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Reaction of Methyl β-Vinylacrylate With Formylcycloalkanones. A New Route To Functionalized Spiro Compounds.

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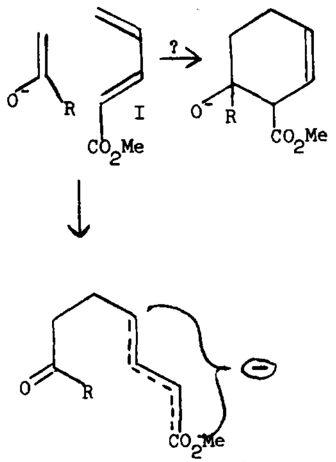
Recently we reported on the reactions of cyclic β-diketones and carbethoxycycloalkanones with compound I under basic catalysis.[2] In monoglyme, the products obtained were, invariably a mixture of tautomers arising from protonation of an initially formed 1,6-adduct. In DMSO the products were derivable from the sequence (i) 1,6-addition; (ii) proton transfer; (iii) intramolecular 1,4-addition. In no case were we able to observe the seemingly plausible sequence (i) 1,6-addition; (ii) aldol condensation which would result in the transformation generalized below. This is noteworthy since just such a transformation occurs in the reaction of enamines with I.[3] We now report that the reaction of formylcycloalkanones with I in $DMSO^{-}$—DMSO does indeed proceed via the latter sequence, enabling a one-step synthesis of functionalized spiro compounds from readily available starting materials.

Reaction of formylcyclohexanone with I in $DMSO^{-}$—DMSO afforded a mixture of three products. Combustion and spectral analysis allowed for their assignment as II[4] (15% yield; DNP mp = 99-100°), III (9% yield; DNP mp = 92-93°) and IV (40% yield; DNP mp = 160-161°).

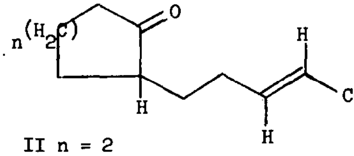
Compounds II and III undoubtedly arise from 1,6-addition followed by deformylation of the resultant β-ketoaldehyde by some, as yet undetermined, nucleophile. No moncyclic product containing the formyl group could be detected. Compound IV must be the result of dehydration on an intermediate carbinol which is in turn the result of cycloaddition (in structural terms) of an enolate and compound I.

Reaction of formylcyclopentanone with I under identical conditions proceeds in a similar fashion in gross terms but with notable differences in detail. A mixture of products was obtained which was determined to consist of V[4](13%; DNP mp = 112-113°); VI (9%; DNP mp = 94-95°); VII (11%; DNP mp = 143°dec); VIII (14%; DNP mp = 97-99°) and IX (7%; DNP mp = 84-85°). The sum total of mono:bicyclic products(22:32) is reasonably comparable to the formylcyclohexanone case. What is notable, is the greater stability of the intermediate carbinols in the latter case. Examination of molecular models failed to suggest a convincing reason for this difference.

The failure to obtain cycloaddition products in the previously studied cases[2] was believed to be due to the fact that the extended enolate produced on 1,6-addition exists primarily as the trans-C_3-C_4 system. Indeed, all monocyclic products isolated from those as well as these reactions contained trans α,β or β,γ double bonds. That cycloaddition does occur with the β-ketoaldehyde, might be a consequence of the greater electrophilicity of the aldehydo carbonyl group. This could allow for cyclization of a small amount of C_3-C_4 cis anion present at equilibrium. Alternatively, the process may be viewed as a concerted cycloaddition. The strong dienophilic capabilities of[3] an alkylidene cycloalkanone (such as is formally embodied in the anion of a formylcycloalkanone) is encouraging in this regard. Studies bearing on this mechanistic issue as well as exploitation of this simple route to spiro systems are in progress.

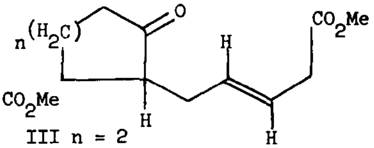


I



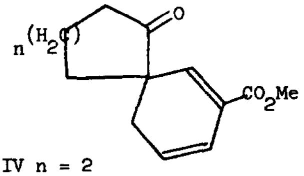
II n = 2

V n = 1



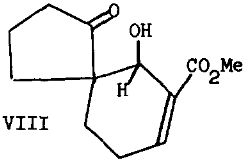
III n = 2

VI n = 1

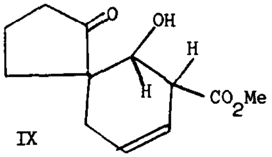


IV n = 2

VII n = 3



VIII



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References

1. (a) National Science Foundation Graduate Trainee, (b) Mobay Fellow.

2. S. Danishefsky, G. A. Koppel and R. Levine, *Tetrahedron Letters*, 2257 (1968).

3. G. Berchtold, J. Ciabattoni and A. A. Tunic, *J. Org. Chem.*, **30**, 3679 (1965); S. Danishefsky and R. Cunningham *ibid.*, **30**, 3676 (1965); S. Danishefsky and R. Cavanaugh, *ibid.*, **33**, 2959 (1968).

4. The yields were determined by quantitative g.l.c. Infrared, nmr, and mass spectra as well as combustion analyses agree with the assignments II-IX.