Supporting information

Efficient Synthesis of Functionalized Aziridinium Salts

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Experimental Section

Instruments and reagents. ^1H , ^{13}C , and DEPT NMR spectra were obtained using a 300 instrument and chemical shifts are reported in parts per million on the δ scale relative to TMS. Fast atom bombardment (FAB) high-resolution mass spectra (HRMS) and electrospray ionization (EI) HRMS were obtained on JEOL double sector JMS-AX505HA mass spectrometer and Bruker micrOTOF II atmospheric pressure Time-of-Flight mass spectrometer using direct infusion, respectively. Optical rotation was measured in a cell with 50mm length and 1 mL capacity on JASCO (DIP-1000). Chiral-HPLC was performed on Agilent 1200 (Agilent, Santa Clara, CA) equipped with a diarray detector ($\lambda = 254$ and 280 nm), thermostat set at 35°C and a Chiralpak® AD-H (4.6 x 150 mm, Chiral Technologies Inc., West Chester, PA). The mobile phase of a binary gradient (0-1.3 %B/20 min; solvent A = Hexanes; solvent B = EtOH) was used.

General procedure for the synthesis of 11 and 12.⁷ A slurry of the ester salt **15** or **16** (10 mmol) in dry methanol (2.5 mL) was treated with Et_3N (10 mL). To the stirred slurry was then added anhydrous ether (100 mL), and the solution was cooled at -10°C for 1 h. The resulting triethylamine hydrochloride salt was filtered off, and the filtrate was concentrated under vacuum to light yellow oil. To the solution of oil in MeOH (50 mL) at 0°C was added in portions NaBH_4 (946 mg, 25 mmol) over 20 min. The resulting mixture was allowed to warm to room temperature and stirred for 4-6 h (while the reaction progress was continuously monitored using TLC). The solvent was removed *via* vacuum, and the residue was treated with H_2O (50 mL) and extracted with EtOAc (3×100 mL). The combined organic layer was treated with MgSO_4 ,

filtered, and concentrated under vacuum to provide amino alcohol **12** that was used for the next step without further purification.

(S)-2-amino-3-phenylpropan-1-ol ((S)-11b).¹⁰ A slurry of the ester salt **(S)-15b**⁸ (3.88g, 18 mmol) in dry methanol (2 mL) was treated with Et₃N (3 mL). To the stirred slurry was then added anhydrous ether (100 mL), and the solution was cooled at -10 °C for 1 h. The resulting triethylamine hydrochloride salt was filtered off, and the filtrate was concentrated under vacuum to light yellow oil (3.16 g, 98 %). To the solution of oil in MeOH (50 mL) at 0 °C was added in portions NaBH₄ (1.701 g, 45 mmol) over 20 min. The reaction provided **(S)-11b** (2.72 g, 100 %) as a white solid.

(R)-2-amino-3-phenylpropan-1-ol ((R)-11b).¹¹ A slurry of the ester salt **(R)-15b**⁹ (3 g, 15 mmol) in dry methanol (2 mL) was treated with Et₃N (3 mL). To the stirred slurry was then added anhydrous ether (100 mL), and the solution was cooled at -10 °C for 1 h. The resulting triethylamine hydrochloride salt was filtered off, and the filtrate was concentrated under vacuum to light yellow oil (2.3 g, 87 %). To the solution of oil in MeOH (20 mL) at 0 °C was added in portions NaBH₄ (2.0 g, 51 mmol) over 20 min. The reaction provided **(R)-11b** (1.7 g, 88 %) as a white solid

(S)-2-aminopentan-1-ol (12a).³ A slurry of the ester salt **16a**¹⁴ (1.20 g, 7.16 mmol) in dry methanol (1.5 mL) was treated with Et₃N (2 mL). To the stirred slurry was then added anhydrous ether (50 mL), and the solution was cooled at -10 °C for 1 h. The resulting triethylamine hydrochloride salt was filtered off, and the filtrate was concentrated under vacuum to colorless oil* (0.86 g, 91 %). To the solution of oil in MeOH (15 mL) at 0 °C was added in portions NaBH₄ (0.30 g, 7.86 mmol) over 20 min. The reaction provided **12a** (0.62 g, 93%) as a white solid.

(S)-2-amino-3-methylbutan-1-ol (12b).⁴ A slurry of L-Valine methyl ester hydrochloride **16b** (2.0 g, 11.9 mmol) in dry methanol (1.5 mL) was treated with Et₃N (2.5 mL). To the stirred slurry was then added anhydrous ether (50 mL), and the solution was cooled at -10 °C for 1 h. The resulting triethylamine hydrochloride salt was filtered off, and the filtrate was concentrated under vacuum to colorless oil* (1.45 g, 93%). To the solution of oil in MeOH (15 mL) at 0 °C was added in portions NaBH₄ (0.54 g, 14.1 mmol) over 20 min. The reaction provided **12b** (0.98 g, 86%) as a white solid.

(S)-2-amino-2-phenylethanol (12c).¹³ A slurry of the ester salt **16c**¹² (8.5 g, 42.2 mmol) in dry methanol (3 mL) was treated with Et₃N (7 mL). To the stirred slurry was then added anhydrous ether (100 mL), and the solution was cooled at -10 °C for 1 h. The resulting triethylamine

hydrochloride salt was filtered off, and the filtrate was concentrated under vacuum to light yellow oil (6.2 g, 89 %). To the solution of oil in MeOH (40 mL) at 0 °C was added in portions NaBH₄ (2.9 g, 76.7 mmol) over 20 min. The reaction provided **12c** (4.4 g, 86 %) as a white solid.

(S)-2-amino-3-(1H-indol-3-yl)propan-1-ol (12e).⁵ A slurry of L-Tryptophan methyl ester hydrochloride 16e (2.0 g, 7.95 mmol) in dry methanol (1.5 mL) was treated with Et₃N (2.5 mL). To the stirred slurry was then added anhydrous ether (50 mL), and the solution was cooled at -10 °C for 1 h. The resulting triethylamine hydrochloride salt was filtered off, and the filtrate was concentrated under vacuum to colorless oil (1.68 g, 98%). To the solution of oil in MeOH (15 mL) at 0 °C was added in portions NaBH₄ (0.35 g, 9.24 mmol) over 20 min. The reaction provided **12e** (1.41 g, 96%) as a white solid.

(S)-4-(2-amino-3-hydroxypropyl)phenol (12f).⁶ To the stirred solution of L-Tyrosine methyl ester hydrochloride 16f (2.0 g, 8.63 mmol) in CH₃CN (20 mL) was added K₂CO₃ (2.98 g, 21.6 mmol). The solution was heated at 45 °C for 14 h. The resulting salt was filtered off, and the filtrate was concentrated under vacuum to orange color solid (1.32 g, 78%). To the solution of solid in MeOH (20 mL) at 0 °C was added in portions NaBH₄ (0.43 g, 11.35 mmol) over 20 min. The reaction provided **12f** (0.71 g, 63%) as a yellow solid.

(1-Benzyl-2-hydroxyethylamino)acetic acid *tert*-butyl ester (13). To a stirred solution of DL-phenyl alaninol **11**¹ (1.02 g, 6.76 mmol) in CH₃CN (10 mL) was added K₂CO₃ (932 mg, 6.76 mmol) at 0 °C. Then a solution of *tert*-butyl bromoacetate (1.32 g, 6.76 mmol) in CH₃CN (10 mL) was added dropwise over a span of 20 min while maintaining the temperature 0 °C. The reaction mixture was then allowed to stir at room temperature for 24 h, while the reaction progress was continuously monitored using TLC. After which the reaction mixture was filtered off to remove K₂CO₃, and the filtrate concentrated under vacuum to provide the light yellow oil. The crude mixture was then purified by silica gel chromatography using 30 % ethyl acetate in hexanes as eluent to afford the pure mono substituted **13** (875 mg, 50 %) as white waxy solid. ¹H NMR (CDCl₃, 300 MHz) δ 1.45 (s, 9H), 2.72-2.78 (m, 2H), 2.80-2.90 (m, 1H), 3.27-3.38 (m, 3H), 3.55 (dd, *J* = 11.2 Hz, 3.3 Hz, 1H), 7.16-7.35 (m, 5H); ¹³C NMR (CDCl₃, 300 MHz) δ 28.3 (q), 38.0 (t), 49.4 (t), 60.7 (d), 62.5 (t), 81.3 (s), 126.3 (d), 128.5 (d), 129.1 (d), 138.7 (s), 172.0 (s). HRMS (positive ion FAB) Calcd for C₁₅H₂₄NO₃ [M + H]⁺ *m/z* 266.1740. Found: [M + H]⁺ *m/z* 266.1751.

General procedure for synthesis of 1. To a solution of amino alcohol **13** (1 mmol) in CH₃CN (5 mL) was added K₂CO₃ (1.2 mmol) at 0 °C. Then, a solution of RBr (1.05 mmol) in CH₃CN (2 mL) was added dropwise over a span of 20 min while maintaining the temperature 0 °C. The

reaction mixture was then warmed to room temperature and stirred for 18 h-24 h while the reaction progress was continuously monitored using TLC. The solvent was removed, and the residue was dissolved in DCM (30 mL). The resulting solution was filtered, and the filtrate was evaporated and purified via column chromatography on silica gel (60-230 mesh, 0-20% EtOAc in hexanes).

[Benzyl-(1-hydroxymethyl-2-phenylethyl)amino]acetic acid *tert*-butyl ester (1a). To a solution of **13** (100 mg, 0.38 mmol) in CH₃CN (2 mL) was added K₂CO₃ (62 mg, 0.45 mmol) at 0 °C. Then, a solution of benzyl bromide (77 mg, 0.45 mmol) in CH₃CN (1 mL) was added, and the resulting solution was stirred for 20 h. After work-up, the crude mixture was then purified via chromatography on silica gel eluted with 20% EtOAc in hexanes to afford **1a** as colorless oil (124 mg, 93 %). ¹H NMR (CDCl₃, 300 MHz) δ 1.47 (s, 9H), 2.45 (dd, *J* = 13.5, 8.4 Hz, 1H), 2.92 (dd, *J* = 13.5, 5.9 Hz, 1H), 3.09-3.20 (m, 2H), 3.34-3.55 (m, 3H), 3.70 (d, *J* = 14.5 Hz, 1H), 3.92 (d, *J* = 14.5 Hz, 1H), 4.02 (br s, 1H), 7.11-7.37 (m, 10H); ¹³C NMR (CDCl₃, 300 MHz) δ 28.0 (q), 33.6 (t), 51.7 (t), 56.0 (t), 61.8 (t), 65.1 (d), 81.5 (s), 126.3 (d), 127.3 (d), 128.4 (d), 128.6 (d), 129.1 (d), 138.7 (s), 139.1 (s), 172.2 (s). HRMS (positive ion FAB) Calcd for C₂₂H₃₀O₃N [M + H]⁺ *m/z* 356.2226. Found : [M + H]⁺ *m/z* 356.2218.

Allyl-(1-hydroxymethyl-2-phenylethyl)amino]acetic acid *tert*-butyl ester (1f**).** To a solution of **13** (100 mg, 0.38 mmol) in CH₃CN (2 mL) was added K₂CO₃ (62 mg, 0.45 mmol) at 0 °C. Then, a solution of allyl bromide (55 mg, 0.45 mmol) in CH₃CN (1 mL) was added, and the resulting solution was stirred for 16 h. After work-up, **1f** (114 mg, 100 %) as a light yellow oil was obtained and was used for the next step without further column chromatographic purification. ¹H NMR (CDCl₃, 300 MHz) δ 1.45 (s, 9H), 2.39 (dd, *J* = 13.5, 8.3 Hz, 1H), 2.78 (dd, *J* = 13.5, 5.9 Hz, 1H), 3.05-3.19 (m, 3H), 3.27-3.41 (m, 4H), 3.98 (br s, 1H (OH)), 5.06-5.17 (m, 2H), 5.70-5.83 (m, 1H), 7.11-7.29 (m, 5H); ¹³C NMR (CDCl₃, 300 MHz) δ 28.0 (q), 33.7 (t), 51.8 (t), 55.0 (t), 61.6 (t), 65.4 (d), 81.4 (s), 117.5 (t), 126.3 (d), 128.5 (d), 129.0 (d), 136.3 (d), 139.0 (s), 172.4 (s). HRMS (positive ion FAB) Calcd for C₁₈H₂₈O₃N [M + H]⁺ *m/z* 306.2069. Found : [M + H]⁺ *m/z* 306.2062.

[(1-Hydroxymethyl-2-phenylethyl)-(4-nitrobenzyl)amino]acetic acid *tert*-butyl ester (1g**).** To a solution of **13** (108 mg, 0.41 mmol) in CH₃CN (3 mL) was added K₂CO₃ (68 mg, 0.49 mmol) at 0 °C. Then, a solution of *p*-nitrobenzyl bromide (105 mg, 0.49 mmol) in CH₃CN (1 mL) was added, and the resulting solution was stirred for 16 h. After work-up, the crude mixture was then purified via chromatography on silica gel eluted with 20% EtOAc in hexanes to afford **1g** as a light yellow oil (134 mg, 82%). ¹H NMR (CDCl₃, 300 MHz) δ 1.40 (s, 9H), 2.52 (dd, *J* = 13.6, 7.4 Hz, 1H), 2.81 (dd, *J* = 13.6, 6.9 Hz, 1H), 3.09-3.20 (m, 2H), 3.37-3.55 (m, 3H), 3.87 (d, *J* = 14.5 Hz, 1H), 3.92 (d, *J* = 14.5 Hz, 1H), 4.02 (br s, 1H, OH), 7.14 (d, *J* = 6.9 Hz, 2H), 7.21-7.32 (m, 3H), 7.36 (d, *J* = 8.5 Hz, 2H), 8.10 (d, *J* = 8.5 Hz, 2H); ¹³C NMR (CDCl₃, 300 MHz) δ 28.0

(q), 34.0 (t), 51.1 (t), 56.1 (t), 62.4 (t), 65.7 (d), 82.0 (s), 123.6 (d), 126.5 (d), 128.7 (d), 129.0 (d), 129.5 (d), 138.9 (s), 146.9 (s), 147.2 (s), 172.4 (s). HRMS (positive ion FAB) Calcd for $C_{22}H_{28}N_2O_5$ $[M + H]^+$ m/z 401.2076. Found: $[M + H]^+$ m/z 401.2073.

General procedure for synthesis of 1. To a solution of DL-phenyl alaninol **11**¹ (1 mmol) in CH_3CN (5 mL) was added K_2CO_3 (2.2 mmol) at 0 °C. Then, a solution of RBr (2.05 mmol) in CH_3CN (2 mL) was added dropwise over a span of 20 min while maintaining the temperature 0 °C. The reaction mixture was then warmed to room temperature and stirred for 18 h-24 h while the reaction progress was continuously monitored using TLC. The solvent was removed, and the residue was dissolved in CH_2Cl_2 (10 mL). The resulting solution was filtered, and the filtrate was purified via column chromatography on silica gel (60-230 mesh, 0-20% EtOAc in hexanes).

(S)-tert-butyl 2,2'-(1-hydroxy-3-phenylpropan-2-ylazanediyl)diacetate ((S)-1b). To the stirred solution of amino alcohol (**S**)-**11b** (500 mg, 3.31 mmol) in CH_3CN (10 mL) was added K_2CO_3 (1.0 g, 7.28 mmol) at 0 °C. Then the solution of *tert*-butyl bromoacetate (1.32 g, 6.8 mmol) in CH_3CN (5 mL) was added dropwise over a span of 20 min while maintaining the temperature 0 °C. After work-up the crude mixture was purified via column chromatography on

silica gel (60-230 mesh) eluted with 15 % EtOAc in hexanes to provide **(S)-1b** as a colorless oil (1.12 g, 88.9%). ^1H NMR (CDCl_3 , 300 MHz) δ 1.47(s, 18H), 2.43 (dd, $J = 13.3, 8.9$ Hz, 1H), 2.89 (dd, $J = 13.3, 5.5$ Hz, 1H), 3.00-3.13 (m, 1H), 3.22-3.52 (m, 6H), 4.20 (dd, $J = 9.5, 2.3$ Hz, 1H), 7.10-7.31 (m, 5H); ^{13}C NMR (CDCl_3 , 300 MHz) δ 28.1 (q), 35.3 (t), 53.7 (t), 61.8 (t), 67.2 (d), 81.4 (s), 126.3 (d), 128.5 (d), 129.0 (d), 138.9 (s), 171.9 (s). The ^1H and ^{13}C NMR data of **(S)-1b** is essentially identical to those of **(rac)-1b** reported in the literature.⁷ HRMS (positive ion ESI) Calcd for $\text{C}_{21}\text{H}_{33}\text{NNaO}_5$ $[\text{M} + \text{Na}]^+$ m/z 402.2251. Found : $[\text{M} + \text{H}]^+$ m/z 402.2226. $[\alpha]_D^{26} = -24.5^\circ$ (C 1.3, CHCl_3)

(R)-tert-butyl 2,2'-(1-hydroxy-3-phenylpropan-2-ylazanediyl)diacetate ((R)-1b). To the stirred solution of amino alcohol **(R)-11b** (1.2 g, 7.9 mmol) in CH_3CN (15 mL) was added K_2CO_3 (2.4 g, 17.4 mmol) at 0°C . Then the solution of *tert*-butyl bromoacetate (3.2 g, 16.2 mmol) in CH_3CN (5 mL) was added dropwise over a span of 20 min while maintaining the temperature 0°C . The reaction mixture was then warmed to room temperature and stirred for 26 h. After work-up the crude mixture was purified via column chromatography on silica gel (60-230 mesh) eluted with 15 % EtOAc in hexanes to provide **(R)-1b** (2.2 g, 73%) as a colorless oil. ^1H NMR (CDCl_3 , 300 MHz) δ 1.43 (s, 18H), 2.40 (dd, $J = 13.3, 8.8$ Hz, 1H), 2.89 (dd, $J = 13.3, 5.5$ Hz, 1H), 2.97-3.08 (m, 1H), 3.20-3.49 (m, 6H), 4.19 (dd, $J = 9.5, 2.3$ Hz, 1H), 7.09-7.29 (m, 5H); ^{13}C NMR (CDCl_3 , 300 MHz) δ 28.0 (q), 35.3 (t), 53.7 (t), 61.8 (t), 67.2 (d), 81.3 (s), 126.2 (d), 128.5 (d), 129.0 (d), 138.9 (s), 171.9 (s). The ^1H and ^{13}C NMR data of **(R)-1b** is essentially

identical to those of (**rac**)-**1b** reported in the literature.⁷ HRMS (positive ion ESI) Calcd for $C_{21}H_{33}NNaO_5$ $[M + Na]^+$ m/z 402.2251. Found : $[M + H]^+$ m/z 402.2232. $[\alpha]_D^{26} = +30.4^\circ$ (C 1.0, $CHCl_3$)

tert-butyl 1-hydroxy-3-phenylpropan-2-ylcarbamate (1e).¹⁵ To a solution of **11** (1 g, 6.6 mmol) in CH_3CN (15 mL) was added $(Boc)_2O$ (1.7 g, 7.9 mmol) at $0^\circ C$. The resulting solution was stirred for 6 h. At which time the reaction mixture was concentrated in vacuo. The residue was treated with 10% aqueous NaOH (10 mL) and extracted with Ether (20 mL X 2). The combined organic layer was treated with $MgSO_4$ and concentrated under vacuum to provide **1e** (1.6 g, 100%) as a white waxy solid.

2-Diallylamino-3-phenylpropan-1-ol (1h). To a solution of **11** (274.5 mg, 1.82 mmol) in CH_3CN (3 mL) was added K_2CO_3 (552.0 mg, 4.04 mmol) at $0^\circ C$. Then, a solution of allyl bromide (450.2 mg, 3.72 mmol) in CH_3CN (2 mL) was added, and the resulting solution was stirred for 20 h. After work-up, the crude mixture was then purified via chromatography on silica gel eluted with 20% EtOAc in hexanes to afford **1h** (374 mg, 89 %) as a colorless oil. 1H NMR ($CDCl_3$, 300 MHz) δ 2.30 (dd, $J = 13.3, 9.8$ Hz, 1H), 2.91-3.02 (m, 3H), 3.15-3.25 (m, 2H), 3.35-3.45 (m, 4H), 5.15-5.25 (m, 4H), 5.74-5.87 (m, 2H), 7.10-7.31 (m, 5H); ^{13}C NMR ($CDCl_3$, 300 MHz) δ 32.0 (t), 52.3 (t), 60.4 (t), 61.6 (d), 117.5 (t), 126.2 (d), 128.5 (d), 129.0 (d), 136.6

(d), 139.3 (s). HRMS (positive ion FAB) Calcd for $C_{15}H_{21}ON$ $[M + H]^+$ m/z 232.1701. Found: $[M + H]^+$ m/z 232.1702.

2-Dibenzylamino-3-phenylpropan-1-ol (1i). To a solution of **11** (157 mg, 1.04 mmol) in CH_3CN (3 mL) was added K_2CO_3 (316 mg, 2.29 mmol) at 0 °C. Then the solution of benzyl bromide (364 mg, 2.13 mmol) in CH_3CN (2 mL) was added, and the resulting solution was stirred for 24 h. After work-up, the crude mixture was then purified via chromatography on silica gel eluted with 20% EtOAc in hexanes to afford **1i** (265 mg, 77%) as a white waxy solid. 1H NMR ($CDCl_3$, 300 MHz) δ 2.46 (dd, J = 13.2, 9.3 Hz, 1H), 3.17-3.19 (m, 3H), 3.34-3.37 (m, 1H), 3.49-3.57 (m, 3H), 3.93 (s, 1H), 3.98 (s, 1H), 7.11-7.38 (m, 15H); ^{13}C NMR ($CDCl_3$, 300 MHz) δ 32.0 (t), 53.4 (t), 60.5 (t), 61.0 (d), 126.4 (d), 127.5 (d), 128.7 (d), 129.2 (d), 139.3 (s), 139.4 (s). HRMS (positive ion FAB) Calcd for $C_{23}H_{26}ON$ $[M + H]^+$ m/z 332.2014. Found: $[M + H]^+$ m/z 332.2036.

2-(2,4-Dimethoxybenzylamino)-3-phenylpropan-1-ol (14).² To a stirred solution of **11** (2.0 g, 10.2 mmol) and 1,4-Dimethoxy benzaldehyde (DMB) (1.7 g, 10.2 mmol) in 1,2-dichloroethane (35 mL), $NaBH(OAc)_3$ (3.0 g, 14.3 mmol) was added portionwise over 40 min at 0 °C. After the addition, the reaction mixture was allowed to stir at room temperature overnight. After which the

reaction mixture was treated with saturated NaHCO₃ (30 mL) and extracted with ethyl Acetate (30 mL × 3). The combined organic layers were dried over MgSO₄, filtered, and concentrated in *vacuo* to the dryness to provide **14** (2.0 g, 65%) as a white waxy solid. ¹H NMR (CDCl₃, 300 MHz) δ 2.26-2.63 (m, 2H), 2.76 (d, *J* = 14 Hz, 2H), 2.85-2.98 (m, 1H), 3.31-3.42 (m, 1H), 3.58-3.84 (m, 10H), 6.35-6.45 (m, 2H), 7.02 (d, *J* = 7.8 Hz, 1H), 7.07-7.34 (m, 5H); ¹³C NMR (CDCl₃, 300 MHz) δ 37.1 (t), 46.4 (t), 55.0 (t), 55.2 (q), 55.3 (q), 58.9 (d), 66.8 (t), 98.5 (d), 103.7 (d), 120.2 (s), 126.2 (d), 128.5 (d), 129.3 (d), 130.5 (d), 138.9 (s), 158.7 (s), 160.3 (s). HRMS (positive ion FAB) Calcd for C₁₈H₂₄NO₃ [M + H]⁺ *m/z* 302.1751. Found: [M + H]⁺ *m/z* 302.1759.

2-[Allyl-(2,4-dimethoxy-benzyl)-amino]-3-phenyl-propan-1-ol (1j). To a solution of **14** (1.01 g, 3.4 mmol) and K₂CO₃ (468 mg, 3.9 mmol) in CH₃CN (5 mL), a solution of allyl bromide (533.8 mg, 3.8678 mmol) in CH₃CN (2 mL) was added dropwise over 20 min at 0 °C. The resulting mixture was allowed to stir at room temperature for overnight and filtered off to remove K₂CO₃, and the filtrate was concentrated under vacuum. The crude mixture was then purified by silica gel chromatography using ethyl acetate/*n*-hexane (1:10) as eluent to afford the pure product **1j** (881 mg, 77%) as a white waxy solid. ¹H NMR (CDCl₃, 300 MHz) δ 2.37 (dd, *J* = 13.2, 10.1 Hz, 1H), 2.99-3.14 (m, 2H), 3.15-3.27 (m, 1H), 3.34-3.47 (m, 3H), 3.54 (t, *J* = 10.5 Hz, 2H), 3.80 (s, 3H), 3.83 (s, 3H), 3.97 (d, *J* = 12.9 Hz, 1H), 5.15 (d, *J* = 10.1 Hz, 1H), 5.24 (d, *J* = 17.1 Hz, 1H), 5.75-5.93 (m, 1H), 6.45-6.55 (m, 2H), 7.09-7.35 (m, 6H); ¹³C NMR (CDCl₃,

300 MHz) δ 31.4 (t), 47.7 (t), 52.6 (t), 55.2 (q), 55.3 (q), 61.6 (t), 63.2 (d), 98.8 (d), 104.0 (d), 117.0 (t), 119.4 (s), 126.1 (d), 128.5 (d), 129.1 (d), 131.7 (d), 139.7 (d), 158.9 (s), 160.4 (s). HRMS (positive ion ESI) Calcd for $C_{21}H_{27}NO_3$ $[M + H]^+$ m/z 342.2064. Found: $[M + H]^+$ m/z 342.2065.

General procedure for synthesis of 9. To a solution of amino alcohol **12** (10 mmol) in CH_3CN (20 mL) was added K_2CO_3 (22 mmol) at 0 °C. Then, a solution of *tert*-butyl bromoacetate (20.5 mmol) in CH_3CN (10 mL) was added dropwise over a span of 20 min while maintaining the temperature 0 °C. The reaction mixture was then warmed to room temperature and stirred for 18 h-24 h while the reaction progress was continuously monitored using TLC. The solvent was removed, and the residue was dissolved in CH_2Cl_2 (10 mL). The resulting solution was filtered and evaporated, and the filtrate was purified via column chromatography on silica gel (60-230 mesh, 0-20% EtOAc in hexanes) to afford *N,N'*-dialkylated amino alcohol **9**.

(S)-*tert*-butyl 2,2'-(1-hydroxypentan-2-ylazanediyl)diacetate (9a). To a solution of L-Norvalinol **12a**³ (0.35 g, 3.39 mmol) in CH_3CN (10 mL) was added K_2CO_3 (1.03 g, 7.46 mmol) at 0 °C. Then, a solution of *tert*-butyl bromoacetate (1.46g, 7.46 mmol) in CH_3CN (5 mL) was added dropwise over a span of 20 min while maintaining the temperature 0 °C. The reaction

mixture was then allowed to stir at room temperature for 24 h. After work-up, the crude mixture was then purified by silica gel chromatography using ethyl acetate/*n*-hexane (1:10) as eluent to afford **9a** (0.79 g, 70%) as a colorless oil. ^1H NMR (CDCl_3 , 300 MHz) δ 0.90 (t, $J = 6.9$ Hz, 3H), 1.06-1.42 (m, 4H), 1.45 (s, 18H), 2.69-2.81 (m, 1H), 3.15-3.55 (m, 6H), 4.30 (d, $J = 8.6$ Hz, 1H); ^{13}C NMR (CDCl_3 , 300 MHz) δ 14.3 (q), 20.1 (t), 28.1 (q), 30.9 (t), 53.3 (t), 62.6 (t), 65.1 (d), 81.3 (s), 172.3 (s). HRMS (positive ion ESI) Calcd for $\text{C}_{17}\text{H}_{34}\text{NO}_5$ $[\text{M}+\text{H}]^+$ m/z 332.2431. Found: $[\text{M} + \text{H}]^+$ m/z 332.2393.

(S)-tert-butyl 2,2'-(1-hydroxy-3-methylbutan-2-ylazanediyl)diacetate (9b). To a solution of **12b⁴** (0.40 g, 3.9 mmol) in CH_3CN (10 mL) was added K_2CO_3 (1.2 g, 8.53 mmol) at 0°C . Then, a solution of *tert*-butyl bromoacetate (1.7 g, 8.5 mmol) in CH_3CN (5 mL) was added to the mixture, and the resulting solution was stirred for 24 h. After work-up, the crude mixture was then purified via column chromatography on silica gel eluted with 10% EtOAc in hexanes to afford **9b** (0.63 g, 49%) as a colorless oil. ^1H NMR (CDCl_3 , 300 MHz) δ 0.84 (d, $J = 6.0$ Hz, 3H), 0.93 (d, $J = 6.0$ Hz, 3H), 1.43 (s, 18H), 2.38 (m, 1H), 3.24 (t, $J = 11.0$ Hz, 1H), 3.37-3.52 (m, 4H), 3.55-3.71 (m, 1H), 4.55-4.67 (m, 1H); ^{13}C NMR (CDCl_3 , 300 MHz) δ 20.0 (q), 21.1 (q), 28.0 (q), 29.4 (d), 54.3 (t), 61.5 (t), 72.8 (d), 81.3 (s), 172.4 (s). HRMS (positive ion FAB) Calcd for $\text{C}_{17}\text{H}_{34}\text{O}_5\text{N}$ $[\text{M} + \text{H}]^+$ m/z 332.2437. Found: $[\text{M} + \text{H}]^+$ m/z 332.2448.

(S)-tert-butyl 2,2'-(2-hydroxy-1-phenylethylazanediyl) (9c) To the stirred solution of **12c** (200 mg, 1.5 mmol) in CH₃CN (5 mL) was added K₂CO₃ (443 mg, 3.2 mmol) at 0 °C. Then, a solution of *tert*-butyl bromoacetate (583 mg, 3.0 mmol) in CH₃CN (1 mL) was added to the mixture, and the resulting solution was stirred for 24 h. After work-up, the crude mixture was then purified via chromatography on silica gel eluted with 10% EtOAc in hexanes to afford **9c** (217 mg, 40 %) as a colorless oil. ¹H NMR (CDCl₃, 300 MHz) δ 1.44 (s, 18H), 3.35-3.52 (m, 4H), 3.75-3.82 (m, 2H), 3.97-4.05 (m, 1H), 7.20-7.38 (m, 5H) ; ¹³C NMR (CDCl₃, 300 MHz) δ 28.1 (q), 54.1 (t), 62.6 (t), 68.0 (d), 81.4 (s), 127.8 (d), 128.2 (d), 128.5 (d), 138.4 (s), 171.8 (s). HRMS (positive ion ESI) Calcd for C₂₀H₃₂O₅N [M + H]⁺ *m/z* 366.2275. Found: [M + H]⁺ *m/z* 366.2293.

(S)-tert-butyl 2,2'-(1-(benzylthio)-3-hydroxypropan-2-ylazanediyl)diacetate (9d). To the stirred solution of S-benzyl-L-cysteinol **12d** (304 mg, 1.54 mmol) in CH₃CN (4 mL) was added K₂CO₃ (468 mg, 3.4 mmol) at 0 °C. Then the solution of *tert*-butyl bromoacetate (616 mg, 3.2 mmol) in CH₃CN (1 mL) was added to the mixture, and the resulting solution was stirred for 24 h. After work-up, the crude mixture was then purified via chromatography on silica gel eluted with 15% EtOAc in hexanes to afford **9d** as a colorless oil (387 mg, 67%). ¹H NMR (CDCl₃, 300

MHz) δ 1.45 (s, 18H), 2.24 (dd, J = 13.2, 8.3 Hz, 1H), 2.62 (dd, J = 13.1, 6.0 Hz, 1H), 2.82-2.96 (m, 1H), 3.24 (dd, J = 11.4, 10.0 Hz, 1H), 3.39 (s, 4H), 3.60-3.65 (m, 1H), 3.69 (s, 2H), 4.24 (bs, 1H), 7.15-7.35 (m, 5H); ^{13}C NMR (CDCl_3 , 300 MHz) 28.0 (q), 30.3 (t), 37.0 (t), 53.3 (t), 61.8 (t), 64.5 (d), 81.5 (s), 127.1 (d), 128.6 (d), 128.9 (d), 138.0 (s), 171.9 (s). HRMS (positive ion ESI) Calcd for $\text{C}_{22}\text{H}_{36}\text{NO}_5\text{S}$ $[\text{M} + \text{H}]^+$ m/z 426.2309. Found : $[\text{M} + \text{H}]^+$ m/z 426.2317.

(S)-tert-butyl 2,2'-(1-hydroxy-3-(1H-indol-3-yl)propan-2-ylazanediyl)diacetate (9e).⁵ To the stirred solution of L-Tryptophanol **12e**⁵ (500 mg, 2.63 mmol) in CH_3CN (10 mL) was added K_2CO_3 (799 mg, 5.78 mmol) at 0 °C. Then the solution of *tert*-butyl bromoacetate (1.1 g, 5.8 mmol) in CH_3CN (5 mL) was added to the mixture, and the resulting solution was stirred for 24 h. After work-up, the crude mixture was then purified via chromatography on silica gel eluted with 10% EtOAc in hexanes to afford **9e** (665 mg, 61 %) as a light yellow oil. ^1H NMR (CDCl_3 , 300 MHz) δ 1.45 (s, 18H), 2.63 (dd, J = 14.2, 9.1 Hz, 1H), 3.03 (dd, J = 14.2, 4.9 Hz, 1H), 3.16-3.30 (m, 1H), 3.31-3.59 (m, 5H), 6.95 (s, 1H) 7.07-7.21 (m, 2H), 7.34 (d, J = 7.9 Hz, 1H), 7.57 (d, J = 7.9 Hz, 1H); ^{13}C NMR (CDCl_3 , 300 MHz) δ 24.4 (q), 28.1 (t), 53.6 (d), 62.2 (t), 65.4 (t), 81.4 (s), 111.2 (d), 112.8 (s), 118.7 (d), 119.3 (d), 122.0 (d), 122.3 (d), 127.3 (s), 136.3 (s), 172.2 (s). HRMS (positive ion FAB) Calcd for $\text{C}_{23}\text{H}_{35}\text{O}_5\text{N}_2$ $[\text{M} + \text{H}]^+$ m/z 419.2546. Found: $[\text{M} + \text{H}]^+$ m/z 419.2562.

(S)-tert-butyl 2,2'-(1-(4-(2-tert-butoxy-2-oxoethoxy)phenyl)-3-hydroxypropan-2-ylazanediyl) diacetate (9f). To the stirred solution of L-Tyrosinol **12f**⁶ (268 mg, 1.60 mmol) in CH₃CN (10 mL) was added K₂CO₃ (558 mg, 4.04 mmol) at 0 °C. Then the solution of *t*-butyl bromoacetate (791 mg, 4.04 mmol) in CH₃CN (5 mL) was added dropwise over a span of 20 min while maintaining the temperature 0 °C. The reaction mixture was then allowed to stir at room temperature for 24 h while the reaction progress was continuously monitored using TLC. After which the reaction mixture was filtered off to remove K₂CO₃, and the filtrate concentrated under vacuum to provide a light yellow oil. The crude mixture was then purified by silica gel chromatography using 1:10 ethyl acetate/*n*-hexane as eluent to afford **9f** (556 mg, 68%) as a light yellow oil. ¹H NMR (CDCl₃, 300 MHz) δ 1.42 (s, 18H), 1.44 (s, 9H), 2.40-2.49 (m, 1H), 2.73-2.82 (m, 1H), 2.91-3.04 (m, 1H), 3.19-3.45 (m, 6H), 4.44 (s, 2H), 6.76 (d, *J* = 8.5 Hz, 2H), 7.01 (d, *J* = 8.6 Hz, 2H); ¹³C NMR (CDCl₃, 300 MHz) δ 28.0 (q), 28.1 (q), 34.3 (t), 53.7 (t), 61.7 (t), 65.8 (t), 67.2 (d) 81.4 (s), 82.2 (s), 114.7 (d), 129.9 (d), 131.8 (s), 156.4 (s), 168.1 (s), 171.9 (s). HRMS (positive ion ESI) Calcd for C₂₇H₄₄NO₈ [M+H]⁺ *m/z* 510.3061. Found: [M + H]⁺ *m/z* 510.3072.

1,2-Dibenzyl-1-tert-butoxycarbonylmethyl aziridinium bromide (2a). To a solution of *N,N*-dialkylated alcohol **1a** (1 eq) and triphenyl phosphine (1.2 eq) in various solvents was portionwise added NBS (1.2 eq) at 0 °C over 20 min. The resulting mixture was stirred for 4 h while being maintained at 0 °C. The ice bath was removed, and the reaction mixture was warmed

to room temperature and stirred for 1 h and evaporated to dryness. The residue was purified via column chromatography on silica gel (60-230 mesh) eluting with 5% EtOAc in hexanes to afford **2a** as a colorless oil. ^1H NMR (CDCl_3 , 300 MHz) δ 1.51 (s, 9H), 2.96 (dd, $J = 14.5, 9.0$ Hz, 1H), 3.15 (dd, $J = 14.1, 7.4$ Hz, 1H), 3.26 (dd, $J = 14.1, 6.6$ Hz, 1H), 3.37 (s, 2H), 3.50 (dd, $J = 14.5, 4.4$ Hz, 1H), 3.89-3.99 (m, 2H), 4.12-4.21 (m, 1H), 7.20-7.43 (m, 10H); ^{13}C NMR (CDCl_3 , 300 MHz) δ 28.3 (q), 42.7 (t), 55.4 (d), 55.9 (t), 58.8 (t), 61.5 (t), 81.2 (s), 126.7 (d), 127.4 (d), 128.4 (d), 128.5 (d), 129.0 (d), 129.3 (d), 138.7 (s), 139.0 (s), 170.7 (s). HRMS (positive ion FAB) Calcd for $\text{C}_{22}\text{H}_{29}\text{BrO}_2\text{N}$ $[\text{M} + \text{H}]^+$ m/z 418.1382. Found: $[\text{M} + \text{H}]^+$ m/z 418.1389.

Synthesis of 2a using CH_3CN as solvent. To a solution of **1a** (82 mg, 0.23 mmol) and PPh_3 (72 mg, 0.28 mmol) in CH_3CN (2 mL) at 0 °C was added NBS (49 mg, 0.28 mmol). The residue was purified by silica gel column chromatography eluted with 5% EtOAc in hexanes to afford **2a** (73 mg, 76 %) as a colorless oil.

Synthesis of 2a using CHCl_3 as solvent. To a solution of **1a** (50 mg, 0.14 mmol) and PPh_3 (45 mg, 0.17 mmol) in CHCl_3 (2 mL) at 0 °C was added NBS (30 mg, 0.17 mmol). The residue was purified by silica gel column chromatography eluted with 5% EtOAc in hexanes to afford **2a** (32 mg, 53 %) as a colorless oil.

Synthesis of 2a using CHCl_3 as solvent (work-up done after storing the reaction mixture at the freezer overnight). To a solution of **1a** (70 mg, 0.20 mmol) and PPh_3 (62 mg, 0.24 mmol) in CHCl_3 (2 mL) at 0 °C was added NBS (42 mg, 0.24 mmol). After the reaction described above, the reaction mixture was kept in the freezer overnight, and the solvent was evaporated. The residue was purified by silica gel column chromatography eluted with 5% EtOAc in hexanes to afford **2a** (78 mg, 95 %) as a colorless oil.

Synthesis of 2a using CH₂Cl₂ as solvent. To a solution of **1a** (87 mg, 0.24 mmol) and PPh₃ (77 mg, 0.29 mmol) in CHCl₃ (2 mL) at 0 °C was added NBS (52 mg, 0.29 mmol). The residue was purified by silica gel column chromatography eluted with 5% EtOAc in hexanes to afford **2a** (45 mg, 45 %) as a colorless oil.

Synthesis of 2a using THF as solvent. To a solution of **1a** (69 mg, 0.20 mmol) and PPh₃ (62 mg, 0.23 mmol) in freshly distilled THF (2 mL) at 0 °C was added NBS (42 mg, 0.23 mmol). The residue was purified by silica gel column chromatography eluted with 5% EtOAc in hexanes to afford **2a** (29 mg, 36 %) as a colorless oil.

2-Benzyl-1,1-bis-*tert*-butoxycarbonylmethyl aziridinium chloride (3b) and [(1-Benzyl-2-chloro-ethyl)-*tert*-butoxycarbonylmethyl amino]acetic acid *tert*-butyl ester (4b). To a solution of amino alcohol **1b** (200 mg, 0.53 mmol) in CHCl₃ (5 mL) was dropwise added SOCl₂ (75.2 mg, 0.63 mmol) at 0 °C over 20 min. The resulting mixture was then warmed to room temperature and stirred for 1 d. After which the reaction mixture was evaporated to dryness and the residue was purified via column chromatography on silica gel (60-230 mesh) eluting with 10% EtOAc in hexanes to afford an inseparable mixture of **3b** and **4b** (91 mg, 43%) as a colorless oil. ¹H NMR (CDCl₃, 300 MHz) δ 1.46 (s, 18H), 2.82-3.02 (m, 2H), 3.14 (dd, *J* = 14.5, 9.0 Hz, 0.5H), 3.25-3.38 (m, 1H), 3.41-3.67 (m, 5H), 4.12-4.26 (m, 0.5H), 7.12-7.29 (m, 5H); ¹³C NMR (CDCl₃, 300 MHz) δ 28.1 (q), 28.2 (q), 36.5 (t), 42.0 (t), 46.0 (t), 53.9 (t), 57.2 (t),

61.5 (t), 62.2 (d), 65.0 (d), 80.9 (s), 81.2 (s), 126.3 (d), 126.6 (d), 128.3 (d), 128.5 (d), 129.2 (d), 129.5 (d), 138.1 (s), 138.9 (s), 170.6 (s), 171.3 (s).

Conversion of 4b to 3b. A solution of inseparable mixture of **3b** and **4b** (15 mg, 0.04 mmol) in CHCl_3 (1 mL) was stirred at room temperature for 10 days. The resulting solution was evaporated to dryness to afford **3b** (15 mg, 100%). ^1H NMR (CDCl_3 , 300 MHz) δ 1.46 (s, 18H), 2.82-3.02 (m, 2H), 3.14 (dd, $J = 14.5, 9.0$ Hz, 1H), 3.35 (dd, $J = 14.2, 4.5$ Hz, 1H), 3.50 (dd, $J = 27.1, 17.4$ Hz, 4H), 4.12-4.26 (m, 1H), 7.12-7.29 (m, 5H); ^{13}C NMR (CDCl_3 , 300 MHz) δ 28.2 (q), 42.0 (t), 57.2 (t), 61.5 (t), 62.2 (d), 81.2 (s), 126.6 (d), 128.3 (d), 129.5 (d), 138.1 (s), 170.7 (s); HRMS (positive ion FAB) Calcd for $\text{C}_{21}\text{H}_{33}\text{ClNO}_4$ $[\text{M} + \text{H}]^+$ m/z 398.2098. Found: $[\text{M} + \text{H}]^+$ m/z 398.2109.

Synthesis of 3b in reflux condition. To a solution of amino alcohol **1b** (100 mg, 0.26 mmol) in CHCl_3 (3 mL) was dropwise added SOCl_2 (37.5 mg, 0.32 mmol) at 0°C over 20 min. The resulting mixture was then reflux for 0.5 h. After which the reaction mixture was evaporated to dryness and the residue was purified via prep-TLC eluting with 20% EtOAc in hexanes to afford **3b** (33 mg, 32%).

To a solution of N,N' -dialkylated amino alcohol **1b** (200 mg, 0.53 mmol) and Et_3N (162 mg, 1.6 mmol) in THF (6 mL) were added catalytic amount of DMAP (1 mg) and MsCl (72 mg, 0.63 mmol) at 0°C . The reaction mixture was then warmed to room temperature and stirred for 3d

while the reaction progress was continuously monitored using TLC. Saturated NaHCO₃ solution (10 mL) was added, and the reaction mixture was extracted with ether (3 × 20 mL). The combined ether layers were washed with saturated citric acid (10 mL), H₂O (10 mL), 5% NaHCO₃ (10 mL), and H₂O (10 mL). The ether layer was dried, filtered, concentrated in vacuo, and the residue was purified via column chromatography on silica gel (60-230 mesh) eluting with 10% EtOAc in hexanes to afford inseparable mixture of **3b** and **4b** (108 mg, 51%).

Synthesis of [tert-Butoxycarbonylmethyl(2-iodo-3-phenylpropyl)amino]acetic acid tert-butyl ester ((rac)-7b).

Using I₂. To a solution of **1b** (200 mg, 0.53 mmol) and PPh₃ (166 mg, 0.63 mmol) in CH₂Cl₂ (5 mL) at 0 °C was added iodine (161 mg, 0.63 mmol). The residue was purified by silica gel column chromatography eluted with 5% EtOAc in hexanes to afford **7b** (83 mg, 32 %) as a colorless oil. ¹H NMR (CDCl₃, 300 MHz) δ 1.46 (s, 18H), 2.95-3.05 (m, 2H), 3.30-3.41 (m, 1H), 3.42-3.60 (m, 5H), 4.22-4.33 (m, 1H), 7.15-7.31 (m, 5H); ¹³C NMR (CDCl₃, 300 MHz) δ 28.2 (q), 36.8 (d), 43.6 (t), 56.9 (t), 63.8 (t), 81.2 (s), 126.6 (d), 128.3 (d), 129.1 (d), 139.9 (s), 170.5 (s); HRMS (positive ion ESI) Calcd for C₂₁H₃₂INNaO₄ [M + Na]⁺ *m/z* 512.1268. Found: [M + H]⁺ *m/z* 512.1238.

Using I₂ and imidazole. To a solution of **1b** (200 mg, 0.53 mmol) and PPh₃ (166 mg, 0.63 mmol) in CH₂Cl₂ (5 mL) at 0 °C was added imidazole (43 mg, 0.63 mmol) and iodine (161 mg, 0.63

mmol). The residue was purified by silica gel column chromatography eluted with 5 % EtOAc in hexanes to afford **7b** (232 mg, 90 %) as a colorless oil.

Using NIS. To the stirred solution of **1b** (200 mg, 0.53 mmol) and PPh₃ (166 mg, 0.63 mmol) in CH₂Cl₂ (5 mL) at 0 °C was added NIS (142 mg, 0.63 mmol). The residue was purified by silica gel column chromatography eluted with 5 % EtOAc in hexanes to afford **7b** (195 mg, 75 %) as a colorless oil.

(S)-tert-butyl 2,2'-(2-iodo-3-phenylpropylazanediyl)diacetate ((S)-7b). To a solution of **(S)-1b** (75 mg, 0.20 mmol) and PPh₃ (63 mg, 0.24 mmol) and imidazole (16.3 mg, 0.24 mmol) in CH₂Cl₂ (3 mL) at 0 °C was added iodine (60.2 mg, 0.24 mmol). The resulting mixture was stirred for 4 h while being maintained at 0 °C. The ice bath was removed, and the reaction mixture was warmed to room temperature and stirred for 1 h and evaporated to dryness. The residue was purified by silica gel column chromatography eluted with 5% EtOAc in hexanes to afford **(S)-7b** (85.4 mg, 88 %) as a yellowish oil. ¹H NMR (CDCl₃, 300 MHz) δ 1.46 (s, 18H), 2.95-3.06 (m, 2H), 3.30-3.41 (m, 1H), 3.45-3.60 (m, 5H), 4.22-4.33 (m, 1H), 7.15-7.31 (m, 5H); ¹³C NMR (CDCl₃, 300 MHz) δ 28.2 (q), 36.7 (d), 43.6 (t), 56.9 (t), 63.9 (t), 81.2 (s), 126.6 (d), 128.3 (d), 129.1 (d), 139.9 (s), 170.5 (s); The ¹H and ¹³C NMR data of **(S)-7b** is essentially identical to those of **(rac)-7b** as reported above. HRMS (positive ion ESI) Calcd for C₂₁H₃₂INNaO₄ [M + Na]⁺ m/z 512.1268. Found : [M + H]⁺ m/z 512.1251. [α]_D²⁶ = -4.2° (C 1.0, CHCl₃)

(R)-tert-butyl 2,2'-(2-iodo-3-phenylpropylazanediyl)diacetate ((R)-7b). To a solution of **(R)-1b** (214 mg, 0.56 mmol) and PPh₃ (178 mg, 0.68 mmol) and imidazole (46.2 mg, 0.68 mmol) in CH₂Cl₂ (6 mL) at 0 °C was added iodine (172 mg, 0.68 mmol). The resulting mixture was stirred for 4 h while being maintained at 0 °C. The ice bath was removed, and the reaction mixture was warmed to room temperature and stirred for 1 h and evaporated to dryness. The residue was purified by silica gel column chromatography eluted with 5% EtOAc in hexanes to afford **(R)-7b** (265 mg, 97 %) as a yellowish oil. ¹H NMR (CDCl₃, 300 MHz) δ 1.47 (s, 18H), 2.95-3.07 (m, 2H), 3.30-3.41 (m, 1H), 3.43-3.60 (m, 5H), 4.22-4.33 (m, 1H), 7.20-7.33 (m, 5H); ¹³C NMR (CDCl₃, 300 MHz) δ 28.2 (q), 36.7 (d), 43.6 (t), 56.9 (t), 63.9 (t), 81.2 (s), 126.6 (d), 128.3 (d), 129.1 (d), 139.9 (s), 170.5 (s); The ¹H and ¹³C NMR of **(S)-7b** is essentially identical to those of **(rac)-7b** as reported above. HRMS (positive ion ESI) Calcd for C₂₁H₃₂INNaO₄ [M + Na]⁺ m/z 512.1268. Found : [M + H]⁺ m/z 512.1253. [α]_D²⁶ = + 5.1° (C 1.0, CHCl₃)

General procedure for synthesis of 1, 6, or 8. To a solution of *N,N*-dialkylated alcohol **1** or **7** (1 eq) and PPh₃ (1.2 eq) in CH₂Cl₂ or CHCl₃ was portionwise added NBS (1.2 eq) at 0 °C over 20 min. The resulting mixture was stirred for 4 h while being maintained at 0 °C. The ice bath was removed, and the reaction mixture was warmed to room temperature and stirred for 1 h and

evaporated to dryness. The residue was purified via column chromatography on silica gel (60-230 mesh) eluting with 5-10% EtOAc in hexanes.

1,1-Bis-*tert*-butoxycarbonylmethyl-2-(4-nitrobenzyl)aziridinium bromide (2c). To a solution of **1c** (200 mg, 0.47 mmol) and PPh₃ (148 mg, 0.57 mmol) in CHCl₃ (3 mL) at 0 °C was added NBS (102 mg, 0.57 mmol). The residue was purified by silica gel column chromatography eluted with 10 % EtOAc in hexanes to afford **2c** (172 mg, 75%) as a colorless oil. The ¹H and ¹³C NMR spectral data of **2c** are essentially identical to those reported previously.⁷

1,1-Bis-benzyloxycarbonylmethyl-2-[3-(4-nitrophenyl)-propyl]aziridinium bromide (2d).

To a solution of **11d** (590 mg, 2.63 mmol) in CH₃CN (10 mL) at 0 °C was added K₂CO₃ (727 mg, 5.26 mmol). A solution of benzyl bromoacetate (1.20 g, 5.26 mmol) in CH₃CN (20 mL) at 0 °C was added dropwise over a span of 30 min. The reaction mixture was then warmed to room temperature and stirred for 24 h. The reaction mixture was filtered, and the filtrate was evaporated, and the residue was purified via column chromatography eluted with 30% EtOAc in hexanes (silica gel 60-230 mesh). Compound **1d** was obtained as slightly brownish oil (1.15 g, 84%). ¹H NMR (CDCl₃, 300 MHz) δ 1.15 -1.80 (m, 4 H), 2.61-2.82 (m, 3 H), 3.20-3.84 (m, 5 H),

5.12 (s, 4 H), 7.26-7.36 (m, 12 H), 8.12 (d, $J = 8.6$ Hz, 2 H); ^{13}C NMR (CDCl_3 , 300 MHz) δ 26.7 (t), 28.4 (t), 35.7 (t), 53.5 (t), 62.8 (d), 66.7 (t), 70.3 (t), 120.6 (d), 128.3 (d), 128.4 (d), 128.6 (d), 129.0 (d), 135.3 (s), 146.3 (s), 149.8 (s), 172.7 (s). Compound **1d** was found to be unstable at room temperature and immediately used for the next step.

To a solution of **1d** (120 mg, 0.23 mmol) and PPh_3 (60 mg, 0.23 mmol) in CH_2Cl_2 (3 mL) at 0 °C was portionwise added NBS (41 mg, 0.23 mmol) over 30 min. The resulting mixture was stirred for 4 h while being maintained at 0 °C and kept in the freezer overnight and warmed to room temperature and stirred for 1 h and evaporated to dryness. The residue was purified by silica gel column chromatography eluted with 10% EtOAc in hexanes to afford **2d** (98 mg, 73%) as a colorless oil. ^1H NMR (CDCl_3 , 300 MHz) δ 1.71- 2.07 (m, 4 H), 2.60-2.78 (m, 2 H), 3.05 (dd, $J = 7.1$ Hz, 7.9 Hz, 1 H), 3.25 (dd, $J = 7.1$ Hz, 7.9 Hz, 1 H), 3.62 (dd, $J = 15.6$, 15.6 Hz, 4 H), 4.01-4.12 (m, 1 H), 5.13 (s, 4 H), 7.26-7.35 (m, 12H), 8.14 (d, $J = 8.2$ Hz, 2H); ^{13}C NMR (CDCl_3 , 300 MHz) δ 24.7 (t), 34.9 (t), 35.3 (t), 54.5 (t), 56.1 (t), 62.3 (d), 66.4 (t), 123.6 (d), 128.2 (d), 128.3 (d), 128.5 (d), 129.1 (d), 135.4 (s), 146.3 (s), 149.7 (s), 170.8 (s). HRMS (positive ion FAB) Calcd for $\text{C}_{29}\text{H}_{32}\text{O}_6\text{N}_2\text{Br}$ $[\text{M} + \text{H}]^+$ m/z 583.1444. Found: $[\text{M} + \text{H}]^+$ m/z 583.1418.

1-Allyl-2-benzyl-1-tert-butoxycarbonylmethyl aziridinium bromide (2f). To a solution of **1f** (110 mg, 0.36 mmol) and PPh_3 (112.7 mg, 0.43 mmol) in CHCl_3 (3 mL) at 0 °C was added NBS (77 mg, 0.43 mmol). The residue was purified by silica gel column chromatography eluted with 5 % EtOAc in hexanes to afford **2f** (116 mg, 87 %) as a colorless oil. ^1H NMR (CDCl_3 , 300 MHz)

δ 1.46 (s, 9H), 2.98 (dd, $J = 14.4, 8.9$ Hz, 1H), 3.03 (dd, $J = 14.1, 7.3$ Hz, 1H), 3.14 (dd, $J = 14.1, 6.9$ Hz, 1H), 3.30-3.37 (m, 4H), 3.47 (dd, $J = 14.5, 4.5$ Hz, 1H), 4.15-4.24 (m, 1H), 5.13-5.24 (m, 2H), 5.79-5.92 (m, 1H), 7.23-7.34 (m, 5H); ^{13}C NMR (CDCl_3 , 300 MHz) δ 28.2 (q), 42.7 (t), 55.4 (d), 56.0 (t), 57.9 (t), 61.1 (t), 81.1 (s), 117.9 (t), 126.7 (d), 128.3 (d), 129.3 (d), 135.7 (d), 138.7 (s), 170.7 (s). HRMS (positive ion FAB) Calcd for $\text{C}_{18}\text{H}_{26}\text{BrO}_2\text{N}$ $[\text{M} + \text{H}]^+$ m/z 368.1225. Found : $[\text{M} + \text{H}]^+$ m/z 368.1209.

2-Benzyl-1-tert-butoxycarbonylmethyl-1-(4-nitrobenzyl)aziridinium bromide (2g). To a solution of **1g** (82 mg, 0.21 mmol) and PPh_3 (64.4 mg, 0.25 mmol) in CHCl_3 (2 mL) at 0°C was added NBS (43.8 mg, 0.25 mmol). The residue was purified by silica gel column chromatography eluted with 5% EtOAc in hexanes to afford **2g** (87 mg, 92 %) as a colorless oil. ^1H NMR (CDCl_3 , 300 MHz) δ 1.46 (s, 9H), 3.01 (dd, $J = 14.4, 8.2$ Hz, 1H), 3.08-3.29 (m, 2H), 3.19-3.36 (m, 3H), 4.00 (s, 2H), 4.09-4.21 (m, 1H), 7.14-7.31 (m, 5H), 7.56 (d, $J = 8.6$ Hz, 2H), 8.18 (d, $J = 8.6$ Hz, 2H); ^{13}C NMR (CDCl_3 , 300 MHz) δ 28.2 (q), 43.0 (t), 54.7 (d), 55.6 (t), 58.1 (t), 61.2 (t), 81.5 (s), 123.7 (d), 126.9 (d), 128.5 (d), 129.1 (d), 129.3 (d), 138.2 (s), 146.8 (s), 147.4 (s), 170.2 (s). HRMS (positive ion FAB) Calcd for $\text{C}_{22}\text{H}_{28}\text{BrO}_4\text{N}_2$ $[\text{M} + \text{H}]^+$ m/z 463.1232. Found : $[\text{M} + \text{H}]^+$ m/z 463.1211.

1,1-Diallyl-2-benzyl aziridinium bromide (2h). To a solution of **1h** (135 mg, 0.58 mmol) and PPh_3 (183 mg, 0.70 mmol) in CHCl_3 (3 mL) at 0 °C was added NBS (125 mg, 0.70 mmol). The residue was purified by silica gel column chromatography eluted with 5% EtOAc in hexanes to afford **2h** (133 mg, 78 %) as a colorless oil. ^1H NMR (CDCl_3 , 300 MHz) δ 2.82 (dd, $J = 13.6, 7.9$ Hz, 1H), 2.90-2.99 (two dd's overlapped, $J = 14.5, 13.6, 7.9, 4.2$ Hz, 2H), 3.16 (dd, $J = 14.1, 6.6$ Hz, 2H), 3.26 (dd, $J = 14.1, 6.6$ Hz, 2H), 3.51 (dd, $J = 14.5, 4.2$ Hz, 1H), 4.18-4.27 (m, 1H), 5.16-5.24 (m, 4H), 5.82-5.95 (m, 2H), 7.24-7.36 (m, 5H); ^{13}C NMR (CDCl_3 , 300 MHz) δ 42.8 (t), 55.2 (d), 57.9 (t), 60.6 (t), 117.8 (t), 126.7 (d), 128.4 (d), 129.3 (d), 135.5 (d), 138.9 (s). HRMS (positive ion FAB) Calcd for $\text{C}_{15}\text{H}_{21}\text{BrN}$ $[\text{M} + \text{H}]^+$ m/z 294.0857. Found: $[\text{M} + \text{H}]^+$ m/z 294.0847.

1,1,2-Tribenzyl aziridinium bromide (2i). To a solution of **1i** (100 mg, 0.30 mmol) and PPh_3 (94 mg, 0.36 mmol) in CHCl_3 (3 mL) at 0 °C was added NBS (64 mg, 0.36 mmol). The residue was purified by silica gel column chromatography eluted with 5% EtOAc in hexanes to afford colorless oil **2i** (104 mg, 87%). ^1H NMR (CDCl_3 , 300 MHz) δ 2.72 (dd, $J = 14.6, 9.4$ Hz, 1H), 2.90 (dd, $J = 13.5, 8.1$ Hz, 1H), 2.97 (dd, $J = 13.5, 6.3$ Hz, 1H), 3.47 (dd, $J = 14.6, 4.2$ Hz, 1H), 3.66 (d, $J = 13.5$ Hz, 2H), 3.73 (d, $J = 13.5$ Hz, 2H), 4.05-4.14 (m, 1H), 7.06-7.41 (m, 15H); ^{13}C NMR (CDCl_3 , 300 MHz) δ 42.7 (t), 54.8 (d), 59.4 (t), 61.4 (t), 126.6 (d), 127.3 (d), 128.3 (d), 128.4 (d), 129.1 (d), 129.1 (d), 138.9 (s), 139.0 (s). HRMS (positive ion FAB) Calcd for $\text{C}_{23}\text{H}_{25}\text{BrN}$ $[\text{M} - \text{Br} + \text{H}]^+$ m/z 314.1909. Found: $[\text{M} - \text{Br} + \text{H}]^+$ m/z 314.1924.

1-Allyl-2-benzyl-1-(2,4-dimethoxybenzyl)aziridinium bromide (2j). To a solution of **1j** (245 mg, 0.72 mmol) and PPh₃ (235 mg, 0.90 mmol) in CHCl₃ (3 mL) at 0 °C was added NBS (160 mg, 0.90 mmol). The resulting mixture was stirred for 4 h while being maintained at 0 °C. The ice bath was removed, and the reaction mixture was warmed to room temperature and stirred for 18 h and evaporated to dryness. The residue was purified by silica gel column chromatography eluted with 5% EtOAc in hexanes to afford **2j** (71 mg, 24.6 %) as a yellowish oil. ¹H NMR (CDCl₃, 300 MHz) δ 2.77-3.02 (m, 3H), 3.08-3.29 (m, 2H), 3.53-3.63 (m, 1H), 3.68 (d, *J* = 10.2 Hz, 2H), 3.80 (s, 3H), 3.83 (s, 3H), 4.16-4.28 (m, 1H), 5.13-5.28 (m, 2H), 5.85-6.01 (m, 1H), 6.45-6.54 (m, 2H), 7.15-7.36 (m, 6H); ¹³C NMR (CDCl₃, 300 MHz) δ 42.6 (t), 52.2 (t), 55.4 (q), 55.5 (q), 58.0 (t), 60.9 (t), 98.5 (d), 104.1 (d), 117.5 (t), 119.3 (s), 126.5 (d), 128.2 (d), 129.2 (d), 131.4 (d), 136.0 (d), 139.2 (s), 158.9 (s), 160.1 (s). HRMS (Positive ion ESI) Calcd for C₂₁H₂₇BrNO₂ [M + H]⁺ *m/z* 404.1220 Found: [M + H]⁺ *m/z* 404.1215.

(S)-1,1-bis(2-tert-butoxy-2-oxoethyl)-2-propylaziridinium bromide (10a). To a solution of **9a** (500 mg, 1.51 mmol) and PPh₃ (475mg, 1.81 mmol) in CH₂Cl₂ (10 mL) at 0 °C was portionwise added NBS (322 mg, 1.81 mmol). The residue was purified by silica gel column chromatography

eluted with 5 % EtOAc in hexanes to afford **10a** (371 mg, 62 %) as a colorless oil. ^1H NMR (CDCl_3 , 300 MHz) δ 0.93 (t, $J = 7.3$ Hz, 3H), 1.46 (s, 18H), 1.56-1.76 (m, 3H), 1.95-2.03 (m, 1H), 3.01 (dd, $J = 14.2, 7.1$ Hz, 1H), 3.19 (dd, $J = 14.2, 6.5$ Hz, 1H), 3.42-3.55 (m, 4H), 4.04-4.11 (m, 1H); ^{13}C NMR (CDCl_3 , 300 MHz) δ 13.5 (q), 20.7 (t), 28.2 (q), 38.2 (t), 55.6 (d), 57.2 (t), 62.6 (t), 81.1 (s), 170.6 (s). HRMS (positive ion FAB) Calcd for $\text{C}_{17}\text{H}_{33}\text{BrNO}_4$ $[\text{M}+\text{H}]^+$ m/z 394.1593. Found: $[\text{M} + \text{H}]^+$ m/z 394.1613.

(S)-1,1-bis(2-tert-butoxy-2-oxoethyl)-2-isopropylaziridinium bromide (10b). To a solution of **9b** (166 mg, 0.50 mmol) and PPh_3 (157 mg, 0.60 mmol) in CHCl_3 (3 mL) at 0°C was added NBS (107 mg, 0.60 mmol). The residue was purified by silica gel column chromatography eluted with 5 % EtOAc in hexanes to afford **10b** (147 mg, 75 %) as a colorless oil. ^1H NMR (CDCl_3 , 300 MHz) δ 0.88 (d, $J = 6.6$ Hz, 3H), 0.98 (d, $J = 6.6$ Hz, 3H), 1.41 (s, 18H), 2.03 (septet further split into d, $J = 6.6, 2.8$ Hz, 1H), 3.00 (dd, $J = 14.4, 7.1$ Hz, 1H), 3.14 (dd, $J = 14.4, 7.1$ Hz, 1H), 3.35-3.48 (m, 4H), 4.10 (td, $J = 7.1, 2.8$ Hz, 1H); ^{13}C NMR (CDCl_3 , 300 MHz) δ 17.0 (q), 21.6 (q), 28.1 (q), 30.7 (d), 56.9 (t), 60.2 (t), 64.0 (d), 81.1 (s), 170.5 (s). HRMS (positive ion FAB) Calcd for $\text{C}_{17}\text{H}_{32}\text{BrNO}_4$ $[\text{M}-\text{Br}]^+$ m/z 314.2331. Found: $[\text{M}-\text{Br}]^+$ m/z 314.2315.

(S)-1,1-bis(2-tert-butoxy-2-oxoethyl)-2-phenylaziridinium bromide (10c). To a solution of **9c** (190 mg, 0.52 mmol) and PPh_3 (162 mg, 0.62 mmol) in CHCl_3 (3 mL) at 0°C was added NBS

(111 mg, 0.62 mmol). The residue was purified by silica gel column chromatography eluted with 5 % EtOAc in hexanes to afford **10c** (134 mg, 60 %) as a colorless oil. ^1H NMR (CDCl_3 , 300 MHz) δ 1.44 (s, 18H), 3.36-3.45 (s, 4H), 3.44 (d, J = 7.2 Hz, 2H), 5.12 (t, J = 7.2 Hz, 1H), 7.26-7.45 (m, 5H); ^{13}C NMR (CDCl_3 , 300 MHz) δ 28.2 (q), 53.8 (d), 57.1 (t), 63.0 (t), 81.1 (s), 128.0 (d), 128.4 (d), 128.6 (d), 140.6 (s), 170.6 (s). HRMS (positive ion ESI) Calcd for $\text{C}_{20}\text{H}_{30}\text{BrNNaO}_4$ $[\text{M} + \text{Na}]^+$ m/z 450.1250. Found: $[\text{M} + \text{H}]^+$ m/z 450.1251.

(S)-2-(benzylthiomethyl)-1,1-bis(2-tert-butoxy-2-oxoethyl)aziridinium bromide (10d). To a solution of **9d** (200 mg, 0.47 mmol) and PPh_3 (148 mg, 0.56 mmol) in CHCl_3 (5 mL) at 0 °C was portionwise added NBS (100 mg, 0.56 mmol). The residue was purified by silica gel column chromatography eluted with 5 % EtOAc in hexanes to afford **10d** (87 mg, 38 %) as a colorless oil. ^1H NMR (CDCl_3 , 300 MHz) δ 1.45 (s, 18H), 2.92-3.10 (m, 2H), 3.11-3.29 (m, 2H), 3.38-3.53 (m, 4H), 3.79 (s, 2H), 4.11-4.20 (m, 1H), 7.20-7.36 (m, 5H); ^{13}C NMR (CDCl_3 , 300 MHz) 28.2 (q), 37.0 (t), 37.1 (t), 53.3 (d), 57.2 (t), 60.9 (t), 81.2 (s), 127.2 (d), 128.6 (d), 129.0 (d), 138.1 (s), 170.8 (s). HRMS (positive ion ESI) Calcd for $\text{C}_{22}\text{H}_{34}\text{BrNNaO}_4\text{S}$ $[\text{M} + \text{H}]^+$ m/z 510.1284. Found: $[\text{M} + \text{H}]^+$ m/z 510.1287.

(S)-2-((1H-indol-2-yl)methyl)-1,1-bis(2-tert-butoxy-2-oxoethyl)aziridinium bromide (10e).

To the stirred solution of **9e** (122 mg, 0.29 mmol) and PPh₃ (91.7 mg, 0.35 mmol) in CHCl₃ (3 mL) at 0 °C was portionwise added NBS (61.9 mg, 0.35 mmol). The residue was purified by silica gel column chromatography eluted with 5 % EtOAc in hexanes to afford **10e** (63 mg, 45 %) as a colorless oil. ¹H NMR (CDCl₃, 300 MHz) δ 1.45 (s, 18H), 3.09-3.34 (m, 3H), 3.41-3.67 (m, 5H), 4.36-4.43 (m, 1H), 7.07-7.21 (m, 3H), 7.35 (d, *J* = 7.9 Hz, 1H), 7.64 (d, *J* = 7.9 Hz, 1H), 8.10 (br s, 1H, NH); ¹³C NMR (CDCl₃, 300 MHz) δ 28.2 (q), 32.4 (t), 55.3 (d), 57.0 (t), 61.9 (t), 81.2 (s), 111.1 (d), 112.8 (s), 118.9 (d), 119.4 (d), 122.0 (d), 123.0 (d), 127.5 (s), 136.1 (s), 170.6 (s). HRMS (positive ion FAB) Calcd for C₂₃H₃₃BrN₂O₄ [M - Br]⁺ *m/z* 401.2440. Found: [M-Br]⁺ *m/z* 401.2465.

(S)-2-(4-(2-tert-butoxy-2-oxoethoxy)benzyl)-1,1-bis(2-tert-butoxy-2-oxoethyl)aziridinium

bromide (10f). To a solution of **9f** (200mg, 0.39 mmol) and PPh₃ (158 mg, 0.61 mmol) in CH₂Cl₂ (5 mL) at 0 °C was added NBS (108 mg, 0.61 mmol). The residue was purified by silica gel column chromatography eluted with 5 % EtOAc in hexanes to afford **10f** (93 mg, 41 %) as a colorless oil. ¹H NMR (CDCl₃, 300 MHz) δ 1.46 (s, 18H), 1.48 (s, 9H), 2.85-3.07 (m, 2H), 3.24 (dd, *J* = 14.2, 6.3 Hz, 1H), 3.37-3.56 (m, 5H), 4.14-4.26 (m, 1H), 4.49 (s, 2H), 6.83 (d, *J* = 8.5 Hz, 2H) 7.26 (d, *J* = 8.5 Hz, 2H); ¹³C NMR (CDCl₃, 300 MHz) δ 28.1 (q), 28.2 (q), 41.5 (t), 55.8(d), 57.1 (t), 62.0 (t), 65.8 (t) 81.2 (s), 82.3 (s), 114.4 (d), 130.4 (d), 131.6 (s), 156.7 (s), 168.1 (s), 170.6 (s). HRMS (positive ion FAB) Calcd for C₂₇H₄₃BrNO₇ [M + H]⁺ *m/z* 572.2223. Found: [M + H]⁺ *m/z* 572.2203.

tert-butyl 1-bromo-3-phenylpropan-2-ylcarbamate (8e). To a solution of **1e** (200 mg, 0.80 mmol) and PPh₃ (252 mg, 0.96 mmol) in CHCl₃ (3 mL) at 0 °C was added NBS (170 mg, 0.96 mmol). The residue was purified by silica gel column chromatography eluted with 10 % EtOAc in hexanes to afford **8e** (117 mg, 47 %) as a colorless oil. ¹H NMR (CDCl₃, 300 MHz) δ 1.44 (s, 9H), 2.82-2.98 (m, 2H), 3.36 (dd, *J* = 10.4, 3.6 Hz, 2H), 3.53 (dd, *J* = 10.2, 3.6 Hz, 1H), 4.05 (br s, 1H), 4.67 (d, *J* = 7.5 Hz, 1H (of NH)), 7.22-7.34 (m, 5H); ¹³C NMR (CDCl₃, 300 MHz) δ 28.4 (q), 37.4 (t), 38.8 (t), 51.5 (d), 79.8 (s), 126.8 (d), 128.7 (d), 129.3 (d), 137.1 (s), 155.0 (s). HRMS (positive ion ESI) Calcd for C₁₄H₂₀BrNNaO₂ [M + Na]⁺ *m/z* 336.0570. Found : [M + Na]⁺ *m/z* 336.0559.

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1. ^1H and ^{13}C NMR spectra

(2a)

(R)-7b

2. Chiral-HPLC spectra of the stereoisomers (rac)-7b, (S)-7b and (R)-7b.