18-Norpregna-8,11,13-trienes: Reaction of 16α,17α-Epoxypregn-8-en-11-ones with Lewis Acids

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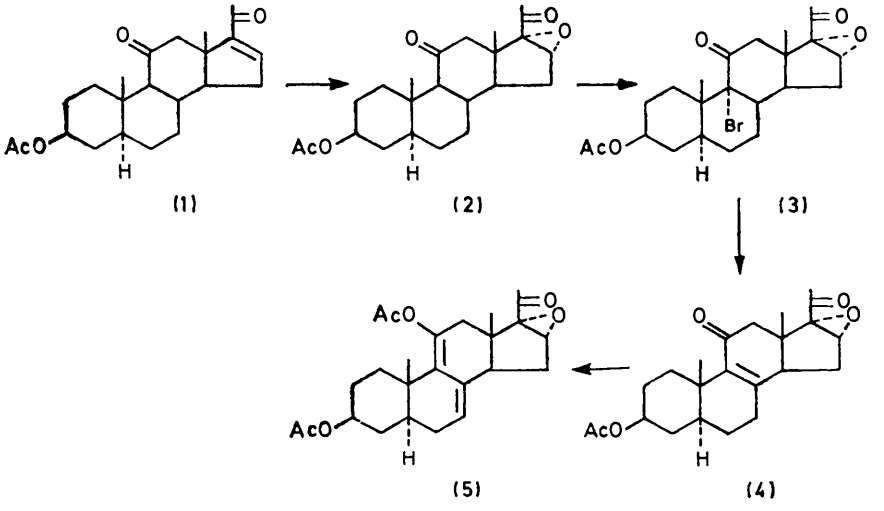
Treatment of 3β-acetoxy-16α,17α-epoxy-5α-pregn-8-ene-7,11,20-trione (6) with acetic anhydride gave 3β,17α-diacetoxy-5α-pregna-8,14-diene-7,11,20-trione (10) and 3β,16α-diacetoxy-11-hydroxy-17β-methyl-18-nor-5α,17α-pregna-8,11,13-triene-7,20-dione (8). Two competing mechanisms for the reaction are proposed. Similar attempts to aromatise 3β-acetoxy-16α,17α-epoxy-5α-pregn-8-ene-11,20-dione (4) were unsuccessful.

In earlier papers [1] we described the aromatisation in ring C of a number of 17β-hydroxyandrostanes, using a Wagner-Meerwein shift [2] of the 13β-methyl group to the 17β-position by dehydration of the 17β-alcohol. Continuing our investigations to evaluate the biological properties of ring-C-aromatic steroids, we have extended this work into the pregnane series. This paper deals with the opening of a pregnane-16α,17α-epoxide containing a Δ^8-11-ketone system to give the corresponding 11-hydroxy-ring-C-aromatic pregnane derivative.

The opening of 16α,17α-epoxides accompanied by a Wagner-Meerwein shift in pregnanes unsubstituted in ring C is well documented,[3] and is claimed to result in 17β-methylpregn-12- or -13-enes, depending on the reagent. A variety of reagents have been used, including toluene-*p*-sulphonic acid in various solvents,[3a,b] hydrogen fluoride,[3c] yeasts,[3d] and sulphuric acid in formic or acetic acid.[3a] In earlier instances there appeared to be some doubt about the position of the double bond in the rearranged product,[3b,e] but a structure proof by Herzog and his co-workers [3f] resolved the controversy in favour of the 13,14-double bond.

It seemed probable therefore that a similar reaction of a 16α,17α-epoxide containing a Δ^8-11-ketone system would proceed *via* a Wagner–Meerwein rearrangement to give the corresponding 17β-methyl-11-hydroxy-17α-pregna-8,11,13-triene.

The intermediate selected for the investigation, 3β-acetoxy-16α,17α-epoxy-5α-pregn-8-ene-11,20-dione (4), was prepared by the method outlined in Scheme 1. Epoxidation of 3β-acetoxy-5α-pregn-16-ene-11,20-dione (1) with alkaline hydrogen peroxide [4] followed by direct bromination of the 16α,17α-epoxide (2) with *N*-bromosuccinimide [5] gave 3β-acetoxy-9α-bromo-16α,17α-epoxy-5α-pregnane-11,20-dione (3) in which the 9α-configuration



SCHEME 1

[1] (*a*) C. L. Hewett, S. G. Gibson, I. M. Gilbert, J. Redpath, and D. S. Savage, *J.C.S. Perkin I*, 1973, 1967; (*b*) C. L. Hewett, I. M. Gilbert, J. Redpath, D. S. Savage, J. Strachan, T. Sleigh, and R. Taylor, *ibid.*, 1974, 897; (*c*) C. L. Hewett, S. G. Gibson, J. Redpath, and D. S. Savage, *ibid.*, p. 1432; (*d*) C. L. Hewett, S. G. Gibson, I. M. Gilbert, J. Redpath, D. S. Savage, T. Sleigh, and R. Taylor, *ibid.*, 1975, 336.

[2] (*a*) A. Cohen, J. W. Cook, and C. L. Hewett, *J. Chem. Soc.*, 1935, 445; (*b*) K. Miescher and H. Kägi, *Helv. Chim. Acta*, 1949, **32**, 761.

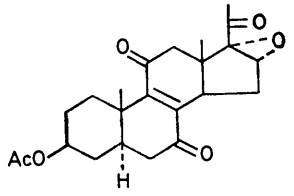
[3] (*a*) K. Heusler and A. Wettstein, *Chem. Ber.*, 1954, **87**, 1301; (*b*) H. L. Herzog, M. J. Gentles, A. Mitchell, E. B. Hershberg, and L. Mandell, *J. Amer. Chem. Soc.*, 1959, **81**, 6478; (*c*) E. L. Shapiro, M. Steinberg, D. Gould, M. J. Gentles, H. L. Herzog, M. Gilmore, W. Charney, E. B. Hershberg, and L. Mandell, *ibid.*, p. 6483; (*d*) B. Camerino and A. Vercellone, *Gazzetta*, 1956, **86**, 260; (*e*) V. Fortorella and A. Romeo, *ibid.*, 1963, **92**, 1118; (*f*) H. L. Herzog, O. Gnoj, L. Mandell, G. G. Nathansohn, and A. Vigevani, *J. Org. Chem.*, 1967, **32**, 2906.

[4] (*a*) J. Pataki, G. Rosenkranz, and C. Djerassi, *J. Amer. Chem. Soc.*, 1952, **74**, 5615; (*b*) H. Martinez, H. J. Ringold, C. Rosenkranz, and C. J. Djerassi, *ibid.*, 1953, **75**, 239.

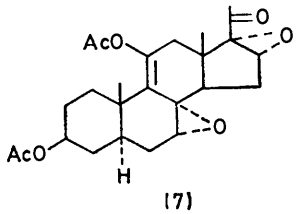
[5] (*a*) Ch. Meystre, L. Ehmann, R. Neher, and K. Miescher, *Helv. Chim. Acta*, 1945, **28**, 1252; Ch. Meystre and K. Miescher, *ibid.*, 1945, **28**, 1497; (*b*) Ch. Meystre and K. Miescher, *ibid.*, 1946, **29**, 33; Ch. Meystre, H. Frey, R. Neher, A. Wettstein, and K. Miescher, *ibid.*, p. 627.

of the bromine atom was confirmed by the n.m.r. spectrum [δ 2.63 (12β-H) and 3.48 (12α-H)].[6] Dehydrobromination of the 9α-bromo-11-ketone (3) with boiling collidine [5d,7] or with calcium carbonate in dimethyl formamide,[7b] gave 3β-acetoxy-16α,17α-epoxy-5α-pregn-8-ene-11,20-dione (4), $\lambda_{max.}$ 257 nm (ε 8 000) (14α-Δ⁸-11-ketone).

Contrary to expectation, however, treatment of the 16α,17α-epoxy-Δ⁸-11-ketone (4), with sulphuric acid or zinc chloride in acetic anhydride, or boron trifluoride–ether complex in benzene gave mixtures which could not be separated or identified, and treatment with toluene-*p*-sulphonic acid in acetic anhydride gave the 7,9(11)-diene 11-acetate (5) with the epoxide group intact. The structure of the dienol acetate (5) was confirmed by the characteristic i.r. absorption at 1 755 cm^{-1}, u.v. absorption at 251 nm (ε 13 000), and n.m.r. absorption at δ 3.75 (16β-H in a 16α,17α-epoxide).



(6)



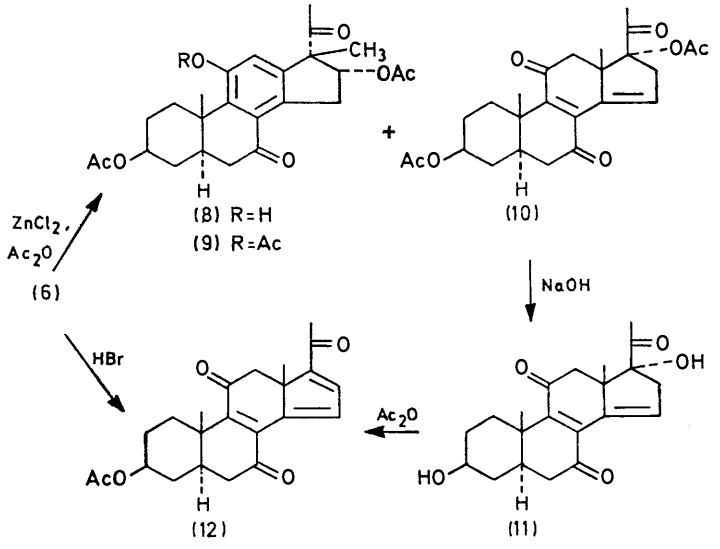
(7)

Because attempted aromatisation of the Δ⁸-11-ketone (4) was unsuccessful, and since our interests extend to 7-oxygenated aromatic steroids,[1d] the investigation was extended to the aromatisation of 3β-acetoxy-16α,17α-epoxy-5α-pregn-8-ene-7,11,20-trione (6), conveniently prepared by oxidation of the dienol acetate (5) with chromic acid. The structure of the oxidation product (6) was confirmed by its u.v. spectrum [$\lambda_{max.}$ 275 nm (ε 7 000) (Δ⁸-7,11-dione)] and by the absence of any vinylic proton n.m.r. absorption. A by-product isolated from the oxidation reaction was the intermediate diepoxide (7), 1 743 cm^{-1} (characteristic of an enolic acetate), δ 2.67 (7β-H).

Treatment of the 16α,17α-epoxy-Δ⁸-7,11,20-trione (6) with boron trifluoride, hydrogen fluoride at −60 °C, toluene-*p*-sulphonic acid, or aluminium trichloride gave no reaction; use of hydrogen fluoride at 0 °C gave an intractable mixture of products.

Treatment of the 16α,17α-epoxy-Δ⁸-7,11,20-trione (6) with anhydrous zinc chloride in acetic anhydride gave a mixture of two components (see Scheme 2) which was separated by column chromatography. The more polar product was the required 3β,16α-diacetoxy-11-hydroxy-17β-methyl-18-nor-5α,17α-pregna-8,11,13-triene-7,20-dione (8), δ 7.2 (11-OH), 6.94 (aromatic 12-H), and 5.53 (16β-H), $\lambda_{max.}$ 263 (ε 6 700) and 338 nm (4 400). The expected 11-acetate (9) was not isolated, presumably having been hydrolysed on the column. The less polar product was the dienedione (10), δ 6.74 (*J* 2.4 Hz, 15-H), 3.67 (*J* 20 and 2.4 Hz, 16α-H), and 3.07 (*J* 20 Hz, 16β-H), $\lambda_{max.}$ 330 nm (ε 4 900) (8,14-diene-7,11-dione).

Confirmatory evidence for the dienedione structure (10) was obtained when the compound was hydrolysed and the dialcohol (11) formed was reacetylated. This resulted in elimination of the hydroxy-group at position 17α along with the adjacent proton to introduce a double bond at position 16 (see Scheme 2), to give the 8,14,16-trienetrione (12), confirming the presence of a tertiary hydroxy-group in the diol (11). The trienetrione (12) was also obtained by treatment of the 16α,17α-epoxide (6) with anhydrous hydrogen bromide. The structure of the trienetrione (12) was demonstrated by the u.v. absorption of the extended conjugated unsaturated

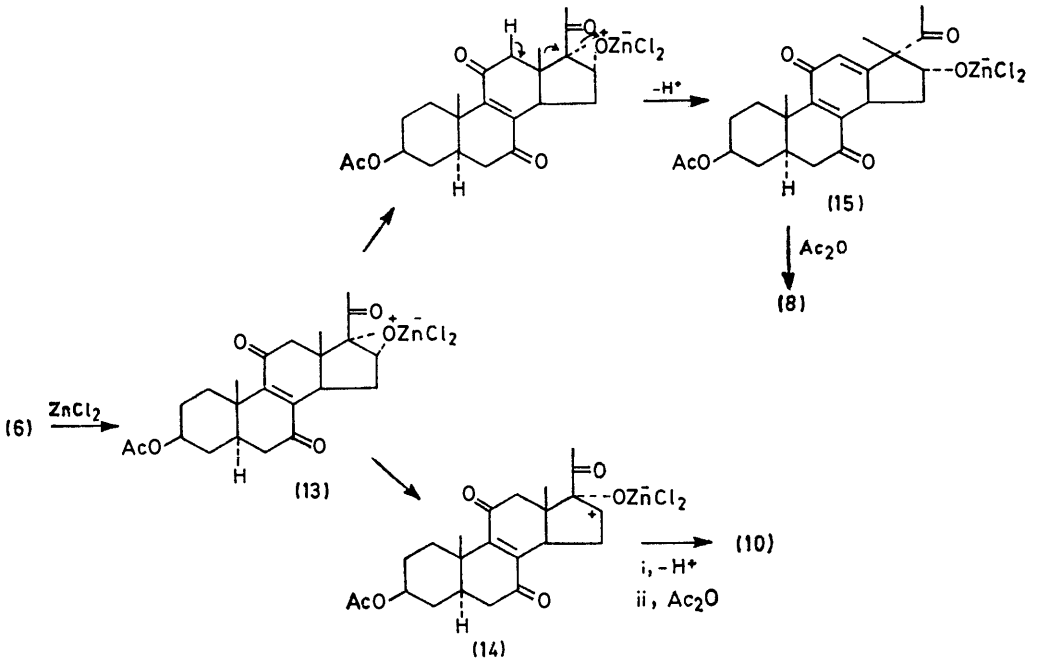


SCHEME 2

[6] E. R. H. Jones and D. A. Wilson, *J. Chem. Soc.*, 1965, 2933.
[7] (*a*) H. B. Henbest, E. R. H. Jones, A. A. Wagland, and T. I. Wrigley, *J. Chem. Soc.*, 1955, 2477; (*b*) G. F. H. Green and A. G. Long, *J. Chem. Soc.*, 1961, 2532.

system at 264 (ε 8 600), 323 (7 700), and 365 nm (8 100) and by the n.m.r. absorption at δ 7.23 and 7.28 (*J* 13.2 Hz, 15- and 16-H).

The opening of the 16α,17α-epoxide (6) with zinc chloride in acetic anhydride is believed to proceed *via* two competing pathways. The intermediate (13) formed by attack of the Lewis acid on the epoxide as shown in Scheme 3 undergoes rearrangement by a concerted mechanism with loss of a 12-proton to give the 17β-methyl intermediate (15). Enolisation followed by attack with acetic anhydride to displace the Lewis acid (12%) and (10) (30%) may be a measure of the energy requirements for the two competing pathways.



SCHEME 3

gives the aromatic 16α-acetate (8). Since carbocation centres adjacent to carbonyl groups are not very stable, this explanation is preferred to one involving the formation of a 17-carbocation followed by rearrangement.

The alternative opening of the intermediate (13) as shown in Scheme 3 gives the 16-carbocation (14), which loses a proton at position 15 to give a Δ^{15}-intermediate. Attack by acetic anhydride on the 17α-oxygen atom to displace the Lewis acid and allylic rearrangement of the 15,16-double bond to bring it into conjugation with the 8,9-double bond, gives the 8,14-diene 17α-acetate (10).

When ring C is unsubstituted and in the normal chair conformation, a concerted mechanism probably predominates giving a rearrangement to the corresponding Δ^{12}- or Δ^{13}-derivative.[3] In the present case however, when there is a strain in rings C and D caused by the Δ^{8}-11-ketone system, the steric relationships for a concerted mechanism may not be completely favourable; hence the alternative pathway *via* the 16-carbocation (14) assumes importance and elimination as well as aromatisation occurs. The relative yields of the two products (8)

EXPERIMENTAL

M.p.s were determined with a Kofler hot-stage apparatus. I.r. spectra were determined with a Perkin-Elmer 457 spectrometer. U.v. spectra were determined with a Perkin-Elmer 402 spectrometer for solutions in ethanol. Optical rotations were measured for solutions in chloroform at room temperature unless otherwise stated. N.m.r. spectra (solvent $CDCl_3$) were determined at 60 Hz with a Varian A-60 spectrometer (tetramethylsilane as internal standard). U.v. irradiations were carried out with a Hanovia U.V.S. 500 medium-pressure lamp.

3β-Acetoxy-9α-bromo-16α,17α-epoxy-5α-pregnane-11,20-dione (3).—A suspension of *N*-bromosuccinimide (38 g) and 3β-acetoxy-16α,17α-epoxy-5α-pregnane-11,20-dione [4a] (2) (38 g) in methylene dichloride (700 ml) was stirred and irradiated for 3 h. The solution was washed in succession with sodium hydrogen sulphite solution, water, potassium hydrogen carbonate solution, and water until neutral, dried (Na_2SO_4), and concentrated. Treatment of the residue with diethyl ether gave the *9α-bromo-16α,17α-epoxide* (3) (33.8 g), m.p. 210—215° (decomp.), $[\alpha]_D$ +152°, $\nu_{max.}$ (KCl) 1 732 and 1 250 (3-acetate), and 1 705 cm^{-1} (11- and 20-ketones), δ 1.0 (3H, s, 13-Me), 1.2 (3H, s, 10-Me), 2.0 (6H, s, 3β-OAc and 17-COMe), 2.63 (1H, d, *J* 13.5 Hz, 12β-H), 3.48 (1H, d, *J* 13.5 Hz, 12α-H), 3.8 (1H, s, 16β-H), and 4.7 (1H, m, 3α-H) (Found: C, 59.2; H, 6.9; Br, 18.7. $C_{23}H_{31}BrO_5$ requires C, 59.1; H, 6.6; Br, 17.1%).

3β-Acetoxy-16α,17α-epoxy-5α-pregn-8-ene-11,20-dione (4). —(*a*) 3β-Acetoxy-9α-bromo-16α,17α-epoxy-5α-pregnane-11,-20-dione (3) (110 g) was heated to reflux in collidine (750 ml) and boiled for 5 min with occasional swirling; the mixture was then cooled and poured into an excess of dilute hydro-

chloric acid (2N). The product was dissolved in methylene dichloride and the solution was washed with hydrochloric acid (2N) and water until neutral, dried (Na_2SO_4), and evaporated under vacuum. Crystallisation of the residue from methanol and then from methylene dichloride–methanol gave the *product* (4) (82.5 g), m.p. 221—224°, $\nu_{max.}$ (KCl) 1 726 and 1 250 (3-acetate), 1 703 (20-ketone), 1 695 (unsaturated 11-ketone), and 1 580 cm^{-1} (8,9-double bond), $\lambda_{max.}$ 257 nm (ε 8 000) (Δ^8-11-ketone), δ 1.05 (3H, s) and 1.09 (3H, s, 10- and 13-Me), 2.05 (6H, s, 3β-OAc and 17-COMe), 2.44 (1H, d, *J* 14.7 Hz, 12β-H), 2.87 (1H, d, *J* 14.7 Hz, 12α-H), 3.83 (1H, s, 16β-H), and 4.7 (1H, m, 3α-H) (Found: C, 71.1; H, 8.1. $C_{23}H_{30}O_5$ requires C, 71.5; H, 7.8%).

(*b*) The 9α-bromo-16α,17α-epoxide (3) (200 g) was added to a stirred suspension of calcium carbonate (200 g) in dimethylformamide (2 l) which had been heated to reflux, and heating and stirring were continued for a further 0.5 h. The mixture was cooled, poured into water (10 l), acidified with acetic acid, and diluted further with water (10 l). The product was filtered off, washed with water, dried, and recrystallised from methanol to give the pregn-8-ene-11,20-dione (4) (148 g), m.p. 220—223°, identical (i.r. and n.m.r.) with the material prepared by method (*a*).

3β,11-*Diacetoxy*-16α,17α-*epoxy*-5α-*pregna*-7,9(11)-*dien*-20-*one* (5).—Toluene-*p*-sulphonic acid (8.0 g) was added to a stirred suspension of 3β-acetoxy-16α,17α-epoxy-5α-pregn-8-ene-11,20-dione (4) (80.0 g) in acetic anhydride (240 ml) at 80 °C to give a clear solution. After 6 min at 80 °C the 3β,11-*diacetoxy-compound* (5) crystallised out, and after 20 min the mixture was cooled to 0 °C and the product (75.5 g) was filtered off. Crystallisation from methylene dichloride–methanol gave a sample m.p. 228—236°, $[\alpha]_D$ +123° (*c* 1.1), $\nu_{max.}$ (KCl) 1 755 and 1 210 (dienol acetate), 1 727 and 1 245 (3-acetate), and 1 700 cm^{-1} (20-ketone), $\lambda_{max.}$ 251 nm (ε 13 400), δ 0.92 (3H, s, 13-Me), 1.02 (3H, s, 10-Me), 2.0 (6H, s, 3β- and 11-OAc), 2.1 (3H, s, 17-COMe), 3.75 (1H, s, 16β-H), and 4.7 (1H, m, 3α-H) (Found: C, 70.1; H, 7.7. $C_{25}H_{32}O_6$ requires C, 70.1; H, 7.5%).

Oxidation of 3β,11-*Diacetoxy*-16α,17α-*epoxy*-5α-*pregna*-7,9-(11)-*dien*-20-*one* (5) *with Chromic Acid*.—A solution of chromium trioxide (39 g) in water (30 ml) and glacial acetic acid (350 ml), was added to a solution of compound (5) (70 g) in glacial acetic acid (2.8 l) at 50 °C with stirring. After 10 min at 50—55 °C the mixture was poured into water (13 l) and the yellow solid (47 g) was filtered off, dried (Na_2SO_4), and crystallised from methylene dichloride-methanol to give 3β-*acetoxy*-16α,17α-*epoxy*-5α-*pregn*-8-*ene*-7,11,20-*trione* (6) (36.6 g). Recrystallisation from methylene dichloride–diethyl ether gave a sample of m.p. 222—225°, $[\alpha]_D$ +88° (*c* 1.0), $\nu_{max.}$ (KCl) 1 735 (3-acetate), 1 705 (20-ketone), and 1 685 and 1 675 cm^{-1} (7- and 11-αβ-unsaturated ketone), $\lambda_{max.}$ 275 nm (ε 7 000) (Δ^8-7,11-dione), δ 1.05 (3H, s, 13-Me), 1.3 (3H, s, 10-Me), 2.03 (6H, s, 3β-OAc and 17-COMe), 3.86 (1H, s, 16β-H), and 4.7 (1H, m, 3α-H) (Found: C, 68.6; H, 6.8. $C_{23}H_{28}O_6$ requires C, 69.0; H, 7.0%). The watered-out aqueous acetic acid from the reaction mixture was extracted with methylene dichloride. The extract was washed neutral and concentrated under vacuum, and the residue (11.5 g) was allowed to crystallise from methanol to give 3β,11-*diacetoxy*-7α,8α,16α,17α-*diepoxy*-5α-*pregn*-9(11)-*en*-20-*one* (7) (1.7 g). Crystallisation from diethyl ether gave a sample of m.p. 193—195°, $[\alpha]_D$ +46° (c 1.0), $\nu_{max.}$ 1 743 (enol acetate), 1 725 and 1 240 (3-acetate), and 1 700 cm^{-1} (20-ketone), $\lambda_{max.}$ 215 nm (ε 4 700) [9(11)-double bond], δ 1.04 (3H, s, 13-Me), 1.3 (3H, s, 10-Me), 1.99 and 2.05 (9H, 2s, 3β- and 11-OAc and 17-COMe), 2.67 (1H, s, 7β-H), 3.75 (1H, s, 16β-H), and 4.7 (1H, m, 3α-H) (Found: C, 67.8; H, 7.4. $C_{25}H_{32}O_7$ requires C, 67.6; H, 7.3%).

Treatment of 3β-*Acetoxy*-16α,17α-*epoxy*-5α-*pregn*-8-*ene*-7,11,20-*trione* (6) *with Aluminium Chloride*.—The epoxide (6) (1.0 g) was added to aluminium trichloride (0.05 g) in acetic anhydride (10 ml) which had previously been heated to reflux, and heating and stirring were continued for a further 0.5 h. The solution was cooled and poured into water and the solid was isolated, dried, and shown to be identical with the starting material (6) by its m.p. (223—225°) and its u.v. and i.r. spectra. Similar results were obtained when the epoxide (6) (1.0 g) was heated with toluene-*p*-sulphonic acid (0.1 g) in acetic anhydride at reflux for 15 min or treated at −60 °C with hydrogen fluoride for 1 h, or with boron trifluoride–ether complex (0.05 ml) at 0 °C in benzene (10 ml) for 4 h. Treatment at 0 °C with hydrogen fluoride gave a mixture of products which could not be separated by chromatography or identified.

Rearrangement of 3β-*Acetoxy*-16α,17α-*epoxy*-5α-*pregn*-8-*ene*-7,11,20-*trione* (6) *with Zinc Chloride*.—The trione epoxide (6) (5.0 g) was added to refluxing anhydrous zinc chloride (0.17 g) in acetic anhydride (50 ml) and heating under reflux was continued for 30 min. The solution was cooled, diluted with water (50 ml), stirred for 1 h to destroy acetic anhydride, and poured slowly into an excess of water to precipitate the product. After drying, the solid was dissolved in benzene and carefully chromatographed on a column (1.5 in diam.) of silica gel (Merck; 200 g) (elution with benzene–ether mixtures and finally with diethyl ether). The fractions were examined by t.l.c. The combined fraction containing the less polar product was concentrated and the residue (3.1 g) was crystallised from diethyl ether to give 3β,17α-*diacetoxy*-5α-*pregna*-8,14-*diene*-7,11,20-*trione* (10) (1.5 g), m.p. 198—203°, $[\alpha]_D$ −136° (*c* 1.0), $\nu_{max.}$ 1 735, 1 725, and 1 710 (3-acetate, 17-acetate, and 20-ketone), 1 690 and 1 680 (7- and 11-ketones), 1 610 (14,15-double bond) and 1 260br cm^{-1} (3- and 17-acetates), $\lambda_{max.}$ 218 (ε 8 900) and 330 nm (4 900), δ 0.82 (3H, s, 13-Me), 1.34 (3H, s, 10-Me), 2.01 (3H, s, 17-COMe), 2.09 [6H, s, 3β,17α-$(OAc)_2$], 3.07 (1H, d, *J* 20 Hz, 16β-H), 3.67 (1H, q, *J* 20 and 2.4 Hz, 16α-H), 4.7 (1H, m, 3α-H), and 6.74 (1H, t, *J* 2.4 Hz, 15-H) (Found: C, 67.7; H, 6.8. $C_{25}H_{30}O_7$ requires C, 67.8; H, 6.8%). The combined fraction containing the more polar product was concentrated, the residue (1.2 g) was combined with the mother liquors from the crystallisation of the 8,14-diene-7,11,20-trione (10), and the material was rechromatographed on a column of silica gel G (Merck t.l.c. grade; 120 g) (elution with benzene–ethyl acetate mixtures). The more polar fractions from the column were combined and the residue (1.3 g) was crystallised from methanol to give 3β-16α-*diacetoxy*-11-*hydroxy*-17β-*methyl*-18-*nor*-5α,17α-*pregna*-8,11,13-*triene*-7,20-*dione* (8) (0.6 g), m.p. 247—248°, $\nu_{max.}$ (KCl) 3 160 (OH), 3 005 (aromatic C–H), 1 750—1 735br (3β- and 16α-acetate), 1 710 (20-ketone), 1 595—1 585 (aromatic C–H), and 1 240 cm^{-1} (3β- and 16α-acetate), $\lambda_{max.}$ 216 (ε 17 530), 239infl (13 000), 263 (6 700), and 338 nm (4 400), δ 1.38 and 1.45 (6H, 2s, 17β- and 10-Me), 2.0, 2.07, and 2.16 (9H, 3s, 3β- and 16α-OAc, and 17α-COMe), 2.4 (2H, m, 15-H_2), 3.5 (2H, m, 6-H_2), 4.7 (1H, m, 3α-H), 5.53 (1H, m, 16β-H), 6.94 (1H, s, 12-H), and 7.2 (1H, s, 11-OH) (Found: C, 67.7; H, 6.6. $C_{25}H_{30}O_7$ requires C, 67.8; H, 6.8%).

3β,17α-*Dihydroxy*-5α-*pregna*-8,14-*diene*-7,11,20-*trione* (11).

—The diacetate (10) (500 mg) was hydrolysed by heating to reflux for 15 min in methanol (25 ml) with sodium hydroxide solution (2.5 ml; 1N). The solution was cooled, acidified with dilute acetic acid, and diluted with water. The product was filtered off, dried, and crystallised from methanol to give the 3β,17α-*dihydroxy*-7,11,20-*trione* (11) (300 mg), m.p. 217—219°, $\nu_{max.}$ (KCl) 1 710 (20-ketone), 1 695 and 1 685 (7- and 11-ketones), and 1 615 cm^{-1} (14,15-double bond), $\nu_{max.}$ (CH_2Cl_2) 3 580 cm^{-1} (OH), $\lambda_{max.}$ 217 (ε 7 800) and 335 nm (4 700) (Found: C, 70.5; H, 7.4. $C_{21}H_{26}O_5$ requires C, 70.4; H, 7.3%).

3β-*Acetoxy*-5α-*pregna*-8,14,16-*triene*-7,11,20-*trione* (12).—(*a*) A solution of 3β-acetoxy-16α,17α-epoxy-5α-pregn-8-ene-7,11,20-trione (6) (10 g) in glacial acetic acid (100 ml) was heated to 90 °C for 0.5 h with a saturated solution of hydrogen bromide in glacial acetic acid (50 ml). After cooling, the solution was poured into water and the crude product was filtered off and crystallised from methylene dichloride–methanol to give the *product* (12) (7.0 g) m.p. 231—232°, $\nu_{max.}$ 1 730 (3β-acetate), 1 690 and 1 680 (Δ^{8}-7,11-dione), 1 650 ($\Delta^{14,16}$-20-one), 1 585 (16,17-double bond), and 1 505 cm^{-1} (14,16-diene), $\lambda_{max.}$ 264 (ε 8 600), 323 (7 700), and 365 nm (8 100), δ 1.17 (3H, s, 10-Me), 1.43 (3H, s, 13-Me), 2.02 (3H, s, 3β-OAc), 2.31 (1H, d, *J* 13.5 Hz, 12β-H), 2.37 (3H, s, 17-COMe), 3.30 (1H, d, *J* 13.5 Hz, 12α-H), 4.7 (1H, m, 3α-H), and 7.15 and 7.38 (2H, 2d, *J* 2.7 Hz, 15- and 16-H) (Found: C, 71.7; H, 7.21. $C_{23}H_{26}O_5$ requires C, 72.2; H, 6.9%).

(*b*) 3β,17α-Dihydroxy-5α-pregna-8,14-diene-7,11,20-trione (11) (300 mg) in pyridine (2 ml) was treated with acetic anhydride (1 ml) at room temperature for 2 h. The product was isolated by addition of water and filtration. Crystallisation from methylene dichloride–methanol gave the 8,14,16-triene-7,11,20-trione (12) (250 mg), m.p. 230—232°, identical with the product prepared by method (*a*) (t.l.c., i.r., and u.v. examination).

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