Synthesis of α-hydroxy ketones using a HOF·MeCN complex

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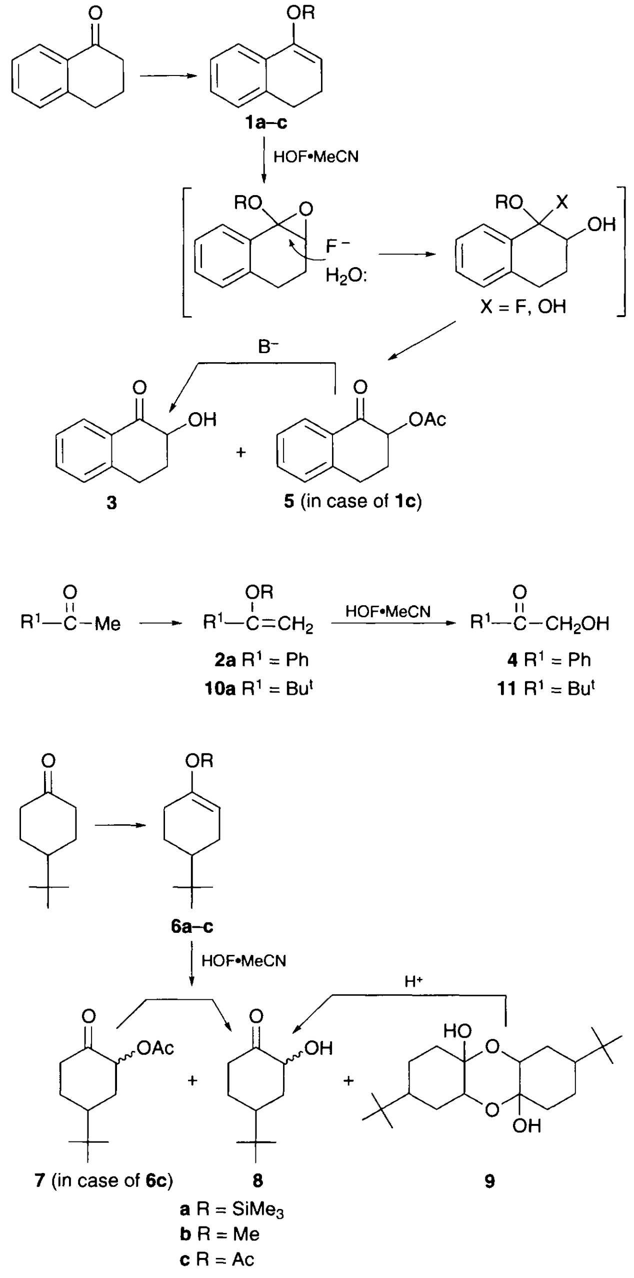
The complex, HOF·MeCN made directly by bubbling fluorine through aqueous acetonitrile, reacts quickly and efficiently with enolic forms of ketones to produce α-hydroxy ketones.

The synthesis of α-hydroxy carbonyl derivatives has been of continuous interest to organic chemists since the beginning of the century.[1] Classical methods have been supplemented in more recent years by several heavy metal-containing oxidants such as MoO$_5$·Py·HMPA[2] and CrO$_2$Cl$_2$,[3] but nowadays chemists are minimizing as much as possible the use of these potentially contaminating agents. An important, different type of reagent is dimethyldioxirane reported to oxidize lithium enolates to acyloins in yields of 50–70%.[4]



The HOF·MeCN complex is rapidly evolving as the best possible oxygen transfer agent, since it contains a truly electrophilic oxygen. Its easy preparation only requires bubbling nitrogen diluted fluorine[5] through aqueous acetonitrile. Its moderate reaction conditions with substrates make it an excellent epoxidizing agent[6] and a unique oxidizer of many functional groups among them amines,[7] alcohols, ketones,[8] amino acids[9] and sulfides.[10] Here we report the reaction of this oxidant with enol derivatives of various ketones.

Benzylic enol derivatives such as tetralone trimethylsilyl enol ether **1a** or its methyl enol ether **1b** and acetophenone trimethylsilyl enol ether **2a** were treated at room temperature with a twofold excess of HOF·MeCN forming α-hydroxytetralone **3**[2] and α-hydroxyacetophenone **4**[4] in higher than 90% yield, each in a 5–10 min.†

Although we have not isolated any intermediates in these reactions it is quite likely that they proceed through the epoxidation of the enolic double bond. The epoxide is opened subsequently by either the nucleophilic fluoride ion or a water molecule present in the reaction mixture. This is supported by the reaction of tetralone enol acetate **1c** with HOF·MeCN under the above conditions. Apart from the expected **3** which was obtained in 50% yield, 2-acetoxytetralone **5** was also isolated in 50% yield. This second product resulted from a known type of rearrangement of enol acetate epoxides,[11] and could be hydrolysed back to **3** bringing the overall hydroxylation yield to near quantitative.

The results of the reaction between HOF·MeCN and the enol acetate of the 4-*tert*-butylcyclohexanone **6c** indicated an acetoxy epoxide intermediate here as well. A mixture of *cis*- and *trans*-2-acetoxy-4-*tert*-butylcyclohexanone **7**[12] was obtained and isolated in 65% yield, while the rest 35% were a mixture of *cis*- and *trans*-2-hydroxy-4-*tert*-butylcyclohexanone **8**[13] and its dimer **9**. The latter, under acidic work-up, could be converted back to the monomer **8**.[14] Repeating the reaction with the corresponding silyl enol ether **6a** and methyl enol ether **6b** yielded only a mixture of **8** and **9** in 90% yield. Dimerization is not favoured with the pinacolone derivatives and only α-hydroxypinacolone **11**[3] was obtained quantitatively after treating **10a** with HOF·MeCN at room temperature for 10 min.

This research was supported by the Israel Science Foundation administrated by the Israel Academy of Science and Humanities.

Footnote

† All physical properties of the products, including ^{1}H NMR, IR and MS are in excellent agreement with the proposed structures and with the properties published in the referenced literature.

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Received, 22nd November 1995; Com. 5/07627G