Experimental Section

**General:** $^1$H NMR spectra were recorded at 300.00 MHz at 20 °C with either tetramethylsilane ($\delta$ 0.00), chloroform ($\delta$ 7.26), methanol ($\delta$ 3.30), acetone ($\delta$ 2.20) or dimethyl sulfoxide ($\delta$ 2.49) as the internal standard. $^{13}$C NMR spectra were recorded at 75.46 MHz at 20 °C with either chloroform ($\delta$ 77.7) methanol ($\delta$ 49.0), acetone ($\delta$ 30.2) or dimethyl sulfoxide ($\delta$ 39.0) as the internal standard. Signal multiplicities were established by DEPT experiments. Melting points were determined through a Büchi instrument and are uncorrected. Specific optical rotations were determined at the D line through a Perkin Elmer 341 polarimeter. Flash chromatographic separations were performed over Merck Silica gel 60 (230-400 mesh), tlc analyses were performed over Merck precoated tlc plates (Silica gel 60 GF$_{254}$ 0.25 mm). HPLC analyses were performed with a LiChrospher Si 60 (5 µm) 250 mm × 4mm ID column and a 4mm × 4mm ID precolumn, UV 254 nm, flow 0.7 or 1.0 mL/min. Tetrahydrofuran was obtained anhydrous over sodium and benzophenone. Unless otherwise stated, other solvents and reagents were used as commercially available.

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\begin{align*}
\text{9} & \stackrel{a}{\rightarrow} \text{OH} & \text{COOMe} & \text{NH$_2$• HCl} \\
\text{b} & \rightarrow \text{OH} & \text{COOMe} & \text{NHTrt} \\
\text{c} & \rightarrow & \text{NHTrt} & \text{COOMe} \\
\end{align*}
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(a) Methyl (2S,3R)-3-Hydroxy-2-triphenylmethylaminobutanoate (10): To a stirred solution of (S)-threonine methyl ester hydrochloride (9, 7.06 g, 41.6 mmol) in chloroform, triethylamine (12.8 mL, 91.5 mmol) and trityl chloride (12.77 g, 41.6 mmol) dissolved in chloroform were added dropwise at 0 °C. After 72 h at 0 °C, the mixture was concentrated in vacuo and the residue was dissolved in ethyl acetate and washed with water. The aqueous layer was back-extracted with ethyl acetate (2×45 mL), the combined organic layers were washed with a 10% w/w solution of citric acid (110 mL), water (120 mL), dried with magnesium sulfate and concentrated in vacuo. The crude product was purified by flash chromatography (ethyl acetate/chloroform = 5/95) to afford 14.28 g (91% yield) of product as a yellowish solid. $[\alpha]_D^{21} +12.8$ (c 0.940, CHCl$_3$); m.p. 40-45 °C; $^1$H NMR (CDCl$_3$): $\delta$ 1.20 (d, 3H, $J = 6.2$ Hz), 2.10 (bs, 1H), 3.14 (s, 3H), 3.39 (d, 1H, $J = 7.3$ Hz), 3.60 (bs, 1H), 3.74-3.87 (m, 1H), 7.11-7.51 (m, 15H); $^{13}$C NMR (CDCl$_3$): $\delta$ 19.45 (CH$_3$), 52.21 (CH$_3$), 63.00 (CH), 70.28 (CH), 71.27 (C), 127.16 (CH), 128.42 (CH), 129.45 (CH), 145.96 (C), 174.21 (C).

(b) (2S,3S)-3-Methyl-2-methoxycarbonyl-1-(triphenylmethyl)aziridine (11): In a three-necked 250 mL flask, N-trityl ester 10 (14.14 g, 37.7 mmol) was dissolved in dry pyridine (113.0 mL) while stirring and under a positive pressure of nitrogen. The mixture was cooled to -10 °C with an ice-salt
bath and methanesulfonyl chloride (5.9 mL, 75.4 mmol) was added dropwise. The mixture was allowed to warm to room temperature; after 24 h tlc analysis (ethyl acetate/chloroform = 5/95) revealed that the starting material was consumed and ethyl acetate was added. A precipitate formed which was dissolved in water; the organic layer was washed with a 10% w/w solution of citric acid (2×50 mL) and with water (2×50 mL), dried with magnesium sulfate and concentrated in vacuo. The residue was dissolved in THF (113.0 mL) while stirring and triethylamine (7.16 mL, 51.4 mmol) was added. The mixture was heated at reflux for 40 h, then it was concentrated in vacuo, the residue was dissolved in ethyl acetate, washed with water (3×30 mL), with a saturated solution of copper sulfate (2×20 mL) and with water (2×20 mL). The organic layer was dried with magnesium sulfate and concentrated in vacuo. The crude product was crystallized from methanol to afford 4.85 g of aziridine 11; the mother liquor was concentrated in vacuo and the residue crystallized from methanol to give a second crop of product (2.49 g); the residue was concentrated in vacuo and purified by flash chromatography (ethyl acetate/petroleum ether = 5/95) to obtain 1.58 g of product. Combined yield 66%: white solid; m.p. 98 °C; [α]D° -90.6 (c 1.096, THF); 1H NMR (CDCl3): δ 1.37 (d, 3H, J = 5.4 Hz), 1.58-1.70 (m, 1H), 1.89 (d, 1H, J = 6.5 Hz), 3.73 (s, 3H), 7.14-7.32 (m, 9H), 7.49-7.56 (m, 6H); 13C NMR (CDCl3): δ 13.84 (CH3), 35.32 (CH), 36.46 (CH), 52.31 (CH3), 75.53 (C), 127.36 (CH), 128.12 (CH), 129.91 (CH), 144.42 (C), 171.21 (C).

(c) (2S,3S)-2-Hydroxymethyl-3-methyl-1-(triphenylmethyl)aziridine (2): In a three-necked 250 mL flask, aziridine ester 11 (5.60 g, 15.7 mmol) was dissolved in dichloromethane (32 mL) while stirring and under a positive pressure of nitrogen. The mixture was cooled to -70 °C with an acetone-dry ice bath and a 1M solution of diisobutylaluminum hydride (DIBAH) in hexane (39.3 mL, 39.3 mmol) was added dropwise in 45 min. The mixture was allowed to warm to room temperature and, after 3 h, the tlc analysis (ethyl acetate/hexane = 1/3) revealed that the starting material was consumed. The mixture was cooled to -70 °C and a saturated solution of ammonium chloride (9.4 mL) was added dropwise. A precipitate formed which was filtered over a Celite pad and washed with diethyl ether; the filtrate was washed with water, dried with magnesium sulfate and concentrated in vacuo. The residue was crystallized from a mixture of dichloromethane/hexane = 1/9 to afford 3.22 g of product; the mother liquors were concentrated in vacuo and crystallized again to give 0.24 g of the same product. Combined yield 67%: white solid m.p. 79-84 °C; [α]D° +16.0 (c 1.058, CHCl3); 1H NMR (CDCl3): δ 1.30-1.51 (m, 5H), 1.80 (bs, 1H), 3.72-3.95 (m, 2H), 7.15-7.30 (m, 9H), 7.45-7.52 (m, 6H); 13C NMR (CDCl3): δ 14.05 (CH3), 31.43 (CH), 36.82 (CH), 61.73 (CH2), 75.05 (C), 127.25 (CH), 128.06 (CH), 129.93 (CH), 145.23 (C).
(2S,3S)-2-Hydroxymethyl-3-methyl-1-(4-methylphenylsulfonyl)aziridine (3a): In a three-necked 25 mL flask, alcohol 2 (0.40 g, 1.2 mmol) was dissolved in a 1:1 mixture of chloroform/methanol (2.0 mL) while stirring. The mixture was cooled to -70 °C and trifluoroacetic acid (TFA, 2.0 mL, 26.3 mmol) was added dropwise. After 15 min, the mixture was allowed to warm to -10 °C; after 2 h the tlc analysis (ethyl acetate/petroleum ether = 1/2) revealed that the starting material was consumed. Then, the mixture was concentrated in vacuo (at a temperature lower than 30 °C) to obtain a white solid which was dissolved in chloroform (2.0 mL). The mixture was cooled to -40 °C and triethylamine (0.51 mL, 3.7 mmol) and p-toluene sulfonyl chloride (0.23 g, 1.2 mmol) dissolved in chloroform (2.0 mL) were added dropwise. The mixture was allowed to warm to 0 °C and, after 16 h, it was concentrated in vacuo. The crude product was purified by flash chromatography (ethyl acetate/petroleum ether = 1/2 then 2/3) to afford 0.23 g (79% yield) of product: white solid; m.p. 68-70 °C; [α]D 21 +4.8 (c 0.991, CHCl3); 1H NMR (CDCl3): δ 1.22 (d, 3H, J = 5.6 Hz), 2.40 (s, 3H), 2.70 (bs, 1H), 2.84-3.05 (m, 2H), 3.63 (dd, 1H, J = 12.1, 6.3 Hz), 3.69 (dd, 1H, J = 12.1, 5.5 Hz), 7.34 (d, 2H, J = 8.1 Hz), 7.81 (d, 2H, J = 8.1 Hz); 13C NMR (CDCl3): δ 12.53 (CH3), 22.11 (CH3), 40.46 (CH), 45.32 (CH), 59.51 (CH2), 128.30 (CH), 130.26 (CH), 135.15 (C), 145.14 (C).

Preparation of N-tosyl-2,3-aziridine alcohols 3b-d

Methyl (S)-3-tert-Butyldimethylsiloxyl-2-(4-methylphenylsulfonamido)propanoate: A stirred mixture of (S)-serine methyl ester hydrochloride (12, 5.00 g, 32.1 mmol) and p-toluene sulfonyl chloride (6.31 g, 32.1 mmol) in a 1:1 mixture of chloroform/dichloromethane (28.0 mL) was cooled to about 0 °C under a positive pressure of nitrogen. Triethylamine (9.0 mL) was then added dropwise in 55 min. A solid formed and the mixture was stirred at 0 °C for 48 h. Imidazole (4.38 g, 64.2 mmol), tert-butyldimethylchlorosilane (4.84 g, 32.1 mmol), and dimethylformamide (2.8 mL) were
successively added and the mixture was stirred at 0 °C for another 20 h. The reaction was then quenched with 14 mL of a saturated solution of ammonium chloride added dropwise at -20 °C under vigorous stirring. The mixture was extracted three times with hexane and the organic layer was washed with a 5% w/w solution of citric acid (50 mL), water (50 mL), a 5% w/w solution of sodium bicarbonate (50 mL), and water (50 mL). The organic layer was dried over magnesium sulfate and concentrated in vacuo to afford a crude white solid which was purified by flash chromatography (ethyl acetate/petroleum ether = 1/2, then 3/2) to obtain 9.45 g (76% yield) of product: white solid; m.p. 55-58 °C; \([\alpha]_D^{18} +5.6\) (c 1.716, CHCl3); \(^1\)H NMR (CDCl3): \(\delta 0.24 (s, 3H), 0.25 (s, 3H), 1.05 (s, 9H), 2.66 (s, 3H), 3.77 (s, 3H), 4.00 (dd, 1H, \(J = 9.9\), 3.5 Hz), 4.19 (dd, 1H, \(J = 9.9\), 2.9 Hz), 4.25-4.32 (m, 1H), 5.66 (d, 1H, \(J = 9.1\) Hz), 7.53 (d, 2H, \(J = 8.1\) Hz), 7.98 (d, 2H, \(J = 8.1\) Hz); \(^{13}\)C NMR (CDCl3): \(\delta -4.69\) (CH3), -4.52 (CH3), 19.16 (C), 22.55 (CH3), 22.67 (CH3), 53.45 (CH3), 58.61 (CH), 65.53 (CH2), 128.16 (CH), 130.65 (CH), 138.23 (C), 144.59 (C), 171.10 (C).

\(\textbf{(R)-3-t\text{-tert\text{-Butyldimethylsilyloxy-2-(4-methylphenyl)sulfonamido-1-propanol (13):}\) A stirred solution of the starting ester (9.27 g, 23.9 mmol) in anhydrous THF (68.0 mL) was cooled to about 0 °C under a positive pressure of nitrogen and a 2M solution of lithium borohydride in THF (35.9 mL, 71.8 mmol) was gradually added. The reaction mixture was stirred at 0 °C for 30 min then the temperature was raised to room temperature. After 16 h the tlc analysis (ethyl acetate/petroleum ether = 3/7) revealed that the starting material was consumed and a saturated solution of ammonium chloride (20 mL) was added dropwise at 0 °C. A white solid formed which was washed with THF. The filtrate was dried over magnesium sulfate and concentrated in vacuo; the residue was dissolved in ethyl acetate, washed with a saturated solution of ammonium chloride and with water, dried over magnesium sulfate and concentrated in vacuo. The crude product was purified by flash chromatography (ethyl acetate/petroleum ether = 3/7) to obtain 8.26 g (96% yield) of product: yellow oil; \([\alpha]_D^{18} +14.1\) (c 1.248, CHCl3); \(^1\)H NMR (CDCl3): \(\delta -0.03 (s, 3H), -0.02 (s, 3H), 0.82 (s, 9H), 2.42 (s, 3H), 2.52 (bs, 1H), 3.20-3.34 (m, 1H), 3.46-3.65 (m, 4H), 5.30 (d, 1H, \(J = 7.6\) Hz), 7.30 (d, 2H, \(J = 8.9\) Hz), 7.77 (d, 2H, \(J = 8.9\) Hz); \(^{13}\)C NMR (CDCl3): \(\delta -5.15\) (CH3), 18.63 (C), 22.00 (CH3), 26.26 (CH3), 56.02 (CH), 63.26 (CH2), 63.66 (CH2), 127.56 (CH), 130.26 (CH), 138.23 (C), 144.06 (C).

\(\textbf{(1S,2S)-3-t\text{-tert\text{-Butyldimethylsilyloxy-2-(4-methylphenyl)sulfonamido-1-phenyl-1-propanol (15):}\) A stirred solution of (1S,2S)-2-amino-1-phenyl-1,3-propanediol (14, 2.50 g, 15.0 mmol) and triethylamine (2.2 mL, 15.6 mmol) in DMF (31 mL) was cooled to about 0 °C and p-toluenesulfonyl chloride (2.99 g, 15.6 mmol) was added in portions in 30 min. The mixture was stirred at room temperature for 21 h, then imidazole (2.04 g, 29.9 mmol) and \textit{tert}-butyldimethylchlorosilane (2.25 g,
(15.0 mmol) in DMF (10 mL) were added successively at -5 °C. The temperature was raised to room temperature and the mixture was stirred for 24 h; it was then cooled to 0 °C and a saturated solution of ammonium chloride (10 mL) was added dropwise. A precipitate formed which was dissolved with water and the mixture was extracted three times with ethyl acetate. The combined organic layers were washed with a 5% w/w solution of citric acid (15 mL), water (15 mL), a 5% w/w solution of sodium bicarbonate (15 mL), and water (15 mL), dried over magnesium sulfate and concentrated in vacuo. The flash chromatography (ethyl acetate/petroleum ether = 1/1, then methanol) afforded 4.22 g of product and 1.38 g of the tosylated diol. This fraction (3.6 mmol) was suspended in dichloromethane (20 mL) and imidazole (0.54 g, 3.9 mmol) and tert-butyldimethylchlorosilane (0.59 g, 3.9 mmol) were added at room temperature. After 63 h the reaction was quenched with a saturated solution of ammonium chloride (2.6 mL) added dropwise at 0 °C. The work up was the same of the previous reaction and the flash chromatography of the crude product (ethyl acetate/petroleum ether = 4/6) afforded another 0.97 g of product; combined yield 80%. White solid; m.p. 133-137 °C; [α]D 23 +58.0 (c 0.788, CHCl3); 1H NMR (CDCl3): δ 0.03 (s, 3H), 0.04 (s, 3H), 0.89 (s, 9H), 2.35 (s, 3H), 3.30 (m, 2H), 3.64 (m, 2H), 4.91 (d, 1H, J = 4.2 Hz), 5.19 (d, 1H, J = 8.1 Hz), 7.03-7.43 (m, 9H); 13C NMR (CDCl3): δ -5.09 (CH3), 18.65 (C), 21.95 (CH3), 26.33 (CH3), 60.17 (CH), 65.15 (CH2), 74.07 (CH), 126.39 (CH), 127.20 (CH), 128.03 (CH), 128.76 (CH), 128.83 (CH), 130.02 (CH), 137.46 (C), 140.54 (C), 143.51 (C).

(1R,2R)-3-tert-Butyldimethylsilyloxy-2-(4-methylphenyl)sulfonamido-1-(4-nitrophenyl)-1-propanol (17): The same procedure described above for the synthesis of 15 was followed to convert (1R,2R)-2-amino-1-(4-nitrophenyl)-1,3-propanediol (16, 4.00 g, 18.8 mmol) into the compound 17, in this case the starting material was scarcely soluble in DMF. tert-Butyldimethylchlorosilane (4.1 equiv) was added and, to drive the protection of the hydroxyl group to completion, the mixture was brought to 50 °C. Flash chromatography (ethyl acetate/petroleum ether = 2/8 than 3/7) afforded 6.96 g of product (77% yield). White solid; m.p. 200-208 °C; [α]D 22 -29.0 (c 0.500, CHCl3); 1H NMR (CDCl3): δ 0.12 (s, 6H), 0.93 (s, 9H), 2.31 (s, 3H), 3.35 (m, 1H), 3.83 (bs, 1H), 3.90 (d, 2H, J = 3.9 Hz), 5.10 (d, 1H, J = 2.3 Hz), 5.24 (d, 1H, J = 8.8 Hz), 6.98 (d, 2H, J = 8.9 Hz), 7.24-7.33 (m, 4H), 7.90 (d, 2H, J = 8.9 Hz); 13C NMR (CDCl3): δ -5.08 (CH3), -5.03 (CH3), 18.63 (C), 21.70 (CH3), 26.31 (CH3), 59.46 (CH), 66.64 (CH2), 73.56 (CH), 123.64 (CH), 126.84 (CH), 127.04 (CH), 129.82 (CH), 137.31 (C), 144.00 (C), 147.52 (C), 148.20 (C). Anal. calcd for C22H32N2O6SSi: C, 54.97; H, 6.71; N, 5.83. Found: C, 55.09; H, 6.71; N, 5.84.
General procedure for aziridine ring closure: A stirred solution of the starting material and triphenylphosphine (1.2 equiv) in THF (2.0 mL/mmol) was cooled to about 0 °C with an ice-water bath and diethyl azodicarboxylate (DEAD, 1.2 equiv) was added dropwise. The mixture was allowed to warm to room temperature and stirred for 4-19 h. It was then concentrated in vacuo, the solid obtained was taken up in petroleum ether, filtered off and washed with petroleum ether for the products obtained from 13 and 15, and with a mixture of ethyl acetate/petroleum ether = 3/7 for the product obtained from 17. The filtrate was concentrated in vacuo and the crude product was purified by flash chromatography.

(R)-2-(tert-Butyldimethylsiloxy)methyl-1-(4-methylphenylsulfonyl)aziridine (O-TBDMS-3b): alcohol 13 (0.50 g, 1.4 mmol) gave the corresponding aziridine (0.44 g, 94% yield); chromatographic conditions: ethyl acetate/petroleum ether = 1/4: white solid; m.p. 39-41 °C; [α]D21 +27.5 (c 0.836, CHCl3); 1H NMR (CDCl3): δ -0.05 (s, 3H), -0.04 (s, 3H), 0.80 (s, 9H), 2.19 (d, 1H, J = 4.5 Hz), 2.43 (s, 3H), 2.62 (d, 1H, J = 7.1 Hz), 2.84-2.95 (m, 1H), 3.56 (dd, 1H, J = 11.6, 5.3 Hz), 3.69 (dd, 1H, J = 11.6, 4.0 Hz; C1Hb), 7.31 (d, 2H, J = 8.1 Hz), 7.81 (d, 2H, J = 8.1 Hz); 13C NMR (CDCl3): δ -4.99 (CH3), 18.73 (C), 22.10 (CH3), 26.23 (CH3), 31.00 (CH2), 41.30 (CH), 62.81 (CH2), 128.48 (CH), 129.12 (CH), 135.23 (C), 144.93 (C).

(2R,3R)-2-(tert-Butyldimethylsiloxy)methyl-1-[4-methylphenylsulfonyl]-3-phenylaziridine (O-TBDMS-3c): alcohol 15 (2.50 g, 5.7 mmol) gave the corresponding aziridine (2.04 g) and 0.25 g of starting material were recovered (92% yield); chromatographic conditions: ethyl acetate/petroleum ether = 3/7: colorless oil; [α]D24 -64.4 (c 1.023, CHCl3); 1H NMR (CDCl3): δ -0.21 (s, 3H), -0.18 (s, 3H), 0.75 (s, 9H), 2.43 (s, 3H), 3.27 (m, 2H), 3.51 (m, 1H), 4.03 (d, 1H, J = 6.6 Hz), 7.26 (m, 5H), 7.33 (d, 2H, J = 8.2 Hz), 7.90 (d, 2H, J = 8.2 Hz); 13C NMR (CDCl3): δ -7.73 (CH3), -5.63 (CH3), 18.18 (C), 21.73 (CH3), 25.75 (CH3), 44.78 (CH), 46.20 (CH), 59.75 (CH2), 127.58 (CH), 128.03 (CH), 128.13 (CH), 128.34 (CH), 129.79 (CH), 132.40 (C), 134.88 (C), 144.65 (C).

(2S,3S)-2-(tert-Butyldimethylsilyloxy)methyl-1-(4-methylphenylsulfonyl)-3-(4-nitrophenyl)aziridine (O-TBDMS-3d): alcohol 17 (1.50 g, 3.1 mmol) gave the corresponding aziridine (2.04 g) and 0.25 g of starting material were recovered (92% yield); chromatographic conditions: ethyl acetate/petroleum ether = 3/7: white solid; m.p. 79-84 °C; [α]D27 +82.7 (c 1.000, CHCl3); 1H NMR (CDCl3): δ -0.21 (s, 3H), -0.15 (s, 3H), 0.75 (s, 9H), 2.46 (s, 3H), 3.27 (m, 2H), 3.51 (m, 1H), 4.08 (d, 1H, J = 6.6 Hz), 7.37 (d, 2H, J = 8.2 Hz), 7.46 (d, 2H, J = 8.6 Hz), 7.90 (d, 2H, J = 8.2 Hz); 13C NMR (CDCl3): δ -5.35 (CH3), -5.19 (CH3), 18.54 (C), 22.16 (CH3), 26.08 (CH3), 44.15 (CH), 46.84 (CH), 60.05 (CH2), 123.93 (CH), 128.54 (CH), 129.12 (CH), 130.39 (CH), 134.86
General procedure for the deprotection of O-TBDMS aziridines to alcohols 3: A stirred solution of the starting TBDMS ether in THF (1.0 mL/mmol) was cooled to 0 °C with an ice-water bath and a 1M solution of tetrabutylammonium fluoride in THF was added dropwise (1.1 equiv). After 30 min at 0 °C the tlc analysis (ethyl acetate/petroleum ether = 1/1) revealed that the starting material was consumed. The reaction mixture was poured into an ice-water bath and extracted four times with ethyl acetate. The combined extracts were washed with a 5% w/w solution of citric acid, water, a 5% w/w solution of sodium bicarbonate and water. Each aqueous layer was back-extracted with ethyl acetate. The combined organic layers were dried over magnesium sulfate and concentrated in vacuo to afford a crude yellow oil which was purified by flash chromatography.

(R)-2-Hydroxymethyl-1-(4-methylphenylsulfonyl)aziridine (3b): 2.78 g (8.1 mmol) of the starting material afforded 1.66 g of the aziridine 3b (90% yield); chromatographic conditions: ethyl acetate/petroleum ether = 6/4: white solid; m.p. 42-43 °C; [α]D24 +32.0 (c 1.228, CHCl3); 1H NMR (CDCl3): δ 2.26 (d, 1H, J = 4.4 Hz), 2.40 (s, 3H), 2.56 (d, 1H, J = 6.7 Hz), 2.80 (bs, 1H), 2.93-3.04 (m, 1H), 3.49-3.80 (m, 2H), 7.33 (d, 2H, J = 8.9 Hz), 7.80 (d, 2H, J = 8.9 Hz); 13C NMR (CDCl3): δ 22.12 (CH3), 31.52 (CH2), 40.96 (CH), 61.31 (CH2), 128.44 (CH), 130.31 (CH), 134.80 (C), 145.36 (C).

(2R,3R)-2-Hydroxymethyl-1-(4-methylphenylsulfonyl)-3-phenylaziridine (3c): 2.01 g (4.8 mmol) of the starting material afforded 1.35 g of the aziridine 3c (92% yield); chromatographic conditions: ethyl acetate/petroleum ether = 4/6: white solid; m.p. 80-82 °C; [α]D22 -124.8 (c 1.320, CHCl3); 1H NMR (CDCl3): δ 2.05 (s, 1H), 2.42 (s, 3H), 3.21-3.50 (m, 3H), 4.02 (d, 1H, J = 7.0 Hz), 7.19-7.30 (m, 5H), 7.35 (d, 2H, J = 8.3 Hz), 7.90 (d, 2H, J = 8.3 Hz); 13C NMR (CDCl3): δ 22.19 (CH3), 45.81 (CH), 46.45 (CH), 59.84 (CH2), 127.76 (CH), 128.58 (CH), 128.63 (CH), 128.98 (CH), 130.38 (CH), 132.62 (C), 134.86 (C), 145.43 (C).

(2S,3S)-2-Hydroxymethyl-1-(4-methylphenylsulfonyl)-3-(4-nitrophenyl)aziridine (3d): 0.99 g (2.1 mmol) of the starting material afforded 0.79 g of the aziridine 3d (94% yield); chromatographic conditions: ethyl acetate/petroleum ether = 4/6: colorless oil; [α]D19 +141.5 (c 1.192, CHCl3); 1H NMR (CDCl3): δ 2.42 (s, 3H; CH3 (Ts)), 2.83 (bs, 1H; OH), 3.40 (m, 3H; C1'Ha, C1'Hb, C2'H), 4.04 (d, 1H, J = 6.6 Hz; C3'H), 7.36 (d, 2H, J = 8.2 Hz; arom.), 7.43 (d, 2H, J = 8.7 Hz; arom.), 7.88 (d, 2H, J = 8.2 Hz; arom.), 8.08 (d, 2H, J = 8.7 Hz; arom.); 13C NMR (CDCl3): δ 21.67 (CH3), 44.41 (CH), 46.23 (CH), 58.88 (CH2), 123.62 (CH), 128.06 (CH), 128.53 (CH), 130.06 (CH), 133.82 (C), 139.80 (C), 145.45 (C).
Anal. calcd for C₁₆H₁₆N₂O₅S: C, 55.16; H, 4.63; N, 8.04. Found: C, 55.26; H, 4.61; N, 8.02.

General procedure for the one-pot direct conversion of N-tosyl-2,3-aziridine alcohols 3 into 4,5-dihydroisoxazole derivatives 4: To a stirred solution of the alcohol 3 in dichloromethane (1.0 mL/mmol) 2,2,6,6-tetramethyl-1-piperidinyloxyl (TEMPO) (0.1 equiv) and bisacetoxyiodobenzene (BAIB, 1.1 equiv) were added successively at room temperature. The course of the reaction was monitored by HPLC (THF/hexane = 35/65, 1.0 mL/min) and after 5 h the alcohol was consumed. At this point imidazole (3.3 equiv) and ethyl nitroacetate (1.1 equiv) were added. After another 20 h of stirring at r.t. the reaction mixture was diluted with dichloromethane, washed twice with a 10% w/w solution of sodium bicarbonate and with water; each aqueous layer was back-extracted with dichloromethane. The organic layer was dried with magnesium sulfate and concentrated in vacuo. The crude product was purified by flash chromatography for the products 4a-c and by crystallization from acetone and hexane for the product 4d.

(4R,5R)- and (4S,5R)-3-Ethoxycarbonyl-4-hydroxy-5-[(S)-methyl-(4-methylphenylsulfonamido)]methyl-4,5-dihydroisoxazole 2-Oxide (4a): Alcohol 3a (0.35 g, 1.4 mmol) afforded 0.44 g of isoxazole trans-4a and 0.06 g of the isoxazole cis-4a. Combined yield 94%; chromatographic conditions: ethyl acetate/petroleum ether = 6/4:

trans-4a: white solid; m.p. 51-53 °C; [α]D²⁵ +120.0 (c 0.990, CHCl₃); ¹H NMR (CDCl₃): δ 0.96 (d, 3H, J = 7.0 Hz; CH₃), 1.34 (t, 3H, J = 7.1 Hz; CH₃ (Et)), 2.42 (s, 3H; CH₃ (Ts)), 3.66-3.73 (m, 1H; C₁'H), 3.91 (bs, 1H; OH), 4.35 (q, 2H, J = 7.1 Hz; CH₂ (Et)), 4.43-4.46 (m, 1H; C⁵H), 5.58 (d, 1H, J = 9.4 Hz; NH), 5.65 (d, 1H, J = 3.0 Hz; C⁴H), 7.31 (d, 2H, J = 8.1 Hz; arom.), 7.76 (d, 2H, J = 8.1 Hz; arom.); ¹³C NMR (CDCl₃): δ 14.60 (CH₃), 17.67 (CH₃), 22.04 (CH₃), 51.24 (CH), 62.76 (CH₂), 75.52 (CH), 85.92 (CH), 111.69 (C), 127.50 (CH), 130.46 (CH), 137.67 (C), 144.45 (C), 159.34 (C). Anal. calcd for C₁₅H₂₀N₂O₇S: C, 48.38; H, 5.41; N, 7.52. Found: C, 48.33; H, 5.40; N, 7.52.  

cis-4a: white solid; m.p. 87 °C; [α]D²⁴ +8.5 (c 0.914, CHCl₃); ¹H NMR (CDCl₃): δ 1.18 (d, 3H, J = 6.9 Hz; CH₃), 1.32 (t, 3H, J = 7.1 Hz; CH₃ (Et)), 2.42 (s, 3H; CH₃ (Ts)), 3.90-4.01 (m, 1H; C¹'H), 4.32 (q, 2H, J = 7.1 Hz; CH₂ (Et)), 4.56 (dd, 1H, J = 7.0 Hz; C⁵H), 5.43 (d, 1H, J = 6.6 Hz; C⁴H), 5.60 (d, 1H, J = 8.9 Hz; NH), 7.31 (d, 2H, J = 8.3 Hz; arom.), 7.78 (d, 2H, J = 8.3 Hz; arom.); ¹³C NMR (CDCl₃): δ 14.61 (CH₃), 17.79 (CH₃), 22.04 (CH₃), 48.74 (CH), 62.68 (CH₂), 73.29 (CH), 81.08 (CH), 110.34 (C), 127.54 (CH), 130.30 (CH), 138.06 (C), 144.26 (C), 159.34 (C). Anal. calcd for C₁₅H₂₀N₂O₇S: C, 48.38; H, 5.41; N, 7.52. Found: C, 48.42; H, 5.43; N, 7.51.
(4R,5S)- and (4S,5S)-3-Ethoxycarbonyl-4-hydroxy-5-(4-methylphenylsulfonamido)methyl-4,5-dihydroisoxazole 2-Oxide (4b): Alcohol 3b (0.18 g, 0.8 mmol) afforded 0.21 g of a mixture of the two diastereomeric isoxazoles cis-4b and trans-4b. Combined yield 75%; chromatographic conditions: ethyl acetate/petroleum ether = 1/1: white solid; $^1$H NMR (CDCl$_3$): $\delta$ 1.35 (m, 3H; CH$_3$ (Et) cis+trans), 2.45 (m, 3H; CH$_3$ (Ts) cis+trans), 3.25 (d, 2H, $J$ = 5.4 Hz; C$^1$H$_2$ trans), 3.40 (dd, 1H, $J$ = 14.1, 6.0 Hz; C$^1$H$_a$ cis), 3.55 (dd, 1H, $J$ = 14.1, 7.0 Hz; C$^1$H$_b$ cis), 4.10 (bs, 1H; OH cis+trans), 4.32 (m, 2H; CH$_2$ (Et) cis+trans), 4.65 (dt, 1H, $J$ = 12.7, 6.5 Hz; C$^5$H cis), 5.52 (d, 1H, $J$ = 2.5; C$^4$H trans), 5.52 (d, 1H, $J$ = 6.5; C$^4$H cis), 5.75, 5.88 (bs, 1H; NH cis+trans), 7.32 (m, 2H; arom.), 7.74 (m, 2H; arom.); $^{13}$C NMR (CDCl$_3$): $\delta$ 14.57 (CH$_3$), 22.03 (CH$_3$), 40.21 (CH$_2$), 43.71 (CH$_2$), 62.74 (CH$_2$), 62.84 (CH$_2$), 72.88 (CH), 75.36 (CH), 82.37 (CH), 111.36 (C), 112.10 (C), 127.52 (CH), 128.50 (CH), 130.36 (CH), 130.44 (CH), 136.62 (C), 136.69 (C), 144.48 (C), 159.44 (C). Anal. calcd for C$_{14}$H$_{18}$N$_2$O$_7$S: C, 46.92; H, 5.06; N, 7.82. Found: C, 47.01; H, 5.05; N, 7.82.

(4R,5S)-3-Ethoxycarbonyl-4-hydroxy-5-[(R)-(4-methylphenylsulfonamido)phenyl]methyl-4,5-dihydroisoxazole 2-Oxide (3c): Alcohol 3c (0.91 g, 3.0 mmol) afforded 1.20 g of the 4,5-trans-4,5-dihydroisoxazole 4c (92% yield); chromatographic conditions: ethyl acetate/petroleum ether = 4/6: white solid; m.p. 77-81 °C; $[^\alpha]_D^{26}$ -135.8 (c 1.001, CHCl$_3$); $^1$H NMR (CDCl$_3$): $\delta$ 1.27 (t, 3H, $J$ = 7.1 Hz; CH$_3$ (Et)), 2.25 (s, 3H; CH$_3$ (Ts)), 3.95 (bs, 1H; OH), 4.27 (q, 2H, $J$ = 7.1 Hz; CH$_2$ (Et)), 4.73 (m, 2H; C$_5$H, C$_1'$H), 5.64 (d, 1H, $J$ = 2.1 Hz; C$_4$H), 6.53 (d, 1H, $J$ = 9.6 Hz; NH), 6.99 (d, 2H, $J$ = 8.0 Hz; arom.), 7.09 (m, 5H; arom.), 7.49 (d, 2H, $J$ = 8.0 Hz; arom.); $^{13}$C NMR (CDCl$_3$): $\delta$ 14.10 (CH$_3$), 21.40 (CH$_3$), 58.59 (CH), 62.25 (CH$_2$), 75.22 (CH), 85.50 (CH), 111.07 (C), 127.03 (CH), 128.13 (CH), 128.56 (CH), 129.36 (CH), 135.50 (C), 136.87 (C), 143.38 (C), 158.81 (C). Anal. calcd for C$_{20}$H$_{22}$N$_2$O$_7$S: C, 55.29; H, 5.10; N, 6.45. Found: C, 55.35; H, 5.09; N, 6.44.

(4R,5S)-3-Ethoxycarbonyl-4-hydroxy-5-[(S)-(4-methylphenylsulfonamido)-(4-nitrophenyl)]-methyl-4,5-dihydroisoxazole 2-Oxide (4d): Alcohol 3d (0.21 g, 0.6 mmol) afforded 0.16 g of the isoxazole trans-4d (55% yield): white solid; m.p. 185 °C (decomposition); $[^\alpha]_D^{22}$ +131.9 (c 0.500, acetone); $^1$H NMR (DMSO-$d_6$): $\delta$ 1.22 (t, 3H, $J$ = 7.1 Hz; CH$_3$ (Et)), 2.22 (s, 3H; CH$_3$ (Ts)), 4.22 (q, 2H, $J$ = 7.1 Hz; CH$_2$ (Et)), 4.54 (dd, 1H, $J$ = 6.6, 1.9 Hz; C$_5^5$H), 4.87-4.98 (m, 1H, C$_1'^1$H), 5.02 (dd, 1H, $J$ = 7.6, 1.9 Hz; C$_4^4$H), 6.32 (d, 1H, $J$ = 7.6 Hz; OH), 7.09 (d, 2H, $J$ = 8.2 Hz; arom.), 7.39 (d, 2H, $J$ = 8.2 Hz; arom.), 7.50 (d, 2H, $J$ = 8.8 Hz; arom.), 8.01 (d, 2H, $J$ = 8.8 Hz; arom.), 8.88 (d, 1H, $J$ = 9.9 Hz; NH); $^{13}$C NMR (DMSO-$d_6$): $\delta$ 14.30 (CH$_3$), 21.00 (CH$_3$), 57.53 (CH), 61.40 (CH$_2$), 74.10 (CH), 85.13 (CH), 111.34 (C), 123.39 (CH), 126.61 (CH), 129.27 (CH), 129.40 (CH), 138.13 (C), 142.80 (C),
Hydroxylated Merrifield-supported Nitroacetic acid (6): Nitroacetic acid: In a 250 mL three-necked round bottomed flask equipped with a thermometer and a condenser, potassium hydroxide (120.97 g, 2.156 mol) was added to water (121 mL). When the temperature reached 67 °C, nitromethane (28.2 mL, 0.524 mol) was added. During the addition the temperature rose to 95 °C. At the end the flask was left open, without the condenser and the temperature was kept between 95 and 100 °C for 5 h. The mixture was then cooled to room temperature and yellow crystals formed. The solid was filtered and washed with cold methanol. The mother liquors were concentrated under reduced pressure and a second crop of crystals was recovered. The product obtained (20.81 g, 44% combined yield) was used without further purification. In a 100 mL three-necked round bottomed flask, potassium nitroacetate (8.00 g, 44.1 mmol) was dissolved in water (20 mL) while stirring. The solution was cooled to -8 °C with an ice-brine bath and a cold solution (-10 °C) of L-tartaric acid (13.24 g, 88.2 mmol) in water (20 mL) was added dropwise, keeping the temperature between -8 and -3 °C. At the end of the addition, the mixture was stirred at -2 °C for 30 min, the solid was filtered and the solution obtained was saturated with sodium chloride. The aqueous solution was extracted twelve times with cold diethyl ether, the organic layer was dried over magnesium sulfate and concentrated under reduced pressure. The oil obtained was taken up in cold chloroform and concentrated in vacuo three times to give 3.51 g (76% yield by mass) of product as white crystals, which was used without further purification. IR (film) ν (cm⁻¹): 1770 (CO), 1550 (NO₂).

In a 100 mL three-necked round bottomed flask equipped with a thermometer and a CaCl₂ tube, hydroxylated Merrifield resin (4.67 g, loading 0.68 mequiv/g, 3.17 mequiv) was suspended in dry THF (35 mL). The mixture was cooled to 0 °C and diisopropylcarbodiimide (DIC, 2.24 mL, 14.3 mmol) was added dropwise. After ten minutes an ice-cold solution of nitroacetic acid (1.50 g, 1.3 mmol) in dry THF (5 mL) was added dropwise keeping the temperature below 10 °C. After two hours the temperature was left rising to room temperature and the mixture was stirred for 15 h. The course of the reaction was monitored by FTIR until complete disappearance of the OH band. At the end the resin was filtered, washed with dichloromethane (3×50 mL), a mixture methanol/DMF = 1/1 (3×50 mL), water

(1) The entire work-up was made below 10 °C. Lower yields were obtained without this temperature control.
(3×50 mL) a mixture methanol/DMF = 1/1 (3×50 mL) and dichloromethane (3×50 mL) and was dried under reduced pressure at 50 °C for 2 h obtaining 4.91 g of resin (theoretical 4.962 g, theoretical loading 0.64 mequiv/g). IR (KBr) ν (cm⁻¹): 3084, 3060, 3030 (CH arom.), 2925, 2951 (CH aliph.), 1755 (CO), 1565 (NO₂).

General method for the synthesis of solid-supported dihydroisoxazoles 7: To a stirred solution of the aziridine alcohol (1.1 equiv) in dichloromethane (1 mL/mmol), TEMPO (0.11 equiv) and BAIB (1.2 equiv) were added at room temperature. After 5 h, imidazole (3.6 equiv) and the supported nitroacetate (1.0 equiv) were added followed by dichloromethane to suspend the resin. After 17 h the resin was filtered, washed with dichloromethane, methanol and dichloromethane and dried under reduced pressure at 50 °C for 2 h.

Polymer-supported 4,5-dihydroisoxazole 7a: IR (KBr) ν (cm⁻¹): 3491 (OH), 3269 (NH), 3056, 3025 (CH arom.), 2921, 2849 (CH aliph.), 1737 (CO), 1625 (CN), 1325, 1155 (SO₂).

Polymer-supported 4,5-dihydroisoxazoles 7b: IR (KBr) ν (cm⁻¹): 3485 (OH), 3300 (NH), 3061, 3025 (CH arom.), 2922, 2847 (CH aliph.), 1738 (CO), 1615 (CN), 1335, 1157 (SO₂).

Polymer-supported 4,5-dihydroisoxazoles 7c: IR (KBr) ν (cm⁻¹): 3498 (OH), 3277 (NH), 3059, 3025 (CH arom.), 2923, 2850 (CH aliph.), 1736 (CO), 1629 (CN), 1327, 1158 (SO₂).

General procedure for the cleavage of solid-supported 4,5-dihydroisoxazoles 7: The resin was suspended in a mixture toluene/methanol/triethylamine = 20/10/1 (15 mL/mequiv) and the mixture was heated to 50 °C until FTIR analysis revealed that the dihydroisoxazole cleavage was complete (48 h). Then it was filtered and washed with dichloromethane (3×15 mL/mequiv), methanol (3×15 mL/mequiv), and dichloromethane (3×15 mL/mequiv) and the filtrate was concentrated under reduced pressure. Flash chromatography of the crude product afforded the desired product.

(4SR,5R)-4-Hydroxy-3-methoxycarbonyl-5-[((S)-methyl(4-methylphenylsulfonamido)]methyl-4,5-dihydroisoxazole 2-Oxide (8a). The cleavage of the polymer-supported dihydroisoxazole 7a, obtained from aziridine alcohol 3a (509 mg, 2.11 mmol) and resin 6 (3.00 g, 1.92 mequiv), afforded dihydroisoxazoles 8a (687 mg, 1.92 mmol, quantitative yield), that were separated by flash column chromatography (ethyl acetate : petroleum ether from 1: 1 to 3 : 2).

(4S,5R)-4,5-trans-8a: colorless oil; [α]D²⁵ +111.6 (c 1.568, CH₃OH); ¹H NMR (CDCl₃): δ 0.97 (d, 3H, J = 7.2 Hz; CH₃C¹), 2.44 (s, 3H; CH₃ (Ts)), 3.41 (d, 1H, J = 4.1 Hz; OH), 3.69 (m, 1H; C¹¹H), 3.90 (s, 3H; OCH₃), 4.42 (dd, 1H, J = 2.2, 3.6 Hz; C⁵H), 5.07 (d, 1H, J = 9.34 Hz; NH), 5.64 (m, 1H; C⁴H), 7.34 (d, 2H, J = 8.5 Hz; arom), 7.76 (d, 2H, J = 8.5 Hz; arom); ¹³C NMR (CDCl₃): δ 18.38 (CH₃), 22.24 (CH₃), 51.46 (CH), 53.55 (CH₃), 75.84 (CH), 85.89 (CH), 111.60 (C), 127.66 (CH), 130.69
(CH), 137.81 (C), 144.80 (C), 159.85 (C). Anal. calcd for C_{14}H_{18}N_{2}O_{7}S: C, 46.92; H, 5.06; N, 7.82. Found: C, 46.95; H, 5.08; N, 7.82.

**4R,5R)-4,5-cis-8a:** colorless oil; \(^{1}H\) NMR (acetone-\(d_{6}\)): \(\delta\) 1.38 (d, 3H, \(J = 6.6\) Hz; \(\text{CH}_{3}C^{1}\)), 2.62 (s, 3H; \(\text{CH}_{3}\)), 3.97 (s, 3H; \(\text{OCH}_{3}\)), 4.18 (\(m\), 1H; \(\text{C}^{1}\)H), 4.72 (\(dd\), 1H, \(J = 5.4, 9.7\) Hz; \(\text{C}^{5}\)H), 5.47-5.63 (\(m\), 2H; \(\text{C}^{4}\)H, NH), 7.59 (\(d\), 2H, \(J = 8.1\) Hz; arom), 7.97 (\(d\), 2H, \(J = 8.1\) Hz; arom). Anal. calcd for C_{14}H_{18}N_{2}O_{7}S: C, 46.92; H, 5.06; N, 7.82.

**(4R,5S)- and (4S,5S)-4-Hydroxy-3-methoxycarbonyl-5-(4-methylphenylsulfonamido)methyl-4,5-dihydroisoxazole 2-Oxide (8b):** The cleavage of polymer-supported dihydroisoxazole 7b, obtained from aziridine alcohol 3b (539 mg, 2.37 mmol) and resin 6 (3.37 g, 2.16 mequiv), afforded dihydroisoxazoles 8b (535 mg, 1.55 mmol, 72% yield). \(^{1}H\) NMR (CDCl\(_3\)): \(\delta\) 2.40 (s, 3H; \(\text{CH}_{3}\)), 3.15-3.25 (\(m\), 2H; \(\text{C}^{1}\)H\(_2\), trans), 3.30-3.39 (\(m\), 1H; \(\text{C}^{1}\)H\(_a\), cis), 3.44-3.52 (\(m\), 1H; \(\text{C}^{1}\)H\(_b\), cis), 3.83 (s, 3H; \(\text{OCH}_{3}\), trans + cis), 4.40 (bs, 1H; OH, trans + cis), 4.59-4.63 (\(m\), 1H; \(\text{C}^{5}\)H, trans), 4.70-4.77 (\(m\), 1H; \(\text{C}^{5}\)H, cis), 5.46 (\(m\), 1H; \(\text{C}^{4}\)H, trans + cis), 5.80 (\(t\), 1H, \(J = 8.8\) Hz; NH, cis), 6.00 (t, 1H, \(J = 8.9\) Hz; NH, trans), 7.31 (\(m\), 2H; arom, trans + cis), 7.74 (\(m\), 2H; arom, trans + cis); \(^{13}C\) NMR (CDCl\(_3\)): \(\delta\) 21.60 (\(\text{CH}_{3}\)), 39.89 (\(\text{CH}_{2}\)), 43.42 (\(\text{CH}_{2}\)), 52.98 (\(\text{CH}_{3}\)), 72.61 (CH), 74.96 (CH), 77.65 (CH), 81.43 (CH), 110.48 (C), 118.81 (C), 127.03 (CH), 130.06 (CH), 136.23 (C), 136.38 (C), 144.12 (C), 144.24 (C), 159.23 (C), 159.41 (C). Anal. calcd for C_{13}H_{16}N_{2}O_{7}S: C, 45.34; H, 4.68; N, 8.14. Found: C, 45.46; H, 4.67; N, 8.17.

**4R,5S)-4-Hydroxy-3-methoxycarbonyl-5-[(R)-(4-methylphenylsulfonamido)phenyl]methyl-4,5-dihydroisoxazole 2-Oxide (8c):** The cleavage of polymer-supported dihydroisoxazole 7c, obtained from aziridine alcohol 3c (465 mg, 1.53 mmol) and resin 6 (2.18 g, 1.39 mequiv), afforded dihydroisoxazole 8c (480 mg, 1.14 mmol, 82% yield). White solid; m.p. 57-60 °C. \([\alpha]_{D}^{27} -124.8\) (c 1.480 CH\(_3\)OH); \(^{1}H\) NMR (CDCl\(_3\)): \(\delta\) 2.20 (s, 3H; \(\text{CH}_{3}\)), 3.73 (s, 3H; \(\text{OCH}_{3}\)), 4.00 (bs, 1H; OH), 4.65 (\(m\), 2H; \(\text{C}^{5}\)H, \(\text{C}^{1}\)H), 5.58 (bs, 1H; \(\text{C}^{4}\)H), 6.28 (\(d\), 1H, \(J = 8.9\) Hz; NH), 6.93 (\(d\), 2H, \(J = 8.1\) Hz; arom), 7.01 (\(m\), 5H; arom), 7.41 (\(d\), 2H, \(J = 8.1\) Hz; arom); \(^{13}C\) NMR (CDCl\(_3\)): \(\delta\) 21.88 (\(\text{CH}_{3}\)), 53.35 (CH\(_3\)), 59.08 (CH), 75.69 (CH), 85.98 (CH), 111.42 (C), 127.49 (CH), 128.67 (CH), 129.08 (CH), 129.85 (CH), 135.91 (C), 137.20 (C), 143.96 (C), 159.68 (C). Anal. calcd for C_{19}H_{20}N_{2}O_{7}S: C, 54.28; H, 4.79; N, 6.66. Found: C, 54.40; H, 4.83; N, 6.63.
4,5-trans-7a
4,5-trans-7a
4,5-cis-7a
4,5-trans- and 4,5-cis-7b
4,5-trans- and 4,5-cis-7b
$O$-TBDMS-6d