

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

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Abstract: By a novel "one pot" fragmentation-cyclization reaction 17 β -hydroxy-17 α -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 work¹ lactone **8** was prepared directly from the corresponding 17 β -hydroxy-16-oximino derivative **3** and potassium hydroxide in boiling ethylene glycol (Scheme 1).

In the present work, examining the chemical behaviour of 17 β -hydroxy-17 α -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 α -hydroxy oximes **4-7** were prepared by stereospecific addition of α -picolyllithium and benzylolithium to the C-17 carbonyl group of **1** and **2** (Scheme 1)².

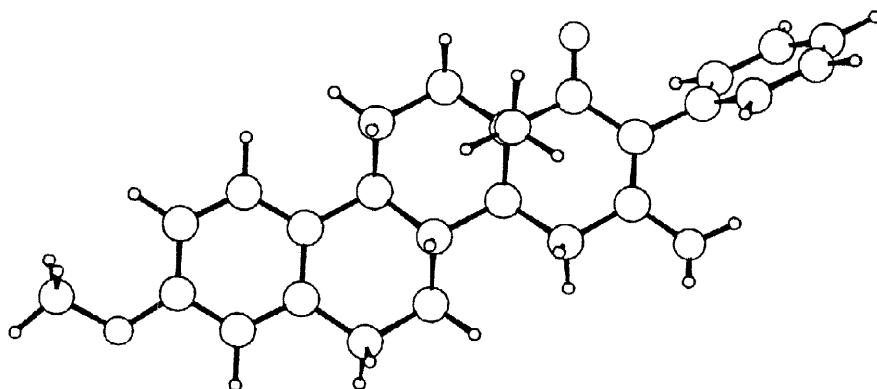
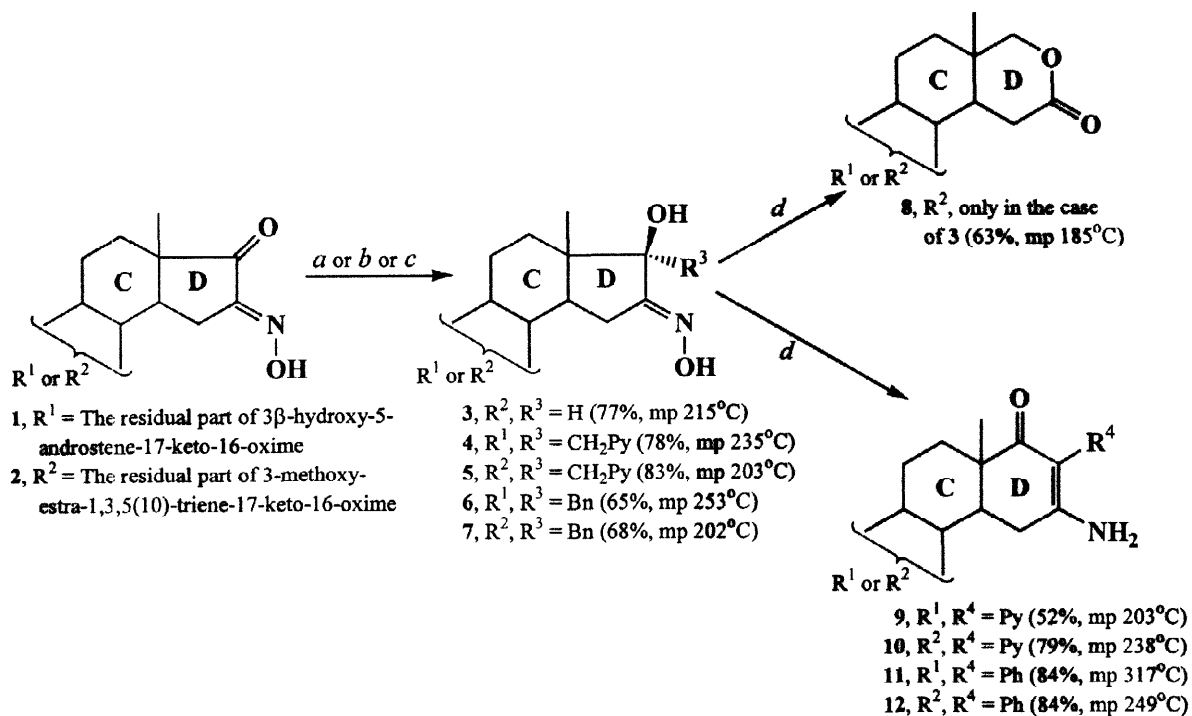


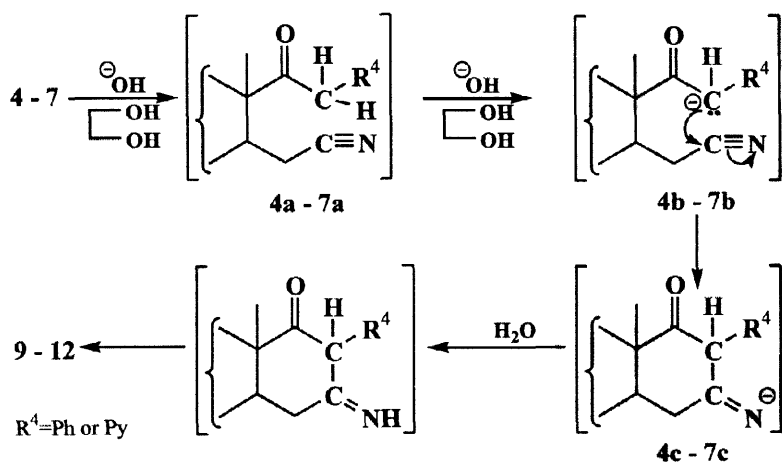
Figure 1 A perspective view of the molecular structure of compound **12**

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.



Scheme 1 a) α -PyCH₂Li, ether, THF, -10°C; b) BnLi, THF, -10°C; c) NaBH₄, H₂O-MeOH, KOH; d) KOH (3-15 mol equiv.), HOCH₂CH₂OH, 160°C, H₂O.

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



Scheme 2

References:

- Miljković, D.; Petrović, J. *J. Org. Chem.* **1977**, *42*, 2101-2102.
- Miljković, D.; Penov-Gaši, K.; Đurendić, E.; Sakač, M.; Medić-Mijačević, Lj.; Pejanović, V.; Stanković, S.; Lazar, D. *Tetrahedron Lett.* **1997**, *38*, 4683-4684.