction conditions were critical; we obtained only the 13 β -propyl compound (XXIV) in another run. As described in the preceding paper,¹⁾ it became necessary to protect the hydroxy group at C-17 prior to Birch reduction. Treatment of XXI with dihydropyran in the presence of boron trifluoride etherate as a catalyst⁶⁾ gave the tetrahydropyranyl ether (XXII) in good yield. Birch reduction of XXII, followed by acid treatment, gave XXIII in 57% yield. The B/C ring juncture of XXIII was assigned *trans* on the basis of our previous work.⁷⁾

Chart 4

5) R.S. Tipson and A. Cohen, *Carbohydrate Res.*, **1**, 338 (1965).

6) H. Alper and L. Dinkes, *Synthesis*, **1972**, 81.

7) T. Miki, K. Hiraga, and T. Asako, *Proc. Chem. Soc.*, **1963**, 139.

Oxidation of XXIII with chromium trioxide-pyridine complex gave the diketone (XXV) in 66% yield; it was identical in all respects to a sample prepared previously.¹⁾

We examined another possible sequence to the 13 β -allylgonanes. Treatment of IV with bromine in chloroform at -10° yielded the dibromide (XXVI), which was converted by treatment with hydrochloric acid in acetone into the gonapentaene (XXVII) in high yield, $\lambda_{\max}$ nm: 312. Attempts to hydrogenate selectively the C-14 double bond of XXVII over Raney nickel or palladium on barium carbonate were unsuccessful, giving debrominated 13 β -propylgonatetraene (XXVIII). When XXVII was hydrogenated over palladium black in acetic acid, the desired gonatetraene dibromide (XXIX) was obtained in high yield, $\lambda_{\max}$ nm: 276.

XXIX was treated with zinc dust in acetic acid⁸⁾ to give the 13 β -allylgonatetraene (XX) in 38% yield; it was identical in all respects to the specimen mentioned above.

Experimental

Reduction of I with NaBH₄—To a solution of I (2.0 g) in tetrahydrofuran (30 ml) and MeOH (20 ml), NaBH₄ was added gradually with stirring at -20° to -30° . The reaction mixture was poured into H₂O and extracted with ether. The ether layer was washed with H₂O and dried. Evaporation of ether gave 1.94 g of oil (a mixture of II and III, in a ratio of 2:1, judging from the spectrum).

II: IR $\nu_{\max}^{\text{liq}}$ cm⁻¹: 3400 (OH), 1740 (C=O). NMR (CCl₄) δ : 3.68 (3H, singlet, OCH₃), 4.15 (1H, quartet, $J_1=6$ Hz, $J_2=9$ Hz, 14 β -H), 4.85–6.00 (4H, multiplet, CH₂=CH and C₁₁-H), 6.4–7.3 (3H, multiplet, arom.H). UV $\lambda_{\max}^{\text{EtOH}}$ nm (ϵ): 266 (19000).

dl-9 α ,14 α -Epoxy-3-methoxy-13 β -allyl-8,14-secogona-1,3,5(10)-trien-17-one (IV)—A mixture (1.9 g) of II and III in dry benzene (50 ml) was stirred with a saturated solution of *p*-TsOH in benzene (2 ml) at room temperature for 2 hr. The mixture was poured into H₂O and extracted with ether. The ether layer was washed with H₂O, dried and evaporated. The residue was chromatographed over silica gel (300 g). Elution with benzene–AcOEt (10:1) gave V (15 mg) as crystals, then IV (930 mg) as crystals. Elution with benzene–AcOEt (8:1) gave unreacted III (537 mg) as an oil.

V: mp 85–89°. IR $\nu_{\max}^{\text{KBr}}$ cm⁻¹: 1750 (C=O). NMR (CDCl₃) δ : 3.78 (3H, singlet, OCH₃), 3.95 (1H, triplet, $J=2$ Hz, C₁₄-H), 4.96–6.00 (3H, multiplet, CH₂=CH), 6.67–7.45 (3H, multiplet, arom.H). UV $\lambda_{\max}^{\text{EtOH}}$ nm (ϵ): 277 (1680), 283 (1640).

The quantitative conversion of V to IV was observed by TLC, when V was treated with conc. HCl in MeOH at room temperature for 5 min.

IV: mp 109–111°. Anal. Calcd. for C₂₁H₂₆O₃: C, 77.27; H, 8.03. Found: C, 77.54; H, 8.25. IR $\nu_{\max}^{\text{KBr}}$ cm⁻¹: 1740 (C=O). NMR (CCl₄) δ : 3.66 (3H, singlet, OCH₃), 4.15 (1H, triplet, $J=2$ Hz, C₁₄-H), 4.90–5.90 (3H, multiplet, CH₂CH), 6.34–7.20 (3H, multiplet, arom.H). UV $\lambda_{\max}^{\text{EtOH}}$ nm (ϵ): 277 (1680), 283 (1640).

III: IR $\nu_{\max}^{\text{liq}}$ cm⁻¹: 3500 (OH), 1740 (C=O). NMR (CDCl₃) δ : 3.74 (3H, singlet, OCH₃), 4.20 (1H, triplet, $J=6$ Hz, 14 α -H), 5.00–6.10 (3H, multiplet, CH₂=CH), 5.66 (1H, multiplet, C₁₁-H), 6.62–7.30 (3H, multiplet, arom.H). UV $\lambda_{\max}^{\text{EtOH}}$ nm (ϵ): 271 (10700).

dl-9 α ,14 α -Epoxy-3-methoxy-13-(2',3'-dihydroxypropyl)-8,14-secogona-1,3,5(10)-trien-17-one (VI)—A mixture of IV (1.1 g) and OsO₄ (1.0 g) in ether (100 ml) was allowed to stand overnight at room temperature in the dark. The dark precipitate was collected by filtration, washed with ether dissolved in EtOH (100 ml) and H₂O (100 ml), and refluxed with Na₂SO₃ (3.0 g) for 3 hr. After EtOH was distilled off, the mixture was extracted with AcOEt. The AcOEt layer was washed with H₂O, dried and evaporated to give crystals, 1.12 g, mp 137–139°. Anal. Calcd. for C₂₁H₂₈O₅: C, 69.97; H, 7.83. Found: C, 69.78; H, 7.86. IR $\nu_{\max}^{\text{KBr}}$ cm⁻¹: 3350 (OH), 1745 (C=O). NMR (CDCl₃) δ : 3.70 (3H, singlet, OCH₃), 4.15 (1H, multiplet, C₁₄-H), 6.5–7.3 (3H, multiplet, arom.H). UV $\lambda_{\max}^{\text{EtOH}}$ nm (ϵ): 277 (1750), 283 (1660).

dl-9 α ,14 α ,17 β ,2'-Diepoxy-3,17 α -dimethoxy-13(3'-hydroxypropyl)-8,14-secogona-1,3,5(10)-triene (VII)—A solution of VI (100 mg) in MeOH (20 ml) was treated with conc. HCl (0.1 ml) at 70° for 5 min. The reaction mixture was poured into H₂O, dried and evaporated. The residue was chromatographed over silica gel (20 g). Elution with benzene–ether (10:1) gave crystals (77 mg), mp 118–122°. IR $\nu_{\max}^{\text{KBr}}$ cm⁻¹: 3450 (OH). NMR (CDCl₃) δ : 3.41 (1/2 $\times$ 3H, singlet, OCH₃), 3.45 (1/2 $\times$ 3H, singlet, OCH₃), 3.74 (3H, singlet, OCH₃), 3.90 (1H, broad singlet, C₁₄-H), 4.0–4.4 (1H, broad singlet, CH₂-CH-CH₂), 6.5–7.5 (3H, multiplet, arom.H). UV $\lambda_{\max}^{\text{EtOH}}$ nm (ϵ): 277 (15400), 284 (1070). Mass Spectrum m/e : 374 (M⁺).

dl-14 β ,2'-Epoxy-17 α -hydroxy-3-methoxy-13 β -(3'-hydroxy)propylgona-1,3,5(10),8-tetraene (VIII)—Preparation from VI: A solution of VI (700 mg) in MeOH (100 ml) was refluxed with conc. HCl (1 ml) for

8) "Organic Syntheses," Coll. Vol IV, ed by N. Rabjohn, John Wiley & Sons, Inc, New York, 1943, p. 195.

1 hr. The AcOEt layer was washed with H₂O, dried and evaporated to give crystals. Yield 670 mg, mp 167—169° (from ether). Anal. Calcd. for C₂₁H₂₆O₄: C, 73.66; H, 7.66. Found: C, 73.95; H, 7.80. IR $\nu_{\text{max}}^{\text{KBr}}$ cm⁻¹: 3400—3500 (OH). NMR (CDCl₃) δ : 3.3—3.7 (2H, multiplet, CH-CH₂-O), 3.78 (3H, singlet, OCH₃), 4.15—4.40 (1H, multiplet, -CH-OH). UV $\lambda_{\text{max}}^{\text{EtOH}}$ nm (ϵ): 274 (13300). Mass Spectrum m/e : 342 (M⁺).

Preparation from IX: IX (500 mg) was treated with conc. HCl in the same way as described above. Yield 380 mg. VIII was also obtained on treatment with HClO₄. On the other hand, the starting material (IX) was recovered in the case of the following reaction conditions: refluxing with *p*-TsOH in benzene for 2 hr or heating with AcOH at 70° for 1 hr or fusion with P₂O₅ at 70° for 20 min.

dl-9,14 α -Epoxy-3-methoxy-13 β (2',3'-diacetoxy)propyl-8,14-secogona-1,3,5(10)-trien-17-one (IX)—A mixture of VI (620 mg), Ac₂O (10 ml) and pyridine (10 ml) was allowed to stand overnight at room temperature. The reaction mixture was evaporated under reduced pressure. The residue was triturated with ether to give crystals. Yield 830 mg, mp 71—74°. IR $\nu_{\text{max}}^{\text{KBr}}$ cm⁻¹: 1740—1760 (acetate). NMR (CDCl₃) δ : 2.06 (3H, singlet, OAc), 2.07 (3H, singlet, OAc), 3.73 (3H, singlet, OCH₃), 3.8—4.3 (3H, multiplet, CH₂OAc and C₁₄-H), 5.3 (1H, multiplet, -CH-OAc). UV $\lambda_{\text{max}}^{\text{EtOH}}$ nm (ϵ): 276 (1800), 283 (1750). Mass Spectrum m/e : 444 (M⁺).

dl-17 α -Acetoxy-3-methoxy-13 β (2',3'-diacetoxy)propylgona-1,3,5(10),8,14-pentaene (Xa, Xb)—Preparation from VI: A mixture of VI (4.5 g) and *p*-TsOH (4.5 g) in Ac₂O (300 ml) was heated at 80° for 1 hr. The mixture was concentrated under reduced pressure. The residue was dissolved in ether and washed successively with aqueous NaHCO₃ soln. and H₂O, then dried and evaporated. The residual oil (4.8 g) was chromatographed over silica gel (300 g). Elution with benzene-AcOEt (8:1) gave Xa as an oil (1.5 g), with benzene-AcOEt (5:1), Xb as an oil (1.9 g) and then with benzene-AcOEt (3:1), XI as crystals (650 mg).

Xa: IR $\nu_{\text{max}}^{\text{liq}}$ cm⁻¹: 1740 (C=O). NMR (CDCl₃) δ : 2.00 (6H, singlet, 2 $\times$ OAc), 2.12 (3H, singlet, OAc), 5.36 (1H, multiplet, CHOAc), 5.58 (1H, doublet, J =5 Hz, 17 β -H), 3.80—4.30 (2H, multiplet, CH₂OAc), 5.62 (1H, singlet, C₁₅-H), 6.65—7.30 (3H, multiplet, arom.H). UV $\lambda_{\text{max}}^{\text{EtOH}}$ nm (ϵ): 312 (24000).

Xb: IR $\nu_{\text{max}}^{\text{liq}}$ cm⁻¹: 1740 (C=O). NMR (CDCl₃) δ : 1.98 (3H, singlet, OAc), 2.03 (3H, singlet, OAc), 2.04 (3H, singlet, OAc), 5.22 (1H, multiplet, CHOAc), 5.31 (1H, doublet, J =5 Hz, 17 β -H), 5.63 (1H, broad singlet, C₁₅-H), 6.65—7.30 (3H, multiplet, arom.H). UV $\lambda_{\text{max}}^{\text{EtOH}}$ nm (ϵ): 310 (20400). Xa and Xb were stereoisomers at C-2'.

XI: mp 149—155°. IR $\nu_{\text{max}}^{\text{KBr}}$ cm⁻¹: 1745 (C=O). NMR (CDCl₃) δ : 1.97 (3H, singlet, OCH₃), 3.88—4.32 (2H, multiplet, CH₂OAc), 5.16 (1H, multiplet, C₂'-H), 5.34 (1H, doublet, J =6 Hz, 17 β -H), 6.69—7.27 (3H, multiplet, arom.H). UV $\lambda_{\text{max}}^{\text{EtOH}}$ nm (ϵ): 350 (17900). XI was also obtained from X (50 mg) on treatment with *p*-TsOH (50 mg) and Ac₂O (5 ml). Yield 45 mg.

Preparation from VIII: A mixture of VIII (150 mg) and *p*-TsOH (150 mg) in Ac₂O (20 ml) was heated at 75° for 20 min. Yields: Xa (70 mg), Xb (85 mg).

Preparation from IX: X (105 mg) was also obtained from IX (100 mg) by treatment with *p*-TsOH and Ac₂O in the manner described above.

Reduction of XI with NaBH₄: To a solution of XI in MeOH (2.5 ml) and tetrahydrofuran (2.5 ml), NaBH₄ was added portionwise. The mixture was poured into H₂O and extracted with ether. Evaporation of ether gave XII as a colorless oil (12 mg). UV $\lambda_{\text{max}}^{\text{EtOH}}$ nm: 316.

dl-17 α -Acetoxy-3-methoxy-13 β (2',3'-diacetoxy)propylgona-1,3,5(10),8-tetraene (XIII)—A suspension of X (a mixture of Xa and Xb, 3.4 g) and Raney Ni (wet 7.0 g) in dioxane (200 ml) was shaken in H₂ until the absorption at 312 nm disappeared from the UV spectrum. When the reaction was over, the catalyst was removed by filtration and the filtrate was concentrated under reduced pressure to give crystals. Yield 3.0 g. UV $\lambda_{\text{max}}^{\text{EtOH}}$ nm (ϵ): 277 (8750).

dl-17 α -Acetoxy-3-methoxy-8-iso-13 β (2',3'-diacetoxy)propylgona-1,3,5(10)-triene (XVIIIa, XVIIIb)—A suspension of XVI (550 mg, a mixture of stereoisomers XVIa and XVIb) and Raney Ni (wet 4 g) in dioxane (60 ml) was hydrogenated at atmospheric pressure. The catalyst was removed by filtration and the filtrate was concentrated. The residual oil (530 mg) was chromatographed on silica gel (100 g). Elution with benzene-AcOEt (8:1) gave XVIIIa (230 mg) and with benzene-AcOEt (5:1), XVIIIb (250 mg).

XVIIIa: mp 181—189°. IR $\nu_{\text{max}}^{\text{KBr}}$ cm⁻¹: 1740 (C=O). NMR (CDCl₃) δ : 1.97, 2.01, 2.07 (9H, each singlet, 3 $\times$ OAc), 3.73 (3H, singlet, OCH₃), 3.75, 4.24 (2H, multiplet, CH₂OAc), 5.19 (1H, doublet, J =6 Hz, 17 β -H), 5.10—5.25 (1H, multiplet, C₂'-H), 6.55—7.10 (3H, multiplet, arom.H). UV $\lambda_{\text{max}}^{\text{EtOH}}$ nm (ϵ): 277 (1990), 286 (1990).

XVIIIb: mp 139—145°. IR $\nu_{\text{max}}^{\text{KBr}}$ cm⁻¹: 1740—1750 (C=O). NMR (CDCl₃) δ : 1.97 (3H, singlet, OAc), 2.03 (6H, singlet, 2 $\times$ OAc), 3.74 (3H, singlet, OCH₃), 3.85—4.26 (2H, multiplet, CH₂OAc), 4.93 (1H, doublet, J =6 Hz, 17 β -H), 5.05—6.34 (1H, multiplet, CHOAc), 6.55—7.12 (3H, multiplet, arom.H). UV $\lambda_{\text{max}}^{\text{EtOH}}$ nm (ϵ): 277 (2350), 285 (2170).

dl-17 α -Acetoxy-3-methoxy-8-iso-13 β (2',3'-dihydroxy)propylgona-1,3,5(10)-triene (XVa, XVb)—A solution of XIVa (100 mg) in 1% KOH-MeOH (10 ml) was allowed to stand at room temperature for 2 hr. The reaction mixture was poured into H₂O and the resultant precipitate (XVa) was collected by filtration. Yield 73 mg. IR $\nu_{\text{max}}^{\text{KBr}}$ cm⁻¹: 3400 (OH), 1720 (C=O). NMR (CDCl₃) δ : 2.05 (3H, singlet, OAc).

XVb was obtained from XIVb (45 mg) in the same manner as above. Yield 33 mg. IR $\nu_{\text{max}}^{\text{KBr}}$ cm⁻¹: 3400 (OH), 1720 (C=O). NMR (CDCl₃) δ : 2.07 (3H, singlet, OAc).

dl-17 α -Acetoxy-3-methoxy-8-iso-13 β -(2'-oxo)ethylgona-1,3,5(10)-triene (XVI)—A mixture of XVa (50 mg) and NaIO₄ (100 mg) in MeOH (5 ml) and H₂O (5 ml) was warmed at 60° for 30 min. The mixture was poured into H₂O and extracted with ether. Evaporation of the solvent gave crystals (33 mg). Identical crystals of XVI were also obtained from XVb (25 mg). Yield 17 mg. mp 152–154°. *Anal.* Calcd. for C₂₂H₂₈O₄: C, 74.13; H, 7.92. Found: C, 73.91; H, 8.03. IR $\nu_{\max}^{\text{KBr}}$ cm⁻¹: 1740, 1720 (C=O). NMR (CDCl₃) δ : 2.06 (3H, singlet, OAc), 3.74 (3H, singlet, OCH₃), 5.13 (1H, doublet, $J=7$ Hz, 17 β -H), 6.55–7.30 (3H, multiplet, arom.H), 9.88 (1H, triplet, $J=3$ Hz, CHO).

dl-17 α -Acetoxy-3-methoxy-13 β (2',3'-dihydroxy)propylgona-1,3,5(10),8-tetraene (XVII)—To a solution of XIII (1.5 g) in MeOH (10 ml), 1% KOH–MeOH (2 ml) was added. The mixture was allowed to stand at room temperature for 55 min, then was poured into H₂O and extracted with CHCl₃. The CHCl₃ layer was washed with H₂O, dried and evaporated to give an oil (1.3 g), which was chromatographed on silica gel (25 g). Elution with benzene–AcOEt (1:1) gave a colorless oil (530 mg). Mass Spectrum C₂₅H₃₄O₅S₂ (542.65) m/e : 447 (M⁺–OMs). IR $\nu_{\max}^{\text{liq}}$ cm⁻¹: no OH, 1730 (C=O), 1360, 1180 (SO₂). NMR (CDCl₃) δ : 2.02, 2.03 (total 3H, two singlets, OAc), 3.00, 3.07 (total 6H, two singlets, OMs), 3.74, 3.76 (total 3H, two singlets, OCH₃), 4.0–4.5 (3H, multiplet, OCH₂CH–O), 5.10 (1H, multiplet, CHOAc), 6.6–7.2 (3H, multiplet, arom.H).

dl-17 α -Acetoxy-3-methoxy-13 β -allylgona-1,3,5(10),8-tetraene (XIX)—A mixture of XVIII (750 mg), NaI (750 mg) and Zn dust (500 mg) in DMF (10 ml) was stirred at 100–110° for 45 min. After the insoluble material had been filtered off, the filtrate was evaporated under reduced pressure. The residue was chromatographed on silica gel (10 g). Elution with benzene–AcOEt (5:1) gave crystals. Yield 390 mg (80%). Recrystallization from ether–*n*-hexane gave columns, mp 118–120°. Mass Spectrum C₂₃H₂₈O₃ (352.45) m/e : 352 (M⁺). IR $\nu_{\max}^{\text{liq}}$ cm⁻¹: 1730 (C=O), 3060, 1640, 910 (allyl). NMR (CDCl₃) δ : 2.08 (3H, singlet, OAc), 3.80 (3H, singlet, OCH₃), 4.70–5.40 (2H, multiplet, CH₂=CH), 5.00 (1H, multiplet, 17 β -H), 5.53–6.35 (1H, multiplet, C=CH), 6.65–7.30 (3H, multiplet, arom.H). UV $\lambda_{\max}^{\text{EtOH}}$ nm (ϵ): 278 (14800).

dl-17 α -Hydroxy-3-methoxy-13 β -allylgona-1,3,5(10),8-tetraene (XX)—Preparation from XIX: A solution of XIX (300 mg) in 2% KOH–MeOH (10 ml) was warmed at 60° for 20 min. MeOH was evaporated under reduced pressure and the residue was extracted with CHCl₃. The CHCl₃ layer was washed with H₂O, dried and evaporated. The residue was chromatographed on silica gel (10 g). Yield 260 mg (98.1%). Mass Spectrum C₂₁H₂₆O₂ (310.42) m/e : 310 (M⁺), 292 (M⁺–H₂O), 269 (M⁺–allyl). IR $\nu_{\max}^{\text{liq}}$ cm⁻¹: 3400 (OH), 3060, 1640, 910 (allyl). UV $\lambda_{\max}^{\text{EtOH}}$ nm (ϵ): 278 (13700). NMR (CDCl₃) δ : 3.78 (3H, singlet, OCH₃), 4.14 (1H, quartet, $J_1=3$ Hz, $J_2=9$ Hz, 17 β -H), 4.75–5.30 (2H, multiplet, CH₂=C), 5.55–6.20 (1H, multiplet, C=CH), 6.55–7.25 (3H, multiplet, arom.H).

Preparation from XXIX: To a solution of XXIX (20 g) in AcOH (10 ml) and CHCl₃ (20 ml), Zn dust was added gradually with vigorous stirring at room temperature. After the Zn dust had been filtered off, the filtrate was evaporated under reduced pressure. The residue was chromatographed on silica gel (100 g) to give a colorless oil (900 mg). IR, NMR and UV spectra were identical with those of the sample prepared from XIX.

dl-17 α -Hydroxy-3-methoxy-13 β -allylgona-1,3,5(10)-triene (XXI)—A mixture of XX (185 mg) and K in liq. NH₃ (40 ml) and tetrahydrofuran (40 ml), was stirred at –40 to –50° for 1 hr. After addition of NH₄Cl (200 mg), NH₃ was allowed to evaporate. The residue was chromatographed on silica gel (10 g). Elution with benzene–AcOEt (8:1) gave crystals. Yield 167 mg (81%). Recrystallization from ether–*n*-hexane gave columns, mp 123–125°. Mass Spectrum C₂₁H₂₈O₂ (312.44) m/c : 312 (M⁺), 394 (M⁺–H₂O), 269 (M⁺–allyl). IR $\nu_{\max}^{\text{liq}}$ cm⁻¹: 3400 (OH), 3060, 1635, 905 (allyl). UV $\lambda_{\max}^{\text{EtOH}}$ nm (ϵ): 278 (3030), 285 (1800). NMR (CDCl₃) δ : 3.80 (3H, singlet, OCH₃), 4.05 (1H, quartet, $J_1=3$ Hz, $J_2=9$ Hz, 17 β -H), 4.80–5.30 (2H, multiplet, CH₂=C), 5.40–6.10 (1H, multiplet, C=CH), 6.55–7.25 (3H, multiplet, arom.H).

dl-3-Methoxy-17 α -tetrahydropyranyloxy-13 β -allylgona-1,3,5(10)-triene (XXII)—A mixture of XXI (37 mg), dihydropyran (0.5 ml) and ether (3 ml) in the presence of a catalytic amount of BF₃ ether, was stirred at room temperature for 2.5 hr. The reaction mixture was evaporated under reduced pressure, and the resulting oil was purified by preparative TLC (benzene: AcOEt=10:1). Yield, oil 37 mg. Mass Spectrum C₂₆H₃₆O₃ (396.55) m/e : 396 (M⁺). IR $\nu_{\max}^{\text{liq}}$ cm⁻¹: 3060, 1640, 905 (allyl), no OH. NMR (CCl₄) δ : 3.76 (3H, singlet, OCH₃), 4.00 (1H, broad singlet, 17 β -H), 4.82 (1H, singlet, –O–CH–O–), 4.80–5.30 (2H, multiplet, CH₂=C), 5.45–6.10 (1H, multiplet, C=CH), 6.5–7.3 (3H, multiplet, arom.H).

dl-17 α -Hydroxy-13 β -allylgona-4-en-3-one (XXIII)—Preparation from XXII: To a mixture of XXII (37 mg), EtOH (1.5 ml), tetrahydrofuran (5 ml) and liq. NH₃ (10 ml), Li was added with stirring between –40 and –50° for 30 min. After evaporation of NH₃, the residue was extracted with ether. After ether had evaporated, the residue was dissolved in MeOH (5 ml) and conc. HCl (1 ml) and allowed to stand at room temperature for 20 min. The reaction mixture was poured into H₂O and extracted with CHCl₃. The CHCl₃ layer was washed with H₂O, dried and evaporated to give an oil (36 mg), which was purified by preparative TLC (benzene: AcOEt=10:1). Yield 16 mg (57%), needles, mp 151–155° (from ether). Mass Spectrum C₂₀H₂₈O₂ (300.44) m/e : 300 (M⁺), 284 (M⁺–H₂O), 259 (M⁺–allyl). IR $\nu_{\max}^{\text{liq}}$ cm⁻¹: 3400 (OH), 1660, 1620 (C=C–C=O), 3050, 1635, 910 (allyl). UV $\lambda_{\max}^{\text{EtOH}}$ nm (ϵ): 234 (15200). NMR (CDCl₃) δ : 3.97 (1H, triplet, $J=5$ Hz, 17 β -H), 4.86–5.15 (2H, multiplet, CH₂=C), 5.45–5.80 (1H, multiplet, C=CH), 5.78 (1H, singlet, C₄-H).

Preparation from XXI: XXI (54 mg) was treated with Li, liq. NH₃ (10 ml) and EtOH (3 ml) as described above. Yield 16 mg (30%). However in another run, XXI (75 mg) was treated with Li, liq. NH₃

(20 ml) and EtOH (3 ml), and gave only XXIV (20 mg). Mass Spectrum $C_{20}H_{30}O_2$ (302.44) m/e : 302 (M^+). IR $\nu_{\max}^{KBr}$ cm^{-1} : 3450 (OH), 1660, 1620 ($C=C=O$). NMR ($CDCl_3$) δ : 0.90 (3H, triplet, $J=5.5$ Hz, CH_3), 3.94 (1H, quartet_{ABX}, $J_{AX}=4$ Hz, $J_{BX}=9$ Hz, 17β -H), 5.77 (1H, singlet, C_4 -H).

dl-13 β -Allylgon-4-ene-3,17-dione (XXV)—A solution of XXIII (19 mg) in pyridine (0.2 ml) was added to CrO_3 -pyridine complex (prepared from 20 mg of CrO_3 and 0.2 ml of pyridine) under ice-cooling. The mixture was allowed to stand overnight at 5° , then was poured into ice-water and extracted with $CHCl_3$. The extract was washed with dilute HCl soln. and H_2O , then dried and evaporated. The residue was purified by preparative TLC (benzene: AcOEt=5:1). Yield 14 mg. Recrystallization from ether gave colorless needles, mp $167-168^\circ$. The mixed mp and IR and NMR spectra were identical with those of a sample obtained previously.¹⁾

9 α ,14 α -Epoxy-3-methoxy-13(2',3'-dibromo)propyl-8,14-secogona-1,3,5(10)-trien-17-one (XXVI)—To a solution of IV (10.0 g) in $CHCl_3$ (500 ml), bromine (6.8 g) in $CHCl_3$ (100 ml) was added dropwise with stirring at -10° . The solvent was concentrated under reduced pressure. The residue was crystallized from ether. Yield 8.5 g. mp $152-156^\circ$. Anal. Calcd. for $C_{21}H_{26}O_3Br_2$: C, 51.87; H, 5.39. Found: C, 51.48; H, 5.03. IR $\nu_{\max}^{KBr}$ cm^{-1} : 1735 ($C=O$). NMR ($CDCl_3$) δ : 3.77 (3H, singlet, OCH_3), 3.4—4.0 (3H, multiplet, $BrCH_2CHBr$), 4.25 (1H, multiplet, C_{14} -H), 6.5—7.4 (3H, multiplet, arom.H). UV $\lambda_{\max}^{EtOH}$ nm (ϵ): 277 (1590), 283 (1500).

dl-17 α -Hydroxy-3-methoxy-13 β (2',3'-dibromo)propylgona-1,3,5(10),8,14-pentaene (XXVII)—A solution of XXVI (2.0 g) in acetone (120 ml) was refluxed with conc. HCl (60 ml) for 20 min. The mixture was poured into ice-water and extracted with ether. The organic solvent was washed with H_2O , dried and evaporated to give an oil (2.0 g). IR $\nu_{\max}^{liq}$ cm^{-1} : 3400 (OH). NMR ($CDCl_3$) δ : 3.80 (3H, singlet, OCH_3), 3.4—4.3 (3H, multiplet, $BrCH_2CHBr$), 4.30 (1H, multiplet, 17β -H), 5.66 (1H, multiplet, C_{15} -H), 6.7—7.3 (3H, multiplet, arom.H). UV $\lambda_{\max}^{EtOH}$ nm: 312.

dl-17 α -Hydroxy-3-methoxy-13 β -propylgona-1,3,5(10),8-tetraene (XXVIII)—A suspension of XXVII (1.3 g) and Raney Ni (wet 10 g) in dioxane (100 ml) was shaken under a stream of hydrogen. After absorption of an equi-mole of hydrogen, the catalyst was filtered off. The filtrate was evaporated to give crystals (1.23 g). Recrystallization from ether-*n*-hexane gave columns, mp $125-127^\circ$. Anal. Calcd. for $C_{21}H_{26}O_2$: C, 80.73; H, 9.03. Found: C, 80.54; H, 8.79. IR $\nu_{\max}^{KBr}$ cm^{-1} : 3300—3450 (OH). UV $\lambda_{\max}^{EtOH}$ nm (ϵ): 278 (18900). Catalytic hydrogenation of XXVII with Pd-BaCO₃ in MeOH gave the same product.

dl-17 α -Hydroxy-3-methoxy-13 β (2',3'-dibromo)propylgona-1,3,5(10),8-tetraene (XXIX)—A suspension of XXVII (2.0 g) and PtO_2 (2.0 g) in AcOH (100 ml) was shaken in hydrogen. After absorption of an equi-mole of hydrogen, the catalyst was filtered off. The filtrate was evaporated to give an oil (2.0 g). IR $\nu_{\max}^{liq}$ cm^{-1} : 3450 (OH). UV $\lambda_{\max}^{EtOH}$ nm (ϵ): 276 (16800).

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