

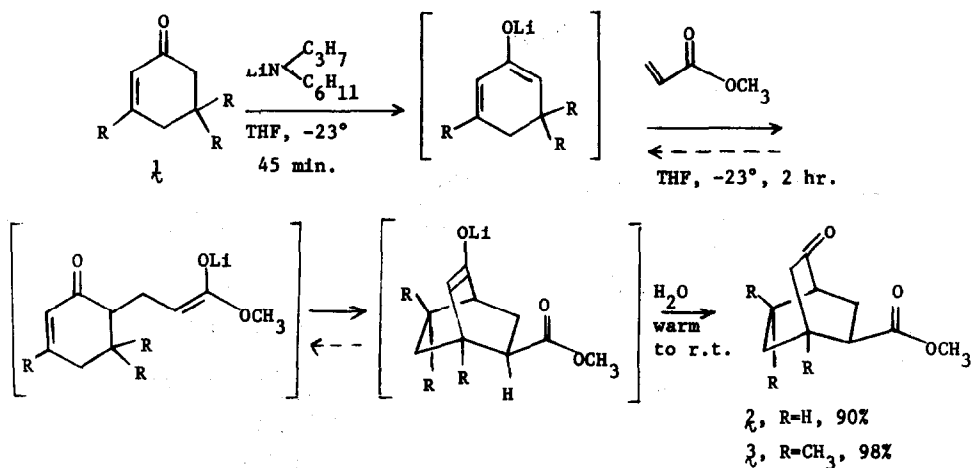
REACTIONS OF α' DIENOLATES WITH MICHAEL ACCEPTORS:
A SYNTHESIS OF BICYCLO [2,2,2] OCTAN-2-ONES.

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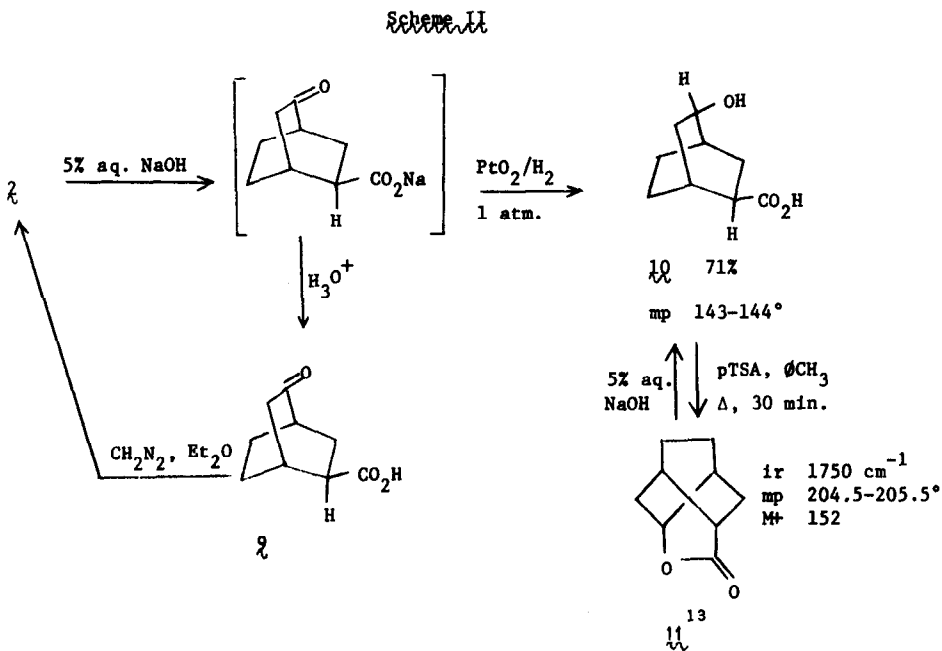
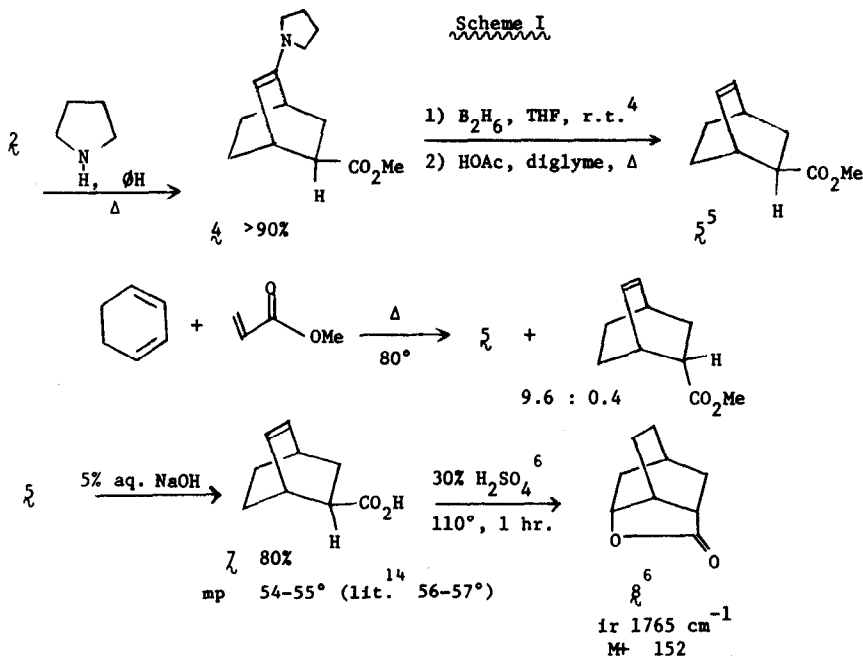
We recently observed that cross-conjugated dienolate anions are formed preferentially from α,β -unsaturated ketones under conditions of kinetic control.² These dienolate bases were methylated in high yield giving α' -methyl derivatives. The intriguing possibility that these intermediate dienolate anions might undergo sequential Michael additions resulting in bicyclic products prompted us to investigate their reaction with Michael acceptors. We now report a facile, high yield synthesis of bicyclo [2,2,2] octan-2-ones involving the reaction of methyl acrylate with the cross-conjugated dienolate bases derived from cyclohexenone and isophorone.



The reaction is highly stereospecific giving rise in each case to a single diastereomer as evidenced by chromatography (glc, tlc); nmr (CCl_4) sharp $-\text{CO}_2\text{CH}_3$, $\text{2} \delta 3.69$, $\text{3} \delta 3.70$; and sharp melting points, 2 (2,4 DNP) $139-140^\circ$, 3 $53-54^\circ$ (lit.³ $54.5-55.5^\circ$). The nmr spectrum

of **3** proved identical to that reported for this compound by H. Nozaki et. al.³

We have established the stereochemistry of the C-5 function in the case of **2** by the reactions presented in Scheme I and Scheme II.



The synthesis of bicyclo [2,2,2] octan-2-ones by Diels Alder cycloadditions to cross conjugated diene derivatives of cyclohexenones has been described by several research groups.^{3,7,8,15} Yields based on starting enone, in most cases have been low due primarily to competing formation of the γ -dienol derivative. The formation of bicyclooctenol acetates by the reaction of maleic anhydride with the cross conjugated dienol acetates of isophorone and cyclohexenone in respective yields (and reaction times) of 32%, (72 hours) and 80% (18 hours) is particularly noteworthy.¹⁵ Reactions in which the α,β -unsaturated ketone acts both as a donor and acceptor in the Michael fashion have also been reported. At least three groups of workers^{9,10,12} have observed the formation of bicyclic products by thermal and base catalyzed double Michael additions in reported yields of 28-40%. Bellamy¹¹ has invoked a similar sequential Michael mechanism to account for the formation of a tri-cyclic dimer in 40% yield by the treatment of 4,4-dimethylcyclopent-2-enone with base. In all but one⁹ of the above cases the observed stereochemistry of the major isomer formed has been reported to be endo.

The mechanism of the cyclization described here is not rigorously defined. Diels Alder cycloaddition is clearly possible; but in view of the very high yields observed under exceptionally mild conditions with substrates of varying steric hindrance, we favor a path involving sequential Michael reactions. If this interpretation proves correct, reactions of cross-conjugated dienolate bases with Michael acceptors should provide a powerful synthetic alternative to the Diels Alder reaction. Further studies and applications of this approach are currently in progress.

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