The hydroboration of some steroidal hydroxymethylene derivatives

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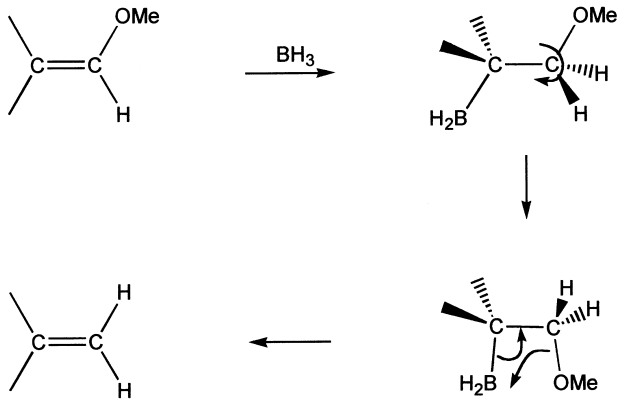
The regio- and stereochemistry of the hydroboration of some methoxymethylene steroids and hydroxymethylene (β-formyl) steroidal ketones and the oxidation of the adducts to form the corresponding hydroxymethyl steroids, are described.

Keywords: hydroboration, steroids, enol ethers

The directing effects of substituents on the regiochemistry of the hydroboration of alkenes has been the subject of a number of studies.[1,2] In a simple enol-ether, the ether directs the addition of the borane to the β-position. The resultant borane may then undergo a β-elimination reaction involving the loss of an alkoxide and the formation of an unsubstituted alkene (Scheme 1). This alkene may then undergo further hydroboration.

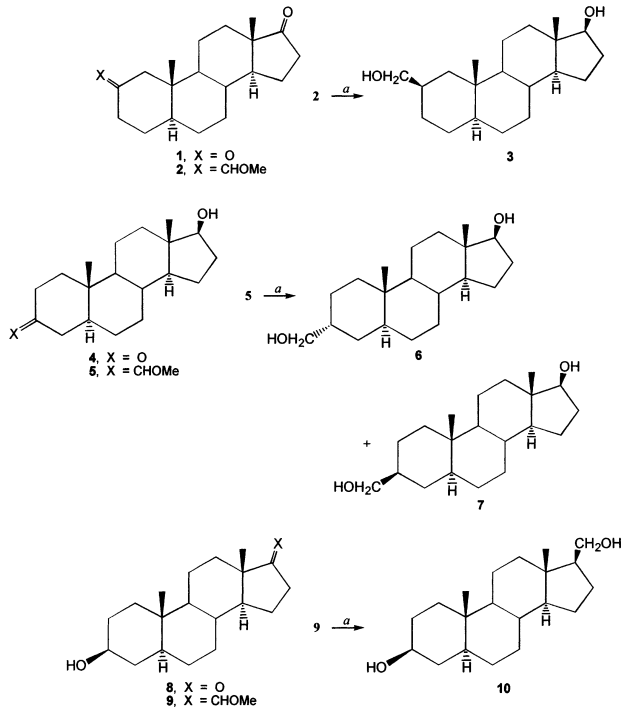


Scheme 1. Diborane demethoxylation of an enol ether.

Hydroboration of a cyclic αβ-unsaturated ketone, and subsequent oxidation with alkaline hydrogen peroxide, affords a *trans* 1,2-diol rather than a 1,3-diol.[3] However, the effect of a hydroxyl substituent attached to an αβ-unsaturated ketone, as in a β-hydroxymethylene ketone (the tautomer of a β-formylketone) or an α-hydroxy-αβ-unsaturated ketone, is less well documented. In this paper we report on the regio- and stereochemistry of the hydroboration of some methoxymethylene steroids, β-hydroxymethylene steroidal ketones, and an α-hydroxy-αβ-unsaturated ketone.

2-Methoxymethylene-5α-androstan-17-one (**2**), 17β-hydroxy-3-methoxymethylene-5α-androstane (**5**) and 3β-hydroxy-17-methoxymethylene-5α-androstane (**9**) were prepared from the 2-, 3- and 17-ketones **1**, **4**, and **8** respectively, by a Wittig reaction with methoxymethyltriphenylphosphonium bromide.[6,7] Hydroboration gave the corresponding 2β-, 3α- and 3β-, and 17β-hydroxymethyl steroids, **3**, **6**, **7**, and **10**, which were identical to samples that had been obtained by the hydroboration of the related 2-, 3- and 17-methylene steroids[8] (see Scheme 2).

17β-Hydroxy-2-hydroxymethylene-5α-androstan-3-one (**11**) and 3β-hydroxy-16-hydroxymethylene-5α-androstan-17-one (**15**) were prepared by formylation of the 3- and 17-



Scheme 2. Hydroboration of compounds 2, 5, and 9.

ketones.[9,10] These β-formylketones exist as their hydroxymethylene tautomers [δ_H 8.67, =CH(OH)]. Hydroboration of compound **11** gave the 2β-hydroxymethyl-2α,3β,17β-triol which was isolated as its triacetate **12**. The 2,17-diacetate **13** afforded the 2β-hydroxymethyl-3β,17β-diol **14**. 3β-Hydroxy-16-hydroxymethylene-5α-androstan-17-one (**15**) gave the 16-hydroxymethyl-3β,16α,17β-triol which was isolated as its diacetate **16**.

Hydroboration of 4,17β-hydroxyandrost-4-en-3-one (**17**)[11] gave 3β,4β,17β-trihydroxy-5α-androstane which was purified as its 3β,17β-diacetate **18**[12] (see Scheme 3).

The hydroboration of the methoxymethylene steroids may be rationalised in terms of the addition of the borane to the β-position relative to the methoxyl group, *i.e.* to the more highly substituted carbon. This is followed by elimination of the methoxyl group and rehydroboration of the alkene. The stereochemistry of the products parallels that of the hydroboration of the corresponding alkenes. In the case of the hydroxymethylene ketones, the enols are probably trapped as their borate esters and the ketones are reduced to the corresponding alcohols. The stereochemistry of this reduction then directs the subsequent addition of the borane to C-2α, or C-16α. Only in the case of the acetate does elimination and rehydroboration take place. The formation of the 3β,4β,17β-trihy-

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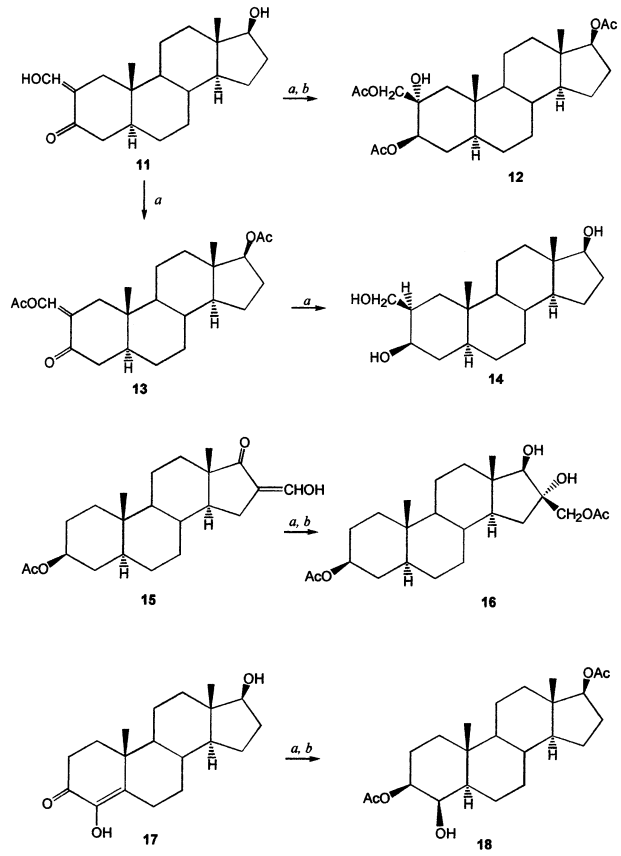

Reagents and conditions: *a*, i) BH_3·THF ii) H_2O_2/NaOH; *b*, Ac_2O/Py

Scheme 3. Hydroboration of compounds 11, 13, 15 and 17.

droxy-5α-androstane may occur by conversion of the 4-enol into a 5α-androstan-4-one and reduction of this ketone from the less-hindered face to generate the 4β-alcohol.

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

Schemes: 3

Table 1, Hydroboration of hydroxymethylene steroids (products, yields)

Table 2, ^{13}C NMR data (compounds **12**, **14**, **16**)

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