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CONTROL OF THE ALKYLATION OF KETONE ENOLATES WITH TRIBUTYL TIN CHLORIDE AND TRIETHYL ALUMINUM

P. A. Tardella (*)
Department of Chemistry, Columbia University
New York, N.Y. 10027

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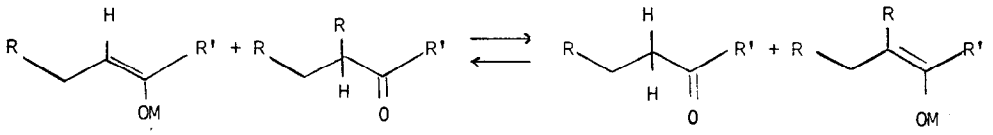
The monoalkylation of enolates is always accompanied by di- and polyalkylation (1). These side reactions are due, in the absence of excess of base, to equilibration of the starting enolate with the monoalkylation product:



Several solutions have been proposed in the past to overcome this problem (2), and, quite recently, the use of lithium enolates generated from trialkylsilyl enol ethers (3) and more special methods, such as the alkylation of α-bromo ketones with boranes, have been suggested (4).

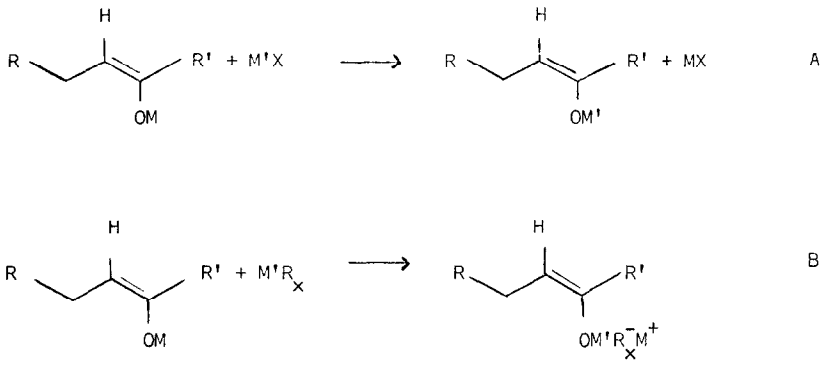
It is known (5) that the rate of the above-mentioned equilibration decreases as the metal is changed from K to Li, i.e. with increasing covalent character of the metal oxygen bond.

It seemed reasonable to ask whether it would be possible to find other metal enolates which could be alkylated faster than they become equilibrated.

Only few cases of alkylation of enolates other than those of Li, Na, K (6,7,8) have been reported and there are no comparative data for any case.

A systematic study in this direction was started, based on the possibility of producing enolates (or complexes) according to the following scheme:

(*) Present address: Istituto di Chimica Organica dell'Università di Roma, Italy



Results are summarized in Tables I and II and show that the addition of one equivalent of Bu_3SnCl (as M'X, scheme A) or Et_3Al)as $M'R_x$, scheme B) to Li (or K) enolates gives, in a number of instances, monoalkylation in good yields.

The lower reaction rates of the tin and aluminum complexes necessitates the addition of some hexamethylphosphoramide (HMP) to the usual solvent - 1,2-dimethoxyethane (DME) - in order to achieve reaction in a reasonable time. It is our conclusion that Et_3Al is more generally useful as an additive to lithium enolates and allows simpler work-up of reaction mixtures than Bu_3SnCl.

Many other metal halides were examined (according scheme A) but gave monoalkylation to the same extent as, or less than did Li enolates.

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References

1) For a review cf.: a) H. O. House, Rec.Chem.Prog., 28, 98, (1967) and
b) H. O. House, Modern Synthetic Reactions, p. 163, W. A. Benjamin, New York 1965
2) Ref. 1b) pages 194-201
3) G. Stork, P. F. Hudrlik, J.Am.Chem.Soc., 90, 4464 (1968)
4) H. C. Brown, M. M. Rogic, M. W. Rathke, J.Am.Chem.Soc., 90, 6218 (1968)
5) G. Stork, P. Rosen, N. Goldman, R. V. Coombs and J. Tsuji, J.Am.Chem.Soc., 87, 275 (1965)
6) J. Fauvarque, J. F. Fauvarque, Compt.Rend., Ser. C, 263, 488 (1966)
7) T. A. Spencer, R. W. Britton, D. S. Watt, J.Am.Chem.Soc., 98, 5727 (1967).
8) E. C. Taylor, G. H. Hawks III, A. McKillop, J.Am.Chem.Soc., 90, 2421 (1968)

TABLE I

Ketone or derivative	Enolate formation	Alkylation conditions	Alkylation products distribution (1) mono- %	di- %
Cyclohexanone trimethylsilyl enol ether (2)	MeLi	DME CH_3I 2 moles 0°, 1 h	89	3
"	MeLi, Bu_3SnCl (3)	"	93 (4)	-
"	MeLi, Et_3Al	DME:HMP = 8:3 CH_3I 2 moles 0°, 45 h	94	-
"	MeLi	DME nBuI 10 moles r.t., 2.5 h (5)	65	8
A "	MeLi, Et_3Al	DME:HMP = 10:1 nBuI 10 moles r.t., 1.5 h (5)	78	2
"	MeLi, Bu_3SnCl	DME:HMP = 10:1 nBuI 2 moles r.t., 2 h	63	6
"	MeLi	DME:HMP = 10:1 iPrI 2 moles r.t., 20 h	54	5
	MeLi, Bu_3SnCl	"	50	-

Notes

1) by VPC analysis, unless otherwise stated

2) The cleavage was performed (cf. ref. 3) in presence of $Ø_3CH$ as indicator

3) After addition of Bu_3SnCl (or Et_3Al) the reaction mixture was stirred 15-25 minutes at r.t.

4) 83% by distillation.

5) The enolate was dropped (50-60 minutes) into the alkylating mixture: in all other cases the reverse order of addition was used.

TABLE II

Ketone or derivative	Enolate formation	Alkylation conditions	Alkylation product distribution (I) mono- %	di-%
Cyclopentanone	$Ø_3CLi$	DME CH_3I 10 moles r.t., 0.5 h	51	24
"	$Ø_3CLi$, Et_3Al	DME:HMP = 20:1 CH_3I 10 moles r.t., 1.2 h (5)	67	14
Cholestanone	$Ø_3CLi$, Bu_3SnCl	DME:HMP = 10:1 CH_3I 2.5 moles r.t., 1 h	32 (6)	2
"	$Ø_3CLi$, Et_3Al	DME:HMP = 10:1 CH_3I 12 moles r.t., 25 h	76 (6)	8
"	$Ø_3CLi$	DME CH_3I, 12 moles r.t., 1 h	69 (6)	16
10-Methyl-decal-2-one (trans)	$Ø_3CK$	DME:HMP = 6:1 CH_3I 2 moles r.t., 1 h	47	33
"	$Ø_3CK$, Bu_3SnCl	"	54	5

Notes

6) From the mass spectrum (weighted mixtures of Cholestanone and 2-Methylcholestanone gave parent peaks in the right ratio).