

SELECTIVE BORANE REDUCTIONS OF PROGESTERONE

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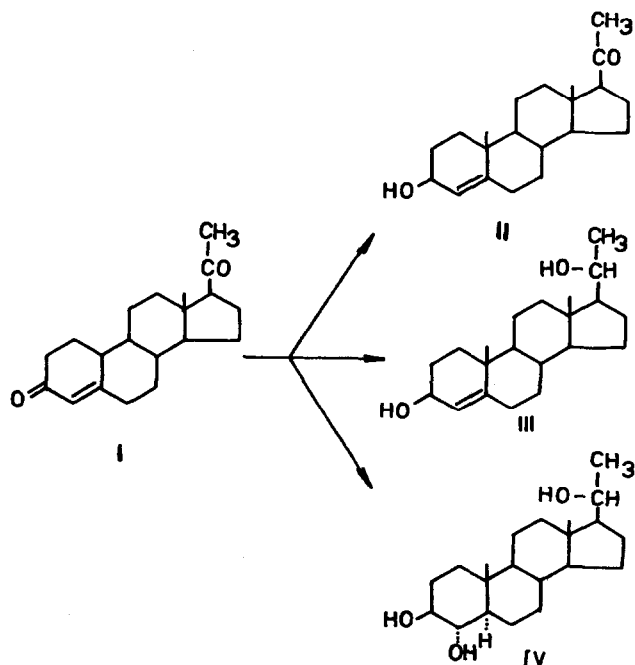
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A number of selective reductions using borane and metal borohydrides has been described (1,2). In our studies of hydroboration of steroid conjugated ketones under different conditions and with different solvents we have found that borane reduces in a good yield the carbonyl group in C-3 of progesterone (I), without affecting the carbonyl in C-20, as well as the Δ^4 double bond, thus giving as the main product, 3 β -hydroxy-20-keto- Δ^4 -pregnene (II), which was obtained in a pure state by direct crystallization of the reaction product from methanol.

3,20-Diketo- Δ^4 -pregnene (progesterone) (I), m.p. 130-131 $^\circ$, dissolved in diglyme was treated at the room temperature for one hour by a stream of borane obtained through the reaction of boron trifluoride etherate with sodium borohydride in the above solvent; after the usual alkali-peroxide treatment 3 β -hydroxy-20-keto- Δ^4 -pregnene (3) (II), was obtained in a yield of about 70%, m.p. 159 $^\circ$ (Koflerblock); $[\alpha]_D^{20} = +138^\circ$ (c=0,8

in CHCl_3); UV - no absorption for conjugated ketone; IR-Spectrum: ν_{max} 1690, 1660 cm^{-1} . Acetylation of II with $\text{Ac}_2\text{O}/\text{Py}$ gave the corresponding acetate, m.p. 125°; $[\alpha]_{\text{D}}^{20} = +114^\circ$ (c=0,8 in CHCl_3).

Beside the main product (II), from the reaction mixture we isolated and identified 3 β , 20 α -dihydroxy- Δ^4 -pregnene (4), (III), m.p. 182°; $[\alpha]_{\text{D}}^{20} = +43^\circ$ (c=1,0 in CHCl_3); IR-Spectrum: $\nu_{\text{max}} = 3330, 1660 \text{ cm}^{-1}$; (no absorption in UV); acetate, m.p. 152°; $[\alpha]_{\text{D}}^{20} = +46^\circ$ (c=1,15 in CHCl_3), and 3 α , 4 α , 20 β -trihydroxy-(5)pregnane (IV), m.p. 240°, $[\alpha]_{\text{D}}^{20} = \pm 0^\circ$ (c=0,79 in



CH₂OH); IR-Spectrum : $\nu_{\max} = 3330 \text{ cm}^{-1}$ (no UV absorption) and acetate, m.p. 178-180°; $[\alpha]_{\text{D}}^{20} = +24,5$ (c=1,0 in CHCl₃) were obtained in yields of 15% and 7%, respectively.

Our results are consistent with the mechanism of electrophylic borane reductions in which the centers of higher electron densities are attacked first. However, the hydride ion reductions gave, with the same substrate—progesterone—after column chromatography, only 25% of the product II (3).

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* Satisfactory analytical data were obtained for all compounds.