Supporting Information for:

A Tandem Semipinacol/Schmidt Reaction Leading to Versatile and Efficient Approach to Azaquaternary Alkaloid Skeletons

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Note: ^1H and ^{13}C NMR spectra were recorded in CDCl_3 solution on Varian Mercury-300 or 400 MHz. The MS data were obtained with EI (70 eV). High-resolution mass spectral analysis (HRMS) data were measured on the Bruker ApexII by means of the ESI technique.

General Procedure for the Synthesis Substrates 1a-1g and Spectral Data

All these substrates were synthesized by normal chemical transformations. Generally vinyl lithium with a transferable function was added to a ketone. Then the transferable function was changed into azido and epoxided following protecting by TMS (Methods A). Alternatively the allylic alcohol was protected by TMS following change to azide, then it was epoxided (Methods B). A Typical Procedure for the Synthesis Substrate 1b was listed as a model (Methods A).

A solution of known compound vinyl bromide **3**¹ (2.00 g, 12.1 mmol) in 100 ml of DMF was treated with *tert*-butylchlorodimethylsilane (TBSCl, 2.22 g, 14.7 mmol), imidazole (4.18 g, 61.5 mmol) at room temperature. After 1 h, the reaction mixture was poured into 400 mL ether and washed with water, dried over Na_2SO_4 , filtered and concentrated. Flash chromatography on silica gel afforded 3.30 g of a new vinyl bromide **4** as a clear oil (98% yield): ^1H NMR (300MHz, CDCl_3) δ 0.04(s, 6H), 0.89(s, 9H), 1.74~1.79(m, 2H), 2.50(t, 2H), 3.63(t, 2H), 5.40(s, 1H), 5.58(t, 1H);

^{13}C NMR (75MHz, CDCl_3) δ -5.3, 18.3, 25.9, 31.0, 37.8, 61.4, 116.7, 134.3; MS (EI) m/e 265, 263, 223, 221, 169, 167, 139, 75, 67.

5e

A solution of the vinyl bromide **4** (2.1 g, 7.53 mmol) in 12 mL of THF was treated dropwise with *n*-butyllithium at $-78\text{ }^\circ\text{C}$ (4.2 mL, 1.8M in hexane 7.56 mmol), followed by addition of cyclopentanone (0.80 mL, 9.04 mmol) after 20 min. The reaction mixture was allowed to warm to ambient temperature, quenched by addition of water (5 mL), extracted with ether ($2 \times 70\text{ mL}$), dried over anhydrous MgSO_4 , filtered and concentrated. The siloxyl ether was treated with tetrabutylammonium fluoride trihydrate (10 g, 31.7 mmol) at room temperature. After 2 h, ether (200 mL) was added, and the mixture was washed with water and brine and then dried (Na_2SO_4) and concentrated. Chromatography gave 0.77 g of the desired compound **5e** (60% yield): ^1H NMR (300MHz, CDCl_3) δ 1.66~1.91(m, 10H), 2.04(bs, 2H), 2.22(t, 2H, $J=7.5\text{ Hz}$), 3.69(t, 2H, $J=6\text{ Hz}$), 4.85(d, 1H, $J=0.9\text{ Hz}$), 5.14(s, 1H); ^{13}C NMR (75MHz, CDCl_3) δ 23.2, 27.6, 31.6, 38.4, 61.9, 84.5, 107.8, 153.1; MS (EI) m/e 170, 152, 137, 125, 111, 85, 67, 55.

6e

Methanesulfonyl chloride (0.55 g, 4.75 mmol) was added to a solution of compound **5e** (0.77 g, 4.53 mmol) and triethylamine (0.95 mL, 6.83 mmol) in CH_2Cl_2 at $0\text{ }^\circ\text{C}$. After 10 min, the mixture was diluted with CH_2Cl_2 and washed with brine, and then dried (Na_2SO_4) and concentrated to give the crude mesylate, which was diluted in dimethyl sulfoxide (DMSO, 5 mL) and treated with NaN_3 . The reaction mixture was stirred for 18 h and 25 mL of H_2O was added. After dilution with ether (150 mL), the organic layer was separated, and washed with water, brine, dried over Na_2SO_4 and concentrated in vacuum, chromatographed to give a clear oil **6e** (478 mg, 84% yield): ^1H NMR (300MHz, CDCl_3) δ 1.33(s, 1H), 1.63~1.89(m, 10H), 2.20(t, 2H, $J=7.8\text{ Hz}$), 3.33(t, 2H, $J=6.9\text{ Hz}$), 4.82(s, 1H), 5.16(s, 1H); ^{13}C NMR (75MHz, CDCl_3) δ 23.4(2C), 28.0, 28.7, 38.7(2C), 51.2, 84.5, 108.4, 152.5; IR 2096.3, 1640.3 cm^{-1} .

1e

The azide **6e** (478 mg, 2.45 mmol) was diluted into CH_2Cl_2 (25 mL). NaHCO_3 (247 mg, 2.94 mmol) was added and then treated with 3-chloroperoxybenzoic acid (*m*-CPBA, 509 mg, 2.94 mmol). After 2.5 h, the reaction mixture was diluted with CH_2Cl_2 and washed with saturated K_2CO_3 solution, dried over Na_2SO_4 , concentrated. The crude product was diluted into DMF (5 mL) and treated trimethylchlorosilane (TMSCl , 400mg, 3.68 mmol) and imidazole (833 mg, 12.25 mmol) at $0\text{ }^\circ\text{C}$. After 2 h, the mixture was quenched with water and then extracted with ether. The organic phase was washed with water, brine, and then dried over Na_2SO_4 and concentrated. The residue was chromatographed to give the desired substrate **1e** (548 mg, 79% yield): ^1H NMR: (300 MHz, CDCl_3) δ 0.09(s, 9H), 1.51~1.84(m, 11H), 1.86~2.02(m, 1H), 2.62(d, 1H, $J=4.2\text{ Hz}$), 2.68(d,

^1H , $J=4.2\text{Hz}$), 3.22~3.30(m, 2H); ^{13}C NMR (75 MHz, CDCl_3) δ 2.1, 23.3, 23.4, 23.8, 26.8, 34.9, 36.9, 49.4, 51.6, 60.8, 87.1; HMRS (ESI, $\text{M}^+\text{+Na}$, $\text{C}_{13}\text{H}_{25}\text{N}_3\text{O}_2\text{NaSi}$) Calcd. : 306.1608; Found: 306.1611; Error: 1.0 ppm; IR 2096.3 cm^{-1} .

A Typical Procedure for the Synthesis Substrate 1f was listed as another model (Methods B).

Methanesulfonyl chloride (0.128 mL, 1.65 mmol) was added to a solution of compound **5c**

(prepared as for **5e**, 1.347 g, 5.7 mmol) and triethylamine (1.2 mL,

8.6 mmol) in CH_2Cl_2 (50 mL) at 0 $^\circ\text{C}$. After 5 min, the mixture was diluted with CH_2Cl_2 and washed with brine, and then dried (Na_2SO_4) and concentrated to give the crude mesylate, which was diluted in dry pyridine (20 mL) and treated with hexamethyl disilazane (HMDS, 2.4 mL, 11.4 mmol) and TMSCl (0.98 mL, 7.7 mmol) subsequently. The reaction mixture was stirred for 30 min and H_2O (10 mL) was added carefully. After dilution with ether (150 mL), the organic layer was separated, and washed with saturated CuSO_4 solution, water, brine, dried over Na_2SO_4 and concentrated in vacuum, chromatographed gave a clear oil (1.122 g, 51%).

The oil (1.122g 2.9 mmol) was dissolved in DMF (5 mL) and treated with sodium azide (470 mg, 2.7 mmol) at room temperature. After 48 h, the mixture was diluted with water (10 mL) and then extracted with ether (150 mL). The organic layer was washed with water, brine, and then dried over Na_2SO_4 , concentrated. The residue (688 mg) was diluted into CH_2Cl_2 , NaHCO_3 (344 mg, 4.1 mmol) was added and then treated with *m*-CPBA (430 mg, 2.5 mmol). After 2.5h, the reaction mixture was diluted with CH_2Cl_2 (100 mL) and washed with saturated K_2CO_3 solution, dried over Na_2SO_4 , concentrated and chromatographed to give the desired Siloxy-Epoxy-Azide **1c** (649 mg, 64% yield). ^1H NMR: (300 MHz, CDCl_3) δ 0.08~0.19(9H), 1.30~1.71(7H), 2.59~2.67(1H), 2.89~3.13(3H), 3.81(s, 3H), 6.78~7.27(3H); ^{13}C NMR (75 MHz, CDCl_3) major δ 2.3, 23.9, 26.7, 47.7, 51.3, 55.1, 63.1, 77.8, 111.8, 112.2, 118.4, 128.8, 147.6, 159.2; HMRS (ESI, $\text{M}^+\text{+Na}$, $\text{C}_{17}\text{H}_{27}\text{N}_3\text{O}_3\text{NaSi}$) Calcd. : 372.1714, Found: 372.1705; Error: 1.2 ppm; IR 2096.3 cm^{-1} .

1a was prepared as for **1e**, as a mixture of diastereomers: ^1H NMR (300 MHz, CDCl_3) diastereoisomer mixture (1:1) δ 0.08~0.17(9H), 1.27~1.72(7H), 2.60~2.68(1H), 2.89~3.14(3H), 7.25~4.47(5H); ^{13}C NMR (75 MHz, CDCl_3) diastereoisomer mixture (1:1) δ : 2.2, 2.3, 23.7, 23.86, 23.92, 25.0, 26.0, 26.7, 47.8, 48.9, 51.3, 51.4, 63.2, 63.3, 77.8, 78.9, 125.6, 126.0, 127.0, 127.1, 127.87, 127.95, 145.7, 146.0; HMRS (ESI, $\text{M}^+\text{+Na}$, $\text{C}_{16}\text{H}_{25}\text{N}_3\text{O}_2\text{NaSi}$) Calcd. : 342.1608, Found: 342.1603, Error: 1.5 ppm; IR: 2095.5 cm^{-1} .

1b was prepared as for **1c**, as a mixture of diastereomers: ^1H NMR (300 MHz, CDCl_3) diastereoisomer mixture (1:3) δ 0.07~0.10(9H), 1.43~1.73(4H), 2.67~2.70(1H), 2.80~2.85(1H), 3.13~3.19(2H), 4.49~4.51(1H), 7.26~7.39(5H); ^{13}C NMR (75 MHz, CDCl_3), diastereoisomer mixture, major δ 0.04, 23.7, 26.7, 50.1, 51.3, 61.0, 76.6, 126.7, 127.7, 128.1, 140.9; HMRS (ESI, $\text{M}^+\text{+Na}$, $\text{C}_{15}\text{H}_{23}\text{N}_3\text{O}_2\text{NaSi}$) Calcd. : 328.1452, Found: 328.1458, Error: 1.8 ppm; IR 2095.8 cm^{-1} .

1d was prepared as for **1e**: ^1H NMR (300 MHz, CDCl_3) δ 0.14(s, 9H), 1.48~1.58(m, 3H), 1.74~1.80(m, 2H), 1.87(t, 1H, $J=6.0\text{Hz}$), 1.98~2.08(m, 3H), 2.18(bs, 1H), 2.66(d, 1H, $J=4.8\text{Hz}$), 2.72(d, 1H, $J=4.8\text{Hz}$), 3.22~3.28(m, 2H); ^{13}C NMR (75 MHz, CDCl_3) δ 1.9, 13.2, 23.9, 25.5, 31.9, 33.1, 48.2, 51.6, 60.1, 79.4; HMRS (ESI, $\text{M}^+\text{+Na}$, $\text{C}_{12}\text{H}_{23}\text{N}_3\text{O}_2\text{NaSi}$) Calcd. : 292.1452, Found: 292.1448, Error: 1.4 ppm; IR 2096.3 cm^{-1} .

1f was prepared as for **1e**: ^1H NMR (300 MHz, CDCl_3) δ 0.13(s, 9H), 1.09~1.15(m, 1H), 1.22~1.37(m, 2H), 1.42~1.65(m, 9H), 1.86~1.94(m, 2H), 2.55(d, 1H, $J=4.5\text{Hz}$), 2.80(d, 1H, $J=4.5\text{Hz}$), 3.21~3.33(m, 2H); ^{13}C NMR (75 MHz, CDCl_3) δ 2.3, 21.48, 21.53, 23.6, 25.6, 25.7, 33.0, 33.6, 47.6, 51.7, 63.0, 76.3; HMRS (ESI, $\text{M}^+\text{+Na}$, $\text{C}_{14}\text{H}_{27}\text{N}_3\text{O}_2\text{NaSi}$) Calcd. : 320.1765, Found: 320.1764, Error: 0.3 ppm; IR 2096.6 cm^{-1} .

1g was prepared as for **1c**, as a mixture of diastereomers: ^1H NMR (300 MHz, CDCl_3) diastereoisomer mixture δ -0.05(9H), 1.48~2.23(6H), 2.26~2.54(2H), 2.79~3.35(4H), 7.15~7.43(4H); ^{13}C NMR (75 MHz, CDCl_3) diastereoisomer mixture (2:1) δ 1.6, 23.9, 26.4, 29.8, 38.3, 48.1, 51.6, 62.7, 87.3, 124.5, 126.0, 126.2, 128.6, 143.2, 143.8; HMRS (ESI, $\text{M}^+\text{+Na}$, $\text{C}_{17}\text{H}_{25}\text{N}_3\text{O}_2\text{NaSi}$) Calcd. : 354.1608; Found: 354.1595, Error: 3.7 ppm; IR 2095.8 cm^{-1} .

Procedure for the Synthesis Substrates 1h and Spectral Data for 1h

Allylmagnesium chloride solution (3.5 mL, 2 M in THF, 7 mmol) was added to the known compound **6**² (1.25 g, 7 mmol) in dry THF at 0 °C. After 30 min, the reaction mixture was diluted with water, and then extracted with ether. The organic phase was washed with NH₄Cl, water, brine, and then dried over Na₂SO₄ and concentrated. The residue was chromatographed to give the desired allyl alcohol **7** (773 mg, 50% yield): ¹H NMR (300 MHz, CDCl₃) δ 1.60~1.64(m, 4H), 1.73~1.82(m, 3H), 1.92~2.11(m, 3H), 2.21~2.32(m, 1H), 2.38(d, 2H, J=6.9Hz), 3.31(t, 2H, J=6.3Hz), 5.10~5.15(m, 2H), 5.55(s, 1H), 5.69~5.84(m, 1H); ¹³C NMR (75 MHz, CDCl₃) δ 18.9, 25.5, 27.4, 28.0, 36.1, 43.6, 51.4, 71.9, 118.6, 125.6, 133.7, 139.8.

The allyl alcohol **7** (773 mg, 3.5 mmol), was diluted with benzene (30 mL), Vanadyl(IV) acetylacetonate (50 mg, 0.19 mmol) was added, following *tert*-butyl hydroperoxide (*t*-BuOOH, 1.75 mL, 4.0 M in pentane, 7.0 mmol), the reaction mixture was diluted with water, then extracted with ether. The organic phase was washed with saturated NaHSO₃ solution, water, brine, and then dried over Na₂SO₄ and concentrated. The residue was chromatographed to give the - hydroxy epoxide **8h** (904 mg, 87% yield): ¹H NMR (300 MHz, CDCl₃) δ 1.23~1.45(m, 5H), 1.47~1.98(m, 4H), 2.06~2.16(m, 1H), 2.21(s, 1H), 2.28~2.35(m, 1H), 2.49~2.56(m, 1H), 3.21~3.34(m, 3H), 5.01~5.15(m, 2H), 5.83~5.97(m, 1H); ¹³C NMR (75 MHz, CDCl₃) δ 17.0, 22.9, 23.5, 26.9, 32.6, 40.4, 51.6, 60.9, 64.3, 73.2, 118.1, 133.2.

The - Hydroxy epoxide **8h** (626 mg, 2.64 mmol) was treated with TMSCl (0.578 mL, 5.28 mmol) and imidazole (854 mg, 13.2 mmol) in 15 mL of DMF at room temperature. After 4 h, the mixture was diluted with ether, and washed with water twice, and dried over Na₂SO₄, concentrated, and chromatographed to give the desired Siloxy-Epoxy-Azide **1h** (750 mg, 92% yield): ¹H NMR (300 MHz, CDCl₃) δ 0.12(s, 9H), 1.21~1.53(m, 4H), 1.56~1.90(m, 5H), 2.00~2.11(m, 1H), 2.21~2.29(m, 1H), 2.41~2.47(dd, 1H, J=13.5 Hz, 3.3 Hz), 3.02(s, 1H), 3.18~3.33(m, 2H), 5.01~5.09(m, 2H), 5.77~5.90(m, 1H); ¹³C NMR (75 MHz, CDCl₃) δ 2.5, 18.3, 21.7, 23.3, 25.7, 29.9, 41.3, 51.7, 58.9, 64.1, 78.0, 117.1, 133.8; HRMS (ESI, M⁺+Na, C₁₅H₂₇N₃O₂NaSi) Calcd. : 332.1765, Found: 332.1771, Error: 1.8 ppm; IR 2096.1 cm⁻¹.

Procedure for the Synthesis Substrates **1i** and **1j** and Spectral Data

The substituted cyclohexanone **8** (7.4 g 19.4 mmol) was added to a stirred solution of TsNHNH₂ (3.8 g, 20.4 mmol) in 50 mL of ethanol. The solution was stirred for 5 h at room temperature, and 5 mL of water was added and the mixture was cooled for 12 h at -20 °C. the white solid was collected by filtration, washed with cold ethanol and then dried in vacuo (8.5 g, 80% yield). *n*-Butyllithium (12.5 mL, 1.4 M in hexane, 17.5 mmol) was slowly added to a stirred solution of tosylhydrazone (2.7 g, 5 mmol) in 35 mL of TMEDA cooled at -60 °C for 15 min. The reaction mixture was warmed up to 10 °C and stirred for 10 min, then cooled to -40 °C. cyclobutanone (0.96 mL, 12.5 mmol) was added. The resulting mixture was warmed to room temperature for additional 30 min and poured into a mixture of water (10 mL)-ether (100 mL). The organic layer was separated and washed with brine dried over Na₂SO₄, filtered and finally evaporated under reduced pressure, flash chromatographed to give allylic alcohol **9** (1.28 g, 57% yield): ¹H NMR (300 MHz, d-acetone) δ 1.05(s, 9H), 1.41~1.62(m, 6H), 1.87~2.16(m, 5H), 2.17~2.40(m, 3H), 2.59(bd, 1H, J=8.7 Hz), 3.74~3.80(m, 3H), 5.71(d, 1H, J=3.6 Hz), 7.40~7.74(m, 10H); ¹³C NMR (75 MHz, d-acetone) δ 13.8, 18.2, 19.1, 25.2, 26.6, 26.9, 30.2, 35.3, 35.9, 37.4, 62.8, 78.2, 120.8, 128.0, 129.9, 134.1, 135.7, 145.6.

The siloxyl ether **9** (1.2 g, 2.62 mmol) was treated with tetrabutylammonium fluoride trihydrate (1.8 g, 5.71 mmol) at room temperature. After 3 h, ether (300mL) was added, and the mixture was washed with water and brine and then dried (Na₂SO₄) and concentrated. Chromatography gave 514 mg of the desired compound **10** (100% yield): ¹H NMR (300 MHz, d-acetone) δ 1.40~1.68(m, 6H), 1.84~2.36(m, 6H), 2.50~2.52(m, 2H), 2.94(bs, 1H), 3.54~3.64(m, 3H), 4.01(s, 1H), 5.67~5.69(m, 1H); ¹³C NMR (75 MHz, d-acetone) δ 13.7, 18.2, 25.1, 27.5, 30.4, 35.3, 36.5, 37.4, 60.7, 78.2, 120.4, 145.7; MS (EI) *m/e* 151, 135, 125, 109, 77.

Methanesulfonyl chloride (0.198 mL, 2.55 mmol) was added to a solution of the compound **10** (500 mg, 2.55 mmol) and triethylamine (0.355 mL, 2.55 mmol) in CH₂Cl₂ at 0 °C. After 10 min, the mixture was diluted with ether and washed with brine, and then dried (Na₂SO₄) and concentrated to give the crude mesylate, which was diluted in dry pyridine (15 mL) and treated with hexamethyl disilazane (HMDS, 1.2 mL, 5.7 mmol) and TMSCl (0.50 mL, 3.9 mmol) subsequently. The reaction mixture was stirred for 30 min and H₂O (10 mL) was added carefully. After dilution with ether (150 mL), the organic layer was separated, and washed with saturated CuSO₄ solution, water, brine, dried over Na₂SO₄ and concentrated in vacuum, gave a clear oil **11** (560 mg, 64% yield): ¹H NMR (300 MHz, CDCl₃) δ 0.08(s, 9H), 1.43~1.61(m, 6H), 1.75~1.81(m, 1H), 2.04~2.31(m, 7H), 2.43(bd, 1H, J=7.5Hz), 2.98(s, 3H), 4.21~4.26(m, 2H), 5.71~5.74(m, 1H); ¹³C NMR (75 MHz, CDCl₃) δ 1.9, 13.7, 18.3, 25.0, 27.1, 30.4, 32.2, 35.5, 37.3, 37.7, 68.9, 80.0, 121.7, 142.6; MS (EI) m/e 256, 219, 145, 131, 117, 91, 79.

The oil **11** (560 mg, 1.62 mmol) was dissolved in DMF and treated with sodium azide (263 mg, 4.05 mmol) at room temperature. After 48 h, the mixture was diluted with water and then extracted with ether. The organic phase was washed with water, brine, and then dried over Na₂SO₄ and concentrated. The residue was chromatographed to give the siloxy azide **12** (342 mg, 72% yield): ¹H NMR (300 MHz, CDCl₃) δ 0.11(s, 9H), 1.44~1.57(m, 6H), 1.61~1.85(m, 1H), 2.07~2.39(m, 8H), 3.23~3.35(m, 2H), 5.73(d, 1H, J=3.6 Hz); ¹³C NMR (75 MHz, CDCl₃) δ 1.9, 13.8, 18.4, 25.1, 27.0, 31.4, 32.0, 35.5, 37.8, 50.0, 80.1, 121.4, 143.2.

The Siloxy-Azide **12** (282 mg, 0.96 mmol) was diluted into CH₂Cl₂, NaHCO₃ (162 mg, 1.93 mmol) was added and then treated with m-CPBA (85%, 197 mg, 0.96 mmol). After 2.5h, the reaction mixture was diluted with CH₂Cl₂ and washed with saturated K₂CO₃ solution, dried over Na₂SO₄, concentrated and chromatographed to give the desired Sily-Epoxy-Azide **1i** (271 mg, 91% yield): ¹H NMR (300 MHz, CDCl₃) diastereoisomer mixture (6:1) δ 0.08~0.18(9H), 1.13~1.58(5H), 1.59~1.76(2H), 1.78~2.31(8H), 3.07~3.08(1H), 3.18~3.39(2H); ¹³C NMR (75 MHz, CDCl₃) diastereoisomer mixture, major δ 2.0, 13.8, 23.4, 25.0, 25.3, 28.6, 29.1, 31.8, 32.5, 49.8, 55.3, 63.2, 80.4; HRMS (ESI, M⁺+Na, C₁₅H₂₇N₃O₂SiNa) Calcd. : 332.1765, Found: 332.1755, Error: 3.0 ppm; IR 2094.5 cm⁻¹.

1j was prepared as for **1i**, as a mixture of diastereomers: ¹H NMR (300 MHz, CDCl₃)

diastereoisomer mixture (8:1) δ 0.09(9H), 1.11~1.21(1H), 1.24~1.38(2H), 1.42~1.48(1H), 1.54~1.75(10H), 1.83~1.93(1H), 2.05(bd, 1H, $J=13.5$ Hz), 2.39~2.44(1H), 2.93~3.03(1H, 3.20~3.38(2H); ^{13}C NMR (75 MHz, CDCl_3) δ 2.1, 14.3, 22.9, 23.6, 25.0, 25.1, 28.0, 28.7, 33.8, 36.8, 49.9, 56.4, 63.8, 87.4; HRMS (ESI, $\text{M}^+ + \text{Na}$, $\text{C}_{16}\text{H}_{29}\text{N}_3\text{O}_2\text{SiNa}$) Calcd. : 346.1921, Found: 346.1922, Error: 0.3 ppm; IR 2094.4 cm^{-1} .

Procedure for the Tandem Semipinacol/intramolecular Aube's type Schmidt reaction

To a cooled (-78 °C) solution of the Siloxy-Epoxy-Azide **1** (0.3 m mol) in CH_2Cl_2 (3 ml) under argon was added TiCl_4 (0.66 ml, 1M in CH_2Cl_2). The result mixture was stirred -78 °C for 15 minutes. Then the mixture was warmed slowly to room temperature (25 °C) for additional times, then it was quenched with 1 ml water. The mixture was partitioned between water and 50 ml CH_2Cl_2 . The organic layer was collected, dried (Na_2SO_4), filtered, and concentrated to give a solid **2**. Chromatography afforded the desired products.

Spectral Data for Tandem Products

2a: Siloxy-Epoxy-Azide **1a** run in the general procedure. The mixture was stirred at room temperature for 1.5 h, and it afforded **2a** as a white solid in 95% yield: ^1H NMR (300 MHz, CDCl_3) δ 1.66~1.94(m, 2H), 1.96~2.01(m, 2H), 2.24(s, 3H), 3.60~3.78(m, 2H), 3.90(d, 1H, $J=12.3$ Hz), 4.26(d, 1H, $J=12.0$ Hz), 7.13~7.37(m, 5H); ^{13}C NMR (75 MHz, CDCl_3) δ 21.2, 23.9, 39.8, 50.7, 68.3, 74.2, 125.9, 126.7, 128.3, 140.4, 171.5; MS (EI) m/e 219, 201, 188, 146; HMRS (ESI, $\text{M}^+ + \text{Na}$, $\text{C}_{13}\text{H}_{17}\text{NO}_2\text{Na}$) Calcd. : 242.1151, Found: 242.1148, Error: 1.2 ppm; IR 1626.0 cm^{-1} .

2b: Siloxy-Epoxy-Azide **1b** run in the general procedure. The mixture was stirred at room temperature for 0.5 h, and it afforded **2b** as a white solid in 80% yield: ^1H NMR (300 MHz, CDCl_3) δ 1.65~1.75(m, 1H), 1.83~1.92(m, 1H), 2.00~2.10(m, 1H), 2.30~2.39(m, 1H), 3.54~3.64(m, 1H), 3.69~3.78(m, 1H), 3.92(d, 1H, $J=12.3$ Hz), 4.25(d, 1H, $J=12.3$ Hz), 7.18~7.38(m, 5H), 8.18(s, 1H); ^{13}C NMR (75 MHz, CDCl_3) δ 21.0, 38.0, 45.6, 66.2, 70.3, 125.7, 127.4, 128.7, 142.9, 163.0; MS (EI) m/e 174, 146, 104; HMRS (ESI, $\text{M}^+ + \text{H}$, $\text{C}_{12}\text{H}_{16}\text{NO}_2$) Calcd. : 206.1176, Found: 206.1176, Error: 0 ppm; IR 1647.3 cm^{-1} .

2c: Siloxy-Epoxy-Azide **1c** run in the general procedure. The mixture was stirred at room temperature for 10 h, and it afforded **2c** as a white solid in 77% yield: ^1H NMR (300MHz, CDCl_3) δ 1.66~1.84(m, 2H), 1.88~2.05(m, 2H), 2.21(s, 3H), 3.57~3.76(m, 2H), 3.78(s, 3H), 3.87(d, 1H, $J=12.3\text{Hz}$), 4.20(t, 1H, $J=10.5\text{Hz}$), 5.65(bd, 1H), 6.66(t, 1H), 6.74~6.78(m, 2H), 7.26(m, 2H), ^{13}C NMR (75MHz, CDCl_3) δ 21.1, 23.9, 39.7, 50.6, 55.0, 68.3, 74.2, 111.0, 112.9, 118.4, 129.3, 142.4, 159.4, 171.3; MS (EI) m/e 249, 231, 218, 176; HMRS (ESI, $\text{M}^+ + \text{Na}$, $\text{C}_{14}\text{H}_{19}\text{NO}_3\text{Na}$) Calcd. : 272.1257, Found: 272.1250, Error: 2.6 ppm; IR 1626.4 cm^{-1} .

2d: Siloxy-Epoxy-Azide **1d** run in the general procedure. The mixture was stirred at room temperature for 3 h, and it afforded **2d** as a white solid in 77% yield. ^1H NMR (300 MHz, CDCl_3) δ 1.28~1.41(m, 1H), 1.47~1.58(m, 1H), 1.72~1.82(m, 1H), 1.86~2.00(m, 3H), 2.20~2.45(m, 4H), 2.55(bs, 1H), 3.34~3.44(m, 2H), 3.51(d, 1H, 11.1 Hz), 3.72~3.81(m, 1H); ^{13}C NMR (75 MHz, CDCl_3) δ 17.5, 20.1, 30.2, 30.3, 35.6, 44.8, 63.6, 64.8, 170.4; MS (EI) m/e 169, 138, 110, 84, 55; HMRS (ESI, $\text{M}^+ + \text{H}$, $\text{C}_9\text{H}_{16}\text{NO}_2$) Calcd. : 170.1176, Found: 170.1173, Error: 1.8 ppm; IR 1607.8 cm^{-1} .

2e: Siloxy-Epoxy-Azide **1e** run in the general procedure. The mixture was stirred at room temperature for 0.5 h, and it afforded **2e** as a white solid in 67% yield. ^1H NMR (400 MHz, CDCl_3) δ 1.44~1.55(m, 2H), 1.63~1.79(m, 5H), 1.80~1.89(m, 1H), 2.01~2.06(dt, $J=10.8\text{Hz}$, 2.4Hz, 1H), 2.25~2.30(m, 1H), 2.41~2.47(ddd, $J=10.8\text{Hz}$, 3.9Hz, 1.5Hz, 1H), 2.63~2.70(td, $J=10.8\text{Hz}$, 2.1Hz, 1H), 3.50~3.58(m, 2H), 3.63(d, 1H, $J=11.6\text{ Hz}$), 3.82(d, 1H, $J=11.6\text{ Hz}$), 4.50(bs, 1H); ^{13}C NMR (100 MHz, CDCl_3) δ 20.9, 23.6(2C), 35.8, 37.0, 38.9, 49.4, 63.9, 65.6, 173.9; MS (EI) m/e 183, 152; HMRS (ESI, $\text{M}^+ + \text{Na}$, $\text{C}_{10}\text{H}_{17}\text{NO}_2\text{Na}$) Calcd. : 206.1151, Found: 206.1148, Error: 1.5 ppm; IR 1600.5 cm^{-1} .

2f: Siloxy-Epoxy-Azide **1f** run in the general procedure. The mixture was stirred at room temperature for 8 h, and it afforded **2f** as a white solid in 66% yield: ^1H NMR (300 MHz, CDCl_3) δ 1.42~1.68(m, 4H), 1.72~1.96(m, 7H), 2.17~2.25(m, 2H), 2.92~3.02(m, 1H), 3.48~3.64(m, 4H), 4.60(bs, 1H); ^{13}C NMR (75 MHz, CDCl_3) δ 19.7, 21.5, 25.0, 25.3, 33.9, 34.0, 35.6, 48.7, 67.3, 68.2, 174.2; MS (EI) m/e 197, 166; HMRS (ESI, $\text{M}^+\text{+H}$, $\text{C}_{11}\text{H}_{20}\text{NO}_2$) Calcd. : 198.1489, Found: 198.1485, Error: 2.0 ppm; IR 1599.5 cm^{-1} .

2g: Siloxy-Epoxy-Azide **1g** run in the general procedure. The mixture was stirred at room temperature for 3 h, and it afforded **2g** as a white solid in 61% yield and a byproduct **2g'** in 20% yield: **2g** ^1H NMR (300 MHz, CDCl_3) δ 1.73~1.82(m, 1H), 2.11~2.24(m, 1H), 2.34~2.44(dt, $J=15.0\text{Hz}$, 7.8Hz, 1H), 2.53~2.63(m, 1H), 2.84~3.19(m, 4H), 3.48~3.58(dt, $J=11.7\text{Hz}$, 8.7Hz, 1H), 3.76(d, 1H, $J=12.3\text{ Hz}$), 3.88~3.96(td, $J=9.3\text{Hz}$, 3.0Hz, 1H), 4.11 (d, 1H, $J=12.3\text{ Hz}$), 4.96(bs, 1H), 7.08~7.26(m, 4H); ^{13}C NMR (75 MHz, CDCl_3) δ 20.6, 30.8, 35.3, 41.4, 49.5, 70.5, 71.4, 126.3, 126.9, 129.2, 130.9, 137.9, 139.4, 174.7; MS (EI) m/e 231, 200, 156, 111; HMRS (ESI, $\text{M}^+\text{+Na}$, $\text{C}_{14}\text{H}_{17}\text{NO}_2\text{Na}$) Calcd. : 254.1151, Found: 254.1157, Error: 2.4 ppm; IR 1617.6 cm^{-1} . **2g'** ^1H NMR (300 MHz, CDCl_3) δ 1.57~1.81(m, 4H), 1.89~1.97(m, 1H), 2.03~2.13(m, 1H), 2.90~2.98(m, 2H), 3.04~3.39(m, 3H), 3.71(s, 2H), 7.17(d, 1H), 7.26(t, 1H), 7.47~7.53(m, 1H), 8.01(d, 1H); ^{13}C NMR (75 MHz, CDCl_3) δ 23.3, 24.7, 27.3, 28.0, 48.6, 51.6, 66.1, 126.8, 127.8, 128.8, 131.3, 133.8, 143.2, 203.7.

2h: Siloxy-Epoxy-Azide **1h** run in the general procedure. The mixture was stirred at room temperature for 1 h, and it afforded **2h** as a white solid in 92% yield: ^1H NMR (300 MHz, CDCl_3) δ 1.57~1.92(m, 5H), 1.97~2.06(m, 2H), 2.31~2.66(m, 6H), 3.54~3.59(m, 2H), 3.76(bs, 1H), 5.11~5.16(m, 2H), 5.62~5.76(m, 1H); ^{13}C NMR: (75 MHz, CDCl_3) δ : 16.6, 21.5, 30.7, 36.3, 37.3, 40.6, 50.2, 67.7, 71.3, 119.3, 132.3, 173.5; MS (EI) m/e 209, 180, 168, 110; HRMS (ESI, $\text{M}^+\text{+Na}$, $\text{C}_{12}\text{H}_{19}\text{NO}_2\text{Na}$) Calcd. : 232.1308, Found: 232.1312, Error: 1.7 ppm; IR 1601.4 cm^{-1} .

2i: Siloxy-Epoxy-Azide **1i** (mixture $\alpha/\beta=1:6$) run in the general procedure. The mixture was stirred at room temperature for 3 h, and it afforded respectively **2i** (mixture $\alpha/\beta=1:7$, β isomer was confirmed by X ray analysis) as white solids in 68% and 10% yields: **2i** ^1H NMR (300 MHz, CDCl_3) δ 1.24~1.34(m, 2H), 1.40~1.76(m, 5H), 1.83~1.94(m, 4H), 1.98~2.07(m, 1H), 2.18~2.43(m, 3H), 3.52~3.57(m, 2H), 3.98(s, 1H), 4.66(bs, 1H); ^{13}C NMR (75 MHz, CDCl_3) δ 13.9, 17.8, 24.5, 25.7, 29.8, 29.9, 31.1, 45.9, 46.4, 64.4, 69.6, 170.4; MS (EI) m/e 209, 150, 137, 122, 84; HRMS (ESI, $\text{M}^+ + \text{Na}$, $\text{C}_{12}\text{H}_{19}\text{NO}_2\text{Na}$) Calcd. : 232.1308, Found: 232.1311, Error: 1.3 ppm; IR 1621.4 cm^{-1} ; **2i2** HNMR (400 MHz, CDCl_3) δ 1.18~1.31(m, 2H), 1.19~1.51(m, 2H), 1.55~1.79(m, 6H), 1.70~1.91(m, 4H), 2.28~2.38(m, 1H), 2.43~2.52(m, 1H), 2.66~2.73(m, 1H), 3.04~3.12(m, 1H), 3.97~4.02(m, 1H), 4.26(s, 1H); CNMR (100 MHz, CDCl_3) δ 15.0, 21.1, 24.67, 24.74, 26.3, 28.6, 29.0, 41.2, 48.3, 67.2, 68.3, 174.3.

2j: Siloxy-Epoxy-Azide **1j** (mixture $\alpha/\beta=1:8$) run in the general procedure. The mixture was stirred at room temperature for 1 h, and it afforded **2j** with a minor diastereoisomer mixture ($\alpha/\beta=1:8$) as white solids in combined 93% yields. ^1H NMR (300 MHz, CDCl_3) δ 1.23~1.32(m, 1H), 1.37~1.72(m, 9H), 1.77~2.02(m, 4H), 2.24~2.37(m, 2H), 2.55~2.65(m, 1H), 3.29~3.39(m, 1H), 3.61~3.70(m, 1H), 4.81(s, 1H), 4.92(bs, 1H); ^{13}C NMR(75 MHz, CDCl_3) δ 13.8, 22.2, 23.4, 24.5, 25.5, 34.5, 35.6, 45.7, 47.7, 65.7, 68.1, 173.4; MS (EI) m/e 223, 164, 151, 136, 122, 95; HRMS (ESI, $\text{M}^+ + \text{Na}$, $\text{C}_{13}\text{H}_{21}\text{NO}_2\text{Na}$) Calcd. : 246.1465, Found: 246.1468, Error: 1.2 ppm; IR 1613.9 cm^{-1} .

Synthesis of azaquaternary 5-7-5 ring skeleton from **2h**

Procedure for Synthesis the Tricyclic Lactam **5h**:

PCC (250 mg, 1.16 mmol), silica (250 mg), and NaOAc (100 mg, 1.22 mmol) were well mixed, then added into the solution of **2h** (132 mg, 0.63 mmol) in CH_2Cl_2 . After 18 h, the mixture was subjected to a column of Al_2O_3 , washed with CHCl_3 , the organic solvent was evaporated and chromatographed to give the ketone **8c** (115 mg, 88% yield): ^1H NMR (300 MHz, CDCl_3) δ 1.87~2.29(m, 6H), 2.30~2.39(m, 2H), 2.44~2.57(m, 2H), 2.61~2.68(m, 1H), 2.79~2.89(m, 1H), 3.57~3.64(m, 1H), 3.68~3.77(m, 1H), 5.07~5.13(m, 2H), 5.71~5.85(m, 1H); ^{13}C NMR (75 MHz, CDCl_3) δ 21.1, 22.9, 33.3, 35.2, 37.2, 39.1, 47.3, 73.9, 119.6, 132.6, 170.9, 211.7; MS (EI) m/e 207, 166, 138, 109, 96, 83, 70, 57, 41; HRMS (ESI, $\text{M}^+ + \text{Na}$, $\text{C}_{12}\text{H}_{17}\text{NO}_2\text{Na}$) Calcd. : 230.1151, Found: 230.1157, Error: 2.6 ppm; IR 1645.8, 1714.0 cm^{-1} .

PdCl_2 (12 mg, 0.07 mmol) and Cu_2Cl_2 (32 mg, 0.16 mmol) were added into a mixture of DMF and water (v/v=7:1, 2 mL). Then saturated with oxygen for 2 h. **3h** (50 mg, 0.24 mmol) was added to the mixture, and the mixture was heated to 60 $^\circ\text{C}$ for 3 h. the solution was acidified to litmus with 10% hydrochloric acid (5 mL) and extracted 3 times with 20 mL CHCl_3 , dried over Na_2SO_4 , concentrated, and chromatographed to give the diketone **4h** (45 mg, 84%): ^1H NMR (300 MHz, CDCl_3) δ 1.88~2.20(m, 5H), 2.24 (s, 2H), 2.29~2.40 (m, 1H), 2.43~2.55(m, 3H), 2.64~2.69(m, 1H), 2.82~2.95(m, 2H), 3.62~3.74(m, 2H); ^{13}C NMR (75 MHz, CDCl_3) δ 21.3, 22.9, 32.8, 33.3, 34.7, 35.2, 44.6, 47.1, 74.2, 170.4, 205.4, 210.8; MS (EI) m/e 223, 195, 180, 167, 152, 138, 126, 96; HRMS (ESI, $\text{M}^+ + \text{Na}$, $\text{C}_{12}\text{H}_{17}\text{NO}_3\text{Na}$) Calcd. : 246.1101, Found: 246.1102, Error: 0.4 ppm; IR 1646.0, 1714.5 cm^{-1} .

4h (45 mg, 0.20 mmol) was treated with KO^tBu (28 mg, 0.24 mmol) in 2 ml of ^tBuOH at 40 °C. After 30 min, water diluted and extracted with CH₂Cl₂, dried over over Na₂SO₄, concentrated, and chromatographed to give the tricyclic lactam **5h** (28 mg, 68% yield): ¹H NMR (300 MHz, CDCl₃) δ 1.61~1.67(m, 1H), 1.84~1.99(m, 2H), 2.00~2.11(m, 3H), 2.15~2.58(m, 5H), 2.69(s, 2H), 2.82(dd, 1H, J=12.0 Hz, 8.7 Hz), 3.55~3.71(m, 2H), 6.01(s, 1H); ¹³C NMR (75 MHz, CDCl₃) δ 21.4, 24.2, 25.2, 32.5, 40.9, 47.0, 50.3, 70.7, 129.2, 170.8, 180.2, 202.7; MS: 205, 150, 134, 122; HMRS (ESI, M⁺+H, C₁₂H₁₆NO₂) Calcd. : 206.1176, Found: 206.1177, Error: 0.5 ppm; IR 1639.3, 1712.1 cm⁻¹.

References:

- (1) Miwako M.; Yumiko W.; Takao U.; Kagari Y.; Katsumi C.; Yoshio B., *J. Org. Chem.* **1983**, 48, 4058-4067.
- (2) Milligan, G.; Mossman C. J.; Aubé, J. *J. Am. Chem. Soc.* **1995**, 117, 10449-10459.

X-Ray Ellipsoid Plots of 2h and 2i have been deposited at the Cambridge Crystallographic Data Centre and allocated the deposition numbers CCDC 616555 & 616556

It is complicated of C10-C12 in the single crystalloid. It is explained that in the crystalloid two conformation exist with the ratio of about 3:1. And it does not influence the relative stereochemistry.

The major product **2i1** was confirmed by X-ray crystallography analysis.

Copies of ^1H NMR and ^{13}C NMR of Substrates and Products

175.805
173.371

77.424
77.000
76.576
68.121
66.370
66.015
65.954
65.683
48.062
47.738
45.685
41.313
36.791
35.566
34.521
29.015
28.683
28.053
25.527
25.123
24.913
24.520
23.745
23.390
22.421
22.212
20.002
13.829