NOTES

A NOVEL ISOMERIZATION OF STEROIDAL $\Delta^{4,9(10)}$-3-KETONES.

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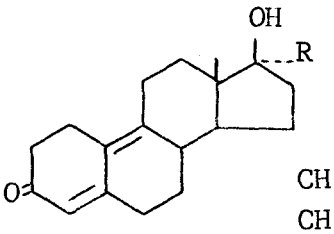
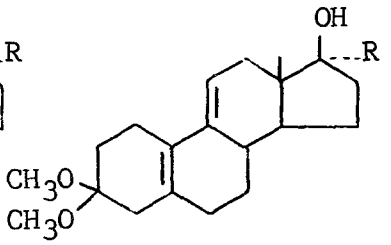
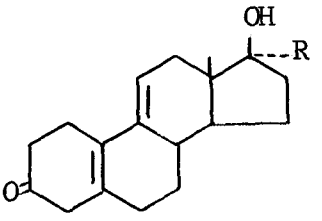
In an attempt to prepare the enol ether of 17β-hydroxy-19-norandrosta-4,9(10)-dien-3-one (Ia),[1] we found that treatment of this compound with hydrogen chloride in methanol at room temperature gave a product IIa, isolated as a gum by chromatography, which showed no carbonyl absorption and very weak bands at 1639 and 1612 $cm.^{-1}$ in the infrared. Hydrolysis of this product using dilute sulfuric acid (8%) in acetone gave an isomer of compound Ia, 17β-hydroxy-19-norandrosta-5(10),9(11)-dien-3-one (IIIa),[2,3] m.p. 111-118° with effervescence (Calcd. for $C_{18}H_{24}O_2$: C, 79.37; H, 8.88. Found: C, 78.81; H, 9.04. $[\alpha]_D^{25}$ + 164° (chloroform), $\lambda_{max.}^{MeOH}$ 240 mμ (ε 17,900), $\nu_{max.}^{KBr}$ 3333 and 1727 $cm.^{-1}$). Further evidence for this structure was found in the proton magnetic resonance spectrum which showed one olefinic hydrogen with a

signal at 5.74 p.p.m. The intermediate IIa was assigned the probable structure of 3,3-dimethoxy-19-norandrosta-5(10),9(11)-dien-17β-ol. The mechanism for its formation is probably similar to that proposed[4,5] for the formation of Δ^5-3-ethyleneketals. Thus the addition of methanol to the 3,4-double bond of the first-formed 3,5(10),9(11)-trienol ether would give compound IIa. Compound IIIa was converted back to the parent compound Ia upon treatment with dilute sulfuric acid (8%) in methanol under reflux.







Ia, R = H IIa, R = H IIIa, R = H

b, R = CH_3 b, R = CH_3 b, R = CH_3

c, R = C≡CH c, R = C≡CH c, R = C≡CH

Similar two-stage treatment of 17β-hydroxy-17α-methyl-19-norandrosta-4,9(10)-dien-3-one (Ib)[1] and of 17α-ethynyl-17β-hydroxy-19-norandrosta-4,9(10)-dien-3-one (Ic)[1] gave 17β-hydroxy-17α-

methyl-19-norandrosta-5(10),9(11)-dien-3-one (IIIb), m.p. 128-130° (Calcd. for $C_{19}H_{26}O_2$: C, 79.68; H, 9.15. Found: C, 79.81; H, 9.51. $[\alpha]_D^{25}$ + 127° (chloroform), $\lambda_{max.}^{MeOH}$ 240 mμ (ε 19,800), $\nu_{max.}^{KBr}$ 3436 and 1698 cm.$^{-1}$), and 17α-ethynyl-17β-hydroxy-19-norandrosta-5(10),9(11)-dien-3-one (IIIc),[2] m.p. 152-154° (Calcd. for $C_{20}H_{24}O_2$: C, 81.04; H, 8.16. Found: C, 81.04; H, 8.48. $[\alpha]_D^{25}$ + 145° (chloroform), $\lambda_{max.}^{MeOH}$ 240 mμ (ε 19,300), $\nu_{max.}^{CHCl_3}$ 3571, 3279, and 1701 cm.$^{-1}$) respectively. The intermediates IIb and IIc were isolated as gums by chromatography. Overall yields were 40-50%.

Compounds IIIa, b, and c gave a positive blue tetrazolium test as did the related $\Delta^{5(10)}$-3-ketones, a Δ^5-3-ketone and a Δ^{14}-17-ketone. Thus it appears that, unlike the α β-unsaturated ketones, steroidal β γ-unsaturated ketones give a positive test.

Further work on these $\Delta^{5(10),9(11)}$-steroids is in progress.

REFERENCES

1. M. Perelman, E. Farkas, E. J. Fornefeld, R. J. Kraay, and R. T. Rapala, J. Am. Chem. Soc., 82, 2402 (1960).

2. Recently, G. Nomine and R. Bucourt, U. S. Pat. 3,033,856/1962 and G. Nomine, R. Bucourt, and M. Vignau, U. S. Pat. 3,052,672/1962 described the conversion of 17β-benzoyloxy-19-norandrosta-4,9(10)-dien-3-one and of compound Ic into the corresponding $\Delta^{5(10),9(11)}$-3-ketones by the formation of the respective intermediate 3-pyrrolidyl-3,5(10),9(11)-trienes followed by acid hydrolysis.

3. These $\Delta^{5(10),9(11)}$-3-ketones were unstable and became yellow on standing overnight at room temperature.

4. C. Djerassi and M. Gorman, J. Am. Chem. Soc., 75, 3704 (1953).

5. J. J. Brown, R. H. Lenhard, and S. Bernstein, Experientia, 18, 309 (1962).