

AUTOXIDATION OF ANDROSTENONES

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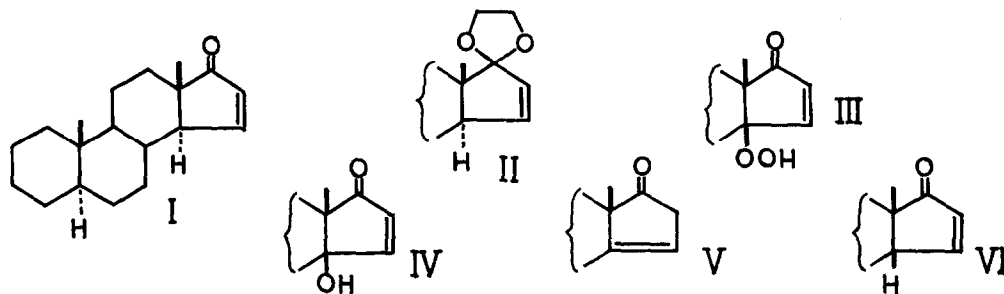
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(Received in UK 26 October 1968; accepted for publication 6 January 1969)

Recently we had occasion to prepare 5 α -androst-15-en-17-one (I) by hydrolysis of the 17-ethylene ketal (II)¹ with p-toluenesulphonic acid in aqueous acetone at 25° (5 hr.). Concentration in vacuo followed by extraction with ether and crystallisation from hexane gave the androstenone (I)¹ (50%). The hexane mother liquor on standing for three days deposited material (20%) which failed to redissolve in hexane but crystallised from methanol to give 14 β -hydroperoxy-5 α -androst-15-en-17-one (III) as plates, m.p. 183-186° (d.), $[\alpha]_D + 62^\circ$ (c, 0.69, MeOH), λ_{max} 216 m μ (ϵ 6,700); ν_{max} 3220 (-O.OH), 1691 (C=C-C=O) and 1582 cm.⁻¹ (C=C). The n.m.r. spectrum in D.M.S.O. showed a singlet (1H) at τ -0.68 (-O-OH),² 2.58 (d, 1H; J = 6.5 Hz -C-16H), 3.67 (d, 1H; J = 6.5 Hz. -C-15H) (Found: M⁺304.2037. C₁₉H₂₈O₃ requires M⁺304.2038).

When the hydroperoxide (III) is treated with potassium iodide in acetic acid and left aside for 1 hr. it is converted quantitatively to 14 β -hydroxy-5 α -androst-15-en-17-one (IV), (from methanol), m.p. 190-191°, $[\alpha]_D + 149^\circ$ (c, 0.7, CHCl₃), λ_{max} 213 m μ (ϵ 4,400); ν_{max} (KBr) 3445 (OH), 1700 cm.⁻¹ (cyclopentenone). The n.m.r. peak at τ -0.68 was absent. (Found: M⁺288.2092. C₁₉H₂₈O₂ requires M⁺288.2089). The assignment of the 14 β -configuration to the hydroxyl group in compound (IV) was in keeping with its optical rotatory dispersion which showed a positive Cotton effect curve characteristic of 14 β -substituted androst-15-en-17-ones.³

When the Δ^{15} -androstenone (I) was heated under reflux in benzene (15 min.) with p-toluenesulphonic acid in a nitrogen atmosphere and the product chromatographed on neutral alumina, light petroleum (40-60°) eluted



5 α -androst-14-en-17-one (V), (from hexane), m.p. 56-57°, $[\alpha]_D + 142^\circ$ ($d, 1.3$); $\lambda_{\text{max.}}^{\text{Hexane}}$ 214 m μ (ϵ 1,600); $\nu_{\text{max.}}$ (KBr) 1738 (non-conjugated cyclopentenone) and 1640 cm.^{-1} (C=C). N.m.r. absorptions (CDCl_3) at τ 4.47 (m, 1H; C-15H coupled to C-16 methylene), 7.08 (m, 2H; C-16 methylene). (Found: $M^+ 272.2140$. $\text{C}_{19}\text{H}_{28}\text{O}$ requires $M^+ 272.2140$). Continued elution with light petroleum (60-80°) afforded 5 α ,14 β -androst-15-en-17-one (VI), m.p. 64-65°, $[\alpha]_D + 253^\circ$ ($d, 0.81$); $\lambda_{\text{max.}}^{\text{Hexane}}$ 226 m μ (ϵ 6,400); $\nu_{\text{max.}}$ (KBr) 1698 (cyclopentenone) and 1586 cm.^{-1} (C=C). (Found: $M^+ 272.2143$. $\text{C}_{19}\text{H}_{28}\text{O}$ requires $M^+ 272.2140$).

Intermediate eluates obtained in the chromatographic separation of the ketones (V and VI) - and which contained only these ketones as shown by t.l.c. - were allowed to stand in air for 14 days. Titration of a portion of the residue with standard thiosulphate indicated that 90% conversion to hydroperoxide had occurred while recrystallisation of the residue from methanol afforded only the hydroperoxide (III) thereby illustrating the ready susceptibility of ring D unsaturated androsten-17-ones to autoxidation.

All new compounds described gave satisfactory elemental analysis.

References

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