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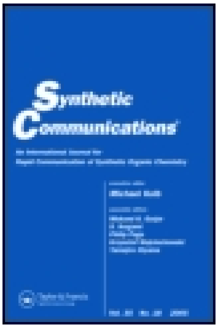

Synthetic Communications: An International Journal for Rapid Communication of Synthetic Organic Chemistry

Publication details, including instructions for authors and subscription information:
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Sulfhydrolysis of Acyl Ketene Dithioacetals: A Convenient Synthesis of β-Oxodithioesters

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Published online: 17 Sep 2007.

To cite this article: Satheesh K. Nair & C. V. Asokan (1999) Sulfhydrolysis of Acyl Ketene Dithioacetals: A Convenient Synthesis of β-Oxodithioesters, Synthetic Communications: An International Journal for Rapid Communication of Synthetic Organic Chemistry, 29:5, 791-798, DOI: 10.1080/00397919908086034

To link to this article: http://dx.doi.org/10.1080/00397919908086034

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SYNTHETIC COMMUNICATIONS, 29(5), 791-798 (1999)

SULFHYDROLYSIS OF ACYL KETENE DITHIOACETALS: A CONVENIENT SYNTHESIS OF β-OXODITHIOESTERS

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Abstract: β-Oxodithioesters are obtained in good yields from acyl ketenedithioacetals on treatment with hydrogen sulphide in the presence of boron trifluoride etherate in refluxing dioxane

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Solvolysis of functionalized ketenedithioacetals catalysed by Lewis or protic acid provide a convenient method for the synthesis of the respective substituted esters or thiolesters. For instance α-oxoketenedithioacetals have been transformed in to α,β-unsaturated esters[1] and thiolesters[2] by reductive as well as alkylative carbonyl group transposition under acid catalysed solvolysis conditions. Alkenoyl ketenedithioacetals on treatment with $HgCl_2$ in methanol afford the

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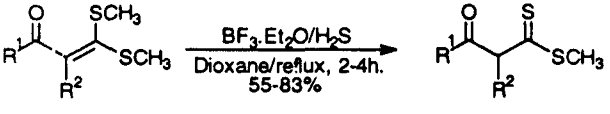
corresponding γ,δ-unsaturated β-ketoesters.[3] We have recently shown that Lewis acid assisted partial hydrolysis of α-oxoketenedithioacetals afford β-oxo-thiolesters.[4] Since esters and thiolesters could be easily derived from ketenedithioacetal functionality, we anticipated that a similar transformation to the corresponding dithioesters could be achieved by acid catalysed sulphydrolysis of functionalized ketenedithioacetals. β-Oxodithioesters are valuable three carbon synthones useful in the synthesis of a veriety of heterocycles.[5] They are also useful in the synthesis of α,β-unsaturated ketones having heteroatom substituants at the β-position.[6] β-Oxodithioesters are usually prepared by the thiocarbonylation[7] of active methylene ketones with dialkyl trithiocarbonates or chlorodithioformates.[8,9] Since a large number of α-oxoketenedithioacetals[10] with diverse structural features are readily available, a method starting from them would provide access to β-oxo-dithioesters with a high variety of substitution patterns.

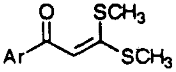
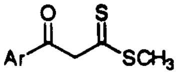
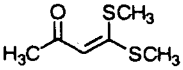
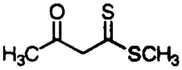
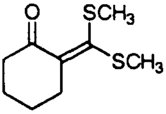
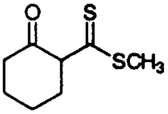
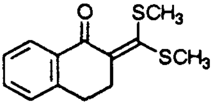
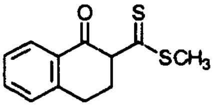


1 2

Scheme 1

When α-oxoketenedithioacetals **1** were treated with hydrogen sulphide in refluxing dioxane in the presence of boron trifluoride etherate for 2-4h. the corresponding substituted dithiocarboxylates **2** could be isolated in good yields (Scheme 1).

Table 1: Methyl β-oxodithiocarboxylates 2 prepared

1,2	Substrate	Product	Yield (%)
			
a	Ar =	C_6H_5	67
b		$4\text{-}CH_3C_6H_4$	71
c		$4\text{-}ClC_6H_4$	83
d		$4\text{-}CH_3OC_6H_4$	57
e		2-naphthyl	55
f		2-thienyl	68
g		$4\text{-}BrC_6H_4$	63
h			67
i			63
j			81

This method has been found to be general to a variety of substituted ketenedithioacetals and several substituted β-oxodithioesters could be synthesised (Table 1). In addition to benzoyl ketenedithioacetals, naphthoyl and thienoyl ketenedithioacetals (**1e** and **1f**) also underwent smooth conversion to the respective dithioesters. Simple acylketenedithoacetal **1h** gave the methyl

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dithioacetate in 67% yield. The ketenedithioacetals from cyclic ketones **1i** and **1j** also gave the respective β-oxodithioesters **2i** and **2j** in good yields.

The reaction apparently involve the complexation of the carbonyl group of the α-oxoketenedithioacetal with the Lewis acid, thus activating the β-carbon atom towards the nucleophilic attack of hydrogen sulphide. However the ketenedithioacetals derived from doubly activated active methylene compounds such as diethyl malonate, ethyl cyanoacetate and malononitrile did not give the expected dithioesters under these conditions. Since α-oxoketenedithioacetals can be easily prepared from any active methylene ketones, the present method would provide an attractive alternative for the synthesis of β-oxodithioesters.

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Experimental

Melting points are uncorrected and were taken on a Buchi-530 melting point apparatus. Infrared spectra were measured with a Shimadzu IR-470 spectrometer and are given as cm^{-1}. Proton NMR spectra were recorded in $CDCl_3$ on a Jeol (90 MHz) or a Bruker WM 300 (300 MHz) spectrometer. Carbon-13 NMR spectra were recorded in $CDCl_3$ on a Jeol (22.4 MHz) or a Bruker WM 300 (75.5 MHz). Chemical shifts are reported in parts per million (ppm) downfield from internal tetramethyl silane. Coupling constants *J* are given in Hz. Electron impact mass spectra were obtained on a Finnigen-Mat 312 instrument.

Preparation of β-Oxodithioesters 2a-j. α-Oxoketenedithioacetals **1** (10 mmol) were taken in dioxane and added 0.13 mL (10mmol).boron trifluoride etherate. The reaction mixture was either stirred at room temperature or refluxed for two to four hours while bubbling hydrogen sulfide. After neutralisation with dilute sodium bicarbonate solution, the mixture was extracted with CH_2Cl_2 , dried, evaporated and the crude dithioesters **2** obtained were purified by column chromatography over silica gel using hexane as the eluent.

S-Methyl 3-oxo-3-phenyl propanedithioate[8] **2a** Obtained as yellow crystals, mp. 58-59 (lit. mp. 55-56°C[8]), yield 67%(1.40g), by the reaction of the ketene-dithioacetal **1a** with hydrogen sulphide in refluxing dioxane in presence of boron trifluoride etherate for 3h.. m/z(EIMS) 210(M^+, 49.9%), 163(100%), 105(90.4%).

S-Methyl 3-oxo-3-(4-methylphenyl)propanedithioate[8] **2b** Obtained as yellow crystals, mp 55-56°C (lit. mp. 54-55°C[8]), yield 71%(1.60g), by the reaction of the ketenedithioacetal **1b** with hydrogen sulphide in refluxing dioxane in presence of boron trifluoride etherate for 2h.

S-Methyl 3-oxo-3-(4-chlorophenyl)propanedithioate[8] **2c** Obtained as yellow crystals, mp 75-76°C (lit. mp. 70-71°C[8]), yield 83%(2.00g), by the reaction of the ketenedithioacetal **1c** with hydrogen sulphide in refluxing dioxane in presence of boron trifluoride etherate for 2.5h.. M/z (EIMS) 244(M^+, 39.4%), 197(85.5%), and 139(100%).

S-Methyl 3-oxo-3-(4-methoxyphenyl)propanedithioate **2d** Obtained as yellow crystals, mp 66-67°C yield 87%(1.37g), by the reaction of the ketenedithioacetal **1d** with hydrogen sulphide in refluxing dioxane in presence of boron trifluoride etherate for 3 h.. ^1H NMR (90MHz, $CDCl_3$) δ= 2.6(s, 3H, SCH_3), 3.9(s, 3H, OCH_3), 6.95(s, 1H, vinylic), 6.96(d, 2H, J = 9Hz), 7.9(d, 2H J = 9Hz)ppm. IR (KBr); ν = 1600, 1590, 1500, 1210 cm^{-1}.

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S-Methyl 3-oxo 3-naphthylpropanedithioate **2e** Obtained as yellow crystals, mp 98-99°C, yield 55% (1.43g), by the reaction of the ketenedithiactal **1e** with hydrogen sulphide in refluxing dioxane in presence of boron trifluoride etherate for 4h.. ^{1}H NMR (300MHz, CDCl$_3$) δ=2.66 (s, 1H, SCH$_3$), 7.08 (s, 1H, vinylic), 7.51-7.55 (m 2H, arom), 7.82-7.92 (m, 4H, arom) 8.44(s, 1H, arom), 15.17(s, 1H, arom) ppm ^{13}C NMR δ = 14.61(SCH$_3$), 108.73(vinylic), 123.23, 127.31, 128.23, 128.46, 129.67, 169.59(arom),. 217.51(C=S) ppm. IR (KBr); ν = 1600, 1550, 1240 cm^{-1}

S-Methyl 3-oxo-3-thienylpropanedithioate[8] **2f** Obtained as yellow crystals, mp 53-54°C(lit. mp. 50-51°C), yield 68%(1.46g) by the reaction of the ketenedithioacetal **1f** with hydrogen sulphide in presence of boron trifluoride etherate in refluxing dioxane for 4hours.

*S-Methyl 3-oxo-3-(4-bromophenyl)propanedithioate.***2g** Obtained as yellow crystals, mp 88-89°C, yield 63% (1.81g), by the reaction of the ketenedithioacetal **1g** with hydrogen sulphide in refluxing dioxane in presence of boron trifluoride etherate for 2h.

^{1}H NMR (90MHz,CDCl$_3$) δ=2.5(s,3H,SCH$_3$), 6.89(s,1H,vinylic)), 7.5(m,4H, arom.) ^{13}C NMR δ=17.09(SCH$_3$), 107.37,(vinylic) 126.31, 127.84, 131.78, 132.89,(arom); 167.00, (C=O); 217.16(C=S) ppm. IR(KBr); ν = 1580, 1470, 1410, 1230cm^{-1}

S-Methyl 3-oxobutanedithioate[8] **2h** Obtained as a red viscous liquid, yield 67%(1.00g), by the reaction of the ketenedithioacetal **1h** with hydrogen sulphide in presence of boron trifluoride etherate in dioxane at 60°C for 3.5 hours.

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S-Methyl cyclohexanone-2-dicarboxylate[8] **2i** Obtained as a reddish-yellow viscous liquid, yield 63% (1.18g), by the reaction of the ketenedithioacetal **1i**. with hydrogen sulphide in presence of boron trifluoride etherate in dioxane at 60°C for 4 hours.

Acknowledgements: SKN thanks UGC for a Junior Research Fellowship. We thank directors of the Regional Sophisticated Instrumentation Centres at IIT Madras, NEHU Shillong and CDRI Lucknow for providing spectral data.

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