

Mottern and Cole's method for the first time in obtaining the best results possible. Full acknowledgment is made to Mottern and Cole for their kindness in letting us use their method and for supplying us with goodly quantities of *d*-galacturonic acid.

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Sterols. LXXIV. Acetic Acid Derivatives of Estrone and α -Estradiol

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Estratriene-1,3,5-one-17-oxyacetic acid-3 was first prepared by Ercoli and Mamoli¹ by treatment of estrone in aqueous potassium hydroxide solution with chloroacetic acid. In the present work the 3-oxyacetic acid derivatives of estratriene-1,3,5-one-17-ol-3 and of estratriene-1,3,5-diol-17(α),3 were prepared by the reaction of these substances with ethyl chloroacetate in the presence of an excess of an ethanolic solution of sodium ethylate. Estratriene-1,3,5-one-17-ol-3 was also caused to react in a similar way with α -chloropropionic acid to yield estratriene-1,3,5-one-17-oxyethylacetic acid-3. The acidic substances were characterized further by the formation of the methyl esters.

We wish to thank Parke, Davis and Company for their generous support and assistance rendered during the course of this work.

Experimental Part

Estratriene-1,3,5-one-17-oxyacetic Acid-3.—To a boiling solution of 1 g. of estrone in 40 cc. of absolute ethanol was added 3.5 cc. of ethyl chloroacetate and a solution of 600 mg. of sodium in 20 cc. of ethanol. The mixture was refluxed on the steam-bath for fourteen hours after which 2 g. of potassium hydroxide was added and the refluxing continued for one hour. The mixture was diluted with water and the clear solution acidified with hydrochloric acid. The white solid was taken up in ether and the ethereal solution washed with water and 5% sodium carbonate solution. Evaporation of the ether yielded approximately 150 mg. of unreacted estrone.

The sodium carbonate washing was acidified with hydrochloric acid and the white solid taken up in ether. Evaporation of the ether gave a product which crystallized from aqueous acetone as small white plates, m. p. 209–211°; yield, 750 mg.

Anal. Calcd. for $C_{20}H_{26}O_4$: C, 73.2; H, 7.4. Found: C, 73.5; H, 7.5.

When the reaction was carried out using equivalent

amounts of sodium and ethyl chloroacetate, only a poor yield of the acid was obtained.

A solution of 50 mg. of the acid in 10 cc. of 80% ethanol was refluxed for one hour with 75 mg. of hydroxylamine hydrochloride and 100 mg. of sodium acetate. The product was crystallized from 80% ethanol to give white crystals of the *oxime*, m. p. 230–232° dec.

Anal. Calcd. for $C_{20}H_{28}O_4N$: C, 69.9; H, 7.3. Found: C, 70.0; H, 7.4.

The **methyl ester** was prepared by treating 150 mg. of the acid in ether-methanol solution with an excess of an ethereal solution of diazomethane. The product was crystallized from aqueous acetone as white crystals, m. p. 130–132°.

Anal. Calcd. for $C_{21}H_{28}O_4$: C, 73.6; H, 7.7. Found: C, 73.5; H, 7.8.

Estratriene-1,3,5-ol-17(α)-oxyacetic Acid-3.—This was prepared from estratriene-1,3,5-diol-3,17(α) as described for estratriene-1,3,5-one-17-oxyacetic acid-3. The product was crystallized from aqueous acetone to give white crystals, m. p. 182–184°.

Anal. Calcd. for $C_{20}H_{26}O_4$: C, 72.7; H, 7.9. Found: C, 72.6; H, 7.9.

Treatment of the acid in ether-methanol solution with diazomethane yielded the **methyl ester** which crystallized as white crystals from ether-pentane, m. p. 94–96°.

Anal. Calcd. for $C_{21}H_{28}O_4$: C, 73.2; H, 8.2. Found: C, 73.3; H, 8.1.

Estratriene-1,3,5-one-17-oxyethylacetic Acid-3.—This was prepared from estrone and α -chloropropionic acid as described for the preparation of estratriene-1,3,5-one-17-oxyacetic acid-3 except that about three times as much sodium was used. The product was crystallized from aqueous acetone as white crystals, m. p. 195–198°.

Anal. Calcd. for $C_{21}H_{28}O_4$: C, 73.6; H, 7.7. Found: C, 73.3; H, 7.7.

Treatment of the acid in methanol-ether solution with diazomethane yielded the **methyl ester** which crystallized from aqueous acetone as small white crystals, m. p. 137–139°.

Anal. Calcd. for $C_{22}H_{28}O_4$: C, 73.9; H, 7.9. Found: C, 74.1; H, 7.9.

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Identification of Propionic Acid in the Presence of Acetic and Butyric Acids

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Pure propionic acid may be tested for readily in a number of ways, namely, as a derivative of *p*-toluidine,¹ benzylisothioureia² and the like; by the formation of 2-ethylbenzimidazole³; by its reac-

(1) R. L. Shriner and R. C. Fuson, "Identification of Organic Compounds," John Wiley & Sons, Inc., New York, N. Y., pp. 95, 144.

(2) S. Veibel and H. Lillielund, *Bull. soc. chim.*, [5] 5, 1153 (1938).

(3) W. O. Pool, H. J. Harwood and A. W. Ralston, *THIS JOURNAL*, 59, 178 (1937).

(1) Ercoli and Mamoli, *Gazz. chim. ital.*, 68, 142 (1938).