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Stereoselective Synthesis of β -Sultams using Chiral Tricarbonyl(η^6 -Arene)Chromium(0) Complexes

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Abstract. The reaction of (-)1*R* or (+)-1*S*-tricarbonyl(2-substituted benzaldehyde)chromium complexes with *tert*butylmethanesulfonamide dianion afforded, after decomplexation and intramolecular cyclization, the enantiomerically pure *N-tert*-butyl-3-(2-phenyl substituted)-1,2-thiazetidine 1,1 dioxides derivatives. The hydrolytic ring opening gave the corresponding enantiopure β -aminosulfonic acid. © 1999 Elsevier Science Ltd. All rights reserved.

Keywords: β -sultam, 1,2-thiazetidine 1,1 dioxides, chiral tricarbonylarene chromium complexes, stereoselective synthesis

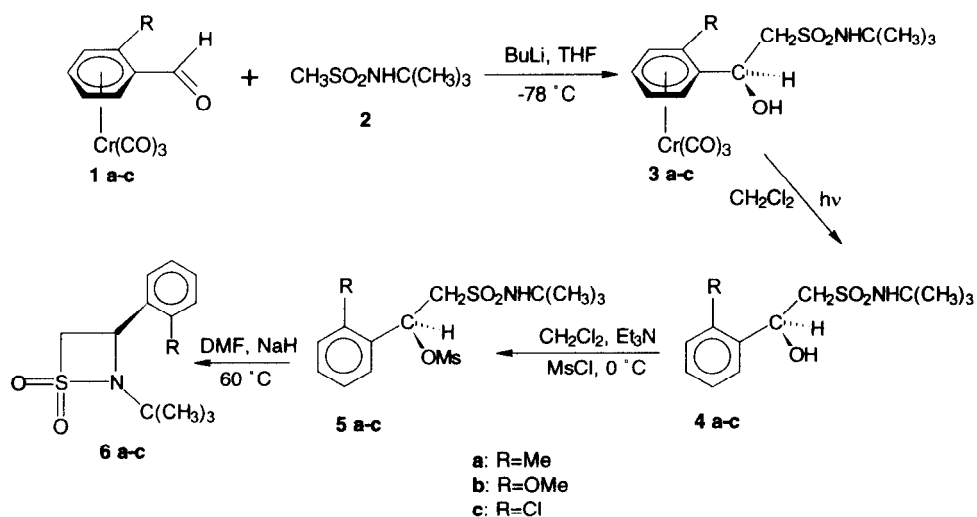
Introduction

The chemical structures of many important antibiotics contain a β -lactam unit as a crucial moiety for their antimicrobial activity. Structurally, the 1,2-thiazetidine 1,1 dioxides (β -sultams) are S-analogues of β -lactam antibiotics and their highly strained and reactive ring makes them promising candidates for biological activity.¹⁻³ However, they have received much less attention. The solid-phase synthesis⁴ of some β -sultams has recently been reported with the aim of producing libraries for the identification of new antibacterial agents. Through the breaking of their strained N-SO₂ bond, β -sultams are also the precursors of taurine analogues; over the last few years, many research groups have attempted to replace the peptide bond with mimetic groups, and the taurine analogues are promising substrates for the synthesis of sulfonamidopseudo peptides.^{5,6} Furthermore, it has been found that the C-S⁷ and C-N⁸ bonds can be broken under different experimental conditions, thus making 1,2-thiazetidine 1,1 dioxides interesting building blocks for the construction of other heterocyclic systems. However, despite their widespread use and applicability in organic synthesis, no data for optically active β -sultams have yet been reported to the best of our knowledge.

The use of chiral tricarbonyl (η^6 -arene) chromium complexes in stereoselective synthesis is well documented,⁹ and we and others have recently reported that the enantiomerically pure tricarbonyl chromium complexes of benzaldehydes and benzaldimines are powerful auxiliaries in stereoselective

cycloadditions¹⁰⁻¹³ and in the synthesis of β -lactam rings.¹⁴⁻¹⁷ With the aim of extending the use of these chiral complexes to the synthesis of different heterocyclic compounds, we studied the preparation of a series of *ortho*-aryl-substituted 1,2-thiazetidines 1,1 dioxides. Among the β -sultam syntheses published in the literature, the method reported by Thompson¹⁸ is considered to be the most suitable for chromium complexed substrates: an α ,*N*-alkanesulfonamide dianion reacts with a large number of electrophiles to afford chemoselective C-alkylation, and particularly with aryl aldehydes to give more highly functionalized β -hydroxysulfonamides that are intermediates for the synthesis of β -styrylsulfonamides or 1,2-thiazetidines 1,1-dioxides. The reaction conditions were compatible with arene chromium derivatives, and the low reaction temperature was instrumental for high diastereoselection. The reaction sequence was first performed starting from racemic substrates and subsequently repeated on the optically pure compounds.

We report here the synthesis of the enantiomerically pure *N-tert*-butyl-3-(2-phenyl substituted) 1,2-thiazetidines 1,1 dioxide derivatives **6a-c**, starting from optically pure tricarbonyl(2-substituted benzaldehyde)chromium(0) complexes **1a-c**.¹⁹ (Scheme 1)



Scheme 1

Results and Discussion

The attack of the *N-tert*-butylmethanesulfonamide dianion generated using BuLi in dry THF solution at -78 °C on *ortho* substituted optically pure benzaldehydes **1a-c** (the 1-(*R*) enantiomer is shown in the

scheme 1 for the sake of simplicity) afforded the corresponding complexed 2-hydroxysulfonamides **3a-c** in good yield. The diastereoselection evaluated by ^1H NMR on the crude reaction mixture was nearly complete in the case of **3b** and **3c**, whereas the 2-hydroxysulfonamide **3a** was obtained only in 60% d.e. However it is worth noting that the two diastereoisomers were easily separated by column chromatography and characterized.

The reaction of the *N-tert*-butylmethanesulfonamide dianion on the pro-stereogenic formyl group is the key step for the diastereoselective formation of the new stereogenic center, and is controlled by means of the planar chirality produced by the $\text{Cr}(\text{CO})_3$ unit. After this center was created in high enantiomeric purity, the organic ligand was therefore removed from the complex and the subsequent reactions were run in a stereoselective manner on the more easily handled substrates. The uncomplexed 2-hydroxysulfonamides **4a-c** were obtained in nearly quantitative yields by exposing a solution of complexed 2-hydroxysulfonamides **3a-c** in CH_2Cl_2 to air and sunlight.

In order to favour the intramolecular ring closure, the 2-hydroxyl group was transformed using mesyl chloride in the presence of Et_3N into the corresponding mesyl derivatives **5**, of which **5a** and **5c** were isolated in good yield; **5b** was used for the subsequent step without any purification.

As expected, the ring closure to form the β -sultam ring, which was performed in DMF solution at 60 °C using NaH as a base, underwent an $\text{S}_{\text{N}}2$ substitution with the complete inversion of the configuration and without any racemization. The β -sultams **6a-c** were recovered in good yield and with unchanged enantiopurity (e.e. $\geq 98\%$) with respect to the 2-hydroxysulfonamides **3a-c**.

It was possible to assign the absolute configuration to β -sultams **6a-c** on the basis of the following considerations: the accepted stereochemical model operating on *ortho* substituted benzaldehyde complexes predicts that the nucleophilic species attacks the formyl group from the opposite side to that of the $\text{Cr}(\text{CO})_3$ unit and on the preferred conformation in which the $\text{C}=\text{O}$ group is *anti* with respect to substituent in the *ortho* position. Therefore, starting from the (-)-(*1R*) tricarbonyl(2-chlorobenzaldehyde)chromium **1c** and (-)-(*1R*) tricarbonyl(2-methoxybenzaldehyde)chromium **1b**, we assigned the (*2R*) configuration to the newly formed stereogenic center of the complexed 2-hydroxysulfonamides **3b,c** the (*2S*) configuration to the corresponding uncomplexed **4b,c**, and consequently, after the $\text{S}_{\text{N}}2$ intramolecular reaction, the (*3R*) absolute configuration to β -sultams **6b,c**.

This hypothesis was further confirmed by X-ray analysis of the optically pure β -sultam **6c**. As shown in the figure, the absolute configuration of C-3 (C1 in the figure) of β -sultam **6c** is (*R*).

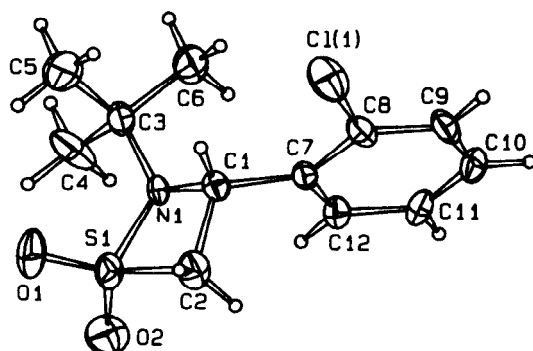
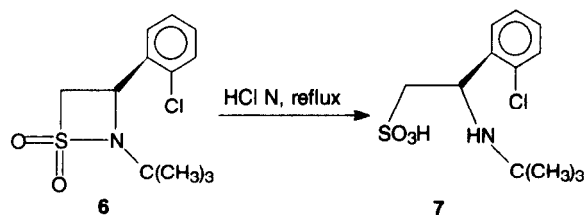


Figure: ORTEP plot of (-)-(3*R*) *N*-tertbutyl-3-(2-chlorophenyl) 1,2-thiazetidone 1,1-dioxide **6c**; heavy atom ellipsoids are at 20% probability level, H atoms not to scale.

Finally as a probe for running further transformations of the above substrates, we hydrolysed the β -sultam **6c** with HCl 1*N*²⁰ to the corresponding optically pure β -amino sulfonic acid in good yield. (Scheme 2)



Scheme 2

Conclusions

These results underline that chiral chromiumtricarbonyl arenes are extremely useful and versatile substrates for the enantioselective synthesis of optically pure β -sultams in excellent yields, and with predictable stereochemistry on the basis of the absolute configuration of the starting aldehydes. In addition, the possibility of transforming these monosubstituted β -sultams into the corresponding β -aminosulfonic acids opens the way to other interesting applications.

Experimental section

All of the reactions were performed under nitrogen. Thermolysis with hexacarbonylchromium(0) was carried out in a round-bottomed flask, equipped with a Liebig air condenser and a water condenser on top. All of the chemicals were used as obtained from commercial sources. Column chromatography and

TLC were carried out using silica gel 60 and silica gel 60 F₂₅₄ pre-coated plates respectively. The melting points were measured using a Buchi apparatus and are uncorrected. The IR spectra were recorded using a 1725X FTIR spectrometer. NMR spectra were recorded in CDCl₃ using a Varian XL 300 spectrometer. Evaluation of enantiomeric excess was performed using Eu(hfc)₃ (tris [3-(heptafluoropropyl)hydroxymethylene]-*d*-camphorato)europium(III) salt. The optical rotations were measured using a Perkin-Elmer 241 Polarimeter, with a 1 dm pathlength at 25 °C. The racemic compounds were prepared as previously reported. The optically pure complexed benzaldehydes were obtained by resolution of the corresponding racemic substrate using a known procedure.¹⁹

Synthesis of complexed 2-hydroxysulfonamides 3a-c General procedure: *n*-BuLi (2.45 mmol, 1.6M solution in hexane) was added dropwise to a solution of *N*-*tert*-butyl methanesulfonamide **2** (1.17 mmol) in 3.5 ml of dry THF at -78 °C. The resulting solution was warmed to -30 °C and maintained at this temperature for about 30 min. After re-cooling to -78 °C, a solution of complexed benzaldehyde **1a-c** (1.17 mmol in 7 ml of THF) was slowly added. The hydroxysulfonamide **3a-c** was immediately formed and, after 10 min, the reaction was quenched by adding at -78 °C a 1:9 mixture of AcOH in THF until acidic pH (about 4 ml). The solution was warmed to room temperature and then the organic layer was washed with water (3 x 20 ml). After evaporation of the solvent under reduced pressure, the crude yellow oil was recrystallised by adding a 2:1 mixture of petroleum ether : diethylether, if no differently specified.

***N*-*tert*-butyl-2-(2-methylphenyl tricarbonyl chromium)-2-hydroxyethansulfonamide 3a:** Yield 95%; yellow solid, mp 140-160 °C; d.e. 60%, ν_{\max} (Nujol) 3460, 3300, 1966, 1897, 1875, 1305, 1146; *Anal.* Calc. For C₁₆H₂₁CrNSO₆ (407.413); C, 47.16; H, 5.20; N, 3.44. Found C, 47.26; H, 5.19; N, 3.45. Starting from (+)-*1S* benzaldehyde **1a** [α]_D = +627 (CHCl₃, *c* 0.1); The two diastereoisomers were separated by chromatography (SiO₂ eluent Et₂O:petroleum ether 3:1). *First diastereoisomer:* yellow solid, mp 158-9 °C; yield 60%. ¹H NMR δ 1.25 (s, 9H, CMe₃); 2.1 (s, 3H, Me); 3.1 (AB part of ABX system, 2H, CH₂); 3.48 (s, 1H, OH); 4.3 (s, 1H, NH); 5.0 (d, 1H, aromCr(CO)₃, J=6.3 Hz); 5.05 (X part of ABX system, 1H, CH); 5.1 (dd, 1H, aromCr(CO)₃, J=6.3 and 6.4 Hz); 5.25 (dd, 1H, aromCr(CO)₃, J=6.4 and 6.3 Hz); 5.61 (d, 1H, aromCr(CO)₃, J=6.3 Hz); [α]_D = +30.3 (CHCl₃, *c* 0.1); d.e. \geq 98%. *Second diastereoisomer:* yellow solid, mp 149-50 °C; yield 15%. ¹H NMR δ 1.4 (s, 9H, CMe₃); 2.3 (s, 3H, Me); 3.45 (AB part of ABX system, 2H, CH₂); 3.85 (s, 1H, OH); 4.4 (s, 1H, NH); 5.05 (d, 1H, aromCr(CO)₃, J=6.6 Hz); 5.09 (X part of ABX system, 1H, CH); 5.12 (dd, 1H, aromCr(CO)₃, J=6.6 and 6.6 Hz); 4.51 (dd, 1H, aromCr(CO)₃, J=6.6 and 6.6 Hz); 5.7 (d, 1H, aromCr(CO)₃, J=6.6 Hz); [α]_D = +40 (CHCl₃, *c* 0.1); d.e. \geq 98%.

(2*R*)-*N*-*tert*-butyl-2-(2-methoxyphenyl tricarbonyl chromium)-2-hydroxyethansulfonamide 3b: Yield 88%; yellow solid, mp 109-110 °C; d.e. \geq 98% ν_{\max} (Nujol) 3408, 3300, 1958, 1889, 1867, 1314, 1143; starting from (-)-*1R* benzaldehyde **1b**, [α]_D = -1047 (CHCl₃, *c* 0.1). ¹H NMR δ 1.4 (s, 9H, CMe₃); 3.21 (dd, 1H, CH₂, J=23.6 and 4.4 Hz); 3.36 (dd, 1H, CH₂, J=23.6 and 2.1 Hz); 3.46 (bs, 1H, OH); 3.76 (s, 3H, OMe); 4.4 (s, 1H, NH); 4.91 (dd, 1H, aromCr(CO)₃, J=6.2 and 6.6 Hz); 5.3 (d, 1H, aromCr(CO)₃, J=6.6); 5.27 (m, 1H, CH); 5.6 (dd, 1H, aromCr(CO)₃, J=6.6 and 6.2 Hz); 5.9 (d, 1H, aromCr(CO)₃, J=6.2 Hz). *Anal.* Calc. For C₁₆H₂₁CrNSO₇ (423.413); C, 45.39; H, 5.00; N, 3.31. Found C, 45.52; H, 4.99; N, 3.32; [α]_D = +107 (CHCl₃, *c* 0.1).

(2*R*)-*N*-*tert*-butyl-2-(2-chlorophenyl tricarbonyl chromium)-2-hydroxyethansulfonamide 3c: Yield 89%; yellow solid, m.p. 151 °C (diethyl ether/ petroleum ether 1/1) d.e. \geq 98% ν_{\max} (Nujol) 3450, 3300, 1983, 1920, 1897, 1330, 1150; Starting from (-)-*1R* benzaldehyde **1c** [α]_D = -1015 (*c* = 0.1 CHCl₃). ¹H NMR δ 1.4 (m, 9H, CMe₃); 3.25 (dd, 1H, CH₂, J=14.2 Hz and 9.8 Hz); 3.49 (dd, 1H, CH₂, J=14.2 and 1.5 Hz); 3.84 (d, 1H, OH, J=2.7 Hz); 4.44 (bs, 1H, NH); 5.1 (t, 1H, aromCr(CO)₃, J=5.8 Hz); 5.27 (m, 1H, CH); 5.4 (m, 2H, aromCr(CO)₃); 5.85 (d, 1H, aromCr(CO)₃, J=7.3 Hz). *Anal.* Calc. For C₁₅H₁₈ClCrNSO₆

(427.831); C, 42.11; H, 4.24; N, 3.27. Found C, 42.23; H, 4.23; N, 3.26; $[\alpha]_D^{25} = +31.1^\circ$ (c= 0.1 CHCl₃).

Decomplexation of 2-hydroxymetansulfonamides 3a-c General procedure: The solution in CH₂Cl₂ of the appropriate complexed 2-hydroxysulfonamides **3a-c**, was exposed to air and sunlight for 3-5h. The solvent was evaporated and the residue treated with Et₂O and filtered over celite. After evaporation of the solvent, the residue was crystallised with petroleum ether.

N-tert-butyl-2-(2-methylphenyl)-2-hydroxyethansulfonamide 4a: From the diastereomeric mixture: yield 97%; white solid, mp 98 °C; ν_{\max} (Nujol) 3469, 3294, 1316, 1146; ¹H NMR δ 1.39 (s, 9H, CMe₃); 2.32 (s, 3H, Me); 3.23 (dd, 1H, CH₂, J=14.4 and 2.2 Hz); 3.33 (dd, 1H, CH₂, J=14.4 and 9.5 Hz); 3.52 (d, 1H, OH, J=2.2 Hz); 4.44 (s, 1H, NH); 5.50 (m, 1H, CH); 7.51-7.10 (m, 4H, arom). $[\alpha]_D^{25} = -29.58$ (c= 0.1 CHCl₃). *Anal.* Calc. For C₁₃H₂₁NSO₃ (271.384); C, 57.53; H, 7.80; N, 5.16. Found C, 57.60; H, 7.78; N, 5.17. The (-)-enantiomer **3a** $[\alpha]_D^{25} = -48.1$ (c= 0.1 CHCl₃) and the (+)-enantiomer $[\alpha]_D^{25} = +45.8$ (c= 0.1 CHCl₃)

(2S)-N-tert-butyl-2-(2-methoxyphenyl)-2-hydroxyethansulfonamide 4b: Yield 94%; white solid, mp 100 °C; ν_{\max} (Nujol) 3500, 3310, 1320, 1142; ¹H NMR δ 1.34 (s, 9H, CMe₃); 3.33 (dd, 1H, CH₂, J=14.4 and 9.1 Hz); 3.48 (dd, 1H, CH₂, J=14.4 and 2.5 Hz); 3.77 (d, 1H, OH, J=4.0 Hz); 3.84 (s, 1H, OMe); 4.30 (s, 1H, NH); 5.43 (m, 1H, CH); 7.42-7.20 (m, 4H, arom). *Anal.* Calc. For C₁₃H₂₁NSO₄ (287.384); C, 54.33; H, 7.36; N, 4.87. Found C, 54.40; H, 7.34; N, 4.88. $[\alpha]_D^{25} = -44.3$ (c= 0.1 CHCl₃)

(2S)-N-tert-butyl-2-(2-chlorophenyl)-2-hydroxyethansulfonamide 4c: Yield 96%; white solid, mp 130-31 °C; ν_{\max} (Nujol) 3500, 3310, 1330, 1140; ¹H NMR δ 1.25 (s, 9H, CMe₃); 3.10 (dd, 1H, CH₂, J=14.4 and 9.8 Hz); 3.34 (dd, 1H, CH₂, J=14.4 and 1.7 Hz); 3.08 (d, 1H, OH, J=2.4 Hz); 4.22 (s, 1H, NH); 5.44 (d, 1H, CH, J=9.8 Hz); 7.52-7.10 (m, 4H, arom). *Anal.* Calc. For C₁₂H₁₈ClNSO₃ (291.802); C, 49.39; H, 6.22; N, 4.80. Found C, 49.48; H, 6.21; N, 4.81. $[\alpha]_D^{25} = +70.7$ (CHCl₃ c= 0.1); e.e. $\geq 98\%$.

Mesylation of 4a-c: To a solution of the appropriate **4a-c**, (1.1 mmol) and Et₃N (freshly distilled, 2.1 mmol), in 5.5 ml of dried CH₂Cl₂ under nitrogen atmosphere cooled to 0 °C, methanesulfonyl chloride (1.64 mmol) was added keeping the temperature under 2 °C. The reaction was immediately complete and was quenched at 0 °C by adding a solution of 5% HCl (about 5 ml) until acidic pH. The organic layer was washed several time with water, dried and evaporated in vacuo. The remaining pale yellow oil was crystallised as white crystals with Et₂O and petroleum ether in the case of **4a,c**. Compound **4b**, however, was directly submitted to the following synthetic step without isolation of the product.

N-tert-butyl-2-(2-methylphenyl)-2-methansulfonyl ethansulfonamide 5a: Yield 98%; white solid, mp 98 °C. ν_{\max} (Nujol) 3304, 1325, 1146; ¹H NMR δ 1.39 (s, 9H, CMe₃); 2.44 (s, 3H, Me); 2.80 (s, 3H, SO₃Me); 3.3 (dd, 1H, CH₂, J=15.1 and 2.9 Hz); 3.72 (dd, 1H, CH₂, J=15.1 and 9.0 Hz); 4.4 (s, 1H, NH); 6.27 (dd, 1H, CH, J=9.0 and 2.9 Hz); 7.42-7.20 (m, 4H, arom.). *Anal.* Calc. For C₁₄H₂₃NS₂O₅ (349.447); C, 48.11; H, 6.63; N, 4.01. Found C, 48.08; H, 6.61; N, 4.00. From the mixture of diastereoisomers $[\alpha]_D^{25} = -29.58$ (CHCl₃, c 0.1).

(2S)-N-tert-butyl-2-(2-chlorophenyl)-2-methansulfonyl ethansulfonamide 5c: Yield 96%; white solid, mp 130-1 °C. ν_{\max} (Nujol) 3310, 1330, 1140; ¹H NMR δ 1.23 (s, 9H, CMe₃); 2.88 (s, 3H, SO₃Me); 3.30 (dd, 1H, CH₂, J=14.9 and 2.9 Hz); 3.48 (dd, 1H, CH₂, J=14.9 and 9.3 Hz); 4.5 (s, 1H, NH); 6.27 (dd, 1H, CH, J=9.3 and 2.9 Hz); 7.41-7.10 (m, 4H, arom.). *Anal.* Calc. For C₁₃H₂₀ClNS₂O₅ (368.895); C, 42.32; H, 5.46; N, 3.80. Found C, 42.29; H, 5.47; N, 3.79. $[\alpha]_D^{25} = +53.48$ (CHCl₃, c 0.1).

Synthesis of β -sultams 6a-c. General procedure: NaH (1.29 mmol, oil suspension) was added to a solution of **5a-c**, (0.86 mmol) in 12 ml of dry DMF. The solution was heated at 60 °C for about 15-20

min (monitored by TLC). The reaction mixture was cooled at room temperature and then diluted with water (30 ml). The aqueous layer was extracted with Et₂O (3x20 ml) and the organic solvent washed with water until neutral pH. After evaporation of the solvent in vacuo, the pale yellow oil was crystallised as white crystals by adding a 3:1 mixture of diethyl ether: petroleum ether.

(+)-*N*-tert-butyl-3-(2-methylphenyl)-thiazetidone 1,1 dioxide 6a: Yield 90%; white solid, mp 100 °C; ν_{\max} (Nujol) 1380, 1167; ¹H NMR δ 1.2 (s, 9H, CMe₃); 1.25 (s, 3H, Me); 3.72 (dd, 1H, CH₂, J=12.1 and 6.0 Hz); 4.34 (dd, 1H, CH₂, J=12.1 and 8.0); 4.77 (dd, 1H, CH, J=8.0 and 6.0 Hz); 7.3-7.05 (m, 4H, arom). *Anal.* Calc. For C₁₃H₁₉NSO₂ (253.368); C, 61.63; H, 7.56; N, 5.53. Found C, 61.58; H, 7.55; N, 5.54. From the first pure diastereoisomer of **3a**, $[\alpha]_D^{25} = +58$ (CHCl₃, c 0.2); e.e. $\geq 98\%$.

(3R)-*N*-tert-butyl-3-(2-methoxyphenyl)-thiazetidone 1,1 dioxide 6b: Yield 90%; white solid, mp 87 °C; ν_{\max} (Nujol) 1317, 1148; ¹H NMR δ 1.21 (s, 9H, CMe₃); 3.74 (dd, 1H, CH₂, J=12.2 and 5.4 Hz); 3.82 (s, 1H, OMe); 4.32 (dd, 1H, CH₂, J=12.2 and 8.3); 5.03 (dd, 1H, CH, J=8.3 and 5.4 Hz); 6.85-7.2 (m, 3H, arom); 7.7 (d, 1H, arom., J=7.8 Hz). *Anal.* Calc. For C₁₃H₁₉NSO₃ (269.368); C, 57.97; H, 7.11; N, 5.20. Found C, 57.95; H, 7.13; N, 5.19. $[\alpha]_D^{25} = +12.57$ (CHCl₃ c=0.1); e.e. $\geq 98\%$.

(3R)-*N*-tert-butyl-3-(2-chlorophenyl)-thiazetidone 1,1 dioxide 6c: Yield 94%; white solid, m.p. 74 °C ν_{\max} (Nujol) 1313, 1143; ¹H NMR (CDCl₃) δ 1.2 (s, 9H, CMe₃); 3.75 (dd, 1H, J=5.2 Hz, J=12.4 Hz); 4.45 (dd, 1H, J=8.3 Hz, J=12.4 Hz); 5.06 (dd, 1H, J=8.3 Hz, J=5.2 Hz); 7.2-7.4 (m, 3H, arom.); 7.85 (d, 1H, arom., J=7.7 Hz); ¹³C NMR (CDCl₃) δ 27.4 (Me₃); 42 (CH); 56.8 (CMe₃); 65.3 (CH₂); 127.6, 127.7, 129.8, 129.5 arom.: 132 (q-C); 137.3 (q-C). *Anal.* Calc. For C₁₂H₁₆ClNSO₂ (273.786); C, 52.64; H, 5.89; N, 5.12. Found C, 52.70; H, 5.90; N, 5.13. $[\alpha]_D^{25} = -107^\circ$ (CHCl₃ c=0.2); e.e. $\geq 98\%$.

Hydrolysis of 6c to (3R)-*N*-tert-butyl- β -aminosulfonic acid 7: 0.16 g (0.59 mmol) of **6c** was suspended in 12 ml of 1N HCl and heated under reflux for about 4h. The water was evaporated under reduced pressure and the remaining white solid was crystallized with ethanol/water giving the amino acid **7** in 50% yield. Mp >240 °C; $[\alpha]_D^{25} = -49$ (CHCl₃ c 0.3). ¹H NMR (CDCl₃ + DMSO) δ 1.2 (s, 9H, Me₃); 2.85 (dd, 1H, CH₂, J=14.2 and 2.3 Hz); 3.16 (dd, 1H, CH₂, J=10.5 and 14.2 Hz); 5.2 (m, 1H, CH); 7.4-8.1 (m, 4H, arom.); 9.6 and 9.25 (2brs, 2H, NH and SO₃H).

X-ray analysis of (3R)-*N*-tert-butyl-3-(2-chlorophenyl)-thiazetidone 1,1 dioxide 6c: C₁₂H₁₆ClNO₂S, $F_w = 273.77$, monoclinic, space group $P2_1$, $a = 11.634(1)$, $b = 10.203(1)$, $c = 12.929(1)$ Å, $\beta = 115.522(5)^\circ$, $V = 1384.9(2)$ Å³, $Z = 4$, $D_x = 1.313$ Mg.m⁻³, $\lambda(\text{Mo-K}\alpha) = 0.417$ nm⁻¹; crystal dimensions 0.48x0.32x0.18 mm³, $\lambda = 0.71073$ Å (Mo-K α radiation, graphite monochromator, Siemens P4 diffractometer). Data collection at room-temperature, ω -2 θ scan mode, $4 < 2\theta < 50^\circ$, h 0 \rightarrow 13, k -12 \rightarrow 12, l -15 \rightarrow 13; 5125 collected reflections, 4873 unique reflections [3521 with $I_o > 2\sigma(I_o)$], merging $R = 0.0144$; no absorption correction. The structure was solved by SIR92²¹ and refined by SHELXL-93,²² by full-matrix least-squares based on F_o^2 , with weights $w = 1/[\sigma^2(F_o)^2 + (0.061P)^2]$, where $P = (F_o^2 + 2F_c^2)$. The final consistency index were $R = 0.0414$ and $R_w = 0.0980$ for the observed reflections (0.0603 and 0.1043 respectively for all reflections), goodness-of-fit = 0.977. The final map showed the maximum peak (0.51 e.Å⁻³) near the SIB atom. The absolute configuration was determined by Flack²³ method [final Flack parameters 0.08(6)].

The structure has two independent molecules, whose main difference is the orientation of the phenyl group (the torsion N1-Cl-C7-C8 is 146.8(3) and 131.7(4) ° for molecules A and B respectively).

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