Kinetics of Intramolecular Alkyl Radical Attack on Sulfur in Disulfides and Thioesters

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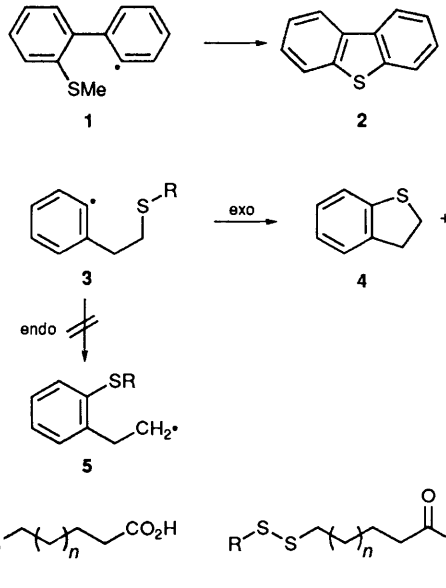
The 4-(alkyldithio)butyl radicals **8a** and **c**, and the 4-(phenyldithio)butyl radical **8b**, generated from the corresponding esters of *N*-hydroxypyridine-2(1*H*)-thione, undergo fast exo-cyclisation by S_Hi attack at sulfur. Similarly, the 5-(alkyldithio)pentyl radical **8d** undergoes 1,6-ring formation. The rate constants for cyclisation were determined by photolysis of the radical precursors in the presence of appropriate thiols. Butyl and pentyl radicals bearing ω-acetylthio or ω-benzoylthio substituents also undergo ring closure but much more slowly. The kinetics of these intramolecular S_H2 reactions are discussed and compared with those for the intermolecular attack of hexyl radicals on diphenyl disulfide and on dibutyl disulfide.

Although ring formation by intramolecular homolytic substitution at a hetero atom is of synthetic utility[1-4] and may have biological significance,[5,6] this type of process has received much less attention than have cyclisations involving intramolecular radical addition to multiple bonds.[7] Recent reports include investigations of the attack of carbon-centred radicals on sulfur in sulfides,[1,2,8-15] disulfides,[6,15,16] sulfoxides,[13,17] thioesters,[13,18-20] sulfinyl esters[21] and *S*-sulfonates,[22] on selenium in selenides,[3,4,15,23] and on oxygen in peroxides[24] and sulfonates.[22] Intramolecular displacements of carbon-centred radicals by attack of iminyl radicals on sulfides and selenides have also been described.[25]

In the first reported study of intramolecular radical substitution at sulfur, Kampmeier found that the radical **1**, derived from the corresponding iodide, gave only dibenzothiophene **2** by substitution in the exo mode,[26] and the same behaviour was observed later for radicals of the general type **3**.[17,27,28] No products derived from the radical **5** generated by endo substitution could be detected. Exclusive exo substitution was also observed for intramolecular attack of alkyl radicals on sulfide sulfur,[12] and in a variety of cases where the endo mode would be expected to be the more exothermic possible pathway.[2]



1 2 3 4 5

6a R = Bu^t, n = 1
b R = Ph, n = 1
c R = Bu, n = 1
d R = Bu^t, n = 2

7a R = Bu^t, n = 1
b R = Ph, n = 1
c R = Bu, n = 1
d R = Bu^t, n = 2

This specificity, together with the observations that the rate of reaction depends on the stability of the radical displaced,[12,15] and that cyclisation by substitution at sulfur in an optically active sulfoxide proceeds with strict inversion of stereochemistry[17] underlies the hypothesis that the reaction proceeds *via* backside attack through a transition structure in which the attacking radical, the sulfur atom, and the leaving group assume an approximately collinear arrangement.[17,27] Such a transition structure cannot be accommodated on the pathway for endo substitution.

Although the possibility that radical displacements at divalent sulfur might involve the intermediacy of short-lived hypervalent sulfuranyl radicals has been discussed,[29] theoretical treatments do not support this view.[29-31] They indicate, in agreement with the experimental evidence, that the reaction proceeds through a T-shaped transition structure. For radical attack on the sulfur of a sulfoxide, calculations located a tetravalent intermediate radical, but the energy well in which it lies is so shallow that it is predicted 'to behave much more like a transition structure than an intermediate'.[31]

Rate constants for intramolecular attack of aryl radicals on sulfide sulfur typically have values of the order of 10^7 s^{-1} at ordinary temperatures.[28] Although other processes sometimes compete with ring closure,[8] the rates of ring closure are usually sufficiently high to afford cyclised products in yields acceptable for synthetic purposes.[2] This is not the case, however, for the corresponding reaction of alkyl radicals where the rate constants are so low (typically $< 10^3$ s^{-1} at 50 °C)[12] that intermolecular reactions intervene under ordinary conditions. In order to define the conditions necessary for cyclisation of alkyl radicals by attack on divalent sulfur we have now examined the kinetics of such reactions for radicals containing suitably disposed disulfide or thioester groups. Also, for comparison the rates of intermolecular attack of hexyl radicals on two representative symmetrical disulfides have been determined.

Results

In our previous studies of intramolecular aryl radical attack on sulfur the radicals were generated by treatment of a halide with tributylstannane.[2,8,10,17] This method was precluded from the

Table 1 Relative yields of products and relative rate constants for reactions of dithio-substituted radicals with thiols in benzene at 50 °C

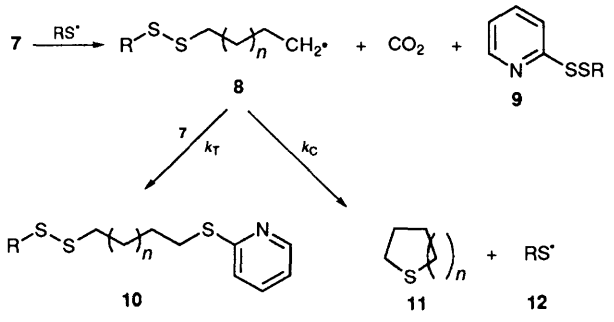
Precursor	Radical	Thiol	$[RSH]_i$[a]/mol dm^{-3}	$[RSH]_f$[b]/mol dm^{-3}	Product[c] Cy	Product[c] UH	$[Cy]_f/[UH]_f$[d]	k_c/k_H
7a	**8a**	Bu^{t}SH	0.54	0.48	**11a**	**13a**	2.32	1.2
			0.41	0.37			3.30	1.3
			0.18	0.16			16.8	2.8
7b	**8b**	PhSH	0.83	0.74	**11a**	**13b**	2.36	1.8
			0.72	0.65			2.63	1.8
			0.60	0.54			3.38	1.9
			0.49	0.44			4.65	1.9
			0.40	0.37			5.33	2.2
			0.29	0.26			6.21	1.8
7d	**8d**	Bu^{t}SH	0.49	0.44	**11d**	**13d**	0.12	0.056
			0.31	0.28			0.18	0.051
			0.19	0.17			0.30	0.053
			0.27	0.25			0.25	0.064
			0.21	0.19			0.34	0.064
			0.16	0.15			0.44	0.068

[a] Initial concentration of thiol. [b] Final concentration of thiol. [c] Cy and UH represent the cyclised and uncyclised products respectively. [d] Relative final concentrations of products.

present work because of the possible incursion of ionic mechanisms and because of the propensity of tributyltin radicals to attack the disulfide or thioester groups. Accordingly, we used carboxylate esters of *N*-hydroxypyridine-2(1*H*)-thione (Barton esters)[32] as radical precursors since it has been established that they generate alkyl radicals in a chain reaction that can be propagated by either alkylthio radicals or alkyl radicals. Furthermore, the rate constants for the chain propagating reactions of various types of alkyl radicals have been determined.[33]

The unsymmetrical disulfides **6a** and **d** were prepared by heating an excess of di-*tert*-butyl disulfide with the appropriate symmetrical disulfide diacid at 100 °C in the presence of a catalytic amount of iodine.[34] Diphenyl disulfide was similarly used for the preparation of **6b**. After a number of other methods had been found to be unsuccessful, the unsymmetrical disulfide **6c** was prepared by treatment of 5-mercaptopentanoic acid with butanethiol in the presence of diethyl azodicarboxylate.[35] In the course of this work it was found that the unsymmetrical disulfides **6a–d** rapidly undergo disproportionation to mixtures of symmetrical disulfides in the presence of base.[36] Hence it was necessary to use silica gel which had been previously washed with buffer at pH 7.6 for the chromatographic purification of **6a–d**. The Barton esters **7a–d** were readily prepared in the usual way *via* the acid chlorides.[37]

The reactions expected to ensue upon homolytic decomposition of the Barton esters **7a–d** are shown in Scheme 1. However,

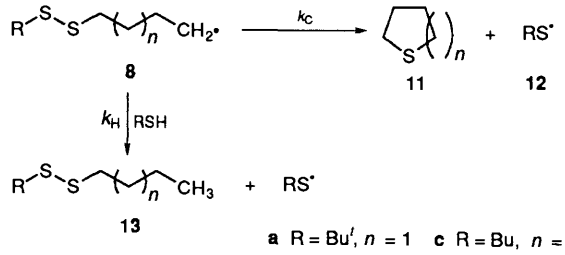


a R = Bu^t, *n* = 1 **c** R = Bu, *n* = 1
b R = Ph, *n* = 1 **d** R = Bu^t, *n* = 2

Scheme 1

heating of a dilute solution (0.2 mol dm^{-3}) of **7a** in benzene gave only tetrahydrothiophene **11a** and *tert*-butyl 2-pyridyl disulfide **9a**. This outcome demonstrated that the addition of an alkyl radical to an hydroxamate is not suitable for use as a radical clock in this system. Since the rate constant for hydrogen atom transfer to an alkyl radical from *tert*-butyl mercaptan (k_H = 1 × 10^7 dm^3 mol^{-1} s^{-1} at 50 °C)[33,38] is greater than that for alkyl radical addition to a Barton ester (k_T = 1.4 × 10^6 dm^3 mol^{-1} s^{-1} at 50 °C)[33,39] we expected that heating of **7a** in the presence of an excess of *tert*-butyl mercaptan would afford the disulfide **13a** as well as the cyclised product **11a**. In the event UV irradiation of a solution of **7a** with 10 molar equivalents of the thiol (0.2 mol dm^{-3}) in degassed benzene gave almost quantitatively a mixture of the cyclised product **11a**, the product of hydrogen atom transfer **13a**, and the pyridyl disulfide **9a**. Traces of di-*tert*-butyl disulfide and dibutyl disulfide were also detected; presumably they arose by disproportionation of **13a**.

The results of a series of experiments conducted under carefully controlled conditions with accurate determination of the yields of products by GC are presented in Table 1. The data are consistent with the reactions of Scheme 2 in which



a R = Bu^t, *n* = 1 **c** R = Bu, *n* = 1
b R = Ph, *n* = 1 **d** R = Bu^t, *n* = 2

Scheme 2

cyclisation of radical **8a** in a unimolecular process with rate constant k_c competes with bimolecular hydrogen-atom transfer from the thiol to **8a** with rate constant k_H. The usual kinetic analysis of Scheme 2 gives the integrated rate eqn. (1) where $[Cy]_f$ is the final concentration of the cyclised product **11**, and $[RSH]_i$ and $[RSH]_f$ are the initial and final concentrations of thiol respectively.

$$[Cy]_f = k_c/k_H \ln \{([RSH]_i + k_c/k_H)/([RSH]_f + k_c/k_H)\} \quad (1)$$

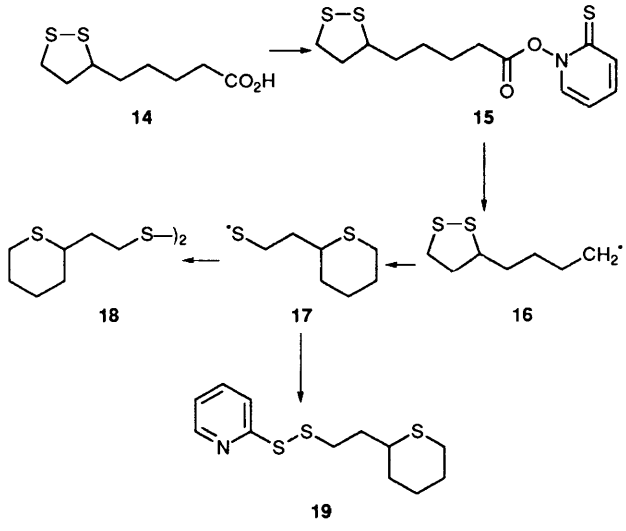
Table 2 Rate constants for inter- and intra-molecular S_H2 reactions at sulfur in benzene

Reaction	T/°C	k
8a→**11a**	50	$(1.70 \pm 0.90) \times 10^7$ s^{-1}
8b→**11a**		$(3.25 \pm 0.27) \times 10^8$ s^{-1}
8d→**11d**		$(6.20 \pm 0.90) \times 10^5$ s^{-1}
22a→**11a**	50	*ca.* 7.0×10^3 s^{-1}
22a→**11a**	104	*ca.* 3.5×10^4 s^{-1}
22b→**11a**	50	*ca.* 2.0×10^2 s^{-1}
22b→**11a**	104	*ca.* 5.0×10^3 s^{-1}
22c→**11c**	104	*ca.* 1.1×10^3 s^{-1}
22d→**11c**	104	*ca.* 2.3×10^2 s^{-1}
27 + PhSSPh→**28a** + PhS$^{\bullet}$	50	$(7.6 \pm 1.0) \times 10^5$ dm^3 mol^{-1} s^{-1}
27 + BuSSBu→**28b** + BuS$^{\bullet}$	50	$(3.8 \pm 0.2) \times 10^4$ dm^3 mol^{-1} s^{-1}

Substitution of the experimental values of $[Cy]_f$, $[RSH]_i$ and $[RSH]_f$ into eqn. (1) allows k_c/k_H to be determined by an iterative method.[40] The results of three experiments conducted at 50 °C with different concentrations of *tert*-butyl mercaptan gave values of k_c/k_H in the range 1.2–2.8 (Table 1). The reason for the spread of values is not clear, but it probably reflects the difficulty of accurately determining the yields of products when the ratio $[\mathbf{11a}]_f/[\mathbf{13a}]_f$ is high. The values (1.2, 1.3) determined at the higher thiol concentrations are expected to be the more reliable. k_c Was obtained (Table 2) by substitution into k_c/k_H of the known value of k_H for the reaction of a primary alkyl radical with *tert*-butyl mercaptan ($k_H = 1 \times 10^7$ dm^3 mol^{-1} s^{-1} at 50 °C).[33,38]

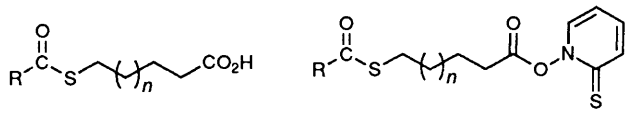
UV irradiation of dilute solutions of **7b** and **d** in benzene at 50 °C with thiophenol ($k_H = 1.7 \times 10^8$ dm^3 mol^{-1} s^{-1} at 50 °C)[33,41] and *tert*-butyl mercaptan respectively gave the products expected from Schemes 1 and 2. The relevant data are listed in Tables 1 and 2. In the absence of a thiol **7c** decomposed smoothly in benzene to give tetrahydrothiophene **11a** and the disulfide **9c**. Since no value for k_H is available for butyl mercaptan, the decomposition of **7c** in the presence of *tert*-butyl mercaptan was examined. However, the mixture of products arising from chain propagation by both the *tert*-butylthio and butylthio radicals was so complex that useful kinetic data could not be obtained.

Intramolecular substitution at sulfur in the radical **16** derived from thioctic acid **14** was also briefly studied (Scheme 3). In this case the Barton ester **15** could not be obtained from the acid chloride. Therefore, it was prepared *in situ* by DCC coupling of



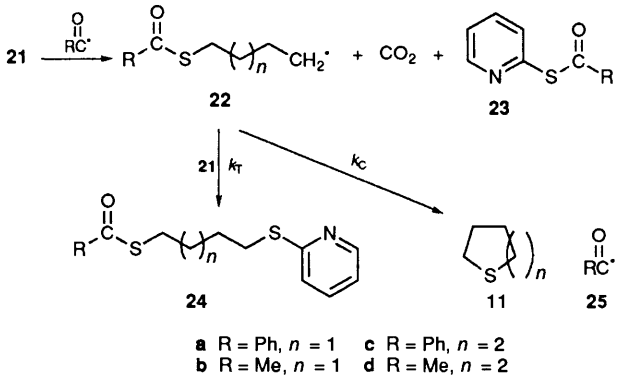
Scheme 3

thioctic acid with *N*-hydroxypyridine-2(1*H*)-thione[37] and was heated in degassed benzene at 80 °C for 3 h. The two major products were identified as **18** and **19** on the basis of their NMR and mass spectra. They arise through six-membered ring formation involving homolytic attack on the disulfide bond in **16**.



20a R = Ph, n = 1 **21a** R = Ph, n = 1
b R = Me, n = 1 **b** R = Me, n = 1
c R = Ph, n = 2 **c** R = Ph, n = 2
d R = Me, n = 2 **d** R = Me, n = 2

The four ω-acylthio acids **20a–d** were readily prepared from the corresponding ω-bromo acids and were converted into their Barton esters by DCC coupling.[37] UV irradiation of the ester **21a** in benzene at 50 °C gave the mixture of **11a**, **23a** and **24a** expected from the reactions of Scheme 4. Clearly, under the



a R = Ph, n = 1 **c** R = Ph, n = 2
b R = Me, n = 1 **d** R = Me, n = 2

Scheme 4

conditions used in this experiment the intermolecular attack of the intermediate radical **22a** on the precursor **21a** is sufficiently fast to compete effectively with the cyclisation **22a**→**11a**. There was no indication that decarbonylation of the radical **25a**, a process expected to be relatively slow,[42] competed with its reaction with **21a**.

A series of reactions was conducted in which the chain decomposition of **21a** in solutions of known concentration was allowed to proceed to completion and the yields of products were accurately determined by GC. If the reactions that occur under these conditions, in which the final concentration of **21a** is zero, are confined to those of Scheme 4 the final concentration of the cyclised product **11a** should be related to the initial

Table 3 Relative yields of products and relative rate constants for reactions of ω-acylthioalkyl radicals in benzene

				Product[b]			
T/°C	Precursor	Radical	$[Pr]_i$[a]/mol dm^{-3}	Cy	UT	$[Cy]_f$[c]/ mol dm^{-3}	$(k_c/k_T)/10^{-4}$ dm^3 mol^{-1}
50	**21a**	**22a**	0.053	**11a**	**24a**	0.011	42
50			0.193			0.018	50
50			0.360			0.024	57
104			0.031			0.0099	50
104			0.071			0.0199	92
50	**21b**	**22b**	0.034	**11a**	**24b**	0.0007	1.25
50			0.050			0.0008	1.35
104			0.029			0.0033	9.6
104			0.050			0.0047	13.0
104	**21c**	**22c**	0.031	**11b**	**24c**	0.0008	1.5
104			0.052			0.0014	2.6
104			0.070			0.0016	2.9
104	**21d**	**22d**	0.031	**11b**	**24d**	0.0003	0.46
104			0.050			0.0003	0.42
104			0.071			0.0004	0.56

[a] Initial concentration of the radical precursor. [b] Cy and UT represent the cyclised and uncyclised products respectively. [c] Final concentration of cyclised product.

concentration of **21a** by the rate eqn. (2) where $[Cy]_f$ represents the final concentration of cyclised product and $[Pr]_i$ is the initial concentration of the radical precursor **21a**.

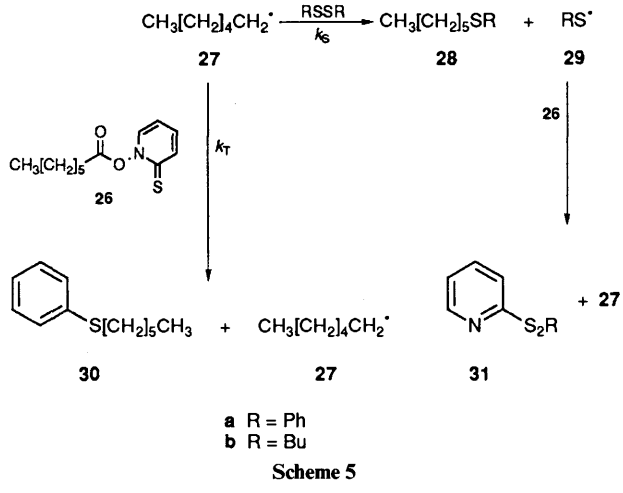
$$[Cy]_f = k_c/k_T \ln (1 + [Pr]_i k_T/k_c) \quad (2)$$

The values of k_c/k_T obtained when the experimental data are substituted into eqn. (2) are given in Table 3, which also includes the corresponding data for homolytic decomposition of the precursors **21b–d** under similar conditions. Because the cyclisations of **22b–d** are so slow the final concentrations of cyclised product were very small even at 104 °C and hence were difficult to measure accurately. Consequently, the kinetic data obtained from them may include relatively large experimental errors. Values of k_c determined from k_c/k_T and from the values of k_T previously reported ($k_T = 1.4 \times 10^6$ dm^3 mol^{-1} s^{-1} at 50 °C and 5.0×10^6 dm^3 mol^{-1} s^{-1} at 104 °C)[33,39] are given in Table 2.

In order to compare the rates of inter- and intra-molecular homolytic substitution on disulfide sulfur a number of experiments were conducted in which the Barton ester **26** of heptanoic acid, a source of hexyl radicals, was irradiated in benzene at 50 °C with diphenyl disulfide. The products detected comprised hexyl phenyl sulfide **28a**, 2-(hexylthio)pyridine **30**, and phenyl 2-pyridyl disulfide **31a**. The expected mechanism of their formation is shown in Scheme 5. Provided that diphenyl disulfide is in large excess, the reaction essentially involves a competition between a second order process, namely the addition of hexyl radicals **27** to the precursor **26** to give **30**, and a first order process, the attack of hexyl radical on diphenyl disulfide to give **28a**. Under these conditions eqn. (3) applies,

$$[SP]_f = k_{app}/k_T \ln (1 + [Pr]_i k_T/k_{app}) \quad (3)$$

where $[Pr]_i$ is the initial concentration of the radical precursor **26**, $[SP]_f$ is the final concentration of homolytic substitution product, and the apparent first order rate constant $k_{app} = k_S[PhSSPh]$. Hence, k_S/k_T can be calculated by an iterative method[40] provided that the final concentration of substitution product $[\mathbf{28a}]_f$, and the average concentration of disulfide, $[PhSSPh]_m$, are accurately determined. The results obtained



Scheme 5

[Table 4 (see Experimental)] gave $k_S/k_T = 0.56 \pm 0.05$ at 50 °C. Since at this temperature[39] $k_T = 1.4 \times 10^6$ dm^3 mol^{-1} s^{-1} it follows that $k_S = 7.6 \times 10^5$ dm^3 mol^{-1} s^{-1}. This value is rather greater than might have been expected on the basis of a very recent determination[15] at 25 °C *viz.* $k_S = 2.0 \times 10^5$ dm^3 mol^{-1} s^{-1}. However, the discordance between the two sets of results does not invalidate the conclusions adumbrated below.

The rate constant for the attack of hexyl radicals on dibutyl disulfide was determined in the same way by irradiation of a mixture of the disulfide and **26** at 50 °C. The results (Table 2) gave $k_S/k_T = 0.027 \pm 0.003$ at 50 °C from which it follows that $k_S = (3.8 \pm 0.4) \times 10^4$ dm^3 mol^{-1} s^{-1}.

Discussion

The results described above and the kinetic data summarised in the Tables reveal a number of interesting features. First, it is noteworthy that all of the cyclisations involve an S_H2 reaction in the exo mode; no trace could be detected of the products expected to arise from intramolecular alkyl radical attack at the remote sulfur atom in the disulfides **7a**, **b** or **c**, or at the carbonyl carbon of the thioesters **22c–d**. These observations, which are congruent with previous reports of exclusive exo substitution by

intramolecular alkyl or aryl radical attack on the sulfur in simple sulfides,[2,12,17,26-28] conform to the hypothesis that S_H2 reactions on sulfur normally proceed through a T-shaped transition structure in which the attacking radical, the sulfur atom, and the leaving group assume an approximately linear disposition.[17,27]

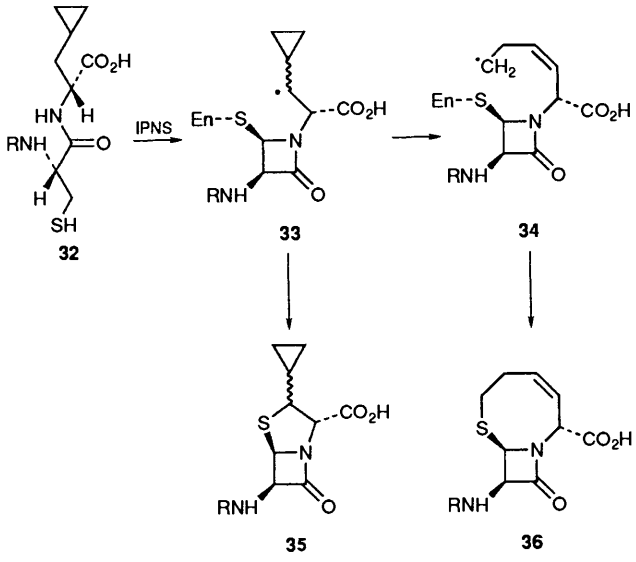
Further support for this view is revealed when our results are combined with those of Franz and his co-workers[12] for 1,5 intramolecular alkyl radical attack on sulfides which show that the value of k_c at 50 °C for cyclisation of $^{\bullet}CH_2[CH_2]_3SAlkyl$ is $1.6 \times 10^2\ s^{-1}$. The relative order of reactivity where R represents alkyl is thus $^{\bullet}CH_2(CH_2)_3SR \approx {}^{\bullet}CH_2[CH_2]_3SCOR < {}^{\bullet}CH_2[CH_2]_3SCH_2Ph \approx {}^{\bullet}CH_2[CH_2]_3SCOPh < {}^{\bullet}CH_2[CH_2]_3SSR < {}^{\bullet}CH_2[CH_2]_3SSPh$. From this it appears that the rates of these reactions reflect the stabilities of the radicals displaced, an observation that is consistent with the view that the S_H2 process at sulfur involves concerted bond formation and bond fission and proceeds through a transition structure rather than through a hypervalent intermediate. A somewhat less plausible hypothesis is that S_H2 generates a hypervalent intermediate in a reversible reaction. The ejection of the leaving radical may then be rate-limiting.

It has been suggested previously that the transition structures for alkyl radical attack on sulfur are dipolar and that their formation involves the attacking species behaving as a nucleophile.[13] However, the observation that the radicals **22a** and **b** containing a thioester function undergo cyclisation with approximately the same rate constants as analogous sulfides, *i.e.* $^{\bullet}CH_2[CH_2]_3S[CH_2]_2CH_3$ and $^{\bullet}CH_2[CH_2]_3SCH_2Ph$,[12] does not support this view. Neither is it consistent with the observation that sulfoxides are not more reactive than sulfides.[13]

Comparison of the rate constant for cyclisation of **8a** with that for **8d**, and of those for **22a** and **b** with those for **22c** and **d** indicates that 6-membered ring formation occurs about 25–30 times more slowly than does 5-membered ring formation. This difference is very similar to that observed between 1,5-cyclisation of the hexenyl radical ($k_c = 5.8 \times 10^5\ s^{-1}$ at 50 °C)[38,43] and 1,6-cyclisation of the heptenyl radical ($k_c = 1.5 \times 10^4\ s^{-1}$ at 50 °C).[44] Presumably, as with alkenyl ring closures, formation of the smaller ring by S_H2 on sulfur has both a more favourable entropy of activation, reflecting a smaller loss of rotational degrees of freedom, and a lower activation enthalpy.

Somewhat similar comparisons can be made between the rate constants for inter- and intra-molecular homolytic substitution at sulfur in a disulfide bond and those for analogous homolytic addition reactions of olefins. Our value for the rate constant for attack of hexyl radicals on diphenyl disulfide (Table 2) is somewhat larger than those previously reported for the same reaction with hexenyl radicals[38,43] or other primary radicals.[15] However, all these data show that the rate constant for 1,5-cyclisation by S_H2 at the SSPh group (**8b**→**11a**) is much greater (*ca.* 400–800 times) than that for intermolecular alkyl radical attack on PhSSPh. Unfortunately it is difficult to find reliable data for the rate of intermolecular alkenyl radical addition to unactivated olefins. For the gas phase reaction of methyl radicals with prop-1-ene Kerr[45] gives a pre-exponential factor of $\log A = 8.52$ and an activation energy of $E_a = 31\ kJ\ mol^{-1}$, each of which is close to the values obtained theoretically.[46,47] Also the rate constant at 50 °C calculated from these parameters ($k_c = 3 \times 10^3\ s^{-1}$) is the same as that derived by Ingold[48] for the reaction of methyl radicals with but-1-ene in solution and is about 200 times smaller than that for 1,5 cyclisation of hexenyl radical. Although the Arrhenius parameters are not available for the S_H2 reactions at sulfur we expect that the major difference between the inter- and intra-molecular processes like that for homolytic addition to alkenes will reflect a much less favourable entropy of activation for the former because of the loss of translational degrees of freedom in the formation of the transition structure.

The observation that intramolecular alkyl radical substitution at sulfur in disulfides occurs rapidly at ordinary temperatures may have implications for the biosynthesis of β-lactam antibiotics. The formation of ring-opened products when substrates containing a cyclopropane ring were incubated with appropriate enzymes has demonstrated that free radicals are intermediates in the enzymic production of both cephalosporins and penicillins.[49,50] For example, incubation of **32** with isopenicillin N synthetase (IPNS) gave mainly **36** the formation of which was ascribed to the intermediacy of the radical **34** formed by ring opening of the enzyme bound radical **33** (Scheme 6). However, the concomitant formation of **35**, albeit



Scheme 6

in small yield, suggests that direct ring-closure in **33** is sufficiently fast to compete with the opening of the cyclopropylcarbinyl radical. It appears, therefore, that ring closure of **33** must have a rate constant of *ca.* $10^7\ s^{-1}$, *i.e.* a little less than the expected rate constant ($k_c \approx 10^8\ s^{-1}$)[38] for the reaction **33**→**34**. A rate constant in this range seems to rule out the possibility of a radical 'rebound' mechanism. Although the rate constant for ring closure by S_H2 on a disulfide bond is of a comparable magnitude, the attachment of the substrate to IPNS through an S–S bridge seems highly unlikely. However, in the light of the present results intramolecular attack on an S–Fe bond is certainly kinetically feasible and is consistent with the evidence already available for binding of the substrate to the enzyme through iron.[5]

Experimental

IR Spectra were recorded on a Perkin-Elmer 683 spectrometer. ^1H NMR spectra were recorded in deuteriochloroform with tetramethylsilane as internal reference at 200 MHz on a Varian XL-200 or JEOL PNM FX-200 spectrometer. All *J* values are given in Hz. ^{13}C NMR spectra were recorded in deuteriochloroform with tetramethylsilane as internal reference at 50 MHz on a JEOL PNM FX-200, or Varian XL-200 instrument. In some cases quaternary aromatic carbons were not detected. Assignment of hydrogen substitution of carbons, where appropriate, was made by use of the 'attached proton test' (APT).[51] Electron impact (EI) mass spectra and chemical ionisation (CI) mass spectra with ammonia as the reagent gas were measured on a VG Micromass 7070F mass spectrometer operating at 70 eV. High resolution mass spectra were recorded

on an AEI MS 902 instrument. Flash chromatography on silica was carried out as previously described.[52] High pressure liquid chromatography (HPLC) was conducted on a Waters Radial-Pak 5μ HPLC cartridge, and the eluate was scanned with a Waters *R403 differential* refractometer. Gas liquid chromatography (GC) was carried out on a 25 μ × 0.2 mm vitreous silica chromatography column (δGE 25QC 2/BP1 1.0) in a Varian 6000 or Varian 3400 gas chromatograph fitted with a flame ionisation detector and a Hewlett Packard 3390A integrator. Melting points were determined on a Reichert hot-stage microscope and are uncorrected. Elemental analyses were carried out by the Australian National University Microanalytical Service. Solvents and reagents were purified according to published procedures.[53] Tetrahydrothiophene, tetrahydrothiapyran, diphenyl disulfide, dibutyl disulphide and *N*-hydroxypyridine-2-thione were commercial samples. The disulfides **13a**,[54] **b**[55] and **d**[56] were prepared by iodine catalysed reactions[34] from the corresponding symmetrical disulfides, while **23b**,[57] **28a**,[58] **28b**,[59] **31a**[60] and **31b**[60] were obtained by established methods.

5,5′-*Dithio*(*dipentanoic Acid*)—5-Mercaptopentanoic acid, prepared from 5-bromopentanoic acid as previously described,[61] was heated in dimethyl sulfoxide at 100 °C (ref. 62) to give the dithio acid[63] as needles from ethanol–water, m.p. 86–87 °C; ν_{max}(CH_2Cl_2 film)/cm^{-1} 2700–3200 and 1695; δ_H 2.70 (4 H, t, *J* 6, 2 × CH_2S), 2.40 (4 H, t, *J* 7, 2 × CH_2CO_2H) and 1.79–1.70 (8 H, m, 4 × CH_2); δ_C 179.7 (CO), 38.6 (SCH_2), 33.5 (CH_2CO_2H), 28.5 and 13.4 (CH_2CH_2); *m*/*z* (CI) 266 (M^+, 6%), 101 (73) and 55 (100).

6,6′-*Dithio*(*dihexanoic Acid*).—Heating of 6-mercaptohexanoic acid in dimethylsulfoxide[62] gave 6,6′-dithio(dihexanoic acid)[63] as plates from ethanol–water, m.p. 78–80 °C; ν_{max}(CH_2Cl_2 film)/cm^{-1} 2650–3450 br and 1715; δ_H 2.68 (4 H, t, *J* 8, 2 × SCH_2), 2.35 (4 H, t, *J* 7, 2 × CH_2CO_2H) and 1.78–1.35 (12 H, m, 6 × CH_2); δ_C 177.4 (CO), 38.4 (SCH_2), 33.6 (CH_2CO_2H), 28.5, 27.5 and 24.0 (3 × CH_2); *m*/*z* 294 (M^+, 8%), 115 (21), 55.1 (100).

5-(tert-*Butyldithio*)*pentanoic Acid* **6a**.—A mixture of the 5,5′-dithio(dipentanoic acid) (1.06 g, 4.0 mmol), di-*tert*-butyl sulfide (2.14 g, 12 mmol) and iodine (125 mg, 0.5 mmol) was heated at 100 °C for 16 h as previously described.[34] Chromatography of the crude product separated the excess of di-*tert*-butyl sulfide (eluted with CH_2Cl_2) from the title compound **6a** (eluted with ethyl acetate) which was obtained as a colourless oil (0.71 g, 80%) (Found: M^+, 222.0748. $C_9H_{18}O_2S_2$ requires *M*, 222.0748); ν_{max}(CH_2Cl_2 film)/cm^{-1} 3400–2900 and 1710; δ_H 2.71 (2 H, t, *J* SCH_2), 2.38 (2 H, t, *J* 6, CH_2CO_2H), 1.71–1.70 (4 H, m, 2 × CH_2) and 1.33 (9 H, s, 3 × CH_3); δ_C 178.9 (CO), 47.8 (*C*Me_3), 40.1 (SCH_2), 33.5 (CH_2CO_2H), 29.9 (3 × CH_3), 28.6 and 23.5 (2 × CH_2); *m*/*z* 222 (M^+, 10%), 170 (18), 148 (20), 101 (16) and 57 (100).

5-(*Phenyldithio*)*pentanoic Acid* **6b**.—Treatment of 5,5′-dithio-(dipentanoic acid) (1.0 g, 3.8 mmol) with diphenyl disulfide as described above gave the required disulfide **6b** as a colourless oil (0.64 g, 70%) (Found: M^+, 242.0436. $C_{11}H_{14}O_2S_2$ requires *M*, 242.0435); δ_H 7.55–7.50 (2 H, m, ArH), 7.35–7.15 (3 H, m, ArH), 2.77–2.70 (2 H, m, SCH_2), 2.31 (2 H, t, *J* 7, CH_2CO_2H) and 1.75–1.67 (4 H, m, 2 × CH_2); δ_C 179.4 (CO), 137.4, 128.9, 127.6, 126.7 (Aryl C), 38.3 (SCH_2), 33.4 (CH_2CO_2H), 28.0 and 23.3 (2 × CH_2), *m*/*z* 242 (M^+, 100%), 142 (73), 109 (81) and 101 (90).

5-(*Butyldithio*)*pentanoic Acid* **6c**.—Treatment of 5-mercaptopentanoic acid (1.60 g, 12 mmol) with butanethiol (1.08 g, 12 mmol) and diethyl azodicarboxylate (2.09 g, 12 mmol) as previously described[35] gave **6c** (1.20 g, 45%) as a colourless solid (Found: M^+, 222.0749. $C_9H_{18}O_2S_2$ requires M, 222.0748); ν_{max}($CHCl_2$ film)/cm^{-1} 3500–2800 and 1715; δ_H 2.69 (4 H, t, *J* 7, 2 × SCH_2), 2.39 (2 H, t, *J* 6, CH_2CO_2), 1.80–1.55 (6 H, m, 3 × CH_2), 1.50–1.24 (2 H, m, CH_2) and 0.93 (3 H, t, *J* 7, CH_3); δ_C 179.3 (C=O), 38.9, 38.5 (2 × SCH_2), 33.5 (*C*H_2CO_2), 31.3, 28.5, 23.4, 21.6 (4 × CH_2) and 13.6 (CH_3); *m*/*z* 222 (M^+, 20%), 176 (30) and 101 (52).

6-(tert-*Butyldithio*)*hexanoic Acid* **6d**.—Treatment of 6,6′-dithio(dihexanoic acid) (2.0 g, 6.8 mmol) with di-*tert*-butyl disulfide (3.63 g, 20.5 mmol) and iodine (212 mg, 0.85 mmol) as described above gave **6d** as a clear oil (Found: M^+, 236.0904. $C_{10}H_{20}O_2S_2$ requires *M*, 236.0905); ν_{max}(CH_2Cl_2 film)/cm^{-1} 3500–2700 and 1710; δ_H 2.7 (2 H, t, *J* 8, SCH_2), 2.37 (2 H, t, *J* 7, CH_2CO_2H), 1.80–1.52 (6 H, m, 3 × CH_2) and 1.39 (3 H, s, 3 × CH_3); δ_C 179.9 (C=O), 47.5 (*C*Me_3), 40.3 (SCH_2), 33.8 (CH_2CO_2H), 29.8 (3 × CH_3), 28.8, 27.8 and 24.1 (3 × CH_2).

1-(tert-*Butyldithiobutylcarbonyloxy*)*pyridine*-2(1H)-*thione* **7a**.—Following the literature procedure[64] for the preparation of carboxylic thiohydroxamic anhydrides, a solution of **6a** (222 mg, 1.0 mmol) and oxalyl chloride (1.0 cm^3) in benzene (10 cm^3) was stirred at ambient temperature for 2 h. The oil remaining after evaporation of the solvent under reduced pressure was then treated with a solution of the sodium salt of *N*-hydroxypyridine-2(1*H*)-thione (177 mg, 1.2 mmol) in dichloromethane (15 cm^3) and the mixture was stirred for 2 h at ambient temperature in the dark. After being filtered, the solution was concentrated under reduced pressure and the residue was chromatographed on silica with dichloromethane to give **7a** as a yellow oil; δ_H 7.82–7.60 (2 H, m), 7.25 (1 H, ddd, *J* 2, 8, 8), 6.70 (1 H, ddd, *J* 2, 8, 8), 2.78–2.62 (4 H, m, SCH_2 and CH_2CO_2), 1.90–1.55 (4 H, m, 2 × CH_2) and 1.33 (9 H, s, 3 × CH_3); δ_C 175.7 (CO_2), 168.6 (C=S), 137.6, 137.2, 133.6, 112.6 (pyridyl), 47.6 (CMe_3), 40.2 (SCH_2), 31.1 (CH_2CO_2), 29.9 (3 × CH_3), 28.0 and 23.1 (2 × CH_2).

1-(*Phenyldithiobutylcarbonyloxy*)*pyridine*-2(1H)-*thione* **7b**.—Consecutive treatment of **6b** (0.60 g, 2.48 mmol) with oxalyl chloride and with the sodium salt of *N*-hydroxypyridine-2(1H)-thione (447 mg, 3.0 mmol) as described in the preceding experiment gave **7b** as a yellow oil (0.48 g, 60%); ν_{max}(neat)/cm^{-1} 1805 and 1610; δ_H 7.67 (1 H, d, *J* 8), 7.56–7.52 (2 H, m), 7.38–7.15 (5 H, m), 6.63 (1 H, ddd, *J* 2, 8, 8), 2.81–2.64 (4 H, SCH_2 and CH_2CO_2H) and 1.96–1.77 (4 H, m, 2 × CH_2); δ_C 175.6 (C=O), 168.4 (C=S), 137.5, 137.1, 133.5, 128.9, 127.4, 127.3, 127.0, 126.7, 112.6 (phenyl, pyridyl), 37.9 (SCH_2), 30.9 (CH_2CO_2H), 27.7 and 22.8 (2 × CH_2).

1-(*Butyldithiobutylcarbonyloxy*)*pyridine*-2(1H)-*thione* **7c**.—Formation of the acid chloride from **6c** (0.54 g, 2.43 mmol) and treatment with the sodium salt of the thione as described above gave **7c** as a yellow oil (0.44 g, 60%); ν_{max}(neat)/cm^{-1} 1710; δ_H 8.10 (1 H, dd, *J* 2, 8), 7.67 (1 H, dd, *J* 2, 8), 7.29 (1 H, ddd, *J* 2, 6, 8), 6.81 (1 H, ddd, *J* 2, 6, 8), 2.69 (4 H, t, *J* 7, 2 × SCH_2), 2.40 (2 H, m, CH_2CO_2H), 1.79–1.59 (6 H, m, 3 × CH_2), 1.51–1.21 (2 H, m, CH_2) and 0.92 (3 H, t, *J* 8, CH_3); δ_C 175.6 (CO_2), 168.4 (C=S), 137.6, 137.2, 133.6, 112.5 (pyridyl), 39.1, 38.6 (2 × SCH_2), 31.4 (*C*H_2CO_2), 31.3, 28.2, 23.2, 21.6 (4 × CH_2) and 13.6 (CH_3); *m*/*z* 222 (M^+, 20%), 176 (30) and 101 (52).

1-(tert-*Butyldithiopentylcarbonyloxy*)*pyridine*-2(1H)-*thione* **7d**.—The acid **6d** (0.50 g, 1.12 mmol) was converted by the procedure described above into **7d** (0.37 g, 55%); δ_H 7.69–7.57 (2 H, m), 7.21 (1 H, ddd, *J* 2, 8, 8), 6.65 (1 H, ddd, *J* 2, 8, 8), 2.72 (4 H, t, *J* 8, SCH_2 and CH_2CO_2), 1.95–1.38 (6 H, m, 3 × CH_2) and 1.33 (9 H, s, 3 × CH_3); δ_C 175.7 (C=O), 168.7 (C=S), 137.6, 137.2, 133.6, 112.6 (pyridyl), 47.7 (*C*Me_3), 40.2 (SCH_2), 31.3 (*C*H_2CO_2), 29.8 (3 × CH_3), 28.6, 27.6 and 23.8 (3 × CH_2).

Photolysis of **7a**.—A solution of **7a** (50 mg, 0.15 mmol) in benzene (0.75 cm^3) was degassed, sealed under nitrogen in a reactivial, placed in a constant temperature bath at 80 °C and irradiated with UV light. After 2 h the solution had become colourless. GC analysis then showed the presence of only two compounds: tetrahydrothiophene, and 2-(*tert*-butyldithio)pyridine **9a**[60] which was obtained after evaporation of the solvent as a clear oil (Found: M^+, 199.0409 $C_9H_{13}NS_2$ requires *M*, 199.0409); δ_H 8.42 (1 H, dd, *J* 2, 8, pyridyl), 7.79 (1 H, dd, *J* 2, 4, pyridyl), 7.65–7.57 (1 H, m, pyridyl), 7.12–7.01 (1 H, m, pyridyl) and 1.34 (9 H, s, 3 × CH_3); δ_C 159.1, 149.1, 136.7, 120.3, 119.6 (5 × pyridyl C), 49.1 (CMe_3) and 29.7 (3 × CH_3); *m*/*z* 199.0 (M^+, 7%) and 142.9 (100).

Photolysis of **7b**.—Photolysis of a solution of **7b** (0.5 cm^3; 0.2 mol dm^{-3}) in benzene at 50 °C as described above gave only tetrahydrothiophene and 2-(phenyldithio)pyridine **9b**[65] which was isolated by chromatography as a clear oil (Found: M^+, 219.0716. $C_{11}H_9NS_2$ *M*, requires 219.0716); δ_H 8.49–8.43 (1 H, m), 7.66–7.58 (2 H, m), 7.57–7.46 (2 H, m), 7.35–7.17 (3 H, m) and 7.13–7.05 (1 H, m); δ_C 160.0, 149.5, 137.2 (pyridyl C), 129.1, 127.4, 127.3 (aryl C), 120.9 and 119.7 (pyridyl C); *m*/*z* 219 (M^+, 100%), 155 (56), 109 (76) and 78 (67).

Photolysis of **7c**.—Photolysis of a 0.4 mol dm^{-3} solution of **7c** in benzene (0.7 cm^3) at 50 °C as described above gave tetrahydrothiophene, dibutyl disulfide, and 2-(butyldithio)pyridine **9c**[60] which was isolated by chromatography as a clear oil (Found: M^+, 199.0490. $C_9H_{13}NS_2$ requires *M*, 199.0489); δ_H 8.53–8.43 (1 H, m, pyridyl), 7.79–7.59 (2 H, m, pyridyl), 7.16–7.03 (1 H, m, pyridyl), 2.80 (2 H, t, *J* 8, SCH_2), 1.77–1.56 (2 H, m, CH_2), 1.52–1.28 (2 H, m, CH_2) and 0.90 (3 H, t, *J* 8, CH_3); δ_C 161.3, 149.5, 137.4, 121.1, 119.6 (5 × pyridyl C), 38.7 (SCH_2), 30.9 (SCH_2CH_2), 21.6 (CH_2CH_3) and 13.6 (CH_3); *m*/*z* 199 (M^+, 2%), 143 (8) and 111 (100).

Preparation and Thermolysis of the Thioctic Acid Ester **15** *of* N-*Hydroxypyridine*-2(1H)-*thione*.—A solution of thioctic acid (1.5 g, 7.3 mmol), DCC (2.25 g, 10.9 mmol), DMAP (1.07 g, 8.7 mmol) and *N*-hydroxypyridine-2(1*H*)-thione (1.11 g, 8.7 mmol) in benzene (50 cm^3) was stirred at room temperature under nitrogen for 1 h, then at reflux for 3 h. Chromatography of the product mixture gave di-2-(thian-2-yl)ethyl disulfide **18** (Found: M^+, 322.0916. $C_{14}H_{26}S_4$ requires, *M*, 322.0917); δ_H 2.83–2.72 (3 H, m, CH_2SCH), 2.67–2.60 (2 H, m, $SSCH_2$), 1.98–1.79 (4 H, m, 2 × CH_2) and 1.64–1.23 (4 H, m, 2 × CH_2); δ_C 41.1 (CH_2SCH), 35.9, 35.3, 34.5, 28.8, 27.2 and 25.8 (6 × CH_2); *m*/*z* 322 (M^+, 1%), 161 (100) and 129 (3).

Further elution of the column gave 2-(thian-2-yl)ethyl 2-pyridyl disulfide **19** (Found: M^+, 271.0523. $C_{12}H_{17}NS_3$ requires *M*, 271.0523); δ_H 8.45 (1 H, dd, *J* 2, 4, pyridyl), 7.74–7.59 (2 H, m, pyridyl), 7.11–7.03 (1 H, m, pyridyl), 2.97–2.75 (3 H, m, CH_2SCH), 2.68–2.54 (2 H, m, $SSCH_2$), 2.00–1.71 (4 H, m, 2 × CH_2) and 1.50–1.27 (4 H, m, 2 × CH_2); δ_C 160.3, 149.5, 136.8, 120.4, 119.6 (5 pyridyl C), 41.0 (CH_2SCH), 36.0, 34.9, 34.4, 28.7, 27.2 and 25.7 (6 × CH_2); *m*/*z* 271 (1%) and 161 (100).

Reactions of **7a**, **b** *and* **d** *with Thiols*.—The radical precursor was added to a solution (1.0 or 2.0 cm^3) of either benzenethiol or *tert*-butyl mercaptan (10 mol equiv.) in benzene in a reactivial fitted with a septum inlet. A fine stream of nitrogen was bubbled through the solution for a few minutes, and the vial was then immersed in a constant temperature bath and irradiated with a sunlamp for 2–3 h. The data obtained on GC of the product mixtures are summarised in Table 1.

Butyl Phenyl Disulfide **13b**.—Treatment of thiophenol (1.1 g, 10 mmol) with butanethiol (0.90 g, 10 mmol) and diethyl azodicarboxylate in the usual way afforded **13b**[55] (1.6 g, 65%) as a clear oil (Found: M^+ 198.0536. $C_{10}H_{14}S_2$ requires *M*, 198.0537); δ_H 7.47–7.18 (5 H, m, aryl), 2.74 (2 H, t, *J* 7, CH_2S), 1.56 (2 H, m, CH_2), 1.50–1.28 (2 H, m, CH_2CH_3) and 0.88 (3 H, t, *J* 7, CH_3); δ_C 128.9, 127.4, 126.6 (aryl C), 38.7 (SCH_2), 30.9 (SCH_2CH_2), 121.6 (CH_2CH_3) and 13.6 (CH_3).

5-(*Benzoylthio*)*pentanoic Acid* **20a**.—5-Bromopentanoic acid (2.54 g, 14 mmol) and potassium thiobenzoate [prepared from thiobenzoic acid (1.9 g, 13.8 mmol)] were stirred in dimethylformamide (25 cm^3) at ambient temperature for 20 h, then poured into aqueous sodium hydrogen carbonate. The aqueous solution was extracted with dichloromethane, then acidified to afford **20a** (2.62 g, 80%) which was extracted with dichloromethane and crystallised from ethyl acetate–hexane as plates, m.p. 48–50 °C (Found: C, 60.6; H, 6.3, S, 13.5%; M^+, 238.0663. $C_{12}H_{14}O_3S$ requires C, 60.5; H, 5.9; S, 13.5%; *M*, 238.0664); ν_{max}(CH_2Cl_2 film)/cm^{-1} 3500–2600 br 1705 and 1665; δ_H 7.97 (2 H, d, *J* 7, aryl), 7.61–7.39 (3 H, m, aryl), 3.09 (2 H, t, *J* 6, SCH_2), 2.46–2.35 (2 H, m, CH_2CO_2) and 1.80–1.72 (4 H, m, 2 × CH_2); δ_C 191.7 (COS), 179.5 (CO_2), 133.2, 128.4, 127 (aryl), 33.4 (CH_2CO_2), 28.9, 28.4 and 23.7 (3 × CH_2); *m*/*z* 238 (M^+, 49%), 116 (78), 105 (100) and 77.2 (89).

5-(*Acetylthio*)*pentanoic Acid* **20b**.—Treatment of 5-bromopentanoic acid (3.62 g, 20 mmol) with the potassium salt of thioacetic acid (1.52 g, 20 mmol) as described above gave **20b** as an oil (2.38 g, 65%) (Found: M^+, 176.0507. $C_7H_{12}O_3S$ requires *M*, 176.0507); ν_{max}(neat)/cm^{-1} 3500–2800 br and 1700 br; δ_H 2.89 (2 H, t, *J* 6, SCH_2), 2.38 (2 H, t, *J* 8, CH_2CO_2H), 2.33 (3 H, S, CH_3) and 1.77–1.60 (4 H, m, 2 × CH_2); δ_C 195.8 (COS), 178.9 (CO_2), 33.2, 30.3, 28.6, 28.4 and 23.4 (4 × CH_2, CH_3); *m*/*z* 176.0 (M^+, 1%), 116 (19) and 83.9 (30).

6-(*Benzoylthio*)*hexanoic Acid* **20c**.—The usual treatment of 6-bromohexanoic acid (1.37 g, 7 mmol) with the potassium salt prepared from thiobenzoic acid (0.97 g, 7 mmol) gave the required acid as an oil (1.45 g, 82%) (Found: M^+, 252.0820. $C_{13}H_{16}O_3S$ requires *M*, 252.0820); ν_{max}(CH_2Cl_2 film)/cm^{-1} 3500–2700 br, 1705 and 1670; δ_H 7.97 (2 H, d, *J* 6, aryl), 7.61–7.39 (3 H, m, aryl), 3.07 (2 H, t, *J* 7, SCH_2), 2.35 (2 H, t, *J* 8, CH_2CO_2) and 1.79–1.40 (6 H, m, 3 × CH_2); δ_C 191.9 (COS), 179.2 (CO_2), 133.1, 128.5, 127.1 (aryl), 33.8, 29.2, 28.7, 28.2 and 24.1 (5 × CH_2); *m*/*z* 252 (M^+, 6%), 192 (4), 130 (76), 105 (100) and 77.1 (85).

6-(*Acetylthio*)*hexanoic Acid* **20d**.—Treatment of 6-bromohexanoic acid (3.9 g, 20 mmol) with the potassium salt prepared from thioacetic acid (1.52 g, 20 mmol) as described above afforded the required acid as an oil (3.2 g, 85%) (Found: C, 50.7; H, 7.4. $C_8H_{14}O_3S$ requires C, 50.5; H, 7.4%); ν_{max}($CHCl_2$ film)/cm^{-1} 3400–2300 br, 1715 and 1695; δ_H 2.87 (2 H, t, *J* 6, SCH_2), 2.39–2.30 (2 H, m, CH_2CO_2), 2.33 (3 H, s, CH_3) and 1.73–1.32 (6 H, m, 3 × CH_2); δ_C 195.9 (COS), 179.1 (CO_2), 33.6, 30.3, 28.9, 28.6, 27.9 and 29.9 (CH_3, 6 × CH_2); *m*/*z* 190 (M^+, 3%), 130.2 (100), 102 (82), 87.1 (40) and 58.1 (55).

1-(*Benzoylthiobutylcarbonyloxy*)*pyridine*-2(1H)-*thione* **21a**.—A solution of the acid **20a** (1.50 g, 6.3 mmol), dicyclohexylcarbodiimide (DCC, 1.95 g, 9.45 mmol), 4-dimethylaminopyridine (DMAP, 1.15 g, 9.45 mmol) and *N*-hydroxypyridine-2(1*H*)-thione (0.96 g, 7.6 mmol) in benzene (50 cm^3) was stirred at room temperature for 1 h. Evaporation of the solvent under reduced pressure and chromatography of the residue gave **21a** as an unstable yellow solid (0.87 g, 40%); ν_{max}(neat)/cm^{-1} 1810, 1660 and 1610; δ_H 7.92 (2 H, d, *J* 8, aryl), 7.72–7.45 (5 H, m, aryl and pyridyl), 7.25–7.17 (1 H, m, pyridyl), 6.64 (1 H, ddd, *J* 2, 8, 8, pyridyl), 3.12 (2 H, t, *J* 7,

Table 4 Relative yields of products and relative rate constants for reactions of hexyl radicals generated from **26** with disulfides in benzene at 50 °C

				Product[b]				
$[Pr]_i$/mol dm^{-3}	$[Pr]_f$/mol dm^{-3}	Disulfide	$[Disulfide]_m$[a]	SP	TP	$[SP]_f/[TP]_f$[c]	(k_{app}/k_T)[d]/dm^3 mol^{-1}	k_S/k_T
0.104	0.052	PhSSPh	2.950	**28a**	**30a**	30.3	1.28	0.44
0.096	0.048		1.948			24.4	1.15	0.59
0.118	0.059		0.941			9.0	0.50	0.53
0.098	0.049		0.759			8.05	0.38	0.50
0.096	0.048		0.555			7.60	0.35	0.63
0.148	0.074	BuSSBu	2.893	**28b**	**30b**	1.47	0.092	0.032
0.132	0.066		1.957			0.90	0.045	0.023
0.100	0.050		0.964			0.72	0.027	0.028
0.128	0.064		1.970			1.06	0.055	0.028
0.064	0.032		0.986			1.04	0.025	0.025
0.032	0.016		0.493			1.06	0.014	0.028

[a] Mean concentration of disulfide. [b] SP and TP respectively represent the products of homolytic substitution on the disulfide and of chain transfer addition to the precursor. [c] Relative final concentrations of products. [d] $k_{app} = k_S$[disulfide], see text.

CH_2CO_2) and 2.04–1.80 (4 H, m, 2 × CH_2); δ_C 191.7 (COS), 175.8 (CO_2), 168.5 (C=S), 137.2, 133.4, 133.3, 128.5, 127.1, 112.4 (aryl, pyridyl), 31.0 (CH_2CO_2), 28.8, 28.2 and 13.3 (3 × CH_2).

1-(*Acetylthiobutylcarbonyloxy*)*pyridine*-2(1H)-*thione* **21b**.—Treatment of 5-(acetylthio)pentanoic acid (1.76 g, 10 mmol) with DCC (3.09 g, 15 mmol), DMAP (1.83 g, 15 mmol) and *N*-hydroxypyridine-2(1*H*)-thione (1.52 g, 12 mmol) as described above gave **21b** (1.30 g, 45%) as a yellow oil; ν_{max}(neat)/cm^{-1} 1805, 1685 and 1605; δ_H 7.71–7.61 (2 H, m, pyridyl), 7.29–7.19 (1 H, m, pyridyl), 6.69 (1 H, ddd, *J*, 2, 8, 8, pyridyl), 2.91 (2 H, t, *J* 7, SCH_2), 2.74 (2 H, t, *J* 8, CH_2CO_2), 2.33 (3 H, s, CH_3COS) and 1.96–1.63 (4 H, m, 2 × CH_2); δ_C 195.7 (COS), 175.7 (C=O), 168.5 (C=S), 137.6, 137.2, 133.5, 112.6 (pyridyl), 30.9, 30.6, 28.7, 28.3 and 23.2 (CH_3, 4 × CH_2).

1-(*Benzoylthiopentylcarbonyloxy*)*pyridine*-2(1H)-*thione* **21c**.—Treatment of 6-(benzoylthio)hexanoic acid (1.15 g, 4.56 mmol) with DCC (1.41 g, 6.8 mmol), DMAP (830 mg, 6.8 mmol) and *N*-hydroxypyridine-2(1*H*)-thione (695 mg, 5.47 mmol) gave **21c** (0.66 g, 40%) as an unstable yellow solid; ν_{max}(neat)/cm^{-1} 1810, 1660 and 1610; δ_H 7.97 (2 H, d, *J* 8, aryl), 7.71–7.40 (5 H, m, aryl and pyridyl), 7.26–7.16 (1 H, m, pyridyl), 6.63 (1 H, ddd, *J* 2, 8, 8, pyridyl), 3.09 (2 H, t, *J* 7, SCH_2), 2.74 (2 H, t, *J* 7, CH_2CO_2) and 1.95–1.54 (4 H, m, 2 × CH_2); δ_C 191.9 (COS), 175.7 (C=O), 168.7 (C=S), 137.6, 137.3, 133.5, 133.2, 128.5, 127.1, 112.5, (aryl, pyridyl), 31.3, 29.1, 28.6, 28.0 and 23.7 (5 × CH_2).

1-(*Acetylthiopentylcarbonyloxy*)*pyridine*-2(1H)-*thione* **21d**.—Treatment of 6-(acetylthio)hexanoic acid (1.93 g, 10 mmol), DCC (3.09 g, 15 mmol), DMAP (1.83 g, 15 mmol) and *N*-hydroxypyridine-2(1*H*)-thione (1.52 g, 12 mmol) in the usual way gave **21d** (1.33 g, 44%) as a yellow oil; ν_{max}(neat)/cm^{-1} 1805, 1685 and 1610; δ_H 7.69 (2 H, ddd, *J* 2, 8, 8, pyridyl), 7.26–7.18 (1 H, m, pyridyl), 6.65 (1 H, ddd, *J* 2, 8, 8, pyridyl), 2.89 (2 H, t, *J* 7, SCH_2), 2.73 (2 H, t, *J* 7, CH_2CO_2), 2.33 (3 H, s, CH_3) and 1.92–1.46 (4 H, m, 2 × CH_2); δ_C 195.8 (COS), 175.6 (C=O), 168.6 (C=S), 137.6, 137.1, 133.5, 112.5 (4 × pyridyl C), 31.2, 30.5, 28.9, 28.6, 27.8 and 23.6 (5 × CH_2, CH_3).

Photolysis of **21a–d**.—In a typical experiment a solution (2.0 cm^3; 0.053 mol dm^{-3}) of **21a** in benzene was placed in a reactivial, degassed, and heated in a constant temperature bath at 50 °C while being irradiated with a sunlamp. After 3 h, by which time the solution had become colourless, the mixture was analysed by GC. The results are given in Table 3. Chromatography of the mixture of products from a reaction conducted on a larger scale gave **23a** and **24a** which were identified by comparison with authentic compounds. Photolyses of **21b–d** were conducted similarly. The results are summarised in Table 3.

2-*Benzoylthiopyridine* **23a**.—Stirring of a solution of benzoyl chloride and pyridine-2-thiol in benzene for 16 h at room temperature, and chromatography of the crude product gave **23a** (60%) as a clear oil (Found: M^+, 215.0405. $C_{12}H_9NOS$ requires *M*, 215.0405); ν_{max}(neat)/cm^{-1} 1680; δ_H 8.67 (1 H, d, *J* 6), 8.00 (2 H, d, *J* 8) and 7.77–7.27 (6 H, m); δ_C 189.1 (C=O), 150.3, 137.0 (pyridyl C), 133.7, 130.6, 128.7, 127.4 and 123.4 (aryl and pyridyl C).

4-(*Benzoylthio*)*butyl* 2-*Pyridyl Sulfide* **24a**.—Following the procedure for the preparation of **7a**, 5-bromopentanoic acid (2.0 g, 12 mmol) was converted into its ester with *N*-hydroxypyridine-2-(1*H*)-thione which was then photolysed as described above to afford 4-bromobutyl 2-pyridyl sulfide as a clear oil (2.4 g, 80%). The bromo-compound (740 mg, 3.0 mmol) was then treated with thiobenzoic acid (500 mg, 3.6 mmol) and sodium hydroxide (150 mg, 7 mmol) in ether as described above to afford **24a** (680 mg, 75%) as an oil (Found: M^+, 303.0751. $C_{16}H_{17}NOS_2$ requires *M*, 303.0752); ν_{max}(neat)/cm^{-1} 1660; δ_H 8.41 (1 H, d, *J* 8), 8.06 (2 H, d, *J* 8), 7.61–7.39 (4 H, m), 7.12 (1 H, d, *J* 8), 7.09–6.92 (1 H, m), 3.31 (2 H, t, *J* 8, CH_2SCO), 3.12 (2 H, t, *J* 8, SCH_2) and 1.89–1.81 (4-H, m, 2 × CH_2); δ_C 191.0 (C=O), 159.0, 149.4 (pyridyl C), 137.1, 135.8, 133.2, 128.5, 127.1, 122.2, 119.2 (aryl and pyridyl C), 29.3, 28.7, 28.6 and 28.5 (4 × CH_2).

4-(*Acetylthio*)*butyl* 2-*Pyridyl Sulfide* **24b**.—A sample (738 mg, 3.0 mmol) of 4-bromobutyl 2-pyridyl sulfide from the preceding experiment was treated with potassium thioacetate [from thioacetic acid (260 mg, 3.4 mmol)] in the usual way to give **24b** (580 mg, 80%) as a clear oil (Found: M^+, 241.0589. $C_{11}H_{15}NOS_2$ requires *M*, 241.0590); ν_{max}(neat)/cm^{-1} 1690; δ_H 8.41 (1 H, d, *J* 8, pyridyl), 7.46 (1 H, ddd, *J* 2,8,8, pyridyl), 7.15 (1 H, d, *J* 8, pyridyl), 6.99–6.92 (1 H, m, pyridyl), 3.17 (2 H, t, *J* 7, CH_2SCO), 2.91 (2 H, t, *J* 7, SCH_2), 2.31 (3 H, s, CH_3) and 1.79–1.71 (4 H, m, 2 × CH_2); δ_C 195.4 (C=O), 158.9, 149.2, 135.6, 122.0, 119.1 (5 × pyridyl C), 30.4, 29.7, 29.1, 28.6 and 28.4 (4 × CH_2, CH_3); *m/z* 241 (4%), 198 (72), 166 (32) and 112 (100).

5-(*Benzoylthio*)*pentyl* 2-*Pyridyl Sulfide* **24c**.—Following the procedure described above for the preparation of **7a**, 6-bromohexanoic acid (1.8 g, 10 mmol) was converted into its

acid chloride and then treated with the sodium salt of *N*-hydroxypyridine-2-(1*H*)-thione (1.8 g, 12 mmol) to afford the ester which was then photolysed as described above to give 5-bromopentyl 2-pyridyl sulfide as a clear oil (2.0 g, 78%). This bromo-compound (788 mg, 3.0 mmol) was then treated with potassium thiobenzoate [prepared from thiobenzoic acid (500 mg, 3.6 mmol)] in the usual way to give **24c** (620 mg, 65%) as an oil (Found: $M^+ - PhCO$, 212.0567. $C_{10}H_{14}NS_2$ requires 212.0568); ν_{max}(neat)/cm^{-1} 1660; δ_H 8.41 (1 H, d, *J* 8), 7.96 (2 H, d, *J* 8), 7.61–7.39 (4 H, m), 7.16 (1 H, d, *J* 8), 6.99–6.92 (1 H, m), 3.17 (2 H, t, *J* 7, CH_2SCO), 3.08 (2 H, t, *J* 7, SCH_2) and 1.85–1.50 (6 H, m, 3 × CH_2); δ_C 159.3 (pyridyl), 149.4 (pyridyl), 135.7, 133.2, 128.5, 127.2, 122.2, 119.2 (aryl and pyridyl), 29.8, 29.2, 29.0, 28.8 and 28.1 (5 × CH_2). *m*/*z* 317 (1%), 212(15), 180(17) and 105 (100).

4-(*Acetylthio*)*pentyl 2-Pyridyl Sulfide* **24d**.—Following the above procedure a sample (740 mg, 3.0 mmol) of 5-bromopentyl 2-pyridyl sulfide from the preceding experiment was treated with potassium thioacetate [prepared from thioacetic acid (260 mg, 3.4 mmol)] in ether to give **24d** (610 mg, 80%) as a clear oil (Found: M^+, 255.0751. $C_{12}H_{17}NOS_2$ requires *M*, 255.0752); ν_{max}(neat)/cm^{-1} 1690; δ_H 8.41 (1 H, d, *J* 8, pyridyl), 7.46 (1 H, ddd, *J* 2, 8, 8, pyridyl), 7.15 (1 H, d, *J* 8, pyridyl), 6.96 (1 H, ddd, *J* 2, 8, 8, pyridyl), 3.17 (2 H, t, *J* 7, $COSCH_2$), 2.87 (2 H, t, *J* 7 CH_2S), 2.32 (3 H, s, CH_3) and 1.81–1.45 (6 H, m, 3 × CH_2); δ_C 195.7 (C=O), 159.2; 149.4; 135.7; 122.1, 119.1 (5 × pyridyl C), 30.5, 29.7, 29.1, 28.9, 28.4 and 27.9 (5 × CH_2, CH_3).

1-(*Hexylcarbonyloxy*)*pyridine*-2-(1*H*)-*thione* **26**.—Heptanoic acid (520 mg, 4.0 mmol) was converted into its acid chloride which was then treated with the sodium salt of *N*-hydroxy-2-(1*H*)-thione (715 mg, 4.8 mmol) as described above to afford **26**[66] (75%) as a dark yellow oil; $\nu_{max}(CH_2Cl_2)$/cm^{-1} 3500–2800 and 1715; δ_H 8.42 (1 H, d, *J* 4, pyridyl), 7.46 (1 H, ddd, *J* 2, 8, 8, pyridyl), 7.12 (1 H, d, *J* 8, pyridyl), 6.96 (1 H, ddd, *J* 2, 8, 8, pyridyl), 3.15 (2 H, t, *J* 7, CH_2S), 1.89–1.73 (2 H, m, $CH_2CH_2CO_2$), 1.78–1.61 (2 H, m, CH_2CH_2S), 1.52–1.23 (6 H, m, 3 × CH_2) and 0.89 (3 H, t, *J* 7, CH_3); δ_C 159.7, 149.3, 135.7, 122.2, 119.1 (5 × pyridyl C), 31.4, 31.2, 22.5, 19.3, 18.6 (5 × CH_2) and 14.0 (CH_3).

Photolysis of Pyridinethione **26**.—A solution of **26** (60 mg) in dry degassed benzene (5 cm^3) was irradiated with UV light for 3 h. The solvent was then removed under reduced pressure and the residue was chromatographed to give 2-hexylthiopyridine **30** as an oil (Found: M^+, 195.1081. $C_{11}H_{17}NS$ requires *M*, 195.1082); δ_H 8.41 (1 H, d, *J* 8, pyridyl), 7.66 (1 H, dd, *J* 2, 8, pyridyl), 7.21 (1 H, ddd, *J* 2, 8, 8, pyridyl), 6.64 (1 H, ddd, *J* 2, 8, 8, pyridyl), 2.71 (2 H, t, *J* 7, CH_2S), 1.89–1.73 (2 H, m, CH_2CH_2S), 1.51–1.27 (6 H, m, 3 × CH_2) and 0.90 (3 H, t, *J* 7, CH_3); δ_C 137.6, 137.2, 133.3, 112.4 (4 × pyridyl C), 31.5, 31.2, 28.5, 24.2, 22.3, (5 × CH_2) and 13.9 (CH_3); *m*/*z* 195.0 (M^+, 24%), 138(61), 125(81) and 111 (100).

Reaction of **26** *with Disulfides*.—In a typical experiment a solution of **26** and diphenyl disulfide (2.95 mol dm^{-3}) in benzene was placed in a reactivial, degassed and heated at 50 °C in a constant temperature bath while being irradiated with a sunlamp. After complete consumpion of **26** (*ca.* 3 h) the mixture was analysed for **28a**, **30** and **31a** by GC. The results, and those obtained from similar experiments are presented in Table 4.

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