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Supporting Information

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Supporting information

Lithiation-Induced Migrations from Nitrogen to Carbon in Terminal Aziridines

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(I) General details

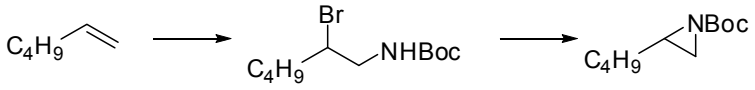
Reactions were performed in flame-dried glassware under an atmosphere of argon. MeCN and CH_2Cl_2 were degassed and dried over alumina under nitrogen.[1] THF was distilled over sodium and benzophenone under an atmosphere of nitrogen. *t*-BuOMe was dried over CaH_2. 2,2,6,6-Tetramethylpiperidine was distilled from CaH_2 under reduced pressure. All other reagents were used as received. Reactions were monitored by TLC (thin layer chromatography) using silica 60 gel aluminium-backed plates. The plates were visualised using ultraviolet light and developed in basic potassium permanganate solution. Column chromatography was performed using the solvent systems indicated. Petroleum ether refers to the fraction that boils at 30–40 ºC. The stationary phase used was silica gel 60. ^{1}H, ^{13}C and ^{31}P spectra were recorded in $CDCl_3$ or CD_3OD as indicated at ambient temperature. Data are

1. Pangborn, A. B.; Giardello, M. A.; Grubbs, R. H.; Rosen, R. K.; Timmers, F. J. *Organometallics* **1996**, *15*, 1518–1520.

expressed as chemical shifts in parts per million (ppm) relative to residual chloroform and $CDCl_3$ (^1H δ 7.27, ^{13}C δ 77.0 respectively) and residual MeOH and CD_3OD (^1H δ 3.31, ^{13}C δ 49.2 respectively) as the internal standard on the δ scale. The multiplicity of each signal is designated using the following abbreviations; s, singlet; d, doublet; dd, doublet of doublets; dt, doublet of triplets; ddt, doublet of doublet of triplets; t, triplet; sept, septlet; br, broad. Coupling constants *J* are given in Hz. Infra-red spectra of the compounds were recorded neat, as a film, or KBr disc as indicated. The intensity of the peaks are reported as s, strong; m, medium; w, weak; br, broad. High-resolution mass spectra were obtained using chemical ionisation techniques (NH_4^+ and Na^+) or by gas chromatography analysis with a BPX5 column-HP 6890 (dimethylsilicon capillary column, 30 m, 0.25 mm i.d.) equipped with a reflectron TOF mass spectrometer operating at 60 eV (flow rate (He) = 1 mL/min). Specific rotations $[\alpha]^T_D$ were measured using a polarimeter with a cell of path length 10.0 cm, at T °C and are given in 10^{-1} deg cm^2 g^{-1}. Concentrations (*c*) are given in g/100 mL.

(II) Characterisation data for *N*-Boc aziridines

Representative procedure 1 : *tert*-Butyl 2-butylaziridine-1-carboxylate 5a



tert-Butyl dibromocarbamate[2] (1 equiv 4.1 mmol) in CH_2Cl_2 (5 mL) was added dropwise *via* syringe pump over 30 min to a stirred refluxing solution of 1-hexene (0.51 mL, 4.1 mmol) in CH_2Cl_2 (5 mL) under argon in the light. Following stirring for 12 h in the light at reflux, the pale yellow solution was cooled to 0 °C and an aqueous solution of Na_2SO_3 (12% w/v, 4.1 mL) was added dropwise. Following stirring at 0 °C for 20 min, the aqueous phase was washed with CH_2Cl_2 (3 × 20 mL), the combined organic phase was washed with H_2O (2 × 10 mL), brine (20 mL), dried ($MgSO_4$) and

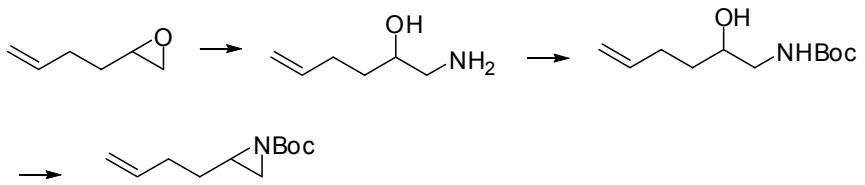
2. Śliwińska, A.; Zwierzak, A. *Tetrahedron* **2003**, *59*, 5927–5934.

then evaporated under reduced pressure. Purification of the residue by column chromatography (petroleum ether/Et_2O 97:3, R_f = 0.21) gave the crude amino bromide as a pale yellow oil (492 mg, 43%).

The crude amino bromide was dissolved in anhydrous DMF (41 mL), cooled to 0 °C and NaH (60% w/w dispersion in mineral oil, 106 mg, 2.6 mmol) was added portion-wise over 1 min. Following stirring for 1 h at 0 °C, the suspension was warmed to room temperature and stirred for a further 1 h. Et_2O (10 mL) and H_2O (10 mL) were then added and the aqueous phase was washed with Et_2O (3 × 20 mL). The combined organic phase was washed with H_2O (3 × 10 mL), brine (30 mL), dried ($MgSO_4$) and then evaporated under reduced pressure. Purification of the residue by column chromatography (petroleum ether/Et_2O 97:3) gave *aziridine* **5a** as a colourless oil (335 mg, 96%).

R_f 0.30 (petroleum ether/Et_2O 97:3); IR (neat) 2933s, 2873s, 1721s (C=O), 1468s, 1413s, 1393s, 1368s, 1311s, 1223s, 1164s and 1065m cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 2.31-2.25 (1H, m, CHN), 2.18 (1H, d, *J* 6, CH(*H*)N, *trans* to alkyl chain), 1.83 (1H, d, *J* 4, C*H*(H)N, *cis* to alkyl chain), 1.39 (9H, s, $C(CH_3)_3$), 1.37−1.29 (6H, m, 3 × CH_2), 0.85 (3H, t, *J* 7, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.6 (C=O), 80.6 (OC), 38.1 (CHN), 31.8 (CH_2N), 31.5 (CH_2), 28.9 (CH_2), 27.8 ($C(CH_3)_3$), 22.2 (CH_2), 13.9 (CH_3); MS CI *m/z* (rel. int.) 200 ($M + H^+$, 45), 117 (20), 100 (100). HRMS *m/z* calcd for $C_{11}H_{22}NO_2$ requires 200.1645, found 200.1643.

Representative procedure 2 : *tert*-Butyl 2-(but-3-enyl)aziridine-1-carboxylate 5b



1-Aminohex-5-en-2-ol

NH_4OH (35% aq, 12 mL) was added to a stirred solution of 1,2-epoxy-5-hexene (2.23 mL, 19.0 mmol) in MeCN (3 mL) at room temperature. The colourless solution was heated at 120 °C in a sealed tube for 1 h. Following cooling and evaporation, bulb-to-bulb distillation (7 mbar, 150 °C) gave 1-aminohex-5-en-2-ol as a colourless oil (1.76 g, 80%).

IR (neat) 3366br.s (O–H, N–H), 2919m, 2499w, 2354w, 1639m (C=C), 1567s, 1453s, 1330m and 1096m cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 5.84-5.71 (1H, m, =CH), 5.02-4.86 (2H, m, H_2C=), 3.52-3.43 (1H, m, C*H*OH), 2.77-2.66 (1H, m, CH(*H*)N), 2.53−2.24 (4 H, m, C*H*(H)N, OH, NH_2), 2.23-2.04 (2H, m, =CHCH_2), 1.53-1.38 (2H, m, CH_2); ^{13}C NMR (100 MHz, $CDCl_3$) δ 138.4 (=CH), 114.7 (H_2C=), 71.3 (CHOH), 47.5 (CH_2N), 36.9 (CH_2), 29.9 (=CH*C*H_2); MS ES *m/z* (rel. int.) 116 (M + H^+, 100), 81 (30), 72 (30), 60 (50), 56 (70), 55 (40), 44 (45), 43 (50), 41 (60); HRMS *m/z* calcd for $C_6H_{14}NO$ requires 116.1070, found 116.1069.

tert-Butyl 2-hydroxyhex-5-enyl carbamate

A solution of 1-aminohex-5-en-2-ol (1.50 g, 13.0 mmol) in CH_2Cl_2 (5 mL) was added dropwise to a stirred solution of di-*tert*-butyl dicarbonate (2.84 g, 13.0 mmol) in CH_2Cl_2 (21 mL) at 0 °C under argon. Following warming to room temperature, the reaction was stirred for 6 h. H_2O (10 mL) was added and the organic phase was washed with H_2O (2 × 50 mL), brine (30 mL), dried ($MgSO_4$) and evaporated under

reduced pressure to give *tert*-butyl 2-hydroxyhex-5-enyl carbamate[3] as a pale yellow oil (2.70 g, 96%).

R_f 0.20 (petroleum ether/Et_2O 4:1); IR (neat) 3451br.m (O–H, N–H), 3079w, 2980m, 2932m, 2251m, 1697s (C=C), 1641w, 1510s, 1457m, 1392m, 1368s, 1251m and 1170s cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 5.85 (1H, ddt, *J* 13, 7, 7, =CH), 5.11-4.96 (3H, m, H_2C=, NH), 3.79-3.77 (1H, m, C*H*OH), 3.35-3.27 (1H, m, CH(*H*)N), 3.09 (1H, dd, *J* 14, 7, C*H*(H)N), 2.33-2.08 (3H, m, =CHCH_2, OH), 1.60-1.50 (2H, m, CH_2), 1.45 (9H, s, $C(CH_3)_3$); ^{13}C NMR (100 MHz, $CDCl_3$) δ 155.8 (C=O), 138.1 (=CH), 115.0 (H_2C=), 79.6 (OC), 71.1 (CHOH), 49.6 (CH_2N), 33.7 (CH_2), 29.8 (=CHCH_2), 28.4 ($C(CH_3)_3$); MS CI *m/z* (rel. int.) 216 ($M + H^+$, 10), 177 (15), 160 (80), 142 (100); HRMS *m/z* calcd for $C_{11}H_{22}NO_3$ requires 216.1600, found 216.1593.

tert-Butyl 2-(but-3-enyl)aziridine-1-carboxylate **5b**

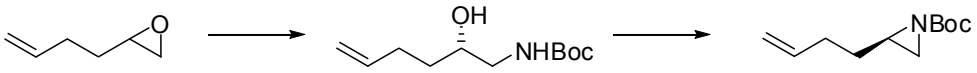
Potassium hydroxide (2.49 g, 44.5 mmol, freshly powdered) was added to a stirred solution of *tert*-butyl 2-hydroxyhex-5-enyl carbamate (1.95 g, 9.1 mmol) and tosyl chloride (2.42 g, 12.7 mmol) in THF (32mL) under argon. Following stirring for 24 h, the suspension was filtered and washed with Et_2O (2 × 30 mL). The filtrate was then evaporated under reduced pressure. Purification of the residue by column chromatography (petroleum ether/Et_2O 95:5) gave *aziridine* **5b** as a colourless oil (1.39 g, 77%).

R_f 0.28 (petroleum ether/Et_2O 95:5); IR (neat) 3077w, 2979s, 2933s, 1720s (C=O), 1642m (C=C), 1477m, 1453m, 1412s, 1393s, 1368s, 1309s, 1224s, 1159s and 1065m cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 5.86 (1H, ddt, *J* 14, 7, 7, =CH), 5.09-4.97 (2H, m, H_2C=), 2.41-2.35 (1H, m, CHN), 2.26 (1H, d, *J* 6, CH(*H*)N, *trans* to alkyl chain), 1.92 (1 H, d, *J* 4, CH(*H*)N, *cis* to alkyl chain), 1.58-1.53 (2H, m, =CHCH_2), 1.48-1.43 (2H, m, CH_2), 1.45 (9H, s, $C(CH_3)_3$); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.6

3. Prudente, C. K.; Hausman, M. C. *Bioconjugate Chem.* **2003**, *14*, 1270–1278.

(C=O), 137.6 (=CH), 115.1 (H_2C=), 80.9 (OC), 37.6 (CHN), 31.6 (=CHCH_2), 31.1 (CH_2N), 29.7 (CH_2), 27.9 (C(CH_3)$_3$); MS CI *m/z* (rel. int.) 198 (M + H^+, 10), 98 (100), 56 (30); HRMS *m/z* calcd for $C_{11}H_{20}NO_2$ requires 198.1494, found 198.1488.

Representative procedure 3 : (*R*)-*tert*-Butyl 2-(but-3-enyl)aziridine-1-carboxylate (–)-5b

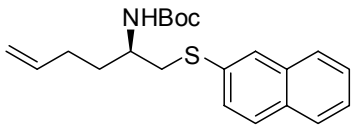


4-Nitrobenzoic acid (74 mg, 0.44 mmol) was added to a stirred suspension of (*R,R*)-(–)-*N,N'*-bis(3,5-di-*tert*-butylsalicylidene)-1,2-cyclohexanediaminocobalt (133 mg, 0.22 mmol) in *t*-BuOMe (1.5 mL) at room temperature with exposure to air. Following stirring for 30 min, *tert*-butyl carbamate (586 mg, 5.00 mmol) and *t*-BuOMe (0.5 mL) were added. Following stirring for 5 min, 1,2-epoxy-5-hexene (1.24 mL, 11.0 mmol) was added and the solution was stirred for 24 h. The suspension was filtered, washed with Et_2O (20 mL) and evaporated under reduced pressure. Purification of the residue by column chromatography (petroleum ether/Et_2O 4:1 to 7:3) gave (*S*)-*tert*-butyl 2-hydroxyhex-5-enyl carbamate as a crude brown oil contaminated with trace amounts of catalyst (1.05 g, 97%).

The brown oil was flushed with argon, dissolved in THF (12 mL), then tosyl chloride (1.29 g, 6.8 mmol) and potassium hydroxide (1.33 g, 23.7 mmol, freshly powdered) were added. Following stirring for 24 h, the suspension was filtered, washed with Et_2O (50 mL) and the filtrate was evaporated under reduced pressure. Purification of the residue by column chromatography (petroleum ether/Et_2O 4:1 to 7:3) gave *(R)-aziridine* (–)-**5b** as a colourless oil (751 mg, 78%).

$[\alpha]^{25}_D$ = –53.3 (*c* 1.0, $CHCl_3$); All other data matches that of racemic *tert*-butyl 2-(but-3-enyl)aziridine-1-carboxylate **5b** above.

(*R*)-*tert*-Butyl 1-(naphthalen-2-ylthio)hex-5-en-2-yl carbamate

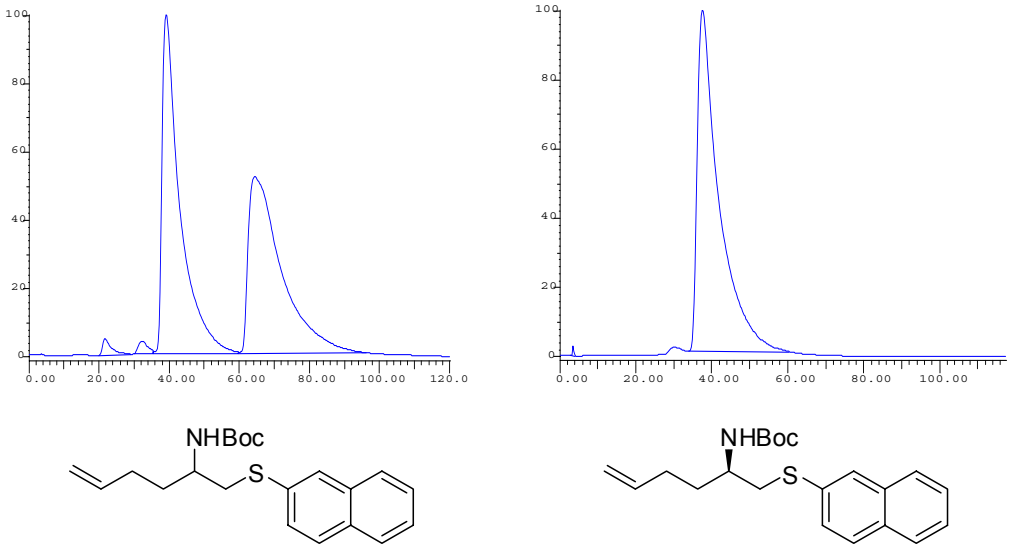


2-Napththalenethiol (89 mg, 0.56 mmol) was added to a stirring solution of *aziridine* (–)-**5b** (100 mg, 0.51 mmol) in MeOH (5 mL). The solution was cooled to 0 ºC and Et_3N (78 µL, 0.56 mmol) was added dropwise. The reaction was warmed to room temperature and stirred for 16 h. H_2O (5 mL) and Et_2O (10 mL) were added and the phases separated. The aqueous phase was extracted with Et_2O (3 × 10 mL). The combined organic phases were washed with H_2O (2 × 10 mL), dried ($MgSO_4$) and evaporated under reduced pressure. Purification of the residue by column chromatography (petroleum ether/Et_2O 96:4 to 94:6) gave (*R*)-*tert*-butyl 1-(naphthalen-2-ylthio)hex-5-en-2-yl carbamate as a white solid (115 mg, 63%).

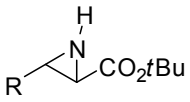
$[\alpha]^{22}_D$ = –10.3 (*c* 1.0, $CHCl_3$); (m.p. = 44–46 °C); R_f 0.15 (petroleum ether/Et_2O 94:6); IR (film) 3345br.m (N–H), 3055m, 2977s, 2931m, 1694s (C=O), 1641w, 1502s, 1416m, 1366m, 1269w, 1248m, 1169s, 1019m and 812s cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.86-7.75 (4H, m, 4 × $C_{Ar}H$), 7.50-7.42 (3H, m, 3 × $C_{Ar}H$), 5.79 (1H, ddt, *J* 14, 7, 7, =CH), 5.04-4.95 (2H, m, H_2C=), 4.67-4.65 (1H, m, NH), 3.93 (1H, br.s, C*H*NH), 3.28-3.14 (2H, m, CH_2S), 2.19-2.04 (2H, m, =CHCH_2), 1.82-1.74 (1H, m, CH(*H*)), 1.67-1.56 (1H, m, C*H*(H)), 1.40 (9H, s, $C(CH_3)_3$); ^{13}C NMR (100 MHz, $CDCl_3$) δ 155.3 (C=O), 137.6 (=CH), 133.9 ($C_{Ar\ quat}$), 133.8 (C_{Ar}), 131.8 (C_{Ar}), 128.5 (C_{Ar}), 127.7 (C_{Ar}), 127.5 (C_{Ar}), 127.3 ($C_{Ar\ quat}$), 127.1 ($C_{Ar\ quat}$), 126.6 (C_{Ar}), 125.7 (C_{Ar}), 115.2 (H_2C=), 79.3 (OC), 49.9 (CHNH), 39.2 (CH_2S), 33.1 (=CH*C*H_2), 30.2 (CH_2), 28.3 ($C(CH_3)_3$); MS CI *m/z* (rel. int.) 375 (M + NH_4^+, 15), 358 (M + H^+, 20), 319 (70), 284 (90), 258 (100); HRMS *m/z* calcd for $C_{21}H_{28}NO_2S$, 358.1835, found 358.1831.

The enantiomeric excess (>99%) was determined by chiral HPLC analysis, Chiralcel OJ column (250 × 4.6 mm), 99:1 heptane:EtOH, 1.0 ml/min. t_R = 37.49 min. Chiral

HPLC analysis of racemic *tert*-butyl 1-(naphthalen-2-ylthio)hex-5-en-2-yl carbamate: Chiralcel OJ column, 99:1 heptane:EtOH, 1.0 ml/min. t_R = 39.10 and 64.56 min.

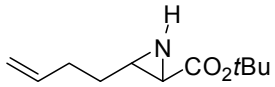


General procedure A: Synthesis of aziridinylesters



n-BuLi (1.6 M in hexanes, 0.94 mL, 1.5 mmol) was added dropwise to a stirred solution of 2,2,6,6-tetramethylpiperidine (0.25 mL, 1.5 mmol) in THF (3.8 mL) at –78 °C under argon. Following warming to room temperature for 30 min, the resulting solution was re-cooled to –78 °C and a solution of aziridine (0.50 mmol) in THF (1.5 mL) was added dropwise over 1 min. Following stirring for 90 min at –78 °C, saturated aqueous NH_4Cl (2 mL) was added and the flask was warmed to room temperature. The aqueous phase was washed with Et_2O (3 × 10 mL). The combined organic phase was dried ($MgSO_4$) and then evaporated under reduced pressure. Purification of the residue by column chromatography (petroleum ether/Et_2O, SiO_2) gave the aziridinylester.

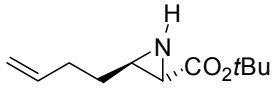
***tert*-Butyl (2*R**, 3*S**)-3-(but-3-enyl)aziridine-2-carboxylate 4b**



Following **General procedure A** using *aziridine* **5b** (99 mg, 0.5 mmol) gave, following purification of the resulting residue by column chromatography (petroleum ether/Et_2O 85:15) *aziridinylester* **4b** as a colourless oil (86 mg, 86%).

R_f 0.26 (petroleum ether/Et_2O 85:15); IR (neat) 3286br.m (N–H), 2980s, 2934m, 1721s (C=O), 1642m (C=C), 1430m, 1394m, 1369s, 1230s and 1163s cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 5.86-5.81 (1H, m, =CH), 5.06-4.97 (2H, m, H_2C=), 2.24-2.14 (4H, m, 2 × CHN, =CHCH_2), 1.54-1.47 (11H, m, CH_2, $C(CH_3)_3$), 1.23-1.21 (1H, m, NH); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.7 (C=O), 137.6 (=CH), 115.2 (H_2C=), 81.8 (OC), 38.6 (CHN), 36.2 (CHN), 31.9 (=CHCH_2), 31.3 (CH_2), 28.0 (OC(CH_3)$_3$); MS CI *m/z* (rel. int.) 198 ($M + H^+$, 100), 142 (30), 52 (90); HRMS *m/z* calcd for $C_{11}H_{20}NO_2$, 198.1489, found 198.1490.

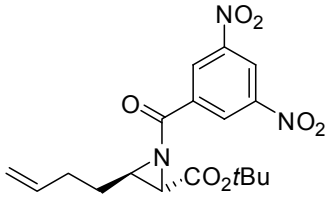
***tert*-Butyl (2*S*, 3*R*)-3-(but-3-enyl)aziridine-2-carboxylate** (+)-**4b**



Following **General procedure A** using *aziridine* (–)-**5b** (197 mg, 1.0 mmol, all other reagents were scaled accordingly) gave, following purification of the resulting residue by column chromatography (petroleum ether/Et_2O 85:15) *aziridinylester* (+)-**4b** as a colourless oil (165 mg, 84%).

$[\alpha]^{21}_D$ = +67.6 (*c* 1.0, $CHCl_3$); All other data matches that of racemic *tert*-butyl 3-(but-3-enyl)aziridine-2-carboxylate **4b** above.

***tert*-Butyl (2*S*,3*R*)-3-(but-3-enyl)-1-(3,5-dinitrobenzoyl)aziridine-2-carboxylate**

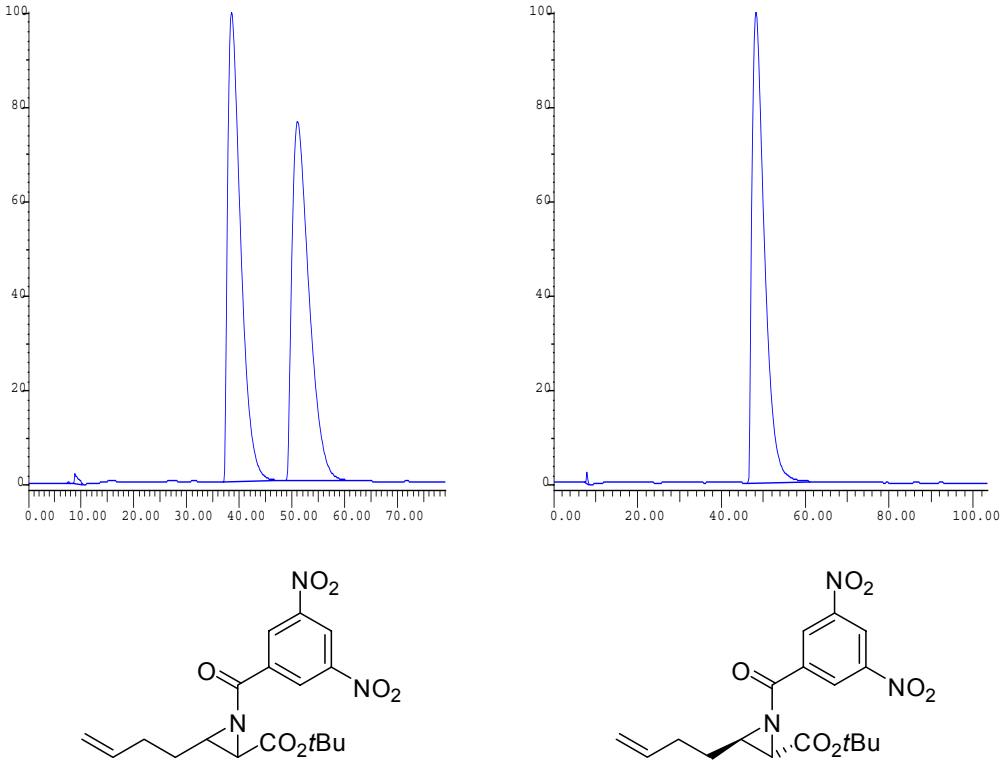


3,5-Dinitrobenzoyl chloride (63 mg, 0.28 mmol) was added in a single portion to a stirred solution of (2*S*, 3*R*)-*aziridinylester* (+)-**4b** (50 mg, 0.25 mmol) and Et_3N (42 µL, 0.30 mmol) in CH_2Cl_2 (4 mL) at room temperature under argon. Following stirring for 3 h, H_2O (10 mL) was added and the aqueous phase was washed with CH_2Cl_2 (2 × 10 mL). The combined organic phase was washed with H_2O (20 mL) dried ($MgSO_4$) and evaporated under reduced pressure. Purification of the residue by column chromatography (petroleum ether/Et_2O 9:1) gave the *aziridine derivative* as a white solid (90 mg, 92%).

$[\alpha]^{21}_D$ = –98.5 (*c* 1.0, $CHCl_3$); (m.p. = 79–81 °C); R_f 0.30 (petroleum ether/Et_2O 9:1); IR (film) 3110m, 2981s, 1725s (C=O), 1687s (C=C), 1546s, 1457m, 1345s, 1249m, 1162m, 1131m, 1075m and 916m cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 9.18 (1H, t, *J* 2, $C_{Ar}H$), 9.06 (2H, d, *J* 2, 2 × $C_{Ar}H$), 5.88 (1H, ddt, *J* 14, 7, 7, =CH), 5.16-5.05 (2H, m, H_2C=), 3.29 (1H, d, *J* 3, CHCO), 3.06 (1H, dt, *J* 7, 3, CHN), 2.36-2.30 (2H, m, =CHC*H*$_2$), 1.92-1.75 (2H, m, CH_2), 1.25 (9H, s, C(*C*H_3)$_3$); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.9 (C=O), 166.3 (C=O), 148.6 (2 × $C_{Ar\ quat}$), 137.6 (=CH), 136.5 ($C_{Ar\ quat}$), 127.9 (2 × C_{Ar}), 121.6 (C_{Ar}), 116.2 (H_2C=), 83.8 (OC), 44.2 (*C*HCO), 43.1 (CHN), 30.9 (=CH*C*H_2), 30.4 (CH_2), 27.6 (C(*C*H_3)$_3$); MS CI *m/z* (rel. int.) 409 (M + NH_4^+, 100), 392 (M + H^+, 30), 198 (45), 134 (35); HRMS *m/z* calcd for $C_{18}H_{22}N_3O_7$, 392.1452, found 392.1452.

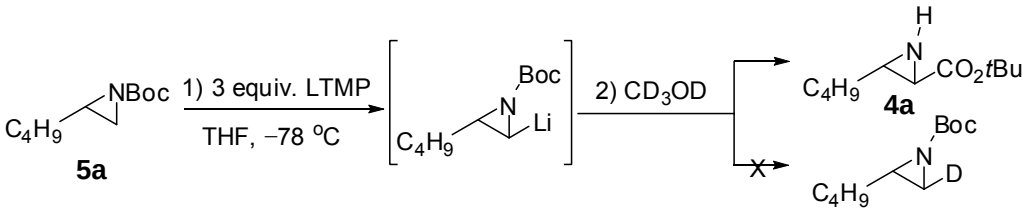
The enantiomeric excess (>99%) was determined by chiral HPLC analysis, Chiralcel OD column (250 × 4.6 mm), 99:1 heptane:EtOH, 0.5 ml/min. t_R = 48.17 min. Chiral HPLC analysis of racemic *tert*-butyl (2*R**,3*S**)-3-(but-3-enyl)-1-(3,5-

dinitrobenzoyl)aziridine-2-carboxylate: Chiralcel OD column, 99:1 heptane:EtOH, 0.5 ml/min. t_R = 38.47 and 51.02 min.



Experiments on the rate of the Boc [1,2] anionic rearrangement

Quenching the lithiation-induced migration reaction after various times with d_4-MeOH failed to show any incorporation of deuterium into starting material **5a** (Table 1, entries 1-4). The results indicate that lithiation is the slow rate-limiting step and that [1,2] shift is rapid, as the postulated intermediate α-lithiated aziridine could not be trapped by deuterium.

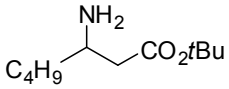


entry	time	yield of 5a (%)	yield of 4a (%)
1	90 s	50	31
2	5 min	42	37
3	60 min	2	88
4	90 min	0	90

Table 1

(III) Characterisation data for aziridinylester transformations (Scheme 3)

***tert*-Butyl 3-aminoheptanoate 8**

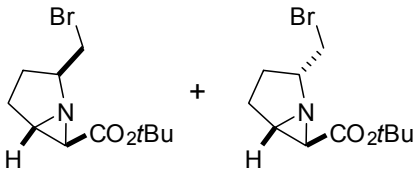


Raney-Ni (~0.1 mL, 50% w/v suspension in H_2O) was added to a stirred solution of *aziridinylester* **4b** (39 mg, 0.2 mmol) in EtOH (8 mL) at room temperature under argon. The flask was flushed with hydrogen twice and the reaction stirred under a balloon of hydrogen for 12 h. Celite (~50 mg) was added and the suspension was filtered through a plug of celite and washed with CH_2Cl_2 (50 mL). Following evaporation of the filtrate under reduced pressure, H_2O (10 mL) and CH_2Cl_2 (10 mL) were added. The aqueous phase was washed with CH_2Cl_2 (2 × 10 mL), the combined organic phase was dried (Na_2SO_4) and evaporated under reduced pressure to give *β-amino acid* **8** as a pale yellow oil (39 mg, 99%).

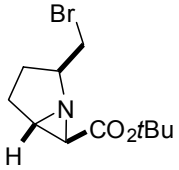
R_f 0.20 (CH_2Cl_2/MeOH/NH_4OH 97:2:1); IR (neat) 3376br.s (N–H), 2960s, 2931s, 2861m, 1727s (C=O), 1558w, 1458w, 1368s and 1153s cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 3.14-3.08 (1H, m, CHN), 2.37 (1H, dd, *J* 16, 4, CH(*H*)CO), 2.15 (1H, dd, *J* 16, 9, C*H*(H)CO), 1.59-1.22 (17H, m, NH_2, 3 × CH_2, $C(CH_3)_3$), 0.88 (3H, t, *J* 7, CH_3);

^{13}C NMR (100 MHz, $CDCl_3$) δ 172.1 (C=O), 80.4 (OC), 48.4 (CHN), 43.9 (*C*H_2CO), 37.2 (CH_2), 28.2 (CH_2), 28.1 (C(*C*H_3)$_3$), 22.7 (CH_2), 14.0 (CH_3); MS CI *m/z* (rel. int.) 202 (M + H^+, 100), 146 (40), 52 (30); HRMS *m/z* calcd for $C_{11}H_{24}NO_2$, 202.1802, found 202.1800.

tert-Butyl (2*R,5*R**,6*S**)-2-(bromomethyl)-1-azabicyclo[3.1.0]hexane-6-carboxylate 9 and _tert_-Butyl (2*R**,5*S**,6*R**)-2-(bromomethyl)-1-azabicyclo[3.1.0]hexane-6-carboxylate 9**

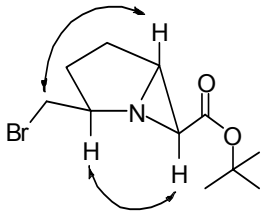


NBS (196 mg, 1.1 mmol) was added to a stirred solution of *aziridinylester* **4b** (197 mg, 1.0 mmol) in CH_2Cl_2 (20 mL) at room temperature under argon. Following stirring for 20 h, the solvent was removed under reduced pressure while maintaining the water bath at 20 °C. Purification of the residue by column chromatography (petroleum ether/Et_2O 4:1 to 7:3) gave *azabicycle syn*-**9** (61 mg, 22%) as a solid and *azabicycle anti*-**9** (201 mg, 73%) as a white solid.

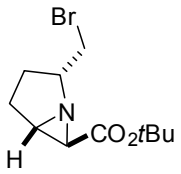


(m.p. = 55–57 °C); R_f 0.33 (petroleum ether/Et_2O 4:1);IR (film) 2976s, 1736s (C=O), 1410m, 1368m, 1327w, 1222m, 1155s and 969m cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.65–3.61 (1H, m, CH(*H*)Br), 3.58-3.53 (1H, m, C*H*CH_2Br), 3.17 (1H, app. t, *J* 9, C*H*(H)Br), 2.73 (1H, dd, *J* 5, 3, CHN), 2.20-2.06 (2H, m, CH_2), 2.04 (1H, d, *J* 3, CHCO), 1.91-1.85 (1H, m, CH(*H*)), 1.62-1.47 (10H, m, C*H*(H), C(CH_3)$_3$); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.5 (C=O), 81.6 (OC), 65.9 (*C*HCH_2Br), 47.1 (CHN), 38.5 (*C*HCO), 35.7 (CH_2Br), 28.1 (C(*C*H_3)$_3$), 24.8 (CH_2), 24.1 (CH_2); MS CI *m/z* (rel. int.)

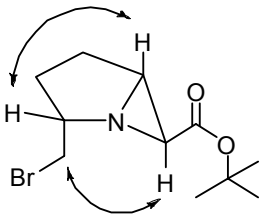
278 (^{81}BrM + H$^+$, 20), 276 (^{79}BrM + H$^+$, 25), 221 (100), 140 (50), 96 (75); HRMS *m/z* calcd for $C_{11}H_{19}NO_2{}^{79}Br$, 276.0599, found 276.0593.



nOe experiments: irradiation at 2.73 (CHN) saw reciprocal signal enhancement at 3.17 (C*H*(H)Br) and 3.65–3.61 (CH(*H*)Br); irradiation at 2.04 (CHCO) saw reciprocal signal enhancement at 3.58-3.53 (C*H*CH_2Br), no signal enhancement was observed at 3.17 (C*H*(H)Br) or 3.65-3.61 (CH(*H*)Br).

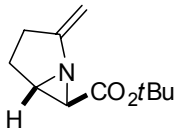


(m.p. = 46–48 °C); R_f 0.23 (petroleum ether/Et_2O 7:3); IR (film) 2977s, 1736s (C=O), 1408m, 1368w, 1333m, 1298m, 1120m, 1157s and 957m cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.70 (1H, dd, *J* 10, 5, CH(*H*)Br), 3.65-3.67 (1H, m, C*H*CH_2Br), 3.31 (1H, dd, *J* 10, 8, C*H*(H)Br), 2.77 (1H, dd, *J* 5, 3, CHN), 2.24 (1H, dd, *J* 14, 8, CH(*H*)), 2.18 (1H, d, *J* 3, CHCO), 2.09-1.99 (1H, m, C*H*(H)), 1.93-1.86 (1H, m, CH(*H*)), 1.46 (9H, s, $C(CH_3)_3$), 1.19-1.08 (1H, m, C*H*(H)); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.6 (C=O), 81.5 (OC), 65.1 (*C*HCH_2Br), 46.5 (CHN), 33.6 (*C*HCO), 32.7 (CH_2Br), 28.0 ($C(CH_3)_3$), 26.5 (CH_2), 25.3 (CH_2); MS CI *m/z* (rel. int.) 278 (^{81}BrM + H$^+$, 45), 276 (^{79}BrM + H$^+$, 45), 198 (100), 196 (40); HRMS *m/z* calcd for $C_{11}H_{19}NO_2{}^{79}Br$, 276.0594, found 276.0592.



nOe experiments: irradiation at 2.77 (CHN) saw reciprocal signal enhancement at 3.65-3.67 (C*H*CH_2Br); irradiation at 2.18 (CHCO) saw reciprocal signal enhancement at 3.31 (C*H*(H)Br), no signal enhancement was observed at 3.65-3.67 (C*H*CH_2Br).

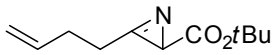
tert-Butyl (5*R,6*S**)-2-methylene-1-azabicyclo[3.1.0]hexane-6-carboxylate 10**



DBU (22 μL, 0.15 mmol) was added to a stirred solution of *azabicycle syn*-**9** (3.3 mg, 0.012 mmol) and *azabicycle anti*-**9** (11.7 mg, 0.038 mmol) in toluene (2 mL) under argon. The resultant emulsion was heated to reflux for 10 h. Following cooling, H_2O (5 mL) was added and the aqueous phase was washed with CH_2Cl_2 (10 mL). The combined organic phase was washed with H_2O (2 × 10 mL), brine (10 mL), dried ($MgSO_4$) and the CH_2Cl_2 was removed under reduced pressure. Purification of the toluene solution by column chromatography (petroleum ether to petroleum ether/Et_2O 4:1) gave *enamine* **10** as a colourless oil (8.9 mg, 92%).

R_f 0.40 (petroleum ether/Et_2O 4:1); IR (neat) 2977s, 1737s (C=O), 1665m (C=C), 1368m, 1327m, 1153s and 870w cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 5.24 (1H, s, =CH(*H*)), 4.64 (1H, s, =C*H*(H)), 2.96-2.94 (1H, m, CHN), 2.41-2.37 (1H, m, CH(*H*)), 2.25 (1H, d, *J* 3, CHCO), 2.21-2.07 (3H, m, C*H*(H), CH_2), 1.48 (9H, s, C(*C*H_3)$_3$); ^{13}C NMR (125 MHz, $CDCl_3$) δ 168.8 (C=O), 158.3 (=C), 101.8 (=CH_2), 81.6 (OC), 48.4 (CHN), 42.7 (CHCO), 27.8 (C(*C*H_3)$_3$, 25.8 (CH_2), 24.9 (CH_2); MS CI *m/z* (rel. int.) 196 (M + H^+, 5), 140 (100), 124 (40), 112 (45), 96 (95), 82 (30); HRMS *m/z* calcd for $C_{11}H_{18}NO_2$, 196.1338, found 196.1329.

tert-Butyl 3-(but-3-enyl)-2*H*-azirine-2-carboxylate 11



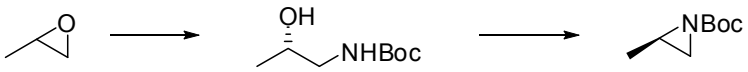
DMSO (0.23 mL, 3.3 mmol) was added to a stirred solution of oxalyl chloride (0.11 mL, 1.3 mmol) in CH_2Cl_2 (4.8 mL) at –78 °C under argon. Following stirring for 5 min, *aziridinylester* **4b** (99 mg, 0.5 mmol) in CH_2Cl_2 (2.4 mL) was added dropwise. Following stirring for a further 15 min, Et_3N (0.70 mL, 5.0 mmol) was added dropwise and the reaction was stirred for 5 min. Following warming to room temperature, the

suspension was stirred for 5 h. The solvent was evaporated, the residue was suspended in Et_2O (20 mL), filtered and washed with Et_2O (3 × 10 mL). The filtrate was then evaporated under reduced pressure. Purification of the residue by column chromatography (petroleum ether/Et_2O 95:5) gave *azirine* **11** as a colourless oil (90 mg, 92%).

R_f 0.18 (petroleum ether/Et_2O 95:5); IR (neat) 2980m, 2934m, 1790w (C=N), 1724m (C=O), 1644m, 1456w, 1393m, 1369s, 1256m, 1219m and 1156s cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 5.89 (1H, ddt, *J* 13, 7, 6, =CH), 5.16-5.07 (2H, m, H_2C=), 2.91 (2H, t, *J* 7, CH_2CN), 2.54-2.48 (2H, m, =CHCH_2), 2.35 (1H, s, CHN), 1.46 (9H, s, $C(CH_3)_3$); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.3 (C=O), 162.1 (C=N), 135.6 (=CH), 116.6 (H_2C=), 81.4 (OC), 29.8 (CHN), 28.2 (=CHCH_2), 28.1 ($C(CH_3)_3$), 26.2 (CH_2CN); MS CI *m/z* (rel. int.) 196 ($M + H^+$, 5), 140 (15), 123 (40), 98 (100), 82 (10); HRMS *m/z* calcd for $C_{11}H_{18}NO_2$, 196.1338, found 196.1346.

(IV) Characterisation data for (*S*)-azirinomycin *tert*-butyl ester (Scheme 4)

***tert*-Butyl (*R*)-2-methylaziridine-1-carboxylate 14**

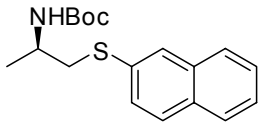


4-Nitrobenzoic acid (147 mg, 0.88 mmol) was added to a stirred suspension of (*R,R*)-(–)-*N,N'*-bis(3,5-di-*tert*-butylsalicylidene)-1,2-cyclohexanediaminocobalt (266 mg, 0.44 mmol) in *t*-BuOMe (3.0 mL) at room temperature with exposure to air. Following stirring for 30 min, *tert*-butylcarbamate (1.17 g, 10.0 mmol) and *t*-BuOMe (1.0 mL) were added. Following stirring for a further 5 min, propylene oxide (1.54 mL, 22.0 mmol) was added and the solution was stirred for 24 h. The suspension was filtered, washed with Et_2O (20 mL) and evaporated under reduced pressure. Purification of the residue by column chromatography (petroleum ether/Et_2O 6:4) gave *tert*-butyl (*S*)-2-hydroxypropyl carbamate **13** as a crude brown oil contaminated with trace

amounts of catalyst (1.75 g, 99%). The enantiomeric excess (>99%) was determined by chiral HPLC analysis of the 2-napthalenethiol derivative of aziridine **14**, see below. The brown oil was flushed with argon, dissolved in THF (25 mL), then tosyl chloride (2.67 g, 14.0 mmol) and potassium hydroxide (2.75 g, 49.0 mmol, freshly powdered) were added. Following stirring for 24 h, the suspension was filtered, washed with Et_2O (70 mL) and the filtrate was evaporated under reduced pressure. Purification of the residue by column chromatography (petroleum ether/Et_2O 95:5) gave *(R)-aziridine* **14** as a colourless oil (979 mg, 62%).

$[\alpha]^{20}_D$ = –40.1 (*c* 1.0, CH_2Cl_2), lit.[4] $[\alpha]^{20}_D$ = +39.2 (*c* 1.0, CH_2Cl_2) for *S*-enantiomer; R_f 0.24 (petroleum ether/Et_2O 95:5); IR (neat) 3065w, 2978s, 1926w, 1716s (C=O), 1458s, 1154s, 1089w and 1063w cm^{-1}; ^1H NMR (400 MHz; $CDCl_3$) δ 2.35-2.30 (1H, m, CHN), 2.13 (1H, d, *J* 6, CH(*H*)N, *trans* to alkyl chain), 1.77-1.75 (1H, m, C*H*(H)N, *cis* to alkyl chain), 1.35 (9H, s, $C(CH_3)_3$), 1.17-1.15 (3H, m, CH_3CHN); ^{13}C NMR (100 MHz; $CDCl_3$) δ 162.3 (C=O), 80.6 (OC), 33.4 (CHN), 32.3 (CH_2N), 27.8 ($C(CH_3)_3$), 17.3 (CH_3CHN); MS CI *m/z* (rel. int.) 280 (90), 190 (50), 158 ($M + H^+$, 100), 151 (100), 90 (50); HRMS *m/z* calcd for $C_8H_{16}NO_2$ requires 158.1176, found 158.1177.

tert-Butyl (_R_)-1-(naphthalen-2-ylthio)propan-2-yl carbamate



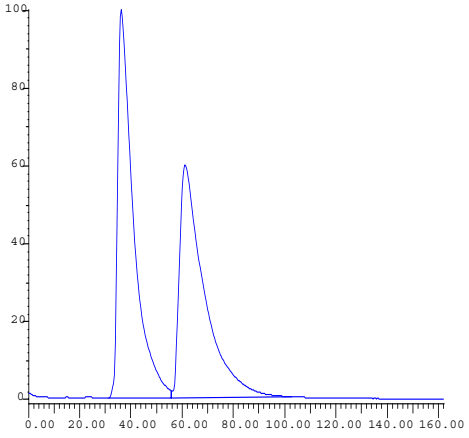
2-Napththalenethiol (88 mg, 0.55 mmol) was added to a stirring solution of *aziridine* **14** (100 mg, 0.50 mmol) in MeOH (5 mL). The solution was cooled to 0 ºC and Et_3N (77 µL, 0.55 mmol) was added dropwise. The reaction was warmed to room temperature and stirred for 16 h. H_2O (5 mL) and Et_2O (10 mL) were added and the phases separated. The aqueous phase was extracted with Et_2O (3 × 10 mL). The combined organic phases were washed with H_2O (2 × 10 mL), dried ($MgSO_4$) and

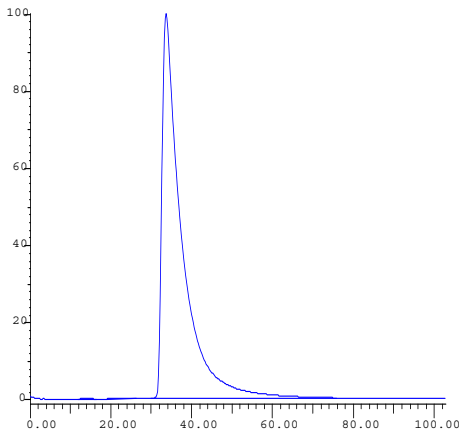
4. Wessig, P.; Schwarz, J. *Synlett* **1997**, 893–894.

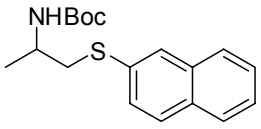
evaporated under reduced pressure. Purification of the residue by column chromatography (petroleum ether/Et_2O 95:5 to 9:1) gave (*R*)-*tert*-butyl 1-(naphthalen-2-ylthio)propan-2-yl carbamate as a white solid (138 mg, 76%).

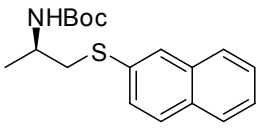
$[\alpha]^{21}_D$ = –22.4 (*c* 1.0, $CHCl_3$); (m.p. = 58–60 °C); R_f 0.21 (petroleum ether/Et_2O 9:1); IR (film) 3346br.m (N–H), 2976m, 1697s (C=O), 1502s, 1454m, 1391w, 1248m, 1170s and 744m cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.88 (1H, s, $C_{Ar}H$), 7.80-7.75 (3H, m, 3 × $C_{Ar}H$), 7.49-7.42 (3H, m, 3 × $C_{Ar}H$), 4.66 (1H, br.s, NH), 3.99 (1H, br.s, C*H*NH), 3.27 (1H, dd, *J* 13, 5, CH(*H*)S), 3.11-3.07 (1H, m, C*H*(H)S), 1.41 (9H, s, $C(CH_3)_3$), 1.27 (3H, d, *J* 7, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ 155.0 (C=O), 133.8 (C_{Ar}), 131.8 (C_{Ar}), 128.5 (2 × C_{Ar}), 127.7 (C_{Ar}), 127.4 (C_{Ar}), 127.1 (2 × C_{Ar}), 126.5 (C_{Ar}), 125.7 (C_{Ar}), 79.4 (OC), 46.2 (CHNH), 40.4 (CH_2S), 28.4 ($C(CH_3)_3$), 19.9 (CH_3); MS CI *m/z* (rel. int.) 318 (M + H+, 5), 244 (100), 218 (75), 201 (30); HRMS *m/z* calcd for $C_{18}H_{24}NO_2S$, 318.1528, found 318.1517.

The enantiomeric excess (>99%) was determined by chiral HPLC analysis, Chiralcel OJ column, 99:1 heptane:EtOH, 1 ml/min. t_R = 33.56 min. Chiral HPLC analysis of racemic *tert*-butyl 1-(naphthalen-2-ylthio)propan-2-yl carbamate: Chiralcel OJ column, 99:1 heptane:EtOH, 1 ml/min. t_R = 36.14 and 61.10 min.

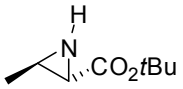








***tert*-Butyl (2*S*,3*R*)-3-methylaziridine-2-carboxylate 15**



Following **General procedure A** using *aziridine* **14** (940 mg, 5.98 mmol, all other reagents were scaled accordingly) gave, following purification of the resulting residue by column chromatography (petroleum ether/Et_2O 85:15) *aziridinylester* **15**[5] as a colourless oil (658 mg, 70%).

$[\alpha]^{20}_D$ = +63.7 (*c* 1.0, $CHCl_3$); R_f 0.19 (petroleum ether/Et_2O 85:15); IR (neat) 3286br.m (N–H), 2978s, 2932s, 1719s (C=O), 1457w, 1424m, 1369m, 1346m, 1229m, 1167s, 1150m, and 1016w cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 2.21-2.16 (2H, m, 2 × CHN), 1.48 (9H, s, $C(CH_3)_3$), 1.27-1.22 (4H, m, NH, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.8 (C=O), 81.9 (OC), 37.1 (CHN), 34.2 (CHN), 28.0 ($C(CH_3)_3$), 17.9 (CH_3); MS CI *m/z* (rel. int.) 175 ($M + NH_4^+$, 5), 158 ($M + H^+$, 100), 102 (15), HRMS *m/z* calcd for $C_8H_{16}NO_2$, 158.1176, found 158.1176.

***tert*-Butyl (*S*)-3-methyl-2H-azirine-2-carboxylate 16**

DMSO (1.79 mL, 25.2 mmol) was added to a stirred solution of oxalyl chloride (0.87 mL, 9.9 mmol) in CH_2Cl_2 (37 mL) at –78 °C under argon. Following stirring for 5 min, *aziridinylester* **15** (600 mg, 3.8 mmol) in CH_2Cl_2 (18 mL) was added dropwise. Following stirring for a further 15 min, Et_3N (5.3 mL, 38.2 mmol) was added dropwise and the reaction was stirred for 5 min. Following warming to room temperature, the suspension was stirred for 12 h. The solvent was evaporated, the residue was suspended in Et_2O (100 mL), filtered and washed with Et_2O (3 × 20 mL). The filtrate was then carefully evaporated under reduced pressure. Purification of the residue by

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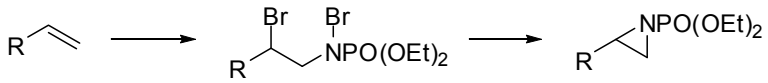
5. Serafin, S. V.; Zhang, K.; Aurelio, L.; Hughes, A. B.; Morton, T. H. *Org. Lett.* **2004**, *6*, 1561–1564.

column chromatography (petroleum ether/CH_2Cl_2 1:1 to 4:6) gave *azirine* **16**[6] as a volatile colourless oil (427 mg, 72%).

$[\alpha]^{21}_D$ = +58.6 (*c* 1.0, $CHCl_3$), lit.[6a] $[\alpha]^{20}_D$ –20.1 (97% pure, *c* 1.1, $CHCl_3$, *R*-enantiomer, 44% *ee*); R_f 0.18 (petroleum ether/CH_2Cl_2 4:6); IR (neat) 2980m, 1797m (C=N), 1724s (C=O), 1458w, 1393m, 1369s, 1346m, 1292w, 1218m and 1158s cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 2.51 (3H, s, CH_3), 2.35 (1H, s, CH), 1.46 (9H, s, $C(CH_3)_3$); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.2 (C=O), 159.4 (C=N), 81.5 (OC), 29.7 (CH), 28.1 ($C(CH_3)_3$), 12.6 (CH_3); MS CI *m/z* (rel. int.) 156 ($M + H^+$, 100), 123 (20), 102 (45), 100 (60), 83 (80); HRMS *m/z* calcd for $C_8H_{14}NO_2$, 156.1025, found 156.1029.

(V) Characterisation data for *N*-phosphonate aziridines and aziridinylphosphonates

General Procedure B: Synthesis of *N*-Phosphonate aziridines[7]



Alkene (1 equiv) was added to a stirred solution of $Br_2NPO(OEt)_2$[8] (1 equiv) in CH_2Cl_2 (15 mL) under argon at room temperature. Following stirring for 4 h under UV irradiation (256 nm) at room temperature, the flask was cooled to 0 °C and NaH (2 equiv) was added slowly. Following stirring at 0 °C for 30 min, the suspension was warmed to room temperature and stirred for a further 1 h. CH_2Cl_2 (10 mL) and H_2O (10 mL) were added and the organic phase was washed with H_2O (2 × 10 mL). The organic phase was dried ($MgSO_4$) and then evaporated under reduced pressure.

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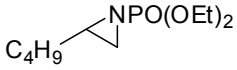
6. a) Verstappen, M. M. H.; Ariaans, G. J. A.; Zwanenburg, B. *J. Am. Chem. Soc*. **1996**, *118*, 8491–8492; b) Takashi Sakai, T.; Liu, Y.; Ohta, H.; Korenaga, T.; Ema, T. *J. Org. Chem.* **2005**, *70*, 1369–1375.
7. Zwierzak, A.; Zawadzki, S. *Synthesis* **1972**, 416–417.
8. Zawadzki, S.; Zwierzak, A. *Tetrahedron* **1973**, *29*, 315–320.

Purification of the residue by column chromatography (EtOAc/$CHCl_3$) gave the *N*-phosphonate aziridine.

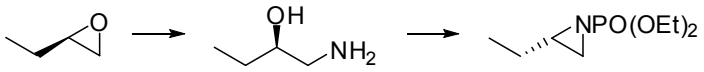
Diethyl 2-butylaziridin-1-ylphosphonate 18a[9]



Following **General procedure B** using 1-hexene (0.64 g, 7.6 mmol) gave, following purification of the resulting residue by column chromatography (EtOAc/$CHCl_3$ 1:2) *aziridine* **18a** as a pale yellow oil (1.02 g, 57%).

R_f 0.54 (EtOAc/$CHCl_3$ 1:2); IR (neat) 2933s, 2873m, 1651w, 1467w, 1394w, 1264s (P=O), 1034s and 967s cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 4.17-4.10 (4H, m, 2 × OCH_2), 2.35-2.33 (1H, m, NCH), 2.31 (1H, dd, *J* 18, 6, CH(*H*)N), 1.88 (1H, dd, *J* 10, 4, C*H*(H)N), 1.51-1.36 (6H, m, 3 × CH_2), 1.33 (6H, t, *J* 7, CH_3), 0.90 (3H, t, *J* 7, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ 63.2 (2 × $POCH_2$, t, $J_{C\text{-}P}$ 8), 36.8 (CHN, d, $J_{C\text{-}P}$ 7), 32.2 (*C*H_2CH), 30.8 (NCH_2, d, $J_{C\text{-}P}$ 7), 29.0 (CH_2), 22.3 (*C*H_2CH_3), 16.3 (2 × OCH_2*C*H_3, t, $J_{C\text{-}P}$ 6), 13.9 (CH_3); ^{31}P NMR (162 MHz, $CDCl_3$) δ 16.3; MS CI *m/z* (rel. int.) 236 (M + H^+, 100), 220 (20), 193 (90), 166 (45), 150 (80), 136 (20), 98 (35); HRMS calcd for $C_{10}H_{23}NO_3{}^{31}P$, 236.1416, found 236.1419.

Diethyl (*S*)-2-ethylaziridin-1-ylphosphonate 18h



(*R*)-1-Aminobutan-2-ol

NH_4OH (25% aq., 6.0 mL) was added to a stirred solution of (*R*)-1,2-epoxybutane (0.86 mL, 10.0 mmol) in MeCN (2.0 mL) at room temperature. The colourless solution was heated in a sealed tube at 100 °C for 1 h. Following cooling and

9. Osowska-Pacewicka, K.; Zwierzak, A. *J. Prakt. Chem.* **1986**, *328*, 441–444.

evaporation, bulb-to-bulb distillation (9 mbar, 125 °C) gave (*R*)-aminobutan-2-ol as a colourless oil (622 mg, 70%).

$[\alpha]^{20}_D$ = +7.3 (*c* 1.0, $CHCl_3$), lit.[10] $[\alpha]^{20}_D$ +7.3 (*c* 0.99, $CHCl_3$); IR (neat) 3353br,m (N–H, O–H), 2928s, 2858m, 1577m, 1467m and 1074w cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 3.46-3.40 (1H, m, OCH), 2.80 (1H, dt, *J* 13, 4, 3, CH(*H*)N), 2.51 (1H, dt, *J* 10, 5, 4 C*H*(H)N), 2.24 (3H, br, NH_2, OH), 1.47-1.39 (2H, m, C$H_2$$CH_3$), 0.94 (3H, t, *J 8*, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ 73.4 (CHO), 46.9 (CH_2N), 27.6 (*C*$H_2$$CH_3$), 10.0 ($CH_3$); MS FI *m/z* (rel. int.) 90 (M + H^+, 100), 60 (40); HRMS calcd for $C_4H_{12}NO$, 90.0919, found 90.0917.

Diethyl (*S*)-2-ethylaziridin-1-ylphosphonate **18h**[11]

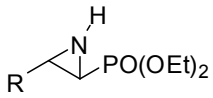
Diethyl chlorophosphate (1.95 mL, 13.5 mmol) was added to a stirred solution of (*R*)-1-aminobutan-2-ol (600 mg, 6.7 mmol) and Et_3N (2.81 mL, 20.2 mmol) in THF (60 mL) at room temperature under argon. Following stirring for 20 h, NaH (60% w/w dispersion in mineral oil, 1.62 g, 40.4 mmol) was added and the suspension was stirred for a further 16 h. H_2O (0.75 mL) was added and the suspension was filtered through a plug of $MgSO_4$ and washed with Et_2O (100 mL). Following removal of the solvent under reduced pressure, column chromatography (EtOAc/$CHCl_3$ 1:2) gave *aziridine* **18h** as a pale yellow oil (725 mg, 52%).

$[\alpha]^{20}_D$ = +2.32 (*c* 1.0, $CHCl_3$); R_f 0.55 (EtOAc/$CHCl_3$ 1:2); IR (neat) 2982s, 1466m, 1394m, 1260s (P=O), 1032s and 971s cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 4.16-4.09 (4H, m, 2 × OCH_2), 2.48-2.38 (1H, m, NCH), 2.29 (1H, dd, *J* 10, 6, CH(*H*)N), 1.88 (1H, dd, *J* 10, 4, C*H*(H)N), 1.57-1.40 (2H, m, CH_2), 1.31 (6H, t, *J* 7, 2 × OCH_2C*H*$_3$), 0.98 (3H, t, *J* 8, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ 63.2 (2 × OCH_2, t, $J_{C\text{-}P}$ 7), 38.1 (CHN, d, $J_{C\text{-}P}$ 6), 30.5 (CH_2N, d, $J_{C\text{-}P}$ 7), 25.5 (CH_2, d, $J_{C\text{-}P}$ 5), 16.3 (2 × OCH_2*C*H_3, d,

10. Iwaneka, W.; Wolftb, C.; Mattayc, J. *Tetrahedron Lett.* **1995**, *36*, 8969–8972.
11. Prepared by analogy with *N*-diphenylphosphinoyl aziridines: Osborn, H. M. I.; Cantrill, A. A.; Sweeney, J. B.; Howson, W. *Tetrahedron Lett.* **1994**, *35*, 3159–3162.

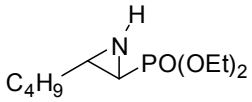
$J_{C\text{-}P}$ 6), 10.9 (CH_3); ^{31}P NMR (162 MHz, $CDCl_3$) δ 15.3; MS CI *m/z* (rel. int.) 208 (M + H^+, 97), 154 (10), 100 (30), 72 (100), 96 (90); HRMS calcd for $C_8H_{19}NO_3{}^{31}P$, 208.1103, found 208.1101.

General procedure C: Synthesis of *N*-H aziridinylphosphonates



n-BuLi (1.6 M in hexanes, 2.30 mL, 3.7 mmol) was added dropwise to a stirred solution of TMP (0.63 mL, 3.7 mmol) in THF (15 mL) at –78 °C under argon. Following warming to room temperature for 30 min, the resulting solution was re-cooled to –78 °C and a solution of aziridine (0.74 mmol) in THF (1 mL) was added dropwise over 1 min. Following stirring for 1 - 4 h at –78 °C, sat. aqueous NH_4Cl (2 mL) was added and the flask was warmed to room temperature. The aqueous phase was washed with Et_2O (3 × 10 mL), the combined organic phase was dried ($MgSO_4$) and then evaporated under reduced pressure. Purification of the residue by column chromatography (EtOAc/$CHCl_3$/MeOH 1:1:0.05, SiO_2) gave the aziridinylphosphonate.

Diethyl (2*R,3*S**)-3-butylaziridin-2-ylphosphonate 19a**

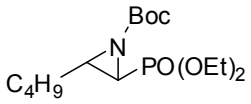


Following **General procedure C** using *aziridine* **18a** (175 mg, 0.74 mmol) for 4 h gave, following purification of the resulting residue by column chromatography (EtOAc/$CHCl_3$/MeOH 1:1:0.05), *aziridinylphosphonate* **19a** as a pale yellow oil (159 mg, 91%).

R_f 0.40 (EtOAc/$CHCl_3$/MeOH 1:1:0.05); IR (neat) 3250br.m (N–H), 2932s, 1653w, 1458m, 1393w, 1233s (P=O), 1127s (P–O–C) and 968s cm^{-1}; ^1H NMR (400 MHz,

$CDCl_3$) δ 4.16-4.07 (4H, m, 2 × OCH_2), 2.33-2.31 (1H, m, CHN), 1.59 (1H, dd, *J* 4, 8, CHP), 1.51-1.32 (13H, m, 3 × CH_2, NH, 2 × OCH_2CH_3), 0.89 (3H, t, *J* 7, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ 62.3 (2 × OCH_2, t, J_{C-P} 7), 34.9 (CHN), 32.8 (CH_2CH), 29.5 (PCHN, d, J_{C-P} 139), 29.3 (CH_2), 22.3 (CH_2), 16.4 (2 × CH_3, d, J_{C-P} 3), 13.9 (CH_3); ^{31}P NMR (162 MHz, $CDCl_3$) δ 27.33; MS CI *m/z* (rel. int.) 236 ($M + H^+$, 100), 206 (83), 98 (99), 84 (24); HRMS calcd for $C_{10}H_{23}NO_3{}^{31}P$, 236.1416, found 236.1408.

tert-Butyl (2*R,3*S**)-2-butyl-3-(diethoxyphosphoryl)aziridine-1-carboxylate**

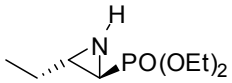


Di-*tert*-butyl dicarbonate (186 mg, 0.85 mmol) was added to a stirred solution of *aziridinylphosphonate* **19a** (50 mg, 0.21 mmol) and DMAP (29 mg, 0.23 mmol) in CH_2Cl_2 (5 mL) at 0 °C under argon. Following stirring for 2 h, the solution was warmed to room temperature and stirred for 48 h. saturated aqueous NH_4Cl (2 mL) was added and the organic phase was washed with H_2O (2 mL), dried (Na_2SO_4) and evaporated under reduced pressure. Purification by column chromatography (EtOAc/$CHCl_3$ 1:2) gave *tert*-butyl (2*R**,3*S**)-2-butyl-3-(diethoxyphosphoryl)aziridine-1-carboxylate as a pale yellow oil (61mg, 85%).

R_f 0.64 (EtOAc/$CHCl_3$ 1:2); IR (neat) 2980s, 1725s (C=O), 1394m, 1321s, 1257s, 1160s (P=O), 1027s and 970s cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 4.24-4.13 (4H, m, 2 × OCH_2), 2.77-2.71 (1H, m, NCH), 2.30 (1H, dd, *J* = 15, 4, CHP), 1.58-1.25 (21H, m, $C(CH_3)_3$, 3 × CH_2, 2 × OCH_2CH_3), 0.92 (3H, t, *J* 7, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.4 (C=O), 81.9 (OC), 62.9 ($POCH_2$, d, J_{C-P} 6), 62.4 ($POCH_2$, d, J_{C-P} 6), 41.5 (CN, d, J_{C-P} 3), 35.3 (CHP, d, J_{C-P} 197), 30.7 (CH_2CH), 28.9 (CH_2), 27.9 ($C(CH_3)_3$), 22.2 (CH_3CH_2), 16.4 (2 × OCH_2CH_3, t, J_{C-P} 5), 13.9 (CH_3); ^{31}P NMR (162 MHz, $CDCl_3$) δ 21.22; MS CI *m/z* (rel. int.) 336 ($M + H^+$, 100); HRMS calcd for $C_{15}H_{30}NNaO_5{}^{31}P$ 358.1754, found 358.1756.

$^3J_{HH}$ = 4 Hz for *tert*-butyl (2*R**,3*S**)-2-butyl-3-(diethoxyphosphoryl)aziridine-1-carboxylate.[12]

Diethyl (2*S*,3*S*)-(3-ethylaziridin-2-yl)phosphonate 19h

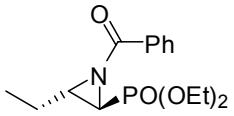


Following **General procedure C** using *aziridine* **18h** (100 mg, 0.48 mmol, all other reagents were scaled accordingly) for 4 h gave, following purification of the resulting residue by column chromatography (EtOAc/$CHCl_3$/MeOH 1:1:0.05) *aziridinylphosphonate* **19h** as a pale yellow oil (89 mg, 89%). The enantiomeric excess (>99% ee) was determined by chiral HPLC analysis of the benzoate derivative, see below.

$[\alpha]^{20}_D$ = –16.5 (*c* 1.0, $CHCl_3$); R_f 0.50 (EtOAc/$CHCl_3$/MeOH 1:1:0.05); IR (neat) 3289br (N–H), 2985s, 1648m, 1464m, 1394m, 1227s (P=O) and 1026s cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 4.17-4.09 (4H, m, 2 × OCH_2), 2.32 (1H, br.s, CHN), 1.61-1.42 (4H, m, CHP, NH, CH_2), 1.34 (6H, t, *J* 7, 2 × OCH_2CH_3), 1.01 (3H, t, *J* 8, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ 62.4 ($POCH_2$, d, $J_{C\text{-}P}$ 6), 62.3 ($POCH_2$, d, $J_{C\text{-}P}$ 6), 36.1 (CHN), 28.2 (PC, d, $J_{C\text{-}P}$ 186), 26.0 (CH_2), 16.4 (OCH_2CH_3, t, $J_{C\text{-}P}$ 5), 11.1 (CH_3); ^{31}P NMR (162 MHz, $CDCl_3$) δ 26.5; MS CI *m/z* (rel. int.) 208 ($M + H^+$, 80), 98 (30), 72 (40), 70 (100); HRMS calcd for $C_8H_{19}NO_3{}^{31}P$, 208.1103, found 208.1103.

12. For related aziridinylphosphonates *trans* $^3J_{HH}$ = 2-3 Hz and cis $^3J_{HH}$ = 6-7 Hz: Pousset, C.; Larcheveque, M. *Tetrahedron Lett.* **2002**, *43*, 5257–5260.

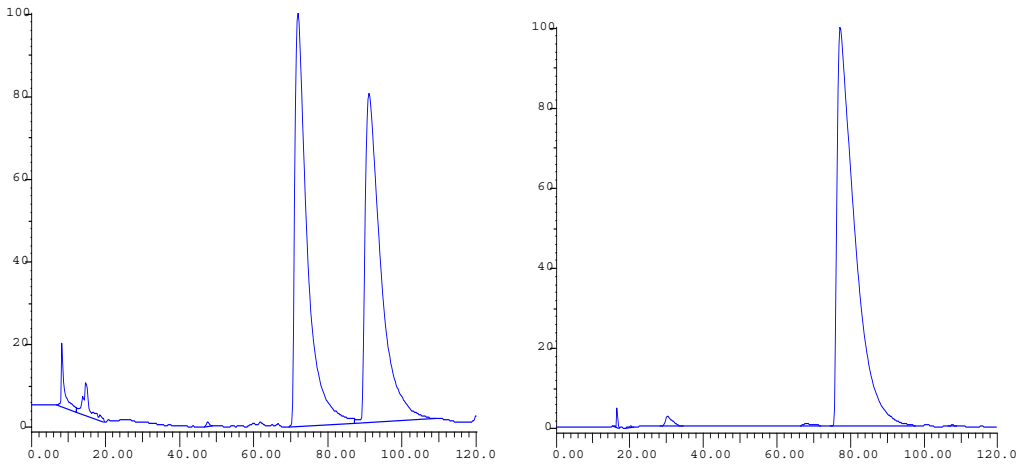
Diethyl (2*R*,3*S*)-1-benzoyl-3-ethylaziridin-2-ylphosphonate



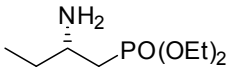
Benzoyl chloride (49 mg, 0.35 mmol) was added to a stirred solution of *aziridinylphosphonate* **19h** (60 mg, 0.29 mmol) and Et_3N (49 μL, 0.35 mmol) in CH_2Cl_2 (3 mL) at room temperature under argon. Following stirring for 2 h, H_2O (10 mL) was added and the aqueous phase was washed with CH_2Cl_2 (3 × 5 mL), the combined organic phase was dried ($MgSO_4$) and evaporated under reduced pressure. Purification of the residue by column chromatography (EtOAc/$CHCl_3$ 1:2) gave diethyl (2*R*,3*S*)-1-benzoyl-3-ethylaziridin-2-ylphosphonate as a colourless oil (81 mg, 90%).

$[\alpha]^{20}_D$ = +14.8 (*c* 1.0, $CHCl_3$); R_f 0.60 (EtOAc/$CHCl_3$ 1:2); IR (neat) 3289br.m (N–H), 2985s, 1678s (C=O), 1451w, 1254s (P=O), 1025s, 968m and 723m cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.05-8.03 (2H, m, 2 × $C_{Ar}H$), 7.58-7.54 (1H, m, $C_{Ar}H$), 7.47-7.43 (2H, m, 2 × $C_{Ar}H$), 4.20-4.09 (4H, m, 2 × OCH_2), 3.16-3.10 (1H, m, NCH), 2.66 (1H, dd, *J* 14, 4, CHP), 1.77-1.66 (1H, m, $CH_3CH(H)$), 1.35 (3H, t, *J* 7, OCH_2CH_3), 1.31 (3H, t, *J* 7, OCH_2CH_3), 1.14-1.03 (1H, m, $CH_3CH(H)$), 0.97 (3H, t, *J* 8, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ 176.3 (C=O), 133.2 ($C_{Ar\ quat}$), 132.9 (2 × C_{Ar}), 129.1 (2 × C_{Ar}), 128.4 (C_{Ar}), 63.1 (OCH_2, d, J_{C-P} 6), 62.5 (OCH_2, d, J_{C-P} 6), 44.9 (CHN, d, J_{C-P} 4), 34.4 (PC, J_{C-P} 201), 24.3 (CH_2), 16.4 (OCH_2CH_3, t, J_{C-P} 6), 11.0 (CH_3); ^{31}P NMR (162 MHz, $CDCl_3$) δ 20.1; MS CI *m/z* (rel. int.) 312 ($M + H^+$, 15), 174 (100), 156 (40), 105 (35); HRMS calcd for $C_{15}H_{23}NO_4{}^{31}P$, 312.1365, found 312.1370.

The enantiomeric excess (>99%) was determined by chiral HPLC analysis, Chiralcel OJ-H column (250 × 4.6 mm), 98:2 hexane:*i*-PrOH, 0.25 ml/min. t_R = 76.2 min. Chiral HPLC analysis of racemic diethyl (2*R**,3*S**)-1-benzoyl-3-ethylaziridin-2-ylphosphonate: Chiralcel OJ-H column, 98:2 hexane:*i*-PrOH, 0.25 ml/min. t_R = 71.8 and 90.1 min.



Diethyl (*S*)-(2-aminobutyl)phosphonate (+)-20



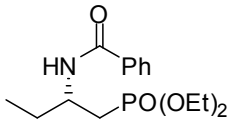
Ammonium formate (304 mg, 4.83 mmol) was added to a stirred suspension of *aziridinylphosphonate* **19h** (50 mg, 0.24 mmol) and Pd/C (10% palladium on carbon, 10 mg, 0.01 mmol) in MeOH (5 mL) at room temperature under argon. Following stirring at reflux for 16 h, the suspension was cooled and NH_4OH (25% aqueous solution) was added until pH > 8. The aqueous phase was washed with CH_2Cl_2 (3 × 5 mL), the combined organic phase was dried ($MgSO_4$) and evaporated under reduced pressure. Purification by column chromatography (CH_2Cl_2 to CH_2Cl_2/MeOH/NH_4OH 96:3:1) gave *β-amino phosphonate* **20**[13] as a colourless oil (34 mg, 68%). The enantiomeric excess (>99% ee) was determined by chiral HPLC analysis of the benzoate derivative, see below.

$[\alpha]^{20}_D$ = +16.3 (*c* 0.58, MeOH), lit.[13b] $[\alpha]^{20}_D$ +7.3 (*c* 2.3, MeOH, 64% ee); R_f 0.12 (CH_2Cl_2/MeOH/NH_4OH 96:3:1); IR (neat) 3423br.m (N–H), 1643m, 1209w (P=O) and

13. a) Palacios, F.; Aparicio, D.; Ochoa de Retana, A. M.; de los Santos, J. M.; Gil, J. I.; de Munain, R. L. *Tetrahedron: Asymmetry* **2003**, *14*, 689–700; b) Yuan, C.; Xu, C.; Zhang, Y. *Tetrahedron* **2003**, *59*, 6095–6102.

1025m cm^{-1}; ^1H NMR (250 MHz, CD_3OD) δ 4.20-4.09 (4H, m, 2 × OCH_2), 3.14-3.04 (1H, m, CHN), 2.09-1.99 (1H, m, CH(*H*)P), 1.88-1.80 (1H, m, C*H*(H)P), 1.63-1.45 (2H, m, CH_2), 1.35 (6H, t, *J* 7, 2 × OCH_2CH_3), 0.97 (3H, t, *J* 8, CH_3); ^{13}C NMR (100 MHz, CD_3OD) δ 63.6 ($POCH_2$, d, J_{C-P} 6), 48.7 (CHN, d, J_{C-P} 4), 33.6 (PCH_2, d, J_{C-P} 138), 31.7 (CH_2, d, J_{C-P} 14), 16.9 (2 × OCH_2CH_3, d, J_{C-P} 6), 10.5 (CH_3); ^{31}P NMR (162 MHz, CD_3OD) δ 31.4; MS CI *m/z* (rel. int.) 210 ($M + H^+$, 100), 193 (30), 153 (35); HRMS calcd for $C_8H_{21}NO_3{}^{31}P$, 210.1259, found 210.1256.

Diethyl (*S*)-2-benzamidobutylphosphonate

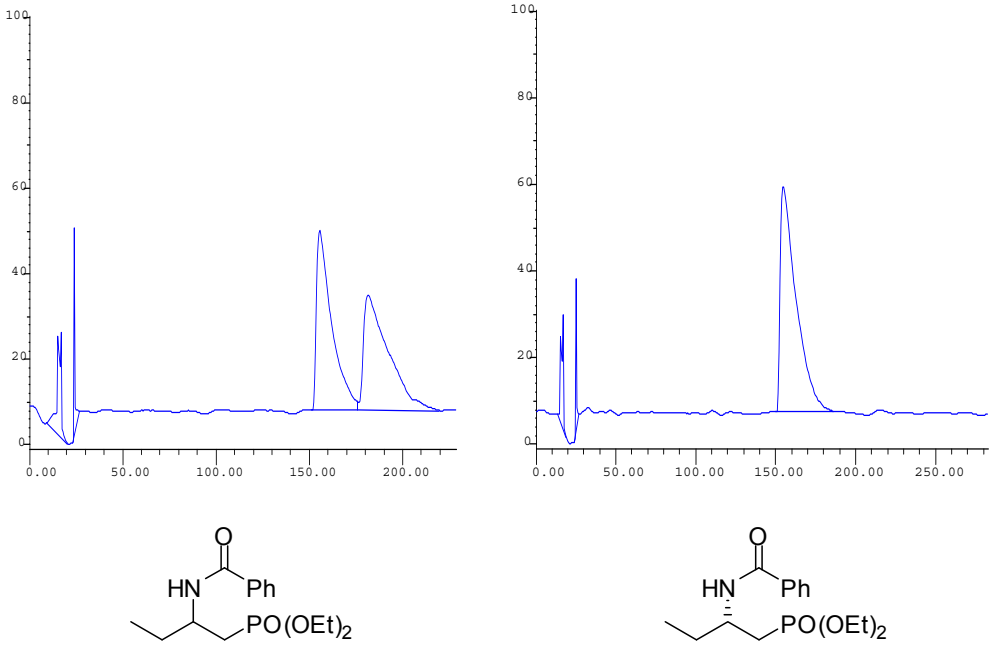


Benzoyl chloride (32 mg, 0.23 mmol) was added to a stirred solution of *β-amino phosphonate* **20** (40 mg, 0.19 mmol) and Et_3N (32 µL, 0.23 mmol) in CH_2Cl_2 (3 mL) at room temperature under argon. Following stirring for 2 h, H_2O (10 mL) was added, the aqueous phase was washed with CH_2Cl_2 (3 × 5 mL), the combined organic phase was dried ($MgSO_4$) and evaporated under reduced pressure. Purification by column chromatography (EtOAc/$CHCl_3$ 1:2) gave diethyl (*S*)-2-benzamidobutylphosphonate as a colourless oil (54 mg, 91%).

$[\alpha]^{20}_D$ = –28.6 (*c* 0.3, $CHCl_3$); R_f 0.36 (EtOAc/$CHCl_3$ 1:2); IR (neat) 3304br.m (N–H), 2934s, 1713s (C=O), 1579s, 1226s (P=O), 1053s, 959s and 712m cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.87-7.84 (2H, m, 2 × $C_{Ar}H$), 7.49-7.38 (3H, m, 3 × $C_{Ar}H$), 4.48-4.32 (1H, m, NCH), 4.20-4.03 (4H, m, 2 × OCH_2), 2.17-2.11 (2H, m, PCH_2), 1.89-1.70 (2H, m, CH_2), 1.34 (3H, t, *J* 7, OCH_2CH_3), 1.28 (3H, t, *J* 7, OCH_2CH_3), 0.98 (3H, t, *J* 8, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.7 (C=O), 134.5 ($C_{Ar\ quat}$), 131.3 (2 × C_{Ar}), 128.5 (2 × C_{Ar}), 127.0 (C_{Ar}), 62.1 (OCH_2, J_{C-P} 6), 61.5 (OCH_2, J_{C-P} 6), 46.9 (CHN, J_{C-P} 6), 29.2 (CHP, J_{C-P} 139), 28.3 (CH_2, J_{C-P} 5), 16.4 (2 × OCH_2CH_3, t, J_{C-P} 6), 10.7 (CH_3); ^{31}P NMR (162 MHz, $CDCl_3$) δ 30.3; MS CI *m/z* (rel. int.) 314 ($M + H^+$, 100), 193 (20),

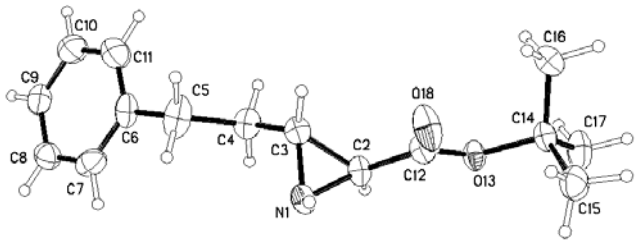
131 (20), 122 (25), 103 (15), 87 (10); HRMS calcd for $C_{15}H_{25}NO_4{}^{31}P$, 314.1521, found 314.1529.

The enantiomeric excess (>99%) was determined by chiral HPLC analysis, Chiralcel OJ-H column, 98:2 hexane:*i*-PrOH, 0.25 ml/min. t_R = 156.2 min. Chiral HPLC analysis of racemic diethyl 2-benzamidobutylphosphonate: Chiralcel OD-H column, 98:2 hexane:*i*-PrOH, 0.25 ml/min. t_R = 155.4 and 181.7 min.



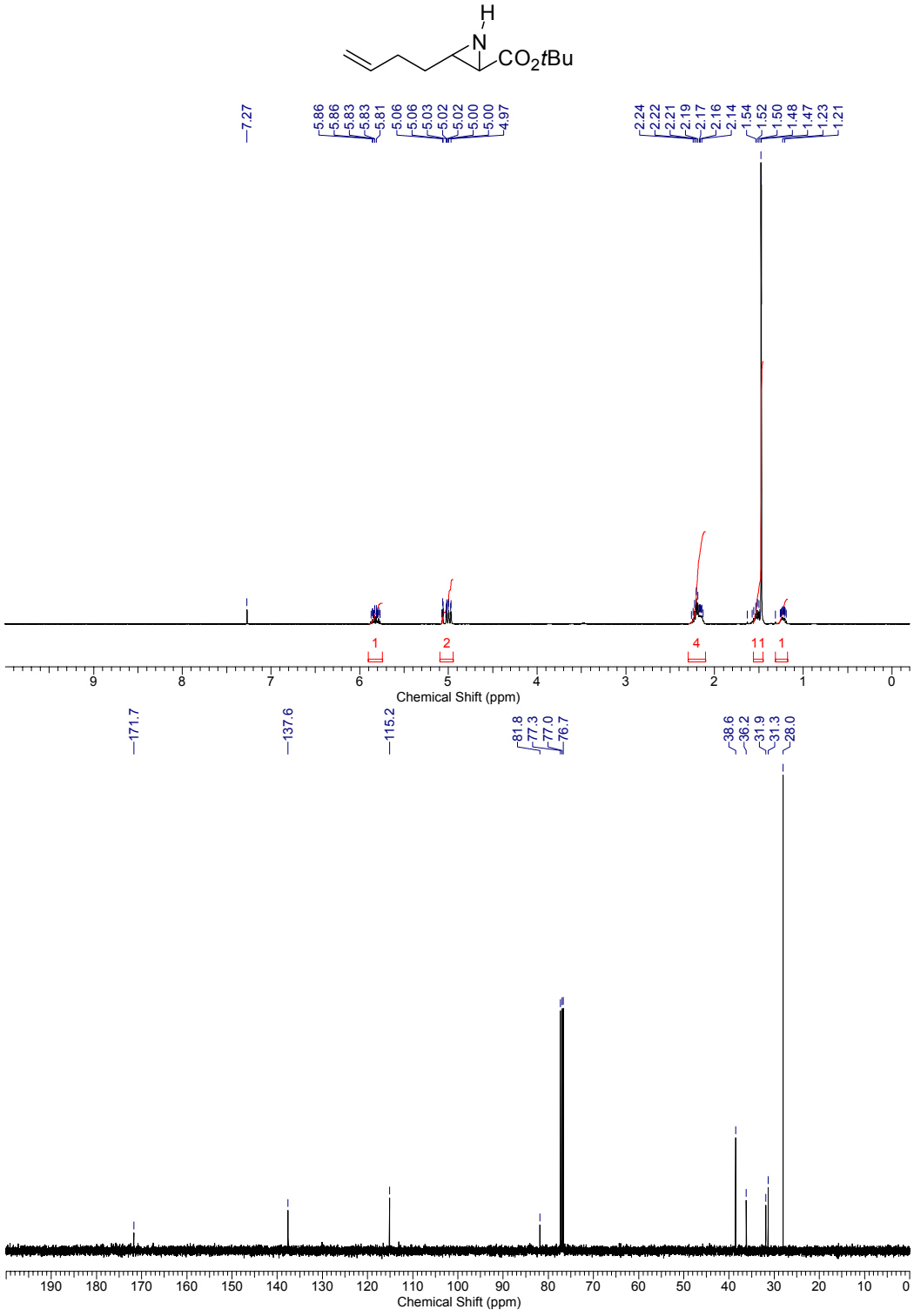
(VI) X-ray structure and representative NMR spectra

X-Ray structure of aziridinylester 4c[14]

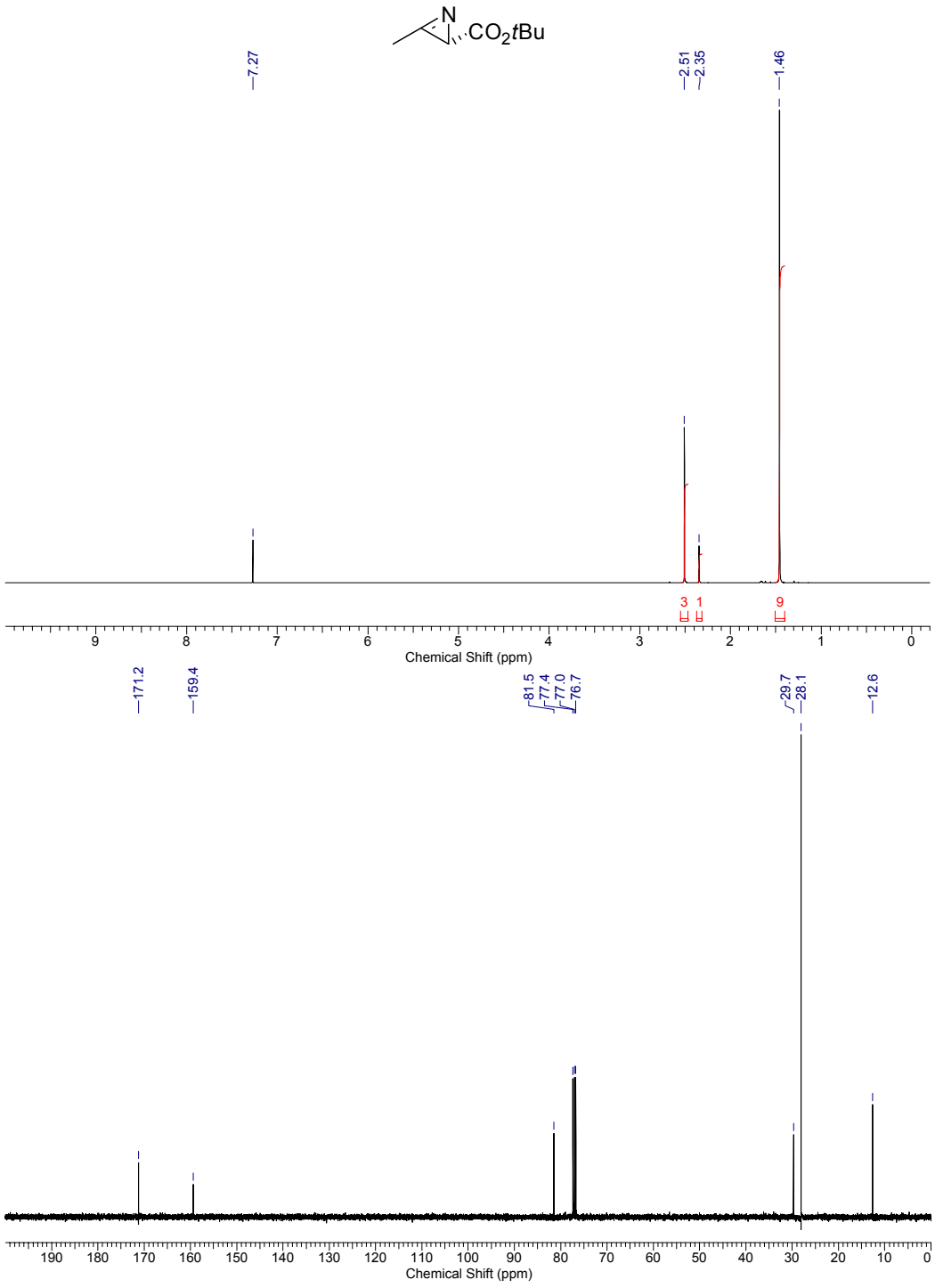


14. CDC 635326 available at http://www.ccdc.cam.ac.uk.

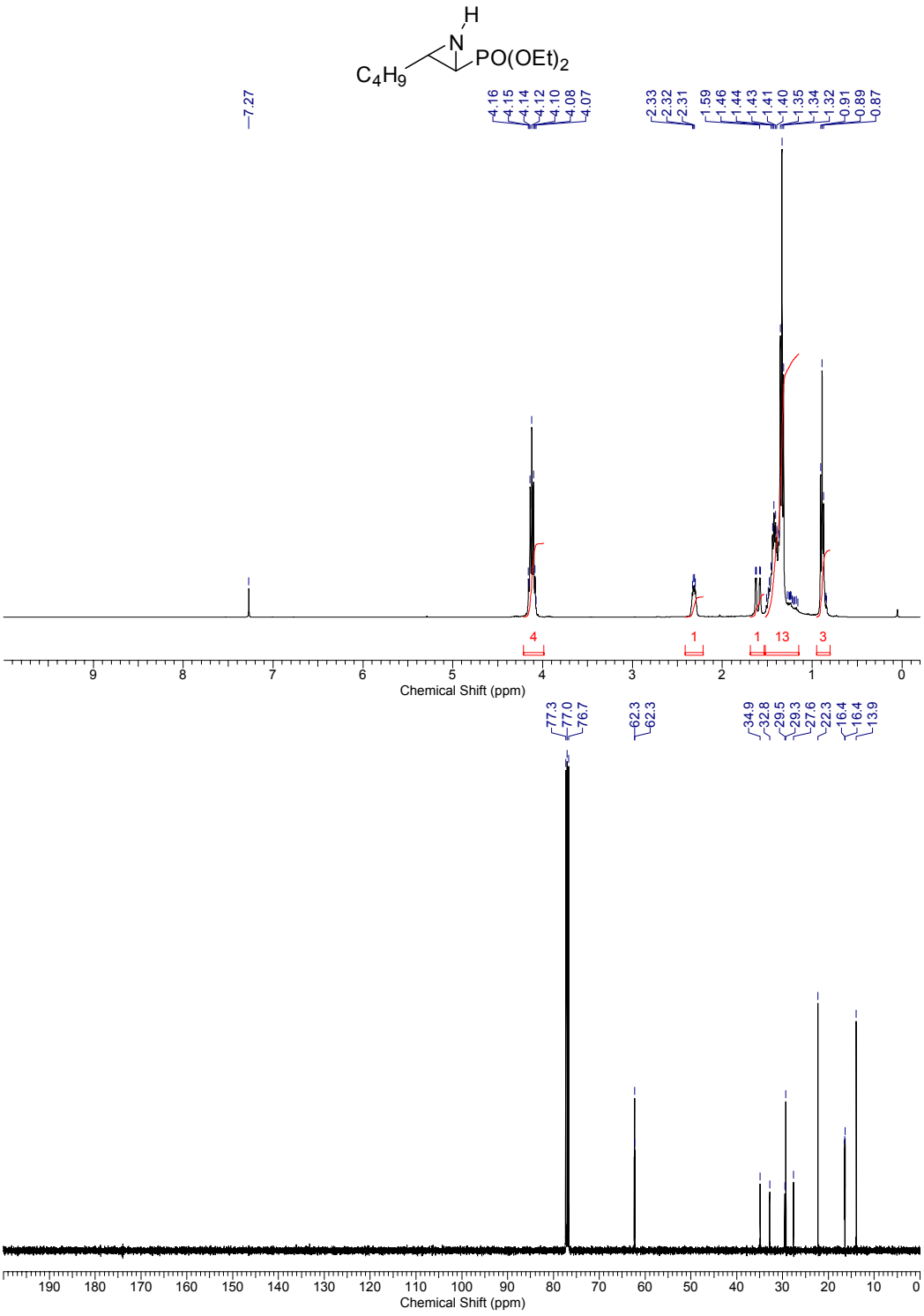
tert-Butyl (2_R_*,3_S_*)-3-(but-3-enyl)aziridine-2-carboxylate 4b



tert-Butyl (_S_)-3-methyl-2H-azirine-2-carboxylate 16



Diethyl (2*R,3*S**)-3-butylaziridin-2-ylphosphonate 19a**



Diethyl (*S*)-2-aminobutylphosphonate (+)-20