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Solvent-mediated selective single and double ring-opening of *N*-tosyl-activated aziridines using benzylamine

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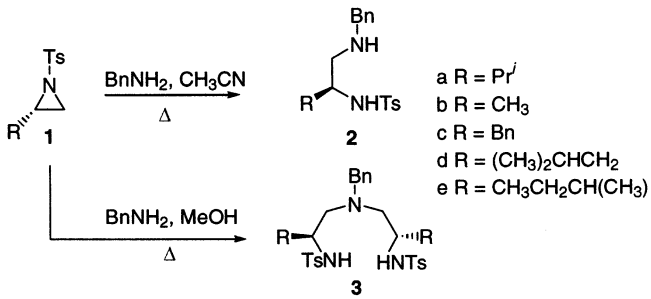
Abstract—An efficient methodology has been developed for the synthesis of a series of new diamine **2** and triamine ligands **3** for application in asymmetric catalysis via selective single or double ring-opening of tosylaziridines **1**, which are derived from chiral pool amino acids. The selectivity of the ring-opening reaction is readily controlled by the solvent employed. Thus, in acetonitrile formation of secondary amines **2** occurs via a single ring-opening step, whilst in methanol the reactions proceed to give the tertiary amines **3** via the ring-opening of two aziridine molecules.

1. Introduction

The development and application of new homochiral ligands in asymmetric catalysis continues to be an area of enormous interest and activity, since this approach represents one of the most efficient means of obtaining enantiopure chiral compounds.[1] We are currently interested in the development of small ligand libraries to enable us to screen the catalytic activity of their transition metal complexes in a number of asymmetric transformations using diversity methods. Aziridines are ideal starting materials for this purpose[2] and our interest in the area has been further stimulated by a number of reports of the successful application of related C_2- and C_3-symmetric ligands, derived from chiral pool amino acids, in asymmetric catalysis; examples include diethylzinc additions to benzaldehyde[3] and aldol-like acyl halide–aldehyde cyclocondensations.[4] To maximise the structural diversity of the ligands available to us, we were particularly interested in developing highly chemoselective routes towards both diamine and triamine ligands, such as **2** and **3**, via single and double ring-opening of activated aziridines. Our rationale for seeking to broaden the scope of the ligands produced lies in the empirical nature of the discovery process for asymmetric catalysts and the consequential requirement for ligand libraries containing as much structural diversity as possible when screening for activity.[5]

2. Results and discussion

The *N*-tosyl-aziridines, **1**, used in this study were prepared in an identical manner from the appropriate



Scheme 1.

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amino alcohol using slight modifications of the reported procedure.[6] We then attempted to facilitate ring opening of these materials at the methylene carbon using benzylamine as the amine nucleophile under a range of classical conditions.[2] The choice of benzylamine was based on our recent experience that had demonstrated it to be an ideal nucleophile and the fact that the benzyl group could be readily removed in related polyamine systems.[7] Therefore, its presence in **2** and **3** would readily allow for the selective introduction of further structural modularity in the ligand library, if needed, through appropriate deprotection/alkylation strategies.

It quickly became apparent from an initial screen of reaction conditions using **1a**, that considerable chemoselectivity could be achieved in the ring-opening reaction simply by modifying the reaction solvent (Scheme 1). Thus, for example, when **1a** was reacted with benzylamine in a 1:1 molar ratio in acetonitrile the secondary amine **2a** was formed almost exclusively, whereas in methanol a mixture of **2a** and **3a** resulted. The observed tendency for double ring-opening in methanol could be exploited and by reacting **1a** with benzylamine in a 2:1 ratio, **3a** was exclusively formed. In contrast, using this 2:1 reactant ratio with acetonitrile as the solvent essentially still resulted in the formation of only the secondary amine **2a**. Only after heating the reaction mixture under reflux in the presence of excess **1a** for a week was **3a** formed. In this case it remained contaminated with **2a** and was difficult to purify and the reaction was consequently low yielding. In contrast, **2a** could be readily converted to **3a** in methanol by the addition of a further equivalent of **1a** at reflux. Optimisation of the results of this initial screen resulted in the isolation of **2a** and **3a** in 62 and 69% yield, respectively (Table 1, entries 1 and 2). The double ring-opening of three *N*-tosyl aziridines using aqueous ammonia and methylamine has been reported by Lin and co-workers.[8] However, this is a more complicated procedure that first requires the single ring-opened product to be prepared, moreover the products are all isolated by column chromatography. In contrast both single, **2a**, and double, **3a**, ring-opened products could be readily isolated from the crude reaction mixture without the need for chromatography; the isolation of **3a** being particularly straightforward through recrystallisation of the crude reaction mixture.

Table 1. Chemoselective ring opening of aziridines **1** with benzylamine

Entry	Ligand	R	Solvent	Yield (%)
1	**2a**	Pr^i	CH_3CN	62
2	**3a**	Pr^i	MeOH	69
3	**2b**	CH_3	CH_3CN	56
4	**3b**	CH_3	MeOH	69
5	**2c**	Bn	CH_3CN	49
6	**3c**	Bn	MeOH	80
7	**2d**	$(CH_3)_2CHCH_2$	CH_3CN	60
8	**3d**	$(CH_3)_2CHCH_2$	MeOH	44
9	**2e**	$CH_3CH_2CH(CH_3)$	CH_3CN	42
10	**3e**	$CH_3CH_2CH(CH_3)$	MeOH	79

The simple procedures optimised for **1a** were then applied to four other activated aziridines **1b–e**. In all cases the ring-opening of the aziridines proceeded in an analogous manner and homogeneous samples of single and double ring-opened products could be prepared in moderate to good yield (Table 1, entries 3–10). To the best of our knowledge only one of these compounds, **3c**, has been previously applied in asymmetric catalysis when an aluminium complex was shown to be a moderately selective catalyst in an asymmetric acyl halide–aldehyde cyclocondensation,[4] although we have been unable to find any experimental data.

3. Conclusion

We have discovered that careful choice of the reaction solvent can provide an extremely simple methodology for controlling the ring-opening of activated *N*-tosyl-aziridines, **1**, by benzylamine to generate the new enantiomerically pure diamine- and triamine-ligands **2** and **3**. The use of acetonitrile results in the exclusive formation of the single ring-opened products **2**, whilst the use of methanol produces the double ring-opened materials **3**. The procedure is particularly convenient, as both products can be isolated in a pure state following a simple work up procedure.

4. Experimental

4.1. General methods

All reagents were commercially available and were used without further purification, unless otherwise stated. CH_3CN was heated under reflux overnight with CaH_2 in an atmosphere of nitrogen and then distilled from CaH_2. Methanol was heated under reflux for 3 h over Mg turnings together with a small quantity of iodine and then distilled. Benzylamine was dried over KOH pellets prior to use. Nitrogen for inert atmosphere use was purified by passing it through anhydrous manganese(II) oxide, 3 Å molecular sieves and highly reduced chromium adsorbed onto a silica support. Thin-layer chromatography (TLC) was performed on silica gel 60 F_{254} plates (Merck). Melting points were determined using an Electrothermal melting point apparatus and are uncorrected. Elemental analyses were obtained using a Carlo Erba 1106 elemental analyser. ^1H NMR and ^{13}C NMR spectra were recorded as $CDCl_3$ solutions on a JEOL JNM-EX spectrometer at 270 and at 67.9 MHz, respectively. All ^1H NMR spectra were referenced to residual $CHCl_3$ as the internal standard with *J* values are given in hertz. IR spectra were recorded on a Perkin–Elmer 1720X FT-IR spectrometer with a solid state ATR attachment. Mass spectra were recorded on a VG Instruments ZAB-SE using xenon gas at 8 kV in a matrix of 3-nitrobenzyl alcohol (MNBA) and sodium iodide (FAB).

4.2. General procedure for the preparation of the secondary amines 2 via the ring-opening of *N*-tosyl-aziridines 1 with benzylamine

All reactions were carried out in an identical manner to yield products that were homogeneous by TLC. All yields are based on the aziridine **1** (Table 1) and the procedure used is typified by the preparation of **2a**. It was found that the addition of a slight excess of benzylamine resulted in cleaner reactions and easier product purification.

4.2.1. *N*-[1-(Benzylaminomethyl)-2-methylpropyl]-4-methylbenzenesulfonamide 2a. *N*-Tosyl-aziridine, **1a** (2.00 g, 8.37 mmol) and benzylamine (1.00 g, 9.35 mmol) were dissolved in dry acetonitrile (30 mL) and the mixture stirred under reflux for 3 days. The solvent was evaporated under reduced pressure and the slightly yellow residue dissolved in diethyl ether (30 mL). Upon the addition of concentrated hydrochloric acid (2 mL) the desired product precipitated as its HCl salt. The colourless crystals were collected, dissolved in H_2O (30 mL), basified to pH 12 with solid KOH and extracted with dichloromethane (3×50 mL). The combined organic extracts were then dried with anhydrous magnesium sulfate and the solvent evaporated under reduced pressure, resulting in a colourless waxy-solid (1.8 g, 5.19 mmol, 62%). $[\alpha]_D^{25}$ −18.8 (*c* 0.5, $CHCl_3$). ^{1}H NMR: δ 7.68 (d, 2H, $J=8.4$), 7.33–7.16 (m, 7H), 3.54 (s, 2H), 3.03–2.97 (m, 1H), 2.55 (dd, 1H, $J=12.4$ and 6.8), 2.38 (dd, 1H, $J=12.4$ and 4.5), 2.36 (s, 3H), 1.83 (octet, 1H, $J=6.8$), 0.84 (d, 3H, $J=6.8$), 0.79 (d, 3H, $J=6.8$). ^{13}C NMR: δ 143.1, 139.8, 137.7, 129.5, 128.4, 127.9, 127.5, 127.1, 58.5, 53.6, 48.6, 30.2, 21.5, 19.1, 18.1. IR (ν_{max}/cm^{-1}): 3237, 2957, 1441, 1321, 1304, 1153, 1090, 1027, 862, 809, 731, 698, 663, 588, 553, 542 cm^{-1}. FABMS (*m*/*z*): 347 (100%) [M+H]. HRMS (FAB) calcd for $C_{19}H_{27}N_2O_2S$ [M+H] 347.1793; found: 347.1783.

4.2.2. *N*-(2-Benzylamino-1-methylethyl)-4-methylbenzenesulfonamide 2b. Colourless oil. $[\alpha]_D^{25}$ −4.8 (*c* 0.5, $CHCl_3$). ^{1}H NMR: δ 7.79 (d, 2H, $J=8.3$), 7.39–7.29 (m, 7H), 3.61 (s, 2H,), 3.38–3.25 (m, 1H), 2.51 (dd, 1H, $J=12.4$ and 8.1), 2.60 (dd, 1H, $J=12.4$ and 4.4), 2.43 (s, 3H), 1.13 (d, 3H, $J=6.7$). ^{13}C NMR: δ 143.8, 140.4, 138.1, 130.2, 129.0, 128.5, 127.7, 127.6, 54.3, 53.7, 49.4, 22.1, 20.1. IR (ν_{max}/cm^{-1}): 3266, 2853, 1598, 1494, 1452, 1320, 1156, 1091, 1027, 985, 883, 814, 736, 698, 662, 574, 550. FABMS (*m*/*z*): 319 (43%) [M+H]. HRMS (FAB) calcd for $C_{17}H_{23}N_2O_2S$ [M+H] 319.1480; found: 319.1485.

4.2.3. *N*-(1-Benzyl-2-benzylaminoethyl)-4-methylbenzenesulfonamide 2c. Colourless oil. $[\alpha]_D^{25}$ −4.0 (*c* 0.5, $CHCl_3$). ^{1}H NMR: δ 7.68 (d, 2H, $J=8.2$), 7.34–7.16 (m, 10H), 7.09–7.03 (m, 2H), 3.54 (AB quartet, 2H, $J=13.1$), 3.48–3.39 (m, 1H), 2.89 (dd, 1H, $J=13.8$ and 5.3), 2.73 (dd, 1H, $J=13.8$ and 8.2), 2.93–2.47 (m, 2H), 2.37 (s, 3H). ^{13}C NMR: δ 143.6, 140.3, 137.8, 130.1, 129.8, 128.9, 128.8, 128.4, 127.5, 127.4, 126.9, 54.9, 53.7, 51.5, 40.1, 21.9. IR (ν_{max}/cm^{-1}): 3257, 3027, 1598, 1494, 1453, 1324, 1157, 1092, 960, 814, 743, 700, 664, 631, 533, 503. Anal. calcd for $C_{23}H_{26}N_2O_2S.0.5\ H_2O$: C, 68.5; H, 6.7; N, 6.9. Found: C, 68.6; H, 6.1; N, 6.6. FABMS (*m*/*z*): 395 (100%) [M+H]. HRMS (FAB) calcd for $C_{23}H_{27}N_2O_2S$ [M+H] 395.1793; found: 395.1810.

14.2.4. *N*-[1-(Benzylaminomethyl)-3-methylbutyl]-4-methylbenzenesulfonamide 2d. Colourless waxy-solid. $[\alpha]_D^{25}$ −19.2 (*c* 0.5, $CHCl_3$). ^{1}H NMR: δ 7.71 (d, 2H, $J=8.2$), 7.32–7.14 (m, 7H), 3.57 (s, 2H), 3.32–3.21 (m, 1H), 2.52–2.40 (m, 2H), 2.36 (s, 3H), 1.52 (nonet, 1H, $J=6.7$), 1.38–1.27 (m, 1H), 1.22–1.12 (m, 1H), 0.77 (d, 3H, $J=6.7$), 0.72 (d, 3H, $J=6.7$). ^{13}C NMR: δ 143.2, 139.9, 138.0, 129.7, 128.5, 128.1, 127.2, 127.1, 53.6, 52.2, 51.7, 43.0, 24.5, 22.7, 22.4, 21.6. IR (ν_{max}/cm^{-1}): 3277, 2955, 1453, 1328, 1160, 1093, 965, 910, 814, 731, 699, 667, 631, 544. Anal. calcd for $C_{20}H_{28}N_2O_2S$: C, 66.6; H, 7.8; N, 7.8. Found: C, 66.8; H, 8.2; N, 7.6. FABMS (*m*/*z*): 361 (100%) [M+H]. HRMS (FAB) calcd for $C_{20}H_{28}N_2O_2S$ [M+H] 361.1950; found: 361.1958.

4.2.5. *N*-[1-(Benzylaminomethyl)-2-methylbutyl]-4-methylbenzenesulfonamide 2e. Colourless waxy-solid. $[\alpha]_D^{25}$ −3.6 (*c* 0.5, $CHCl_3$). ^{1}H NMR: δ 7.70 (d, 2H, $J=8.2$), 7.31–7.15 (m, 7H), 3.51 (s, 2H), 3.13–3.06 (m, 1H), 2.52 (dd, 1H, $J=12.4$ and 7.4), 2.39 (dd, 1H, $J=12.4$ and 4.2), 2.34 (s, 3H), 1.67–1.52 (m, 1H), 1.46–1.31 (m, 1H), 1.11–0.95 (m, 1H) 0.83–0.75 (m, 6H). ^{13}C NMR: δ 143.2, 139.9, 137.7, 129.7, 128.5, 128.1, 127.2, 127.1, 57.2, 53.5, 48.0, 37.2, 25.8, 21.6, 14.4, 11.9. IR (ν_{max}/cm^{-1}): 3534, 3312, 3065, 2963, 2877, 1674, 1597, 1493, 1475, 1453, 1381, 1317, 1302, 1208, 1182, 1157, 1130, 1111, 1090, 1046, 1030, 954, 868, 811, 752, 697, 577, 541 cm^{-1}. FABMS (*m*/*z*): 361 (100%) [M+H]. HRMS (FAB) calcd for $C_{20}H_{28}N_2O_2S$ [M+H] 361.1950; found: 361.1958.

4.3. General procedure for the preparation of the tertiary amine 3 via the double ring opening of the *N*-tosyl-aziridines 1 with benzylamine

All reactions were carried out in an identical manner and the procedure used is typified by that described for the preparation of compound **3a** as detailed below. Yields are given in Table 1.

4.3.1. *N*-(1-{*N*′-Benzyl-*N*′-[(2-{4-methylbenzenesulfonylamino}-3-methyl-butyl]aminomethyl}-2-methyl-propyl)-4-methylbenzenesulfonamide 3a. *N*-Tosyl-aziridine **1a** (1.6 g, 6.7 mmol,) and benzylamine (0.360 g, 3.35 mmol) were dissolved in dry methanol (30 mL) and the mixture stirred under reflux for 3 days. The solvent was evaporated under reduced pressure, leaving an off-white oil. Upon trituration with diethyl ether (30 mL) the desired product precipitated as colourless crystals, which were recrystallised from ethanol in 69% yield (1.36 g, 2.36 mmol). Mp 135–136°C. $[\alpha]_D^{25}$ −37.6 (*c* 0.5, $CHCl_3$). ^{1}H NMR: δ 7.81 (d, 4H, $J=8.3$), 7.29–7.22 (m, 9H), 5.21 (d, 2H, $J=6.7$), 3.74 (d, 1H, $J=13.3$), 3.49–3.41 (m, 2H), 3.28 (d, 1H, $J=13.3$), 2.48 (dd, 2H, $J=13.3$ and 8.9), 2.41 (s, 6H), 2.32 (dd, 2H $J=13.3$ and 6.5),1.94–1.78 (m, 2H), 0.66 (t, 12H, $J=7.1$). ^{13}C NMR:

δ 143.6, 139.2, 138.4, 130.1, 128.9, 127.8, 127.6, 59.0, 56.6, 55.0, 30.1, 22.1, 18.6, 17.7. IR (ν_{max}/cm^{-1}): 3247, 2961, 1599, 1456, 1319, 1184, 1158, 1094, 1074, 1040, 1023, 915, 812, 745, 700, 664, 627, 590, 552, 542, 503, 492. Anal. calcd for $C_{31}H_{43}N_3O_4S_2$: C, 63.6; H, 7.4; N, 7.2. Found: C, 63.8; H, 7.4; N, 6.9%. FABMS (m/z): 586 (47%) [M+H], 359 (100). HRMS (FAB) calcd for $C_{31}H_{44}N_3O_4S_2$ [M+H] 586.2773; found: 586.2750.

4.3.2. *N*-(1-{*N*′-Benzyl-*N*′-[(2-{4-methylbenzenesulfonyl-amino}-propyl]aminomethyl}ethyl)-4-methylbenzenesulfonamide 3b. Colourless crystals. Mp 91–92°C. $[\alpha]_D^{25}$ −43.2 (*c* 0.5, $CHCl_3$). ^{1}H NMR: δ 7.79 (d, 4H, J= 8.2), 7.26–7.20 (m, 7H), 7.08–7.04 (m, 2H), 5.08 (d, 2H, J=4.2), 3.56 (d, 1H, J=13.4), 3.48–3.40 (m, 2H), 3.09 (d, 1H, J=13.4), 2.40–2.31 (m, 8H), 2.21 (dd, 2H, J=13.4 and 4.5), 0.94 (d, 6H, J=6.2). ^{13}C NMR: δ 143.3, 138.1, 137.4 129.7, 129.3, 128.5, 127.4, 127.2, 59.5, 57.9, 47.0, 21.6, 19.9. IR (ν_{max}/cm^{-1}): 3279, 3225, 2927, 1596, 1494, 1444, 1413, 1345, 1316, 1158, 1092, 1019, 992, 944, 861, 813, 734, 666, 591, 572, 553, 533. Anal. calcd for $C_{27}H_{35}N_3O_4S_2{\cdot}0.5H_2O$: C, 60.2; H, 7.1; N, 7.8. Found: C, 60.2; H, 6.7; N, 7.7%. FABMS (m/z): 530 (43%) [M+H], 331 (33). HRMS (FAB) calcd for $C_{27}H_{36}N_3O_4S_2$ [M+H] 530.2147; found: 530.2120.

4.3.3. *N*-(1-{*N*′-Benzyl-*N*′-[(2-{4-methylbenzenesulfonyl-amino}-3-phenyl-propyl]aminomethyl}-2-phenyl-ethyl)-4-methylbenzenesulfonamide 3c. Colourless crystals. Mp 119–120°C. $[\alpha]_D^{25}$ −18.0 (*c* 0.5, $CHCl_3$). ^{1}H NMR: δ 7.63 (d, 4H, J=8.2), 7.20–7.13 (m, 13H), 7.06–7.01 (m, 2H), 6.94–6.91 (m, 4H), 5.22 (bs, 2H), 3.63 (bs, 2H), 3.54 (d, 1H, J=13.5), 3.10 (d, 1H, J=13.5), 2.71 (dd, 2H, J=13.9 and 5.9), 2.55–2.30 (m, 12H). ^{13}C NMR: δ 143.2, 138.0, 137.5, 129.7, 129.6, 129.4, 128.6, 128.5, 127.4, 127.1, 126.5, 58.3, 58.0, 53.3, 40.1, 21.6. IR (ν_{max}/cm^{-1}): 3343, 3219, 1599, 1494, 1450, 1415, 1319, 1149, 1090, 1041, 985, 949, 817, 756, 735, 703, 663, 592, 546. FABMS (m/z): 682 (55%) [M+H], 407 (93), 395 (100). HRMS (FAB) calcd for $C_{39}H_{44}N_3O_4S_2$ [M+H] 682.2773; found: 682.2750.

4.3.4. *N*-(1-{*N*′-Benzyl-*N*′-[(2-{4-methylbenzenesulfonyl-amino}-4-methyl-pentyl]aminomethyl}-3-methyl-butyl)-4-methylbenzenesulfonamide 3d. Colourless crystals. Mp 112–113°C. $[\alpha]_D^{25}$ −39.6 (*c* 0.5, $CHCl_3$). ^{1}H NMR: δ 7.76 (d, 4H, J=8.2), 7.28–7.15 (m, 9H), 5.13 (bs, 2H), 3.55 (d, 1H, J=13.4), 3.38 (bs, 2H), 3.28 (d, 1H, J=13.4), 2.48–2.30 (m, 10H), 1.42–1.34 (m, 2H), 1.19–1.14 (m, 4H) 0.72 (d, 6H, J=6.7), 0.62 (d, 6H, J=6.3). ^{13}C NMR: δ 143.2, 138.5, 138.0, 129.6, 128.4, 127.3, 127.1, 59.3, 58.8, 50.3, 43.4, 24.5, 22.8, 22.4, 21.6. IR (ν_{max}/cm^{-1}): 3251, 2950, 1598, 1495, 1452, 1429, 1323, 1305, 1157, 1091, 1041, 1016, 962, 909, 813, 746, 729, 700, 664, 574, 551. Anal. calcd for $C_{33}H_{47}N_3O_4S_2{\cdot}0.5H_2O$: C, 63.6; H, 7.7; N, 6.8. Found: C, 63.7; H, 8.1; N, 6.6%. FABMS (m/z): 614 (32%) [M+H], 373 (100). HRMS (FAB) calcd for $C_{33}H_{48}N_3O_4S_2$ [M+H] 614.3086; found: 614.3110.

4.3.5. *N*-(1-{*N*′-Benzyl-*N*′-[(2-{4-methylbenzenesulfonyl-amino}-3-methyl-pentyl]aminomethyl}-2-methylbutyl)-4-methylbenzenesulfonamide 3e. Colourless solid. Mp 145–146°C. $[\alpha]_D^{25}$ −15.6 (*c* 0.5, $CHCl_3$). ^{1}H NMR: δ 7.82 (d, 4H, J=8.5), 7.30–7.17 (m, 9H), 5.27 (d, 2H, J=5.8), 3.75 (d, 1H, J=13.3), 3.58–3.53 (m, 2H), 3.17 (d, 1H, J=13.3), 2.50–2.41 (m, 2H), 2.41 (s, 6H), 2.25 (dd, 2H, J=13.2 and 4.8), 1.63–1.58 (m, 2H), 1.29–1.10 (m, 2H), 1.01–0.88 (m, 2H), 0.80 (t, 6H, J=7.3), 0.64 (d, 6H, J=7.1). ^{13}C NMR: δ 143.3, 139.0, 138.0, 129.8, 129.7, 128.7, 127.6, 127.4, 58.5, 54.9, 53.2, 37.3, 25.5, 21.9, 14.2, 12.5. IR (ν_{max}/cm^{-1}): 3256, 2957, 1597, 1451, 1329, 1300, 1182, 1158, 1123, 1093, 1043, 930, 916, 811, 746, 701, 666, 631, 603, 554, 543. Anal. calcd for $C_{33}H_{47}N_3O_4S_2$: C, 64.6; H, 7.7; N, 6.9. Found: C, 64.5; H, 8.1; N, 6.5%. FABMS (m/z): 614 (56%) [M+H], 373 (100). HRMS (FAB) calcd for $C_{33}H_{48}N_3O_4S_2$ [M+H] 614.3086; found: 614.3110.

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References

1. *Comprehensive Asymmetric Catalysis*; Jacobsen, E. N.; Pfaltz, A.; Yamamoto, H., Eds.; Springer: Berlin, Heidelberg, New York, 1999.
2. Tanner, D. *Angew. Chem., Int. Ed. Engl.* **1994**, *33*, 599–619.
3. (a) Cernerud, M.; Adolfson, H.; Moberg, C. *Tetrahedron: Asymmetry* **1997**, *8*, 2655–2662; (b) Cernerud, M.; Skrinning, A.; Bérgère, I.; Moberg, C. *Tetrahedron: Asymmetry* **1997**, *8*, 3437–3441; (c) Lake, F.; Moberg, C. *Tetrahedron: Asymmetry* **2001**, *12*, 755–760.
4. Nelson, S. G.; Peelan, T. J.; Wan, Z. *J. Am. Chem. Soc.* **1999**, *121*, 9742–9743.
5. (a) Crabtree, R. H. *Chem. Commun.* **1999**, 1611–1616; (b) Muñiz, K.; Bolm, C. *Chem. Eur. J.* **2000**, *6*, 2309–2316.
6. Berry, M. B.; Craig, D. *Synlett*. **1992**, 41–44, neat THF was used for the reduction of the protected amino acid. Aziridines **1a** and **1c** were purified by recrystallisation from ethanol and all other aziridines were used after filtration through a short pad of silica gel.
7. Pulacchini, S.; Watkinson, M. *Eur. J. Org. Chem.* **2001**, 4333–4338.
8. Wang, J.-Q.; Zhong, M.; Lin, G.-Q. *Chinese J. Org. Chem.* **1998**, *16*, 65–77.