[CONTRIBUTION FROM THE COLLIP MEDICAL RESEARCH LABORATORY AND THE DEPARTMENT OF CHEMISTRY, UNIVERSITY OF WESTERN ONTARIO]

Steroids and Related Products. XV.[1] The Introduction of the Δ^{11}-Double Bond. II[2,3]

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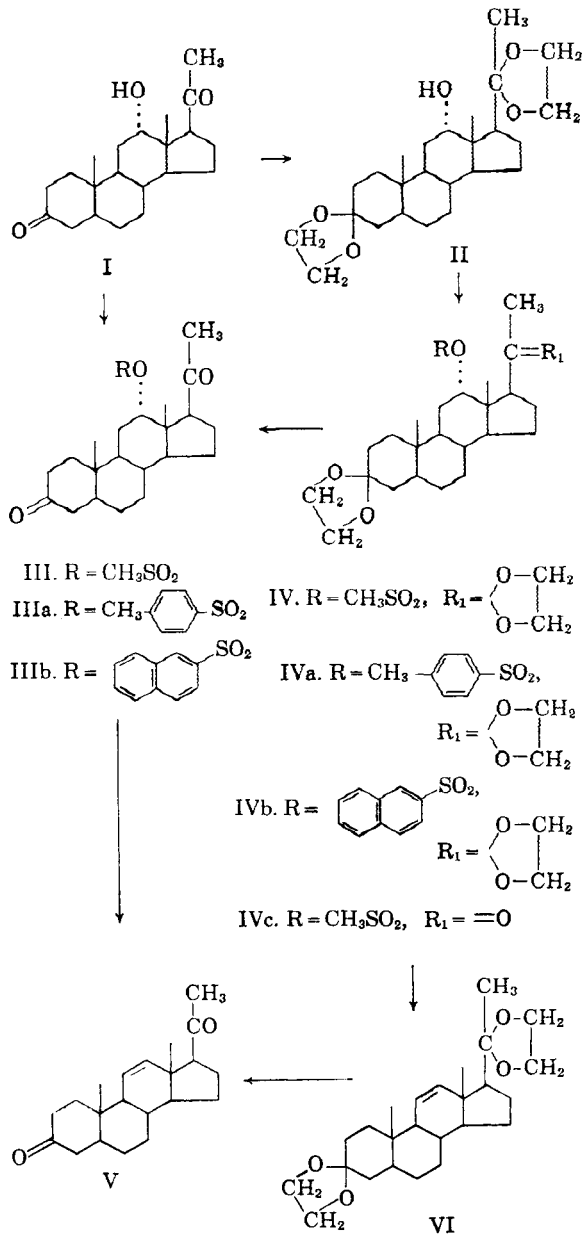
Further evidence is presented for the postulate, formulated in Part I of this study, that dehydrosulfonylations of steroidal 12α-sulfonates, with aluminum oxide, are prone to steric acceleration. It is shown that in the case of A/B-*cis*-fused steroids, this reaction proceeds smoothly from bulky sulfonates, such as tosylates and naphthalenesulfonates, but only under vigorous conditions from small-sized mesylates.

In Part I of this investigation,[2] our group reported that an 11,12-double bond could conveniently be introduced into the steroid molecule by dehydrotosylation with aluminum oxide,[6] and suggested that this reaction was prone to steric acceleration. We showed that the reaction proceeded readily, at room temperature, either in the presence of a bulky, quasi-axial 17α-substituent which subjects the 12α-sulfonate to a marked (1:3) diaxial interaction, or in the case of *cis*-fusion of rings A and B, when the main plane of ring A is parallel to, and on the same side as, the axial 12α-C—O bond of the sulfonate. From an inspection of models, it is clear that a *cis*-fused A-ring can exert steric compression on a 12α-sulfonate only when the latter is bulky. Therefore, in such an A/B *cis*-fused system, the elimination reaction should proceed smoothly from large-sized 12α-sulfonates, such as tosylates and naphthalenesulfonates, but only with difficulty from small-sized 12α-mesylates. The experiments described in this paper prove that this is indeed the case.

When 12α-mesyloxypregnane-3,20-dione (III) was subjected to the action of alkaline aluminum oxide, under conditions which lead in high yield to the transformation of tosylate IIIa to Δ^{11}-pregnene-3,20-dione (V),[2] an elimination reaction did not take place to an appreciable extent. In order to effect the elimination of methanesulfonic acid, the reaction had to be carried out at an elevated temperature, as in the case of the elimination of *p*-toluenesulfonic acid without steric assistance, for instance in the absence of a bulky 17α-substituent



(1) Paper XIV of this series: Ch. R. Engel, R.-M. Hoegerle, and R. Deghenghi, *Can. J. Chem.*, **38**, 1199 (1960).

(2) Part I: G. Just and Ch. R. Engel, *J. Org. Chem.*, **23**, 12 (1958).

(3) The main aspects of this work were included in a communication presented before the 40th Annual Conference of the Chemical Institute of Canada, Vancouver, Canada, June 1957.

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(5) This paper is abbreviated from part of the M.Sc. thesis submitted by S. F. Papadopoulos to the Faculty of Graduate Studies of the University of Western Ontario in May 1960.

(6) Compare also: (a) Ch. R. Engel, K. F. Jennings, and G. Just, *J. Am. Chem. Soc.*, **78**, 6153 (1956) and (b) A. Ruff and T. Reichstein, *Helv. Chim. Acta*, **34**, 70 (1951).

and in the presence of a Δ^{4}-3-keto moiety.[2] On the other hand, we confirmed the facile elimination, at room temperature, of *p*-toluenesulfonic acid from tosylate IIIa and, furthermore, we were able to introduce the 11,12-double bond, in even higher yield, by treating the 12α-(2-naphthalenesulfonate) IIIb with aluminum oxide under conditions identical to those employed in the dehydrotosylation. We thus obtained further, convincing, evidence that the elimination proceeds smoothly, under mild conditions, from sulfonates which are exposed to steric compression and only with difficulty in the case of unhindered 12α-sulfonates.[7]

The naphthalenesulfonate IIIb was prepared from pregnane-12α-ol-3,20-dione (I) *via* the 3,20-diketal II,[8] because we found that naphthalenesulfonyl chloride in pyridine attacked a free 3-keto group. Also, it was necessary to prepare the methanesulfonate III in pyridine-chloroform, as described by Fried and Sabo,[9] since the 3-ketone was likewise attacked when the mesylation was carried out under the usual reaction conditions, in the absence of chloroform.[10] The deketalization of the intermediate diketals IV, IVa, and IVb, giving the free diketo derivatives III, IIIa, and IIIb, was achieved by an exchange reaction with acetone in the presence of *p*-toluenesulfonic acid.[11,12]

The naphthalenesulfonates IIIb and IVb, which could not be obtained in the crystalline form, showed a characteristic absorption maximum in the ultraviolet at 226–228 mμ, similar to that exhibited by tosylates,[6a] but with a higher extinction coefficient: in the case of purified naphthalenesulfonate IIIb, log ϵ was 5.0, as compared to 4.4 for the pure tosylate IIIa.

EXPERIMENTAL[13–16]

3,20-Bisethylenedioxypregnane-12α-ol (II). (*a*) A solution of 3 g. of pregnane-12α-ol-3,20-dione (I),[17] m.p. 179–180°, in 200 cc. of absolute benzene, was reduced to 185 cc. There was added 55 cc. of freshly distilled ethylene glycol and 120 mg. of *p*-toluenesulfonic acid monohydrate and the mixture was refluxed under exclusion of moisture for 30 hr., with vigorous stirring. During this period, moist benzene was removed periodically with the help of a water trap. After cooling, the product was poured into an iced sodium bicarbonate solution and the mixture was extracted with ether. The organic layer was washed with iced 1% sodium bicarbonate solution and with water, dried over sodium sulfate and taken to dryness. The residue (3.75 g., 99.7%), representing diketal II, crystallized upon trituration with ether; m.p. 78–80°; ν_{max}^{KBr} 3415 cm.$^{-1}$ (12α-hydroxyl), 1190, 1162, 1104, 1085, 1060 cm.$^{-1}$ (ketal bands). A sample was recrystallized three times from ether-hexane for analysis; m.p. 78–79°, $[\alpha]_D^{23}$ 31–32°.

Anal. Calcd. for $C_{25}H_{40}O_5$: C, 71.39; H, 9.59. Found: C, 71.23; H, 9.47.

(*b*) In another experiment, 2.0 g. of I was treated in an analogous fashion in 134 cc. of absolute benzene with 33 cc. of ethylene glycol and 80 mg. of *p*-toluenesulfonic acid, for 18 hr. The amorphous reaction product (2.7 g.) was chromatographed on 82 g. of aluminum oxide (*p*H 8.5, activity II–III). Benzene-ether (4:1) eluted 700 mg. of crude amorphous *3-ethylenedioxypregnane-12α-ol-20-one*, which resisted all attempts of crystallization; ν_{max}^{KBr} 1700 cm.$^{-1}$ (20-ketone, single band). Elutions with benzene-ether mixtures (1:1 and 1:4) gave 1.25 g. of crystalline diketal II, m.p. 78–80°, identical with the product described under (a).

12α-Hydroxy-3,20-bisethylenedioxypregnane-12α-methanesulfonate (IV). To a solution of 850 mg. of 3,20-bisethylenedioxypregnane-12α-ol (II), m.p. 77–78.5°, in 5.3 cc. of pyridine, was added at −15°, 4.2 cc. of a mixture prepared at −5° from 4.2 cc. of pyridine and 2.22 cc. of freshly distilled methanesulfonyl chloride. The product was allowed to stand for 4 hr. at 0° and then for another 48 hr. at −4°. Ice and ice water were added and after 4 hr. the mixture was extracted with ether. The ethereal solution was washed with

(7) Because of the qualitative nature of our experiments, based on the establishment of relative yields and not on actual reaction rates; also, because the yields in both the dehydrotosylation and dehydronaphthalenesulfonylation experiments were high, the observation of higher yields in the case of the elimination of 2-naphthalenesulfonic acid might not seem truly significant. However, this observation was confirmed in every set of experiments and in different series. Furthermore, while it is possible to purify, in reasonable yields, a 12α-tosylate by rapid chromatography on slightly acid aluminum oxide,[2] 12α-naphthalenesulfonates are transformed even under those circumstances, in relatively high yield, to the corresponding 11,12-unsaturated products.

(8) In order to obtain a complete transformation of the diketone I to the diketal II, the starting material had to be refluxed for thirty to thirty-six hours with ethylene glycol in benzene, in the presence of *p*-toluenesulfonic acid and with constant removal of water. After a reaction time of eighteen hours, an appreciable amount of 3-monoketal was still present; this product could only be obtained in the amorphous form, but its 12α-mesylate derivative IVc crystallized well.

(9) J. Fried and E. F. Sabo, *J. Am. Chem. Soc.*, **79**, 1130 (1957).

(10) Compare for instance: H. P. Sigg and T. Reichstein, *Helv. Chim. Acta*, **39**, 1507 (1956).

(11) H. Schinz and G. Shäppi, *Helv. Chim. Acta*, **30**, 1483 (1947). Compare also: C. Djerassi, E. Batres, J. Romo, and G. Rosenkranz, *J. Am. Chem. Soc.*, **74**, 3664 (1952); G. Rosenkranz, J. Pataki, and C. Djerassi, *J. Org. Chem.*, **17**, 290 (1952); H. J. Dauben, Jr., B. Löken, and H. J. Ringold, *J. Am. Chem. Soc.*, **76**, 1339 (1954); Ch. R. Engel, *Can. J. Chem.*, **35**, 131 (1957).

(12) Results similar to those obtained in the above-described series of transformations of the 12α-sulfonates III, IIIa, and IIIb with aluminum oxide were encountered when the corresponding diketals IV, IVa, and IVb were subjected to the action of aluminum oxide: dehydromesylation took place only at elevated temperatures, whereas the tosylate IVa and the naphthalenesulfonate IVb gave readily, at room temperature, the unsaturated diketal VI, which was transformed with acetone and *p*-toluenesulfonic acid to Δ^{11}-pregnene-3,20-dione (V).

(13) The melting points were taken in evacuated capillaries and the temperatures were corrected.

(14) We are indebted to Mr. J. F. Alicino, Metuchen, N. J., for the excellent microanalytical work.

(15) The aluminum oxide used was a gift of Merck and Company, Montreal, to whom we express our sincere thanks. The commercial product was treated before use, as described in footnote 18 of reference 2; compare also footnote 18 of the first article of this series [Ch. R. Engel, *J. Am. Chem. Soc.*, **76**, 4909 (1954)].

(16) For chromatographic purifications with silica gel, Davison's product No. 923 was used.

(17) We extend sincere thanks to Canada Packers Ltd., Toronto, for a generous gift of 3α,12α-diacetoxypregnane-20-one, which was used as starting material for the preparation of I.

water, iced dilute hydrochloric acid, iced 1*N* sodium carbonate solution and with water, was dried over sodium sulfate, and was taken to dryness *in vacuo*. The crude crystalline reaction product (925 mg., 92%) was recrystallized three times from ether-hexane for analysis; m.p. 134–135°, $[\alpha]_D^{23}$ 69°.

Anal. Calcd. for $C_{26}H_{42}O_7S$: C, 62.62; H, 8.49; S, 6.43. Found: C, 62.55; H, 8.60; S, 6.22.

3-Ethylenedioxypregnane-12α-ol-20-one-12α-methanesulfonate (IVc). At −5°, 1.95 cc. of freshly distilled methanesulfonyl chloride was dissolved in 3.84 cc. of absolute pyridine. A quantity of 3.8 cc. of this solution was added, at −15°, to a solution of 700 mg. of amorphous 12α-hydroxy-3-ethylenedioxypregnane-20-one (see above), in 4.8 cc. of pyridine. The product was treated and worked up as described for the preparation of the 12α-mesyloxy diketal IV. Thus, there was obtained 800 mg. (94% yield) of crystalline 3-ethylenedioxypregnane-12α-ol-20-one-12α-methanesulfonate (IVc), m.p. 134–135°. The product was recrystallized four times from ether-hexane for analysis; m.p. 147.5–148°; ν_{max}^{KBr} 1700 cm.$^{-1}$ (20-ketone), 1360, 1325, and 1164 cm.$^{-1}$ (mesylate), 1102, 1087,1062 cm.$^{-1}$ (ketal bands), $[\alpha]_D^{23}$ 86.5°.

Anal. Calcd. for $C_{24}H_{38}O_6S$: C, 63.40; H, 8.43; S, 7.05. Found: C, 63.28; H, 8.22; S, 6.91.

Pregnane-12α-ol-3,20-dione-12α-methanesulfonate (III). To a solution of 1.0 g. of pregnane-12α-ol-3,20-dione (I), m.p. 179–180°, in 4.5 cc. of absolute chloroform and 1.1 cc. of pyridine, there was added 0.35 cc. of methanesulfonyl chloride in 0.8 cc. of chloroform, at 0°. The mixture was allowed to stand for 16 hr. at 0° and was then poured into 800 cc. of ice water. The organic product was extracted with ether, the ethereal solution was washed with water, iced 2*N* hydrochloric acid and iced sodium carbonate solution and with water. After drying with sodium sulfate the solvent was removed. The crude amorphous residue (1.3 g.) showed no hydroxy absorption in the infrared and a double keto band. The product was rapidly chromatographed on 40 g. of aluminum oxide (*p*H 6.5, activity II–III). Benzene-ether mixtures eluted 956 mg. (78%) of crystalline mesylate III, m.p. 105–109°. Elutions with ethyl acetate gave 264 mg. of impure starting material I, m.p. 158–161°, melting after one recrystallization at 176–178°; the product was identified by mixed melting point and infrared analysis. (Considering this recovery of starting material, the yield of III was practically quantitative.) A sample of mesylate III was recrystallized four times from ether for analysis; m.p. 114–114.5°; ν_{max}^{KBr} 1705 and 1697 cm.$^{-1}$ (double band of 3- and 20-ketones), 1345 and 1172 cm.$^{-1}$ (mesylate), $[\alpha]_D^{23}$ 92.4°.

Anal. Calcd. for $C_{22}H_{34}O_6S$: C, 64.36; H, 8.35; S, 7.81. Found: C, 64.66; H, 8.31; S, 7.71.

Reaction of 12α-mesyloxypregnane-3,20-dione (III) *with aluminum oxide at room temperature.* A quantity of 560 mg. of mesylate III, m.p. 111–113°, was chromatographed, at room temperature, on 16 g. of aluminum oxide (*p*H 8.5, activity II) (compare the preparation of V from IIIa[2]). The majority of the starting material (387 mg.) was recovered in the pure state, m.p. 114–115°. No Δ^{11}-pregnene-3,20-dione (V) was isolated. The experiment was repeated with 350 mg. of the recovered mesylate III; again no 11-unsaturated product could be isolated and 274 mg. of pure mesylate was recovered.

Δ^{11}-Pregnene-3,20-dione (V)[2,18] *by dehydromesylation with aluminum oxide at elevated temperatures.* (a) *From 12α-mesyloxypregnane-3,20-dione* (III). A quantity of 274 mg. of mesylate III, m.p. 114–115°, was treated with 21 g. of aluminum oxide (*p*H 8.5, activity II) at 55°, as described for the dehydrotosylation of 12α-tosyloxyprogesterone.[2] There was obtained 107 mg. of impure Δ^{11}-pregnene-3,20-dione (V), m.p. 109–117°; the product was again treated with aluminum oxide at 55°, and thus there was obtained 33 mg. of Δ^{11}-pregnene-3,20-dione, m.p. 124–127°, identified by mixed melting point and comparison of the infrared spectrum with that of an authentic sample.

(b) *From 12α-mesyloxy-3,20-bisethylenedioxypregnane* (IV). A quantity of 870 mg. of mesyloxy diketal IV, m.p. 134–136°, was treated with 50 g. of aluminum oxide (*p*H 8.5, activity II), for 6 hr. at 55°, according to the procedure previously described[2] (see also above). There was obtained 430 mg. of an oily product, which gave a positive tetranitromethane reaction and which was rechromatographed, at room temperature, on 13 g. of aluminum oxide (*p*H 8). The purified, but amorphous Δ^{11}-*3,20-bisethylenedioxypregnene* (VI) thus obtained (413 mg.) was dissolved in 71 cc. of absolute acetone and treated for 36 hr. with 90 mg. of *p*-toluenesulfonic acid at room temperature. From the crude reaction product (275 mg.), 100 mg. of pure, authentic Δ^{11}-*pregnene-3,20-dione* (V), m.p. 128–129°, was obtained by crystallization from ether-hexane.

(c) *From 12α-mesyloxy-3-ethylenedioxypregnane-20-one* (IVc). Treatment of 265 mg. of 12α-mesyloxy-3-ethylenedioxypregnane-20-one (IVc), m.p. 147–148°, with 40 g. of aluminum oxide (*p*H 8.5, activity II) at 55°, for 6 hr., gave 201 mg. of amorphous Δ^{11}-*3-ethylenedioxypregnene-20-one*, which was rechromatographed at room temperature to give 150 mg. of purified, but still amorphous product; ν_{max}^{smear} 1695 cm.$^{-1}$ (20-ketone), 1623 and 723 cm.$^{-1}$ (Δ^{11}-double bond). A solution of this product in 15.5 cc. of absolute acetone was treated for 36 hr. with 20 mg. of *p*-toluenesulfonic acid at room temperature. Precipitation in a dilute sodium bicarbonate solution gave 35 mg. of Δ^{11}-*pregnene-3,20-dione* (V), m.p. 127–129°. The filtrate gave, upon extraction with ether, 100 mg. of impure product which yielded, after chromatography, another 31 mg. of V, m.p. 128–130°, and 51 mg. of less pure product, m.p. 110–120°. Both portions gave a positive tetranitromethane reaction. Recrystallization of the higher melting fraction from ether-hexane raised the m.p. to 133.5–134.5°. The product was sublimed at 110° in high vacuum for analysis; m.p. 133–134°; ν_{max}^{KBr} 3000 cm.$^{-1}$ (Δ^{11}-double bond), 1711 and 1693 cm.$^{-1}$ (3,20-diketone), 1623 and 723 cm.$^{-1}$ (Δ^{11}-double bond).

Anal. Calcd. for $C_{21}H_{30}O_2$: C, 80.18; H, 9.61. Found: C, 79.97; H, 9.85.

Δ^{11}-Pregnene-3,20-dione (V) *from pregnane-12α-ol-3,20-dione-12α-(p-toluenesulfonate)* (IIIa).[2,8b,19] The 12α-tosyloxypregnane-3,20-dione (IIIa), used in this experiment, was prepared from diketal II as follows: A solution of 3 g. of 3,20-bisethylenedioxypregnane-12α-ol (II), m.p. 77–78°, and 3.16 g. of *p*-toluenesulfonyl chloride in 16.3 cc. of pyridine was stored for 6 days at 50°. The usual working up gave 3.8 g. of crude amorphous *12α-tosyloxy-3,20-bisethylenedioxypregnane* (IVa), $\lambda_{max}^{C_2H_5OH}$ 225 mμ (log ε 3.9), containing some 3-monoketal as evidenced by a small 20-keto band in the infrared. The product was chromatographed on silica gel and gave 1.78 g. of purified tosyloxy diketal IVa, $\lambda_{max}^{C_2H_5OH}$ 225 mμ (log ε 4.4). This product was subjected to an exchange reaction with acetone and *p*-toluenesulfonic acid, as described above, and the resulting amorphous reaction product (1.5 g.) was chromatographed on silica gel. Thus 890 mg. of authentic, crystalline *12α-tosyloxypregnane-3,20-dione* (IIIa), m.p. 124–127°, $\lambda_{max}^{C_2H_5OH}$ 226 mμ (log ε 4.4), was obtained. The melting point was raised by one recrystallization from methanol to 129–131°.

A quantity of 610 mg. of pure tosyloxy diketone IIIa, m.p. 129–131°, was chromatographed on 20 g. of aluminum oxide (*p*H 8.5, activity II), as previously described.[2] The benzene-ether fractions (4:1) gave 276 mg. of Δ^{11}-*pregnene-3,20-dione* (V), m.p. 125–127° (70% yield). The rest of the chromatogram fractions (334 mg.) still showed an ultraviolet absorption spectrum typical of a tosylate[6a] and was rechromatographed on 10 g. of aluminum oxide, as before. Benzene-ether eluted 60 mg. (15% from the 610 mg. of

(18) P. Hegner and T. Reichstein, *Helv. Chim. Acta*, **26**, 721 (1943).

(19) J. v. Euw and T. Reichstein, *Helv. Chim. Acta*, **29**, 654 (1946).

starting material IIIa) of Δ^{11}-pregnene-3,20-dione (V), m.p. 124–127° (total yield after two chromatograms 85.5%).

Δ^{11}-Pregnene-3,20-dione (V) *from pregnane-12α-ol-3,20-dione-12α-(2-naphthalenesulfonate)* (IIIb). The diketonaphthalenesulfonate IIIb used in this experiment was prepared as follows: A solution of 1.2 g. of 3,20-bisethylenedioxypregnane-12α-ol (II), m.p. 78–80°, and 1.56 g. of 2-naphthalenesulfonyl chloride in 6.3 cc. of pyridine was kept for 6 days at 50°. The product was extracted with ether and the organic solution was washed with iced dilute hydrochloric acid, iced sodium bicarbonate solution and with water and was dried over sodium sulfate. Evaporation of the solvent gave 1.63 g. of amorphous product, $\lambda_{max}^{C_2H_5OH}$ 227–228 mμ (log ε 4.8), representing crude *12α-hydroxy-3,20-bisethylenedioxypregnane-12α-(2-naphthalenesulfonate)* (IVb). In another run, 2 g. of diketal II gave 2.5 g. of IVb, $\lambda_{max}^{C_2H_5OH}$ 226 mμ (log ε 4.5). This product was chromatographed on 100 g. of silica gel. Benzene–ethyl acetate (84:16) eluted 1.5 g. of a clear oil, $\lambda_{max}^{C_2H_5OH}$ 227–228 mμ (log ε 4.9), which was dissolved in 141 cc. of absolute acetone and treated for 36 hr. with 197 mg. of *p*-toluenesulfonic acid. The usual working up gave an amorphous reaction product (1.25 g.) which was chromatographed on 50 g. of silica gel. Benzene–ethyl acetate fractions eluted 694 mg. of a clear, amorphous product, representing *pregnane-12α-ol-3,20-dione-12α-(2-naphthalenesulfonate)* (IIIb), $\lambda_{max}^{C_2H_5OH}$ 227–228 mμ (log ε 5.0), ν_{max}^{smear} 1700 and 1695 cm.$^{-1}$ (3,20-diketone).

A quantity of 655 mg. of this purified diketonaphthalenesulfonate IIIb (equivalent to 610 mg. of tosylate IIIa) was chromatographed on 20 g. of aluminum oxide (*p*H 8.5, activity II) under conditions identical to those employed for the reaction of tosylate IIIa with this reagent. Benzene-ether (4:1) eluted 300 mg. (76% yield) of *Δ^{11}-pregnene-3,20-dione* (V), m.p. 124–127°. The rest of the chromatogram fractions (355 mg.) was rechromatographed, as described in the case of the tosylate IIIa. Thus, another 50 mg. (13% from 655 mg. of naphthalenesulfonate IIIb) of Δ^{11}-pregnene-3,20-dione, m.p. 124–127°, was obtained (total yield after two chromatograms 89%).

Rapid chromatography of naphthalenesulfonate IVb *on acidic aluminum oxide.* A quantity of 500 mg. of 12α-hydroxy-3,20-bisethylenedioxypregnane-12α-(2-naphthalenesulfonate) (IVb) was dissolved in a small amount of benzene and absorbed on 15 g. of acidic aluminum oxide (*p*H 6, activity III). The product was rapidly chromatographed, the first elutions being made with petroleum ether (b.p. 30–60°)–benzene (1:4) mixtures. Thus, there was obtained 268 mg. (77%) of crude 11-unsaturated product which was subjected to the usual exchange reaction with acetone and *p*-toluenesulfonic acid. From the reaction mixture, 116 mg. of crystalline *Δ^{11}-pregnene-3,20-dione* (V) was obtained; m.p. 126–127.5°, not depressed upon admixture of an authentic sample; the mother liquors amounted to 84 mg.

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[CONTRIBUTION FROM THE DIVISION OF STEROID RESEARCH, THE JOHN HERR MUSSER DEPARTMENT OF RESEARCH MEDICINE, UNIVERSITY OF PENNSYLVANIA]

Investigations on Steroids. XXXIV. 8,19-Epoxyprogesterone and 8,19-Epoxycortexone[1,2]

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Ethyl 8,19-epoxy-3β,5-dihydroxy-5β-etianate (III), which is obtainable as a minor reaction product in the selective dehydration of 3β,5,14,19-tetrahydroxy-5β,14β-etianic acid (I) leading mainly to ethyl 3β,5,19-trihydroxy-Δ^{14}-5β-etienate (II), has been transformed by conventional methods into 8,19-epoxyprogesterone (X) and 8,19-epoxycortexone (XVII). A conspicuous feature of the 8,19-epoxy series is the pronounced, abnormal levorotatory shift which occurs when the 5β-hydroxy-3-oxo compounds are converted into the Δ^4-3-ketones. As the analogous 19:8-lactone compounds behave normally in this respect, no explanation for this phenomenon can be given at present.

The degradation of strophanthidol to 3β,5,14,19-tetrahydroxy-5β, 14β-etianic acid (I) was described from this laboratory some time ago.[4] Treatment of I with 0.1 *N* ethanolic hydrogen chloride resulted mainly in simultaneous esterification and selective

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(2) The findings of this paper were presented on Sept. 5, 1958, at the 4th International Congress of Biochemistry in Vienna (*cf.* Maximilian Ehrenstein: Biochemistry of the Corticoids, Proceedings of the Fourth International Congress of Biochemistry, Vol. 4 [Symposium: Biochemistry of Steroids], Pergamon Press, p. 259 (1959).

(3) Dr. Klaus Otto was the recipient of a Fulbright Travel Grant and was on leave of absence from the Physiologisch-chemisches Institut der Universität Bonn, West Germany.

(4) M. Ehrenstein and A. R. Johnson, *J. Org. Chem.*, 11, 823 (1946).