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A FACILE ROUTE TO CYCLOPENTENONES BY FRIEDEL-CRAFTS ACYLATION

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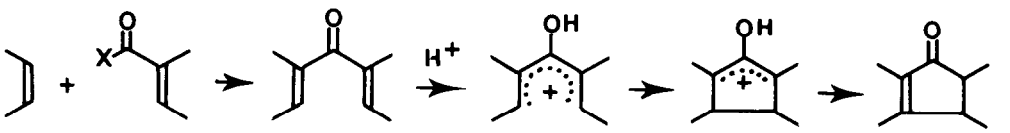
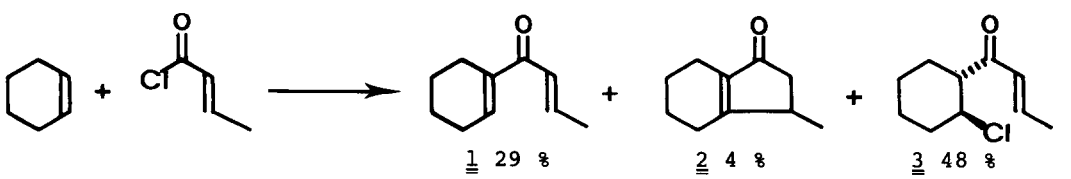
Summary: Various cyclopentenones are obtained in fair to high yields when ethylenic acyl bromides are condensed with cyclohexene at low temperature. With less reactive reagents, condensation occurs at 0 °C, leading to β-chloroketones. A muscone precursor is obtained in two steps with excellent yields.

Cyclopentenones are useful intermediates in the synthesis of a wide range of compounds as prostaglandins (1), muscone (2), terreins (3), antitumoral substances (4), rethrolones (5) etc.

Usually, cyclopentenones have been produced in good yields by intramolecular aldol ring closures of 1,4-diones (6). The route to cyclopentenones via cyclisation of divinylketones (NAZAROV-type conrotatory electrocyclisation (7) is an attractive one, limited only by the availability of the divinylketones (generally prepared by a RUPE rearrangement of acetylenic diols (2,8), acylation of alkenes with unsaturated acids in polyphosphoric acide (9) or acylation of vinylsilanes (10)).One another route can be found in the FRIEDEL-CRAFTS acylation of alkenes by ethylenic acid halides in the presence of $AlCl_3$ (earlier studies had shown that polyhalogenated ketones are produced (11)).



Results: In a preliminary experiment, condensation of cyclohexene with crotonoyl chloride, at 0 °C, gave a mixture, the main component of which is trans-β-chloroketone 3 (12) :



1 29 % 2 4 % 3 48 %

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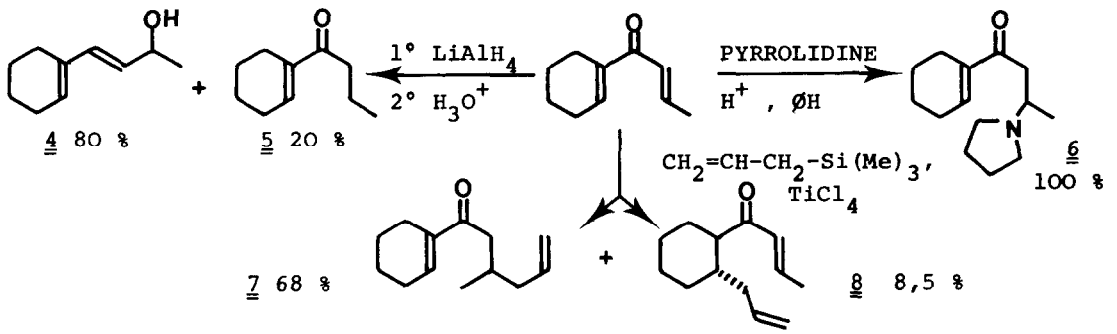
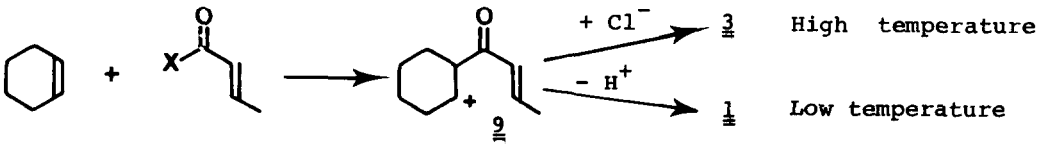
Chloroketone 3 is practically the only primary product, ketones 1 (13) and 2 (9a) resulting from the work-up.

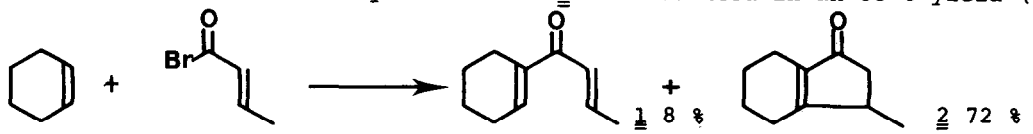
Nucleophilic reagents, such as complex hydrides, pyrrolidine or trimethylallylsilane (14), have been found to add very easily to the dienone 1 on the propenyl moiety :



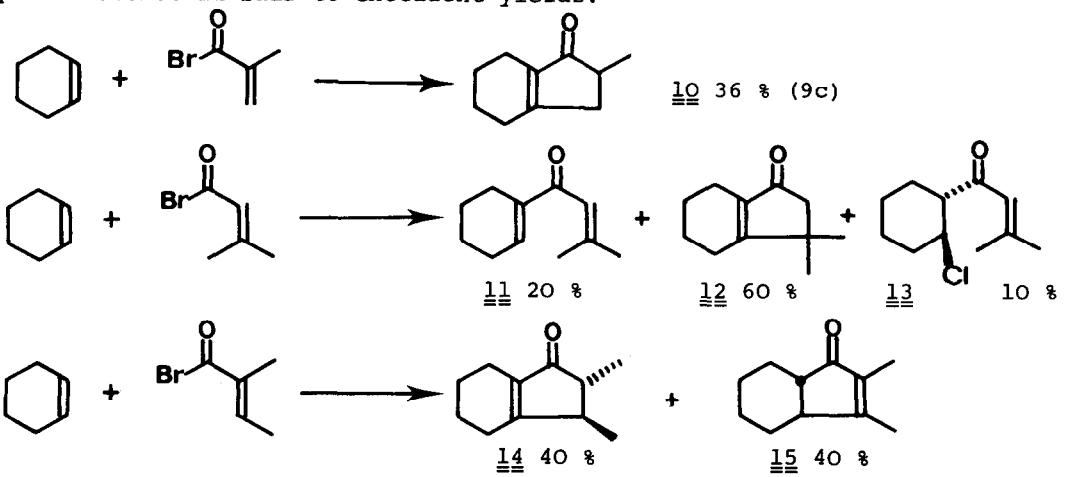
For this reason, we conclude that the chloroketone 3 is not produced by conjugate addition of HCl on the dienone 1. Accordingly, we were led to consider the β-ketocarbenium ion 9 as precursor of chloroketone 3 and dienone 1 :



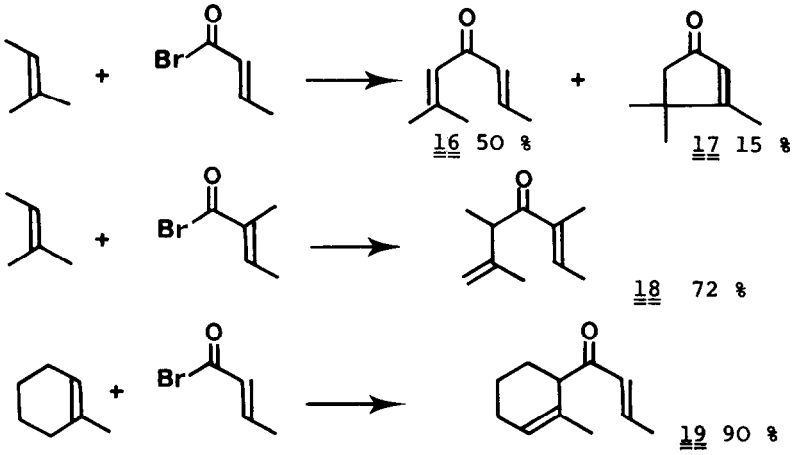
These were reasons to expect that the importance of the competing H^+ abstraction reaction could be increased by lowering the reaction temperature. In fact, by using the more reactive crotonoyl bromide (15), condensation occurs at low temperature (-78 °C) and bicyclic ketone 2 was isolated in an 80 % yield (16):



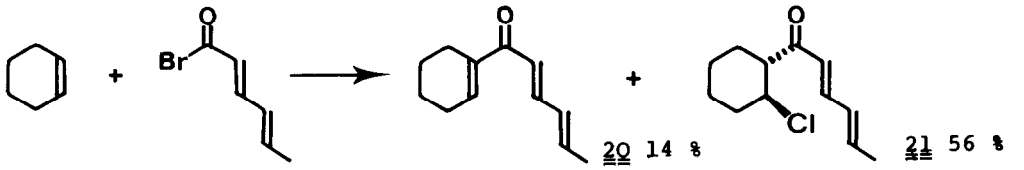
The present reaction is useful especially for the preparation of 6/5 fused bicyclic ketones in fair to excellent yields:



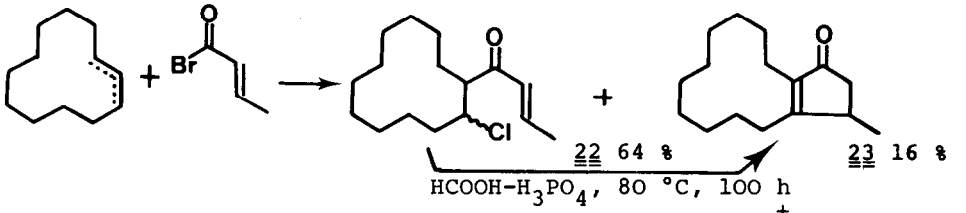
When the same reaction conditions were applied to the trisubstituted alkenes, the main product is in fact often the allylvinylketone (17):



Condensation of cyclohexene with sebacoyl bromide at low temperature does not occur, and warming up to 0 °C (during 18 h) is necessary; chloroketone 21 is, as expected, the major product:



In the same way, cyclododecene (cis + trans) reacts slowly with crotonoyl bromide at -78 °C :



Ketone 23 is an important intermediate in the synthesis of (±)-muscone (2). By acid treatment ($HCOOH\text{-}H_3PO_4$ 3/1 (w/w), 80 °C, 100 h), the chloroketone 22 is converted easily to the cyclopentenone 23 (quantitative yield). This method has the advantage of a direct and simple synthesis using very cheap reagents, in contrast to previous more sophisticated methods (2, 10, 18)

It is clear that the FRIEDEL-CRAFTS acylation with unsaturated acyl bromides has still a large scope in synthesis.

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