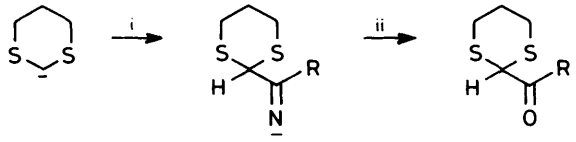
Reactions of Metallated 1,3-Dithianes with Carboxylic Acid Derivatives

Philip C. Bulman Page,* Monique B. van Niel, and Donald Westwood
Department of Organic Chemistry, Robert Robinson Laboratories, University of Liverpool, P.O. Box 147, Liverpool L69 3BX

2-Lithio-1,3-dithiane and 2-lithio-2-trimethylsilyl-1,3-dithiane react with nitriles to afford primary aminoketene dithioacetals in good yields; these compounds exhibit marked ambident nucleophilicity. Use of other carboxylic acid derivatives as electrophiles normally produces acyl dithianes, however 2-lithio-2-trimethylsilyl-1,3-dithiane reacts with benzoyl cyanide to give a cyanoketene dithioacetal.

Since the early work of Corey and Seebach,[1] metallated 1,3-dithianes have become the most widely known and used of available acyl anion equivalents. A wide range of electrophiles react successfully including alkyl halides, aldehydes and ketones, esters, acyl halides, amides, carbon dioxide, and epoxides.[2] 2-Lithio-2-trimethylsilyl-1,3-dithiane has also found use as a reagent for the preparation of ketene thioacetals[3] but has otherwise not been extensively studied.

Surprisingly few examples of reactions of metallated 1,3-dithianes with nitriles have been reported.[4] These universally report the formation of acyldithianes by nucleophilic attack of dithiane anion at the nitrile group followed by hydrolysis of the resulting primary imine upon work-up (Scheme 1). A similar reaction of the anion derived from 2-trimethylsilyl-1,3-oxathiane using s-butyl-lithium has also been reported.[5]

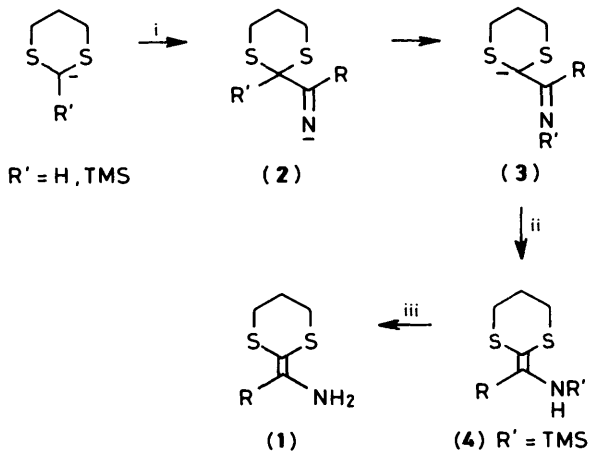


Scheme 1. *Reagents:* i, RCN; ii, H_3O^+

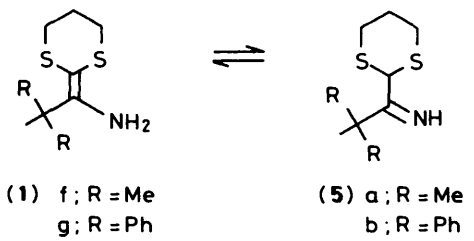
We have reinvestigated the reactions of 2-lithio-1,3-dithiane and 2-lithio-2-trimethylsilyl-1,3-dithiane with nitriles and have observed notably different results.

Results and Discussion

In our hands both 2-lithio-1,3-dithiane and 2-lithio-2-trimethylsilyl-1,3-dithiane react with non-enolisable nitriles to produce primary aminoketene dithioacetals (**1**) upon normal work-up (Table 1).[6] The compounds appear interesting as they are at once ketene dithioacetals and primary enamines. As ketene dithioacetals may be hydrolysed to give carboxylic acids, aminoketene dithioacetals are formally equivalents of α-amino acids. Tertiary aminoketene dithioacetal (**19**) may be prepared by the reaction of 2-lithio-2-trimethylsilyl-1,3-dithiane with dimethyl formamide.[7] We believe that these reactions proceed by initial formation of the corresponding imine anions (**2**), inter- or intramolecular migration of the silicon entity from carbon to nitrogen (or the related proton transfer) to give dithiane carbanions (**3**), and subsequent protonation at the nitrogen atom. Hydrolytic cleavage of the nitrogen-silicon bond of products (**4**) occurs on work-up to give primary aminoketene dithioacetals (**1**) (Scheme 2); alternatively the trimethylsilyl compounds (**4**) may be isolated by recrystallisation from the product mixture. A tautomerism is observed between the aminoketene dithioacetals (**1f**) and (**1g**), derived from use of pivalonitrile and 2,2-diphenylpropionitrile as substrates, and the primary imines (**5a**) and (**5b**) (Scheme 3).

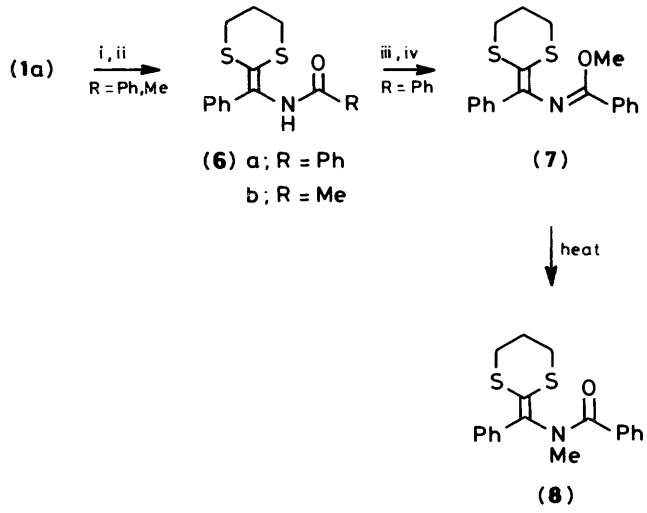


Scheme 2. *Reagents:* i, RCN; ii, H_3O^+; iii, SiO_2/H_2O

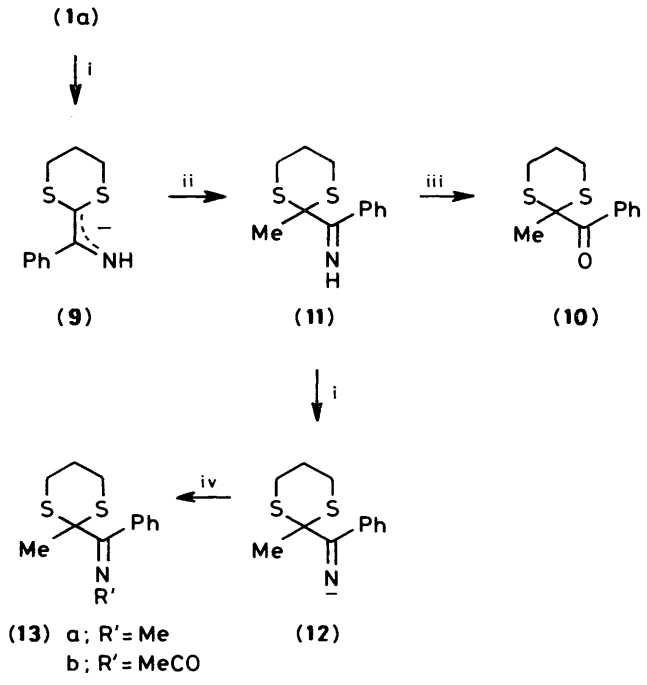


Scheme 3.

In common with many enamines, aminoketene dithioacetals display marked ambident nucleophilicity. Acylation of compound (**1a**) using benzoyl chloride or acetyl chloride in tetrahydrofuran (THF) in the presence of one equivalent of triethylamine gave the corresponding amide (**6**) (Scheme 4). Conversely, treatment of (**1a**) with one equivalent of n-butyllithium in THF at −78 °C gave the delocalised anion (**9**) which reacted with alkyl halides to exclusively provide singly protected diketones (**10**) after hydrolytic work-up (0.1M HCl) (Scheme 5). Aminoketene dithioacetals are therefore synthetic equivalents of α-ketoacyl anions (**20**). Deprotonation of compound (**6a**) with one equivalent of base and treatment of the resulting anion with methyl iodide (1 equiv.) provided iminoether (**7**), by reaction at oxygen, rather than the nitrogen-quenched material (**8**) (Scheme 4). An unusually facile migration of the methyl group from oxygen to nitrogen occurred on heating compound (**7**) in ethanolic solution under reflux to give the thermodynamically favoured N-alkylated material (**8**). Chapman rearrangements of this type normally require temp-



Scheme 4. *Reagents:* i, Et_3N; ii, RCOCl (R = Ph, Me); iii, Ph_3C^-; iv, MeI

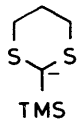
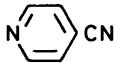
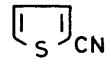


Scheme 5. *Reagents:* i, n-BuLi; ii, MeI; iii, H_3O^+; iv, R'X

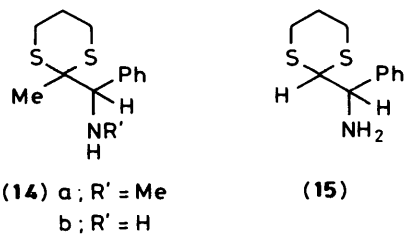
eratures in excess of 300 °C;[8] however the reaction is known to be catalysed by alkyl halides.[8]

A particularly interesting discovery was that rapid work-up of the alkylation reaction mixture with saturated aqueous ammonium chloride solution gave not the ketone (**10**) but rather the primary imines (**11**).[9] We were astonished to find these primary imines to be remarkably stable under normal laboratory conditions; they may even be purified by flash column chromatography using silica gel (Merck 9385) as adsorbent without any unusual precautions. We know of few other examples of primary imines with this degree of stability.[10] Although readily hydrolysed using dilute acid to give ketones (**10**), imines (**11**) are resistant to reduction and we have been quite unable to convert them into the corresponding amines

Table 1.

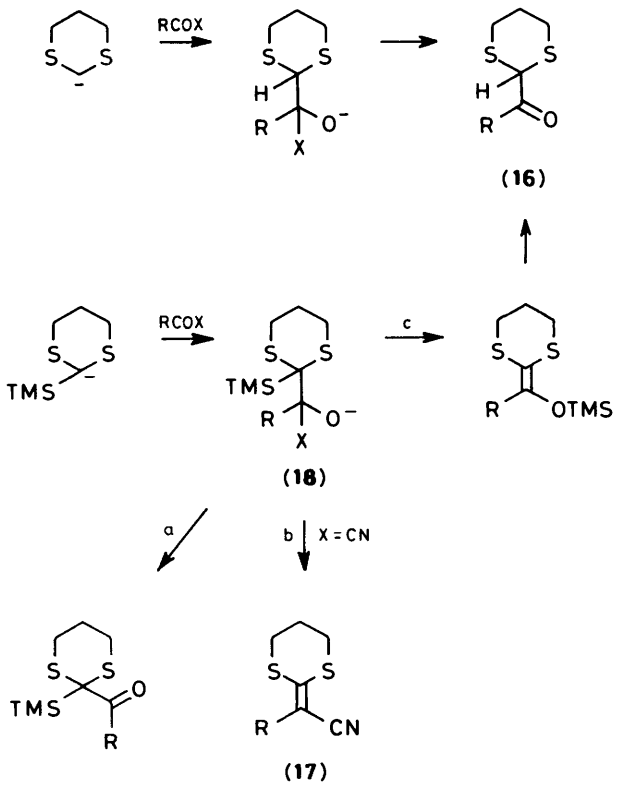
	RCN		
		Yield of compound (1) (%)	
a;	PhCN	87	67
b;	*p*-MeC_6H_4CN	81	78
c;	*p*-BrC_6H_4CN	60	48
d;		69	61
e;		65	27
f;	Me_3CCN	55	40
g;	$MePh_2CN$	68	57

(**14**) using hydride reducing agents, perhaps due to steric hindrance[11] or preferential removal of the acidic imine proton. Indeed, treatment of imine (**11**) with n-butyl-lithium resulted exclusively in deprotonation to give anion (**12**), no nucleophilic addition being observed. Addition of electrophiles to THF solutions of (**12**) gave the expected products of alkylation at the nitrogen atom (**13**) in reasonable yields (Scheme 5).



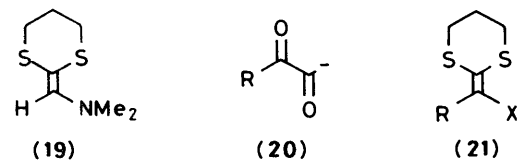
The amines (**14**) proved to be accessible in quantitative yields by reduction of the imines (**11**) and (**13a**) with borane–THF complex at room temperature. A similar reduction of the parent aminoketene dithioacetal (**1a**) provided the protected α-amino aldehyde (**15**) in good yield.

2-Lithio-1,3-dithiane reacts with various other carboxylic acid derivatives including acyl halides, esters, thioesters, and isocyanates to give acyl dithianes in reasonable yields.[2] We have found that use of 2-lithio-2-trimethylsilyl-1,3-dithiane generally gives similar products which also do not contain silicon (Table 2). An interesting divergence of reaction pathway was observed when nitriles were used as electrophiles. The normal acyl dithiane product (**16**, R = Ph) was observed on treatment of benzoyl cyanide with the parent dithiane anion, while reaction with the silylated anion gave the cyanoketene dithioacetal (**17**, R = Ph) as the only product in 45% yield, the breakdown of the tetrahedral intermediate (**18**) with loss of the leaving group (Scheme 6, path a) presumably being slower than the competing Peterson elimination (path b). It is conceivable that the loss of the silicon entity observed in the reactions of other acyl



Scheme 6.

derivatives could also be explained by invoking this pathway, the initially formed enol ethers (**21**) undergoing subsequent hydrolysis. However, we have been unable to find any trace of such enol ether intermediates in the product mixtures. We



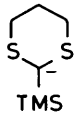
therefore suggest that these reactions normally proceed by an intramolecular transfer of the silicon grouping from carbon to oxygen followed by expulsion of the leaving group to form sensitive trimethylsilyl enol ethers of the observed acyl dithiane products (Scheme 6, path c).

Experimental

I.r. spectra were recorded in solution or for liquids as thin films and for solids as Nujol mulls on Perkin-Elmer 298 and 1320 spectrophotometers, and calibrated against polystyrene. ^{1}H N.m.r. spectra were recorded using Jeol PMX60, Perkin-Elmer R34, and Bruker WM250 instruments using tetramethylsilane as reference. ^{13}C N.m.r. spectra were recorded using Jeol JNM-FX60Q and Bruker WM250 instruments with tetramethylsilane as reference. Mass spectra were obtained using a VG Micromass 7070E machine. M.p.s were obtained using a Reichert hot stage apparatus.

Flasks, syringes, needles, and stirring bars were dried for a minimum of four hours at 150 °C and allowed to cool in a desiccator over self-indicating silica gel. Anhydrous THF was freshly distilled from the sodium-benzophenone ketyl radical prior to use. All reactions requiring the use of organolithium

Table 2.

		
	Yield of acyl dithiane	
MeCOEt	43	33
PhCOEt	55	33
PhCOCN	77	—
PhCOSMe	24	81
MeNCO	40	—

reagents were conducted under a small static positive pressure of nitrogen or argon and cooled externally using a Camlab/Fryka KB300 cooling bath, carbon dioxide pellets, or liquid nitrogen.

All yields quoted refer to isolated products purified by recrystallisation, flash column chromatography on silica gel (Merck 9385), dry flash column chromatography on silica gel (Merck 15111), vacuum distillation with conventional or Buchi Kugelrohr GKR50 apparatus, or preparative m.p.l.c. using a Gilson 303 metering pump, a Gilson 803C pressure module, a Rheodyne 7125 injection valve, a Waters R403 refractive index detector, a Gilson TDC80 fraction collector, a Chessel B082 chart recorder and Buchi, Corning, Omnifit, and BDH glass columns.

General Procedure for the Preparation of 2-Lithio-1,3-dithiane and 2-Lithio-2-trimethylsilyl-1,3-dithiane.—A solution of n-butyl-lithium in hexane (1.2 equiv.) was added to a solution of 2-trimethylsilyl-1,3-dithiane or 1,3-dithiane in dry THF (0.2 molar) at −40 °C. After being stirred for 2 h the solution of the anion was transferred by cannula for subsequent reaction.

2-Trimethylsilyl-1,3-dithiane. The anion generated from 1,3-dithiane (3.5 g, 29.1 mmol) was transferred *via* cannula to a solution of chlorotrimethylsilane (4.07 g, 32 mmol) in THF (50 ml) at −78 °C. The mixture was left to reach room temperature with stirring and saturated aqueous ammonium chloride (100 ml) added. The mixture was extracted with chloroform (3 × 150 ml) and the combined organic layers were dried ($MgSO_4$). Evaporation of the solvent gave an oily residue which was purified by distillation to give the title compound as a colourless oil (4.7 g, 84%), b.p. 78—80 °C at 1.2 mmHg (Found: C, 43.5; H, 8.45. $C_7H_{16}S_2Si$ requires C, 43.70; H, 8.38%); $\nu_{max.}$ 2 900, 1 425, 1 250, and 850 cm^{-1}; $\delta_H(CD_2Cl_2)$ 0.16 (9 H, s), 1.9—2.2 (2 H, m), 2.6—3.0 (4 H, m), and 3.7 (1 H, s).

General Procedure for the Preparation of Primary Aminoketene Dithioacetals.—The anion generated from 1,3-dithiane or 2-trimethylsilyl-1,3-dithiane was transferred *via* cannula to a solution of the nitrile in THF at −78 °C. The mixture was allowed to reach room temperature with stirring and saturated aqueous ammonium chloride (100 ml) added. The mixture was extracted with chloroform (3 × 100 ml) and the combined organic layers were dried ($MgSO_4$). Evaporation of the solvent gave crude aminoketene dithioacetals which were purified by column chromatography.

α-(1,3-*Dithian*-2-*ylidene*)*benzylamine* (**1a**).—(*a*) *From* 1,3-*dithiane*. 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 at −78 °C. Work-up and chromatography using ethyl acetate–light petroleum (1:5) as eluant gave the title compound (**1a**) as yellow crystals (14.0 g, 87%), m.p. 118—120 °C (Found: C, 59.05; H, 5.9; N, 6.2. $C_{11}H_{13}NS_2$ requires C, 59.15; H, 5.87; N, 6.27%); $\nu_{max.}$ 3 450, 3 320, and 1 610 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); $\delta_C(CD_2Cl_2)$ 25.59, 31.72, 32.69, 127.84, 128.47, 137.39, and 149.88 (Found: *m/z* 223.048960 (M^+), 149, 121, 105, 77, 68, and 51. $C_{11}H_{13}NS_2$ requires 223.048939.

(*b*) *From* 2-*trimethylsilyl*-1,3-*dithiane*. The anion generated from 2-trimethylsilyl-1,3-dithiane (1.94 g, 10.1 mmol) was added to a solution of benzonitrile (1.25 g, 12.1 mmol) in THF at −78 °C. Work-up and chromatography using ethyl acetate–light petroleum (1:5) as eluant gave the title compound (**1a**) (1.51 g, 67%).

α-(1,3-*Dithian*-2-*ylidene*)(p-*tolyl*)*methylamine* (**1b**).— (*a*) *From* 1,3-*dithiane*. The anion generated from 1,3-dithiane (2.77 g, 23.1 mmol) was added to a solution of *p*-toluonitrile (2.7 g, 23.1 mmol) in THF at −78 °C. Work-up and chromatography using ethyl acetate–light petroleum (1:10) as eluant gave the title compound (**1b**) as colourless crystals (3.52 g, 81%), m.p. 98—99 °C (Found: C, 60.5; H, 6.35; N, 5.85. $C_{12}H_{15}NS_2$ requires C, 60.72; H, 6.37; N, 5.90%); $\nu_{max.}$ 3 410, 3 300, and 1 585 cm^{-1}; $\delta_H(CDCl_3)$ 2.07—2.2 (2 H, m), 2.35 (3 H, s), 2.55—2.65 (2 H, m), 2.75—2.85 (2 H, m), 4.3 (2 H, br s), 7.1 (2 H, d, *J* 7 Hz), and 7.23 (2 H, d, *J* 7 Hz); Found: *m/z* 237.0645932 (M^+). $C_{12}H_{15}NS_2$ requires 237.064588.

(*b*) *From* 2-*trimethylsilyl*-1,3-*dithiane*. The anion generated from 2-trimethylsilyl-1,3-dithiane (1.88 g, 9.8 mmol) was added to a solution of 4-toluonitrile (1.17 g, 10 mmol) in THF at −78 °C. Work-up and chromatography using ethyl acetate–light petroleum (1:10) as eluant gave the title compound (**1b**) as colourless crystals (1.82 g, 78%).

α-(1,3-*Dithian*-2-*ylidene*)(p-*tolyl*)*methylamine* (**1b**).— (*a*) (*a*) *From* 1,3-*dithiane*. The anion generated from 1,3-dithiane (1.43 g, 11.9 mmol) was added to a solution of *p*-bromobenzonitrile (2.17 g, 11.9 mmol) in THF at −78 °C. Work-up and chromatography using ethyl acetate–light petroleum (1:5) as eluant gave the title compound (**1c**) as a red oil which crystallised on standing (2.15 g, 60%); m.p. 95—96 °C (Found: C, 43.8; H, 4.0; N, 4.45. $C_{11}H_{12}NS_2Br$ requires C, 43.71; H, 4.00; N, 4.63%); $\nu_{max.}$ 3 460, 3 320, 1 600, and 1 585 cm^{-1}; $\delta_H(CDCl_3)$ 2.15—2.25 (2 H, m), 2.6—2.7 (2 H, m), 2.85—2.95 (2 H, m), 4.35 (2 H, br s), 7.29 (2 H, d, *J* 8.9 Hz), and 7.48 (2 H, d, *J* 8.9 Hz). Found: *m/z* 302.9579 (M^+), 229, 184, 149, 130, and 120. $C_{11}H_{12}NS_2Br$ requires 302.9574.

(*b*) *From* 2-*trimethylsilyl*-1,3-*dithiane*. The anion generated from 2-trimethylsilyl-1,3-dithiane (3.88 g, 20.2 mmol) was added to a solution of *p*-bromobenzonitrile (3.68 g, 20.2 mmol) in THF at −78 °C. Work-up and chromatography using ethyl acetate–light petroleum (1:10) as eluant gave the title compound (**1c**) as orange crystals (2.93 g, 48%).

α-(1,3-*Dithian*-2-*ylidene*)(4-*pyridyl*)*methylamine* (**1d**).—(*a*) *From* 1,3-*dithiane*. The anion generated from 1,3-dithiane (4.92 g, 41 mmol) was added to a solution of 4-cyanopyridine (4.26 g, 41 mmol) in THF at −78 °C. Work-up and chromatography using ethyl acetate–petroleum (1:3) as eluant gave the title compound as brown crystals (**1d**) (4.55 g, 69%); m.p. 111—113 °C (Found: C, 53.6; H, 5.5; N, 12.5; $C_{10}H_{12}N_2S_2$ requires C, 53.54; H, 5.39; N, 12.49%); $\nu_{max.}$ 3 430, 3 300, and 1 600 cm^{-1}; $\delta_H(CDCl_3)$, 2.1—2.2 (2 H, m), 2.6—2.7 (2 H, m), 2.8—2.9 (2 H, m), 4.5 (2 H, br s), 7.3 (2 H, d, *J* 5 Hz), and 8.53 (2 H, d, *J* 5 Hz). Found: *m/z* 224.043 045 0 (M^+). $C_{10}H_{12}N_2S_2$ requires 224.044 188.

(*b*) *From* 2-*trimethylsilyl*-1,3-*dithiane*. The anion generated from 2-trimethylsilyl-1,3-dithiane (1.72 g, 9 mmol) was added to a solution of 4-cyanopyridine (1.12 g, 10.8 mmol) in THF at −78 °C. Work-up and chromatography using ethyl acetate–light petroleum (1:2) as eluant gave the title compound (**1d**) as orange crystals (1.23 g, 61%).

α-(1,3-*Dithian*-2-*ylidene*)(2-*thienyl*)*methylamine* (**1e**).—(*a*) *From* 1,3-*dithiane*. The anion generated from 1,3-dithiane (5.08 g, 42.3 mmol) was added to a solution of 2-cyanothiophene (4.61 g, 42.3 mmol) in THF at −78 °C. Work-up and chromatography using ethyl acetete–light petroleum (1:3) as eluant gave the title compound (**1e**) as an orange oil (6.37 g, 65%); $\nu_{max.}$ 3 400, 3 320, 3 200, 3 100, 3 080, and 1 600 cm^{-1}; $\delta_H(CDCl_3)$, 2.1—2.25 (2 H, m), 2.7—2.8 (2 H, m), 2.8—2.9 (2 H, m), 4.35 (2 H, br s), 7.0—7.05 (1 H, m), and 7.25—7.4 (2 H, m). Found: *m/z* 229.0064 (M^+), 155, 119, and 106. $C_9H_{11}NS_3$ requires 229.0054.

(*b*) *From* 2-*trimethylsilyl*-1,3-*dithiane*. The anion generated from 2-trimethylsilyl-1,3-dithiane (1.9 g, 9.9 mmol) was added to a solution of 2-cyanothiophene (1.3 g, 11.9 mmol) in THF at −78 °C. Work-up and chromatography using ethyl acetate–light petroleum (1:3) as eluant gave the title compound (**1e**) as a yellow oil (0.6 g, 27%).

α-(1,3-*Dithian*-2-*ylidene*)-β,β-*dimethylpropylamine* (**1f**).—(*a*) *From* 1,3-*dithiane*. The anion generated from 1,3-dithiane (2.77 g, 23.1 mmol) was added to a solution of trimethylacetonitrile (1.92 g, 2.55 ml, 23.1 mmol) in THF at −78 °C. Work-up and chromatography using ethyl acetate–light petroleum (1:5), as eluant gave the title compound (**1f**) as a yellow oil (1.46 g, 55%); $\nu_{max.}$ 3 400, 3 350, 3 250, 2 220, 1 680, 1 600, and 1 480 cm^{-1}; $\delta_H(CDCl_3)$, 1.15 (s), 1.8—2.15 (m), 2.8—3.05 (m), 4.5 (s), and 4.85 (s).

(*b*) *From* 2-*trimethylsilyl*-1,3-*dithiane*. The anion generated from 2-trimethylsilyl-1,3-dithiane (1.84 g, 9.6 mmol) was added to a solution of trimethylacetonitrile (0.8 g, 9.6 mmol) in THF at −78 °C. Work-up and chromatography using ethyl acetate–light petroleum (1:5) as eluant gave the title compound (**1f**) as an orange oil (0.78 g, 40%).

α-(1,3-*Dithian*-2-*ylidene*)-β,β-*diphenylpropylamine* (**1g**).—(*a*) *From* 1,3-*dithiane*. The anion generated from 1,3-dithiane (1.22 g, 10.2 mmol) was added to a solution of 2,2-diphenylpropionitrile (2.53 g, 12.2 mmol) in THF at −78 °C. Work-up and chromatography using ethyl acetate–light petroleum (1:9) as eluant gave the title compound (**1g**) as a pale yellow oil (1.42 g, 68%); $\nu_{max.}$ 3 060, 3 040, and 2 980 cm^{-1}; $\delta_H(CDCl_3)$, 1.85—2.05 (m), 2.0—2.1 (m), 2.7—2.8 (m), 3.25 (t, *J* 10 Hz), 4.45 (s), and 7.2—7.4 (m).

(*b*) *From* 2-*trimethylsilyl*-1,3-*dithiane*. The anion generated from 2-trimethylsilyl-1,3-dithiane (0.70 g, 3.6 mmol) was added to a solution of 2,2-diphenylpropionitrile (0.81 ml, 4.3 mmol) in THF at −78 °C. Work-up and chromatography using ethyl acetate–light petroleum (1:9) as eluant gave the title compound (**1g**) as a pale yellow oil (0.57 g, 57%).

N-*Trimethylsilyl*-α-(1,3-*dithian*-2-*ylidene*)*benzylamine* (**4**, R = Ph).—The anion generated from 2-trimethylsilyl-1,3-dithiane (0.62 g, 3.21 mmol) was added to a solution of benzonitrile (0.36 g, 3.5 mmol) in THF at −78 °C. Work-up and recrystallization gave the title compound (**4**, R = Ph) as colourless crystals, (0.26 g, 27%); m.p. 89—94 °C; $\nu_{max.}$ 3 340, 3 300, 1 610, and 1 600 cm^{-1}; $\delta_H(CD_2Cl_2)$, 0.4 (9 H, s), 1.9—2.1 (2 H, m), 2.3—2.4 (2 H, m), 2.55—2.65 (2 H, m), 4.7 (1 H, br s),

7.1—7.2 (2 H, m), and 7.2—7.3 (3 H, m). Found: *m/z* 295.087 310 8 (M^+). $C_{14}H_{21}NSiS_2$ requires 295.088 465.

α-(1,3-*Dithian*-2-*ylidene*)*benzyl Cyanide* (**17**, R = Ph).—The anion generated from 2-trimethylsilyl-1,3-dithiane (2.4 g, 12.5 mmol) was added to a solution of benzoyl cyanide (1.7 g, 13 mmol) in THF (50 ml) at −78 °C. The mixture was allowed to warm to room temperature with stirring and quenched with saturated aqueous ammonium chloride. The mixture was extracted with chloroform (3 × 150 ml) and the combined organic layers were dried ($MgSO_4$). Evaporation of the solvent gave an oily residue which was purified by chromatography using ethyl acetate–light petroleum (1:5) as eluant to yield the title compound (**17**, R = Ph) as colourless crystals (1.3 g, 45%), m.p. 126—127 °C (Found: C, 62.05; H, 4.95; N, 5.7. $C_{12}H_{11}NS_2$ requires C, 61.77; H, 4.75; N, 6.00%); $\nu_{max.}$ 2 200 cm^{-1}; $\delta_H(CDCl_3)$ 2.1—2.3 (2 H, m), 2.9—3.1 (2 H, m), 3.0—3.2 (2 H, m), and 7.3—7.5 (5 H, m); $\delta_C(CDCl_3)$ 23.37, 29.54, 106.66, 118.15, 128.80, 129.20, 133.70, and 158.22. Found: *m/z* 233.029 998 8 (M^+). $C_{12}H_{11}NS_2$ requires 233.033 298 4.

N-*Benzoyl*-α-(1,3-*dithian*-2-*ylidene*)*benzylamine* (**6a**).—A solution of compound (**1a**) (1.06 g, 4.8 mmol) in dry THF was stirred with triethylamine (0.73 g, 1.5 equiv.), under a positive pressure of nitrogen. Benzoyl chloride (0.81 g, 1.2 equiv.) was added slowly and stirring was continued for 5 h. The precipitate was removed by filtration and washed with cold ethanol to give the title compound (**6a**) as colourless needles (1.39 g, 89%), m.p. 212—214 °C (Found: C, 66.0; H, 5.25; N, 4.3. $C_{18}H_{17}NOS_2$ requires: C, 65.86; H, 5.23; N, 3.98%); $\nu_{max.}$ 3 300 and 1 650 cm^{-1}; $\delta_H[(CD_3)_2SO]$ 2.0—2.13 (2 H, m), 2.85—2.95 (2 H, m), 2.95—3.05 (2 H, m), 7.2—7.6 (8 H, m), 7.95 (2 H, d, *J* 9.8 Hz), and 9.93 (1 H, s). Found: *m/z* 327.074 737 5 (M^+). $C_{18}H_{17}NOS_2$ requires 327.075 151 5.

N-*Acetyl*-α-(1,3-*dithian*-2-*ylidene*)*benzylamine* (**6b**).—A solution of compound (**1a**) (1.50 g, 6.72 mmol) in dry THF was stirred with triethylamine (0.75 g, 1.1 equiv.), under a positive pressure of nitrogen. Acetyl chloride (0.63 g, 1.2 equiv.) was added slowly and stirring continued for 5 h. The precipitate was removed by filtration and washed with cold ethanol to give the title compound as colourless needles (**6b**) (1.38 g, 77%), m.p. 204—206 °C; (Found: C, 58.65; H, 5.7; N, 5.1. $C_{13}H_{15}NOS_2$ requires C, 58.84; H, 5.70; N, 5.28%); $\nu_{max.}$ 3 250 and 1 660 cm^{-1}; $\delta_H[(CD_3)_2SO]$ 1.90 (3 H, s), 2.0—2.1 (2 H, m), 2.8—3.0 (4 H, m), and 7.3 (5 H, s). Found *m/z* 265.058 85. $C_{13}H_{15}NOS_2$ requires 265.0595.

2-*Benzoyl*-2-*methyl*-1,3-*dithiane* (**10**).—A solution of n-butyllithium in hexane (1.2 equiv.) was added to a solution of compound (**1a**) (1.00 g, 4.5 mmol) in THF at −78 °C. After being stirred for 15 min, the solution of the anion was quenched by addition of iodomethane (0.76 g, 5.4 mmol). The mixture was allowed to reach room temperature with stirring and quenched with dilute aqueous hydrochloric acid. After being stirred for a further 15 min the mixture was extracted with chloroform (3 × 120 ml) and the combined organic layers were dried ($MgSO_4$). Evaporation of the solvent gave a crystalline residue which was purified by recrystallisation from methanol or by chromatography using ethyl acetate–light petroleum (1:10) as eluant to yield colourless crystals of the title compound (**10**) (0.97 g, 91%), m.p. 99–100 °C (Found: C, 60.2; H, 5.9. $C_{12}H_{14}OS_2$ requires C, 60.47; H, 5.92%); $\nu_{max.}$ 1 675 cm^{-1}; $\delta_H(CDCl_3)$ 1.8 (3 H, s), 1.85—2.0 (1 H, m), 2.1—2.22 (1 H, m), 2.65—2.8 (2 H, m), 3.25—3.4 (2 H, m), 7.35—7.55 (3 H, m), and 8.0 (2 H, m). Found: *m/z* 238.048 706 1 (M^+). $C_{12}H_{14}OS_2$ requires 238.048 60.

2-*Acetyl*-1,3-*dithiane* (**16**, R = Me).—The anion generated from 1,3-dithiane (4.0 g, 33.3 mmol) was added to a solution of ethyl acetate (5.87 g, 66.6 mmol) in THF at −78 C. The mixture was allowed to warm to room temperature with stirring and quenched with saturated aqueous ammonium chloride. The mixture was extracted with several portions of chloroform and the combined organic layers dried ($MgSO_4$). Evaporation of the solvent gave a residue which was purified by chromatography using ethyl acetate–light petroleum (1:2) as eluant to yield 2-acetyl-1,3-dithiane (**16**, R = Me) as a pale yellow oil (2.33 g, 43%), b.p. 250 °C (0.5 mmHg); $\nu_{max.}$ 3 500 and 1 710 cm^{-1}; $\delta_H(CDCl_3)$ 2.0—2.2 (2 H, m), 2.4 (3 H, s), 2.5—2.7 (2 H, m), 3.2—3.3 (2 H, m), and 4.3 (1 H, s).

2-*Benzoyl*-1,3-*dithiane* (**16**, R = Ph).—(*a*) *From* 1,3-*dithiane and ethyl benzoate*. The anion generated from 1,3-dithiane (2.32 g, 19.3 mmol) was added to a solution of ethyl benzoate (4.35 g, 29 mmol) in THF at −78 °C. The mixture was allowed to warm to room temperature with stirring and quenched with saturated aqueous ammonium chloride. The mixture was extracted with chloroform (3 × 150 ml) and the combined organic layers were dried ($MgSO_4$). Evaporation of the solvent gave a residue which was purified by chromatography using ethyl acetate–light petroleum (1:3) as eluant to yield colourless crystals of 2-benzoyl-1,3-dithiane (**16**; R = Ph) (2.38 g, 55%), m.p. 94—95 °C (Found: C, 59.29; H, 5.60; $C_{11}H_{12}S_2O$ requires: C, 58.93; H, 5.36%); $\nu_{max.}$ 1 670, 1 600, and 1 585 cm^{-1}; $\delta_H(CDCl_3)$ 2.0—2.2 (2 H, m), 2.6—2.75 (2 H, m), 3.30—3.45 (2 H, m), 5.17 (1 H, s), 7.4—7.6 (3 H, m), and 7.95 (2 H, d, *J* 9.8 Hz). Found: *m/z* 224.032 958 7 (M^+). $C_{11}H_{12}S_2O$ requires 224.032 954 7.

(*b*) *From* 2-*trimethylsilyl*-1,3-*dithiane and ethyl benzoate*. The anion generated from 2-trimethylsilyl-1,3-dithiane (2.84 g, 14.8 mmol) was added to a solution of ethyl benzoate (2.22 g, 14.8 mmol) in THF at −78 °C. The mixture was allowed to warm to room temperature with stirring and quenched with saturated aqueous of ammonium chloride. Usual work-up and chromatography using ethyl acetate–light petroleum (1:9) as eluant gave colourless crystals of 2-benzoyl-1,3-dithiane (**16**, R = Ph) (3.52 g, 33%).

(*c*) *From* 1,3-*dithiane and benzoyl cyanide*. The anion generated from 1,3-dithiane (2.62 g, 21.8 mmol) was added to a solution of benzoyl cyanide (3.43 g, 26.2 mmol) in THF at −78 °C. The mixture was allowed to warm to room temperature with stirring and quenched with saturated aqueous ammonium chloride. Usual work-up and chromatography gave colourless crystals of 2-benzoyl-1,3-dithiane (**16**, R = Ph) (3.75 g, 77%).

(*d*) *From* 1,3-*dithiane and methyl thiobenzoate*. The anion generated from 1,3-dithiane (0.18 g, 1.50 mmol) was added to a solution of methyl thiobenzoate (0.25 g, 1.64 mmol) in THF at −78 °C. The mixture was allowed to warm to room temperature with stirring, and quenched with saturated aqueous ammonium chloride. Usual work-up and chromatography gave colourless crystals of 2-benzoyl-1,3-dithiane (**16**, R = Ph) (0.08 g, 24%).

(*e*) *From* 2-*trimethylsilyl*-1,3-*dithiane and methyl thiobenzoate*. The anion generated from 2-trimethylsilyl-1,3-dithiane (0.526 g, 2.74 mmol) was added to a solution of methyl thiobenzoate (0.50 g, 3.29 mmol) in THF at −78 °C. The mixture was allowed to warm to room temperature with stirring, and quenched with saturated aqueous ammonium chloride. Usual work-up and chromatography gave colourless crystals of 2-benzoyl-1,3-dithiane (**16**, R = Ph) (0.50 g, 81%).

N-*Methyl*-α-(1,3-*dithian*-2-*yl*)*formamide* (**16**, R = NHMe).—The anion generated from 1,3-dithiane (2.16 g, 18 mmol) was added cautiously to a solution of methyl isocyanate (1.23 g, 21.6 mmol) in THF at −78 °C. The mixture was allowed to warm to room temperature with stirring. Usual work-up and

chromatography using ethyl acetate as eluant gave the title compound (**16**, R = NHMe) as colourless crystals (1.28 g, 40%); m.p. 175—177 °C (Found: C, 40.55; H, 6.30; N, 7.90. $C_6H_{11}NOS_2$ requires: C, 40.65; H, 6.25; N, 7.90%); $\nu_{max.}$ 3 300 and 1 650 cm^{-1}; δ_H[$(CD_3)_2SO$] 1.9—2.0 (2 H, m), 2.6—2.7 (3 H, m), 2.7—2.8 (2 H, m), 3.2—3.32 (2 H, m), 4.5 (1 H, s), and 8.0 (1 H, br s). Found: *m/z* 177.027 862 5 (M^+). $C_6H_{11}NOS_2$ requires 177.028 203 9.

(2-*Methyl*-1,3-*dithian*-2-*yl*)*benzylimine* (**11**).—n-Butyl lithium in hexane solution (2.91 mmol, 1.1 equiv.) was added to a solution of α-(1,3-dithian-2-ylidene)benzylamine (0.59 g, 2.65 mmol) in THF (20 ml) at −40 °C. After 15 min the mixture was cooled to −78 °C and methyl iodide (0.18 ml, 1.1 equiv.) was introduced. After being warmed to room temperature the mixture was quenched with a saturated aqueous solution of ammonium chloride and extracted with methylene dichloride (× 3). The combined organic extracts were dried ($MgSO_4$) and the solvents evaporated off to yield a yellow oil. Thin layer chromatography showed a quantitative reaction with formation of a product sufficiently pure for further reaction. Chromatography using ethyl acetate–light petroleum (1:3) as eluant provided the title compound (**11**) as a yellow oil (0.480 g, 76%); $\nu_{max.}$ 3 200 and 1 620 cm^{-1}; δ_H($CDCl_3$), 1.60 (3 H, s), 1.75—2.05 (2 H, m), 2.55—2.65 (2 H, m), 2.75—3.05 (2 H, m), 7.30—7.40 (3 H, m), and 7.50—7.60 (2 H, m). Found: *m/z* 237.064 459 (M^+). $C_{12}H_{15}NS_2$ requires 237.064 59.

N-*Methyl*-α-(2-*methyl*-1,3-*dithian*-2-*yl*)*benzylimine* (**13a**).—A solution of α-(2-methyl-1,3-dithian-2-yl)benzylimine (0.330 g, 1.39 mmol) in THF (25 ml) at −40 °C was treated with n-butyllithium in hexane solution (1.53 mmol, 1.1 equiv.) and stirred for one hour to yield a deep red solution. The solution was cooled to −78 °C and methyl iodide (0.10 ml, 1.1 equiv.) added. The mixture was allowed to warm to room temperature, quenched with saturated aqueous ammonium chloride and extracted with methylene dichloride (× 3). The combined organic extracts were dried ($MgSO_4$) and the solvents evaporated off to yield a yellow oil. Purification by recrystallisation from light petroleum (40—60 °C) or by chromatography using ethyl acetate–light petroleum (1:5) as eluant gave the title compound (**13a**) as a pale yellow solid (6.22 g, 63%), m.p. 78—79 °C (Found: C, 62.1; H, 6.85; N, 5.35. $C_{13}H_{17}NS_2$ requires C, 62.11; H, 6.82; N, 5.57%); $\nu_{max.}$ 1 640 cm^{-1}; δ_H($CDCl_3$), 1.60 (3 H, s), 1.80—2.15 (2 H, m), 2.70—2.85 (2 H, m), 3.00 (3 H, s), 3.10—3.30 (2 H, m), 7.1—7.2 (2 H, m), and 7.3—7.4 (3 H, m). Found: *m/z* 251.077 10 (M^+). $C_{13}H_{17}NS_2$ requires 251.077 10.

N-*Acetyl*-α-(2-*methyl*-1,3-*dithian*-2-*yl*)*benzylimine* (**13b**).—A solution of the anion of α-(2-methyl-1,3-dithian-2-yl)benzylimine (0.440 g, 1.86 mmol), prepared as described above, was treated at −78 °C with acetyl chloride (0.292 g, 3.72 mmol). After being warmed to room temperature the mixture was quenched with saturated aqueous ammonium chloride and extracted with methylene dichloride (× 3). The combined organic extracts were dried ($MgSO_4$) and the solvents evaporated off to yield a brown oil. Purification by recrystallisation from diethyl ether or by chromatography using ethyl acetate–light petroleum yielded the title compound (**13b**) as a colourless solid (0.15 g, 33%), m.p. 112—113 °C (Found: C, 60.1; H, 6.15; N, 4.8. $C_{14}H_{17}NOS_2$ requires C, 60.18; H, 6.13; N, 5.01%); $\nu_{max.}$ 1 650 and 1 700 cm^{-1}; δ_H($CDCl_3$), 1.55 (3 H, s), 1.85—2.0 (1 H, m), 1.92 (3 H, s), 2.10—2.25 (1 H, m), 2.65—2.75 (2 H, m), 3.3—3.45 (2 H, m), and 7.35 (5 H, s).

N-*Methyl*-α-(2-*methyl*-1,3-*dithian*-2-*yl*)*benzylamine* (**14a**).—A solution of compound (**13a**) (0.56 g, 2.23 mmol) in THF (75 ml) was treated with borane–THF complex (5.0 ml, 5.0 mmol) and the reaction mixture stirred at room temperature for 16 h. Water was added dropwise until all the excess of borane was destroyed and the solvents were evaporated off under reduced pressure. The residue was stirred with dilute hydrochloric acid (2M) for 12 h at room temperature and neutralised using concentrated potassium hydroxide solution (10M). The mixture was extracted with methylene dichloride (× 3) and the combined organic phases dried ($MgSO_4$). Evaporation of the solvent under reduced pressure gave colourless crystals of the title compound (**14a**) requiring no further purification, (0.56 g, 100%), m.p. 95—96 °C (Found: C, 61.85; H, 7.7; N, 5.45. $C_{13}H_{14}NS_2$ requires C, 61.61; H, 7.56; N, 5.53%); $\nu_{max.}$ 3 300 cm^{-1}; δ_H($CDCl_3$) 1.5 (3 H, s), 1.95—2.05 (2 H, m), 2.25 (3 H, s), 2.8—3.1 (4 H, m), 3.95 (1 H, s), 7.25—7.35 (3 H, m), and 7.4—7.5 (2 H, m); *m/z* (c.i.) 254 ($M^+ + 1$).

α-(2-*Methyl*-1,3-*dithian*-2-*yl*)*benzylamine* (**14b**).—A solution of compound (**11**) (0.48 g, 2.03 mmol) in THF (40 ml) was treated with borane–THF complex (6.0 ml, 6.0 mmol) and the reaction mixture stirred at room temperature for 16 h. Water was added dropwise until all the excess of borane was destroyed and the solvents were evaporated off under reduced pressure. The residue was stirred with dilute hydrochloric acid (2M) for 12 h at room temperature and neutralised using concentrated potassium hydroxide solution (10M). The mixture was extracted with methylene dichloride (× 3) and the combined organic phases dried ($MgSO_4$). Evaporation of the solvent under reduced pressure gave the title compound (**14b**) as a colourless oil requiring no further purification (0.48 g, 100%), b.p. 220 °C (1.3 mmHg) (Found: C, 60.55; H, 7.25; N, 5.85. $C_{12}H_{17}NS_2$ requires C, 60.21; H, 7.16; N, 5.85%); $\nu_{max.}$ 3 340 and 3 270 cm^{-1}; δ_H($CDCl_3$) 1.5 (3 H, s), 1.90—2.05 (4 H, m), 2.7—3.05 (4 H, m), 4.40 (1 H, s), 7.25—7.35 (3 H, m), and 7.40—7.50 (2 H, m); *m/z* (c.i.) 240 ($M^+ + 1$).

α-(1,3-*Dithian*-2-*yl*)*benzylamine* (**15**).—A solution of compound (**1a**) (0.40 g, 1.79 mmol) in THF (50 ml) was treated with borane–THF complex (7.2 ml, 7.2 mmol) for 16 h at 50 °C. The solution was cooled, water was added dropwise until all the excess of borane was destroyed and the solvents were evaporated off under reduced pressure. The residue was heated under reflux with hydrochloric acid (5M) for 4 h. On cooling, colourless crystals of the title compound (**15**) were precipitated as the hydrochloric acid salt (0.28 g, 71%), m.p. 239—240 °C (Found: C, 50.35; H, 6.3; N, 5.2. $C_{11}H_{16}ClNS_2$ requires C, 50.46; H, 6.16; N, 5.35%); $\nu_{max.}$ 3 500 cm^{-1}; δ_H($CDCl_3$–CD_3OD) 1.75—1.95 (1 H, m), 2.00—2.15 (1 H, m), 2.80—2.95 (6 H, m), 4.15—4.25 (2 H, m), 7.30—7.40 (5 H, m); *m/z* (c.i.) 226 ($M^+ + 1$).

N-*Benzoyl*-N-*methyl*-α-(1,3-*dithian*-2-*ylidene*)*benzylamine* (**8**).—A solution of compound (**6a**) (0.4 g, 1.2 mmol) in dry DMF (10 ml) at −40 °C was treated with a solution of trityllithium (2 equiv.) in THF and the mixture stirred for 30 min. Iodomethane (0.34 g, 2.2 mmol) was added in one portion and the reaction allowed to reach room temperature. The solvent was evaporated off under reduced pressure to give an oily residue which was purified by column chromatography to give *N*-[α-(1,3-dithian-2-ylidene)benzyl]-α-methoxybenzylimine (**7**) as a yellow oil (0.26 g, 64%) which was heated under reflux in dry ethanolic solution for 2 h. Evaporation of the solvent under reduced pressure gave colourless crystals of the title compound (**8**) (0.24 g, 92%); m.p. 215—217 °C; $\nu_{max.}$ 1 640 cm^{-1}; δ_H[$(CD_3)_2CO$] 1.95—12.10 (2 H, m), 2.50—2.65 (1 H, m), 2.75—2.85 (2 H, m), 2.90—3.00 (1 H, m), 3.2 (3 H, s), and 7.2—7.5 (10 H, m). Found: *m/z* 341.0871, 236, 150, and 118. $C_{19}H_{19}NOS_2$ requires 341.0908.

Acknowledgements

We are indebted to the S.E.R.C. for financial support.

References

1 E. J. Corey and D. Seebach, *Angew. Chem., Int. Ed. Engl.*, 1965, **4**, 1075,1077.
2 B. T. Grobel and D. Seebach, *Synthesis*, 1977, 357.
3 D. Seebach, M. Kolb, and B. T. Grobel, *Chem. Ber.*, 1973, **106**, 2277; F. A. Carey and A. S. Court, *J. Org. Chem.*, 1972, **37**, 1926.
4 (*a*) D. N. Crouse and D. Seebach, *Chem. Ber.*, 1968, **101**, 3113; (*b*) K. Ogura and G. Tsuchihashi, *J. Am. Chem. Soc.*, 1974, **96**, 1960; (*c*) I. Kawamoto, S. Muramatsu, and Y. Yura, *Tetrahedron Lett.*, 1974, 4223.
5 (*a*) K. Fuji, M. Ueda, and E. Fujita, *J. Chem. Soc., Chem. Commun.*, 1983, 49; (*b*) K. Fuji, M. Ueda, K. Sumi, K. Kajiwara, E. Fujita, T. Iwashita, and I. Miura, *J. Org. Chem.*, 1985, **50**, 657; (*c*) K. Fuji, M. Ueda, K. Sumi, and E. Fujita, p. 663.
6 P. C. B. Page, M. B. van Niel, and P. H. Williams, *J. Chem. Soc., Chem. Commun.*, 1985, 742; P. C. B. Page and M. B. van Niel, *ibid.*, 1987, 43; P. C. B. Page, D. J. Chadwick, M. B. van Niel, and D. Westwood, *Acta Crystallogr.*, 1987, 803.
7 P. F. Jones, M. F. Lappert, and A. C. Szary, *J. Chem. Soc., Perkin Trans. 1*, 1973, 2272.
8 B. C. Challis and A. D. Frenkel, *J. Chem. Soc., Perkin Trans. 2*, 1978, 192.
9 P. C. B. Page, M. B. van Niel, and D. Westwood, *J. Chem. Soc., Chem. Commun.*, 1987, 775.
10 J. Barluenga, F. Lopez, and F. Palacios, *J. Chem. Res.*, 1985, (*S*) 211; (*M*) 2541.
11 A. Dondoni and G. Barbaro, *J. Chem. Soc., Chem. Commun.*, 1975, 761.

Received 19*th February* 1987; *Paper* 7/312