

# Simple Routes to Keto-norsteroids

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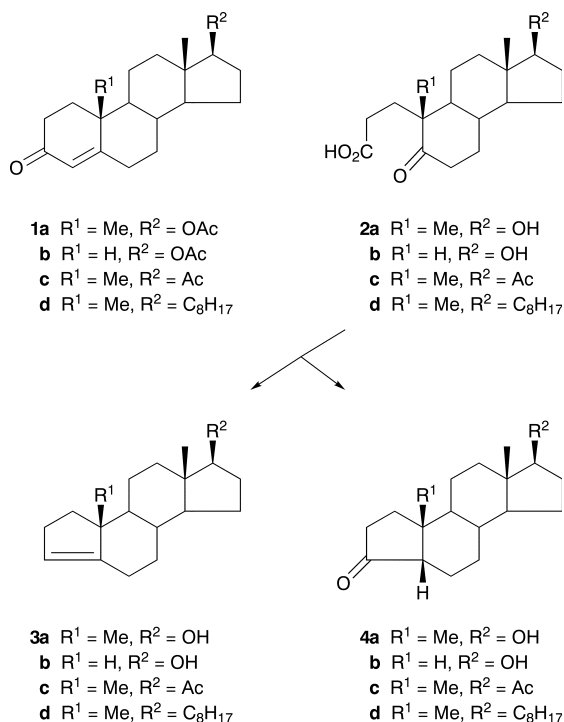
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*J. Chem. Research (S)*,  
1998, 221  
*J. Chem. Research (M)*,  
1998, 1032–1042

Ring A and B keto-norsteroids have been obtained by applying the McMurray low valency titanium cyclization to steroidal seco ring A and ring B nor-keto-esters which were readily available by cleaving the corresponding unsaturated ketones.

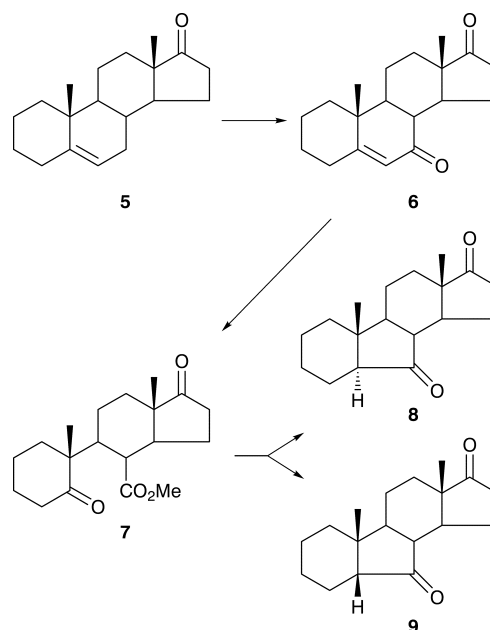
Nor-steroids often have an interesting pharmacological profile when compared to their six-membered analogues.<sup>1</sup> The established methods<sup>2</sup> for the preparation of keto-norsteroids involve a series of steps which do not always proceed in good yield. Here we describe simple alternative routes to these compounds utilizing the McMurray reaction.<sup>4</sup>

Oxidative cleavage of steroidal  $\Delta^4$ -3-ketones **1** with potassium permanganate–sodium periodate afforded the 5-oxo-3,5-seco-4-nor-3-oic acids **2** in good yield. The acids were methylated with caesium fluoride and methyl iodide.<sup>6</sup> The resultant keto-esters were then reductively cyclized with a low-valency titanium reagent derived from the titanium trichloride:dimethoxyethane complex and a zinc:copper couple.<sup>7</sup> This afforded the 5 $\beta$ -A-nor-3-ketone **4** as the major product (67%) accompanied by the 3(5)-alkene **3** as the minor product. The sequence was applied to testosterone acetate **1a**, 19-nortestosterone acetate **1b**, progesterone **1c** and cholest-4-en-3-one **1d** which were converted to their respective 5 $\beta$ -A-nor-3-ketones **4a–d** together with small amounts of the 3(5)-alkenes.



A similar sequence was applied to the preparation of a B-norsteroid. The readily available dehydroisoandrosterone (3 $\beta$ -hydroxyandrost-5-en-17-one) was converted via its 3 $\beta$ -iodo derivative into androst-5-en-17-one **5**.<sup>9</sup> The latter was oxidized with the chromium trioxide–3,5-dimethyl-

pyrazole complex<sup>10</sup> to androst-5-en-7,17-dione **6**. Cleavage of the unsaturated ketone with potassium permanganate–sodium periodate and methylation with caesium fluoride–methyl iodide gave methyl 5,17-dioxo-5,7-seco-6-nor-androstan-7-oate **7**. This keto-ester was reductively cyclized with low valency titanium to the B-norketone. The major product (47%) was the B-nor-5 $\alpha$ -androstan-6,17-dione **8** accompanied by the *cis* isomer **9** (15%).



C.U. wishes to thank Kocaeli University, Izmit, Turkey, for study leave and financial assistance.

Techniques used: IR, <sup>1</sup>H NMR, chromatography

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Received, 25th November 1997; Accepted, 30th December 1997  
 Paper E/7/08520F

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