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MICHAEL ADDITIONS OF DIENOLATE ANIONS
- A NEW ANNELATION REACTION

George A. Kraus* and Hirohiko Sugimoto
Department of Chemistry
Iowa State University
Ames, Iowa 50011

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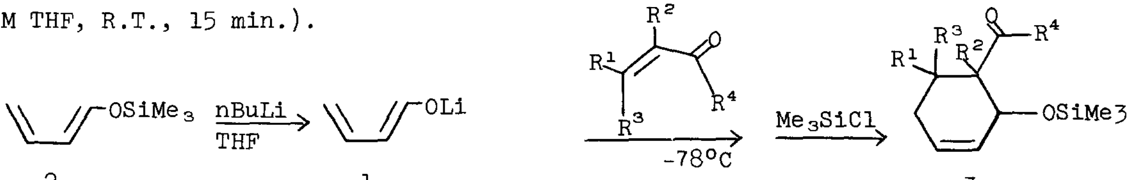
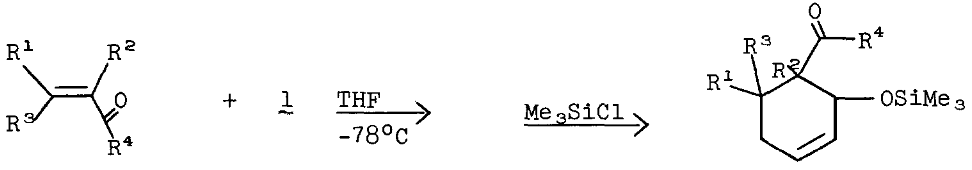
The use of enolate anions generated in aprotic media has become an established technique in organic synthesis.[1] Although many papers have described the scope of alkylation[2] and aldol condensations,[3] surprisingly few reports have appeared about Michael additions.[4] We have embarked upon a study of Michael addition reactions of dienolate anions and have encountered unusual selectivity with dienolate anion 1. This anion can be conveniently generated by reaction of n-butyllithium with the readily available[5] enol silyl ether 2 (1M THF, R.T., 15 min.).



2 1 3

Reaction of 1 with Michael acceptors, followed by trapping of the intermediate with chlorotrimethylsilane[6] yields adduct 3. The site of initial Michael addition is especially notable in view of both theoretical predictions and experimental observations[7] that the preferred site of electrophilic attack on a dienolate anion is at the α carbon. Interestingly, 1 did not react with saturated ketones. This scheme represents an attractive alternative to a Diels-Alder approach using 2 or other alkoxybutadienes due to the much lower temperatures employed and the absence of side reactions such as elimination and diene polymerization. One explanation for this novel reaction would be that the Michael addition is reversible and that the observed product represents the most stable one. Another possibility would be a metal-assisted Diels-Alder reaction[8] which would form adduct 3 after silation. We have previously proposed this concept to explain our results of Michael additions with angelicalactone, which also occur at the γ carbon. In addition, we have performed Michael additions of unsaturated sulfones.[9] For these compounds, conjugate additions occur almost exclusively at the α-carbon. Experiments using dienolate anions constrained to react in a transoid conformation are in progress.

TABLE



R^1	R^2	R^3	R^4	% Yield	
H	H	H	OCH_3	60	a
CH_3	H	H	CH_3	44	a
H	CH_3	H	CH_3	45	a
CH_3	CO_2CH_3	H	OCH_3	70	b
H	H	$-CH_2-CH_2-CH_2-$	--	--	

a = mixture of diastereomers

b = a small amount of acyclic product (unsaturated aldehyde) formed.

In a typical reaction, 10 millimoles of n-butyllithium was added over 5 minutes to a solution of 10 millimoles of 2 in 10 ml THF. The yellow solution was stirred at R.T. for 15 min., cooled to -78°C and 10 millimoles of ethyl acrylate in 3 ml THF was added over 5 min. The solution was allowed to warm to 0°C and quenched at that temperature with chlorotrimethylsilane. The solution was then diluted with pentane, washed twice with water, dried over sodium sulfate and concentrated. The product was isolated by bulb to bulb distillation. The product obtained was identical (NMR, IR, TLC) to an authentic sample prepared by a Diels-Alder reaction of 2 with ethyl acrylate.[10]

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References and Notes

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6. This is necessary to avoid complicated product mixtures due to intermolecular reactions of the free aldehyde.
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