Tetrahedron Vol. 44, No. 2, pp. 619 to 624, 1988
Printed in Great Britain.

0040-4020/88 $3.00+.00
Pergamon Journals Ltd.

FROM AZIRIDINES TO CARBAPENEMS VIA A NOVEL β-LACTAM RING CLOSURE

AN ENANTIOSELECTIVE SYNTHESIS OF (+)-PS-5

DAVID TANNER* AND PETER SOMFAI

Department of Organic Chemistry

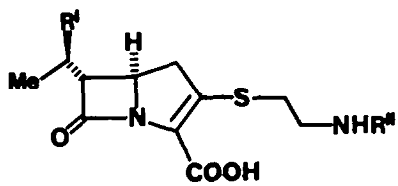
Chalmers University of Technology

S-412 96 Göteborg, Sweden

(*Received in UK* 12 *October* 1987)

Abstract - An enantioselective synthesis of the carbapenem antibiotic (+)-PS-5 is described. The starting point is the chiral Sharpless epoxy-alcohol 3 which is transformed stereospecifically to the aziridine 6. Regioselective ring-opening of 6 by $LiEt_2Cu$ followed by RuO_4 oxidation yields the β-sulfonamido carboxylic acid 8 which is cyclised under mild conditions and in excellent yield to the N-tosyl azetidinone 9. Deprotection at nitrogen, unmasking of the side-chain hydroxyl and oxidation then furnishes 11, a known advanced intermediate for (+)-PS-5.

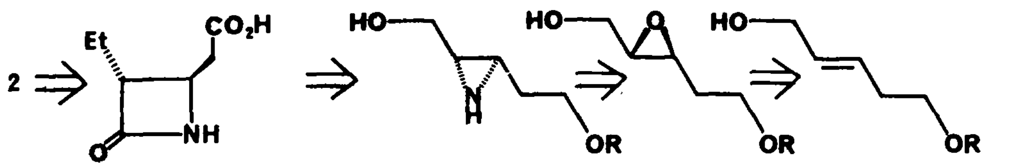
Due to their unique structure, potent antibacterial activity, and often low natural abundance, the carbapenem antibiotics (exemplified below by thienamycin, 1 and PS-5, 2) continue to fascinate organic chemists as regards the total synthesis of these important biomolecules[1], two central problems in any totally synthetic approach being control of absolute stereochemistry and efficient formation of the β-lactam ring system.



1 R^{I}=OH R^{II}=H

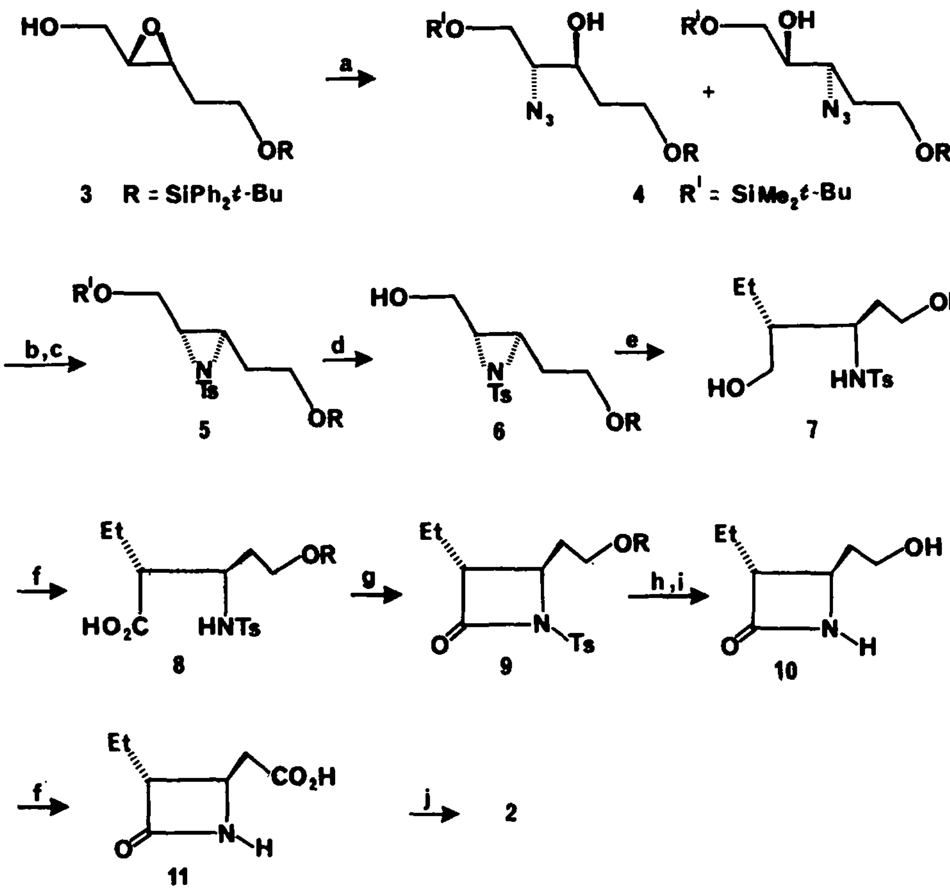
2 R^{I}=H R^{II}=Ac

We recently described[2] a novel enantioselective entry to (+)-thienamycin, 1, which relied on the use of a chiral 2,3-aziridino alcohol as a key intermediate. The aziridine in question was itself easily procured in enantiomerically pure form from an epoxy alcohol synthesised using the Sharpless asymmetric epoxidation technique[3a]. The present paper describes a continuation of our work which has culminated in a highly stereocontrolled route to the natural form of the related carbapenem PS-5, 2, a simplified retrosynthetic analysis of the problem being shown in Scheme 1.



Scheme 1

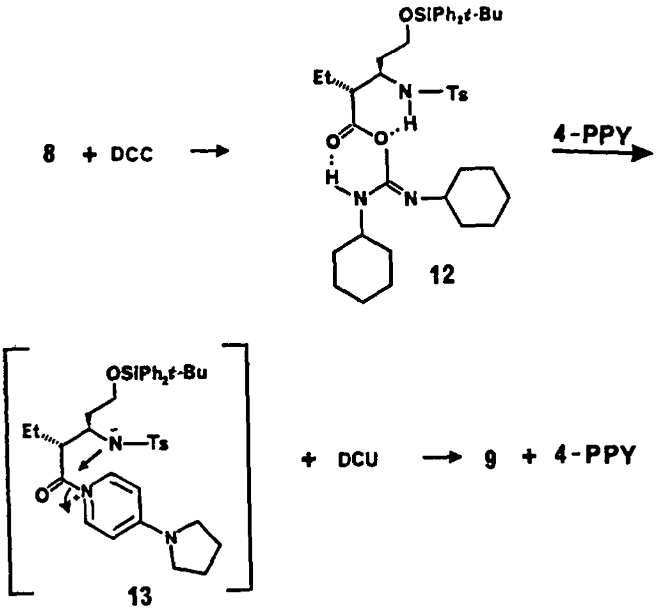
In the synthetic direction (see Scheme 2) the two major features are (i) the highly regio-selective ring-opening of the chiral aziridine 6 which dictates relative and absolute stereo-chemistry and (ii) the novel cyclisation of the β-sulfonamido carboxylic acid 8 to form the azetidinone ring under extremely mild conditions and in excellent (83%) yield.



Scheme 2

(a) NaN_3, $MeO(CH_2)_2OH/H_2O$, 94% yield, then TBDMSCl, DMAP, NEt_3, CH_2Cl_2, 95% (b)Ph_3P, toluene, reflux, 98% (c) TsCl, pyridine, 96% (d) $HOAc/THF/H_2O$ (3:1:1) 82% (e) $LiEt_2Cu$ Et_2O, 80% (f) $RuCl_3$ (2 mol%) $NaIO_4$, $CCl_4/CH_3CN/H_2O$, RT, 82% (g) DCC, 4-pyrrolidino-pyridine (cat.) CH_2Cl_2, RT, 15 min., 83% (h) Na-naphthalide, DME, -78°C, 85% (i) HCl, MeOH, RT, 91% then (f) 73% (j) see ref. 12.

The chiral epoxy alcohol 3, itself readily available in at least 97% e.e. by the Sharpless asymmetric epoxidation technique[3a,b], was transformed by our modification[2] of the Blum procedure[4] to the key 2,3-aziridino alcohol 6 which underwent highly regioselective[2,5] ring-opening upon exposure to $LiEt_2Cu$, the resultant β-sulfonamido alcohol being then oxidised smoothly[6] to the carboxylic acid 8. In the preceding paper[7] we have described the intramolecular coupling of ω-sulfonamido carboxylic acids to give the relevant N-tosyl lactams, a technique which we discovered in an attempt to esterify 8 under the Hassner conditions[8] (MeOH, DCC, 4-pyrrolidinopyridine, CH_2Cl_2, RT). This yielded only a modest amount of the expected methyl ester along with, to our surprise, significant amounts of the N-tosyl β-lactam 9. Gratifyingly, simply repeating this experiment in the absence of methanol led to smooth and rapid formation of 9 in no less than 83% isolated yield (CH_2Cl_2, RT, 15 min.). High-dilution methods were unnecessary but the presence of the 4-pyrrolidinopyridine (4-PPY) was essential since in its absence little or no β-lactam formation occurred and the relevant N-acyl urea could be isolated chromatographically in high yield. Significantly, we were unable to detect the formation of the anhydride in the reactions run in the absence of 4-PPY, and this may indicate that the mechanism suggested[7] in the preceding paper is indeed operative in the present case (see also Scheme 3).



Scheme 3

Thus, the initially-formed O-acyl species 12 (which may well enjoy the intramolecular hydrogen bonding indicated) is attacked by 4-PPY. After expulsion of the (insoluble) DCU, the zwitterionic acylpyridinium species 13 undergoes rapid ring-closure to 9 with simultaneous regeneration of the 4-PPY catalyst.

The N-tosyl β-lactam 9 is characterised by an unusually high frequency carbonyl stretch in the IR (1790 cm^{-1}) and by the expected small coupling constant for the ring protons in the ^1H NMR (J_{trans} = 3 Hz). Deprotection at nitrogen was achieved easily with no adverse effects on the azetidinone ring by use of sodium naphthalide in DME at low temperature[9], the hydroxyl was then unmasked by dilute mineral acid, and the resultant primary alcohol oxidised[6,10] in good yield to the desired 11 ($[\alpha]_D$ +46.7°, c 0.9, $CHCl_3$, lit.[11] +48.98°, c 1.14, $CHCl_3$). Since enantiomerically pure 11, obtained via resolution, has already been transformed into (+)-PS-5 by Favara[12], the present work constitutes a convenient formal total synthesis of the antibiotic in its natural form.

In conclusion, we note that since the present approach relies on the Sharpless technique[3a] for initial introduction of chirality, simple variation of the starting allylic alcohol (Z or E) and tartrate (D or L) geometries in harness with the stereospecificity[2,4] of the epoxide-to-aziridine transformation and the excellent regioselectivity observed in the aziridine ring-opening should allow the enantioselective synthesis of all possible diastereomers of the desired carbapenem. The present route should also be amenable to the preparation of other non-natural congeners, a matter of no little importance in the β-lactam antibiotic field.

Acknowledgements - We thank the Swedish Natural Science Research Council for financial support.

EXPERIMENTAL

All reactions were run under argon, using flame- or oven-dried glassware. Solvents were purified and dried using standard procedures.

Epoxy alcohol 3 was obtained from the corresponding allylic alcohol (94% yield) according to the general procedure described in ref. 3a. The material was shown to be at least 97% optically pure by the method described in ref. 3b.

^{1}H NMR (270 MHz, $CDCl_3$/TMS): δ 7.57 (4H, m, aromatic) 7.30 (6H, m, aromatic) 3.88 (1H, dd, J=12.5, 2.5Hz, CHOH) 3.77 (2H, m, CH_2OSi) 3.59 (1H, dd, J=12.5, 4, CHOH) 3.10 (1H, td, J=6, 2, epoxide) 2.95 (1H, ddd, J=4, 2.5, 2, epoxide) 1.82 (2H, apparent qt, J=6, CH_2CH_2OSi) 1.04 (9H, s, t-Bu).
IR: 3400 (b, OH) 1260 (epoxide) 1100 (OSi) 930 (epoxide) cm^{-1}.
MS: (m/z) 299 (M - t-Bu)
$[\alpha]_D$ -17.56° (c 1.13, CH_2Cl_2).

Azides 4. Epoxy alcohol 3 (4.252g, 11.9 mmol) was dissolved with stirring in an 8:1 mixture of $MeO(CH_2)_2OH$ and H_2O. Sodium azide (3.882g, 59.7 mmol) and ammonium chloride (1.266g, 23.9 mmol) were added and the mixture was refluxed for 80 min. The reaction mixture was then partitioned between ether and water, the layers were separated and the aq.phase was back-extracted with four portions of ether. The combined organics were washed twice with water and once with brine, and dried over Na_2SO_4. Removal of solvents and flash chromatography of the residue (silica gel, ether-pentane gradient 60 to 100%) yielded an inseparable 1:1 mixture of regioisomeric azidodiols (^{1}H NMR analysis) which was used directly in the next step. Yield: 4.493g, 94%.
IR: 3400 (b,s,OH) and 2100 (s,azide).
The mixture of azidodiols (4.130g, 10.4 mmol) was dissolved in CH_2Cl_2 (40 ml) and stirred at 0°C. Triethylamine (1.59 ml, 11.4 mmol) and DMAP (50mg, 0.4 mmol) were added and the mixture was stirred for 5 min before addition of TBDMSCl (1.872g, 12.4 mmol). The reaction mixture was allowed to reach RT and was then stirred overnight. After partitioning between CH_2Cl_2 and water, the organic phase was separated and washed once with NH_4Cl.aq. dried over Na_2SO_4 and the solvent was removed. Flash chromatography of the residue (ether-pentane 10 to 20%) yielded the regioisomeric azides 4 as an inseparable mixture which was carried on directly. Yield: 5.044g, 95%.
IR: 3500 (b,OH) 2100(s,azide) 1100 (vs,OSi).

N-tosyl aziridine 5. The mixture of azides 4 (4.970g, 9.7 mmol) was dissolved in toluene (40 ml) and triphenylphosphine (3.049g, 11.6 mmol) was added. The resultant solution was refluxed for 50 min, cooled, and the solvent removed. The oily residue was triturated with ether to precipitate triphenylphosphine oxide which was filtered off, and the filtrate was evaporated to dryness to yield a residue which was flash chromatographed (ether-pentane 40 to 80%). There was obtained 4.465g (98%) of a single aziridine as an oil.

^{1}H NMR: 7.70 (4H, m, aromatic) 7.39 (6H, m, aromatic) 3.92 (2H, m, CH_2CH_2OSi) 3.75 (2H, bd, J=3.5, CH_2OSi) 2.05 (1H, bm, aziridine) 1.83 (1H, apparent qt, J=3.5, aziridine) 1.65 (3H, m, CH_2CH_2OSi and NH) 1.06 (9H, s, t-Bu) 0.89 (9H, s, t-Bu) 0.05 (6H, s, $SiMe_2$).
IR: 3300 (vb,NH) 1100 (vs,OSi).
MS: 412 (M - t-Bu).
$[\alpha]_D$ +19.6° (c 1.40, CH_2Cl_2).
The aziridine (2.009g, 4.3 mmol) was dissolved with stirring in pyridine (5 ml) and cooled to -20°C. Tosyl chloride (0.898g, 4.7 mmol) was added and the resultant mixture stored in the freezer overnight. The reaction mixture was partitioned between ether and $CuSO_4$.aq. and the separated organic phase washed once with $CuSO_4$.aq., once with water, and once with brine. The organics were died over Na_2SO_4 and the solvent was removed to yield an oily residue which was purified by flash chromatography (ether-pentane 5 to 30%). This furnished 2.572g (96%) of 5 as a colourless oil.

^{1}H NMR: 7.85 (2H, "d", J=8.5, tosyl) 7.65 (4H, m, phenyl) 7.40 (6H, m, phenyl) 7.23 (2H, "d", J=8.5 tosyl) 3.83 (1H, dd, J=11, 4.5, CH_2OSi) 3.80 (1H, dd, J=11, 5, CH_2OSi) 3.74 (2H, t, J=6, CH_2CH_2OSi) 2.93 (2H, m, aziridine) 2.40 (3H, s, tosyl-Me) 2.10 (2H, m, CH_2CH_2OSi) 1.05 (9H, s, t-Bu) 0.92 (9H, s, t-Bu) -0.05 (6H, 2xs, $SiMe_2$).
IR: 1320 (s,sulfonamide) 1160 (s,sulfonamide) 1100 (s,OSi).
MS: 566 (M - t-Bu).
$[\alpha]_D$ +6.71° (c 1.13, CH_2Cl_2).

Aziridino alcohol 6. Aziridine 5 (1.349g, 2.2 mmol) was dissolved in a 3:1:1 mixture of acetic acid, THF and water (total volume 25 ml) and the mixture stirred at RT for 3 days. The mixture was then poured into ether-water and solid Na_2CO_3 was added in small portions to neutralise the acid. The phases were separated and the organics washed once with brine and then stripped down to yield a residue which was flash chromatographed (ether-pentane 60%). There was obtained 0.908g (82%) of the aziridino alcohol 6 as an oil.

^{1}H NMR: 7.80 (2H, "d", J=8, tosyl) 7.59 (4H, m, phenyl) 7.38 (6H, m, phenyl) 7.24 (2H, "d", J=8, tosyl) 4.08 (1H, ddd, J=13.5, 9, 3, CHOH) 3.89 (1H, ddd, J=13.5, 8, 5, CHOH) 3.63 (2H, apparent dd, J=6.5, 5, CH_2OSi) 3.15 (1H, ddd, J=6.5, 6, 4.5, aziridine) 3.01 (1H, ddd, J=8, 4.5, 3, aziridine) 2.59 (1H, dd, OH) 2.44 (3H, s, tosyl-Me) 1.90 (1H, dtd, J=14, 6.5, 6, $CHCH_2OSi$) 1.74

(1H, ddt, J=14, 6.5, 5, C<u>H</u>CH$_2$OSi) 1.05 (9H, s, t-Bu).
IR: 3500 (b,OH) 1320 (s,sulfonamide) 1160 (s,sulfonamide) 1100 (s,OSi).
MS: 452 (M - t-Bu).
$[\alpha]_D$ +23.0° (c 1.40, CH_2Cl_2).

Alcohol 7. Freshly purified CuI (2.151g, 11.3 mmol) was slurried in ether (70 ml) and cooled with stirring to -78°C. A solution of freshly prepared ethyllithium (1.32M in ether, 17.1 ml, 22.6 mmol) was added via syringe and the resultant pale brown solution was stirred at -78°C for 10 min. A solution of aziridino alcohol 6 (1.917g, 3.8 mmol) in ether (10 ml) was added dropwise and the resultant solution stirred at -78°C for 1h (complete according to TLC). After the usual work-up, the residue was purified by flash chromatography (ether-pentane 70%, 3 runs) which separated the desired regioisomer 7 from minor amounts of the (less polar) regioisomer. There was obtained 1.63g (80%) of 7 as an oil. The ratio of regioisomers was ca. 15:1 in favour of the desired component.

^{1}H NMR: 7.73 (2H, "d", J= 8, tosyl) 7.59 (4H, m, phenyl) 7.40 (6H, m, phenyl) 5.91 (1H, d, J=8.5, N<u>H</u>) 4.05 (1H, bdd, J=12, 3, C<u>H</u>OH) 3.65 (2H, m, C<u>H</u>OH and C<u>H</u>NTs) 3.50 (2H, m, C<u>H</u>$_2$OSi) 2.41 (3H, s, tosyl-Me) 2.29 (1H, b, O<u>H</u>) 1.57 (2H, m, C<u>H</u>$_2$CH$_2$OSi) 1.46 (1H, m, methine) 1.32 (2H, m, C<u>H</u>$_2$CH$_3$) 1.05 (9H, s, t-Bu) 0.86 (3H, t, J=7, CH$_2$C<u>H</u>$_3$).
IR: 3500 (b,s,OH) 3250 (b,s,N-H) 1320(s,sulfonamide) 1160(s,sulfonamide) 1100(s,OSi).
MS: 482 (M - t-Bu)
$[\alpha]_D$ +9.15° (c 1.33, CH_2Cl_2).

β-sulfonamido carboxylic acid 8. This material was sensitive towards silica gel column chromatography, so on larger scales it was not purified and the crude product was used directly in the next step. However, a small sample of the acid was obtained pure by preparative TLC (ether-pentane 80%). Alcohol 7 (0.108g, 0.2 mmol) was dissolved with stirring in a mixture of CCl_4 (0.5 ml) acetonitrile (0.5 ml) and water (0.75 ml). $NaIO_4$ (0.176g, 0.82 mmol) was added and the mixture stirred for 5 min before the addition of $RuCl_3$ (1mg). The resultant mixture was then stirred vigorously for 1h at RT. The phases were separated and the aqueous layer was back-extracted with two portions of CH_2Cl_2. The organics were dried over Na_2SO_4 and stripped down to yield a residue which was taken up in ether (10 ml). The ethereal mixture was filtered through Celite and the filtrate evaporated to dryness. Preparative TLC of the residue yielded the desired carboxylic acid as a clear colourless oil. Yield: 0.091g, (82%).

^{1}H NMR: 7.73 (2H, "d", J=8, tosyl) 7.58 (4H, m, phenyl) 7.38 (6H, m, phenyl) 7.19 (2H, "d", J=8, tosyl) 5.62 (1H, d, J=9, N<u>H</u>) 3.80 (1H, dtd, J=9, 7, 3.9, C<u>H</u>-NTs) 3.52 (2H, m, C<u>H</u>$_2$OSi) 2.62 (1H, td, J=7, 3.9, C<u>H</u>-COO) 2.40 (3H, s, tosyl-Me) 1.65 (4H, complex m, methylenes) 1.05 (9H, s, t-Bu) 0.92 (3H, t, Me).
IR: 3500-2500 (vb,COOH) 3250(b,N-H) 1710 (s,COOH) 1320 (s,sulfonamide) 1165 (s,sulfonamide) 1100 (s,OSi).
$[\alpha]_D$ +0.50° (c 2.50, CH_2Cl_2).

The actual oxidation step could be carried out easily on a gram scale,the yield being typically 80 - 90% of crude acid (pure according to ^{1}H NMR spectroscopy).

N-tosyl β-lactam 9. The crude acid 8 (0.525mg, 0.95 mmol) was dissolved in CH_2Cl_2 (9.5ml,i.e. 0.1 M solution of the acid) and stirred at RT during addition of DCC (0.223g, 1.08 mmol) and 4-PPY (15mg). The resultant solution was stirred for 15 min at RT (reaction complete according to TLC) and the precipitated DCU was filtered off. The filtrate was washed twice with water, once with 5% aqueous acetic acid, and once with water. The organics were dried over Na_2SO_4 and stripped down to yield a residue which was purified by flash chromatography (ether-pentane 20 to 30%). There was obtained 0.422g (83%) of the N-tosyl β-lactam 9 as a colourless oil.

^{1}H NMR: 7.86 (2H, "d", J=8, tosyl) 7.63 (4H, m, phenyl) 7.42 (6H, m, phenyl) 7.33 (2H, "d", J=8, tosyl) 3.89 (1H, ddd, J=9, 4, 3, C<u>H</u>-N) 3.75 (2H, m, J_{gem}=8, C<u>H</u>$_2$OSi) 3.00 (1H, td, J=7, 3, C<u>H</u>-C=O) 2.45 (3H, s, tosyl-Me) 2.39 (1H, m, C<u>H</u>CH$_2$OSi) 1.80 (1H, ddt, J=13, 9, 4.5, C<u>H</u>CH$_2$OSi) 1.55 (2H, 2xdq, J=14, 7, Et methylenes) 1.05 (9H, s, t-Bu) 0.83 (3H, t, Me). The value of 3Hz for the vicinal coupling constant between the azetidinone protons confirms the trans stereochemistry.
IR: 1790 (s, β-lactam) 1360 (s,sulfonamide) 1160 (s,sulfonamide) 1100 (s,OSi).
MS: 478 (M - t-Bu)
$[\alpha]_D$ -15.2° (c 2.14, CH_2Cl_2).

Alcohol 10. The tosyl group in 9 was removed as follows. Recrystallised naphthalene (0.525g, 4.1 mmol) was dissolved with stirring in 1,2-dimethoxyethane (10 ml) and sodium metal (0.095g) was added. The mixture was stirred for 1h at RT and the resultant blue-green solution of sodium naphthalide was cooled to -78°C before addition of a solution of 9 (0.366g, 0.68 mmol) in DME (ca. 1 ml).The reaction mixture was stirred for 20 min at -78°C (reaction complete according to TLC) and then water was added dropwise until the colour of the anion was discharged. The resultant colourless mixture was then partitioned between ether and water, the layers were separated, and the aqueous layer was back-extracted with three portions of ether. The combined organics were dried over Na_2SO_4 and then stripped down to afford a residue which was purified by flash chromatography (ether-pentane 40 to 80%). There was obtained 0.216g (85%) of the deprotected β-lactam.

^{1}H NMR: 7.65 (4H, m, phenyl) 7.42 (6H, m, phenyl) 5.75 (1H, b, -N<u>H</u>) 3.77 (2H, symmetrical 10-line m, C<u>H</u>$_2$OSi) 3.48 (1H, ddd, J=7.5, 6, 2, C<u>H</u>-N) 2.75 (1H, dddd, J=8, 6, 2, 1.5, C<u>H</u>CON) 1.83 (2H, m,

CH_2CH_2OSi) 1.81 (1H, dqd, J=14, 7, 6, Et methylene) 1.71 (1H, ddq, J=14, 8, 7, Et methylene) 1.04 (9H, s, t-Bu) 0.99 (3H, t, J=7, Me).
IR: 3300 (b,N-H) 1750(s, β-lactam) 1110(s,OSi).
MS: 324 (M - t-Bu).
$[\alpha]_D$ +11.6° (c 0.80, CH_2Cl_2).
The silyl ether protecting group was hydrolysed as follows. The β-lactam from above (0.228g, 0.598 mmol) was dissolved with stirring in methanol (5 ml). Concentrated hydrochloric acid (a total of 8 drops) was added carefully over a period of 6h, the reaction being monitored carefully by TLC. When the reaction was complete according to TLC analysis, a small amount of powdered sodium bicarbonate was added, the mixture was filtered, and the filtrate evaporated to dryness. Flash chromatography of the residue yielded the alcohol 10 (0.078g, 91%).
^{1}H NMR: 6.48 (1H, b, -NH) 3.76 (2H, m, CH_2OSi) 3.48 (1H, ddd, J=8, 5, 2, CH-N) 2.79 (1H, dddd, J=8.5, 6, 2, 1.1, CH-CON) 2.40 (1H, b, OH) 1.90 (2H, m, CH_2CH_2OSi) 1.81 (1H, dqd, J=15, 7, 6, Et methylene) 1.71 (1H, ddq, J=15, 8.5, 7, Et methylene) 1.02 (3H, t, J=7, Me). The values for the vicinal coupling between the azetidinone protons (2 Hz) and the long-range coupling between CHCON and NH (1.1 Hz) show clearly that the β-lactam ring has the required trans geometry. (See also the previous compound).
IR: 3350-3200 (b,vs,OH and NH) 1730 (s, β-lactam).
MS: 143 (M^+).
$[\alpha]_D$ +24.3° (c 1.33, CH_2Cl_2).

Carboxylic acid 11. This material was obtained from 10 by the RuO_4 oxidation procedure described above for the conversion of 7 to 8. The yield was 73%, m.p. 110 - 112°C (lit. 113 - 115°C,ref.12).
^{1}H NMR: 6.78 (1H, b, NH) 3.65 (1H, ddd, J=9.5, 4, 2, CH-N) 2.83 (1H, dddd, J=8, 6.5, 2, 0.5, CH-CON) 2.79 (1H, dd, J=16, 4, CHCOOH) 2.61 (1H, dd, J=16, 9.5, CHCOOH) 1.84 (1H, dqd, J=14, 7, 6.5 Et methylene) 1.71 (1H, ddq, J=14, 8, 7, Et methylene) 1.04 (3H, t, J=7, Me).
IR: 1750 (s,β-lactam) 1725 (s,COOH).
$[\alpha]_D$ +46.7° (c 0.90, $CHCl_3$; lit. +48.98°, c 1.14, $CHCl_3$, ref. 11).

REFERENCES

1. For a recent review, see: Nagahara, T. and Kametani, T. Heterocycles (1987) 25 729.

2. Tanner, D. and Somfai, P. Tetrahedron Lett. (1987) 28 1211.

3. (a) Katsuki, T. and Sharpless, K.B. J.Am.Chem.Soc. (1980) 102 5974. (b) The e.e. of epoxy alcohol 3 was estimated to at least 97% by ^{1}H NMR spectroscopy on the corresponding acetate in the presence of Eu(tfc)$_3$, after a suitable control experiment on the racemic acetate.

4. Ittah, Y., Sasson, Y., Shahak, I., Isaroom, S. and Blum, J. J.Org.Chem. (1978) 43 4271.

5. For related examples of ring-opening in the corresponding epoxy alcohol series, see: Nagaoka, H. and Kishi, Y. Tetrahedron (1981) 37 3873.

6. Carlsen, P.H.J., Katsuki, T., Martin, V.S. and Sharpless, K.B. J.Org.Chem. (1981) 46 3939.

7. Tanner, D. and Somfai, P. Preceding paper.

8. Hassner, A. and Alexanian, V. Tetrahedron Lett. (1978) 4475.

9. For recent related examples, see: (a) Nagashima, H., Ozaki, N., Washiyama, M. and Itoh, K. Tetrahedron Lett. (1985) 26 657. (b) Trost, B.M. and Sudhakar, A.R. J.Am.Chem.Soc. (1987) 109 3792.

10. For a related example of this oxidation applied to a β-lactam having no N-protecting group, see: Ito, Y. and Terashima, S. Chem. Lett. (1987) 445.

11. Okano, K., Izawa, T. and Ohno, M. Tetrahedron Lett. (1983) 24 217.

12. Favara, D., Omodei-Sale, A., Consonni, P. and Depaoli, A. Tetrahedron Lett. (1982) 23 3105.