Studies Related to Penicillins. Part XV.[1] Reactions of 2-Oxa-4,7-diazabicyclo[3.2.0]hept-3-en-6-ones with Thiols[2]

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(1*R*,5*S*)-3-Benzyl-7-(2-methylprop-1-enyl)-2-oxa-4,7-diazabicyclo[3.2.0]hept-3-en-6-one (2) is converted, probably by way of the azetinium ion (27), into a mixture of (3*R*,4*R*)-1-(2-methylprop-1-enyl)-4-methylthio-3-phenylacetamidoazetidin-2-one (7) and the (3*R*,4*S*)-isomer (17) by methanethiol in the presence of a Lewis acid. Corresponding reactions occur when the oxazoline (2) is similarly treated with ethanethiol, butane-1-thiol, butane-2-thiol, 2-methylpropane-2-thiol, prop-2-ene-1-thiol, ethane-1,2-dithiol, 2-mercaptoethyl acetate, methyl mercaptoacetate, and methyl 3-mercaptopropionate.

(1*R*,5*S*)-7-(2-Methylprop-1-enyl)-3-phenoxymethyl-2-oxa-4,7-diazabicyclo[3.2.0]hept-3-en-6-one (3) and methyl 2-{(1*R*,5*S*)-3-benzyl-6-oxo-2-oxa-4,7-diazabicyclo[3.2.0]hept-3-en-7-yl}-3-methylbut-2-enoate (4) also react with methanethiol to give mixtures of the corresponding *cis*- and *trans*-4-methylthioazetidin-2-ones.

The methylpropenyl substituents of derivatives (7) and (17) and of (3*R*,4*R*)-4-allylthio-1-(2-methylprop-1-enyl)-3-phenylacetamidoazetidin-2-one (12) and the (3*R*,4*S*)-isomer (22) are removed by treatment with either ozone–ammonium hydroxide or *N*-bromoacetamide–triethylamine.

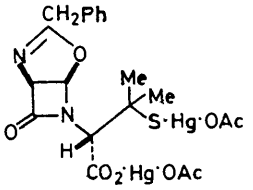
RECENTLY it was shown [3] that the salt (1), obtained from the reaction of potassium benzylpenicillinate with mercury(II) acetate, was converted into the oxazoline (2) by dimethyl sulphoxide. The derivative (2) is a potentially valuable precursor of β-lactam antibiotic

[1] Part XIV, R. J. Stoodley and N. S. Watson, *J.C.S. Perkin I*, 1974, 1632.

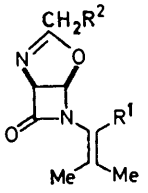
[2] Preliminary communication, D. F. Corbett, and R. J. Stoodley, *J.C.S. Chem. Comm.*, 1974, 438.

[3] R. J. Stoodley and N. R. Whitehouse, *J.C.S. Chem. Comm.*, 1973, 477; *J.C.S. Perkin I*, 1974, 181.

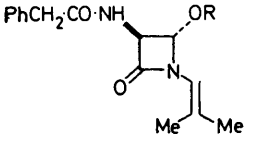
analogues if nucleophiles can be introduced at position 1 with retention of configuration. A study of the reaction of the oxazoline (2) with acidified alcohols and organic



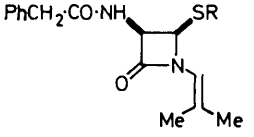
(1)



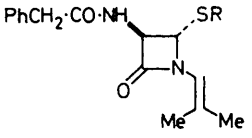
(2) $R^1 = H, R^2 = Ph$
(3) $R^1 = H, R^2 = PhO$
(4) $R^1 = MeO_2C, R^2 = Ph$



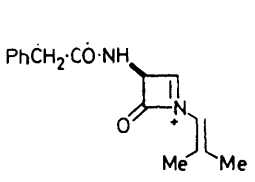
(5) R = Me
(6) R = p-$MeC_6H_4 \cdot SO_2$



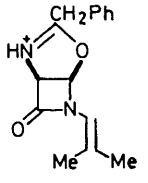
(7) R = Me
(8) R = Et
(9) R = Bu^n
(10) R = EtCH(Me)
(11) R = Bu^t
(12) R = $CH_2{:}CH{\cdot}CH_2$
(13) R = $HS{\cdot}CH_2{\cdot}CH_2$
(14) R = $AcO{\cdot}CH_2{\cdot}CH_2$
(15) R = $MeO_2C{\cdot}CH_2$
(16) R = $MeO_2C{\cdot}CH_2{\cdot}CH_2$



(17) R = Me
(18) R = Et
(19) R = Bu^n
(20) R = EtCH(Me)
(21) R = Bu^t
(22) R = $CH_2{:}CH{\cdot}CH_2$
(23) R = $HS{\cdot}CH_2{\cdot}CH_2$
(24) R = $AcO{\cdot}CH_2{\cdot}CH_2$
(25) R = $MeO_2C{\cdot}CH_2$
(26) R = $MeO_2C{\cdot}CH_2{\cdot}CH_2$



(27)



(28)

acids had demonstrated that, although the 1,2-bond is cleaved, the nucleophiles enter with inversion of configuration; for example, the *trans*-azetidinone (5) was formed with methanol in the presence of toluene-*p*-sulphonic acid.[4]

When treated with methanethiol and a trace of toluene-*p*-sulphonic acid, the oxazoline (2) afforded a more polar product (41% after silica gel chromatography) which, although it ran as a single entity on t.l.c., was shown to be a mixture (1·8 : 1) of two components by n.m.r. spectroscopy. The major component crystallised from the mixture on addition of ether; it was considered to be the *cis*-azetidinone (7) on the basis of analytical and spectroscopic evidence. Fractionation of the mother liquor (silica gel chromatography) yielded the pure minor constituent, which was considered to be the *trans*-azetidinone (17).

Under corresponding conditions the oxazoline (2) reacted with several other thiols. A mixture of the *cis*- and *trans*-azetidinones was produced in each case (Table 1).

TABLE 1

Reaction of the oxazoline (2) with thiols in the presence of toluene-*p*-sulphonic acid

Thiol	Azetidinones produced	Yield (%) [a]	Ratio (*cis* : *trans*) [b]
Ethanethiol	(8) and (18)	52	1·5 : 1
Butane-1-thiol	(9) and (19)	46	1·5 : 1
Butane-2-thiol	(10) and (20)	30	2·0 : 1
2-Methylpropane-2-thiol	(11) and (21)	20	1·5 : 1
Prop-2-ene-1-thiol	(12) and (22)	34	1·8 : 1
Ethane-1,2-dithiol	(13) and (23)	57	1·2 : 1
2-Mercaptoethyl acetate	(14) and (24)	34	1 : 1
Methyl mercaptoacetate	(15) and (25)	18	1 : 1·5
Methyl 3-mercaptopropionate	(16) and (26)	29	1 : 1·1

[a] Based upon the weight of azetidinones isolated after silica gel chromatography. [b] Estimated by n.m.r. spectroscopy.

The formation of mixtures of the *cis*- and *trans*-azetidinones may be explicable in two ways: either both products are derived from the azetinium ion (27), or else the *trans*-azetidinone is produced from the reaction of the oxazolinium ion (28) with the thiol and the *cis*-azetidinone arises by way of the tosylate (6) formed by attack of toluene-*p*-sulphonate anion on the oxazolinium ion (28). In an attempt to distinguish between these pathways, the reaction of the oxazoline (2) with methanethiol was examined further. It was established that no reaction occurred in the absence of toluene-*p*-sulphonic acid. Furthermore, the ratio of *cis*- to *trans*-azetidinone was constant throughout the reaction and was independent of the concentration of the catalyst. Consequently, the cation (27) is probably the precursor of the azetidinones.

Azetinium ions, analogous to species (27), are likely intermediates in the reactions of penicillanic acid esters [5] and anhydropenicillins [6] with chlorine, in the cyclisation,[7] equilibrations,[6,8] and solvolyses [9] of 4-chloroazetidin-2-ones, and in the degradation of penicillins with mercury(II) acetate.[3]

[4] D. F. Corbett and R. J. Stoodley, *J.C.S. Perkin I*, 1974, 185.
[5] S. Kukolja, *J. Amer. Chem. Soc.*, 1971, **93**, 6267; S. Kukolja and S. R. Lammert, *Croat. Chem. Acta*, 1972, **44**, 423.
[6] S. Wolfe, W. S. Lee, G. Kannengiesser, and J.-B. Ducep, *Canad. J. Chem.*, 1972, **50**, 2894.
[7] S. Kukolja, *J. Amer. Chem. Soc.*, 1972, **94**, 6270, 7590.
[8] S. Wolfe, J.-B. Ducep, G. Kannengiesser, and W. S. Lee, *Canad. J. Chem.*, 1972, **50**, 2902.
[9] S. Wolfe and M. P. Goeldner, *Tetrahedron Letters*, 1973, 5153.

In the hope of improving the yield of the *cis*-azetidinone (7) with respect to the *trans*-isomer (17), the influence of Lewis acids on the reaction of the oxazoline (2) with methanethiol was investigated (Table 2). Although several other types of reagent were effective in promoting the reaction, the *cis*- to *trans*-isomer ratio was less satisfactory. However, boron trifluoride–ether complex, which produced a 68% yield of equal amounts of the *cis*- and *trans*-azetidinones, gave the cleanest product.

TABLE 2

Influence of Lewis acids on the reaction of the oxazoline (2) with methanethiol

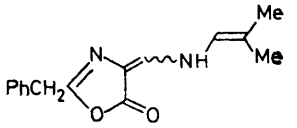
Lewis acid	Yield (%) of (7) and (17) [a]	Ratio of (7) to (17) [b]
Toluene-*p*-sulphonic acid	41	1·8 : 1
Sulphuric acid	48	1·2 : 1
Methanesulphonic acid	24	1 : 1
Boron trifluoride	68	1 : 1
Zinc chloride	57	1 : 1·5
Tin(II) chloride	65	1 : 1·5
Tin(IV) chloride	83	1 : 2·8

[a] Based upon the weight of the azetidinones isolated after silica gel chromatography. [b] Estimated by n.m.r. spectroscopy.

The reactions of the oxazoline (2) with prop-2-ene-1-thiol, 2-mercaptoethyl acetate, and methyl mercaptoacetate were re-examined with boron trifluoride–ether used as the Lewis acid. In each case, although the ratio of *cis*- to *trans*-azetidinone was less, the overall yield was improved. The oxazolinone (29), a derivative obtained previously [4] by the trifluoroacetic-acid-induced isomerisation of the oxazoline (2), was also produced in the reactions involving 2-mercaptoethyl acetate and methyl mercaptoacetate.

In order to determine the generality of the reaction of 2-oxa-4,7-diazabicyclo[3.2.0]hept-3-en-6-ones with thiols, the behaviour of compounds (3) and (4) towards methanethiol was examined briefly. In the presence of toluene-*p*-sulphonic acid, the former derivative afforded (33% after silica gel chromatography) a 1 : 2 mixture of the azetidinones (30) and (32). Under corresponding conditions the latter derivative was recovered unchanged; however, it was transformed (77% after silica gel chromatography) into a 1 : 1·3 mixture of the azetidinones (31) and (33) by boron trifluoride–ether.

The foregoing reactions are of interest in two respects. First, they illustrate that the 1,2-bonds of the oxazolines (2)—(4) can be cleaved by thiols with retention as well as with inversion of configuration; evidently the 1,2-bonds are completely cleaved to give the azetinium ions, *e.g.* (27), in these processes. By contrast, the formation of only inverted products in the reactions of the derivative (2) with alcohols and acids suggests that the nucleophilic attack is coupled with the 1,2-bond rupture. Secondly, the reactions exemplify a new general route to 1-substituted *cis*- and *trans*-3-acylamino-4-alkylthioazetidin-2-ones. The *cis*-derivatives, which are of considerable current interest,[10] have been prepared previously from



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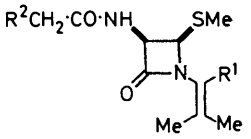
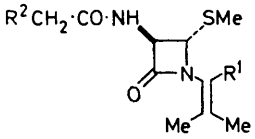
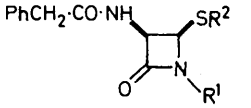


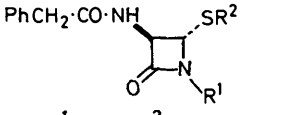
(30) R^1 = H, R^2 = PhO
(31) R^1 = MeO_2C, R^2 = Ph



(32) R^1 = H, R^2 = PhO
(33) R^1 = MeO_2C, R^2 = Ph



(34) R^1 = CHO, R^2 = Me
(35) R^1 = CHO, R^2 = CH_2:CH·CH_2
(36) R^1 = H, R^2 = Me
(37) R^1 = H, R^2 = CH_2:CH·CH_2
(38) R^1 = Me_2CBr·CH(OH), R^2 = Me



(39) R^1 = CHO, R^2 = Me
(40) R^1 = CHO, R^2 = CH_2:CH·CH_2
(41) R^1 = H, R^2 = Me
(42) R^1 = H, R^2 = CH_2:CH·CH_2
(43) R^1 = Me_2CBr·CH(OH), R^2 = Me

penicillanic acid esters,[11] penicillin esters [12] and their sulphoxides,[13] 3-hydroxypenams,[14] and a cepham,[15] and by total synthesis.[16]

If the reactions of the oxazolines (2)—(4) with thiols are to be of value in the synthesis of β-lactam antibiotic analogues, the 1-substituents of the products must be removed. Of the reagents which have been employed previously for this purpose, potassium permanganate [17] and ozone–sodium methoxide [18] appeared to hold the most promise for the present examples. Treatment of the mixture of azetidinones (7) and (17) with potassium permanganate afforded a complex array of products. However, ozonolysis of the mixture yielded two major compounds which were considered to be the formyl

[10] 'Cephalosporins and Penicillins,' ed. E. H. Flynn, Academic Press, New York, 1972; R. J. Stoodley, *Progr. Org. Chem.*, 1973, **8**, 102; J. H. C. Nayler, *Adv. Drug Res.*, 1973, **7**, 1.

[11] J. P. Clayton, J. H. C. Nayler, R. Southgate, and P. Tolliday, *Chem. Comm.*, 1971, 590; J. H. C. Nayler, M. J. Pearson, and R. Southgate, *J.C.S. Chem. Comm.*, 1973, 57.

[12] M. Yoshimoto, S. Ishihara, E. Nakayama, E. Shoji, H. Kuwano, and N. Soma, *Tetrahedron Letters*, 1972, 4387; M. Nomato, Y. Imashiro, I. Minamida, and M. Yamaoka, *ibid.*, p. 5097.

[13] D. H. R. Barton, D. G. T. Greig, G. Lucente, P. G. Sammes, M. V. Taylor, C. M. Cooper, G. Hewitt, and W. G. E. Underwood, *Chem. Comm.*, 1970, 1683; D. H. R. Barton, P. G. Sammes, M. V. Taylor, C. M. Cooper, G. Hewitt, B. E. Looker, and W. G. E. Underwood, *ibid.*, 1971, 1137; I. Ager, D. H. R. Barton, G. Lucente, and P. G. Sammes, *J.C.S. Chem. Comm.*, 1972, 601; I. Ager, D. H. R. Barton, D. G. T. Greig, G. Lucente, P. G. Sammes, M. V. Taylor, and G. H. Hewitt, B. E. Looker, A. Mowatt, C. A. Robson, and W. G. E. Underwood, *J.C.S. Perkin I*, 1973, 1187.

[14] K. Heusler, *Helv. Chim. Acta*, 1972, **55**, 388; J. C. Sheehan, D. Ben-Ishai, and J. U. Piper, *J. Amer. Chem. Soc.*, 1973, **95**, 3064; J. C. Sheehan and J. U. Piper, *J. Org. Chem.*, 1973, **38**, 3492.

[15] R. J. Stoodley and N. S. Watson, *J.C.S. Perkin I*, 1973, 2105.

[16] R. Lattrell, *Angew. Chem. Internat. Edn.*, 1973, **12**, 925.

[17] E. G. Brain, A. J. Eglington, J. H. C. Nayler, M. J. Pearson, and R. Southgate, *J.C.S. Chem. Comm.*, 1972, 229.

[18] R. D. G. Cooper and F. L. José, *J. Amer. Chem. Soc.*, 1972, **94**, 1021.

derivatives (34) and (39) on the basis of spectroscopic evidence. Although sodium methoxide failed to remove the formyl groups in a satisfactory manner, the reaction was accomplished with ammonium hydroxide by Heusler's procedure.[14] Addition of ether to the derived mixture of azetidinones (36) and (41) (18%) afforded the crystalline *cis*-isomer (36) in 7% yield; compound (36) has been described previously.[19]

The allylthioazetidinones (37) and (42) were also obtained (19% after silica gel chromatography) by treatment of a mixture of the derivatives (12) and (22) with ozone followed by ammonium hydroxide. The greater reactivity of the methylpropenyl group towards ozone presumably reflects the enamine character of the substituent.

In view of the low yields realised in the foregoing experiments, an alternative procedure for the removal of the *N*-methylpropenyl substituent was sought. A similar yield resulted when the mixture of the azetidinones (7) and (17) was treated with *N*-bromoacetamide followed by triethylamine; the mixture of azetidinones (36) and (41) was recovered in 20% yield and the crystalline *cis*-isomer (36) was isolated in 7% yield. Application of this procedure to the mixture of the allylthioazetidinones (12) and (22) was more successful and the purified mixture of azetidinones (37) and (42) was obtained in 39% yield. Although not characterised, the bromohydrins, *e.g.* (38) and (43), are evidently formed in the reactions of the azetidinones with *N*-bromoacetamide.

EXPERIMENTAL

For general experimental details see Part I.[20] Ozonisations were performed with a Wallace and Tieman Ozonator operating with an input voltage of 150 V and a flow rate of 50 l h^{-1}.

Reaction of the Oxazoline (2) *with Methanethiol.*—(*a*) *General procedure.* The oxazoline (2) [3] (0·100 g, 0·39 mmol) was treated with methanethiol (*ca.* 1 ml) and a trace of the appropriate Lewis acid at 0°. After 10 min the mixture was diluted with chloroform and washed with sodium hydrogen carbonate solution followed by water. The residue, obtained by evaporation of the dried ($MgSO_4$) organic layer, was fractionated by silica gel chromatography (benzene–ether as eluant) to give a mixture of the azetidinones (7) and (17), which ran as a single entity on t.l.c. The composition of the mixture was deduced by n.m.r. spectroscopy (see Table 1).

(*b*) The oxazoline (2) [3] (0·600 g, 2·35 mmol) was treated with methanethiol (*ca.* 3 ml) and toluene-*p*-sulphonic acid monohydrate (0·05 g, 0·26 mmol) at 0° for 1 h. Work-up and fractionation of the product [method (*a*)] yielded a 1·8 : 1 mixture of the *cis*- (7) and *trans*-azetidinones (17) (0·293 g, 41%). Addition of ether to the mixture afforded (3R,4R)-1-(2-*methylprop*-1-*enyl*)-4-*methylthio*-3-*phenylacetamidoazetidin*-2-*one* (7) (0·119 g, 17%), m.p. 120—122° (from Et_2O), $[\alpha]_D$ −19° (1·0% in $CHCl_3$), $\nu_{max.}$ (KBr) 3260 (NH), 1750 (azetidinone C=O), 1660 (amide C=O), and 1540 cm^{-1} (amide II), τ ($CDCl_3$) 8·26 (6H, s, *gem*-Me_2), 8·15 (3H, s, MeS), 6·38 (2H, s, CH_2·CO), 5·13 (1H, d, *J* 4·5 Hz, 4-H), 4·55 (1H, dd, *J* 8 and 4·5 Hz, 3-H), 4·4br (1H, s, vinylic), 3·2br (1H, d, *J* 8 Hz, NH), and 2·70 (5H, s, aromatic) [addition of D_2O caused the signal at τ 4·55 to collapse to a doublet (*J* 4·5 Hz) and that at 3·2 to disappear] (Found: C, 63·4; H, 6·5; N, 9·1%; M^+, 304. $C_{16}H_{20}N_2O_2S$ requires C, 63·2; H, 6·6; N, 9·2%; *M*, 304).

The mother liquor was refractionated by silica gel chromatography (fractions were monitored by n.m.r. spectroscopy) to give (3R,4S)-1-(2-*methylpropen*-1-*yl*)-4-*methylthio*-3-*phenylacetamidoazetidin*-2-*one* (17) (0·038 g, 5%), $[\alpha]_D$ −12° (3·0% in $CHCl_3$), $\nu_{max.}$ (film) 3300 (NH), 1760 (azetidinone C=O), 1665 (amide C=O), and 1540 cm^{-1} (amide II), τ ($CDCl_3$) 8·27 (6H, s, *gem*-Me_2), 7·92 (3H, s, MeS), 6·44 (2H, s, CH_2·CO), 5·39 (1H, dd, *J* 7·5 and 1 Hz, 3-H), 5·30 (1H, d, *J* 1 Hz, 4-H), 4·4br (1H, s, vinylic), 3·4br (1H, d, *J* 7·5 Hz, NH), and 2·73 (5H, s, aromatic) [addition of D_2O caused the signal at τ 5·39 to collapse to a doublet (*J* 1 Hz) and that at 3·4 to disappear] (Found: M^+, 304·1232. $C_{16}H_{20}N_2O_2S$ requires *M*, 304·1255).

(*c*) The oxazoline (2) [3] (0·100 g, 0·39 mmol) was treated with methanethiol (*ca.* 1 ml) and 1 or 3 mol. equiv. of toluene-*p*-sulphonic acid monohydrate for 10 min. The purified [method (*a*)] mixtures (1·9 : 1) of the azetidinones (7) and (17) were obtained in respective yields of 43 and 40%.

(*d*) The oxazoline (2) [3] (0·100 g, 0·39 mmol) was treated with methanethiol (*ca.* 1 ml) and toluene-*p*-sulphonic acid monohydrate (0·074 g, 0·39 mmol) for 0·5 min. Work-up and fractionation of the product [method (*a*)] gave a 2 : 1 mixture of the azetidinones (7) and (17) (0·051 g, 43%).

(*e*) The oxazoline (2) [3] was treated with methanethiol and boron trifluoride–ether [method (*a*)]. Work-up after 10 min and purification of the products as before gave a 1 : 1 mixture of the azetidinones (7) and (17) in 68% yield.

Reaction of the Oxazoline (2) *with Ethanethiol.*—The oxazoline (2) [3] (0·400 g, 1·56 mmol) was treated with ethanethiol (*ca.* 2 ml) and a trace of toluene-*p*-sulphonic acid monohydrate at 0°. After 45 min the mixture was diluted with ether and washed with sodium hydrogen carbonate solution followed by water. The product, obtained by evaporation of the dried ($MgSO_4$) organic layer, was fractionated by silica gel chromatography [light petroleum (b.p. 60—80°)–ethyl acetate as eluant] to give a 1·5 : 1 mixture of (3R,4R)-4-*ethylthio*-1-(2-*methylprop*-1-*enyl*)-3-*phenylacetamidoazetidin*-2-*one* (8) and the (3R,4S)-*isomer* (18) (0·256 g, 52%) as a chromatographically homogeneous syrup, $\nu_{max.}$ ($CHCl_3$) 3380 and 3260 (each NH), 1755 (azetidinone C=O), 1675 (amide C=O), and 1515 cm^{-1} (amide II), τ ($CDCl_3$) [*cis*-azetidinone (8)] 8·79 (3H, t, *J* 7·5 Hz, *Me*CH_2·S), 8·26 (6H, s, *gem*-Me_2), 7·65 (2H, q, *J* 7·5 Hz, MeCH_2·S), 6·40 (2H, s, CH_2·CO), 5·06 (1H, d, *J* 4·5 Hz, 4-H), 4·56 (1H, dd, *J* 9 and 4·5 Hz, 3-H), 4·4br (1H, s, vinylic), 2·9br (1H, d, *J* 9 Hz, NH), and 2·75 (5H, s, aromatic); *trans*-azetidinone (18) as for the *cis*-isomer except 8·90 (3H, t, *J* 7·5 Hz, *Me*CH_2·S), 7·52 (2H, q, *J* 7·5 Hz, MeCH_2·S), 6·48 (2H, s, CH_2·CO), and 5·25 (2H, m, 3- and 4-H) (Found: M^+, 318·1410. $C_{17}H_{22}N_2O_2S$ requires *M*, 318·1402).

Reaction of the Oxazoline (2) *with Butane*-1-*thiol.*—The oxazoline (2) [3] (0·275 g, 1·08 mmol) was treated with butane-1-thiol (*ca.* 1 ml) and a trace of toluene-*p*-sulphonic acid monohydrate for 1 h. Work-up and purification of the product [as described for the reaction of the oxazoline (2) with ethanethiol] gave a 1·5 : 1 mixture of (3R,4R)-4-*butylthio*-1-(2-*methylprop*-1-*enyl*)-3-*phenylacetamidoazetidin*-2-*one* (9) and the (3R,4S)-*isomer* (19) (0·169 g, 46%) as a

[19] R. D. Allan, D. H. R. Barton, M. Girijavallabhan, P. G. Sammes, and M. V. Taylor, *J.C.S. Perkin I*, 1973, 1182.
[20] I. McMillan and R. J. Stoodley, *J. Chem. Soc.* (*C*), 1968, 2533.

chromatographically homogeneous syrup, $\nu_{max.}$ ($CHCl_3$) 3430 and 3320 (each NH), 1765 (azetidinone C=O), 1685 (amide C=O), and 1520 cm^{-1} (amide II), τ ($CDCl_3$) [*cis*-azetidinone (9)] 9·3—8·4br (7H, m, $MeCH_2{\cdot}CH_2$), 8·27 (6H, s, *gem*-Me_2), 7·9—7·3 (2H, m, $CH_2{\cdot}S$), 6·40 (2H, s, $CH_2{\cdot}CO$), 5·17 (1H, d, *J* 4·5 Hz, 4-H), 4·56 (1H, dd, *J* 9 and 4·5 Hz, 3-H), 4·4br (1H, s, vinylic), 2·9br (1H, d, *J* 9 Hz, NH), and 2·72 (5H, s, aromatic); *trans*-azetidinone (19) as for the *cis*-isomer except 6·49 (2H, s, $CH_2{\cdot}CO$), 5·30 (2H, m, 3- and 4-H), and 2·76 (5H, s, aromatic) (Found: M^+, 346·1731. $C_{19}H_{26}N_2O_2S$ requires *M*, 346·1715).

Reaction of the Oxazoline (2) *with Butane-2-thiol.*—The oxazoline (2) [3] (0·250 g, 0·98 mmol) was treated with butane-2-thiol (1 ml) and a trace of toluene-*p*-sulphonic acid monohydrate for 45 min. Work-up [as described for the reaction of the oxazoline (2) with ethanethiol] and silica gel fractionation of the product (benzene–ether as eluant) afforded a 1·9 : 1 mixture of (3R,4R)-1-(2-*methylprop*-1-*enyl*)-4-(1-*methylpropylthio*)-3-*phenylacetamidoazetidin*-2-*one* (10) and the (3R,4S)-*isomer* (20) (0·097 g, 29%) as a chromatographically homogeneous syrup, $\nu_{max.}$ (film) 3320 (NH), 1755 (azetidinone C=O), 1670 (amide C=O), and 1525 cm^{-1} (amide II), τ ($CDCl_3$) [*cis*-azetidinone (10)] 8·65—8·20 (8H, m, *Et*CH*Me*), 8·28 (6H, s, *gem*-Me_2), 7·53—7·08 (1H, m, Et*CH*Me), 6·40 (2H, s, $CH_2{\cdot}CO$), 5·06 (1H, d, *J* 4·5 Hz, 4-H), 4·53 (1H, dd, *J* 8 and 4·5 Hz, 3-H), 4·4br (1H, s, vinylic), 3·3br (1H, d, *J* 8 Hz, NH), and 2·72 (5H, s, aromatic); *trans*-azetidinone (20) as for the *cis*-isomer except 6·48 (2H, s, $CH_2{\cdot}CO$), 5·36 (1H, dd, *J* 8 and 2 Hz, 3-H), 5·25 (1H, d, *J* 2 Hz, 4-H), and 2·76 (5H, s, aromatic) [addition of D_2O caused the signals at τ 5·36 and 5·06 to collapse to doublets (*J* 2 and 4 Hz, respectively) and that at 3·3 to disappear] (Found: M^+, 346·1714. $C_{19}H_{26}N_2O_2S$ requires *M*, 346·1715).

Reaction of the Oxazoline (2) *with 2-Methylpropane-2-thiol.*—The oxazoline (2) [3] (0·250 g, 0·98 mol) was treated with 2-methylpropane-2-thiol (1 ml) and a trace of toluene-*p*-sulphonic acid monohydrate for 50 min. Work-up [as described for the reaction of the oxazoline (2) with ethanethiol] and silica gel fractionation of the product (benzene–ether as eluant) gave a 1·3 : 1 mixture of (3R,4R)-4-(1,1-*dimethylethylthio*)-1-(2-*methylprop*-1-*enyl*)-3-*phenylacetamidoazetidin*-2-*one* (11) and the (3R,4S)-*isomer* (21) (0·071 g, 21%) as a chromatographically homogeneous syrup, $\nu_{max.}$ (film) 3320 (NH), 1755 (azetidinone C=O), 1670 (amide C=O), and 1535 cm^{-1} (amide II), τ ($CDCl_3$) [*cis*-azetidinone (11)] 8·86 (9H, s, Bu^t), 8·28 (6H, s, *gem*-Me_2), 6·39 (2H, s, $CH_2{\cdot}CO$), 5·06 (1H, d, *J* 4·5 Hz, 4-H), 4·51 (1H, dd, *J* 8 and 4·5 Hz, 3-H), 4·5br (1H, s, vinylic), 3·6br (1H, d, *J* 8 Hz, NH), and 2·76 (5H, s, aromatic); *trans*-azetidinone (21) 8·75 (9H, s, Bu^t), 8·28 (6H, s, *gem*-Me_2), 6·46 (2H, s, $CH_2{\cdot}CO$), 5·54 (1H, dd, *J* 8 and 2 Hz, 3-H), 5·13 (1H, d, *J* 2 Hz, 4-H), 4·5br (1H, s, vinylic), 3·4br (1H, d, *J* 8 Hz, NH), and 2·79 (5H, s, aromatic) [addition of D_2O caused the signals at τ 5·54 and 4·51 to collapse to doublets (*J* 2 and 4·5 Hz, respectively) and those at 3·6 and 3·4 to disappear] (Found: M^+, 346·1721. $C_{19}H_{26}N_2O_2S$ requires *M*, 346·1715).

Reaction of the Oxazoline (2) *with Prop-2-ene-1-thiol.*—(*a*) The oxazoline (2) [3] (0·250 g, 0·98 mmol) was treated with prop-2-ene-1-thiol (1 ml) and a trace of toluene-*p*-sulphonic acid monohydrate for 45 min. Work-up and fractionation of the product [as described for the reaction of the oxazoline (2) with methanethiol: method (*a*)] gave a 1·8 : 1 mixture of (3R,4R)-3-*allylthio*-1-(2-*methylprop*-1-*enyl*)-3-*phenylacetamidoazetidin*-2-*one* (12) and the (3R,4S)-*isomer* (22) (0·110 g, 34%) as a chromatographically homogeneous syrup, $\nu_{max.}$ (film) 3320 (NH), 1750 (azetidinone C=O), 1665 (amide C=O), and 1530 cm^{-1} (amide II), τ ($CDCl_3$) [*cis*-azetidinone (12)] 8·29 (6H, s, *gem*-Me_2), 7·05 (2H, d, *J* 7 Hz, $CH_2{\cdot}S$), 6·39 (2H, s, $CH_2{\cdot}CO$), 5·4—4·0 (6H, m, 3-H, 4-H, $CH_2{\cdot}CH$, and vinylic), 3·2br (1H, d, *J* 9 Hz, NH), and 2·7 (5H, s, aromatic); *trans*-azetidinone (22) as for the *cis*-isomer except 6·76 (2H, d, *J* 7 Hz, $CH_2{\cdot}S$) and 6·48 (2H, s, $CH_2{\cdot}CO$) (addition of D_2O caused the signal at τ 3·2 to disappear) (Found: M^+, 330·1415. $C_{18}H_{22}N_2O_2S$ requires *M*, 330·1402).

(*b*) The oxazoline (2) [3] (0·250 g, 0·98 mmol) was treated with prop-2-ene-1-thiol (1 ml) and a trace of boron trifluoride–ether complex for 15 min. Work-up and purification of the product [method (*a*)] yielded a 1 : 1·1 mixture of the azetidinones (12) and (22) (0·196 g, 61%) as a chromatographically homogeneous syrup.

Reaction of the Oxazoline (2) *with Ethane-1,2-dithiol.*—The oxazoline (2) [3] (0·300 g, 1·17 mmol) was treated with ethane-1,2-dithiol (1 ml) and a trace of toluene-*p*-sulphonic acid monohydrate for 45 min. Work-up and fractionation of the product [as described for the reaction of the oxazoline (2) with ethanethiol] gave a 1·2 : 1 mixture of (3R,4R)-4-(2-*mercaptoethylthio*)-1-(2-*methylprop*-1-*enyl*)-3-*phenylacetamidoazetidin*-2-*one* (13) and the (3R,4S)-*isomer* (23) (0·235 g, 57%) as a chromatographically homogeneous syrup, $\nu_{max.}$ ($CHCl_3$) 3370 and 3250 (each NH), 1755 (azetidinone C=O), 1675 (amide C=O), and 1510 cm^{-1} (amide II), τ ($CDCl_3$) [*cis*-azetidinone (13)] 8·26 (6H, s, *gem*-Me_2), 7·6—7·2 (4H, m, $CH_2{\cdot}CH_2{\cdot}S$), 6·40 (2H, s, $CH_2{\cdot}CO$), 5·01 (1H, d, *J* 4·5 Hz, 4-H), 4·57 (1H, dd, *J* 8 and 4·5 Hz, 3-H), 4·4br (1H, s, vinylic), and 2·70 (5H, s, aromatic); *trans*-azetidinone (23) as for the *cis*-isomer except 6·49 (2H, s, $CH_2{\cdot}CO$), 5·31 (1H, dd, *J* 8 and 1 Hz, 3-H), 5·24 (1H, d, *J* 1 Hz, 4-H), and 2·74 (5H, s, aromatic) (Found: M^+, 350·1126. $C_{17}H_{22}N_2O_2S_2$ requires *M*, 350·1123).

Reaction of the Oxazoline (2) *with 2-Mercaptoethyl Acetate.*—(*a*) The oxazoline (2) [3] (0·100 g, 0·39 mmol) was treated with 2-mercaptoethyl acetate (1 ml) and a trace of toluene-*p*-sulphonic acid monohydrate for 1 h. Work-up [as described for the reaction of the oxazoline (2) with ethanethiol] and silica gel fractionation of the product (benzene–ether as eluant) yielded a 1 : 1·5 mixture of (3R,4R)-4-(2-*acetoxyethylthio*)-1-(2-*methylprop*-1-*enyl*)-3-*phenylacetamidoazetidin*-2-*one* (14) and the (3R,4S)-*isomer* (24) (0·049 g, 34%) as a chromatographically homogeneous syrup, $\nu_{max.}$ (film) 3310 (NH), 1750 (azetidinone C=O), 1670 (amide C=O), and 1535 cm^{-1} (amide II), τ ($CDCl_3$) [*cis*-azetidinone (14)] 8·26 (6H, s, *gem*-Me_2), 8·0 (3H, s, MeCO), 7·47 (2H, t, *J* 6 Hz, CH_2OAc), 6·42 (2H, s, $CH_2{\cdot}CO$), 6·0 (2H, t, *J* 6 Hz, $CH_2{\cdot}S$), 5·06 (1H, d, *J* 4·5 Hz, 4-H), 4·66 (1H, dd, *J* 7·5 and 4·5 Hz, 3-H), 4·5br (1H, s, vinylic), 3·0br (1H, d, *J* 7·5 Hz, NH), and 2·72 (5H, s, aromatic); *trans*-azetidinone (24) as for the *cis*-isomer except 7·22 (2H, t, *J* 6 Hz, $CH_2{\cdot}OAc$), 6·49 (2H, s, $CH_2{\cdot}CO$), 5·88 (2H, t, *J* 6 Hz, $CH_2{\cdot}S$), 5·4 (1H, dd, *J* 7·5 and 2 Hz, 3-H), 5·25 (1H, d, *J* 2 Hz, 4-H), and 2·78 (5H, s, aromatic) [addition of D_2O caused the signal at τ 3·0 to disappear and those at 5·4 and 4·66 to collapse to doublets (*J* 2 and 4·5 Hz, respectively)] (Found: M^+, 376·1458. $C_{19}H_{24}N_2O_4S$ requires *M*, 376·1457).

(*b*) The oxazoline (2) [3] (0·100 g, 0·39 mmol) was treated with 2-mercaptoethyl acetate (1 ml) and a trace of boron trifluoride–ether for 30 min. Work-up and purification of the product [method (*a*)] gave two fractions, each as a chromatographically homogeneous syrup. The less polar material

(0·026 g, 26%) was identical with the oxazolinone (29) [4] (t.l.c. and n.m.r. spectroscopy). The more polar material (0·046 g, 31%) was a 1 : 2·5 mixture of the *cis*- (14) and *trans*-azetidinones (24).

Reaction of the Oxazoline (2) *with Methyl Mercaptoacetate.*—(*a*) The oxazoline (2) [3] (0·200 g, 0·78 mmol) was treated with methyl mercaptoacetate (1 ml) and a trace of toluene-*p*-sulphonic acid monohydrate for 45 min. Work-up and fractionation of the product [as described for the reaction of the oxazoline (2) with methanethiol: method (*a*)] yielded a 1 : 1·5 mixture of *methyl* α-[(2R,3R)-1-(2-*methylprop*-1-*enyl*)-4-*oxo*-3-*phenylacetamidoazetidin*-2-*ylthio*]*acetate* (15) and the (2S,3R)-*isomer* (25) (0·051 g, 18%) as a chromatographically homogeneous syrup, $\nu_{max.}$ (film) 3300 (NH), 1750 (azetidinone and ester C=O), 1655 (amide C=O), and 1530 cm^{-1} (amide II), τ ($CDCl_3$) [*cis*-azetidinone (15)] 8·31 (6H, s, *gem*-Me_2), 6·99 (2H, s, CH_2·S), 6·42 (2H, s, CH_2·CO), 6·36 (3H, s, MeO_2C), 4·90 (1H, d, *J* 4 Hz, 2-H), 4·65 (1H, dd, *J* 8 and 4 Hz, 3-H), and 2·67 (5H, s, aromatic); *trans*-azetidinone (25) as for the *cis*-isomer except 6·67 (2H, ABq, *J* 14 Hz, CH_2·S), 6·47 (2H, s, CH_2·CO), 5·35 (1H, dd, *J* 8 and 2 Hz, 3-H), 5·15 (1H, d, *J* 2 Hz, 2-H), and 2·70 (5H, s, aromatic) (Found: M^+, 362·1303. $C_{18}H_{22}N_2O_4S$ requires *M*, 362·1300).

(*b*) The oxazoline (2) [3] (0·100 g, 0·39 mmol) was treated with methyl mercaptoacetate (1 ml) and a trace of boron trifluoride–ether. Work-up and purification of the product [method (*a*)] gave two fractions, each as a chromatographically homogeneous syrup. The less polar component (0·022 g, 22%) was identical with the oxazolinone (29) [4] (t.l.c. and n.m.r. spectroscopy). The more polar material (0·056 g, 40%) was a 1 : 1·9 mixture of the *cis*- (15) and *trans*-azetidinones (25).

Reaction of the Oxazoline (2) *with Methyl* 3-*Mercaptopropionate.*—The oxazoline (2) [3] (0·250 g, 0·98 mmol) was treated with methyl 3-mercaptopropionate (1 ml) and a trace of toluene-*p*-sulphonic acid monohydrate for 45 min. Work-up [as described for the reaction of the oxazoline (2) with ethanethiol] and silica gel fractionation of the product (benzene–ether as eluant) gave a 1 : 1·1 mixture of *methyl* 3-[(2R,3R)-1-(2-*methylprop*-1-*enyl*)-4-*oxo*-3-*phenylacetamidoazetidin*-2-*ylthio*]*propionate* (16) and the (2S,3R)-*isomer* (26) (0·107 g, 29%) as a chromatographically homogeneous syrup, $\nu_{max.}$ (film) 3310 (NH), 1760 (azetidinone C=O), 1735 (ester C=O), 1655 (amide C=O), and 1525 cm^{-1} (amide II), τ ($CDCl_3$) [*cis*-azetidinone (16)] 8·28 (6H, s, *gem*-Me_2), 7·6—7·15 (4H, m, CH_2·CH_2·S), 6·39 (2H, s, CH_2·CO), 6·35 (3H, s, MeO_2C), 5·03 (1H, d, *J* 4 Hz, 2-H), 4·62 (1H, dd, *J* 8 and 4 Hz, 3-H), 4·4br (1H, s, vinylic), and 2·75br (6H, s, aromatic and NH); *trans*-azetidinone (26) as for the *cis*-isomer except 6·48 (2H, s, CH_2·CO), 5·36 (1H, dd, *J* 8 and 2 Hz, 3-H), and 5·27 (1H, d, *J* 2 Hz, 2-H) [addition of D_2O caused the signals at τ 5·36 and 4·62 to collapse to doublets (*J* 2 and 4 Hz, respectively)] (Found: M^+, 376·1455. $C_{19}H_{24}N_2O_4S$ requires *M*, 376·1457).

Reaction of the Oxazoline (3) *with Methanethiol.*—The oxazoline (3) [3] (0·250 g, 0·91 mmol) was treated with methanethiol (*ca.* 1 ml) and a trace of toluene-*p*-sulphonic acid monohydrate at 0° for 30 min. Work-up and fractionation of the product [as described for the reaction of the oxazoline (2) with methanethiol: method (*a*)] gave a 1 : 2 mixture of (3R,4R)-1-(2-*methylprop*-1-*enyl*)-4-*methylthio*-3-*phenoxyacetamidoazetidin*-2-*one* (30) and the (3R,4S)-*isomer* (32) (0·100 g, 33%) as a chromatographically homogeneous syrup, $\nu_{max.}$ (film) 3340 (NH), 1760 (azetidinone C=O), 1675 (amide C=O), and 1525 cm^{-1} (amide II), τ ($CDCl_3$) [*cis*-azetidinone (30)] 8·23 (6H, s, *gem*-Me_2), 8·02 (3H, s, MeS), 5·43 (2H, s, CH_2·CO), 5·07 (1H, d, *J* 4·5 Hz, 4-H), 4·47 (1H, dd, *J* 8 and 4·5 Hz, 3-H), 5·3br (1H, s, vinylic), and 3·2—2·4 (6H, m, aromatic H and NH); *trans*-azetidinone (32) as for the *cis*-isomer except 7·90 (3, s, MeS), 5·50 (2H, s, CH_2·CO), and 5·25—5·18 (2H, m, 3- and 4-H) (Found: M^+, 320·1213. $C_{16}H_{20}N_2O_3S$ requires *M*, 320.1195).

Reaction of the Oxazoline (4) *with Methanethiol.*—The oxazoline (4) [3] (0·200 g, 0·64 mmol) was treated with methanethiol (*ca.* 1 ml) and a trace of boron trifluoride–ether at 0° for 15 min. Work-up and fractionation of the product [as described for the reaction of the oxazoline (2) with methanethiol: method (*a*)] gave a 1 : 1·3 mixture of *methyl* 3-*methyl*-2-[(2R,3R)-2-*methylthio*-4-*oxo*-3-*phenylacetamidoazetidin*-1-*yl*]*but*-2-*enoate* (31) and the (2S,3R)-*isomer* (33) (0·177 g, 77%) as a chromatographically homogeneous syrup, $\nu_{max.}$ (film) 3300 (NH), 1760 (azetidinone C=O), 1720 (ester C=O), 1670 (amide C=O), and 1525 cm^{-1} (amide II), τ ($CDCl_3$) [*cis*-azetidinone (31)] 8·14 and 8·06 (each 3H, s, *gem*-Me_2), 7·91 (3H, s, MeS), 6·43 (2H, s, CH_2·CO), 6·32 (3H, s, MeO_2C), 4·98 (1H, d, *J* 4·5 Hz, 2-H), 4·61 (1H, dd, *J* 8 and 4·5 Hz, 3-H), 3·0 (1H, d, *J* 8 Hz, NH), and 2·80 (5H, s, aromatic); *trans*-azetidinone (32) as for the *cis*-isomer except 8·06 (6H, s, *gem*-Me_2), 7·80 (3H, s, MeS), 6·49 (2H, s, CH_2·CO), 5·18 (1H, dd, *J* 8 and 2 Hz, 3-H), 5·12 (1H, d, *J* 2 Hz, 2-H), and 2·72 (5H, s, aromatic) (Found: M^+, 262·1319. $C_{18}H_{22}N_2O_4S$ requires *M*, 362·1300).

Reaction of the Methylthioazetidinones (7) *and* (17) *with Ozone–Ammonium Hydroxide.*—A cooled (acetone–solid carbon dioxide) solution of a 1 : 1 mixture of the azetidinones (7) and (17) (0·300 g, 0·99 mmol) in dichloromethane (10 ml) was treated with ozone for 7 min. Evaporation left a syrup which was mainly a 1 : 1 mixture of (3*R*,4*R*)-1-formyl-4-methylthio-3-phenylacetamidoazetidin-2-one (34) and the (3*R*,4*S*)-isomer (39), $\nu_{max.}$ (film) 3340 (NH), 1820 (azetidinone C=O), 1710 (formyl C=O), 1685 (amide C=O), and 1515 cm^{-1} (amide II), τ ($CDCl_3$) *inter alia* 7·78 and 7·68 (each 3H, s, MeS), 6·49 and 6·45 (each 2H, s, CH_2·CO), 5·73 (1H, dd, *J* 8 and 4 Hz, 3-H of *cis*-isomer), 4·8 (1H, d, *J* 4 Hz, 4-H of *cis*-isomer), 4·8—4·7 (2H, m, 3- and 4-H of *trans*-isomer), 2·8br (12H, s, aromatic and 2 NH), and 1·32 and 1·28 (each 1H, s, CHO).

A solution of the formyl derivatives in dichloromethane (15 ml) was stirred vigorously with 0·5% ammonium hydroxide solution (15 ml). After 5 h the aqueous layer was extracted (twice) with dichloromethane and the extracts were combined with the original organic layer. Evaporation of the dried ($MgSO_4$) solution left a residue which was purified by silica gel chromatography [light petroleum (b.p. 40—60°)–ethyl acetate as eluant] to give a 1 : 1 mixture of (3*R*,4*R*)-4-methylthio-3-phenylacetamidoazetidin-2-one (36) and the (3*R*,4*S*)-isomer (41) (0·044 g, 18%) as a chromatographically homogeneous syrup, $\nu_{max.}$ (film) 3410 and 3300 (NH), 1765 (azetidinone C=O), 1675 (amide C=O), and 1510 cm^{-1} (amide II), τ ($CDCl_3$) [*cis*-azetidinone (36)] 8·15 (3H, s, MeS), 6·35 (2H, s, CH_2·CO), 5·25 (1H, d, *J* 4 Hz, 4-H), 4·5 (1H, dd, *J* 9 and 4 Hz, 3-H), 3·6br (2H, s, 2 NH), and 2·7br (5H, s, aromatic); *trans*-azetidinone (41) as for the *cis*-isomer except 7·90 (3H, s, MeS), 6·40 (2H, s, CH_2·CO), 5·37 (1H, dd, *J* 9 and 2 Hz, 3-H), 5·31 (1H, d, *J* 2 Hz, 4-H), and 3·4br (2H, s, 2 NH).

Addition of ether to the mixture afforded the *cis*-azetidinone (36) (0·016 g, 7%), m.p. 175—177° (from benzene) (lit.,[14] 187—189°), $\nu_{max.}$ (KBr) 3300 (NH), 1775 (azetidinone

C=O), 1730, 1655 (amide C=O), and 1525 cm^{-1} (amide II) (Found: M^+, 250·0769. Calc. for $C_{12}H_{14}N_2O_2S$: M, 250·0776).

Reaction of the Methylthioazetidinones (7) *and* (17) *with* N-*Bromoacetamide–Triethylamine*.—*N*-Bromoacetamide (0·300 g, 2·08 mmol) was added to a stirred solution of a 1 : 1 mixture of the azetidinones (7) and (17) (0·500 g, 1·64 mmol) in 90% aqueous acetone (10 ml). After 10 min the mixture was diluted with dichloromethane and washed (twice) with water. Evaporation of the dried ($MgSO_4$) organic layer left a residue which was dissolved in dichloromethane (10 ml) and treated with triethylamine (0·170 g, 1·68 mmol) for 20 min. The solution was then diluted with dichloromethane, washed with N-hydrochloric acid followed by water, dried ($MgSO_4$), and concentrated. Fractionation of the residue by silica gel chromatography [light petroleum (b.p. 40—60°)–ethyl acetate as eluant] gave a 1 : 1 mixture of the *cis*- (36) and *trans*-azetidinones (41) (0·082 g, 20%) as a chromatographically homogeneous syrup.

Addition of ether to the mixture afforded a crystalline material (0·030 g, 7%), which was identical with the *cis*-azetidinone (36) (t.l.c., i.r., and n.m.r. spectroscopy).

Reaction of the Allylthioazetidinones (12) *and* (22) *with Ozone–Ammonium Hydroxide*.—A cooled (acetone–solid carbon dioxide) solution of a 1 : 1 mixture of the azetidinones (12) and (22) (0·100 g, 0·30 mmol) in dichloromethane (5 ml) was treated with ozone for 1·5 min. Evaporation left a syrup which was mainly a 1 : 1 mixture of (3*R*,4*R*)-4-allylthio-1-formyl-3-phenylacetamidoazetidin-2-one (35) and the (3*R*,4*S*)-isomer (40), $\nu_{max.}$ (film) 3350 (NH), 1820 (azetidinone C=O), 1710 (formyl C=O), 1680 (amide C=O), and 1530 cm^{-1} (amide II), τ ($CDCl_3$) *inter alia* 7·0—6·0 (4H, m, 2 CH_2·S), 6·47 and 6·40 (each 2H, s, CH_2·CO), 5·68 (1H, dd, J 7 and 4 Hz, 3-H of *cis*-isomer), 5·1—4·0 (9H, m, 2 CH_2:CH, 4-H of *cis*-isomer, and 3- and 4-H of *trans*-isomer), 2·7br (10H, s, aromatic), and 1·30 and 1·25 (each 1H, s, CHO).

The mixture of the *N*-formylazetidinones was treated with ammonium hydroxide [as described for the derivatives (34) and (39)] to give a product which was fractionated by silica gel chromatography [light petroleum (b.p. 40—60°)–ethyl acetate as eluant]. The derived chromatographically homogeneous syrup (0·016 g, 19%) was a 1 : 1 mixture of (3R,4R)-4-*allylthio*-3-*phenylacetamidoazetidin*-2-*one* (37) and the (3R,4S)-*isomer* (42), $\nu_{max.}$ (film) 3290 (NH), 1765 (azetidinone C=O), 1665 (amide C=O), and 1515 cm^{-1} (amide II), τ ($CDCl_3$) [*cis*-azetidinone (37)] 7·03 (2H, d, J 7 Hz, CH_2·S) 6·46 (2H, s, CH_2·CO), 5·55—4·05 (5H, m, 3-H, 4-H, and CH_2:CH), and 3·25—2·7 (7H, m, aromatic and 2 NH); *trans*-azetidinone (42) as for the *cis*-isomer except 6·80 (2H, d, J 7 Hz, CH_2·S), and 6·54 (2H, s, CH_2·CO) (Found: M^+, 276·0946. $C_{14}H_{16}N_2O_2S$ requires M, 276·0932).

Reaction of the Allylthioazetidinones (12) *and* (22) *with* N-*Bromoacetamide–Triethylamine*.—A 1 : 1 mixture of the azetidinones (12) and (22) (0·500 g, 1·52 mmol) was treated with *N*-bromoacetamide-triethylamine [as described for derivatives (7) and (17)]. Fractionation of the product as before gave a syrup (0·162 g, 39%), which was identical with the mixture of azetidinones (37) and (42) (t.l.c. and n.m.r. spectroscopy).

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