

INTRODUCTION OF A  $\Delta 14$  DOUBLE BOND INTO  $5\beta$ -H STEROIDS  
BY SELECTIVE FREE-RADICAL HALOGENATION

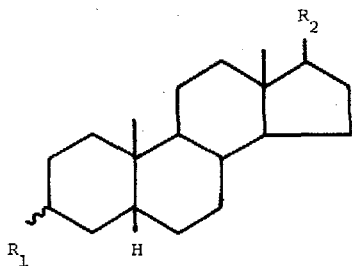
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Previous investigation has shown that the intramolecular free-radical halogenation of steroids of  $5\alpha$ -H configuration can be directed by proximity effects arising from geometric constraints introduced by the use of aryl iodine dichloride reagents attached to the  $3\alpha$ -position via an ester linkage.<sup>1</sup> Subsequently, a radical relay mechanism<sup>2</sup> was described in which the intermediate aryl iodide-chlorine  $\sigma$ -complex is formed by chlorine atom transfer from an external chlorinating radical. These methods have been used for the selective halogenation of steroids at C-9, 14,<sup>1,2</sup> and 17.<sup>3</sup>

This process, remote oxidation, has now been extended to substrates with  $5\beta$ -H configuration. Irradiation for 30 min. using a 275-W sunlamp, of a  $10^{-2}$  M solution of *m*-iodophenylacetate I together with 1 equiv. of  $\text{PhICl}_2$  in  $\text{CCl}_4$  gave, after standard base treatment, acetylation and chromatography on  $\text{AgNO}_3$ -impregnated silica gel, a 45% yield of  $\Delta 14$ - $3\alpha$ -coprostenyl acetate<sup>4</sup> ( $3\alpha$ -ol, mp 172.5-173<sup>o</sup>) as the only identifiable olefin and a 48% recovery of unreacted steroid. The result is consistent with the prediction of calculations from X-ray data which show that the  $3\alpha$ -oxygen to  $14\alpha$ -hydrogen distance in the steroid ( $5.93\text{\AA}$ <sup>5</sup>) is close to the oxygen-chlorine distance in the reagent *m*-iodophenylacetate-chlorine  $\sigma$ -complex ( $5.24\text{\AA}$ ).<sup>3</sup> The same photolysis in  $\text{CH}_2\text{Cl}_2$  failed to give chlorinated steroids, suggesting effects similar to those found in irradiations of  $3\alpha$ -coprostanyl esters of benzophenone carboxylic acids in which no intramolecular attack occurred,<sup>6</sup> possibly a result of the intervention of a solvent molecule between reagent and substrate.



	$R_1$	$R_2$
I	$3\alpha$ <i>m</i> -IPhCH <sub>2</sub> COO-	$-C_8H_{17}$
II	$3\alpha$ -OAc	$-C_8H_{17}$
III	$3\beta$ -OAc	$-C_8H_{17}$
IV	$3\beta$ -OAc	$-COCH_3$

Photolysis of a  $10^{-2}$  M solution of II and  $\text{PhICl}_2$  in benzene gave attack at C-14 and C-17 in yields of 9% and 32% respectively, but not at C-9. The AB-cis ring fusion of the steroid apparently blocks abstraction of the  $9\alpha$ -H. The possibility that the  $3\alpha$ -OAc group might also block this position was eliminated by the photolysis of III together with  $\text{PhICl}_2$  under the same conditions. Again, no  $\Delta 9(11)$  olefin formed upon dehydrohalogenation, only the  $\Delta 14^7$  and  $\Delta 16$  olefins were obtained along with starting material.

Since it was known that the presence of a 17-keto group in  $3\alpha$ -androstanylone acetate inhibits  $14\alpha$ -hydrogen abstraction,<sup>1</sup> it was predicted that IV, with a 20-keto group, should not be attacked at C-17 in an intermolecular reaction. A  $10^{-2}$  M benzene solution of IV and 1.1 equiv. of  $\text{PhICl}_2$  was irradiated for 8 min. at  $25^\circ$ . Dehydrohalogenation using silver perchlorate gave a 52% yield of  $\Delta 14$ -5 $\beta$ -pregnen-3 $\beta$ -yl-20-one acetate,<sup>8</sup> an intermediate in the synthesis of digi-toxigenin<sup>8a</sup> and bufalin.<sup>9</sup>

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