Transformations of Penicillins: Reactions with Chloramine T

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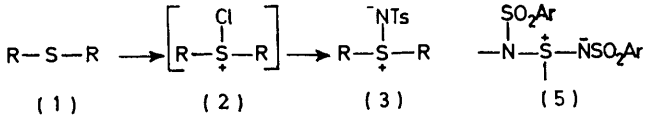
Reaction of chloramine T trihydrate with certain 6β-amidopenicillanates affords β-lactam-fused thiadiazine *S*-imides. The structure of one *S*-imide was established by *X*-ray crystallography and those of the others were deduced by spectroscopic comparison. Penicillanates lacking a secondary amide group at C-6 did not undergo comparable reaction. The β-lactam-fused heterocyclic *S*-imides were particularly stable towards a series of reactants, including oxidising and reducing reagents. Trichloroethyl 6β-phenylacetamidopenicillanate was significantly different in its reactivity towards chloramine T, affording β-lactam-fused oxazolines and a monocyclic chloroazetidinone. A by-product in these reactions was identified as *NN'*-thiobis(toluene-*p*-sulphonamide).

As part of a programme [1] aimed at developing methods of chemically modifying the thiazolidine ring of penicillins, without cleaving the β-lactam ring, we have investigated the reactions of chloramine T (sodium *N*-chlorotoluene-*p*-sulphonamidate trihydrate) with a series of 6β-substituted penicillanates. We anticipated that chloramine T would react at sulphur, affording an *S*-chlorosulphonium intermediate from which chloride ion would be displaced by toluene-*p*-sulphonamidate ion to form sulphimides † or products derived therefrom. [Reactions of chloramine T with sulphides (1) giving *S*-chlorosulphonium species (2)

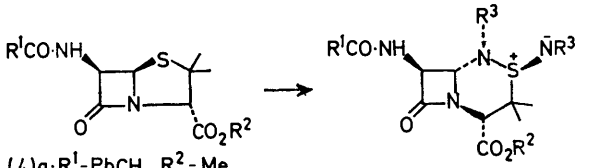
† During this investigation, the reaction of an ethoxycarbonylnitrene with a penicillin affording a transient sulphimide which rearranged to a sulphenamide was reported.[2]

[1] Preliminary report, M. M. Campbell, G. Johnson, A. F. Cameron, and I. S. Cameron, *J.C.S. Chem. Comm.*, 1974, 868.
[2] M. Numata, Y. Imashiro, I. Minamida, and M. Yamaoka, *Tetrahedron Letters*, 1972, 5097.

and thence sulphimides (3) are well established.[3] Related electrophilic reactions at sulphur in penicillins have previously been effected by the use of reagents such as

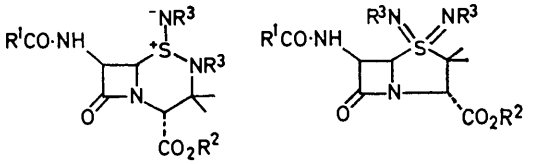


(1) (2) (3) (5)

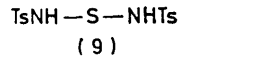


(4)a; R^1 = $PhCH_2$, R^2 = Me
b; R^1 = $PhO{\cdot}CH_2$, R^2 = Me
c; R^1 = Me, R^2 = $PhCH_2$
d; R^1 = $PhO{\cdot}CH_2$, R^2 = $PhCH_2$
e: R^1 = $PhCH_2$, R^2 = $CCl_3{\cdot}CH_2$

(6a–d) R^3 = Ts



(7) (8)



(9)

t-butyl hypochlorite,[4–6] chlorine,[7a–d] sulphuryl chloride,[7a] iodobenzene dichloride,[5,8] 1-chlorobenzotriazole,[5,8,9] and *N*-bromosuccinimide.[5,6] These reagents formed *S*-halogenosulphonium intermediates which either underwent ring opening to form halides or sulphenyl halides, or were hydrolysed during work-up to afford sulphoxides. We now report that chloramine T affords new reactions and rearrangements of penicillins leading to β-lactam-fused heterocycles.

A typical reaction involved treating a methanolic solution of the methyl penicillanate (4a) at room temperature with chloramine T (2 mol. equiv.) in methanol. Under certain conditions the major product crystallised from the solution. Elemental analysis indicated the formula $C_{31}H_{34}N_4O_8S_3$, implying incorporation of two molecules of toluene-*p*-sulphonyl 'nitrene' into the penicillin. No molecular ion was detected in the mass spectrum. The i.r. spectrum indicated a β-lactam ring (1790 cm^{-1}) and possibly the functional group (5) [10] (1360, 1168, 1150, and 990 cm^{-1}). The n.m.r. spectrum indicated a bicyclic system containing a *gem*-dimethyl system (τ 8·90 and 8·42), two tosyl units (τ 7·60), and *trans*-β-lactam protons [τ 4·70 and 4·80 ($J < 1$ Hz)]. The signal at τ 4·70 appeared as a doublet (J 6 Hz) because of coupling to the amide NH. A methine singlet was observed at τ 5·25. An extensive series of chemical reactions aimed at oxidation or reduction of the sulphimide showed the molecule to be relatively unreactive. Three closely related structures were plausible, but could not be distinguished unambiguously. An *X*-ray crystallographic structure determination was therefore undertaken, and proved the structure to be (6a) with stereochemistry as depicted. The thiadiazine ring of (6a) adopts a chair conformation with torsion angles in the range |51·2°|—|64·1°|, distorted by the presence of the heteroatoms. Atoms C-2, C-3, N-5, and C-6 form an approximately planar set, with the sulphur and the β-lactam nitrogen atoms respectively −0·965 and +0·500 Å removed from the calculated least-squares plane through the former set of four atoms. The alternative possibilities (7) and (8) were thereby excluded.

The related penicillins (4b—d) were also shown to react readily with chloramine T in methanol to give the sulphimides (6b—d). An interesting by-product was identified as *NN'*-thiobis(tosylamine) (9) by elemental and spectroscopic analysis. This unusual compound, the dihydro-derivative of a sulphodi-imide, is to our knowledge known only as its disodium salt.[11,*]

Penams lacking a secondary amide function at C-6, including methyl 6β-phthalimidopenicillanate, benzyl 6β-triphenylmethylaminopenicillanate, and methyl 6,6-dibromopenicillanate did not react under the conditions employed for (4a—d), indicating that a 6β-secondary amide is necessary for reaction. Possible mechanisms to explain the formation of (6) therefore require an *S*-chlorosulphonium intermediate (10) formed *either* by initial *N*-chlorination [8] of the secondary amide followed by stereochemically favourable intramolecular transfer of chlorine to sulphur *or* by formation of a hydrogen-bonded complex.[8] Subsequent displacement of chloride by toluene-*p*-sulphonamidate ion (which would be present in equilibrium with chloramine T and related *N*-chloro-species [3b]) would afford a sulphimide intermediate (11) or the corresponding *N*-protonated aminosulphonium compound. Ring-opening of either of those species to a cation (12) [7a,12] or (13) [13] followed by cyclisation from the

* Compound (9), formed by an alternative process, has recently been reported (G. Kresze and N. Schonberger, *Annalen*, 1974, **6**, 874).

[3] See, for example, (*a*) A. W. Johnson, 'Ylid Chemistry,' Academic Press, New York, 1966, p. 356; (*b*) K. Tsujihara, N. Furukawa, K. Oae, and S. Oae, *Bull. Chem. Soc. Japan*, 1969, **42**, 2631.

[4] J. C. Sheehan in 'Molecular Modifications of Drug Design,' Advances in Chemistry Series, No. 45, American Chemical Society, Washington, D.C., 1964, p 15.

[5] 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.

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

[7] (*a*) S. Kukolja, *J. Amer. Chem. Soc.*, 1971, **93**, 6267; (*b*) S. Kukolja and S. R. Lammert, *ibid.*, 1972, **94**, 7169; (*c*) S. Kukolja and S. R. Lammert, *Croat. Chem. Acta*, 1972, **44**, 423; (*d*) S. Wolfe, W. S. Lee, G. Kannengiesser, and J.-B. Ducep, *Canad. J. Chem.*, 1972, **50**, 2894.

[8] D. H. R. Barton, F. Comer, and P. G. Sammes, *J. Amer. Chem. Soc.*, 1969, **91**, 1529.

[9] S. Kukolja and S. R. Lammert, *Croat. Chem. Acta*, 1972, **44**, 299.

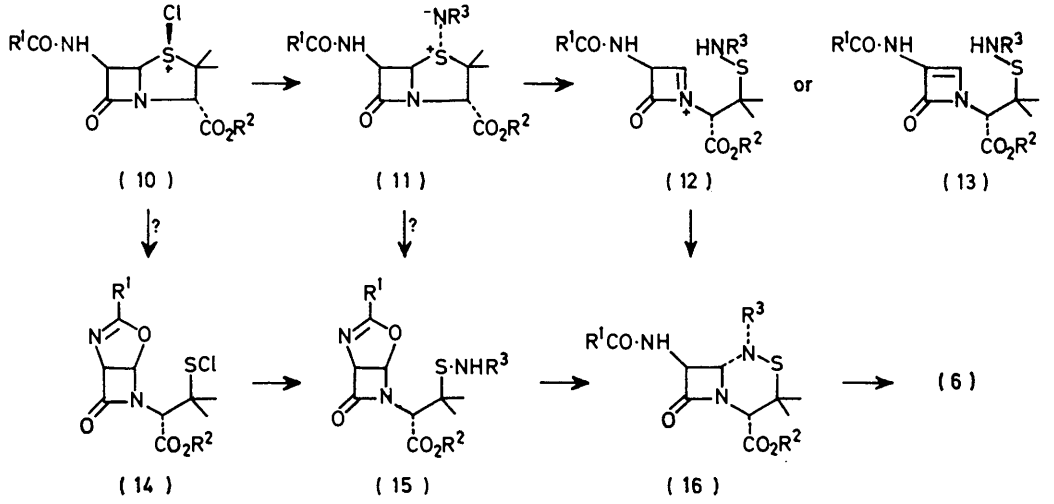
[10] (*a*) A. Kucsman, I. Kapovits, and F. Ruff, *Acta Chim. Acad. Sci. Hung.*, 1967, **54**, 153; (*b*) W. Wucherpfennig and G. Kresse, *Tetrahedron Letters*, 1966, 1671.

[11] K. Bederke, Diploma Thesis, T.U. Berlin, 1961.

[12] (*a*) R. J. Stoodley and N. R. Whitehouse, *J.C.S. Perkin I*, 1974, 181; (*b*) D. F. Corbett and R. J. Stoodley, *ibid.*, p. 185.

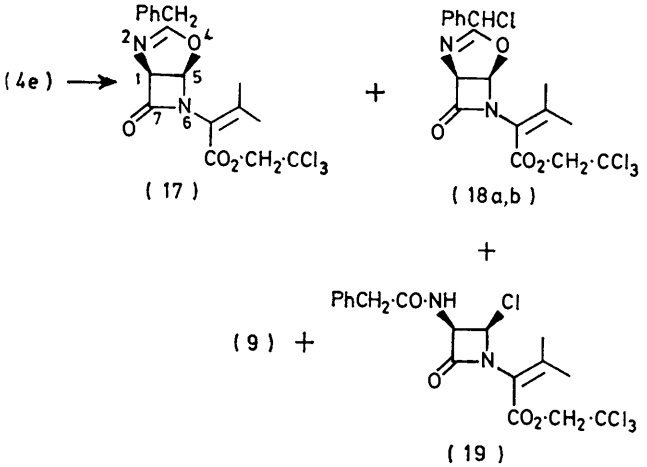
[13] (*a*) R. D. Allen, D. H. R. Barton, M. Girijavallabhan, P. G. Sammes, and M. V. Taylor, *J.C.S. Perkin I*, 1973, 1182; (*b*) R. J. Stoodley and N. S. Watson, *J.C.S. Perkin I*, 1974, 252.

α-face would afford (16). Conversion of (16) into (6) may involve displacement of chloride from an α-chlorosulphonium intermediate by toluene-*p*-sulphonamidate ion approaching from the sterically less-hindered β-face.

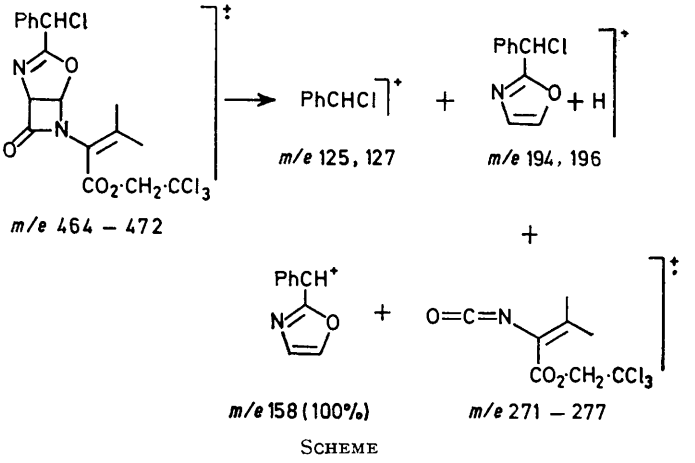


Alternative mechanisms involve the oxazolines (14) or (15) as intermediates. It is also possible that the sulphenamide group in (15) is converted by chloramine T into an *S*-imide which then cyclises to (6). We do not favour a mechanism involving Stevens rearrangement of (11) to give (16) directly. The postulated intermediates in the reactions of penicillins (4a—d) could not be isolated although a variety of reaction conditions and chromatographic techniques were investigated. Some credence for oxazoline intermediates was, however, obtained from a study of the reaction of chloramine T with (4e).

The reaction of chloramine T and (4e) in methanol was extremely complex. In methanol–acetone transesterification of (4e) giving (4a) was observed. It was then found that use of acetonitrile as solvent afforded several products the distribution of which was highly dependent



on the concentration of reactants, temperature, and reaction time. One reaction gave the oxazoline (17) together with an inseparable mixture of the diasterioisomeric α-chlorinated oxazolines (18a and b), presumably formed by benzylic chlorination of (17). The structures of (18a and b) were readily assigned by elemental analysis of the mixture, together with i.r. [1790 and 1645 cm^{-1} (β-lactam and oxazoline, respectively)], n.m.r. (*cis*-disubstituted β-lactam, α-chlorobenzyl, and trichloroethyl-αβ-didehydrovalinate functional groups) and mass



Scheme

spectrometry (Scheme). Another product was characterised as the *cis*-disubstituted chloroazetidinone (19), possibly formed by nucleophilic attack of chloride on the β-face of (6) or (16) or on an intermediate 3-tosylaminoazetidinone. The isomeric *trans*-chloride was not detected. (Related chlorides have been formed by other procedures.[7]) The final product was *NN'*-thiobis(ditosylamine) (9). No sulphimide of structure (6) was observed in any of the reactions of (4e) with chloramine T, perhaps because in an intermediate such as (15) base-catalysed elimination of *N*-tosylthiohydroxylamine is a more favourable process owing to the greater acidity of the methine proton α to the ester group. Chloramine T, an oxidising reagent,[14] would cause the thiohydroxyl-

[14] M. M. Campbell and D. M. Evgenios, *J.C.S. Perkin I*, 1973, 2866.

amine to dimerise to *NN'*-dithiobis(tosylamine), disproportionation of which could afford (9).

Our investigations of chloramine T reactions with penicillins [1] and with seco-penicillins [15] thus complement other workers' [4-9] studies on penicillin chlorosulphonium species and, in addition, have uncovered some new modes of reaction of penicillins.

EXPERIMENTAL

I.r. spectra were recorded with a Perkin-Elmer 157G spectrophotometer. Mass spectra were obtained from A.E.I. MS30 and MS902 machines. ^{1}H N.m.r. spectra were recorded on both Perkin-Elmer R12 60 MHz and JEOL JNM-MN-100 instruments for solutions in deuteriochloroform containing tetramethylsilane as internal reference. Reactions were monitored by t.l.c. on Merck Kieselgel HF_{254} with ethyl acetate–light petroleum as eluant. Light petroleum refers to the fraction of boiling range 60—80°. Column chromatographic separations were achieved by using pressurised short-path columns with Kieselgel H(nach Stahl)Typ 60 as adsorbent. M.p.s were determined with a Kofler hot-stage apparatus. Chloramine T was used in its trihydrate form. Solvents were reagent grade unless otherwise stated.

Reaction of Chloramine T with Methyl 6β-Phenylacetamidopenicillanate (4a).—To the ester (4a) (6·4 g, 20 mmol) in methanol (25 ml) was added chloramine T (11·0 g, 39 mmol) in methanol (50 ml). The solution was stirred till a heavy precipitate had formed. The precipitate was filtered off and dissolved in chloroform, leaving insoluble sodium chloride which was removed by further filtration. The filtrate was evaporated *in vacuo* affording an oil which was dissolved in ethanol and set aside to crystallise, giving white crystals of (2S,4R,6S,7S)-*methyl* 3,3-*dimethyl*-8-*oxo*-7-*phenylacetamido*-5-p-*tolylsulphonyl*-4-*thia*-1,5-*diazabicyclo*[4.2.0]*octane*-2-*carboxylate* S-p-*tolylsulphonylimide* (6a) (2·6 g), m.p. 151—152°, $[\alpha]_D^{20}$ +77° (*c* 1·00 in $CHCl_3$), $\nu_{max.}$ (KBr) 3320 (amide NH, sharp), 1790 (β-lactam C=O), 1750 (ester C=O), 1690 (amide C=O), and 1360, 1168, 1150, and 990 cm^{-1} (all *S*-tosylimide [10]) τ 8·90 and 8·42 (each 3H, s, *gem*-dimethyl), 7·60 (6H, s, two tosyl methyls), 6·40 (2H, s, $PhCH_2$), 6·20 (3H, s, OCH_3), 5·25 (1H, s, 2-H), 4·80 (1H, s, 6-H), 4·70 (1H, d, *J* 6 Hz, 7-H), and 3·30—2·00 (14H, m, aromatic and amide NH) (Found: C, 53·9; H, 5·1; N, 8·2; S, 13·7. $C_{31}H_{34}N_4O_8S_3$ requires C, 54·2; H, 5·0; N, 8·2; S, 14·0%). No attempt was made to recover additional (6a), which was shown by t.l.c. to be a major component of the mother liquors. This reaction could not be effected in acetone. Crystals of (6a) suitable for *X*-ray crystallography were obtained by slow recrystallisation from methanol–chloroform.

Reaction of Chloramine T with Methyl 6β-Phenoxyacetamidopenicillanate (4b).—The ester (4b) (3·0 g, 8·2 mmol) and chloramine T (5·1 g, 17·6 mmol) reacted in methanol and the reaction was worked up as described above. (2S,4R,6S,7S)-*methyl* 3,3-*dimethyl*-8-*oxo*-7-*phenoxyacetamido*-5-p-*tolylsulphonyl*-4-*thia*-1,5-*diazabicyclo*[4.2.0]*octane*-2-*carboxylate* S-p-*tolylsulphonylimide* (6b) was obtained as crystals (1·55 g), m.p. 141—142°, $[\alpha]_D^{20}$ +35° (*c* 1·00 in $CHCl_3$), $\nu_{max.}$ (KBr) 3400 (amide NH), 1790 (β-lactam C=O), 1750 (ester C=O), 1698 (amide C=O), and 1365, 1165, 1150, and 1010 cm^{-1} (*S*-tosylimide [10]), τ 8·84 and 8·46 (each 3H, s, *gem*-dimethyl), 7·64 (6H, s, two tosyl methyls), 6·25 (3H, s, OCH_3), 5·53 (2H, s, $PhOCH_2$), 5·29 (1H, s, 2-H), 4·70 (1H, s, 6-H), 4·65 (1H, d, *J* 10 Hz, 7-H), and 3·20—2·00 (14H, m, aromatic and amide NH) [Found: C, 52·8; H, 5·0; N, 7·9; S, 13·8%; *M* (vapour phase osmometry), 684. $C_{31}H_{34}N_4O_9S_3$ requires C, 53·0; H, 4·9; N, 8·0; S, 13·6%; *M*, 702]. No useful mass spectrum could be obtained because of thermal decomposition in the ion source.

In order to characterise the minor constituents of the reaction the crude residue (1 g) obtained from evaporation of the mother liquors was subjected to *rapid* short-path column chromatography. (Conventional column chromatography led to substantial decomposition of some of the constituents.) The first product eluted was obtained as white needles (0·06 g), m.p. 116—119°, identified as *NN'-thiobis*(*toluene*-p-*sulphonamide*) (9), $\nu_{max.}$ (KBr) 3260 (SO_2·NH), and 1365, 1300, 1165, and 1090 cm^{-1} (all Ts [10]), τ 7·60 (6H, s, two tosyl methyls), 2·75 and 2·25 (each 4H, d, *J* 10 Hz, *p*-disubstituted aromatic), and 0·00br (2H, s, NH, exchanged by D_2O), $\lambda_{max.}$ (EtOH) 230 nm (ε 17,700) (Found: C, 45·0; H, 4·5; N, 7·7; S, 25·9. $C_{14}H_{16}H_2O_4S$ requires C, 45·2; H, 4·3; N, 7·5; S, 25·8%); no molecular ion in mass spectrum. The next components eluted were toluene-*p*-sulphonamide and the starting ester (1a) (estimated quantity of ester 0·10 g) as an inseparable mixture. Further elution afforded (3*S*,4*S*)-1-(1-methoxycarbonyl-2-methylprop-2-enyl)-3-phenoxyacetamido-4-[*N*-(*p*-tolylsulphonylaminothio)-*p*-tolylsulphonylamino]azetidin-2-one [16] (0·12 g) followed by the sulphimide (6b) (0·13 g). Further elution gave a highly unstable β-lactam component (0·11 g), $\nu_{max.}$ (film) 3300 (amide NH), and 1160 and 1090 cm^{-1} (Ts), which was not characterised. Final elution of the column with acetone gave highly polar products as a dark oil (*ca.* 0·3 g) which was shown by i.r. to contain β-lactam cleaved products.

Reaction of Chloramine T with Benzyl 6β-Acetamidopenicillanate (4c).—The ester (4c) was treated in methanol with chloramine T as described above. Work-up and column chromatography gave (2*S*,4*R*,6*S*,7*S*)-benzyl 3,3-dimethyl-8-oxo-7-methylacetamido-5-*p*-tolylsulphonyl-4-thia-1,5-diazabicyclo[4.2.0]octane-2-carboxylate *S*-*p*-tolylsulphonylimide (6c) in 20% yield. No attempt was made to improve the yield by rechromatographing the mixed fractions, which were shown by t.l.c. to contain more sulphimide, $\nu_{max.}$ ($CHCl_3$) 1785 (amide C=O), 1740 (ester C=O), 1700 (amide C=O), and 1360, 1165, 1145, and 1000 cm^{-1} *S*-tosylimide [10]), τ 8·88 and 8·50 (each 3H, s, *gem*-dimethyl), 8·02 (3H, s, CH_3·CONH), 7·60 (6H, s, two tosyl methyls), 5·23 (1H, s, 2-H), 4·80 (1H, s, 6-H), 4·70 (1H, d, *J* 6 Hz, 7-H), and 3·00—2·00 (13H, m, aromatic). This compound was chromatographically unstable and could not be obtained in analytically pure form. Spectroscopic data quoted are for material slightly impure according to t.l.c.

Reaction of Chloramine T with Benzyl 6β-Phenoxyacetamidopenicillanate (4d).—Reaction in methanol, as described for (4a and b) afforded the *S*-imide (6d) in 30% yield (no attempt was made to rechromatograph mixed fractions from the column chromatography), $\nu_{max.}$ (film) 3350 (amide NH), 1795 (β-lactam C=O), 1740 (ester C=O), 1690 (amide C=O), and 1370, 1300, 1150, and 995 cm^{-1} (*S*-tosylimide [10]), τ 8·83 and 8·50 (each 3H, s, *gem*-dimethyl), 7·68 (6H, s, two tosyl methyls), 5·54 (2H, s, $PhOCH_2$), 5·20 (1H, s, 2-H), 4·82 (1H, s, 6-H), 4·60br (3H, s, 7-H and $PhCH_2$), and 3·20—2·00 (19H, aromatic and NH). This compound was of comparable instability to (4c) and could not be obtained in pure crystalline form.

[15] M. M. Campbell and G. Johnson, *J.C.S. Perkin I*, in the press.
[16] M. M. Campbell and G. Johnson, *J.C.S. Chem. Comm.*, 1974, 974; see also following paper for full characterisation.

Reaction of Chloramine T *with Trichloroethyl* 6β-*Phenylacetamidopenicillanate* (4e).—The trichloroethyl ester (4e) (1·0 g, 2·16 mmol) in methanol–acetone was treated with chloramine T (2·5 g, 8·8 mmol) in acetone and stirred at room temperature till t.l.c. indicated partial reaction. Column chromatography afforded the major product, identified as methyl 6β-phenylacetamidopenicillanate (4a) by spectroscopic comparison with an authentic sample.

The reaction was repeated in acetonitrile (4 h stirring). The solution was diluted with ethyl acetate, washed with brine, dried ($MgSO_4$), and concentrated *in vacuo*. T.l.c. indicated that the resultant oil was identical in composition with the solute. Chromatography afforded first an inseparable mixture of diastereoisomers (18a and b), (1S,5R)-3-(α-*chlorobenzyl*)-6-(2-*methyl*-1-βββ-*trichloroethoxycarbonylprop*-1-*enyl*)-4-*oxa*-2,6-*diazabicyclo*[3.2.0]*hept*-2-*en*-7-*one* (0·13 g) as an oil, $\nu_{max.}$ (mixture; film) 1790 (β-lactam C=O), 1760 (ester C=O), and 1645 cm^{-1} (oxazoline), τ (major diastereoisomer) 8·13 and 7·67 (each 3Hs, $=CMe_2$), 5·36 (1H, d, *J* 12 Hz, *H*CH·CCl_3), 5·10 (1H, d, *J* 12 Hz, HC*H*·CCl_3), 4·66 (1H, d, *J* 3·5 Hz, 5- or 1-H), 4·26 (1H, s, PhC*H*Cl), 3·72 (1H, d, *J* 3·5 Hz, 5- or 1-H), and 2·4 (5H, m, Ph); τ (minor diastereoisomer) 8·61 and 7·75 (each 3H, s, $=CMe_2$), 5·37 (1H, d, *J* 12 Hz, *H*CH·CCl_3), 5·00 (1H, d, *J* 12 Hz, HC*H*·CCl_3), 4·66 (1H, d, *J* 3·5 Hz, 5- or 1-H), 4·26 (1H, s, PhC*H*Cl), 3·68 (1H, d, *J* 3·5 Hz, 5- or 1-H), and 2·3 (5H, m, Ph) (ratio of isomers 6 : 5) (Found for mixture: C, 47·0; H, 3·5; Cl, 29·7%; N, 5·9. $C_{18}H_{16}Cl_4N_2O_4$ requires C, 46·5; H, 3·4; Cl, 30·5; N, 6·0%). In the mass spectrum a complex molecular ion region was observed because of intermolecular H-transfer in the ion source: *m/e* 465 (*M* + 1, 6%, $C_{18}H_{17}{}^{35}Cl_4N_2O_4$, 271 (16%, $C_8H_8{}^{35}Cl_3NO_3$), 194 (56%, $C_{10}H_9{}^{35}ClNO$), 158 (100%, $C_{10}H_8NO$), and 125 (70%, $C_7H_6{}^{35}Cl$).* The next compound eluted was starting material (4e) (0·20 g), followed by (1S,5R)-3-*benzyl*-6-(2-*methyl*-1-βββ-*trichloroethoxycarbonylprop*-1-*enyl*)-4-*oxa*-2,6-*diazabicyclo*[3.2.0]*hept*-2-*en*-7-*one* (17) as an oil (0·20 g), $\nu_{max.}$ (film) 1790 (β-lactam C=O), 1740 (ester C=O), and 1650 cm^{-1} (oxazoline C=N), τ 8·48 and 7·74 (each 3Hs, $=CMe_2$), 6·22 (2H, s, PhCH_2), 5·31 (1H, d, *J* 12 Hz, *H*CH·CCl_3), 4·93 (1H, d, *J* 12 Hz, HC*H*·CCl_3), 4·69 (1H, d, *J* 3·5 Hz, 5- or 1-H), 3·76 (1H, d, *J* 3·5 Hz, 5- or 1-H), and 2·55 (5H, s, Ph) (Found: M^+, 430·0286. $C_{18}H_{17}Cl_3N_2O_4$ requires *M*, 430·0254). Further elution provided (3R,4R)-4-*chloro*-1-(2-*methyl*-1-βββ-*trichloroethoxycarbonylprop*-1-*enyl*)-3-*phenylacetamidoazetidin*-2-*one* (19) as white crystals (0·10 g), m.p. 121—123°, $[\alpha]_D^{22}$ −12° (*c* 1·00 in $CHCl_3$), $\nu_{max.}$ (KBr) 3300 (amide NH), 1790 (β-lactam C=O), 1740 (ester C=O), and 1665 cm^{-1} (amide C=O), τ 7·93 and 7·63 (each 3H, s, $=CMe_2$), 6·3 (2H, s, PhCH_2), 5·30 (1Hz, d, *J* 12 Hz, *H*CH·CCl_3), 5·00 (1H, d, *J* 12 Hz, HC*H*·CCl_3), 4·31 (1H, dd, *J* 5 and 9 Hz, 3-H), 3·75 (1H, d, *J* 5 Hz, 4-H), 3·1 (1H, d, *J* 9 Hz, amide NH), and 2·50 (5H, s, Ph) (Found: C, 46·0; H, 4·0; Cl, 30·7; N, 5·8. $C_{18}H_{18}Cl_4N_2O_4$ requires C, 46·2; H, 3·9; Cl, 30·3; N, 6·0%). Subsequent fractions afforded *NN'*-thiobis-(toluene-*p*-sulphonamide) (9) (0·10 g).

The yields quoted for this experiment are not optimised; many of the chromatographic fractions contained mixtures.

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* Low resolution data.