Studies Related to Penicillins. Part XII.[1] Reactions of (1*R*,5*S*)-3-Benzyl-7-(2-methylprop-1-enyl)-2-oxa-4,7-diazabicyclo[3.2.0]hept-3-en-6-one with Alcohols and with Acids

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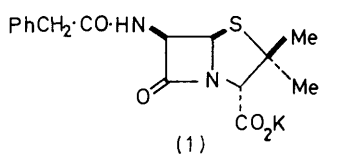
(1*R*,5*S*)-3-Benzyl-7-(2-methylprop-1-enyl)-2-oxa-4,7-diazabicyclo[3.2.0]hept-3-en-6-one (12) is converted into (3*S*,4*S*)-4-ethoxy-1-(2-methylprop-1-enyl)-3-phenylacetamidoazetidin-2-one (4) by ethanol containing toluene-*p*-sulphonic acid. The oxazoline (12) undergoes an analogous reaction with acidic methanol and with acidic 2-mercaptoethanol to give the derivatives (5) and (6), respectively. Reagent-grade chloroform and toluene-*p*-sulphonic acid transform the derivatives (12) and (4) into (2*S*)-3,3-diethoxy-*N*-(2-methylprop-1-enyl)-2-phenylacetamidopropionamide (15).

The oxazoline (12) is also converted into (3*R*,4*S*)-4-acetylthio-1-(2-methylprop-1-enyl)-3-phenylacetamidoazetidin-2-one (8) by thioacetic acid; a corresponding reaction occurs with 2-mercaptoacetic and with trifluoroacetic acid to give the derivatives (9) and (10), respectively. The azetidinone (9) rearranges to (2*R*)-*N*-(2-methylprop-1-enyl)-2-(5-oxo-1,3-oxathiolan-2-yl)-2-phenylacetamidoacetamide (16) when chromatographed on silica gel, and the azetidinone (10) yields 2-benzyl-4-[(2-methylprop-1-enyl)aminomethylene]-Δ^2-1,3-oxazolin-5-one (19) when left in the presence of trifluoroacetic acid. Derivative (19) is also obtained from *S*-chloromercurio(II)benzylpenicillenic acid (22) and dimethyl sulphoxide.

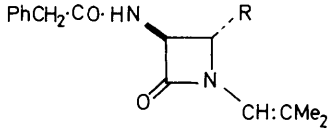
RECENTLY it was shown [2] that penicillins, *e.g.* (1) are degraded to monocyclic azetidinones, *e.g.* (2), by mercury(II) acetate in hot acetic acid. When the reaction was conducted at room temperature, the salt (11) was isolated; it was converted into the acetate (2) by hot acetic acid and into the methylpropenyl derivative (12) by dimethyl sulphoxide.[1]

The oxazoline (12) incorporates two features which render it a potentially useful precursor of β-lactam antibiotic analogues. First, it is expected to undergo ring-opening reactions in which the 1,2-bond is ruptured. If the cation (13) is an intermediate in this process, it may be possible to introduce nucleophiles at position 1 with either retention or inversion of the original configuration. Secondly, the oxazoline (12) can in principle undergo a hydrolytic cleavage of the 2,3-bond to give the azetidinol (14). We now describe the results of some attempts to achieve the first objective.

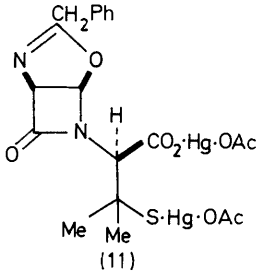
Initially, we examined the possibility of introducing a nucleophile which might subsequently be displaced. In an attempt to prepare the tosylate (3), the oxazoline (12) was treated with 1 mol. equiv. of toluene-*p*-sulphonic acid in chloroform. However, the major product was the acetal (15), identified on the basis of analytical and spectroscopic evidence [in particular, *m/e* 103·0760; $(EtO)_2CH$ requires 103·0759)]. Compound (15) is presumably formed from the reaction of the oxazoline (12) with the ethanol present in reagent-grade chloroform.



(1)



(2) R = OAc (7) R = S·CH_2·CH_2·OH
(3) R = OTs (8) R = SAc
(4) R = OEt (9) R = O_2C·CH_2·SH
(5) R = OMe (10) R = O_2C·CF_3
(6) R = O·CH_2·CH_2·SH



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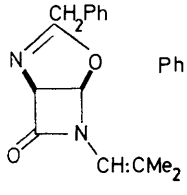

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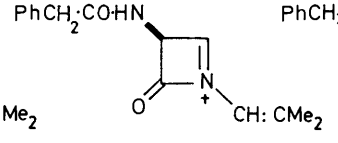

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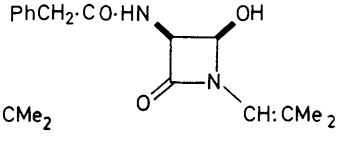


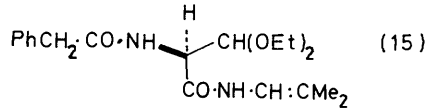
(14)

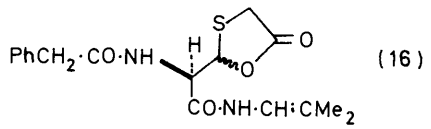
In ethanol containing a trace of toluene-*p*-sulphonic acid, the oxazoline (12) was transformed into the azetidinone (4), identified on the basis of its spectroscopic properties. The *trans* orientation of the β-lactam

[1] Part XI, R. J. Stoodley and N. R. Whitehouse, preceding paper.

[2] R. J. Stoodley and N. R. Whitehouse, *J.C.S. Perkin I*, 1973, 32.

protons was indicated[3] by their coupling constant of 1·0 Hz. The ethoxy-derivative (4) afforded the acetal (15) in the presence of chloroform and toluene-*p*-sulphonic acid; consequently, it is a likely intermediate in the first-described reaction.


(15)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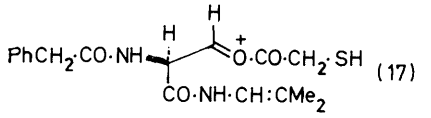
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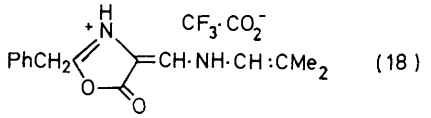
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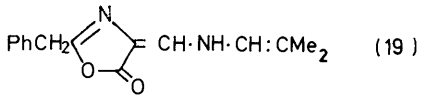
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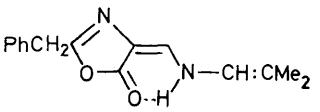
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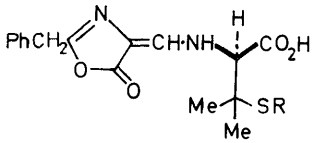
(21) R = H
(22) R = HgCl

The acid-catalysed scission of the oxazoline 1,2-bond by alcohols appears to be a general process, which proceeds with inversion of configuration at position 1. Thus, the oxazoline (12) was converted into the derivatives (5) and (6) by acidic methanol and by acidic 2-mercaptoethanol, respectively. In the latter case there was also evidence for the formation of the alcohol (7).

Previously, it was shown [1] that acetic acid also induced the fission of the 1,2-bond of the oxazoline (12) with inversion of configuration to give the acetate (2). Similar reactions occurred with thioacetic and with 2-mercaptoacetic acid to give the derivatives (8) and (9), respectively.

When chromatographed on silica gel, the thiol (9) was converted into a slightly less-polar material, which was considered to be the lactone (16) on the basis of elemental analysis and spectroscopic evidence. N.m.r. spectroscopy indicated that the lactone (16) was present as a mixture (*ca.* 1 : 1) of isomers. The isomer ratio was altered by recrystallisation and, therefore, the mixture was not at equilibrium.

The formation of the lactone (16) as a mixture of diastereoisomers, which presumably differed in the configuration at position 2 of the oxathiolan ring, can be accounted for by invoking the intermediacy of the cation (17). It is not clear why the thiol (6) does not undergo a similar reaction.

In an attempt to prepare the trifluoroacetate (10), the oxazoline (12) was treated with trifluoroacetic acid in chloroform. The product was considered to be the oxazolinium trifluoroacetate (18), on the basis of its elemental analysis, its spectroscopic properties, and its conversion into the oxazolinone (19) by sodium hydrogen carbonate. The derivative (19) showed carbonyl absorptions at 1745 and 1690 cm^{-1} and absorbed strongly at 352 nm (ε 21,200); these data are characteristic of aminoalkylideneoxazolinones.[4] N.m.r. spectroscopy indicated that the oxazolinone (19) was a mixture (*ca.* 1·4 : 1) of diastereoisomers. The major isomer was obtained in low yield when the mixture was crystallised from methanol. Its carbonyl group absorbed at 1690 cm^{-1} (*cf.* 1745 cm^{-1} for the minor isomer) and its imino proton n.m.r. signal appeared at τ 1·0 (τ 2·2 for the minor isomer). This suggested that these groups were involved in intramolecular hydrogen bonding,[5] and the major oxazolinone was thus tentatively considered to be the (*E*)-isomer (20).

With a view to providing chemical evidence in support of its structure, an attempt was made to interrelate the oxazolinone (19) and benzylpenicillenic acid (21).[6] Since it was recently shown that the salt (11) was converted into the methylpropenyl derivative (12) by dimethyl sulphoxide,[1] *S*-chloromercurio(II)benzylpenicillenic acid (22) [7] was treated in a similar manner. The oxazolinone (19) was obtained as a mixture (*ca.* 1·4 : 1) of isomers, after silica gel chromatography. In consequence, there is little doubt that the oxazoline (12) rearranges to the oxazolinone (19) in the presence of trifluoroacetic acid.

When the conversion of the oxazoline (12) into the oxazolinone (19) was followed by n.m.r. spectroscopy, an intermediate was detected. Although attempts to isolate this intermediate were unsuccessful, its n.m.r. spectrum was in accord with structure (10). It seems likely, therefore, that the first step in the rearrangement involves the formation of the trifluoroacetate (10). This proposal was supported by the observation that the acetate (2) was also converted into the oxazolinone (19) by trifluoroacetic acid.

[3] H. B. Kagan, J. J. Basselier, and J. L. Luche, *Tetrahedron Letters*, 1964, 941; J. L. Luche, H. B. Kagan, R. Parthasarathy, G. Tsoucaris, C. De Rango, and C. Zelwer, *Tetrahedron*, 1968, **24**, 275; K. D. Barrow and T. M. Spotswood, *Tetrahedron Letters*, 1965, 3325.

[4] D. C. Cook and A. Lawson, *J.C.S. Perkin I*, 1973, 465 and references therein.

[5] G. C. Pimentel and A. L. McClennan, ' The Hydrogen Bond,' W. H. Freeman and Co., London, 1960.

[6] R. L. Peck and K. Folkers in ' The Chemistry of Penicillins,' eds. H. T. Clarke, J. R. Johnson, and R. Robinson, Princeton University Press, Princeton, New Jersey, 1949, p. 161.

[7] B. B. Levine, *Arch. Biochem. Biophys.*, 1961, **93**, 50.

EXPERIMENTAL

For general experimental details see Part I.[8]

(2S)-3,3-*Diethoxy*-N-(2-*methylprop*-1-*enyl*)-2-*phenylacetamidopropionamide* (15).—(*a*) A solution of the oxazoline (12) [1] (0·102 g, 0·4 mmol) in chloroform (3 ml) was stirred with toluene-*p*-sulphonic acid (0·069 g, 0·4 mmol). After 5 min the solution was diluted with chloroform, washed with sodium hydrogen carbonate solution followed by water, and dried ($MgSO_4$). Evaporation left a residue (0·110 g), which was purified by silica gel chromatography (benzene–ether as eluant) to give the *amide* (15) (0·046 g, 33%), m.p. 138—140° (from benzene–ether), $[\alpha]_D$ +7° (1% in $CHCl_3$), $\nu_{max.}$ (KBr) 3270 (NH) and 1650sh and 1635 cm^{-1} (each amide C=O), $\lambda_{max.}$ (EtOH) 237 nm (ε 9000), τ ($CDCl_3$) 8·95 and 8·78 (each 3H, t, *J* 8 Hz, *Me*CH_2), 8·40 and 8·29 (each 3H, s, *gem*-Me_2), 6·72—6·02 (4H, m, 2CH_2Me), 6·35 (2H, s, CH_2·CO), 5·4 (1H, dd, *J* 7 and 3 Hz, 2-H), 5·15 (1H, d, *J* 3 Hz, 3-H), 3·45br (1H, d, *J* 11 Hz, vinylic proton), 3·35br (1H, d, *J* 7 Hz, NH), 2·6 (5H, s, aromatic protons), and 1·75br (1H, d, *J* 11 Hz, NH) [addition of deuterium oxide caused the signal at τ 5·4 to collapse to a doublet (*J* 3 Hz), that at 3·45 to collapse to a singlet, and those at 3·35 and 1·75 to disappear] [Found: C, 65·3; H, 8·0; N, 8·1%; *M* (mass spectrum), 348. $C_{19}H_{28}N_2O_4$ requires C, 65·5; H, 8·1; N, 8·1%; *M*, 348].

(*b*) A solution of the ethoxy-derivative (4) (0·100 g, 0·33 mmol) (prepared by the method described below) was treated with toluene-*p*-sulphonic acid, as in procedure (*a*). Work-up gave the acetal (15) (0·077 g, 67%), m.p. 138—140° (from benzene–ether).

Reaction of the Oxazoline (12) *with Ethanol.*—The oxazoline (12) [1] (0·255 g, 1 mmol) was dissolved in ethanol (10 ml) and a trace of toluene-*p*-sulphonic acid was added. Work-up after 30 min gave a syrup (0·260 g), which was purified by silica gel chromatography (benzene–ether as eluant) to give (3S,4S)-4-*ethoxy*-1-(2-*methylprop*-1-*enyl*)-3-*phenylacetamidoazetidin*-2-*one* (4) (0·120 g, 40%), $\nu_{max.}$ (film) 3260 (NH), 1750 (azetidinone C=O), and 1655 cm^{-1} (amide C=O), τ ($CDCl_3$) 8·77 (3H, t, *J* 7 Hz, *Me*CH_2), 8·25 and 8·23 (each 3H, s, *gem*-Me_2), 6·55—6·07 (2H, m, CH_2Me), 6·43 (2H, s, CH_2·CO), 5·38 (1H, dd, *J* 7 and 1 Hz, 3-H), 5·01 (1H, d, *J* 1 Hz, 4-H), 4·2br (1H, s, vinylic proton), 3·4br (1H, d, *J* 7 Hz, NH), and 2·65 (5H, s, aromatic protons) [addition of deuterium oxide caused the signal at τ 5·41 to collapse to a doublet (*J* 1 Hz) and that at 3·4 to disappear] [Found: *M* (mass spectrum), 302·1644. $C_{17}H_{22}N_2O_3$ requires *M*, 302·1630].

Reaction of the Oxazoline (12) *with Methanol.*—The oxazoline (12) [1] (0·102 g, 0·4 mmol) was dissolved in methanol (3 ml) and a trace of toluene-*p*-sulphonic acid was added. Work-up after 30 min gave a syrup (0·100 g), which was fractionated by silica gel chromatography (benzene–ether as eluant) to give (3S,4S)-4-*methoxy*-1-(2-*methylprop*-1-*enyl*)-3-*phenylacetamidoazetidin*-2-*one* (5) (0·036 g, 31%), $\nu_{max.}$ (film) 3260 (NH), 1750 (azetidinone C=O), and 1655 cm^{-1} (amide C=O), τ ($CDCl_3$) 8·23 and 8·20 (each 3H, s, *gem*-Me_2), 6·45 (3H, s, MeO), 6·37 (2H, s, CH_2·CO), 5·3 (1H, dd, *J* 8 and 1 Hz, 3-H), 5·01 (1H, d, *J* 1 Hz, 4-H), 4·16br (1H, s, vinylic proton), 2·8br (1H, d, *J* 8 Hz, NH), and 2·58 (5H, s, aromatic protons) [addition of deuterium oxide caused the signal at τ 5·4 to collapse to a doublet (*J* 1 Hz), and that at 2·8 to disappear] [Found: *M* (mass spectrum), 288·1501. $C_{16}H_{20}N_2O_3$ requires *M*, 288·1474].

Reaction of the Oxazoline (12) *with 2-Mercaptoethanol.*—The oxazoline (12) [1] (0·154 g, 0·6 mmol) was dissolved in 2-mercaptoethanol (1 ml) and a trace of toluene-*p*-sulphonic acid was added. Work-up after 15 min gave a syrup (0·138 g), which was purified by silica gel chromatography (benzene–ether as eluant) to yield (3S,4S)-4-(2-*mercaptoethoxy*)-1-(2-*methylprop*-1-*enyl*)-3-*phenylacetamidoazetidin*-2-*one* (6) (0·045 g, 22%), $\nu_{max.}$ (film) 3300 (NH), 1765 (azetidinone C=O), and 1665 cm^{-1} (amide C=O), τ ($CDCl_3$) 8·22 and 8·20 (each 3H, s, *gem*-Me_2), 7·44—7·10 (2H, m, CH_2·S), 6·45—6·00 (2H, m, CH_2·O), 6·38 (2H, s, CH_2·CO), 5·35 (1H, dd, *J* 7 and 1 Hz, 3-H), 4·95 (1H, d, *J* 1 Hz, 4-H), 4·21br (1H, s, vinylic proton), 3·2br (1H, d, *J* 7 Hz, NH), and 2·65br (5H, s, aromatic protons) [addition of deuterium oxide caused the signal at τ 5·35 to collapse to a doublet (*J* 1 Hz) and that at 3·2 to disappear] [Found: *M* (mass spectrum), 334·1355. $C_{17}H_{22}N_2O_3S$ requires *M*, 334·1351].

Further elution afforded (3R,4S)-4-(2-*hydroxyethylthio*)-1-(2-*methylprop*-1-*enyl*)-3-*phenylacetamidoazetidin*-2-*one* (7) (0·075 g, 37%), $\nu_{max.}$ (film) 3400 and 3300 (OH and NH), 1750 (azetidinone C=O), and 1660 cm^{-1} (amide C=O), τ ($CDCl_3$) 8·26 (6H, s, *gem*-Me_2), 7·28 (2H, t, *J* 5·5 Hz, S·CH_2), 6·5—6·2 (4H, m, CH_2CO and CH_2·OH), 5·31 (1H, d, *J* 7 Hz, 3-H), 5·24 (1H, s, 4-H), 4·45br (1H, s, vinylic proton), 2·95br (1H, d, *J* 7 Hz, NH), and 2·77 (5H, s, aromatic protons) (addition of deuterium oxide caused the signal at 5·31 to collapse to a singlet and that at 2·95 to disappear) [Found: (mass spectrum), 334·1351. $C_{17}H_{22}N_2O_3S$ requires *M*, 334·1351].

Reaction of the Oxazoline (12) *with Thioacetic Acid.*—The oxazoline (12) [1] (0·102 g, 0·4 mmol) was dissolved in thioacetic acid (1 ml). Work-up after 30 min yielded a syrup, which was fractionated by silica gel chromatography (benzene–ether as eluant) to give (3R,4S)-4-*acetylthio*-1-(2-*methylprop*-1-*enyl*)-3-*phenylacetamidoazetidin*-2-*one* (8) (0·070 g, 53%), $\nu_{max.}$ (film) 3300 (NH), 1775 (azetidinone C=O), 1705, and 1665 cm^{-1} (amide C=O), τ ($CDCl_3$) 8·27 (6H, s, *gem*-Me_2), 7·65 (3H, s, MeCO), 6·42 (2H, s, CH_2·CO), 5·1 (1H, dd, *J* 8 and 2 Hz, 3-H), 4·61 (1H, d, *J* 2 Hz, 4-H), 4·5br (1H, s, vinylic proton), 3·05br (1H, d, *J* 8 Hz, NH), and 2·65 (5H, s, aromatic protons) [addition of deuterium oxide caused the signal at τ 5·1 to collapse to a doublet (*J* 2 Hz) and that at 3·05 to disappear] [Found: *M* (mass spectrum), 332·1202. $C_{17}H_{20}N_2O_3S$ requires *M*, 332·1195].

Reaction of the Oxazoline (12) *with 2-Mercaptoacetic Acid.*—The oxazoline (12) [1] (0·510 g, 2 mmol) was dissolved in 2-mercaptoacetic acid (5 ml). Work-up after 30 min yielded crude (3*S*,4*S*)-4-(2-mercaptoacetoxy)-1-(2-methylprop-1-enyl)-3-phenylacetamidoazetidin-2-one (9) (0·490 g, 71%), $\nu_{max.}$ (film) 3300 (NH), 1770 (azetidinone C=O), and 1665 cm^{-1} (amide C=O), τ ($CDCl_3$) 8·28 and 8·25 (each 3H, s, *gem*-Me_2), 6·7 (2H, d, *J* 8 Hz, CH_2·S), 6·4 (2H, s, CH_2·CO), 5·3 (1H, dd, *J* 8 and 1 Hz, 3-H), 4·3 (1H, s, vinylic proton), 3·8 (1H, d, *J* 1 Hz, 4-H), 2·9br (1H, d, *J* 8 Hz, NH), and 2·68 (5H, s, aromatic protons) [addition of deuterium oxide caused the signal at 6·7 to collapse to a singlet, that at 5·3 to collapse to a doublet (*J* 1 Hz), and that at 2·9 to disappear].

An attempt to purify the crude thiol (9) (0·48 g, 1·38 mmol) by silica gel chromatography [ethyl acetate–light petroleum (b.p. 40—60°) as eluant] led to the isolation of (2R)-N-(2-*methylprop*-1-*enyl*)-2-(5-*oxo*-1,3-*oxathiolan*-2-*yl*)-2-*phenylacetamidoacetamide* (16) (0·208 g, 43%), as a mixture (*ca.* 1 : 1) of isomers. After recrystallisation from ethyl acetate–light petroleum (b.p. 40—60°) the mixture (*ca.*

[8] I. McMillan and R. J. Stoodley, *J. Chem. Soc.* (*C*), 1968, 2533.

1·5 : 1) had m.p. 157—160°, $\nu_{max.}$ (KBr) 3300 (NH), 1785 (γ-lactone C=O), and 1640 cm^{-1} (amide C=O), τ ($CDCl_3$; major isomer) 8·40 and 8·30 (each 3H, s, *gem*-Me_2), 6·5 (2H, s, CH_2·S), 6·32 (2H, s, CH_2·CO), 4·8 (1H, dd, *J* 10 and 5 Hz, 2-H), 4·2 (1H, d, *J* 5 Hz, O·CH·S), 3·6 (1H, d, *J* 10 Hz, vinylic proton), 3·0br (1H, d, *J* 10 Hz, NH), 2·7 (5H, s, aromatic protons), and 1·7br (1H, d, *J* 10 Hz, NH), τ ($CDCl_3$; minor isomer) as for major isomer except 6·6 (2H, ABq, *J* 18 Hz, CH_2·S) [addition of deuterium oxide caused the signal at τ 4·8 to collapse to a doublet (*J* 5 Hz), that at 3·6 to collapse to a singlet, and those at 3·0 and 1·7 to disappear] [Found: C, 58·9; H, 6·0; N, 8·0%; *M* (mass spectrum), 348. $C_{17}H_{20}N_2O_4S$ requires C, 58·6; H, 5·8; N, 8·1%; *M*, 348].

Reaction of the Oxazoline (12) *with Trifluoroacetic Acid.*—(*a*) The oxazoline (12) [1] (0·500 g, 1·95 mmol) was dissolved in ethanol-free chloroform (1 ml) and trifluoroacetic acid (0·7 g, 6·15 mmol) in ethanol-free chloroform (5 ml) was added. After 5 min the solution was concentrated and the residue was dissolved in chloroform (10 ml). Evaporation left 2-*benzyl*-4-[(2-*methylprop*-1-*enyl*)*aminomethylene*]-5-*oxo*-Δ^2-1,3-*oxazolinium trifluoroacetate* (18). After recrystallisation from chloroform–light petroleum (b.p. 40—60°) the sample (0·349 g; 47%) had m.p. 102—104° (decomp.), $\nu_{max.}$ (KBr) 1765 and 1690sh (each unsat. C=O) and 1655 cm^{-1}, $\lambda_{max.}$ (EtOH) 245 (ε 4900), 343sh (24,700), and 352 nm (27,600), τ (C_6D_6) 8·70 and 8·54 (each 3H, s, *gem*-Me_2), 6·50 (2H, s, CH_2Ph), 4·97br (1H, d, *J* 10 Hz, CH·CMe_2), 3·44 (1H, d, *J* 14 Hz, CH·N), 2·93br (m, aromatic protons), and 1·35br (1H, NH) (Found: C, 54·8; H, 4·7; N, 7·5. $C_{17}H_{15}F_3N_2O_4$ requires C, 55·1; H, 4·6; N, 7·6%).

The salt (18) (0·291 g, 0·87 mmol) was dissolved in chloroform and the solution was washed with sodium hydrogen carbonate solution followed by water. Evaporation of the dried ($MgSO_4$) organic layer left 2-benzyl-4-[(2-methylprop-1-enyl)aminomethylene]-Δ^2-1,3-oxazolin-5-one (19) (0·186 g, 92%), as a mixture (*ca.* 1·4 : 1 by n.m.r. spectroscopy) of isomers, $\nu_{max.}$ (film) 3300 (NH), 1750sh, 1730 and 1690 (each unsat. C=O), and 1655 cm^{-1}, $\lambda_{max.}$ (EtOH), 243 (ε 5500) and 352 nm (21,200), τ (C_6D_6) 8·7br (6H, s, *gem*-Me_2), 6·53 and 6·40 (2H, s, CH_2Ph for minor and major isomer, respectively), 4·74br (1H, d, *J* 11 Hz, CH·CMe_2), 3·3—2·8 (m, CH·N and aromatic protons), and 2·2br and 1·0br (1H, NH for minor and major isomer, respectively) (addition of deuterium oxide caused the signal at τ 4·74 to collapse to a singlet and those at 2·2 and 1·0 to disappear), τ [$(CD_3)_2SO$] 8·3br (6H, s, *gem*-Me_2), 6·15 (2H, s, CH_2Ph), 3·75br (1H, d, *J* 11 Hz, CH·CMe_2), 3·2 and 2·15 (1H, d, *J* 8 and 14 Hz, CH·N for minor and major isomer, respectively), and 2·65br (5H, s, aromatic protons) (addition of deuterium oxide caused the signals at τ 3·75, 3·2, and 2·15 to collapse to singlets) [Found: *M* (mass spectrum), 256·1231. Calc. for $C_{15}H_{16}N_2O_2$: *M*, 256·1212].

Addition of a small volume of methanol to the foregoing mixture (0·150 g) induced crystallisation of the (E)-*isomer* (20) (0·020 g, 13%), m.p. 111—114°, $\nu_{max.}$ (KBr) 3400 (NH), 1695 (unsat. C=O), and 1640 cm^{-1}, $\lambda_{max.}$ (EtOH) 245 (ε 6500) and 352 nm (32,000), τ (C_6D_6) 8·75 and 8·72 (each 3H, s, *gem*-Me_2), 6·4 (2H, s, CH_2Ph), 4·85br (1H, d, *J* 11 Hz, CH·CMe_2), 3·2 (1H, d, *J* 14 Hz, CH·N), 2·8br (m, aromatic protons), and 1·0br (1H, NH) (addition of deuterium oxide caused the signals at τ 4·85 and 3·2 to collapse to singlets and that at 1·0 to disappear) [Found: C, 70·0; H, 6·2; N, 10·6%; *M* (mass spectrum), 256. $C_{15}H_{16}N_2O_2$ requires C, 70·3; H, 6·3; N, 10·9%; *M*, 256].

(*b*) The oxazoline (12) [1] (0·051 g, 0·2 mmol) was dissolved in deuteriochloroform (0·5 ml) and one drop of trifluoroacetic acid was added. Immediately the n.m.r. signals due to the starting material were replaced by those of a new substance, which was considered to be (3*S*,4*S*)-1-(2-methylprop-1-enyl)-3-phenylacetamido-4-trifluoroacetylazetidin-2-one (10), τ 8·25 (6H, s, *gem*-Me_2), 6·4 (2H, s, CH_2·CO), 5·5 (1H, dd, *J* 7 and 1 Hz, 3-H), 4·4br (1H, s, vinylic proton), 3·7 (1H, d, *J* 1 Hz, 4-H), 3·4br (1H, d, *J* 7 Hz, NH), and 2·7 (5H, s, aromatic protons). The trifluoroacetate (10) decomposed when attempts were made to isolate it. Further addition of trifluoroacetic acid to the deuteriochloroform solution of the trifluoroacetate (10) gave a solution the n.m.r. spectrum of which was characteristic of the oxazolinium salt (18).

Reaction of (3S,4S)-4-*Acetoxy*-1-(2-*methylprop*-1-*enyl*)-3-*phenylacetamidoazetidin*-2-*one* (2) *with Trifluoroacetic Acid.*—The acetate (2) [2] (0·050 g, 0·157 mmol) was dissolved in trifluoroacetic acid (0·5 ml). Work-up after 12 h yielded a syrup (0·032 g, 79%), which was identical with the oxazolinone (19) (t.l.c. and n.m.r. spectroscopy).

Reaction of S-*Chloromercurio*(II)*benzylpenicillenic Acid* (22) *with Dimethyl Sulphoxide.*—The salt (22) [7] (0·8 g, 1·41 mmol) was stirred in dimethyl sulphoxide (5 ml) for 18 h. Methanol was added and the mixture was filtered over Hiflo. The filtrate was diluted with ether and extracted (3 times) with water. Evaporation of the dried ($MgSO_4$) organic layer left a residue, which was fractionated by silica gel chromatography (benzene–ether as eluant). The derived syrup (0·036 g, 10%) was identical with the oxazolinone (19) [t.l.c. and n.m.r. spectroscopy (ratio of isomers *ca.* 1·4 : 1)].

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