Available online at www.sciencedirect.com

ScienceDirect

Mendeleev Commun., 1994, **4(5)**, 187–188

Mendeleev Communications

A New One-pot Synthesis of 17-Oxo-13α-steroids of the Androstane Series from their 13β-Analogues

Feodor G. Yaremenko*[a] and Alexandr V. Khvat[b]

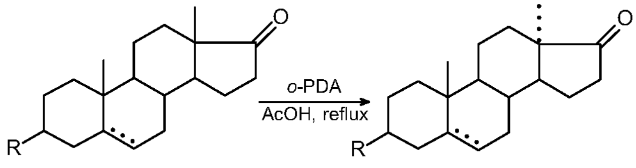
[a] Ukrainian Scientific Research Institute of Endocrinological Diseases Pharmacotherapy, 310002 Khar'kov, Ukraine.
Fax: +7 057 247 5121
[b] Department of Chemistry, Khar'kov State University, 310077 Khar'kov, Ukraine.

A conversion of 17-oxosteroids of the androstane series into the corresponding 13α-steroids by refluxing in acetic acid containing 1,2-phenylenediamine has been developed.

13α,14α-Steroids of the androstane series attract attention as antiprogesterone agents,[1,2] but at the same time they remain rather obscure subjects for investigation.

Previously developed synthetic methods of 13α-steroid production involved partial or complete steroid synthesis,[3–5] irradiation of 17-ketones[6–8,16] and isomerisation of 17-ketosteroid acyloximes of the 13β-series by heating in a mixture of acetic acid and pyridine[9,10] or reduction by zinc in acetic acid medium.[11] In some cases, the reactions were complicated by comparatively low yields, a complex procedure for reaction product separation (especially 13α- and 13β-epimers) as well as possible side-reactions including Beckmann rearrangement and D-ring cleavage.[12,13]

We have developed a one-pot synthesis of 13α-epimers of



1a–d **2a–d**

a R = H,5α
b R = AcO,5α
c R = AcO,Δ^5
d R = OH,Δ^5

Scheme 1

17-oxosteroids[†] which involves heating under reflux equimolar amounts of a 17-oxo-13β-steroid and *o*-phenylenediamine (*o*-PDA) in acetic acid for 3–4 h to give a good yield (~ 50%) of the 13α-derivatives in high purity. The nature of the reaction was indicative of an ion–radical mechanism of interaction. This was verified by the development and disappearance of the blue colour in the course of the reaction and the appearance of two absorption bands in the visible UV spectral region of the reaction mixture (*ca.* 580 and 625 nm), similar to Wurster's colours in their absorption nature (560 and 606 nm for Wurster's Blue). The existence of organic paramagnetic particles was recorded by EPR but the structure of the ion–radical observed was not determined because of poor spectral resolution. The same mechanism of ion–radical formation in the course of C_{13}–C_{17} bond cleavage and subsequent cyclization in the more stable 13α-isomer has been discussed by Barton *et al.*[9]

We thank Professor V. V. Minin for help with EPR spectroscopic measurements.

References

1 C. P. Puri, R. K. Patil, W. A. G. Elger, A. D. Vadigoppula and M. Rp. Jagen, *Contraception*, 1989, **39**, 227.
2 Fang Li, Fang Xu, Qingjiang Liao and Weicheng Wang, *Zhongguo Yaoke Daxue Xuebao*, 1992, **23(6)**, 329 (*Chem. Abstr.*, 1993, **119**, 49722b).
3 J. R. Billeter and K. Miescher, *Helv. Chim. Acta*, 1951, **34**, 2053.
4 W. S. Johnson and L. J. Chinn, *J. Am. Chem. Soc.*, 1951, **73**, 4987; W. S. Johnson, B. Bannister, R. Pappo and J. E. Pike, *J. Am. Chem. Soc.*, 1969, **78**, 6354.
5 I. I. Eliseev, E. A. Zhukovskii and A. G. Shavva, *Vest. St.-Peterb. Univ., Ser. 4: Fiz. Khim.*, 1992, 67 (in Russian).
6 D. N. Kirk and M. Hartshorn, *Steroid Reaction Mechanisms*, Elsevier, Amsterdam, 1968, p. 420.
7 M. Fetizon and J.-L. Gramain, *Bull. Soc. Chim. Fr.*, 1967, 1003.
8 G. Neef, A. Seeger and H. Vierhufe, *Synth. Commun.*, 1993, **24**, 931.
9 R. B. Boar, F. K. Jetuah, J. F. McGhie, M. S. Robinson and D. H. R. Barton, *J. Chem. Soc., Perkin Trans. 1*, 1977, 2163.
10 Y. Ohue and K. Orito, *J. Chem. Soc., Perkin Trans. 1*, 1987, 1247.
11 J. Boivin, A. M. Schiano and S. Z. Zard, *Tetrahedron Lett.*, 1992, 7849.
12 S. Hiroshi and U. Tsutomu, *Bull. Soc. Chem. Jpn.*, 1974, **47**, 687; S. Hiroshi and U. Tsutomu, *Tetrahedron Lett.*, 1973, 2289.
13 G. Quinkert, A. Moschel and G. Buhr, *Chem. Ber.*, 1965, **98**, 2742.
14 J.-C. Gramain and J.-C. Qurion, *Magn. Reson. Chem.*, 1986, **24**, 938.
15 E. Colinaud, J.-L. Gramain and J.-C. Qurion, *J. Chem. Soc., Perkin Trans. 2*, 1987, 921.
16 J. P. L. Bots, *Recl. Trav. Chim. Pays-Bas*, 1958, **77**, 1010.

Received: Moscow, 25th April 1994
Cambridge, 14th June 1994; Com. 4/02909G

[†] *Experimental.* 5α,13α-*Androstan*-17-*one* **2a**. 5α-Androstan-17-one (2.00 g, 0.0073 mol) was dissolved in acetic acid (20 ml), then *o*-PDA (0.80 g, 0.0074 mol) was added and the mixture was heated under reflux for 4 h. The mixture was diluted with water and extracted with $CHCl_3$, then separated on silica gel (50 g) with $CHCl_3$ as eluent to give 1.15 g of 5α,13α-androstan-17-one **2a** and 0.76 g of 5α,13β-androstan-17-one **1a**. The yield of compound **2a** was 57.5%, m.p.123–124 °C (MeOH) (lit.,[7] 120–122 °C). IR, ν/cm^{-1} (KBr): 1730 (C=O); ^{1}H NMR, ($CHCl_3$, δ, ppm): 0.57 (s, 3H, 19-Me), 0.91 (s, 3H, 18-Me); ^{13}C NMR ($CHCl_3$, δ, ppm): 11.84 (19-Me), 25.28 (18-Me), 221.94 (C=O).

Under such (or similar) conditions the following have also been obtained: 3β-hydroxy-5α,13α-androstan-17-one acetate **2b**, yield 56%, m.p. 129–130 °C (lit.,[7] 133–135 °C), 3β-hydroxy-13α-androst-5-en-17-one acetate **2c**, yield 35%, m.p. 143–144 °C (lit.,[16] 143–144 °C), 3β-hydroxy-13α-androst-5-en-17-one **2d**, yield 58%, m.p. 189.5–190.5 °C (lit.,[16] 187–189 °C). The spectral characteristics of compounds **2a–d** are in agreement with the literature data.[14,15]