New Routes to Heterocycles *via* Sulphenylation of Unsaturated Amides

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The reaction of manganese(III) acetate with diphenyl disulphide in dichloromethane–trifluoroacetic acid in the presence of *N*-allylacetamide, followed by hydrolysis, affords a vicinal hydroxy sulphide. Similarly, addition to *N*-allyltrifluoroacetamide affords hydroxy sulphide adducts, but with different regioselectivity. *N*-Allylbenzamide and other unsaturated benzamides under similar conditions give cyclic products, 4,5-dihydro-1,3-oxazoles. Homoallylic amides give 5,6-dihydro-4*H*-1,3-oxazines. Amides derived from pent-4-enylamine give substituted pyrrolidines by cyclisation through nitrogen, but *N*-hex-5-enylbenzamide gives only an acyclic adduct. Unsaturated carboxylic acids and unsaturated carboxamides are transformed in good yield into lactones under similar conditions.

Neighbouring group participation permitting sulphenylcyclisation in the reactions of sulphur electrophiles with substituted alkenes is much less developed than the equivalent methodology based on selenium electrophiles. Thus selenyl-lactonisation is well established[1] and widely used, but sulphenyl-lactonisation, in spite of a few reports,[2,3] has been less used. As previously recognised[4] this contrast can be attributed in part to the lesser stability of sulphenyl chlorides relative to selenenyl chlorides. The contrasting use of these reagents extends to other types of cyclisation. Thus selenenylcyclisation is observed on reaction of areneselenenyl halides or related electrophiles with unsaturated amides[5,6] and unsaturated imidates.[7] No equivalent methodology has been developed for the synthesis of sulphenylated nitrogen heterocycles.

As described elsewhere,[8,9] we have developed an alternative methodology for functionalisation of substituted alkenes by sulphur electrophiles based on the use of manganese((III) salts to permit the generation of sulphur electrophiles from organic disulphides, rather than one based on sulphenyl halides. In this paper we describe the functionalisation of a variety of unsaturated amides with sulphur electrophiles generated by reaction of manganese(III) salts with organic disulphides. We show that by appropriate choice of amide either products of vicinal addition without cyclisation by the neighbouring group may be obtained with good regiocontrol, or products of sulphenylcyclisation may be isolated. Such heterocyclic products are 4,5-dihydro-1,3-oxazines, 5,6-dihydro-4*H*-1,3-oxazines, or pyrrolidines, as described in a preliminary communication.[10] In addition we show that these conditions permit efficient sulphenylcyclisation with unsaturated acids, and hence provide an attractive alternative to the use of sulphenyl halides in sulphenyl-lactonisation.

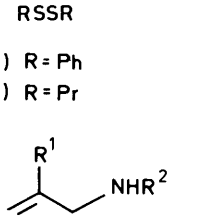
In the light of our observations[8] that additions of diphenyl disulphide (**1**) and dipropyl disulphide (**2**) to allyl acetate give products in which the regiochemistry is determined by neighbouring group participation, and that in the corresponding reactions of allyl trifluoroacetate regiochemistry is determined by the inductive effect of the trifluoroacetate group, it was interesting to establish the consequences of addition to allylacetamide (**3**) and allyltrifluoroacetamide (**4**).

The results of these and other trifluoroacetoxysulphenylation experiments are shown in Table 1. In each case the starting amide was obtained by acetylation or trifluoroacetylation of the appropriate amine. Additions of disulphides in dichloromethane–trifluoroacetic acid were conducted as previously described,[8] and products were isolated either directly after work-up, by chromatography, or in the case of trifluoroacetates by initial hydrolysis, and subsequent work-up and chromatography. Allylacetamide (**3**) gave the hydroxy sulphide (**23**) in 87% yield. The Markovnikov addition agrees with the analogous addition to allyl acetate[8] and other results in the literature. In additions of tellurium tetrachloride[11] to *N*-allyl amides the isolation of both cyclic and acyclic products shows that neighbouring group participation is important. Further evidence of neighbouring group participation in additions to *N*-allyl amides is found in

Table 1. Sulphenylation of unsaturated amides

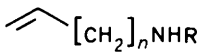
Alkene	Disulphide	Product(s)	Yield (%)[a]
CH_2=$CHCH_2NHCOCH_3$ (**3**)	(**1**)	(**23**)	87
CH_2=$CHCH_2NHCOCF_3$ (**4**)	(**1**)	(**25**)	19
		(**24**)	68
CH_2=$CMeCH_2NHCOCH_3$ (**6**)	(**1**)	(**31**)	10
		(**28**)	60
CH_2=$CH[CH_2]_2NHCOCH_3$ (**9**)	(**1**)	(**37**)	42
CH_2=$CHCH_2NHCOPh$ (**5**)	(**1**)	(**30**)	76
CH_2=$CHCH_2NHCOPh$ (**5**)	(**2**)	(**32**)	67
		(**27**)	8
CH_2=$CMeCH_2NHCOPh$ (**7**)	(**1**)	(**33**)	85
CH_2=$CMeCH_2NHCOPh$ (**7**)	(**2**)	(**34**)	78
CH_2=$CH[CH_2]_2NHCOPh$ (**10**)	(**1**)	(**36**)	67
CH_2=$CH[CH_2]_3NHCOPh$ (**12**)	(**1**)	(**38**)	54
CH_2=$CH[CH_2]_3NHCOC_6H_4OMe$-*p* (**13**)	(**1**)	(**39**)	48
CH_2=$CHCH_2CHMeCH_2NHCOPh$ (**17**)	(**1**)	(**40**)	71[b]
CH_2=$CH[CH_2]_4NHCOPh$ (**15**)	(**1**)	(**29**)	60

[a] Yields of material isolated after chromatographic separation. [b] Mixture of diastereoisomers.

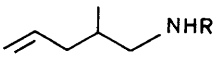


(1) R = Ph
(2) R = Pr

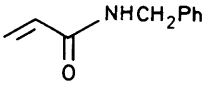
(3) R^1 = H, R^2 = $COCH_3$
(4) R^1 = H, R^2 = $COCF_3$
(5) R^1 = H, R^2 = COPh
(6) R^1 = Me, R^2 = $COCH_3$
(7) R^1 = Me, R^2 = COPh



(8) n = 2, R = H
(9) n = 2, R = $COCH_3$
(10) n = 2, R = COPh
(11) n = 3, R = H
(12) n = 3, R = COPh
(13) n = 3, R = COC_6H_4OMe-p
(14) n = 4, R = H
(15) n = 4, R = COPh



(16) R = H
(17) R = COPh



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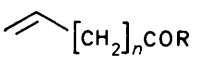
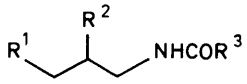
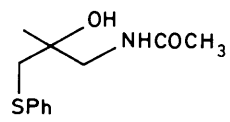


(19) n = 2, R = OH
(20) n = 3, R = OH
(21) n = 2, R = NHPh
(22) n = 2, R = NHBu



(23) R^1 = PhS, R^2 = OH, R^3 = CH_3
(24) R^1 = OH, R^2 = PhS, R^3 = CF_3
(25) R^1 = PhS, R^2 = OH, R^3 = CF_3
(26) R^1 = PhS, R^2 = OH, R^3 = Ph
(27) R^1 = PrS, R^2 = OH, R^3 = Ph



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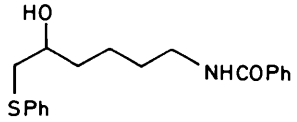

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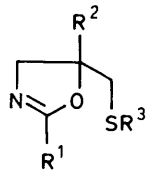
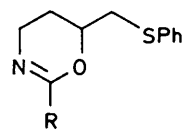
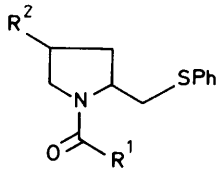


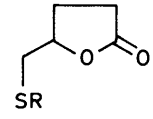
(30) R^1 = R^3 = Ph, R^2 = H
(31) R^1 = R^2 = Me, R^3 = Ph
(32) R^1 = Ph, R^2 = H, R^3 = Pr
(33) R^1 = R^3 = Ph, R^2 = Me
(34) R^1 = Ph, R^2 = Me, R^3 = Pr
(35) R^1 = Me, R^2 = H, R^3 = Ph



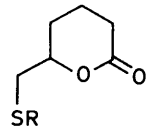
(36) R = Ph
(37) R = Me



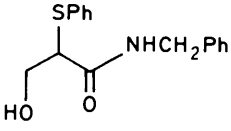
(38) R^1 = Ph, R^2 = H
(39) R^1 = p-$MeOC_6H_4$, R^2 = H
(40) R^1 = Ph, R^2 = Me



(41) R = Ph
(42) R = Pr



(43) R = Ph
(44) R = Pr



(45)

the acid-catalysed cyclisation[12] of *N*-allylacetamides to give 4,5-dihydro-1,3-oxazoles, and in their halogenation.[13] In the case of the addition to allylacetamide (**3**) to give the adduct (**23**) no other acyclic product was isolated, but traces of a second product were observed (t.l.c.) suggestive of the formation of a 4,5-dihydro-1,3-oxazole (see later). In marked contrast the addition to allyltrifluoroacetamide (**4**) afforded the adduct (**25**) as a minor product (19%) and, by anti-Markovnikov addition, the adduct (**24**) as the major product (68%). With the trifluoroacetyl substituent neighbouring group participation is less favoured and the inductive effect of this group controls the regiochemistry in favour of formation of the anti-Markovnikov adduct (**24**). The magnitude of this inductive effect is less with an amide substituent than with an ester substituent. Hence a decrease in selectivity in addition to allylic amides relative to allylic esters is to be expected. The formation of the adduct (**25**) in 19% yield contrasts with the absence of any Markovnikov adduct in addition to allyl trifluoroacetate.

The possibility of neighbouring group participation in an *N*-allylacetamide was confirmed by the behaviour of the amide (**6**). Although the major product was the Markovnikov adduct (**28**), isolated in 60% yield, a minor product was the 4,5-dihydro-1,3-oxazole (**31**), isolated in 10% yield. Subsequently the oxazole (**35**) was synthesized independently from the hydroxy sulphide adduct (**23**) and found to be identical (t.l.c.) with the very minor product of addition to allylacetamide (**3**). Thus the formation of cyclic products is a minor pathway in addition to the two allylic acetamides (**3**) and (**6**). There is good literature precedent[5] for neighbouring group participation in additions to the amide derivatives of homoallylic amines. We found that addition to the homoallylic amide (**9**) gave the oxazine (**37**) in 42% yield.

In the light of the efficient participation of *N*-allylbenzamides in electrophilic additions[11] we examined the additions of diphenyl disulphide (**1**) and dipropyl disulphide (**2**) to the benzamides (**5**) and (**7**). From the appropriate reactions the oxazoles (**30**) and (**32**—(**34**) were isolated in good yield. In one case a small amount of the minor Markovnikov adduct (**27**) was isolated. The greater electron release by the phenyl substituent in the benzamides than by the methyl substituent in the acetamides facilitates formation of the 4,5-dihydro-1,3-oxazoles. The effect of modification of the reaction conditions was briefly investigated. In addition to the *N*-allylbenzamide (**5**) an increase in the amount of trifluoroacetic acid present led to the preferential formation of the Markovnikov adduct (**26**). This adduct was isolated as the only product (47% yield) in the presence of an excess of acid and with a long reaction time (3 days). These results suggest that the 4,5-dihydro-1,3-oxazoles are formed under conditions of kinetic control and can react further to give the vicinal trifluoroacetoxy sulphides and hence the hydroxy sulphides. Control experiments established that neither ring-opening of the 4,5-dihydro-1,3-oxazoles nor ring closure of the vicinal adducts occurred on work-up or chromatography. However some of the 4,5-dihydro-1,3-oxazoles and the 5,6-dihydro-4*H*-1,3-oxazines described later are unstable.

Under conditions similar to those employed for the formation

Table 2. Sulphenylation of unsaturated acids and amides

Alkene	Disulphide	Product	Yield (%)[a]
CH_2=CH[CH_2]$_2$CONHPh (**21**)	(**1**)	(**41**)	66
CH_2=CH[CH_2]$_2$CONHBu (**22**)	(**1**)	(**41**)	52
CH_2=CH[CH_2]$_2$$CO_2$H (**19**)	(**1**)	(**41**)	88
CH_2=CH[CH_2]$_2$$CO_2$H (**19**)	(**2**)	(**42**)	91
CH_2=CH[CH_2]$_3$$CO_2$H (**20**)	(**1**)	(**43**)	85
CH_2=CH[CH_2]$_3$$CO_2$H (**20**)	(**2**)	(**44**)	84
CH_2=CHCONHCH_2Ph (**18**)	(**1**)	(**45**)	45

[a] Yields of material isolated after chromatographic separation.

of the oxazole (**30**) from the allylic benzamide (**5**), the homoallylic benzamide (**10**) afforded the oxazine (**36**). Further chain extension offers competition by neighbouring group participation to give a seven-membered ring by reaction at oxygen or a five-membered tetrahydropyrrole by reaction at nitrogen. Reactions of the three amides (**12**), (**13**), and (**17**) with diphenyl disulphide (**1**) gave in each case the appropriate tetrahydropyrrole (**38**)—(**40**). However the amide (**15**) did not give the corresponding piperidine, but instead the adduct (**29**), by Markovnikov addition. The formation of substituted tetrahydropyrroles by reaction of unsaturated amides with electrophiles has good literature precedent. The closest analogy is the cyclisation with areneselenenyl halides.[5,6] Similarly, addition of mercury(II) salts[14] leads to substituted tetrahydropyrroles. In contrast with the failure of addition to the unsaturated amide (**15**) to give a piperidine, cyclisations with other electrophiles permit direct formation of piperidines from unsaturated amides.[5,15]

The possibility of cyclisation of the three unsaturated amides (**18**), (**21**), and (**22**) to give lactams or lactones was examined. The acryloylamide (**18**) gave simply the hydroxy sulphide (**45**) with the expected regioselectivity. The two amides (**21**) and (**22**) gave the lactone (**41**) in 66 and 52% yield, respectively. Results are shown in Table 2.

The isolation of lactones suggested the possibility of sulphenyl-lactonisation of unsaturated acids under our reaction conditions. Table 2 shows that the acids (**19**) and (**20**) react with both diphenyl disulphide (**1**) and dipropyl disulphide (**2**) to give high yields of lactones (**41**)—(**44**).

Related cyclofunctionalisations have been reported[1,5,16] in reactions of unsaturated amides and carboxylic acids with benzeneselenenyl chloride. Similarly, although less used, the analogous reactions of unsaturated carboxylic acids[2,3,17] with benzenesulphenyl chloride and related compounds are well known. However the limitations[4] in the use of arenesulphenyl halides suggest the need for other methods of sulphenyl-lactonisation. In certain cases the alternative sulphenyl-lactonisation procedure described here may have value in synthesis. Our results establish that the conditions of generation of sulphur electrophiles by manganese(III) acetate with disulphides in dichloromethane–trifluoroacetic acid are generally applicable to the synthesis of a variety of heterocyclic systems including lactones. Other methods of sulphenyl-lactonisation based on different electrophiles are being developed, *e.g.* with dimethyl(methylthio)sulphonium tetrafluoroborate.[18]

Experimental

General experimental details are described in the preceding paper.[8]

Preparation of Amines.—With the exception of the following compounds amines were obtained from commercial sources.

But-3-enylamine (**8**). Reaction of but-3-enonitrile in ether with lithium aluminium hydride and aluminium chloride (1:1) for 2 h, followed by work-up and distillation afforded but-3-enylamine (63%) as a colourless liquid, b.p. 81 °C.

Pent-4-enylamine (**11**). Reaction of pent-4-enonitrile in ether with lithium aluminium hydride for 2 h followed by work-up and distillation afforded pent-4-enylamine (**11**) (69%) as a colourless liquid, b.p. 105 °C.

2-Methylpent-4-enylamine (**16**). Reaction of propiononitrile with lithium di-isopropylamide in tetrahydrofuran followed by addition of allyl bromide afforded (after reaction at 20 °C for 8 h and work-up) 2-methylpent-4-enonitrile (37% with respect to propiononitrile) as a colourless liquid, b.p. 148 °C. Reduction with lithium aluminium hydride, work-up, and distillation afforded 2-methylpent-4-enylamine (**16**) (72%) as a colourless liquid, b.p. 120—121 °C.

Hex-5-enylamine (**14**). Reduction of hex-5-enonitrile with lithium aluminium hydride in ether for 2 h followed by work-up and distillation afforded hex-5-enylamine (**14**) (73%) as a colourless liquid, b.p. 130—132 °C.

Preparation of Amides.—All the acetamides described here are known compounds, and were prepared from the appropriate amines by reaction with acetic anhydride in dichloromethane in the presence of triethylamine, or with trifluoroacetic anhydride. All the benzamides with the exception of the following compounds are known, and were prepared from the appropriate amines by reaction with benzoyl chloride in aqueous sodium hydroxide.

N-(Pent-4-enyl)-4-methoxybenzamide (**13**). Aroylation of pent-4-enylamine (**11**) afforded compound (**13**), $\nu_{max.}$($CHCl_3$) 3 470, 3 370, 1 655, 1 610, and 1 580 cm^{-1}; δ_H(60 MHz) 1.4—2.3 (4 H, complex, CH_2CH_2CH_2N), 3.15—3.45 (2 H, m, CH_2N), 3.65 (3 H, s, CH_3), 4.75—5.15 (2 H, m, CHCH_2), 5.4—6.0 (1 H, m, CHCH_2), 6.8 (2 H, aromatic), 7.2 (1 H, br s, NH), and 7.7 (2 H, aromatic).

N-(2-Methylpent-4-enyl)benzamide (**17**). Benzoylation of 2-methylpent-4-enylamine (**16**) afforded *N-(2-methylpent-4-enyl)benzamide* (**17**) (Found: M^+, 203.2110. $C_{13}H_{17}NO$ requires M, 203.1305); $\nu_{max.}$(CCl_4) 3 470, 3 340, 1 650, 1 610, and 1 585 cm^{-1}; δ_H 0.94 (3 H, d, J 6.5 Hz, CH_3), 1.85 (1 H, m) and 1.94 (1 H, m) (CH_2CCH_3), 2.13 (1 H, m, CHCH_3), 3.2—3.5 (2 H, m, CH_2N), 5.02 (2 H, m, CHCH_2), 5.76 (1 H, m, CHCH_2), 6.74 (1 H, s, NH), and 7.3—7.85 (5 H, complex, aromatic).

N-(Hex-5-enyl)benzamide (**15**). Benzoylation of hex-5-enylamine (**14**) afforded *N-(hex-5-enyl)benzamide* (**15**) (Found: M^+, 203.1302. $C_{13}H_{17}NO$ requires M, 203.1310); m/z 203 (M^+, 3%), 162 (25), and 105 (100); $\nu_{max.}$($CHCl_3$) 3 455, 3 345, and 1 645 cm^{-1}; δ_H 1.38 (2 H, m, CH_2), 1.56 (2 H, m, CH_2), 2.00 (2 H, m, CH_2), 3.38 (2 H, q, CH_2N), 4.88 (2 H, m, CHCH_2), 5.73 (1 H, m, CHCH_2), and 7.2—7.85 (6 H, complex, aromatic and NH); δ_C 26.17 (CH_2), 28.97 (CH_2), 33.18 (CH_2), 39.88 (CH_2N), 114.51 (CHCH_2), 126.93 (CHCH_2), 128.17, 130.95, 134.85, and 138.25 (aromatic), and 167.65 (CO).

Preparation of Carboxylic Acids.—Hex-5-enoic acid (**19**) was obtained by hydrolysis of hex-5-enonitrile. Pent-4-enoic acid (**20**) was obtained from a commercial source.

Preparation of N-Substituted Alkenamides.—Amides were prepared by reaction of unsaturated acid with thionyl chloride followed by the appropriate amine. The known *N*-benzylacrylamide (**18**), m.p. 91 °C, and *N*-phenylpent-4-enamide (**21**), m.p. 90—91 °C, were prepared in 83 and 86% yield, respectively.

N-Butylpent-4-enamide (**22**) was isolated as an oil in 84% yield (Found: M^+, 155.1287. $C_9H_{17}NO$ requires M, 155.1310); m/z 155 (12%), 113 (26), and 55 (100); $\nu_{max.}$($CHCl_3$) 3 455, 3 340, and 1 655 cm^{-1}; δ_H 0.90 (3 H, t, J 7 Hz, CH_3), 1.34 (2 H, m, CH_2CH_3), 1.47 (2 H, m, NCH_2CH_2), 2.27 (2 H, m, CH_2), 2.36 (2

H, m, CH_2), 3.21 (2 H, q, CH_2N), 5.00 (2 H, m, CH_2=C), 5.82 (1 H, m, C*H*=CH_2), and 6.54 (1 H, br s, NH); δ_C 13.50 (CH_3), 19.96 (CH_3CH_2), 29.63 (CH_2), 31.65 (CH_2), 31.65 (CH_2), 35.75 (CH_2), 39.15 (CH_2N), 115.06 (CH_2=C), 137.15 (*C*H=CH_2), and 172.33 (CO).

General Procedure for Sulphenylcyclisation of Unsaturated Amides and Acids.—Diphenyl disulphide (5.55 mmol) or another appropriate disulphide in dichloromethane (100 ml) containing trifluoroacetic acid (4 ml) was treated with manganese(III) acetate dihydrate (5.55 mmol) in the presence of the added amide or acid (3.7 mmol) at 0 °C for 4 h. The mixture was poured into water (100 ml) and extracted with ether (3 × 50 ml). The organic phase was washed with aqueous potassium hydrogen carbonate (3 × 50 ml) and then water (3 × 50 ml), dried ($MgSO_4$), filtered, and evaporated under reduced pressure. The crude product was purified by column chromatography [silica gel; eluant ethyl acetate–light petroleum (b.p. 40—60 °C)] in all cases except those which gave trifluoroacetates ($\nu_{max.}$ 1 790 cm^{-1}). In the latter cases the crude product was hydrolysed (aqueous potassium carbonate) and purified after work-up by column chromatography.

Addition of diphenyl disulphide to N-*allylacetamide* (**3**). Diphenyl disulphide (0.81 g) was oxidised by manganese(III) acetate dihydrate (1.48 g) in the presence of *N*-allylacetamide (**3**) (0.73 g). Work-up, hydrolysis of the crude product with sodium carbonate, and subsequent purification by chromatography afforded as a colourless oil, N-(2-*hydroxy*-3-*phenylthiopropyl*)-*acetamide* (**23**) (725 mg, 87% w.r.t. diphenyl disulphide) (Found: M^+, 225.0642. $C_{11}H_{15}NO_2S$ requires *M*, 225.3050); *m*/*z* 225 (M^+, 0.5%), 207 (13), and 98 (100); $\nu_{max.}$($CHCl_3$) 3 460, 3 350, 1 665, and 1 590 cm^{-1}; δ_H 1.99 (3 H, s, CH_3), 2.96 (1 H, dd, *J* 14 and 7 Hz) and 3.03 (1 H, dd, *J* 14 and 6 Hz) (CH_2S), 3.25 (1 H, m) and 3.53 (1 H, m) (CH_2N), 3.81 (1 H, m, CHO), 4.07 (1 H, br s, OH), 6.50 (1 H, s, NH), and 7.1—7.4 (5 H, complex, aromatic); δ_C 22.97 (CH_3), 38.96 (CH_2S), 44.64 (CH_2N), 69.51 (CHO), 126.64, 129.13, 129.94, and 135.53 (aromatic carbon), and 171.61 (CO).

Addition of diphenyl disulphide to N-*allyltrifluoroacetamide* (**4**). Diphenyl disulphide (0.81 g) was oxidised by manganese(III) acetate dihydrate (1.48 g) in the presence of the amide (**4**) (1.1 g). Work-up, hydrolysis of the crude product with sodium carbonate, and subsequent purification by chromatography afforded (as the less polar fraction) as a white solid N-(2-*hydroxy*-3-*phenylthiopropyl*)*trifluoroacetamide* (**25**) (188 mg 19% w.r.t. diphenyl disulphide), m.p. 94 °C (from ethyl acetate–light petroleum) (Found: C, 47.3; H, 4.3; N, 5.0; S, 11.4. $C_{11}H_{12}F_3NO_2S$ requires C, 47.3; H, 4.3; N, 5.0; S, 11.5%); $\nu_{max.}$($CHCl_3$) 3 515, 3 440, 1 775, and 1 590 cm^{-1}; δ_H 2.90 (1 H, dd, *J* 14 and 8 Hz) and 3.08 (1 H, dd, *J* 14 and 5 Hz) (CH_2S), 3.19 (1 H, br s, OH), 3.32 (1 H, m) and 3.65 (1 H, m) (CH_2N), 3.84 (1 H, m, CHO), 7.04 (1 H, s, NH), and 7.2—7.5 (5 H, complex, aromatic); δ_C 39.48 (CH_2S), 44.26 (CH_2N), 68.19 (CHOH), 117.56 (CF_3), 127.32, 129.39, 130.61, and 134.44 (aromatic carbon), and 157.66 (CO); and (as the more polar fraction) as a colourless oil N-(3-*hydroxy*-2-*phenylthiopropyl*)*trifluoroacetamide* (**24**) (663 mg, 68% w.r.t. diphenyl disulphide) (Found: M^+, 279.1257. $C_{11}H_{12}F_3NO_2S$ requires *M*, 279.2865); *m*/*z* 279 (M^+, 11%), 261 (32), and 135 (100); $\nu_{max.}$($CHCl_3$) 3 440, 1 730, and 1 590 cm^{-1}; δ_H 3.35 (1 H, m, CHS), 3.51 (1 H, br s, OH), 3.58—3.85 (4 H, complex, CH_2N and CH_2O), and 7.2—7.5 (5 H, complex, aromatic); δ_C 44.44 (CH_2OH) 128.12, 129.40, 132.51, and 132.69 (aromatic carbon), and 159.85 (CO).

Preparation of Dihydro-1,3-*oxazoles.*—The following dihydro-1,3-oxazoles were prepared by the same procedure.

2-*Phenyl*-5-*phenylthiomethyl*-4,5-*dihydro*-1,3-*oxazole* (**30**) (76%) (Found: M^+, 269.0907. $C_{16}H_{15}NOS$ requires *M*, 269.0870); $\nu_{max.}$($CHCl_3$) 1 645, 1 600, and 1 580 cm^{-1}; δ_H 3.05 (1 H, dd, *J* 14 and 7 Hz) and 3.29 (1 H, dd, *J* 14 and 6 Hz) (CH_2S), 3.86 (1 H, dd, *J* 15 and 7 Hz) and 4.13 (1 H, dd, *J* 15 and 10 Hz) (CH_2N), 4.82 (1 H, m, CHO), and 7.15—7.9 (10 H, complex, aromatic); δ_C 38.70 (CH_2S), 59.75 (CH_2N), 78.36 (CHO), 126.81, 127.06, 127.76, 128.54, 129.09, 130.48, 131.30, and 135.28 (aromatic carbon), and 163.82 (C=N). In the presence of an excess of trifluoroacetic acid *N*-(2-hydroxy-3-phenylthiopropyl)benzamide (**26**) was formed instead (see later).

2,5-*Dimethyl*-5-*phenylthiomethyl*-4,5-*dihydro*-1,3-*oxazole* (**31**) (10%) (Found: M^+, 221.0880. $C_{11}H_{13}NOS$ requires *M*, 221.0870); $\nu_{max.}$($CHCl_3$) 1 675, and 1 590 cm^{-1}; δ_H 1.45 (3 H, s, CH_3), 1.85 (3 H, s, CH_3), 3.12 (1 H, d, *J* 14 Hz) and 3.22 (1 H, d, *J* 14 Hz) (CH_2S), 3.51 (1 H, d, *J* 14 Hz) and 3.81 (1 H, d, *J* 14 Hz) (CH_2N), and 7.2—7.45 (5 H, complex, aromatic); δ_C 14.02 (CH_3), 25.45 (CH_3), 44.25 (CH_2S), 64.84 (CH_2N), 85.32 (*C*CH_3), 126.49, 128.94, 130.10, and 136.59 (aromatic carbon), and 163.97 (C=N). This (less polar) minor product, separated by chromatography from the major (more polar) product, was N-(2-*hydroxy*-2-*methyl*-3-*phenylthiopropyl*)*acetamide* (**28**) (60%) (Found: M^+, 221.0909. $C_{12}H_{17}NO_2S{\cdot}H_2O$ requires *M*, 221.0972); *m*/*z* 221 (11%), 149 (15), 112 (83), 70 (38), and 43 (100); $\nu_{max.}$($CHCl_3$) 3 450, 3 350, 1 665, and 1 590 cm^{-1}; δ_H 1.29 (3 H, s, CH_3), 2.00 (3 H, s, CH_3CO), 3.15 (2 H, s, CH_2S), 3.39 (2 H, m, CH_2N), 3.85 (1 H, br, s, OH), 6.20 (1 H, br s, NH), and 7.15—7.5 (5 H, complex, aromatic); δ_C 23.08 (CH_3), 24.93 (CH_3), 44.85 (CH_2), 48.72 (CH_2), 73.12 (COH), 126.61, 129.19, 129.94, and 136.90 (aromatic carbon), and 171.56 (CO).

2-*Phenyl*-5-*propylthiomethyl*-4,5-*dihydro*-1,3-*oxazole* (**32**) (67%) (Found: M^+, 235.1048. $C_{13}H_{17}NOS$ requires *M*, 235.1026); $\nu_{max.}$($CHCl_3$) 1 650 and 1 560 cm^{-1}; δ_H 0.96 (3 H, t, *J* 7 Hz, CH_3), 1.58 (2 H, m, C*H*$_2$ CH_3), 2.55 (2 H, t, *J* 7 Hz, CH_2S), 2.66 (1 H, dd, *J* 14 and 7 Hz) and 2.83 (1 H, dd, *J* 14 and 6 Hz) (CH_2CO), 3.82 (1 H, dd *J* 15 and 7 Hz) and 4.12 (1 H, dd, *J* 15 and 9.5 Hz) (CH_2N), 4.80 (1 H, CHO, m), 7.3—7.5 (3 H, complex, aromatic), and 7.95 (2 H, m, aromatic); δ_C 12.98 (CH_3), 22.72 (*C*H_2CH_3), 34.57 (CH_2S), 36.15 (CH_2S), 59.56 (CH_2N), 79.02 (CHO), 127.65, 127.84, 127.94, and 130.87 (aromatic carbon), and 163.19 (C=N). Further elution afforded, in low yield, the more polar N-(2-*hydroxy*-3-*propylthiopropyl*)*benzamide* (**27**) (8%), m.p. 92 °C (from ethyl acetate–light petroleum) (Found: C, 61.8; H, 7.5; N, 5.6; S, 12.6. $C_{13}H_{19}NO_2S$ requires C, 61.6; H, 7.6; N, 5.5; S, 12.6%); $\nu_{max.}$($CHCl_3$) 3 460, 3 390, and 1 655 cm^{-1}; δ_H 0.94 (3 H, t, *J* Hz, CH_3), 1.55 (2 H, m, CH_3CH_2), 2.46 (2 H, t, *J* 7 Hz, CH_2CH_2S), 2.55 (1 H, dd, *J* 14 and 8 Hz), and 2.66 (1 H, dd, *J* 14 and 5 Hz) (CH_2S), 3.41 (1 H, m) and 3.74 (1 H, m) (CH_2N), 3.90 (1 H, m, CHO), 4.26 (1 H, d, *J* 4 Hz, OH), and 7.25—7.8 (6 H, complex, aromatic and NH); δ_C 13.24 (CH_3), 22.97 (CH_3CH_2), 34.66 (CH_2CH_2S), 37.20 (CH_2S), 45.09 (CH_2N), 69.55 (CHO), 127.06, 128.44, 131.46, 134.26 (aromatic carbon), and 168.51 (CO).

5-*Methyl*-2-*phenyl*-5-*phenylthiomethyl*-4,5-*dihydro*-1,3-*oxazole* (**33**) (85%) (Found: M^+, 283.09961. $C_{17}H_{17}NOS$ requires *M*, 283.1026); $\nu_{max.}$($CHCl_3$) 1 645, 1 605, and 1 585 cm^{-1}; δ_H 1.50 (3 H, s, CH_3), 3.18 (1 H, d, *J* 14 Hz) and 3.24 (1 H, d, *J* 14 Hz) (CH_2S), 3.73 (1 H, d, *J* 15 Hz) and 4.20 (1 H, d, *J* 15 Hz) (CH_2N), and 7.1—7.85 (10 H, complex, aromatic); δ_C 25.23 (CH_3), 44.04 (CH_2S), 65.06 (CH_2N), 85.48 (*C*CH_3), 126.26, 127.98, 128.76, 129.97, 130.92, 131.02, 131.05, and 136.32 (aromatic carbon), and 162.72 (C=N).

5-*Methyl*-2-*phenyl*-5-*propylthiomethyl*-4,5-*dihydro*-1,3-*oxazole* (**34**) (78%) (Found: M^+, 249.1206. $C_{14}H_{19}NOS$ requires *M*, 249.1182); $\nu_{max.}$($CHCl_3$) 1 650, 1 610, and 1 590 cm^{-1}; δ_H 0.94 (3 H, t, *J* 7 Hz, CH_3), 1.53 (3 H, s, CH_3CO), 1.59 (2 H, m, C*H*$_2CH_3$), 2.57 (2 H, t, *J* 7 Hz, CH_2S), 2.78 (1 H, d, *J* 14 Hz) and 2.84 (1 H, d, *J* 14 Hz) (CH_2CO), 3.75 (1 H, d, *J* 15 Hz) and 4.02 (1 H, d, *J* 15 Hz) (CH_2N), and 7.35—8.00 (5 H, complex, aromatic); δ_C 13.02 (CH_3), 22.90 (*C*H_2CH_3), 25.26 (*C*H_3CO),

35.91 (CH_2S), 41.18 (CH_2S), 65.11 (CH_2N), 86.01 ($OCCH_3$), 127.45, 127.64, 127.83, and 130.18 (aromatic carbon), and 162.70 (C=N).

Preparation of Dihydro-1,3-oxazines.—The following dihydro-1,3-oxazines were prepared by the same procedure.

2-*Phenyl*-6-*phenylthiomethyl*-5,6-*dihydro*-4H-1,3-*oxazine* (**36**) (67%) (Found: M^+, 283.1091. $C_{17}H_{17}NOS$ requires M, 283.1026); $\nu_{max.}$($CHCl_3$) 1 660, 1 590, and 1 485 cm^{-1}; δ_H 1.67 (1 H, m) and 1.96 (1 H, m) (CH_2CH_2N), 3.03 (1 H, dd, J 15 Hz) and 3.23 (1 H, dd, J 15 Hz) (CH_2S), 3.47 (1 H, m) and 3.61 (1 H, m) (CH_2N), 4.27 (1 H, m, CHO), and 7.1—8.0 (10 H, complex, aromatic); δ_C 26.16 (CH_2CH_2N), 38.77 (CH_2S), 42.43 (CH_2N), 73.62 (HCO), 126.34, 126.92, 127.76, 128.91, 129.76, 130.12, 133.72, and 135.86 (aromatic carbon), and 154.92 (C=N).

2-*Methyl*-6-*phenylthiomethyl*-5,6-*dihydro*-4H-1,3-*oxazine* (**37**) (42%) (Found: M^+, 221.0942. $C_{12}H_{15}NOS$ requires M, 221.0870); $\nu_{max.}$($CHCl_3$) 1 680 and 1 590 cm^{-1}; δ_H 1.60 (1 H, m) and 1.95 (1 H, m) (CH_2CH_2N), 1.84 (3 H, s, CH_3), 2.96 (1 H, dd, J 14 and 7 Hz) and 3.17 (1 H, dd J 14 and 6 Hz) (CH_2S), 3.27 (1 H, m) and 3.37 (1 H, m) (CH_2N), 4.13 (1 H, m, CHO), and 7.13—7.43 (5 H, complex, aromatic); δ_C 21.16 (CH_3), 25.49 (CH_2CH_2N), 38.42 (CH_2S), 41.66 (CH_2N), 72.98 (CHO), 126.16, 128.68, 129.52, and 135.65 (aromatic carbon), and 156.87 (C=N).

Preparation of Pyrrolidines.—The following pyrrolidines were prepared by the same procedure.

N-*Benzoyl*-2-*phenylthiomethylpyrrolidine* (**38**) (54%), m.p. 107 °C (from ethyl acetate–light petroleum) (Found: C, 72.3; H, 6.5; N, 4.6; S, 11.0. $C_{18}H_{19}NOS$ requires C, 72.7; H, 6.4; N, 4.7; S, 10.8%); $\nu_{max.}$($CHCl_3$) 1 620 and 1 580 cm^{-1}; δ_H 1.57—2.18 (4 H, complex, $CH_2CH_2CH_2N$), 3.13 (1 H, dd, J 14 and 8 Hz) and 3.35 (1 H, m) (CH_2S), 3.42 (1 H, m) and 3.62 (1 H, dd, J 14 and 3 Hz) (CH_2N), 4.48 (1 H, m, CHN), and 7.0—7.55 (10 H, complex, aromatic); δ_C 24.81 (CH_2), 29.52 (CH_2), 35.67 (CH_2S), 50.51 (CH_2N), 56.71 (CHN), 125.47, 126.97, 127.97, 128.26, 128.76, 129.63, 132.72, and 136.94 (aromatic), and 169.80 (CO).

N-(4-*Methoxybenzoyl*)-2-*phenylthiomethylpyrrolidine* (**39**) (48%), m.p. 67—70 °C (from ethyl acetate–light petroleum) (Found: C, 69.6; H, 6.5; N, 4.2; S, 9.8. $C_{19}H_{21}NO_2S$ requires C, 69.7; H, 6.5; N, 4.3; S, 9.8%); (Found: M^+, 327.1289. $C_{19}H_{21}NO_2S$ requires M, 327.1287); $\nu_{max.}$($CHCl_3$) 1 615, 1 575, and 1 515 cm^{-1}; δ_H 1.6—2.25 (4 H, complex, $CH_2CH_2CH_2N$), 3.1—3.7 (4 H, complex, CH_2S and CH_2N), 3.78 (3 H, s, OCH_3), 4.50 (1 H, m, CHN), and 6.8—7.55 (9 H, complex, aromatic); δ_C 25.25 (CH_2), 29.71 (CH_2), 36.04 (CH_2S), 50.98 (CH_2N), 55.18 (CH_3), 57.06 (CHN), 125.57, 128.43, 128.82, and 129.08 (aromatic), 161.10 ($COCH_3$), and 169.72 (CO).

N-*Benzoyl*-4-*methyl*-2-*phenylthiomethylpyrrolidine* (**40**) (71%) (Found: M^+, 311.3700. $C_{19}H_{21}NOS$ requires M, 311.1343); $\nu_{max.}$($CHCl_3$) 1 620 and 1 585 cm^{-1}; δ_H 0.95 (3 H, two d, J 7 Hz, CH_3 of two isomers), 1.5—3.5 (7 H, complex), 4.51 (1 H, complex, CHN of two isomers), and 7.0—7.5 (10 H, complex, aromatic); δ_C 16.29 and 17.97 (CH_3), 32.01 and 33.52 ($CHCH_3$), 35.52 (CH_2), 36.50 (CH_2), 37.01 and 38.75 (CH_2), 56.36 (CHN), 57.20 (CH_2N), 57.44 (CHN), 58.15 (CH_2N), 169.61, and 169.85 (CO), and other aromatic signals.

N-[(5-*Hydroxy*-6-*phenylthio*)*hexyl*]*benzamide* (**29**).—The *amide* (**29**) was obtained from the amide (**15**); yield 60%; m.p. 78—81 °C (from ethyl acetate–light petroleum) (Found: C, 69.4; H, 7.0; N, 4.2; S, 10.1. $C_{19}H_{23}NO_2S$ requires C, 69.3; H, 7.0; N, 4.2; S, 9.7%); m/z 206 (15%) and 105 (100); δ_H 1.25—1.63 (6 H, complex, $CH_2CH_2CH_2CH_2N$), 2.88 (1 H, dd, J 13 and 8 Hz) and 2.99 (1 H, dd, J 13 and 5 Hz) (CH_2S), 3.33 (2 H, m, CH_2N), 3.66 (2 H, m, $CHOH$), and 7.05—7.8 (11 H, complex, aromatic and NH); δ_C 22.77 (CH_2), 29.23 (CH_2), 35.44 (CH_2), 39.73 (CH_2), 41.60 (CH_2), 69.48 (CHO), 126.07, 126.85, 128.22, 128.80, 129.42, 131.03, 134.61, and 135.92 (aromatic carbon), and 167.68 (CO).

Preparation of Lactones.—5-Phenylthiomethylfuran-2(3*H*)-one (**41**) was obtained in 88% yield from pent-4-enoic acid (**19**) by the same procedure. Similarly hex-5-enoic acid (**20**) afforded 6-phenylthiomethyl-3,4,5,6-tetrahydro-2-pyrone (**43**) in 84% yield. 5-Propylthiomethyl-4,5-dihydrofuran-2(3*H*)-one (**42**) was obtained in 91% yield from pent-4-enoic acid (**19**) and dipropyl disulphide (**2**). 6-Propylthiomethyl-3,4,5,6-tetrahydro-2-pyrone (**44**) was obtained in 84% yield from hex-5-enoic acid (**20**) and dipropyl disulphide (**2**). Similarly, *N*-phenylpent-4-enamide (**21**) afforded 5-phenylthiomethyl-4,5-dihydrofuran-2(3*H*)-one (**41**) in 66% yield, and *N*-butylpent-4-enamide (**22**) afforded 5-phenylthiomethyl-4,5-dihydrofuran-2(3*H*)-one (**41**) in 52% yield.

Under the same reaction conditions the acrylamide (**18**) afforded N-*benzyl*-3-*hydroxy*-2-*phenylthiopropanamide* (**45**) (45%), m.p. 85—87 °C (from ethyl acetate–light petroleum) (Found: C, 66.8; H, 6.0; N, 4.7; S, 11.3. $C_{16}H_{17}NO_2S$ requires C, 66.9; H, 5.9; N, 4.9; S, 11.1%); $\nu_{max.}$($CHCl_3$) 3 400, 3 290, 1 660, 1 605, and 1 590 cm^{-1}; δ_H 3.81—4.01 (3 H, complex, CHS and CH_2O), 4.14 (1 H, br s, OH), 4.38 (2 H, d, J 6 Hz, CH_2N), and 7.05—7.5 (11 H, complex, aromatic and NH); δ_C 43.65 (CH_2N), 53.87 (CHS), 62.95 (CH_2OH), 127.55, 128.53, 131.62, and 137.89 (aromatic carbon), and 170.44 (CO).

Preparation of Hydroxy Amides.—The following hydroxy amide was prepared by the same procedure, but with a longer reaction period (72 h) and a larger amount of trifluoroacetic acid (10 ml): N-(2-*hydroxy*-3-*phenylthiopropyl*)*benzamide* (**26**) (47%), m.p. 136 °C (from ethyl acetate–light petroleum) (Found: C, 66.8, H, 5.7; N, 4.9; S, 11.1. $C_{16}H_{17}NO_2S$ requires C, 66.9; H, 6.0; N, 4.9; S, 11.2%); $\nu_{max.}$($CHCl_3$) 3 450, 3 360, 1 655, 1 605, and 1 580 cm^{-1}; δ_H 3.03 (1 H, dd, J 13 and 7 Hz) and 3.11 (1 H, dd, J 13 and 6 Hz) (CH_2S), 3.45 (1 H, m) and 3.63 (1 H, m) (CH_2N), 3.93 (1 H, m, CHO), 5.1 (1 H, br s, OH), 7.1—7.9 (10 H, complex, aromatic), and 8.20 (1 H, s, NH); δ_C 37.06 (CH_2S), 43.93 (CH_2N), 67.84 (CHO), 124.32, 125.99, 126.81, 127.30, 127.50, 129.76, 133.31, and 135.55 (aromatic carbon), and 166.23 (CO).

2-*Methyl*-5-*phenylthiomethyl*-4,5-*dihydro*-1,3-*oxazole* (**35**).—Methanesulphonyl chloride (170 mg) was added to a stirred solution of *N*-(2-hydroxy-3-phenylthiopropyl)acetamide (**23**) (225 mg) in dry pyridine (10 ml) at 0 °C. After 1 h water (30 ml) was added and the mixture was extracted with ether (5 × 30 ml). The combined extracts were washed with aqueous saturated copper sulphate (4 × 20 ml), then with water (3 × 30 ml), dried (Na_2SO_4), and filtered. The solvent was removed under reduced pressure to afford, after column chromatography (eluant ethyl acetate), as a colourless oil, the *oxazole* (**35**) (175 mg, 84%) (Found: M^+, 207.0782. $C_{11}H_{13}NOS$ requires M, 207.0717); $\nu_{max.}$($CHCl_3$) 1 680 and 1 590 cm^{-1}; δ_H 1.90 (3 H, s, CH_3), 2.99 (1 H, dd, J 14 and 7 Hz) and 3.18 (1 H, dd, J 14 and 6 Hz) (CH_2S), 3.62 (1 H, m) and 3.88 (1 H, m) (CH_2N), 4.62 (1 H, m, CHO), and 7.2—7.45 (5 H, complex, aromatic); δ_C 13.83 (CH_3), 38.70 (CH_2S), 59.43 (CH_2N), 77.98 (CHO), 126.80, 129.08, 130.34, and 135.30 (aromatic carbon), and 164.66 (C=N).

Acknowledgements

We thank the Egyptian Educational Bureau for financial support through the Channel Scheme, and Mrs. J. Street for n.m.r. spectra.

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Received 12*th October* 1987; *Paper* 7/1822