

KETENE THIOACETAL MONOXIDES: A NOVEL AND VERSATILE CLASS OF TWO-CARBON MICHAEL RECEPTORS

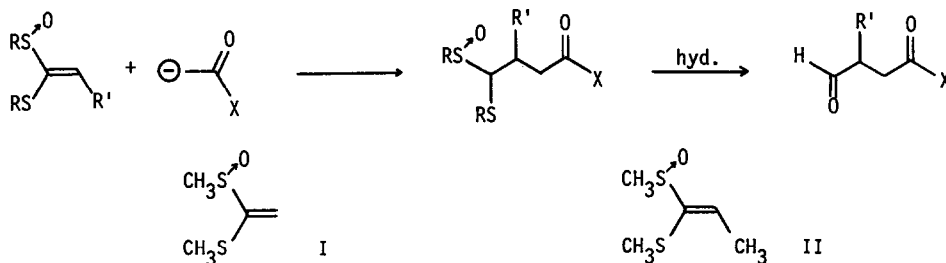
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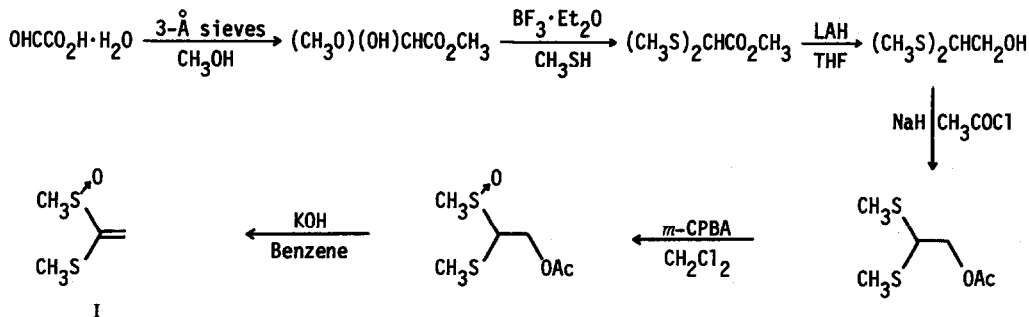
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In the preceding communication we outlined the preparation of an unusual class of electron deficient olefins, ketene thioacetal monoxides.¹ Our interest in these olefins arose from the possibility that compounds of this type might be used as receptors in the Michael addition reaction. In principle, combination of these olefins with enolates derived from carbonyl systems could result in the formation of 1,4-dicarbonyl compounds in which one of the carbonyl groups is an aldehyde residue.² To realize this proposition, we have studied compounds I and II and herein wish to describe the successful conjugate addition of several enolate species to them. These results provide the first examples of an extremely efficient assemblage of unsymmetrical 1,4-dicarbonyl systems by utilization of a two-carbon Michael receptor.³

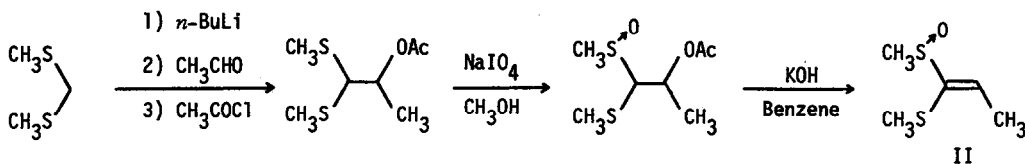


We have carefully investigated the most convenient and efficient means of obtaining quantities of I and have found the method of choice to be that starting from glyoxylic acid.⁴



77% overall yield

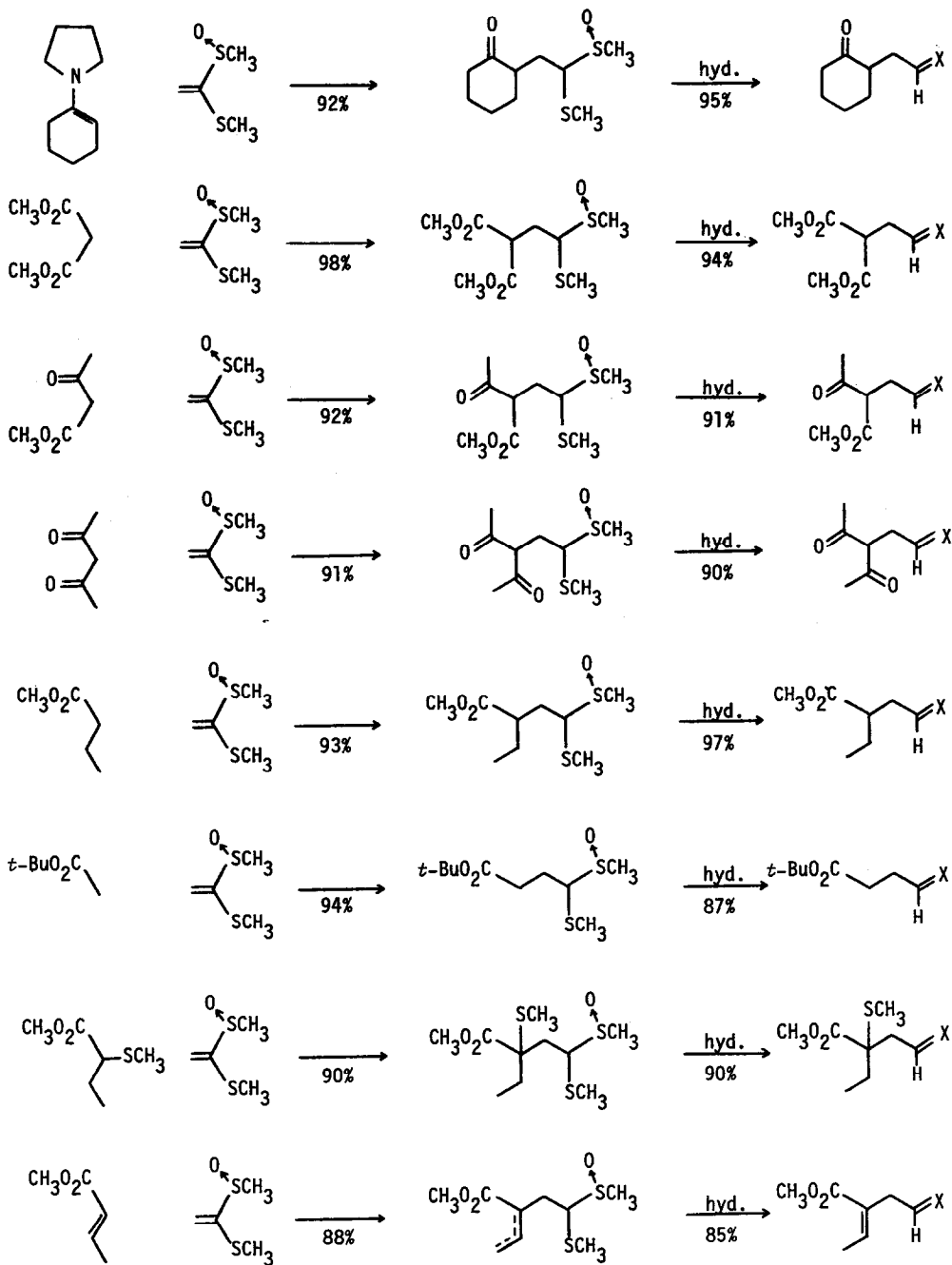
Ketene thioacetal monoxides such as II which are derived from low molecular weight aldehydes are best prepared by the method outlined below.⁵

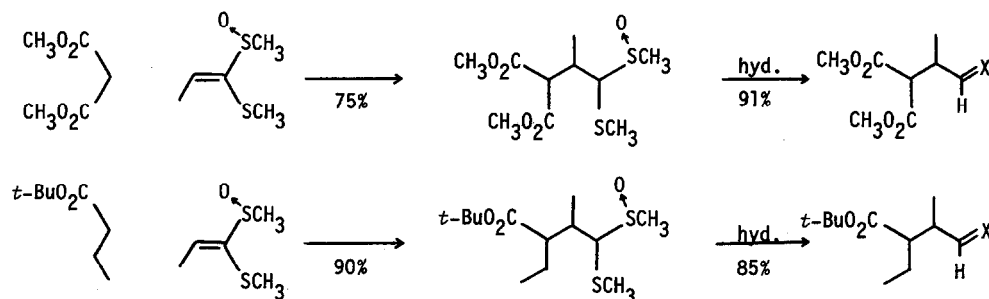


50% overall yield

Experimentally, the Michael addition reactions of I and II fall into three classes: a) reactions with enamines, b) reactions with sodium enolates derived from β -dicarbonyl compounds, and c) reactions with lithium enolates derived from simple ester systems.

The reactions of enamines (1 equivalent) with I (1 equivalent) are best carried out in refluxing acetonitrile (1 molar).⁶ β -Dicarbonyl compounds (1 equivalent) react with either I or II (1 equivalent) in THF solution (1 molar) using sodium hydride (0.3 equivalents) as the base.⁷ Addition (at -78°) of either ketene thioacetal monoxide (2 molar in THF, 1 equivalent) to solutions of lithium enolates of simple esters (1 equivalent) prepared in THF solution (0.5 molar) by reaction with lithium diisopropylamide (1 equivalent) affords very high yields of the corresponding Michael adducts in 30 minutes or less.⁸ A summary of some typical Michael reactions of this type are given below.





Hydrolysis of the above addition products in aqueous acetonitrile containing perchloric acid yields the corresponding aldehydes [X = O].⁹ Alternatively, conversion of these adducts into their corresponding dimethylacetal analogues [X = (OCH₃)₂] may be carried out in a mixture of trimethyl orthoformate, methanol, and perchloric acid.⁹

On the basis of these results, it is clear that efficient construction of 1,4-dicarbonyl compounds in which one of the carbonyl groups is an aldehyde residue can be easily realized using two-carbon Michael receptors such as I and II. Additionally, this new synthetic method should be of preparative significance since the reactions described occur under conditions of ideal stoichiometry.

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REFERENCES

1. J. L. Herrmann, J. E. Richman, P. J. Wepplo, and R. H. Schlessinger, *Tetrahedron Letts.*, in press.
2. Ketene thioacetals are reported to add alkyl and aryl organolithium reagents but reactions of these systems with other types of anions are unknown. For examples, see D. Seebach, M. Kolb, and B. T. Grobel, *Angew. Chem. Intern. Ed. Engl.*, 12, 69 (1973).
3. This construction of a 1,4-dicarbonyl system is much more efficient than that obtained by alkylation with the acetal of chloroacetaldehyde. For a high yield example of the latter reaction, see W. D. Woessner and R. A. Ellison, *Tetrahedron Letts.*, 3735 (1972).
4. Acylation of the carbonyl anion equivalent described in reference 1 with formaldehyde also gives a good yield of I. However, we have found that anhydrous formaldehyde is not convenient to handle on a large scale.
5. An alternative and comparable method of preparing II is described in reference 1.
6. Hydrolysis of these adducts to the intermediate keto thioacetal monoxide is done in refluxing water.
7. These reactions require between 5 and 15 hours at room temperature.
8. These reactions are worked up using saturated ammonium chloride. The yields reported are for isolated products. All compounds exhibited satisfactory spectral and physical properties.
9. For more detailed hydrolysis conditions, see reference 1 and references cited therein.