Tetrahedron Vol. 45, No. 12, pp. 3819 to 3838, 1989
Printed in Great Britain.

0040-4020/89 $3.00+.00

ADDITION OF AMINOKETENE DITHIOACETALS TO α,β-UNSATURATED KETONES. SYNTHESIS AND REACTIONS OF CYCLOHEX-2-EN-1,4-DIONE MONODITHIOACETALS

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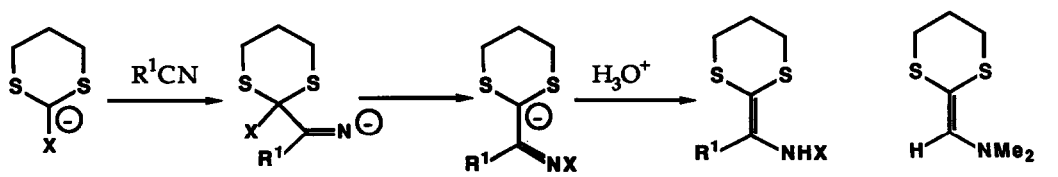
(*Received in UK* 15 *March* 1989)

Aminoketene dithioacetals add to α,β-unsaturated ketones to give 1,5-diketones after hydrolytic work-up. Upon treatment with acid or base, these diketones suffer intramolecular aldol reactions yielding cyclohex-2-en-1,4-dione monodithioacetals, interesting and useful synthetic equivalents of cyclohex-2-en-1,4-diones which readily undergo conjugate addition and cycloaddition reactions.

We have recently reported a synthesis of primary and secondary aminoketene dithioacetals (1) from the reaction of 2-lithio-1,3-dithiane or 2-lithio-2-trimethylsilyl-1,3-dithiane with non-enolisable nitriles (Scheme 1) [1]. These compounds, at once ketene dithioacetals and enamines, appear to be of some potential as intermediates for organic synthesis [2]. Tertiary aminoketene dithioacetals, e.g. (2), may be prepared by the Peterson reaction of 2-lithio-2-trimethylsilyl-1,3-dithiane with tertiary amides [3].



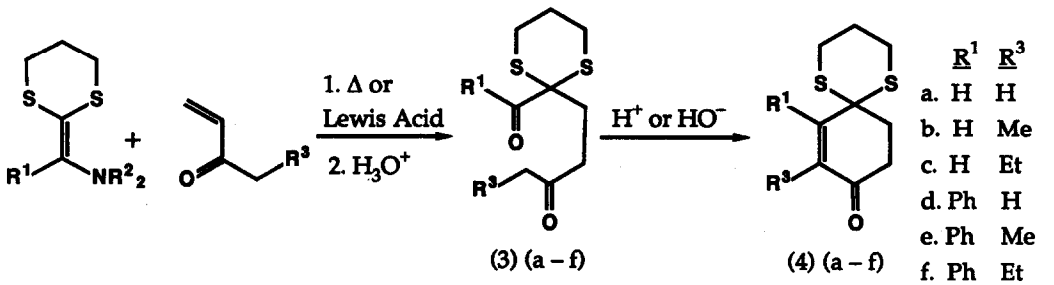
Scheme 1

(1)
a. R^1 = Ph, X = H

(2)

Enamines are well-known in the literature to react with α,β-unsaturated ketones by cycloaddition or conjugate addition mechanisms [4] and ketene acetals have been reported to undergo cycloaddition with α,β-unsaturated carbonyl compounds under high pressure [5]. Stable primary enamines are rather unusual; however we have found that aminoketene dithioacetals

follow a similar pattern of reactivity, providing 1,5-diketones (3) after aqueous work-up. These 1,5-diketones undergo intramolecular aldol reaction under acidic or basic conditions to give cyclohex-2-en-1,4-dione monodithioacetals (4) in up to quantitative yields (Scheme 2) [6].



Scheme 2

Table 1 : Uncatalysed

Aminoketene dithioacetal	Enone R3	Product	Yield/%
(2)	H	(3a)	53
(2)	Me	(3b)	57
(1a)	H	(3d)	50
(1a)	Me	(3e)	0

Table 2 : Catalysed

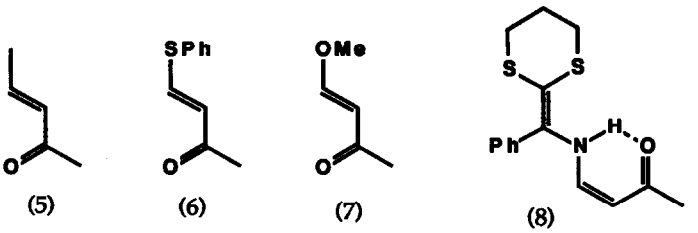
Aminoketene dithioacetal	Enone R3	Product	Yield/%
(2)	H	(3a)	58
(2)	Me	(3b)	28
(2)	Et	(3c)	35
(1a)	H	(3d)	98
(1a)	Me	(3e)	100
(1a)	Et	(3f)	57

Preparation of cyclohex-2-en-1,4-dione monodithioacetals

Our initial experiments centred on primary aminoketene dithioacetal (1a) and but-3-en-2-one. A mixture of these reagents in 1:2 molar ratio boiled under reflux in toluene solution gave 1,5-diketone (3d) in 50% yield after aqueous work-up. While this reaction could be carried out on a multigram scale, we were unable to improve the yield, even by use of a considerable excess of the enone or by its slow generation *in situ* from 4-chlorobutan-2-one [7]. Tertiary aminoketene dithioacetal (2) also readily reacted with but-3-en-2-one and pent-1-en-3-one under similar conditions and in similar yields. The reaction did not occur with enones bearing substituents at the β-terminus (Table 1). But-3-yn-2-one and cyclohex-2-enone were unreactive under a variety of reaction conditions.

Our results suggest that one limitation of this interesting reaction is the introduction of further substituents at the β-terminus of the enone. For example, no 1,5-diketone could be prepared from any of enones (5), (6), or (7). Enone (7) was unusual in that a reaction did occur with aminoketene dithioacetal (1a) to give an excellent yield of the product (8) resulting from a conjugate addition by the nitrogen atom of (1a), followed by loss of methanol. Examination of the NMR spectrum of (8) indicated exclusive Z double bond geometry, presumably favoured by

intramolecular hydrogen bonding, as indicated.



(5) (6) (7) (8)

We were pleased to discover that addition reactions between aminoketene dithioacetals and enones are also catalysed by Lewis acids [8]. While aluminium chloride does not successfully mediate any reaction between aminoketene thioacetal (1a) and but-3-en-2-one in toluene solution, addition of one equivalent of anhydrous zinc chloride to a solution of these two materials in dichloromethane at room temperature for two days induced smooth conversion to diketone (3d) in 98% yield after normal work-up. The quantity of Lewis acid used is most important; use of 0.1 equivalents in this reaction gave only 29% yield after two days and 34% after 12 days while use of 10 equivalents gave 85%. The reaction is more general under these conditions than in the absence of Lewis acids (Table 2). For example, zinc chloride in dichloromethane mediated a reaction between aminoketene thioacetal (1a) and pent-1-en-3-one which did not take place in toluene solution under reflux when no Lewis acid was present. Other Lewis acids were in general much less effective, as indicated in Table 3 for the reaction between aminoketene dithioacetal (1a) and but-3-en-2-one. Overall the best results were obtained using ethereal zinc chloride solution.

Table 3 : Lewis Acid Catalysis

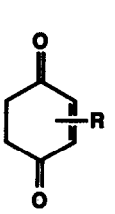
Lewis acid	Proportion/equiv.	Time/days	Temp/°C	Yield/%
$AlCl_3$	1	4	0	14
$ZnCl_2$	0.1	4	0	28
$ZnCl_2$	0.1	12	0	34
$ZnCl_2$	1	2	0	98
$ZnCl_2$	2	4	0	97
$ZnCl_2$	4.5	4	0	80
$ZnCl_2$	10	2	0	85
$ZnBr_2$	2	2	0	41
$SnCl_4$	2	4	-78	0
$SnCl_4$	2	4	0	14
$BF_3.Et_2O$	2	4	0	47
$TiCl_4$	2	1	-78	0
$TiCl_4$	2	3	0	5

The 1,5-dicarbonyl compounds formed in these reactions undergo rapid and efficient intramolecular adol reaction under both acidic and basic conditions to form the novel cyclohex-

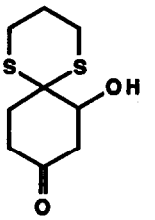
2-en-1,4-dione monoacetals (4) (Table 4). The compounds are singly protected equivalents of the hydroquinone tautomers (9) and therefore show promise as synthetic intermediates. Thus, treatment of dilute solutions of (3d) and (3e) with sodium ethoxide in ethanolic solution under reflux gave up to quantitative formation of the corresponding cyclohex-2-en-1,4-dione monoacetals (4d) and (4e). This reaction could also successfully be carried out in boiling toluene as the solvent using para-toluene sulphonic acid as catalyst. Compound (4d) was also prepared by a Robinson annelation reaction of 2-benzoyl-1,3-dithiane [9] with but-3-en-2-one using sodium ethoxide as the base.

Table 4 : Preparation of (4) from (3)

Diketone	Cyclohexendione monodithioacetal	Yield/%
(3a)	(4a)	75
(3b)	(4b)	69
(3c)	(4c)	78
(3d)	(4d)	100
(3e)	(4e)	100
(3f)	(4f)	91



(9)



(10)

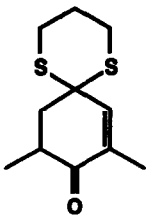
Interestingly, when ketoaldehyde (3a) was treated with sodium methoxide in methanolic solution under reflux the intermediate ketoalcohol (10) could be isolated in good yield (62%). Treatment of (3a) with LDA also produced this material. Conversion of (10) to the cyclohex-2-en-1,4-dione monoacetal (4a) took place in quantitative yield by dehydration in a Dean-Stark apparatus using para-toluene sulphonic acid as catalyst.

In the case of ketoaldehyde (3b), treatment with sodium ethoxide in ethanol under reflux did not effect aldol reaction; however cyclohex-2-en-1,4-dione monoacetal (4b) was isolated in 69% yield when 5% ethanolic potassium hydroxide solution was employed. The reaction also proceeded in acetic acid solution under reflux, although in lower yield.

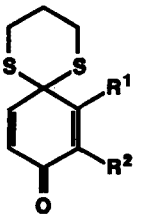
Reactions of cyclohexenedione monodithioacetals

Cyclohexendione monodithioacetals readily undergo enolate chemistry. For example, treatment of (4b) with LDA followed by reaction of the enolate with methyl iodide gave the substituted product (11) in 50% yield.

Benzoquinone monoacetals have been used for the synthesis of a number of natural products including anthracyclinones [10]. Although they are of obvious value as building blocks in such syntheses they have not been widely adopted, perhaps because their preparation usually requires somewhat unfamiliar electrochemical techniques.



(11)



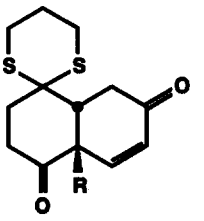
(12) a. $R^1 = R^2 = H$
b. $R^1 = H$, $R^2 = Me$
c. $R^1 = Ph$, $R^2 = H$

Introduction of further unsaturation into cyclohexendione monoacetals clearly would provide a new method of synthesis of quinone monoacetals. Accordingly, we attempted a reaction of aminoketene thioacetal (1a) with 4-(phenylthio)-but-3-en-2-one (6) in the expectation that addition and cyclisation to give the cyclohexendione monoacetal could be followed by oxidation of the sulphur atom and elimination of benzene sulphenic acid. Unfortunately no addition to the enone took place under our normal reaction conditions. Similar treatment of 4-methoxybut-3-en-2-one resulted in exclusive nitrogen alkylation to give (8) (see above). However, introduction of a phenylseleno group into each of aminoketene dithioacetals (4a), (4b), and (4d) took place smoothly using enolate chemistry and phenylselenenyl bromide as the electrophile. Selenoxide elimination occurred readily although in variable yields using either hydrogen peroxide or MCPBA as the oxidant; quinone monodithioacetals (12a), (12b), and (12c) were isolated as highly crystalline solids. Reich [11] has suggested that such syn eliminations are poor reactions in cyclic enones because of difficulty in attaining the correct conformation required for eliminations to occur. Reich has also reported that poor yields of elimination products were observed in cyclic α-seleno ketones which did not bear substituents at carbon atom 3.

Cyclohex-2-en-1,4-dione monoacetals appear to have some potential as synthetic building blocks, for example as dienophiles in the Diels-Alder reaction. They are stable crystalline synthetic equivalents of cyclohex-2-en-1,4-diones with built-in chemodifferentiation of the two carbonyl groups. They are therefore attractive substrates for cycloaddition and conjugate addition reactions, for example in the preparation of substituted decalin systems. Cyclohexenones are known to be sluggish substrates when used as dienophiles [12] and we therefore selected the highly reactive 1-methoxy-3-trimethylsilyloxybuta-1,3-diene (Danishefsky's diene) [12,13] as a suitable diene for a study of their reactivity in Diels-Alder reactions. Best results were obtained by carrying out cycloaddition reactions in sealed tubes at 220 °C for two days using dry degassed xylene as solvent and by using 3 to 5 equivalents of diene (Table 5); cycloadducts were isolated along with para-hydroxyacetophenone. Two types of product could be obtained from these reactions depending upon the work-up conditions used: increasing the concentration of acid used in the work-up favoured the production of methoxyketones (13) at the expense of the expected enones (14). Very high field proton NMR

data including proton decoupling and COSY spectra obtained for (13a) indicate cis stereochemistry at the ring fusion and trans stereochemistry between the ring junction protons and the methoxy group, as would be expected from an endo transition state.

(13)
a. R = H
b. R = Me

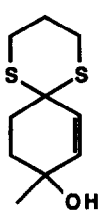


(14)
a. R = H
b. R = Me

Table 5

Product	Yield/%
13a	35
13b	29
14a	47
14b	25

Cyclohex-2-en-1,4-dione monodithioacetals also undergo conjugate addition reactions upon treatment with organocuprate reagents. However, we observed an unusually fine balance between the reactivity and selectivity of the cuprate reagents used. For example, while addition of dimethyl lithium cuprate to cyclohex-2-en-1,4-diones (4a) and (4d) gave only deprotonation in both thf and ether solvents, a copper-catalysed addition of methyl magnesium iodide to (4a) resulted in exclusive 1,2 addition to give alcohol (15).



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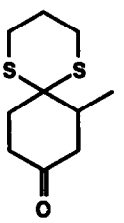

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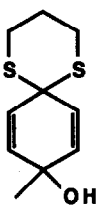
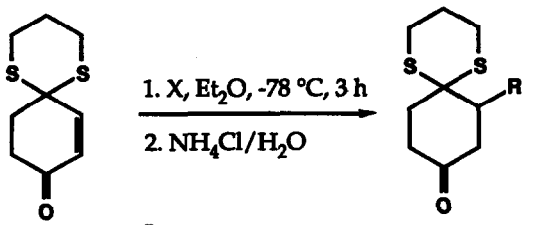


(17)

An excellent review by Lipschutz [14] indicates that higher order mixed organocuprates react with α,β-unsaturated ketones cleanly and with high selectivity. These reagents do not require the use of additives to aid solubility. This is an obvious advantage since organocopper reactivity profiles are generally controlled by several parameters (for example temperature, solvent, source of Cu(I)), and the number of possible combinations of variables can be reduced if additives are unnecessary. We were encouraged to find that the higher order reagent dimethyl dilithium cyano cuprate provided the correct spectrum of reactivity to give 1,4 addition product (16) in 78% yield upon reaction with (4a). Interestingly, when larger alkyl groups were used copper catalysed Grignard reagents proved more suitable (equation 1). Treatment of quinone monodithioacetal (12a) with dimethyl lithium cuprate gave only (17), the product of 1,2 addition.



Equation 1

X = $^{n}Bu_2Cu(CN)Li_2$ 39%

pent-5-enylmagnesium bromide/ CuBr.DMS 77%

We believe that these experiments demonstrate some of the synthetic potential of aminoketene dithioacetals and cyclohex-2-en-1,4-dione monoacetals, and we hope that they will find further and wider use in the future.

General Experimental Details

IR spectra were recorded in the range 4 000-600 cm^{-1} on a Perkin Elmer 298 spectrophotometer, and were calibrated against polystyrene. Solid samples were run as nujol mulls and liquids as thin films.

^{1}H NMR spectra were recorded on Perkin Elmer R34, Bruker WM250, Bruker AC200, or Jeol PMX60 instruments using deuteriochloroform solutions and tetramethylsilane as internal reference.

^{13}C NMR spectra were recorded on Bruker WM250, Bruker AC200, or Jeol JNM-FX60Q instruments using deuteriochloroform solutions and tetramethylsilane as internal reference.

Mass spectra were obtained on VG Micromass 7070E or AEI MS 902 mass spectrometers.

Microanalyses were performed in the University of Liverpool Department of Chemistry microanalytical laboratory.

Melting points were determined on a Reichert hot stage apparatus and are uncorrected. Solvents used for recrystallisation are indicated in brackets after the melting point.

Flash column chromatography was carried out using Merck 9385 silica gel, using hand-bellows or an air line to apply pressure to the column. Mixtures of ethyl acetate and petroleum ether (bp 40-60 °C) in proportions ranging from 1:1 to 1:10 were used as eluant, unless otherwise stated.

Dry flash column chromatography was carried out using Merck 15111 silica gel using petroleum ether (bp 40-60 °C) containing an increasing proportion of ethyl acetate as eluant.

Thin layer chromatography was carried out on glass and aluminium backed plates coated with a 0.25 mm layer of silica gel 60H, using mixtures of ethyl acetate and petroleum ether (bp 40-60 °C) as eluant unless otherwise stated. Uv inactive compounds were visualised by spraying with dodeca-molybdophosphoric acid (15% w/v in EtOH) followed by charring.

Purification of Solvents

Tetrahydrofuran and diethyl ether were freshly distilled under nitrogen from the sodium/benzophenone ketyl radical immediately prior to use.

Toluene and dichloromethane were allowed to stand over calcium hydride overnight prior to distillation under nitrogen.

Dimethylformamide was distilled from calcium hydride. The distillate was flash distilled from alumina activated by heating to 150 °C overnight. Dry solvent was stored over activated type 4Å molecular sieve under an atmosphere of nitrogen.

Ethanol was distilled under nitrogen from activated magnesium.

Purification of Reagents

n-Butyllithium

n-Butyllithium was purchased from the Lithium Corporation of Europe in one gallon quantities and decanted into 500 mL oven baked bottles stoppered with septa. The molarity of the n-butyllithium was determined by the Gilman double titration method.

Chlorotrimethylsilane

Chlorotrimethylsilane was distilled from calcium hydride under nitrogen and stored over activated type 4Å molecular sieve.

1,3-Dithiane

1,3-Dithiane was stored in a desiccator over self-indicating silica gel. It was occasionally necessary to recrystallise the reagent from petroleum ether (bp 40-60 °C).

Triethylamine

Triethylamine was distilled from potassium hydroxide pellets under nitrogen, and stored over activated type 4Å molecular sieve.

Copper (I) bromide-dimethyl sulphide complex

Copper (I) bromide (5 g) was purified by dissolution in hydrobromic acid. The resultant purple solution was stirred for five minutes before being treated with sodium sulphite (2 g). The mixture was allowed to stand for ten minutes before being poured into water (500 mL). The

colourless precipitate of pure copper (I) bromide was allowed to settle and was collected by filtration. The purified copper (I) bromide was placed in a flask fitted with a reflux condenser, and dimethyl sulphide was added carefully until all the solid had dissolved. The solution was gradually poured into petroleum ether (100 mL), and the colourless precipitate of copper (I) bromide-dimethyl sulphide complex collected by filtration.

Preparation of glassware

All organometallic reactions were carried out in two or three necked round bottom flasks which were baked at 150 °C for a minimum of four hours. The flasks were allowed to cool in a desiccator over self-indicating silica gel, and were purged with nitrogen prior to being stoppered with septum caps. Syringes, needles, cannulas, and magnetic stirring bars used in organometallic reactions were also baked and allowed to cool in a desiccator. All organometallic reactions were carried out under a slight static positive pressure of nitrogen. Resealable Carius tubes were carefully washed with 1M aqueous sodium hydroxide solution and rinsed with copious quantities of water. They were then baked at 150 °C for a minimum of twenty-four hours, and allowed to cool in a desiccator containing self-indicating silica gel.

Normal work-up procedures

Reactions were usually worked-up by addition of a saturated aqueous solution of ammonium chloride, followed by extraction of the aqueous phase using several portions of chloroform or dichloromethane. The combined organic extracts were dried over anhydrous magnesium sulphate which was later removed by filtration. The filtrate was reduced in volume on a rotary evaporator to give the crude reaction mixture which was purified by chromatography or distillation.

Preparation of 2-lithio-1,3-dithiane and 2-lithio-2-trimethyl-silyl-1,3-dithiane

To a solution of 2-trimethylsilyl-1,3-dithiane or 1,3-dithiane in dry thf (0.2 molar) at -40 °C was added dropwise a solution of n-butyllithium (1.2 equiv.) in hexane. After stirring for two hours the solution of the anion was transferred by cannula for subsequent reaction.

N,N-Dimethyl-(2-(1,3-dithianylidene))-methylamine (2)

To the anion generated from 2-trimethylsilyl-1,3-dithiane (prepared from 1,3-dithiane (3.0 g, 25 mmol) and treated sequentially with 1.2 equivalents each of n-butyllithium and chlorotrimethylsilane) was added N,N-dimethylformamide (3.87 mL, 50 mmol) at -78 °C. The reaction was allowed to reach room temperature slowly before being worked-up in the usual manner. N,N-Dimethyl-(2-(1,3-dithianylidene))-methylamine (2) was obtained as a yellow oil exhibiting a pleasant aroma. It is not stable to chromatography on silica gel and was therefore used without purification; $\nu_{max.}$ 1 605 cm^{-1}; $\delta_H(CDCl_3)$, 1.73-3.33 (6 H, m), 2.87 (6 H, s), and 6.58 (1 H, s).

(2-(1,3-Dithianylidene))-phenylmethylamine (1a)

The anion generated from 1,3-dithiane (8.66 g, 72.2 mmol) was added to a solution of benzonitrile (7.45 g, 72.2 mmol) in thf (50 mL) at -78 °C. Work-up and chromatography using ethyl acetate-petroleum ether (1:5) as eluant gave (2-(1,3-dithianylidene))-phenylmethylamine (1a) as a crystalline solid (14.0 g, 87%), mp 118-120 °C (ethyl acetate) (Found: C, 59.07; H, 5.89; N, 6.21. $C_{11}H_{13}NS_2$ requires: C, 59.15; H, 5.87; N, 6.27%); $\nu_{max.}$ 3 450, 3 320, 1 610, and 1 600 cm^{-1}; $\delta_H(CD_2Cl_2)$ 1.95-2.1 (2 H, m), 2.5-2.6 (2 H, m), 2.7-2.8 (2 H, m), 4.3 (2 H, br s), and 7.25-7.4 (5 H, m); $\delta_C(CD_2Cl_2)$ 26.59, 31.72, 32.69, 127.84, 128.47, 137.29, and 149.88. Found: *m/z* 223.048 996 0 (M^+), 149, 121, 105, 77, 69, and 51. $C_{11}H_{13}NS_2$ requires 223.048 939 4.

2-Benzoyl-2-(4-(butan-2-onyl))-1,3-dithiane (3d)

(a) Uncatalysed

(2-(1,3-Dithianylidene))-phenylmethylamine (1a) (0.6 g, 2.7 mmol) and but-3-en-2-one (0.45 mL, 5.4 mmol) were heated to reflux in toluene (50 mL) for twenty-four hours. The reaction was worked up as usual and purified by chromatography to give 2-benzoyl-2-(4-(butan-2-onyl))-1,3-dithiane (3d) as needles (0.4 g, 50%), mp 63-66 °C (diethyl ether) (Found: C, 61.06; H, 6.12. $C_{15}H_{18}O_2S_2$ requires C, 61.19; H, 6.16%); $\nu_{max.}$ 1 720, 1 680, 1 600, and 1 570 cm^{-1}; δ_H ($CDCl_3$, 250 MHz), 1.85-2.05 (1 H, m), 2.05 (3 H, s), 2.05-2.18 (1 H, m), 2.45-2.52 (2 H, m), 2.56-2.62 (2 H, m), 2.74-2.83 (2 H, m), 3.13-3.24 (2 H, m), 7.27-7.53 (3 H, m), and 8.06-8.10 (2 H, m); δ_C ($CDCl_3$), 24.71, 27.89, 30.01, 32.66, 38.49, 60.21, 129.63, 130.69, 133.34, 137.05, 197.46, and 207.00. Found: *m/z* (CI, NH_4^+), 312 [$(M+18)^+$], 295 [$(M+1)^+$], 208, 191, 175, and 105.

(b) Zinc chloride catalysis

To a solution of (2-(1,3-dithianylidene))-phenylmethylamine (1a) (0.3 g, 1.35 mmol) in dry dichloromethane (30 mL) was added zinc chloride (0.18 g, 1.35 mmol). The mixture was cooled to 0 °C and but-3-en-2-one (0.19 g, 2.7 mmol) added in aliquots over a period of 2 days. The reaction was worked up in the usual manner and purified by chromatography to give 2-benzoyl-2-(4-(butan-2-onyl))-1,3-dithiane (3d) (0.39 g, 98%).

2-Benzoyl-2-(1-(pentan-3-onyl))-1,3-dithiane (3e)

To a solution of (2-(1,3-dithianylidene))-phenylmethylamine (1a) (0.5 g, 2.24 mmol) in dry dichloromethane (30 mL) was added zinc chloride (1.42 g, 10.4 mmol). The mixture was cooled to 0 °C and pent-1-en-3-one (0.38 g, 4.47 mmol) added in aliquots over a period of 2 days. The reaction was worked up in the usual manner and purified by chromatography to give 2-benzoyl-2-(1-(pentan-3-onyl))-1,3-dithiane (3e) as needles (0.69 g, 100%), mp 81-83 °C (diethyl ether) (Found: C, 62.09; H, 6.53. $C_{16}H_{20}O_2S_2$ requires C, 62.34; H, 6.49%); $\nu_{max.}$ 1 700 and 1 655 cm^{-1}; δ_H ($CDCl_3$, 250 MHz), 0.94-1.00 (3 H, t, *J* 7.32 Hz), 1.91-1.99 (1 H, m), 2.06-2.12 (1 H, m), 2.27-2.36 (2 H, q, *J* 7.32 Hz), 2.45-2.63 (4 H, m), 2.69-2.88 (2 H, m), 3.02-3.23 (2 H, m), 7.36-7.53 (3 H, m), and 8.07-8.10 (2 H, d, *J* 7.81 Hz). Found: *m/z* (CI, NH_4^+), 326 [$(M+18)^+$], 309 [$(M+1)^+$], 291, 222, and 203.

2-Benzoyl-2-(1-(hexan-3-onyl))-1,3-dithiane (3f)

To a solution of (2-(1,3-dithianylidene))-phenylmethylamine (1a) (0.30 g, 1.35 mmol) in dry

dichloromethane (30 mL) was added ethereal zinc chloride (1 M, 2.69 ml, 2.70 mmol). The mixture was cooled to 0 °C and hex-1-en-3-one (0.264 g, 2.70 mmol) added in aliquots over a period of 2 days. The reaction was worked up in the usual manner and purified by chromatography to give 2-benzoyl-2-(1-(hexan-3-onyl))-1,3-dithiane (3f) as needles (0.258 g, 57%), mp 51-52 °C (diethyl ether) (Found: C, 63.15; H, 6.89. $C_{17}H_{22}O_2S_2$ requires C, 63.35; H, 6.83%); $\nu_{max.}$ 1 710, 1 670, 1 600, and 1 580 cm^{-1}; δ_H ($CDCl_3$, 200 MHz), 0.80-1.00 (3 H, t, *J* 7.3 Hz), 1.25-1.35 (1 H,m), 1.40-1.60 (2 H, m), 1.80-2.30 (4 H, m), 2.40-2.60 (2 H, q, *J* 7.32 Hz), 2.65-2.85 (2 H, m), 3.10-3.30 (2 H, m), 7.30-7.50 (3 H, m), and 8.00-8.20 (2 H, m). Found: *m/z* (CI, NH_4^+), 340 [(*M*+18)$^+$], 323 [(*M*+1)$^+$], 305, 291, 236, 219, and 105.

cis-N-(4-(But-3-en-2-onyl))-(2-(1,3-dithianylidene))-phenylmethylamine (8)
(2-(1,3-Dithianylidene))-phenylmethylamine (1a) (0.75 g, 3.3 mmol) and 4-methoxybut-3-en-2-one (9) (1.5 g, 15 mmol) were heated to reflux in solution in chloroform (25 mL) for nine days. Usual work-up and purification by chromatography gave cis-N-(4-(but-3-en-2-onyl))-(2-(1,3-dithianylidene))-phenylmethylamine (8) as a crystalline solid (0.7 g, 73%), mp 154-155 °C (absolute alcohol) (Found: C, 62.05; H, 5.98; N, 4.72. $C_{15}H_{17}NOS_2$ requires C, 61.82; H, 5.88; N, 4.81%); $\nu_{max.}$ 1 635, 1 585, and 1 550 cm^{-1}; δ_H ($CDCl_3$, 250 MHz), 2.12 (3 H, s), 2.15-2.22 (2 H, m), 2.67-2.71 (2 H, m), 2.95-2.99 (2 H, m), 5.06 (1 H, d, *J* 7.76 Hz), 6.35 (1 H, dd, *J* 7.76 and 12.34 Hz), 7.20-7.27 (2 H, m), 7.39-7.50 (3 H, m), and 12.35 (1 H, br d, *J* 11.75 Hz, exchangeable with D_2O); δ_C ($CDCl_3$), 25.74, 29.33, 30.98, 31.60, 97.32, 110.81, 128.69, 129.09, 129.95, 141.85, 143.39, 197.99, 205.62, and 219.35. Found: *m/z* 291.074 4 (*M*$^+$). $C_{15}H_{17}NOS_2$ requires 291.075 2.

Cyclohex-2-en-4-one spiro-1,2'-(1',3'-dithiane) (4a)
(a) To a solution of 2-carboxaldehyde-2-(4-(butan-2-onyl))-1,3-dithiane (3a) (2.0 g, 9.2 mmol) in ethanol (50 mL) under reflux was added slowly sodium ethoxide (1 equiv.) in ethanolic solution. When all the starting material had reacted according to TLC analysis, usual work-up was followed by purification by chromatography to remove baseline residues to give cyclohex-2-en-4-one spiro-1,2'-(1',3'-dithiane) (4a) as a crystalline solid (1.37 g, 75%), mp 75-77 °C (diethyl ether) (Found: C, 53.74; H, 6.05. $C_9H_{12}OS_2$ requires C, 53.96; H, 6.04%); $\nu_{max.}$ 1 670 cm^{-1}; δ_H ($CDCl_3$), 2.0-2.15 (2 H, m), 2.5-2.6 (2 H, m), 2.6-2.7 (2 H, m), 2.9-3.0 (4 H, m), 5.9 (1 H, d, *J* 10 Hz), and 7.1 (1 H, d, *J* 10 Hz). Found: *m/z* 200.032 562 3 (*M*$^+$), 162, 126, 97, and 74. $C_9H_{12}OS_2$ requires 200.032 958 7.

(b) A solution of 2-hydroxycyclohexan-4-one spiro-2'-(1',3'-dithiane) (10) (0.43 g, 2 mmol) in toluene (25 mL) was heated to reflux with para-toluene sulphonic acid (one crystal). After six hours the reaction was worked up in the usual manner and purified by chromatography to remove baseline residues to give cyclohex-2-en-4-one spiro-1,2'-(1',3'-dithiane) (4a) (250 mg, 63%).

3-Methylcyclohex-2-en-4-one spiro-1,2'-(1',3'-dithiane) (4b)
(a) A solution of 2-carboxaldehyde-2-(1-(pentan-3-onyl))-1,3-dithiane (3b) (1.18 g, 5.1 mmol) in

ethanol (125 mL) under reflux was treated with 5% ethanolic potassium hydroxide solution (0.75 mL/mmol substrate) over one hour. The reaction mixture was neutralised by addition of dilute sulphuric acid after six hours, and the organic phase was washed with water before being dried over magnesium sulphate. Removal of the solvent gave an oily residue which was purified by dry flash column chromatography to give 3-methylcyclohex-2-en-4-one spiro-1,2'-(1',3'-dithiane) (4b) as an undistillable oil (0.75 g, 69%) (Found: C, 56.13; H, 6.87. $C_{10}H_{14}OS_2$ requires C, 56.04; H, 6.58%); $\nu_{max.}$ 3 400 and 1 680 cm^{-1}; δ_H ($CDCl_3$), 1.8 (3 H, s), 1.9-2.1 (2 H, m), 2.5-2.6 (2 H, m), 2.6-2.7 (2 H, m), 2.8-2.95 (4 H, m), and 6.7 (1 H, s). Found: *m/z* 214.048 3 (M^+), 140, 111, 97, and 74. $C_{10}H_{14}OS_2$ requires 214.048 6.

(b) 2-Carboxaldehyde-2-(1-(pentan-3-onyl))-1,3-dithiane (3b) (200 mg, 0.9 mmol) was heated to reflux for twenty-four hours in solution in acetic acid (25 mL). The reaction mixture was washed successively with sodium bicarbonate solution and water before being dried over magnesium sulphate. Following removal of solvent, chromatography to remove baseline residues gave 3-methylcyclohex-2-en-4-one spiro-1,2'-(1',3'-dithiane) (4b) (70 mg, 36%).

3-Ethylcyclohex-2-en-4-one spiro-1,2'-(1',3'-dithiane) (4c)

To a solution of 2-carboxaldehyde-2-(1-(hexan-3-onyl))-1,3-dithiane (3c) (0.50 g, 2.03 mmol) in ethanol (50 mL) under reflux was added slowly sodium ethoxide (1 equiv.) in ethanolic solution. When all the starting material had reacted according to TLC analysis, usual work-up was followed by purification by chromatography to remove baseline residues to give 3-ethylcyclohex-2-en-4-one spiro-1,2'-(1',3'-dithiane) (4c) as an oil (0.36 g, 78%), $\nu_{max.}$ 1 675 cm^{-1}; δ_H ($CDCl_3$), 0.95-1.05 (3 H, m), 1.8-2.1 (2 H, m), 2.1-2.3 (2H, m), 2.4-2.7 (4 H, m), 2.7-3.0 (4 H, m), and 6.55 (1H, s).

2-Phenylcyclohex-2-en-4-one spiro-1,2'-(1',3'-dithiane) (4d)

(a) 2-Benzoyl-2-(4-(butan-2-onyl))-1,3-dithiane (3d) (0.25 g, 0.9 mmol) in ethanol (100 mL) at 0 °C was slowly treated with sodium ethoxide (1 equiv.) in ethanolic solution. When the reaction had reached completion according to TLC analysis usual work-up gave 2-phenylcyclohex-2-en-4-one spiro-1,2'-(1',3'-dithiane) (4d) (0.23 g, 100%) as an oil which crystallised on standing; mp 137-140 °C (hexane) (Found: C, 65.03; H, 5.93. $C_{15}H_{16}OS_2$ requires C, 65.18; H, 5.83%); $\nu_{max.}$ 1 680, 1 600, and 1 570 cm^{-1}; δ_H ($CDCl_3$), 1.8-2.0 (1 H, m), 2.0-2.2 (1 H, m), 2.6-2.7 (2 H, m), 2.7-2.9 (4 H, m), 3.0-3.2 (2 H, m), 6.05 (1 H, s), 7.3-7.5 (3 H, m), and 7.7-7.9 (2 H, m). Found: *m/z* 276.063 980 1 (M^+), 202, 174, 160, and 145. $C_{15}H_{16}OS_2$ requires 276.064 258 8.

(b) A solution of 2-benzoyl-1,3-dithiane (0.32 g, 1.4 mmol) in ethanol (25 mL) under reflux was slowly treated with a solution of sodium ethoxide (2 equiv.) in ethanol (30 mL). But-3-en-2-one (0.10 g, 1.4 mmol) was added after ten minutes. When TLC analysis indicated that all the 2-benzoyl-1,3-dithiane had reacted, the solvent was removed *in vacuo* and the reaction mixture was purified by chromatography to give 2-phenylcyclohex-2-en-4-one spiro-1,2'-(1',3'-dithiane) (4d) (0.18 g, 47%).

3-Methyl-2-phenylcyclohex-2-en-4-one spiro-1,2'-(1',3'-dithiane) (4e)

To a solution of 2-benzoyl-2-(4-(pentan-2-onyl))-1,3-dithiane (3e) (0.065 g, 0.21 mmol) in ethanol (30 mL) under reflux was added slowly sodium ethoxide (1 equiv.) in ethanolic solution. When all the starting material had reacted according to TLC analysis, usual work-up was followed by purification by chromatography to remove baseline residues to give 3-methyl-2-phenylcyclohex-2-en-4-one spiro-1,2'-(1',3'-dithiane) (4e) as a crystalline solid (0.061 g, 100%), mp 169-171 °C (diethyl ether). $\nu_{max.}$ 1 670 cm^{-1}; δ_H ($CDCl_3$), 1.5 (3H, s), 1.8-2.0 (1 H, m), 2.4-2.6 (2 H, m), 2.7-3.1 (5 H, m), and 7.2-7.6 (5 H, m). Found: *m/z* (CI, NH_4^+), 308 (M^++18), 291 (M^++1), 278, 204, and 187.

3-Ethyl-2-phenylcyclohex-2-en-4-one spiro-1,2'-(1',3'-dithiane) (4f)

To a solution of 2-benzoyl-2-(1-(hexan-3-onyl))-1,3-dithiane (3f) (0.060 g, 0.18 mmol) in ethanol (30 mL) under reflux was added slowly sodium ethoxide (1 equiv.) in ethanolic solution. When all the starting material had reacted according to TLC analysis, usual work-up was followed by purification by chromatography to remove baseline residues to give 3-ethyl-2-phenylcyclohex-2-en-4-one spiro-1,2'-(1',3'-dithiane) (4f) as a crystalline solid (0.052 g, 91%), mp 133-135 °C (diethyl ether). $\nu_{max.}$ 1 670 cm^{-1}; δ_H ($CDCl_3$), 0.7-1.1 (3H, m), 1.2-1.4 (1H, m), 1.5-2.2 (5 H, m), 2.2-2.7 (1 H, m), 2.7-3.1 (5 H, m), and 7.1-7.6 (5 H, m).

2-Carboxaldehyde-2-(4-(butan-2-onyl))-1,3-dithiane (3a)

(a) Uncatalysed

A solution of N,N-dimethyl-(2-(1,3-dithianylidene))-methylamine (2) (prepared from 1,3-dithiane (3.0 g, 25 mmol) as described previously) in chloroform solution under reflux was treated with aliquots of but-3-en-2-one (total of 3 mL, 3.6 mmol) over three days. Usual work-up and chromatography gave 2-carboxaldehyde-2-(4-(butan-2-onyl))-1,3-dithiane (3a) as an oil (2.89 g, 53% based on 1,3-dithiane), bp 200 °C at 0.1 mmHg (Found: C, 49.76; H, 6.63. $C_9H_{14}O_2S_2$ requires C, 49.51; H, 6.46 %); $\nu_{max.}$ 1 715 cm^{-1}; δ_H ($CDCl_3$), 1.6-1.9 (1 H, m), 2.2-2.2 (6 H, m), 2.6-2.8 (4 H, m), 2.9-3.1 (2 H, m), and 9.0 (1 H, s). Found: *m/z* 218.043 304 4 (M^+), 189, 119, and 106. $C_9H_{14}O_2S_2$ requires 218.043 523 4.

(b) Zinc chloride catalysis

To a solution of N,N-dimethyl-(2-(1,3-dithianylidene))-methylamine (2) (prepared from 1,3-dithiane (0.37 g, 3.08 mmol) as described previously) in dichloromethane (30 mL) was added zinc chloride (0.84 g, 6.18 mmol). The mixture was cooled to 0 °C and but-3-en-2-one (0.39 g, 5.6 mmol) added in aliquots over a period of 4 days. The reaction was worked up in the usual manner and purified by chromatography to give 2-carboxaldehyde-2-(4-(butan-2-onyl))-1,3-dithiane (3a) (0.39 g, 58% based on dithiane).

2-Hydroxycyclohexan-4-one spiro-1,2'-(1',3'-dithiane) (10)

(a) To a solution of 2-carboxaldehyde-2-(4-(butan-2-onyl))-1,3-dithiane (3a) (0.68 g, 3.1 mmol) in methanol (50 mL) under reflux was added slowly a solution of sodium methoxide in methanol

until all the starting material had reacted according to TLC analysis. Usual work-up and chromatography to remove baseline residues gave 2-hydroxycyclohexan-4-one spiro-1,2'-(1',3'-dithiane) (10) as colourless crystals (0.42 g, 62%); mp 104-105 °C (diethyl ether) (Found: C, 49.46; H, 6.48. $C_9H_{14}O_2S_2$ requires C, 49.51; H, 6.46%); $\nu_{max.}$ 3 480 and 1 715 cm^{-1}; δ_H ($CDCl_3$), 1.8-2.5 (5 H, m), 2.5-2.7 (5 H, m-reduces to 4 H on D_2O shake), 2.9-3.15 (3 H, m), and 4.5 (1 H, s). Found: *m/z* 218.042 877 2 (M^+), 189, 145, and 132. $C_9H_{14}O_2S_2$ requires 218.043 523 4.

(b) A solution of 2-carboxaldehyde-2-(4-(butan-2-onyl))-1,3-dithiane (3a) (0.62 g, 2.8 mmol) in thf (25 mL) at -78 °C was treated with lithium diisopropylamide (1.2 equiv.). The reaction mixture was allowed to attain room temperature slowly. Usual work-up and chromatography gave 2-hydroxycyclohexan-4-one spiro-1,2'-(1',3'-dithiane) (10) (230 mg, 38%).

2-Carboxaldehyde-2-(1-(pentan-3-onyl))-1,3-dithiane (3b)

(a) Uncatalysed

To a solution of N,N-dimethyl-(2-(1,3-dithianylidene))-methylamine (2) (prepared from 1,3-dithiane (2 g, 15.5 mmol) as described previously) in toluene (25 mL) under reflux was added pent-1-en-3-one (1.64 mL, 16.5 mmol). After boiling under reflux for four days, the reaction mixture was worked up in the usual manner and purified by chromatography to give 2-carboxaldehyde-2-(1-(pentan-3-onyl))-1,3-dithiane (3b) as an undistillable oil (2.22 g, 57% based on 1,3-dithiane); $\nu_{max.}$ 1 715 and 1 670 cm^{-1}; δ_H ($CDCl_3$), 1.05 (3 H, t, *J* 7.3 Hz), 1.7-1.9 (1 H, m), 1.95-2.2 (3 H, m), 2.45 (2 H, q, *J* 7.3 Hz), 2.5-2.75 (4 H, m), 2.9-3.15 (2H, m), and 9.0 (1 H, s). Found: *m/z* (EI), 203 [$(M-29)^+$], 120, 84, and 57; *m/z* (CI, NH_4^+), 250 [$(M+18)^+$].

(b) Zinc chloride catalysis

To a solution of N,N-dimethyl-(2-(1,3-dithianylidene))-methylamine (2) (prepared from 1,3-dithiane (0.34 g, 2.86 mmol) as described previously) in dichloromethane (30 mL) under a nitrogen atmosphere was added zinc chloride (0.78 g, 5.72 mmol). The mixture was cooled to 0 °C and pent-1-en-3-one (0.48g, 5.72 mmol) added in aliquots over a period of two days. The reaction mixture was worked up in the usual manner and purified by chromatography to give 2-Carboxaldehyde-2-(1-(pentan-3-onyl))-1,3-dithiane (3b) (0.197 g, 28% based on 1,3-dithiane).

2-Carboxaldehyde-2-(1-(hexan-3-onyl))-1,3-dithiane (3c)

To a solution of N,N-dimethyl-(2-(1,3-dithianylidene))-methylamine (2) (0.46 g, 2.63 mmol) in dry dichloromethane (50 mL) was added zinc chloride (0.715 g, 5.26 mmol). The mixture was cooled to 0 °C and hex-1-en-3-one (0.52 g, 5.26 mmol) added in aliquots over a period of 2 days. The reaction was worked up in the usual manner and purified by chromatography to give 2-carboxaldehyde-2-(1-(hexan-3-onyl))-1,3-dithiane (3c) as an oil (0.22 g, 35%), (Found: C, 53.56; H, 7.40. $C_{11}H_{18}O_2S_2$ requires C, 53.62; H, 7.31%); $\nu_{max.}$ 1 730 and 1 720 cm^{-1}; δ_H ($CDCl_3$, 200 MHz), 0.80 (3 H, t, *J* 7.2 Hz), 1.25-1.35 (1 H, m), 1.50-2.00 (3 H, m), 2.10 (2 H, t, *J* 7.2 Hz), 2.40 (2 H, t, *J* 7.2 Hz), 2.50-2.70 (4 H, m), 2.90-3.10 (2 H, m), and 9.10 (1 H, s). Found: *m/z* (CI, NH_4^+), 264 [$(M+18)^+$], 247 [$(M+1)^+$], 229, 217, 160, and 143.

3,5-Dimethylcyclohex-2-en-4-one spiro-1,2'-(1',3'-dithiane) (11)

A solution of 3-methylcyclohex-2-en-4-one spiro-1,2'-(1',3'-dithiane) (4b) (1.0 g, 4.7 mmol) in thf (20 mL) was transferred *via* cannula into a stirred solution of LDA (prepared from 0.79 mL diisopropylamine and n-butyllithium (1.2 equiv.) in thf (3 mL), at -78 °C for half an hour) at -78 °C. The reaction mixture was allowed to warm to 0 °C before being cooled to -78 °C again, and then treated with iodomethane (0.35 mL, 5.6 mmol). The reaction was allowed to attain room temperature slowly before usual work-up. Chromatography using ethyl acetate/petroleum ether (1:2) as eluant gave 3,5-dimethylcyclohex-2-en-4-one spiro-1,2'-(1',3'-dithiane) (11) as an undistillable oil (0.54 g, 50%); $\nu_{max.}$ 3 440 and 1 670 cm^{-1}; δ_H ($CDCl_3$), 1.8 (3 H, s), 2.0-2.3 (4 H, m), 2.3-2.7 (3 H, m), 2.7-3.0 (5 H, m), and 6.75 (1 H, s). Found: *m/z* 228.063 9 (M^+), 154, 84, and 49. $C_{11}H_{16}OS_2$ requires 228.064 3.

Cyclohexa-2,5-dien-4-one spiro-1,2'-(1',3'-dithiane) (12a)

A solution of cyclohex-2-en-4-one spiro-1,2'-(1',3'-dithiane) (4a) (0.5 g, 2.5 mmol) in thf (25 mL) was transferred *via* cannula into a stirred solution of LDA (prepared from diisopropylamine (0.42 mL) and n-butyllithium (1. 3 equiv.) in thf (2 mL) at -78 °C for one hour) at -78 °C. The reaction was allowed to stir for one hour at -78 °C before being treated with a solution of phenylselenenyl bromide (prepared from diphenyl diselenide (0.39 g, 1.25 mmol) and bromine (1.25 mmol, 0.06 mL)) in thf (20 mL). The reaction was allowed to attain room temperature slowly, and stirring was continued overnight. Following the usual work-up procedure, purification by chromatography using ethyl acetate/petroleum ether (1:2) as eluant gave 4-phenylselenenyl cyclohex-2-en-4-one spiro-1,2'-(1',3'-dithiane) as an undistillable brown oil (0.48 g, 54%). A solution of the selenide (prepared from cyclohex-2-en-4-one spiro-1,2'-(1',3'-dithiane) (1.0 g, 5 mmol)) in dichloromethane (30 mL) was cooled in an ice/salt bath and treated slowly with a solution of meta-chloroperbenzoic acid (0.78 g, 5 mmol) in dichloromethane. When all the starting material had reacted as indicated by TLC analysis, the reaction was washed with saturated aqueous sodium bicarbonate solution and extracted with several portions of dichloromethane. The combined organic extracts were dried over magnesium sulphate and the solvents removed *in vacuo*. Purification by chromatography using ethyl acetate/petroleum ether (1:2) as eluant gave cyclohexa-2,5-dien-4-one spiro-1,2'-(1',3'-dithiane) (12a) as colourless crystals (0.43 g, 43% based on enone (4a)), mp 185-186 °C (ethyl acetate/petroleum ether) (Found: C, 54.51; H, 5.07. $C_9H_{10}OS_2$ requires C, 54.51; H, 5.08%); $\nu_{max.}$ 1 660, 1 640, 1 610, and 860 cm^{-1}; δ_H ($CDCl_3$), 2.1-2.2 (2 H, m), 3.0-3.1 (4 H, m), 6.3 (2 H, d, *J* 10 Hz), and 7.25 (2H, d, *J* 10 Hz). Found: m/z 198.017 9. $C_9H_{10}OS_2$ requires 198.017 3).

3-Methylcyclohexa-2,5-dien-4-one spiro-1,2'-(1',3'-dithiane) (12b)

A solution of 3-methylcyclohex-2-en-4-one spiro-1,2'-(1',3'-dithiane) (4b) (1.0 g, 4.7 mmol) in thf (15 mL) was transferred *via* cannula into a stirred solution of LDA (prepared from diisopropylamine (0.79 mL) and n-butyllithium (1.3 equiv.) in thf (2 mL) at -78 °C for one hour) at -78 °C. The anion was allowed to form over thirty minutes before being quenched by addition of phenyl selenenyl bromide (prepared from diphenyldiselenide (0.88 g, 2.8 mmol) and

bromine (0.14 mL, 2.8 mmol)) in thf (10 mL). The reaction was maintained at -78 °C for thirty minutes before being allowed to reach 0 °C. Following the usual work-up procedure, water (3 mL) containing acetic acid (0.2 mL) was added to the crude selenide in dichloromethane (10 mL). Hydrogen peroxide (30% w/v) was added slowly until all starting matrial had reacted according to TLC analysis. The reaction was then worked up by addition of saturated aqueous sodium hydrogen carbonate solution and extracted with dichloromethane. The combined organic extracts were dried over magnesium sulphate and the solvents removed *in vacuo*. Purification by chromatography using ethyl acetate/petroleum ether (1:2) as eluant gave 3-methylcyclohexa-2,5-dien-4-one spiro-1,2'-(1',3'-dithiane) (12b) as crystalline plates (0.25 g, 25%), mp 112-114 °C (diethyl ether) (Found: C, 56.26; H, 5.69. $C_{10}H_{12}OS_2$ requires C, 56.57; H, 5.70%); $\nu_{max.}$ 1 670 and 1 640 cm^{-1}; δ_H ($CDCl_3$), 2.0 (3 H, s), 2.05-2.2 (2 H, m), 2.9-3.3 (4 H, m), 6.25 (1 H, d, *J* 10 Hz), 6.95 (1 H, s), and 7.3 (1 H, d, *J* 10 Hz). Found: *m/z* 212.034 0 (M^+), 179, 170, 138, and 74; $C_{10}H_{12}OS_2$ requires 212.032 9.

2-Phenylcyclohexa-2,5-dien-4-one spiro-1,2'-(1',3'-dithiane) (12c)

A solution of 2-phenylcyclohex-2-en-4-one spiro-1,2'-(1',3'-dithiane) (4d) (0.27 g, 1.0 mmol) in thf (20 mL) was transferred *via* cannula into a stirred solution of LDA (prepared from diisopropylamine (0.16 mL) and n-butyllithium (1.2 equiv.) in thf (2 mL) for three quarters of an hour) at -78 °C. The anion was allowed to form over thirty minutes before being quenched by addition of phenyl selenenyl bromide (prepared from diphenyl diselenide (0.15 g, 0.5 equiv.) and bromine (0.03 mL, 0.5 equiv.)) in thf (10 mL). The reaction was maintained at -78 °C for thirty minutes before being allowed to reach 0 °C. Following the usual work-up procedure, water (3 mL) containing acetic acid (0.2 mL) was added to the crude selenide in dichloromethane (10 mL). Hydrogen peroxide (30% w/v) was added slowly until all starting material had reacted according to TLC analysis. The reaction was then quenched by addition of saturated aqueous sodium hydrogen carbonate solution and extracted with dichloromethane. The combined organic extracts were dried over magnesium sulphate and the solvents removed *in vacuo*. Purification by chromatography using ethyl acetate/petroleum ether (1:2) as eluant gave 2-phenylcyclohexa-2,5-dien-4-one spiro-1,2'-(1',3'-dithiane) (12c) as an unstable clear oil (100 mg, 36%); $\nu_{max.}$ 1 700 cm^{-1}; δ_H ($CDCl_3$), 1.9-2.2 (2 H, m), 2.5-2.7 (2 H, m), 2.9-3.2 (2 H, m), 6.8 (1 H, s, 7.05 (1 H, d, *J* 10 Hz), 7.2-7.6 (3 H, m), 7.65-7.75 (2 H, m), and 7.8 (1 H, d, *J* 10 Hz).

1-Methoxy-3-trimethylsilyloxybuta-1,3-diene (Danishefsky's diene)

Anhydrous powdered zinc chloride (0.54 g, 4.0 mmol) was added to dry triethylamine (37.8 mL, 0.27 mol) under a static positive pressure of nitrogen at room temperature. To this mixture was added 4-methoxybut-3-en-2-one (9) (13.35 g, 0.133 mol) in dry toluene (20 mL), followed immediately by trimethylchlorosilane (33.38 mL, 0.26 mol) in one portion. A slight exothermic reaction was noted. After thirty minutes, the reaction temperature was raised to 40 °C and stirring was continued overnight. The reaction was allowed to cool, and then added to dry ether (250 mL) before being filtered through a pad of Celite. The filtrate and combined ethereal washings were concentrated *in vacuo* to a volume of ca. 100 mL. The brown reaction mixture

was rediluted with dry ether (200 mL) and again filtered through Celite. The cycle was repeated twice until no more solid precipitated when the oil was diluted. Distillation through a Vigreux column gave 1-methoxy-3-trimethylsilyloxybuta-1,3-diene as a clear oil (18.85 g, 82%); bp 36-40 °C at 2 mmHg; $\nu_{max.}$ (dry $CHCl_3$ solution), 1 656, 1 618, 1 597, 1 567, 1 538, 1 300, 1 234, 1 010, and 950 cm^{-1}; δ_H ($CDCl_3$) 0.23 (9 H, s), 3.57 (3 H, s), 4.03-4.17 (2 H, br d, *J* 1 Hz), 5.36 (1 H, d, *J* 12 Hz), and 6.81 (1 H, d, *J* 12 Hz).

Diels-Alder reaction of cyclohex-2-en-4-one spiro-1,2'-(1',3'-dithiane) (4a) with 1-methoxy-3-trimethylsilyloxybuta-1,3-diene

(a) Formation of bicyclo-[4.4.0]-dec-2-en-4,10-dione spiro-7,2'-(1',3'-dithiane) (14a)

A baked resealable Carius tube was charged with cyclohex-2-en-4-one spiro-1,2'-(1',3'-dithiane) (4a) (1.0 g, 5 mmol), 1-methoxy-3-trimethylsilyloxybuta-1,3-diene (3.44 g, 20 mmol) and dry degassed xylene (10 mL). The tube was then sealed under a blanket of nitrogen and heated to 220 °C for forty-eight hours. The tube was allowed to cool to room temperature and the contents poured into water (100 mL) containing silica gel (ca. 1 g). After stirring for sixty hours the aqueous phase was extracted with chloroform and the combined organic layers dried over magnesium sulphate. Removal of solvents gave an oily residue which was purified by chromatography using ethyl acetate/petroleum ether (1:1) as eluant to give bicyclo-[4.4.0]-dec-2-en-4,10-dione spiro-7,2'-(1',3'-dithiane) (14a) as an oil (0.42 g, 31%); bp 250 °C at 0.05 mmHg; $\nu_{max.}$ 3 200, 1 710, and 1 620 cm^{-1}; δ_H ($CDCl_3$, 250 MHz), 2.2-2.55 (5 H, m), 2.79 (1 H, ddd, *J* 1.5, 4.9, and 6.6 Hz), 2.95-3.04 (2 H, m), 3.25-3.43 (4 H, m), 4.02-4.15 (2 H, m), 6.89 (1 H, d, *J* 8.8 Hz), and 7.89 (1 H, d, *J* 8.8 Hz). Found: *m/z* 268.059 5 (M^+), 145, 132, and 69. $C_{13}H_{16}O_2S_2$ requires 268.059 2.

(b) Formation of 2-methoxybicyclo-[4.4.0]-deca-4,10-dione spiro-7,2'-(1',3'-dithiane) (13a)

A baked resealable Carius tube was charged with cyclohex-2-en-4-one spiro-1,2'-(1',3'-dithiane) (4a) (2.0 g, 10 mmol), 1-methoxy-3-trimethylsilyloxybuta-1,3-diene (5.2 g, 30 mmol), and dry degassed xylene (10 mL). The reactants were then sealed under a blanket of nitrogen and heated to 200 °C for thirty-two hours. The tube was carefully opened when it had cooled to room temperature, and the contents stirred for one and a half hours with dry tetrahydrofuran (25 mL) containing concentrated hydrochloric acid (one drop). Purification by chromatography using ethyl acetate/petroleum ether (1:1) as eluant gave 2-methoxybicyclo-[4.4.0]-deca-4,10-dione spiro-7,2'-(1',3'-dithiane) (13a) as a crystalline solid (1.05 g, 35%), mp 130-133 °C (Found: C, 55.76; H, 6.80. $C_{14}H_{20}O_3S_2$ requires C, 55.97; H, 6.71%); $\nu_{max.}$ 1 710 and 1 100 cm^{-1}; δ_H($CDCl_3$, 250 MHz), 1.97-2.20 (2 H, m), 2.23-2.37 (2 H, m), 2.47-2.56 (1 H, m), 2.7-3.02 (9 H, m), 3.20-3.28 (1 H, m), 3.38 (3 H, s), 3.40-3.45 (1 H, m), and 3.91-3.92 (1 H, m); δ_C($CDCl_3$), 25.23, 26.28, 26.47, 34.28, 38.66, 40.33, 43.55, 43.67, 48.05, 51.88, 57.42, 78.12, 206.94, and 208.01. Found: *m/z* 300.031 5 (M^+), 268, 145, and 132. $C_{14}H_{20}O_3S_2$ requires 300.085 4.

Diels-Alder reaction of 3-methylcyclohex-2-en-4-one spiro-2'-(1',3'-dithiane) (13) with 4-methoxy-2-trimethylsilyloxybuta-1,3-diene

(a) Formation of 1-methylbicyclo-[4.4.0]-dec-2-en-4,10-dione spiro-7,2'-(1',3'-dithiane) (14b)

A baked resealable Carius tube was charged with 3-methylcyclohex-2-en-4-one spiro-1,2'-(1',3'-dithiane) (4b) (0.75 g, 3.5 mmol) and 1-methoxy-3-trimethylsilyloxybuta-1,3-diene (1.8 g, 10.5 mmol). The tube was sealed under a blanket of nitrogen and heated to 220 °C for fifty-five hours. The contents were then stirred with thf (25 mL) containing concentrated hydrochloric acid (one drop) and water (two drops) for one hour. The aqueous phase was extracted with several portions of dichloromethane. The combined organic phase was dried over magnesium sulphate and reduced in volume. The residue was purified by chromatography to give 1-methylbicyclo-[4.4.0]-dec-2-en-4,10-dione spiro-7,2'-(1',3'-dithiane) (14b)as an oil (0.25 g, 25%); $\nu_{max.}$1 675 and 1 720 cm^{-1}; $\delta_H(CDCl_3)$, 1.9-2.1 (2 H, m), 2.3 (3 H, s), 2.5-3.2 (11 H, m), 6.1 (1 H, d, *J* 5 Hz), and 6.6 (1 H, d, *J* 5 Hz). Found: *m/z* 282.073 2 (M^+), 214, 45, and 132. $C_{14}H_{18}O_2S_2$ requires 283.075 4.

(b) Formation of 2-methoxy-1-methylbicyclo-[4.4.0]-deca-4,10-dione spiro-7,2'-(1',3'-dithiane) (13b)

A baked resealable Carius tube was charged with 3-methyl-cyclohex-2-en-4-one spiro-1,2'-(1',3'-dithiane) (4b) (0.86 g, 4 mmol) and 1-methoxy-3-trimethylsilyloxybuta-1,3-diene (3.44 g, 20 mmol) and dry degassed xylene (10 mL). The tube was sealed under a blanket of nitrogen and heated to 220 °C for ninety-one hours. The tube was allowed to cool to room temperature and the contents poured into water (100 mL) containing silica gel (8 g). After stirring for one hour the aqueous phase was extracted with several portions of chloroform. The combined organic extracts were dried over magnesium sulphate and reduced in volume. The residue was purified by chromatography to give 2-methoxy-1-methylbicyclo-[4.4.0]-deca-4,10-dione spiro-7,2'-(1',3'-dithiane) (13b)as colourless crystals (0.36 g, 29%), mp 180-182 °C (methanol) (Found: C, 57.51; H, 7.29. $C_{15}H_{22}O_3S_2$ requires C, 57.29; H, 7.05%); $\nu_{max.}$ 1 700 and 1 720 cm^{-1}; $\delta_H(CDCl_3$, 250 MHz), 1.36 (3 H, s), 1.98-2.04 (2 H, m), 2.26-3.02 (13 H, m), 3.20 (3 H, s), and 3.59 (1 H, t, *J* 2.67 Hz). Found: *m/z* 314.101 2 (M^+), 282, 214, 145, and 132. $C_{15}H_{22}O_3S_2$ requires 314.101 0.

2-Methylcyclohexan-4-one spiro-1,2'-(1',3'-dithiane) (16)

Copper (I) cyanide (0.27 g, 3 mmol) in diethyl ether (3 mL) was cooled to -78 °C and treated with methyllithium (2.4 equiv.). The slurry was allowed to warm to 0 °C at which point it became a colourless solution. This solution was cooled to -78 °C and treated with a solution of cyclohex-2-en-4-one spiro-1,2'-(1',3'-dithiane) (4a) (0.5 g, 2.5 mmol) in diethyl ether (15 mL). The reaction mixture was stirred for three hours at -78 °C before being quenched by the addition of saturated aqueous ammonium chloride solution and extracted with several portions of dichloromethane. The combined organic extracts were dried over magnesium sulphate and reduced in volume to give 2-methylcyclohexan-4-one spiro-1,2'-(1',3'-dithiane) (16) as a colourless crystalline solid (0.42 g, 78%); mp 75-78 °C (methanol) (Found: C, 55.44; H, 7.44. $C_{10}H_{16}OS_2$ requires C, 55.52; H, 7.45%); $\nu_{max.}$ 1 710 cm^{-1}; $\delta_H(CDCl_3$, 250 MHz), 1.22 (3 H, d, *J* 6.4 Hz), 1.84-2.00 (1 H, m), 2.04-2.37 (2 H, m), 2.40-2.66 (5 H, m), and 2.70-3.12 (5 H, m). Found: *m/z* 216.064 3 (M^+), 159, 145, 132, 100, and 74. $C_{10}H_{16}OS_2$ requires 216.064 2.

2-Butylcyclohexan-4-one spiro-1,2'-(1',3'-dithiane)

A slurry of copper (I) cyanide (0.27 g, 3 mmol) in diethyl ether (3 mL) stirring at -78 °C was treated with n-butyllithium (2 equiv.). The reaction was allowed to warm to -20 °C at which point a brown solution was formed. The solution was cooled to -78 °C and stirring was continued for half an hour. A solution of cyclohex-2-en-4-one spiro-1,2'-(1',3'-dithiane) (4a) (0.5 g, 2.5 mmol) in diethyl ether (15 mL) was added dropwise. The reaction was held at -78 °C for three hours before being quenched and worked up in the usual manner. Chromatography gave 2-butylcyclohexan-4-one spiro-1,2'-(1',3'-dithiane) as a clear oil which crystallised reluctantly on standing (0.25 g, 39%) (Found: C, 60.44; H, 8.69. $C_{13}H_{22}OS_2$ requires C, 60.42; H, 8.58%); $\nu_{max.}$ 3 500 and 1 710 cm^{-1}; $\delta_H(CDCl_3$, 250 MHz), 0.90 (3 H, t, *J* 7 Hz), 1.10-1.40 (5 H, m), and 1.68-3.15 (14 H, m). Found: *m/z* 258.110 7 (M^+), 201, 145, and 128. $C_{13}H_{22}OS_2$ requires 258.111 2.

2-(5-(Pent-1-enyl))cyclohexan-4-one spiro-1,2'-(1',3'-dithiane)

Pent-4-enyl magnesium bromide was prepared from 5-bromopentene (0.pp g, 6.25 mmol) and magnesium turnings (0.15 g, 6.25 mmol) in dry diethyl ether (3 mL); the Grignard reagent was then diluted with diethyl ether (5 mL) and cooled to -78 °C. Freshly prepared copper (I) bromide-dimethyl sulphide complex (1.03 g, 5 mmol) was then added *via* a Schlenk tube and stirring was continued for thirty minutes. A solution of cyclohex-2-en-4-one spiro-1,2'-(1',3'-dithiane) (4a) (0.5 g, 2.5 mmol) in dry diethyl ether (15 mL) was added dropwise over twenty minutes. When addition was complete, the reaction was allowed to reach room temperature over two hours. Usual work-up gave 2-(5-(pent-1-enyl))-cyclohexan-4-one spiro-1,2'-(1',3'-dithiane) as an oil (0.52 g, 77%) (Found: C, 62.60; H, 8.42. $C_{14}H_{22}OS_2$ requires C, 62.41; H, 8.23%); $\nu_{max.}$ 3 500, 3 080, 1 740, and 1 680 cm^{-1}; $\delta_H(CDCl_3$, 250 MHz), 1.83-2.22 (8 H, m), 2.31-3.20 (11 H, m), 4.93-5.06 (2 H, m), and 5.72-5.88 (1 H, m). Found: *m/z* 270.111 6 (M^+), 195, 162, 145, and 106. $C_{14}H_{22}OS_2$ requires 270.111 2.

4-Methylcyclohexa-2,5-dien-4-ol spiro-1,2'-(1',3'-dithiane) (17)

Copper (I) iodide (0.47 g, 2.47 mmol) in thf (10 mL) at -78 °C was treated with methyllithium (2.2 equiv.) and the solution was stirred at 0 °C until all the yellow precipitate of methylcopper had reacted to form a clear solution. The solution was stirred for a further hour at -78 °C, before being treated with a solution of cyclohexa-2,5-dien-4-one spiro-1,2'-(1',3'-dithiane) (12a) (0.41 g, 2.1 mmol) in thf (15 mL) . The reaction was allowed to attain room temperature slowly, and stirring was continued overnight. Purification by chromatography following the usual work-up procedure gave 4-methylcyclohexa-2,5-dien-4-ol spiro-1,2'-(1',3'-dithiane) (17) as an oil (140 mg, 31%), bp 250 °C at 0.5 mmHg; $\nu_{max.}$ 3 360, 1 700, 1 600, and 1 580 cm^{-1}; $\delta_H(CDCl_3)$, 1.9 (2 H, q, *J* 5 Hz), 2.15 (3 H, s), 2.65 (2 H, t, *J* 5 Hz), 3.0 (2 H, t, 5 Hz), 6.7 (1 H, s, exchangeable with D_2O), 6.85 (2 H, d, *J* 10 Hz), and 7.35 (2 H, d, *J* 10 Hz). Found: *m/z* 214.049 3 (M^+), 199, 125, and 89. $C_{10}H_{14}OS_2$ requires 214.048 6.

Acknowledgements

This investigation has enjoyed support from the SERC and from Shell Research Ltd.

References

1. Page, P. C. B.; van Niel, M. B.; Williams, P. H. *J. Chem. Soc., Chem. Commun* **1985**, 742; Page, P. C. B.; van Niel, M. B.; Westwood, D. *J. Chem. Soc., Perkin Trans. 1*, **1988**, 269.
2. Page, P. C. B.; van Niel, M. B.; Westwood, D. *J. Chem. Soc., Chem. Commun.*,**1987**, 775.
3. Jones, P. F.; Lappert, M. F.; Szary, A. C. *J. Chem. Soc., Perkin Trans. 1*, **1973**, 2272.
4. Desimoni, G.; Tacconi, G. *Chem. Rev.*, **1975**, *75*, 651; Sauer, J. *Angew. Chem., Int. Ed. Engl.*, **1966**, *5*, 211; Fleming, I.; Harley-Mason, J. *J. Chem. Soc.*, **1964**, 2165.
5. Aben, R. W. N.; Scheeren, H. W. *Tetrahedron Lett.*, **1985**, *26*, 1889.
6. Page, P. C. B.; van Niel, M. B. *J. Chem. Soc., Chem. Commun.*, **1987**, 43.
7. Paquette, L. A.; Belmont, D. T.; Hsu, Y.-L. *J. Org. Chem.*, **1985**, *50*, 4667.
8. Page, P. C. B.; Harkin, S.; Marchington, A. P. *Synth. Commun.*, **1989**, in press.
9. Prepared by the reaction of 2-lithio-1,3-dithiane with ethyl benzoate. See Corey, E. J.; Seebach, D. *Angew. Chem., Int. Ed. Engl.*, **1965**, *4*, 1075; idem, *ibid*, 1077.
10. see, for example, Chenard, B. L.; Dolson, M. G.; Sercel, A. D.; Swenton, J. S. *J. Org. Chem.*, **1984**, *49*, 318; Evans, D. A.; Truesdale, L. K.; Carroll, G. L. *J. Chem. Soc., Chem. Commun.*, **1973**, 55.
11. Reich, H. J.; Renga, R. M.; Reich, K. *J. Am. Chem. Soc.*, **1975**, *97*, 5434.
12. Danishefsky, S.; Kitahara, T.; Yan, C. F.; Morris, J. *J. Am. Chem. Soc.*, **1979**, *101*, 6996; idem, *ibid*, 7001; idem, *ibid*, 7008.
13. Danishefsky, S.; Kitahara, T. *J. Am. Chem. Soc.*, **1974**, *96*, 7807.
14. Lipschutz, B. H.; Wilhelm, R. S.; Kozlowsky, J. A. *Tetrahedron*, **1984**, *40*, 5005.