

Tetrahedron Letters 39 (1998) 9759-9760

TETRAHEDRON LETTERS

## A Novel Fragmentation-Cyclization Reaction of Steroidal α-Hydroxy Oximes

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Received 9 July 1998; accepted 12 October 1998

Abstract: By a novel "one pot" fragmentation-cyclization reaction  $17\beta$ -hydroxy- $17\alpha$ -substituted-16-oximino derivatives in the androstane and estrane series were converted to a new type of D-homo derivative. © 1998 Elsevier Science Ltd. All rights reserved.

In our previous work<sup>1</sup> lactone **8** was prepared directly from the corresponding  $17\beta$ -hydroxy-16-oximino derivative **3** and potassium hydroxide in boiling ethylene glycol (Scheme 1).

In the present work, examining the chemical behaviour of  $17\beta$ -hydroxy- $17\alpha$ -substituted-16-oximino derivatives 4-7 and potassium hydroxide in boiling ethylene glycol, we unexpectedly discovered a novel "one pot" fragmentation-cyclization reaction. Instead of the formation of the corresponding lactones, a new type of D-homo derivative 9-12 possessing 16-amino functionality were obtained. Starting  $\alpha$ -hydroxy oximes 4-7 were prepared by stereospecific addition of  $\alpha$ -picolyllithium and benzyllithium to the C-17 carbonyl group of 1 and 2 (Scheme 1)<sup>2</sup>.



The X-ray structural analysis of 12 unambiguously proved the structure of these new D-homo steroids (Fig. 1). Detailed X-ray structural analysis of 12 will be published separately.

Figure 1 A perspective view of the molecular structure of compound 12

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Scheme 1 *a*) α-PyCH<sub>2</sub>Li, ether, THF, -10°C; *b*) BnLi, THF, -10°C; *c*) NaBH<sub>4</sub>, H<sub>2</sub>O-MeOH, KOH; *d*) KOH (3-15 mol equiv.), HOCH<sub>2</sub>CH<sub>2</sub>OH, 160°C, H<sub>2</sub>O.

We suppose that the relative thermodynamic instability of initial compounds (4-7), having  $17\alpha$ -bulky substituents ( $\mathbb{R}^3 \neq H$ ), and the relatively high reaction temperature lead to the formation of the intermediate seco-cyano ketones (4a-7a) which, underwent intramolecular addol cyclization through the intermediates **b** and **c**, and finally afforded the D-homo derivatives (Scheme 2).



References:

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