

Rearrangement in the Substitution Reaction of 3-Keto-4 $\beta$ -bromo-5 $\beta$ -steroids

By Yasuo SATOH, Masaaki MUKOH, Yuichi OGAKI, Tomoyoshi TAKAHASHI  
Takako KIMURA, Hiromitsu AOKI and Akira HAGITANI

*Department of Chemistry, St. Paul's University (Rikkyo Daigaku), Toshima-ku, Tokyo*

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The authors wish to report on a new rearrangement in the substitution reaction of 3-keto-4 $\beta$ -bromo-5 $\beta$ -steroids with potassium acetate.

4 $\beta$ -Bromo-5 $\beta$ -cholestan-3-one (8 g.) in acetic acid (280 ml.) was refluxed with potassium acetate (56 g.) in a nitrogen atmosphere for 6 hr. The reaction mixture was then evaporated under reduced pressure, and the residue was extracted with ether. The ethereal extracts were washed with an aqueous sodium bicarbonate solution and water, dried, and evaporated. Two crystallizations of the residue from ethanol gave needles (2.6 g.), m. p. 149–151°C. Found: C, 78.37; H, 10.85. Calcd. for C<sub>29</sub>H<sub>48</sub>O<sub>3</sub>: C, 78.33; H, 10.88%. IR (KBr disk): 1765 ( $\nu_{C=O}$ ), 1743 ( $\nu_{C=O}$ ) and 1224 cm<sup>-1</sup> ( $\nu_{C-O-C}$ ); ORD in dioxane ( $c$  1.00) at 18°,  $[\alpha]_{589}^{18} + 8.0^\circ$ ,  $[\alpha]_{400}^{18} + 8.0^\circ$ ,  $[\alpha]_{308}^{18} - 195.0^\circ$ ,  $[\alpha]_{285}^{18} + 205.0^\circ$ ; NMR  $\delta$ : 5.24 (one proton, quartet) (=C<sub>2</sub>H-OAc), 2.15 (three protons, singlet) (C<sub>2</sub>-OOCCH<sub>3</sub>).

By treating a mixture of methyl 4 $\beta$ -bromo-3-ketocholanoate (2 g.), potassium acetate (11 g.) and acetic acid (55 ml.) as described above, needles (1.3 g.), m. p. 168.5–170°C were obtained. Found: C, 72.68; H, 9.50. Calcd. for C<sub>27</sub>H<sub>42</sub>O<sub>5</sub>: C, 72.61; H, 9.48%. IR (KBr disk): 1750 ( $\nu_{C=O}$ ), 1722 ( $\nu_{C=O}$ ), 1227 ( $\nu_{C-O-C}$ ), 1150 cm<sup>-1</sup> ( $\nu_{C-O-C}$ ); ORD in dioxane at 19°:  $[\alpha]_{589}^{19} + 5.5^\circ$ ,  $[\alpha]_{380}^{19} + 9.0^\circ$ ,  $[\alpha]_{309}^{19} - 190.0^\circ$ ,  $[\alpha]_{285}^{19} + 230.0^\circ$ ; NMR  $\delta$ : 5.24 (one proton, quartet) (=C<sub>2</sub>H-OAc), 3.68 (three protons, singlet) (C<sub>23</sub>-COOCH<sub>3</sub>), 2.15 (three protons, singlet) (C<sub>2</sub>-OOCCH<sub>3</sub>).

Both products of this reaction are 2 $\beta$ -acetoxy-3-keto-5 $\beta$ -steroids, not 4-substituted isomers. This has been confirmed by the signs of the Cotton effect and its specific rotations in ORD, and by the patterns of the splitting and its coupling con-

stants in NMR spectra (Fig. 1).<sup>1,2)</sup>

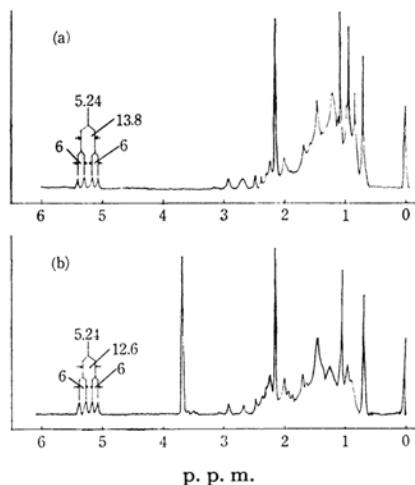


Fig. 1. Nuclear magnetic resonance spectra.

- (a) 2 $\beta$ -Acetoxy-5 $\beta$ -cholestan-3-one  
(b) Methyl 2 $\beta$ -acetoxy-3-ketocholanoate

We may conclude that the substitution reaction of 4 $\beta$ -Br in 3-keto-5 $\beta$ -steroids with potassium acetate is accompanied by the rearrangement of C<sub>4</sub> to C<sub>2</sub>.

This result is contrary to that reported by Fieser and Romero concerning the C<sub>2</sub>–C<sub>4</sub> rearrangement of 2 $\alpha$ -bromo-5 $\alpha$ -cholestan-3-one with potassium acetate.<sup>3)</sup>

Further details will be published later.

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- 3) L. F. Fieser and M. A. Romero, *ibid.*, **75**, 4716 (1953).