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A Novel and Selective Oxidation of Steroidal Allylic Alcohols to the Corresponding Ketones

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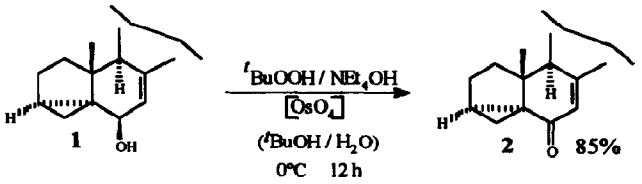
Abstract: The oxidation of steroidal allylic alcohols with ^{t}BuOOH and catalytic amounts of OsO_4 yielded the corresponding α,β-unsaturated ketones in good yields.

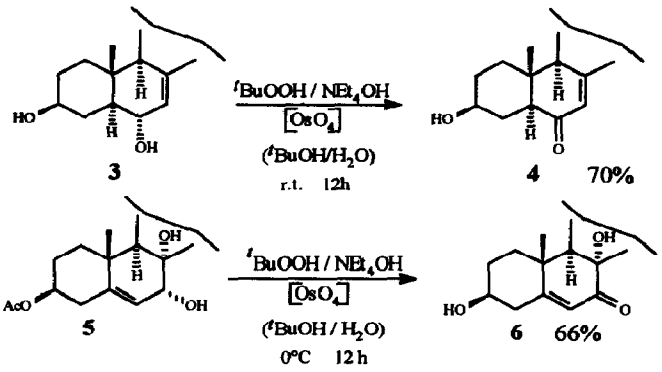
Osmium-tetroxide is a well known reagent for *cis*-dihydroxylation of olefins[1]. Due to its cost and toxicity several procedures were developed using only catalytic amounts of OsO_4 and various co-oxidants, like H_2O_2,[2] *N*-methylmorpholino-*N*-oxide[3] or ^{t}BuOOH,[4] to regenerate the reduced Os species.
Attempted dihydroxylation of the double-bond in 3α,5α-cyclocholest-7-en-6β-ol (**1**), according to the procedure of Sharpless, with ^{t}BuOOH and catalytic amounts of OsO_4 in the presence of aqueous NEt_4OH yielded unexpectedly 3α,5α-cyclocholest-7-en-6-one (**2**)[5] in a good yield (**Scheme 1**).



Scheme 1.

Hydroxylated derivatives could be detected neither by NMR spectroscopy nor by analytical TLC.
In control experiments it was shown that OsO_4 is essential for the reaction. A mixture of unchanged **1** and its elimination product 3α,5α-cyclocholest-6,8(14)-diene were received with ^{t}BuOOH / ^{t}BuOH or ^{t}BuOOH / ^{t}BuOH / NEt_4OH / H_2O only.

On the basis of these findings we tried to prove the general validity of this method for steroidal allylic alcohols. 5α-Cholest-7-ene-3β,6α-diol (**3**) and 3β-acetoxycholest-5-ene-7α,8α-diol (**5**) were selectively oxidized in the same way to 3β-hydroxy-5α-cholest-7-en-6-one (**4**) and 3β,8α-dihydroxycholest-5en-7-one (**6**) with good yields without over-oxidation (C-C-splitting) in the case of **5** or reaction at the hydroxy group 3 (**Scheme 2**).



Scheme 2.

The advantages of this method are good yields, easy working up, the fact that only small amounts of the very toxic and expensive OsO_4 are needed and the selectivity of the reaction leaving saturated secondary hydroxy groups unchanged. Especially the conversion of **1** into **2** is of some interest due to its applicability in the synthesis of brassinosteroids.

References and Notes.

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5. 3α,5α-Cyclocholest-7-en-6β-ol (**1**, 300 mg, 0.78 mmol) was dissolved in 2 ml of ^{t}BuOH and 0.1 ml of 20% aqueous NEt_4OH, 0.53 ml (1.6 mmol) of ^{t}BuOOH (3 M in iso-octane) and 0.04 ml (0.0031 mmol) of OsO_4 solution (2.5% in ^{t}BuOH) were added. After standing for 12 h in a cooling box (0° - +5°C) 1 ml 5% Na_2SO_3 solution was given to the reaction mixture and stirred for 1 h at 20°C. The reaction mixture was extracted with Et_2O, the ethereal phase was washed with sat. NaCl solution, dried over Na_2SO_4 and the solvent was distilled in vacuo. The crude product (331 mg) was purified by chromatography on 40 g of silica gel and **2** (254 mg, 0.66 mmol, 85%) was obtained.

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