Conversion of Secopenicillanic Acid Derivatives into β-Lactam Sulphimides and Oxazolines

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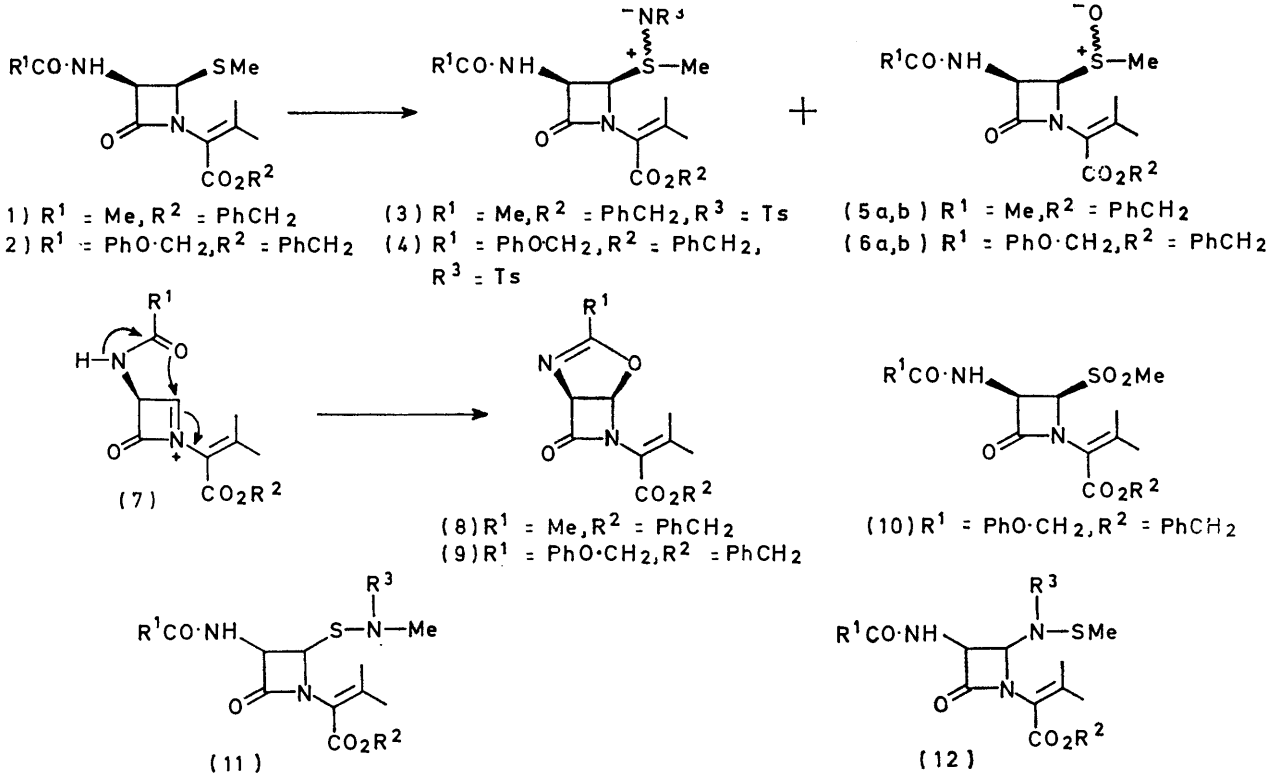
4-(Methylthio)azetidin-2-ones when treated with chloramine T gave in each case a single sulphimide enantiomer, together with both possible sulphoxides. The sulphimides were readily converted by heating, or by attempted oxidation or reduction, into β-lactam fused oxazolines. The 4-methylthio-3-(triphenylmethylamino)azetidin-2-one derivative did not undergo comparable reaction with chloramine T.

WE have recently shown [1,2] that reactions of chloramine T (*N*-chloro-*N*-sodiotoluene-*p*-sulphonamide trihydrate) with penicillins afford novel β-lactam fused heterocyclic sulphimides and rearrangement products. We now report the extension of these studies to seco-penicillins and describe the formation of new sulphimides which can readily be transformed into β-lactam fused oxazolines.



Such oxazolines have been investigated by other workers [3] and are particularly interesting as potential precursors of β-lactam antibiotic analogues.

Chloramine T reacts with sulphides to form sulphimides.[4] Accordingly, the 4-(methylthio)azetidin-2-one (1) [5] was treated with 1 mol. equiv. of chloramine T in absolute ethanol at room temperature in an attempt to form a sulphimide, but t.l.c. indicated the presence of several major products. Column chromatography afforded first the desired sulphimide (3), the structure of which was established by elemental analysis and i.r. and n.m.r. spectroscopy (τ 4·72 and 4·80, *J* 6 Hz, 3- and 4-H) (Table). The sulphimide structure, rather than one of the alternative sulphenamide structures (11) and (12) was assigned as a consequence of i.r. absorptions [6] at 1000, 1150, and 1280 cm^{-1}, and the n.m.r. chemical shifts for 3- and 4-H.† Only *one* of the possible sulphimide enantiomers, $[\alpha]_D^{20}$ −15° (*c* 1·00 in

† The signal due to 4-H in a structure related to (6), *i.e.* a 4-sulphenamido-1-(1-benzyloxycarbonyl-2-methylprop-1-enyl)-3-phenoxyacetamidoazetidin-2-one, has been recorded [7] at τ 5·01.

[1] M. M. Campbell, G. Johnson, A. F. Cameron, and I. R. Cameron, *J.C.S. Chem. Comm.*, 1974, 868.
[2] M. M. Campbell and G. Johnson, *J.C.S. Chem. Comm.*, 1974, 974.
[3] (*a*) J. C. Sheehan in 'Molecular Modifications of Drug Design.' American Chemical Society Advances in Chemistry Series, No. 45, Washington, D.C., 1964, p. 15; (*b*) E. G. Brain, A. J. Eglington, J. H. C. Nayler, M. J. Pearson, and R. Southgate, *J.C.S. Chem. Comm.*, 1972, 229; (*c*) D. H. R. Barton, F. Comer, D. G. T. Greig, P. G. Sammes, C. M. Cooper, G. Hewitt, and W. G. E. Underwood, *J. Chem. Soc.* (*C*), 1971, 3540; (*d*) R. J. Stoodley and N. R. Whitehouse, *J.C.S. Perkin I*, 1974, 181; (*e*) D. F. Corbett and R. J. Stoodley, *ibid.*, p. 185.
[4] M. M. Campbell and D. M. Evgenios, *J.C.S. Perkin I*, 1973, 2866, and references cited therein.
[5] J. P. Clayton, J. H. C. Nayler, M. J. Pearson, and R. Southgate, *J.C.S. Perkin I*, 1974, 22.
[6] W. Wucherpfennig and G. Kresse, *Tetrahedron Letters*, 1966, 1671.
[7] M. Numata, Y. Imashiro, I. Minamida, and M. Yamaoka, *Tetrahedron Letters*, 1972, 5097.

$CHCl_3$), was present in the reaction mixture.* This sulphimide (3), whose stereochemistry at sulphur remains to be determined, is probably formed from an *S*-chlorosulphonium intermediate from which chloride ion is displaced by toluene-*p*-sulphonamidate anion, possibly with inversion of configuration.

^{1}H N.m.r. data [a] (τ values)

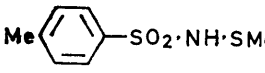
Compound	3-H	4-H	S·CH_3	S(:NTs)·CH_3	SO·CH_3	SO_2·CH_3
(1)	4·48 (5, 12, dd) [b]	4·92 (5, d)	7·96			
(2)	4·50 (5, 12, dd)	4·91 (5, d)	8·14			
(17)	4·32 (5, d)	4·70 (5, d)	7·68			
(3)	4·72 (6, d)	4·80 (6, d)		7·80 [c]		
(4)	4·37 (6, 12, dd)	4·65 (6, d)		7·70 [c]		
(18)	4·00 (5, d)	4·36 (5, d)		7·74 [c]		
(5a)	4·06 (6, 12, dd)	5·35 (6, d)			7·73	
(5b)	4·30 (6, 12, dd)	5·05 (6, dd)			7·69	
(6a)	3·76 (6, 12, dd)	5·19 (6, d)			7·63	
(6b)	4·30 (6, 12, dd)	5·00 (6, d)			7·95	
(19a)	4·21 (6, d)	5·09 (6, d)			7·70	
(19b)	4·20 (6, d)	5·26 (6, d)			7·82	
(10)	4·02 (5·5, 12, dd)	4·72 (5·5, d)				7·42

[a] See Experimental section for chemical shift data not quoted in Table. [b] *J*/Hz in parentheses. [c] CH_3·S(:NTs) signal tends to appear in the region τ 7·4—7·9 in a series of alkylsulphinides (unpublished results). The signal for the methyl group attached to sulphide, sulphimide, sulphoxide, or sulphone was consistently higher in intensity than the signals for the methyl groups of the didehydrovalinyl unit, owing to fine coupling in the latter cases. The methylthio signal of one compound (17) was identified from the n.m.r. spectrum of the [$^2H_3$]methylthio-compound, synthesised by treating benzyl 6β-tritylaminopenicillinate with CD_3I–NaOH.

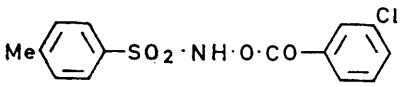
Further elution of the chloramine T reaction products afforded as a chromatographically inseparable mixture the two sulphoxide enantiomers (5a and b) in the ratio 6 : 1 as determined by n.m.r. analysis (Table). The sulphoxides are probably also derived from the *S*-chlorosulphonium species, by hydrolysis and configurational inversion. Chloramine T trihydrate supplies the necessary molecules of water. A separate experiment showed that the sulphoxides (5a and b) could also be formed from the 4-(methylthio)azetidin-2-one (1) by oxidation with *m*-chloroperbenzoic acid, but with the proportions reversed.

The sulphimide (3) was heated in dry toluene in an attempt to effect Stevens rearrangement to either (11) or (12). The major product was, however, the oxazoline (8), possibly formed as depicted. Cation intermediates such as (7) have previously been invoked [3d,e] to explain the formation of β-lactam fused oxazolines. An unstable by-product was tentatively assigned the sulphenamide structure (13) on the basis of n.m.r. spectroscopic analysis.

Attempts to oxidise (3) to a sulphoximide with *m*-chloroperbenzoic acid also afforded the oxazoline (8) as the main β-lactam product. This oxidation gave also, as a by-product, a very unstable compound whose mass



(13)

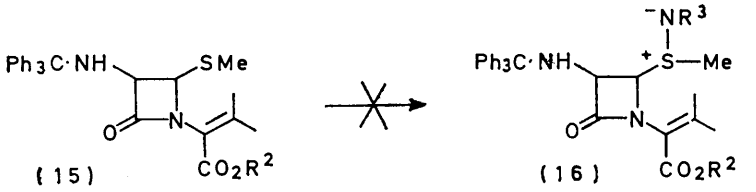


(14)

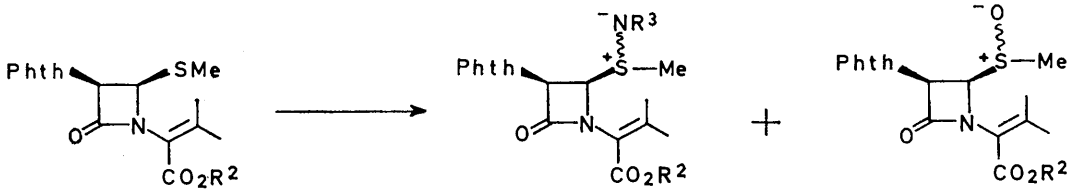
and n.m.r. spectra suggested structure (14). Hydrogenation of (3) over 10% palladium–charcoal also gave the oxazoline (8).

Other 4-(methylthio)azetidin-2-ones were treated with chloramine T. The (3*R*)-phenoxyacetamido-derivative (2) gave a chromatographically inseparable mixture of a sulphimide (4) and the enantiomeric sulphoxides (6a and b). Oxidation of the mixture with *m*-chloroperbenzoic acid followed by column chromatography afforded mainly the oxazoline (9) and the sulphone (10) derived from (6a and b).

In an attempt to determine whether the secondary amide group at C-3 was implicated in the formation of an *S*-chlorosulphonium species, and thence the sulphimide and sulphoxide products, the reaction of chloramine T with (3*R*)-tritylamino- (15) and (3*R*)-phthalimido- (17) derivatives was investigated. The (3*R*)-(tritylamino)azetidin-2-one was relatively unreactive, being recovered largely unchanged from a room temperature reaction. The (3*R*)-(phthalimido)azetidin-2-one, however, rapidly reacted giving a sulphimide (18)



(15) (16)



(17) (18) (19 a,b)

Phth = phthalimido

* *Note added in proof.* In certain subsequent experiments using a different batch of chloramine T an inseparable mixture of the sulphimide enantiomers was obtained.

together with an enantiomeric sulphoxide mixture (19a and b). It was therefore concluded that in the seco-penicillin reactions with chloramine T direct formation of an *S*-chlorosulphonium intermediate was possible, leading to the isoelectronic sulphimides and sulphoxides. In the presence of a secondary amide group at C-3 the initial formation of an *N*-chloro-, or a hydrogen-bonded chloramine T complex, could not be precluded.

EXPERIMENTAL

I.r. spectra were recorded with a Perkin-Elmer 157G grating spectrophotometer, mass spectra with A.E.I. MS 30 and MS 902 machines, and ^{1}H n.m.r. spectra with both Perkin-Elmer R12 60 MHz and JEOL JNM-MH-100 instruments for solutions in deuteriochloroform containing tetramethylsilane as internal reference. Reactions were monitored by t.l.c. on Merck Kieselgel H with ethyl acetate–light petroleum and acetone–light petroleum as solvents. Light petroleum refers to the fraction of boiling range 60—80°. M.p.s were determined with a Kofler hot-stage apparatus. Column chromatographic separations were achieved by using pressurised short-path columns with Kieselgel H (nach Stahl) type 60 as adsorbent.

Reaction of Chloramine T with (3R,4R)-3-*Acetamido*-1-(1-*benzyloxycarbonyl*-2-*methylprop*-1-*enyl*)-4-*methylthioazetidin*-2-*one* (1).—To a solution of the acetamido-derivative (1) (9·0 g, 24·8 mmol) in absolute ethanol (60 ml) was added chloramine T (7·2 g, 25·5 mmol) in absolute ethanol (40 ml). When t.l.c. indicated the absence of starting material the solution was filtered and evaporated *in vacuo* to give an oil. Chromatography on silica gel (24 g) [light petroleum–ethyl acetate (2 : 1)] afforded (3R,4R)-3-*acetamido*-1-(1-*benzyloxycarbonyl*-2-*methylprop*-1-*enyl*)-4-*methylthioazetidin*-2-*one* S-p-*tolylsulphonylimide* (3) as a solid foam (4·05 g, 30·6%), $[\alpha]_D^{20}$ −15° (*c* 1·00 in $CHCl_3$) which could not be recrystallized without decomposition; $\nu_{max.}$ (film) 1800 (β-lactam), 1740 (ester C=O), 1700 (amide C=O), 1280 (SO_2),[6] 1150 (SO_2),[6] and 1000 cm^{-1} (S=N);[6] τ ($CDCl_3$) 7·93 (6H, s), 7·80 (3H, s), 7·66 (3H, s), and 7·62 (3H, s) (5 × Me), 4·72 and 4·80 (2H, dd, *J* 6 Hz, 3- and 4-H), 4·80 (2H, s, PhCH_2), and 2·90—2·10 (10H, m, aromatic and secondary amido) (Found: C, 56·6; H, 5·8; N, 7·7; S, 12·1. $C_{25}H_{29}N_3S_2O_6$ requires C, 56·5; H, 5·5; N, 7·9; S, 12·0%).

The second product eluted was also obtained as a solid foam (3·0 g, 32%), $\nu_{max.}$ (film) 1780 (β-lactam), 1723 (ester C=O), 1680 (amide C=O), and 1070 cm^{-1} (sulphoxide),[8] shown to be a mixture of two sulphoxide isomers (5a and b) by n.m.r.: τ ($CDCl_3$) (5a) 7·9 (3H, s), 7·86 (3H, s), 7·73 (3H, s), and 7·46 (3H, s) (4 × Me), 5·35 (1H, d, *J* 7 Hz, 4-H), 4·79 (2H, m, PhCH_2), 4·06 (dd, *J* 6 and 12 Hz, 3-H), 2·74 (5H, s, *Ph*CH_2), and 2·8 and 2·3 (each 2H, d, *J* 10 Hz, tosyl aromatic); τ (5b) 7·90 (3H, s), 7·80 (3H, s), 7·69 (3H, s), 7·61 (3H, s), 5·05 (1H, d, *J* 6 Hz, 4-H), 4·83 (1H, d, *J* 12 Hz, PhCH_aH_b), 4·52 (1H, d, *J* 12 Hz, PhCH_aH_b), 4·30 (1H, dd, *J* 6 and 9 Hz, 3-H), 3·08 (1H, d, *J* 9 Hz, amide), and 2·54 (5H, s, *Ph*CH_2). The ratio of (5a) to (5b) was 6 : 1.

Oxidation of (3R,4R)-3-*Acetamido*-1-(1-*benzyloxycarbonyl*-2-*methylprop*-1-*enyl*)-4-*methylthioazetidin*-2-*one* (1) *with* m-*Chloroperbenzoic Acid*.—To a solution of the acetamido-derivative (1) (0·150 g, 0·4 mmol) in ether (10 ml) at 0° was added *m*-chloroperbenzoic acid (0·090 g, 0·5 mmol). The solution was stirred and the reaction monitored by t.l.c. The solution was washed with aqueous sodium hydrogen carbonate and water, dried ($MgSO_4$), and evaporated *in vacuo* to yield a clear oil. Preparative t.l.c. afforded a mixture of the two sulphoxide isomers (5a and b) (0·040 g) in the ratio 1 : 6 as determined by n.m.r.

Action of Heat on the Sulphimide (3).—The sulphimide (3) (0·200 g, 0·375 mmol) was refluxed in dry toluene (5 ml) for 0·3 h. The solution was chromatographed on Kieselgel (12 g) [light petroleum–ethyl acetate (2·5 : 1)], affording as the sole β-lactam product (1S,5R)-6-(1-*benzyloxycarbonyl*-2-*methylprop*-1-*enyl*)-3-*methyl*-4-*oxa*-2,6-*diazabicyclo*[3.2.0]-*hept*-2-*en*-7-*one* (8) as an oil, $[\alpha]_D^{20}$ +29° (*c* 1·00 in $CHCl_3$), $\nu_{max.}$ 1790 (β-lactam), 1730 (ester C=O), 1665 (oxazoline C=N), and 1640 cm^{-1}, τ ($CDCl_3$) 8·32 (3H, s), 8·10 (3H, s), and 7·72 (3H, s) (3 × Me), 4·93 (1H, d, *J* 3·5 Hz, 1-H or 5-H), 4·87 (2H, s, *J* 12 Hz, PhCH_2), 4·16 (1H, d, *J* 3·5 Hz, 1-H or 5-H), and 2·69 (5H, s, *Ph*CH_2) (Found: M^+, 314·1274. $C_{17}H_{18}N_2O_4$ requires *M*, 314·1267). A highly unstable by-product eluted from the column contained *p*-tolylsulphonyl and methylthio absorptions in the n.m.r. spectrum, and is tentatively assigned the sulphenamide structure (13). Its decomposition afforded toluene-*p*-sulphonamide with evolution of volatile sulphurous product(s).

(3R,4R)-1-(1-*Benzyloxycarbonyl*-2-*methylprop*-1-*enyl*)-4-*methylthio*-3-*triphenylmethylaminoazetidin*-2-*one* (15).—To a stirred suspension of benzyl (triphenylmethylamino)-penicillanate (26 g, 0·05 mol) in dry tetrahydrofuran (300 ml) were added methyl iodide (26 g, 0·19 mol) and then powdered sodium hydroxide (4 g, 0·1 mol). The mixture was stirred till it became homogeneous, and was then diluted with ethyl acetate (500 ml), washed twice with water (300 ml), dried ($MgSO_4$), and evaporated *in vacuo* to yield a dark oil (17·5 g). Chromatography afforded the *product* (15) (12·4 g). Crystallization from methanol gave a solid, m.p. 131·5—132°, $[\alpha]_D^{20}$ −38° (*c* 1·00 in $CHCl_3$), $\nu_{max.}$ (KBr) 1770 (β-lactam) and 1730 cm^{-1} (ester C=O), τ ($CDCl_3$) 8·50 (3H, s), 8·03 (3H, s), and 7·80 (3H, s) (3 × Me), 7·05br (1H, s, NH), 5·55 (2H, d, *J* 4 Hz, 3- and 4-H), 5·10 (1H, d, *J* 12 Hz, PhCH$_a$H$_b$), 4·75 (1H, d, *J* 12 Hz, PhCH_aH_b), and 3·00—2·30 (20H, m, aromatic) (Found: M^+, 562·2355. $C_{35}H_{34}N_2O_3{}^{32}S$ requires *M*, 562·2291).

(3R,4R)-3-*Amino*-1-(1-*benzyloxycarbonyl*-2-*methylprop*-1-*enyl*)-4-*methylthioazetidin*-2-*one*.—To a solution of compound (15) (10 g, 0·02 mol) in dry acetone (50 ml) at −20° was slowly added a solution of toluene-*p*-sulphonic acid (3·4 g, 0·02 mol) in dry acetone (50 ml). The solution was maintained at −15 °C for 2 h and at 5 °C for 15 h, then diluted with ethyl acetate, washed with aqueous sodium hydrogen carbonate and water, dried ($MgSO_4$), and evaporated *in vacuo* to yield a dark oil. This was shown by t.l.c. to contain only triphenylmethanol and the unstable aminoazetidinone. The oil was dissolved in dry methylene chloride and the solution divided for subsequent reactions. (The aminoazetidinone underwent ready reaction with atmospheric CO_2.)

(3R,4R)-1-(1-*Benzyloxycarbonyl*-2-*methylprop*-1-*enyl*)-4-*methylthio*-3-*phenoxyacetamidoazetidin*-2-*one* (2).—A portion of the solution prepared as described above, calculated to contain the aminoazetidinone (0·73 g, 0·002 mol), was cooled to −20 °C, and triethylamine (0·49 g, 0·005 mol) was added. Phenoxyacetyl chloride (0·4 g, 0·002 mol) in methylene chloride (20 ml) was added and the temperature was maintained at −20 °C for 1 h. The solution was

[8] L. J. Bellamy, 'Advances in Infrared Group Frequencies,' Methuen, London, 1968, pp. 191 and 220.

washed with dilute hydrochloric acid and water, dried ($MgSO_4$), and evaporated *in vacuo* to give an oil. Chromatography afforded *compound* (2) (0·63 g), which was crystallized from diethyl ether–light petroleum; m.p. 113·5—114°, $[\alpha]_D^{20}$ −13° (*c* 1·00 in $CHCl_3$), $\lambda_{max.}$ (KBr) 1765 (β-lactam), 1705 (ester C=O), and 1690 cm^{-1} (amide C=O), τ ($CDCl_3$) 8·15 (3H, s), 8·00 (3H, s), and 7·40 (3H, s) (3 × Me), 5·45 (2H, s, PhOCH_2), 4·95 (1H, d, *J* 5 Hz, 4-H), 4·84 (1H, s, PhC$H_a$$H_b$), 4·76 (1H, s, PhC$H_a$$H_b$), 4·55 (1H, dd, *J* 5 and 8·5 Hz, 3-H), and 3·20—2·50 (11H, m, aromatic and NH) (Found: M^+, 454·1570. $C_{24}H_{26}N_2O_5{}^{32}S$ requires *M*, 454·1562).

(3R,4R)-3-*Acetamido*-1-(1-*benzyloxycarbonyl*-2-*methylprop*-1-*enyl*)-4-*methylthioazetidin*-2-*one* (1).—By the procedure described above, reaction with acetyl chloride gave, as a yellow oil, *compound* (1), $[\alpha]_D^{20}$ +26° (*c* 1·00 in $CHCl_3$), $\nu_{max.}$ (film) 1775 (β-lactam), 1730 (ester C=O), and 1670 cm^{-1} (amide C=O), τ ($CDCl_3$) 8·15 (3H, s), 8·08 (3H, s), 8·05 (3H, s), and 7·81 (3H, s) (4 × Me), 5·05 (1H, d, *J* 5 Hz, 4-H), 5·04 (1H, d, *J* 12 Hz, PhC$H_a$$H_b$), 4·81 (1H, d, *J* 12 Hz, PhC$H_a$$H_b$), 4·61 (1H, dd, *J* 5 and 8 Hz, 3-H), 3·20br (1H, d, *J* 8 Hz, NH), and 2·83 (5H, s, *Ph*CH_2) (Found: M^+, 362·1293. $C_{18}H_{22}N_2O_4{}^{32}S$ requires *M*, 362·1309).

(3R,4R)-1-(1-*Benzyloxycarbonyl*-2-*methylprop*-1-*enyl*)-4-*methylthio*-3-*phthalimidoazetidin*-2-*one* (17).—To a portion of the aminoazetidinone solution was added an equimolar quantity of *N*-ethoxycarbonylphthalimide, and the solution was stirred at room temperature for 24 h, then washed with hydrochloric acid (2M), dilute sodium hydroxide (0·5M), and water. The solution was dried ($MgSO_4$) and evaporated *in vacuo* to yield an oil. Chromatography afforded *compound* (17) as a yellow oil, $[\alpha]_D^{20}$ −21° (*c* 1·00 in $CHCl_3$), $\nu_{max.}$ (film) 1785 and 1775 (β-lactam and phthalimido C=O), and 1730 and 1725 cm^{-1} (ester and phthalimido C=O), τ ($CDCl_3$) 8·14 (3H, s) and 7·68 (6H, s) (3 × Me), 4·85 (1H, d, *J* 12 Hz, PhC$H_a$$H_b$), 4·71 (1H, d, *J* 5·5 Hz, 3-H or 4-H), 4·57 (1H, d, *J* 12 Hz, PhC$H_a$$H_b$), 4·35 (1H, d, *J* 5·5 Hz, 3-H or 4-H), 2·60 (5H, s, *Ph*CH_2), and 2·18 (4H, m, phthalimide) (Found: M^+, 450·1251. $C_{24}H_{22}N_2O_5{}^{32}S$ requires *M*, 450·1249).

Oxidation of the Sulphimide (3).—The sulphimide (3) (0·250 g, 0·470 mmol) in methylene chloride (10 ml) at −10 °C was treated with *m*-chloroperbenzoic acid (0·123 g, 0·72 mmol) in cold methylene chloride (10 ml). The stirred solution was allowed to attain room temperature, filtered, and evaporated *in vacuo*, and the resultant oil chromatographed on Kieselgel [light petroleum–ethyl acetate (2·5 : 1)]. Unchanged sulphimide (0·020 g) was recovered, together with the oxazoline (8) (0·080 g, 58%). A minor product eluted as an unstable solid exhibited molecular ions in the mass spectrum at *m/e* 325 and 327 (3 : 1), τ ($CDCl_3$) 2·4—2·9 (8H, m, aromatic) and 7·60 (3H, s, tosyl CH_3), and $\nu_{max.}$ 3300 (NH) and 1710 cm^{-1} (C=O), and is tentatively assigned the hydroxylamine structure (14).

Hydrogenation of the Sulphimide (3).—The sulphimide (3) (0·050 g, 0·10 mmol) was hydrogenated at 1 atm over 10% palladium–charcoal. After 1 h, filtration, evaporation *in vacuo*, and preparative t.l.c. gave toluene-*p*-sulphonamide and the oxazoline (8) (i.r. and n.m.r.).

Reaction of Chloramine T with (3R,4R)-1-(1-*Benzyloxycarbonyl*-2-*methylprop*-1-*enyl*)-4-*methylthio*-3-*phenoxyacetamidoazetidin*-2-*one* (2).—The phenoxyacetamido-derivative (2) (2 g, 4·4 mmol) in methanol (25 ml) was treated with chloramine T (1·1 g, 3·9 mmol) in methanol. After stirring for 3 h at room temperature the solution was filtered and evaporated *in vacuo* to give an oil. Chromatography on Kieselgel (20 g) [light petroleum–ethyl acetate (2 : 1)] gave starting material (0·140 g) and fractions containing the sulphimide (4) together with the enantiomeric sulphoxides (6a and b) as an inseparable mixture (1·2 g).

In an attempt to remove the sulphoxides from the sulphimide, the mixture (400 mg) was dissolved in dry methylene chloride and cooled to 0°. *m*-Chloroperbenzoic acid (0·080 g, 0·45 mmol) was added with stirring and after 10 min the solution was filtered and evaporated *in vacuo*. The resultant oil was chromatographed on Kieselgel (6 g) [light petroleum–ethyl acetate (2 : 1)]. (1S,5R)-6-(1-*Benzyloxycarbonyl*-2-*methylprop*-1-*enyl*)-3-*phenoxymethyl*-4-*oxa*-2,6-*diazabicyclo*[3.2.0]*hept*-2-*en*-7-*one* (9) was obtained as an unstable oil (0·100 g), $\nu_{max.}$ (film) 1790 (β-lactam), 1720 (ester C=O), 1660 (C=N), and 1640 cm^{-1}, τ ($CDCl_3$) 8·18 (3H, s) and 7·75 (3H, s) (2 × Me), 5·34 (2H, s, PhOCH_2), 4·75 (2H, s, PhCH_2), 4·70 (1H, d, *J* 3 Hz, 1-H or 5-H), 3·92 (1H, d, *J* 3 Hz, 1-H or 5-H), and 3·20—2·40 (10H, m, aromatic) (Found: M^+, 406·1539. $C_{23}H_{22}N_2O_5$ requires *M*, 406·1529). The second product eluted was (3R,4R)-1-(1-*benzyloxycarbonyl*-2-*methylprop*-1-*enyl*)-4-*methylsulphonyl*-3-*phenoxyacetamidoazetidin*-2-*one* (10) (0·090 g), $\nu_{max.}$ (film) 1790 (β-lactam), 1725 (ester C=O), and 1700 cm^{-1} (amide), τ ($CDCl_3$) 7·83 (3H, s), 7·71 (3H, s), and 7·42 (3H, s) (3 × Me), 5·40 (2H, s, PhOCH_2), 4·72 (1H, d, *J* 5·5 Hz, 4-H), 4·72 (2H, dd, *J* 12 Hz, PhCH_2), 4·02 (1H, dd, *J* 5·5 and 12 Hz, 3-H), 3·10—2·40 (10H, m, aromatic), and 2·04 (1H, d, *J* 12 Hz, amide) [Found: *m/e*, 406·1528. $C_{23}H_{22}N_2O_5$ (*M* − CH_3SO_2H) requires 406·1529]. The third product eluted was a sulphoxide (6a) (0·150 g) slightly contaminated by the sulphimide (4). N.m.r. data obtained by subtraction were, for (6a): τ ($CDCl_3$) 7·76 (3H, s), 7·63 (3H, s), and 7·58 (3H, s) (3 × Me), 5·29 (2H, s, PhOCH_2), 5·19 (1H, d, *J* 6 Hz, 4-H), 4·60 (2H, t, *J* 2 Hz, PhCH_2), 3·76 (1H, dd, *J* 6 and 12 Hz, 3-H), 3·00—2·00 (10H, m, aromatic), and 0·90 (1H, d, *J* 12 Hz, amide); and for (4): τ ($CDCl_3$) 7·93 (3H, s), 7·78 (3H, s), 7·70 (3H, s), and 7·64 (3H, s) (4 × Me), 5·43 (2H, s, PhOCH_2), 4·80 (2H, dd, *J* 2 Hz, PhCH_2), 4·65 (1H, d, *J* 6 Hz, 4-H), 4·37 (1H, dd, *J* 6 and 12 Hz, 4-H), 3·20—2·20 (10H, m, aromatic), and 1·62 (1H, d, *J* 12 Hz, amide).

Attempted Reaction of (3R,4R)-1-(1-*Benzyloxycarbonyl*-2-*methylprop*-1-*enyl*)-4-*methylthio*-3-*triphenylmethylaminoazetidin*-2-*one* (15) *with Chloramine T*.—The tritylamino-derivative (15) (0·280 g, 0·50 mmol) in methanol (30 ml) was treated with chloramine T (0·140 g, 0·50 mmol) at room temperature with stirring for 2 h. No reaction was detected by t.l.c. A further 0·50 mmol of chloramine T was added but after 15 h (15) was largely unchanged. Column chromatography afforded (15) (0·200 g), together with non-β-lactams.

Reaction of (3R,4R)-1-(1-*Benzyloxycarbonyl*-2-*methylprop*-1-*enyl*)-4-*methylthio*-3-*phthalimidoazetidin*-2-*one* (17) *with Chloramine T*.—The phthalimido-derivative (17) (0·700 g, 1·55 mmol) was treated with chloramine T (0·440 g, 1·55 mmol) in methanol and the products were chromatographed and isolated as described above. Starting material (17) (0·100 g) was recovered, then (3R,4R)-1-(1-*benzyloxycarbonyl*-2-*methylprop*-1-*enyl*)-4-*methylthio*-3-*phthalimidoazetidin*-2-*one* S-p-*tolylsulphonylimide* (18) (0·150 g, 18%), $[\alpha]_D^{20}$ +5° (*c* 1·00 in $CHCl_3$), was eluted, and was obtained as an unstable oil, $\nu_{max.}$ (film) 1800 (β-lactam), 1785 (phthalimido), 1725 (ester C=O), 1390 (=N–SO_2),[6] 1143 (=N–SO_2),[6] and 990 cm^{-1} (S=N),[6] τ ($CDCl_3$) 7·74 (3H, s),

7·68 (6H, s), and 7·52 (3H, s) (4 × Me), 4·63 (2H, s, PhCH_2), 4·36 (1H, d, J 5 Hz, 3-H), 4·00 (1H, d, J 5 Hz, 4-H), and 3·00—2·00 (13H, m, aromatic). The third product eluted was a mixture of two sulphoxide enantiomers (19a and b), $\nu_{max.}$ (film) 1790vbr (β-lactam and phthalimido), 1730 (ester C=O), and 1050 cm^{-1} (sulphoxide);[8] n.m.r. data, obtained by subtraction: major isomer (19a), τ ($CDCl_3$) 7·76 (3H, s), 7·70 (3H, s), and 7·65 (3H, s) (3 × Me), 5·09 (1H, d, J 6 Hz, 4-H), 4·71 (2H, s, PhCH_2), 4·21 (1H, d, J 6 Hz, 3-H), and 2·70—1·90 (9H, m, aromatic); minor isomer (19b), 7·98 (3H, s), 7·82 (3H, s), and 7·26 (3H, s) (3 × Me), 5·26 (1H, d, J 6 Hz, 4-H), 4·71 (2H, s, PhCH_2), 4·20 (1H, d, J 6 Hz, 3-H), and 2·70—1·90 (9H, m, aromatic).

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