Synthesis of Novel Fused β-Lactams by Intramolecular 1,3-Dipolar Cycloadditions. Part 8.[1] 6,7,7a,7b-Tetrahydro-3-methyl-6-oxo-1*H*-azeto-[1,2-*a*]azirino[2,1-*c*]pyrazine-4-carboxylic Acids

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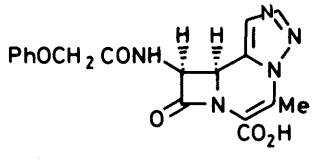
4-Vinylazetidin-2-one (**4**) was converted into t-butyl (7a*RS*, 7b*RS*)-6,7,7a,7b-tetrahydro-3-methyl-6-oxo-1*H*-azeto[1,2-*a*]azirino[2,1-*c*]pyrazine-4-carboxylate (**12**; R = Bu^t) *via* thermolysis of the vinyl azide (**9**) in refluxing benzene. The configuration of the aziridine ring was assigned on the basis of nuclear Overhauser enhancement difference spectroscopy. t-Butyl was not an appropriate acid protecting group, but the corresponding diphenyl-t-butylsilyl ester (**12**; R = $SiPh_2Bu^t$) was cleanly deprotected to give potassium (7a*RS*,7b*RS*)-6,7,7a,7b-tetrahydro-3-methyl-6-oxo-1*H*-azeto[1,2,*a*]-azirino[2,1-*c*]pyrazine-4-carboxylate (**12**; R = K).

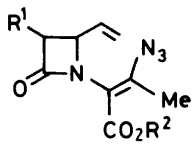
The known (3*RS*, 4*SR*)-3-azido-1-(1-benzyloxycarbonyl-2,2-ethylenedioxypropyl)-4-styryl-azetidin-2-one (**21**) was used to prepare benzyl (1*RS*, 7*SR*, 7a*SR*, 7b*SR*)-6,7,7a,7b-tetrahydro-3-methyl-6-oxo-7-phenoxyacetamido-1-phenyl-1*H*-azeto[1,2-*a*]azirino[2,1-*c*]pyrazine-4-carboxylate (**15**) *via* the vinyl azide (**19**). In the 7-acylamino series neither benzyl nor diphenyl-t-butylsilyl proved amenable acid protecting groups, but 2,2,2-trichloroethyl was found to be a convenient alternative. Thus heating (3*RS*, 4*SR*)-1-[2-azido-1-(2,2,2-trichloroethoxycarbonyl)prop-1-enyl]-3-phenoxy-acetamido-4-vinylazetidin-2-one (**20**) in refluxing benzene provided 2,2,2-trichloroethyl (7*RS*, 7a*RS*, 7b*RS*)-6,7,7a,7b-tetrahydro-3-methyl-6-oxo-7-phenoxyacetamido-1*H*-azeto[1,2-*a*]azirino[2,1-*c*]-pyrazine-4-carboxylate (**17**), which was deprotected to give the corresponding acid (**18**). The 4-vinyl functionality of the azide (**20**), was introduced at an earlier stage by semi-hydrogenation of an ethynyl group present in a suitably substituted precursor.

The potassium salt (**12**; R = K) and the acid (**18**) were both antibacterially inactive.

The intramolecular cycloaddition between an acetylene and a vinyl azide has been used to prepare the tricyclic triazole (**1**), which was antibacterially active.[1] In the hope of further exploiting the process for the synthesis of β-lactam antibiotic analogues, the case in which the triple bond was replaced by a double bond was investigated.[2] By analogy with our earlier work,[3] it was envisaged that the thermolysis of (**2**) would lead to the imine (**3**), a system of potential biological interest. Although an acylamino side-chain was considered a necessary prerequisite for antibacterial activity, the initial studies were performed on the readily available 4-vinylazetidinone (**4**).[4]



(**1**)



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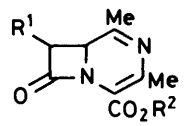
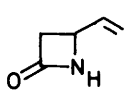
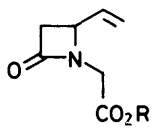


(**3**)



(**4**)

Alkylation of (**4**) with t-butyl bromoacetate in dry tetrahydrofuran–dimethylformamide (THF–DMF, 3:1) using powdered potassium hydroxide afforded the ester (**5**; R = Bu^t). The ester enolate of (**5**; R = Bu^t), generated by means of lithium



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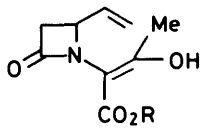
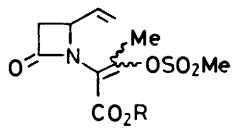
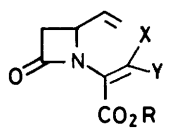


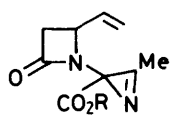
(**6**)



(**7**)



(**8**) Y = N_3, X = Me
(**9**) Y = Me, X = N_3

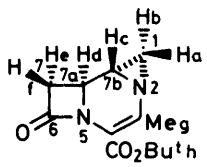


(**10**)

hexamethyldisilazide in THF at −76 °C, was quenched with acetyl chloride to provide the β-keto ester (**6**; R = Bu^t). The i.r. [$\nu_{max.}$($CHCl_3$) 1 750, 1 650, and 1 625 cm^{-1}] and ^1H n.m.r. spectra indicated that (**6**; R = Bu^t) existed primarily in the enol form. Further elaboration of (**6**; R = Bu^t) by successive treatment with methanesulphonyl chloride and sodium azide as previously described,[1,2] gave the desired *N*-functionality. Rapid fractionation of the crude product on silica gel afforded unchanged methanesulphonate (**7**; R = Bu^t) (20%), and the vinyl azide as a mixture of separable geometrical isomers (**8**) and (**9**) (ratio *ca.* 1:1). The *E*-isomer (**8**) was stable at room temperature but was converted into the azirine (**10**; R = Bu^t) on heating at reflux in benzene for 20 min.

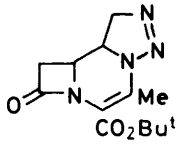
When the *Z*-isomer (**9**) was stored in ethyl acetate for 18 h, complete loss of the azide band in the i.r. spectrum was observed. Removal of the solvent and ether trituration afforded a good yield of a white solid, which from the n.m.r. spectrum was

Table. ^{1}H N.m.r. data* for vinyl aziridine (**12**; R = Bu^t)

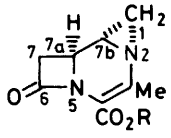
Structure	Chemical shifts (p.p.m.)	Coupling constants (Hz)
	a 2.56	J_{ab} 0.93
	b 1.39	J_{ac} 4.70
	c 2.69	J_{bc} 3.60
	d 3.03	J_{ad} 0.41
	e 3.42	J_{bd} 0.32
	f 2.82	J_{de} 3.77
	g 2.30	J_{ce} 5.43
	h 1.53	J_{df} 2.52
		J_{ef} 15.07

* Solvent $CDCl_3$; Me_4Si as internal standard; Bruker WM250 spectrometer.

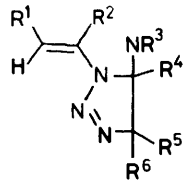
substantially the 1,2,3-triazoline (**11**). The NCH_2 appeared as an AB quartet at δ 4.34 and 4.64, (*J* 18 Hz), each part showing further coupling of 7 and 11 Hz respectively. When the material was briefly refluxed in benzene, quantitative conversion into a less polar (t.l.c.) component occurred. The product was isolated as a crystalline solid and the n.m.r. spectrum was exceptional in that the lowest field signal was at δ 3.42, and only one olefinic methyl group was indicated. The imine type structure (**3**) was therefore discounted in favour of the aziridine (**12**; R = Bu^t). This observation is in accord with a recent literature report[5] on the intermolecular reaction of vinyl azides with electron deficient olefins. Although in that study the initial 1,3-dipolar adduct of the azide was never isolated, electron rich olefins have been very recently shown[6] to give relatively stable 1,2,3-triazolines of type (**13**).



(**11**)



(**12**)



(**13**)

The ^{1}H n.m.r. spectrum of the vinylaziridine (**12**; R = Bu^t) was extremely complex. The chemical shifts and coupling constants of all the protons (Table) were ascertained from an analysis of the highly resolution enhanced 250 MHz ^{1}H n.m.r. spectra, which included pertinent homonuclei decoupling by irradiation, and the use of nuclear Overhauser enhancement difference spectroscopy. Some of our original assignments,[2] based on less comprehensive data, were thus shown to be incorrect.

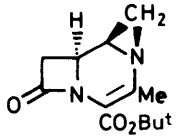
Lanthanide induced shifts have been used to delineate stereochemical assignments in β-lactam ring systems,[7] but in this case the technique provided no clear-cut information. It appeared that two binding sites were being occupied at about the same rate, leading to inconsistent shift results.

The *cis*-orientation of the aziridine ring and the C-7a proton was tentatively deduced from the following evidence. Models indicated that the Karplus angles between the C-7a and C-7b protons for the structures (**12**; R = Bu^t) and (**14**) are respectively *ca.* 110° and 10—20°. A coupling constant of *ca.* 6—8 Hz would be predicted for a dihedral angle of 10—20°, and since the observed $J_{7a,7b}$ is 3.77 Hz, this leads to the assignment of (**12**; R = Bu^t) as the more likely structure for the aziridine product. This *cis*-disposition of the C-7a proton and the aziridine ring also provides a slightly better coupling path for the W-coupling between the C-7a proton and the aziridine methylene protons.

Nuclear Overhauser enhancement difference spectroscopy was instrumental in confirming these tentative ideas, and also allowed definitive assignment for the chemical shifts of the aziridine protons. Irradiation at δ 1.39 produced a strong positive nuclear Overhauser effect (n.O.e.) in the resonance at δ 2.56, as well as a significant enhancement of the signal at δ 3.03. Similarly, irradiation at δ 2.56 gave a strong positive enhancement of the resonance at δ 1.39, and a definite, but weaker, effect at δ 2.69. Significantly no n.O.e. was observed on the C-7 protons in either experiment. However an n.O.e. was evident on the C-7 β-proton when the resonance at δ 2.69 was irradiated. Inspection of models clearly show that only a *cis* relationship between the C-7a proton and the aziridine ring can accommodate these data. The *trans* orientation would favour a considerable enhancement of the C-7 β-proton on irradiation of one or both of the aziridine methylene resonances.

On irradiation at δ 3.03 the predicted n.O.e.'s of the C-7 protons were masked by INDOR effects, but an n.O.e. was produced at δ 1.39 but not at δ 2.56, indicating that the C-1 α-proton (δ 1.39) was significantly higher field than the C-1 β-proton (δ 2.56). This remarkable shift of the C-1 α-proton was attributed to two factors. First, shielding by the orbitals of the double bond, and secondly, its *trans*-diaxial relationship with the nitrogen lone pair.

The removal of the t-butyl ester protecting group from (**12**; R = Bu^t) could not be achieved without concomitant disruption of the vinyl aziridine system. The instability of (**12**; R = Bu^t) *per se* to conditions of hydrogenolysis or alkaline hydrolysis precluded the use of benzyl or simple alkyl as a blocking group. However, earlier work in these laboratories[8] indicated that diphenyl-t-butylsilyl was an ideal carboxy protecting group for penicillins, and since the vinyl aziridine (**12**; R = Bu^t) was unaffected by the required deprotection procedure, the following approach was adopted. The intermediate methanesulphonate (**7**; R = Bu^t) was treated with trifluoroacetic acid to give the acid (**7**; R = H) which was immediately re-esterified with diphenyl-t-butylsilyl chloride to provide the ester (**7**; R = $SiPh_2Bu^t$) as a mixture of geometrical isomers (ratio 1:1). The same compound was available *via* a different route. The t-butyl ester of the lactam (**5**; R = Bu^t) was replaced by diphenyl-t-butylsilyl as described for the methanesulphonate (**7**; R = Bu^t), and the resultant ester (**5**; R = $SiPh_2Bu^t$) converted into the methanesulphonate (**7**; R = Bu^t) (2:1 isomer ratio), *via* the enol (**6**; R = $SiPh_2Bu^t$). The methanesulphonate (**7**; R = $SiPh_2Bu^t$), derived from either route was then treated as previously described to provide the azirine (**10**; R = $SiPh_2Bu^t$) and the aziridine (**12**; R = $SiPh_2Bu^t$). It was then a simple matter to remove the ester protecting group using potassium fluoride–18-crown-6 in THF, to afford the potassium salt (**12**; R = K). The i.r. and ^{1}H n.m.r. spectra of the final product were in accord with the desired structure, and the u.v. spectrum [$\lambda_{max.}$(EtOH) 261 nm (ε 11 199)] confirmed the presence of the vinylaziridine



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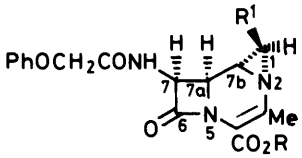


(15) R^1 = Ph, R^2 = CH_2Ph
(16) R^1 = Ph, R^2 = H
(17) R^1 = H, R^2 = CH_2CCl_3
(18) R^1 = R^2 = H

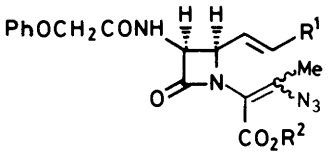
chromophore. Although the material (12; R = K) was devoid of antibacterial activity, it was hoped that the acylamino analogues would be more potent.

Contemporaneous with our work in the unsubstituted series, the aziridine (15) was prepared from the vinyl azide (19). The synthesis of the vinyl azide (19) involved the same totally synthetic approach as that already reported for the preparation of triazolocephems (1),[1] using the known acetal (21)[9] as starting material. Thus, reduction of the azide (21) with hydrogen sulphide–triethylamine,[10] followed by acylation with phenoxyacetyl chloride gave the amide (22). Removal of the acetal with 95% aqueous trifluoroacetic acid and treatment of the resulting enol (23) with methanesulphonyl chloride gave methanesulphonate (24), as a mixture of geometrical isomers in a ratio 9:1. The methanesulphonate (24) then provided the vinyl azide (19) on reaction with sodium azide. Thermolysis of the vinyl azide (19) in benzene for 10 min gave the azirines (27) and the aziridine (15).

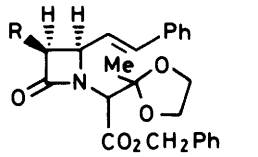
Although the compound (15) was not an appropriate precursor for the corresponding free acid (16), owing to the aforementioned instability of the system to hydrogenolysis, the ^{1}H n.m.r. spectrum was of interest. Long range coupling was not evident (90 MHz spectrum), but the two aziridine methine protons at C-7b and C-1 respectively gave resonances at δ 2.55 (*J* 2.9 and 3.9 Hz) and δ 2.67 (*J* 2.9 Hz). In the derivative (17) (*vide infra*) lacking the phenyl group in the aziridine ring, the α- and β-protons of the aziridine methylene group appeared at δ 1.58 and 2.55 respectively (see the Experimental section). Since an aromatic group would be expected to produce both spatial and inductive deshielding effects, the phenyl ring must be substituted on the β-face of the aziridine, deshielding the α-proton by *ca.* δ 1.1.

At this time it was thought that phenyl substitution of the aziridine ring could be detrimental to biological activity, and the synthetic target became the free acid (18). Our first requirement was therefore a *cis* 3-acylamino monocyclic β-lactam substituted with a vinyl group at C-4. As an initial approach it was decided to examine the introduction of an azido group into the 3-position of the 4-vinylazetidinone (4). Accordingly, the azetidinone (4) was silylated using dimethyl-t-butylsilyl chloride, and the product (28) treated successively with lithium diisopropylamide, tosyl azide, and chlorotrimethylsilane,[11] to provide the *trans* azide (29) as the only product. The Merck group[12] have reported a method for the kinetically controlled isomerisation of 6α(7α)-aminopenicillins and cephalosporins to their β-epimers, and Bachi[13] has demonstrated its applicability to non-fused β-lactams. Thus, the azide (29) was reduced to the amine (30) which was converted into the Schiff base (31), but application of the Merck procedure proved unrewarding. Consequently we returned to the route involving modification of a suitably functionalised *N*-substituent. The selection of an appropriate carboxy protecting group became of paramount importance. Work in the non-acylamino series ruled out t-butyl, benzyl, and simple alkyl. Since the synthetic sequence also demanded that the group be stable to trifluoroacetic acid, diphenyl-t-butylsilyl was also of little utility. However, 2,2,2-trichloroethyl, which has been used widely in cephalosporin synthesis, proved advantageous.

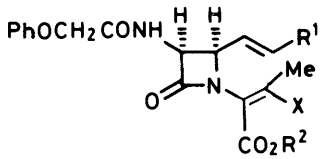
Attempts at the preparation of the Schiff base (32) derived from acrolein were not fruitful, but a 4-vinyl substituent was successfully introduced *via* semi-hydrogenation of an ethynyl group. The ethyl ester (34) was available from our earlier studies on triazolocephems, and was synthesised *via* an identical



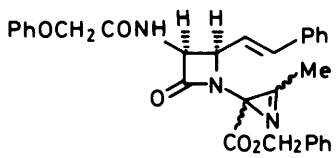
(19) R^1 = Ph, R^2 = CH_2Ph
(20) R^1 = H, R^2 = CH_2CCl_3



(21) R = N_3
(22) R = $NHCOCH_2OPh$



(23) R^1 = Ph, R^2 = CH_2Ph, X = OH
(24) R^1 = Ph, R^2 = CH_2Ph, X = OSO_2Me
(25) R^1 = H, R^2 = CH_2CCl_3, X = OH
(26) R^1 = H, R^2 = CH_2CCl_3, X = OSO_2Me



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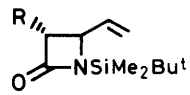
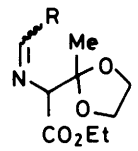
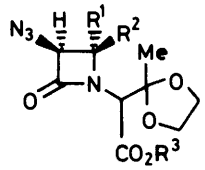


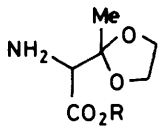
(28) R = H
(29) R = N_3
(30) R = NH_2
(31) R = $NCHC_6H_4NO_2$-*p*-



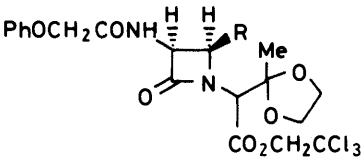
(32) R = $CH=CH_2$
(33) R = $C\equiv CSiMe_3$



(34) R^1 = H, R^2 = $C\equiv CSiMe_3$, R^3 = Et
(35) R^1 = H, R^2 = $C\equiv CSiMe_3$, R^3 = CH_2Ph
(36) R^1 = $C\equiv CSiMe_3$, R^2 = H, R^3 = Et
(37) R^1 = R^3 = H, R^2 = $C\equiv CH$
(38) R^1 = H, R^2 = $C\equiv CH$, R^3 = CH_2CCl_3



(39) R = Et
(40) R = CH_2Ph



(41) R = C≡CH
(42) R = CH=CH_2
(43) R = Et

sequence to the previously reported benzyl analogue (**35**).[1] Thus, the amine (**39**) was transformed *via* the Schiff base (**33**), into the *trans* and *cis* β-lactams (**36**) and (**34**), both of which were inseparable mixtures of stereoisomers.

Hydrolysis of the ester (**34**) with 0.25M sodium hydroxide in THF proceeded smoothly with concomitant cleavage of the trimethylsilyl group, to give the crude acid (**37**). Re-esterification with 2,2,2-trichloroethanol–dicyclohexylcarbodiimide (DCC) then provided the ester (**38**) as a single crystalline isomer, of undefined stereochemistry at the carboxylate functionality. The azide (**38**) was conveniently converted into the amide (**41**) at this stage using the established methodology. Hydrogenation of the amide (**41**) in dioxane using 10% Pd–$BaSO_4$ gave the required olefin (**42**) in 75% yield, along with some completely hydrogenated material (**43**) (10%). Successive treatment of the acetal (**42**) with trifluoroacetic acid, methanesulphonyl chloride, and sodium azide afforded the vinyl azide (**20**), *via* the crystalline enol (**25**) and the methanesulphonate (**26**). Brief thermolysis of the azide (**20**) in benzene, gave the aziridine (**17**) as the only isolable product. Finally reaction of the ester (**17**) with activated zinc dust in THF containing potassium dihydrogenphosphate,[14] removed the carboxy protecting group, to give the desired free acid (**18**) in 60% yield. The product (**18**) possessed the expected spectroscopic properties, but was antibacterially inactive.

Experimental

General procedures were as in Part 1 [15] except where indicated otherwise. 250 MHz n.m.r. spectra were recorded on a Bruker WM 250 instrument. All the compounds are racemic.

Esters of 2-*Oxo*-4-*vinylazetidin*-1-*ylacetic Acid* (**5**).—4-Vinylazetidin-2-one (**4**) (1.94 g) was dissolved in a mixture of dry THF and DMF (75 ml, 3:1) at 0 °C, containing t-butyl bromoacetate (3.9 g). Powdered potassium hydroxide (1.12 g) was added and the mixture vigorously stirred. The cooling bath was removed and after 30 min the reaction mixture was poured into ethyl acetate and brine. The organic layer was separated, washed successively with water and brine, dried, and evaporated. Chromatography of the residue afforded *the ester* (**5**; R = Bu^t) as an oil (2.89 g) (Found: M^+, 211.1200. $C_{11}H_{17}NO_3$ requires *M*, 211.1208); $\nu_{max.}$ 1 755 and 1 738 cm^{-1}; δ_H(60 MHz) 1.47 (9 H, s), 2.7 and 3.28 (2 H, ABq, *J* 15 Hz, each arm showing further coupling of 3 and 5 Hz respectively), 3.51 and 4.11 (2 H, ABq, *J* 18 Hz), and 5.2—6.25 (3 H, m, typical vinyl pattern).

The ester (**5**; R = Bu^t) (1 g) was dissolved in trifluoroacetic acid (10 ml). After 30 min the solution was evaporated, the residue treated with toluene, and the mixture re-evaporated (× 2). The crude product was dissolved in dichloromethane (15 ml) and the solution cooled to −10 °C. Triethylamine (510 mg) was added followed by diphenyl-t-butylsilyl chloride (1.39 g) in dichloromethane (2 ml). The solution was warmed to room temperature and after 30 min, water was added. The organic layer was separated, washed successively with water and brine, dried, and evaporated. Chromatography of the residue provided *the ester* (**5**; R = $SiPh_2Bu^t$) as a thick oil (1.08 g) (Found: $M^+ - Bu^t$, 336.1045. $C_{19}H_{18}NO_3Si$ requires $M^+ - Bu^t$, 336.1054); $\nu_{max.}$ 1 755 and 1 738 cm^{-1}; δ_H(90 MHz) 1.1 (9 H, s), 2.68 and 3.12 (2 H, ABq, *J* 15 Hz, each part showing further coupling of *J* 2.5 and 5 Hz respectively), 3.7 and 4.33 (2 H, ABq, *J* 19 Hz), 4.15 (1 H, m), 5.15—5.4 (2 H, m), 5.58—6.0 (1 H, m), and 7.22—7.8 (10 H, m).

Esters of 1-(1-*Carboxy*-2-*hydroxyprop*-1-*enyl*)-4-*vinylazetidin*-2-*one* (**6**).—Hexamethyldisilazane (4.602 g) was dissolved in dry THF (70 ml), under argon, at 0 °C and n-butyl-lithium (17.9 ml; 1.6M-solution in hexane) was added. After 10 min the solution was cooled to −76 °C and the ester (**5**; R = Bu^t) (2.74 g) in dry THF (15 ml) was added dropwise during 10 min. The mixture was stirred for a further 15 min and then acetyl chloride (1.12 g) in THF (5 ml) added dropwise during 10 min. After 5 min the solution was poured into ethyl acetate–0.01M-hydrochloric acid. The organic layer was separated, washed successively with water and brine, dried, and evaporated. Chromatography afforded the *product* (**6**; R = Bu^t) as an oil (2.15 g) (Found: M^+, 253.1319. $C_{13}H_{19}NO_4$ requires *M*, 253.1312); $\nu_{max.}$ 1 750, 1 650, and 1 625 cm^{-1}; δ_H(60 MHz) 1.53 (9 H, s), 2.04 (3 H, s), 2.17 and 3.70 (2 H, ABq, *J* 15 Hz, each arm showing further coupling of 3 and 5 Hz respectively), 3.95—4.42 (1 H, m), 5.12—6.25 (3 H, m, typical vinyl pattern), and 12.53 (1 H, s, exch. D_2O).

Using the same procedure, the corresponding diphenyl-t-butylsilyl derivative (**5**; R = $SiPh_2Bu^t$) (4.6 g) was converted into 1-(1-*diphenyl*-t-*butylsilyloxycarbonyl*-2-*hydroxyprop*-1-*enyl*)-4-*vinylazetidin*-2-*one* (**6**; R = $SiPh_2Bu^t$), which was isolated as a thick oil (2.74 g) (Found: M^+, 435.1875. $C_{25}H_{29}NO_4Si$ requires *M*, 435.1863); $\nu_{max.}$ 1 750 and 1 640 cm^{-1}; δ_H(90 MHz) 1.11 (9 H, s), 2.08 (3 H, s), 2.79 and 3.19 (2 H, ABq, *J* 15 Hz, each part showing further coupling of *J* 3 and 5 Hz respectively), 4.25 (1 H, m), 5.15—5.4 (2 H, m), 5.65—6.06 (1 H, m), 7.2—7.8 (10 H, m), and 12.56 (1 H, s, exch. D_2O).

Esters of 1-(1-*Carboxy*-2-*methylsulphonyloxyprop*-1-*enyl*)-4-*vinylazetidin*-2-*one* (**7**).—The enol (**6**; R = Bu^t) (1.484 g) was dissolved in dry dichloromethane (100 ml) and the solution was cooled to 0 °C. Triethylamine (888 mg) was added, followed by methanesulphonyl chloride (1.008 g) in dichloromethane (10 ml). The solution was washed successively with dilute hydrochloric acid (0.01M) and brine, then dried and evaporated. Chromatography of the residue afforded the *methanesulphonate* (**7**; R = Bu^t) as a foam (1.94 g) (Found: M^+, 331.1079. $C_{14}H_{21}NO_6S$ requires *M*, 331.1089); $\nu_{max.}$ 1 760, 1 720, and 1 640 cm^{-1}; the n.m.r. spectrum indicated that the material was a *ca.* 1:1 mixture of geometrical isomers, δ_H(90 MHz) *inter alia* 1.52 (9 H, s), 2.21 and 2.46 (together 3 H, both s), 3.17 and 3.18 (together 3 H, both s), 4.38—4.6 (1 H, m), and 5.18—6.14 (3 H, m, typical vinyl pattern).

Similar reaction of the enol (**6**; R = $SiPh_2Bu^t$) (2 g) afforded 1-(1-*diphenyl*-t-*butylsilyloxycarbonyl*-2-*methylsulphonyloxyprop*-1-*enyl*)-4-*vinylazetidin*-2-*one* (**7**; R = $SiPh_2Bu^t$) as a thick oil (2.41 g) (Found: $M^+ - Bu^t$ 456.0928. $C_{22}H_{22}NO_6SSi$ requires $M - Bu^t$ 456.0934); $\nu_{max.}$ 1 760, 1 720, 1 640, 1 365, and 1 165 cm^{-1}; the n.m.r. spectrum showed that the material was a 1:1 mixture of geometrical isomers, δ_H(250 MHz) *inter alia* 1.10 (9 H, s), 2.30 and 2.53 (together 3 H, both s), 2.85 and 3.23 (together 3 H, both s), 4.40—4.54 (1 H, m), 5.21—5.28 (2 H, m), 5.79—6.0 (1 H, m), and 7.3—7.7 (10 H, m).

Successive treatment of the methanesulphonate (**7**; R = Bu^t) (350 mg) with trifluoroacetic acid and diphenyl-t-butylsilyl chloride as described for (**5**; R = Bu^t), provided the methanesulphonate (**7**; R = $SiPh_2Bu^t$) (441 mg), in an isomer ratio of 2:1.

Esters of (7*a*RS,7*b*RS)-6,7,7*a*,7*b*-*Tetrahydro*-3-*methyl*-6-*oxo*-1H-*azeto*-[1,2-a] *azirino* [2,1-c]*pyrazine*-4-*carboxylic Acid* (**12**) *and* 1-(1-*Carboxy*-3-*methyl*-2H-*azirin*-2-*yl*)-4-*vinylazetidin*-2-*one* (**10**).—*Method A*. The methanesulphonate (**7**; R = Bu^t) (662 mg) was dissolved in dry DMF (15 ml) and powdered sodium azide (163 mg) added. The mixture was vigorously stirred for 1 h, and then poured into ethyl acetate and water. The organic layer was separated, washed with brine, dried, and evaporated. Rapid chromatography gave the *Z*-vinyl azide (**9**; R = Bu^t) (81 mg), the *E*-vinyl azide (**8**; R = Bu^t) (180 mg), and starting material (**7**; R = Bu^t) (106 mg).

The *Z*-isomer (**9**; R = Bu^t) (81 mg) was dissolved in ethyl acetate (2 ml) and after 16 h the i.r. spectrum showed no azide band. Removal of the solvent, followed by ether trituration gave the 1,2,3-triazoline (**11**) as a white solid (38 mg), $\nu_{max.}$ 1 765, 1 700, and 1 605 cm^{-1}; δ_H(90 MHz) *inter alia* 1.54 (9 H, s), 2.67 (3 H, s), 4.34 and 4.64 (2 H, ABq, *J* 18 Hz, each arm showing further coupling of 7 and 11 Hz). The solid (**11**) (35 mg) was dissolved in dry benzene (2 ml) and the solution refluxed for 20 min. The solvent was evaporated and the residue chromatographed to provide the *aziridine* (**12**; R = Bu^t) as a white solid (25 mg), m.p. 142—144 °C (ethyl acetate–light petroleum) (Found: C, 62.3; H, 7.4; N, 11.3. $C_{13}H_{18}N_2O_3$ requires C, 62.4; H, 7.2; N, 11.2%); $\lambda_{max.}$ 277 nm (ε 13 000 dm^3 mol^{-1} cm^{-1}); $\nu_{max.}$ (Nujol) 1 750, 1 695, and 1 595 cm^{-1}; δ_H(250 MHz) see Table and text.

The *E*-isomer (**8**; R = Bu^t) (175 mg) was dissolved in toluene (15 ml) and the solution was refluxed for 20 min. The solvent was evaporated off and the residue chromatographed to give the *azirine* (**10**; R = Bu^t) as an oil (191 mg) (Found: M^+, 250.1307. $C_{13}H_{18}N_2O_3$ requires *M*, 250.1316); $\nu_{max.}$ 1 760, 1 733, and 1 650 cm^{-1}; δ_H(90 MHz) 1.45 (9 H, s), 2.6 (3 H, s), 2.69 and 3.03 (2 H, ABq, *J* 15 Hz, each part showing further coupling of *J ca.* 3 and 5 Hz), 4.0—4.5 (1 H, m), 5.15—5.5 (2 H, m), and 5.67—6.32 (1 H, m). *Method B*. The methanesulphonate (**7**; R = Bu^t) (1.94 g) was dissolved in dry DMF (40 ml) and treated with powdered sodium azide (762 mg) as previously described in Method A. The crude product was dissolved in dry benzene (50 ml) and the solution refluxed for 20 min. The solution was evaporated and the residue chromatographed on silica-gel to provide the azirine (**10**; R = Bu^t) (477 mg), the methanesulphonate (**7**; R = Bu^t) (121 mg), and the aziridine (**12**; R = Bu^t) (309 mg). Method B was used to convert the methanesulphonate (**7**; R = SiPh$_2$Bu^t) (2.74 g) into 1-(1-*diphenyl*-*t*-*butylsilyloxycarbonyl*-3-*methyl*-2H-*azirin*-2-*yl*)-4-*vinylazetidin*-2-*one* (**10**; R = SiPh$_2$Bu^t) which was isolated as a thick oil (600 mg); (Found: M^+, 432.1863 $C_{25}H_{28}N_2O_3Si$ requires *M*, 432.1869); $\nu_{max.}$ 1 755, 1 725, and 1 650 cm^{-1}; δ_H(90 MHz) 1.05 (9 H, s), 2.63 (3 H, s), 2.68 and 3.02 (2 H, ABq, *J* 15 Hz, each part showing further coupling of 3 and 5 Hz), 4.0—4.25 (1 H, m), 5.0—5.45 (2 H, m), 5.8—6.3 (1 H, m), and 7.2—7.8 (10 H, m). Further elution of the column provided *diphenyl*-*t*-*butylsilyl*-(7*a*RS,7*b*RS)-6,7,7*a*,7*b*-*tetrahydro*-3-*methyl*-6-*oxo*-1H-*azeto*[1,2-a]*azirino*[2,1-c]*pyrazine*-4-*carboxylate* (**12**; R = SiPh$_2$Bu^t) as a crystalline solid (691 mg), m.p. 145—146 °C (ethyl acetate–light petroleum) (Found: C, 69.7; H, 6.5; N, 6.5. $C_{25}H_{28}N_2O_3Si$ requires C, 69.4; H, 6.5; N, 6.5%); $\lambda_{max.}$ 284 nm (ε 13 390 dm^3 mol^{-1} cm^{-1}); $\nu_{max.}$ 1 765, 1 690, and 1 590 cm^{-1}; δ_H(250 MHz) 1.12 (9 H, s), 1.45 (1 H, m, *J* 3.4 Hz and unresolved fine coupling), 2.28 (3 H, s), 2.59 (1 H, m, *J* 4.4 Hz and unresolved fine coupling), 2.73 (1 H, q), 2.85 and 3.48 (2 H, ABq, *J* 15 Hz, each arm showing further coupling of *J* 2.4 and 5.3 Hz respectively), 7.07 (6 H, m), and 7.15 (4 H, m).

Potassium (7*a*RS,7*b*RS)-6,7,7*a*,7*b*-*Tetrahydro*-3-*methyl*-6-*oxo*-1H-*azeto*[1,2-a]*azirino*[2,1-c]*pyrazine*-4-*carboxylate* (**12**; R = K).—The ester (**12**; R = SiPh$_2$Bu^t) (51 mg) was dissolved in dry THF (2 ml) and anhydrous potassium fluoride (9 mg) and 18-crown-6 (3 mg) were added. After 4 h, filtration gave the *potassium salt* (**12**; R = K) as a buff solid (18 mg) [Found: M^+ + H, (FAB), 233. $C_9H_{10}N_2O_3K$ requires *M* + H, 233]; $\lambda_{max.}$ 261 nm (ε 11 120 dm^3 mol^{-1} cm^{-1}); $\nu_{max.}$ (KBr) 3 420br, 1 750, 1 615, and 1 580 cm^{-1}; δ_H(250 MHz) 1.5 (1 H, m, *J* 3.8 Hz and further unresolved fine coupling), 2.0 (3 H, s), 2.39 (1 H, m, *J* 4.9 Hz and further unresolved fine coupling), 2.69 (1 H, q), 2.78 (2 H, ABq, *J* 15 Hz, and each arm showing further coupling of *J* 2.7 and 5.3 Hz).

(3RS, 4SR)-1-(1-*Benzyloxycarbonyl*-2,2-*ethylenedioxypropyl*)-3-*phenoxyacetamido*-4-*styrylazetidin*-2-*one* (**22**).—The azide (**21**) (5.75 g; 2:1 ratio of carboxylate epimers) was dissolved in dry dichloromethane (200 ml) at 0 °C, and triethylamine (1.38 g) added. Hydrogen sulphide was bubbled through the solution for 5 min, and the reaction left for 1 h at 0 °C and 45 min at 10—15 °C. The solution was evaporated and the residue treated with dichloromethane and the mixture re-evaporated (× 2). The residue was dissolved in dry dichloromethane (200 ml) and the solution cooled to −5 °C. Triethylamine (1.38 g) was added, followed by phenoxyacetyl chloride (2.38 g) in dichloromethane (20 ml). The solution was washed with water, dried, and evaporated. Chromatography gave a foam (5.78 g), from which the *major isomer* (**22**) (3.6 g) was isolated by trituration with ethyl acetate–hexane, m.p. 124 °C (ethyl acetate–hexane) (Found: C, 69.1; H, 6.1; N, 5.0. $C_{32}H_{32}N_2O_7$ requires C, 69.1; H, 5.8; N, 5.0%); $\nu_{max.}$ 3 425, 1 760, 1 740sh, 1 690, and 1 660sh cm^{-1}; δ_H(90 MHz) 1.5 (3 H, s), 3.89 (4 H, s), 4.35 (1 H, s), 4.31 and 4.55 (2 H, ABq, *J* 15 Hz), 4.85 (1 H, dd, *J* 5 and 9 Hz), 5.22 (2 H, s), 5.41 (1 H, dd, *J* 5 and 9 Hz), 6.02 (1 H, dd, *J* 9 and 16 Hz), 6.65 (1 H, d, *J* 16 Hz), and 6.67—7.5 (16 H, m).

(E)-(3RS, 4SR)-1-(1-*Benzyloxycarbonyl*-2-*hydroxyprop*-1-*enyl*)-3-*phenoxyacetamido*-4-*styrylazetidin*-2-*one* (**23**).—The amide (**22**) (929 mg) was dissolved in trifluoroacetic acid (10 ml). After 90 min the solution was poured into dichloromethane–ice–water and the organic layer separated. The aqueous layer was extracted with dichloromethane (× 3) and the combined organic extracts washed with water (× 3), dried, and evaporated. Chromatography afforded the *enol* (**23**) as a solid (564 mg) m.p. 147—148 °C (ethyl acetate–light petroleum) (Found: C, 70.0; H, 5.9; N, 5.4. $C_{30}H_{28}N_2O_6$ requires C, 70.3; H, 5.5; N, 5.5%); $\nu_{max.}$ 3 420, 1 765, 1 695, and 1 660 cm^{-1}; δ_H(90 MHz) 2.16 (3 H, s), 4.45 (2 H, s), 4.58 (1 H, dd, *J* 5 and 9 Hz), 5.12 and 5.29 (2 H, ABq, *J* 12 Hz), the C-3 β-lactam proton is obscured by the ABq of the ester, 6.02 (1 H, dd, *J* 9 and 16 Hz), 6.7—7.5 (16 H, m), and 12.26 (1 H, s, exch. D_2O).

(3RS, 4SR)-1-(1-*Benzyloxycarbonyl*-2-*methylsulphonyloxyprop*-1-*enyl*)-3-*phenoxyacetamido*-4-*styrylazetidin*-2-*one* (**24**).—The enol (**23**) (561 mg) was converted into the *methanesulphonate* (**24**) (453 mg) as described for (**6**; R = Bu^t) (Found: M^+, 590.1721. $C_{31}H_{30}N_2O_8S$ requires *M*, 590.1722); $\nu_{max.}$ 3 410, 1 765, 1 725, 1 685, and 1 635 cm^{-1}; the n.m.r. spectrum showed the material was essentially a single isomer, δ_H(90 MHz) 2.5 (3 H, s), 3.23 (3 H, s), 4.42 (2H, s), 4.82 (1 H, dd, *J* 5 and 8 Hz), 5.10 and 5.33 (2 H, ABq, *J* 12 Hz), 5.37 (1 H, dd, *J* 5 and 9 Hz), 6.16 (1 H, dd, *J* 8 and 15 Hz), 6.42 (1 H, d, *J* 15 Hz), and 6.7—7.5 (16 H, m).

Benzyl (1RS,7RS,7*a*RS,7*b*RS)-6,7,7*a*,7*b*-*Tetrahydro*-3-*methyl*-6-*oxo*-7-*phenoxyacetamido*-1-*phenyl*-1H-*azeto*[1,2-a]*azirino*-[2,1-c]*pyrazine*-4-*carboxylate* (**15**) and (3RS,4SR)-1-(1-*Benzyloxycarbonyl*-3-*methyl*-2H-*azirin*-2-*yl*)-3-*phenoxyacetamido*-4-*styrylazetidin*-2-*one* (**27**).—The methanesulphonate (**24**) (422 mg) was converted as described for (**7**; R = Bu^t) (Method B) *via* the vinyl azide (**19**), into the *aziridine* (**15**), which was isolated, after chromatography, as a solid (152 mg), m.p. 192 °C (ethyl

acetate–light petroleum) (Found: C, 70.6; H, 5.6; N, 8.5. $C_{30}H_{27}N_3O_5$ requires C, 70.7; H, 5.3; N, 8.3%); $\lambda_{max.}$ 286 nm (ε 18 900 dm^3 mol^{-1} cm^{-1}); $\nu_{max.}$ 3 400, 1 772, and 1 695br cm^{-1}; δ_H(90 MHz) 2.34 (3 H, s), 2.55 (1 H, dd, *J* 2.9 and 3.9 Hz), 2.67 (1 H, d, *J* 2.9 Hz), 3.47 (1 H, d, *J* 3.9 and 5.3 Hz), 4.47 (2 H, s), 5.17 and 5.33 (2 H, ABq, *J* 12 Hz), 5.43 (1 H, dd, *J* 5.3 and 7.6 Hz), and 6.7—7.6 (16 H, m).

Further elution of the column provided the two isomers of the azirine (**27**). The *less polar isomer* (**27**) was an amorphous solid (43 mg) (Found: M^+, 509.1938 $C_{30}H_{27}N_3O_5$ requires *M*, 509.1948); $\nu_{max.}$ 3 405, 1 765, 1 730, 1 690, and 1 650 cm^{-1}; δ_H(90 MHz) 2.67 (3 H, s), 4.39 (2 H, s), 5.04 and 5.27 (2 H, ABq, *J* 12 Hz), the latter signal obscures a one proton multiplet, 5.41 (1 H, dd, *J* 5 and 9 Hz), 5.98 (1 H, dd, *J* 8 and 16 Hz), 6.64 (1 H, d, *J* 16 Hz), and 6.6—7.5 (16 H, m). The *more polar isomer* (**27**) (56 mg) was obtained as needles, m.p. 157—158 °C (ethyl acetate–light petroleum) (Found: C, 70.7; H, 5.0; N, 8.1. $C_{30}H_{27}N_3O_5$ requires, C, 70.7; H, 5.3; N, 8.3%); $\nu_{max.}$ 3 420, 1 770, 1 735, 1 692, and 1 655 cm^{-1}; δ_H(90 MHz) 2.59 (3 H, s), 4.44 (2 H, s), 4.61 (1 H, dd, *J* 5 and 9 Hz), 5.08 (2 H, s), 5.32 (1 H, dd, *J* 5 and 9 Hz), 6.15 (1 H, dd, *J* 9 and 16 Hz), 6.65 (1 H, d, *J* 16 Hz), and 6.7—7.5 (16 H, m).

1-(*Dimethyl-t-butylsilyl*)-4-*vinylazetidin*-2-*one* (**28**).—4-Vinylazetidin-2-one (**4**) (485 mg) and dimethyl-t-butylsilyl chloride (828 mg) were dissolved in dry DMF (15 ml). The solution was cooled to 0 °C and triethylamine (555 mg) in DMF (3 ml) added dropwise over 15 min. After a further 15 min the mixture was poured into ethyl acetate–water. The organic layer was separated, washed successively with dilute hydrochloric acid (0.01M) and brine, then dried, and evaporated. Chromatography gave the *product* (**28**) as a clear oil (924 mg) (Found: M^+, 211.1403. $C_{11}H_{21}NOSi$ requires *M*, 211.1390); $\nu_{max.}$ 1 730 cm^{-1}; δ_H(60 MHz) *inter alia* 0.18 (3 H, s), 0.21 (3 H, s), 0.97 (9 H, s), 2.73 and 3.31 (2 H, ABq, *J* 16 Hz, each arm showing further coupling of *J* 3 and 5.5 Hz), 4.0 (1 H, m), and 5.0—6.2 (3 H, m, typical vinyl pattern).

(3RS, 4RS)-3-*Azido*-1-(*dimethyl-t-butylsilyl*)-4-*vinylazetidin*-2-*one* (**29**).—Di-isopropylamine (111 mg) was dissolved in dry THF (3 ml) and the solution cooled to 0 °C. n-Butyl-lithium (0.68 ml of 1.6M-solution in hexane) was added and after 3—4 min the solution was cooled to −76 °C. The azetidin-2-one (**28**) (211 mg) was added dropwise in THF during 5 min. After 2 h at −76 °C, toluene-*p*-sulphonyl azide (218 mg) in THF (1 ml) was added, followed after a further 30 min by chlorotrimethylsilane (238 mg) in THF (1 ml). The solution was allowed to warm to room temperature and after 17 h the solution was evaporated, and partitioned between ethyl acetate and water. The organic layer was separated, washed with brine, dried, and evaporated. Chromatography gave the *azide* (**29**) as an oil (62 mg) (Found: M^+ + H, 253.1660. $C_{22}H_{23}N_4OSi$ requires *M* + H, 253.1641); $\nu_{max.}$ 2 125, and 1 745 cm^{-1}; δ_H(60 MHz) *inter alia* 3.9 (1 H, dd, *J* 3 and 8.5 Hz), 4.27 (1 H, d, *J* 3 Hz), and 5.1—6.2 (3 H, m, typical vinyl pattern).

Ethyl 2-*Trimethylsilylpropynylideneamino*-3,3-*ethylenedioxybutanoate* (**33**).—Trimethylsilylprop-2-ynal (12.6 g) (prepared from trimethylsilylethynyl-lithium and ethyl formate according to the procedure of Hauptmann [16]) was treated with the amine (**39**) in dry dichloromethane (250 ml) to give a 1:1 mixture of *syn*- and *anti*-isomers of the Schiff base (**33**) as previously reported [1] for the corresponding benzyl ester (**40**). The *product* (**33**) was an orange gum (29.2 g) of sufficient purity for the next stage. A small sample was rapidly chromatographed for characterisation (Found: M^+ + H, 298.1490. $C_{14}H_{24}NO_4Si$ requires *M* + H, 298.1474); $\nu_{max.}$ 1 735 and 1 605 cm^{-1}; δ_H(90 MHz) 0.23 (9 H, s), 1.29 (3 H, t, *J* 7 Hz), 1.52 and 1.54 (together 3 H, s), 3.94 and 4.70 (together 1 H, s and d respectively, *J* 2 Hz), 3.98 and 4.01 (together 4 H, s), 4.24 (2 H, q, *J* 7 Hz), 7.48 and 7.66 (together 1 H, s and d respectively, *J ca.* 2 Hz).

(3RS, 4RS)- *and* (3RS, 4SR)-3-*Azido*-1-(2,2-*ethylenedioxy*-1-*ethoxycarbonyl*)*propyl*-4-*trimethylsilylethynylazetidin*-2-*one* (**36**) *and* (**34**).—Azidoacetic acid (15.12 g) in dry dichloromethane (150 ml) was cooled to 0 °C and trifluoroacetic anhydride (21.15 ml) in dichloromethane (20 ml) added during 10 min. After 15 min triethylamine (20.7 ml) was added in dichloromethane (30 ml) during 15—20 min, and stirring was continued for a further 45 min. The solution was transferred to a dropping-funnel jacketted with solid carbon dioxide and added dropwise during 2 h to the Schiff base (**33**) (29.2 g) in dichloromethane (500 ml) containing triethylamine (20.7 ml) at 0 °C. Stirring was continued for a further 1 h, and then the solution was washed successively with water, dilute aqueous sodium hydrogen carbonate, dilute hydrochloric acid, and brine, then dried and evaporated. Chromatography gave the two inseparable isomers (ratio 4:1) of the trans-β-*lactam* (**36**) as a gum (12.2 g) (Found: C, 50.3; H, 6.1; N, 14.4. $C_{16}H_{24}N_4O_5Si$ requires C, 50.5; H, 6.3; N, 14.7%); $\nu_{max.}$ 2 120, 1 775, and 1 740 cm^{-1}; δ_H(90 MHz) (minor isomer resonance indicated first in paired signals) 0.18 (9 H, s), 1.28 and 1.30 (together 3 H, both t, *J* 7 Hz), 1.42 and 1.54 (together 3 H, both s), 3.99 (4 H, s), 4.24 and 4.28 (together 2 H, both q, *J* 7 Hz), 4.40 and 4.30 (together 1 H, both s), 4.47 (1 H, d, *J* 2 Hz), and 4.57 (1 H, d, *J* 2 Hz).

Further elution of the column gave the cis-β-*lactam* (**34**) as a gum (11.85 g). The material was an inseparable mixture of carboxylate epimers in a ratio of *ca.* 3:2 (Found: C, 50.2; H, 6.2; N, 15.0%); $\nu_{max.}$ 2 115, 1 770, and 1 740 cm^{-1}; δ_H(90 MHz) (minor isomer resonance indicated first in paired signals) 0.18 (9 H, s), 1.28 and 1.30 (together 3 H, both t, *J* 7 Hz), 1.46 and 1.54 (together 3 H, both s), 3.98 (4 H, s), 4.22 (2 H, q, *J* 7 Hz), 4.48 and 4.44 (1 H, both s), 4.51 (1 H, d, *J* 5 Hz), and 4.75 and 4.97 (1 H, both *J* 5 Hz).

(3RS, 4SR)-3-*Azido*-1-(2,2-*ethylenedioxy*-1-*ethoxycarbonylpropyl*)-4-*ethynylazetidin*-2-*one* (**38**).—The azide (**34**) (11.85 g) was dissolved in THF (220 ml) at 0 °C and sodium hydroxide (0.25M; 284 ml) added dropwise over 20 min. The reaction was allowed to warm to room temperature. After 30 min the solution was diluted with brine and dichloromethane and then acidified to pH 2. The organic layer was separated and the aqueous solution extracted with further dichloromethane (× 2). The combined organic extracts were washed with brine, dried and evaporated. The total crude product was dissolved in dichloromethane (150 ml) at 0 °C and pyridine (2.46 g), 2,2,2-trichloroethanol (4.66 g) and dicyclohexylcarbodi-imide (6.43 g) added in dichloromethane (50 ml). The cooling-bath was removed and after 2 h the mixture was filtered. The filtrate was washed successively with aqueous citric acid and brine, then dried, and evaporated. Chromatography gave the *product* (**38**) as a single isomer which was a crystalline solid (5 g), m.p. 107 °C (ethyl acetate–light petroleum) (Found: C, 37.8; H, 3.2; N, 13.5. $C_{13}H_{13}Cl_3N_4O_5$ requires C, 37.9; H, 3.2; N, 13.6%); $\nu_{max.}$ 3 300, 2 115, 1 780, and 1 765sh cm^{-1}; δ_H(90 MHz) 1.50 (3 H, s), 2.70 (1 H, d, *J* 2.2 Hz), 4.03 (4 H, s), 4.62 (1 H, d, *J* 0.2 Hz), 4.81 (1 H, d, *J* 5.2 Hz), 4.72 and 4.88 (2 H, ABq, *J* 12 Hz), and 5.02 (1 H, ddd, *J* 5.2, 2.2 and 0.2 Hz).

(3RS, 4SR)-1-[2,2-*Ethylenedioxy*-1-(2,2,2-*trichloroethoxycarbonyl*)*propyl*]-4-*ethynyl*-3-*phenoxyacetamidoazetidin*-2-*one* (**41**).—The azide (**38**) (2.06 g; single isomer) was reduced and acylated as described for (**21**) to give *the amide* (**41**) as a crystalline solid (2.6 g), m.p. 121 °C (ethyl acetate–light petroleum) (Found: C, 48.6; H, 4.0; Cl, 21.1; N, 5.3. $C_{21}H_{21}Cl_3N_2O_7$ requires C, 48.5; H, 4.0; Cl, 20.5; N, 5.4%); $\nu_{max.}$ 3 410, 3 300,

1 775, 1 760sh, and 1 695 cm^{-1}; δ_H(90 MHz) 1.48 (3 H, s), 2.4 (1 H, d, *J* 2 Hz), 4.01 (4 H, s), 4.56 (3 H, s), 4.78 (2 H, AA' system), 4.98 (1 H, dd, *J* 2 and 5 Hz), 5.6 (1 H, dd, *J* 5 and 10 Hz), and 6.85—7.45 (6 H, m).

(3RS, 4SR)-1-[2,2-*Ethylenedioxy*-1-(2,2,2-*trichloroethoxycarbonyl*)*propyl*]-4-*ethyl*-3-*phenoxyacetamidoazetidin*-2-*one* (**43**), *and* (3RS,4SR)-1-[2,2-*Ethylenedioxy*-1-(2,2,2-*trichloroethoxycarbonyl*)*propyl*]-3-*phenoxyacetamido*-4-*vinylazetidin*-2-*one* (**42**).—The ethynyl derivative (**41**) (2.28 g) was hydrogenated over 10% Pd–$BaSO_4$ (1.14 g) in dioxane (100 ml) for 1.5 h (t.l.c. control). The catalyst was removed by filtration through Kieselguhr and the filtrate evaporated. Chromatography gave the 4-*ethyl derivative* (**43**) as an amorphous solid (250 mg) (Found: C, 48.2; H, 4.6; N, 5.4. $C_{21}H_{25}Cl_3N_2O_7$ requires C, 48.1; H, 4.8; N, 5.3%); $\nu_{max.}$ 3 425, 1 780sh, 1 760, and 1 690 cm^{-1}; δ_H(90 MHz) 0.82 (1 H, t, *J* 7 Hz), 1.1—2.2 (2 H, m), 1.5 (3 H, s), 3.98 (4 H, s), 3.95—4.2 (1 H, m), 4.42 (1 H, s), 4.52 (2 H, s), 4.77 (2 H, s), 5.38 (1 H, dd, *J* 5 and 9 Hz), and 6.85—7.5 (6 H, s).

Further elution of the column provided the 4-*vinyl derivative* (**42**) as an amorphous solid (1.7 g) (Found: C, 48.4; H, 4.4; N, 5.2. $C_{21}H_{23}Cl_3N_2O_7$ requires C, 48.3; H, 4.4; N, 5.4%); $\nu_{max.}$ 3 425, 1 770, 1 760, and 1 690 cm^{-1}; δ_H(90 MHz) *inter alia* 1.55 (3 H, s), 3.98 (4 H, s), 4.22 (1 H, s), 4.49 (2 H, s), 4.68 (1 H, dd, *J* 5.5 and 7 Hz), 4.79 (2 H, s), 5.33 (1 H, dd, *J ca.* 3 and 10 Hz), 5.42 (1 H, dd, *J* 5.5 and 8.5 Hz), 7.02 (1 H, d, *J* 8.5 Hz), and 6.8—7.4 (5 H, m).

(E)-(3RS, 4SR)-1-[2-*Hydroxy*-1-(2,2,2-*trichloroethoxycarbonyl*)-*prop*-1-*enyl*]-3-*phenoxyacetamido*-4-*vinylazetidin*-2-*one* (**25**).—The amide (**42**) (1.67 g) was treated with trifluoroacetic acid (30 ml) and water (1.5 ml) as described for (**22**) to give the *enol* (**25**) as a white solid (1.23 g), m.p. 154—156 °C (ethyl acetate–hexane) (Found: C, 47.8; H, 4.1; Cl, 22.4; N, 5.7. $C_{19}H_{19}Cl_3N_2O_6$ requires C, 47.7; H, 4.0; Cl, 22.3; N, 5.7%); $\nu_{max.}$(Nujol) 3 325, 1 755, 1 690, and 1 665 cm^{-1}; δ_H(90 MHz) 2.2 (3 H, s), 4.51 (2 H, s), *ca.* 4.55 (1 H, partially obscured dd), 4.63 and 4.97 (2 H, ABq, *J* 12 Hz), 5.16—5.5 (3 H, m), 5.65—6.05 (1 H, m), 6.8—7.45 (6 H, m), and 11.85 (1 H, s, exch. D_2O).

(3RS, 4SR)-1-[2-*Methylsulphonyloxy*-1-(2,2,2-*trichloroethoxycarbonyl*)*prop*-1-*enyl*]-3-*phenoxyacetamido*-4-*vinylazetidin*-2-*one* (**26**).—The enol (**25**) (1.47 g) was converted into the methanesulphonate (**26**) as described for (**23**). The *product* (**26**) was an amorphous solid (1.39 g) (Found: C, 43.0; H, 3.9; N, 5.1; S, 5.5. $C_{20}H_{21}Cl_3N_2O_8S$ requires C, 43.2; H, 3.8; N, 5.0; S, 5.8%); $\nu_{max.}$ 3 420, 1 770, 1 750, 1 690, and 1 635 cm^{-1}; δ_H(90 MHz) (major isomer) 2.62 (3 H, s), 3.32 (3 H, s), 4.52 (2 H, s), 4.73 and 4.94 (2 H, ABq, *J* 12 Hz), 4.86 (1 H, dd, *J* 5.5 and 8 Hz), 5.28—5.44 (3 H, m), 5.76—5.96 (1 H, m), and 6.8—7.5 (6 H, m).

2,2,2-*Trichloroethyl* (7*RS*,7*a*RS,7*b*RS)-6,7,7*a*,7*b*-*Tetrahydro*-3-*methyl*-6-*oxo*-7-*phenoxyacetamido*-1H-*azeto*[1,2-a]*azirino*[2,1-c]*pyrazine*-4-*carboxylate* (**17**).—The methanesulphonate (**26**) (278 mg) was converted into the *aziridine* (**17**) as described for (7; R = Bu^t) (Method B). The material (**17**) was the sole β-lactam containing product and was isolated as an amorphous solid (75 mg) (Found: C, 47.8; H, 3.9; N, 8.9. $C_{19}H_{18}Cl_3N_3O_5$ requires C, 48.05; H, 3.8; N, 8.85%); $\lambda_{max.}$ 284 nm (ε 12 040 dm^3 mol^{-1} cm^{-1}); $\nu_{max.}$ 3 410, 1 770, 1 725, and 1 690br cm^{-1}; δ_H(250 MHz). 1.58 (1 H, m), 2.4 (3 H, s), 2.55 (1 H, m), 2.61 (1 H, m), 3.36 (1 H, m), 4.58 (2 H, s), 4.8 and 4.92 (2 H, ABq, *J* 12 Hz), 5.52 (1 H, dd, *J* 5 and 6.9 Hz), and 6.88—7.4 (6 H, m).

(7RS,7*a*RS,7*b*RS)-6,7,7*a*,7*b*-*Tetrahydro*-3-*methyl*-6-*oxo*-7-*phenoxyacetamido*-1H-*azeto*[1,2-a]*azirino*[2,1-c]*pyrazine*-4-*carboxylic Acid* (**18**).—The aziridine (**17**) (42 mg) was dissolved in THF (0.42 ml) and zinc dust (84 mg) was added, followed by potassium dihydrogenphosphate solution (1M; 0.084 ml). The mixture was vigorously stirred, and after 30 min was filtered through Kieselguhr, and washed well with ethyl acetate. The filtrate was washed successively with dilute citric acid solution and brine, dried, and evaporated. The residue was triturated with ether to give the acid (**18**) as a buff solid (16 mg); $\lambda_{max.}$ 268 and 274 nm (ε 9 785 and 9 653 dm^3 mol^{-1} cm^{-1}); $\nu_{max.}$ 3 400, 1 760br, and 1 700br; δ_H(250 MHz) [$CDCl_3$ + 2 drops $(CD_3)_2SO$] 1.48 (1 H, m), 2.33 (3 H, s), 2.51 (1 H, m), 2.61 (1 H, m), 3.28 (1 H, m), 3.5—4.5 (1 H, very br s), 4.57 (2 H, s), 6.55 (1 H, dd, *J* 5.2 and 8.2 Hz), 6.85—7.4 (5 H, m), and 8.38 (1 H, d, *J* 8.2 Hz).

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