The Stereochemistry of the Hydroboration of 2- and 3-Methylene-5α-androstanes

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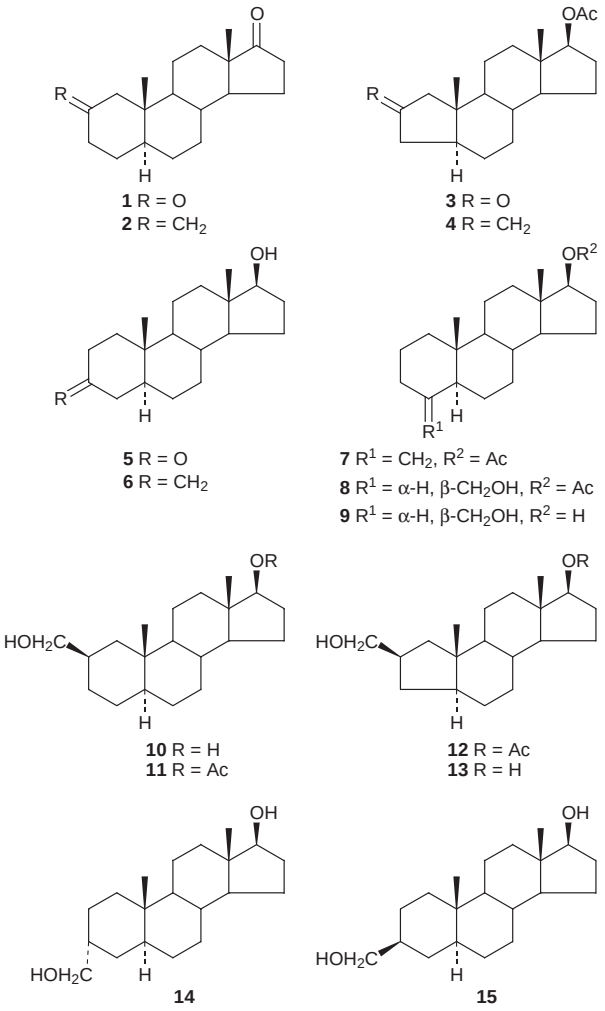
The *exo* facial selectivity in the hydroboration of 2-, 3- and 4-methylene-5α-androstanes is rationalized in terms of the easier steric access and a hyperconjugative interaction of the alkene with the adjacent axial C–H bonds enhancing the electron density on one face of the alkene.

Theoretical considerations have suggested that there are two stages to the hydroboration of an alkene.[1,2] The first stage involves the formation of a π-complex between the alkene and the boron hydride. The second step involves the collapse of this *via* a four-membered cyclic transition state to give the alkylborane. Under kinetic conditions the facial selectivity in the hydroboration of an alkene will be determined by the relative ease of formation of this π-complex on each face. Steric access and the facial anisotropy of the relevant HOMO will be two contributory features in determining this. The origin of the facial selectivity in the electrophilic attack on methylene cyclohexanes has been attributed[3,4] to hyperconjugative contributions made to the HOMO by the adjacent periplanar C–H σ-bonds. Hydroboration of an exocyclic methylene may take place from either the *exo* or the *endo* face of the alkene to generate, after oxidation of the borane, an axial or an equatorial hydroxymethyl group. Kinetic considerations including reagent access and the hyperconjugative interaction of an adjacent axial C–H bond would, for a chair ring system, favour the formation of an axial hydroxymethyl group. However thermodynamic considerations based on the stability of the borane, would favour the formation of an equatorial substituent.

We have examined the stereochemistry of hydroboration of 2-methylene-5α-androstan-17-one **2**, 17β-acetoxy-2-methylene-A-nor-5α-androstane **4**, and 3-methylene-5α-androstan-17β-ol **6** in order to assess the relative contribution of steric and electronic factors in the steroids. The substrates were prepared by a Wittig reaction on the corresponding ketones **1**, **3**, and **5**.[11] The results of the hydroboration experiments are given in Table 1.

These results may be rationalized as follows. The hyperconjugative contribution to the HOMO of the alkene by the adjacent axial C–H σ bonds would lead to a facial anisotropy that would favour the formation of the initial π-complex on the α-face in the case of the C–2 alkene, the β-face of the C–3 alkene, and the α-face of a C–4 alkene (Fig. 1). This coupled with the easier access from the *exo* face, would lead to the stereochemistry of the observed major



1 R = O
2 R = CH_2
3 R = O
4 R = CH_2
5 R = O
6 R = CH_2
7 R^1 = CH_2, R^2 = Ac
8 R^1 = α-H, β-CH_2OH, R^2 = Ac
9 R^1 = α-H, β-CH_2OH, R^2 = H
10 R = H
11 R = Ac
12 R = Ac
13 R = H
14
15

Table 1 The hyroboration of methylene-5α-androstanes

Substrate	Product(s)	Yield(%)
2-Methylene-5α-androstane **2**	17β-Hydroxy-2β-hydroxymethyl-5α-androstane **10**	64
17β-Acetoxy-2-methylene-A-nor-5α-androstane **4**	17β-Acetoxy-2β-hydroxymethyl-A-nor-5α-androstane **12**	46
	17β-Hydroxy-2β-hydroxymethyl-A-nor-5α-androstane **13**	39
17β-Hydroxy-3-methylene-5α-androstane **6**	17β-Hydroxy-3α-hydroxymethyl-5α-androstane **14**	66
	17β-Hydroxy-3β-hydroxymethyl-5α-androstane **15**	23
17-Acetoxy-4-methylene-5α-androstane **7**[10]	17β-Acetoxy-4β-hydroxymethyl-5α-androstane **8**	14
	17β-Hydroxy-4β-hydroxymethyl-5α-androstane **9**	48

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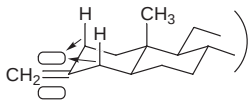

Fig. 1

products. In the case of the 2-methylene, the steric factors arising from the interactions of the intermediate borane with the angular methyl group are not sufficiently great to preclude reaction.

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Techniques used: IR, ^{1}H NMR, chromatography.

References: 13

Figures: 1

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