

Kinetic 1,4-Addition of a Dithioacetate Enolate to α -Enones

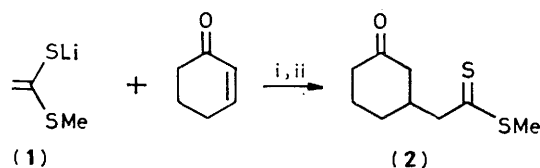
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Lithium methyl dithioacetate reacts with enones at low temperature *via* a selective 1,4-C-addition to give 5-oxodithioesters; further elaboration by thiophilic addition and alkylation furnishes masked 1,5-dicarbonyl compounds.

Dithioesters have recently been introduced as synthetically useful reagents,¹⁻⁵ but studies of their metal enolates have been limited to reactions with alkyl halides,⁶ giving sulphur alkylation, and with some aldehydes,^{3,7} yielding aldols by carbon addition. No report deals with their behaviour towards Michael acceptors. Assuming that dithioester enolates are soft nucleophiles, as compared with carbonyl enolates, 1,4-addition to the conjugated system of α -enones should be favoured⁸ relative to 1,2-addition. The expected reacting site of the ambident nucleophile, whether carbon or sulphur, was unknown.⁹

I report that selective carbon 1,4-addition is observed for the lithium thioenolate (**1**) (Scheme 1). Deprotonation of methyl dithioacetate with lithium di-isopropylamide in tetrahydrofuran (THF), followed by treatment with various enones at low temperature and quenching with aqueous ammonium chloride gave 5-oxodithiocarboxylates (Table 1).[†] Side reactions were not observed. Control experiments at low conversion rates indicated that this process was kinetically controlled. Its mode contrasts with the reported 1,2-addition of lithium carboxylic ester enolates with enones under comparable conditions.¹⁰ Dithioesters are therefore one of the rare examples of carbonyl derivatives¹¹ whose enolates give Michael additions, without being doubly stabilized, as for malonates.



Scheme 1. Reagents: i, tetrahydrofuran (THF), -45°C , 15 min; ii, NH_4Cl , H_2O .

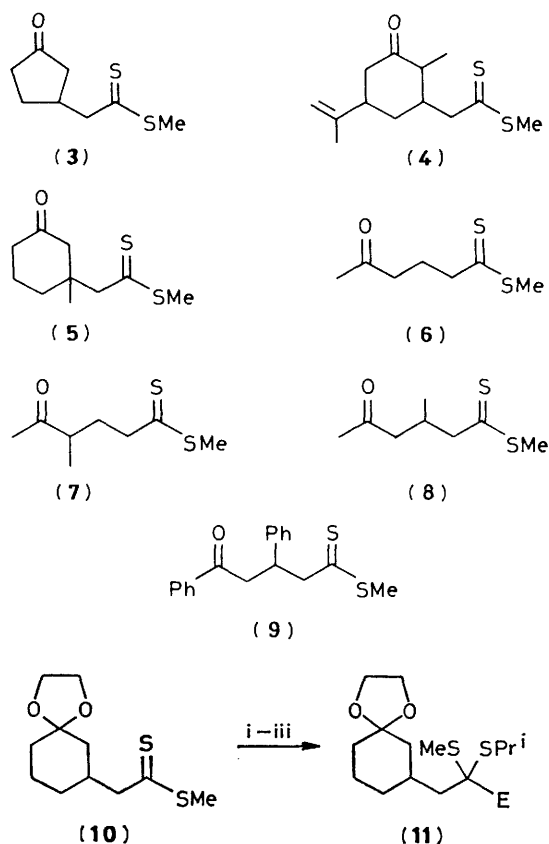
Table 1. Addition of lithium methyl dithioacetate to α -unsaturated ketones.

Enone	$T/^\circ\text{C}^a$	Time/ min	Product %	Yield ^b
Cyclopent-2-enone	-50	15	(3)	78
Cyclohex-2-enone	-45	15	(2)	86
(-)-Carvone	-30	10	(4)	70 ^c
3-Methylcyclohex-2-en-1-one	-10	30	(5)	52
But-3-en-2-one	-98	15	(6)	30
3-Methylbut-3-en-2-one	-55	15	(7)	73
Pent-3-en-2-one	-60	15	(8)	74
Chalcone	-78	10	(9)	73

^a Deprotonation of methyl dithioacetate has been carried out at the same temperature. ^b Yield of the isolated product. ^c Mixture of two stereoisomers in a 3:1 ratio.

[†] All new compounds (**2**)–(**11**) had satisfactory elemental analyses and gave the expected spectroscopic data (i.r., u.v., and ^1H and ^{13}C n.m.r.).

The readily prepared 5-oxodithiocarboxylates (**2**)–(**9**) are 1,5-dicarbonyl precursors with functional differentiation as shown by the following reactions (Scheme 2). Selective protection of the carbonyl moiety in (**2**) was carried out quantitatively by acetalization with ethylene glycol under acidic conditions [$\text{Me}(\text{C}_6\text{H}_4)\text{SO}_3\text{H}$ or $\text{NC}_5\text{H}_5^+\text{Me}(\text{C}_6\text{H}_4)\text{SO}_3^-$, benzene, reflux]. Thiophilic addition¹² of isopropylmagnesium bromide to the dithioester (**10**) gave a dithioacetal carbanion, which could be alkylated by various electrophiles (E) to afford protected 1,5-dicarbonyl compounds of potential synthetic use (Table 2).



Scheme 2. Reagents and conditions: i, Pr^iMgBr , THF, -17°C , 20 min; ii, E^+ , -17°C , 1–4 h; iii, NH_4Cl , H_2O .

Table 2. Thiophilic addition and alkylation (**10**) \rightarrow (**11**).

Electrophile	% Yield ^a
H_2O	87
MeI	78
EtBr^b	85
Allyl Br	77

^a Isolated product. ^b 6 mol. equiv. of hexamethylphosphoramide were added.

Thus, the overall scheme (1) → (11) makes possible the 1,4-addition of a regiocontrolled ketone enolate equivalent, by use of the synthon $^{-}\text{CH}_2\text{-C(=O)}^{-}$?

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