A General Process for the Haloamidation of Olefins. Scope and Mechanism

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Supplementary Materials

Materials and Methods. Unless stated otherwise, reactions were performed in flame-dried glassware under a positive pressure of nitrogen using freshly distilled dry solvents. Thin-layer chromatography (TLC) was performed using E. Merck silica gel 60 F₂₅₄ precoated plates (0.25 mm). Flash chromatography was performed using Baker silica gel (40 μ m particle size). NMR spectra were recorded on Varian Mercury-300 and Varian Mercury-400 instruments and calibrated using residual undeuterated solvent as an internal reference. IR spectra were recorded on Avatar 360 FT-IR spectrometer. Low-resolution and high-resolution mass spectral analyses were performed at the Harvard University Mass Spectrometry Center. Commercial grade reagents and solvents were used without further purification except as indicated below. Dichloromethane and MeCN were distilled from calcium hydride. DME and THF were distilled from sodium.

General Procedure for Bromoamidation using acetonitrile. To a solution of *N*-bromoacetamide (164 mg, 1.2 mmol) in dry acetonitrile (10 mL) at 0 °C in dark was added SnCl₄ (1.0 M in CH₂Cl₂, 0.4 mL, 0.4 mmol) or BF₃·Et₂O (1.0 M in CH₂Cl₂, 0.4 mL, 0.4 mmol) and

deionized water (0.022 mL, 1.2 mmol) successively. After 5 min, olefin (1.0 mmol) was added at once to the reaction mixture. The reaction was followed by TLC or NMR. After the reaction was complete, saturated NaHCO₃ (3 mL) and Na₂SO₃ (3 mL) were added. The organic layer was separated and the aqueous layer was extracted with CH₂Cl₂ (3 × 20 mL). The combined extracts were washed with brine (10 mL), dried (MgSO₄), filtered and concentrated *in vacuo*. The residue was purified by flash column chromatography to yield the corresponding haloamide or oxazoline.

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***N*-(*trans*-2-bromocyclohexyl)acetamide (4).** White solid; ¹H NMR (400 MHz, CDCl₃) δ 5.56 (1H, brs), 3.93 (1H, dddd, *J* = 10.6, 10.6, 8.0, 4.0 Hz), 3.86 (1H, ddd, *J* = 10.6, 10.6, 4.0 Hz), 2.42-2.35 (1H, m), 2.25-2.18 (1H, m), 2.01 (3H, s), 1.96-1.86 (1H, m), 1.78-1.70 (1H, m), 1.50-1.18 (4H, m); ¹³C NMR (100 MHz, CDCl₃) δ 169.8, 55.6, 55.3, 37.3, 33.6, 26.7, 24.5, 23.7; MS (AP+) C₈H₁₅BrNO (MH⁺) 219.8; mp 122-123 °C. (The physical data were in full accordance with the literature value in all respects: Bellucci, G.; Bianchini, R.; Chiappe, C. *J. Org. Chem.* **1991**, *56*, 3067-3073.)

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***N*-(*trans*-2-bromocyclohexyl)propionamide (5).** To a solution of *N*-bromoacetamide (164 mg, 1.2 mmol) in dry propionitrile (10 mL) at 0 °C in dark was added SnCl₄ (1.0 M in CH₂Cl₂, 0.4 mL, 0.4 mmol) and deionized water (0.022 mL, 1.2 mmol) successively. After 5 min, cyclohexene (0.1 mL, 1.0 mmol) was added at once to the reaction mixture. The reaction was followed by NMR. After 1 h, the reaction was quenched with saturated NaHCO₃ (3 mL) and Na₂SO₃ (3 mL). The organic layer was separated and the aqueous layer was extracted with CH₂Cl₂ (3 × 20 mL). The combined extracts were washed with brine (10 mL), dried (MgSO₄), filtered and concentrated *in vacuo*. The residue was purified by flash column chromatography to yield **5** as a white solid. IR (film) 3246, 2939, 1643, 1558, 1264, 1189 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 5.53 (1H, brs), 3.96 (1H, dddd, *J* = 10.8, 10.8, 7.6, 4.0 Hz), 3.88 (1H, ddd, *J* = 10.8, 10.8, 4.0 Hz), 2.42-2.35 (1H, m), 2.25-2.18 (3H, m), 1.96-1.86 (1H, m), 1.78-1.70 (1H, m), 1.50-1.20 (4H, m), 1.16 (3H, t, *J* = 7.6 Hz); ¹³C NMR (100 MHz, CDCl₃) δ 173.4, 55.7, 55.2, 37.3, 33.6, 30.1, 26.7, 24.6, 10.1; HRMS (ES⁺) calcd for C₉H₁₇BrNO (MH⁺) 234.0493, found 234.0485; mp 113-114 °C.

6

***N'*-(*trans*-2-bromocyclohexyl)-*N,N*-dimethylurea (6).** To a solution of *N*-bromoacetamide (164 mg, 1.2 mmol) in dry CH₂Cl₂ (2 mL) and *N,N*-dimethylcyanamide (0.4 mL, 5.0 mmol) at 0 °C in dark was added SnCl₄ (1.0 M in CH₂Cl₂, 0.4 mL, 0.4 mmol) and deionized water (0.022 mL, 1.2 mmol) successively. After 5 min, cyclohexene (0.1 mL, 1.0 mmol) was added at once to the reaction mixture. After 1 h, the reaction was quenched with saturated NaHCO₃ (3 mL) and Na₂SO₃ (3 mL). The organic layer was separated and the aqueous layer was extracted with CH₂Cl₂ (3 × 20 mL). The combined extracts were washed with brine (10 mL), dried (MgSO₄), filtered and concentrated *in vacuo*. The residue was purified by flash column chromatography to yield **6** as a white solid. IR (film) 3281, 2936, 1698, 1540, 1391, 1050 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 4.52 (1H, d, *J* = 6.0 Hz), 3.95 (1H, dt, *J* = 10.4, 4.4 Hz), 3.79-3.71 (1H, m), 2.90 (6H, s), 2.39-2.34 (1H, m), 2.32-2.25 (1H, m), 1.95-1.85 (1H, m), 1.74-1.68 (2H, m), 1.44-1.19 (3H, m); ¹³C NMR (100 MHz, CDCl₃) δ 158.0, 57.1, 56.8, 37.4, 36.4, 34.3, 26.8, 24.6; HRMS (ES+) calcd for C₉H₁₈BrN₂O (MH⁺) 249.0602, found 249.0610; mp 140-142 °C.

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***N*-(*trans*-2-iodocyclohexyl)acetamide (7).** To a solution of iodine (254 mg, 1.2 mmol) in dry acetonitrile (10 mL) at 0 °C in dark was added BF₃·Et₂O (1.0 M in CH₂Cl₂, 1.0 mL, 1.0 mmol) and deionized water (0.022 mL, 1.2 mmol) successively. After 5 min, cyclohexene (0.1 mL, 1.0 mmol) was added at once to the reaction mixture. The reaction was followed by NMR. After 1 h, the reaction was quenched with saturated NaHCO₃ (3 mL) and Na₂SO₃ (3 mL). The organic layer was separated and the aqueous layer was extracted with CH₂Cl₂ (3 × 20 mL). The

combined extracts were washed with brine (10 mL), dried (MgSO₄), filtered and concentrated *in vacuo*. The residue was purified by flash column chromatography to yield **7** as a white solid. IR (film) 3266, 2930, 1649, 1631, 1371, 1168, 1037, 971 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 6.39 (1H, d, *J* = 8.0 Hz), 4.07-3.92 (2H, m), 2.50-2.45 (1H, m), 2.10-2.02 (2H, m), 2.00 (3H, s), 1.81-1.76 (1H, m), 1.56-1.20 (4H, m); ¹³C NMR (100 MHz, CDCl₃) δ 169.8, 55.9, 39.7, 36.0, 33.7, 28.1, 24.9, 23.7; HRMS (ES+) calcd for C₈H₁₅INO (MH⁺) 268.0198, found 268.0201; mp 119-121 °C (lit. 121-123 °C, Radner, F. *Acta Chem. Scand.* **1989**, 43,902-907).

***N*-(trans-2-chlorocyclohexyl)acetamide (8).** To a solution of *N*-chloroacetamide (112 mg, 1.2 mmol) in dry acetonitrile (10 mL) at 0 °C in dark was added BF₃-Et₂O (1.0 M in CH₂Cl₂, 1.0 mL, 1.0 mmol) and deionized water (0.022 mL, 1.2 mmol) successively. After 5 min, cyclohexene (0.1 mL, 1.0 mmol) was added at once to the reaction mixture and it was allowed to raise to 23 °C. The reaction was followed by NMR. After 20 h, the reaction was quenched with saturated NaHCO₃ (3 mL) and Na₂SO₃ (3 mL). The organic layer was separated and the aqueous layer was extracted with CH₂Cl₂ (3 × 20 mL). The combined extracts were washed with brine (10 mL), dried (MgSO₄), filtered and concentrated *in vacuo*. The residue was purified by flash column chromatography to yield **8** as a white solid. ¹H NMR (300 MHz, CDCl₃) δ 5.46 (1H, brs), 3.86 (1H, dddd, *J* = 10.6, 10.6, 7.5, 4.0 Hz), 3.72 (1H, ddd, *J* = 10.6, 10.6, 4.0 Hz), 2.30-2.13 (2H, m), 2.01 (3H, s), 1.82-1.65 (2H, m), 1.78-1.70 (1H, m), 1.48-1.16 (4H, m); ¹³C NMR (100 MHz, CDCl₃) δ 170.0, 62.8, 55.2, 36.3, 33.0, 25.6, 24.4, 23.7; MS (AP+) C₈H₁₅ClNO (MH⁺) 175.8; mp

122-124 °C. (The physical data were in full accordance with the literature value in all respects:

Driguez, H.; Paton, J. M.; Lessard, J. *Can. J. Chem.* **1977**, *55*, 700-717.)

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cis-3a,5,6,6a-Tetrahydro-2-methyl-4H-cyclopentoxazole (9). Colorless oil; IR (film) 2959, 1668, 1385, 1230, 953 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 4.90 (1H, dd, $J = 6.6, 6.0$ Hz), 4.46 (1H, dd, $J = 7.0, 6.6$ Hz), 2.00-1.80 (5H, m), 1.66-1.38 (4H, m); ^{13}C NMR (100 MHz, CDCl_3) δ 164.9, 84.8, 71.6, 34.8, 33.9, 22.3, 13.9; MS (AP+) $\text{C}_7\text{H}_{13}\text{NO}$ (MH^+) 125.8. (The physical data were in full accordance with the literature value in all respects: Hu, N. X.; Aso, Y.; Otsubo, T.; Ogura, F. *J. Chem. Soc. Perkin Trans. 1* **1989**, 1775-1780.)

10

N-(trans-2-bromocyclooctyl)acetamide (10). Colorless oil. IR (film) 3269, 2929, 1635, 1541, 1369, 1225, 957 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 6.39 (1H, d, $J = 7.6$ Hz), 4.36-4.30 (1H, m), 3.88-3.80 (1H, m), 2.10-2.04 (2H, m), 1.87 (3H, s), 1.73-1.43 (10H, m); ^{13}C NMR (100 MHz, CDCl_3) δ 169.4, 57.1, 49.5, 34.9, 33.5, 30.5, 29.7, 24.5, 23.6, 23.3; HRMS (ES+) calcd for $\text{C}_{10}\text{H}_{19}\text{BrNO}$ (MH^+) 248.0650, found 248.0643.

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***cis*-4,5,6,7,7a-pentahydro-2,3a-dimethylbenzoxazole (11).** Colorless oil. IR (film) 2932, 1658, 1441, 1384, 1229, 1023, 951 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 4.84 (1H, t, $J = 4.0$ Hz), 2.20 (3H, s), 2.09-1.73 (5H, m), 1.59 (3H, s), 1.57-1.42 (3H, m); ^{13}C NMR (100 MHz, CDCl_3) δ 175.9, 91.3, 64.1, 32.1, 25.0, 24.0, 17.5, 16.4, 14.3; HRMS (ES+) calcd for $\text{C}_9\text{H}_{16}\text{NO}$ (MH^+) 154.1232, found 154.1225.

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***N*-(*trans*-2-bromo-3-cyclohexenyl)acetamide (12).** White solid; IR (film) 3270, 2924, 1648, 1542, 1373, 1312, 733 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 5.73-5.62 (2H, m), 5.61-5.55 (1H, m), 4.26-4.20 (2H, m), 2.86-2.76 (2H, m), 2.70-2.60 (1H, m), 2.01 (3H, s), 2.03-1.99 (1H, m); ^{13}C NMR (100 MHz, CDCl_3) δ 169.9, 124.6, 124.5, 49.9, 48.9, 34.1, 30.5, 23.7; HRMS (ES+) calcd for $\text{C}_8\text{H}_{13}\text{BrNO}$ (MH^+) 218.0180, found 218.0185; mp 86-88 $^\circ\text{C}$.

13

cis-4,7,7a-trihydro-2,3a-dimethylbenzoxazole (13). Colorless oil. IR (film) 2927, 1657, 1546, 1382, 1014, 881 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 5.93-5.86 (1H, m), 5.83-5.78 (1H, m), 5.10 (1H, brs), 2.75 (1H, dd, $J = 16.4, 6.8$ Hz), 2.62 (1H, ddd, $J = 16.4, 6.8, 2.0$ Hz), 2.35 (3H, s), 2.26 (1H, m), 1.99-1.94 (1H, m), 1.63 (3H, s); ^{13}C NMR (100 MHz, CDCl_3) δ 175.2, 128.1, 125.1, 91.9, 65.8, 33.0, 27.3, 26.7, 13.6; MS (AP+) $\text{C}_9\text{H}_{14}\text{NO}$ (MH^+) 151.9.

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N-[3-(benzyloxy)-2-bromocyclohexyl]acetamide (15). White solid. IR (film) 3261, 2939, 1718, 1652, 1268, 1026, 707 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 8.05 (2H, d, $J = 7.6$ Hz), 7.53 (1H, t, $J = 7.2$ Hz), 7.42 (2H, t, $J = 7.6$ Hz), 7.09 (1H, d, $J = 8.4$ Hz), 5.51 (1H, brs), 4.44 (1H, dq, $J = 10.0, 4.0$ Hz), 4.26 (1H, dd, $J = 10.0, 2.8$ Hz), 2.21-2.17 (1H, m), 2.01 (3H, s), 1.75-1.43 (5H, m); (400 MHz, $\text{CDCl}_3+\text{D}_2\text{O}$) δ 8.05 (2H, d, $J = 7.6$ Hz), 7.53 (1H, t, $J = 7.2$ Hz), 7.42 (2H, t, $J = 7.6$ Hz), 5.48 (1H, brs), 4.40 (1H, dt, $J = 10.0, 4.0$ Hz), 4.23 (1H, dd, $J = 10.0, 2.8$ Hz), 2.21-2.17 (1H, m), 2.01 (3H, s), 1.75-1.43 (5H, m); ^{13}C NMR (100 MHz, CDCl_3) δ 170.4, 165.9, 133.6, 130.0, 128.8, 128.7, 73.1, 56.2, 51.3, 30.0, 23.7, 19.5; HRMS (ES+) calcd for $\text{C}_{15}\text{H}_{19}\text{BrNO}_3$ (MH^+) 340.0548, found 340.0535; mp 145-147 $^\circ\text{C}$. (The corresponding starting material was prepared according to the literature method: Yasui, K.; Fugmi, K.; Tanaka, S.; Tamaru, Y. *J. Org. Chem.* **1995**, 60, 1365-1380.)

***N*-[3-(3,5-dinitrobenzyloxy)-2-bromocyclohexyl]acetamide (16).** White solid. IR (film) 3248, 2927, 2845, 1736, 1543, 1347, 1275, 1161, 718 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 9.25 (1H, t, $J = 2.0$ Hz), 9.16 (2H, t, $J = 2.0$ Hz), 5.70 (1H, d, $J = 7.6$ Hz), 5.61 (1H, brs), 4.47 (1H, dd, $J = 9.2, 2.4$ Hz), 4.30 (1H, dq, $J = 9.2, 4.0$ Hz), 2.35-2.16 (2H, m), 2.04 (3H, s), 1.85-1.60 (4H, m); (400 MHz, $\text{CDCl}_3 + \text{D}_2\text{O}$) δ 9.25 (1H, t, $J = 2.0$ Hz), 9.16 (2H, t, $J = 2.0$ Hz), 5.60 (1H, brs), 4.45 (1H, dd, $J = 9.2, 2.4$ Hz), 4.30 (1H, dt, $J = 9.2, 4.0$ Hz), 2.35-2.16 (2H, m), 2.04 (3H, s), 1.85-1.60 (4H, m); ^{13}C NMR (100 MHz, CDCl_3) δ 170.1, 161.9, 133.8, 129.8, 123.0, 75.0, 54.6, 52.0, 29.4, 23.8, 19.7; HRMS (ES+) calcd for $\text{C}_{15}\text{H}_{17}\text{BrN}_3\text{O}_7$ (MH^+) 447.0515, found 447.0502; mp 172-174 $^\circ\text{C}$. (The corresponding starting material was prepared according to the literature method: Yasui, K.; Fugmi, K.; Tanaka, S.; Tamaru, Y. *J. Org. Chem.* **1995**, *60*, 1365-1380.)

4-Bromohexahydro-2(3H)-benzoxoazolinone (17). To a solution of *N*-bromoacetamide (164 mg, 1.2 mmol) in dry acetonitrile (10 mL) at 0 $^\circ\text{C}$ in dark was added SnCl_4 (1.0 M in CH_2Cl_2 , 0.1 mL, 0.1 mmol) and deionized water (0.022 mL, 1.2 mmol) successively. After 5 min, olefin (1.0

mmol) was added at once to the reaction mixture. The reaction was followed by TLC or NMR. After the reaction finished, it was quenched with saturated NaHCO₃ (3 mL) and Na₂SO₃ (3 mL). The organic layer was separated and the aqueous layer was extracted with CH₂Cl₂ (3 × 20 mL). The combined extracts were washed with brine (10 mL), dried (MgSO₄), filtered and concentrated *in vacuo*. The residue was purified by flash column chromatography to yield a 1:1 (based on ¹H NMR) mixture of **17** and **20** as a colorless oil. The mixture was dissolved in CH₂Cl₂ (0.5 mL) and *n*-hexane (5 mL) and the solution was stirred vigorously for 10 min. The two layers were separated, in which the upper *n*-hexane layer contained **20** and the lower CH₂Cl₂ layer contained **17**.

17 Colorless crystals. IR (film) 3258, 2943, 1743, 1387, 1026, 903, 726 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 4.66 (1H, t, *J* = 6.0 Hz), 4.27 (1H, m), 4.04 (1H, q, *J* = 5.2 Hz), 2.20-2.12 (1H, m), 1.95-1.55 (5H, m); ¹³C NMR (100 MHz, CDCl₃) δ 159.8, 80.7, 52.2, 49.2, 31.4, 27.4, 18.8; MS (AP+) C₉H₁₄BrN₂O₂ (M+CH₃CN+H⁺) 262.9; HRMS (ES+) calcd for C₇H₁₁BrNO₂ (MH⁺) 219.9973, found 219.9966; mp 100-101 °C.

***N*-tert-butylacetamide (20)** White solid. ¹H NMR (400 MHz, CDCl₃) δ 5.34 (1H, brs), 1.90 (3H, s), 1.33 (1H, s); ¹³C NMR (100 MHz, CDCl₃) δ 169.7, 51.4, 29.0, 24.7; mp 95-97 °C. (The physical data were in full accordance with the literature value in all respects: Newcomb, M.; Varick, T. R.; Goh, S.-H. *J. Am. Chem. Soc.* **1990**, 5186-5193.)

3-Acetylamino-4-bromo-6-oxabicyclo[3.2.1]octan-7-one (18). White solid. IR (film) 3293, 2923, 1765, 1670, 1532, 1225, 967 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 6.38 (1H, d, $J = 6.8$ Hz), 4.85 (1H, dd, $J = 5.6, 3.6$ Hz), 4.47 (1H, brt, $J = 6.8$ Hz), 4.22 (1H, brs), 2.60-2.54 (2H, m), 2.35-2.30 (2H, m), 1.95-1.91 (1H, m) 1.88 (3H, s); ^{13}C NMR (100 MHz, CDCl_3) δ 178.7, 169.6, 79.8, 50.2, 46.5, 35.8, 31.6, 30.0, 23.3; HRMS (ES+) calcd for $\text{C}_9\text{H}_{13}\text{BrNO}_3$ (MH^+) 262.0079, found 262.0087; mp 167-169 $^\circ\text{C}$. (The corresponding starting material was prepared according to the literature method: Hatcher, M. A.; Peleg, S.; Dolan, P.; Kensler, T. W.; Sarjeant, A.; Posner, G. H. *Bioorg. Med. Chem.* **2005**, *13*, 3964-3976.)

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***N*-(trans-2-bromo-1,2,3,4-tetrahydro-1-**

naphthalenyl)acetamidodecyclohexyl)trimethylacetamide (19). White solid; IR (film) 3264, 2932, 1642, 1530, 1371, 1272, 1038, 749 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 7.27-7.12 (4H, m), 5.70 (1H, brs), 5.33 (1H, dd, $J = 7.8, 4.9$ Hz), 4.52 (1H, ddd, $J = 5.3, 4.9, 3.9$ Hz), 3.10 (1H, ddd, $J = 17.1, 8.9, 5.9$ Hz), 2.86 (1H, ddd, $J = 17.1, 5.4, 5.4$ Hz), 2.36-2.21 (2H, m), 2.03 (3H, s); ^{13}C NMR (100 MHz, CDCl_3) δ 169.4, 135.8, 133.5, 129.8, 129.2, 128.3, 127.0, 54.5, 51.0, 28.3, 26.6, 23.5; HRMS (ES+) calcd for $\text{C}_{12}\text{H}_{15}\text{BrNO}$ (MH^+) 268.0337, found 268.0327; mp 132-133 $^\circ\text{C}$.

General Procedure for Bromoamidation using various nitriles. To a solution of *N*-bromoacetamide (164 mg, 1.2 mmol) in dry CH_2Cl_2 (2 mL) and nitrile (15 mmol) at 0 $^\circ\text{C}$ in dark

was added $\text{BF}_3\text{-Et}_2\text{O}$ (1.0 M in CH_2Cl_2 , 0.4 mL, 0.4 mmol) and deionized water (0.022 mL, 1.2 mmol) successively. After 5 min, cyclohexene (0.1 mL, 1.0 mmol) was added at once to the reaction mixture. The reaction was followed by NMR. After the reaction finished, it was quenched with saturated NaHCO_3 (3 mL) and Na_2SO_3 (3 mL). The organic layer was separated and the aqueous layer was extracted with CH_2Cl_2 (3×20 mL). The combined extracts were washed with brine (10 mL), dried (MgSO_4), filtered and concentrated *in vacuo*. The residue was purified by flash column chromatography to yield the corresponding bromoamide.

21a

***N*-(*trans*-2-bromocyclohexyl)trimethylacetamide (21a).** White solid; IR (film) 3297, 2939, 1631, 1542, 1321, 1197, 953 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 5.62 (1H, brs), 3.96-3.82 (2H, m), 2.42-2.35 (1H, m), 2.22-2.18 (1H, m), 1.96-1.86 (1H, m), 1.78-1.70 (1H, m), 1.50-1.18 (4H, m), 1.20 (9H, m); ^{13}C NMR (100 MHz, CDCl_3) δ 178.0, 55.8, 55.3, 39.0, 37.4, 33.5, 27.8, 26.8, 24.6; HRMS (ES⁺) calcd for $\text{C}_{11}\text{H}_{21}\text{BrNO}$ (MH^+) 262.0806, found 262.0800; mp 123-124 °C.

21b

***N*-(*trans*-2-bromocyclohexyl)benzamide (21b).** To a solution of *N*-bromoacetamide (164 mg, 1.2 mmol) in dry benzonitrile (2 mL) at 0 °C in dark was added $\text{BF}_3\text{-Et}_2\text{O}$ (1.0 M in CH_2Cl_2 , 0.4

mL, 0.4 mmol) and deionized water (0.022 mL, 1.2 mmol) successively. After 5 min, cyclohexene (0.1 mL, 1.0 mmol) was added at once to the reaction mixture. After 1 h, the reaction was quenched with saturated NaHCO₃ (3 mL) and Na₂SO₃ (3 mL). The organic layer was separated and the aqueous layer was extracted with CH₂Cl₂ (3 × 20 mL). The combined extracts were washed with brine (10 mL), dried (MgSO₄), filtered and concentrated *in vacuo*. The residue was purified by flash column chromatography to yield **21b** as a white solid. IR (film) 3219, 2934, 1632, 1547, 1236, 1192, 702 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 7.82-7.78 (2H, m), 7.56-7.42 (3H, m), 6.16 (1H, brs), 4.13 (1H, dddd, *J* = 10.6, 10.6, 8.0, 4.0 Hz), 4.03 (1H, ddd, *J* = 10.6, 10.6, 4.0 Hz), 2.48-2.32 (2H, m), 2.03-1.92 (1H, m), 1.83-1.75 (2H, m), 1.56-1.45 (1H, m), 1.42-1.30 (2H, m); ¹³C NMR (100 MHz, CDCl₃) δ 167.3, 135.0, 131.7, 128.8, 127.2, 56.0, 55.6, 37.4, 33.6, 26.8, 24.6; HRMS (ES⁺) calcd for C₁₃H₁₇BrNO (MH⁺) 282.0493, found 282.0504; mp 140-141 °C.

N-(*trans*-2-bromocyclohexyl)acrylamide (**21c**). White solid. IR (film) 3220, 2963, 1657, 1234, 1187, 1035 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 6.29 (1H, dd, *J* = 16.8, 0.8 Hz), 6.15 (1H, d, *J* = 10.4 Hz), 6.11 (1H, d, *J* = 10.4 Hz), 6.08 (1H, brs), 5.64 (1H, dd, *J* = 10.4, 1.2 Hz), 4.07-3.98 (1H, m), 3.93 (1H, dt, *J* = 10.8, 4.4 Hz), 2.40-2.36 (1H, m), 2.23-2.19 (1H, m), 1.96-1.72 (3H, m), 1.49-1.22 (3H, m); ¹³C NMR (100 MHz, CDCl₃) δ 165.2, 131.2, 126.9, 55.4, 37.3, 33.5, 26.7, 24.5; HRMS (ES⁺) calcd for C₉H₁₅BrNO (MH⁺) 232.0337, found 232.0335; mp 136-138 °C.

21d

***N*-(*trans*-2-bromocyclohexyl)cyclohexanecarboxamide (21d).** White solid; IR (film) 3284, 2941, 2263, 2214, 1658, 1544, 1348, 1176 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 6.22 (1H, brs), 4.02-3.86 (2H, m), 3.41 (2H, s), 2.45-2.35 (1H, m), 2.22-2.13 (1H, m), 2.01 (3H, s), 1.96-1.85 (1H, m), 1.82-1.72 (2H, m), 1.50-1.25 (3H, m); ^{13}C NMR (100 MHz, CDCl_3) δ 160.6, 114.9, 56.5, 54.7, 37.4, 33.3, 26.7, 26.3, 24.5; HRMS (ES+) calcd for $\text{C}_{11}\text{H}_{17}\text{BrN}_3\text{O}$ ($\text{M}+\text{CH}_3\text{CN}+\text{H}^+$) 286.0555, found 286.0566; mp 129-130 $^\circ\text{C}$.

21e

***N*-(*trans*-2-bromocyclohexyl)cyclohexanecarboxamide (21e).** White solid; IR (film) 3274, 2936, 1640, 1539, 1326, 1195, 775 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 6.60 (1H, brs), 4.03 (2H, ABq, $J = 15.0$ Hz), 4.02-3.88 (2H, m), 2.42-2.35 (1H, m), 2.23-2.16 (1H, m), 1.96-1.86 (1H, m), 1.80-1.72 (2H, m), 1.50-1.26 (3H, m); ^{13}C NMR (100 MHz, CDCl_3) δ 165.5, 55.8, 54.7, 42.9, 37.2, 33.2, 26.6, 24.5; HRMS (ES+) calcd for $\text{C}_8\text{H}_{14}\text{ClBrNO}$ (MH^+) 253.9947, found 253.9951; mp 127-128 $^\circ\text{C}$.

General Procedure for the Synthesis of Aziridines. To a solution of bromoamide (0.1 mmol) in dry THF (2 mL) at 0 $^\circ\text{C}$ was added at once lithium hexamethyldisilazane (LiHMDS) (1.0 M in

THF, 0.12 mL, 0.12 mmol). After 30 min, the reaction was quenched with pH 7 buffer solution (potassium phosphate monobasic sodium hydroxide, 0.2 mL). The organic layer was separated and the aqueous layer was extracted with Et₂O (3 × 2 mL). The combined extracts were washed with brine (0.5 mL), dried (MgSO₄), filtered and concentrated *in vacuo*. The residue was purified by flash column chromatography on a short plug of silica gel to yield the corresponding aziridine.

22a

N-Pivaloyl-7-azabicyclo[4.1.0]heptane (22a). Colorless oil. IR (film) 2931, 1680, 1411, 1288, 1191, 1149 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 2.64-2.61 (2H, m), 1.96-1.89 (2H, m), 1.82-1.78 (2H, m), 1.44-1.40 (4H, m), 1.28-1.24 (4H, m), 1.23 (9H, s); ¹³C NMR (100 MHz, CDCl₃) δ 192.7, 41.4, 36.1, 28.3, 23.9, 20.2; HRMS (ES⁺) calcd for C₁₁H₂₀NO (MH⁺) 182.1545, found 182.1548. (The physical data were in full accordance with the literature value in all respects: Mordini, A.; Russo, F.; Valacchi, M.; Zani, L.; Degl'Innocenti, A.; Reginato, G. *Tetrahedron* **2002**, 58, 7153-7163.)

22b

***N*-Phenyl-7-azabicyclo[4.1.0]heptane (22b).** Colorless oil. IR (film) 2924, 1667, 1409, 11285, 1227, 1115, 703 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 7.98 (2H, d, J = 8.0 Hz), 7.53 (1H, t, J = 7.3 Hz), 7.44 (2H, t, J = 7.6 Hz), 2.75 (2H, m), 2.11-2.04 (2H, m), 1.94-1.88 (2H, m), 1.58-1.53 (2H, m), 1.37-1.34 (2H, m); ^{13}C NMR (100 MHz, CDCl_3) δ 180.5, 133.9, 132.7, 129.3, 128.6, 37.3, 24.2, 20.2; HRMS (ES+) calcd for $\text{C}_{13}\text{H}_{16}\text{NO}$ (MH^+) 202.1232, found 202.1240.

General Procedure for the Synthesis of Oxazolines. To a solution of bromoamide (0.3 mmol) in dry DME (1 mL) was added Et_3N (0.08 mL, 0.6 mmol) and 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) (0.01 mL, 0.03 mmol) successively. The resultant solution was heated to reflux for 4 h. After cooling down to room temperature, the salt was filtered and washed thoroughly with ethyl acetate. The filtrate was concentrated *in vacuo* and the residue was purified by flash column chromatography on a short plug of silica gel to yield the corresponding oxazoline.

23a

***cis*-3a,4,5,6,7,7a-Hexahydro-2-*tert*-butylbenzoxazole (23a).** Colorless oil. IR (film) 2933, 1646, 1457, 1137, 1098, 973, 920 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 4.42 (1H, dt, J = 5.2, 10.0 Hz), 3.85 (1H, dt, J = 5.6, 8.0 Hz), 1.79-1.66 (4H, m), 1.53-1.27 (4H, m), 1.17 (9H, s); ^{13}C NMR (100 MHz, CDCl_3) δ 174.5, 78.5, 63.0, 33.3, 27.8, 27.6, 26.2, 19.6, 19.0; HRMS (ES+) calcd for $\text{C}_{11}\text{H}_{20}\text{NO}$ (MH^+) 182.1545, found 182.1549.

23b

cis-3a,4,5,6,7,7a-Hexahydro-2-phenylbenzoxazole (23b). Colorless oil. IR (film) 2933, 1637, 1448, 1345, 1061, 971, 774, 694 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 7.94 (2H, d, $J = 7.2\text{Hz}$), 7.45 (1H, t, $J = 7.6\text{ Hz}$), 7.38 (2H, t, $J = 8.0\text{ Hz}$), 4.66 (1H, dt, $J = 5.2, 8.0\text{ Hz}$), 4.10 (1H, dt, $J = 6.0, 8.0\text{ Hz}$), 1.94-1.78 (4H, m), 1.66-1.33 (4H, m); ^{13}C NMR (100 MHz, CDCl_3) δ 164.4, 131.4, 128.6, 128.5, 128.3, 79.0, 63.8, 27.9, 26.4, 20.1, 19.3. (The physical data were in full accordance with the literature value in all respects: Hu, N. X.; Aso, Y.; Otsubo, T.; Ogura, F. *J. Chem. Soc. Perkin Trans. I* **1989**, 1775-1780.)

Part II X-ray Structure

X-ray Structure of (18)

18

X-ray Structure of (17)

17