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A NEW SYNTHESIS OF
3-METHOXY-17β-CARBOXYOESTRA-1,3,5(10),6,8-PENTAENE*

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A SYNTHESIS of 3-methoxy-17β-carboxyoestra-1,3,5(10),6,8-pentaene (I, R=2H) was described (1) earlier by Banerjee and Johnson and coworkers. The recent publication (2) of Harnik *et al.* on the applications of 2-methyl-3-carboxycyclopentanone-2-acetic acid (II) derivatives in steroid synthesis has prompted us to report the present new synthesis of I, (R=2H), using ethyl *trans*-2-methyl-3-carbethoxycyclopentanone-2-acetate (IIa, R=C_2H_5) as the starting material; the isomeric *trans*- and *cis*-keto diacids (IIa and IIb, R=H) and the anhydride (III) were reported (3) for the first time by Banerjee and Das Gupta in 1952 as useful synthetic steroid intermediates.

2-Methoxy-6-lithionaphthalene was condensed with the keto diester (IIa, R=C_2H_5) following the procedure (4) of Newman *et al.* Treatment of the resulting crude product with *p*-toluenesulphonic acid in benzene followed by saponification afforded the unsaturated diacid (IV, R=H), m.p. 201-203°; IR ν_{max}^{nujol} 2600 cm^{-1}, 1704 cm^{-1}, 1631-1634 cm^{-1}, 1600 cm^{-1}, 1250 cm^{-1}, 830 cm^{-1}. Cyclisation of IV, R=H, and the corresponding dimethyl ester (IV, R=CH_3),** m.p. 109-110°; UV λ_{max}^{EtOH} 235 mμ (log ε 4.1), 285 mμ (log ε 3.6), 320 mμ (log ε 2.9), 329 mμ (log ε 2.9); IR ν_{max}^{nujol} 1745 cm^{-1}, 1645 cm^{-1}, 1613 cm^{-1}, 1258 cm^{-1}, 814 cm^{-1}, with polyphosphoric acid gave the unsaturated

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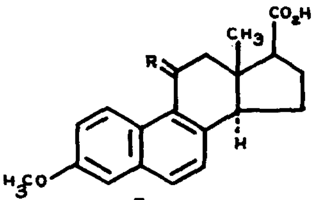
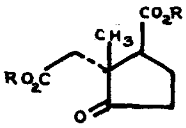
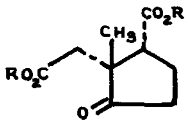
[*] Melting points are not corrected.



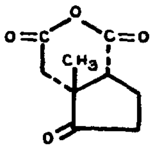
I



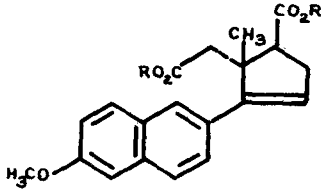
IIa



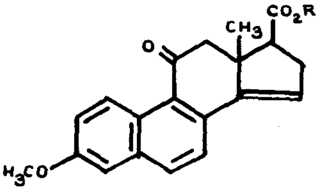
IIb



III



IV



V

keto acid (V, R=H), m.p. 256-258° (evacuated sealed tube); UV λ^{EtOH}_{max} 238 mμ (log ε 4.4), 273 mμ (log ε 4.6), 312 mμ (log ε 3.8), 375 mμ (log ε 3.8); IR ν^{nujol}_{max} 1724 cm^{-1}, 1678 cm^{-1}, 1629-1634 cm^{-1}, 1603 cm^{-1}, 1245 cm^{-1}, 809 cm^{-1}, and its ester (V, R=CH_3), m.p. 168.5°; UV λ^{EtOH}_{max} 240 mμ (log ε 4.5), 275 mμ (log ε 4.6), 316 mμ (log ε 3.8), 322 mμ (log ε 3.8), 326 mμ (log ε 3.8), 372 mμ (log ε 3.8); IR ν^{nujol}_{max} 1748 cm^{-1}, 1684 cm^{-1}, 1629 cm^{-1}, 1608 cm^{-1}, 1244 cm^{-1}, 809 cm^{-1}. Catalytic hydrogenation of V, R=H, in presence of 30% Pd-C catalyst furnished the saturated keto acid (I, R=O), m.p. 277-278° (evacuated sealed tube); UV λ^{EtOH}_{max} 220 mμ (log ε 4.7), 248 mμ (log ε 4.5), 279.5 mμ (log ε 3.6), 282 mμ (log ε 3.6), 284 mμ (log ε 3.6), 316 mμ (log ε 3.8), 355 mμ (log ε 3.5); IR ν^{nujol}_{max} 2660 cm^{-1}, 1718 cm^{-1}, 1661 cm^{-1}, 1623 cm^{-1}, 1597 cm^{-1}, 1245 cm^{-1}. When the aforementioned hydrogenation was allowed to proceed following the uptake of one mole of hydrogen, the absorption

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** This compound has been reported by Harnik _et_ _al_. (2).

slowed down and stopped after two more moles of hydrogen were absorbed to give I, R=2H, m.p. 281-282° (evacuated sealed tube); UV λ_{max}^{EtOH} 231 mμ (log ε 4.8), 268 mμ (log ε 3.7), 278 mμ (log ε 3.7), 323 mμ (log ε 3.3), 338 mμ (log ε 3.4); IR ν_{max}^{nujol} 2833 cm^{-1}, 1700 cm^{-1}, 1623 cm^{-1}, 1598 cm^{-1}, 1244 cm^{-1}. IR spectrum of I, R=2H, was identical with that of the compound (1) prepared earlier and whose configuration was proved by identity with an authentic material (1) prepared from dl-equilenin methyl ether (5).

Work is in progress to prepare naphthalene analogues of 11-keto steroids from the keto acid (I, R=O).

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