[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, WABASH COLLEGE]

Pseudocholesterol. II. *i*-Pseudocholesterol and *i*-Steroid Rearrangement[1]

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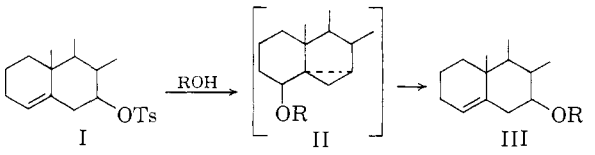
The stereospecific retrograde *i*-steroid rearrangement has been demonstrated to take place in the pseudocholesterol system. By an indirect method, 4-ξ-hydroxy-5,7-cyclocholestane (*i*-pseudocholesterol) has been prepared. This compound has been found to rearrange readily in acid solution to provide 7β-hydroxy-4-cholestene (pseudocholesterol.) The *i*-pseudo steroids show other behavior similar to the *i*-steroids. The possible observation of the epimer of *i*-pseudocholesterol is described.

Pseudocholesteryl tosylate (I), when treated with methanol[2,3] or acetate ion[3,4] under basic conditions fails to provide a 5,7-cyclo derivative (II) in a fashion analogous to the formation of the characteristic 3,5-cyclo derivatives (*i*-steroids) obtained from cholesteryl tosylate when the latter compound is treated with these reagents.[5] Because the homoallylic system is found in very different steric environments in cholesterol and pseudocholesterol, this result was not entirely unexpected. However, the retention of the β-configuration during the transformation

pseudocholesteryl tosylate (I) ⟶ pseudocholesteryl acetate (III)

has been demonstrated unequivocally.[3,4] This retention suggests, but does not demonstrate, participation of the π-electrons of the 4,5-double bond in a transitory 5,7-cyclo intermediate (II) which, not being stable even under basic conditions, rapidly rearranges to the normal pseudocholesteryl derivative as



I II III

The purpose of the work described in this paper was to determine the degree of analogy existing between the pseudocholesteryl system and the cholesteryl system with respect to these particular rearrangement reactions.

The *i*-Cholesterols.—The *i*-steroids of the cholesterol system have been studied extensively.[5] Wallis prepared both of the epimers *i*-cholesterol[6] and epi-*i*-cholesterol[7] and carried out the key methylation[8] of *i*-cholesterol to produce the *i*-cholesteryl methyl ether of Stoll.[9] The experiments of Wallis thus definitely established which of the two epimers was involved in the rearrangement. The configuration of this epimer was established by Shoppee[10] who produced 6α- and 6β-cholestanol by catalytic hydrogenation of the epimers epi-*i*-cholesterol and *i*-cholesterol, respectively. Thus, it was demonstrated that the *i*-ethers of Stoll[9] and the rearrangement produced *i*-cholesterol[6] were of the 6β-configuration. Winstein has offered some indirect evidence for the same configurational assignment.[5]

Wallis[7] prepared the 6α-compound (epi-*i*-cholesterol) as the sole product of lithium aluminum hydride reduction of *i*-cholestenone. Shoppee,[10] however, in repeating this work found that about 10% of the 6β-alcohol accompanied its epimer in this reduction.

Both *i*-cholesterol and epi-*i*-cholesterol are stable in neutral or basic solution but readily undergo acid-catalyzed rearrangement to cholesterol.[5] Winstein[11] has recently compared the reactivities of these substances and has found the β-epimer to be more reactive by a factor of 10^1 to 10^2.

Because both *i*-cholesterol epimers undergo the same rearrangement,[4] the problem of extension to the pseudocholesterol system is simplified. The synthesis of *either* 4α- or 4β-*i*-pseudocholesterol would permit examination of the analogous rearrangement in that system.

The *i*-Pseudocholesterols.—Inasmuch as base-buffered displacement did not provide a source of either *i*-pseudocholesterol or any of its derivatives, it appeared that the existence of the stereospecific rearrangement in the pseudocholesteryl system would have to be examined by the indirect preparation of an *i*-pseudocholesterol, preferably the more stable 4α, equatorial, epimer shown as XI, followed by the observation of its acid-catalyzed rearrangement to pseudocholesteryl acetate (III).

The sequence used by Dodson and Riegel[12] in the cholesteryl system led to the compounds shown below. The reactions used for structural assignment will be discussed.

Nitration of pseudocholesteryl acetate (III) provided an amorphous, hygroscopic 4-nitro-7β-acetoxycholest-4-ene (IIIa). Reduction of IIIa by zinc in acetic acid produced a mixture of 4-keto-7β-acetoxycholestane (V), m.p. 102–103°, $[\alpha]_D$ + 75° and 7β-acetoxycholestane (VI). Basic hydrolysis of the keto ester V provided 4-keto-7β-hydroxy cholestane (VII), m.p. 152–153°, $[\alpha]_D$ + 59°. The structure of VII was established by oxidation to the

(1) (a) Part I, Q. R. Petersen and C. T. Chen, THIS JOURNAL, **77**, 2557 (1955). (b) Presented, in part, to the Division of Organic Chemistry, Boston, Mass., April, 1959.

(2) R. J. W. Cremlyn, R. W. Rees and C. W. Shoppee, *J. Chem. Soc.*, 3790 (1954).

(3) Unpublished experiments of Q. R. Petersen and R. Tinus.

(4) C. W. Shoppee, G. H. R. Summers and R. J. W. Williams, *J. Chem. Soc.*, 1893 (1956).

(5) For excellent reviews and leading references on this topic see: (a) C. W. Shoppee and G. H. R. Summers, *ibid.*, 3361 (1952), and (b) E. M. Kosower and S. Winstein, THIS JOURNAL, **78**, 4347 (1956).

(6) E. S. Wallis, E. Fernholz and F. T. Gephart, *ibid.*, **59**, 137 (1937).

(7) A. F. Wagner and E. S. Wallis, *ibid.*, **72**, 1047 (1950).

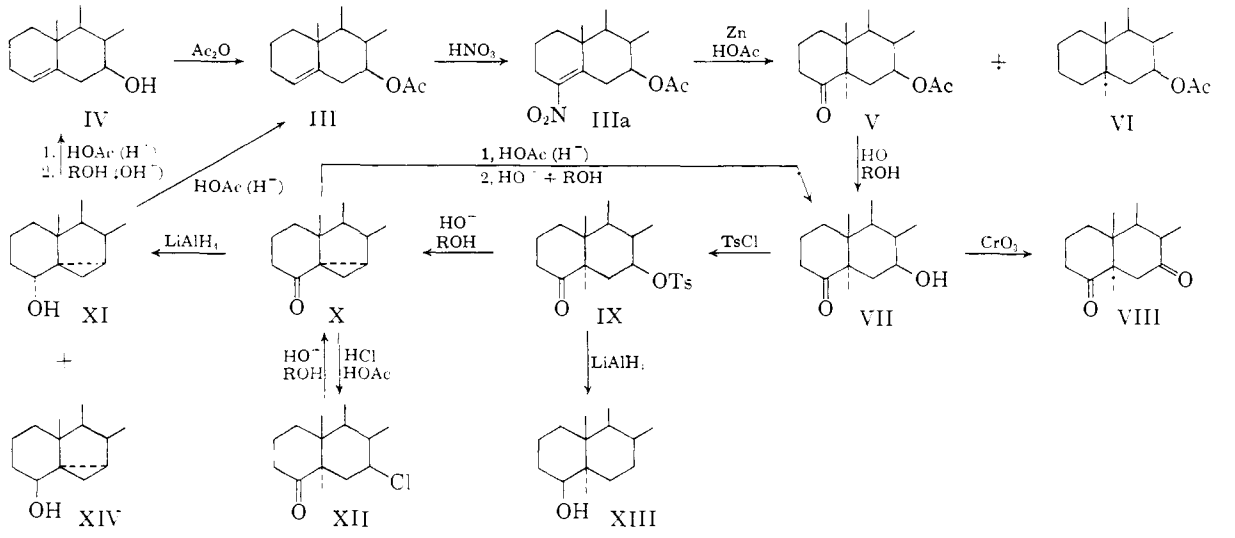
(8) E. G. Ford and E. S. Wallis, *ibid.*, **59**, 1415 (1937).

(9) W. Stoll, *Z. physiol. Chem.*, **207**, 147 (1932).

(10) C. W. Shoppee and G. H. R. Summers, *J. Chem. Soc.*, 3361 (1952); for objections to this work see ref. 5b.

(11) S. Winstein and E. M. Kosower, THIS JOURNAL, **81**, 4399 (1959).

(12) R. M. Dodson and B. Riegel, *J. Org. Chem.*, **13**, 424 (1948).



known[13] cholestane-4,7-dione (VIII). The keto alcohol VII formed a heat-stable *p*-toluenesulfonate ester (IX), m.p. 128–129° to 135–136° (depending upon the rate of heating), $[\alpha]_D + 51°$. The tosylate IX was reduced to 4β-cholestanol (XIII) by the action of lithium aluminum hydride, confirming the assignment of the 4-position to the keto group and the assignment of a *trans* ring juncture at C-5. The keto tosylate, when refluxed with alcoholic potassium hydroxide, provided 4-keto-5,7-cyclocholestane (X), m.p. 84–85°, $[\alpha]_D + 122°$. An acetic acid solution of the ketone X, when treated with concentrated hydrochloric acid, provided a chloro ketone, presumably 4-keto-7β-chlorocholestane (XII), m.p. 109–111°, $[\alpha]_D + 88.°$ The chloro ketone XII readily was reconverted to the *i*-ketone X by alcoholic base.

Lithium aluminum hydride reduction of the cycloketone X produced an oil which was chromatographed on alumina. Benzene eluted 4ξ-hydroxy-5,7-cyclocholestane (XI) (*i*-pseudocholesterol), m.p. 91–92°, $[\alpha]_D + 6°$. An acetic acid solution of XI, when treated with a drop of concentrated sulfuric acid, produced an oily compound which, upon chromatography, provided a crystalline material, m.p. 96–98°. When this material was mix-melted with authentic pseudocholesteryl acetate (III), m.p. 96–97°, the melting point was not depressed. X-Ray powder diagrams and infrared spectra of this compound and authentic pseudocholesteryl acetate were superimposable. The rearrangement-produced acetate was hydrolyzed in alcoholic base to produce pseudocholesterol (IV), demonstrated to be genuine by melting point, X-ray and infrared comparison with authentic material. Thus, the retrograde *i*-steroid rearrangement was demonstrated to take place in the pseudocholesterol system.

It was hoped that the reduction of XI to either 4α- or 4β-cholestanol would firmly establish the configuration of the hydroxyl group in XI. However, hydrogenation of this compound produced an oil which was refractory to crystallization, chromatographic separation or derivative formation.

(13) A. Windaus, *Ann.*, **536**, 116 (1938).

Further elution of the product of the hydride reduction of X with benzene–ether (4:1) provided an oil which, on trituration with aqueous methanol, produced needles of an unstable, hygroscopic substance XIV with the approximate m.p. 50–55°, $[\alpha]_D + 89°$. This substance, even though not well characterized, shows behavior worthy of further discussion. Because of its reactivity, hygroscopicity and low yield, XIV proved to be refractory to quantitative study. However, in addition to the chromatographic behavior and physical constants reported above, these qualitative observations could be made.

Upon the standard acid treatment XIV rearranged promptly to pseudocholesterol (IV).

Although it appeared that the substance XIV could be recrystallized from methanol–water in the cold, upon exposure to air crystals of XIV rapidly lost form and changed into a glassy transparent mass. When this mass was permitted to stand overnight in contact with the atmosphere it was again crystalline, but proved to have been transformed entirely into pure pseudocholesterol (IV).

The possibility that XIV is simply a mixture of XI and IV, the latter compound resulting from rearrangement of XI on the column, was eliminated by comparison of XIV with a synthetic mixture of XI and IV. In addition, rechromatography of pure XI did not produce additional XIV as would be expected if such rearrangement on the column had taken place.

The transformation of XIV to IV would be difficult to explain on any basis other than that XIV is, in fact, an *i*-pseudocholesterol.

By the previously discussed analogy with the cholesteryl system, the production of *i*-pseudocholesterol by a hydride ion reduction of the ketone would be expected to provide the 4α-alcohol as a major product and the 4β-alcohol as a minor product, suggesting the assignment of the 4α-configuration of XI and the 4β-configuration to XIV.

With the exception of the apparent stability of cold aqueous methanol, the experiments and observations reported above justify using the analogy.

TABLE I

SPECIFIC ROTATION OF DERIVATIVES

Cholestane	α	β
6-Hydroxy-3,5-cyclo-[6,7]	+76	+50
6-Hydroxy-[14,10]	+35	+ 8
4-Hydroxy-5,7-cyclo-	+ 6	+89
4-Hydroxy-[15]	+ 4	+29

The direction of changes in rotation as summarized in Table I support the configurational assignments. The later elution of an axial alcohol is contrary to theory but consistent with the observation of Shoppee[10] on epimeric *i*-cholesterols. Winstein,[5b] however, has reported opposite chromatographic behavior. The difference in reactivity of XI and XIV agrees with that described by Winstein[11] for the *i*-cholesterol epimers.

If this cholesteryl–pseudocholesteryl analogy then holds, pseudocholesteryl tosylate (I) would be expected to produce the less stable 4β-alcohol (II or XIV) shown above as an intermediate in the transformation of I into III. The experiments described support the suggestion, made earlier in the text, that the 4β-intermediate is not sufficiently stable to the normal displacement conditions to permit its isolation as an intermediate product.

NOTE ADDED IN PROOF.—The recent communication by C. H. P. Summers on "4-Substituted 5,7-Cyclocholestanes," *Proc. Chem. Soc.*, 24 (1960), prompts me to state that a preliminary report of the present work was submitted for publication in the same journal but declined (on November 7, 1958) on the ground "that it did not reach the required standard of urgency or general importance."—Q. R. P.

Acknowledgment.—The author is indebted to a Frederick Gardner Cottrell grant for financial support of this work and to the Eli Lilly Co. for the infrared and X-ray studies described.

Experimental[16]

4-Nitro-7β-acetoxycholest-4-ene (IIIa).—To 20.0 g. of pseudocholesteryl acetate[1a] was added 600 ml. of concd. nitric acid, and the mixture stirred briefly to wet the acetate. With constant stirring, 2.0 g. of powdered potassium nitrite was added at once. After 0.5 hour, an additional 2.0 g. of potassium nitrite was added. Stirring was continued for a total of 2 hours. The addition of an equal volume of water to the resulting oily mixture precipitated an oil which hardened upon standing overnight in the refrigerator. When rubbed with pure water the hardened oil underwent rapid change to an off-white granular solid which was found to be hygroscopic and refractory to recrystallization. It was washed free of nitric acid by treatment with distilled water in a Waring Blendor. The resulting white solid melted 55–60° and, after drying over Drierite, analyzed approximately for the monohydrate.

Anal. Calcd. for $C_{29}H_{47}O_4N \cdot H_2O$: C, 70.84; H, 9.42. Found: C, 71.65; H, 9.49.

After one month the analytical sample had altered to a yellow gum.

4-Keto-7β-acetoxycholestane (V).—The nitro compound from the previous synthesis was dissolved in 500 ml. of refluxing glacial acetic acid containing 30 ml. of water. To this refluxing solution 40.0 g. of powdered zinc was added during 3 hours. After a total of 4.5 hours of reflux, and while still hot, the mixture was filtered free of unreacted zinc and diluted with twice its volume of water. The resulting suspension was cooled overnight to give an oil which was decanted from the aqueous layer, dissolved in petroleum ether and washed with 10% sodium bicarbonate and water. The petroleum ether solution was chromatographed on a Florisil column.

A solvent of benzene–petroleum ether (1:4) removed 0.49 g. of material melting at 53–56°. Although it could not be recrystallized to a higher melting compound, the material was shown to be 7β-acetoxycholestane[17] (VI) by hydrolysis to 7β-hydroxycholestane and oxidation of that compound to 7-ketocholestane.

With pure benzene there was eluted 6.0 g. of the directly pure keto acetate V, m.p. 102–103°, $[\alpha]_D$ + 75°. Recrystallization from methanol–water did not raise the melting point.

Anal. Calcd. for $C_{29}H_{48}O_3$: C, 78.32; H, 10.88. Found: C, 78.84; H, 11.28.

4-Keto-7β-hydroxycholestane (VII).—Five grams of the acetate V was dissolved in 300 ml. of ethanol containing 10 g. of potassium hydroxide. The solution was refluxed for 1 hour. Water was added to the hot solution well past turbidity. Upon cooling in the refrigerator overnight, 4.5 g. of the keto alcohol VII was precipitated. Very slow recrystallization from ethanol–water provided fine needles, m.p. 152–153°, $[\alpha]_D$ + 50°.

Anal. Calcd. for $C_{27}H_{46}O_2$: C, 80.54; H, 11.52. Found: C, 79.98; H, 11.54.

The keto alcohol VII (0.10 g.) was permitted to stand overnight in 10 ml. of 2% chromic acid solution. Dilution with water and recrystallization of the solid produced gave 0.05 g. of cholestane-4,7-dione (VIII) as unrefractive plates, m.p. 144–146°.[18]

4-Ketocholestane-7β-ol Tosylate (IX).—One-half gram of the keto alcohol from the previous reaction was mixed dry with 0.50 g. of tosyl chloride. Ten ml. of freshly distilled pyridine was added to the mixture to produce a yellow solution which now was permitted to stand at room temperature for 18 hours and then diluted with two volumes of water. The precipitated oil solidified on standing in the cold and was filtered and washed with water. Crystallization from acetone–water provided 0.52 g. of plates melting sharply but variously, 128–129° to 135–136°, depending upon the rate of heating.[18a] The tosylate could be melted and frozen without change and had to be held at 200° to effect the red decomposition characteristic[18b] of steroid tosylates. The rotation of this compound is $[\alpha]_D$ + 51°.

Anal. Calcd. for $C_{34}H_{52}O_4S$: C, 73.34; H, 9.41. Found: C, 73.64; H, 9.30.

A dry mix of 0.150 g. of the tosylate IX and 0.200 g. of lithium aluminum hydride was dissolved in 30 ml. of dry ether. The mixture was refluxed 18 hours and worked up in the usual way to provide, upon chromatography, a trace of cholestane, 0.085 g. (82%) of 4β-hydroxycholestane and a trace of 4α-hydroxycholestane.

4-Keto-5,7-cyclocholestane (X).—Four grams of the tosylate IX was dissolved in 250 ml. of ethanol and 4 g. of potassium hydroxide was added. After a 1-hour reflux period the product was precipitated by addition of water to the hot solution. Recrystallization from acetone–water provided 2.60 g. of the cycloketone X as plates, m.p. 84–85°, $[\alpha]_D$ + 122°.

Anal. Calcd. for $C_{27}H_{44}O$: C, 84.31; H, 11.53. Found: C, 84.20; H, 11.51.

Demonstration of hydrolysis of the *i*-ketone X to the hydroxy ketone VII proved to be surprisingly difficult, the very slow crystallization of slightly impure VII being in part responsible. In one experiment 32 mg. of X was refluxed for 3.5 hours in 10 ml. of acetic acid containing one drop of concd. sulfuric acid. The product was a brown oil which was hydrolyzed in alcoholic potassium hydroxide to give 5 mg. of crystalline VII. The mother liquor remained cloudy and deposited additional crystalline material over a period of months.

(14) R. Tschesche, *Ber.*, **65B**, 1842 (1932).

(15) D. H. R. Barton and W. J. Rosenfelder, *J. Chem. Soc.*, 1048 (1951).

(16) Melting points were taken on the hot-stage of a polarizing microscope and are corrected ±1°. Rotations were taken in chloroform solution at room temperature. Microanalyses were by Midwest Microlab, Inc., and Eli Lilly Co. Some rotations were determined by Eli Lilly Co.

(17) R. O. W. Cremlyn and C. W. Shoppee, *J. Chem. Soc.*, 3515 (1954), report m.p. 66° for this compound.

(18) Dodson and Riegel, ref. 12, describe: (a) almost identical behavior for the melting point of the cholesteryl analog of this compound, but (b) quite different heat stability.

4-Keto-7β-chlorocholestane (XII).—A sample of 0.1017 g. of the *i*-ketone X was dissolved in 30 ml. of hot glacial acetic acid and concd. hydrochloric acid was added to turbidity. Sufficient ether was added to clear the turbidity and the solution was cooled to give a crystalline product. Upon recrystallization from acetone–water, 0.0778 g. of the chloro ketone as matted needles, m.p. 109–111°, $[\alpha]D + 88°$, was produced.

Anal. Calcd. for $C_{27}H_{45}OCl$: C, 77.00; H, 10.77. Found: C, 77.34; H, 10.88.

Twenty ml. of an ethanolic solution of 0.060 g. of XII was treated with two pellets of potassium hydroxide and heated for 0.5 hour. After standing at room temperature overnight, the solution was diluted with water to precipitate 0.050 g. of directly pure *i*-ketone X.

4ξ-Hydroxy-5,7-cyclocholestane (XI).—To 0.26 g. of the *i*-ketone X contained in 50 ml. of dry ether was added 1.0 g. of lithium aluminum hydride. The mixture was refluxed for 1 hour and then the excess hydride was destroyed with wet methanol. The resulting suspension was filtered free of solids and evaporated to a pale yellow oil. This oil was chromatographed on a 1 inch × 7 inch alumina column. Petroleum ether elution produced a small amount of yellow oil. Benzene eluted an oil which, upon trituration with methanol, produced book-like plates, m.p. 89–90°. Recrystallization of the combined benzene eluates from acetone–water or methanol–water gave slow crystallization of 0.10 g. of the *i*-alcohol XI as chunky prisms, m.p. 91–92°, $[\alpha]D + 5.8°$.

Anal. Calcd. for $C_{27}H_{46}O$: C, 83.85; H, 11.92. Found: C, 84.20; H, 12.00.

Hydrogenation of XI by the procedure of Shoppee[10] produced an oil. No solid products could be obtained from this oil.

By addition of benzene–ether (4:1) to the column there was eluted an oil which, upon methanol–water trituration, produced clumps of needle crystals of XIV. The study of this substance is reported adequately in the Discussion portion of this paper. It should be pointed out that the hygroscopicity of XIV prevented accurate weighing, and thus the $[\alpha]D + 89°$ should be considered a minimum rotation.

Rearrangement of *i*-Pseudocholesterol.—(a) To 10 ml. of an acetic acid solution of 0.03 g. of the *i*-steroid XI was added one drop of concd. sulfuric acid. The resulting solution was heated at 70° for 1 hour and then evaporated to an oily solid. This mixture was washed with water to remove the acid and the solid remaining was recrystallized from acetone–water to give 0.02 g. of diamond-shaped crystals, m.p. 95–98°. When mix-melted with authentic pseudocholesteryl acetate (m.p. 96–97°),[1a] the m.p. of the authentic material was not depressed. X-Ray powder diagrams and infrared spectra of this compound and authentic pseudocholesteryl acetate were superimposable.

(b) In another experiment the solution of XI, after acid treatment, was made basic with ethanolic potassium hydroxide, filtered to remove inorganic salts, and refluxed for one hour. Addition of water produced needle-like crystals, m.p. 119–123°. This was demonstrated to be authentic pseudocholesterol by melting point, X-ray and infrared comparison with authentic material.

CRAWFORDSVILLE, IND.

[CONTRIBUTION FROM THE ORGANIC CHEMICAL RESEARCH SECTION, LEDERLE LABORATORIES DIVISION, AMERICAN CYANAMID CO.]

16-Hydroxylated Steroids. XV.[1] Synthetic Corticoids Related to 9α-Fluoro-16α-hydroxy-hydrocortisone and -prednisolone (Triamcinolone)

BY SEYMOUR BERNSTEIN AND ROBERT H. LENHARD

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A number of synthetic variants of 9α-fluoro-16α-hydroxy-hydrocortisone (Ia) and -prednisolone (triamcinolone) (IIa) have been prepared. These include 9α-fluoro-11β,16α,17α,21-tetrahydroxy-4,6-pregnadiene-3,20-dione (IVa) and 6-dehydrotriamcinolone (VIIa).

In this paper we wish to describe the preparation of certain compounds related to 9α-fluoro-16α-hydroxyhydrocortisone (Ia) and triamcinolone (9α-fluoro-16α-hydroxyprednisolone) (IIa).[2]

Bromination of 16α,21-diacetoxy-9α-fluoro-11β,17α-dihydroxy-4-pregnene-3,20-dione (Ib)[2a] in cold acetic acid–ether[3] with one equivalent of bromine gave the 6-bromo compound III (not characterized) which was dehydrobrominated in refluxing *s*-collidine to afford the 4,6-diene diacetate IVb. Saponification with potassium hydroxide in methanol gave 9α-fluoro-11β,16α,17α,21-tetrahydroxy-4,6-pregnadiene-3,20-dione (IVa), isomeric with triamcinolone (IIa). Chromic anhydride–pyridine oxidation of the 4,6-diene diacetate IVb yielded the 11-ketone V. The free tetrol IVa in acetone containing a trace of perchloric acid readily formed an acetonide VI.

Selenium dioxide dehydrogenation[4] of 16α,21-diacetoxy-9α-fluoro-11β,17α-dihydroxy-4,6-pregnadiene-3,20-dione (IVb) in *t*-butyl alcohol and acetic acid gave the expected 1,4,6-triene diacetate VIId together with an approximately equal amount of a by-product assigned the structure 11β,16α,21-triacetoxy-9α-fluoro-17α-hydroxy-1,4,6-pregnatriene-3,20-dione (VIIb).[5]

Saponification of the 1,4,6-triene diacetate VIId gave 6-dehydro-triamcinolone (9α-fluoro-11β,16α,17α,21-tetrahydroxy-1,4,6-pregnatriene-3,20-dione, VIIa). Oxidation of VIIa afforded 16α,21-diacetoxy-9α-fluoro-17α-hydroxy-1,4,6-pregnatri-

(1) Paper XIV, S. Bernstein and R. Littell, THIS JOURNAL, **82**, 1235 (1960).

(2) For previously described modifications or related compounds, see: (a) S. Bernstein, R. H. Lenhard, W. S. Allen, M. Heller, R. Littell, S. M. Stolar, L. I. Feldman and R. H. Blank, *ibid.*, **78**, 5693 (1956); **81**, 1689 (1959); (b) S. Bernstein, M. Heller, R. Littell, S. M. Stolar, R. H. Lenhard and W. S. Allen, *ibid.*, **79**, 4555 (1957); (c) S. Bernstein, *Recent Progress in Hormone Research*, **14**, 1 (1958); (d) J. Fried, A. Borman, W. B. Kessler, P. Grabowich and E. F. Sabo, THIS JOURNAL, **80**, 2338 (1958); (e) S. Bernstein, M. Heller, R. Littell, S. M. Stolar, R. H. Lenhard, W. S. Allen and I. Ringler, *ibid.*, **81**, 1696 (1959); (f) S. Bernstein and R. Littell, *J. Org. Chem.*, **24**, 429 (1959); (g) S. Bernstein, J. J. Brown, L. I. Feldman and N. E. Rigler, THIS JOURNAL, **81**, 4956 (1959); (h) G. R. Allen, Jr., and M. J. Weiss, *ibid.*, **81**, 4968 (1959); and (i) S. Bernstein, M. Heller and S. M. Stolar, *ibid.*, **81**, 1256 (1959).

(3) C. Djerassi, G. Rosenkranz, J. Romo, S. Kaufmann and J. Pataki, *ibid.*, **72**, 4534 (1950).

(4) (a) C. Meystre, H. Frey, W. Voser and A. Wettstein, *Helv. Chim. Acta*, **39**, 734 (1956); (b) S. Szpilfogel, T. Posthumus, M. DeWinter and D. Van Dorp, *Rec. trav. chim.*, **75**, 475 (1956).

(5) Acetylation in a selenium dioxide–acetic acid dehydrogenation is not without precedent; M. E. Urion, *Compt. rend.*, **199**, 363 (1934), found that under these conditions 1-methylcyclohexene was converted into 1-methylcyclohexene-6-ol acetate in 40% yield.