Unprecedented Reaction of a Thiocarbonyl Ylide with Carbonyl Compounds: a Novel Synthesis of 1,3-Oxathiolanes

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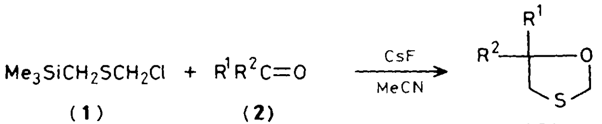
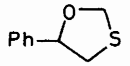
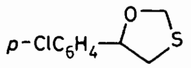
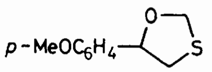
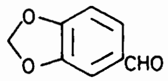
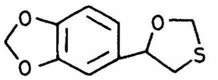
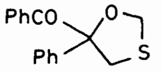
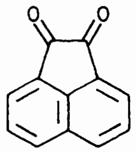
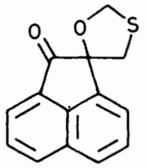
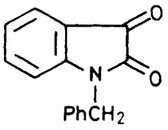
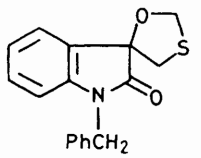
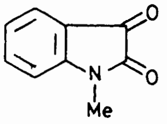
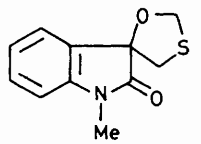
Thioformylium methylide, readily generated from chloromethyl trimethylsilylmethyl sulphide with the aid of fluoride ion, reacts with carbonyl compounds such as aldehydes, α-diketones, and α-oxo amides to give the corresponding 1,3-oxathiolanes in good yields.

Thiocarbonyl ylides and related ylides are important and interesting 1,3-dipolar reagents from both synthetic and theoretical points of view.[1] However the reaction of thiocarbonyl ylides with heterodipolarophiles has not been described hitherto, though activated alkenes and alkynes readily react to give hydrogenated thiophenes. During studies on the application of thiocarbonyl ylides to organic synthesis,[2] we have found that chloromethyl trimethylsilylmethyl sulphide (**1**) readily reacts with carbonyl compounds under mild conditions to afford the corresponding 1,3-oxathiolane derivatives which are important as intermediates in organic synthesis, as radioprotectants, and for their biological activities[3] [reaction (1)]. To our knowledge, this constitutes not only an unprecedented example of the addition of a thiocarbonyl ylide synthon to the carbonyl groups of aldehydes and ketones, but also a new synthetic method for 1,3-oxathiolanes.[3]



(1) (2) (3) (1)

Table 1. Reaction of the sulphide (**1**) with carbonyl compounds[a]

Entry	Carbonyl compound	Time / h	Product (% Yield)[b]	
1	PhCHO	94		(35)
2	*p*-ClC$_6$H$_4$CHO	194		(54)
3	*p*-MeOC$_6$H$_4$CHO	71		(83)
4		192		(49)
5	PhCOCOPh	38		(61)
6		19		(76)
7		22		(86)
8		44		(66)

[a] Reaction was carried out with 2 equiv. of (**1**) and caesium fluoride at room temperature in acetonitrile. [b] Yield after isolation by t.l.c. All the products gave satisfactory n.m.r., i.r., and mass spectra.

Reactions of the sulphide (**1**) with carbonyl compounds (**2**) proceed very smoothly in the presence of dried caesium fluoride in acetonitrile at room temperature to give the corresponding [3 + 2] cycloadducts, the 1,3-oxathiolanes (**3**), in high yield. Representative results are listed in Table 1. Among the various carbonyl compounds studied, α-diketones and α-oxo amides are especially good acceptors of the parent thiocarbonyl ylide synthon. In particular, cyclic diketones and oxoamides such as acenaphthenequinone and isatin derivatives reveal high reactivity towards (**1**). Simple ketones and oxo esters do not undergo the reaction under the present reaction conditions. However reactions with aromatic aldehydes proceed smoothly at room temperature to give the corresponding 1,3-oxothiolanes in moderate to high yield. Acetonitrile is the most suitable solvent for the reaction.

Although further study is required before the mechanistic details can be fully understood, the results are compatible with a [3 + 2] cycloaddition of the *in-situ*-generated thiocarbonyl ylide, similar to the reaction with activated alkenes. The synthetic utility is apparent from the novelty of this route to otherwise inaccessible 1,3-oxathiolanes. The present methodology might be applicable to the synthesis of other heterocyclic compounds containing two or more heteroatoms; this is currently under investigation.

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