706. *Steroids. Part XVIII.* The Preparation of Some 11-Ethynyl-steroids.*

By C. W. Shoppee and Ruth E. Lack.

The preparation of some 11α-ethynyl-11β-hydroxy-steroids by the action of ethynylmagnesium bromide on the corresponding 11-keto-steroids is described. These 11β-hydroxy-compounds are readily dehydrated by thionyl chloride in pyridine.

Although the lack of reactivity of 11-keto-steroids with normal carbonyl reagents is well known,[1] the reactions of several 11-keto-steroids with methyl-lithium and methylmagnesium bromide have been described.[2-5] Methyl-lithium has generally given high yields of the 11α-methyl derivatives, *e.g.*, with 11-oxotigogenin,[6] 3β-hydroxy-5α-ergost-22-en-11-one,[6] and derivatives of 5α- and 5β-pregnan-11-one.[4,7] Variable results have, however, been reported with methylmagnesium bromide; Fonken, Hogg, and McIntosh [4,5] found it not to react with a series of 11-keto-steroids, and Elks [6] recovered only starting material when methyl-lithium was replaced by methylmagnesium iodide in the treatment of 11-oxotigogenin. Although Kirk and Petrow [8] report good yields of 11α-methyl derivatives from 11-oxotigogenin acetate and from 3β,20β-diacetoxy-5α-pregnan-11-one with this reagent, they found the Δ^5-3,17-bisketal from androst-4-ene-3,11,17-trione and various derivatives of 5β-pregnan-11-one to be completely unreactive.

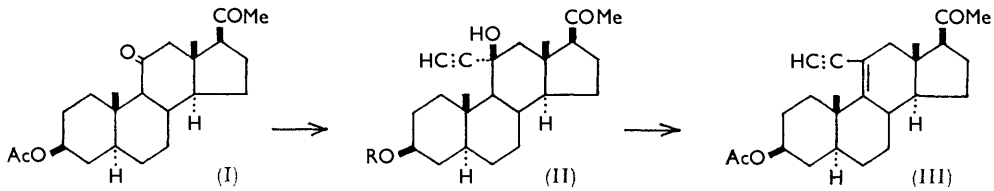
After the successful reaction of ethynylmagnesium bromide [9] with the hindered keto-group in an α-ethyldeoxyanisoin and related compounds,[10] we have investigated the reactions of a series of 11-keto-steroids with this reagent.

3β-Acetoxy-5α-pregnane-11,20-dione (I) was converted [11] into the 20-ketal, whose structure follows from the similarity in shape and amplitude of its optical rotatory dispersion curve to those described by Djerassi *et al.*[12] for 11-keto-groups in the same

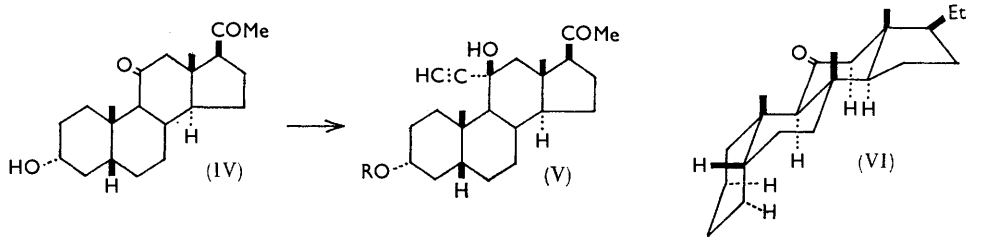
* Part XVII, preceding paper.

[1] Steiger and Reichstein, *Helv. Chim. Acta*, 1937, **20**, 817; Huang-Minlon, *J. Amer. Chem. Soc.*, 1949, **71**, 3301.
[2] Ringold, Batres, and Zderic, *Tetrahedron*, 1958, **2**, 164.
[3] Fonken and Hogg, *Tetrahedron*, 1958, **2**, 365.
[4] Fonken, *J. Org. Chem.*, 1958, **23**, 1075.
[5] Fonken, Hogg, and McIntosh, *J. Org. Chem.*, 1959, **24**, 1600.
[6] Elks, *J.*, 1960, 3333.
[7] Aderic, Batres, Limon, Cartio, Lisci, Monroy, Necoechea, and Ringold, *J. Amer. Chem. Soc.*, 1960, **82**, 3404.
[8] Kirk and Petrow, *J.*, 1961, 2091.
[9] Jones, Skattebol, and Whiting, *J.*, 1956, 4765.
[10] Shoppee, Craig, and Lack, *J.*, 1961, 1311, 2291.
[11] Allen, Bernstein, and Littel, *J. Amer. Chem. Soc.*, 1954, **76**, 6116; Campbell, Babcock, and Hogg, *ibid.*, 1958, **80**, 4717.
[12] Folz, Lippman, and Djerassi, *J. Amer. Chem. Soc.*, 1955, **77**, 4359; Djerassi and Closson, *ibid.*, 1956, **78**, 3761; Djerassi, Osiecki, Riniker, and Riniker, *ibid.*, 1958, **80**, 1216.

stereochemical environment. The 20-ketal, on treatment with ethynylmagnesium bromide, gave a good yield of the 20-ketal of 3β,11β-dihydroxy-11α-ethynyl-5α-pregnan-20-one (II; R = H), characterised as the 20-ketal 3-monoacetate. Brief hydrolysis of



the latter with toluene-*p*-sulphonic acid in acetone at 55° gave the 20-ketone (II; R = Ac), which was readily dehydrated by thionyl chloride in pyridine at 0° to 3β-acetoxy-



11-ethynyl-5α-pregn-9(11)-en-20-one (III). The ease of ionic dehydration of axial 11β-hydroxy-steroids, originally observed in 1940 by Shoppee,[13] has been confirmed [2-7] and is consistent with the configuration assigned in (II) at position 11.

Although 5β-pregnan-11-one failed to react with methylmagnesium bromide,[8] we find that 3α-hydroxy-5β-pregnane-11,20-dione (IV) as the 20-ketal, whose optical rotatory dispersion curve by its shape and amplitude [12] discloses the presence of an 11-keto-group, is converted by ethynylmagnesium bromide in low yield into the 20-ketal of 11α-ethynyl-3α,11β-dihydroxy-5β-pregnan-20-one (V; R = H). The product was isolated as the 20-ketal 3-monoacetate, which on brief hydrolysis with toluene-*p*-sulphonic acid in acetone at 55° gave 3α-acetoxy-11α-ethynyl-11β-hydroxy-5β-pregnan-20-one (V; R = Ac).

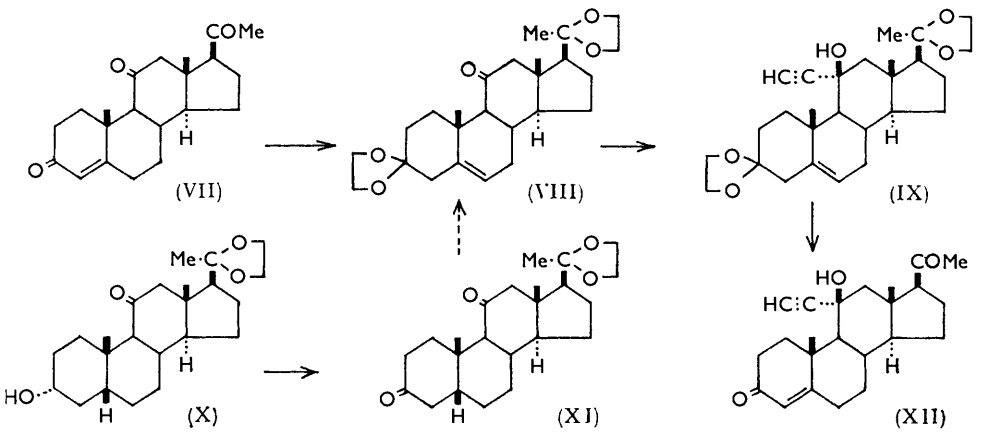
The lower yield of 11α-ethynyl derivative in the 5β- than in the 5α-pregnane series, and the similar finding for the reaction with methylmagnesium bromide,[8] suggest increased steric hindrance to the α-approach of the alkyl group with both reagents in the 5β-series (VI or with ring A as a boat), compared with the 5α-series; there appears to be equal hindrance in the two series on the β-side of the molecule. These results may represent a long-range conformational transmission effect; the lack of reactivity of Δ^5-compounds, *e.g.*, the Δ^5-3,20-diketal of cortisone (see below), is probably due to such an effect.

Although several Δ^5-11-keto-steroids,[7] including the Δ^5-3,20-bisketal from pregn-4-ene-3,11,20-trione,[14] failed to react with methyl-lithium, Fonken *et al.*[5] found that the Δ^5-3-ketal from 21-triphenylmethoxypregna-4,17(20)[*cis*]-diene-3,11-dione formed the 11α-methyl derivative with this reagent. We therefore examined the reaction of the Δ^5-3-ketal from an 11-ketone with ethynylmagnesium bromide.

Pregn-4-ene-3,11,20-trione [15] (VII), prepared from 3α-hydroxy-5β-pregnane-11,20-dione by oxidation, bromination, and dehydrobromination, was converted into the known Δ^5-3,20-diketal (VIII) as described by Constantine *et al.*,[14] or, more conveniently, by using ethylene glycol as both reagent and solvent.[8] The 3,20-diketal (VIII) had the m. p. 175—178° previously reported [14] but showed a positive Cotton curve of molecular amplitude

[13] Shoppee, *Helv. Chim. Acta*, 1940, **23**, 740; cf. Shoppee, *J.*, 1946, 1134.
[14] Constantine, Haven, and Sarett, *J. Amer. Chem. Soc.*, 1953, **75**, 1716.
[15] Hegner and Reichstein, *Helv. Chim. Acta*, 1943, **26**, 721; von Euw, Lardon, and Reichstein, *ibid.*, 1944, **27**, 821.

$10^{-2}a + 47$. The shape of the curve at first led us to suspect the presence of a free 20-keto-group since ketalisation of an 11-keto-group under forcing conditions has been described.[16] We now attribute the shape of the curve to the change in steric environment of the 11-keto-group caused by the presence of the isolated 5,6-double bond, which is known to affect the shape of Cotton curves.[17] A similarly shaped curve has been observed for the 3,20-bisketal of cortisone, in which the 11-keto-group has the same steric environment as in (VIII). An attempt was made to prepare the 3,20-bisketal (VIII) by an alternative route; the 20-ketal (X) was smoothly oxidised by chromium trioxide in pyridine to 5β-pregnane-3,11,20-trione 20-ketal (XI), but monobromination gave only inseparable oils, which could not be dehydrobrominated satisfactorily.[18]



The 3,20-diketal (VIII) with ethynylmagnesium bromide in tetrahydrofuran gave a good yield of a carbonyl-free amorphous product, which had the correct spectral properties ($\nu_{max.}$ 3600, 3310 cm.$^{-1}$) and gave correct analyses for 11α-ethynyl-11β-hydroxypregn-5-ene-3,20-dione diketal (IX). This crude product was hydrolysed by toluene-*p*-sulphonic acid in acetone at 55°, to give after chromatography on silica gel 11α-ethynyl-11β-hydroxypregn-4-ene-3,20-dione (XII); this compound was difficult to crystallise and was also obtained as a hydrate.

Elks [6] found the Δ^5-3,20-diketal [19] of cortisone and the 3,20-diketal of 4,5α-dihydrocortisone did not react with methyl-lithium, and similar results were obtained by Fonken *et al.*[5] with the 20-ketal of 3β,17α-dihydroxy-5α-pregnane-11,20-dione. The Δ^5-3,20-diketal of cortisone [19] with a large excess of ethynylmagnesium bromide, under the same forcing conditions as previously employed, gave no trace of 11-ethynyl derivative, although the 17,20:20,21-bismethylenedioxy-derivative of the Δ^5-3-ketal from cortisone has been reported [20] to react with allylmagnesium bromide. The lack of reactivity of the 11-keto-group in these compounds may be related to the ease of enolisation [5] but may also be attributed [6] to the presence of the 17α-hydroxy-group. Examination of a model shows little 1,4-steric interaction between the 11-keto- and the 17α-hydroxyl group, but considerable steric hindrance to rearside α-approach to the 11-keto-group could result from initially formed 17α-metallic complexes with methyl-lithium and methylmagnesium bromide.

[16] Magerlein and Levin, *J. Amer. Chem. Soc.*, 1955, **77**, 1904.
[17] Djerassi, Closson, and Lippman, *J. Amer. Chem. Soc.*, 1956, **78**, 3163; Chaudhry, Halsall, and Jones, *J.*, 1961, 2727.
[18] Evans, Green, Hunt, Long, Mooney, and Phillipps, *J.*, 1958, 1529.
[19] Antonucci, Bernstein, Hiller, Linbad, Littel, and Williams, *J. Org. Chem.*, 1953, **17**, 70.
[20] Beyler, Hoffman, and Sarett, *J. Amer. Chem. Soc.*, 1960, **82**, 178.

Experimental

For general directions see *J.*, 1959, 345. Ultraviolet absorption spectra were measured for EtOH solutions on a Perkin–Elmer 4000 A spectrophotometer, infrared absorption spectra were determined for CCl_4 solutions in a Perkin–Elmer model 221 spectrophotometer. Analysis samples were dried at 20°/0·5 mm. for 2—8 hr.

3β-*Acetoxy*-20,20-*ethylenedioxy*-5α-*pregnan*-11-*one*.—3β-Acetoxy-5α-pregnane-11,20-dione (5 g.) in ethylene glycol (60 ml.) containing toluene-*p*-sulphonic acid (250 mg.) was slowly distilled under reduced pressure at 90° for 15 min. After addition of sodium hydrogen carbonate solution to the cooled residue, the product was filtered off, dried, and recrystallised from methanol, to give 3β-*acetoxy*-20,20-*ethylenedioxy*-5α-*pregnan*-11-*one* (4·4 g.), m. p. 155—157°, $\nu_{max.}$ 1735 (OAc), 1710 (C=O) cm.$^{-1}$ (Found: C, 71·4; H, 9·1. $C_{25}H_{38}O_5$ requires C, 71·7; H, 9·15%). After further purification by chromatography on neutral aluminium oxide the m. p. was raised to 165—166°. Optical rotary dispersion (in MeOH), positive Cotton effect: $[\phi]$ + 2470° (322·5 mμ), — 2360° (275 mμ), $10^{-2}a$ + 48.

3β-*Acetoxy*-20,20-*ethylenedioxy*-11α-*ethynyl*-5α-*pregnan*-11β-*ol*.—The above 20-ketal (2 g., 0·005 mole) was treated with ethynylmagnesium bromide in tetrahydrofuran [prepared from magnesium (2·43 g., 0·1 g.-atom) and ethyl bromide (13·1 g.)] at 65° for 18 hr. Decomposition of the complex with a saturated solution of ammonium chloride, acidification with sulphuric acid, and ether-extraction gave the product which was then treated with acetic anhydride (5 ml.) at 130° for 10 min. After the usual working-up the crude acetate was chromatographed on neutral aluminium oxide (60 g.) prepared in hexane. Elution with benzene gave unchanged 20-ketal 3-acetate (320 mg.), m. p. 164·5°; elution with ether–benzene (1 : 20; 7 × 25 ml.) gave 3β-*acetoxy*-20,20-*ethylenedioxy*-11α-*ethynyl*-5α-*pregnan*-11β-*ol* (1·4 g.), m. p. 190—191°, $\nu_{max.}$ 3600 (OH), 3305 (C≡CH), 1735 (OAc), 1109 (ketal) cm.$^{-1}$ (Found: C, 72·85; H, 9·25. $C_{27}H_{40}O_5$ requires C, 72·95; H, 9·05%). Further elution with ether–benzene (1 : 1) and ether gave only oils (300 mg.), $\nu_{max.}$ 3500 (OH), 3250 (C≡CH) cm.$^{-1}$, but these gave more material of m. p. 190—191° after treatment with acetic anhydride at 130° for 10 min.

When the above 20-ketal (4·18 g., 0·01 mole) was treated with ethynylmagnesium bromide in tetrahydrofuran [prepared from magnesium (2·43 g., 0·1 g.-atom) and ethyl bromide (13·1 g.)] for 1 hr. at 65° and the product isolated as above, the only product was 3β-*hydroxy*-20,20-*ethylenedioxy*-5α-*pregnan*-11-*one* (3·45 g.), m. p. 210° (from ether), $\nu_{max.}$ 3400, 1710 cm.$^{-1}$ (Found: C, 73·3; H, 9·5. $C_{23}H_{36}O_4$ requires C, 73·35; H, 9·6%). This was treated with acetic anhydride (10 ml.) at 130° for 10 min., to give the 20-ketal 3-monoacetate, m. p. and mixed m. p. 165°.

3β-*Acetoxy*-11α-*ethynyl*-11β-*hydroxy*-5α-*pregnan*-20-*one*.—3β-Acetoxy-11α-ethynyl-20,20-ethylenedioxy-5α-pregnan-11β-ol (100 mg.) was treated with toluene-*p*-sulphonic acid (10 mg.) in acetone (10 ml.) at 55° for 15 min. Addition of water gave 3β-*acetoxy*-11α-*ethynyl*-11β-*hydroxy*-5α-*pregnan*-20-*one* (88 mg.), m. p. 235—237°, $\nu_{max.}$ (in Nujol) 3440 (OH), 3285 (C≡CH), 1730 (OAc), 1705 (C=O), 1365 (Ac) cm.$^{-1}$ (Found: C, 74·9; H, 9·1. $C_{25}H_{36}O_4$ requires C, 74·95; H, 9·05%).

3β-*Acetoxy*-11-*ethynylpregn*-9(11)-*en*-20-*one*.—3β-Acetoxy-11α-ethynyl-11β-hydroxy-5α-pregnan-20-one (40 mg.) in pyridine (4 ml.) was treated with thionyl chloride (0·5 ml.) at 0° for 5 min. The mixture was poured into water and extracted with ether, to give 3β-*acetoxy*-11-*ethynylpregn*-9(11)-*en*-20-*one* (32 mg.), m. p. 182—183° (from acetone), $\nu_{max.}$ 3300 (C≡CH), 3080 (C≡C), 1732 (OAc), 1707 (C=O) cm.$^{-1}$ (Found: C, 78·6; H, 8·75. $C_{25}H_{34}O_3$ requires C, 78·5; H, 8·95%).

20,20-*Ethylenedioxy*-3α-*hydroxy*-5β-*pregnan*-11-*one*.—3α-Hydroxy-5β-pregnane-11,20-dione (500 mg.) in ethylene glycol (20 ml.) containing toluene-*p*-sulphonic acid (50 mg.) was slowly distilled under reduced pressure at 90° for 15 min. The cooled residue was diluted with sodium hydrogen carbonate solution and filtered. The crude solid product was purified by chromatography on neutral aluminium oxide (15 g.) in hexane. Elution with benzene gave 20,20-*ethylenedioxy*-3α-*hydroxy*-5β-*pregnan*-11-*one* (580 mg.), m. p. 143—145° (from ether), $\nu_{max.}$ 3500 (OH), 1709 (C=O) cm.$^{-1}$ (Found: C, 73·2; H, 9·6. $C_{23}H_{36}O_4$ requires C, 73·35; H, 9·6%). Optical rotatory dispersion: in MeOH, $[M]$ +640° (322·5—320 mμ, peak), +160° (287·5 mμ, trough), $10^{-2}a$ +5.

3α-*Acetoxy*-20,20-*ethylenedioxy*-11α-*ethynyl*-5β-*pregnan*-11β-*ol*.—20,20-Ethylenedioxy-3α-hydroxy-5β-pregnan-11-one (1·0 g.) was treated with ethynylmagnesium bromide in tetrahydrofuran [prepared from magnesium (1·2 g., 0·05 mole) and ethyl bromide (6·5 g.)] at 65° for 18 hr.

The product was isolated in the usual way, but chromatography on neutral aluminium oxide gave no pure product although spectral properties showed that it probably was a mixture of unchanged ketal and 20,20-ethylenedioxy-11α-ethynyl-5β-pregnane-3α,11β-diol. All fractions were combined and treated with acetic anhydride at 130° for 15 min. The usual isolation procedure gave a crude product which was chromatographed on aluminium oxide (30 g.) in pentane. Elution with benzene–pentane (1 : 1; 5 × 20 ml.) gave only oils (450 mg.), but elution with benzene (3 × 25 ml.) gave 3α-*acetoxy*-20,20-*ethylenedioxy*-11α-*ethynyl*-5β-*pregnan*-11β-*ol* (385 mg.), m. p. 185° (from pentane–ether), $\nu_{max.}$ 3600 (OH), 3300 (C≡CH), 1730 (OAc) cm.$^{-1}$ (Found: C, 72·85; H, 9·2. $C_{27}H_{40}O_5$ requires C, 72·95; H, 9·05%).

3α-*Acetoxy*-11α-*ethynyl*-11β-*hydroxy*-5β-*pregnan*-20-*one*.—3α-Acetoxy-20,20-ethylenedioxy-11α-ethynyl-5β-pregnan-11β-ol (100 mg.) in acetone (10 ml.) was treated with toluene-*p*-sulphonic acid (10 mg.) at 55° for 10 min. Dilution with water and extraction with ether, followed by chromatography on silica gel (10 g.) in pentane and elution with ether–pentane (1 : 20), gave 3α-*acetoxy*-11α-*ethynyl*-11β-*hydroxy*-5β-*pregnan*-20-*one* (68 mg.), m. p. 215° (from ether–pentane), $\nu_{max.}$ 3400 (OH), 3300 (C≡CH), 1735 (OAc), 1705 (C=O) cm.$^{-1}$ (Found: C, 74·9; H, 9·1. $C_{25}H_{36}O_4$ requires C, 74·95; H, 9·05%).

5β-*Pregnane*-3,11,20-*trione*.—3α-Hydroxy-5β-pregnane-11,20-dione (4 g.) in acetic acid (50 ml.) was treated with a 2% solution of chromium trioxide in acetic acid (50 ml.) for 18 hr. at 20°. The solution was concentrated by distillation under reduced pressure, poured into water, and extracted with ether. Evaporation of the solvent gave 5β-pregnane-3,11,20-trione [15] (3·2 g.), m. p. 158—160°.

Pregn-4-*ene*-3,11,20-*trione*.—5β-Pregnane-3,11,20-trione (4 g.) in acetic acid (50 ml.) was treated with 1 drop of a saturated solution of hydrogen bromide in acetic acid and then dropwise with a solution of bromine (1·85 g.) and sodium acetate (950 mg.) at 20° during 10 min. The usual isolation procedure gave 4β-bromo-5β-pregnan-3,11,20-trione,[15] m. p. 158—159°. This bromo-ketone (2·5 g.) was heated with *s*-collidine (10 ml.) in nitrogen at 180° for 30 min. The usual isolation procedure gave a brown oil, which was chromatographed on silica gel (300 g.) prepared in pentane. Elution with ether–pentane (1 : 20) gave pregn-4-ene-3,11,20-trione (1·75 g.), m. p. 172—175°, $\nu_{max.}$ 1710, 1685, 1640 cm.$^{-1}$.

3,3:20,20-*Bisethylenedioxypregn*-5-*en*-11-*one*.—(*a*) Pregn-4-ene-3,11,20-trione (1·75 g.) in benzene (30 ml.) was refluxed under a Dean and Stark apparatus with ethylene glycol (4 ml.) and toluene-*p*-sulphonic acid (175 mg.) for 10 hr. The usual isolation procedure gave a crude product, which was chromatographed on neutral aluminium oxide (50 g.) in hexane. Elution with benzene–hexane (1 : 1; 7 × 50 ml.) gave the diketal (1·35 g.), m. p. 176—178° (from hexane), $\nu_{max.}$ 1710 cm.$^{-1}$ (Found: C, 72·1; H, 8·65. Calc. for $C_{25}H_{36}O_5$: C, 72·1; H, 8·7%). Optical rotatory dispersion: in MeOH, [*M*] +1660° (325—322·5 mμ, peak), −3320° (275 mμ, trough), $10^{-2}a$ +50. Further elution with ether–benzene (1 : 20) gave only oils (500 mg.).

(*b*) Pregn-4-ene-3,11,20-trione (1 g.), in ethylene glycol (30 ml.) containing toluene-*p*-sulphonic acid (100 mg.), was slowly distilled at 90° under reduced pressure for 30 min. The residue was cooled, diluted with sodium hydrogen carbonate solution. and extracted with ether. The residual oil was chromatographed on neutral aluminium oxide (30 g.) in hexane. Elution with benzene–hexane gave the diketal (950 mg.), m. p. and mixed m. p. 174—175°.

20,20-*Ethylenedioxy*-5β-*pregnane*-3,11-*dione*.—20,20-Ethylenedioxy-3α-hydroxy-5β-pregnan-11-one (3·2 g.) in pyridine (100 ml.) was slowly added to chromium trioxide (5·9 g.) in pyridine (100 ml.) at 20° and the mixture was left for 24 hr. After the usual isolation procedure, crystallisation from ether gave 20,20-*ethylenedioxy*-5β-*pregnane*-3,11-*dione* (2·7 g.), m. p. 147° (Found: C, 73·7; H, 9·15. $C_{23}H_{34}O_4$ requires C, 73·75; H, 9·15%).

3,3:20,20-*Bisethylenedioxy*-11α-*ethynylpregn*-5-*en*-11β-*ol*.—3,3:20,20-Bisethylenedioxypregn-5-en-11-one (1 g., 0·05 mole) was treated with ethynylmagnesium bromide in tetrahydrofuran [prepared from magnesium (1·2 g., 0·05 g.-atom) and ethyl bromide (6·5 g.)] at 65° for 18 hr. After the usual working-up, the product was chromatographed on neutral aluminium oxide (30 g.). Elution with benzene gave unchanged ketal (250 mg.), m. p. 174—175°; elution with ether–benzene (1 : 1; 200 ml.) gave the amorphous 3,3:20,20-*bisethylenedioxy*-11α-*ethynylpregn*-5-*en*-11β-*ol* (500 mg.), m. p. 90—92° (after precipitation from ether with pentane), $\nu_{max.}$ 3600 (OH), 3300 (C≡CH), 1080 (ketal) cm.$^{-1}$ (Found: C, 73·0; H, 8·8. $C_{27}H_{38}O_5$ requires C, 73·3; H, 8·65%). A part, azeotropically distilled from benzene, was crystallised from ether, then having m. p. 210°, $\nu_{max.}$ 3550, 3250, 1080 cm.$^{-1}$ (Found: C, 73·1; H, 8·8%).

11α-*Ethynyl*-11β-*hydroxypregn*-4-*ene*-3,20-*dione*.—3,3:20,20-Bisethylenedioxy-11α-ethynylpregn-5-en-11β-ol (300 mg.) in acetone (30 ml.) was treated with toluene-*p*-sulphonic acid (30 mg.) at 55° for 15 min. Dilution with water and extraction with chloroform gave a brown oil, which was chromatographed on silica gel (30 g.) in pentane. Elution with ether–pentane (1 : 20; 160 ml.) gave 11α-*ethynyl*-11β-*hydroxypregn*-4-*ene*-3,20-*dione hydrate* (after precipitation from an ether solution with pentane) (250 mg.), m. p. 98—100°, $\nu_{max.}$ (in Nujol) 3400 (OH), 3300 (C≡CH), 1712 (C=O), 1680 (C=C–C=O), 1640 (C=C) cm.$^{-1}$ (Found: C, 74·0; H, 8·6. $C_{23}H_{30}O_3,H_2O$ requires C, 74·15; H, 8·65%).

After rechromatography on silica gel, crystallisation from ether gave 11α-*ethynyl*-11β-*hydroxypregn*-4-*ene*-3,20-*dione*, m. p. 235°, $\nu_{max.}$ 3500 (OH), 3300 (C≡CH), 1710 (C=O), 1685 (C=C–C=O), 1640 (C=C) cm.$^{-1}$ (Found: C, 77·6; H, 8·5. $C_{23}H_{30}O_3$ requires C, 77·9; H, 8·5%).

3,3:20,20-*Bisethylenedioxy-derivative of Cortisone*.—Cortisone (3 g.) in ethylene glycol (100 ml.) and toluene-*p*-sulphonic acid (93 mg.) were stirred and slowly distilled under reduced pressure at 90° for 1 hr. The dark solution was made alkaline with saturated sodium hydrogen carbonate solution and the dark solid was filtered off and purified by chromatography on neutral aluminium oxide (90 g.). Elution with benzene (250 ml.) gave a non-hydroxylic product, possibly 3,3:17,20:20,21-trisethylenedioxypregn-5-en-11-one [21] (220 mg.), m. p. 167—169° (from ether), $\nu_{max.}$ 1706 cm.$^{-1}$ (Found: C, 67·95; H, 8·1. $C_{27}H_{38}O_7$ requires C, 68·3; H, 8·05%). Further elution with benzene gave an oil (150 mg.); then use of ether–benzene (1 : 10) gave the 3,3:20,20-bisethylenedioxy-derivative (1·5 g.), m. p. 240—241°, of cortisone (Found: C, 66·8; H, 7·95. Calc. for $C_{25}H_{36}O_7$: C, 66·9; H, 8·1%). Optical rotatory dispersion (in MeOH): positive Cotton effect: $[\phi]$ + 2720 (320 mμ), — 3540 (272·5 mμ), $10^{-2}a$ +63.

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[21] Bernstein, Heller, and Allen, *J. Org. Chem.*, 1961, **26**, 1331.