

A VERSATILE AND REACTIVE MICHAEL RECEPTOR FOR THE SYNTHESIS OF 1,4 -DICARBONYL COMPOUNDS

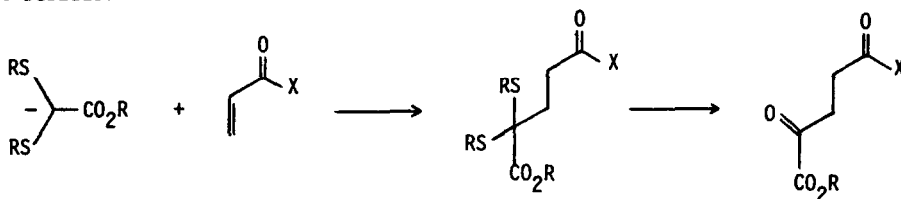
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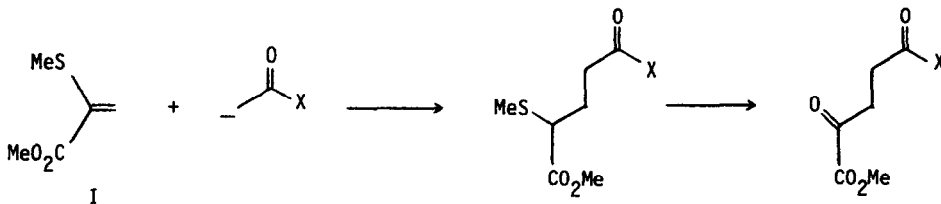
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In the preceding communications we described the novel conjugate addition reactions of two glyoxalate derived carbonyl anion equivalents.¹ These anions were applied to the efficient preparation of a variety of 1,4-dicarbonyl compounds in which one of the carbonyl groups is part of an oxalate residue.

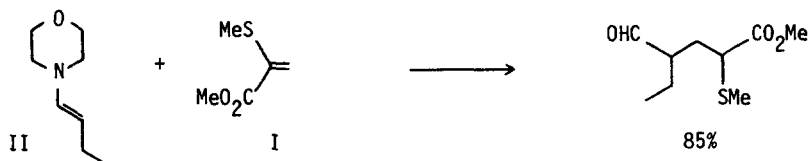


We have also investigated the possibility of realizing the same synthetic result from the opposite tactical direction by examining the conjugate addition behavior of nucleophilic species towards the Michael receptor, methyl 2-methylthioacrylate (I).² Herein, we wish to report that

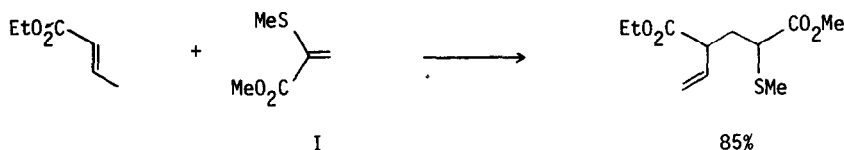


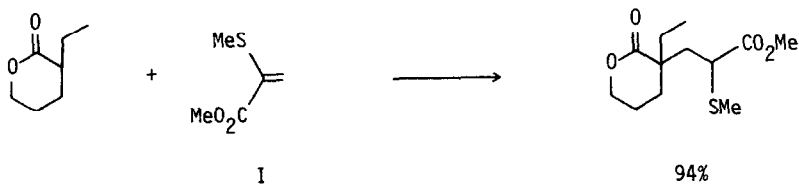
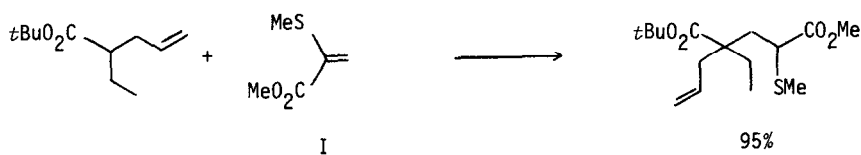
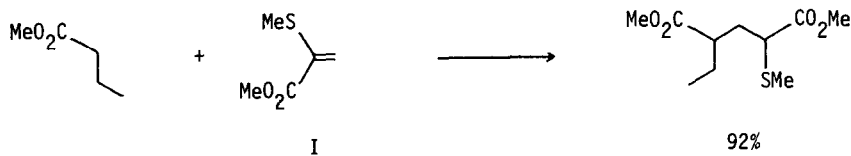
I undergoes remarkably facile and high yield conjugate addition with nucleophiles of widely diverse reactivity. Furthermore, the adducts obtained from I are readily converted by a simple two step process into 1,4-dicarbonyl compounds.

Weakly nucleophilic systems such as the enamines II and III react in high yield with acrylate I under conditions of ideal stoichiometry.³ Interestingly, the rates of these reactions are quite fast relative to methyl acrylate. Most noteworthy, however, is the observation that only monoadducts are obtained in these reactions and no trace of higher molecular weight products could be found.⁴

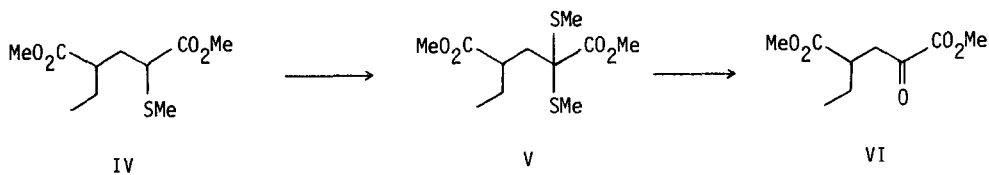


Strongly nucleophilic species, *e.g.*, lithium enolates derived from esters and lactones, also undergo smooth high yield conjugate addition to I. These reactions are carried out at -78° by adding the ester or lactone (1 equivalent, 1 molar in THF) to a 1 molar THF solution of lithium diisopropylamide (1 equivalent).⁵ After enolate formation is complete (15 to 40 minutes), a 2 molar THF solution of the acrylate I (1 equivalent) is added and the resulting mixture stirred at -78° for 1 to 3 hours. In all cases only monoadducts were obtained. The behavior of ethyl crotonate is particularly interesting in that this enolate reacts exclusively at its α -carbon atom.⁶





Conversion of the above Michael adducts into their corresponding 1,4-dicarbonyl analogues is readily accomplished. For example, the diester sulfide IV is converted into the thioketal V by treatment of IV with lithium diisopropylamide followed by S-methylation with methyl *p*-toluenethiolsulfonate.⁷ Hydrolysis of V with *N*-bromosuccinimide in aqueous acetonitrile⁸ affords the ketone VI. The overall yield for the transformation of IV into VI is 94%. The same reaction se-



quence may be applied to the products obtained from enamines II and III. In these cases, however, the aldehyde or ketone residue must be protected as a 1,3-dioxolane before the S-methylation step.⁹

Clearly, the variety of nucleophilic species which conjugatively add to the acrylate I suggests that this versatile Michael receptor will allow the ready synthesis of a variety of 1,4-dicarbonyl compounds. The application of I to the construction of complex molecules should be quite advantageous since it undergoes the Michael addition reaction under very mild conditions with ideal stoichiometry.

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REFERENCES

1. a) R. J. Cregge, J. L. Herrmann, J. E. Richman, R. F. Romanet, and R. H. Schlessinger, *Tetrahedron Letts.*, in press; b) J. L. Herrmann, J. E. Richman, and R. H. Schlessinger, *ibid.*, in press.
2. A convenient and high yield preparation of this compound is described by K. D. Gundermann and H. Schulze, *Chem. Ber.*, **94**, 3254 (1961).
3. These reactions were carried out in acetonitrile at a 1 molar concentration using 1 equivalent of the enamine and 1 equivalent of the acrylate. Yields given are for isolated products. All compounds exhibited satisfactory spectral and physical properties.
4. Double Michael addition reactions are somewhat difficult to prevent with enamines derived from aldehydes. For examples, see M. E. Kuehne in "Enamines: Synthesis, Structure, and Reactions," ed. A. G. Cook, Marcel Dekker, New York, 1969 page 359.
5. Lithium diisopropylamide was prepared by treatment of diisopropylamine with *n*-butyllithium at 4° for 15 minutes. The reagent when properly prepared is colorless to faintly yellow.
6. Similar behavior has been observed for the alkylation of ethyl crotonate. For examples, see J. L. Herrmann, G. R. Kieczkowski, and R. H. Schlessinger, *Tetrahedron Letts.*, in press, and references cited therein.
7. A preparation of methyl *p*-toluenethiolsulfonate is described by D. T. Gibson, *J. Chem. Soc.*, 2637 (1931). The S-methylation reactions occur in high yield for all of the adducts described herein.
8. E. J. Corey and B. W. Erickson, *J. Org. Chem.*, **36**, 3553 (1971).
9. The overall yields of these reaction sequences are in excess of 90%.