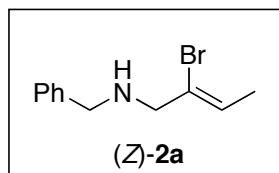


Rare Example of Nucleophilic Substitution at Vinylic Carbon with Inversion: Mechanism of Methyleneaziridine Formation by Sodium Amide Induced Ring Closure Revisited

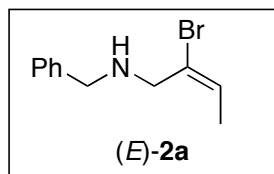
Jason J. Shiers, Michael Shipman,* Jerome F. Hayes, and Alexandra M.Z. Slawin

Supporting Information

General Method A: Preparation of Allylic Amines 2, 10. To the alcohol and triethylamine (2.5 eq.) in THF (n mL) cooled to -30 °C was added methanesulfonyl chloride (1.05 eq.) dropwise. The reaction mixture was warmed to 0 °C over the course of 1 h and then maintained at this temperature for a further 30 min. The amine (2 eq.) was added dropwise to the mixture and after stirring at 0 °C for 10 min, the mixture heated under reflux for 18h. The mixture was cooled and partitioned between diethyl ether (n mL) and 10% NaOH solution ($2n$ mL). The organic phase was washed 10% NaOH solution ($2n$ mL) and brine ($2n$ mL), dried (MgSO_4) and evaporated to give the crude product which was purified by column chromatography on silica gel.

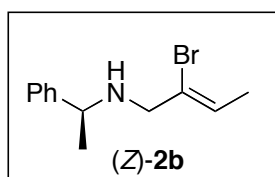


(Z)-Benzyl-(2-bromobut-2-enyl)-amine 2a. Methanesulfonyl chloride (2.40 mL, 31.0 mmol), (Z)-2-bromobut-2-en-1-ol (4.46 g, 29.5 mmol), benzylamine (6.45 mL, 59.1 mmol) and triethylamine (10.3 mL, 73.8 mmol) were reacted together in THF (50 mL) as described in General Method A. Purification (10% EtOAc in petroleum ether) gave (Z)-2a (6.48 g, 92%) as a clear colourless oil. R_f 0.45 (40% EtOAc in petroleum ether); ν_{max} (film) 3318, 1658, 1495, 1454 cm^{-1} ; δ_{H} (400 MHz, CDCl_3) 7.35-7.26 (5H, m, Ph), 5.93 (1H, qt, $J = 6.5, 0.9$ Hz, CH), 3.71 (2H, s, CH_2Ph), 3.49 (2H, s, CH_2CBr), 2.02 (1H, bs, NH), 1.80 (3H, d, $J = 6.5$ Hz, CH_3); δ_{C} (100 MHz, CDCl_3) 139.8 (C, aryl), 128.4 (CH, aryl), 128.3 (CH, aryl), 128.2 ($=\text{CBr}$), 127.1 (CH), 125.7 ($=\text{CH}$), 57.1 (CH_2Ph), 51.4 (CBrCH_2), 16.7 (CH_3); HRMS (Cl^+) calcd for $\text{C}_{11}\text{H}_{15}^{79}\text{BrN}$ $[\text{MH}]^+$ 240.0364, found 240.0388.



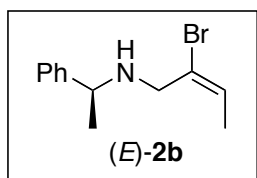
(E)-Benzyl-(2-bromobut-2-enyl)-amine 2a. Methanesulfonyl chloride (3.77 mL, 48.7 mmol), (E)-2-bromobut-2-en-1-ol (7.00 g, 46.4 mmol), benzylamine (10.2 mL, 93.4 mmol) and triethylamine (16.0 mL, 115 mmol) were reacted together in THF (100 mL) as described in General Method A. Purification (10% ether in petroleum ether) gave (E)-2a (9.28 g, 83%) as a clear colourless oil. R_f 0.20 (40% ether in petroleum ether); ν_{max} (film) 3329, 3059, 3026, 1644, 1603,

1494, 1452 cm^{-1} ; δ_{H} (400 MHz, CDCl_3) 7.35-7.15 (5H, m, Ph), 6.12 (1H, q, $J = 7.3$ Hz, =CH), 3.72 (2H, s, CH_2Ph), 3.51 (2H, CH_2CBr), 2.03 (1H, bs, NH), 1.60 (3H, d, $J = 7.3$ Hz, CH_3); δ_{C} (100 MHz, CDCl_3) 139.7 (C, aryl), 129.7 (CH), 128.44 (CH, aryl), 128.36 (CH, aryl), 127.1 (=CH), 125.3 (=CBr), 51.3 (CH_2Ph), 50.1 (CBrCH_2), 15.1 (CH_3); HRMS (EI^+) calcd for $\text{C}_{11}\text{H}_{13}^{79}\text{BrN}$ $[\text{M}-\text{H}]^+$ 238.0231, found 238.0231. Anal. Calcd for $\text{C}_{11}\text{H}_{14}\text{BrN}$: C, 55.0%; H, 5.9%; N, 5.8%. Found: C, 54.7%; H, 5.8%; N, 5.7%.



[(Z)-2-bromobut-2-enyl]-[(S)-1-phenylethyl]-amine 2b.

Methanesulfonyl chloride (3.07 mL, 39.7 mmol), (Z)-2-bromobut-2-en-1-ol (5.70 g, 37.7 mmol), (S)-1-phenylethylamine (9.73 mL, 75.5 mmol) and triethylamine (13.2 mL, 94.7 mmol) were reacted together in THF (75 mL) as described in General Method A. Purification (10% EtOAc in petroleum ether) gave **(Z)-2b** (6.55 g, 68%) as a clear colourless oil. R_f 0.46 (20% EtOAc in petroleum ether); $[\alpha]_{\text{D}}^{21} -55$ (c 1.0, CHCl_3); ν_{max} (film) 3335, 3082, 3062, 3024, 1657, 1602, 1492, 1450 cm^{-1} ; δ_{H} (400 MHz, CDCl_3) 7.36-7.23 (5H, m, Ph), 5.79 (1H, q, $J = 6.5$ Hz, =CH), 3.78 (1H, q, $J = 6.6$ Hz, NCHCH_3), 3.39 (1H, d, $J = 14.5$ Hz, NCHH), 3.29 (1H, d, $J = 14.5$ Hz, NCHH), 1.86 (1H, br s, NH), 1.77 (3H, d, $J = 6.5$ Hz, = CHCH_3), 1.36 (3H, d, $J = 6.6$ Hz, CHCH_3); δ_{C} (100 MHz, CDCl_3) 145.0 (C, aryl), 128.5 (CH, aryl), 128.4 (=CBr), 127.1 (CH, aryl), 126.9 (CH), 125.5 (CH), 55.6 (NCHAr), 55.5 (CH_2), 24.3 (NCHCH_3), 16.6 (=CH CH_3); MS (CI^+) m/z 254 (100%, $[\text{MH}]^+$), 238 (25%, $[\text{M}-\text{CH}_3]^+$), 174 (10%, $[\text{M}-\text{Br}]^+$); HRMS (CI^+) calcd for $\text{C}_{12}\text{H}_{17}^{79}\text{BrN}$ $[\text{MH}]^+$ 254.0544, found 254.0522. Anal. Calcd for $\text{C}_{12}\text{H}_{16}\text{BrN}$: C, 56.7%; H, 6.3%; N, 5.5%. Found: C, 56.7%; H, 6.7%; N, 5.5%.

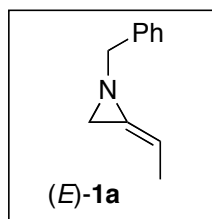


[(E)-2-bromobut-2-enyl]-[(S)-1-phenylethyl]-amine 2b.

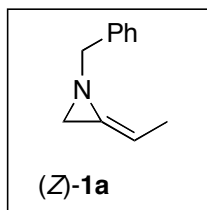
Methanesulfonyl chloride (1.24 mL, 16.0 mmol), (E)-2-bromobut-2-en-1-ol (2.30 g, 15.2 mmol), (S)-1-phenylethylamine (3.93 mL, 30.5 mmol) and triethylamine (5.30 mL, 38.0 mmol) were reacted together in THF (30 mL) as described in General Method A. Purification (10% ether in petroleum ether) gave **(E)-2b** (2.89 g, 75%) as a clear colourless oil. R_f 0.32 (20% EtOAc in petroleum ether); $[\alpha]_{\text{D}}^{21} -36.5$ (c 1.0, CHCl_3); ν_{max} (film) 3334, 3062, 3025, 1645, 1603, 1492, 1449 cm^{-1} ; δ_{H} (400 MHz, CDCl_3) 7.37-7.24 (5H, m, Ph), 6.05 (1H, q, $J = 7.2$ Hz, =CH), 3.78 (1H, q, $J = 6.5$ Hz, NCHCH_3), 3.40 (1H, d, $J = 14.7$ Hz, NCHH), 3.28 (1H, d, $J = 14.7$ Hz, NCHH), 1.92 (1H, br s, NH), 1.41 (3H, d, $J = 7.2$ Hz, =CH CH_3), 1.35 (3H, d, $J = 6.5$ Hz, NCHCH_3); δ_{C} (100 MHz, CDCl_3) 145.0 (C, aryl), 129.3 (CH), 128.4 (CH, aryl), 127.1 (CH, aryl), 127.0 (CH, aryl), 125.8 (C), 55.5 (NCHAr), 48.6 (CH_2), 24.8 (NCHCH_3), 14.9 (=CH CH_3); MS (CI^+) m/z 254 (100%, $[\text{MH}]^+$), 238 (30%, $[\text{M}-\text{CH}_3]^+$); HRMS (CI^+) calcd for $\text{C}_{12}\text{H}_{17}^{79}\text{BrN}$ $[\text{MH}]^+$ 254.0544, found

254.0522. Anal. Calcd for C₁₂H₁₆BrN: C, 56.7%; H, 6.3%; N, 5.5%. Found: C, 56.7%; H, 6.4%; N, 5.2%.

General Method B: Synthesis of Methyleneaziridines 1. A three-necked flask was fitted with a cold-finger condenser and a gas inlet. Iron(III) nitrate nonahydrate (0.25 mol%) was added and the system was flushed with CaCl₂ dried ammonia. A dry-ice/acetone mixture was added to the condenser and ammonia (50 mL) was condensed into the flask. Freshly cut sodium (2.5 eq.) was added in small portions. The initially formed blue solution slowly faded to give a grey suspension of sodium amide. After cooling to –78°C, the allylamine (50% w/v in diethyl ether) was added slowly to the mixture, which was subsequently stirred for 1 h. The mixture was diluted with diethyl ether (10 mL) and quenched by the dropwise addition of water (5 mL) (CAUTION). After the ammonia had evaporated, diethyl ether (50 mL) was added and the mixture was stirred for 2 min. The organic phase was separated and washed 0.1M acetic acid (5 x 50 mL), then 10% NaOH (2 x 50 mL) and finally brine (50 mL), then dried (MgSO₄). Removal of the solvent under reduced pressure and subsequent bulb-to-bulb distillation yielded the product.

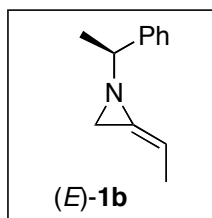


(E)-1-Benzyl-2-ethylideneaziridine 1a. Generation of sodium amide from sodium (600 mg, 26.1 mmol) and iron(III) nitrate nonahydrate (12.0 mg, 0.03 mmol) in ammonia (50 mL) and subsequent reaction with (*Z*)-**2a** (2.50 g, 10.4 mmol) for 1 h at –78 °C as described in General Method B, followed by work-up and bulb-to-bulb distillation (*ca* 60 °C / 1 mmHg) gave (*E*)-**1a** (603 mg, 37%) as a pale yellow oil. *R*_f 0.54 (40% EtOAc in petroleum ether); *v*_{max} (film) 1781, 1496, 1453 cm⁻¹; *δ*_H (400 MHz, CDCl₃) 7.45-7.25 (5H, m, Ph), 5.20 (1H, qt, *J* = 6.7, 1.4 Hz, =CH), 3.64 (2H, br s, NCH₂Ph), 2.18 (2H, br s, aziridine), 1.78 (3H, d, *J* = 6.7 Hz, =CHCH₃); *δ*_C (75 MHz, CDCl₃) 138.7 (C, aryl), 130.1 (=CN), 128.4 (CH, aryl), 128.2 (CH, aryl), 127.2 (CH, aryl), 95.0 (=CH), 63.4 (CH₂Ph), 30.5 (CH₂, aziridine), 14.2 (CH₃); HRMS (Cl⁺) calcd for C₁₁H₁₄N [MH]⁺ 160.1126, found 160.1119.

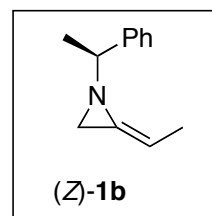


(Z)-1-Benzyl-2-ethylideneaziridine 1a. Generation of sodium amide from sodium (600 mg, 26.1 mmol) and iron(III) nitrate nonahydrate (12.0 mg, 0.03 mmol) in ammonia (50 mL) and subsequent reaction with (*E*)-**2a** (2.50 g, 10.4 mmol) for 1 h at –78 °C in ammonia as described in General Method B, followed by work-up and bulb-to-bulb distillation (*ca* 50 °C / 0.4 mmHg) gave (*Z*)-**1a** (1.28 g, 77%) as a pale yellow oil. The isolated (*Z*)-**1a** contained (*E*)-**1a** (8%) which

reflects the presence of (*Z*)-**2a** (7%) in the starting material. R_f 0.42 (40% EtOAc in petroleum ether); ν_{\max} (film) 1778, 1495, 1453 cm^{-1} ; δ_H (400 MHz, CDCl_3) 7.39-7.24 (5H, m, Ph), 5.11 (1H, q, $J = 6.8$ Hz, $=\text{CHCH}_3$), 3.71 (2H, br s, CH_2Ph), 2.10 (2H, br s, aziridine), 1.70 (3H, d, $J = 6.8$ Hz, CH_3); δ_C (75 MHz, CDCl_3) 138.5 (C, aryl), 129.9 ($=\text{CN}$), 128.4 (CH, aryl), 128.3 (CH, aryl), 127.3 (CH, aryl), 95.2 ($=\text{CHCH}_3$), 62.1 (CH_2Ph), 31.3 (CH_2 , aziridine), 13.4 (CH_3); MS (EI^+) 159 (6%, M^+), 91 (100%, $[\text{PhCH}_2]^+$); HRMS (CI^+) calcd for $\text{C}_{11}\text{H}_{14}\text{N}$ $[\text{MH}]^+$ 160.1121, found 160.1120.

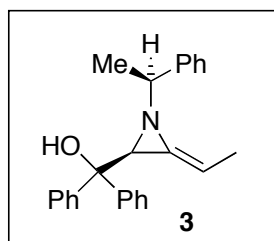


(E)-1-[(S)-1-phenylethyl]-2-ethylideneaziridine 1b. Generation of sodium amide from sodium (500 mg, 21.7 mmol) and iron(III) nitrate nonahydrate (8.8 mg, 0.02 mmol) in ammonia (50 mL) and subsequent reaction with (*Z*)-**2b** (2.21 g, 8.69 mmol) for 1 h at -78 °C as described in General Method B, followed by work-up and bulb-to-bulb distillation (*ca* 50 °C / 0.1 mmHg) gave (*E*)-**1b** (865 mg, 57%) as a pale yellow oil. The isolated (*E*)-**1b** contained (*Z*)-**1b** (6%) which reflects the presence of (*E*)-**2b** (6%) in the starting material. R_f 0.46 (20% EtOAc in petroleum ether); $[\alpha]_D^{21} -152$ (*c* 1.0, CHCl_3); ν_{\max} (film) 1777, 1604, 1492, 1450 cm^{-1} ; δ_H (400 MHz, d_6 -DMSO) 7.36-7.21 (5H, m, Ph), 4.98 (1H, br s, $=\text{CH}$), 2.84 (1H, q, $J = 6.6$ Hz, NCHCH_3), 2.05 (1H, br s, aziridine), 1.95 (1H, br s, aziridine), 1.66 (3H, d, $J = 6.6$ Hz, $=\text{CHCH}_3$), 1.36 (3H, d, $J = 6.6$ Hz, CHCH_3Ph); δ_C (100 MHz, d_6 -DMSO) 144.7 (C, aryl), 131.3 ($=\text{CN}$), 128.6 (CH, aryl), 127.4 (CH, aryl), 127.1 (CH, aryl), 93.1 ($=\text{CHCH}_3$), 68.1 (CHAr), 29.3 (CH_2 , ring), 23.8 (CHCH_3Ph), 14.7 ($=\text{CHCH}_3$); HRMS (CI^+) calcd for $\text{C}_{12}\text{H}_{16}\text{N}$ $[\text{MH}]^+$ 174.1283, found 174.1278. Enantiomeric excess determined by treatment of (*E*)-**1b** (5 mg) with (*S*)-2,2,2-trifluoro-1-(9-anthryl)-ethanol (16 mg) in CDCl_3 (0.75 mL) and subsequent integration of the following ^1H NMR regions: δ_H (500 MHz) 1.375-1.345 (0.03H, minor), 1.335-1.295 (0.97H, major). Racemic material used to spike the mixture and verify the analysis.



(Z)-1-[(S)-1-phenylethyl]-2-ethylideneaziridine 1b. Generation of sodium amide from sodium (600 mg, 26.1 mmol) and iron(III) nitrate nonahydrate (12.0 mg, 0.03 mmol) in ammonia (50 mL) and subsequent reaction with (*E*)-**2b** (2.64 g, 10.4 mmol) for 1 h at -78 °C as described in General Method B, followed by work-up and bulb-to-bulb distillation (*ca* 75 °C / 1 mmHg) gave (*Z*)-**1b** (1.67 g, 93%) as a pale yellow oil. The isolated (*Z*)-**1b** contained (*E*)-**1b** (9%) which reflects the presence of (*Z*)-**2b** (8%) in the starting material. R_f 0.46 (20% EtOAc in petroleum ether); $[\alpha]_D^{21} -213$ (*c* 1.0, CHCl_3); ν_{\max} (film) 1780, 1601, 1493, 1450 cm^{-1} ; δ_H (400 MHz, d_6 -DMSO) 7.38-7.22 (5H, m, Ph), 4.93 (1H, q, $J = 6.7$ Hz, $=\text{CH}$), 2.98 (1H, q, $J = 6.6$ Hz, NCHCH_3), 2.06 (1H, br s, aziridine), 1.94 (1H, br s, aziridine), 1.39 (3H, d, $J = 6.6$ Hz,

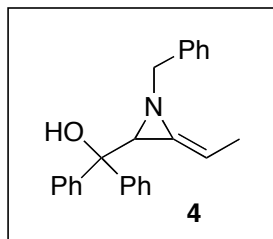
CHCH₃Ph), 1.26 (3H, br s, =CHCH₃); δ_C (100 MHz, d₆-DMSO) 145.0 (C, aryl), 130.6 (=CN), 128.7 (CH, aryl), 127.5 (CH, aryl), 127.4 (CH, aryl), 93.9 (=CHCH₃), 67.4 (CHAr), 29.4 (CH₂, aziridine), 23.9 (CHCH₃Ph), 14.2 (=CHCH₃); HRMS (CI⁺) calcd for C₁₂H₁₆N [MH]⁺ 174.1283, found 174.1290. Enantiomeric excess determined by treatment of (Z)-**1b** (5 mg) with (S)-2,2,2-trifluoro-1-(9-anthryl)-ethanol (32 mg) in CDCl₃ (0.75 mL) and subsequent integration of the following ¹H NMR regions: δ_H (500 MHz) 1.485-1.450 (0.05H, minor), 1.450-1.415 (0.95H, major). Racemic material used to spike the mixture and verify the analysis.



[(Z)-2-ethylidene-1-[(S)-1-phenylethyl]aziridin-3-yl]diphenylmethanol 3.

To a stirred solution of (Z)-**1b** (218 mg, 1.26 mmol) and TMEDA (227 μ L, 1.50 mmol) in THF (10 mL) at -78°C was added *sec*-butyllithium (1.3M in hexanes, 1.25 mL, 1.63 mmol) dropwise. The resulting solution was stirred at -78°C for 5 h, then benzophenone (297 mg, 1.63 mmol) in THF (1 mL) added dropwise.

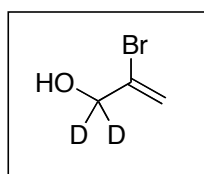
After 10 min, the mixture was warmed to room temperature and stirred overnight. The mixture was partitioned between water (25 mL) and diethyl ether (25 mL), and the aqueous layer washed with diethyl ether (2 x 25 mL). The combined organic phases were washed with brine (75 mL), dried (MgSO₄) and the solvent removed *in vacuo*. To remove unreacted benzophenone, the crude product was dissolved in ethanol (20 mL) and cooled to 0°C . Sodium borohydride (108 mg, 2.85 mmol) was added and the mixture warmed to room temperature and stirred for 4 h. The reaction was quenched by the dropwise addition of ammonium chloride solution, then basified using sodium hydrogen carbonate solution. The mixture was extracted with diethyl ether (3 x 25 mL) and the combined organic extracts washed with brine (75 mL), dried (MgSO₄) and the solvent removed *in vacuo*. Column chromatography (10% ether in petroleum ether) gave **3** (371 mg, 83%) as a colourless oil. Crystals suitable for X-ray crystallography were grown from diethyl ether (slow evaporation). R_f 0.35 (20% Et₂O in petroleum ether); $[\alpha]_D^{21} -11.4$ (c 2.2, CHCl₃); m.p. 102-105 $^\circ\text{C}$; ν_{max} (film) 3422, 3053, 3028, 1782, 1595, 1490, 1445 cm^{-1} ; δ_H (300 MHz, CDCl₃) 7.55-7.20 (15H, m, Ph), 5.09 (1H, q, $J = 6.6$ Hz, =CHCH₃), 3.88 (1H, s, OH), 3.16 (1H, q, $J = 6.8$ Hz, CHCH₃Ph), 2.93 (1H, s, aziridine), 1.08, (3H, d, $J = 6.8$ Hz, =CHCH₃), 0.85 (3H, d, $J = 6.6$ Hz, NCHCH₃); δ_C (75 MHz, CDCl₃) 146.7 (C, aryl), 144.5 (C, aryl), 143.8 (C, aryl), 129.3 (=CN), 128.2 (CH, aryl), 128.0 (CH, aryl), 127.8 (CH, aryl), 127.23 (CH, aryl), 127.17 (CH, aryl), 127.0 (CH, aryl), 126.9 (CH, aryl), 126.7 (CH, aryl), 126.0 (CH, aryl), 97.2 (=CHCH₃), 74.6 (CPh₂OH), 66.3 (CHCH₃Ph), 50.0 (aziridine), 22.9 (NCHCH₃), 12.9 (=CHCH₃); MS (EI⁺) m/z 355 (30%, M⁺), 250 (70%, [M-PhCHCH₃]⁺), 105 (100%, [PhCHCH₃]⁺); HRMS (EI⁺) calcd for C₂₅H₂₅NO [M]⁺ 355.1936, found 355.1918; Anal. Calcd for C₂₅H₂₅NO: C, 84.5; H, 7.1; N, 3.9%. Found: C, 84.4; H, 7.1; N, 3.9%.



[(Z)-1-benzyl-2-ethylideneaziridin-3-yl]diphenylmethanol 4. To a stirred solution of (Z)-**1a** (200 mg, 1.26 mmol) and TMEDA (227 μ l, 1.50 mmol) in THF (10 mL) at $-78\text{ }^{\circ}\text{C}$ was added *sec*-butyllithium (1.3M in hexanes, 1.25 mL, 1.63 mmol) dropwise. The resulting solution was stirred at $-78\text{ }^{\circ}\text{C}$ for 5 h, then benzophenone (297 mg, 1.63 mmol) in THF (1 mL) added dropwise. After 10 min, the mixture was warmed to room temperature and stirred overnight. The mixture was partitioned between water (25 mL) and ether (25 mL), and the aqueous layer washed with diethyl ether (2 x 25 mL). The combined organic phases were washed with brine (75 mL), dried (MgSO_4) and the solvent removed *in vacuo*. To remove unreacted benzophenone, the crude product was dissolved in ethanol (20 mL) and cooled to $0\text{ }^{\circ}\text{C}$. Sodium borohydride (108 mg, 2.85 mmol) was added and the mixture warmed to room temperature and stirred for 4 h. The reaction was quenched by the dropwise addition of ammonium chloride solution, then basified using sodium hydrogen carbonate solution. The mixture was extracted with diethyl ether (3 x 25 mL) and the combined organic extracts washed with brine (75 mL), dried (MgSO_4) and the solvent removed *in vacuo*. Column chromatography (2% EtOAc in petroleum ether) gave **4** (267 mg, 62%) as a colourless oil, which crystallised on standing. Crystals suitable for X-ray crystallography were grown from diethyl ether (slow evaporation). R_f 0.46 (40% Et_2O in petroleum ether); m.p. $87\text{--}89\text{ }^{\circ}\text{C}$; ν_{max} (film) 3444, 3058, 3028, 1785, 1600. 1493, 1447 cm^{-1} ; δ_{H} (400 MHz, CDCl_3) 7.36–7.08 (15H, m, Ph), 5.13 (1H, q, $J = 6.8\text{ Hz}$, =CH), 4.03 (1H, d, $J = 13.1\text{ Hz}$, CHHPh), 3.66 (1H, s, OH), 3.63 (1H, d, $J = 13.1\text{ Hz}$, CHHPh), 2.93 (1H, s, aziridine), 1.69, (3H, d, $J = 6.8\text{ Hz}$, CH_3); δ_{C} (75 MHz, CDCl_3) 146.4 (C, aryl), 144.7 (C, aryl), 137.0 (C, aryl), 129.8 (=CN), 128.9 (CH, aryl), 128.3 (CH, aryl), 128.1 (CH, aryl), 128.0 (CH, aryl), 127.5 (CH, aryl), 127.3 (CH, aryl), 126.8 (CH, aryl), 126.3 (CH, aryl), 97.0 (=CH CH_3), 74.8 (CPh_2OH), 60.3 (CH_2Ph), 50.2 (CHCPh_2OH), 13.4 (CH_3); HRMS (ES^+) calcd for $\text{C}_{24}\text{H}_{24}\text{NO}$ $[\text{MH}]^+$ 342.1852, found 342.1855; Anal. Calcd for $\text{C}_{24}\text{H}_{23}\text{NO}$: C, 84.4; H, 6.8; N, 4.1%. Found: C, 84.3; H, 6.8; N, 4.0%.

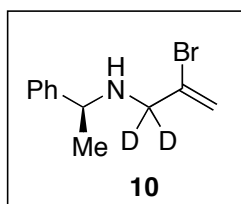
X-ray Crystallographic Structure Determinations. **3:** $\text{C}_{25}\text{H}_{25}\text{NO}$, colourless prism, $0.1 \times 0.1 \times 0.1\text{ mm}$, orthorhombic, space group $P2_12_12_1$, $Z=4$, $a = 9.8665(15)$, $b = 12.1832(18)$, $c = 16.897(3)\text{ \AA}$, $V = 2031.2(5)\text{ \AA}^3$, $\rho_{\text{calcd}} 1.162\text{ Mg m}^{-3}$, $2\theta_{\text{max}} = 51\text{ }^{\circ}$, graphite monochromated MoK_{α} radiation ($\lambda = 0.71073\text{ \AA}$), $\mu(\text{MoK}_{\alpha}) = 0.070\text{ mm}^{-1}$, $T = 125\text{ K}$. Bruker SMART CCD, Lorentzian, polarization and absorption corrections applied (max./min. transmission 1.0000/0.587127). Of 12970 measured data, 3680 were unique and 3075 observed [$I > 2\sigma(I)$]. $R_1 = 0.0368$ and $wR_2 = 0.0763$ for 250 parameters with a residual electron extremes of -0.151 and 0.159 e\AA^{-3} Flack

parameter $-0.7(14)$. **4**: $C_{24}H_{23}NO$, colourless prism, $0.1 \times 0.1 \times 0.1$ mm, monoclinic, space group $P2_1/c$, $Z=4$, $a = 7.4715(8)$, $b = 11.4568(12)$, $c = 21.543(2)$ Å, $V = 1838.8(3)$ Å³, ρ_{calcd} 1.233 Mgm⁻³, $2\theta_{max} = 50.8^\circ$, graphite monochromated MoK_α radiation ($\lambda = 0.71073$ Å), $\mu(MoK_\alpha) = 0.074$ mm⁻¹, $T = 125$ K. Bruker SMART CCD, Lorentzian, polarization and absorption corrections applied (max./min. transmission 1.0000/0.922477). Of 11001 measured data, 3304 were unique and 2932 observed [$I > 2\sigma(I)$]. $R_1 = 0.0331$ and $wR_2 = 0.0788$ for 241 parameters with a residual electron extremes of -0.181 and 0.271 eÅ⁻³. The structures were solved by direct methods. The non-hydrogen atoms were refined anisotropically, the C-H hydrogen atoms were idealized and refined isotropically using a riding model. Structural refinements were performed with the full-matrix least-squares method on F^2 for all data (G M Sheldrick, SHELXTL Version 6.10, Bruker AXS, Madison WI, 2002).



2-Bromo-1,1-dideuterioprop-2-en-1-ol. Aluminium chloride (1.73 g, 13.0 mmol) was added portionwise to a vigorously stirred solution of lithium aluminium deuteride (1.60 g, 38.1 mmol) in diethyl ether (200 mL) at 0°C .

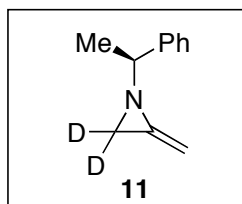
The resulting mixture was allowed to warm to room temperature. After stirring for 10 min, the mixture was cooled to -78°C and ethyl 2-bromoacrylate (9.12 g, 50.9 mmol) in diethyl ether (30 mL) was added dropwise. The mixture was warmed to 0°C , stirred for 1 h then quenched by dropwise addition of water (7 mL), followed by 10% NaOH solution (3 mL). The mixture was warmed to room temperature whereupon it was filtered and the precipitate washed with diethyl ether (100 mL). The supernatant was dried ($MgSO_4$), filtered and evaporated. Column chromatography (10% ether in petroleum ether) gave the *title compound* (5.29 g, 75%) as a clear colourless oil. R_f 0.35 (20% diethyl ether in petroleum ether); ν_{max} (film) 3286, 1632 cm^{-1} ; δ_H (400 MHz, $CDCl_3$) 5.93 (1H, d, =CHH), 5.58 (1H, s, =CHH), 2.52 (1H, br s, OH); δ_C (100 MHz, $CDCl_3$) 132.3 (=CBr), 116.4 (CH_2), 66.8 (CD_2); GC-MS (EI^+) m/z 138 (20%, M^+), 59.1 (100%, $[M-Br]^+$); HRMS (EI^+) calcd for $C_3H_3BrD_2O$ $[M]^+$ 137.9644, found 137.9645.



(2-Bromo-1,1-dideuterioprop-2-enyl)-[(S)-1-phenylethyl]-amine 10.

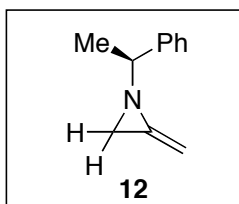
Methane-sulfonyl chloride (2.84 mL, 36.7 mmol), 2-bromo-1,1-dideuterioprop-2-en-1-ol (4.75 g, 34.2 mmol), α -methylbenzylamine (8.94 mL, 69.3 mmol) and triethylamine (12.0 mL, 86.1 mmol) were reacted together in THF (75 mL) as described in General Method A. Purification (10% EtOAc in petroleum ether) gave **10** (5.73 g, 69%) as a clear colourless oil. Material judged to have 95%D incorporation by integration of the residual hydrogen signals at δ 3.36 and 3.25 in the 1H NMR spectrum. $[\alpha]_D^{21} -31.6$ (c 10, $CHCl_3$); R_f 0.41 (10% EtOAc in petroleum ether); ν_{max}

(film) 3334, 3060, 1624, 1492, 1450 cm^{-1} ; δ_{H} (300 MHz, CDCl_3) 7.29-7.20 (5H, m, aromatics), 5.66 (1H, d, $J = 1.8$ Hz, =CHH), 5.55 (1H, d, $J = 1.8$ Hz, =CHH), 3.79 (1H, q, $J = 6.6$ Hz, CHCH_3Ph), 1.77 (1H, bs, NH), 1.35 (3H, d, $J = 6.6$ Hz, CHCH_3Ph); δ_{C} (75 MHz, CDCl_3) 145.2 (C, aryl), 134.2 (=CBr), 128.9 (CH, aryl), 127.5 (CH, aryl), 127.3 (CH, aryl), 118.2 (=CH₂), 55.9 (CHCH_3Ph), 55.1 (CD_2), 24.7 (CH_3); δ_{D} (75 MHz, CHCl_3) 3.33 (s), 3.23 (s); HRMS (EI^+) calcd for $\text{C}_{11}\text{H}_{12}\text{D}_2\text{N}^{79}\text{Br}$ $[\text{M}]^+$ 241.0435, found 241.0441.



3,3-Dideutero-2-methylene-1-[(1S)-1-phenylethyl]aziridine 11.

A three-necked flask was fitted with a dry-ice condenser and a gas inlet. Iron(III) chloride (2.0 mg, 0.01 mmol) was added and the system purged with CaCl_2 dried ammonia. A dry-ice/acetone mixture was added to the condenser and ammonia (25 mL) condensed into the flask. Freshly cut sodium (118 mg, 5.13 mmol) was added in small portions. The initially formed blue solution slowly faded to give a grey suspension of sodium amide. **10** (1.00 g, 4.13 mmol) in ether (1 mL) was added slowly to the mixture, which was then stirred for 5 min. The mixture was diluted with diethyl ether (5 mL) and quenched by the dropwise addition of water (2 mL) (CAUTION). After the ammonia had evaporated, diethyl ether (25 mL) was added and the mixture was stirred for 2 min. The organic phase was separated and washed with 0.1M acetic acid (3 x 50 mL), 10% NaOH (2 x 50 mL) and brine (50 mL), then dried (MgSO_4). Removal of the solvent *in vacuo* and subsequent bulb-to-bulb distillation gave **11** (565 mg, 85%) as a clear colourless oil. Material judged to have 92%D incorporation by integration of the residual hydrogen signals at 2.11, 2.09, 2.01 and 2.00 ppm in the ^1H NMR spectrum (average of three experiments). R_f 0.52 (10% EtOAc in petroleum ether); ν_{max} (film) 3060, 1769, 1492, 1448 cm^{-1} ; δ_{H} (300 MHz, CDCl_3) 7.38-7.25 (5H, m, Ph), 4.66 (1H, s, =CHH), 4.64 (1H, s, =CHH), 2.93 (1H, q, $J = 6.6$ Hz, CHCH_3Ph), 1.51 (3H, d, $J = 6.6$ Hz, CHCH_3Ph); δ_{C} (75 MHz, CDCl_3) 144.3 (C, aryl), 137.4 (=CN), 128.8 (CH, aryl), 127.6 (CH, aryl), 127.2 (CH, aryl), 83.5 (=CH₂), 68.8 (CHCH_3Ph), 29.7 (CD_2), 23.9 (CH_3); MS (CI^+) m/z 162 (100%, $[\text{MH}]^+$), 105 (40%, $[\text{PhCHCH}_3]^+$); HRMS (CI^+) calcd for $\text{C}_{11}\text{H}_{12}\text{D}_2\text{N}$ $[\text{MH}]^+$ 162.1246, found 162.1244.



Preparation of 2-methylene-1-[(1S)-1-phenylethyl]aziridine **12 from (2-bromo-1,1-dideuterioprop-2-enyl)-[(S)-1-phenylethyl]-amine **10**.**

A three-necked flask was fitted with a dry-ice condenser and a gas inlet. Iron(III) chloride (2.0 mg, 0.01 mmol) was added and the system was purged with CaCl₂ dried ammonia. A dry-ice/acetone mixture was added to the condenser and ammonia (25 mL) condensed into the flask. Freshly cut sodium (236 mg, 10.3 mmol) was added in small portions. The initially formed blue solution slowly faded to give a grey suspension of sodium amide. After cooling to -78°C , **10** (1.00 g, 4.13 mmol) [94%D as judged by integration of the ¹H NMR signal at 2.70 ppm] in ether (1 mL) was added slowly to the mixture, which was then stirred for 1 h. The mixture was diluted with diethyl ether (5 mL) and quenched by the dropwise addition of water (2 mL) (CAUTION). After the ammonia had evaporated, diethyl ether (25 mL) was added and the mixture was stirred for 2 min. The organic phase was separated and washed with 0.1M acetic acid (3 x 50 mL), 10% NaOH (2 x 50 mL) and brine (50 mL), then dried (MgSO₄). Removal of the solvent *in vacuo* and bulb-to-bulb distillation gave **12** (601 mg, 91%) as a clear colourless oil. Material judged to have 12%D incorporation by integration of the signals at 2.11, 2.09, 2.01 and 2.00 ppm in the ¹H NMR spectrum. δ_{H} (300 MHz, CDCl₃) 7.38-7.25 (5H, m, Ph) 4.66 (1H, s, =CHH), 4.64 (1H, s, =CHH), 2.93 (1H, q, $J = 6.6$ Hz, CHCH₃Ph), 2.15-2.07 (0.94H, 2 x s, aziridine CHD and CHH), 2.04-1.98 (0.82H, 2 x s, aziridine CDH and CHH), 1.51 (3H, d, $J = 6.6$ Hz, CHCH₃Ph). All other data consistent with those previously reported.

Sodium Amide Induced Exchange: Conversion of **11 to **12**.** A three-necked flask was fitted with a dry-ice condenser and a gas inlet. Iron(III) chloride (2.0 mg, 0.01 mmol) was added and the system purged with CaCl₂ dried ammonia. A dry-ice/acetone mixture was added to the condenser and ammonia (25 mL) condensed into the flask. A small, freshly cut piece of sodium (18 mg, 0.78 mmol) was added to the flask and the initially formed blue solution slowly faded to give a grey suspension of sodium amide. **11** (500 mg, 3.10 mmol) [92%D incorporation] in ether (1 mL) was added slowly to the mixture, which was then stirred for 1.5 h. The mixture was diluted with diethyl ether (5 mL) and quenched by the dropwise addition of water (2 mL) (CAUTION). After the ammonia had evaporated, diethyl ether (25 mL) was added and the mixture was stirred for 2 min. The organic phase was separated and washed with 10% NaOH (2 x 50 mL) and brine (50 mL), dried over MgSO₄ and the solvent removed *in vacuo*. Bulb-to-bulb distillation gave **12** (462 mg, 94%) as a clear colourless oil. The material was judged to have 2.5%D incorporation by integration of the signals at 2.11, 2.09, 2.01 and 2.00 ppm in the ¹H NMR spectrum (average of two experiments). R_{f} 0.52 (10% EtOAc in petrol); ν_{max} (film) 3060, 1769, 1492, 1448 cm⁻¹; δ_{H} (300 MHz, CDCl₃) 7.38-7.25 (5H, m, Ph), 4.66 (1H, s, =CHH), 4.64

(1H, s, =CHH), 2.93 (1H, q, $J = 6.6$ Hz, CHCH₃Ph), 2.15-2.07 (0.99H, 2 x s, aziridine CHD and CHH), 2.04-1.98 (0.96H, 2 x s, aziridine CDH and CHH), 1.51 (3H, d, $J = 6.6$ Hz, CHCH₃Ph); δ_c (75 MHz, CDCl₃) 144.3 (C, aryl), 137.4 (=CN), 128.8 (CH, aryl), 127.6 (CH, aryl), 127.2 (CH, aryl), 83.5 (=CH₂), 68.8 (CHCH₃Ph), 29.8 (NCH₂), 23.9 (CH₃); MS (EI⁺) m/z 159 (10%, M⁺), 105 (100%, [PhCHCH₃]⁺); HRMS (ES⁺) calcd for C₁₁H₁₄N [MH]⁺ 160.1121, found 160.1122.