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Introduction

The increasing availability of enantiopure vic-diols and vicaminoalcohols has stimulated interest in developing synthetic chemistry which makes use of these substances.^{1,2} In particular, activation of the C-O bonds to nucleophilic attack at carbon opens up routes to a-substituted alcohols and amines. Thus, cyclic sulfate esters 1, prepared from vic-diols in two steps, undergo ring opening with a variety of nucleophiles to give hemisulfates 2 which can be hydrolysed to the substituted alcohols 3.3 In some cases two nucleophilic substitutions lead to complete displacement of sulfate.4-7 Similarly, vic-aminoalcohols can be converted into cyclic sulfamidates e.g. 4 which also undergo nucleophilic substitution with breaking of the C-O(SO₂) bond to produce sulfamate salts 5 which, after hydrolysis with concentrated sulfuric acid, yield substituted amines 6 (Scheme 1).4,8,9 Cyclic phosphate esters prefer attack at phosphorus by hard nucleophiles, but some examples of ring opening at carbon with soft or bulky nucleophiles have been recognized.10 Ko has introduced the cyclic thionocarbonate derivative of a vic-diol, e.g. 7 from diisopropyl tartrate, which undergoes nucleophilic substitution with azide, phenylthiolate and benzoate to give the substituted alcohol 9 directly without an acidic hydrolysis step since the intermediate thiocarbonate salt 8 loses COS in situ or during aqueous work up (Scheme 2).11 The ring C-O bond can also be reduced to give malates.12 In contrast, cyclic thionocarbonates of tartrate esters react with secondary amines to give enantiopure acyclic thionocarbamates via initial addition to the thione

attack

group.¹³ We report here an investigation of the reactions of nucleophiles with five-membered cyclic thionocarbamates, to determine their reactivity and regioselectivity. Cyclic thionocarbamates have been used synthetically in other ways, primarily as chiral auxiliaries,¹⁴ but also as intermediates in the synthesis of enantiopure protected aryl-β-hydroxyl-α-amino acids¹⁵ and 1-(Boc)-amino-1-alkenylphosphonate esters,¹⁶ as derivatives for kinetic resolutions,¹⁷ as pseudo-C-nucleosides,¹⁸ in radical reactions,¹⁹ and as precursors for other oxazolidines.²⁰ Carbon disulfide,²¹ thiophosgene^{18,22} or bis(imidazolyl)thione^{19,20} have been used to prepare them from the corresponding aminoalcohols, as well as hydroxyl addition to isothiocyanates¹⁸ and cycloaddition of aldehydes to anions of substituted methyl isothiocyanates.^{15,16}

Activation and regioselectivity of five-membered cyclic

The cyclic thionocarbamate of alaninol undergoes nucleophilic attack by sulfur nucleophiles at 5-C to give 1-thiopropyl-2-amine derivatives when derivatised on nitrogen with a Boc group. Iodide under microwave conditions causes a rearrangement to the isomeric thiazolidinone, while "hard"

nucleophiles react at the thione group to yield a variety of product types by subsequent C-N or C-O

cleavage. X-ray crystallography studies showed that the N-Boc group reduces delocalisation of electron

density from nitrogen into the thione group, and thus promotes activation of the ring to nucleophilic

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thionocarbamates to nucleophilic attack[†]





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Results and discussion

N-Benzylalaninol **10** was converted to its cyclic thionocarbamate **11** in 56% yield by treatment with thiophosgene and pyridine in dichloromethane at 0 °C (Scheme 3). The reactions of **11** with a variety of nucleophiles under a range of conditions was attempted but none was successful. For example, reactions with sodium thiophenolate, potassium phthalimide and lithiated acetonitrile all showed unreacted starting material even at 60 °C. To understand more about this heterocyclic system the molecular structure was measured by single crystal X-ray diffraction at 120 K.

The structure of **11** is shown in Fig. 1, with selected molecular geometry in Table 1. The five-membered ring adopts a



shallow half chair conformation with the two sp³ carbon atoms deviating most from the best ring plane (by 0.073 and -0.074 Å). The bonding geometry at nitrogen in 11 is planar, and it is notable that the bond from nitrogen to the thione carbon (1.3319(18) Å) is 0.025 Å shorter than that from the oxygen atom (1.3574(17) Å) in contrast to the usual trend of bond lengths from these atoms to carbon. A similar trend is observed in the structures of eight low temperature high quality measurements of N-unsubstituted 1,3-oxazolidine-2-thiones in the Cambridge Structural Database²³ (CSD): N-C: 1.326(8), O-C: 1.352(7) Å.²⁴ There is thus substantial electron donation of the nitrogen atom's lone pair into the thiocarbonyl group, which is consistent with the longer thiocarbonyl bond in 11 (1.6558(14) Å) and the eight other cyclic thionocarbamates (1.658(10) Å) compared to those in accurate low temperature measurements of cyclic thionocarbonates (1.623(2)–1.638(2) Å).²⁵ This strong conjugation from the nitrogen atom suppresses the activating effect of the thione on the ring oxygen atom so that it does not promote its leaving group ability. This is in accord with the O-C(=S)bond length in **11** being 0.02 Å longer than in the cyclic thionocarbonates (average 1.331(6) Å for three measurements).25 In contrast to the cyclic thionocarbamates, the X-ray diffraction



Fig. 1 Molecular structures of 11 (left), 14 (right) and 17 (below) determined by X-ray diffraction.

Table 1 Selected molecular geometry for molecules 11, 14 and 17, bond lengths in Å, bond angles in $^\circ$

	11	14	17
S1=C1/O4=C	1.6558(14)	1.6370(12)	1.1992(19)
O1-C1	1.3574(17)	1.3434(14)	1.348(2)
O1-C3	1.455(2)	1.4637(14)	1.448(2)
O2-C5	_	1.1974(13)	1.206(2)
N1-C1	1.3319(18)	1.3722(14)	1.389(2)
N1-C2	1.4659(17)	1.4860(14)	1.477(2)
N1-C5	1.4625(17)	1.4069(14)	1.400(2)
C2-C3	1.513(2)	1.5180(16)	1.532(2)
C1-O1-C3	109.12(11)	109.50(8)	111.28(12)
C1-N1-C2	112.75(11)	110.97(9)	112.24(13)
C1-N1-C5	124.93(11)	125.74(9)	127.93(13)
C2-N1-C5	122.05(11)	123.29(9)	119.12(13)
N1-C1-S1/N1-C1-O4	129.01(10)	130.50(9)	129.36(15)
N1-C1-O1	109.96(12)	108.68(9)	108.75(13)
O1-C1-S1/O1-C1-O4	121.03(10)	120.79(8)	121.88(15)
N1-C2-C3	100.72(12)	99.30(8)	100.94(13)
O1-C3-C2	105.72(12)	103.59(9)	106.25(13

studies of the cyclic sulfamidates 4,²⁶ and 12,²⁷ show longer bonds from the nitrogen atom to the sulfur atom than from the ring oxygen atom (4: S–N 1.612(2); S–O 1.565(2) Å, 12 S–N 1.661(2); S–O 1.580(2) Å). The interaction of the N atom with the SO₂ group is not sufficient to prevent nucleophilic displacement of the O(SO₂) group from the 5-C atom.

To reduce the delocalisation of electron density from the nitrogen atom the *N*-Boc cyclic thionocarbamates of alaninol and serine methyl ester **14** and **16** were prepared in two steps, first forming the cyclic thionocarbamates **13** and **15** by reaction with thiophosgene and triethylamine, and then reaction with di-*tert*-butyl dicarbonate, pyridine and 4-dimethylaminopyridine to give the final products as recently described by one of us (Scheme 4).²⁸ The structure of **14** was measured by X-ray diffraction at 120 K, and the results are shown in Fig. 1 and in Table 1.

The heterocyclic ring of the cyclic thionocarbamate 14 adopts an approximate half chair conformation, significantly more puckered than in 11, with the ring sp³ carbon atoms



deviating most from the ring's best plane (by 0.154 and -0.164 Å). The bonding at the nitrogen atom is planar and the Boc group is well aligned for conjugation with the ring nitrogen, with torsion angles about the N-C(Boc) bond of 7.67(18) and 8.04(14)°. In contrast to 11 the ring bond from nitrogen to the thiocarbonyl group (1.3722(14) Å) is *longer* than the ring bond from oxygen to the thiocarbonyl group (1.3464(14) Å). There is clear evidence of less electron delocalization from the nitrogen atom into the thione bond than in the N-benzyl derivative 11 from the longer N-C(=S) bond (by 0.040 Å) and the shorter thiocarbonyl bond (by 0.019 Å) in 14. There is a small contraction in the O–C(=S) bond (by 0.014 Å), signifying an increase in the electron delocalization from oxygen into the thiocarbonyl group. However, conjugation of nitrogen with the thione group is not eliminated in 14; the bond from the nitrogen to the thione group is still shorter than that to the Boc group (by 0.035 Å), and the latter (1.4069(14) Å) is notably longer (by ca. 0.05 Å) than in N-Boc compounds which do not carry a second electron attracting group *e.g.* carrying two sp³ carbons for which C–N: 1.357(12) Å (168 examples measured at T < 150 K).²³ The structures of three oxazolidine-2-thiones bearing N-acyl substituents have been reported, and all show the exocyclic N-C bond to be longer than the endocyclic one.²⁹ The corresponding structure where the thione is replaced by a carbonyl group, 17, prepared from 14 with mercuric acetate, was also determined (Fig. 1) and shows a longer endocyclic N-C bond (1.389(2) Å) than 14, consistent with slightly better conjugation of nitrogen with a thione than with a carbonyl group.

Reactions of cyclic thionocarbamates 14 and 16 with several nucleophiles have been investigated and, in contrast to the Nbenzyl derivative 11, some successful ring openings at 5-C observed (Scheme 5). Thus, 14 reacted with sodium pyridine-2thiolate in THF at 60 °C to give the substituted N-Boc amine 19 (60%) accompanied by a small amount of the corresponding N,NdiBoc analogue 20 (6%). The reaction proceeds by ring opening of 14 by the nucleophile at 5-C followed by loss of COS leading to anion 18 which is then protonated in the work up to give the major product. Presumably, a small amount of anion 18 abstracts a Boc group from starting material to give the diBoc material 20. Some unactivated thionocarbamate 13 was also isolated. Sodium phenylthiolate reacted with 14 under similar conditions, giving the ring-opened product 22 (32%), a small amount of the corresponding diBoc compound 23 (4%) and a significant yield of the 1,3,5-triazinetrione derivative 24 (38%). The latter may be formed by the reaction of initially formed anion 21 with the isocyanate 25 derived from further 21 by loss of t-butoxide. Trimersations of isocyanates catalysed by nucleophiles are known.30 Sodium ethanethiolate reacted with 14 to give the ring opened product 26 in 25% yield at room temperature, but under microwave conditions in xylene (145 °C) the yield rose to 58%. 14 also reacted with potassium thioacetate in DMF at 20 °C to give the ring opened product 28 in which the sulfur carries the Boc group and the nitrogen carries the acetate. Ring opening gives the anion 27 which then abstracts the acetyl group from the sulfur to leave a thiolate which abstracts the Boc group from nitrogen (Scheme 6). The structural assignment is supported by IR and NMR data. The ¹³C signals for the carbonyl carbons are observed at δ_c : 169.5



(S–C=O) and 159.8 (N–C=O) while a *S*-acetyl carbonyl C would be observed at *ca.* δ_c : 195 (S–C=O). Furthermore, the infrared absorption at 1645 cm⁻¹ is only compatible with an amide and not with a *N*-Boc group (expected *ca.* 1680 cm⁻¹). Cyclic thionocarbamate **16** also undergoes ring opening with sodium 2-pyridinethiolate and phenylthiolate to give the *N*-Boc protected esters **29** and **30** in yields of 57% and 70% (Scheme 6).

The reaction of **14** with iodide was also investigated since ring opening at 5-C by iodide could be followed by an intramolecular substitution of iodide by the thiocarbamate anion *via* sulfur to give thiazolidin-2-one **31** (Scheme 7). Thionocarbonates such as 7 are known to undergo the corresponding reaction with the bromide ion.^{11a} Reaction of **14** with tetrabutylammonium iodide

in THF or toluene under refluxing conditions was unsuccessful, but transferring the reaction to microwave conditions in xylene at 145 °C gave a 57% yield of the thiazolidin-2-one **31**, the structure of which was confirmed by a crystal structure determination (Fig. 2). Compound **31** is a potential precursor to *vic*aminothiols, which are useful heterocyclic building blocks, linkers and ligands.³¹ In the crystal structure of **31** the ring system adopts an approximate envelope conformation with the methine carbon lying 0.51 Å out of the plane of the other four atoms. The bond lengths from nitrogen to the ring and Boc carbonyls are similar: 1.391(3) and 1.403(3) Å respectively.

Given the success of the above rearrangement reaction with iodide, the reaction was attempted with the unactivated cyclic





thionocarbamate, which did not carry a Boc group on the ring nitrogen 13. Under microwave conditions in xylene (145 $^{\circ}$ C, one hour) the reaction is indeed successful providing the thiazolidinone 32 in 95% yield. However, when the reaction was carried out in almost solvent free conditions, the dimeric product 33 was isolated in 27% yield which has been formed by reaction between two molecules of the initial product of ring opening with iodide. Thus under forcing conditions even the unactivated system 13 will undergo reaction with iodide.

Given the presence of thione and urethane functionalities in molecule **14** we were interested to see how "harder" nucleophiles selected between attack at these groups and attack at the ring 5-C atom. Thus, reaction with a range of organolithium and organomagnesium nucleophiles were investigated which unveiled a rather selective and interesting chemistry, leading to unusual products in some cases. The reaction of **14** with these "harder" nucleophiles all start by attack of the organometallic on the thione group to give **43** but the precise product produced depends on the subsequent reactions of this addition product (Scheme 10). Thus, *n*-butyl lithium, *sec*-butyl lithium, *t*-butyl lithium and lithium dimethylamide react with **14** at -78 °C by

addition to the thione followed by collapse of the tetrahedral intermediate **43** with breakage of the ring C–N bond to give **34–37** in yields of 46, 53, 95 and 32% respectively, **35** being obtained as a 1 : 1 mixture of diastereomers. The high yield of **36** reflects the known high reactivity of *t*-butyl organometallics, and addition to the thione in this case may go *via* a single electron transfer mechanism (Scheme 8). It was important to exclude the isomeric structural assignments of these products as alcohols of type **39** which would be formed by breaking the ring C–O bond rather than the ring C–N bond. Examination of the literature suggested that there was no clearly ambiguous spectroscopic method for this, for example based on the infrared stretch of the C=S group or on the ¹³C chemical shift of the thione carbon atom, so the structures of **36** and **37** were determined by X-ray crystallography (Fig. 3).





Fig. 3 Molecular structure of **36** (above) and **37** (below) determined by X-ray diffraction. The conformations differ by a rotation about the central CH–CH₂ bond.

Fia. 2

The adduct 37 from the reaction of thionocarbamate 14 with lithium dimethylamide was accompanied by a significant yield of 38 the corresponding compound which carried an extra Boc group on the nitrogen atom, the structure of which was also confirmed by X-ray crystallography. This material has probably arisen by the anion formed on ring cleavage then removing a Boc group from starting material 14.

The structures of 36-38 were measured at 150 K (Fig. 3 and 4), and for 36 there were two independent molecules in the asymmetric unit. All molecules show a planar arrangement involving the thiocarbonyl group and the attached oxygen and carbon or nitrogen atoms. For the two thiourethanes 37 and 38 the thiocarbonyl group is much longer (1.6710(15) & 1.6788(15) Å) than for the two molecules of thionoester 36 (1.602(3) and 1.629(3) Å) due to the strong conjugation of nitrogen with the thione group. The O-C(=S) bond in thionoester 36 (1.327(3) and 1.315(4) Å) is significantly shorter than in the thiourethanes (1.3408(17) and 1.3415(17) Å) since there is no competition for conjugation with the thione group. In the compound 38 which has two Boc groups attached to the nitrogen atom, the two carbonyl groups are directed away from each other but there is a short 1,5 contact between the butoxy O atoms of just 2.545 Å. The bonding geometry at the nitrogen and the two carbonyl carbons are all planar, but one of the Boc group has twisted about its N-C bond by ca. 32° to maximise the O···O separation. The structure of 34, a liquid at room temperature, is supported by comparison of spectral data with those **36**. The O-methylene group has a chemical shift of δ_c : 74.3 ppm very close to that of 36 (δ_c : 74.8 ppm), whereas the alternative structure 39 (R = n-Bu) would be expected to have a lower shift for its -CH₂OH group. The thione group for 34 shows a stretching frequency of 1175 cm⁻¹ and ¹³C chemical shift of 224.2 ppm similar to the values for **36** of 1163 cm⁻¹ and δ_c : 231 ppm.

Interestingly, the reaction of 14 with phenyl lithium led to a different type of product i.e. the thiazoline 40 in 95% yield, which was also obtained by reaction with phenyl magnesium bromide in 38%. Reaction with phenylethynyl lithium gave the corresponding thiazoline product, the disubstituted alkyne, 41 in 59% yield (Scheme 9). The structural assignment is supported by ¹³C resonance of the 4-C at δ_c : 72.7 similar to that shown for a series of closely related thiazolines.³² In contrast,



Fig. 4 Molecular structure of 38 determined by X-ray diffraction, showing the mutual arrangement of the two Boc groups on the nitrogen atom.



reaction of 14 with isopropyl magnesium chloride gave the oxazolidinone 42 in 47% yield. These products arise from initial addition of the organometallic reagent to the thione to give 43 and subsequent ring opening by ring O-C bond cleavage, rather than N-C bond cleavage, followed by attack of the oxyanion on the Boc carbonyl group to give a five-membered ring as an intermediate anion. In the case of the thiazolines, the Boc group is transferred to oxygen making the latter a good leaving group which is displaced by the thioamide anion to form the ring system (Scheme 10). In the case of the oxazolidinone the attack of the oxyanion on the Boc group is followed by expulsion of the butoxide ion. All processes following the attack on the thiocarbonyl group may well be reversible, with the exception of the loss of t-BuO₂CO to give the thiazolines, which may be favoured by groups which conjugate with the thioamide anion. In contrast, phenyl lithium reacts with the ester substituted thionocarbamate 16 to give the alkene 44, formed by initial deprotonation next to the ester group, and the phenyl substituted material 45 (Scheme 11).

In summary, sulfur centred 'soft' nucleophiles attack the cyclic thionocarbamate by ring-opening at 5-C followed by loss



Scheme 10

8



of COS to give beta-substituted N-Boc amines, including a vicaminothiol derivative via the reaction with iodide, while 'hard' organolithium and Grignard reagents give a variety of unusual products which are all derived from attack on the thione group. The former has potential applications to the preparation of novel chiral ligands for metal binding and catalysis, while the latter provides access to new derivatives of heterocyclic systems.

Experimental

General

NMR spectra were measured on a JEOL JNM-EX270 spectrometer at 270 MHz for ¹H and at 67.8 MHz for ¹³C or on a JEOL ECLIPSE 400 spectrometer at 400 MHz for ¹H and at 100 MHz for ¹³C using CDCl₃ as solvent, and measured in ppm downfield from TMS, unless otherwise stated. IR spectra were recorded on Perkin Elmer Spectrum 100 FT-IR Spectrometer using an ATR window, and are reported in cm⁻¹. Mass spectra were recorded at the EPSRC Mass Spectrometry Centre at Swansea University. Melting points were recorded on a Stuart SMP30 melting point apparatus. Chemical analysis data were obtained from Mr Stephen Boyer, London Metropolitan University. Optical rotations were measured on a Perkin Elmer 241 polarimeter at 21 °C using sodium D line radiation and are reported in 10^{-1} deg. cm² g⁻¹. Flash chromatography was performed on 40-63 silica gel (Merck). Microwave experiments were carried out in CEM Discover SP synthesis system.

Preparation of 11

Thiophosgene (3.48 g, 2.31 ml, 30.3 mmol) in dichloromethane (15 ml) was added dropwise to a stirred solution of dry pyridine (4.82 g, 60.1 mmol) and S-2-benzylaminopropanol (5.00 g, 30.3 mmol) in dichloromethane (50 ml) at 0 °C under nitrogen. The mixture was stirred at 0 °C for 3 h. and left to warm up to room temperature overnight. Water (50 ml) was added and the organic layer separated and washed with hydrochloric acid $(1 \text{ M}, 2 \times 30 \text{ ml})$ and brine. After drying over sodium sulfate, the organic extract was evaporated to give a brown oil which was purified by chromatography using hexane-ethyl acetate (1:1) as eluent to furnish S-3-benzyl-4-methyl-1,3-oxazolidine-2-thione (3.50 g, 55.8%) as a clear oil which slowly crystallised, m.p. 77-79 °C. Anal. calcd for C₁₁H₁₃NSO: C: 63.7, H: 6.3, N: 6.8%, found C: 63.8, H: 6.4, N: 6.7%; $\delta_{\rm H}$ (400 MHz, CDCl₃): 7.22–7.35 $(5H, m, Ar-H_5)$, 5.38 $(1H, d, J = 15.1 \text{ Hz}, PhCH_{\alpha})$, 4.53 (1H, t, J =8.8 Hz, $5H_{\alpha}$), 4.34 (1H, d, J = 15.1 Hz, PhCH_B), 4.03 (1H, dd, J =8.8, 7.4 Hz, 5- H_{β}), 3.79–3.92 (1H, m, 4-H), 1.25 (3H, d, J = 6.4 Hz, 4-CH₃); δ_C: (100 MHz, CDCl₃): 188.0 (2-C), 134.6, 128.8, 128.0 and 127.9 (Ar-C₆), 72.7 (5-C), 53.9 (4-C), 49.1 (N-CH₂), 17.5 (CH₃); v_{max}: 1583, 1481, 1450, 1431, 1348, 1306, 1285, 1235,

Preparation of 13

91; $[\alpha]_{\rm D} = -161^{\circ}$ (c = 0.5 in CH₂Cl₂).

A solution of thiophosgene (2.0 ml, 25.6 mmol) in dichloromethane (2 ml) was added dropwise to a solution of 2-amino-1propanol (1.93 g, 2.0 ml, 25.6 mmol) and triethylamine (6.51 g, 9.0 ml, 64.4 mmol) in dry dichloromethane (50 ml) at 0 °C, and stirred for 3 h at room temperature. The reaction was quenched with 10% HCl, the organic layer separated and the aqueous layer extracted with dichloromethane (2 \times 40 ml). The combined organic fractions were washed with water (40 ml) and dried over Na₂SO₄. The crude material was purified by chromatography using cyclohexane-ethyl acetate (1:1) as eluent to provide 4-methyloxazolidine-2-thione 1333 as a yellow solid (1.09 g, 36%), m.p. 76–78 °C; $\delta_{\rm H}$ (400 MHz, CDCl₃): 8.21 (1H, br-s, NH), 4.66–4.74 (1H, m, 5-C H_{α}), 4.13–4.20 (2H, m, 4-H, 5-C H_{β}), 1.30 (3H, d, J = 5.8 Hz, CH_3); δ_C (400 MHz, $CDCl_3$): 189.0 (2-C), 76.8 (5-C), 52.5 (4-C), 19.9 (CH₃); v_{max}: 3168, 3021, 1646, 1532, 1181; m/z: (EI) 117 (M⁺), 102, 86, 42; *HRMS*: (EI) for $[M + H]^+$ C₄H₈NOS requires 118.0321, found: 118.0320.

806, 769, 725, 700, 675, 664, 585 cm⁻¹; m/z: (EI) 207 (M⁺), 132,

Preparation of 14

4-(Dimethylamino)pyridine (0.64 g, 5.16 mmol) in dichloromethane (18 ml) was added dropwise to a solution of 13 (6.00 g, 51.6 mmol), triethylamine (5.20 g, 50.6 mmol) and di-t-butyl dicarbonate (11.6 g, 51.6 mmol) in dichloromethane (120 ml) under nitrogen at 0 °C. The solution was stirred at room temperature for 7 h. The volatilities were removed and residue was purified by chromatography using hexane-ethyl acetate (2:1) as eluent to give 3-t-butyloxycarbonyl-4-methyl-oxazolidine-2-thione 14 as a yellow solid (4.80 g, 44%). m.p. 102-103 °C. Anal. calcd for C₉H₁₅NO₃S: C, 49.75; H, 6.96; N, 6.45, S: 14.76%; found: C, 50.01; H, 6.71; N, 6.36, S: 14.35%; δ_H (400 MHz, $CDCl_3$: 4.49–4.58 (1H, m, 4-*H*), 4.47 (1H, t, J = 7.8 Hz, 5- H_{α}), 4.08 $(1H, dd, J = 8.4, 3.0 Hz, 5-H_{B}), 1.50 (9H, s, 3 \times CH_{3}), 1.38 (3H, d, J)$ J = 6.2 Hz, 4-CH₃); $\delta_{\rm C}$ (400 MHz, CDCl₃): 184.4 (C=S), 149.3 (N-C=O), 84.8 ($C(CH_3)_3$), 72.9 (5-C), 55.4 (4-C), 28.0 (3 × CH_3), 19.3 (4-CH₃); v_{max}: 2986, 2930, 1759, 1157; m/z: (ESI) 240 ([M + Na]⁺), 162.

Preparation of 15

Triethylamine (9.94 g, 98.4 mmol) was added to a stirring solution of DL-serine methyl ester hydrochloride (5.00 g, 32.8 mmol) in dichloromethane (50 ml) under nitrogen at 0 °C. Thiophosgene (3.77 g, 2.52 ml, 32.8 mmol) in dichloromethane (15 ml) was added dropwise and the resulting mixture was allowed to stir at 0 °C for 3 h gradually warming to room temperature overnight. Water was added to the mixture. The organic layer was separated and washed with 1 M hydrochloric acid $(2 \times 30 \text{ ml})$ and brine (50 ml) and dried over sodium sulphate. Final purification was achieved by column chromatography with ethyl acetate-dichloromethane (1:5) as eluent to give methyl 2-thioxooxazolidine-4-carboxylate 15 (3.50 g, 66%) as a colourless oil. Anal. calcd for C5H7NO3S: C, 37.26, H, 4.38, N:

8.69%, found: C, 37.60, H: 4.31, N: 8.43%; $\delta_{\rm H}$ (270 MHz, CDCl₃): 8.27 (1H, br-s, N–H), 4.62–4.90 (3H, m, 4-H, 5-H₂), 3.85 (3H, s, OCH₃); $\delta_{\rm C}$ (400 MHz, CDCl₃): 189.7 (C=S), 169.4 (C=O), 72.4 (5-C), 57.4 (4-C), 53.5 (OCH₃); $\nu_{\rm max}$: 3315, 2960, 1745, 1602, 1509, 1361, 1265, 1178, 1101, 1037, 958; *m*/*z*: (CI) 179 ([M + NH₄]⁺), 162 ([M + H]⁺), 147, 130.

Preparation of 16

Triethylamine (4.32 g, 42.6 mmol), di-t-butyl dicarbonate (18.77 g, 85.2 mmol) and 4-dimethylaminopyridine (0.52 g, 4.28 mmol) were added to a stirred solution of 15 (6.86 g, 42.6 mmol) in dichloromethane (80 ml) under nitrogen at 25 °C and the mixture stirred for 7 h. The mixture was evaporated, and the residue purified by chromatography using ethyl acetatedichloromethane (1:5) followed by crystallization from ethanol to give methyl S-3-t-butyloxycarbonyl-2-thioxooxazolidine-4-carboxylate 16 (8.70 g, 78%) as fine white crystals, m.p. 101-103 °C. Anal. calcd for C₁₀H₁₅NO₅S: C, 45.97; H: 5.79; N: 5.36%, found C, 46.05; H, 5.94; N, 5.42%; $\delta_{\rm H}$ (400 MHz, DMSO-d₆): 5.09 $(1H, dd, J = 9.6, 4.2 Hz, 4-H), 4.74 (1H, t, J = 9.6 Hz, 5-H_{\alpha}), 4.52$ $(1H, dd, J = 9.6, 4.2 Hz, 5-H_{\beta}), 3.84 (3H, s, OCH_3), 1.52 (9H, s, s)$ $C(CH_3)_3$; δ_C (100 MHz, DMSO-d₆): 183.5 (C=S), 168.8 (CO₂Me), 148.4 (N-C=O), 85.4 (CMe₃), 68.8 (5-C), 59.9 (4-C), 53.3 (OCH₃), 27.7 (C(CH₃)₃); v_{max}: 1752, 1314, 1258, 1222, 1142, 1063, 1024, 967, 843, 773, 591; m/z: (ESI) 284 ([M + Na]⁺), 162; *HRMS*: (ESI) for $[M + H]^+ C_{10}H_{16}NO_5S$ requires 262.0744, found 262.0736.

Preparation of 17

To a solution of the thione 14 (217 mg, 1.0 mmol) in chloroform (10 ml) was added mercuric (II) acetate (435 mg, 1.4 mmol). The reaction mixture was stirred for 2 h before being filtered and the solid residue washed with chloroform. The filtrate was collected, mixed with water (10 ml), and the solution was neutralised with solid sodium bicarbonate. The organic layer was separated, dried over magnesium sulphate and concentrated by evaporation to give 3-t-butyloxycarbonyl-4-methyl-oxazolidine-2one 17 (187 mg, 93%) as a white solid, m.p. 94-95 °C. Anal. calcd for C₉H₁₅NO₄: C, 49.75; H, 6.96; N: 6.40%; found: C, 49.87; H, 7.01; N: 6.39%; $\delta_{\rm H}$ (400 MHz, CDCl₃): 4.28–4.36 (2H, m, 4-,5- H_{α}), 3.86 (1H, dd, J = 2.8, 7.8 Hz, 5- H_{β}), 1.48 (9H, s, 3 × C H_{3}), 1.36 (3H, d, J = 6.2 Hz, 4-CH₃); $\delta_{\rm C}$ (100 MHz, CDCl₃): 152.2 (2-C), 149.3 (N-C=O), 83.8 (C(CH₃)₃), 68.3 (5-C), 51.2 (4-C), 28.0 (3 × CH₃), 19.7 (4-CH₃); v_{max:} 2989, 1773, 1719, 1354, 1217, 1151, 1108, 1086, 1049, 984, 846, 773, 758, 749 cm⁻¹; *HRMS*: (ESI) for $[M + H]^+ C_9 H_{16} NO_4$ requires 202.1074, found 202.1074.

Reactions of 14

(a) With sodium pyridine-2-thiolate. A solution of the sodium salt of 2-mercaptopyridine in dry THF (15 ml), formed from 2-mercaptopyridine (101.4 mg, 0.108 ml, 0.92 mmol) and sodium hydride (60% dispersion in oil, 74 mg, 1.84 mmol), was added to a solution of 14 (200 mg, 0.92 mmol) in dry THF (10 ml). The mixture was stirred and heated to reflux overnight. The pale red solution was left to cool to room temperature, several drops of water were added, and the mixture stirred for 30 min. The solvent was evaporated, and the residue was extracted with

dichloromethane (2 \times 20 ml) and the extract washed with water (30 ml) and dried with sodium sulfate. The crude product was purified by chromatography using cyclohexane-ethyl acetate (1:1, increasing to 1:4) to give 19 (60.0%) and 20 (6.5%). N-t-Butyloxycarbonyl-1-(pyrid-2'-ylthio)prop-2-ylamine, 19, pale yellow solid (148 mg, 60.0%); m.p. 56-57 °C. Anal. calcd for C13H20N2O2S: C, 58.20; H, 7.46; N, 10.44%; found: C, 58.33; H, 7.41; N, 10.36%; $\delta_{\rm H}$ (400 MHz, CDCl₃): 8.40 (1H, br-d, J = 4.0 Hz, 6'-*H*), 7.46 (1H, dt, *J* = 1.8, 7.8 Hz, 4'-*H*), 7.23 (1H, d, *J* = 8.0 Hz, 3'-H), 6.97-7.00 (1H, m, 5'-H), 5.49 (1H, s, NH), 3.90-4.05 (1H, m, 2-*H*), 3.22–3.40 (2H, m, 1-*H*₂), 1.39 (9H, s, 3 × C*H*₃), 1.25 (3H, d, $J = 6.8, 3-H_3$; δ_C (100 MHz, CDCl₃): 155.4 (N-C=O), 158.7, 149.1, 135.9, 122.3 & 119.5 (Ar-C₅), 78.8 (C-(CH₃)₃), 47.1 (2-C), 36.0 (1-C), 28.3 (3 × CH₃), 20.3 (3-C); ν_{max} : 3359, 2973, 1678, 1581, 1519, 1415, 1167, 1154, 1125, 1059, 1053, 752, 578, 399 cm^{-1} ; m/z: (ESI) 269 ([M + H]⁺), 152; HRMS: (ESI) for [M + H]⁺ C13H21N2O2 requires 269.1318, found: 269.1324. N,N-Di(tbutoxycarbonyl)-1-(pyrid-2'-ylthio)propyl-2-amine 20, pale thick oil, (22 mg, 6.5%). $\delta_{\rm H}$ (400 MHz, CDCl₃): 8.38 (1H, d, J = 4.0 Hz, 6'-H), 7.40-7.44 (1H, m, 4'-H), 7.11-7.15 (1H, m, 3'-H), 6.91-6.95 (1H, m, 5'-H), 4.49-4.58 (1H, m, 2-H), 3.47-3.56 (2H, m, 1-H₂), 1.43 (18H, s, 6 × CH₃), 1.39 (3H, d, J = 7.2 Hz, 3-H₃); $\delta_{\rm C}$ (100 MHz, $CDCl_3$): 157.1 (2 × N-C=O), 159.1, 149.1, 135.7, 122.3 & 119.5 (Ar- C_5), 82.0 (2 × C(CH₃)₃), 52.2 (2-C), 34.6 (1-C), 27.9 (6 × CH₃), 17.9 (3-C); v_{max}: 3049, 2978, 1942, 1699, 1577, 1553, 1454, 1337, 1212, 1142, 1121, 1039, 985, 752 & 395 cm⁻¹; *m/z*: (ESI) 369 $([M + H]^{+})$, 269, 213, 152; *HRMS*: (ESI) for $[M + H]^{+}$, $C_{18}H_{29}N_2O_4S$ requires 369.1843; found: 369.1838.

(b) With sodium phenylthiolate. To a solution of the sodium salt of thiophenol in dry THF (15 ml), formed from thiophenol (101.4 mg, 0.108 ml, 0.92 mmol) and sodium hydride (60% dispersion in oil, 74 mg, 1.84 mmol), was added to a solution of 14 (200 mg, 0.92 mmol) in dry THF (10 ml). The mixture was stirred and heated to 60 °C for 4 h. After adding some drops of water, the mixture was left stirring for 30 min. The clear solution was diluted with water (30 ml) and extracted with dichloromethane (2 \times 20 ml). The organic layer was evaporated, and the crude product was purified by chromatography eluting with cyclohexane-ethyl acetate (10:1). The separation gave three compounds 22 (32.0%), 23 (4.5%) and 24 (38.3%). N-1-t-Butoxycarbonyl-1-phenylthiopropyl-2-amine 22 is a white solid (78 mg, 32.0%), m.p. 62-63 °C. Anal. calcd for C14H21NO2S: C, 62.92; H, 7.86; N, 5.24%; found: C, 63.00; H, 7.96; N, 5.21%; $\delta_{\rm H}$ (400 MHz, CD₃OD): 7.37 (2H, d, J = 8.0 Hz, ortho Ar- H_2), 7.27 (2H, t, J = 8.0 Hz, meta Ar- H_2), 7.15 (1H, t, J =7.2 Hz, para Ar-H), 3.68–3.77 (1H, m, 2-H), 3.09 (1H, br-dd, J = 6.0, 13.0 Hz, $1-H_{\alpha}$), 2.88 (1H, dd, J = 7.2, 13.0 Hz, $1-H_{\beta}$), 1.41 (9H, s, $3 \times CH_3$), 1.18 (3H, d, J = 6.8 Hz, $3 \cdot H_3$); δ_C (100 MHz, CD₃OD): 157.6 (N-C=O), 137.8, 130.3, 129.9 & 127.0, (Ar-C₆), 79.9 (C- $(CH_3)_3$, 48.6 (2-C), 40.8 (1-C), 28.8 (3 × CH₃), 20.0 (3-C); ν_{max} : 3368, 2976, 1681, 1518, 1244, 1153, 1026, 737, 610, 468 cm^{-1} ; m/z: (EI) 290 ([M + Na]⁺), 212, 151; *HRMS*: (EI) for [M + Na]⁺ C₁₄H₂₁NO₂SNa requires 290.1185; found: 290.1189.

N,*N*-*Bis*(*t*-butoxycarbonyl)-1-(phenylthio)propyl-2-amine 23, clear colourless liquid (15 mg, 4.45%). Anal. calcd for C₁₉H₂₉NO₄S: C, 62.12; H, 7.90; N, 3.81%; found: C, 62.14; H, 7.83; N, 3.96%; $\delta_{\rm H}$ (400 MHz, CDCl₃): 7.29 (2H, d, *J* = 7.8 Hz,

ortho Ar- H_2), 7.19 (2H, t, J = 7.8 Hz, meta Ar- H_2), 7.10 (1H, t, J =7.2 Hz, para Ar-H), 4.28–4.37 (1H, m, 2-H), 3.35 (1H, dd, J = 8.0, 13.6, 1- H_{α}), 3.06 (1H, dd, J = 7.2, 13.6 Hz, 1- H_{β}), 1.39 (18H, s, 6 × CH₃), 1.30 (3H, d, J = 6.8 Hz, 3-H₃); $\delta_{\rm C}$ (100 MHz, CDCl₃): 152.8 $(2 \times N-C=0)$, 135.8, 129.5, 128.8 & 126.1, (Ar-C₆), 82.2 (2×10^{-6}) $C(CH_3)_3$, 52.2 (2-C), 38.6 (1-C), 27.9 (6 × CH₃), 17.6 (CH₃); ν_{max} : 2978, 1736, 1699, 1367, 1345, 1273, 1142, 740, 691 cm⁻¹; m/z: (ESI) 390 ($[M + Na]^+$), 268, 151; *HRMS*: (ESI) for $[M + H]^+$ C19H30NO4S requires 368.1890, found: 368.1890. rac-R,R,R- and rac-R,R,S-1,3,5-tris(1'-(phenylthio)prop-2'-yl)hexahydro-1,3,5-triazine-2,4,6-trione 24, clear colourless liquid (68 mg, 12.8%). $\delta_{\rm H}$ (400 MHz, CDCl₃): 7.35 (6H, d, J = 7.8 Hz, $3 \times ortho$ Ar- H_2), 7.33 (6H, t, J = 7.8 Hz, $3 \times meta$ Ar- H_2), 7.25 (3H, t, J = 7.2 Hz, $3 \times para$ Ar- H_1), 4.88–4.98 (3H, m, $3 \times 2'$ -H), 3.53–3.62 (3H, m, $3 \times 1'$ -H_{α}), 3.15–3.23 $(3H, m, 3 \times 1'-H_{\beta}), 1.44 (9H, d, J = 6.8 \text{ Hz}, 3 \times 3'-H_{3}); \delta_{C} (100 \text{ MHz},$ CDCl₃): 159.4 (3 × N₂-C=O), 135.3, 130.4, 130.2, & 126.8 (3 × Ar- C_6), 51.1 (3 × 2'-C), 37.1 (3 × 1'-C), 17.3 (3 × 3'-C); ν_{max} : 2975, 1683, 1425, 1369, 1024, 762, 734, 689, 421 cm⁻¹; m/z: (EI) 579 $([M]^+)$, 151, 150; *HRMS*: (ESI) for $[M + H]^+$, $C_{30}H_{34}N_3O_3S_3$ requires 580.1749, found 580.1749. The multiplicities of resonances in region $\delta_{\rm H}$ 3–4ppm indicate that two diastereomers are present.

(c) With sodium ethanethiolate. 14 (200 mg, 0.92 mmol) and sodium ethanethiolate (339 mg, 0.92 mmol) were dissolved in dry xylene (10 ml) and the mixture was stirred and irradiated in a microwave oven at 145 °C for 1 h. After cooling to room temperature the reaction mixture was dissolved in dichloromethane (15 ml) and was washed with distilled water (2 \times 10 ml). The organic layer was dried over sodium sulfate, and solvent removed in vacuo. The crude residue was purified by chromatography using cyclohexane-ethyl acetate (2:1) as eluent to give N-t-butoxycarbonyl-1-(ethylthio)propyl-2-amine 26 as a pale yellow oil (116 mg, 57.6%). Anal. calcd for $C_{10}H_{21}NO_2S$: C, 54.76; H, 9.65; N, 6.39%; found: C, 54.82; H, 9.49; N, 6.27%; $\delta_{\rm H}$ (400 MHz, CDCl₃): 4.59 (1H, s, NH), 3.71–3.80 (1H, br-m, 2-*H*), 2.63 (1H, dd, J = 5.0, 13.3 Hz, 1- H_{α}), 2.47–2.53 (3H, m, 1- H_{β} , -CH₂Me), 1.37 (9H, s, $3 \times CH_3$), 1.20 (3H, t, J = 7.3 Hz, CH₂CH₃), 1.14 (3H, d, J = 6.8 Hz, 3- H_3); δ_C (100 MHz, CDCl₃): 155.1 (N-C= O), 79.2 (C-(CH₃)₃), 45.9 (2-C), 38.4 (1-C), 28.3 ($3 \times CH_3$), 26.7 (S-CH₂Me), 19.8 (3-C), 14.8 (CH₂CH₃); v_{max}: 3332, 2972, 2928, 1689, 1506, 1365, 1246, 1166, 1048, 1025 cm⁻¹; m/z: (ESI) 220 $[M + H]^+$, 164, 146; *HRMS*: (ESI) for $[M + H]^+$ C₁₀H₂₂NO₂S requires 220.1366, found: 220.1368.

(d) With potassium thioacetate. Potassium thioacetate (116 mg, 1.01 mmol) was added to a solution of 14 (200 mg, 0.92 mmol) dissolved in dry DMF (20 ml) under anhydrous conditions. The mixture was stirred at 20 °C for 12 h. After adding some drops of water, and stirring for 30 min, the mixture was concentrated in vacuo. The crude material was purified by chromatography (cyclohexane-ethyl acetate 4:1) to give Nacetyl-S-t-butoxycarbonyl-1-mercaptopropyl-2-amine 28 as а yellow liquid (70 mg, 32.6%). Anal. calcd for C₁₀H₁₉NO₃S: C, 51.48; H, 8.21; N, 6.00%; found: C, 51.33; H, 7.92; N, 5.92%; $\delta_{\rm H}$ (400 MHz, CDCl₃): 5.76 (1H, s, NH), 4.06-4.16 (1H, m, 2-H), 2.87–2.90 (2H, m, 1- H_2), 1.86 (3H, s, COC H_3), 1.43 (9H, s, 3 \times CH₃), 1.14 (3H, d, J = 6.4 Hz, 3-H₃); $\delta_{\rm C}$ (100 MHz, CDCl₃): 169.5 (S-C=O), 159.8 (N-C=O), 85.3 (C-(CH₃)₃), 46.0 (2-C), 36.3 (1-C),

28.1 (3 × *C*H₃), 23.3 ((O=C)*C*H₃), 19.9 (3-*C*); ν_{max} : 3278, 2979, 1702, 1645, 1547, 1369, 1200, 1123, 838, 732 cm⁻¹; *m/z*: (ESI) 234 ([M + H]⁺), 178, 156; *HRMS*: (ESI) for [M + H]⁺ C₁₀H₂₀NO₃S requires 234.1158, found: 234.1159.

(e) With tetrabutylammonium iodide. Tetrabutylammonium iodide (339 mg, 0.92 mmol) and 14 (200 mg, 0.92 mmol) were dissolved in dry xylene (10 ml) and the mixture was stirred and irradiated in a microwave oven at 145 °C for 1 h. After cooling to room temperature the reaction mixture was dissolved in dichloromethane (15 ml) and was washed with distilled water $(2 \times 10 \text{ ml})$. The organic layer was dried over sodium sulfate, and solvent removed in vacuo. The crude residue was purified by chromatography using cyclohexane-ethyl acetate (2:1) as eluent to give N-t-butoxycarbonyl-4-methyl-1,3-thiazolidin-2-one 31 as a white solid (114 mg, 57.0%), which was crystallized from ethyl acetate, m.p. 77-78 °C. Anal. calcd for C9H15NO3S: C, 49.75; H, 6.96; N, 6.45%, found: C, 49.87; H, 7.03; N, 6.39%; $\delta_{\rm H}$ $(400 \text{ MHz}, \text{CDCl}_3)$: 4.50–4.57 (1H, quin., J = 6.8 Hz, 4-H), 3.51 $(1H, dd, J = 11.0, 7.8 Hz, 5-H_{\alpha}), 2.72 (1H, d, J = 11.0 Hz, 5-H_{\beta}),$ 1.45 (9H, s, 3 × CH₃), 1.35 (3H, d, J = 6.2 Hz, 4-CH₃); $\delta_{\rm C}$ (100 MHz, CDCl₃): 169.6 (2-C), 148.5 (N-C=O), 83.3 (C(CH₃)₃), 54.6 (4-C), 31.6 (5-C), 27.7 (3 × CH₃), 18.7 (4-CH₃); ν_{max} : 2977, 1755, 1672, 1369, 1354, 1326, 1278, 1245, 1169, 1147, 942, 859, 768, 672, 548 cm⁻¹; m/z: (ESI) 235 ([M + NH₄]⁺), 218 ([M + H]⁺), 162, 144; *HRMS*: (ESI) for $[M + NH_4]^+ C_9 H_{19} N_2 O_3 S$ requires 235.1111, found: 235.1114.

(f) With *n*-butyl lithium. *n*-Butyl lithium (0.37 ml, 2.5 M, 0.92 mmol) was added to a stirred solution of 14 (200 mg, 0.92 mmol) in anhydrous tetrahydrofuran (20 ml), under a nitrogen atmosphere at -78 °C. The solution was allowed to warm to 20 °C and was stirred overnight and became yellow. After adding some drops of a mixture of THF and water, and stirring for 30 min, the solvent was evaporated. The residue was extracted with dichloromethane (2 \times 20 ml) and the extract was washed with water (30 ml). The organic layer was evaporated and the resulting residue was chromatographed using cyclohexaneethyl acetate (2:1) to give the product O-(2'-((tert-butoxycarbonyl)amino)propyl) thiopentanoate 34 (116 mg, 45.9%) as a yellow liquid. Anal. calcd for C13H25NO3S: C, 56.72; H, 9.09; N, 5.09%; found: C, 56.68; H, 9.15; N, 5.05%; $\delta_{\rm H}$ (400 MHz, CD₃OD): 4.36 (1H, dd, J = 10.8, 4.9 Hz, 1'- H_{α}), 4.24–4.30 (1H, brdd, J = 10.8, 7.8 Hz, 1'- H_{β}), 3.96–4.04 (1H, m, 2'-H), 2.72 (2H, t, $J = 8.0 \text{ Hz}, 2-H_2$, 1.67–1.75 (2H, m, 3- H_2), 1.41 (9H, s, 3 × C H_3), 1.32–1.41 (2H, m, 4- H_2), 1.16 (3H, d, J = 6.8 Hz, 3'- H_3), 0.90 (3H, t, J = 6.8 Hz, 5- H_3); δ_C (100 MHz CD₃OD): 224.2 (C=S), 157.3 (N-C=O), 78.7 (C(CH₃)₃), 74.3 (1'-C), 46.8 (2'-C), 45.4 (2-C), 31.7 (3-C), 27.5 (3 × CH₃), 21.6 (4-C), 16.3 (3'-C), 12.9 (5-C); ν_{max} : 3333, 2963, 2934, 1688, 1505, 1490, 1442, 1387, 1366, 1351, 1246, 1188, 1164, 1101, 1068, 1032, 930, 921, 804 cm⁻¹; *m/z*: (EI) 276 $([M + H]^+)$, 260, 220, 204, 186, 180, 160; *HRMS*: (EI) for $[M + H]^+$ C₁₃H₂₆NO₃S requires 276.1629, found: 276.1631.

(g) With sec-butyl lithium. Prepared following procedure for 34 above, but using sec-butyl lithium (0.79 ml, 1.4 M, 1.1 mmol) instead of *n*-butyl lithium. The product was isolated by chromatography using cyclohexane–ethyl acetate (19:1) to give *O-(N-t-butoxycarbonyl)-2'-aminopropyl 2-methylthiobutanonate* 35 (134 mg, 53%) as a white solid, m.p. 58–59 °C, two

diastereomers (*ca.* 1 : 1), $\delta_{\rm H}$ (400 MHz, CDCl₃): 4.47 (1H, br, N*H*), 4.24–4.37 (2H, m, 1'-*H*₂), 4.03–4.21 (1H, br, 2'-*H*), 2.76 (1H, hex., *J* = 6.9 Hz, 2-*H*), 1.37 (9H, s, 3 × C*H*₃), 1.62–1.75 (1H, m, 3-*H*_α), 1.52–1.41 (1H, m, 3-*H*_β), 1.16 (6H, 2 × d, *J* = 7.3 Hz, 3'-*H*₃, 2-C*H*₃), 0.82 (3H, t, *J* = 7.4 Hz, 4-*H*₃); $\delta_{\rm C}$ (100 MHz, CDCl₃): 229.12 and 229.09 (*C*=S), 155.0 (N–*C*=O), 79.5 (O–*C*(CH₃)₃), 74.44 and 74.38 (1'-*C*), 52.25 and 52.21 (2-*C*), 45.4 and 45.3 (2'-*C*), 29.6 and 29.5 (3-C), 28.3 (O–C-(*C*H₃)₃), 19.92 and 19.90 (2-*C*H₃), 18.0 (3'-C), 11.7 (4-C); $\nu_{\rm max}$: 3345, 2975, 2936, 1682, 1528, 1455, 1368, 1345, 1291, 1271, 1267, 1235, 1192, 1154, 1101, 1052, 1007, 982, 851, 753, 636 cm⁻¹; *HRMS*: (ESI) for [M + H]⁺ C₁₃H₂₆NO₃S requires 276.1628, found 276.1631.

(h) With *t*-butyl lithium. Prepared following procedure for 34 above, but using tert-butyl lithium (0.69 ml, 1.6 M, 1.1 mmol) instead of *n*-butyl lithium. The product was isolated by chromatography using cyclohexane-ethyl acetate (4:1) to give O-(Nt-butoxycarbonyl)-2'-aminopropyl 2,2-dimethylthiopropionate 36 (240 mg, 94.8%) as a yellow solid, m.p. 67–68 °C. Anal. calcd for C13H25NO3S: C, 56.69; H, 9.15; N, 5.09%; found: C, 57.00; H, 9.21; N, 4.96%. δ_H (400 MHz, CDCl₃): 4.47 (1H, br, NH), 4.24-4.31 (2H, m, 1'- H_2), 4.03–4.12 (1H, br, 2'-H), 1.37 (9H, s, 3 × CH_3 , 1.23 (9H, s, 3 × CH_3), 1.14 (3H, d, J = 6.8 Hz, 3'-H); δ_C (100 MHz, CDCl₃): 231.1 (C=S), 155.0 (N-C=O), 81.5 (O-C(CH₃)₃), 74.8 (1'-C), 67.0 (1-C), 47.3 (2'-C), 29.7 (O-C-(CH₃)₃), 28.3 (C-(CH₃)₃), 17.9 (3'-C), v_{max}: 3314, 2975, 1681, 1539, 1368, 1255, 1211, 1163, 1114, 1059, 658 cm⁻¹; m/z: (ESI) 276 ([M + H]⁺), 260; *HRMS*: (ESI) for $[M + H]^+ C_{13}H_{26}NO_3S$ requires 276.1628, found 276.1629.

(i) With lithium dimethylamide. Prepared following procedure for 34 above but using lithium dimethylamide (1.0 ml, 5 wt% in hexane, 0.92 mmol). The product was isolated by flash column chromatography using cyclohexane-ethyl acetate (4:1) The separation gave two compounds 37 and 38. N-t-Butoxycarbonyl-O-(dimethylaminothiocarbonyl)-2-aminopropanol 37 (75 mg, 31.1%), a yellow solid, m.p. 87 °C. $\delta_{\rm H}$ (400 MHz, CDCl₃): 4.55 (1H, br-s, NH), 4.30-4.41 (2H, m, 1-H₂), 3.99-4.14 (1H, br, 2-H), 3.29 (3H, s, N-CH₃), 3.06 (3H, s, N-CH₃), 1.36 (9H, s, $3 \times CH_3$), 1.13 (3H, d, J = 6.8 Hz, $3-H_3$); δ_C (100 MHz, CDCl₃): 189.6 (C=S), 155.1 (N-C=O), 79.2 (C(CH₃)₃), 76.7 (1-C), 46.0 (2-*C*), 42.7 (N–*C*H₃), 37.7 (N–*C*H₃), 28.3 (C(*C*H₃)₃), 17.7 (3-*C*); *v*_{max}: 3357, 2977, 1684, 1526, 1366, 1271, 1163, 1025, 634, 549 cm⁻¹; m/z: (ESI) 263 ([M + H]⁺), 207; *HRMS*: (ESI) for [M + H]⁺ C11H23N2O3S requires 263.1424, found 263.1420. N,N-Di-(t-butoxycarbonyl)-O-(dimethylaminothiocarbonyl)-2-aminoethanol 38 (103 mg, 30.9%), a yellow solid, m.p. 100-102 °C. Anal. calcd for C₁₆H₃₀N₂O₅S: C, 53.01; H, 8.34; N, 7.73%; found: C, 53.28; H, 8.47; N, 7.60%; $\delta_{\rm H}$ (400 MHz, CDCl₃): 4.48–4.64 (3H, 2-H, 1-H₂), $3.27 (3H, s, N-CH_3), 3.01 (3H, s, N-CH_3), 1.42 (18H, s, 6 \times CH_3),$ 1.24 (3H, d, J = 6.8 Hz, 3- H_3); δ_C (100 MHz, CDCl₃): 187.6 (C = S), 152.8 (2 × N-C=O), 82.2 (2 × $C(CH_3)_3$), 72.2 (1-C), 51.0 (2-C), 42.5 (N-CH₃), 37.6 (N-CH₃), 27.9 (2 × C(CH₃)₃), 15.2 (3-C); ν_{max} : 2977, 1734, 1691, 1539, 1396, 1378, 1367, 1353, 1294, 1276, 1234, 1200, 1174, 1158, 1123, 1045, 1021, 766 cm⁻¹; m/z: (ESI) $363 ([M + H]^+)$, 307, 263; *HRMS*: (ESI) for $[M + H]^+ C_{16}H_{31}N_2O_5S$ requires 363.1948, found: 363.1940.

(j) With phenyl lithium. Prepared following procedure for 34 above, but using phenyl lithium (0.52 ml, 1.8 M in diethyl

ether, 0.92 mmol). The product was isolated by chromatography using cyclohexane–ethyl acetate (2 : 1) to give 4-methyl-2-phenylthiazoline³² **40** (155 mg, 95.0%) as a yellow oil. $\delta_{\rm H}$ (400 MHz, CDCl₃): 7.79–7.84 (2H, m, 2'-,6'-H), 7.33–7.43 (3H, m, 3'-,4'-,5'-H), 4.72 (1H, hex., J = 6.8 Hz, 4-CH), 3.46 (1H, dd, J = 6.8, 8.4 Hz, 5-H_{α}) 2.98 (1H, dd, J = 7.2, 8.4 Hz, 5-H_{β}), 1.43 (3H, d, J = 6.2 Hz, 4-CH₃); $\delta_{\rm C}$ (100 MHz, CDCl₃): 166.1 (2-C), 133.1, 130.8, 128.2, 128.1 (Ar-C₆), 72.7 (4-C), 39.6 (5-C), 20.2 (4-CH₃); $\nu_{\rm max}$: 2967, 1446, 1300, 1249, 1107, 948, 765, 690, 612, 396 cm⁻¹; m/z: (ESI) 178 ([M + H]⁺), 162, 131, 77; *HRMS*: (ESI) for [M + H]⁺ C₁₀H₁₂NS requires 178.0683, found: 178.0679.

(k) With phenyl magnesium bromide. Prepared following procedure for 34 above, but using phenyl magnesium bromide (3.0 ml in diethyl ether), gave 40 (38%).

(1) With phenylethynyl lithium. Prepared following procedure for 34 above but using lithium phenylacetylide (1.0 ml, 1 M in THF, 0.92 mmol). The product was purified by chromatography cyclohexane–ethyl acetate (2 : 1) to yield 4-methyl-2-(phenylethynyl)thiazoline 41 as a yellow oil (110 mg, 59.5%). $\delta_{\rm H}$ (400 MHz, CDCl₃): 7.44 (2H, d, J = 7.8 Hz, ortho Ar- H_2), 7.27 (2H, t, J =7.8 Hz, meta Ar- H_2), 7.25 (1H, t, J = 7.2 Hz, para Ar- H_1), 4.54–4.58 (1H, m, 4-H), 3.44 (1H, dd, J = 7.0, 8.3 Hz, 5- H_{α}), 2.96 (1H, dd, J =6.8, 8.3 Hz, 5- H_{β}), 1.43 (3H, d, J = 6.2 Hz, 4-CH₃); $\delta_{\rm C}$ (100 MHz, CDCl₃): 163.5 (2-*C*), 132.1, 129.8, 128.3 and 122.7 (Ar- C_6), 93.0 (sp-*C*), 81.9 (sp-*C*) 72.5 (4-*C*), 40.6 (5-*C*), 20.0 (4-CH₃); $\nu_{\rm max}$: 2980, 2210, 1704, 1369, 1299, 1205, 1149, 756, 689 cm⁻¹; m/z: (EI) 201 ([M]⁺), 186, 155, 127; *HRMS*: (ESI) for [M + H]⁺ C₁₂H₁₂NS requires 202.0692, found: 202.0685.

(m) With isopropyl magnesium chloride. Prepared following the procedure for 34 above, but using isopropyl magnesium chloride (0.47 ml, 2 M in THF, 0.94 mmol). The product was purified by column chromatography cyclohexane-ethyl acetate (2 : 1) to give 3-(2'-methylpropanethioyl) 4-methyl-1,3-oxazolidin-2-one 42 as a yellow oil. Anal. calcd for C₈H₁₃NO₂S: C, 51.31; H, 7.00; N, 7.48%; found: C, 51.26; H, 7.11; N, 7.58%. $\delta_{\rm H}$ (400 MHz, CDCl₃): 5.10–5.17 (1H, m, 4-H), 4.29–4.40 (2H, m, 2'-,5- H_{α}), 3.99 (1H, dd, J = 1.8, 8.6 Hz, 5- H_{β}), 1.42 (3H, d, J = 6.3 Hz, 4-CH₃), 1.16 (6H, d, J = 6.4 Hz, 2 × -CH₃); $\delta_{\rm C}$ (100 MHz, CDCl₃): 219.5 (C=S), 150.4 (2-C), 68.4 (5-C), 55.8 (4-C), 38.4 (2'-C), 24.0 (-CH₃), 23.4 (-CH₃), 17.6 (4-CH₃), $\nu_{\rm max}$: 2973, 1777, 1371, 1312, 1242, 1161, 1120, 1046, 914, 761, 698 cm⁻¹; m/z: (EI) 187 ([M]⁺), 102, 85, 70, 68, 44; *HRMS*: (EI) for [M]⁺ C₈H₁₃NO₂S requires 187.0662, found: 187.0663.

Rearrangement of 13 with tetrabutylammonium iodide to give 32 and 33

(a) Bu_4NI (550 mg, 1.7 mmol) was added to a solution of *rac* 4-methyl-1,3-oxazolidine-2-thione **13** (200 mg, 1.7 mmol) dissolved in dry xylene (10 ml). The mixture reaction was stirred for 30 min. The glass tube was placed in an alumina bath inside the microwave oven (CEM Discover SP), and irradiated so that the internal temperature reached 145 °C for 1 h. After cooling to room temperature, the reaction mixture was dissolved in dichloromethane and filtered, the solvent was evaporated and the crude compound purified by column chromatography using cyclohexane–ethyl acetate (3 : 1) which afforded the pure *rac* 4-

methyl-1,3-thiazolidin-2-one **32** (190 mg, 95%) as a yellow oil. Anal. calcd for C₄H₇NOS: C, 41.00; H, 6.02; N, 11.95%; found: C, 41.02; H, 6.03; N, 11.89%; $\delta_{\rm H}$ (400 MHz, CDCl₃): 7.07 (1H, br-s, NH), 3.95 (1H, hex., J = 6.7 Hz, 4-H), 3.42 (1H, dd, J = 7.1, 10.8 Hz, 5-H_{α}), 2.96 (1H, dd, J = 7.2, 10.8 Hz, 5-H_{β}), 1.28 (3H, d, J = 6.3 Hz, CH₃); $\delta_{\rm C}$ (100 MHz, CDCl₃): 175.4 (2-C), 51.2 (4-C), 36.4 (5-C), 20.3 (CH₃); $\nu_{\rm max}$: 3230, 2971, 1654, 1355, 1217 and 684 cm⁻¹; m/z: (GC-EIP) 117 (M⁺), 102; *HRMS*: (GC-EIP) for [M]⁺ C₄H₇NOS requires 117.0243, found: 117.0241.

(b) Using the procedure above but using a much smaller amount of dry xylene (2 ml) and 1.5 eq. Bu₄NI to obtain a *rac -R,R* and *R,S- 4,9-dimethyl-1,6,3,8-dithiadiazocyclodecane-2,7-dione* **33** as a pale brown oil (110 mg, 27.7%). Anal. calcd for $C_8H_{14}N_2O_2S_2$: C, 41.00; H, 6.02; N, 11.95%; found: C, 41.14; H, 6.03; N, 11.89%; δ_H (400 MHz CDCl₃): 6.72 (2H, br-s, 2 × NH), 3.87 (2H, hex., J = 6.7 Hz, 4-,9-H), 3.64 (2H, dd, J = 10.1, 7.0 Hz, 5-,10- H_{α}), 3.17 (2H, dd, J = 10.1, 6.4 Hz, 5-,10- H_{β}), 1.28 (2 × 3H, d, J = 6.7 Hz, 2 × CH₃); δ_C (100 MHz, CDCl₃): 176.2 (2 × C=O), 50.6 (4-,9-C), 41.6 (5-,10-C), 20.8 (2 × CH_3); ν_{max} : 3231, 2966, 1869, 1661, 1215, 1060, 681 and 615 cm⁻¹; m/z: (ESI) 235 ([M + H]⁺), 201, 158, 140. *HRMS*: for [M + H]⁺ C₈H₁₅N₂O₂S₂ requires 235.0569, found: 235.0571.

Reactions of 16

(a) With pyridine-2-thiolate. A solution of the sodium salt of 2-mercaptopyridine in dry THF (15 ml), formed from 2-mercaptopyridine (122 mg, 1.1 mmol) and sodium hydride (60% dispersion in mineral oil, 71 mg, 1.78 mmol), was added to a solution of thionocarbamate 16 (261 mg, 1.0 mmol). After stirring at room temperature overnight, drops of 20% acetic acid were added, and the mixture left to stir for 30 min. The solvent was evaporated, and the residue was extracted with dichloromethane $(2 \times 20 \text{ ml})$ and the extract washed with water (30 ml). The crude product was purified by chromatography using cyclohexane-ethyl acetate (1:2) to furnish rac methyl 2-((tertbutoxycarbonyl)amino)-3-(pyridin-2-ylthio)propanoate 29 (177 mg, 56.7%) as a yellow oil. Anal. calcd for $C_{14}H_{20}N_2O_4S$: C, 53.62; H, 6.45; N, 8.97%, found: C, 53.62; H, 6.47; N, 8.88%. $\delta_{\rm H}$ (400 MHz, CDCl₃): 8.32 (1H, br-d, *J* = 4.0 Hz, 6'-*H*), 7.41 (1H, dt, J = 1.8, 7.3 Hz, 4'-H), 7.14 (1H, d, J = 8.0 Hz, 3'-H), 6.93-6.97 (1H, d, J = 8.0 Hz, 3'-H)m, 5'-H), 6.26 (1H, s, NH), 4.50 (1H, m, 2-H), 3.63 (3H, s, OCH₃), 3.48–3.58 (2H, m, 3- H_2), 1.33 (9H, s, 3 × C H_3); δ_C (400 MHz, CDCl₃): 171.4 (1-C), 157.6 (2'-C), 155.5 (N-C=O), 149.7 (6'-C), 136.2 (4'-C), 122.5 (3'-C), 119.9 (5'-C), 79.9 (C-(CH₃)₃), 54.4 (2-C), 52.2 (OCH₃), 31.9 (3-C), 28.2 (3 \times CH₃), ν_{max} : 3352, 2961, 1744, 1711, 1578, 1454, 1416, 1365, 1258, 1164, 1017, 797, 761 and 401 cm⁻¹; m/z: (EI) 312 ([M]⁺), 239, 219, 196; *HRMS*: (EI) for [M]⁺ C₁₄H₂₀N₂O₄S requires 312.1138, found: 312.1136.

(b) With phenylthiolate. Sodium hydride (60% dispersion in mineral oil, 71 mg, 1.78 mmol) was added to anhydrous methanol (10 ml) and the mixture stirred at room temperature for 30 min. Dry thiophenol (0.28 ml, 2.67 mmol) was added and the mixture was stirred for a further 30 min after which time thionocarbamate **16** (261 mg, 1.0 mmol) was added. After stirring at room temperature overnight, a few drops of 20% acetic acid were added and the reaction mixture was evaporated. The

residue was extracted with diethyl ether, dried and concentrated in vacuo. Final purification was achieved by column chromatography with ethyl acetate as eluent to give rac methyl 2-((tertbutoxycarbonyl)amino)-3-(phenylthio)propanoate 30 (216 mg, 69.5%) as clear oil. Anal. calcd for C₁₅H₂₁NO₄S: C, 57.86; H, 6.80; N, 4.50%; found: C, 57.85; H, 6.81; N, 4.41%; $\delta_{\rm H}$ (400 MHz, CDCl₃): 7.39-7.15 (5H, m, Ar-H₅), 5.32 (1H, s, NH), 4.50-4.58 (1H, m, 2-H), 3.45 (3H, s, OCH₃), 3.28-3.32 (2H, m, 3-H₂), 1.43 (9H, s, $3 \times CH_3$); δ_C (100 MHz, CDCl₃): 170.8 (1-*C*), 154.8 (N-*C*= O), 134.8 (ipso-C), 130.5 (2 × meta-C), 129.0 (2 × ortho-C), 126.8 (para-C), 79.9 (C-(CH₃)₃), 53.7 (2-C), 52.1 (OCH₃), 37.0 (3-C), 28.2 $(3 \times CH_3)$; ν_{max} : 3373, 2977, 1746, 1712, 1499, 1438, 1366, 1161, 1053, 1011, 742 and 691 cm⁻¹; m/z: (EI) 311 ([M]⁺), 193, 122, 56; HRMS: (EI) for [M]⁺ C₁₅H₂₁NO₄S requires 311.1186, found: 311.1183. Compound 30 has been briefly referred to before.34

(c) With phenyl lithium. Phenyl lithium (84 mg, 0.56 ml, 1.1 mmol) was added to a stirred solution of thionocarbamate 16 (261 mg, 1.0 mmol) in anhydrous tetrahydrofuran (15 ml) under a nitrogen atmosphere at -78 °C, and the solution was stirred under anhydrous conditions. The solution was allowed to warm to 20 °C and was stirred overnight and became yellow. After adding some drops of a mixture of aqueous THF and stirring for 30 min, the solvent was evaporated, the residue was extracted with dichloromethane $(2 \times 20 \text{ ml})$ and the extract was washed with water (30 ml). The organic layer was evaporated and the resulting residue was chromatographed on silica using ethyl acetate-cyclohexane (1:2) to give two known products: 2-tertbutoxycarbonylamino-acrylic acid methyl ester 4434,35 as a yellow oil $(105 \text{ mg}, 52.3\%), \delta_{H}$ (400 MHz, CDCl₃): 6.96 (1H, s, NH), 6.10 (1H, br-s, $3-H_{\alpha}$), 5.65 (1H, d, J = 1.5 Hz, $3-H_{\beta}$), 3.74 (3H, s, OCH₃), 1.31 (9H, s, $3 \times CH_3$), δ_C (100 MHz, CDCl₃): 164.4 (1-*C*), 152.4 (N-*C*= O), 131.2 (2-C), 105.1 (3-C), 80.6 (C-(CH₃)₃), 52.7 (OCH₃), 28.2 (3 × *C*H₃); *v*_{max}: 3356, 2973, 1741, 1700, 1510, 1366, 1222, 1151, 1055, 1018, 751, 699, 498 and 382 cm⁻¹ and methyl 2-((tert-butoxycarbonyl)amino)-3-phenylpropanoate 45³⁶ as a pale yellow solid (81 mg, 29.1%), m.p. 89-91 °C. Anal. calcd for C₁₅H₂₁NO₄: C, 64.50; H, 7.58; N, 5.00%; found: C, 64.42; H, 7.63; N, 4.95%; $\delta_{\rm H}$ (400 MHz, CDCl₃): 7.05-7.28 (5H, m, Ar-H₅), 4.91 (1H, s, NH), 4.49-4.53 (1H, m, 2-H), 3.63 (3H, s, OCH₃), 2.92-3.06 (2H, m, 3-*H*₂), 1.39 (9H, s, $3 \times CH_3$); δ_C (100 MHz, CDCl₃): 172.0 (1-*C*), 155.1 (N-C=O), 135.9 (*ipso-C*), 129.2 (2 × meta-C), 128.5 (2 × ortho-C), 126.9 (para-C), 79.9 (C-(CH₃)₃), 54.3 (2-C), 52.2 (OCH₃), 38.3 (3-C), 28.2 (3 × CH_3); ν_{max} : 3356, 2973, 1741, 1700, 1510, 1366, 1222, 1151, 1055, 1018, 751, 699, 498 and 382 cm^{-1} ; m/z: (ESI) 302 ([M + Na^{+} , 180, 149.

X-ray crystallography

Data was collected with MoKα radiation at 120–150 K on a Bruker Nonius diffractometer equipped with a rotating anode source, and a 95 mm CCD camera by the EPSRC National X-ray Crystallography Service at Southampton University for **11** and **14** or on an Agilent Xcalibur diffractometer equipped with a Sapphire detector at Nottingham Trent University for **17**, **31** and **35–37**. Structures were solved and refined with the SHELXS and SHELXL suite of programs³⁷ using the XSEED³⁸ interface, and

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molecular illustrations are prepared with Mecury $^{\rm 39}$ and POV-RAY. $^{\rm 40}$

Crystal data for **11**: C₁₁H₁₃NSO, $M_r = 207.3$, orthorhombic, a = 19.5407(9), b = 8.0050(4), c = 6.7851(3) Å, V = 1061.35(9) Å³, $P2_12_12$, Z = 4, $D_{calc.} = 1.297$ g cm⁻³, T = 120 K, $\mu = 0.271$ mm⁻¹, F(000) = 440, 2439 unique reflections, 2242 with $I > 2\sigma(I)$, max. (sin θ)/ $\lambda = 0.65$ Å⁻¹, final R = 0.027, wR = 0.069. Crystals grown from dichloromethane.

Crystal data for **14**: C₉H₁₅NSO₃, $M_r = 217.2$, monoclinic, a = 7.4816(2), b = 15.2728(4), c = 9.6621(3) Å, $\beta = 97.115(2)^{\circ}$, V = 1095.54(5) Å³, $P2_1/a$, Z = 4, $D_{calc.} = 1.317$ g cm⁻³, T = 120 K, $\mu = 0.278$ mm⁻¹, F(000) = 464, 2506 unique reflections, 2183 with $I > 2\sigma(I)$, max. (sin θ)/ $\lambda = 0.65$ Å⁻¹, final R = 0.029, wR = 0.070. Crystals grown from ethyl acetate.

Crystal data for 17: C₉H₁₅NO₄, $M_r = 201.2$, orthorhombic, a = 9.1981(4), b = 9.2778(3), c = 23.4543(11) Å, V = 2001.55(14) Å³, *Pbca*, Z = 8, $D_{calc.} = 1.34$ g cm⁻³, T = 120 K, $\mu = 0.105$ mm⁻¹, F(000) = 864, 2376 unique reflections, 1819 with $I > 2\sigma(I)$, final R = 0.049, wR = 0.095. Crystals grown from ether.

Crystal data for **31**: C₉H₁₅NO₃S, $M_r = 217.3$, monoclinic, a = 9.6972 (6), b = 6.7661 (3), c = 17.4884(10) Å, $\beta = 100.177$ (3)°, V = 1129.40(11) Å³, $P2_1/n$, Z = 4, $D_{calc.} = 1.28$ g cm⁻³, T = 120 K, $\mu = 0.270$ mm⁻¹, F(000) = 464, 2390 unique reflections, 1996 with $I > 2\sigma(I)$, final R = 0.052, wR = 0.119. Crystals grown from ethyl acetate.

Crystal data for **36**: C₁₃H₂₅NO₃S, $M_r = 275.4$, monoclinic, a = 11.4804(3), b = 9.9540(3), c = 28.7919(8) Å, $\beta = 90.00(3)^{\circ}$, V = 3290.22(16) Å³, $P2_1/c$, Z = 8, $D_{calc.} = 1.11$ g cm⁻³, T = 150 K, $\mu = 0.198$ mm⁻¹, F(000) = 1200, 7791 unique reflections, 5508 with $I > 2\sigma(I)$, final R = 0.064, wR = 0.15. Twinned crystal, twin law 1 0 0 0 -1 0 0 0 -1, with 0.41 : 0.59 distribution. Crystals grown from ethyl acetate.

Crystal data for 37: $C_{11}H_2N_2O_3S$, $M_r = 262.37$, monoclinic, a = 13.1321(4), b = 11.0452(3), c = 10.1525(3) Å, $\beta = 100.532(3)^\circ$, V = 1447.78(7)Å³, $P2_1/c$, Z = 4, $D_{calc.} = 1.20$ g cm⁻³, T = 150 K, $\mu = 0.223$ mm⁻¹, F(000) = 568, 3569 unique reflections, 2818 with $I > 2\sigma(I)$, final R = 0.039, wR = 0.11. Crystals grown from ethyl acetate.

Crystal data for **38**: C₁₆H₃₀N₂O₅S, $M_r = 362.48$, monoclinic, $a = 5.9611(2), b = 19.2487(6), c = 17.6222(5) \text{ Å}, \beta = 94.909(3)^{\circ},$ $V = 2014.61(11) \text{ Å}^3, P2_1/n, Z = 4, D_{calc.} = 1.19 \text{ g cm}^{-3}, T = 150 \text{ K},$ $\mu = 0.186 \text{ mm}^{-1}, F(000) = 784, 4614$ unique reflections, 3514 with $I > 2\sigma(I)$, final R = 0.040, wR = 0.010. Crystals grown from ethyl acetate.

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