tion 3: 72–82° (100–50 mm.), 3.8 g.; Fraction 4: 82–83° (50 mm.), 17.3 g.; Residue, 3 g.

Fraction 2 was recovered mesityl oxide (0.21 mole); its refractive index indicated the absence of any enol ester (II).[8] Analysis of Fraction 4 indicated it to be a mixture composed of 78% w. 3,3-dimethyl-2-acetoxyoxirane and 22% w. 4-methyl-3,4-epoxy-2-pentanone.

Anal. Calcd. for 78% $C_6H_{10}O_3$ and 22% $C_6H_{10}O_2$: C, 57.1; H, 8.0. Found: C, 57.1; H, 8.0.

The infrared spectrum showed ester carbonyl absorption at 5.73μ with a shoulder at 5.84μ. A sample of 4-methyl-3,4-epoxy-2-pentanone[3] exhibited carbonyl absorption at 5.84μ.

Fraction 4 (15 g.) was washed with three 25-ml. portions of water, dried over magnesium sulfate and Claisen distilled to give 7 g. of 3,3-dimethyl-2-acetoxyoxirane, b.p. 60° (20 mm.), n_D^{20} 1.4128, which, by analysis, was substantially free of the ketone epoxide.

Anal. Calcd. for $C_6H_{10}O_3$: C, 55.4; H, 7.7. Found: C, 55.8; H, 7.9.

A 2,4-dinitrophenylhydrazone was prepared[9] from Fraction 4 and recrystallized from ethyl acetate, m.p. 199–200° (dec.). The same derivative was prepared from freshly distilled 2-methylpropenal, m.p. 200–201° (dec.). The mixed m.p. was 199–200° (dec.). The derivative from Fraction 4 was subjected to analysis.

Anal. Calcd. for $C_{10}H_{10}N_4O_4$: C, 48.0; H, 4.0; N, 22.4. Found: C, 47.8; H, 4.2; N, 22.3.

Reaction of methyl isopropenyl ketone with peroxyacetic acid. A solution of 84 g. (1.0 mole) of methyl isopropenyl ketone[10] (b.p. 98–99°; 98% purity by bromine number) and 1.0 mole of 45% peroxyacetic acid in 500 ml. of chloroform was allowed to stand at room temperature for 5 days. Iodometric titration at that time indicated that 96% of the theoretical amount of peracid had been consumed. The mixture was worked up as above and distilled through a 10-tray Oldershaw column to give, after removal of solvent and 10.0 g. of crude starting material, b.p. 50–54° (150 mm.), 22.2 g. (22% yield) of product, b.p. 58–59° (50 mm.); n_D^{20} 1.4171. Analysis of the product indicated it to be a mixture containing 89% of 3-methyl-3,4-epoxy-2-butanone[11] and 11% of 2-methyl-2-acetoxyoxirane.

Anal. Calcd. for 89% $C_5H_8O_2$ and 11% $C_5H_8O_3$: C, 59.2; H, 7.9. Found: C, 59.1; H, 8.0.

A 1.96 g. sample of the product was allowed to stand overnight with 50.0 ml. of 0.102*N* sodium hydroxide. Back titration with standard acid indicated the presence of 10.8% by weight of ester calculated as 2-methyl-2-acetoxyoxirane.

The infrared spectrum of the product was virtually identical with that of the epoxy ketone obtained from the alkaline epoxidation of methyl isopropenyl ketone[11]: maxima at 5.84, 7.35, 8.87, 9.92, 10.56, 10.88, and 11.92μ. The only significant difference was a shoulder at 5.71μ, consistent with the presence of small amount of ester impurity.

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[8] A. P. Terent'ev, A. N. Kost, A. M. Yurkevich, and E. E. Khaskina (Moscow State University) *Zhur. Obshchei Khim.* **23**, 746 (1953); *Chem. Abstr.* **48**, 4430 (1954) report b.p. 121–124°, n_D^{20} 1.4106 for isobutyraldehyde enol acetate (II).

[9] R. L. Shriner and R. C. Fuson, "The Systematic Identification of Organic Compounds," 2nd Ed., John Wiley & Sons, Inc., New York 1948, p. 143.

[10] Prepared by liquid phase alkali-catalyzed condensation between methyl ethyl ketone and formaldehyde (Shell Development Co., unpublished results).

[11] Wilder and Dolnick (reference 3) report b.p. 130–138°; n_D^{20} 1.4192. We repeated their alkaline epoxidation and found b.p. 58–59° (50 mm.); n_D^{20} 1.4182.

7α-Hydroxy-Reichstein's Substance S

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ROBERT H. LENHARD, LOUIS I. FELDMAN,
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During an extensive investigation of the microbiological transformation of Reichstein's substance S (I) with a variety of organisms, several monohydroxylated products were obtained.[1] The fermentation of this substrate with *Cephalosporium sp.* (Lederle No. Z-164) to form 7α-hydroxy-Reichstein's substance S (IIa)[2] and the tentative proof of its structure is elaborated in this paper.

The structure of IIa was assigned on the basis of the following considerations. Elemental analysis indicated the addition of one oxygen to the parent compound. Treatment of IIa in pyridine with acetic anhydride (one equivalent or an excess over two equivalents) at room temperature provided a monoacetate IIb or a diacetate IIc, respectively, which indicated the addition of an acylable hydroxyl group. Furthermore, reaction of IIa in methanol with 8% (v/v) sulfuric acid at reflux temperature gave in 79% yield 17α,21-dihydroxy-4,6-pregnadiene-3,20-dione (IIIa). An attempt to prepare the 3-monoketal of the monoacetate IIb by treatment with ethylene glycol (benzene reflux, *p*-toluenesulfonic acid) led only to the known 21-acetoxy-17α-hydroxy-4,6-pregnadiene-3,20-dione (IIIb).[3] It is interesting to note that the $\Delta^{4,6}$-3-one moiety is apparently unreactive under these conditions to ethylene glycol.

Since the physical constants of IIa did not agree with either 6α- or 6β-hydroxy-Reichstein's substance S,[4] it seemed obvious that the new group must be on the C7 carbon atom in order to permit

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[1] The microbiological synthesis of 15α- and 15β-hydroxy substance S has been announced by this laboratory: S. Bernstein, L. I. Feldman, W. S. Allen, R. H. Blank, and C. E. Linden, *Chem. & Ind. (London)*, 111 (1956).

[2] Other observed microbiological hydroxylations at C7 of various steroids have been reported: (a) A. Krámli and J. Horváth, *Nature*, **162**, 619 (1948); **163**, 219 (1949); (b) F. W. Kahnt, Ch. Meystre, R. Neher, E. Vischer, and A. Wettstein, *Experientia*, **8**, 422 (1952); (c) Ch. Meystre, E. Vischer, and A. Wettstein, *Helv. Chim. Acta*, **38**, 381 (1955); (d) J. Fried, R. W. Thoma, D. Perlman, J. E. Herz, and A. Borman, *Recent Progress in Hormone Research*, **11**, 157 (1955); (e) H. C. Murray and D. H. Peterson, U. S. Patent **2,702,809** (Feb. 22, 1955); (f) W. J. McAleer, M. A. Kozlowski, T. H. Stoudt, and J. M. Chemerda, Meeting-in-Miniature of the American Chemical Society, New York Section, March 14, 1958; (g) W. J. McAleer, M. A. Kozlowski, T. H. Stoudt, and J. M. Chemerda, *J. Org. Chem.*, **23**, 958 (1958).

[3] F. Sondheimer, C. Amendola, and G. Rosenkranz, *J. Am. Chem. Soc.*, **75**, 5932 (1953).

[4] D. H. Peterson, S. H. Eppstein, P. D. Meister, B. J. Magerlein, H. C. Murray, H. Marian Leigh, A. Weintraub, and L. M. Reineke, *J. Am. Chem. Soc.*, **75**, 412 (1953); K. Florey and M. Ehrenstein, *J. Org. Chem.*, **19**, 1331 (1954).

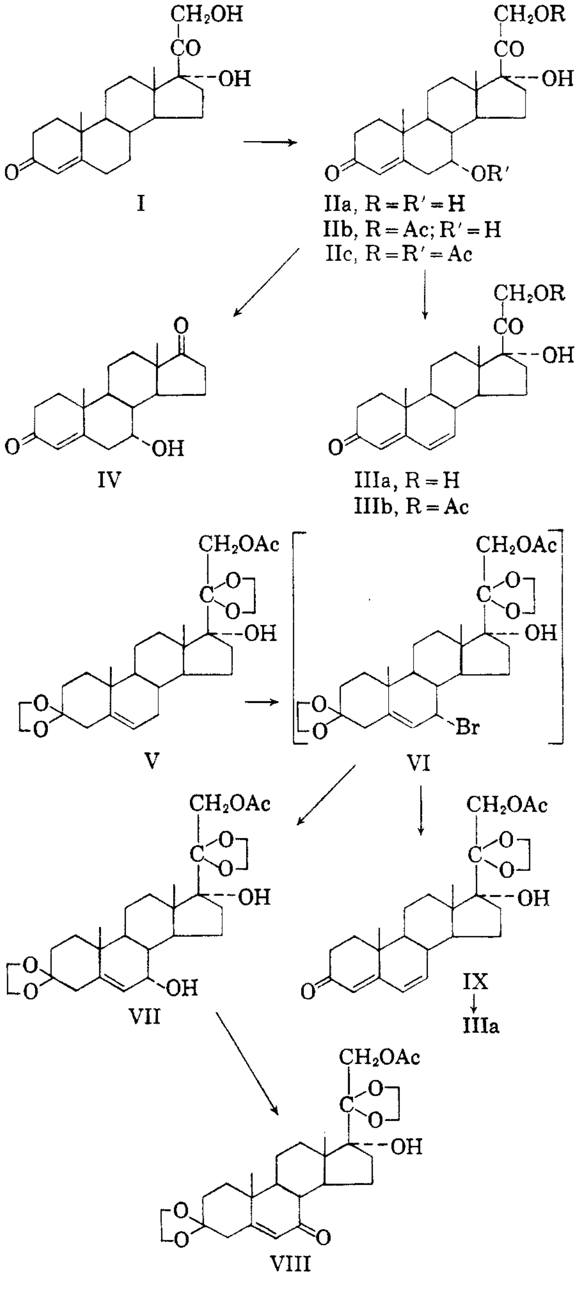
dehydration to the $\Delta^{4,6}$-3-one IIIa under acidic conditions. Moreover, in accordance with the observation[5] that the $[M]_D$ (7-hydroxy steroid) $-[M]_D$ (parent steroid) is negative for a 7α-hydroxyl substituent and positive for a 7β-hydroxyl substituent, the ΔM_D (IIa − Reichstein's substance S[6]) was calculated to be −110 suggestive that IIa is 7α,17α,21-trihydroxy-4-pregnene-3,20-dione. Thus, it follows that IIb is 21-acetoxy-7α,17α-dihydroxy-4-pregnene-3,20-dione and IIc is the 7α,21-diacetate. Further support of the configurational assignment was furnished by sodium bismuthate[7] treatment of IIa to form 7α-hydroxy-4-androstene-3,17-dione (IV). The ΔM_D (IV − 4-androstene-3,17-dione[8]) is −30 again suggestive that the added hydroxyl group at C7 is in the α-configuration.

The absorption spectrum of IIa in sulfuric acid[9] showed a new maximum at *ca.* 340 mμ which could indicate the introduction of a $\Delta^{4,6}$-3-one system similar to the case of the 6β-hydroxy-3-ones. However, it should be mentioned that the sulfuric acid spectrum of 7α-hydroxy-4-androstene-3,17-dione (IV) was essentially similar to that of 4-androstene-3,17-dione in the 2-hr. period used as a standard time. Consequently, some caution must be observed in anticipating a typical acid reaction (*i.e.*, dehydration) under the conditions of determining the sulfuric acid spectrum.

Concurrent with the microbiological hydroxylation experiments, an investigation was carried out to introduce by chemical means an oxygen function in the C7 position of Reichstein's substance S. According to an already published procedure[10] 21-acetoxy-3,20-bisethylenedioxy-5-pregnene-17α-ol (V)[11] was brominated in the allylic position (C7) with *N*-bromosuccinimide. The bromination product VI (not purified) was treated with alumina to give 21-acetoxy-3,20-bisethylenedioxy-5-pregnene-7α,17α-diol (VII). The latter was ozidized with chromic acid–pyridine reagent to 21-acetoxy-3,20-bisethylenedioxy-17α-hydroxy-5-pregnene-7-one (VIII).

In one run, a collection of the mother liquors from the alumina treatment of the bromination product VI gave after oxidation a compound whose ultraviolet spectrum revealed the presence of a $\Delta^{4,6}$-3-one moiety. Accordingly, the product was assigned the structure 21-acetoxy-20-ethylenedioxy-17α-hydroxy-4,6-pregnadiene-3-one (IX), although it could never be brought to a satisfactory elemental analysis. Saponification of IX followed by acid hydrolysis furnished 17α,21-dihydroxy-4,6-pregnadiene-3,20-dione (IIIa) identical to the sample described above. It is most probable that in this particular run an accidental hydrolysis of

Flow sheet



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[5] (a) H. J. Ringold, G. Rosenkranz, and C. Djerassi, *J. Am. Chem. Soc.*, **74**, 3318 (1952); (b) A. E. Bide, H. B. Henbest, E. R. H. Jones, and P. A. Wilkinson, *J. Chem. Soc.*, 1788 (1948); (c) C. W. Greenhalgh, H. B. Henbest, and E. R. H. Jones, *J. Chem. Soc.*, 2375 (1952), and (d) Ch. Meystre, E. Vischer, and A. Wettstein, *Helv. Chim. Acta*, **38**, 381 (1955).

[6] The molecular rotation of Reichstein's substance *S* in methanol as determined in this Laboratory was +450.

[7] C. J. W. Brooks and K. Norymberski, *Biochem. J.*, **55**, 371 (1953).

[8] The molecular rotation of 4-androstene-3,17-dione in chloroform is +567 as reported in J. P. Mathieu and A. Petit, *Tables de Constantes et Données Numeriques 6. Constantes Selectionnées Pouvoir Rotatoire Naturel I. Steroides*, Masson & Cie, Editeurs, Paris, 1956, p. 15.

[9] S. Bernstein and R. H. Lenhard, *J. Org. Chem.*, **19**, 1269 (1954).

[10] R. H. Lenhard and S. Bernstein, *J. Am. Chem. Soc.*, **78**, 989 (1956).

[11] R. Antonucci, S. Bernstein and R. H. Lenhard, *J. Am. Chem. Soc.*, **76**, 2956 (1954).

the 3-ketal function followed by dehydrobromination occurred possibly in the *N*-bromosuccinimide treatment or work-up. The alumina treatment and the oxidation most likely did not contribute to the structure of the final product.

In view of the unlikely possibility of obtaining a 7α-ol-Δ^4-3,20-dione by a strictly chemical method[10] no further work was done on this approach.

Bioassays.[12] In the electrolyte assay (K/Na) ratio on adrenalectomized rats 7α-hydroxy-Reichstein's substance S (IIa) showed no activity at total dose levels of 15 and 60 μg. In the same assay desoxycorticosterone gave significant responses at 6 and 25 μg. dose levels.

In the thymus involution assay (adrenalectomized and ovariectomized mice) IIa was inactive at a total dose level of 600 μg., whereas hydrocortisone acetate gave significant responses at 75 and 150 μg. dose levels.

7α-Hydroxy-4-androstene-3,17-dione (IV) was inactive in the baby chick comb test for androgenic activity (inunction method, propylene glycol, daily dose of 20 μg. for 7 days). Dehydroisoandrosterone at the same dose level showed significant activity.

EXPERIMENTAL

Melting points. All melting points are uncorrected.

Optical rotations. The rotations are for chloroform solutions (unless otherwise noted), and were determined at 24–25°.

Absorption spectra. The ultraviolet spectra were determined in absolute alcohol; the infrared spectra were determined in a potassium bromide disk (unless otherwise indicated).

Petroleum ether. The fraction used had a b.p. 60–70° (Skellysolve B).

7α-Hydroxy-Reichstein's substance S (7α,17α,21-trihydroxy-4-pregnene-3,20-dione) (IIa). A 5-gal. fermentation bottle containing a paddle stirrer and aerating assembly was charged with 12 l. of the following medium: Edamin lactalbumin digest (Sheffield), 2%; cerelose, 2%; corn steep liquor, 0.6%; pH adjusted to 7.0. The bottle was sterilized by autoclaving at 120° for 1 hr. The fermentation vessel was inoculated with 300 ml. of a 72-hr. mycelial growth of *Cephalosporium sp.* and incubated at 28° with a stirring rate of 200 r.p.m. and an aeration rate of 0.2 vol. of air/vol. of medium/min. Forty-eight hr. after inoculation, 6 g. of Reichstein's substance S (I) dissolved in 120 ml. of methanol was added to the mash. The bottle was harvested 125 hr. later when paper chromatography showed an almost complete conversion of Reichstein's substance S to the more polar product. The mash was filtered, and the mycelial cake was washed with 2 l. of acetone. The acetone extract and mash filtrate were pooled, and the acetone was removed by distillation. The resulting aqueous mixture was extracted with four successive 2-l. portions of methylene chloride which were subsequently combined, washed with saturated saline, and evaporated. This furnished 5 g. of a gummy solid which was subjected to partition chromatography on Celite[13] (320 g.) in the following manner. The stationary phase consisted of 6 parts of methanol and 4 parts of water, whereas the mobile phase consisted of 8 parts of ethyl acetate and 3 parts of petroleum ether (b.p. 90–100°). Both phases were equilibrated with each other. The gummy solid was dissolved in 20 ml. of the stationary phase and mixed with 40 g. of diatomaceous earth, and the mixture was added to the column. Chromatography was then initiated with the mobile phase, and 160 fractions of 20-ml. vol. each were collected. Fractions 76–120 (inclusive) contained the desired product as shown by paper chromatographic analysis, and were combined and evaporated. The residue consisted of 4.5 g. of a gummy solid which was slurried with cold chloroform and filtered. This afforded 0.99 g. of crystalline crude IIa, m.p. 197–200°. Crystallization from acetone–petroleum ether raised the melting point to 209–211°; λ_{max} 242–243 mμ (ε 14,800); ν_{max} 3420, 1720, 1667, 1628, and 1034 cm.$^{-1}$; $[\alpha]_D$ +94° (*c*, 0.839 in methanol), $[M]_D$ +340.

Anal. Calcd. for $C_{21}H_{30}O_5$ (362.45): C, 69.58; H, 8.34. Found: C, 69.40; H, 8.56.

21-Acetoxy-7α,17α-dihydroxy-4-pregnene-3,20-dione (IIb). A solution of 7α-hydroxy-Reichstein's substance S (IIa, 100 mg.) in pyridine (1 ml.) was treated with acetic anhydride (0.026 ml.), and the mixture was allowed to stand at room temperature overnight. Water was added, and the resultant crystals were collected and washed with water; 60 mg. (54%), m.p. 197–203°. Recrystallization from acetone–petroleum ether provided the analytical sample, m.p. 210–211.5°; λ_{max} 242 mμ (ε 15,300); ν_{max} 3510, 1740, 1712, 1688, 1630, 1240, and 1070 cm.$^{-1}$; $[\alpha]_D$ +111° (*c*, 1.146), $[M]_D$ +448.

Anal. Calcd. for $C_{23}H_{32}O_6$ (404.49): C, 68.29; H, 7.97. Found: C, 67.92; H, 8.15.

7α,21-Diacetoxy-17α-hydroxy-4-pregnene-3,20-dione (IIc). A mixture of IIa (60 mg.), pyridine (5 ml.) and acetic anhydride (2 ml.) was allowed to stand overnight at room temperature. The solution was poured into ice water, and the resultant crystals were collected and washed with water; 60 mg. (81%), m.p. 253–256°. Recrystallization from acetone–petroleum ether changed the melting point to 246–248°; λ_{max} 238 mμ (ε 16,100); ν_{max} 3550, 1754 (shoulder), 1740, 1660, 1632, 1235, and 1042 cm.$^{-1}$; $[\alpha]_D$ +107° (*c*, 0.936), $[M]_D$ +478.

Anal. Calcd. for $C_{25}H_{34}O_7$ (446.52): C, 67.24; H, 7.68; OAc, 19.3. Found: C, 67.50; H, 7.90; OAc, 19.3.

17α,21-Dihydroxy-4,6-pregnadiene-3,20-dione (IIIa). *A.* A solution of IIa (0.1 g.) in methanol (15 ml.) and 8% (v./v.) sulfuric acid (10 ml.) was refluxed for 1 hr. Water was added to the cooled solution, and the methanol was evaporated. The residual gummy mixture was neutralized with sodium bicarbonate, and the product was extracted with chloroform. The extract was washed with saturated saline, dried, and evaporated to afford crystals which were recrystallized from acetone–petroleum ether to afford 75 mg. (79%) of IIIa, m.p. 218.5–221°. Further recrystallization furnished pure diene IIIa, m.p. 223.5–225°; λ_{max} 283 mμ (ε 26,400); ν_{max} 3580, 1726, 1656, 1631, 1602, and 1096 cm.$^{-1}$

Anal. Calcd. for $C_{21}H_{28}O_4$ (344.44): C, 73.22; H, 8.19. Found: C, 73.10, 73.16; H, 8.52, 8.48.

B. The 21-acetate IX (150 mg.) was saponified by refluxing for 0.5 hr. with 5 ml. of 2.5% alcoholic potassium hydroxide. The addition of water to the cooled reaction mixture yielded 115 mg. of the presumed free alcohol, m.p. 250–253°. Recrystallization from acetone (petroleum ether wash) did not alter the melting point. A solution of 100 mg. of the free alcohol in 8 ml. of methanol and 0.8 ml. of 8% sulfuric

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[12] We are indebted to the following and their associates for the bioassays; Dr. R. I. Dorfman, Worcester Foundation for Experimental Biology (electrolyte and thymus assays), and Dr. F. I. Dessau, Experimental Therapeutics Research Section of these Laboratories (androgen assay).

[13] The adsorbent was specially treated Celite 545 diatomaceous earth which was slurried in 6*N* hydrochloric acid and allowed to stand overnight. It was then filtered and washed with water, followed by 3 A alcohol and/or acetone. Finally, it was dried at 100°. Celite is the trade-mark of Johns-Manville Co. for diatomaceous silica products.

acid (v./v.) was refluxed for 30 min. Water was added to the cooled solution and it was allowed to stand overnight at 5°. The product was filtered and washed with water to afford 68 mg. of the dione IIIa, m.p. 222.5–225.5°. Recrystallization from acetone–petroleum ether gave 56 mg., m.p. 225–228°. One additional crystallization from the same solvent pair did not alter the melting point; λ_{max} 283.5 mμ (ϵ 26,800); $[\alpha]_D$ +88° (*c*, 0.614). The infrared spectrum was identical to that of the sample prepared above.

21-Acetoxy-17α-hydroxy-4,6-pregnadiene-3,20-dione (IIIb). A mixture of the 7α-hydroxy-21-acetate IIb (0.3 g.), benzene (125 ml.), ethylene glycol (8 ml.), and *p*-toluenesulfonic acid (25 mg.) was refluxed and stirred for 5 hr. with constant water removal. The mixture was cooled, neutralized with sodium bicarbonate, and extracted with chloroform. The extract was washed with saturated saline, dried, and evaporated. The crystalline residue was recrystallized from acetone–petroleum ether to give 240 mg. (83%) of IIIb, m.p. 219–221°; λ_{max} 283 mμ (ϵ 29,000). Further crystallization raised the m.p. to 223.5–224.5°[14]; ν_{max} 3484, 1757, 1650, 1623, 1592, 1236, and 1095 cm.$^{-1}$.

7α-Hydroxy-4-androstene-3,17-dione (IV). A solution of IIa (0.5 g.) in glacial acetic acid (50 ml.) was shaken with sodium bismuthate (5 g.) for 25 min. After the addition of water, a solution of potassium hydroxide (35 g.) in water (30 ml.) was added, and the mixture was finally neutralized with solid sodium bicarbonate. The product was extracted with chloroform, and the extract was washed once with saturated sodium bicarbonate solution, and three times with saturated saline, dried, and evaporated. The residue was crystallized from acetone–petroleum ether to furnish 107 mg. of crude IV, m.p. 214–215°. Further recrystallization raised the m.p. to 220–222.5°; λ_{max} 241–242 mμ (ϵ 16,800); ν_{max} 3390, 1748, 1652, and 1087 cm.$^{-1}$; $[\alpha]_D$ +178° (*c*, 1.205), $[M]_D$ +537.

Anal. Calcd. for $C_{19}H_{26}O_3$ (302.40): C, 75.46; H, 8.67. Found: C, 75.71; H, 8.91.

21-Acetoxy-3,20-bisethylenedioxy-5-pregnene-7α,17α-diol (VII). A mixture of the bisethylene ketal of Reichstein's substance S acetate (V, 1.0 g.), *N*-bromosuccinimide (0.46 g.) and anhydrous potassium carbonate (0.2 g.) in carbon tetrachloride (30 ml.) and petroleum ether (b.p. 62–64°) (10 ml.) was refluxed and irradiated for 4 min. by the heat and light of a photospot lamp (Type RSP-2A, General Electric Co.). The filtered solution was stirred at room temperature for 2 hr. with ethyl acetate washed alumina (8 g.), filtered, and evaporated to a glass which was crystallized from ether–petroleum ether to afford 167 mg. of material having a negative Beilstein test, m.p. below 110°; λ_{max} 241 and 285 mμ. The alumina was stirred for 20 min. with approximately 150 ml. of acetone, filtered, and evaporated to a white crystalline solid. Crystallization of the residue from acetone–petroleum ether gave 433 mg. of product, m.p. 193.5–196° with previous softening. Four additional crystallizations from the same solvent pair afforded 190 mg. of the pure diol VII, m.p. 201.5–203.5°; λ_{max} none; ν_{max}^{Nujol} 3550, 3450, 1755, 1680, 1265, 1245, and 1103 cm.$^{-1}$; $[\alpha]_D$ −71° (*c*, 0.973).

Anal. Calcd. for $C_{27}H_{40}O_8$ (492.59): C, 65.83; H, 8.19. Found: C, 65.75; H, 8.12.

21-Acetoxy-3,20-bisethylenedioxy-17α-hydroxy-5-pregnen-7-one (VIII). *A.* A solution of 240 mg. of VII (obtained by evaporation of the mother liquors of the preceding experiment) in 10 ml. of pyridine was added to a slurry of 170 mg. of chromic anhydride in 17 ml. of cold pyridine. After standing at room temperature for 16 hr., the reaction mixture was poured into ice water and extracted with ethyl acetate. The extract was washed with 10% acetic acid (v./v.) and with water, dried, and evaporated. The residue was crystallized from ether–petroleum ether to afford 130 mg. of product, m.p. 185–186.5°; λ_{max} 240 mμ (ϵ 12,700). Recrystallization from ether–petroleum ether gave 98 mg., m.p. 186–187.5°. Two additional crystallizations from the same solvent pair did not alter the melting point; λ_{max} 240 mμ (ϵ 13,000); ν_{max}^{Nujol} 3650, 1761, 1683, 1642, 1242, and 1093 cm.$^{-1}$; $[\alpha]_D$ −63° (*c*, 0.590).

Anal. Calcd. for $C_{27}H_{38}O_8$ (490.57): C, 66.10; H, 7.81. Found: C, 66.43; H, 7.96.

B. In another run, the 7α-hydroxy-bis-ketal VII (685 mg.) was oxidized in the same manner as above and the residue obtained from a benzene extract was crystallized from acetone–ether–petroleum ether to afford 495 mg. of product, m.p. 183–185°. An additional 74 mg., m.p. 179–182°, was obtained by concentration of the mother liquor to bring the total yield to 83%.

21-Acetoxy-20-ethylenedioxy-17α-hydroxy-4,6-pregnadien-3-one (IX). In an attempt to salvage more of the 7-keto analog VIII, several mother liquors from the alumina hydrolysis of the 7α-bromo compound VI were evaporated and the residue (3.8 g.) was oxidized in the same manner as above. The benzene extract was evaporated and the oily residue was treated with acetone–ether–petroleum ether to give a semisolid. After decanting the supernatant liquid, the semisolid residue was triturated with ether to afford 0.22 g. of solid, m.p. 183–187°. Addition of petroleum ether to the decantate precipitated 0.50 g. which was recrystallized from acetone–petroleum ether to give 0.35 g., m.p. 182.5–187.5°. The latter fraction was combined with the above 0.22 g. and recrystallized from acetone–petroleum ether to afford 0.33 g., m.p. 184–189.5°; ν_{max}^{Nujol} 3550, 1737, 1682, 1633, 1600, and 1102 cm.$^{-1}$ One recrystallization from ether–petroleum ether, one from aqueous methanol and two from acetone–petroleum ether gave 0.18 g. of the 4,6-diene-3-one IX, m.p. 191.5–194°; λ_{max} 283–284 mμ (ϵ 25,100); $[\alpha]_D$ +39° (*c*, 0.536).

Anal. Calcd. for $C_{25}H_{34}O_6$(430.52): C, 69.74; H, 7.96. Found: C, 68.49, 68.82; H, 7.75, 7.97.

Acknowledgment. We wish to thank Louis M. Brancone and associates for the analyses, and William Fulmor and associates for the infrared and ultraviolet absorption spectra and optical rotation data.

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p-Thiolcinnamic Acid and S-Acyloxy Derivatives[1]

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Received October 2, 1958

During work relating to the preparation of poly-*p*-thiolstyrene by Overberger and Lebovits,[4] *p*-

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[14] Ref. 3 gives m.p. 220–222°, λ_{max} 284 mμ, log ϵ 4.47 (95% ethanol).

[1] This note comprises portions of the Ph.D. dissertation of H. Biletch, Polytechnic Institute of Brooklyn, 1953, and of a thesis submitted by F. W. Orttung in partial fulfillment of the requirements for the degree of Master of Science in the Graduate School of the Polytechnic Institute of Brooklyn, June 1959.

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[4] C. G. Overberger and A. Lebovits, *J. Am. Chem. Soc.*, **77**, 3675 (1955); **78**, 4792 (1956).