The Effect of Allylic Methoxyl Groups on the Hydroboration of a Steroidal Alkene

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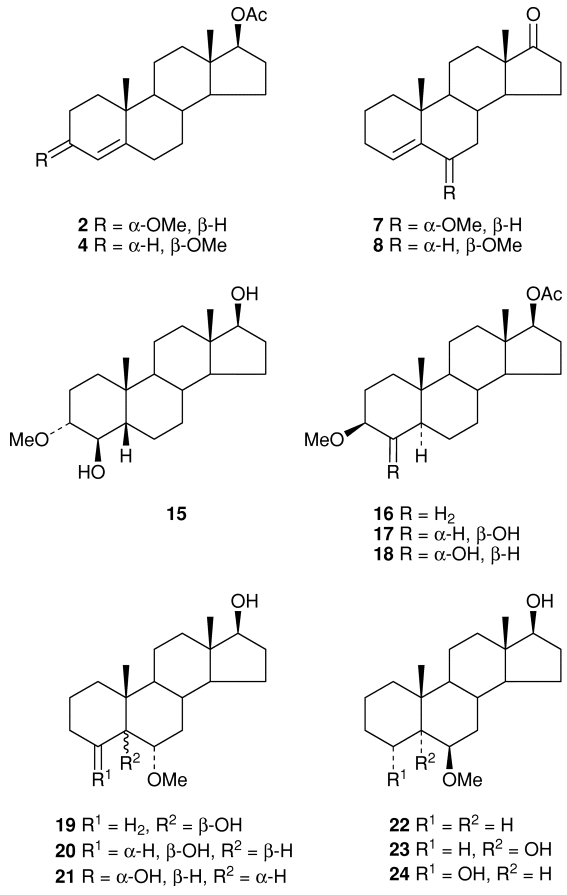
The hydroboration of 3α-, 3β-, 6α- and 6β-methoxyandrost-4-enes has been shown to proceed predominantly *trans* to the methoxy group with, in the case of the 6-methoxy compounds, some Markownikoff hydration to form the tertiary C-5 alcohols, thus parallelling results obtained with the corresponding alcohols.

An allylic hydroxy group has a marked effect on both the regio- and stereo-specificity of the hydroboration of an alkene directing the addition of the boron to the carbon atom adjacent to the substituent and to the *trans* face of the alkene.[1–6] In the steroid series the directing effect of C-3 and C-6 alcohols on the hydroboration of androst-4-enes counterbalances the steric effect of the C-10 methyl group and also, in the case of the C-6α alcohol, leads to some Markownikoff hydration of the double bond.[7,8] These facial and positional effects may arise from borate ester formation, hydrogen bonding to the alkene or from the interaction of the oxygen lone pairs with the π-system of the alkene. A comparison with the effect of an allylic methyl ether could shed some light on these possible contributions (see Scheme).

The substrates were prepared by methylation of the corresponding alcohols with silver oxide and iodomethane or *via* the methanolysis of a 5α,6α-epoxide catalysed by tetracyanoethylene.[9] The results of the hydroboration of the C-3α-, C-3β-, C-6α- and C-6β-methoxyandrost-4-enes are given in Table 1. The structures of the products were established by ^{1}H and ^{13}C NMR methods.

The results from the hydroboration of the allylic methyl ethers parallel those obtained with the corresponding allylic alcohol in which the addition was directed to the *trans* face of the alkene despite unfavourable steric interactions with the angular methyl group. This suggests that hydrogen bonding or borate ester formation do not play a major role in directing the stereochemistry of hydroboration of these allylic alcohols. Theoretical calculations have suggested[10] that the hydroboration of an alkene proceeds *via* the initial formation of a π-complex from which the four-centre transition state evolves that leads to the organoborane. Factors which affect the initial formation of the π-complex will determine the facial and regioselectivity of hydroboration. The repulsive interaction between the lone pairs on the oxygen and the alkene π-system will increase the electron density on the opposite face of the alkene and hence favour *trans* face addition. It has been pointed out that the regioselectivity of boron–carbon bond formation correlates with the atomic orbital coefficient size in the alkene HOMO[11] and this will clearly be affected by these interactions possibly accounting for the formation of the C-5 alcohols.



Scheme

Table 1 Hydroboration of 3- and 6-methoxyandrost-4-enes

Substrate	Product	Yield (%)
17β-Acetoxy-3α-methoxyandrost-4-ene **2**	4β,17-dihydroxy-3α-methoxy-5β-androstane **15**	68
17β-Acetoxy-3β-methoxyandrost-4-ene **4**	17β-acetoxy-3β-methoxy-5α-androstane **16**	6.5
	17β-acetoxy-4β-hydroxy-3β-methoxy-5α-androstane **17**	9.8
	17β-acetoxy-4α-hydroxy-3β-methoxy-5α-androstane **18**	53.2
6α-Methoxyandrost-4-en-17-one **7**	5β,17β-dihydroxy-6α-methoxyandrostane **19**	16
	4β,17β-dihydroxy-6α-methoxy-5β-androstane **20**	38
	4α,17β-dihydroxy-6α-methoxy-5α-androstane **21**	21.4
6β-Methoxyandrost-4-en-17-one **8**	17-hydroxy-6-methoxy-5α-androstane **22**	4
	5α,17β-dihydroxy-6β-methoxyandrostane **23**	4
	4α,17β-dihydroxy-6β-methoxy-5α-androstane **24**	64

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Techniques used: chromatography, IR, ^{1}H and ^{13}C NMR spectroscopy

References: 11

Table 2: ^{13}C NMR data for some hydroboration products

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