Enantioselective Synthesis of (3*S*)-trans-4-(Substituted Methyl)monobactams from 2,3-*O*-Isopropylidene-D-glyceraldehyde

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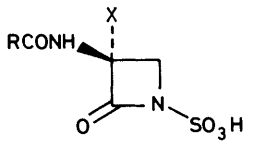
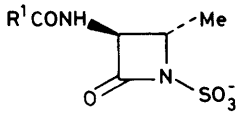
The enantioselective synthesis of various (3*S*)-*trans*-4-(substituted methyl)-2-oxoazetidine-1-sulphonic acid derivatives from 2,3-*O*-isopropylidene-D-glyceraldehyde is described. Reaction of this aldehyde with trimethylsilyl cyanide gave a 80:20 ratio of the corresponding *threo* and *erythro* α-amino-nitriles, which by amino protection and subsequent treatment with basic hydrogen peroxide provided the corresponding α-amino carboxamides. Successive selective protection, activation, sulphonation and, finally, stereospecific cyclization of the *threo* α-carboxamide yielded (2*S*,4*R*)-3-benzyloxycarbonylamino-4-hydroxymethyl-2-oxoazetidine-1-sulphonic acid, an intermediate for the synthesis of the corresponding 4-acyloxymethyl-, 4-carbamoyloxymethyl-, 4-methylsulphonyloxymethyl-, 4-iodomethyl-, and 4-methyl-2-oxozetidines.

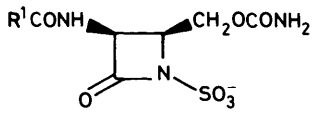
The discovery of various 3-acylamino-2-oxoazetidine-1-sulphonic acids (**1**) (monobactams), isolated from certain bacteria,[1] has stimulated much interest in the isolation and synthesis of new monobactams during the last few years, because of their antibacterial activity as well as their simple structures. Since previous observations[2] revealed that 4-unsubstituted-2-oxoazetidine-1-sulphonic acid derivatives appear to lack activity against β-lactamase-producing strains of gram-negative bacteria, the main synthetic efforts have been directed to the preparation of monobactams bearing different C-4 substituents, with *cis* or *trans* stereochemistry, and with improved antibacterial activity. Among these compounds, aztreonam (**2**)[3] and carumonam (**3**)[4] have been selected for clinical studies on the basis of their improved antibacterial spectrum and pharmacokinetic characteristics.



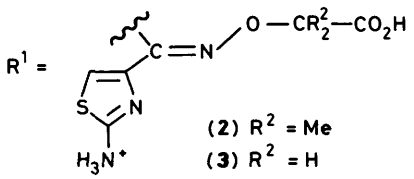
(**1**) X = H, OMe



(**2**)



(**3**)



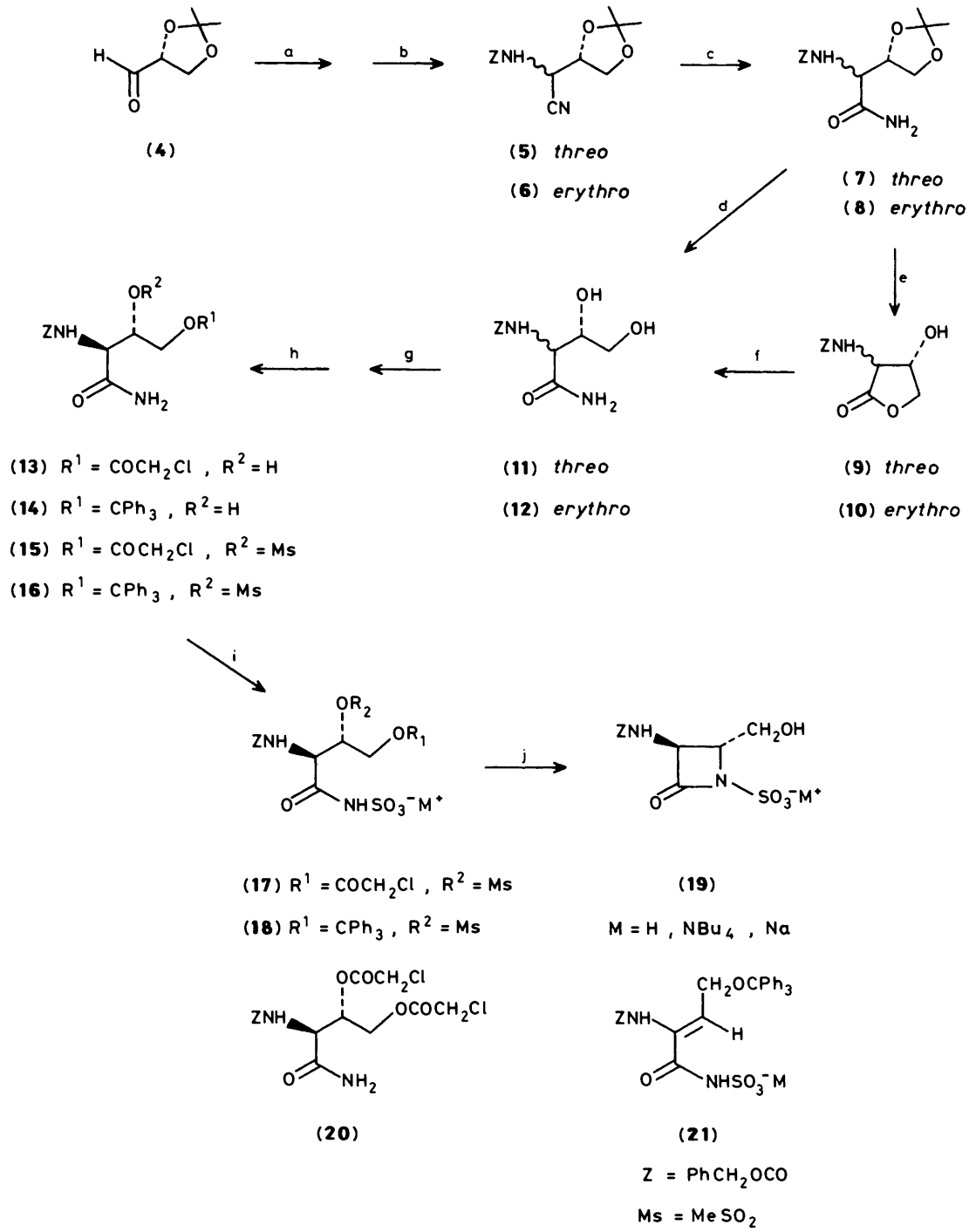
(**2**) R^2 = Me
(**3**) R^2 = H

As part of a synthetic programme directed towards the chiral synthesis of C-4-substituted monobactams, we report here the enantioselective preparation of several 3,4-*trans*-4-(substituted methyl)monobactams *via* the corresponding 4-hydroxymethyl derivative (**19**), a chiral intermediate for the synthesis of other monobactams, by chemical modification of the hydroxymethyl side chain. Optically active compound (**19**) was obtained from 2,3-*O*-isopropylidene-D-glyceraldehyde (**4**), a very versatile chiral synthon for the synthesis of optically active natural products,[5] which is easily prepared from D-mannitol,[6] a naturally occurring and inexpensive starting material.

Results and Discussion

As indicated in Scheme 1, following the precedents of Mai[7] and Ojima[8] for the synthesis of α-amino-nitriles from aldehydes, reaction of the aldehyde (**4**) with trimethylsilyl cyanide (TMSCN) and methanolic ammonia at 50 °C for 24 h provided an 80:20 ratio of *threo* and *erythro* α-amino nitriles. Owing to the instability of these compounds, they were transformed into their corresponding benzyloxycarbonyl derivatives (**5**) and (**6**) in 80% overall yield. With a reaction time of 1 h instead of 24 h, the α-amino-nitriles were obtained in 1.5% yield, along with a 71% yield of the *threo* and *erythro* cyanohydrins[9] in a 20:80 ratio. These results suggest that the cyanohydrins are the first reaction products,[10] and that they suffer S_N2 nucleophilic substitution with inversion of configuration at C-2. The separation of the α-benzyloxycarbonylamino nitriles (**5**) and (**6**) was very difficult and was only possible by preparative t.l.c. (p.l.c.), developing the plates at least fifteen times, such that a small amount of the reaction mixture was separated for identification purposes and the remainder was used as a mixture for the following reaction. The assignment of *threo* and *erythro* configuration to (**5**) and (**6**) respectively was not possible from their ^{1}H n.m.r. data. However, the assignment was unequivocally established on the basis of the following reaction sequences, which in the case of *threo* compound (**5**) led to the *trans* β-lactam (**19**).

The mixture of the *threo* and *erythro* α-amino nitriles (**5**) and (**6**) was converted into the corresponding α-amino carboxamides (**7**) and (**8**) by oxidative hydrolysis with basic hydrogen peroxide at 0 °C, in phase-transfer-catalysed conditions,[11] in 80% yield. The two isomers (**7**) and (**8**) were easily separated and purified by fractional crystallization. Both compounds were then deprotected with mild acid (0.02M-HCl in acetonitrile, at room temperature) to give the D-threonamide (**11**) and the D-erythronamide (**12**) respectively in 80% yield. The hydrolysis



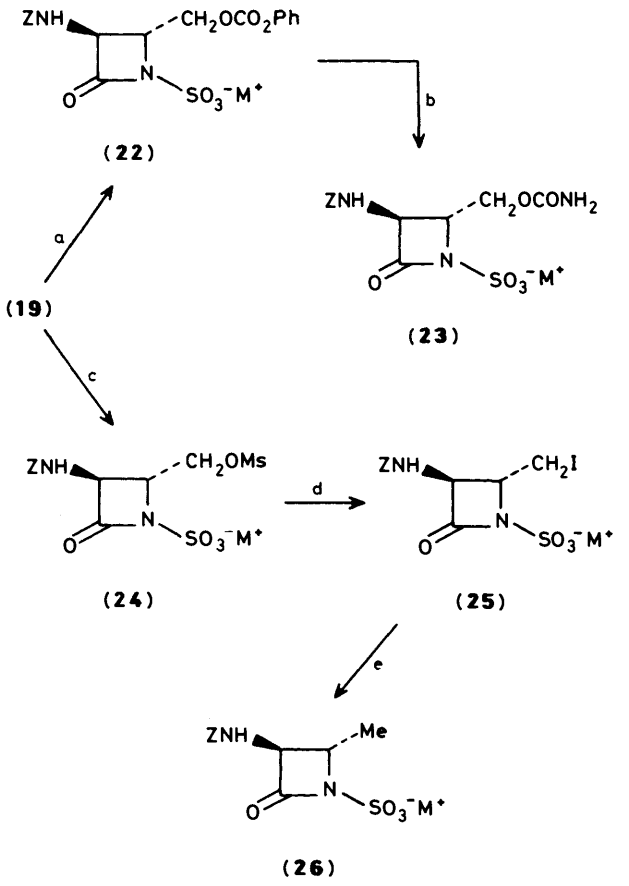
Scheme 1. *Reagents and conditions:* a, TMSCN, NH_3, MeOH, 24 h, 50 °C; b, $PhCH_2OCOCl$, propylene oxide, CH_2Cl_2, 1 h, 0 °C; c, H_2O_2, NaOH, water–CH_2Cl_2, $Bu^n_4N^+$ HSO_4^-, 1 h, 0 °C; d, 0.02 M-HCl, acetonitrile, 24 h, room temp.; e, 1 M-HCl, acetonitrile, 24 h, room temp.; f, NH_4OH, water–hexane, 1 h, 0 °C; g, $ClCH_2COCl$, triethylamine, 4-dimethylaminopyridine (DMAP), DMF, 5 h, −20 °C; h, $MeSO_2Cl$, triethylamine, CH_2Cl_2, 1 h, −20 °C; i, 2-picoline·SO_3 complex, 1,2-dichloroethane, 1 h, 75 °C; j, $KHCO_3$, water–1,2-dichloroethane, 30 min, reflux

conditions were critical, since at higher acid concentration or higher temperature the lactones (**9**) and (**10**) were favoured. In this case (**9**) and (**10**) were transformed again into (**11**) and (**12**), by ammonolysis in a hexane suspension with ammonium hydroxide, in good yield.

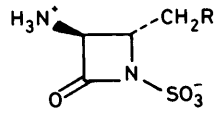
Conversion of the threonamide (**11**) into (3*S*, 4*R*)-3-benzyloxycarbonylamino-4-hydroxymethyl-2-oxoazetidine-1-sulphonic acid (**19**; M = H), a key intermediate for preparing 4-substituted monobactams, was achieved by the procedure reported by Cimarusti *et al.*[12] with slight modifications (Scheme 1). First, selective protection of the primary hydroxy group in compound (**11**) was necessary. Initially, this was carried out by tritylation, with very good yield and selectivity, but in the following reactions the mesyl derivatives (**16**), and, particularly,

(**18**) eliminated[13] the mesyl group, giving the butenamide (**21**) and none of the β-lactamic compound was obtained. As an alternative protection method, chloroacetylation was chosen; thus, treatment of compound (**11**) with chloroacetyl chloride (1.2 equiv.) and triethylamine (1.2 equiv.) in *N*,*N*-dimethylformamide (DMF) at −20 °C for 5 h gave monoester (**13**) in 75% yield. With a higher molar ratio of chloroacetyl chloride the bischloroacetylated product (**20**) was also obtained, and unchanged (**11**) was recovered when the ratio was lowered; in both cases the yield was poorer. Mesylation of the alcohol (**13**) with methanesulphonyl chloride and triethylamine in dichloromethane at −20 °C gave compound (**15**) in 95% yield, which was further converted into the acylsulphamate (**17**) by sulphonation with 2-picoline·SO_3 complex and treatment with tetrabutylammonium hydrogen sulphate. Stereospecific β-lactam formation, by intramolecular S_N2 with inversion of configuration at C-3, proceeded at reflux in a two-phase system of 1,2-dichloroethane and aqueous potassium hydrogen carbonate, with concomitant hydrolysis of the chloroacetyl protecting group, giving the β-lactam (**19**). The *trans* configuration of the product (**19**) was unequivocally assigned by the $J_{3,4}$ value of 2.5 Hz in the ^{1}H n.m.r. spectrum, characteristic of monocyclic *trans* β-lactams.[14] While this synthesis was in progress in our laboratory, the preparation of (3*S*, 4*S*)-3-benzyloxycarbonylamino-4-hydroxymethyl-2-oxoazetidine-1-sulphonic acid, the *cis* epimer of (**19**) from L-ascorbic acid, was reported by Wei *et al.*[15]

As summarized in Scheme 2, the chemical versatility of the hydroxymethyl group in compound (**19**) allowed the preparation of the monobactams (**22**)—(**26**) which could be used as intermediates for other new 4-substituted monobactams by easy chemical modifications. Thus, following the carbamoylation procedure reported by Baker *et al.*,[16] acylation of compound (**19**) with phenyl chloroformate in pyridine at −20 °C afforded the carbonate (**22**), which by ammonolysis with ammonium hydroxide in methanol at room temperature gave the carbamate (**23**). Mesylation of the alcohol (**19**) gave mesyl ester (**24**), which was then transformed into the 4-iodomethyl derivative† (**25**) by reaction with sodium iodide. Attempts to obtain the 4-fluoromethyl analogue (**25**), which would allow preparation of active 4-fluoromethylmonobactams, by treatment with an excess of potassium fluoride[17] in the presence of 18-crown-6, were unsuccessful. Dehalogenation of the iodide (**25**) with tributyltin hydride[18] in tetrahydrofuran (THF) at room temperature provided compound (**26**), which gives access to aztreonam (**2**).



Scheme 2. *Reagents and conditions:* a, PhOCOCl–pyridine, 1 h, −20 °C; b, NH_4OH, water–MeOH, 2 h, room temp.; c, $MeSO_2Cl$–pyridine, 1 h, −20 °C; d, NaI, acetonitrile, 3 h, reflux; e, Bu^n_3SnH, THF, 2 h, room temp.



(**27**) R = OH
(**28**) R = $OCONH_2$
(**29**) R = OMs
(**30**) R = I
(**31**) R = H

Catalytic hydrogenolysis of the benzyloxycarbonyl-protected compounds (**19**), (**23**), (**24**), and (**26**) with 10% Pd/C in a (1:1) water–methanol mixture, and then acidification to pH 2 with 1M-HCl, gave the zwitterions (**27**), (**28**), (**29**), and (**31**). Unexpectedly, the 4-iodomethyl derivative (**25**) did not hydrogenate in the same conditions as before, and was recovered unchanged, so it was deprotected by treatment with trimethylsilyl iodide (TMSI) to give compound (**30**).

In conclusion, the results presented here show the enantioselective synthesis of various *trans*-4-(substituted methyl)monobactams *via* the (3*S*, 4*R*)-3-benzyloxycarbonylamino-4-hydroxymethyl-2-oxoazetidine-1-sulphonic acid (**19**), an intermediate obtained from the chiral synthon 2,3-*O*-isopropylidene-D-glyceraldehyde. The α-amino nitriles (**5**) and (**6**), as well as the corresponding cyanohydrins, could be used as starting materials for the chiral synthesis of other monocyclic β-lactams or carbapenems.

Experimental

M.p.s were determined with a Kofler hot-stage apparatus and are uncorrected. Optical rotations were measured on a Perkin-Elmer 141 polarimeter. I.r. spectra were recorded on a Perkin-Elmer 580 spectrometer. ^{1}H N.m.r. spectra were recorded on a Bruker WP 80 SY or a Varian XL-300 spectrometer, with Me_4Si as internal standard. Analytical t.l.c. was performed on Merck Silica gel 60 F_{254} pre-coated plates (0.2 mm) and spots were detected in u.v. light, or by spraying with 30% sulphuric acid in ethanol, or ninhydrin reagent. Preparative chromatographic purifications were performed on a medium-pressure preparative column of Merck Silica gel 60 (230—400 mesh) or on 20 × 20 cm glass plates coated with a 2 mm layer of Merck Silica gel PF_{254}.

2-Benzyloxycarbonylamino-2-deoxy-3,4-O-*isopropylidene*-D-*threononitrile* (**5**) *and* *2-Benzyloxycarbonylamino-2-deoxy*-3,4-O-*isopropylidene*-D-*erythrononitrile* (**6**).—A mixture of 2,3-*O*-isopropylidene-D-glyceraldehyde (**4**) (65 g, 0.5 mol), TMSCN (78.7 ml, 0.62 mol), and a catalytic amount of zinc iodide (0.2 g) was stirred at room temperature for 15 min, and then was added slowly to a saturated solution of methanolic ammonia (700 ml) at −60 °C. The resulting solution was left to reach room temperature, and then was warmed to 50 °C and stirred at this temperature for 24 h. After evaporation to dryness, the amber-coloured syrup was dissolved in dry dichloromethane (600 ml), propylene oxide (425 ml) was added, the solution was cooled to 0 °C, and benzyl chloroformate (76.69 ml, 0.56 mol) was added dropwise. The reaction mixture was stirred at 0 °C for 1 h and evaporated to dryness to give a syrup, which was purified by medium-pressure chromatography with an ethyl acetate–hexane gradient as eluant to yield a (4:1) mixture of nitriles (**5**) and (**6**) as a syrup (116 g, 80%). This mixture (0.5 g) of (**5**) and (**6**) was separated by p.l.c., developing the plates fifteen times with hexane–ethyl acetate (9:1). Elution of the major band gave the threo-*isomer* (**5**) (0.400 g, 80%) as a white crystalline solid, m.p. 61—62 °C (from cyclohexane); $[\alpha]_D^{25}$ −15.1° (*c* 1 in MeOH) (Found: C, 61.85; H, 6.4; N, 9.8. $C_{15}H_{18}N_2O_4$ requires C, 62.05; H, 6.2; N, 9.7%); $\nu_{max.}$ (Nujol) 3 320 (NH), 2 260 (CN), and 1 705 cm^{-1} (CO); δ_H (300 MHz; $CDCl_3$), 1.36 (3 H, s, Me), 1.47 (3 H, s, Me), 3.88 (1 H, dd, *J* 5.5 and 9 Hz, 4-H), 4.11 (1 H, dd, *J* 6.5 and 9 Hz, 4-H), 4.39 (1 H, m, 3-H), 4.73 (1 H, dd, *J* 3.5 and 9 Hz, 2-H), 5.15 (2 H, s, C*H*$_2$Ph), 5.40 (1 H, br d, *J* 9 Hz, NH), and 7.36 (5 H, s, CH_2*Ph*).

Elution of the minor band yielded the erythro-*isomer* (**6**) (0.100 g, 20%) as a white crystalline solid, m.p. 90 °C (from cyclohexane); $[\alpha]_D^{25}$ +10.78° (*c* 1.015 in MeOH) (Found: C, 62.0; H, 6.4; N, 9.75%); $\nu_{max.}$(Nujol) 3 320 (NH), 2 250 (CN), 1 705 cm^{-1} (CO); δ_H (300 MHz; $CDCl_3$) 1.36 (3 H, s, Me), 1.51 (3 H, s, Me), 3.94 (1 H, dd, *J* 5 and 9 Hz, 4-H), 4.15 (1 H, dd, *J* 6.5 and 9 Hz, 4-H), 4.28 (1 H, m, 3-H), 4.74 (1 H, dd, *J* 3.5 and 9 Hz, 2-H), 5.16 (2 H, s, C*H*$_2$Ph), 5.58 (1 H, br d, *J* 9 Hz, NH), and 7.36 (5 H, s, CH_2*Ph*).

2-Benzyloxycarbonylamino-2-deoxy-3,4-O-*isopropylidene*-D-*threonamide* (**7**) and *2-Benzyloxycarbonylamino-2-deoxy*-3,4-O-*isopropylidene*-D-*erythronamide* (**8**).—Tetrabutylammonium hydrogen sulphate (21.7 g) and 30% hydrogen peroxide (174 ml) were added to a solution of the mixture of (**5**) and (**6**) (87 g, 0.3 mol) in dichloromethane (1.5 l). The reaction mixture was stirred at 0 °C and 20% aq. sodium hydroxide (120 ml) was added dropwise. After the mixture had been stirred at 0 °C for 1 h the organic layer was separated and the aqueous phase was extracted with dichloromethane (2 × 750 ml). The combined extracts were washed successively with water (300 ml), 1M-HCl (300 ml), and brine (600 ml), and dried over $MgSO_4$. Evaporation to dryness gave a white solid, which was recrystallized from benzene to yield the erythro-*isomer* (**8**) (15.7 g, 17%), m.p. 180—181 °C (from benzene); $[\alpha]_D^{25}$ −1.2° (*c* 0.995 in MeOH) (Found: C, 58.5; H, 6.7; N, 9.1. $C_{15}H_{20}N_2O_5$ requires C, 58.45; H, 6.5; N, 9.1%); $\nu_{max.}$(Nujol) 3 460, 3 340, 3 220 (NH), 1 710, and 1 665 cm^{-1} (CO); δ_H(300 MHz; $CDCl_3$) 1.38 (3 H, s, Me), 1.48 (3 H, s, Me), 4.10 (2 H, m, 4-H), 4.18—4.38 (2 H, m, 2- and 3-H), 5.15 (2 H, s, C*H*$_2$Ph), 5.60 (1 H, br d, *J* 9 Hz, 2-NH), 5.60 and 6.40 (2 H, br s, NH_2), and 7.38 (5 H, s, CH_2*Ph*).

Evaporation of the mother waters and recrystallization of the residue from tetrachloromethane gave the threo-*isomer* (**7**) (65 g, 70%), m.p. 137—138 °C (from CCl_4); $[\alpha]_D^{25}$ +10.58° (*c* 1.04 in MeOH) Found: C, 58.2; H, 6.5; N, 8.8%); $\nu_{max.}$(Nujol) 3 410, 3 320, 3 210 (NH), 1 690, and 1 670 cm^{-1} (CO); δ_H (80 MHz; $CDCl_3$) 1.33 (3 H, s, Me), 1.41 (3 H, s, Me), 3.72 (1 H, dd, *J* 6.5 and 9 Hz, 4-H), 4.09 (1 H, dd, *J* 6.5 and 9 Hz, 4-H), 4.34 (1 H, dd, *J* 3.5 and 7.5 Hz, 2-H), 4.64 (1 H, dt, *J* 3.5 and 6.5 Hz, 3-H), 5.10 (2 H, s, C*H*$_2$Ph), 5.68 (1 H, br d, *J* 7.5 Hz, 2-NH), 6.19 and 6.54 (2 H, each br s, NH_2), and 7.30 (5 H, s, CH_2*Ph*).

General Procedure for the Preparation of γ-Butyrolactones (**9**) *and* (**10**).—A solution of the butanamide derivative (**7**) or (**8**) (3.08 g, 10 mmol) in a mixture of acetonitrile (75 ml) and 2M-HCl (25 ml) was stirred at room temperature for 24 h. Evaporation to dryness and crystallization from benzene yielded the corresponding γ-butyrolactone (**9**) or (**10**).

2-Benzyloxycarbonylamino-2-deoxy-D-*threono*-1,4-*lactone* (**9**). This compound was obtained from amide (**7**) in 80% yield, m.p. 137—138 °C (from benzene); $[\alpha]_D^{25}$ −59.2° (*c* 1.01 in MeOH) (Found: C, 57.55; H, 5.3; N, 5.5. $C_{12}H_{13}NO_5$ requires C, 57.4; H, 5.2; N, 5.6%); $\nu_{max.}$(Nujol) 3 390 (OH), 3 300 (NH), 1 800, and 1 780 (CO lactone), and 1 690 cm^{-1} (CO); δ_H (300 MHz; $CDCl_3$) 4.03 (1 H, t, *J* 12 Hz, 4-H), 4.23 (1 H, dd, *J* 2 and 8 Hz, 2-H), 4.57 (2 H, m, 3- and 4-H), 4.95 (1 H, br s, OH), 5.61 (1 H, br d, *J* 8 Hz, NH), 5.16 (2 H, s, C*H*$_2$Ph), and 7.37 (5 H, s, CH_2*Ph*).

2-Benzyloxycarbonylamino-2-deoxy-D-*erythrono*-1,4-*lactone* (**10**). This compound was obtained from amide (**8**) in 86% yield, m.p. 126—127 °C (from benzene); $[\alpha]_D^{25}$ −30.2° (*c* 0.995 in MeOH) (Found: C, 57.6; H, 5.4; N, 5.8%); $\nu_{max.}$(Nujol) 3 430 (OH), 3 320 (NH), 1 750 (CO lactone), and 1 690 cm^{-1} (CO); δ_H (300 MHz; $CDCl_3$), 2.73 (1 H, br s, OH), 4.38 (2 H, d, *J* 1.5 Hz, 4-H_2), 4.49 (1 H, t, 2-H), 4.64 (1 H, m, 3-H), 5.15 (2 H, s, C*H*$_2$Ph), 5.46 (1 H, br d, NH), and 7.36 (5 H, s, CH_2*Ph*).

Preparation of the threo *and* erythro *Amides* (**11**) *and* (**12**).—*Procedure A: deprotection of the* threo *and* erythro *amides* (**7**) *and* (**8**). A solution of the corresponding butanamide (**7**) or (**8**) (77 g, 0.25 mol) in a mixture of acetonitrile (980 ml) and 1M-HCl (20 ml) was stirred at room temperature for 24 h. The solution was concentrated to *ca.* 50 ml and cooled at 0 °C overnight. The resulting precipitate was filtered off to give the desired deprotected butanamide (**11**) or (**12**) in 80% yield.

Procedure B: from the γ-butyrolactones (**9**) *and* (**10**). Cold 25% aq. ammonium hydroxide (5 ml) was added to a stirred suspension of the γ-butyrolactone (**9**) or (**10**) (2.25 g, 9 mmol) in hexane (20 ml) cooled to 0 °C, and the mixture was stirred for 1 h at 0—5 °C. After further addition of 25% aq. ammonium hydroxide (2.5 ml), the reaction mixture was stirred for 30 min at the same temperature. After evaporation of the hexane under reduced pressure, the mixture was cooled to 0 °C and stirred at this temperature for 30 min. The resulting precipitate was filtrated off, washed with cold water (4 ml), and dried over P_2O_5 for 24 h *in vacuo* to yield the butanamide (**11**) or (**12**) in 83% yield.

2-Benzyloxycarbonylamino-2-deoxy-D-*threonamide* (**11**). This compound was obtained from (**7**) or (**9**), m.p. 124—125 °C (from ethyl acetate); $[\alpha]_D^{25}$ −2.85° (*c* 0.965 in MeOH) (Found: C, 53.8; H, 6.1; N, 10.2. $C_{12}H_{16}N_2O_8$ requires C, 53.7; H, 6.0; N, 10.45); δ_H [80 MHz; $(CD_3)_2SO$] 3.24—3.48 (2 H, m, 4-H_2), 3.67—3.98 (1 H, m, 3-H), 4.10 (1 H, dd, *J* 3 and 9 Hz, 2-H), 4.62 (1 H, t, *J* 5.5 Hz, 4-OH), 4.90 (1 H, d, *J* 6.5 Hz, 3-OH), 5.06 (2 H, s, C*H*$_2$Ph), 6.66 (1 H, br d, *J* 9 Hz, 2-NH), 7.07 and 7.25 (2 H, each br s, NH_2), and 7.34 (5 H, s, CH_2*Ph*).

2-Benzyloxycarbonylamino-2-deoxy-D-*erythronamide* (**12**). This compound was obtained from (**8**) or (**10**), m.p. 176—177 °C (from acetonitrile); $[\alpha]_D^{25}$ +3° (*c* 1.025 in MeOH) (Found: C, 53.75; H, 6.1; N, 10.3%); δ_H [80 MHz; $(CD_3)_2SO$] 3.42 (2 H, dd, *J* 5 and 6 Hz, 4-H_2), 3.69 (1 H, m, 3-H), 4.06 (1 H, dd, *J* 6 and 7 Hz, 2-H), 4.62 (1 H, t, *J* 4.5 Hz, 4-OH), 4.93 (1 H, d, *J* 5 Hz, 3-OH), 5.03 (2 H, s, C*H*$_2$Ph), 7.08 (1 H, br d, *J* 7 Hz, 2-NH), 7.08 and 7.2 (2 H, each br s, NH_2), and 7.35 (5 H, s, CH_2-*Ph*).

2-Benzyloxycarbonylamino-4-O-*chloroacetyl*-*2-deoxy*-D-*threonamide* (**13**).—A solution of (**11**) (53.6 g, 0.2 mol) and 4-

dimethylaminopyridine (DMAP) (0.7 g) in a mixture of dry DMF (500 ml) and triethylamine (33.4 ml, 0.24 mol) was cooled to −20 °C and chloroacetyl chloride (20 ml, 0.24 mol) was added dropwise. The reaction mixture was stirred at −20 °C for 5 h, then was evaporated under high vacuum and below 40 °C. The residue was partitioned between ethyl acetate (1.5 l) and cold water (250 ml). The organic phase was washed with brine (500 ml), dried over Na_2SO_4, and evaporated to dryness. The residue was purified by flash chromatography with an ethyl acetate–hexane gradient as eluant to yield *compound* (**13**) (52 g, 75%), m.p. 95—96 °C (from benzene); $[\alpha]_D^{25}$ +5° (*c* 1.005 in MeOH) (Found: C, 48.7; H, 5.0; N, 8.2. $C_{14}H_{17}ClN_2O_6$ requires C, 48.8; H, 4.95; N, 8.15%); δ_H (80 MHz; $CDCl_3$) 2.23 (1 H, br s, 3-OH), 4.03 (2 H, s, CH_2Cl), 4.15—4.30 (2 H, m, 4-H_2), 4.30—4.55 (2 H, m, 2- and 3-H), 5.11 (2 H, s, C*H*$_2$Ph), 5.83 (1 H, br d, *J* 8 Hz, 2-NH), 5.73 and 6.48 (2 H, each br s, NH_2), and 7.38 (5 H, s, CH_2*Ph*).

2-*Benzyloxycarbonylamino*-3,4-di-O-*chloroacetyl*-2-*deoxy*-D-*threonamide* (**20**).—This compound was obtained by the procedure used for the preparation of monoester (**13**) with double proportions of chloroacetyl chloride and triethylamine; this yielded monoester (**13**) in 30% yield and the *diester* (**20**) in 40% yield, m.p. 120—122 °C (from benzene); $[\alpha]_D^{25}$ +28.8° (*c* 0.996 in MeOH) (Found: C, 45.8; H, 4.4; N, 6.4. $C_{16}H_{18}Cl_2N_2O_7$ requires C, 45.6; H, 4.3; N, 6.65%); δ_H (80 MHz; $CDCl_3$) 4.05 (4 H, m, CH_2Cl), 4.13—4.81 (3 H, m, 2-H and 4-H_2), 5.14 (2 H, s, C*H*$_2$Ph), 5.66 (3 H, m, 3-H, 2-NH, N*H*H), 6.28 (1 H, br s, NH*H*), and 7.34 (5 H, s, CH_2*Ph*).

2-*Benzyloxycarbonylamino*-2-*deoxy*-4-O-*trityl*-D-*threonamide* (**14**).—Trityl chloride (2.3 g, 8.3 mmol) was added to a solution of compound (**11**) (2.01 g, 7.5 mmol) and DMAP (0.1 g) in dry DMF (20 ml) containing triethylamine (1.3 ml, 9 mmol) cooled to 0 °C. The reaction mixture was left to reach room temperature and was stirred for 24 h. Then it was treated with cold water (40 ml) and extracted with chloroform (2 × 150 ml). These extracts were washed successively with water (50 ml) and brine (50 ml), and dried over $MgSO_4$. After evaporation to dryness, the residue was purified by flash chromatography with an EtoAc–hexane gradient as eluant to give *compound* (**14**) (2.68 g, 70%) as a foam, which crystallized after some time, m.p. 107—108 °C (from aq. ethanol); $[\alpha]_D^{25}$ −4.2° (*c* 0.77 in MeOH) (Found: C, 72.8; H, 6.0; N, 5.3. $C_{31}H_{30}N_2O_5$ requires C, 72.95; H, 5.9; N, 5.5%); δ_H (80 MHz; $CDCl_3$) 3.05—3.37 (2 H, m, 4-H_2), 3.54 (1 H, br s, 3-OH), 4.19—4.49 (2 H, m, 2- and 3-H), 5.06 (2 H, s, C*H*$_2$Ph), 5.77 (1 H, br d, *J* 8 Hz, 2-NH), 5.77 and 6.39 (2 H, br s, NH_2), 7.29 (5 H, s, CH_2*Ph*), and 7.15—7.38 (15 H, m, CPh_3).

General Procedure of Mesylation of Compounds (**13**) *and* (**14**).—Triethylamine (27 ml, 0.19 mol), and methanesulphonyl chloride (13.5 ml, 0.135 mol) were added to a solution of compound (**13**) or (**14**) (0.09 mol) in dry dichloromethane (800 ml) cooled to −20 °C, and the reaction mixture was stirred at this temperature for 1 h. Then it was washed successively with cold water (200 ml) and brine (200 ml), and dried over $MgSO_4$. Evaporation to dryness and flash chromatography purification with an EtoAc–hexane gradient as eluant yielded the desired mesyl derivative (**15**) or (**16**) in 95% yield.

2-*Benzyloxycarbonylamino*-4-O-*chloroacetyl*-2-*deoxy*-3-O-*mesyl*-D-*threonamide* (**15**). This compound was prepared from the alcohol (**13**), m.p. 103—104 °C (from ethanol); $[\alpha]_D^{25}$ +19.70° (*c* 1.005 in MeOH) (Found: C, 42.9; H, 4.6; N, 6.4. $C_{15}H_{19}ClN_2O_8S$ requires C, 42.6; H, 4.5; N, 6.65%); δ_H (80 MHz; $CDCl_3$) 3.05 (3 H, s, Me), 4.10 (2 H, s, CH_2Cl), 4.18—4.55 (2 H, m, 4-H_2), 4.68 (1 H, dd, *J* 3 and 8 Hz, 2-H), 5.18 (2 H, s, C*H*$_2$Ph), 5.35 (1 H, m, 3-H), 5.98 (1 H, d, *J* 8 Hz, 2-NH), 6.03 and 6.63 (2 H, each br s, NH_2), and 7.38 (5 H, s, CH_2*Ph*).

2-*Benzyloxycarbonylamino*-2-*deoxy*-3-O-*mesyl*-4-O-*trityl*-D-*threonamide* (**16**). This compound was obtained from alcohol (**14**) as a unstable foam, which although homogeneous by analytical t.l.c. proved impossible to obtain as an analytically pure compound; δ_H (80 MHz, $CDCl_3$) 2.96 (3 H, s, Me), 3.29—3.51 (2 H, m, 4-H_2), 4.66 (1 H, dd, *J* 3 and 8 Hz, 2-H), 5.07 (2 H, s, C*H*$_2$Ph), 5.07 (1 H, m, 3-H), 5.58 (1 H, br d, *J* 8 Hz, 2-NH), 5.58 and 6.23 (2 H, each br s, NH_2), 7.26 (5 H, s, CH_2*Ph*), and 7.18—7.37 (15 H, m, CPh_3).

General Procedure for Sulphonation of the Amides (**15**) *and* (**16**).—A solution of 2-picoline (75 ml, 0.76 mol) in 1,2-dichloroethane (650 ml) was cooled to between −20 and −10 °C and chlorosulphonic acid (23 ml, 0.38 mol) was added dropwise under nitrogen, at such a rate as to maintain the internal temperature below −5 °C. The resulting solution was stirred for 15 min at −5 °C and then the α-aminobutanamide (**15**) or (**16**) (0.085 mol) was added. The reaction mixture was heated at 75—80 °C for 1 h and then quickly cooled. The mixture was washed with 0.6M-aq. potassium hydrogen sulphate (750 ml), and then was extracted with 2% aq. sodium hydrogen carbonate (2 × 450 ml). The aqueous basic phase was treated with tetrabutylammonium hydrogen sulphate (28.5 g, 0.085 mol) and extracted with 1,2-dichloroethane (2 × 600 ml). The organic phase was dried over Na_2SO_4 and evaporated to dryness to give the tetrabutylammonium salt (**17**) or (**18**) as analytical t.l.c.-homogeneous foams. These tetrabutylammonium salts (4 mmol) were converted into the corresponding sodium salts on being stirred with the sodium form of Dowex 50W × 4 resin (100—200 mesh) (30 ml) in a (1:2) ethanol–water mixture (30 ml) for 30 min. The resin was removed by filtration and washed with water (30 ml). The filtrate was concentrated to about half of the original volume and washed with ethyl acetate (2 × 10 ml). The aqueous solution was evaporated to dryness under highly reduced pressure. The residue was slurried with methanol and the resulting solid was filtered off and washed with cold methanol and ether, then dried to give the sodium salt (**17**).

2-*Benzyloxycarbonylamino*-4-O-*chloroacetyl*-2-*deoxy*-3-O-*mesyl*-D-*threonamide*-N-*sulphonic Acid Sodium Salt* (**17**). This compound was prepared from amide (**15**) as the tetrabutylammonium salt in 90% yield, which was transformed into the sodium salt in 80% yield, m.p. 123—124 °C (from EtOH); $[\alpha]_D^{25}$ +3.2° (*c* 0.990 in water) (Found: C, 33.2; H, 3.35; N, 5.4. $C_{15}H_{18}ClN_2NaO_{11}S_2 \cdot H_2O$ requires C, 33.2; H, 3.7; N, 5.15%); $\nu_{max.}$(Nujol) 3 420 and 3 240 (NH), 1 740, 1 730, and 1 700 (CO), 1 270, 1 245, 1 180, and 1 050 cm^{-1} (SO); δ_H [80 MHz; $(CD_3)_2SO$] 3.13 (3 H, s, Me), 4.33 (2 H, s, CH_2Cl), 4.19—4.56 (3 H, m, 2-H and 4-H_2), 4.93—5.17 (1 H, m, 3-H), 5.08 (2 H, s, C*H*$_2$Ph), 7.34 (5 H, s, CH_2*Ph*), and 7.50 (1 H, br d, *J* 9 Hz, 2-NH).

2-*Benzyloxycarbonylamino*-2-*deoxy*-3-O-*mesyl*-4-O-*trityl*-D-*threonamide*-N-*sulphonic acid tetrabutylammonium salt* (**18**) *and* (*Z*)-2-*benzyloxycarbonylamino*-4-*trityloxybut*-2-*enamide*-N-*sulphonic Acid Tetrabutylammonium Salt* (**21**). Sulphonation of compound (**16**) by the previous general procedure gave the sulphamate in 80% yield as a white unstable foam; δ_H (80 MHz; $CDCl_3$) 0.97 (12 H, t, *J* 6 Hz, CH_2*Me*), 1.51 (16 H, m, [C*H*$_2$]$_2$Me), 3.05 (3 H, s, SO_2Me), 3.10—3.35 (8 H, m, NCH_2), 3.30—3.60 (2 H, m, 4-H_2), 4.70 (1 H, dd, *J* 2 and 9 Hz, 2-H), 5.00 (2 H, s, C*H*$_2$Ph), 5.30 (2 H, m, 3-H and 2-NH), 7.30 (5 H, s, CH_2*Ph*), 7.10—7.55 (15 H, m, CPh_3), and 8.50 (1 H, br s, 1-NH). Attempts to purify compound (**18**) by crystallization or flash chromatography transformed it into *compound* (**21**), m.p. 156—158 °C (from ethyl acetate) (Found: C, 69.25; H, 7.75; N, 5.05. $C_{47}H_{63}N_3O_7S$ requires C, 69.35; H, 7.75; N, 5.15%); δ_H (80

MHz; $CDCl_3$) 0.97 (12 H, t, *J* 6 Hz, CH_2Me), 1.51 (16 H, m, $[CH_2]_2Me$), 3.24 (8 H, m, NCH_2), 3.77 (2 H, d, *J* 6 Hz, 4-H_2), 4.95 (2 H, s, CH_2Ph), 6.13 (1 H, t, *J* 6 Hz, 3-H), 6.64 (1 H, br s, 2-NH), 7.24 (5 H, s, CH_2Ph), and 7.14—7.32 (15 H, m, CPh_3).

(3R,4R)-3-*Benzyloxycarbonylamino*-4-*hydroxymethyl*-2-*oxoazetidine*-1-*sulphonic Acid Sodium Salt* (**19**).—A solution of the tetrabutylammonium salt of (**17**) (37.18 g, 50 mmol) in 1,2-dichloroethane (700 ml) was refluxed with a solution of potassium hydrogen carbonate (19.3 g, 193 mmol) in water (260 ml) for 30 min. The mixture was cooled, the layers were separated, and the aqueous layer was extracted with 1,2-dichloroethane (2 × 400 ml). The combined organic layers were dried over Na_2SO_4 and evaporated to dryness under reduced pressure to give the tetrabutylammonium salt of (**19**) (27 g, 95%) as an amber oil, which was used for later transformations without further purification. A small portion of this tetrabutylammonium salt was transformed into the corresponding *sodium salt* by treatment with Dowex 50W × 4 resin (Na^+ form) as in the case of compound (**17**), m.p. 129—131 °C (from MeOH); $[\alpha]_D^{25}$ −8.9° (*c* 1.020 in water) (Found: C, 39.7; H, 3.75; N, 7.5. $C_{12}H_{13}N_2NaO_7S\cdot\frac{1}{2}H_2O$ requires C, 39.9; H, 3.9; N, 7.75%); $\nu_{max.}$(Nujol) 3 330br (NH and OH), 1 770 (β-lactam CO), 1 710 (CO), 1 260br (C–O and SO), 1 160, and 1 060 cm^{-1} (SO); δ_H [300 MHz; $(CD_3)_2SO$] 3.67—3.72 (3 H, m, 4-H and 4-CH_2), 4.44 (1 H, dd, *J* 2.5 and 9 Hz, 3-H), 4.54 (1 H, t, *J* 6 Hz, OH), 5.04 (2 H, s, CH_2Ph) 7.36 (5 H, s, CH_2Ph), and 8.07 (1 H, d, *J* 9 Hz, 3-NH).

(3S,4R)-3-*Benzyloxycarbonylamino*-2-*oxo*-4-*phenoxycarbonyloxymethylazetidine*-1-*sulphonic Acid Sodium Salt* (**22**).—Phenyl chloroformate (2.5 ml, 20 mmol) was slowly added to a solution of the tetrabutylammonium salt (**19**) (5.71 g, 10 mmol) in dry pyridine (50 ml) cooled to −20 °C, and the solution was stirred at this temperature for 1 h. After evaporation of the pyridine under highly reduced pressure and below 50 °C, the residue was partitioned between dichloromethane (500 ml) and cold water (200 ml). The organic phase was washed with brine (200 ml), dried over Na_2SO_4, and evaporated to dryness to give the tetrabutylammonium salt of (**22**) as a foam (6.56 g, 95%). Flash chromatography of this salt with a (10:0—9:1) ethyl acetate–methanol gradient gave the free acid (**22**) (82%). A small portion of the tetrabutylammonium salt was transformed into the corresponding *sodium salt* as in the case of compound (**17**), m.p. 168—171 °C (from EtOH); $[\alpha]_D^{25}$ −26.7° (*c* 1.010 in water) (Found: C, 47.1; H, 3.55; N, 5.65. $C_{19}H_{17}N_2NaO_9S\cdot\frac{1}{2}H_2O$ requires C, 47.4; H, 3.75; N, 5.80%); δ_H [300 MHz; $(CD_3)_2SO$] 4.02 (1 H, m, 4-H), 4.54 (2 H, m, 4-CH_2), 4.55 (1 H, dd, *J* 3 and 8 Hz, 3-H), 5.06 (2 H, s, CH_2Ph), 7.37 (5 H, s, CH_2Ph), 7.18—7.46 (5 H, m, OPh), and 8.18 (1 H, d, *J* 8 Hz, 3-NH).

(3S,4R)-3-*Benzyloxycarbonylamino*-4-*carbamoyloxymethyl*-2-*oxoazetidine*-1-*sulphonic Acid Sodium Salt* (**23**).—25% Aq. ammonium hydroxide (100 ml) was added to a solution of the tetrabutylammonium salt (**22**) (3.45 g, 5 mmol) in methanol (30 ml) and the mixture was stirred at room temperature for 2 h. The ammonium salt of (**23**) (0.39 g, 20%) precipitated in the reaction mixture and was filtered off. The filtrate was evaporated to dryness under reduced pressure to give the tetrabutylammonium salt of (**23**) (2.45 g, 80%) as a foam. This salt was transformed into the corresponding *sodium salt* by the procedure used in the preparation of compounds (**17**), m.p. 160—162 °C (from MeOH); $[\alpha]_D^{25}$ 0° (*c* 0.980 in water) (Found: C, 37.5; H, 4.0; N, 10.4. $C_{17}H_{14}N_3NaO_8S\cdot H_2O$ requires C, 37.8; H, 3.85; N, 10.2%); $\nu_{max.}$(Nujol) 3 460, 3 330, 3 260 (NH), 1 770 (β-lactam CO), 1 690, and 1 630 cm^{-1} (CO); δ_H [80 MHz; $(CD_3)_2SO$] 3.68—4.18 (3 H, m, 4-H and 4-CH_2O), 4.61 (1 H, dd, *J* 1 and 7 Hz, 3-H), 5.05 (2 H, s, CH_2Ph), 6.50 (2 H, br s, NH_2), 7.38 (5 H, s, CH_2Ph), and 7.81 (1 H, br d, *J* 7 Hz, 3-NH).

(3S,4R)-3-*Benzyloxycarbonylamino*-4-*mesyloxymethyl*-2-*oxoazetidine*-1-*sulphonic Acid Sodium Salt* (**24**).—Methanesulphonyl chloride (3.8 ml, 38 mmol) was slowly added to a solution of the tetrabutylammonium salt (**19**) (11.42 g, 20 mmol) in dry pyridine (50 ml) cooled to −20 °C, and the solution was stirred at this temperature for 1 h. The work-up as in the case of salt (**22**) yielded the tetrabutylammonium salt of (**24**) (12.72 g, 98%). Flash chromatography of this salt with a (10:0—9:1) ethyl acetate–methanol gradient gave the free acid (**24**) (70%). A small portion of the tetrabutylammonium salt was transformed into the corresponding *sodium salt* (**24**) by the procedure used in the preparation of salt (**17**), m.p. 127—129 °C (from EtOH); $[\alpha]_D^{25}$ −12.6° (*c* 1 in water) (Found: C, 33.25; H, 4.2; N, 5.9. $C_{13}H_{15}N_2NaO_9S_2\cdot 2H_2O$ requires C, 33.5; H, 4.1; N, 6.0%); δ_H [80 MHz; $(CD_3)_2SO$] 3.20 (3 H, s, Me), 3.90 (1 H, m, 4-H), 4.46—4.61 (3 H, m, 3-H and 4-CH_2O), 5.09 (2 H, s, CH_2Ph), 7.38 (5 H, s, CH_2Ph), and 8.12 (1 H, br d, *J* 8 Hz, 3-NH).

(3S,4R)-3-*Benzyloxycarbonylamino*-4-*iodomethyl*-2-*oxoazetidine*-1-*sulphonic Acid Sodium Salt* (**25**).—Sodium iodide (8.90 g, 57 mmol) was added to a solution of the tetrabutylammonium salt (**24**) (6.49 g, 10 mmol) in dry acetonitrile (150 ml) and the mixture was refluxed for 3 h. After evaporation, the residue was partitioned between ethyl acetate (900 ml) and saturated aq. sodium thiosulphate (120 ml). The organic phase was dried over Na_2SO_4 and evaporated. The residue was purified by flash chromatography with a (1:0—1:1) chloroform–acetone gradient to give the tetrabutylammonium salt of (**25**) as a foam (3.40 g, 50%). A small portion of this salt was transformed into the corresponding *sodium salt* (**25**) by the procedure used in the preparation of salt (**17**), m.p. 168—169 °C (decomp.) (from EtOH); $[\alpha]_D^{25}$ 0° (*c* 1.078 in water) (Found: C, 31.1; H, 2.7; N, 5.8. $C_{12}H_{12}IN_2NaO_6S$ requires C, 31.2; H, 2.6; N, 6.1%); δ_H [300 MHz; $(CD_3)_2SO$] 3.17 (2 H, m, CH_2I), 3.79 (1 H, dt, *J* 3 and 9.5 Hz, 4-H), 4.36 (1 H, dd, *J* 3 and 9 Hz, 3-H), 5.05 (2 H, s, CH_2Ph), 7.36 (5 H, s, CH_2Ph), and 8.16 (1 H, br d, *J* 9 Hz, 3-NH).

(3S,4S)-3-*Benzyloxycarbonylamino*-4-*methyl*-2-*oxoazetidine*-1-*sulphonic Acid Sodium Salt* (**26**).—Tributyltin hydride (2.92 g, 10 mmol) was slowly added, under nitrogen, to a solution of the tetrabutylammonium salt (**25**) (1.36 g, 2 mmol) in dry THF (100 ml) and the solution was stirred at room temperature for 2 h. After evaporation, the residue was dissolved in ethyl acetate (250 ml), then the solution was washed successively with water (50 ml) and brine (50 ml), and dried over Na_2SO_4. Evaporation and flash chromatography purification with a (1:1) hexane–acetone mixture provided the tetrabutylammonium salt of (**26**) (0.56 g, 50%), which was transformed into the corresponding *sodium salt* by the procedure used for salt (**17**), m.p. 127—129 °C (from MeOH); $[\alpha]_D^{25}$ −8.7° (*c* 1.250 in water) (Found: C, 42.55; H, 4.2; N, 8.5. $C_{12}H_{13}N_2NaO_6S$ requires C, 42.85; H, 3.9; N, 8.3%); δ_H [80 MHz; $(CD_3)_2SO$] 1.37 (3 H, d, *J* 6 Hz, 4-Me), 3.73 (1 H, dq, *J* 3 and 6 Hz, 4-H), 4.13 (1 H, dd, *J* 3 and 8 Hz, 3-H), 5.08 (2 H, s, CH_2Ph), 7.38 (5 H, s, CH_2Ph), and 8.05 (1 H, br d, *J* 8 Hz, 3-NH).

General Procedure of Amino Deprotection by Hydrogenolysis.—A mixture of the sodium salt of the 3-benzyloxycarbonylaminoazetidin-2-ones (**19**), (**23**), (**24**), or (**26**) (2 mmol) and 10% Pd/C (0.17 g) in a (1:1) methanol–water mixture (25 ml) was treated with hydrogen at atmospheric pressure and room temperature for 2 h. The catalyst was removed by filtration and washed with water (10 ml). The filtrate was evaporated under reduced pressure and the residue was slurried with ethanol (50

ml). This suspension was cooled to 0 °C and was then adjusted to pH 2 with 1M-HCl. The precipitate was filtered off, washed with cold ethanol, and dried to give the deprotected monobactams (**27**), (**28**), (**29**), or (**31**) respectively.

(3S,4R)-3-*Amino*-4-*hydroxymethyl*-2-*oxoazetidine*-1-*sulphonic acid* (**27**). This was obtained by hydrogenolysis of compound (**19**) in 90% yield, m.p. 180 °C (decomp.); $[\alpha]_D^{25}$ −1° (*c* 1.00 in water) (Found: C, 20.4; H, 5.45; N, 11.9. $C_4H_8N_2O_5S\cdot 2H_2O$ requires C, 20.70; H, 6.2; N, 12.1%); δ_H [80 MHz; $(CD_3)_2SO$] 3.50—3.89 (3 H, m, 4-H and 4-CH_2OH), 4.13 (1 H, d, *J* 1 Hz, 3-H), and 5.00 (4 H, br s, OH and 3-NH_3^+).

(3S,4R)-3-*Amino*-4-*carbamoyloxymethyl*-2-*oxozetidine*-1-*sulphonic acid* (**28**) was obtained by hydrogenolysis of compound (**23**) in 90% yield, m.p. 180—181 °C (decomp.) (from aq. MeOH); $[\alpha]_D^{25}$ +6.4° (*c* 1.065 in water) (Found: C, 24.6; H, 4.65; N, 17.4. $C_5H_9N_3O_6S\cdot H_2O$ requires C, 24.9; H, 4.55; N, 17.4%); $\nu_{max.}$(Nujol) 3 460, 3 350, 3 280, and 3 200 (NH), 1 755 (β-lactam CO), 1 710, and 1 690 (CO), 1 240, 1 200, and 1 050 cm^{-1} (SO); δ_H [80 MHz; $(CD_3)_2SO$] 3.75—4.09 (3 H, m, 4-H and 4-CH_2O), 4.18 (1 H, d, *J* 3 Hz, 3-H), 5.52 (2 H, br s, $CONH_2$), and 7.78 (3 H, br s, 3-NH_3^+).

(3S,4R)-3-*Amino*-4-*mesyloxymethyl*-2-*oxoazetidine*-1-*sulphonic acid* (**29**) was obtained by hydrogenolysis of compound (**24**) in 80% yield, m.p. 140 °C (decomp.); $[\alpha]_D^{25}$ 0° (*c* 0.990 in water) (Found: C, 19.2; H, 4.65; N, 8.8. $C_5H_{10}N_2O_7S_2\cdot 2H_2O$ requires C, 19.35; H, 4.5; N, 9.05%); δ_H [80 MHz; $(CD_3)_2SO$] 3.25 (3 H, s, Me), 4.00—4.20 (1 H, m, 4-H), 4.30 (1 H, d, *J* 2 Hz, 3-H), 4.42—4.73 (2 H, m, 4-CH_2O), and 7.88 (3 H, br s, 3-NH_3^+).

(3S,4S)-3-*Amino*-4-*methyl*-2-*oxoazetidine*-1-*sulphonic acid* (**31**)[19] was obtained by hydrogenolysis of compound (**26**), m.p. > 230 °C (decomp.); $[\alpha]_D^{25}$ −39° (*c* 0.105 in water) (lit.,[19] −41.1°); δ_H [80 MHz; $(CD_3)_2SO$] 1.39 (3 H, d, *J* 6.5 Hz, 4-Me), 3.79 (1 H, dq, *J* 2 and 6.5 Hz, 4-H), 3.90 (1 H, d, *J* 2 Hz, 3-H), and 8.67 (3 H, br s, 3-NH_3^+). This compound was identical with an authentic sample[19] by ^{1}H n.m.r. and h.p.l.c.

(3S,4R)-3-*Amino*-4-*iodomethyl*-2-*oxoazetidine*-1-*sulphonic Acid* (**30**).—TMSI (0.42 ml, 2.4 mmol) was added under nitrogen to a suspension of the sodium salt (**25**) (0.92 g, 2 mmol) in dry acetone (80 ml) and the mixture was stirred at room temperature for 30 min. After evaporation to dryness, the residue was purified by flash chromatography with a (4:1) chloroform–methanol mixture to give *compound* (**30**) (0.52 g, 85%), m.p. > 230 °C (decomp.); $[\alpha]_D^{25}$ −15° (*c* 0.800 in water) (Found: C, 13.85; H, 3.45; N, 8.0. $C_4H_7IN_2O_4S\cdot 2H_2O$ requires C, 14.05; H, 3.2; N, 8.2%); δ_H [80 MHz; $(CD_3)_2SO$] 4.20 (1 H, dt, *J* 3 and 9 Hz, 4-H), 4.35—4.60 (3 H, m, 3-H and 4-CH_2I), and 7.37 (3 H, br s, 3-$\dot{N}H_3$).

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