

zinc dust in dilute alcohol<sup>12</sup> at room temperature furnished a mixture of III and 17 $\alpha$ -hydroxycorticosterone acetate, m.p. 217–20°;  $[\alpha]^{25}_D +156^\circ$  (*c*, 0.36 in CHCl<sub>3</sub>);  $\lambda_{\max}^{\text{alc.}}$  241 m $\mu$  ( $\epsilon = 16,700$ ); (Anal. Calcd. for C<sub>23</sub>H<sub>32</sub>O<sub>6</sub>: C, 68.29; H, 7.97. Found: C, 68.47; H, 8.14), identified further by infrared comparison with an authentic sample.

Similarly, 11-epicorticosterone<sup>1,2,13</sup> on monoacetylation, followed by tosylation and elimination of toluenesulfonic acid with sodium acetate in acetic acid yielded the known  $\Delta^{4,9(11)}$ -pregnadiene-21-ol-3,20-dione 21-acetate,<sup>14</sup> m.p. 160–160.5°;  $[\alpha]^{25}_D +128^\circ$  (*c*, 0.76 in acetone),  $+150^\circ$  (*c*, 0.80 in CHCl<sub>3</sub>); which on treatment with N-bromoacetamide afforded 9 $\alpha$ -bromocorticosterone acetate, m.p. 152–53° (dec.);  $[\alpha]^{25}_D +178^\circ$  (*c*, 0.94 in CHCl<sub>3</sub>); (Anal. Calcd. for C<sub>23</sub>H<sub>31</sub>O<sub>5</sub>Br: C, 59.10; H, 6.68; Br, 17.10. Found: C, 59.15; H, 6.70; Br, 17.03).

An attractive feature of this synthetic route is that it permits the introduction of radioactive halogen or tritium into the stable 9-position in the final step.

(12) The use of other reagents commonly employed for reductive dehalogenations such as Raney nickel with or without hydrogen, chromous chloride, zinc in acetic acid and others, led to III, V and/or their 4,5-dihydro products. Of particular interest is the reaction of IV with potassium iodide in acetone, which at the boiling point yielded III and V, while at room temperature it afforded in almost quantitative yield  $\Delta^{4,6,8(9)}$ -pregnatriene-17 $\alpha$ ,21-diol-3,20-dione acetate, m.p. 188–191°;  $[\alpha]^{25}_D +531^\circ$  (*c*, 1.02 in CHCl<sub>3</sub>);  $\lambda_{\max}^{\text{alc.}}$  244 m $\mu$  ( $\epsilon = 14,300$ ), 285–300 m $\mu$  ( $\epsilon = 3,100$ ), 385 m $\mu$  ( $\epsilon = 6,700$ ), *cf.* R. Yashin, G. Rosenkranz and C. Djerassi, *THIS JOURNAL*, **73**, 4654 (1951).

(13) S. H. Eppstein, P. D. Meister, D. H. Peterson, H. C. Murray, H. M. Leigh, D. A. Lyttle, L. M. Reineke and A. Weintraub, *ibid.*, **75**, 408 (1953).

(14) C. W. Shoppee and T. Reichstein, *Helv. Chim. Acta*, **26**, 1316 (1943).

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#### DECATETRAENEDIOIC ACID, A FUMAGILLIN DEGRADATION PRODUCT

Sir:

The antibiotic fumagillin<sup>1,2,3</sup> has been shown to be an acid with an empirical formula of C<sub>26</sub>–27H<sub>34</sub>–36O<sub>7</sub>. We have found that fumagillin can be hydrolyzed under mild alkaline conditions liberating a highly unsaturated acid C<sub>10</sub>H<sub>10</sub>O<sub>4</sub> with the properties of 2,4,6,8-decatetraenedioic acid.<sup>4</sup>

This appears to be the first isolation of this acid from a natural source. The ultraviolet absorption spectrum shows peaks at 336 m $\mu$  and 351 m $\mu$  similar to fumagillin. On hydrogenation, fumagillin absorbs about 5 moles of hydrogen. Hydrolysis of hydrogenated fumagillin yields sebatic acid. These facts lead us to the conclusion that fumagillin is a mono-ester of decatetraenedioic acid: [C<sub>16</sub>–17H<sub>25</sub>–27O<sub>3</sub>]–O–CO–(CH=CH)<sub>4</sub>COOH.

**Isolation of Decatetraenedioic Acid from Fumagillin.**—One gram of fumagillin was sus-

(1) T. E. Eble and F. R. Hanson, *Antibiotics & Chemotherapy*, **1**, 54 (1951).

(2) I. N. Asheshov, F. Strelitz and E. A. Hall, *ibid.*, **2**, 361 (1952).

(3) Our titration and elementary analyses agree best for C<sub>27</sub>H<sub>34</sub>O<sub>7</sub>, as do the data of Eble and Hanson; Asheshov, *et al.*, however, prefer C<sub>26</sub>H<sub>32</sub>O<sub>7</sub>.

(4) R. Kuhn and C. Grundmann, *Ber.*, **69**, 1737 (1936).

ended in 50 ml. of alcohol, and 12 ml. of *N* NaOH added. The fumagillin dissolved, and the solution became red. The solution was boiled under reflux for 15 minutes, diluted with 35 ml. of water to redissolve a precipitate, boiled for ten minutes more, filtered, cooled and acidified. The precipitate (305 mg.) was dissolved in 3.5 ml. of *N* NaOH, treated with Darco G-60, filtered and acidified: yield, 288 mg. of a yellow powder, insoluble in chloroform, alcohol, or water, m. p. 295–297° dec.

Anal. Calcd. for C<sub>10</sub>H<sub>10</sub>O<sub>4</sub>: C, 61.85; H, 5.19. Found: C, 61.68; H, 5.27.

The infrared spectrum showed bands at 3.65, 3.76 and 3.90 (carboxylic OH), 5.93 (carbonyl), and 6.13 and 6.32 microns (C=C) in Nujol mulls.

The methyl ester<sup>4</sup> was prepared through the acid chloride, m. p. 214–217°;  $E_{1\text{cm}}^{1\%}$  3180 at 335 m $\mu$  and  $E_{1\text{cm}}^{1\%}$  2950 at 351 m $\mu$  in alcohol containing 2% chloroform.

Anal. Calcd. for C<sub>12</sub>H<sub>14</sub>O<sub>4</sub>: C, 64.85; H, 6.35. Found: C, 65.10, 64.88; H, 6.60, 6.43.

This ester was compared directly with a synthetic sample kindly supplied by Prof. R. Kuhn. The two were shown to be identical by mixed melting point, infrared (Nujol mull) and ultraviolet spectra.

**Isolation of Sebatic Acid from Hydrogenated Fumagillin.**—Fumagillin (10.1 g.) was hydrogenated with Adams catalyst in alcohol at room temperature and three atmospheres pressure. After 15 minutes over 5 molar equivalents of hydrogen had been consumed. The solution was filtered and concentrated with addition of water to remove alcohol. A solution of 1.67 g. (2 molar equivalents) of sodium hydroxide in 250 ml. was added and the solution heated for one hour on a steam-bath. The cooled solution was extracted with ether, evaporated to 50 ml. and acidified. A white solid (3.32 g.) precipitated, m. p. 132–133°, showing no depression with authentic sebatic acid.

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(5) Abbott Laboratories Fellow for 1952–1953.

#### A NEW CLASS OF ANTITUBERCULAR COMPOUNDS

Sir:

During the screening of a large number of substances chosen from a wide range of chemical types, the discovery was made by Dr. R. L. Mayer and co-workers of the Division of Microbiology that 4,4'-diethoxythiocarbonyl (2) had high anti-tuberculous activity in mice infected with the H37RV strain.<sup>1</sup> The synthesis and testing of over 300 thiocarbonyls and related substances revealed the rather specific structural features necessary for activity.

Shortening the 4-substituent to methoxy (1) (see

(1) R. L. Mayer, P. C. Eisman and E. A. Konopka, *Proc. Soc. Exp. Biol.*, in press.