

## Simple Preparation of Cyclohex-2-ene-1,4-dione Monoacetals

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Aminoketene dithioacetals react with  $\alpha,\beta$ -unsaturated ketones to give  $\delta$ -diketones which undergo Robinson annelation to provide monoacetals of cyclohex-2-ene-1,4-diones in up to quantitative yields.

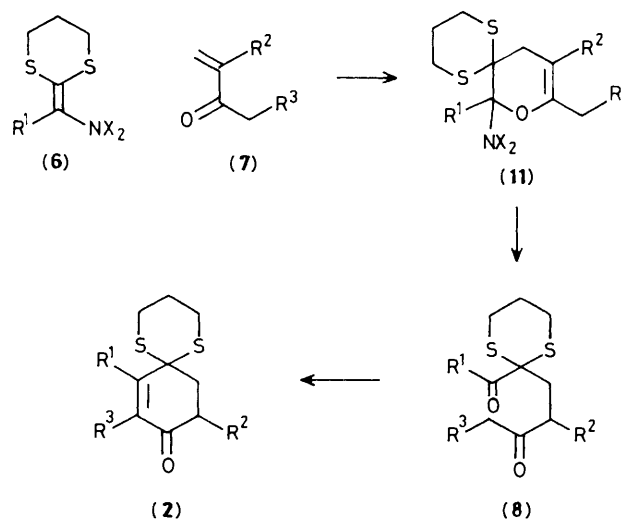
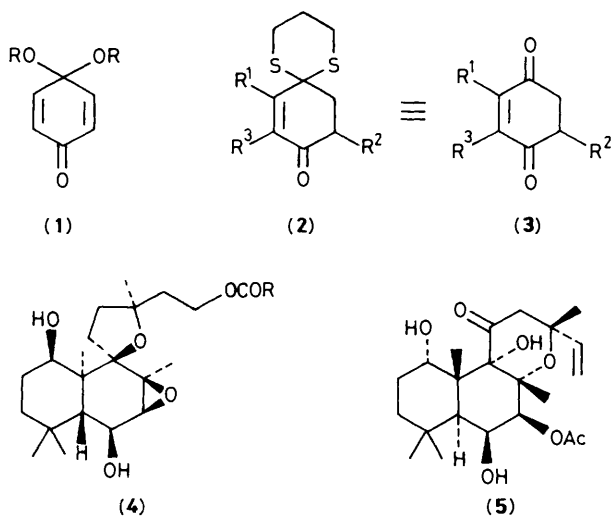
Quinone monoacetals (1) have found some use in organic synthesis in recent years, particularly in the preparation of anthracyclines.<sup>1</sup> They represent synthetic equivalents of quinones and hydroquinones with built-in chemodifferentiation of the two oxidised carbon atoms, allowing their regiospecific use as dienophiles in Diels–Alder reactions. Generally, however, their use has not been widespread, perhaps owing to a lack of simple preparative procedures: normally they are produced by the electrochemical oxidation of hydroquinone methyl ethers,<sup>1</sup> a type of chemistry still unfamiliar to many synthetic chemists.

Cyclohex-2-ene-1,4-dione monodithioacetals (2) appear to be unknown in the chemical literature, but could similarly be regarded as regiospecific synthons for the hydroquinone tautomers (3), and therefore appear to be of considerable interest, for example in the construction by Diels–Alder reaction of decalin systems oxidised at the C-1 and C-4 positions. Erigerol (4)<sup>2</sup> and forskolin (5)<sup>3</sup> are typical examples

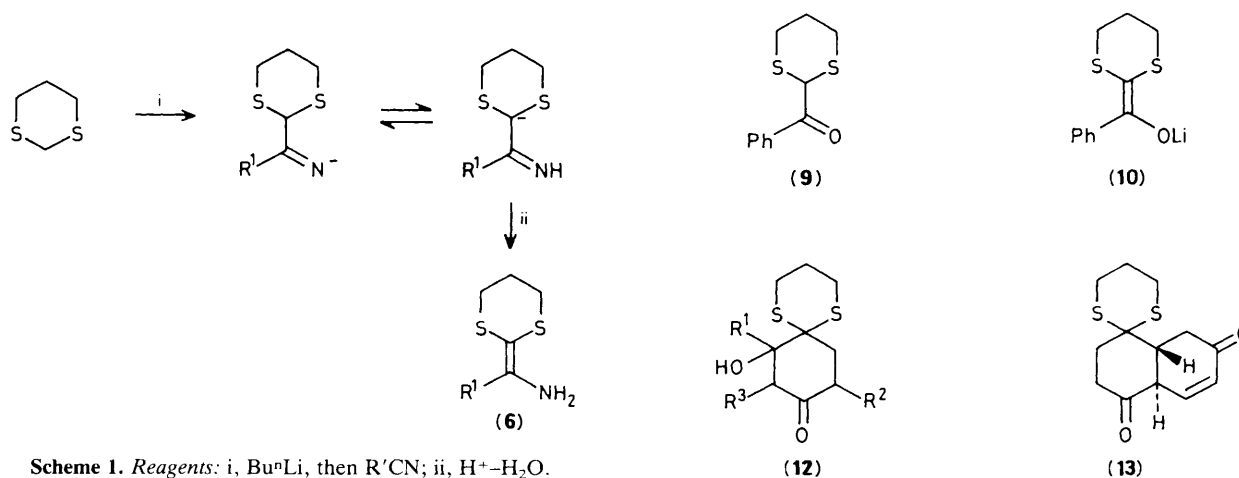
of the many natural products containing such a structural feature.

We now report a simple procedure for the preparation of cyclohex-2-ene-1,4-dione monodithioacetals using enamine chemistry. We have recently reported the synthesis of primary aminoketene dithioacetals (6) by the reaction of metallated dithianes with nitriles (Scheme 1).<sup>4</sup> The present communication describes the first synthetic use of these materials.

The reactions of enamines with  $\alpha,\beta$ -unsaturated ketones and aldehydes are well documented and are commonly supposed to proceed by cycloaddition or conjugate addition mechanisms.<sup>5</sup> We have found that aminoketene dithioacetals react similarly to give the  $\delta$ -diketones (8) in excellent yields (Table 1) upon normal work-up (Scheme 2). No reaction was



Scheme 2



Scheme 1. Reagents: i, Bu<sup>n</sup>Li, then R'CN; ii, H<sup>+</sup>–H<sub>2</sub>O.

Table 1.

Ketene dithioacetal	Enone	X	R <sup>1</sup>	R <sup>2</sup>	R <sup>3</sup>	% Yield	
						Diketone	Dione dithioacetal
(6a)	(7a)	H	Ph	H	H	(8a), 50	(2a), 100 <sup>a</sup>
(6a)	(7b)	H	Ph	Bu <sup>n</sup>	(—) <sup>b</sup>	(8b), 74	— <sup>c</sup>
(6b)	(7c)	Me	H	H	H	(8c), 53	(2c), 100 <sup>a</sup>
(6b)	(7d)	Me	H	H	Me	(8d), 57	(2d), 69 <sup>a</sup>

<sup>a</sup> From (8). <sup>b</sup> R<sup>3</sup>CH<sub>2</sub> replaced by H. <sup>c</sup> Not applicable.

observed when enamine (6a) was treated with but-3-yn-2-one<sup>†</sup> or with cyclohex-2-en-1-one. Further, the corresponding conjugate addition of the lithium enolate (10) of acyl dithiane (9)<sup>6</sup> to methyl vinyl ketone took place in only poor yield. We therefore suggest that the enamine reaction in this case occurs by a cycloaddition process to give the azalactols (11) initially. Tautomerisation and imine hydrolysis upon work-up would then result in the isolation of diketones (8).

Upon treatment with alkoxide (Na-EtOH or KOH-EtOH), or with toluene-*p*-sulphonic acid in benzene solution under reflux, diketones undergo smooth Robinson annelation providing the title compounds (2) in up to quantitative yields

<sup>†</sup> Prepared by the pyridinium chlorochromate oxidation of but-3-yn-2-ol.

(Table 1), no aromatisation being observed. Use of sodium methoxide in refluxing methanolic solution allows isolation of the intermediate ketoalcohols (12) which may be subsequently dehydrated to provide enediones (2). Cyclohex-2-ene-1,4-dione monoacetal (2c) underwent Diels-Alder cycloaddition to Danishefsky's diene<sup>7</sup> to give enone (13) in 40% yield.

We hope that this simple method of access to monoacetals of cyclohex-2-ene-1,4-diones will encourage greater use of these interesting materials in organic synthesis.

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## References

- 1 See, for example, B. L. Chenard, M. G. Dolson, A. D. Sercel, and J. S. Swenton, *J. Org. Chem.*, 1984, **49**, 318.
- 2 T. G. Waddell, C. B. Osborne, R. Collinson, M. J. Levine, M. C. Cross, J. V. Silverton, H. M. Fales, and E. A. Sokoloski, *J. Org. Chem.*, 1983, **48**, 4450.
- 3 S. V. Bhat, B. S. Bajwa, H. Dornauer, N. J. de Souza, and H. W. Fehlhaber, *Tetrahedron Lett.*, 1977, 1669.
- 4 P. C. B. Page, M. B. van Niel, and P. H. Williams, *J. Chem. Soc., Chem. Commun.*, 1985, 742.
- 5 G. Desimoni and G. Tacconi, *Chem. Rev.*, 1975, **75**, 651; J. Sauer, *Angew. Chem., Int. Ed. Engl.*, 1966, **5**, 211; I. Fleming and J. Harley-Mason, *J. Chem. Soc.*, 1964, 2165.
- 6 E. J. Corey and D. Seebach, *Angew. Chem., Int. Ed. Engl.*, 1965, **4**, 1075, 1077.
- 7 S. Danishefsky, T. Kitahara, C. F. Yan, and J. Morris, *J. Am. Chem. Soc.*, 1979, **101**, 6996, 7001, 7008.