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SYNTHESIS AND PRELIMINARY ODOUR EVALUATION OF THE 14β-EPIMER OF THE BOAR TAINT STEROID[1]

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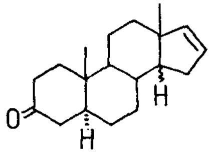
5α,14β-Androst-16-en-3-one (14-*epi*-androstenone) has been prepared from 3β-hydroxy-5α,14β-androstan-17-one by the vinyl iodide route in an overall yield of 35%. Its odour is similar to, but significantly less intense than, that of the naturally occurring 14α-epimer.

Androstenone (1) has an intense musky and urinous odour.[2] It is present in the saliva of male pigs and accumulates in their fatty tissues,[3] producing the off-flavour of the cooked meat known as "boar taint". The molecular parameters required for the release of a steroid-type scent have recently been discussed by Ohloff.[4] Only steroids with normal ring junctions and configuration were found to be odourants, whereas those having *cis*-junctions between rings A and B, or rings C and D, were almost inactive. For C_{19}-steroid odourants of the natural series the perception threshold is very low (<6 p.p.b.), whereas the unnatural enantiomers are odourless.[4] Since inversion of configuration at C-14 of androstenone would be expected to produce a significant change in the conformation of the molecule without greatly affecting its volatility, we have synthesized 14β-androstenone (2) in order to evaluate its sensory properties.

5α,14β-Androst-16-en-3-one (2) was prepared from 14β-androsterone (3) in four steps using the general reaction sequence devised by Barton[5] for the conversion of ketones to alkenes *via* the corresponding hydrazones and vinyl iodides. Application of the method to 17-oxo-androstanes provided a convenient route to androst-16-enes,[5] and yields in the conversion of the intermediate hydrazones to the vinyl iodides have recently been optimized.[6]

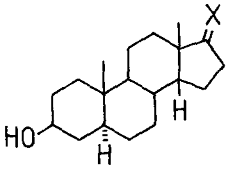
Reaction of 14β-androsterone (3)[7] with hydrazine hydrate in refluxing ethanol in the presence of triethylamine gave the hydrazone (4) in 89% yield.[8] The hydrazone (4) reacted vigorously with iodine in tetrahydrofuran solution to give the vinyl iodide (5) in 76% yield; m.p. 188-190°, ∂_H(CDCℓ_3) 0.82 (s, 19-Me), 1.07 (s, 18-Me), 6.04 (m, 16-H). Reduction of the vinyl iodide (5) with sodium in boiling ethanol gave 5α,14β-androst-16-en-3β-ol (6) in 70% yield; m.p. 135-137°, ∂_H(CDCℓ_3) 0.82 (s, 19-Me), 1.11 (s, 18-Me), 5.55-5.71 (m, 16- and 17-H). Finally, oxidation of the alcohol (6) using chromium trioxide-sulphuric acid in acetone solution[9] gave 14-*epi*-androstenone (2) in 75% yield; m.p. 101.5-103°, ∂_H(CDCℓ_3) 1.03 (s, 19-Me), 1.14 (s, 18-Me), 5.56-5.72 (m, 16- and 17-H). A mixture of the epimers (1) and (2) could not be separated by gas-liquid chromatography using a packed column,[10] but good resolution was achieved on a capillary column.[11]

The odour of the 14β-epimer (2) was reminiscent of that of 14α-androstenone (1) from preliminary tests, although much less intense. The threshold level of natural androstenone (1) was found to be at least two orders of magnitude lower than that of 14β-androstenone (2) in suitable subjects. Thus the presence of a C/D-*cis* ring fusion does not entirely eliminate the steroid odour, in contrast to the results of introducing the A/B-*cis* ring junction.[12]



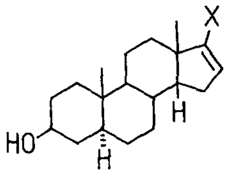
(1) 14α-H

(2) 14β-H



(3) X= O

(4) X= N-NH$_2$



(5) X = I

(6) X = H

References and notes

[1] Steroids. Part 40. For Part 39, see A.B. Turner, R.A. Howie and P.J. Cox, *J. Chem. Soc., Perkin Trans. 1*, 1983, 985

[2] V. Prelog, L. Ruzicka and P. Wieland, *Helv. Chim. Acta*, 1944, *27*, 66

[3] R.L.S. Patterson, *J. Sci. Food Agric.*, 1968, *19*, 31

[4] G. Ohloff, B. Maurer, B. Winter and W. Giersch, *Helv. Chim. Acta*, 1983, *66*, 192

[5] D.H.R. Barton, R.E. O'Brien and S. Sternhell, *J. Chem. Soc.*, 1962, 470

[6] D.H.R. Barton, G. Bashiardes and J.-L. Fourrey, *Tet. Letters*, 1983, 1605

[7] A.F. St. André, H.B. MacPhillary, J.A. Nelson, A.C. Shabica and C.R. Scholz, *J. Amer. Chem. Soc.*, 1952, *74*, 5506.

[8] Satisfactory analytical and spectroscopic data have been obtained for all new compounds.

[9] A. Bowers, T.G. Halsall, E.R.H. Jones and A.J. Lemin, *J. Chem. Soc.*, 1953, 2548

[10] 2 m 3% OV-1 at 250°: (R_T 14α : 380 sec; 14β : 370 sec)

[11] 25 m CP-SIL 5 at 250°: (R_T 14α : 577 sec; 14β : 566 sec). We thank Dr. J. Redpath, Organon Laboratories, for this determination.

[12] V. Prelog, L. Ruzicka, P. Meister and P. Wieland, *Helv. Chim. Acta*, 1945, *28*, 618

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