A General, High Yield Synthesis of α-Oxoketene Dithioacetals and *O*-(1-Alkoxy-2,2-dialkyl)vinyl *S*-Alkyl Dithiocarbonates from Carboxylic Esters

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α-Oxoketene dithioacetals (**5**) and *O*-(1-alkoxy-2,2-dialkyl)vinyl *S*-alkyl dithiocarbonates (**4**) were prepared in high yields from carboxylic esters by the reaction of their lithium enolates (**2**) with carbon disulphide at −78 °C followed by alkylation.

The conjugated ketene dithioacetals contain a masked ester functionality and hold considerable potential as substrates for sequential C–C bond forming reactions and functional group manipulation. α-Oxoketene dithioacetals, derived from ketones, have previously been employed in the synthesis of heterocycles,[1] Diels-Alder dienes,[2] and in the indirect synthesis of α-tertiary alkylated ketones.[3] Aromatic (or heteroaromatic) annelation involving their reaction with Grignard and Reformatsky reagents has been shown to be of general applicability.[4] On the other hand, α-oxoketene dithioacetals derived from carboxylic esters have received little attention and few are known.

The ketones can easily be converted to α-oxoketene dithioacetals by reaction with carbon disulphide in the presence of a base,[1b,3,5] generally sodium hydride,[6] followed by alkylation. However, the reaction of simple esters with the sodium hydride–carbon disulphide–methyl iodide combination has been reported to yield the products which arise from Claisen condensation.[6] There is one report which describes the preparation of some conjugated ketene dithioacetals by the use of non-nucleophilic bases like lithium di-isopropylamide (LDA), lithium dicyclohexylamide (LCA), and lithium hexamethyldisilazide (LHDS).[7] Significant amounts of condensation products and low yields of the desired product were obtained from ester and lactone when LDA was used as base.

We have developed and report here a method for the high yield preparation of *O*-(1-alkoxy-2,2-dialkyl)vinyl *S*-alkyl dithiocarbonates (4) and α-oxoketene dithioacetals (5) from carboxylic esters having one and two α-hydrogen atoms, respectively, adapting a known procedure for the generation of lithium enolates.[8] The key step is the formation of lithium dithiocarbonate (3) by the reaction of lithium enolates (2), generated with LDA, with carbon disulphide at −78 °C. This is the first example of nucleophilic attack by the oxygen of the enolate ion on carbon disulphide.

In a typical experiment, isopropyl isobutyrate (**1b**) (1 equiv.) was added to LDA (1 equiv.) in tetrahydrofuran (THF) for 15 min at 0 °C. The mixture was stirred for 0.5 h and the contents were then cooled down to −78 °C. Carbon disulphide (3 equiv.) was added for 0.5 h and the mixture stirred for an additional 0.5 h followed by addition of methyl iodide (3 equiv.) for 5 min. The contents were then allowed to warm to room temperature and stirred for one day. The reaction was worked up by adding water and extracting with ethyl acetate. Evaporation of the solvent after drying over Na_2SO_4 furnished crude product which was distilled to give

Table 1. Preparation of *O*-(1-alkoxy-2,2-dialkyl)vinyl *S*-alkyl dithiocarbonates (**4a**—**g**) from carboxylic esters (**1a**—**g**).[a]

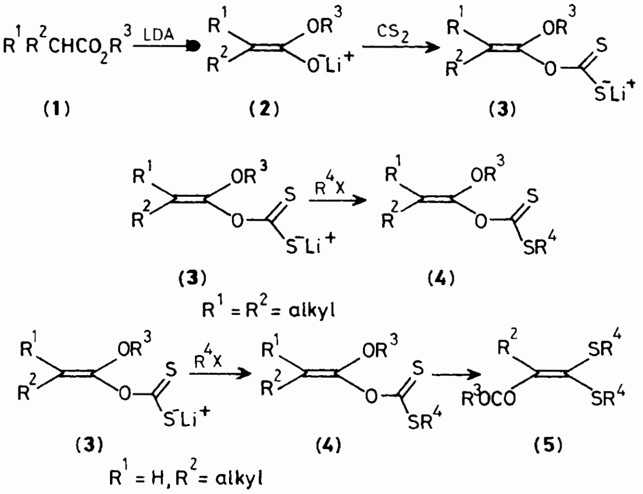
	Substrate/product					Product[b]	
	R^1	R^2	R^3	R^4	X	Yield[c]/%	B.p./°C[d]
(**a**)	Me	Me	Me	n-C_3H_7	Br	84	96—100
(**b**)	Me	Me	*iso*-C_3H_7	Me	I	91	89—93
(**c**)	Me	C_2H_5	Me	C_2H_5	Br	89	97—101
(**d**)	C_2H_5	C_2H_5	C_2H_5	Me	I	86	113—118
(**e**)	C_2H_5	n-C_4H_9	n-C_4H_9	C_2H_5	Br	93	142—147
(**f**)	$(CH_2)_4$		C_2H_5	n-C_3H_7	Br	92	126—132
(**g**)	$(CH_2)_5$		*iso*-C_3H_7	C_2H_5	Br	95	134—139

[a] All the reactions were carried out on a 0.03 molar scale. [b] Satisfactory analytical and spectral data were obtained for all products. [c] Isolated yields. [d] At 3 mm Hg.

Table 2. Preparation of α-oxoketene dithioacetals (**5h**—**m**) from carboxylic esters (**1h**—**m**).[a]

	Substrate/product					Product[b]	
	R^2	R^3	R^4	X	Time/days	Yield[c]/%	B.p./°C[d]
(**h**)	Me	Me	C_2H_5	Br	1	87	104—108
(**i**)	C_2H_5	C_2H_5	Me	I	1	82	106—112
(**j**)	n-C_3H_7	Me	C_2H_5	Br	2	83	102—106
(**k**)	n-C_4H_9	C_2H_5	Me	I	1	80	122—127
(**l**)	n-C_8H_{17}	C_2H_5	Me	I	1	84	153—157
(**m**)	Ph	Me	C_2H_5	Br	2	79	Decomposed

[a] All the reactions were carried out on a 0.03 molar scale. [b] Satisfactory analytical and spectral data were obtained for all products. [c] Isolated yields. [d] At 3 mm Hg.



pure *O*-(1-isopropoxy-2,2-dimethyl)vinyl *S*-methyl dithiocarbonate (**4b**) in 91% yield. Table 1 shows various compounds prepared by this method. The crude products obtained, in all cases, were almost pure as revealed by ^{1}H-n.m.r. spectra and were purified by distillation.

Similarly, when the carboxylic esters having two α-hydrogen atoms were subjected to almost identical conditions, the products obtained after the usual work-up and distillation were characterized as α-oxoketene dithioacetals (**5**). In the case of methyl n-valerate (**1j**), after work-up for 24 h, the crude liquid obtained was analysed to be a mixture of (**4j**) (50%) and (**5j**) (50%) by the ^{1}H-n.m.r. spectrum. However, when the reaction period was extended to 2 days no trace of (**4j**) was obtained. Table 2 shows the α-oxoketene dithioacetal derivatives prepared accordingly.

The formation of (**4**) from carboxylic esters can be explained by the reaction of lithium enolates (**2**) with carbon disulphide to furnish (**3**), which is stable at −78 °C, to be trapped with alkyl halides. In one experiment, the reaction mixture, after addition of carbon disulphide at −78 °C, was warmed to −20 °C and stirred for 0.5 h followed by addition of alkyl halide and further stirring for one day. The ^{1}H-n.m.r. spectrum of the crude product obtained after usual work-up indicated the absence of the desired product and the presence of a significant amount of condensation products suggesting that (**3**) is not stable at that temperature. The formation of α-oxoketene dithioacetals (**5**) can be explained through the intermediacy of (**4**), but the exact nature of the conversion of (**4**) to (**5**) is not clear at this stage. Detailed mechanistic studies and the extension of the work to other substrates are in progress.

In conclusion, a general, high yield synthesis of α-oxoketene dithioacetals and hitherto unknown *O*-(1-alkyl-2,2-dialkyl)vinyl *S*-alkyl dithiocarbonates is described. The fact that enolate ions attack carbon disulphide through oxygen will be useful for a better understanding of the reaction of carbon disulphide with active methylene compounds.

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References

1 (a) M. Augustin and Ch. Groth, *J. Prak. Chem.*, 1979, **321**, 215; (b) M. Augustin, Ch. Groth, H. Kristen, K. Peseke, and Ch. Wiechmann, *ibid.*, 1979, **321**, 205; (c) J. P. Marino and J. L. Kostusyk, *Tetrahedron Lett.*, 1979, 2489 and 2493.

2 S. Masson and A. Thuillier, *Tetrahedron Lett.*, 1980, 4085.

3 E. J. Corey and R. H. K. Chen, *Tetrahedron Lett.*, 1973, 3817.

4 A. Datta, H. Ila, and H. Junjappa, *Tetrahedron Lett.*, 1988, 497; M. P. Babu, D. Pooranchand, H. Ila, and H. Junjappa, *ibid.*, 1988, 501; A. K. Gupta, H. Ila, and H. Junjappa, *ibid.*, 1987, 1459; M. P. Balu, G. Singh, H. Ila, and H. Junjappa, *ibid.*, 1986, 117.

5 S. M. S. Chauhan and H. Junjappa, *Tetrahedron*, 1976, **32**, 1779.

6 I. Shahak and Y. Sasson, *Tetrahedron Lett.*, 1973, 4207.

7 R. K. Dieter, *J. Org. Chem.*, 1981, **46**, 5031.

8 C. Ainsworth, F. Chen, and Y.-N. Kuo, *J. Organomet. Chem.*, 1972, **46**, 59.