(b.p. 80–85°/15 mm.), 2.2 g. (14% or 17% based on unrecovered starting material) of *p*-cresyl benzyl ether (IX),[14] b.p. 98–105°/0.2 mm., m.p. 41–42°, and 0.6 g. (3%) of *benzyl 2-benzyl-4-methylphenyl ether* (VII), b.p. 160–180°/0.3 mm. The ultraviolet spectrum of this compound in cyclohexane shows maxima at 278 mμ (ε 2.6 × 10³) and 287 mμ (ε 2.33 × 10³).

Anal. Calcd. for $C_{21}H_{20}O$: C, 87.46; H, 6.99. Found: C, 87.60; H, 7.24.

Separation of the phenolic fraction of the reaction mixture by distillation gave unreacted *p*-cresol (1.5 g., 7%), b.p. 92–100°/20 mm., *2-benzyl-4-methylphenol* (VI) (8.1 g., 51% or 62% based on unrecovered starting material), b.p. 122–125°/0.1 mm. and *2,6-dibenzyl-4-methylphenol* (VIII) (1.7 g., 7% or 9% based on unrecovered *p*-cresol), b.p. 170–180°/0.1 mm.

2-Benzyl-4-methylphenol (VI) was a colorless viscous oil. The reported b.p.[4] was 180–182°. The ultraviolet spectrum (cyclohexane) shows an absorption maximum at 282 mμ (ε 2.9 × 10³).

Anal. Calcd. for $C_{14}H_{14}O$: C, 84.81; H, 7.12. Found: C, 84.89; H, 7.33.

2,6-Dibenzyl-4-methylphenol (VIII) has been reported[4] to have b.p. 250–252°. The ultraviolet spectrum in cyclohexane shows a maximum at 283 mμ (ε 2.7 × 10³).

3-Benzyl-2-hydroxy-5-methylazobenzene (X). To a solution of 1.0 g. (0.0050 mole) of VI and 800 mg. (0.00488 mole) of *N*-nitrosoacetanilide in methanol in an ice bath was added 450 mg. of piperidine with stirring. The solution immediately became a deep red color. After 10 min., it was diluted with water and extracted with ether. After washing of the ether layer with water and drying over magnesium sulfate the ether was removed by distillation to leave 1.3 g. of red oil which was chromatographed on 30 g. of alumina. With 300 ml. of benzene was eluted 800 mg. (57% yield) of crystalline azo compound, m.p. 89°, and further purified by molecular distillation (160°/0.02 mm.).

The ultraviolet spectra showed the following absorption. In ethanol: λ_{max} 333, 395; ε 2.9 × 10⁴, 1.0 × 10⁴. In acetic acid: λ_{max} 332, 397; ε 2.5 × 10⁴, 8.6 × 10³. In 0.1*N* sodium hydroxide solution: λ_{max} 335, 497; ε 1.1 × 10⁴; 1.1 × 10⁴. The infrared spectrum of a 10% solution in chloroform showed the following medium-to-large bands other than the usual C—H bending and stretching and the OH stretching which has spread over the region from 3100–2100 cm.$^{-1}$: 1607, 1587, 1493, 1420, 1272, 1140, 871, 687, 697 cm.$^{-1}$

Anal. Calcd. for $C_{20}H_{18}N_2O$: C, 79.44; H, 6.00; N, 9.27. Found: C, 79.57; H, 5.98; N, 9.08.

3-Benzyl-4-hydroxy-5-methylazobenzene (IV) was prepared by coupling 1 g. (0.00488 mole) of (II) with benzenediazonium acetate prepared from the addition of 450 mg. of piperidine to 800 ml. (0.005) of nitrosoacetanilide in 50 ml. of methanol. After removal of the ether as in the preceding experiment, 1.3 g. of red oil was obtained and chromatographed on 60 g. of alumina. With 300 ml. of a benzene-ethanol (9/1) mixture was eluted 800 mg. (57%) of viscous red oil, molecularly distilled at 175°/0.002 mm., which failed to crystallize.

The ultraviolet spectra showed the following. In ethanol: λ_{max} 255, 352; ε 1.4 × 10⁴, 2.6 × 10⁴. In acetic acid: λ_{max} 351, 284; ε 2.3 × 10⁴, 1.1 × 10⁴. In 0.1*N* sodium hydroxide solution: λ_{max} 465; ε 2.9 × 10⁴. The infrared spectrum showed, in addition to the usual carbon-hydrogen bending and stretching bands the following: 3605, 1600, 1500, 1295, 1190, 1122, 692, 700 (shoulder) cm.$^{-1}$

Anal. Calcd. for $C_{20}H_{18}N_2O$: C, 79.44; H, 6.00; N, 9.27. Found: C, 79.70; H, 6.07; N, 9.32.

3,5-Dimethyl-2-hydroxyazobenzene (XI), m.p. 90°, was prepared by the method of Auwers.[15] The ultraviolet spectra were as follows. In ethanol: λ_{max} 332, 395 mμ; ε 2.4 × 10⁴, 8.5 × 10³. In acetic acid: λ_{max} 331, 395, ε 2.2 × 10⁴, 6.8 × 10³. In 0.1*N* NaOH: λ_{max} 335, 495; ε 8.5 × 10³, 9.3 × 10³. The infrared spectrum (10% in chloroform) showed moderate to strong bands at 1590, 1608, 1425, 1280, 1272, 1152, 868, and 687 cm.$^{-1}$ in addition to the usual C—H bending and stretching bands and the general absorption from 3100 to 2100 cm.$^{-1}$ of the hydrogen-bonded OH group.

4-Hydroxy-3,5-dimethylazobenzene (XII), m.p. 94–95°, was prepared according to the directions of Auwers and Markovits.[16] The ultraviolet absorption spectra showed the following. In ethanol: λ_{max} 351, ε 2.8 × 10⁴. In acetic acid: λ_{max} 351, 280 mμ; ε 2.5 × 10⁴, 6.9 × 10³. In 0.1*N* sodium hydroxide solution: λ_{max} 464; ε 2.5 × 10⁴. The infrared spectrum of a 10% solution in chloroform showed strong to medium bands at 3615, 1600, 1315, 1193, 1122, 1025, 897, and 689 cm.$^{-1}$

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(14) W. Staedel, *Ann.*, **217**, 44 (1883) reports m.p. 41°.

(15) K. Auwers, *Ann.*, **365**, 295 (1909).

(16) K. Auwers and T. Markovits, *Ber.*, **41**, 2340 (1908)

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

Steroids and Related Products. IX.[1] The Introduction of the Δ^{11}-Double Bond. I[2]

G. JUST AND CH. R. ENGEL[3]

Received June 6, 1957

A general method for the introduction of the Δ^{11}-double bond, consisting in the dehydrotosylation of a 12α-tosylate with aluminum oxide, is described. Differences in reactivity of the 12α-tosylate toward aluminum oxide in the presence and in the absence of a 17α-methyl substituent, and in the presence and in the absence of a Δ^4-double bond are discussed.

In a recent paper in this series[4] we reported that in the case of 17α-methylated steroids the Δ^{11}-double bond could be introduced easily and in good

(1) Paper VIII of this series: Ch. R. Engel and R. L. Noble, *Endocrinology*, **61**, 318 (1957).

(2) Some of the results of this work were described in a communication presented before the Division of Medicinal Chemistry at the 126th National Meeting of the AMERICAN CHEMICAL SOCIETY in Dallas, Tex., April 1956; others were included in a paper given before the Division of Organic Chemistry at the annual meeting of the Chemical Institute of Canada, in Vancouver, June 1957.

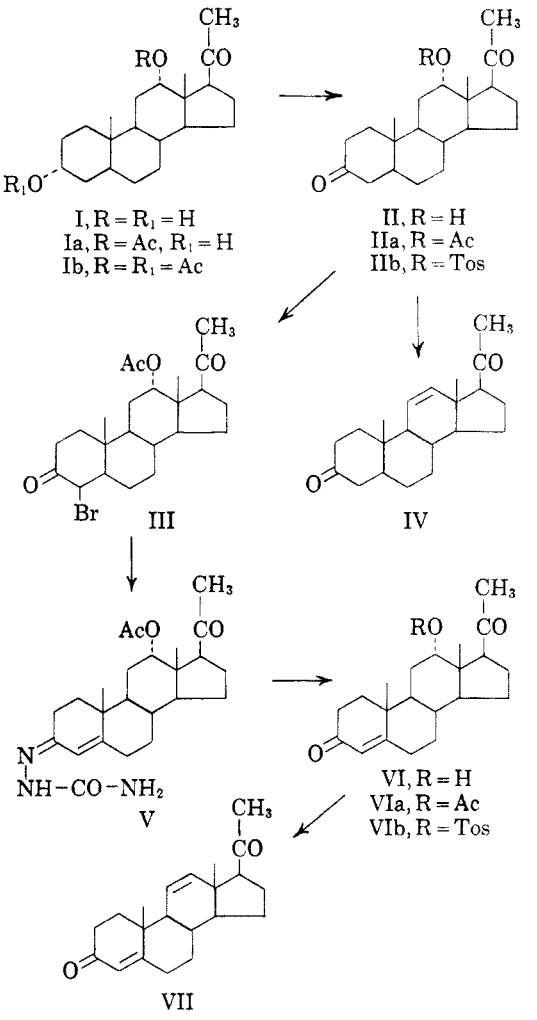
(3) Correspondence concerning this communication should be addressed to this author.

(4) Ch. R. Engel, K. F. Jennings, and G. Just, *J. Am. Chem. Soc.*, **78**, 6153 (1956).

yield by subjecting a 12α-tosylate to the action of slightly alkaline, activated aluminum oxide. It appeared attractive to investigate the application of this method, which had proved far superior to the classical dehydrotosylation with collidine, to the 17-nonmethylated series; for indeed 11,12-unsaturated analogs of progesterone are highly active luteoids,[4,5a,b,6] the corresponding analogs of cortical hormones are likewise biologically active products,[7] and 11,12-unsaturated steroids can readily be converted to the important 11-oxygenated cortical hormones by purely chemical means[8]; furthermore, steroids with an 11,12-double bond represent logical starting materials for the preparation of the biologically highly active 12α-halogenated 11-oxygenated hormone analogs.[9,10]

Ruff and Reichstein[11] have already observed that the elimination of *p*-toluenesulfonic acid from 12α-tosyloxy-3,20-dioxopregnane (IIb) could be effected by prolonged treatment with activated aluminum oxide. We decided to reinvestigate this reaction of the saturated tosylate IIb and to study the dehydrotosylation with aluminum oxide of the Δ^4-unsaturated diketo tosylate VIb which leads to the potent luteoid 11-dehydroprogesterone (VII).[5,6]

The diketones IIb and VIb were prepared by classical methods from the readily available 3α,12α-diacetoxy-20-oxopregnane (Ib). The diketo acetate IIa was obtained from Ib *via* the 3α-hydroxy compound Ia, according to Reichstein's procedure.[12] The Δ^4-unsaturated diketone VIa was prepared *via* the 4β-bromide III; whereas in experiments described in the literature, the introduction of the double bond had proceeded in poor yields,[5a,13] we obtained excellent results when the intermediate bromide III was purified, its mother liquors reconverted to the diketone IIa and when McGuckin's and Kendall's method of dehydrobromination with semicarbazide[14] was used. The 12α-acetoxy diketones IIa and VIa were transformed to the corresponding tosylates *via* the respective alcohols II and VI in the usual manner.[6]



Using the slightly alkaline activated aluminum oxide ordinarily employed in our laboratory, we were able to effect the dehydrotosylation of the saturated diketo tosylate IIb smoothly by subjecting the product to ordinary adsorption chromatography; prolongation of the reaction period[11] or the use of an excess of aluminum oxide[4] was not found to be necessary. In contrast to this, the treatment of the unsaturated diketo tosylate VIb with aluminum oxide, under conditions which had led in good yield to the 11-unsaturated product in the 17α-methylated series, did not result in the formation of the Δ^{11}-double bond in appreciable amounts. After numerous chromatograms on substantial amounts of aluminum oxide of various degrees of activity and of various *p*H values, only unchanged starting material and no 11-unsaturated product could be isolated in the pure state. However, we were able to accomplish the desired dehydrotosylation by changing the reaction conditions, particularly by raising the temperature during the reaction.

An inspection of the molecular models makes the difference between the reactivity of the unsaturated diketo tosylate and of its 17α-methyl homolog[4]

(5) (a) P. Hegner and T. Reichstein, *Helv. Chim. Acta*, **26**, 715 (1943). (b) J. von Euw and T. Reichstein, *Helv. Chim. Acta*, **29**, 654 (1946).

(6) Ch. Meystre, E. Tschopp, and A. Wettstein, *Helv. Chim. Acta.*, **31**, 1463 (1948).

(7) Ch. Meystre and A. Wettstein, *Helv. Chim. Acta*, **31**, 1890 (1948).

(8) A. Fürst and R. Scotoni, Jr., *Helv. Chim. Acta*, **36**, 1410 (1953).

(9) J. E. Herz, J. Fried, and E. F. Sabo, *J. Am. Chem. Soc.*, **78**, 2017 (1956).

(10) D. Taub, R. D. Hoffsommer, and N. L. Wendler, *J. Am. Chem. Soc.*, **78**, 2912 (1956).

(11) A. Ruff and T. Reichstein, *Helv. Chim. Acta*, **34**, 70 (1951).

(12) (a) T. Reichstein and E. von Arx, *Helv. Chim. Acta*, **23**, 747 (1940). (b) C. W. Shoppee and T. Reichstein, *Helv. Chim. Acta*, **24**, 351 (1941).

(13) G. Ehrhart, H. Ruschig and W. Aumüller, *Zeitschr. angew. Chemie* **52**, 363 (1939).

(14) W. F. McGuckin and E. C. Kendall, *J. Am. Chem. Soc.*, **74**, 5811 (1952).

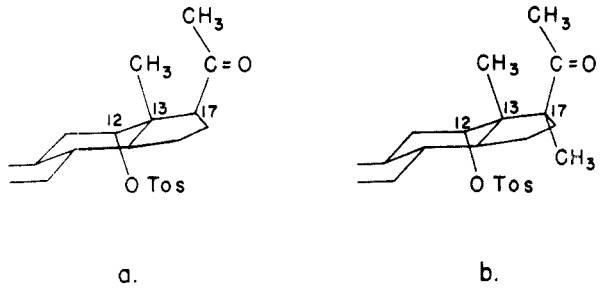


FIG. 1. PARTIAL FORMULAS OF (a) Δ^4-12α-tosyloxy-3,20-dioxopregnene and (b) Δ^4-12α-tosyloxy-3,20-dioxo-17α-methylpregnene.

quite plausible (compare Fig. 1). It can indeed be seen that the quasi-axial 17α-methyl group (Fig. 1b) should exert an enhancing action on the elimination of the axial and closely located tosyloxy substituent. It is further possible to assume that the difference in reactivity of the saturated (*A/B cis*) diketo tosylate IIb and of the unsaturated diketo tosylate VIb is due, at least to an appreciable extent, to a similar stereochemical effect. Indeed, in the case of the saturated tosylate the general plane of ring A is almost perpendicular to the general plane of the rest of the ring system and therefore parallel to and also on the same side as the axial 12α-substituent (Fig. 2b). Even though the distance between this substituent and ring A is greater than the distance between the 12α-tosyloxy group and a 17α-methyl substituent, it seems evident that ring A should exert an appreciable enhancing action on the elimination of the bulky tosyloxy group. In contrast to this situation, when a Δ^4-double bond is present, ring A lies in the same general plane as the rest of the ring system (compare Fig. 2a) and does not facilitate the elimination of *p*-toluenesulfonic acid. However, attention has to be given also to the possibility that the Δ^4-double bond influences the reaction in ring C by "conformational transmission."[15] Further investigations of this problem are to be published at a later date.

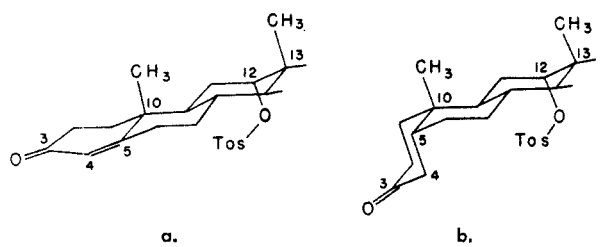


FIG. 2. PARTIAL FORMULAS OF (a) Δ^4-12α-tosyloxy-3,20-dioxopregnene and (b) 12α-tosyloxy-3,20-dioxopregnane.

(15) D. H. R. Barton, *Experientia*, **Supplementum II**, 121 (1955).

EXPERIMENTAL[16–18]

12α-Acetoxy-3,20-dioxopregnane (IIa). The partial hydrolysis of 20 g. of 3α,12α-diacetoxy-20-oxopregnane (Ib), according to Reichstein's procedure,[12a] afforded 9.46 g. of *3α-hydroxy-12α-acetoxy-20-oxopregnane* (Ia), crystallizing in prisms and melting at 199–201°, and 2.475 g. melting between 187 and 200°. Reacetylation of the mother liquors of this substance gave 5.3 g. of the starting material Ib, m.p. 132.5–135.5°. (Total yield of Ia from Ib, considering the recovery of starting material, 92.3%.) It was found that the starting material, 3α,12α-diacetoxy-20-oxopregnane, crystallizes also in a modification melting at 122–123°.[19]

The monohydroxy ketone Ia (11.84 g.) was oxidized with chromic acid, as described in the literature,[12] yielding 9 g. of *12α-acetoxy-3,20-dioxopregnane* (IIa), m.p. 125–128° (81%). A sample was recrystallized four times for analysis; prisms, m.p. 130–131°, $[\alpha]_D^{23}$ 159° (*c*, 0.925 in $CHCl_3$).

Anal. Calcd. for $C_{23}H_{34}O_4$: C, 73.76; H, 9.09. Found: C, 74.01; H, 9.18.

12α-Hydroxy-3,20-dioxopregnane (II). The acetoxy diketone IIa (7.43 g., m.p. 127–129°) was refluxed for 4 hr. with potassium carbonate (28.27 g.) in 225 cc. of methanol and 187 cc. of water. There was obtained 5.73 g. of hydroxy diketone II, m.p. 178–181° (87% yield), part of which crystallized out of the reaction mixture. A sample was recrystallized four times for analysis; needles, m.p. 180.5–181°, $[\alpha]_D^{25}$ 123° (*c*, 0.976 in C_2H_5OH).

Anal. Calcd. for $C_{21}H_{32}O_3$: C, 75.86; H, 9.70. Found: C, 75.80; H, 9.70.

12α-Tosyloxy-3,20-dioxopregnane (IIb). A solution of 1.235 g. of the hydroxy diketone II in 8.2 cc. of pyridine was heated with 1.65 g. of *p*-toluenesulfonyl chloride for 6 days at 40°. The usual working up afforded 1.774 g. of a crude amorphous product showing the ultraviolet absorption spectrum typical of a tosylate[4] [λ_{max}^{EtOH} 226 mμ (log ϵ 4.7)]. When the product was chromatographed very rapidly over slightly acidic aluminum oxide (*p*H 6.5) part of it could be obtained in crystalline form, m.p. 120–125°, λ_{max}^{EtOH} 227 mμ (log ϵ 4.8). The product was used without further purification in the following reaction.

Δ^{11}-3,20-Dioxopregnene (IV).[20] Crude, partly crystalline 12α-tosyloxy diketone IIb (611 mg.) was dissolved in a small amount of benzene and chromatographed on 18 g. of slightly alkaline (*p*H 7.5–8) activated aluminum oxide. Benzene and benzene-ether eluted 426 mg. of crude dioxopregnene IV, m.p. 94–124.5°, giving a positive tetranitromethane test and not showing the ultraviolet absorption typical of tosylates.[4] Repeated chromatography and recrystallizations from ether-hexane afforded a product melting at 128.5–130°. A sample was sublimed under high vacuum at 102–103° for analysis; m.p. 133–134°, $[\alpha]_D^{24}$ 91.2° (*c* 0.535 in $CHCl_3$), ν_{max}^{KBr} 2995 cm.$^{-1}$ (C—H stretching, double bond), 1705 cm.$^{-1}$ (3-ketone), 1690 cm.$^{-1}$ (20-ketone), 1623 cm.$^{-1}$ (double bond), 723 cm.$^{-1}$ (Δ^{11}-double bond).

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

(17) The microanalyses were performed by Mr. J. Alicino, Metuchen, N. J., to whom we wish to express our sincere appreciation.

(18) Sincere thanks are due to Messrs. Merck and Co., Montreal, for providing us with activated aluminum oxide for chromatography. The product was neutralized with ethyl acetate and reactivated as described under footnote 18 of the first article in this series [Ch. R. Engel and G. Just, *J. Am. Chem. Soc.*, **76**, 4909 (1954)]. Desired alterations of the *p*H values of the absorbent were obtained by varying the time of reaction with ethyl acetate.

(19) Dr. P. Ziegler, Canada Packers Ltd., Toronto, kindly corroborated this observation.

(20) Compare also P. Hegner and T. Reichstein, *Helv. Chim. Acta*, **26**, 721 (1943) and the articles cited under footnotes 5b and 11.

Anal. Calcd. for $C_{21}H_{30}O_2$: C, 80.18; H, 9.61. Found: C, 80.11; H, 9.61.

12α-Acetoxyprogesterone (VIa). The acetoxy diketone IIa (2.082 g.) was dissolved in 22 cc. of acetic acid and brominated in the usual manner[4] with one equivalent of bromine in 11.3 cc. of acetic acid. The usual working up[4] gave 1.6 g. of pure *bromo ketone* III, m.p. 175–176.5°; the mother liquors were debrominated with 2 g. of zinc and 22 cc. of 90% acetic acid at 100° and thus afforded 293 mg. of starting material melting at 126.5–128° and 122 mg. of the same product of slightly lesser purity (m.p. 123.5–125.5°) (total yield of the bromination 78.5%). The crystalline bromide (1.6 g.) was treated in the usual fashion[4,14] with 530 mg. of semicarbazide base in 53 cc. of chloroform and 86 cc. of *t*-butyl alcohol. The usual working up gave 1.409 g. of *semicarbazone* V, m.p. 200–203°. The product was hydrolyzed with 48 cc. of acetic acid and 17 cc. of water in the presence of 4.1 cc. of 1.66 *N* pyruvic acid, under carbon dioxide. There was obtained 1.11 g. of *Δ⁴-12α-acetoxy-3,20-dioxopregnene* (VIa), m.p. 170.5–176° (96% yield from bromide III). Two recrystallizations from ether-hexane raised the m.p. to 180.5–182°; $[\alpha]_D^{22}$ 214° (*c*, 0.893 in $CHCl_3$); λ_{max}^{EtOH} 240 mμ (log ε 4.3).

Anal. Calcd. for $C_{23}H_{32}O_4$: C, 74.16; H, 8.66. Found: C, 74.26; H, 8.71.

12α-Tosyloxyprogesterone (VIb). A solution of 2.373 g. of the acetoxy diketone VIa in 80 cc. of methanol was refluxed for four hours with a solution of 9 g. of potassium carbonate in 60 cc. of water. The usual working up afforded 2.006 g. of *12α-hydroxyprogesterone* (VI), m.p. 192–194°, (quantitative yield). The product was tosylated in the usual way[6,7] and there was obtained 2.658 g. of an amorphous reaction product. Chromatography on slightly acid (*p*H 6.5) aluminum oxide[18] afforded 1.49 g. of crystalline tosylate VIb and 567 mg. of crude starting material, yielding upon purification 398 mg. of pure hydroxy ketone VI. The tosylate was rechromatographed and recrystallized twice from ether-hexane for analysis; m.p. 175–175.5° dec., $[\alpha]_D^{22}$ 117° (*c*, 0.932 in $CHCl_3$), λ_{max}^{EtOH} 228 mμ (log ε 4.4), shoulder at 242 mμ (log ε 4.2).

Anal. Calcd. for $C_{28}H_{36}O_5S$: C, 69.39; H, 7.45; S, 6.62. Found: C, 69.20; H, 7.69; S, 6.66.

Unsuccessful attempts to dehydrotosylate 12α-tosyloxyprogesterone (VIb) *with aluminum oxide.* A sample of tosylate VIb (48 mg.) was chromatographed as described previously[4] on 6 g. of slightly alkaline (*p*H of supernatant water 7.5), activated aluminum oxide[18] (activity 2–3, according to Brockmann[21]). There was recovered 46 mg. of unchanged tosylate VIb. The experiment was repeated twice with the same sample, using alkaline aluminum oxide (*p*H 8–9); again only tosylate was recovered. None of the chromatogram fractions showed a clearly positive tetranitromethane test. In another experiment, 49 mg. of tosylate VIb was chromatographed on 20 g. of slightly alkaline aluminum oxide (*p*H 7.5). Again, only the starting material could be recovered in the pure state. A similar result was obtained when 82 mg. of tosylate VIb was chromatographed on 30 g. of alkaline aluminum oxide "Woelm," activity 1.

Successful dehydrotosylation of 12α-tosyloxyprogesterone (VIb) *to 11-dehydroprogesterone* (VII) *with aluminum oxide.* A sample of tosylate VIb (193 mg.) was dissolved in a few cc. of benzene and absorbed in the usual manner on a column of 15 g. of activated, slightly alkaline aluminum oxide (*p*H 7.5) at 22°; the column had been filled prior to the adsorption with petroleum ether-benzene (4:1) up to the surface of the aluminum oxide. The diameter of the column which was provided with a heating jacket was 1 cm. After the adsorption of the substance the column was washed with petroleum ether-benzene (4:1), and subsequently the solvent was drained through the stopcock. The column was now heated for 5 hr. to 45° and was allowed to stand for further 15 hr. at room temperature. Subsequently, ordinary chromatographic elutions were performed. Benzene-ether (4:1 and 1:1) mixtures eluted 122 mg. of crude, crystalline 11-dehydroprogesterone (VII),[5a,b,6] giving a positive tetranitromethane test and showing the ultraviolet absorption spectrum typical of a Δ⁴-3-keto steroid without a tosyl group. The first chromatogram fractions melted between 148 and 154°, the following had a lower melting point and their ultraviolet spectrum indicated traces of tosylate. They were subjected anew to a similar treatment with aluminum oxide and thus there was obtained 51 mg. of pure 11-dehydroprogesterone (VII), m.p. 155–160°. In another series of experiments, 30 mg. of VII was obtained from 100 mg. of tosylate VIb (46.5% yield). The product was subjected to an ordinary chromatographic purification at room temperature and the resulting crystals recrystallized twice from ether-hexane, for analysis; m.p. 169–171°, not depressed upon admixture with authentic 11-dehydroprogesterone[22]; λ_{max}^{EtOH} 239 mμ (log ε 4.2); ν_{max}^{KBr} 3020 cm.$^{-1}$ (C—H stretching, double bond), 1693 cm.$^{-1}$ (20-ketone), 1666 and 1614 cm.$^{-1}$ (Δ⁴-3-ketone doublet), 723 cm.$^{-1}$ (Δ¹¹-double bond); this infrared spectrum was identical with one taken of an authentic sample.[22]

Anal. Calcd. for $C_{21}H_{28}O_2$: C, 80.73; H, 9.03. Found: C, 80.68; H, 8.85.

Acknowledgments. Some of the experiments were carried out with the assistance of Mr. S. Papadopoulos, an M.Sc. candidate of this laboratory; the authors wish to extend their sincere thanks to him and to Mrs. J. Capitaine and Mr. R. Heckadon for technical assistance. The kind cooperation of Mr. R. W. White, Science Service Laboratory, London, Ont., in performing and discussing the infrared analyses reported in this paper is gratefully acknowledged. Sincere thanks are rendered to the Ontario Division of the National Cancer Society of Canada and to Ayerst, McKenna and Harrison, Ltd., Montreal, for supporting this work, and to Canada Packers Company Ltd., Toronto, for kindly providing the starting material. Dean J. B. Collip's interest in this project and Professor J. A. Gunton's kindness in extending the facilities of his department to our group were highly appreciated. One of us (C.R.E.) wishes to express his gratitude to the Canadian Life Insurance Officers' Association for financial assistance.

LONDON, ONT., CANADA

(21) H. Brockmann and H. Schodder, *Ber.*, **74**, 73 (1941).

(22) We wish to express sincere thanks to Dr. A. Wettstein, Ciba Ltd., Basle, Switzerland, for kindly providing material for comparison.