

(48% yield) as pale yellow needles, mp 205–206° (lit.<sup>11</sup> mp 204–205°). *n*-Butyl nitrite (2.50 ml) was added slowly to a stirred solution (N<sub>2</sub> atmosphere) of androsta-4,6-dien-17 $\beta$ -ol-3-one (5.00 g) and potassium *t*-butoxide (6.00 g) in dry *t*-butyl alcohol. After 2 hr, the thick suspension was diluted with water (250 ml) and the solution was extracted with two 250-ml portions of ether. The aqueous phase was covered with ethyl acetate (500 ml) and the stirred mixture was acidified with dilute hydrochloric acid. The organic phase was washed successively with aqueous sodium bicarbonate and water, dried, and evaporated *in vacuo*. Crystallization of the resulting residue (4.10 g) from acetone afforded oximino ketone XIII (3.80 g, 69%) as yellow needles: mp 241–242° dec;  $[\alpha]_D^{25} + 8.3^\circ$  (*c* 0.78);  $\lambda_{\max} 2.96$ – $3.05$ ,  $6.03$ ,  $6.17$ , and  $6.25 \mu$ ;  $\lambda_{\max}^{\text{neutral}} 310 \text{ m}\mu$  ( $\epsilon$  20,400);  $\lambda_{\max}^{\text{basic}} 297 \text{ m}\mu$  ( $\epsilon$  20,000) and  $343 \text{ m}\mu$  ( $\epsilon$  11,400).

*Anal.* Calcd for C<sub>10</sub>H<sub>25</sub>O<sub>2</sub>N: C, 72.35; H, 7.99; N, 4.44. Found: C, 72.28; H, 8.01; N, 4.41.

Using a solution (6 mg/ml) of XIII in ethanol, the following metal complexes were observed, indicative of the *anti* configuration of the oxime function: Ni<sup>2+</sup> (brown), Co<sup>2+</sup> (crimson), Cu<sup>2+</sup> (green), and Fe<sup>2+</sup> (blue, becoming green).

The acetylation of 2-oximinoandrosta-4,6-dien-17 $\beta$ -ol-3-one with acetic anhydride in pyridine at room temperature afforded, after the usual work-up (see preparation of VIII), yellow rosettes (from benzene-ether) of 17 $\beta$ -acetoxy-2-acetoximinoandrosta-4,6-dien-3-one: mp 185–187° dec;  $\lambda_{\max} 5.64$ ,  $5.79$ ,  $5.97$ ,  $6.22$ , and  $6.34 \mu$ ;  $\lambda_{\max} 222 \text{ m}\mu$  ( $\epsilon$  8500) and  $313 \text{ m}\mu$  ( $\epsilon$  22,500).

*Anal.* Calcd for C<sub>23</sub>H<sub>29</sub>O<sub>5</sub>N: C, 69.15; H, 7.32; N, 3.51. Found: C, 69.30; H, 7.41; N, 3.60.

**2-Diazoandrosta-4,6-dien-17 $\beta$ -ol-3-one (XIV).**—To a stirred solution of 2-oximinoandrosta-4,6-dien-17 $\beta$ -ol-3-one (0.700 g) in tetrahydrofuran (10 ml) and 1 *N* sodium hydroxide (5 ml) was added ether (500 ml, precooled to 5°), followed by concentrated ammonium hydroxide (3 ml) and 5.25% sodium hypochlorite (10 ml of Clorox). The two-phase system was stirred at 0–5° for 1 hr and then at room temperature for 2 hr. The washed and dried ethereal phase, on concentration to a small volume, deposited diazo ketone XIV as long yellow needles, decomposing at *ca.* 165° without melting;  $[\alpha]_D^{20} - 77.0^\circ$  (*c* 1.00);  $\lambda_{\max} 2.92$ ,  $4.77$ ,  $6.22$ ,  $6.37$ ,  $7.25$ , and  $7.34 \mu$ ;  $\lambda_{\max} 243 \text{ m}\mu$  ( $\epsilon$  7960),  $287 \text{ m}\mu$  ( $\epsilon$  20,500), and  $345 \text{ m}\mu$  ( $\epsilon$  10,700).

*Anal.* Calcd for C<sub>19</sub>H<sub>24</sub>O<sub>2</sub>N<sub>2</sub>: C, 73.04; H, 7.74; N, 8.97. Found: C, 72.62; H, 7.54; N, 8.85.

**Registry No.**—II, 13341-54-3; IV, 566-93-8; V, 13341-55-4; VI, 6901-58-2; VII, 13341-57-6; VIII, 13341-58-7; X, 13341-59-8; XIII, 5541-21-9; XIV, 13341-61-2; 17 $\beta$ -acetoxy-2-acetoximinoandrosta-4,6-dien-3-one, 13341-62-3.

**Acknowledgment.**—This investigation was supported by Public Health Service Research Grants CY-4498 and CA-04498, National Institutes of Health.

(11) C. Djerassi, G. Rosenkranz, J. Romo, S. Kaufmann, and J. Pataki, *J. Am. Chem. Soc.*, **72**, 4334 (1950).

## Autoxidation of Steroid $\Delta^{3,5}$ -dien-3-ol Ethers. A Simple Route to 6 $\beta$ -Hydroxy $\Delta^4$ -3-Ketones

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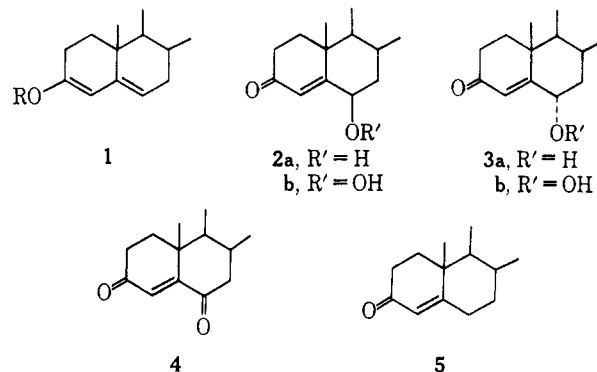
Steroids hydroxylated at C-6 are of current interest for metabolic studies. Formation of 6-hydroxy  $\Delta^4$ -3-ketones from the enol ethers of the corresponding  $\Delta^4$ -3-ketones by per acid oxidation<sup>1,2</sup> has been reported by

(1) For the same reaction on  $\Delta^2$ - and  $\Delta^4$ -enol ethers of 5 $\alpha$ -3-ketones, see R. Gardi, P. P. Castelli, and A. Ercoli, *Tetrahedron Letters*, 497 (1962).

(2) Similar results have been obtained by *t*-butyl chromate oxidation of  $\Delta^4$ -3-ketone enol ethers and enol acetates by K. Ysuda, *Chem. Pharm. Bull.* (Tokyo), **11**, 1167 (1963); *Chem. Abstr.*, **59**, 12864 (1963).

Smith, *et al.*,<sup>3</sup> and by Dusza, *et al.*<sup>4</sup> We wish to report on the preparation of 6 $\beta$ -hydroxy  $\Delta^4$ -3-keto steroids by a different reaction, still starting from  $\Delta^{3,5}$ -dienol ethers.

The main degradative process of enol ethers **1**, of course in the absence of acids, is autoxidation to give 6 $\beta$ - and 6 $\alpha$ -hydroxy  $\Delta^4$ -3-ketones (**2a** and **3a**). This occurs in both solution and solid state.



Experiments carried out in different solvents and the analogy to other autoxidations suggest that the reaction is a free-radical chain process. It is initiated by the light and by radical generators such as benzoyl peroxide or azobisisobutyronitrile and inhibited by antioxidants such as tocopherols or butylhydroxyanisol and by inorganic and organic bases, the latter being effective only if having a  $pK_b$  lower than 6. The time required for the complete disappearance of the enol ether, as shown by thin layer chromatography, varied in the light between 2 and 35 hr according to the nature of the solvent and of the irradiation (direct sunlight, diffuse daylight, fluorescent lamp, incandescent photolamp), being least in direct sunlight. In the dark and in the presence of radical generators, at least 50 hr are necessary. As to the solvent, autoxidation proceeded at the highest rate in alcoholic solution. In direct sunlight, in ethanol, and without initiators, enol ethers **1** reacted practically completely in 2 hr at an average temperature of 30°, yielding 6 $\beta$ -hydroxy  $\Delta^4$ -3-ketones (**2a**) as the main products.

The nature of the etherifying alcohol did not seem to affect sensibly the reaction rate, at least for the aliphatic and cycloaliphatic types.<sup>5</sup> Among the enol ethers tested, only the phenyl and benzyl ethers survived autoxidation conditions. Except for the substitutions at C-6, the influence of the nature of the parent steroid could not be easily settled, although it seemed generally unimportant. The marked increase of reaction time observed with certain compounds was very likely due to their low solubility and to the necessity of using different solvent mixtures. As to the 6-substituted derivatives, enol ethyl ether of 6-chloroprogesterone did not undergo autoxidation, while enol ethyl ether of 6-methyl-17 $\alpha$ -hydroxy-pregn-4-ene-3,20-dione did, but only in low yield, owing to the formation of remarkable amounts of the hydrolysis product.

Iodometric titration of the alcoholic solution after autoxidation revealed variable amounts of active

(3) L. L. Smith, J. J. Goodman, H. Mendelsohn, J. P. Dusza, and S. Bernstein, *J. Org. Chem.*, **26**, 974 (1961).

(4) J. P. Dusza, J. P. Joseph, and S. Bernstein, *ibid.*, **27**, 4046 (1962).

(5) Experiments carried out on suitable derivatives proved that the non-steroidal alcoholic moiety of the enol ethers can be recovered as alcohol.

TABLE I  
 YIELDS AND PHYSICAL PROPERTIES FOR 6 $\beta$ -HYDROXY STEROIDS

Starting compound	Condi- tions <sup>a</sup>	Conversion, <sup>b</sup> %	Yield, <sup>c</sup> %	Product	Mp, <sup>d</sup> °C	[\alpha] <sub>D</sub> , <sup>d</sup> deg	$\lambda_{\max}$ , <sup>d</sup> m $\mu$
Androst-4-ene-3,17-dione 3-ethyl enol ether <sup>e</sup>	A	80	60	6 $\beta$ -Hydroxyandrost-4-ene-3,17-dione <sup>f</sup>	193-195	+105	237
17 $\beta$ -Hydroxyandrost-4-en-3-one ethyl enol ether <sup>e</sup>	A	90	76	6 $\beta$ ,17 $\beta$ -Dihydroxyandrost-4-en-3-one <sup>g</sup>	216-218	+32	237-238
17 $\beta$ -Acetoxyandrost-4-en-3-one ethyl enol ether <sup>h</sup>	A	72	50	17 $\beta$ -Acetoxy-6 $\beta$ -hydroxyandrost-4-en-3-one <sup>i</sup>	213-215	+19	237
17 $\alpha$ -Methyl-17 $\beta$ -hydroxyandrost-4-en-3-one <i>n</i> -hexyl enol ether <sup>j</sup>	A	70	55	17 $\alpha$ -Methyl-6 $\beta$ ,17 $\beta$ -dihydroxyandrost-4-en-3-one <sup>k</sup>	250-252	+4.5	238
17 $\alpha$ -Ethynyl-17 $\beta$ -acetoxyestr-4-en-3-one cyclopentyl enol ether <sup>l</sup>	B	70	29	17 $\alpha$ -Ethynyl-17 $\beta$ -acetoxy-6 $\beta$ -hydroxyestr-4-en-3-one <sup>m</sup>	183-185	-115	238
Pregn-4-ene-3,20-dione 3-cyclopentyl enol ether <sup>j</sup>	A	90	75	6 $\beta$ -Hydroxypregn-4-ene-3,20-dione <sup>n</sup>	180-181	+99.5	237
Pregn-4-ene-3,20-dione 3-methyl enol ether <sup>o</sup>	A	80-90 <sup>p</sup>	...	6 $\beta$ -Hydroxypregn-4-ene-3,20-dione <sup>n</sup>	...	...	...
Pregn-4-ene-3,20-dione 3-allyl enol ether <sup>q</sup>	A	80-90 <sup>p</sup>	...	6 $\beta$ -Hydroxypregn-4-ene-3,20-dione <sup>n</sup>	...	...	...
Pregn-4-ene-3,20-dione 3- <i>n</i> -hexyl enol ether <sup>r</sup>	A	80-90 <sup>p</sup>	...	6 $\beta$ -Hydroxypregn-4-ene-3,20-dione <sup>n</sup>	...	...	...
Pregn-4-ene-3,20-dione 3-cyclohexyl enol ether <sup>j</sup>	A	80-90 <sup>p</sup>	...	6 $\beta$ -Hydroxypregn-4-ene-3,20-dione <sup>n</sup>	...	...	...
Pregn-4-ene-3,20-dione 3-phenyl enol ether <sup>s</sup>	B, C	No reaction	...	...	...	...	...
Pregn-4-ene-3,20-dione 3-benzyl enol ether <sup>t</sup>	B, C	No reaction	...	...	...	...	...
6-Chloropregn-4-ene-3,20-dione 3-ethyl enol ether <sup>u</sup>	C	No reaction	...	...	...	...	...
6-Methyl-17 $\alpha$ -hydroxypregn-4-ene-3,20-dione 3-ethyl enol ether <sup>v</sup>	A	45	9 <sup>w</sup>	6 $\alpha$ -Methyl-6 $\beta$ ,17 $\alpha$ -dihydroxypregn-4-ene-3,20-dione <sup>x</sup>	262-264	+31.5	239-240
21-Acetoxy-17 $\alpha$ -hydroxypregn-4-ene-3,20-dione 3-ethyl enol ether <sup>y</sup>	A	66	60	21-Acetoxy-6 $\beta$ ,17 $\alpha$ -dihydroxypregn-4-ene-3,20-dione <sup>z</sup>	270-272	+75.5	236
21-Acetoxy-17 $\alpha$ -hydroxypregn-4-ene-3,11,20-trione 3-ethyl enol ether <sup>y</sup>	A	70	35	21-Acetoxy-6 $\beta$ ,17 $\alpha$ -dihydroxypregn-4-ene-3,11,20-trione <sup>aa</sup>	268-269	+144.5	232
21-Acetoxy-11 $\beta$ ,17 $\alpha$ -dihydroxypregn-4-ene-3,20-dione 3-ethyl enol ether <sup>j</sup>	A	60	32	21-Acetoxy-6 $\beta$ ,11 $\beta$ ,17 $\alpha$ -trihydroxypregn-4-ene-3,20-dione <sup>bb</sup>	232-234	+107.5	237
Cholest-4-ene-3-one ethyl enol ether <sup>cc</sup>	B	60	34	6 $\beta$ -Hydroxycholest-4-en-3-one <sup>dd</sup>	194-196	+34	238

<sup>a</sup> A, 3-hr exposure to direct sunlight, av temp 30°, solvent ethanol; B, 7-hr exposure to direct sunlight, av temp 30°, solvent ethanol-tetrahydrofuran (85:15); C, 50-hr exposure to direct sunlight, av temp 30°, solvent ethanol, in the presence of benzoyl peroxide. <sup>b</sup> Calculated by thin layer chromatography of the reaction mixture. <sup>c</sup> Obtained as crystalline product, purity on thin layer chromatography at least 98%. <sup>d</sup> For the analytical sample homogeneous on thin layer chromatography. Literature data are reported in the footnotes only if significantly different from ours. <sup>e</sup> A. Serini and H. Köster, *Ber.*, **71**, 1766 (1938). <sup>f</sup> See ref 15, [\alpha]<sub>D</sub> +109° (CHCl<sub>3</sub>),  $\lambda_{\max}$  235.5 m $\mu$ . <sup>g</sup> See ref 4, mp 213-215°, [\alpha]<sub>D</sub> +30 (CHCl<sub>3</sub>). <sup>h</sup> See ref 1. <sup>i</sup> See ref 4, mp 210-212°, [\alpha]<sub>D</sub> +21° (CHCl<sub>3</sub>). <sup>j</sup> See ref 13. <sup>k</sup> *Anal.* Calcd for C<sub>29</sub>H<sub>50</sub>O<sub>3</sub>: C, 75.43; H, 9.50. Found: C, 75.29; H, 9.55. <sup>l</sup> Mp 186-188°, [\alpha]<sub>D</sub> -215°,  $\lambda_{\max}$  245 m $\mu$  ( $\epsilon$  20,600). *Anal.* Calcd for C<sub>27</sub>H<sub>38</sub>O<sub>3</sub>: C, 79.37; H, 8.88. Found: C, 79.28; H, 8.75. <sup>m</sup> *Anal.* Calcd for C<sub>22</sub>H<sub>32</sub>O<sub>4</sub>: C, 74.13; H, 7.92. Found: C, 74.37; H, 8.00. <sup>n</sup> See ref 15, mp 178-179°, [\alpha]<sub>D</sub> +107 (CHCl<sub>3</sub>),  $\lambda_{\max}$  235.5 m $\mu$ . <sup>o</sup> Mp 170-172°, [\alpha]<sub>D</sub> -56°,  $\lambda_{\max}$  240 m $\mu$  ( $\epsilon$  19,000). *Anal.* Calcd for C<sub>22</sub>H<sub>32</sub>O<sub>2</sub>: C, 80.44; H, 9.83. Found: C, 80.69; H, 9.82. <sup>p</sup> Reaction mixture not worked up. <sup>q</sup> R. Gardi and P. P. Castelli, *Gazz. Chim. Ital.*, **93**, 1681 (1963). <sup>r</sup> Mp 77-78°, [\alpha]<sub>D</sub> -47.5°,  $\lambda_{\max}$  241 m $\mu$  ( $\epsilon$  20,400). *Anal.* Calcd for C<sub>27</sub>H<sub>42</sub>O<sub>2</sub>: C, 81.35; H, 10.62. Found: C, 81.31; H, 10.32. <sup>s</sup> Mp 169-171.5°, [\alpha]<sub>D</sub> -57°,  $\lambda_{\max}$  242-243 m $\mu$  ( $\epsilon$  19,900). *Anal.* Calcd for C<sub>27</sub>H<sub>34</sub>O<sub>2</sub>: C, 83.03; H, 8.78. Found: C, 81.31; H, 8.76. <sup>t</sup> H. Köster, U. S. Patent 2,363,338 (Nov 21, 1944). <sup>u</sup> Mp 104-106°, [\alpha]<sub>D</sub> -82°,  $\lambda_{\max}$  252 m $\mu$  ( $\epsilon$  20,200). *Anal.* Calcd for C<sub>23</sub>H<sub>38</sub>O<sub>2</sub>Cl: C, 73.28; H, 9.03; Cl, 9.4. Found: C, 73.05; H, 8.91; Cl, 9.53. <sup>v</sup> Mp 100-102°, [\alpha]<sub>D</sub> -157°,  $\lambda_{\max}$  247-248 m $\mu$  ( $\epsilon$  18,000). *Anal.* Calcd for C<sub>24</sub>H<sub>36</sub>O<sub>3</sub>: C, 77.37; H, 9.74. Found: C, 76.91; H, 9.62. <sup>w</sup> Pure product isolated after chromatography on alumina column. <sup>x</sup> Mp 262-264°, [\alpha]<sub>D</sub> +31.5°,  $\lambda_{\max}$  239-240 m $\mu$  ( $\epsilon$  12,500). *Anal.* Calcd for C<sub>22</sub>H<sub>32</sub>O<sub>4</sub>: C, 73.30; H, 8.95. Found: C, 73.28; H, 8.86. Configuration at C-6 inferred on the basis of ultraviolet maximum; cf. R. Sciaky and A. Consonni, *Gazz. Chim. Ital.*, **92**, 547 (1962). <sup>y</sup> P. L. Julian, E. W. Meyer, W. J. Karpel, and W. Cole, *J. Am. Chem. Soc.*, **73**, 1982 (1951). <sup>z</sup> See ref 4, [\alpha]<sub>D</sub> +49 (pyridine). <sup>aa</sup> See ref 4, [\alpha]<sub>D</sub> +130° (pyridine). <sup>bb</sup> See ref 4, mp 219-221°, [\alpha]<sub>D</sub> +100° (pyridine). <sup>cc</sup> E. Schwenk, G. Fleischer, and B. Whitman, *J. Am. Chem. Soc.*, **60**, 1702 (1938). <sup>dd</sup> L. F. Fieser, *J. Am. Chem. Soc.*, **75**, 4377 (1953).

oxygen, mostly present as nonsteroidal, water-soluble peroxides. Thin layer chromatography showed only traces of steroidal hydroperoxides, identified as the 6 $\beta$ - and 6 $\alpha$ -hydroperoxy  $\Delta^4$ -3-ketones **2b** and **3b** by comparison with the products prepared from  $\Delta^5$ -3-ketones according to Fieser, *et al.*<sup>6,8</sup> Anyway, the analogy

(6) L. F. Fieser, T. W. Greene, F. Bischoff, G. Lopez, and J. J. Rupp, *J. Am. Chem. Soc.*, **77**, 3928 (1955); L. F. Fieser and M. Fieser, "Steroids," Reinhold Publishing Corp., New York, N. Y., 1959, p 235; see also ref 7.

(7) A. J. Cox, *J. Org. Chem.*, **30**, 2052 (1965).

(8) For the formation of **2b** and **3b** by oxygenation of 5-en-3-ones and related problems, see also A. Nickon and W. L. Mendelsohn, *ibid.*, **30**, 2087 (1965), and the herein quoted references.

with other autoxidations of steroid  $\Delta^5$ -enes and other factors suggest that reaction proceeds *via* hydroperoxides **2b** and **3b**. Thus, the little amount of  $\Delta^4$ -ene-3,6-dione (**4**) which was isolated as by-product very likely results from the breakdown of  $\Delta^4$ -3-keto 6-hydroperoxides,<sup>8,9</sup> in this connection, inhibition of the autooxidation of enol ethers by bases may be rationalized as owing to the removal of the proton at C-6

(9) For the formation of enedione **4** also by copper-catalyzed oxygenation of  $\Delta^5$ -cholestenone, see H. C. Volger and W. Brackman, *Rec. Trav. Chim.*, **84**, 579 (1965).

from **2b** and **3b** to give enedione **4**.<sup>10</sup> Other minor products are the  $6\alpha$ -hydroxy  $\Delta^4$ -3-ketones (**3a**) and the parent  $\Delta^4$ -3-ketone (**5**). Generally the ratio between the  $6\beta$  and  $6\alpha$  epimers was never lower than 8–10, a rather high value for a free-radical oxygenation giving as a rule comparable amounts of epimers.<sup>7,11</sup> Higher amounts of  $6\alpha$ -hydroxy compound were found only on autoxidation of cortisol 21-acetate 3-ethyl enol ether.

Also in solvents other than alcohols, for instance in benzene or tetrahydrofuran, transformation of the enol ethers was complete in a brief time, although longer than in alcohol.  $6\beta$ -Hydroxy  $\Delta^4$ -3-ketone **2a** could not be isolated in satisfactory yield, but it was still the major component of the reaction mixture, which contained other compounds besides those cited above and peroxides other than **2b** and **3b**.<sup>12</sup> The results obtained in autoxidations carried out for preparative purpose in direct sunlight and mainly without radical generators are reported in Table I. The new enol ethers employed as starting compounds have been prepared according to already described procedures.<sup>13</sup>

#### Experimental Section<sup>14</sup>

The following example is given to illustrate the method used to perform autoxidation and to prepare the compounds listed in Table I.

**Autoxidation of 3-Ethoxyandrosta-3,5-dien-17-one.**—In a 1-l. Roux bottle, 2 g of androstenedione 3-ethyl enol ether and 150 ml of ethanol were added and the bottle was placed on a suitable shaker and exposed to direct sunlight (average temperature, 30°). After about 1 hr the initially suspended product dissolved completely; after 2 hr thin layer chromatography revealed the presence of about 5% of the starting enol ether and about 85% of hydroxylated compounds, mainly  $6\beta$ -hydroxyandrostenedione. Spraying of the chromatogram with potassium iodide–acetic acid visualized trace amounts of peroxides, identical with the  $6$ -hydroperoxyandrost-4-ene-3,17-dione, prepared as an epimeric mixture from androst-5-ene-3,17-dione by benzoyl peroxide initiated autoxidation according to Fieser, *et al.*<sup>6</sup>

After 3 hr the solvent was evaporated under vacuum and digestion of the residue with ether yielded 1.1 g (60%) of  $6\beta$ -hydroxyandrost-4-ene-3,17-dione, mp 185–192°, purity on thin layer at least 98%. Recrystallization from acetone–hexane gave the analytical sample, mp 193–195°,  $[\alpha]_D +105^\circ$ ,  $\lambda_{max}$  237  $m\mu$  ( $\epsilon$  14,200), identical with the product prepared according to Dusza, *et al.*<sup>4</sup> Evaporation of the collected mother liquors gave a residue which by thin layer chromatography was found to contain at least 50% of  $6\beta$ -hydroxyandrostenedione, about 5% of androstenedione, about 10% of  $6\alpha$ -hydroxyandrostenedione and 1–2% of androst-4-ene-3,6,17-trione.

Besides the  $R_f$  values, the by-products were identified as follows. Androstenedione was identified by elution from the chromatogram and comparison of ultraviolet and infrared spectra with those of an authentic specimen.  $6\alpha$ -Hydroxyandrostenedione was eluted and compared with the product prepared from the  $6\beta$  epimer by epimerization of the acetate according to Balantan and Ehrenstein.<sup>15</sup> Moreover, after refluxing in methanol with hydrochloric acid, the rearrangement product<sup>16</sup> was com-

pared with a specimen of  $5\alpha$ -androstene-3,6,17-trione<sup>15</sup> obtained from  $6\beta$ -hydroxyandrostenedione by the same treatment. Androst-4-ene-3,6,17-trione was identified by comparing the ultraviolet ( $\lambda_{max}$  252  $m\mu$ ) and infrared spectra of the eluted material with those of the authentic specimen, mp 229–230°,  $[\alpha]_D +38^\circ$  (acetone) [lit. mp 216–217°,<sup>17</sup> 220–225°<sup>18</sup>, 223–225°;<sup>19</sup>  $[\alpha]_D +42.1^\circ$ ,<sup>17</sup>  $+32.3^\circ$ ,<sup>18</sup>  $+43^\circ$ <sup>19</sup> (acetone)], prepared by oxidation of  $6\beta$ -hydroxyandrostenedione with 8 *N* chromic acid in acetone.

**Registry No.**— $6\beta$ -Hydroxyandrost-4-ene-3,17-dione, 63-00-3;  $6\beta,17\beta$ -dihydroxyandrost-4-en-3-one, 62-99-7;  $17\beta$ -acetoxy- $6\beta$ -hydroxyandrost-4-en-3-one, 13096-48-5;  $17\alpha$ -methyl- $6\beta,17\beta$ -dihydroxyandrost-4-en-3-one, 13096-49-6;  $17\alpha$ -ethynyl- $17\beta$ -acetoxy- $6\beta$ -hydroxyestr-4-en-3-one, 6856-27-5;  $6\alpha$ -methyl- $6\beta,17\alpha$ -dihydroxypregn-4-ene-3,20-dione, 13096-50-9; 21-acetoxy- $6\beta,17\alpha$ -dihydroxypregn-4-ene-3,11,20-trione, 13096-52-1; 21-acetoxy- $6\beta,11\beta,17\alpha$ -trihydroxypregn-4-ene-3,20-dione, 13096-53-2;  $6\beta$ -hydroxycholest-4-en-3-one, 570-89-8;  $6\beta$ -hydroxypregn-4-ene-3,30-dione, 604-19-3.

(17) A. Butenandt and B. Riegel, *Ber.*, **69**, 1163 (1936).

(18) D. H. Peterson, S. H. Eppstein, P. D. Meister, B. J. Magerlein, H. C. Murray, H. M. Leigh, A. Weintraub, and L. M. Reineke, *J. Am. Chem. Soc.*, **75**, 412 (1953).

(19) C. Amendolla, G. Rosenkranz, and F. Sondheimer, *J. Chem. Soc.*, 1226 (1954).

#### Autoxidative Cleavage of Isopropyl Mesityl Ketone

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In the course of some other studies<sup>3</sup> with isopropyl mesityl ketone (I), a colorless, crystalline compound was frequently observed to form in the liquid ketone which gradually turned dark on standing or following various manipulations. The phenomenon with this ketone has not been previously reported to our knowledge. The compound was identified as mesitoic acid (II) by its neutralization equivalent and comparison of the melting point and the infrared curve with those of authentic mesitoic acid. Although acetone was the expected product from the 3-carbon fragment, conclusive evidence for its presence was difficult to obtain from the original liquid mixtures. However, when oxidation was carried out under controlled conditions by bubbling oxygen gas into the liquid ketone and passing the exit gas through a 2,4-dinitrophenylhydrazine solution, a 2,4-dinitrophenylhydrazone was obtained which was identified as the acetone derivative from its melting point and mixture melting point with authentic material and its  $R_f$  value on thin layer chromatography compared with the  $R_f$  of 2,4-dinitrophenylhydrazone of acetone. Further identification was made by condensing a liquid from the exit gas in a low-temperature trap and comparing the infrared spectrum with acetone's. By this means, water was also found to be a product of the oxidation, the mole ratio of acetone–water being

(1) Research Corp. Predoctoral Fellow.

(2) Welch Foundation Predoctoral Fellow.

(3) A. G. Pinkus and W. C. Servoss, presented at the Kansas City Chemical Conference, Nov 16, 1962.

(10) For a complete review on autoxidation inhibition, see K. U. Ingold, *Chem. Rev.*, **61**, 563 (1961).

(11) A. Nickon, N. Schwartz, J. B. Di Giorgio, and D. A. Widdowson, *J. Org. Chem.*, **30**, 1711 (1965).

(12) Preliminary experiments on photosensitized oxygenation of enol ethers, carried out according to A. Nickon and J. F. Bagli, *J. Am. Chem. Soc.*, **83**, 1498 (1961), showed that in these conditions too  $6\beta$ -hydroxy  $\Delta^4$ -3-ketones (**2a**) were the main products.

(13) A. Ercoli and R. Gardi, *J. Am. Chem. Soc.*, **82**, 746 (1960).

(14) Rotations are in dioxane unless otherwise indicated. Thin layer chromatographies have been carried out in the following systems, according to the polarity of the compounds: ethyl ether–chloroform (1:9), benzene–ethyl acetate (1:1), benzene–ethyl acetate (1:4). We are indebted to Dr. Sergio Cairoli for the microanalyses and to Dr. Cesare Pedrali for the infrared spectra.

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