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Reactions of 2-acyl-1,3-dithianes with α,β-unsaturated ketones: Simple preparation of cyclohexendione monoacetals

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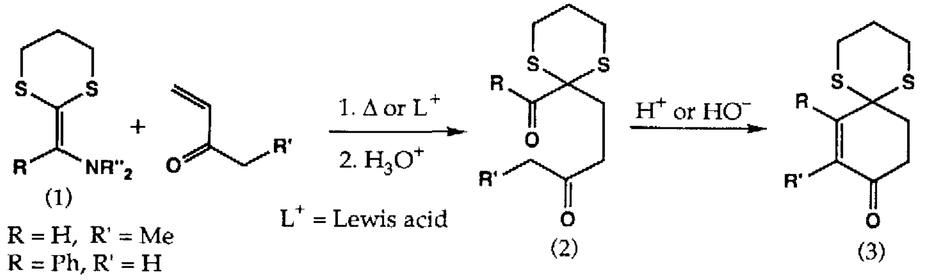
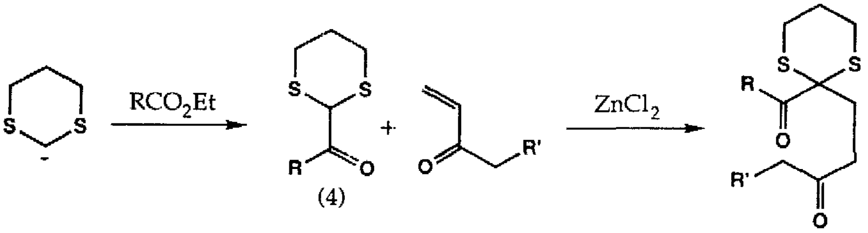
2-Acyl-1,3-dithianes undergo efficient Lewis acid-catalysed addition to α,β-unsaturated ketones giving δ-diketones which suffer intramolecular aldol reaction to produce cyclohex-2-en-1,4-dione monoacetals and/or cyclohex-3-en-1,2-dione monoacetals.

Recently we have reported the Lewis acid-mediated addition of α-aminoketene dithioacetals (1)[3] to α,β-unsaturated ketones to give δ-diketones(2) after hydrolytic work-up[4]. These diketones undergo intramolecular aldol reaction under acidic or basic conditions to give the interesting cyclohex-2-en-1,4-dione monodithioacetals (3) in up to quantitative yields (Scheme 1)[4,5]. Cyclohexendione monoacetals have potential as synthetic building blocks – they readily undergo enolate, conjugate addition, and cycloaddition chemistry – but their synthesis is limited in generality to proton or aryl substituents at position 2 of the products by the difficulty of preparation of alkyl α-aminoketene dithioacetals. We are therefore pleased to report that 2-acyl-1,3-dithianes (4) also undergo Lewis acid-catalysed addition to enones to give analogous δ-diketones suitable for cyclisation (Scheme 2).



Scheme 1

Zinc chloride proved to be a highly efficient mediator of the reaction between acyldithianes and enones. While simple deprotonation of acyldithiane followed by addition of enone is not effective, use of zinc chloride and two or three equivalents of enone provided a very clean and general reaction at room temperature, up to quantitative yields of δ-diketones being obtained (Table 1). Interestingly, under these conditions no reaction could be obtained using 2-benzoyl-1,3-dithiane; this method is therefore complementary to our earlier α-aminoketene dithioacetal route[4,5].



Scheme 2

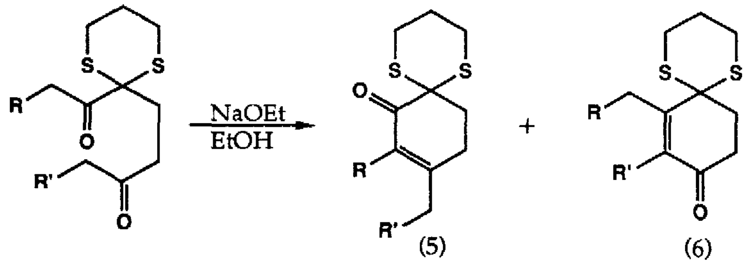
Table 1. Reactions of acyl dithianes with enones (Scheme 2)[6]

Entry	R	R′	Time / days	Yield / %
a	H	CH_3	3	77
b	CH_3	CH_3	1	75
c	CH_3	CH_3CH_2	2	74
d	CH_3	$CH_3CH_2CH_2$	1	75
e	CH_3	OCH_3	7	24
f	CH_3CH_2	CH_3	3	65
g	CH_3CH_2	CH_3CH_2	4	70
h	CH_3CH_2	$CH_3CH_2CH_2$	4	75
i	$CH_3CH_2CH_2$	CH_3	3	59
j	$CH_3CH_2CH_2$	CH_3CH_2	4	79
k	$CH_3CH_2CH_2$	$CH_3CH_2CH_2$	4	79
l	CH_3OCH_2	CH_3	1	100

Table 2. Cyclisations of δ-diketones (Scheme 3)[6]

Entry	R	R′	Yield of (5) / %	Yield of (6) / %
a	H	H	60	0
b	H	CH_3	74	6
c	H	CH_3CH_2	78	4
d	CH_3	H	51	23
e	CH_3	CH_3	75	13
f	CH_3	CH_3CH_2	70	12
g	CH_3CH_2	H	57	25
h	CH_3CH_2	CH_3	13	76
i	CH_3CH_2	CH_3CH_2	11	85
j	CH_3O	H	86	0

Cyclisation of the δ-diketones was carried out by treatment with sodium ethoxide in ethanolic solution and generally took place in about five minutes at room temperature. However, unlike our previous investigation (Scheme 1), two possible cyclisation modes are available leading to two possible regioisomeric products (Scheme 3; Table 2). In most cases the major product observed was the cyclohex-3-en-1,2-dione acetal (5), although in two cases (entries h and i) the regioselectivity was reversed to give mainly (6). In one case this reversal of selectivity is consequent upon a very minor structural change (compare entries g and h). Presumably the cyclisation reaction is under thermodynamic control; however the observed pattern of results is difficult to understand. Further experiments are underway.



Scheme 3

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1. PCBP is currently a Nuffield Foundation Science Research Fellow.
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4. P.C.B.Page, S.Harkin, A.P.Marchington, and M.B.van Niel, *Tetrahedron*, 1989, 3819; P.C.B.Page, S.Harkin, and A.P.Marchington, *Synthetic Commun.*, 1989, 1655.
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6. All new compounds gave satisfactory ^1H nmr and ir spectra, and correct mass spectral and/or combustion analysis data.

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