Studies Related to Penicillins. Part 23.[1] Preparation of the *N*-Phenylacetyl and *N*-Triphenylmethyl Derivatives of (3*R*,4*R*)-3-Amino-4-t-butylthioazetidin-2-one[2]

David F. Corbett, Arun C. Kaura, Christopher D. Maycock, and Richard J. Stoodley*†
Department of Organic Chemistry, The University, Newcastle upon Tyne NE1 7RU

Addition of hypobromous acid to the alkene moiety of the 6-substituent of (1*S*,5*R*)-3-benzyl-6-(2-methylprop-1-enyl)-4-oxa-2,6-diazabicyclo[3.2.0]hept-2-en-7-one (**7a**) was effected by the action of *N*-bromoacetamide in aqueous acetone. On the basis of ^{1}H n.m.r. spectroscopy, the resultant bromohydrin (**14d**) was partially converted by triethylamine in deuteriochloroform into a mixture of (1*S*,5*R*)-3-benzyl-4-oxa-2,6-diazabicyclo[3.2.0]hept-2-en-7-one (**7b**) and 2-bromo-2-methylpropanal, but attempts to isolate compound (**7b**) were without avail.

The bromohydrin (**14d**) was treated with 2-methylpropane-2-thiol in dichloromethane containing triethylamine to give 2-methyl-2-t-butylthiopropanal and a 4:1 mixture of (3*R*,4*R*)-4-phenylacetamido-4-t-butylthioazetidin-2-one (**6a**) and its (3*R*,4*S*)-diastereoisomer (**8b**).

(3*R*,4*R*)-4-Methylsulphinyl-3-triphenylmethylaminoazetidin-2-one (**23b**) underwent thermolysis in 2-methylpropane-2-thiol to give 1-triphenylmethylimidazol-2(3*H*)-one (**28**). However, treatment of (3*R*,4*R*)-4-methylsulphonyl-3-triphenylmethylaminoazetidin-2-one (**23c**) with 2-methylpropane-2-thiol and potassium t-butoxide gave a *ca.* 1.5:1 mixture of (3*R*,4*R*)-4-t-butylthio-3-triphenylmethylaminoazetidin-2-one (**6b**) and its (3*R*,4*S*)-diastereoisomer (**8c**). Compound (**6b**) was converted into the phenylacetyl derivative (**6a**) by a hydrolysis and phenylacetylation sequence.

Species of type (**1**) are valuable intermediates in β-lactam chemistry, undergoing two important intramolecular reactions.[3] Under thermal conditions, they afford penicillanate oxides of type (**2**) by a pericyclic process. Under dehydrative conditions and in the presence of HX, they are converted into penams of type (**3**), cephams of type (**4**), and/or cephems of type (**5**). Only the latter reactions are of preparative value since intermediates of type (**1**) are usually generated by thermolysis of penicillanate oxides of type (**2**).

In principle, as well as analogues of compounds of types (**3**), (**4**), and (**5**), relatives of penicillanate oxides of type (**2**) would become accessible if an alternative route to counterparts of species of type (**1**) could be devised. Two problems must be solved to achieve such an objective. Firstly, it is necessary to unmask the reactive sulphenic acid function under conditions in which it will undergo the appropriate intramolecular reaction. Second, the modified *N*-substituent must be capable of being elaborated in the presence of the latent sulphenic acid moiety. The t-butylsulphinyl group is known to serve as a precursor of the sulphenic acid function and, indeed, 5-t-butylsulphinylpent-1-ene has been shown to afford *cis*-2-methylthiolane 1-oxide when thermolysed.[4] Furthermore, the 1-alkylation,[5] 1-hydroxyalkylation[6] and 1-acylation[7] of 1-unsubstituted 3-acylamino-4-alkylthioazetidin-2-ones are documented reactions. Accordingly, the azetidinones (**6a**) and (**6b**) were selected as candidates to test the afore-cited possibilities. In this paper we described our efforts to prepare these compounds.

Results and Discussion

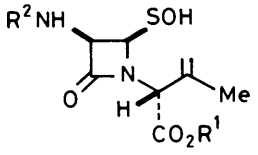
Previously, the oxadiazabicycloheptenone (**7a**)[8] was shown to react with 2-methylpropane-2-thiol in the presence of toluene-*p*-sulphonic acid to give a 1.5:1 mixture of the t-butylthioazetidinones (**6c**) and (**8a**).[9] Although the yield of the compounds was poor (20%), the preference for the formation of the *cis*-isomer (**6c**) was encouraging. It suggested that the intermediate (**9a**) was attacked preferentially from the most-hindered face and, possibly, reflected a directing role of the acylamino group. In the hope that the species (**9b**) would show a corresponding or improved diastereofacial reactivity, efforts were made to prepare the oxadiazabicycloheptene (**7b**).

In earlier work, it was shown that the butenoate (**10a**) was converted into the derivative (**10b**) by the action of potassium permanganate;[10] compound (**10b**) was also prepared by methanolysis of the oxamide (**10c**), obtained by treating the butenoate (**10a**) with ozone.[11] When the afore-mentioned procedures were applied to the butenoate (**7c**),[12] there was no evidence for the formation of compound (**7b**). Thus non-β-lactam products were recovered in low yield when the butenoate (**7c**) was treated with potassium permanganate in either aqueous acetone–pyridine or aqueous *N*,*N*-dimethylformamide–pyridine. Although the oxamide (**7d**) was probably produced, on the basis of i.r. spectroscopic evidence [$\nu_{max.}$(film) 1 820 cm^{-1}], when the butenoate (**7c**) was treated with ozone in dichloromethane at −78 °C, the material rapidly decomposed, during attempted isolation, to products which lacked the β-lactam entity. In the hope of effecting the methanolysis of the presumed oxamide (**7d**), methanol was added to the ozonolysis mixture at −78 °C (with and without the prior addition of Me_2S); however, non-β-lactam materials were again produced.

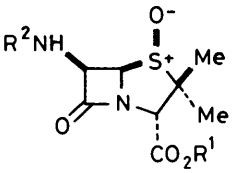
Barton and his co-workers have developed a mild method for the removal of the butenoate group from azetidinones; the procedure involves a reductive or basic cleavage of dihydropyrazoles, *e.g.* (**11**), formed from butenoates by the action of diazomethane.[13] However, the dihydropyrazole (**12**), obtained as a 1:1 mixture of diastereoisomers by treating the butenoate (**7c**) with diazomethane in diethyl ether, afforded complex mixtures of non-β-lactam products when treated with either zinc in aqueous acetic acid or potassium t-butoxide in t-butyl alcohol.

In view of the lack of success in deriving the oxadiazabicycloheptenone (**7b**) from the butenoate (**7c**), efforts were directed to the removal of the propenyl substituent from compound (**7a**). The use of potassium permanganate again led to degradation products. Although it was possible to isolate the formamide (**7e**), albeit in a slightly impure state, from the

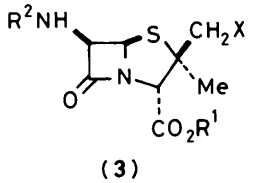
† *Present address:* Department of Chemistry, UMIST, P.O. Box 88, Manchester M60 1QD.



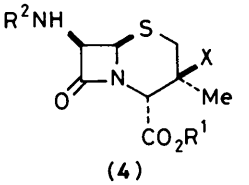
(1)



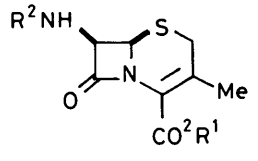
(2)



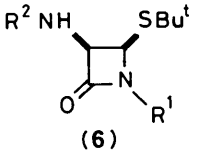
(3)



(4)



(5)

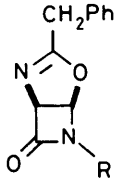


(6)

a; R^1 = H, R^2 = $COCH_2Ph$

b; R^1 = H, R^2 = CPh_3

c; R^1 = $CH{=}CMe_2$, R^2 = $COCH_2Ph$



(7)

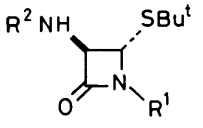
a; R = $CH{=}CMe_2$

b; R = H

c; R = $C(CO_2Me){=}CMe_2$

d; R = $COCO_2Me$

e; R = CHO

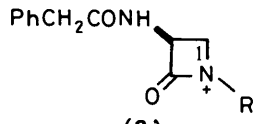


(8)

a; R^1 = $CH{=}CMe_2$, R^2 = $COCH_2Ph$

b; R^1 = H, R^2 = $COCH_2Ph$

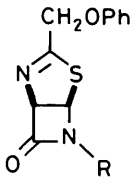
c; R^1 = H, R^2 = CPh_3



(9)

a; R = $CH{=}CMe_2$

b; R = H

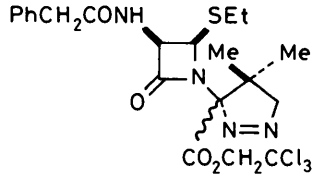


(10)

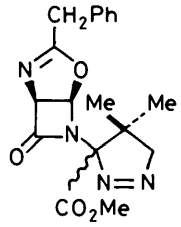
a; R = $C(CO_2CH_2CCl_3){=}CMe_2$

b; R = H

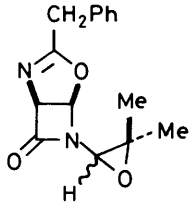
c; R = $COCO_2CH_2CCl_3$



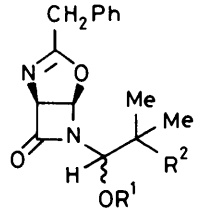
(11)



(12)



(13)



(14)

a; R^1 = H, R^2 = OH

b; R^1 = COC_6H_4Cl-*m*, R^2 = OH

c; R^1 = H, R^2 = $OCOC_6H_4Cl$-*m*

d; R^1 = H, R^2 = Br

reaction of the propenyl derivative (**7a**) with ozone in dichloromethane at −78 °C, conditions for its conversion into compound (**7b**) could not be devised. The formamide (**7e**) was an unstable entity; it underwent substantial decomposition at room temperature over 24 h and failed to survive chromatography on silica gel.

In an attempt to prepare the oxirane (**13**), which might undergo hydrolysis to the oxadiazabicycloheptenone (**7b**) by way of the diol (**14a**), compound (**7a**) was treated with *m*-chloroperoxybenzoic acid in dichloromethane. Subjection of the product to silica-gel chromatography led to the isolation of two crystalline materials in yields of 40% and 20%. On the basis of analytical and spectroscopic evidence, the compounds were considered to be diastereoisomers of the structure (**14b**). The alternative formulation (**14c**) was rendered unlikely by the chemical shifts of the methine proton of the *N*-substituent [δ6.08 and 5.68 ($CDCl_3$) for the major and minor diastereoisomers, respectively (*vide infra*)] in the ^1H n.m.r. spectra and by the presence of prominent ions at *m/z* 59 [attributed to the fragment $(Me_2COH)^{+\bullet}$] in the mass spectra.

Efforts to transform the *m*-chlorobenzoates (**14b**) into the oxadiazabicycloheptenone (**7b**) were again unsuccessful.

The formation of the *m*-chlorobenzoates (**14b**) may be accounted for by postulating the intermediacy of the oxirane (**13**) which undergoes ring opening with *m*-chlorobenzoic acid. Analogous products have previously been encountered in reactions of enol-ether—derived oxiranes with carboxylic acids.[14]

An attempt to stop the reaction at the oxirane stage, by performing it in the presence of sodium carbonate, was ineffective. In the hope of bringing about a solvent-induced ring opening of the presumed intermediate, the reaction was performed in aqueous dioxane and in methanol. Whilst a complex array of products was formed in the former instance, the oxazole (**15**) was the major product (62% yield after SiO_2 chromatography) in the latter case. The oxazole (**15**) was also produced when the oxadiazabicycloheptenone (**7a**) was treated with *m*-chlorobenzoic acid in methanol, suggesting that the last-cited reagent was responsible for the isomerisation.

The oxazole (**15**) probably arises from the oxadiazabicycloheptenone (**7a**) by way of the intermediates (**16**) and (**17**).* Although there is precedent for such reactions,[12] it is worth noting that compound (**7a**) reacts with trifluoroacetic acid[15] or

* We thank a referee for this suggestion.

boron trifluoride[9] to give the dihydro-oxazole (**18**), presumably by way of the species (**9a**). Comparable rearrangements have recently been observed[16] with related compounds.

Earlier, some success was achieved in the removal of the propenyl group from monocyclic azetidinones, *e.g.* (**19a**), by sequential reactions with *N*-bromoacetamide in aqueous acetone and triethylamine in dichloromethane.[9] Although not characterised, bromohydrins, *e.g.* (**19b**), were presumed to be intermediates in the transformations. Treatment of the propenyl derivative (**7a**) with *N*-bromoacetamide in aqueous acetone afforded two less-mobile products (t.l.c.). Although undergoing substantial decomposition when subjected to silica-gel chromatography, the mixture was isolated in a crystalline state by adding diethyl ether to the crude product. Analytical and spectroscopic considerations left little doubt that the material was the bromohydrin (**14d**) as a 2.8:1 mixture of diastereoisomers. In particular, in the 300 MHz ^{1}H n.m.r. spectrum ($CDCl_3$), the methine proton of the *N*-substituent appeared at δ 4.99 for the major diastereoisomer and at δ 4.77 for the minor diastereoisomer. Furthermore, the mass spectrum incorporated prominent ions at *m/z* 123 and 121 [attributed to the fragment $(Me_2CBr)^+$].

Since the rate of formation of the bromohydrin (**14d**) was somewhat variable [requiring different induction periods which, presumably, reflected different purities of the precursor (**7a**)] and the yield of the bromohydrin (**14d**) declined if the reaction time was too long [presumably, reflecting further reactions of the bromohydrin (**14d**)], it was expedient to monitor the transformation by t.l.c. By quenching the reaction when the starting material had almost disappeared, it was possible to isolate the crystalline bromohydrin (**14d**) in yields of up to 75%.

Following various work-up procedures, only non-β-lactam products were isolated from the reaction of the bromohydrin (**14d**) with triethylamine in dichloromethane. However, when the reaction was performed in deuteriochloroform and monitored by 300 MHz ^{1}H n.m.r. spectroscopy, two new materials were rapidly produced in a 1:1 ratio. One of these corresponded to 2-bromo-2-methylpropanal.[17] The other was presumed to be the oxadiazabicycloheptenone (**7b**) on the basis of the double doublets at δ 5.12 and 5.70 (each *J* 3 Hz) which were attributed to the 3- and 5-protons [the corresponding protons of the bromohydrin (**14d**) appeared at δ 5.08 and 5.95 (each *J* 3.5 Hz) for the major diastereoisomer and at δ 5.13 and 6.27 (each *J* 3.5 Hz) for the minor diastereoisomer]. The formation of the new materials proceeded to *ca.* 56% completion, suggesting that the compounds were in equilibrium with the precursor (**14d**). However, over a period of several hours, the intensity of the signals for compounds (**14d**) and (**7b**) decreased considerably, implying that the materials were undergoing other reactions.

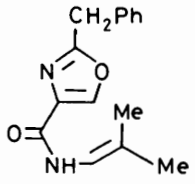
On the basis of the foregoing results, it seems reasonable to conclude that the oxadiazabicycloheptenone (**7b**) is a very reactive chemical entity. If its isolation is to be achieved, exceptionally mild conditions must be employed in its generation. It is interesting to note that compound (**20a**) was recently prepared from the butenoate (**20b**) by an ozonolysis-methanolysis sequence.[18] Evidently, the system is rendered less reactive by the presence of the conjugating phenyl substituent at position 3.

In the hope that a major decomposition pathway of the oxadiazabicycloheptenone (**7b**) proceeded by way of the azetone intermediate (**21a**), the bromohydrin (**14d**) was treated with 2-methylpropane-2-thiol (2 mol equiv.) and triethylamine (1 mol equiv.) in tetrahydrofuran (THF). Following silica-gel purification of the product, a syrupy 1:1 mixture of the azetidinones (**6a**) and (**8b**) was isolated in 23% yield. Interestingly, when the reaction was conducted in dichloromethane, a 9:1 mixture of the azetidinones (**6a**) and (**8b**) was formed in 24% yield. Finally, although the ratio of compounds was reduced to 4:1, the yield of the azetidinones (**6a**) and (**8b**) was improved to 66% by performing the reaction in a 1:1 mixture of dichloromethane and 2-methylpropane-2-thiol; after crystallisation, the azetidinone (**6a**) was isolated in 35% yield. 2-Methyl-2-t-butylthiopropanal was also obtained (31% yield after SiO_2 chromatography) from the last-cited reaction.

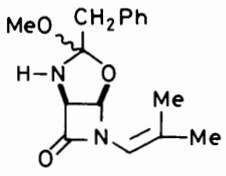
The azetidinone (**6a**) was optically active {$[\alpha]_D$ −55° ($CHCl_3$)}.* Although, of course, this finding does not reveal whether the compound is optically pure, it does exclude the total involvement of the species (**22a**) as a reaction intermediate; moreover, complete racemisation of the species (**21a**) is also precluded.

On the basis of the foregoing results, it is clear that substantial diastereocontrol can be achieved in the reaction of the bromohydrin (**14d**) with 2-methylpropane-2-thiol. Possibly, the acylamino group of the presumed intermediate (**21a**) co-ordinates with the thiol by H-bonding and directs the attack from the most-hindered face to give the *cis*-azetidinone (**6a**).

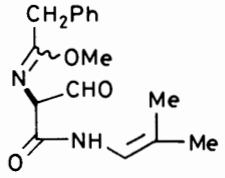
Because of the possibility of replacing its triphenylmethyl group by a wide variety of acyl substituents, efforts were made



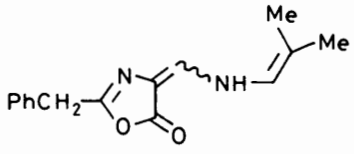
(15)



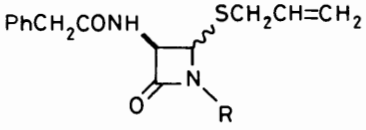
(16)



(17)



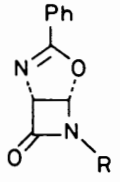
(18)



(19)

a; R = $CH{=}CMe_2$

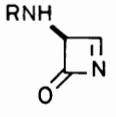
b; R = $CH(OH)C(Br)Me_2$



(20)

a; R = H

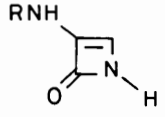
b; R = $C(CO_2CH_2Ph){=}CMe_2$



(21)

a; R = $COCH_2Ph$

b; R = CPh_3



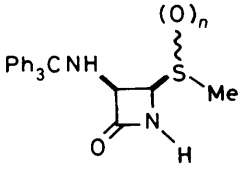
(22)

a; R = $COCH_2Ph$

b; R = CPh_3

* The value quoted in the preliminary communication is incorrect.

to prepare the *cis*-azetidinone (**6b**). Workers at Beecham Pharmaceuticals have shown[10] that the azetidinone (**23a**) is readily obtained from the penicillanate (**24**) by a two-step sequence. It was hoped that the derived sulphoxide (**23b**), when heated in the presence of 2-methylpropane-2-thiol, would give rise to the azetidinones (**6b**) and (**8c**) by way of the intermediate (**21b**).

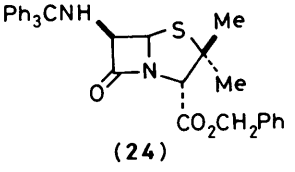


(**23**)

a; *n* = 0

b; *n* = 1

c; *n* = 2



(**24**)

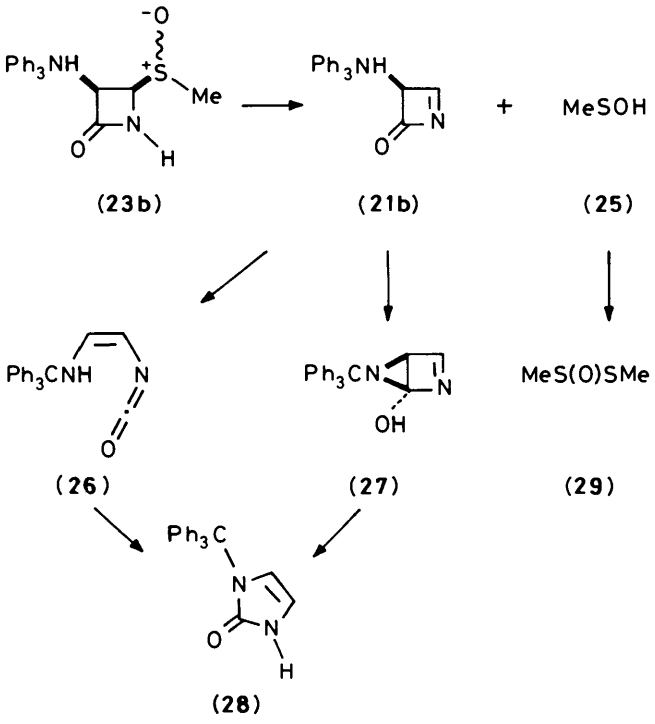
Oxidation of the methylthioazetidinone (**23a**) with sodium periodate in aqueous methanol gave the sulphoxide (**23b**) as a mixture of diastereoisomers. Following silica-gel chromatography, the constituents of the mixture were isolated in yields of 7% and 70%. Thermolysis of the major sulphoxide (**23b**) in 2-methylpropane-2-thiol failed to give the azetidinones (**6b**) and (**8c**); instead, a non-lactam product was isolated (54% yield after SiO_2 chromatography) as needle-like crystals. The constitution of the compound, as $C_{22}H_{18}N_2O$, was established by elemental analysis. Its structure, as the imidazolone (**28**), rests upon its spectroscopic properties. In particular, the ^1H n.m.r. spectrum [$(CD_3)_2CO$] showed the presence of two one-proton multiplets at δ 6.02 and 6.34 for the olefinic protons and a broad one-proton singlet at δ 9.9 for the NH group; addition of deuterium oxide to the solution caused the signal at δ 9.9 to disappear and those at δ 6.02 and 6.34 to collapse to doublets (each *J* 3.5 Hz).

Apparently, 2-methylpropane-2-thiol was playing no role in the (**23b**) → (**28**) transformation and, indeed, thermolysis of the major sulphoxide (**23b**) in boiling benzene again provided the dihydroimidazole (**28**) (77% yield after SiO_2 chromatography). A low yield (15%) of the thiosulphinate (**29**)[19] was also isolated.

The formation of compounds (**28**) and (**29**) from the sulphoxide (**23b**) can be explained by invoking the involvement of intermediates (**21b**) and (**25**) as shown in the Scheme. Possibly, the dihydroazetone (**21b**) undergoes ring expansion to the dihydroimidazole (**28**) by way of either the isocyanate (**26**) or the diazabicyclopentene (**27**); the thiosulphinate (**29**) probably arises by dimerisation of the sulphenic acid (**25**).

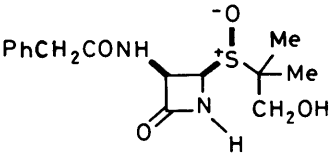
It is noteworthy that Barton[20] and Long[21] reported that thermolysis of the sulphoxide (**30**) in the presence of thiols gave predominantly *trans*-azetidinones of type (**31**).

The methylsulphonyl group of the azetidinone (**23c**)[10] has been displaced by alcohols, in the presence of Lewis acids, to give azetidinones of type (**32**) as *ca.* 1:1 mixtures of diastereoisomers.[22] In the hope of deriving the azetidinones (**6b**) and (**8c**), the reaction of the sulphone (**23c**) with 2-methylpropane-2-thiol was investigated. The most successful outcome as achieved by briefly treating a solution of the azetidinone (**23c**) in 2-methylpropane-2-thiol with freshly sublimed potassium t-butoxide (2 mol equiv.). Silica-gel purification of the product led to the isolation of the *cis*-azetidinone (**6b**) as a foam in 23% yield, and the *trans*-azetidinone (**8c**) as needle-like crystals in 16% yield. The *cis*-azetidinone (**6b**) showed $[\alpha]_D$ +57° (EtOH)

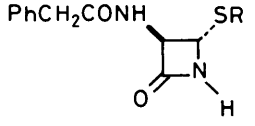


(**23b**) (**21b**) (**25**) (**26**) (**27**) (**29**) (**28**)

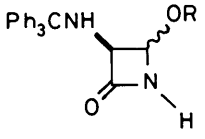
Scheme



(**30**)



(**31**)



(**32**)

and the *trans*-azetidinone (**8c**) showed $[\alpha]_D$ −117° (EtOH). Related displacements of alkylsulphonyl moieties from azetidinones by sulphur nucleophiles have been reported by Sheehan.[23]

To provide an inter-relationship between compounds (**6a**) and (**6b**), the latter material was treated with toluene-*p*-sulphonic acid in methanol–dichloromethane; addition of phenylacetyl chloride and triethylamine to the crude product dissolved in dichloromethane gave the *cis*-azetidinone (**6a**) (44% yield after SiO_2 chromatography). The optical rotation of the recrystallised material {$[\alpha]_D$ −57° ($CHCl_3$)} was very similar to that of the product obtained by way of the bromohydrin (**14d**). Since it is highly unlikely that the same degree of racemisation would accompany the (**14d**) → (**6a**) and (**23c**) → (**6d**) transformations, we conclude that stereochemical integrity is maintained in both reactions. Evidently, the species (**21a**) and (**21b**) show no tendency to undergo epimerisation or to isomerise to the species (**22a**) and (**22b**).

Experimental

Dry solvents, referred to in the ensuing experiments, were prepared as follows: dichloromethane was stored over calcium chloride flakes; THF was dried over calcium hydride and, immediately prior to use, was distilled. Light petroleum refers to that fraction boiling in the range 40—60 °C. Ethereal diazomethane was prepared by adding a solution of Diazald in diethyl ether to potassium hydroxide in aqueous ethanol.[24] 300 MHz ^{1}H N.m.r. spectra were measured on a Bruker WM-300 WB spectrometer. Ozone was generated with a Wallace and Tieman ozonator operating at 150 V and a flow rate of 50 dm^3 h^{-1}. For chromatographic and other instrumental details, see Part 20.[25]

Reaction of the Butenoate (**7c**) *with Diazomethane.*—The butenoate (**7c**)[12] (0.250 g, 0.80 mmol) was dissolved in an ethereal solution of diazomethane (100 cm^3) at *ca.* 5 °C. Evaporation, after 2 weeks, left a syrup (0.260 g) that was predominantly a 1:1 mixture of the (3*R*)- and (3*S*)-diastereoisomers of methyl 3-{(1*S*,5*R*)-3-benzyl-7-oxo-4-oxa-2,6-diazabicyclo[3.2.0]hept-2-en-6-yl}-4,4-dimethyl-4,5-dihydropyrazole-3-carboxylate (**12**). The syrup possessed the following properties: $\nu_{max.}$(film) *inter alia* 1 785 (β-lactam C=O), 1 740 (ester C=O), and 1 645 cm^{-1} (C=N and N=N); δ (60 MHz, $CDCl_3$) *inter alia* 0.55, 0.85, 1.11, and 1.14 (each 0.75 H, s, together 4-Me_2), 3.59, 3.65, and 3.67 (2.5, 1, and 1.5 H, each s, together PhCH_2 and OMe), 4.08—4.73 (2 H, m, 5-H_2), 5.10—5.20 (1 H, m, NCHCO), 6.08 and 6.20 (each 0.5 H, d, *J* 3 Hz, together OCHN), and 7.13 and 7.20 (each 2.5 H, s, together Ph); *m/z inter alia* 357 (MH^+), 328 ($M^+ - N_2$), 169, 160, 159, and 91 ($C_7H_7^+$, base peak) (Found: MH^+, 357.1574. $C_{18}H_{21}N_4O_4$ requires *m/z* 357.1563).

Reaction of the Propenyl Derivative (**7a**) *with Ozone.*—A cooled (Me_2CO–solid CO_2) solution of the propenyl derivative (**7a**)[8] (0.200 g, 0.78 mmol) in dichloromethane (10 cm^3) was treated with ozone until a blue colouration developed. After removal of excess ozone with a stream of nitrogen, dimethyl sulphide (10 drops) was added and the solution allowed to warm to room temperature. Following dilution with dichloromethane, the solution was washed with water, dried ($MgSO_4$), and concentrated. The resultant syrup (0.168 g, *ca.* 93%), which was predominantly (1*S*,5*R*)-3-benzyl-6-formyl-4-oxa-2,6-diazabicyclo[3.2.0]hept-2-en-7-one (**7e**), possessed the following properties: $\nu_{max.}$(film) *inter alia* 1 815 (β-lactam C=O), 1 710 (formyl C=O), and 1 650 cm^{-1} (C=N); δ (60 MHz, $CDCl_3$) *inter alia* 3.65 (2 H, s, PhCH_2), 5.13 and 5.95 (each 1 H, d, *J* 4 Hz, together 1- and 5-H), 7.15 (5 H, s, Ph), and 8.47 (1 H, s, CHO); *m/z inter alia* 230 (M^+) and 159 ($C_{10}H_9NO^+$, base peak).

Reaction of the Propenyl Derivative (**7a**) *with* m-*Chloroperoxybenzoic Acid.*—(*a*) To a stirred solution of the propenyl derivative (**7a**) (0.156 g, 0.61 mmol) in dry dichloromethane (5 cm^3) was added 85% *m*-chloroperoxybenzoic acid (0.210 g, 1.03 mmol). After 3 h, the mixture was diluted with dichloromethane and washed with sodium hydrogen carbonate solution followed by water. Evaporation of the dried ($MgSO_4$) organic layer left a syrup that was a mixture of two components (t.l.c.). The mixture was fractionated by silica-gel chromatography (PhH–Et_2O, gradient elution).

The first-eluted material, isolated as a solid (0.105 g, 40%), was the *major isomer* of (1S,5R)-3-*benzyl*-6-[1-(3-*chlorobenzoyloxy*)-2-*hydroxy*-2-*methylpropyl*]-4-*oxa*-2,6-*diazabicyclo*[3.2.0]-*hept*-2-*en*-7-*one* (**14b**). The sample, after recrystallisation from benzene–diethyl ether, showed the following properties: m.p. 154—156 °C; $[\alpha]_D$ −39° (0.5% in $CHCl_3$); $\nu_{max.}$(KBr) *inter alia* 1 775 (β-lactam C=O), 1 715 (ester C=O), and 1 640 cm^{-1} (C=N); $\lambda_{max.}$ (EtOH) 215 (ε 11 800), 233 (10 900), 285 (1 300), and 293 nm (1 100); δ (60 MHz, $CDCl_3$) 1.03 and 1.18 (each 3 H, s, together CMe_2), 2.6 br (1 H, s, OH), 3.65 (2 H, s, PhCH_2), 5.22 and 5.90 (each 1 H, *J* 3 Hz, together 1- and 5-H), 6.08 (1 H, s, NC*H*OCOC$_6$H$_4$), 7.30 (5 H, s, Ph), and 7.40—8.10 (4 H, m, C_6H_4) (addition of D_2O caused the signal at δ 2.6 to disappear); *m/z inter alia* 229, 139 ($C_7H_4{}^{35}ClO^+$, base peak), and 59 ($C_3H_7O^+$) (Found: C, 61.7; H, 4.8; N, 6.3. $C_{22}H_{21}ClN_2O_5$ requires C, 61.6; H, 4.9; N, 6.5%).

The second-eluted material, isolated as a syrup (0.053 g, 20%), was the *minor isomer* of compound (**14b**). The sample, after crystallisation from diethyl ether, showed the following properties: m.p. 130—132 °C; $[\alpha]_D$ +17° (0.5% in $CHCl_3$); $\nu_{max.}$(KBr) *inter alia* 1 775 (β-lactam C=O), 1 720 (ester C=O), and 1 640 cm^{-1} (C=N); $\lambda_{max.}$(EtOH) 234 (ε 11 300), 285 (1 600), and 293 nm (1 500); δ (60 MHz, $CDCl_3$) 1.03 and 1.23 (each 3 H, s, together CMe_2), 3.3br (1 H, s, OH), 3.58 (2 H, s, PhCH_2), 5.15 and 6.11 (each 1 H, d, *J* 3 Hz, together 1- and 5-H), 5.68 (1 H, s, NC*H*OCOC$_6$H$_4$), 7.23 (5 H, s, Ph), and 7.40—8.05 (4 H, m, C_6H_4) (addition of D_2O caused the signal at δ 3.3 to disappear); *m/z inter alia* 139 ($C_7H_4{}^{35}ClO^+$, base peak) and 59 ($C_3H_7O^+$) (Found: C, 61.9, H, 4.9; N, 6.6).

(*b*) To a stirred solution of the propenyl derivative (**7a**) (0.200 g, 0.78 mmol) in methanol (2 cm^3) was added a solution of 85% *m*-chloroperoxybenzoic acid (0.140 g, 0.69 mmol) in methanol (2 cm^3). When the starting material had disappeared (t.l.c.), the solution was diluted with dichloromethane and washed with aqueous sodium hydrogen carbonate followed by water. Evaporation of the dried ($MgSO_4$) organic layer and purification of the product by silica-gel chromatography (light petroleum–EtOAc, gradient elution) gave N-(2-*methylprop*-1-*enyl*) 2-*benzyloxazole*-4-*carboxamide* (**15**) (0.124 g, 62%). The sample, after recrystallisation from diethyl ether–light petroleum, possessed the following properties: m.p. 72—74 °C; $\nu_{max.}$(KBr) *inter alia* 3 415 (NH) and 1 670 cm^{-1} (amide C=O); $\lambda_{max.}$(EtOH) 216 (ε 9 600) and 267 nm (10 200); δ (60 MHz, $CDCl_3$) 1.7br (6 H, s, CMe_2), 3.98 (2 H, s, PhCH_2), 6.5br (1 H, d, *J* 11 Hz, NHC*H*=C), 7.10 (5 H, s, Ph), 7.90 (1 H, s, 5-H), and 8.1br (1 H, s, CON*H*CH); *m/z inter alia* 256 (M^+) and 91 ($C_7H_7^+$, base peak) (Found: C, 70.6; H, 6.4; N, 11.1. $C_{15}H_{16}N_2O_2$ requires C, 70.3; H, 6.3; N, 10.9%).

Reaction of the Propenyl Derivative (**7a**) *with* m-*Chlorobenzoic Acid.*—To a stirred solution of the propenyl derivative (**7a**) (0.200 g, 0.78 mmol) in methanol (2 cm^3) was added a solution of *m*-chlorobenzoic acid (0.122 g, 0.78 mmol) in methanol (2 cm^3). When the starting material had disappeared (t.l.c.), the solution was diluted with dichloromethane and washed with aqueous sodium hydrogen carbonate followed by water. Evaporation of the dried ($MgSO_4$) organic layer and purification of the residue by silica-gel chromatography (light petroleum–EtOAc, gradient elution) gave a solid (0.105 g, 53%) which was identical (^{1}H n.m.r. spectroscopy) with the oxazole (**15**). The sample, after recrystallisation from diethyl ether–light petroleum, showed m.p. 71—73 °C.

Reaction of the Propenyl Derivative (**7a**) *with* N-*Bromoacetamide.*—To a stirred solution of the propenyl derivative (**7a**) (2.06 g, 8.05 mmol) in acetone (20 cm^3) and water (4 cm^3) was added *N*-bromoacetamide (1.21 g, 8.77 mmol). When the reaction was almost complete (t.l.c.), the mixture was diluted with chloroform and washed (2 ×) with water. Evaporation of the dried ($MgSO_4$) organic layer and addition of diethyl ether gave (1S,5R)-3-*benzyl*-6-(2-*bromo*-1-*hydroxy*-2-*methylpropyl*)-4-*oxa*-2,6-*diazabicyclo*[3.2.0]*hept*-2-*en*-7-*one* (**14d**) (2.14 g, 75%) as a 2.8:1 mixture of diastereoisomers. The sample showed the following properties: m.p. 111—114 °C; $[\alpha]_D$ +14 (2% in $CHCl_3$); $\nu_{max.}$(KBr) *inter alia* 3 240br (OH), 1 770 (β-lactam C=O), and 1 645 cm^{-1} (C=N); $\lambda_{max.}$(EtOH) 210 nm (ε 6 700); δ

(300 MHz, $CDCl_3$) 1.42, 1.48, 1.70, and 1.74 (2.2, 2.2, 0.8, and 0.8 H, each s, together CMe_2), 3.59, 3.69, and 3.70 [0.74 H (d, *J* 15 Hz), 0.52 H (s), and 0.74 H (d, *J* 15 Hz), together $PhCH_2$], 4.4br and 5.6br (0.74 and 0.26 H, each, s, together *CH*OH), 5.08, 5.13, 5.95, and 6.27 (0.74, 0.26, 0.74, and 0.26 H, each d, *J* 3.5 Hz, together 1- and 5-H), and 7.19—7.32 (5 H, m, Ph); *m/z inter alia* 354 and 352 (M^+), 336 and 332 ($M^+ - H_2O$), 256 ($M^+ - HBrO$), 202 ($M^+ - C_4H_7BrO$), 159 ($C_{10}H_9NO^+$, base peak), and 123 and 121 ($C_3H_6Br^+$) (Found: C, 51.3; H, 4.8; N, 7.7. $C_{15}H_{17}BrN_2O_3$ requires C, 51.0; H, 4.8; N, 8.0%).

Reaction of the Bromohydrin (**14d**) *with Triethylamine.*—To a solution of the bromohydrin (**14d**) (0.050 g, 0.14 mmol) in deuteriochloroform (1 cm^3) was added triethylamine (0.01 cm^3, 0.007 mmol). The reaction was monitored by 300 MHz^1 n.m.r. spectroscopy and, after 30 min, a mixture containing a 1:1.3:1.3 ratio of the bromohydrin (**14d**) (as a 2.8:1 mixture of diastereoisomers), the oxadiazabicycloheptenone (**7b**) [δ 3.66 (s, $PhCH_2$), 5.12 and 5.70 (each d, *J* 3 Hz, together 1- and 5-H)] and 2-bromo-2-methylpropanal [δ 1.77 (s, CMe_2) and 9.34 (s, CHO) (these signals were coincident with those of a sample of the bromo-aldehyde prepared by the literature method [17])] was present. After 8 h, the intensity of the signals attributed to compounds (**7b**) and (**14d**) was considerably reduced.

Reaction of the Bromohydrin (**14d**) *with 2-Methylpropane-2-thiol.*—(*a*) To a stirred solution of the bromohydrin (**14d**) (0.200 g, 0.57 mmol) in dry THF (10 cm^3) was added 2-methylpropane-2-thiol (0.13 cm^3, 1.2 mmol) followed by triethylamine (0.08 cm^3, 0.57 mmol). After 4 h, the mixture was concentrated and the residue subjected to silica-gel chromatography (light petroleum–EtOAc, gradient elution) to give a syrup (0.038 g, 23%) which was a 1:1 mixture of (3*R*,4*R*)- and (3*R*,4*S*)-3-phenylacetamido-4-t-butylthioazetidin-2-ones (**6a**) and (**8b**); δ (60 MHz, $CDCl_3$) 1.20 and 1.30 (each 4.5 H, s, together $SCMe_3$), 3.58 and 3.63 (each 1 H, s, together $PhCH_2$), 4.45 and 5.52 [0.5 H, (dd, *J* 8 and 2.5 Hz) and 0.5 H (dd, *J* 9 and 4.5 Hz), together 3-H], 4.92 and 4.97 [0.5 H (d, *J* 2.5 Hz) and 0.5 H (d, *J* 4.5 Hz), together 4-H], 6.3—6.6br (2 H, m, CON*H*CH and 1-H), and 7.23 and 7.28 (each 2.5 H, s, together Ph) [addition of D_2O caused the signals at δ 6.3—6.6 to disappear, those at δ 4.45 to collapse to a d (*J* 2.5 Hz), and those at δ 5.52 to collapse to a d (*J* 4.5 Hz)].

(*b*) To a stirred suspension of the bromohydrin (**14d**) (0.200 g, 0.57 mmol) in dichloromethane (10 cm^3) was added 2-methylpropane-2-thiol (0.13 cm^3, 1.2 mmol) followed by triethylamine (0.08 cm^3, 0.57 mmol). After 4 h, the mixture was concentrated and the residue subjected to silica-gel chromatography (light petroleum–EtOAc, gradient elution) to give a syrup (0.040 g, 24%) which was found to be a 9:1 mixture of the azetidinones (**6a**) and (**8b**) on the basis of 300 MHz ^1H n.m.r. spectroscopy. The mixture possessed the following properties: $[\alpha]_D$ −55° (2.3% in $CHCl_3$); $\nu_{max.}$(film) *inter alia* 3 400 (NH), 1 760 (β-lactam C=O), and 1 660 cm^{-1} (amide C=O); *m/z inter alia* 292 (M^+), 235 ($M^+ - C_4H_9$), and 91 ($C_7H_7^+$, base peak).

(*c*) To a stirred suspension of the bromohydrin (**14d**) (0.500 g, 1.42 mmol) in dichloromethane (5 cm^3) and 2-methylpropane-2-thiol (5 cm^3) was added triethylamine (0.21 cm^3, 1.5 mmol). Within 15 min, a solution was formed which gradually deposited a precipitate (presumed to be $Et_3\overset{+}{N}H\ Cl^-$). Evaporation, after 8 h, and purification of the residue by silica-gel chromatography (light petroleum–EtOAc, gradient elution) gave two fractions.

The first-eluted material, isolated as a syrup (0.069 g, 31%), was 2-*methyl*-2-*t*-*butylthiopropanal*. It possessed the following properties: $\nu_{max.}$(film) *inter alia* 1 730 and 1 715 cm^{-1} (aldehyde C=O); $\lambda_{max.}$(EtOH) 209 (ε 1 800) and 245 nm (600); δ (60 MHz, $CDCl_3$) 1.30 (9 H, s, CMe_3), 1.38 (6 H, s, CMe_2), and 9.12 (1 H, s, CHO); *m/z inter alia* 160 (M^+), 131 (M^+ − CHO), 75, and 57 ($C_4H_9^+$, base peak).

The second-eluted material, also isolated as a syrup (0.273 g, 66%), was a 4:1 mixture of the azetidinones (**6a**) and (**8b**) on the basis of 300 MHz ^1H n.m.r. spectroscopy. Crystallisation of the material from diethyl ether–light petroleum gave (3R,4R)-3-*phenylacetamido*-4-*t*-*butylthioazetidin*-2-*one* (**6a**) (as a hemi-solvate with diethyl ether) (0.165 g, 35%) which possessed the following properties; m.p. 59—60 °C; $[\alpha]_D$ −55° (2% in $CHCl_3$); $\nu_{max.}$(KBr) *inter alia* 3 280 and 3 220 (NH), 1 775 (β-lactam C=O), and 1 655 cm^{-1} (amide C=O); $\lambda_{max.}$(EtOH) 210 nm (ε 6 100); δ (300 MHz, $CDCl_3$) 1.21 (3 H, t, *J* 7 Hz, CH_2Me) 1.22 (9 H, s, $SCMe_3$), 3.48 (2 H, q, *J* 7 Hz, OCH_2Me), 3.64 (2 H, s, $PHCH_2$), 4.98 (1 H, d, *J* 4.5 Hz, 4-H), 5.62 (1 H, dd, *J* 9.5 and 4.5 Hz, 3-H), 6.1br (1 H, s, 1-H), 6.2br (1 H, d, *J* 9.5 Hz, CON*H*CH), and 7.27—7.39 (5 H, m, Ph); *m/z inter alia* 292 (M^+), 235 ($M^+ - C_4H_9$), and 91 ($C_7H_7^+$, base peak) (Found: M^+, 292.1258. $C_{15}H_{20}N_2O_2S$ requires *M*, 292.1245). The material failed to give an acceptable elemental analysis.

Reaction of the Methylthioazetidinone (**23a**) *with Sodium Periodate.*—A solution of the methylthioazetidinone (**23a**) [10] (0.980 g, 2.62 mmol) in methanol (75 cm^3) was treated with sodium periodate (2.50 g, 11.7 mmol) dissolved in the minimum volume of water. After 48 h, water was added to the mixture (to dissolve the precipitate of sodium iodate) which was then extracted (5×) with chloroform. Evaporation of the dried ($MgSO_4$) organic extract left a yellow syrup which was fractionated by silica-gel chromatography (PhH–Et_2O, gradient elution) to give two fractions.

The first-eluted material, isolated as a chromatographically homogeneous foam (0.073 g, 7%), was the minor isomer of (3*R*,4*R*)-4-methylsulphinyl-3-triphenylmethylaminoazetidin-2-one (**23b**). The sample possessed the following properties: $[\alpha]_D$ +79° (1.6% in EtOH); $\nu_{max.}$(film) *inter alia* 3 300 (NH) and 1 780 cm^{-1} (β-lactam C=O); $\lambda_{max.}$(EtOH) 225 nm (ε 11 000); δ (60 MHz, $CDCl_3$) 2.64 (3 H, s, SMe), 3.53 (1 H, d, *J* 9.5 Hz, Ph_3CNH), 4.43 (1 H, d, *J* 4 Hz, 4-H), 4.73 (1 H, dd, *J* 9.5 and 4 Hz, 3-H), and 7.00—7.40 (16 H, m, CPh_3 and 1-H) [addition of D_2O caused the signal at δ 3.53 to disappear and that at δ 4.73 to collapse to a d (*J* 4 Hz)]; *m/z inter alia* 326 ($M^+ - CH_4OS$), 243 ($C_{19}H_{15}^+$, base peak), and 165 ($C_{13}H_9^+$).

The second-eluted material, also isolated as a chromatographically homogeneous foam (0.713 g, 70%), was the major isomer of the azetidinone (**23b**). It possessed the following properties: $[\alpha]_D$ +179° (1.5% in EtOH); $\nu_{max.}$(KBr) *inter alia* 3 400 (NH) and 1 765 cm^{-1} (β-lactam C=O); $\lambda_{max.}$(EtOH) 216 nm (ε 10 200); δ (60 MHz, $CDCl_3$) 2.26 (3 H, s, SMe), 3.33 (1 H, d, *J* 10 Hz, Ph_3CNH), 3.82 (1 H, d, *J* 4 Hz, 4-H), 4.54 (1 H, dd, J 10 and 4 Hz, 3-H), 7.10—7.50 (15 H, m, CPh_3), and 8.13 (1 H, s, 1-H) [addition of D_2O caused the signals at δ 3.33 and 8.13 to disappear and that at δ 4.54 to collapse to a d (*J* 4 Hz)]; *m/z inter alia* 326 ($M^+ - CH_4OS$), 243 ($C_{19}H_{15}^+$, base peak), and 165 ($C_{13}H_9^+$).

Thermolysis of the Sulphoxide (**23b**).—(*a*) A solution of the major sulphoxide (**23b**) (0.098 g, 0.25 mmol) in 2-methylpropane-2-thiol (5 cm^3) was heated under reflux until the starting material had disappeared (t.l.c., *ca.* 2 h). Evaporation and purification of the residue by silica-gel chromatography (PhH–Et_2O, gradient elution) gave 1-*triphenylmethylimidazol*-2(3H)-*one* (**28**) (0.044 g, 54%) as a solid. The material, after recrystallisation from chloroform–diethyl ether, was obtained as colourless needles with the following properties: m.p. 220—225 °C (decomp.); $\nu_{max.}$(KBr) *inter alia* 1 680 cm^{-1} (imidazolone C=O); $\lambda_{max.}$(EtOH) 216 nm (ε 17 700); δ (60 MHz, $CDCl_3$) 6.10 (2 H, d, separation 2 Hz, 4- and 5-H), 7.30 (15 H, s, Ph_3C), and

10.3br (1 H, s, 3-H) (addition of D_2O caused the signal at δ 10.3 to disappear and that at δ 6.10 to collapse to a s); δ [60 MHz, $(CD_3)_2CO$] 5.97—6.07 and 6.30—6.38 (each 1 H, m, together 4- and 5-H), 7.17 (15 H, s, CPh_3), and 9.9br (1 H, s, 3-H) [irradiation at δ 9.9 caused the signals at δ 6.34 and 6.02 to collapse to d (each *J* 3.5 Hz), irradiation at δ 6.02 caused the signal at δ 9.9 to sharpen, addition of D_2O and Et_3N caused the signal at δ 9.9 to disappear and those at δ 6.34 and 6.02 to collapse to d (each *J* 3.5 Hz)]; *m/z inter alia* 243 ($C_{19}H_{15}^+$, base peak) and 165 ($C_{13}H_9^+$) (Found: C, 81.1; H, 5.6; N, 8.9. $C_{22}H_{18}N_2O$ requires C, 81.0; H, 5.5; and N, 8.6%).

(*b*) A solution of the sulphoxide (**23b**) (0.947 g, 2.43 mmol) in benzene (50 cm^3) was heated under reflux until the starting material had disappeared (t.l.c., *ca.* 4.5 h). Evaporation and purification of the residue by silica-gel chromatography (PhH–Et_2O, gradient elution) gave two fractions.

The first-eluted material, isolated as an oil (0.041 g, 15%), was methyl methanethiosulphinate (**29**).[19] It possessed the following properties: δ (60 MHz, $CDCl_3$) 2.64 and 2.96 (each 3 H, s, 2 × SMe); *m/z inter alia* 110 (M^+, base peak) and 95 ($M^+ - O$) (Found: M^+, 109.9857. Calc. for $C_2H_6OS_2$: *M*, 109.9860).

The second-eluted material, isolated as a crystalline solid (0.611 g, 77%), was identical (t.l.c. and ^1H n.m.r. spectroscopy) with the imidazolone (**28**).

Reaction of the Methylsulphonylazetidinone (**23c**) *with* 2-*Methylpropane-2-thiol.*—To a stirred solution of the methylsulphonylazetidinone (**23c**)[10] (1.02 g, 2.51 mmol) in 2-methylpropane-2-thiol (15 cm^3) was added freshly sublimed potassium t-butoxide (0.562 g, 5.02 mmol). After 2 min, the mixture was diluted with chloroform and washed (3 ×) with aqueous sodium hydrogen carbonate followed by water. Evaporation of the dried ($MgSO_4$) organic layer and purification of the resultant syrup by silica-gel chromatography (PhH–Et_2O, gradient elution) gave two β-lactam-containing fractions.

The first-eluted material, isolated as a pale-yellow chromatographically homogeneous syrup (0.236 g, 23%), was identified as (3R,4R)-4-*t-butylthio-3-triphenylmethylaminoazetidin-2-one* (**6b**). It displayed the following properties: $[\alpha]_D$ +57° (3.5% EtOH); $\nu_{max.}$(film) *inter alia* 3 400 (NH) and 1 760 cm^{-1} (β-lactam C=O); $\lambda_{max.}$(EtOH) 225 nm (ε 13 000); δ (90 MHz, $CDCl_3$) 1.23 (9 H, s, $SCMe_3$), 2.75 (1 H, d, *J* 7 Hz, Ph_3CNH), 4.44—4.62 (2 H, m, 3- and 4-H), 6.3br (1 H, s, 1-H), and 7.10—7.60 (15 H, s, CPh_3) [irradiation at δ 4.55 caused the signal at δ 2.75 to collapse to a s, addition of D_2O caused the signals at δ 2.75 and 6.3 to disappear and those at δ 4.44—4.62 to collapse to an AB q (*J* 4 Hz, separation of inner lines 2 Hz); *m/z inter alia* 416 (M^+), 373 (M^+ – CHNO), 243 ($C_{19}H_{15}^+$, base peak), and 165 ($C_{13}H_9^+$) (Found: M^+, 416.1898. $C_{26}H_{28}N_2OS$ requires *M*, 416.1922).

The second-eluted material, isolated as a solid (0.167 g, 16%), was (3R,4S)-4-*t-butylthio-3-triphenylmethylaminoazetidin-2-one* (**8c**). The sample, after recrystallisation from chloroform–diethyl ether, was isolated as colourless needles with the following properties: m.p. 148—150 °C (decomp.); $[\alpha]_D$ −117° (1% in EtOH); $\nu_{max.}$(KBr) *inter alia* 3 400 and 3 320 (NH), 1 750 cm^{-1} (β-lactam C=O); $\lambda_{max.}$(EtOH) 219 nm (ε 9 000); δ (90 MHz, $CDCl_3$) 1.18 (9 H, s, $SCMe_3$), 2.8br (1 H, s, Ph_3CNH), 3.9br (1 H, s, 3-H), 4.36 (1 H, d, *J* 2 Hz, 4-H), 6.6br (1 H, s, 1-H), and 7.10—7.60 (15 H, m, CPh_3) [addition of D_2O caused the signals at δ 2.8 and 6.6 to disappear and that at δ 3.9 to collapse to a d (*J* 2 Hz)]; *m/z inter alia* 416 (M^+), 373 (M^+ – CHNO), 243 ($C_{19}H_{15}^+$, base peak), and 165 ($C_{13}H_9^+$) (Found: C, 74.9; H, 6.7; N, 6.7%; M^+, 416.1922. $C_{26}H_{28}N_2OS$ requires C, 75.0; H, 6.8; N, 6.7%; *M*, 416.1919).

Conversion of the Triphenylmethylaminoazetidinone (**6b**) *into the Phenylacetamidoazetidinone* (**6a**).—To a solution of the triphenylmethylaminoazetidinone (**6b**) (0.190 g, 0.46 mmol) in dry dichloromethane was added toluene-*p*-sulphonic acid monohydrate (0.085 g, 0.45 mmol) dissolved in methanol (0.5 cm^3). When the starting material had disappeared (t.l.c.), the solution was concentrated and the residue dissolved in dry dichloromethane (5 cm^3). To the stirred solution was added phenylacetyl chloride (0.06 cm^3, 0.45 mmol) followed by triethylamine (0.13 cm^3, 0.93 mmol). After 30 min, the mixture was diluted with dichloromethane and washed with aqueous sodium hydrogen carbonate followed by water. Evaporation of the dried ($MgSO_4$) organic layer and purification of the residue by silica-gel chromatography (light petroleum–EtOAc, gradient elution) gave a syrup (0.058 g, 44%) which was identical with the azetidinone (**6a**) by ^1H n.m.r. spectroscopy. The material, after recrystallisation from diethyl ether–light petroleum, showed m.p. 60—61 °C and $[\alpha]_D$ −57° (2.9% in $CHCl_3$).

Acknowledgements

We thank the S.E.R.C. and Beecham Pharmaceuticals for a CAPS studentship (to D. F. C.) and a CASE studentship (to C. D. M.). Acknowledgements are also due to Beecham Pharmaceuticals for a research studentship (to A. R. K.). We are also grateful to Messrs. P. Kelly and S. Addison for the determination of the mass spectra, Dr. S. Hill and Mr. I McKeag for measuring the 300 MHz ^1H n.m.r. spectra, Mr. J. Muers for the microanalytical results, and Mr. E. Hart for technical assistance.

References

1 Part 22, J. Steele and R. J. Stoodley, *J. Chem. Soc., Perkin Trans. 1*, 1983, 2241.
2 Preliminary communication, A. C. Kaura, C. D. Maycock, and R. J. Stoodley, *J. Chem. Soc., Chem. Commun.*, 1980, 34.
3 R. J. Stoodley, *Tetrahedron*, 1975, **31**, 2321.
4 D. N. Jones and D. A. Lewton, *J. Chem. Soc., Chem. Commun.*, 1974, 457; D. N. Jones, D. R. Hill, D. A. Lewton, and C. Sheppard, *J. Chem. Soc., Perkin Trans. 1*, 1977, 1574.
5 R. B. Woodward, K. Heusler, J. Gosteli, P. Naegeli, W. Oppolzer, R. Ramage, S. Ranganathan, and H. Vorbrüggen, *J. Am. Chem. Soc.*, 1966, **88**, 852.
6 R. Scartazzini, H. Peter, H. Bickel, K. Heusler, and R. B. Woodward, *Helv. Chim. Acta*, 1972, **55**, 408.
7 K. Heusler, *Helv. Chim. Acta.*, 1972, **55**, 388.
8 R. J. Stoodley and N. R. Whitehouse, *J. Chem. Soc., Perkin Trans. 1*, 1974, 181.
9 D. F. Corbett and R. J. Stoodley, *J. Chem. Soc., Perkin Trans. 1*, 1975, 432.
10 E. G. Brain, A. J. Eglington, J. H. C. Nayler, M. J. Pearson, and R. Southgate, *J. Chem. Soc., Chem. Commun.*, 1972, 229; *J. Chem. Soc., Perkin Trans. 1*, 1976, 447.
11 R. D. G. Cooper and F. L. José, *J. Am. Chem. Soc.*, 1972, **94**, 1021.
12 R. J. Stoodley and N. S. Watson *J. Chem. Soc., Perkin Trans. 1*, 1975, 883.
13 D. H. R. Barton, D. G. T. Greig, P. G. Sammes, and M. V. Taylor, *Chem. Commun.*, 1971, 845; R. D. Allan, D. H. R. Barton, M. Girijavallabhan, P. G. Sammes, and M. V. Taylor, *J. Chem. Soc., Perkin Trans. 1*, 1973, 1182.
14 C. L. Stevens and S. J. Dykstra, *J. Am. Chem. Soc.*, 1953, **75**, 5975.
15 D. F. Corbett and R. J. Stoodley, *J. Chem. Soc., Perkin Trans. 1*, 1974, 185.
16 M. M. L. Crilley and R. J. Stoodley, *J. Chem. Soc., Perkin Trans. 1*, 1984, 1127.
17 L. N. Yanovskaya and A. P. Terent'ev, *Zhur. Obshchei Khim.*, 1952, **22**, 1598 (*Chem. Abstr.*, 1953, **47**, 9258).
18 D. Habich, *Angew. Chem., Int. Ed. Engl.*, 1983, **22**, 711.
19 T. L. Moore and D. E. O'Connor, *J. Org. Chem.*, 1966, **31**, 3587.

20 D. H. R. Barton, P. G. Sammes, M. V. Taylor, C. M. Cooper, G. Hewitt, B. E. Looker, and W. G. E. Underwood, *Chem. Commun.*, 1971, 1137.
21 A. G. Long in 'Recent Advances in the Chemistry of β-Lactam Antibiotics,' ed. J. Elks, Special Publication No. 28, The Chemical Society, London, 1977, p. 214.
22 E. G. Brain, C. L. Branch, A. J. Eglington, J. H. C. Nayler, N. F. Osborne. M. J. Pearson, T. C. Smale, R. Southgate, and P. Tolliday in 'Recent Advances in The Chemistry of β-Lactam Antibiotics,' ed. J. Elks, Special Publication No. 28, The Chemical Society, London, 1977, p. 204; C. L. Branch and M. J. Pearson, *J. Chem. Soc., Perkin Trans. 1*, 1979, 2268.
23 J. C. Sheehan and C. A. Panetta, *J. Org. Chem.*, 1973, **38**, 940; J. C. Sheehan, H. C. Dalzell, J. M. Greenwood, and D. R. Ponzi, *J. Org. Chem.*, 1974, **39**, 277.
24 A. I. Vogel, 'Practical Organic Chemistry,' 3rd edn., Longman, London, 1979, p. 771.
25 R. Sharma and R. J. Stoodley, *J. Chem. Soc., Perkin Trans. 1*, 1980. 2001.

Received 29*th August* 1986; *Paper* 6/1746