Heterocyclic Transformations. Part 3.[1] Thiolate Ion-induced Transformations of 6-Methyl-1,3-oxazine-2,4(3*H*)-diones to 3-(Alkyl/arylthio)but-2-enamides

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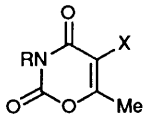
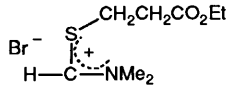
Thiolate ions generated under phase-transfer catalytic conditions react exclusively at C-6 of 3-alkyl-6-methyl-1,3-oxazine-2,4(3*H*)-diones to give (*E*)- and (*Z*)-3-(alkylthio)but-2-enamides. With binucleophiles having at least one thiol group, the *E* + *Z* thiobutenamides are initially formed and their further transformation depends on the nature of the second nucleophile. The bulk of the N-3 substituent of the oxazine and the thiol exercise steric control on the rate and mode of the reaction.

6-Methyl-1,3-oxazine-2,4(3*H*)-dione **1c** constitutes a unique heterocyclic intermediate giving synthetically useful reactions unexpected from its precursors—urethane and ethyl acetoacetate. The regioselectivity of its reactions towards nucleophiles has been rationalised on the basis of the relative 'hardness' of its acidic sites (C-2 > C-4 > C-6)[2] and that of the reacting bases.[2–7] The 'hard' bases, *viz.* ammonia,[3,4] alkylamines,[3,4] hydrazines,[5] carbanions,[6] hydroxide ion[4] and alcohols,[7] react at C-2 to give pyrimidines; pyrazoles; pyridines and alkyl carbamates, respectively. In the presence of triethylamine,[7] alcohols react mainly at C-4 of substrate **1c** to give alkyl acetoacetates and alkyl carbamates. The 'soft' bases cyanide ion[2] and t-butylalcohol in the presence of triethylamine[7] react with compound **1a** at C-6 to give 5-iminopyrrol-2-ones and the corresponding 3-t-butoxybut-2-enamide, respectively. Here, we report that, despite their bulky nature, 'soft' thiolate ions generated from thiols† and α-thioiminium salts under phase-transfer catalytic conditions react exclusively at C-6 of substrates **1** to furnish 3-(alkylthio)but-2-enamide derivatives, thus providing a route to their direct synthesis.[1]



1

a; R = CH_2Ph, X = H
b; R = Me, X = H
c; R = X = H
d; R = Me, X = Br
e; R = Me, X = SPr



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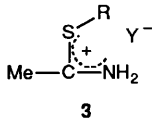
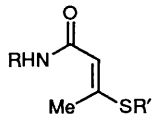
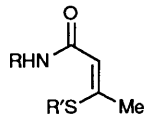


3

a; R = CH_2Ph, Y = Cl
b; R = Me, Y = I
c; R = CH_2CO_2Et, Y = Br



(*E*)-**4**



(*Z*)-**5**

a; R = R' = CH_2Ph
b; R = CH_2Ph, R' = Me
c; R = CH_2Ph, R' = CH_2CO_2Et
d; R = CH_2Ph, R' = $CH_2CH_2CO_2Et$
e; R = CH_2Ph, R' = Pr
f; R = CH_2Ph, R' = Ph
g; R = Me, R' = Pr
h; R = Me, R' = Ph
i; R = H, R' = CH_2Ph
j; R = H, R' = Pr
k; R = H, R' = Ph
l; R = CH_2Ph, R' = CH_2CH_2OH
m; R = H, R' = CH_2CH_2OH
n; R = CH_2Ph, R' = $CH_2CH_2CH_2SH$
o; R = H, R' = $CH_2CH_2CH_2SH$

Results and Discussion

3-Benzyl-6-methyl-1,3-oxazine-2,4(3*H*)-dione **1a** reacted with phenylmethanethiolate ion, generated *in situ* from benzyl ethanimidothioate hydrochloride **3a** under phase-transfer catalytic (PTC) conditions‡ using anhydrous potassium carbonate as base and tetrabutylammonium hydrogen sulphate ($TBA^+ HSO_4^-$) as catalyst in dimethylformamide (DMF) at 30–40 °C, to give two isomeric compounds, (*E*)-*N*-benzyl-3-(benzylthio)but-2-enamide **4a**§ and (*Z*)-*N*-benzyl-3-(benzylthio)but-2-enamide **5a**.

Likewise, reaction of compound **1a** with methanethiolate, ethoxycarbonylmethanethiolate, β-ethoxycarbonylethanethiolate and propanethiolate ions generated from substrates **3b**, **3c**, **2** and propanethiol, respectively, gave the corresponding derivatives of **4b–e** and **5b–e**. However, benzenethiolate ion failed to react with compound **1a** at 30 °C and at 50–60 °C gave only (*E*)-isomer **4f**. Similarly, reaction of 3,6-dimethyl-1,3-oxazine-2,4(3*H*)-dione **1b** with propanethiolate and benzenethiolate ions gave compound **4g** along with its isomer **5g**, and compound **4h**, respectively. These results show that the more nucleophilic methanethiolate and propanethiolate ions gave butenamides **4** and **5** in better yields than did the less nucleophilic benzenethiolate and ethoxycarbonylmethanethiolate ions (Table 1). Also, owing to steric interactions, the *Z*/*E* ratios of the products were lowered by the increase in bulk of the alkylthio groups. Other poorly nucleophilic ions, acetophenone-ω-thiolate and prop-2-ene-1-thiolate ions and sterically hindered *o*-aminobenzenethiolate and 1,1-dimethylethanethiolate ions did not react with a substrate **1a**, **1b** or **1d** at 30–40 °C, and at higher temperatures (>60 °C) multitudes of products were formed.

6-Methyl-1,3-oxazine-2,4(3*H*)-dione **1c** in the presence of thiolate ions under PTC conditions did not give 3-(alkylthio)-but-2-enamide derivatives but underwent decomposition. We have previously reported[7] that the presence of triethylamine increases the reactivity of alcohols towards substrate **1c** to provide alkyl acetoacetates and alkyl carbamates. However, in DMF, in the presence of triethylamine, thiolate ions did not react with compound **1c**. We argued that in ethanol–triethylamine, if 'soft' thiolate ions could exhibit greater reactivity than do alcohols, products incorporating the thiol unit would be obtained.

Phenylmethanethiolate ion, generated from compound **3a**, on reaction with the oxazine **1c** in ethanol containing 3 mol equiv. of triethylamine gave a major product, m.p. 90–92 °C, M^+ 207. Its ^1H NMR spectrum showed two singlets, at δ 2.35 and

† Only one reaction of 1,3-oxazine-2,4(3*H*)-dione, present in oxazinomycin, with thioglycol under relatively drastic conditions is on record.[8]

‡ Compound **1a** decomposed on treatment with strong bases. With benzyl(triethyl)ammonium chloride, the yields of compounds **4** and **5** were lowered, and with CH_2Cl_2, MeCN or PhMe as solvent, reaction did not occur at all.

§ Stereochemistry was determined by NOE experiments.

Table 1 Physical and spectral data of compounds **4** and **5**

Compound[a]	M.p. (°C)[b]	Yield (%)	$\delta_H(CDCl_3)$[c] ArH	NH/NH_2	C=CH	NCH_2 NMe[d]	SCH_2/SMe	Me	ν_{max}/cm^{-1}	M^+ (m/z) (R.I.)
4a	120–122(A)	40	7.27	5.68	5.49	4.43	3.94	2.44	1650, 1590, 1105	297(5)
5a	90–92(A)	23	7.27	6.08	5.72	4.40	4.01	2.13	1645, 1580	297(1)
4b	80–82(A)	64	7.25	5.87	5.33	4.42	2.21	2.42	1660, 1600, 1110	221(22)
5b	102–104(A)	20	7.27	5.92	5.74	4.43	2.28	2.13	1650, 1580	221(42)
4c	liquid	5	7.15	5.90	5.53	4.35	3.40	2.40	1730, 1650, 1610, 1100	293(4)
5c	liquid	4	7.17	6.15	5.70	4.37	3.36	2.26	1730, 1645, 1600	293(4)
4d	liquid	17	7.17	5.83	5.42	4.35	2.55(t)	2.35	1730, 1650, 1610, 1100	307(10)
5d	liquid	6	7.37	6.10	5.78	4.53	2.55(t)	2.20	1730, 1650, 1590	307(15)
4e	85–87(A)	68	7.10–7.40	5.57	5.33	4.40	2.63(t)	2.40	1660, 1600, 1110	249(12)
5e	68–70(A)	16	7.16	6.13	5.70	4.40	2.73(t)	2.13	1650, 1580	249(14)
4f	78–80(A)	20	7.06–7.57	5.42	5.17	4.37		2.46	1650, 1600, 1100	283(30)
4g	72–74(A)	60		5.65	5.40	2.80	2.68(t)	2.40	1650, 1600	173(100)
5g	liquid	12		6.00	5.70	2.76	2.70(t)	2.13	1650, 1590	173(100)
4h	65–66(A)	16	7.10–7.58	5.55	5.27	2.73		2.39	1640, 1600	207(24)
4i + 5i	90–92(C)	60	7.18	5.67	(*E*) 5.48 (*Z*) 5.60		(*E*) 3.92	(*E*) 2.35 (*Z*) 2.13	3300, 1660, 1650, 1075	207(5)
4j + 5j	104–106(C)	62		5.67	(*E*) 5.47 (*Z*) 5.77		2.70(t)	(*E*) 2.40 (*Z*) 2.17	3300, 1650, 1630, 1090	159(28)
4k	137–138(C)	40	7.30	5.20	5.15			2.36	3300, 1665, 1600	193(15)
5k	147–148(C)	15	7.00–7.53	5.70	5.76			1.74	3300, 1650, 1570	193(24)
4l[e]	103–105(B)	25	7.24	7.64	5.71	4.38	2.90(t)	2.40	3390, 1650, 1610, 1120	251(5)
5l	liquid	6	7.22	6.55	5.80	4.38	2.90(t)	2.10	3300, 1635, 1585	251(5)
4m[e]	109(B)	56		5.87–6.97	5.64		2.87(t)	2.33	3300, 1670, 1120	161(70)
4n + 5n	liquid	50	7.19	6.50	(*E*) 5.45 (*Z*) 5.70	4.33	2.76(t)	(*E*) 2.40 (*Z*) 2.10	1640, 1600	281(10)
4o + 5o	liquid	18		5.70–6.40	(*E*) 5.46 (*Z*) 5.73		2.71(t)	(*E*) 2.43 (*Z*) 2.31	3365, 1690, 1580, 1120	191(100)

[a] Elemental analysis: **4a** (Found: C, 72.8; H, 6.3; N, 4.5. $C_{18}H_{19}NOS$ requires C, 72.72; H, 6.40; N, 4.71%); **4b** (Found: C, 64.8; H, 6.6. $C_{12}H_{15}NOS$ requires C, 65.15; H, 6.78%); **5b** (Found: C, 64.8; H, 6.6. $C_{12}H_{15}NOS$ requires C, 65.15; H, 6.78%); **4e** (Found: C, 67.2; H, 7.5; N, 5.5. $C_{14}H_{19}NOS$ requires C, 67.47; H, 7.63; N, 5.62%); **5e** (Found: C, 67.7; H, 7.5; N, 5.7. $C_{14}H_{19}NOS$ requires C, 67.47; H, 7.63; N, 5.62%); **4f** (Found: M^+, 283.1035. $C_{17}H_{17}NOS$ requires 283.1030); (**4i + 5i**) (Found: C, 63.4; H, 6.2. $C_{11}H_{13}NOS$ requires C, 63.77; H, 6.28%); **4l** (Found: C, 62.3; H, 6.9. $C_{13}H_{17}NO_2S$ requires C, 62.15; H, 6.77%). [b] Solvents for crystallisation: (A) Dichloromethane–light petroleum (b.p. range 40–60 °C). (B) Chloroform. (C) Chloroform–light petroleum. (D) Chloroform–ethanol–diethyl ether. [c] Other signals in the ^1H NMR spectra are: **4c** δ 1.24 (3 H, t, *J* 7, Me), 4.06 (2 H, q, *J* 7, CH_2); **5c** δ 1.24 (3 H, t, *J* 7, Me), 4.06 (2 H, q, *J* 7, CH_2); **4d** δ 1.21 (3 H, t, *J* 7, Me), 2.90 (2 H, t, *J* 7, $COCH_2$), 4.07 (2 H, q, *J* 7, OCH_2); **5d** δ 1.26 (3 H, t, *J* 7, Me), 3.16 (2 H, t, *J* 7, $COCH_2$), 4.17 (2 H, q, *J* 7, OCH_2); **4e** δ 0.97 (3 H, t, *J* 7, Me), 1.50 (2 H, sext, *J* 7, CH_2Me); **5e** δ 0.97 (3 H, t, *J* 7, Me), 1.50 (2 H, sext, *J* 7, CH_2Me); **4g** δ 1.00 (3 H, t, *J* 7, Me), 1.65 (2 H, sext, *J* 7, CH_2Me); **5g** δ 1.00 (3 H, t, *J* 7, Me), 1.62 (2 H, sext, *J* 7, CH_2Me); **4l** δ 3.70 (2 H, t, *J* 7, OCH_2), 3.16 (1 H, br, OH, exchangeable with D_2O); **5l** δ 3.40 (1 H, OH, exchangeable with D_2O), 3.70 (2 H, t, *J* 7, OCH_2); **4m** δ 3.46 (1 H, br, OH, exchangeable with D_2O), 3.65 (2 H, t, *J* 7, OCH_2); **4n** δ 2.02 (2 H, quint, *J* 7, CH_2); **4o** δ 2.06 (2 H, quint, *J* 7, CH_2). [d] In each case the signal appears as a doublet (*J* 5), which changed to singlet on addition of D_2O. [e] $\delta_H[^2H_6]$-DMSO + $CDCl_3$.

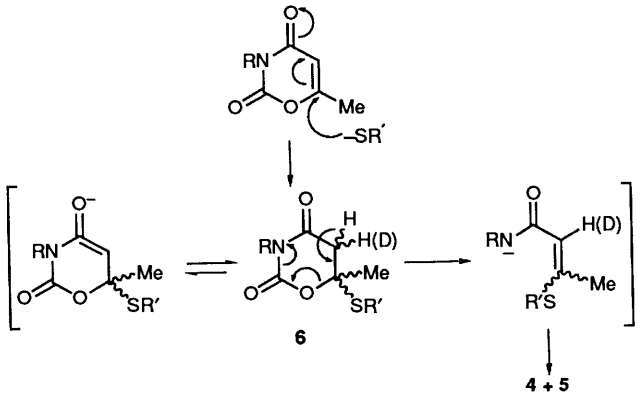
2.13, due to =CMe groups, and two singlets, at δ 5.48 and 5.60, due to olefinic Hs in a 2:1 ratio, along with signals for a benzyl group. Therefore, the product was a mixture of compounds **4i** and **5i** (2:1) which could not be separated by repeated chromatography. A minor component (< 3%), m.p. 66–67 °C, was identical with an authentic sample of ethyl *N*-acetoacetylcarbamate.[9] Hence, in the reaction of an ethanol–thiol mixture with the oxazine **1c**, the thiol reacts much faster than does ethanol to give the product of reaction at C-6, as well as minor component due to reaction of ethanol at the C-2 centre of substrate **1c**. Similarly, reaction of compound **1c** with propanethiol gave a mixture of products **4j** and **5j** in the ratio 2:1 (^1H NMR), which could not be separated. However, reaction of compound **1c** with benzenethiol gave two isomeric (M^+ 193) products, m.p. 137 °C (73%) and m.p. 147–148 °C (27%), in 55% total yield. In analogy with earlier observations, these compounds were assigned the structures (*E*)-**4k** and (*Z*)-**5k**, (*E*)- and (*Z*)-3-(phenylthio)but-2-enamide, respectively. The formation of both the *Z*- and the *E*-isomer of butenamide derivatives in the reaction of benzenethiol with compound **1c**, but only the *E*-isomer in its reactions with oxazines **1a** and **1b**, indicated that the substituent at N-3 of the substrate oxazine **1** also had an effect on the *Z*/*E* ratio.

In the ^1H NMR spectra of all these products the relatively upfield signal of the olefinic H in the *E*-isomer **4** compared with the *Z*-isomer **5** constituted a general structure-distinguishing feature. The maximum upfield shift for the olefinic H noticed in products **4f**, **4h** and **4k** (δ 5.17) could be ascribed to a diamagnetic anisotropic effect due to its proximity to the phenyl ring. The replacement of the aryl group with a benzyl group (**4a** and **4i**) placed the olefinic H outside the influence of the phenyl ring and it appeared downfield (δ 5.48) due to the paramagnetic anisotropic effect. In compounds **5** the olefinic H did not experience any significant change in chemical shift (Table 1; δ 5.70). The appearance of upfield SCH_2/SMe signals in products **4** could be due to their presence in the diamagnetic region as against those in isomers **5**, where SCH_2/SMe remained in the paramagnetic region of the double bond. However, this effect was less pronounced (δ 0.05–0.10) because of the larger distance of the SCH_2/SMe group from the olefin region. In the IR spectra of the (*Z*)-3-(alkylthio)but-2-enamides **5**, absorption bands due to C=O and C=C bonds appeared at lower frequencies than in spectra of the *E*-isomers **4**. Furthermore, the *E*-isomers showed an additional band at 1100 cm^{-1} which was absent in the spectra of the corresponding *Z*-isomers. In the mass spectra of derivatives **4** and **5**, weak parent-ion peaks underwent prominent elimination of alkyl and thioalkyl groups. However, arylthiobutenamides **4f**, **4h**, **4k** and **5f**, **5h**, **5k** could undergo elimination of only the thioaryl group, and the aryl group was not lost.

An analogous reaction of 5-bromo-3,6-dimethyl-1,3-oxazine-2,4(3*H*)-dione **1d** with propanethiolate ion under PTC con-

ditions in DMF gave two products. The higher-R_f product (3%), M^+ 215, in its ^{1}H NMR spectrum exhibited signals due to SPr (δ 2.63, t; 1.54, sextet; 0.97, t), NMe (δ 3.40) and =CMe (δ 2.53). From these data and the absence of an olefinic H signal for compound **1d** (δ 5–6), the product was assigned the structure 3,6-dimethyl-5-(propylthio)-1,3-oxazine-2,4(3*H*)-dione **1e**. The lower-R_f component was found to be compound **1b** (27%). Similarly, reaction of compound **1d** with benzenethiolate and phenylmethanethiolate ions under PTC conditions gave compound **1b** in 20 and 35% yield as the only isolable product. Therefore, as in their reactions with 5-bromouracil,[10] thiolate ions mainly caused debromination of substrate **1d**.

A mechanism of the reactions of thiolate ions with substrates **1** could involve attack at C-6 followed by C-5 protonation and deprotonation, C(6)–O bond cleavage and decarboxylation to form products **4** and **5** (Scheme 1). Compounds **4e** and **5e**,

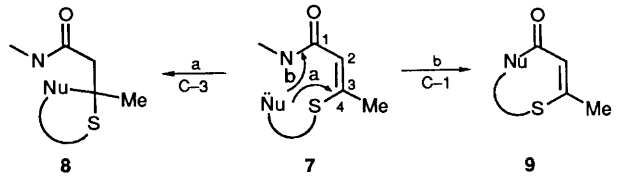


Scheme 1

formed in the reaction of the oxazine **1a** with propanethiolate ion in DMF–D_2O (20:0.8 cm^3), showed the incorporation of deuterium at C-2 (65%) and C-4 (33%). A blank reaction of compound **1a** in DMF–D_2O showed the incorporation of deuterium at C-5 (33%) and C-6 (33%) in compound **1a**. The increased deuterium exchange at C-2 of compounds **4e** and **5e**, stemming from C-5 of the oxazine **1a**, clearly demonstrated the participation of intermediate **6** in these reactions.

In comparison with relatively nonregiospecific reactions of oxazines **1** with *O*- and *N*-nucleophiles, the reactivity and regiospecificity of thiolate ions at C-6 of compounds **1** could be of significant synthetic consequence. We envisaged that in the reactions of oxazines **1** with binucleophiles containing at least one thiol group the initially formed intermediate **7** could undergo cyclisation to provide novel synthetic routes to heterocycles **8** and **9**. We have studied the reactions of oxazines **1** with ethane-1,2-dithiol, propane-1,3-dithiol, 2-mercaptoethanol and 2-aminoethanethiol.

The reaction of compound **1a** with ethane-1,2-dithiol under PTC conditions using potassium carbonate as base, DMF as solvent and TBA^+ HSO_4^- as catalyst gave two products. The higher-R_f compound, m.p. 55–56 °C, M^+ 267 (20%), in its ^{1}H NMR spectrum exhibited an upfield (δ 1.85) Me signal as compared with the chemical shift of the Me group in compounds **4** and **5** (δ 2.1–2.4) and showed an additional 2-H singlet at δ 2.85 due to a $COCH_2$ group. Hence it could be assigned the structure **10a**. The second component, m.p. 178–180 °C, M^+ 440 (4%), showed =CMe (δ 2.34) and SCH_2-CH_2S (δ 3.00) signals in the ratio 3:2. These data corroborate structure **11a** for the second product. Thus, ethane-1,2-dithiol and compound **1a** provided the 1:1 stoicheiometric reaction product **10a** as the major component along with a 1:2 reaction product **11a** as the minor component. On increasing the concentration of ethane-1,2-dithiol (2–3 mol equiv.), the formation of compound **10a** increased only marginally. Similarly, reaction of compound **1a** with propane-1,3-dithiol under PTC conditions (24 h) gave compound **10b** (40%) and **11b** (8%). On intercepting the reaction after 1 h, a liquid product, M^+ 281 (10%), could be isolated. From its ^{1}H NMR spectrum it was found to be a mixture of products **4n** and **5n** which could not be separated. The mixture under PTC conditions in DMF–K_2CO_3–TBA^+ HSO_4^- gave compound **10b**. Therefore, an SH group of the dithiol attacks at C-6 of substrate **1a** and the second SH group in the initially formed intermediate **4** and **5** undergoes (i) intramolecular cycloaddition at the β-carbon of the α,β-unsaturated amide to form compound **10** (path a from **7**) or (ii) reaction at C-6 of another molecule of substrate **1** to form compound **11** (Scheme 2). Owing to the ease of formation of the five-membered ring in the reaction of substrates **1** with ethane-1,2-dithiol, the corresponding derivatives **4** and **5** could not be isolated.



Scheme 2

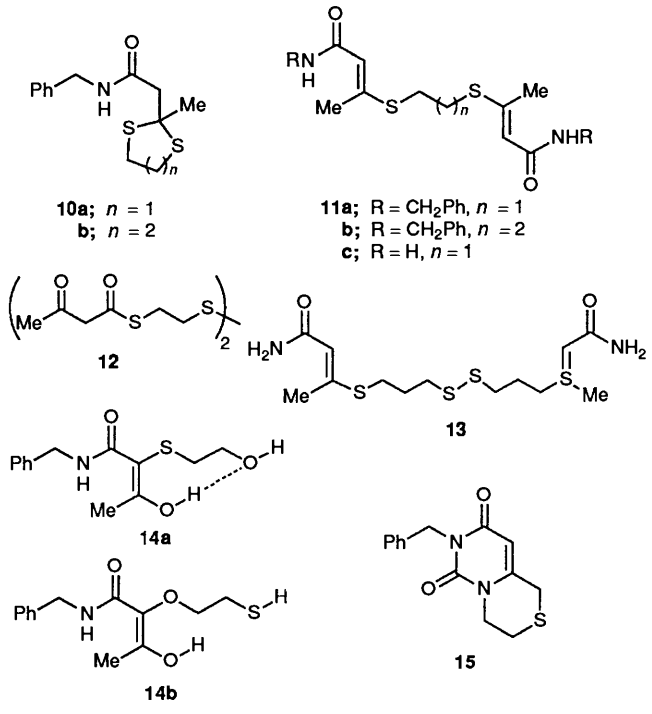
An analogous reaction of compound **1c** with ethane-1,2-dithiol in ethanol containing triethylamine at room temperature gave (i) ethyl *N*-acetoacetylcarbamate, (ii) compound **12**, M^+ 354 (5%), mol. formula $C_{12}H_{18}O_4S_4$—a dimer of *S*-2-(mercaptoethyl) 3-oxo(thiobutyrate), and (iii) compound **11c**. Similarly, reaction of compound **1c** with propane-1,3-dithiol gave compound **4o** and its dimer **13**, which was also formed on storage of compound **4o** in air. Therefore, under non-PTC conditions, the reaction of a dithiol with compound **1c** takes place at C-6 but further reaction is inhibited.

Another binucleophile, 2-mercaptoethanol, upon reaction with the oxazine **1a** under PTC conditions gave products **4l** (25%) and **5l** (6%) along with another minor, liquid product. The latter could tentatively be assigned the structure **14a** or **14b** from the following data: M^+ 267 (10%); δ 2.30 (3 H, s, Me), 4.42 (2 H, d, $NHCH_2$), 2.55 and 3.62 (t, OCH_2CH_2S), 7.56 and 16.30 (exchangeable with D_2O) and 7.3 (m, ArH); δ_C 181.7 (s), 172.3 (s), 138.03 (s) and 92.85 (s), 128.66 (d), 127.47 (d), 20.91 (q), 38.95 (t), 43.44 (t) and 60.02 (t). One aromatic carbon could not be seen in the ^{13}C NMR spectrum, and the mode of formation of product **14a**/**14b** is not evident. An analogous reaction of 2-mercaptoethanol with compound **1c** gave the product **4m** only.

Reaction of 2-aminoethanethiol hydrochloride with the oxazine **1a** under PTC conditions gave a multitude of products. The highest-R_f component, m.p. 120–122 °C, M^+ 274 (100%),* molecular formula $C_{14}H_{14}N_2O_2S$, in its ^{1}H NMR spectrum exhibited two triplets, at δ 4.16 and 2.98 (NCH_2CH_2S), one singlet at δ 5.66 (=CH), two singlets, at δ 3.46 and 5.04 (SCH_2, NCH_2), and a multiplet at δ 7.24 (ArH). Its ^{13}C NMR spectrum† exhibited four methylene carbons, at δ 26.32 (t), 26.79 (t), 39.50 (t) and 44.57 (t), four quaternary carbons, at δ 126.06 (s, arom. C), 136.71 (s, pyrimidine C), 150.87 (s, C=O) and 162.09 (s, C=O), and four CH groups, at δ 98.64 (d, pyrimidine CH), 127.61 (d, arom. C), 128.35 (d, arom. C) and 129.00 (d, arom. C). From these data the product was assigned structure **15**.

* Figures in parentheses pertain to the relative abundance of peaks in the mass spectrum.

† Multiplicities pertain to the off-resonance proton-decoupled spectra.



Thus, thiols–'soft' bases react exclusively at the 'soft' C-6 of 6-methyl-1,3-oxazine-2,4(3*H*)-diones **1** to give (*E*)- and (*Z*)-3-(alkyl/arylthio)but-2-enamides **4** and **5**. In the case of dithiols, the second thiol group, under PTC conditions, undergoes intramolecular cyclisation at the β-carbon of the α,β-unsaturated amide intermediate to give cyclic products **10**, but such intramolecular cyclisation was not observed under non-PTC conditions. Other binucleophiles, *viz.* 2-mercaptoethanol (OH) and 2-aminoethanethiol (NH_2), did not show similar intramolecular additions.

Experimental

IR and ^1H and ^{13}C NMR spectra were recorded on Pye-Unicam SP3-300, JEOL-JNM 60 MHz and Bruker AC-200 instruments, respectively. *J*-Values are given in Hz. Mass spectra were recorded on a JEOL JMS-D-300 spectrometer at 70 eV ionisation voltage at CDRI, Lucknow. M.p.s were determined in capillaries and are uncorrected. Silica gel-G or silica gel 60 HF_{254} plates were used for monitoring of the reactions. Silica gel column chromatography was used for purification of products.

6-Methyl-1,3-oxazine-2,4(3*H*)-dione **1c**[4] and its 3-benzyl-**1a**,[6] 3-methyl-**1b**[6] and 5-bromo-3-methyl-**1d**[2] derivatives were prepared by reported procedures. Thioiminium salts **2** and **3** were obtained by heating of thioacetamide or *N*,*N*-dimethylthioformamide[11] with the respective halides. DMF and ethanol were dried over calcium oxide and were freshly distilled before use. Other chemicals and solvents used were available commercially (LR grade) and were used as such without further purification.

Phase-transfer-catalysed Reactions of Compounds **1a** *and* **1b** *with Thiolate Ions.*—A solution of a 3-substituted-6-methyl-1,3-oxazine-2,4(3*H*)-dione **1a** or **1b** (0.01 mol) and a thioiminium salt **2** or **3** or a thiol (0.012 mol) in DMF (20 cm^3) containing anhydrous potassium carbonate (0.02 mol) and $TBA^+ HSO_4^-$ (15–20 mg) was stirred at 30–40 °C. In the case of thiophenol, the reaction temperature was maintained at 50–60 °C. The progress of the reaction was monitored by TLC. After completion of the reaction (8–12 h), the reaction mixture was diluted with ethyl acetate (50 cm^3) and the suspended solid was filtered off and washed with ethyl acetate. The filtrate was distilled off under reduced pressure and the residual product mixture was chromatographed on a silica gel column with benzene and benzene–ethyl acetate mixtures as eluent to separate the products. The data for these compounds are given in Table 1.

Reaction of Compound **1c** *with Thiols in Ethanol.*—A solution of compound **1c** (0.01 mol) and a thioiminium salt **2** or **3** or a thiol (0.012 mol) in ethanol (20 cm^3) containing triethylamine (0.03 mol) was stirred at 30–40 °C. The progress of the reaction was monitored by TLC on fluorescent silica gel-coated plates. After completion of the reaction (8–12 h), ethanol was removed and the residue was chromatographed on a silica gel column with benzene–ethyl acetate mixtures as eluent to isolate the respective products given in Table 1.

Reaction of Compound **1d** *with Propane-1-thiol.*—A solution of 5-bromo-3,6-dimethyl-1,3-oxazine-2,4(3*H*)-dione **1d** (2.2 g, 0.01 mol) and propane-1-thiol (0.8 cm^3, 0.01 mol) in DMF (15–20 cm^3), containing anhydrous potassium carbonate (2.76 g, 0.02 mol) and $TBA^+ HSO_4^-$ (15–20 mg) was stirred under N_2 at 30–40 °C. After completion of the reaction (TLC, 4–6 h) the reaction mixture was diluted with ethyl acetate (50 cm^3) and the suspended solid was filtered off and washed with ethyl acetate. The solvent was removed from the combined filtrate, and products were isolated and purified by column chromatography to give the debromination product **1b**, identical with an authentic sample, and compound **1e** (see Results and Discussion section).

Reaction of Compound **1a** *with Propane-1-thiolate Ion in* DMF–D_2O.—A solution of compound **1a** (2.17 g, 0.01 mol) and propane-1-thiol (0.8 cm^3, 0.012 mol) in DMF (20 cm^3)–D_2O (1 cm^3) containing anhydrous potassium carbonate (2.76 g, 0.02 mol) and $TBA^+ HSO_4^-$ (15–20 mg) was stirred under N_2 at 30–40 °C. After completion of the reaction (TLC, 8 h) the mixture was diluted with ethyl acetate, suspended solid was filtered off and the solvent was distilled off from the filtrate. The residue was chromatographed on a silica gel column to isolate compounds **4e** and **5e**.

Compound **4e**. M^+ 249 (10%) and 251 (8, $C_{14}H_{17}D_2NOS$); δ($CDCl_3$) 0.97 (3 H, t, *J* 7, Me), 1.50 (2 H, sext, *J* 7, CH_2Me), 2.40 (2 H, s, $\frac{2}{3}$ Me), 2.63 (2 H, t, *J* 7, SCH_2), 4.40 (2 H, d, NCH_2), 5.33 ($\frac{1}{3}$ H, s, $\frac{1}{3}$ 2-H), 5.57 (1 H, br, NH) and 7.10–7.40 (5 H, m, Ph).

Compound **5e**. M^+ 249 (10%) and 251 (8, M^+, $C_{14}H_{17}D_2NOS$); δ($CDCl_3$) 0.97 (3 H, t, *J* 7, Me), 1.50 (2 H, sext, *J* 7, CH_2Me), 2.13 (2 H, s, $\frac{2}{3}$ Me), 2.73 (2 H, t, *J* 7, SCH_2), 4.40 (2 H, d, NCH_2), 5.70 ($\frac{1}{3}$ H, s, $\frac{1}{3}$ 2-H), 6.13 (1 H, br, NH) and 7.16 (5 H, s, Ph).

Phase-transfer-catalysed Base-induced Reaction of Compound **1a** *with* D_2O.—A solution of compound **1a** (2.17 g, 0.01 mol) in DMF (20 cm^3)–D_2O (1 cm^3) containing anhydrous potassium carbonate and $TBA^+ HSO_4^-$ (15–20 mg) was stirred under N_2 for 8 h. The reaction mixture was worked up and chromatographed to give reagent **1a** (1.0 g recovery), δ($CDCl_3$) 2.06 (2 H, s, $\frac{2}{3}$ Me), 5.00 (2 H, s, NCH_2), 5.73 ($\frac{2}{3}$ H, s, $\frac{2}{3}$ 6-H) and 6.85–7.67 (5 H, m, Ph), and *N*-benzylacetoacetamide, m.p. 99 °C (lit.,[12] 101–102 °C).

Reaction of Compound **1a** *with Ethane-1,2-dithiol.*—A solution of compound **1a** (2.17 g, 0.01 mol) and ethane-1,2-dithiol (1.2 cm^3, 0.012 mol) in DMF (15–20 cm^3) containing anhydrous potassium carbonate (2.76 g, 0.02 mol) and $TBA^+ HSO_4^-$ (15–20 mg) was stirred under N_2 at 30–40 °C. After completion of the reaction (TLC, 7–8 h) the mixture was diluted with ethyl acetate (50 cm^3), and suspended solid was filtered off and washed with ethyl acetate. The solvent was distilled from the

combined filtrate and the residue was chromatographed to afford compounds **10a** and **11a**.

N-Benzyl(2-methyl-1,3-dithiolan-2-yl)acetamide **10a** (35%); m.p. 55–56 °C; R_f 0.51 (EtOAc); M^+ 267 (20%); δ($CDCl_3$) 1.85 (3 H, s, Me), 2.85 (2 H, s, $COCH_2$), 3.23 (4 H, s, 2 × SCH_2), 4.35 (2 H, d, *J* 6, NCH_2, collapses to s on D_2O exchange) and 6.47 (1 H, br, NH, exchanges with D_2O); ν(KBr)/cm^{-1} 3280 and 1640.

N,N'-Dibenzyl-3,3'-(ethylenedithio)dibut-2-enamide **11a** (6%); m.p. 178–180 °C; R_f 0.33 (EtOAc); M^+ 440 (4%); δ[$CDCl_3$ + $(CD_3)_2SO$] 2.34 (3 H, s, Me), 3.00 (2 H, s, SCH_2), 4.32 (2 H, d, NCH_2, collapses to s on D_2O exchange), 5.67 (1 H, s, =CH), 7.37 (5 H, s, Ph) and 7.80 (1 H, t, NH, exchanges with D_2O); ν(KBr)/cm^{-1} 3250, 1640 and 1100.

Reaction of Compound **1a** *with Propane*-1,3-*dithiol*.—The reaction was performed in the manner described for the above reaction. On quenching of the reaction after 1 h, a mixture of products **4n** and **5n** could be isolated. However, on quenching of the reaction after 24 h, compounds **10b** and **11b** could be isolated. Data for compounds **4n** and **5n** are given in Table 1.

(i) *N*-Benzyl-(2-methyl-1,3-dithian-2-yl)acetamide **10b** (40%); m.p. 68–69 °C; R_f 0.53 (EtOAc); M^+ 281 (26%); δ($CDCl_3$) 1.70 (3 H, s, Me), 1.96 (2 H, m, CH_2), 2.72 (4 H, m, SCH_2), 2.87 (2 H, s, $COCH_2$), 4.30 (2 H, d, NCH_2, collapses to s on D_2O exchange), 6.63 (1 H, br, NH, exchanges with D_2O) and 7.04 (5 H, s, Ph); ν(KBr)/cm^{-1} 3280 (NH) and 1630 (C=O).

(ii) *N,N'*-Dibenzyl-3,3'-(trimethylenedithio)dibut-2-enamide **11b** (8%); m.p. 115–116 °C; R_f 0.35 (EtOAc): M^+ 454 (4%); δ($CDCl_3$) 0.94 (2 H, quint, *J* 7, CH_2), 2.37 (6 H, s, 2 × Me), 2.83 (4 H, t, *J* 7, 2 × SCH_2), 4.83 (4 H, d, *J* 6, 2 × NCH_2, collapses to s on D_2O exchange), 5.45 (2 H, s, 2 × CH), 5.85 (2 H, t, 2 × NH, exchanges with D_2O) and 7.23 (10 H, s, Ph); ν(KBr)/cm^{-1} 3280 (NH), 1640 (C=O) and 1110.

Reaction of Compound **1c** *with Ethane*-1,2-*dithiol*.—A solution of compound **1c** (1.27 g, 0.01 mol) and ethane-1,2-dithiol (1.2 cm^3, 0.012 mol) in ethanol (20 cm^3) containing triethylamine (4.17 cm^3, 0.03 mol) was stirred at 30–40 °C. After completion of the reaction (TLC, 8–10 h) the ethanol was distilled off and the residue was chromatographed to give (i) ethyl *N*-(acetoacetyl)carbamate (11%), m.p. 66–67 °C (lit.,[9] 72–74 °C), identical with an authentic sample, (ii) compound **12**, and (iii) compound **11c**.

(ii) 5,8,9,12-*Tetrathiohexadecane*-2,4,13,15-*tetraone*/S-2-*mercaptoethyl* 3-*oxo*(*thiobutyrate*) **12** (18%); m.p. 105–106 °C; R_f 0.46 (EtOAc); M^+ 354 (5%); δ($CDCl_3$) 1.85 (3 H, s, Me), 2.85 (2 H, s, CH_2), 3.37 (4 H, s, 2 × SCH_2) and 6.00 (1 H, br, SH); ν(KBr)/cm^{-1} 1660 (C=O) (Found: C, 40.1; H, 6.2. $C_6H_{10}O_2S_2$ requires C, 40.45; H, 5.62%).

(iii) 3,3'-(*Ethylenedithio*)*dibut*-2-*enamide* **11c** (8%); m.p. 138 °C; R_f 0.11 (EtOAc); δ($CDCl_3$) 2.43 (6 H, s, 2 × Me), 3.11 (4 H, s, 2 × SCH_2) and 5.53 (2 H, s, 2 × =CH); ν(KBr)/cm^{-1} 3440, 3200 (NH_2), 1655 (C=O) and 1110 (Found: C, 46.1; H, 5.7; N, 10.6. $C_{10}H_{16}N_2O_2S_2$ requires C, 46.15; H, 6.15; N, 10.76%).

Reaction of Compound **1c** *with Propane*-1,3-*dithiol*.—The reaction was performed in the manner as described in the above experiment. After work-up the residue was chromatographed to afford compounds **4o**, **5o** and **13**.

(i) (*E*)- *and* (*Z*)-3-(3-Mercaptopropylthio)but-2-enamide **4o** + **5o** (18%); liquid; R_f 0.30 (EtOAc); M^+ 191 (100%); δ($CDCl_3$) 1.93 (2 H, quint, CH_2), 2.43 [2 H, s, ⅔ Me (**4o**)], 2.31 [1 H, s, ⅓ Me (**5o**)], 2.71 (4 H, t, 2 × SCH_2), 5.46 [s, ⅔ H, ⅔ =CH (**4o**)], 5.73 [⅓ H, s, ⅓ =CH (**5o**)] and 5.90–6.40 (1 H, br, NH, exchanges with D_2O); ν(KBr)/cm^{-1} 3365 (d, NH_2), 1690 (C=O) and 1120.

(ii) 3,3'-Dithiobis(trimethylenethio)dibut-2-enamide **13** (34%); m.p. 148 °C; R_f 0.11 (EtOAc); M^+ 380 (4%); δ($CDCl_3$ + CF_3CO_2H) 2.06 (2 H, quint, *J* 7, CH_2), 2.31 (*Z*) and 2.43 (*E*) [3 H, s, (1:3) Me], 2.93 (4 H, t, *J* 7, 2 × SCH_2) and 5.46 (*E*) and 5.73 (*Z*) [1 H, s, (3:1) CH]; ν(KBr)/cm^{-1} 3300 (d, NH_2), 1610 (C=O) and 1100.

Reaction of Compound **1a** *with* 2-*Aminoethanethiol Hydrochloride*.—A solution of compound **1a** (2.17 g, 0.01 mol) and 2-aminoethanethiol hydrochloride (2.27 g, 0.02 mol) in DMF (20 cm^3) containing anhydrous potassium carbonate (4.14 g, 0.03 mol) and TBA^+ HSO_4^- (15–20 mg) was stirred under N_2 at 30–40 °C. After work-up as given above, the residue was likewise chromatographed to afford compound **15** and *N*-benzylacetoacetamide (20%), m.p. 97 °C (lit.,[12] 101–102 °C), identical with an authentic sample.

Compound **15** (4%); m.p. 120–122 °C; R_f 0.01 (EtOAc); M^+ 274 (100%); δ($CDCl_3$) 2.98 (2 H, t, *J* 6, SCH_2), 3.43 (2 H, s, SCH_2), 4.16 (2 H, t, *J* 6, NCH_2), 5.04 (2 H, s, NCH_2), 5.66 (1 H, s, =CH) and 7.24 (5 H, m, Ph); δ($CDCl_3$) 26.32 (t, CH_2), 26.79 (t, CH_2), 39.50 (t, CH_2), 44.57 (t, CH_2), 98.64 (d, pyrimidine CH), 126.06 (s, ArC), 127.61 (d, ArCH), 128.35 (d, ArCH), 129.00 (d, ArCH), 136.71 (s, pyrimidine C=CH), 150.87 (s, C=O) and 162.09 (s, C=O); ν_{max}(KBr)/cm^{-1} 1700 (C=O) and 1655 (C=O) (Found: C, 61.0; H, 5.1. $C_{14}H_{14}N_2O_2S$ requires C, 61.3; H, 5.11%).

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