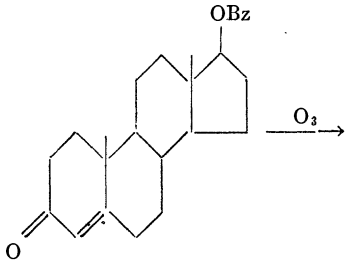
IN THE LABORATORY

Radioactive Testosterone[1]

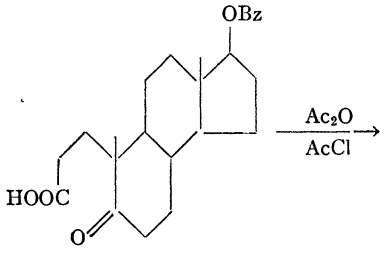
RICHARD B. TURNER

Department of Chemistry, Harvard University

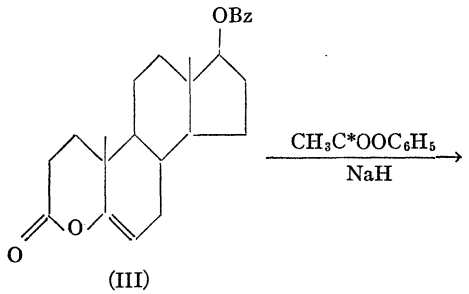
A method for the preparation of steroids labeled with isotopic carbon in ring A has recently been reported from this laboratory (*3*). This work has now been extended to the preparation of 3-radiotestosterone (IV), which is the first example of a synthetic radioactive sex hormone.



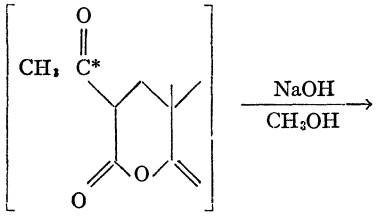
(I)

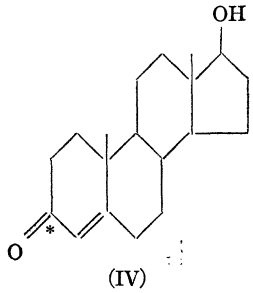


(II)



(III)





(IV)

The procedure employed, outlined in the accompanying diagram, was essentially that reported previously for cholestenone (*3*). Ozonization (cf. *1*) of testosterone benzoate (I) afforded the keto acid II (m.p., 147–148°; $[\alpha]_D = +79°$) in a yield of about 65 per cent. *Anal.* Calc'd for $C_{25}H_{32}O_5$: C, 72.79; H, 7.82. Found: C, 72.83; H, 7.84. This substance was treated with acetic anhydride and acetyl chloride, and an enol-lactone (III) was obtained (80 per cent yield) which melted at 202–202.5°; $[\alpha]_D = -19°$. *Anal.* Calc'd for $C_{25}H_{30}O_4$: C, 76.11; H, 7.66. Found: C, 75.98; H, 7.74.

Condensation of III with phenyl acetate containing C^{14} in the carboxyl group proceeded smoothly in the presence of sodium hydride, yielding an oil which was treated directly with a methanolic solution of sodium hydroxide. The product, isolated by chromatographic separation on alumina, melted at 153–154° and did not depress the melting point of an authentic sample of testosterone. The identity of the substance was further established by measurements of specific rotation (+110°) and ultraviolet absorption ($\lambda_{max.} = 241$ mμ, $\log_{10} \epsilon = 4.21$). Testosterone acetate (m.p., 139–140°) was prepared as a derivative.

The above condensation reaction gave testosterone with an activity of 1.45×10^4 counts/min./mmole[2] in a yield of 48 per cent based on the enol-lactone (III). This substance and compounds of a similar nature may be expected to be of importance in connection with investigations of the intermediary metabolism of the steroid hormones and the relation of these hormones to cancer.

References

1. BOLT, C. C. *Rec. trav. chim.*, 1938, **57**, 906.
2. MILLER, W. W. *Science*, 1947, **105**, 123.
3. TURNER, R. B. *J. Amer. chem. Soc.*, 1947, **69**, 726.

[1] This work was supported by funds provided by the American Cancer Society on the recommendation of the Committee on Growth, National Research Council. The testosterone used in the investigation was made available through the generosity of Erwin Schwenk, Schering Corporation, and C. R. Scholz, Ciba Pharmaceutical Products, Inc.

[2] The author is indebted to Warren W. Miller, Radioactivity Center, Massachusetts Institute of Technology, for activity measurements. For a description of the counting method see reference *2*.