

REGIOCHEMISTRY OF THE THIOENOLATES REACTION WITH UNSATURATED KETONES :
C-VERSUS S-1,4-ADDITION OF A DISUBSTITUTED DITHIOESTER THIOENOLATE.

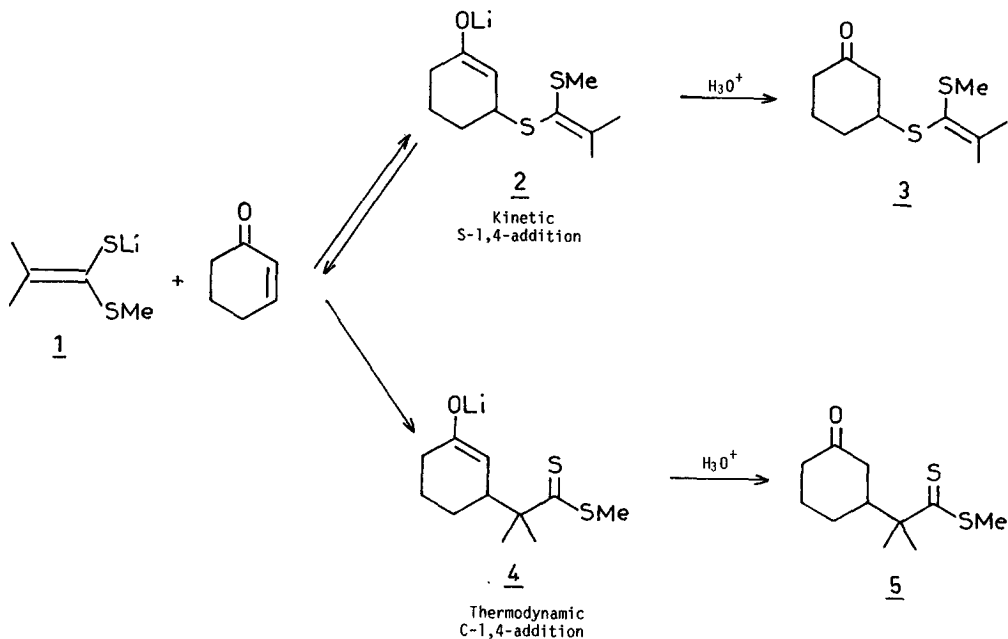
Patrick METZNER* and Rosé RAKOTONIRINA.

Laboratoire de Chimie des Composés Thioorganiques (associé au CNRS), ISMRA, Université de CAEN,
14032 CAEN Cedex, France.

Reaction of the lithium thioenolate of methyl 2-methyldithiopropoate with enones gives kinetic sulphur 1,4-addition or thermodynamic carbon 1,4-addition, with the exception of cyclopent-2-enone which gives kinetic carbon 1,4-addition. In all cases 5-oxodithioesters can be prepared in good yields. No 1,2-addition is observed, confirming the soft nucleophilic character of dithioester thioenolates.

We recently reported ¹ that lithium methyl dithioacetate gives a kinetic 1,4-C-addition with enones, in contrast with the 1,2-mode observed for the analogous oxygen enolates. This promising result, coupled with the versatility of the resulting 5-oxodithioesters, prompted us to examine the scope of this reaction. During this investigation we observed that a disubstituted thioenolate leads to C-or S-1,4-addition, depending on the reaction conditions. Just before we submitted this paper, Bertz and coworkers ² reported the C-1,4-addition of lithium *isopropyl* 2-methyldithiopropoate to cyclopentenones and used it elegantly in synthesis. They also concluded that the presence of two methyl groups α to the thiocarbonyl does not modify the C-*vs* S-reactivity of the dithioester towards cyclopent-2-enone. We wish to report here that other enones behave differently.

Deprotonation of methyl 2-methyldithiopropoate at -78° under aprotic conditions (LDA, THF) gave the colourless and thermally stable thioenolate 1, that was reacted with enones. Let us first consider cyclohex-2-enone and pent-3-en-2-one for which analogous result were observed. At low temperature (-55° : entry 1 and -78°: entry 4), reaction is not complete and, after hydrolysis, we separated from the starting materials two compounds : the predominant oxoketenedithioacetals 3, 6, accompanied by the 5-oxodithioesters 5, 7 (table). This provides evidence for the kinetic sulphur-1,4-addition of a disubstituted thioenolate. Under similar conditions, methyl dithioacetate ¹ and dithiopropoate thioenolates ³ afford carbon conjugate addition. This regiochemistry of the attack of the ambident nucleophile is probably controlled by steric hindrance, though electronic factors may also be involved.



When the reaction mixture is warmed up to -20° (entry 3) or the reaction directly carried out at higher temperatures (-20° : entry 2 ; -30° : entry 5), we isolated fair yields of 5-oxodithioesters **5**, **7**. This shows the reversibility of the reaction : the enolate, *e.g.* **2**, equilibrates to the more stable enolate **4** (-C(=S)-SMe moiety versus =C(SR)-SMe). So far only one exemple⁴ of a reversible thioenolate reaction has been reported : sulfenylation with dimethyl disulphide.

Confirmation of the reversibility was brought by the following experiment. The ketenedithioacetal **3** was deprotonated by LDA in THF at -78° and warmed up to -20° . Hydrolysis afforded mostly dithioester **5** together with some starting material **3** (isolated yield : 72 %).

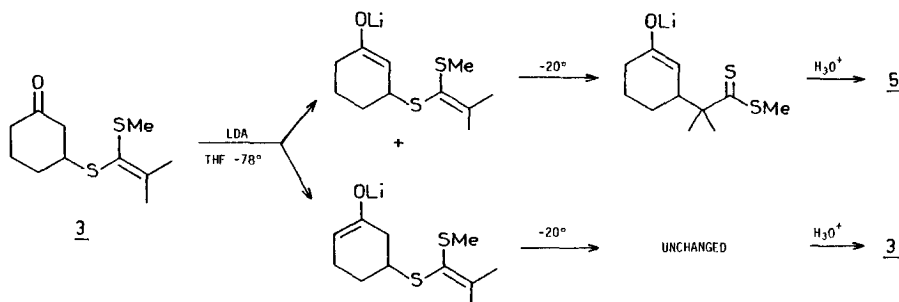
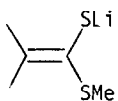
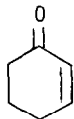
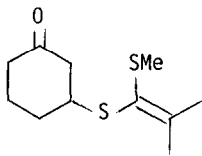
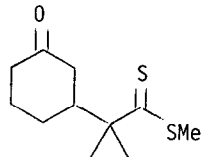
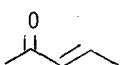
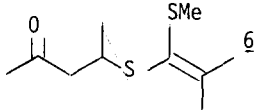
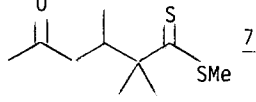
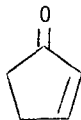
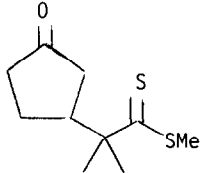


TABLE.

 ADDITION OF  TO UNSATURATED KETONES.

Entry	Enone	Reactions conditions		Addition Ratio		Products
		T °C	Time/min.	Yield	S-add./C-add.	
1		-55	15	66	86 : 14	 <u>3</u>  <u>5</u>
2		-55	15	82	4 : 96	
3		and then -20	15	72	1 : 99	
4		-78	20	39	85 : 15	 <u>6</u>  <u>7</u>
5		-30	20	70	5 : 95	
6		-78	10	45	0 : 100	 <u>8</u>
7		-20	10	70	0 : 100	

This result is in agreement with deprotonation α and α' to the cyclohexanone carbonyl (not totally equilibrated) : the α enolate reverts to the starting thioenolate and enone at -20° to yield the C-addition compound 5 whereas the α' enolate is stable towards retro Michael reaction and gives the starting material 3 after hydrolysis.

Cyclopent-2-enone exhibited a different regioselectivity. At low temperatures (-126° , -94° and -78°) the reaction was not complete and the product was composed of starting materials and of the oxodithioester 8 from C-1,4-addition ; no compound from S-addition was detected. At -20° the compound 8 was isolated with a good yield. So, the kinetic (and thermodynamic ?) reactivity is carbon conjugate addition. The result is similar to the report of Bertz ² for the thioenolate of the corresponding *isopropyl* dithioester.

Thus, kinetically, cyclopent-2-enone behaves differently from cyclohex-2-enone and pent-3-en-2-one which react *via* S-1,4-addition.

It is remarkable that no 1,2-addition is observed here : dithioester enolates are confirmed as soft enolates, ¹ though they are not doubly stabilized carbanions.

On the synthetic point of view, the compounds from C-1,4-addition are obtained easily and bear an interesting tetragonal carbon. ⁵ Their further elaboration via thiophilic addition ^{1,6} will extend the use of dithioester thioenolates as regiocontrolled ketone enolate equivalents suitable for Michael additions.¹

References

- ¹ P. Metzner, *J.C.S. Chem. Comm.*, 1982, 335.
- ² S.H. Bertz, L.W. Jelinski, and G. Dabbagh, *J.C.S. Chem. Comm.*, 1983, 388.
- ³ P. Metzner and R. Rakotonirina, to be published
- ⁴ R.S. Sukhai, R. de Jong, J. Meijer, and L. Brandsma, *Recl. Trav. Chim. Pays-Bas*, 1980 99, 191.
- ⁵ S.F. Martin, *Tetrahedron*, 1979, 36, 419.
- ⁶ L. Léger and M. Saquet, *Bull. Soc. Chim. Fr.*, 1975, 657 ; S. Masson, M. Saquet, and A. Thuillier, *Tetrahedron*, 1977, 33, 2949 ; P. Gosselin, S. Masson, and A. Thuillier *Tetrahedron Letters*, 1978, 2717 ; *J. Org. Chem.*, 1979, 44, 2807.

(Received in France 27 June 1983)