

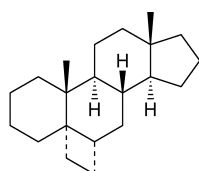
Factors Affecting Facial Selectivity in the Hydroboration of Steroidal Δ^5 -Alkenes

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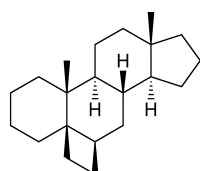
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A comparison between the α - and β -facial selectivity observed in the hydroboration of some androst-5-enes and B-norandrost-5-enes does not parallel the difference between the calculated force field energies for α - and β -cyclobutane models suggesting that the facial selectivity is not determined by the four-centre transition state but by the relative ease of formation of the initial π -complex between the alkene and the borane.

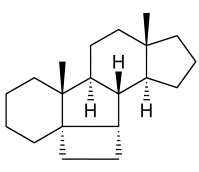
The initial stage in the hydroboration of an alkene involves the formation of a π -complex between the alkene and the borane which rearranges in the second stage to the four-centre transition state that leads to the intermediate borane.¹ Oxidation of the borane with alkaline hydrogen peroxide then affords the alcohol. Calculations on the first two stages^{2–4} have shown that the formation of the four-membered transition state is the rate determining step for the hydroboration. A cyclobutane ring may afford an approximate model for the four-centre transition state.⁶ Differences between the calculated force field energies of the α - and β -oriented four-membered ring adducts derived from androst-5-ene, **1** and **2**, on the one hand, and B-norandrost-5-ene, **3** and **4**, on the other, suggest that the α -oriented four-membered transition state for hydroboration is more stable for the 6:6 fused A/B ring system whilst the β -oriented system is more stable for the 6:5 fused A/B ring system paralleling the known order of stability of *cis* and *trans* fused 6:6 and 6:5 ring systems.⁸



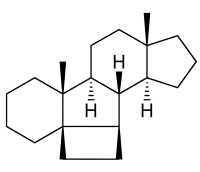
1 625 kJ mol⁻¹



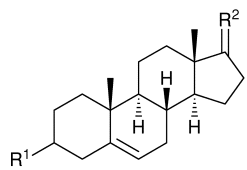
2 641 kJ mol⁻¹



3 652 kJ mol⁻¹



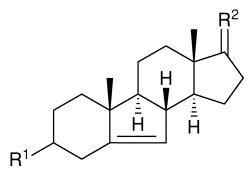
4 607 kJ mol⁻¹



5 R¹ = β -OAc, R² = H₂

6 R¹ = H, R² = O

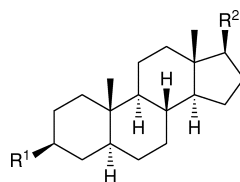
7 R¹ = α -OH, R² = O



8 R¹ = β -OAc, R² = H₂

9 R¹ = α -OH, R² = O

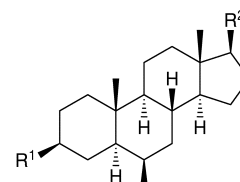
the α -face to afford 5 α -cholestan-6 α -ols. The results of the hydroboration and oxidation of a series of androst-5-ene and B-norandrost-5-enes, **5–9**, are given in Table 1. The stereochemistry of the products was established by their ¹H NMR spectra.¹⁵



10 R¹ = OAc, R² = H

11 R¹ = OH, R² = H

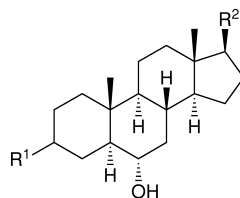
12 R¹ = H, R² = OH



13 R¹ = OAc, R² = H

14 R¹ = OH, R² = H

15 R¹ = H, R² = OH

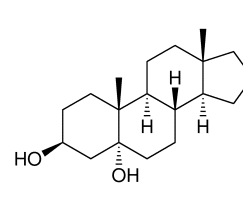


16 R¹ = β -OAc, R² = H

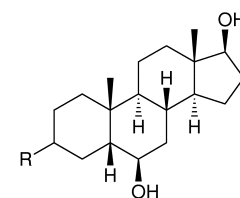
17 R¹ = β -OH, R² = H

18 R¹ = H, R² = OH

19 R¹ = α -OH, R² = OH

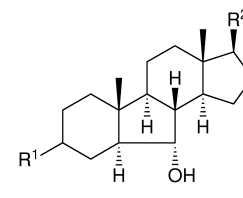


20



21 R = H

22 R = α -OH



23 R¹ = β -OAc, R² = H

24 R¹ = β -OH, R² = H

25 R¹ = α -OH, R² = OH

Prior work on the hydroboration of cholest-5-enes^{9,10} has shown that the predominant direction of attack was from

Except for **7**, the major products of hydroboration of both the six-membered and B-norsteroids arise from reaction on the α -face of the molecule. This suggests that the formation of the four-membered transition state is not determining the facial selectivity and consequently we suggest that the facial selectivity may be determined by the relative ease of formation on the initial π -complex on each face. This interpretation of these results could also accommodate the observed influence of an allylic hydroxy group on the facial selectivity which, in other studies,¹⁷ has been shown to direct the borane to the *trans*

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Table 1 Hydroboration of steroidal Δ^5 -enes

Substrate	Product	Yield (%)
3 β -Acetoxyandrost-5-ene 5	3 β -acetoxy-5 α -androstane 10	1.2
	3 β -acetoxy-6 β -hydroxy-5 α -androstane 13	1.0
	3 β -acetoxy-6 α -hydroxy-5 α -androstane 16	4.9
	3 β -hydroxy-5 α -androstane 11	2.3
	3 β ,5 α -dihydroxyandrostane 20	1.1
	3 β ,6 β -dihydroxy-5 α -androstane 14	1.9
	3 β ,6 α -dihydroxy-5 α -androstane 17	68.2
Androst-5-en-17-one 6	17 β -hydroxy-5 α -androstane 12	3.0
	6 β ,17 β -dihydroxy-5 α -androstane 15	5.0
	6 β ,17 β -dihydroxy-5 β -androstane 21	11.0
	6 α ,17 β -dihydroxy-5 α -androstane 18	44.0
	3 α ,6 β ,17 β -trihydroxy-5 β -androstane 22	64.0
3 α -Hydroxyandrost-5-en-17-one 7	3 α ,6 α ,17 β -trihydroxy-5 α -androstane 19	7.5
	3 β -acetoxy-6 α -hydroxy-B-nor-5 α -androstane 23	34.4
3 β -Acetoxy-B-norandrost-5-ene 8	3 β ,6 α -dihydroxy-B-nor-5 α -androstane 24	49.7
	3 α ,6 α ,17 β -trihydroxy-B-nor-5 α -androstane 25	71.0

face. A repulsive interaction between the oxygen lone pairs and the π -system would enhance the π -electron density on the *trans* face. The regiochemistry of the hydroboration would however be influenced by the relative energies of the orbitals involved in the conversion of the π -complex to the four-membered transition state. In particular the interaction between the oxygen lone pairs of the allylic alcohol and the π -complex as it rearranged to the four-membered transition state would favour the addition of the electron-deficient boron to the adjacent, rather than the distant, carbon. This effect on the electron density might be counter-balanced by the substitution pattern of the alkene.

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Techniques used: ^1H NMR, IR, elemental analysis, chromatography

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