Studies on the Structure of Some Derivatives of 1,3-Thiazolidine-2-thione and Δ^2-1,3-Thiazoline-2-thiol

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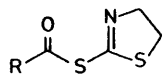
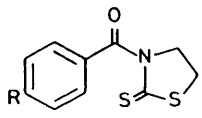
Two types of reactions have been observed for the ambident anion of 1,3-thiazolidine-2-thione: regioselective *N*-acylation and *S*-alkylation. The structures of the products, amides and thioethers, were determined by *X*-ray crystallographic analysis and by assignment of the ^{13}C n.m.r. chemical shifts. The regioselectivity of the reactions is rationalised in terms of the hard–soft acid-base principle and has been exemplified by model experiments.

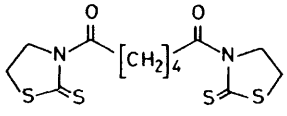
In an earlier paper the Kyoto authors [1] described a procedure for converting carboxylic acids, *via* the Δ^2-1,3-thiazoline-2-thiol ester (1), into alcohols or aldehydes through reduction with sodium borohydride or diisobutylaluminium hydride. However, a single-crystal *X*-ray analysis of the *p*-bromobenzoyl intermediate [2] prepared by treatment of the thallium(I) salt of thiazolidine-2-thione with *p*-bromobenzoyl chloride revealed an amide structure (2) instead of the expected Δ^2-1,3-thiazoline-2-thiol ester (1a). Therefore, the structure of the intermediate in this reaction was revised.[3]



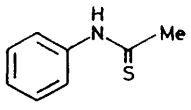
(1) R = C_6H_4Br-*p*



(2) R = Br
(7) R = H



(3)



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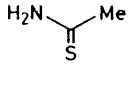

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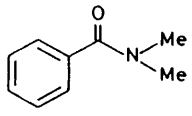


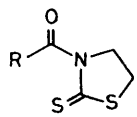
(6)

To further confirm the structural assignments a compound obtained by the reaction of the thallium(I) salt of 1,3-thiazolidine-2-thione with adipic acid dichloride was subjected to a single crystal *X*-ray structural analysis by the Texas authors. The diamide structure (3) was demonstrated unequivocally (see Experimental section).†

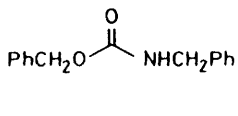
† Sykes *et al.*[4] have discussed methods of distinguishing between S–COR and N–COR structures, but it seemed important to confirm the structural assignments in the above series of compounds.

RESULTS AND DISCUSSION

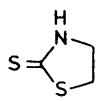
Since the amide structures of compounds (2) and (3) are firmly established, an investigation of the ^{13}C n.m.r. spectra of these and related compounds was undertaken. The thione carbon atoms in compounds (2) and (3) were assigned by comparison with the ^{13}C n.m.r. chemical shifts of the thione groups in compounds (4) and (5),[5] which are found at δ 200.4 and 207.2, respectively. The chemical shifts of the carbonyl carbon atoms were assigned by comparison with the chemical shift of the carbonyl carbon (δ 170.8) in compound (6).[5] Two additional compounds obtained by the treatment of the thallium(I) salt of 1,3-thazolidine-2-thione with benzoyl chloride and hexadecanoyl chloride in tetrahydrofuran were assigned the amide structures (7) and (8) by their ^{13}C chemical shifts. The ^{13}C chemical shifts of the thione and carbamoyloxy carbon atoms in compound (9), prepared from benzyloxycarbonyl chloride, could be assigned with the latter shift based upon comparison with compound (10).[5] The chemical shift of the thione



(8) R = $C_{15}H_{31}$
(9) R = $PhCH_2O$



(10)



(11)

carbon atom in the parent 1,3-thiazolidine-2-thione indicates a thioketo-type structure (11) rather than a thioenol-type formulation. The ^{13}C n.m.r. chemical shifts are given in Table 1.

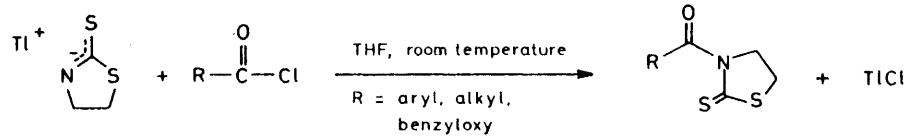
The reaction of the thallium(I) salt of 1,3-thiazolidine-2-thione with acid chlorides can be formulated as indi-

TABLE 1

^{13}C N.m.r. chemical shifts of carbonyl and thione carbon atoms in the 1,3-thiazolidine-2-thione derivatives (δ from $SiMe_4$)

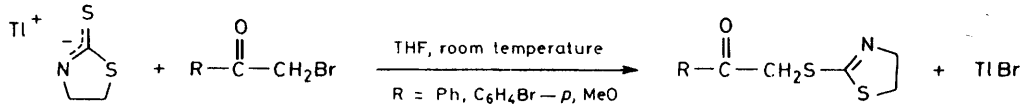
Compound	C=O	C=S	Compound	C=O	C=S
(2)	170.0	201.8	(7)	171.2	201.9
(3)	174.3	201.5	(8)	174.7	201.2
(4)		200.4	(9)	150.6	199.9
(5)		207.2	(10)	156.4	
(6)	170.8		(11)		201.8

cated in Scheme 1. All products of the reaction show a characteristic thione carbon resonance at δ 200 which is consistent with the amide formulation.



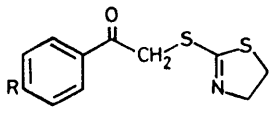
SCHEME 1

The room-temperature reactions between the thallium(I) salt of 1,3-thiazolidine-2-thione and α-bromocarbonyl compounds in tetrahydrofuran were investigated. The ^{13}C n.m.r. spectra of the products exhibited a signal consistent with an imine carbon atom, and a thioether structure formed according to Scheme 2 is indicated.

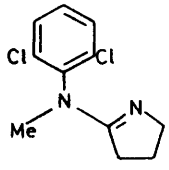


SCHEME 2

The ^{13}C chemical shifts of the imine carbon atoms in compounds (12) and (13) resemble closely those reported for compounds (14) [6] and (15),[7] while the chemical shifts of the carbonyl carbon atoms are analogous to those in



(12) R = H
(13) R = Br



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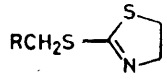
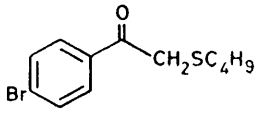


(15) R = Ph
(18) R = CO_2Me

R^1COR^2

(16) R^1 = Ph, R^2 = Me
(19) R^1 = OMe, R^2 = Me
(20) R^1 = Ph, R^2 = SPh



(17)

acetophenone (16) [5] and compound (17). The structure of compound (18) was based upon the comparison of the ^{13}C chemical-shift values of the imine carbon atom with those in compounds (14) and (15), and of the carbonyl carbon atom with that in methyl acetate (19) [5] (see Table 2).

The absence of an imine-carbon resonance [*cf.* (14), δ 166.6; and (15), δ 164.7] and thioester carbonyl resonance [*cf.* (20), δ 189.9] is consistent with the formulation of compounds (7), (8), and (9) as non-thioester structures (1).

The reaction of the thallium(I) salt of 1,3-thiazolidine-2-thione with thiophosgene gave the two major products (21) and (22). The latter, on heating with histamine in tetrahydrofuran for 4 h, afforded the *N*-norderivative (23) of zapotidine,[8] a sulphur-containing alkaloid isolated from the seeds of *Casimiroa edulis*. The ^{13}C n.m.r. spectra were used to assign the structures of these compounds (see Scheme 3 and Table 3).

TABLE 2

^{13}C N.m.r. chemical shift of imine and carbonyl carbon atoms in the Δ^2-1,3-thiazoline-2-thiol derivatives (δ from $SiMe_4$)

Compound	C=N	C=O
(12)	163.8	192.7
(13)	163.8	192.0
(14)	166.6	
(15)	164.3	
(16)		196.9
(17)		192.8
(18)	163.4	168.7
(19)		171.0

TABLE 3

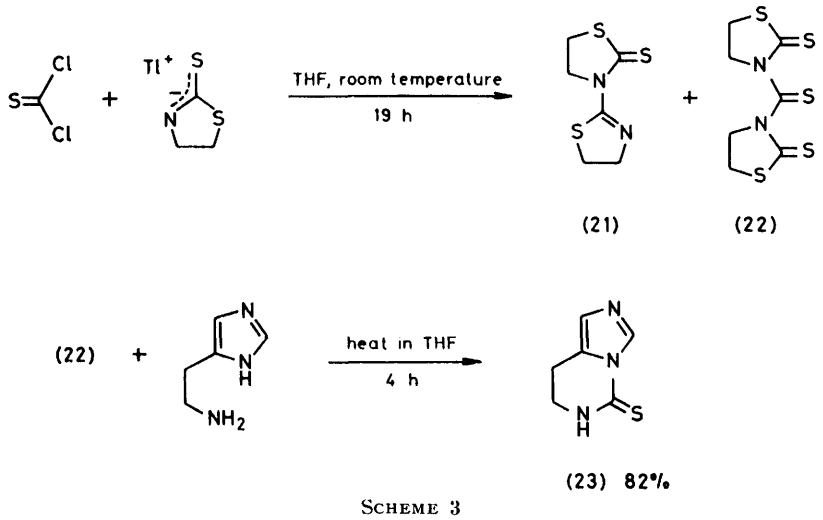
^{13}C N.m.r. chemical shift of imine and thione carbon atoms in compounds (21)—(24) (δ from $SiMe_4$)

Compound	C=N	S–C(:S)–N	N–C(:S)–N
(21)	158.5	198.1	
(22)		198.8	180.8
(23)			173.1
(24) *			180.1

* $PhCH_2NH–C(:S)–NHC_6H_{11}$ (see Experimental section for synthesis).

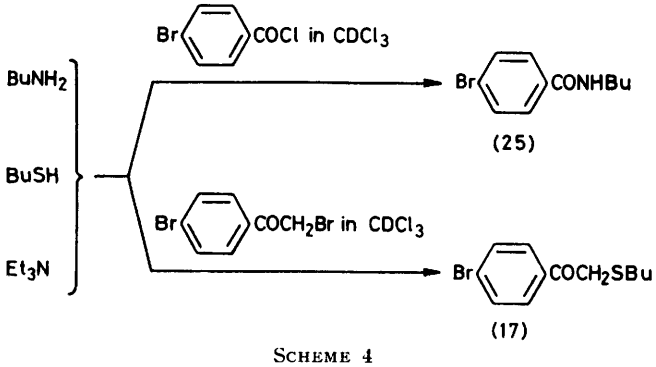
Finally, the regioselective *N*-acylation (Scheme 1) and *S*-alkylation (Scheme 2) with the ambident anion of 1,3-thiazolidine-2-thione can be rationalised in terms of hard and soft acid-base theory. The nitrogen atom in 1,3-thiazolidine-2-thione is classified as a ' hard base ',

while the thione sulphur atom in the same molecule is a ' soft base '. The carbonyl carbon atom in acyl chloride is a ' hard acid ', while the α-carbon atom in the α-bromocarbonyl compound may be regarded as a soft (less



SCHEME 3

hard) acid. Thus the foregoing regioselective reactions can be rationalised by the preferential reaction of hard acids with hard bases and soft acids with soft bases.[9] A solution containing 0.22 mmol each of butylamine (hard



SCHEME 4

base), butanethiol (soft base), and triethylamine in deuteriochloroform was added to a ^{13}C n.m.r. tube containing a 0.2 mmol solution of *p*-bromobenzoyl chloride in the same solvent. The room temperature spectrum, taken after 15 min, indicated the formation of amide (25) only. On the other hand, a similar competitive reaction with *p*-bromophenacyl bromide resulted in the formation of only the thioether (17) (Scheme 4).

The differences between the reactions shown in Schemes 1 and 2 are exemplified by these experiments.

EXPERIMENTAL

Melting points were determined with a Yanagimoto microapparatus. I.r. spectra were measured on a Jasco A-202 spectrophotometer. ^1H N.m.r. and ^{13}C n.m.r. spectra were taken with Varian T-60 and JEOL JM-FX100 instruments in $CDCl_3$, [$^2H_5$]pyridine, and [$^2H_6$]DMSO ($SiMe_4$ as internal standard). Mass spectra were determined on a JEOL JMS-IOSG double-focusing mass spectrometer. Extracts were dried over anhydrous Na_2SO_4. A mixture of Kieselgel 60 (70—230 mesh) (Merck) and silicic acid (Mallinckrodt) (3 : 1) was used for column chromatography.

Synthesis of Amide (3).—The thallium(I) salt of thiazolidine-2-thione (2.838 g, 2.2 mol equiv.) was added to a solution of adipic acid dichloride (732 mg) in THF (10 ml). The mixture was stirred at room temperature for 24 h. The solid material (TlCl) was filtered off and washed with CH_2Cl_2. After addition of water, the filtrate was extracted with CH_2Cl_2. The CH_2Cl_2 extract was washed with brine, dried, and concentrated *in vacuo* to leave a yellow residue, which was purified on a silica gel column to give amide (3) (1.175 g, 84%) as yellow prisms (from $CHCl_3$), m.p. 127—128 °C; $\nu_{max.}$ (KBr) 1 695 (C=O) cm^{-1}, δ_H ($CDCl_3$) 1.65—1.85 (4 H, m, $CH_2 \times 2$), 3.10—3.4 (4 H, m, $COCH_2 \times 2$), 3.30 (4 H, t, *J* 7.5 Hz, $SCH_2 \times 2$), and 4.39 (4 H, t, *J* 7.5 Hz, $NCH_2 \times 2$); δ_C ($CDCl_3$) 24.1 (t), 28.4 (t), 38.1 (t), 56.1 (t), 174.3 (s), and 201.5 (s) (Found: C, 41.3; H, 4.6; N, 7.85%; M^+, 348. $C_{12}H_{16}N_2O_2S_4$ requires C, 41.4; H, 4.65; N, 8.05%; *M*, 348).

X-*Ray Analysis of Amide* (3).—A crystal of dimensions 0.25 × 0.25 × 0.35 mm was mounted on a Syntex $P2_1$ diffractometer. Room-temperature lattice parameters were refined by a least-squares technique utilising 15 reflexions whose angles were measured by a centring routine associated with the Syntex diffractometer. Systematic absences were consistent with space group $P2_12_12_1$.

Crystal data. $C_{12}H_{16}S_4N_2O_2$, $M = 348.5$, $a = 11.903(2)$, $b = 16.171(4)$, $c = 8.072(2)$ Å, $U = 1\,553.7(7)$ Å^3, $D_m = 1.490$ g cm^{-3}, $Z = 4$, $D_c = 1.486$ g cm^{-3}, $F(000) = 728$. Space group $P2_12_12_1$ (D_2^4, No. 19).

Intensity data were collected by the θ—2θ scanning technique using a variable scan speed with Mo-K_α radiation ($\lambda = 0.710\,69$ Å) and a graphite monochromator. 1 829 independent reflexions were measured and 1 616 had $I > 3\sigma(I)$. Lorentz and polarisation corrections were applied, but no absorption corrections were made. A reference reflexion was monitored, but no significant crystal deterioration was observed. The direct-methods program MULTAN [10] was used to calculate phases for the 200 $|E|$-values greater than 1.5. The phase set with the largest combined figure-of-merit was selected, and the *E*-map calculated with these phases revealed the positions of

a 13-atom fragment. Alternate least-squares and Fourier calculations yielded the co-ordinates of the missing 7 heavy atoms and the 16 hydrogen atoms. Least-squares refinement yielded a final R of 0.060 (R' 0.071) for 1 616

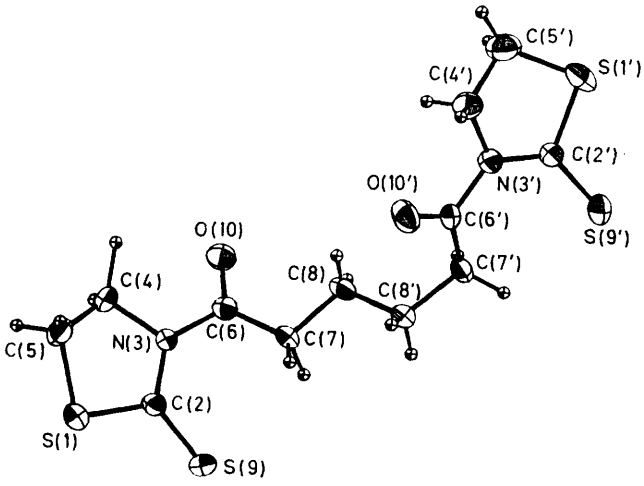


FIGURE ORTEP drawing of amide (3) (thermal ellipsoids are drawn at 35% probability level. Hydrogen thermal parameters are represented by spheres of arbitrary size)

reflexions where $R = \Sigma||F_o| - |F_c||/\Sigma|F_o|$. The function minimised in the refinement was $\Sigma\omega(|F_o| - |F_c|)^2$ where $\omega = [1/\sigma\ (F_o)]^2$ was determined from counting statistics. Hydrogen atom thermal parameters were refined isotropically.

TABLE 4

Atomic coordinates ($\times 10^4$, H $\times 10^3$)

Atom	x/a	y/b	z/c
S(1)	14 074(1)	−2 252(1)	5 518(2)
C(2)	12 749(4)	−1 971(3)	6 188(6)
N(3)	12 685(4)	−1 119(3)	6 403(6)
C(4)	13 798(5)	−0 702(3)	6 405(9)
C(5)	14 532(5)	−1 192(4)	5 255(8)
C(6)	11 737(5)	−0 634(3)	6 828(7)
C(7)	10 591(5)	−0 909(3)	6 276(8)
C(8)	9 750(5)	−0 201(3)	6 280(8)
S(9)	11 776(1)	−2 669(1)	6 572(2)
O(10)	11 920(4)	0 017(3)	7 523(8)
S(1′)	6 089(2)	2 867(1)	4 527(2)
C(2′)	6 428(5)	1 831(3)	4 876(7)
N(3′)	7 474(4)	1 659(3)	4 283(6)
C(4′)	7 990(6)	2 329(4)	3 282(7)
C(5′)	7 491(7)	3 131(4)	3 924(11)
C(6′)	8 049(4)	0 893(3)	4 264(6)
C(7′)	7 744(4)	0 225(3)	5 485(8)
C(8′)	8 638(4)	−0 461(3)	5 546(8)
S(9′)	5 488(1)	1 218(1)	5 754(2)
O(10′)	8 824(4)	0 824(3)	3 284(6)
H(4a)	1 376(9)	004(7)	614(12)
H(4b)	1 401(7)	−072(5)	745(10)
H(5a)	1 456(6)	−105(5)	404(9)
H(5b)	1 530(7)	−117(5)	541(9)
H(7a)	1 023(9)	−135(7)	700(13)
H(7b)	1 050(6)	−122(5)	515(9)
H(8a)	992(7)	022(6)	538(11)
H(8b)	970(8)	−007(6)	745(11)
H(4a′)	808(9)	218(6)	202(12)
H(4b′)	870(8)	231(4)	340(8)
H(5a′)	794(11)	355(8)	301(16)
H(5b′)	776(9)	319(7)	488(14)
H(7a′)	785(9)	041(7)	660(14)
H(7b′)	697(6)	000(5)	515(9)
H(8a′)	843(7)	−093(5)	625(10)
H(8b′)	882(10)	−059(8)	439(14)

TABLE 5

Bond distances (Å) and valence angles (°)

S(1)–C(2)	1.728(5)	S(1′)–C(2′)	1.746(5)
S(1)–C(5)	1.812(7)	S(1′)–C(5′)	1.790(9)
C(2)–N(3)	1.390(7)	C(2′)–N(3′)	1.363(7)
C(2)–S(9)	1.646(5)	C(2′)–S(9′)	1.644(6)
N(3)–C(4)	1.487(7)	N(3′)–C(4′)	1.485(8)
N(3)–C(6)	1.417(7)	N(3′)–C(6′)	1.415(7)
C(4)–C(5)	1.501(9)	C(4′)–C(5′)	1.518(9)
C(6)–O(10)	1.213(8)	C(6′)–O(10′)	1.220(7)
C(6)–C(7)	1.502(8)	C(6′)–C(7′)	1.508(8)
C(7)–C(7)	1.521(8)	C(7′)–C(8′)	1.538(8)
C(8)–C(8′)	1.511(8)		
S(1)–C(2)–N(3)	110.5(3)	S(1′)–C(2′)–N(3′)	110.5(4)
S(1)–C(2)–S(9)	121.3(3)	S(1′)–C(2′)–S(9′)	119.2(3)
N(3)–C(2)–S(9)	128.1(4)	N(3′)–C(2′)–S(9′)	130.2(4)
C(2)–N(3)–C(4)	113.6(4)	C(2′)–N(3′)–C(4′)	114.9(5)
C(2)–N(3)–C(6)	128.1(4)	C(2′)–N(3′)–C(6′)	128.7(4)
C(4)–N(3)–C(6)	117.3(4)	C(4′)–N(3′)–C(6′)	115.6(4)
N(3)–C(4)–C(5)	106.2(5)	N(3′)–C(4′)–C(5′)	106.0(5)
C(4)–C(5)–S(1)	104.6(4)	C(4′)–C(5′)–S(1′)	104.7(5)
C(5)–S(1)–C(2)	93.6(3)	C(5′)–S(1′)–C(2′)	93.3(3)
N(3)–C(6)–O(10)	116.7(5)	N(3′)–C(6′)–O(10′)	117.0(5)
N(3)–C(6)–C(7)	119.2(5)	N(3′)–C(6′)–C(7′)	120.3(4)
C(7)–C(6)–O(10)	123.9(5)	C(7′)–C(6′)–O(10′)	122.7(5)
C(6)–C(7)–C(8)	112.0(5)	C(6′)–C(7′)–C(8′)	111.8(4)
C(7)–C(8)–C(8′)	111.5(5)	C(7′)–C(8′)–C(8)	114.7(5)

TABLE 6

Torsion angles (°)

S(1)–C(2)–N(3)–C(4)	−13.7(6)
C(2)–N(3)–C(4)–C(5)	32.3(7)
N(3)–C(4)–C(5)–S(1)	−34.3(5)
C(4)–C(5)–S(1)–C(2)	24.4(4)
C(5)–S(1)–C(2)–N(3)	−6.9(4)
S(9)–C(2)–N(3)–C(6)	−7.6(8)
C(5)–C(4)–N(3)–C(6)	−155.7(5)
C(2)–N(3)–C(6)–O(10)	154.0(6)
C(2)–N(3)–C(6)–C(7)	−31.3(8)
C(4)–N(3)–C(6)–O(10)	−16.6(8)
C(4)–N(3)–C(6)–C(7)	158.2(5)
N(3)–C(6)–C(7)–C(8)	−159.7(5)
O(10)–C(6)–C(7)–C(8)	14.7(9)
C(6)–C(7)–C(8)–C(8′)	173.7(5)
C(7)–C(8)–C(8′)–C(7)	−179.3(5)
S(1′)–C(2′)–N(3′)–C(4′)	−8.9(6)
C(2′)–N(3′)–C(4′)–C(5′)	28.3(7)
N(3′)–C(4′)–C(5′)–S(1′)	−33.2(6)
C(4′)–C(5′)–S(1′)–C(2′)	25.7(5)
C(5′)–S(1′)–C(2′)–N(3′)	−10.7(5)
S(9′)–C(2′)–N(3′)–C(6′)	−0.1(7)
C(5′)–C(4′)–N(3′)–C(6′)	−161.5(5)
C(2′)–N(3′)–C(6′)–O(10′)	159.9(5)
C(2′)–N(3′)–C(6′)–C(7′)	−23.6(8)
C(4′)–N(3′)–C(6′)–O(10′)	−8.7(7)
C(4′)–N(3′)–C(6′)–C(7′)	167.7(5)
N(3′)–C(6′)–C(7′)–C(8′)	−166.1(5)
O(10′)–C(6′)–C(7′)–C(8′)	10.1(8)
C(6′)–C(7′)–C(8′)–C(8)	68.5(6)

A final difference map showed no peak larger than 0.3 e Å^{-3}, except for peaks of *ca.* 0.5 e Å^{-3} near the S atoms. All shifts during the final cycle of refinement were $<0.5\sigma$. Atomic scattering factors and anomalous dispersion corrections were taken from ref. 11. Atomic positional parameters are given in Table 4 while bond distances, valence angles, and torsion angles are given in Tables 5 and 6.*

3-*Benzyloxycarbonyl*-1,3-*thiazolidine*-2-*thione* (9).—This was synthesised in 84% yield by the same procedure as above, yellow prisms from THF–acetone–EtOH, m.p. 80—80.5 °C; $\nu_{max.}$ (KBr) 1 750 (C=O) cm^{-1}; δ_H ($CDCl_3$)

* Thermal parameters and structure factors have been deposited as Supplementary Publication No. SUP 23012 (14 pp.). For details see Notice to Authors No. 7, *J. Chem. Soc., Perkin Trans. 1*, 1979, Index issue.

3.28 (2 H, t, J 7.5 Hz, SCH_2), 4.53 (2 H, t, J 7.5 Hz, NCH_2), 5.30 (2 H, s, CH_2O), and 7.20—7.50 (5 H, m, aromatic); δ_C ($CDCl_3$) 28.2 (t), 55.6 (t), 68.9 (t), 128.3 (d), 128.4 (d), 134.5 (s), 150.6 (s), and 199.9 (s) (Found: C, 52.1; H, 4.35; N, 5.65%; M^+, 253. $C_{11}H_{11}NO_2S_2$ requires C, 52.15; H, 4.4; N, 5.55%; M, 253).

Typical Preparation of Δ^2-1,3-*Thiazolin*-2-*yl Thioethers*.—The thallium(I) salt of 1,3-thiazolidine-2-thione (418 mg, 1.2 mol equiv.) was added to a solution of *p*-bromophenacyl bromide (300 mg) in THF (20 ml)–HMPA (0.3 ml). The mixture was stirred at room temperature for 24 h. The solid material (TlBr) was filtered off and washed with CH_2Cl_2. After addition of water, the filtrate was extracted with CH_2Cl_2. The CH_2Cl_2 extract was washed with brine, dried, and evaporated *in vacuo* to leave an oily residue, which was chromatographed on silica gel to afford the thioether (13) (310 mg).

Physical Data of Δ^2-1,3-*Thiazolin*-2-*yl Thioethers*.[7]—Thioether (12): yield 85%, pale yellow prisms from n-hexane, m.p. 56—57.5 °C; $\nu_{max.}$ (KBr) 1 690 (C=O) and 1 580 cm^{-1} (C=N); δ_H ($CDCl_3$) 3.35 (2 H, dt, J 7.8 and 0.7 Hz, $-SCH_2-CH_2N=$), 4.11 (2 H, dt, J 7.8 and 0.7 Hz, $=NCH_2-CH_2S-$), 4.65 (2 H, s, $COCH_2S$), 7.31—7.68 (3 H, m, aromatic), and 7.89—8.05 (2 H, m, aromatic); δ_C ($CDCl_3$) 36.0 (t), 40.2 (t), 63.9 (t), 128.3 (d), 128.6 (d), 133.5 (d), 135.3 (s), 163.8 (s), and 192.7 (s) (Found: C, 55.5; H, 4.55; N, 5.85%; M^+, 237. $C_{11}H_{11}NOS_2$ requires C, 55.65; H, 4.65; N, 5.9%; M, 237). Thioether (13): yield 91%, pale yellow needles from $CHCl_3$, m.p. 104—105 °C, $\nu_{max.}$ (KBr) 1 700 (C=O), 1 580, and 1 570 cm^{-1}; δ_H ($CDCl_3$) 3.41 (2 H, t, J 8 Hz, $-SCH_2-CH_2N=$), 4.17 (2 H, t, J 8 Hz, $=NCH_2-CH_2S-$), 4.62 (2 H, s, $COCH_2S$), and 7.60 and 7.85 (each 2 H, AB quartet, J 9 Hz, aromatic); δ_C ($CDCl_3$) 36.2 (t), 39.9 (t), 63.9 (t), 128.8 (d), 129.9 (d), 131.9 (d), 134.2 (s), 163.8 (s), and 192.0 (s) (Found: M^+, 315 and $M^+ + 2$, 317. $C_{11}H_{10}BrNOS_2$ requires M, 315 and $M + 2$, 317). Thioether (18): yield 63%, pale yellow oil; $\nu_{max.}$ ($CHCl_3$) 1 740 (C=O) and 1 515 (C=N) cm^{-1}, δ_H ($CDCl_3$) 3.44 (2 H, dt, J 7.8 and 0.7 Hz, $-SCH_2-CH_2N=$), 3.52 (3 H, s, OMe), 3.73 (2 H, s, $COCH_2S$), and 4.17 (2 H, dt, J 7.8 and 0.7 Hz, $=NCH_2-CH_2S-$); δ_C ($CDCl_3$) 34.2 (t), 36.2 (t), 52.6 (q), 64.0 (t), 163.4 (s), and 168.7 (s) (Found: M^+, 191.008. $C_6H_9NO_2S_2$ requires M, 191.007).

2-*Benzylthio*-Δ^2-1,3-*thiazoline* (15).—This compound was prepared by a literature procedure;[7] colourless prisms from n-hexane, m.p. 48 °C; $\nu_{max.}$ ($CHCl_3$) 1 560 cm^{-1}; δ_H ($CDCl_3$) 3.27 (2 H, dt, J 8 and 0.7 Hz, $-SCH_2CH_2N=$), 4.07 (2 H, dt, J 8 and 0.7 Hz, $=NCH_2CH_2S-$), 4.32 (2 H, s, CH_2S), and 7.14—7.39 (5 H, m, aromatic); δ_C ($CDCl_3$) 35.5 (t), 36.9 (t), 64.1 (t), 127.0 (d), 128.1 (d), 128.6 (d), 136.6 (s), and 164.3 (s) (Found: M^+, 209. $C_{10}H_{11}NS_2$ requires M, 209).

Benzyl N-*Benzylcarbamate* (10).[12]—Benzylamine (140 mg, 1.1 mol equiv.) was added to a yellow solution of 3-benzyloxycarbonyl-1,3-thiazolidine-2-thione (9) (286 mg) in $CHCl_3$ (7 ml). The mixture was stirred at room temperature for 4 days and condensed *in vacuo* to give an oily residue, which was chromatographed on a column prepared from silica gel impregnated with 10% $AgNO_3$ to afford amide (10) (249 mg, 87%) as colourless plates from MeOH–n-hexane, m.p. 61—62 °C; $\nu_{max.}$ (KBr) 3 330 (NH), 1 690 (C=O), and 1 550 (CO–NH) cm^{-1}; δ_H ($CDCl_3$) 4.37 (2 H, d, J 6 Hz, $CONHCH_2$), 5.14 (2 H, s, OCH_2), 7.33 (5 H, s, aromatic), and 7.37 (5 H, s, aromatic); δ_C ($CDCl_3$) 45.0 (t), 66.6 (t), 127.2 (d), 127.9 (d), 128.3 (d), 128.5 (d), 136.4 (s), 138.5 (s), and 156.4 (s) (Found: C, 74.5; H, 6.15; N, 5.5%; M^+, 241. $C_{15}H_{15}NO_2$ requires C, 74.65; H, 6.25; N, 5.8%; M, 241).

2-(2-*Thioxo*-1,3-*thiazolidin*-3-*yl*)-Δ^2-1,3-*thiazoline* (21) *and Bis*-(2-*thioxo*-1,3-*thiazolidin*-3-*yl*) *Thioketone* (22).—A solution of thiophosgene (0.633 ml) in anhydrous THF (10 ml) was added at 0 °C to a suspension of the thallium(I) salt of 1,3-thiazolidine-2-thione (6.17 g, 2.2 mol. equiv.) in THF (40 ml) with stirring in N_2. After 30 min at 0 °C, the mixture was further stirred at room temperature for 19 h. The solid material (TlCl) was filtered off and the filtrate was condensed *in vacuo* to give an oily residue, which was chromatographed on a silica gel column with CH_2Cl_2. The first eluate gave compound (22) (340 mg) as deep red needles from CH_2Cl_2, m.p. 156—157 °C; δ_H ($CDCl_3$) 3.40 (4 H, t, J 8 Hz, $SCH_2-CH_2N \times 2$), and 4.68 (4 H, t, J 8, Hz $NCH_2-CH_2S \times 2$); δ_C ([$^2H_5$]pyridine) 29.1 (t), 61.6 (t), 180.8 (s), and 198.8 (s) (Found: C, 30.2; H, 2.9; N, 10.65%; M^+, 280. $C_7H_8N_2O_5$ requires C, 30.0; H, 2.9; N, 10.0%; M, 280). The second eluate gave compound (21) (168 mg) as pale yellow needles from acetone, m.p. 76—78° (lit.,[4] 78—80 °C); $\nu_{max.}$ (KBr) 1 582 (C=N) cm^{-1}; δ_H ($CDCl_3$) 3.30 (2 H, dt, J 8.5 and 1.5 Hz), 3.38 (2 H, t, J 8 Hz), 3.98 (2 H, dt, J 8.5 and 1.5 Hz), 4.64 (2 H, t, J 8 Hz), 3.98 (2 H, dt, J 8.5 and 1.5 Hz), and 4.64 (2 H, t, J 8 Hz); δ_C ($CDCl_3$) 28.7 (t), 36.2 (t), 56.8 (t), 58.7 (t), 158.5 (s), and 198.1 (s) (Found: C, 35.35; H, 3.95; N, 13.7%; M^+, 203.984. $C_6H_8N_2S_3$ requires C, 35.30; H, 3.95; N, 13.72; M, 203.985).

Demethylzapotidine Derivative (23).—Histamine (168 mg, 1.1 mol. equiv.) was added to a solution of compound (22) (385 mg) in THF (30 ml). The mixture was refluxed for 4 h in N_2 and the solvent was evaporated *in vacuo* to give an oily residue, which was chromatographed on a silica gel column with $CHCl_3$ to yield the demethylzapotidine derivative (23) (172 mg, 81.8%) as colourless plates from $CHCl_3$–MeOH, m.p. 235—236 °C; $\nu_{max.}$ (KBr) 3 150, 3 050, 1 600, and 1 570 cm^{-1}, δ_H ([$^2H_6$]DMSO) 2.96 (2 H, t, J 6 Hz, $=CCH_2CH_2-$), 3.2—3.5 (2 H, m, $-NHCH_2CH_2-$), 6.83 (1 H, d, J 1.5 Hz, $>C=CHN=$), and 8.31 (1 H, d, J 1.5 Hz, $>NCH=N-$); δ_C ([$^2H_6$]DMSO) 18.3 (t), 39.6 (t), 124.3 (s), 125.0 (d), 136.3 (d), and 173.1 (s) (Found: C, 47.0; H, 4.55; N, 27.4%; M^+, 153. $C_6H_7N_3S$ requires C, 47.05; H, 4.6; N, 27.45%; M, 153).

4-*Bromobenzoylmethyl Butyl Sulphide* (17).—Butanethiol (0.11 ml, 1 mol equiv.) and Et_3N (0.14 ml, 1 mol equiv.) were added to a solution of *p*-bromophenacyl bromide (280 mg) in $CHCl_3$ (20 ml). The mixture was stirred at room temperature for 1 h. Evaporation of the solvent *in vacuo* gave an oily residue, which was chromatographed on silica gel to afford the thioether (17) (280 mg, 98%) as colourless needles from MeOH, m.p. 27—27.5 °C; $\nu_{max.}$ (KBr) 1 675 (C=O) cm^{-1}; δ_H ($CDCl_3$) 0.88 (3 H, t, J 7 Hz, $MeCH_2$), 1.10—1.70 (4 H, m), 2.54 (2 H, t, J 7 Hz, SCH_2CH_2), 3.73 (2 H, s, SCH_2CO), and 7.58, 7.83 (each 2 H, AB type, J 8.5 Hz, aromatic); δ_C ($CDCl_3$) 13.5 (q), 21.7 (t), 30.8 (t), 31.9 (t), 36.9 (t), 128.0 (s), 129.9 (d), 131.5 (d), 133.6 (s), and 192.8 (s) (Found: C, 50.2; H, 5.3%; M^+, 286 and $M^+ + 2$, 288. $C_{12}H_{15}BrOS$ requires C, 50.2; H, 5.25%; M, 286 and $M^+ + 2$, 288).

N-*Benzyl*-N′-*cyclohexylthiourea* (24).—A solution of benzylamine (107 mg, 1 mol equiv.) in dry CH_2Cl_2 (10 ml) was added to a solution of cyclohexyl isothiocyanate (141 mg) in dry CH_2Cl_2 (10 ml). The mixture was stirred at room temperature for 3 h and evaporated *in vacuo* to give an

oily residue, which was purified on a silica gel column to yield a colourless oil (239 mg, 96%); $\nu_{max.}$ ($CHCl_3$) 3 450 (NH), 3 230 (NH), and 1 551 cm^{-1}; δ_H ($CDCl_3$) 0.9—2.0 (11 H, m), 4.59 (2 H, d, J 6 Hz, CH_2NH), and 7.28 (5 H, s, aromatic) (Found: M^+, 248. $C_{14}H_{20}N_2S$ requires M, 248).

N-*Butyl*-4-*bromobenzamide* (25).—Butylamine (0.1 ml, 1 mol equiv.) and Et_3N (0.14 ml, 1 mol equiv.) were added to a solution of *p*-bromobenzoyl chloride (220 mg). The mixture was stirred at room temperature for 1 h and treated as usual to afford the amide (25) (250 mg, 98%) as colourless plates from Et_2O–n-hexane, m.p. 88.5—89 °C; $\nu_{max.}$ (KBr) 3 340 (NH), 1 625 (CONH), and 1 545 (CONH) cm^{-1}; δ_H ($CDCl_3$) 0.91 (3 H, t, J 6 Hz, CH_2Me), 1.10—1.70 (4 H, m), 3.42 (2 H, q-like, J 6 Hz, $NHCH_2CH_2$), 6.98 (1 H, br s, NH), and 7.48, 7.63 (each 2 H, AB type, J 8.5 Hz aromatic); δ_C ($CDCl_3$) 13.7 (q), 20.1 (t), 31.5 (t), 39.8 (t), 125.5 (s), 128.3 (d), 131.2 (d), 133.4 (s), and 166.4 (s) (Found: C, 51.5; H, 5.55; N, 5.15%; M^+, 255 and $M^+ + 2$, 257. $C_{11}H_{14}BrNO$ requires C, 51.6; H, 5.5; N, 5.45%; M, 255 and $M^+ + 2$, 257).

Competitive Reaction with p-*Bromobenzoyl Chloride*.—A dry n.m.r. tube was charged with a solution of *p*-bromobenzoyl chloride (44 mg, 0.2 mmol) in $CDCl_3$ (0.2 ml). ' Reagent solution ' [a mixture of buthanethiol (0.11 ml), butylamine (0.1 ml), triethylamine (0.14 ml), and $CDCl_3$ (0.65 ml)] (0.22 ml, each 0.22 mmol) was added *via* syringe. After 15 min at room temperature, a ^{13}C n.m.r. spectrum was taken at 28 °C. Its comparison with ^{13}C n.m.r. spectrum of the authentic sample (25) led to a conclusion that the product was only the amide (25).

Competitive Reaction with p-*Bromophenacyl Bromide*.—The reaction of a solution of *p*-bromophenacyl bromide (28 mg, 0.1 mmol) in $CDCl_3$ (0.2 ml) with 0.11 ml (0.11 mmol) of the ' Reagent solution ' was allowed to take place at room temperature for 15 min in an n.m.r. tube, and its ^{13}C n.m.r. spectrum was checked as in the above experiment; it was proved that thioether (17) was a sole product.

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