Stereoselective Reduction of α-Alkoxycarbonylketene Dithioacetals with the Use of $Me_2Cu(CN)Li_2$

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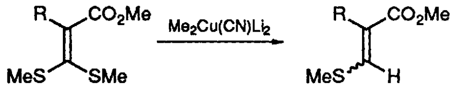
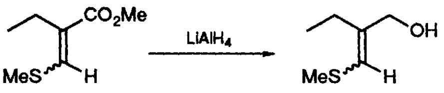
α-Alkoxycarbonylketene dithioacetals (**1**) were smoothly reduced by the higher order cyanocuprate $Me_2Cu(CN)Li_2$ at −20 °C to the corresponding vinyl sulphides (**2**) in high yields, with high stereoselectivity and generality.

The use of organocopper reagents has played a significant synthetic role in forming carbon–carbon bonds. Organocuprates formally act as nucleophiles in substitution reactions and Michael additions.[1] These reactions have been extensively studied, and high regio- and/or stereo-selectivities have been reported.[2] Organocuprates may also serve as reductants and the 'metal–halogen exchange reaction' is representative.[3] This process has not received much attention, since it is regarded as an unwanted side reaction, but it could be a useful synthetic tool if it proceeded stereoselectively.

We now report the stereoselective reduction of α-alkoxycarbonylketene dithioacetals (**1**), prepared according to an established method,[4] to the corresponding vinyl sulphides (**2**) (equation i). Although the addition–elimination sequence of enones bearing leaving groups at their β-position has been widely explored,[5] examples of reduction of enone systems are rare, being limited to a few special cases.[5,6] As shown in Table 1, α-alkoxycarbonylketene dithioacetals of wide structural varieties react with the higher order cyanocuprate $Me_2Cu(CN)Li_2$ and are converted stereoselectively† to the corresponding sulphides (**2**)‡ in high yields.



(**1**) (**2**) (i)



(**2a**) (**3a**) (ii)

The present reduction is in marked contrast to the reactions of α-oxoketene dithioacetals with cuprates which proceed by an addition–elimination sequence.[5] Because both reactions were carried out under similar conditions, this contrast seems to be especially significant. Although the cuprate stoichiometry was not determined accurately, two moles of the cuprate are enough for completion, and over-reduction was not observed in any reaction. When one mole of the cuprate was used, the ^1H NMR spectrum of the crude reaction mixture using (**1a**) showed (**1a**)/(**2a**) = 48/52, suggesting a single electron transfer mechanism.[7] Lower order cyanocuprates were not effective in this reaction. With regard to the

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† In a typical example, using (**1a**), to the solution of the cuprate in ether, prepared by adding ethereal methyl-lithium (1.1 M; 3.6 ml) to a suspension of CuCN (2 mmol) in ether (10 ml) at −20 to 0 °C, was added by syringe a solution of the dithioacetal (**1a**) (1 mmol) in ether (2 ml). The mixture was stirred at −20 °C for 30 min. Extraction with ethyl acetate after quenching at −20 °C with saturated aqueous NH_4Cl, washing with saturated aqueous $NaHCO_3$, drying over $MgSO_4$, and evaporation afforded the crude product which was chromatographed on a basic alumina column (hexane–ethyl acetate, 35 : 1 as eluent) to afford the pure sulphide (**2a**) in 94% yield: b.p. 120 °C at 6 mmHg; IR (film), ν_{max} 1700s, 1590s, 1305s, 1225s, 1120s, 750s; ^1H NMR ($CDCl_3$) δ 1.01 (t, *J* 7.6 Hz, 3H), 1.28 (t, *J* 7.2 Hz, 3H), 2.31 (q, *J* 7.6 Hz, 2H), 2.40 (s, 3H), 4.17 (q, *J* 7.2 Hz, 2H), 7.38 (s, 1H); satisfactory elemental analyses were obtained.

‡ The vinyl sulphides (**2**) are hitherto unknown except (**2d**).[8] Thus, the present reaction should provide a new synthetic route to vinyl sulphides (**2a**—**c**) having an alkoxycarbonyl group, which could not be obtained from (**2d**).

Table 1. Reduction of α-alkoxycarbonylketene dithioacetals (**1**).[a]

	Product		
Substrate (**1**)		Yield[b] (%)	*E*/*Z*[c]
a; R = Et	(**2a**)	94	88/12
		0[d]	—
b; R = Allyl	(**2b**)	95	93/7
c; R = Ph	(**2c**)	97	85/15
d; R = H	(**2d**)	55[e]	97/3

[a] All reactions were carried out at −20 °C for 30 min unless otherwise noted (see text). [b] Isolated yield by column chromatography. [c] Isomer ratio was determined by ^{1}H NMR integration of the unsaturated proton of the crude product. [d] Reduction was attempted using MeCu(CN)Li instead of Me$_2$Cu(CN)Li$_2$ at −20 °C for 1 h. [e] Tetrahydrofuran was used as solvent.

stereochemistry around the carbon–carbon double bond of the products, the unsaturated proton of the major isomer resonates at > 0.5 ppm to lower field than that of the minor isomer in all cases. The major isomer of (**2d**) was determined to be the (*E*)-compound from its coupling constant (14.8 Hz). The product (**2a**) was reduced to (**3a**)§ (equation ii) and a ^{1}H nuclear Overhauser enhancement (NOE) experiment on the major isomer of (**3a**) showed (*E*)-stereochemistry around the double bond (^{1}H NOE for 1-H, but none for 3-H on irradiation of the unsaturated proton; ^{1}H NOE for the unsaturated proton but none for 3-H on irradiation of 1-H). Because many factors are involved it seems premature to discuss the stereoselectivity of this reaction, although it makes it a valuable synthetic tool.

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§ Compound (**3a**) is known, although its synthesis is somewhat tedious.[9]

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