Supporting Information

Tandem Base-Promoted Ring-Opening/Brook Rearrangement/Allylic Alkylation of *O*-Silyl Cyanohydrins of β -Silyl- α,β -epoxyaldehyde: Scope and Mechanism

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General. IR spectra were recorded on Horiba FT-710 spectrometer. ^1H NMR spectra were taken on JEOL Delta-500 (500 MHz) spectrometer, or JEOL Alpha-400 (400 MHz) in CDCl_3 with reference to CHCl_3 (δ 7.26) unless otherwise noted. ^{13}C NMR spectra were measured with JEOL Delta-500 (125 MHz) spectrometer or JEOL Alpha-400 (100 MHz) in CDCl_3 with reference to the CDCl_3 triplet (δ 77.2). Resonance patterns were described as s = singlet, d = doublet, t = triplet, q = quartet, sep = septet, m = multiplet, and br = broad. The assignment of ^1H and ^{13}C NMR spectra is based on H-H decoupling and HMQC experiments. Low- and high-resolution mass spectra (EI-MS) were obtained with a JEOL JMS-D-300 spectrometer or a JEOL JMS-SX102 spectrometers. For routine chromatography, the following adsorbents were used: Fuji-Silysia silica gel BW-200 (150-325 mesh) for column chromatography; Merck precoated silica gel 60 F-254 plates for analytical thin-layer chromatography. All moisture sensitive reactions were performed under a positive pressure of nitrogen. Anhydrous MgSO_4 was used for drying all organic solvent extracts in workup, and the removal of the solvents was performed with a rotary evaporator. Dry solvents and reagents were obtained by using standard procedures.

3-(*tert*-butyldimethylsilyl)-2,3-propene-1-ol

To a cooled ($-80\text{ }^\circ\text{C}$) solution of 3-(1-ethoxyethoxy)-1-propyne (25.0 g, 195 mmol) in THF (200 mL) was added dropwise a solution of LDA prepared from diisopropylamine (31.5 mL, 224 mmol) and *n*-BuLi (2.66 M in hexane, 80.7 mL, 215 mmol) in THF (150 mL) over 50 min. The solution was stirred at the same temperature for 30 min before addition of *t*-butyldimethylsilyl chloride (32.3 g, 215 mmol) in THF (80 mL). After being stirred at the same temperature for 10 min, the reaction mixture was allowed to warm to $20\text{ }^\circ\text{C}$. The mixture was diluted with saturated aqueous NaHCO_3 solution (200 mL), and then extracted with Et_2O (150 mL x 3). The combined organic phases were washed with saturated brine (200 mL), dried, and concentrated to give crude silylated compound (49.6 g). The product was used in the following step without further purification.

To a solution of the above compound in acetone- H_2O (70:30, 250 mL) was added *p*-toluenesulfonic acid monohydrate (5.6 g, 29.3 mmol). After being refluxed for 70 min, the reaction mixture was diluted with saturated aqueous NaHCO_3 solution (200 mL) and extracted with Et_2O (100 mL x 3). The combined organic phases were washed with saturated brine, dried, and concentrated to give crude 3-(*tert*-butyldimethylsilyl)-2-propyn-1-ol (32.8 g). The product was used in the following step without further purification.

To a cooled (ice-water) solution of Red-Al® (65% in toluene, 82.3 g, 268 mmol) in Et_2O (115 mL) was added dropwise a solution of the above compound (30.0 g) in Et_2O (115 mL) over 70 min. After

stirring at the same temperature for 15 min, the cooling bath was removed, and stirring was continued for 90 min. After addition of 3% aqueous H_2SO_4 solution (200 mL), the mixture was filtered through a pad of Celite. The filtrate was separated, and the aqueous phase was extracted with Et_2O (150 mL x 3). Combined organic phases were successively washed with water (100 mL) and saturated brine (100 mL), dried, and concentrated. The residual oil was distilled under reduced pressure to give the title compound (24.0 g, 78%), bp 62 °C/0.15 mmHg, a colorless clear oil. R_f = 0.28 (hexane:AcOEt = 5:1). IR (film) 3318 cm^{-1} . ^1H NMR δ 0.03 (6H, s, SiMe_2), 0.87 (9H, s, $t\text{-Bu}$), 1.71 (1H, br s, OH), 4.18 (1H, dd, J = 4.4, 1.7 Hz, H-1), 5.90 (1H, dt, J = 18.8, 1.7 Hz, H-2), 6.19 (1H, dt, J = 18.8, 4.4 Hz, H-2). ^{13}C NMR δ -6.00 (SiMe_2), 16.6 (CMe_3), 26.6 (CMe_3), 65.8 (C-1), 126.8 (C-3), 146.4 (C-2). HRMS calcd for $\text{C}_9\text{H}_{20}\text{OSi}$ 172.1283, found 172.1322.

(2R*,3R*)-3-(*tert*-butyldimethylsilyl)-2,3-epoxypropanol

To a cooled (ice-water) solution of 3-(*tert*-butyldimethylsilyl)-2-propene-1-ol (24.0 g, 139 mmol) and $\text{Na}_2\text{HPO}_4 \cdot \text{H}_2\text{O}$ (59.8 g, 167 mmol) in CH_2Cl_2 (278 mL) was added mCPBA (77% purity, 38.0 g, 167 mmol). After the cooling bath was removed, the reaction mixture was stirred at room temperature for 12 h. The mixture was diluted with saturated aqueous NaHCO_3 solution (250 mL), separated, and the aqueous phase was extracted with CH_2Cl_2 (150 mL x 3). Combined organic phases were washed with saturated brine (150 mL), dried, and concentrated. The residual oil was subjected to column chromatography (silica gel 350 g, elution with hexane:AcOEt = 3:1) to give the title compound (23.3 g, 89%), a colorless clear oil. R_f = 0.35 (hexane:AcOEt = 2:1). IR (neat) 3425, 1283 cm^{-1} . ^1H NMR δ -0.04 and 0.02 (each 3H, s, SiMe_2), 0.96 (9H, s, $t\text{-Bu}$), 1.73 (1H, dd, 7.1, 5.9 Hz, OH), 2.34 (1H, d, J = 3.7 Hz, H-3), 3.02 (1H, ddd, J = 4.6, 3.7, 2.4 Hz, H-2), 3.60 (1H, ddd, J = 12.5, 7.1, 4.6 Hz, H-1), 3.99 (1H, ddd, J = 12.5, 5.9, 2.4 Hz, H-1). ^{13}C NMR δ -8.34 (SiMe_2), 16.6 (CMe_3), 26.5 (CMe_3), 46.3 (C-3), 55.5 (C-2), 63.3 (C-1). Anal. Calcd for $\text{C}_9\text{H}_{20}\text{O}_2\text{Si}$: C, 57.40; H, 10.70. found: C, 57.19; H, 10.74.

(2R*,3R*)-3-(*tert*-butyldimethylsilyl)-2,3-epoxypropanal (22)

To a cooled (ice-water) solution of 3-(*tert*-butyldimethylsilyl)-2,3-epoxypropanol (7.38 g, 39.18 mmol), DMSO (55.9 mL, 0.79 mol), and NEt_3 (44.2 mL, 10.32 mol) in CH_2Cl_2 (96 mL) was added $\text{SO}_3 \cdot \text{pyridine}$ (98%, 14.6 g, 90.1 mmol). After stirring at the same temperature for 1 hr, the mixture was diluted with hexane- Et_2O (1:1, 100 mL). Phases were separated, and the aqueous phase was extracted with Et_2O -hexane (1:1, 100 mL x 3). Combined organic phases were successively washed with water (100 mL) and 1M hydrochloric acid (100 mL), dried, and concentrated. The residual oil was subjected to column chromatography (silica gel 200 g, elution with hexane:AcOEt = 3:1) to give **22** (6.0 g, 82%), a pale yellow oil. R_f = 0.35 (hexane: Et_2O = 5:1). IR (film) 1730, 1252 cm^{-1} . ^1H NMR δ 0.00 and 0.04 (each 3H, s, SiMe_2), 0.97 (9H, s, $t\text{-Bu}$), 2.56 (1H, d, J = 3.4 Hz, H-3), 3.15 (1H, dd, J = 6.6, 3.4 Hz, H-2), 8.82 (1H, d, J = 6.6 Hz, CHO). ^{13}C NMR δ -8.2 and -8.1 (SiMe_2), 17.0 (CMe_3), 26.6 (CMe_3), 46.6 (C-3), 56.2 (C-2), 199.2 (CHO). HRMS calcd for $\text{C}_9\text{H}_{18}\text{O}_2\text{Si}$ ($\text{M}^+ - \text{C}_4\text{H}_9$) 129.0372, found 129.0343.

(1R*,2S*,3S* and 1R*,2R*,3R*)-2-(*tert*-butyldimethylsiloxy)-4-(*tert*-butyldimethyl-silyl)-3,4-epoxybutanenitriles (21a,b)

To a solution of **22** (214 mg, 1.15 mmol) in CH_2Cl_2 (2.3 mL) was added KCN (15 mg, 0.23 mmol), $n\text{-Bu}_4\text{PBr}$ (78 mg, 0.23 mmol), and TBSCN (97%, 201 mg, 1.38 mmol). After stirring at room temperature for 40 min, the mixture was diluted with saturated aqueous NaHCO_3 solution (10 mL), separated, and the aqueous phase was extracted with CH_2Cl_2 (10 mL x 3). Combined organic phases were washed with saturated brine (10 mL), dried, and concentrated. The residual oil was subjected to column

chromatography (silica gel 45 g, elution with hexane: Et₂O = 20:1) to give **21a** (162 mg, 43%) and **21b** (166 mg, 44%). The relative stereochemistry in **21a** and **21b** was determined on the basis of X-ray analysis of **21b**. **21a**: plates (hexane), mp 32.4-35.8 °C, R_f = 0.33 (hexane:Et₂O = 20:1). IR (KBr) 1253 cm⁻¹. ¹H NMR δ-0.04 and 0.05 (each 3H, s, SiMe₂Bu), 0.17 and 0.19 (each 3H, s, SiMe₂Bu), 0.93(9H, s, *t*-Bu), 0.97(9H, s, *t*-Bu), 2.31 (1H, d, J = 3.4 Hz, H-4), 3.11 (1H, dd, J = 5.9, 3.4 Hz, H-3), 4.23 (1H, d, J = 5.9 Hz, H-2). ¹³C NMR δ-8.6 and -7.9 (SiMe₂), -5.1 and -5.0 (OSiMe₂), 16.7 (CMe₃), 18.3 (OSiCMe₃), 25.7 (CMe₃), 26.6(OSiCMe₃), 47.1 (C-4), 56.7 (C-3), 66.2 (C-2), 117.2 (CN). MS (APCI-LC/MS) 345 (M+NH₄). Anal Calcd for C₁₆H₃₃NO₂Si₂ C, 58.66; H, 10.15; N, 4.28. found C, 58.37; H, 10.13; N, 4.37. **21b**: plates (hexane), mp 38.3-40.5 °C. R_f = 0.28 (hexane:Et₂O = 20:1). IR (KBr) 1257 cm⁻¹. ¹H NMR δ-0.03 and 0.03 (each 3H, s, SiMe₂Bu), 0.14 and 0.19 (each 3H, s, SiMe₂Bu), 0.91 (9H, s, *t*-Bu), 0.97 (9H, s, *t*-Bu), 2.37 (1H, d, J = 3.2 Hz, H-4), 3.09 (1H, dd, J = 4.4, 3.2 Hz, H-3), 4.39 (1H, d, J = 4.4 Hz, H-2). ¹³C NMR δ -8.4 and -8.1 (SiMe₂), -5.1 and -5.1 (OSiMe₂), 16.8 (CMe₃), 18.3 (OSiCMe₃), 25.6 (CMe₃), 26.6 (OSiCMe₃), 48.0 (C-4), 55.9 (C-3), 64.1 (C-2), 117.7 (CN). MS (APCI-LC/MS) 345 (M+NH₄). Anal Calcd for C₁₆H₃₃NO₂Si₂ C, 58.66; H, 10.15; N, 4.28. found C, 58.35; H, 10.29; N, 4.28.

General Procedure for alkylation of 21: Reaction of 21b with MeI and NHMDS

This procedure is representative for the alkylation. To a cooled (-80 °C) solution of **21b** (100 mg, 0.305 mmol) and MeI (23 μL, 0.369 mmol) in THF (0.7 mL) was added a solution of NHMDS (1.02 M in THF, 0.330 mL, 0.337 mmol). After stirring at the same temperature for 5 min, the mixture was diluted with saturated aqueous NH₄Cl solution (10 mL), and extracted with Et₂O (10 mL x 3). Combined organic phases were washed with saturated brine (10 mL), dried, and concentrated. The residual oil was subjected to column chromatography (silica gel 10 g, elution with hexane: Et₂O = 20:1) to give **27** (R = Me) (102 mg, 98%).

(*E*)-**27** (R = Me):

For separation of *E/Z* isomers, MPLC (elution with hexane:Et₂O = 60:1) was used. a colorless clear oil. R_f = 0.36 (hexane: Et₂O = 30:1). IR (film) 1662, 1472, 1258, 1195, 1114 cm⁻¹. ¹H NMR δ 0.16 and 0.21 (each 3H, s, SiMe₂), 0.17 (6H, s, SiMe₂), 0.88 (9H, s, *t*-Bu), 0.92 (9H, s, *t*-Bu), 1.64 (3H, s, CH₃), 5.07 (1H, d, J = 12.0 Hz, H-3), 6.79 (1H, d, J = 12.0 Hz, H-4). ¹³C NMR δ -5.1, -5.0, -3.4, and -2.9 (SiMe₂), 18.1 and 18.4 (CMe₃), 25.7 and 25.7 (CMe₃), 31.9 (CH₃), 67.7 (C-2), 113.4 (C-3), 121.3 (CN), 144.0 (C-4). HRMS calcd for C₁₆H₃₂NO₂Si₂(M⁺ - CH₃), 326.1972, found 326.1929.

(*Z*)-**27** (R = Me):

For separation of *E/Z* isomers, MPLC (elution with hexane:CH₂Cl₂ = 6:1) was used. a colorless clear oil, R_f = 0.36 (hexane:Et₂O = 30:1). IR (film) 658, 1472, 1258, 1146, 1124, 1092 cm⁻¹. ¹H NMR δ 0.18 and 0.22 (each 3H, s, SiMe₂), 0.19 (6H, s, SiMe₂), 0.88 (9H, s, *t*-Bu), 0.96 (9H, s, *t*-Bu), 1.72 (3H, s, CH₃), 4.51 (1H, d, J = 6.4 Hz, H-3), 6.21 (1H, d, J = 6.1 Hz, H-4). ¹³C NMR δ -5.3, -5.2, -3.4, and -3.2 (SiMe₂), 18.1 and 18.3 (CMe₃), 25.7 (CMe₃), 30.6 (CH₃), 66.0 (C-2), 111.8 (C-3), 121.9 (CN), 140.8 (C-4). HRMS calcd for C₁₆H₃₂NO₂Si₂(M⁺ - CH₃), 326.1972, found 326.1929.

(*E*)-**27** (R = Et):

a colorless clear oil, R_f = 0.37 (hexane:Et₂O = 30:1). IR (film) 1661, 1472, 1257, 1208, 1118, 1090 cm⁻¹. ¹H NMR δ 0.14 and 0.22 (each 3H, s, SiMe₂), 0.18 (6H, s, SiMe₂), 0.88 (9H, s, *t*-Bu), 0.93 (9H, s, *t*-Bu), 1.03 (3H, t, J = 7.3 Hz, CH₃), 1.76 and 1.85 (each 1H, dq, J = 14.6, and 7.3 Hz, CH₂CH₃), 4.99 (1H, d, J = 12.0 Hz, H-3), 6.79 (1H, d, J = 12.0 Hz, H-4). ¹³C NMR δ -5.1, -3.7, and -2.8 (SiMe₂), 8.6

(CH₃), 18.2 and 18.4 (CMe₃), 25.7 (CMe₃), 37.5 (CH₂), 72.1 (C-2), 112.3 (C-3), 120.3 (CN), 144.4 (C-4). HRMS calcd for C₁₆H₃₂NO₂Si₂, (M⁺ - CH₂CH₃), 326.1972, found 326.1929.

(Z)-27 (R = Et):

For separation of *E/Z* isomers, MPLC (elution with hexane:CH₂Cl₂ = 7:1) was used. a colorless clear oil, *R_f* = 0.37 (hexane:Et₂O = 30:1). IR (film) 1657, 1472, 1257, 1134, 1098 cm⁻¹. ¹H NMR δ 0.17 (6H, s, SiMe₂), 0.19 and 0.24 (each 3H, s, SiMe₂), 0.89 (9H, s, *t*-Bu), 0.96 (9H, s, *t*-Bu), 1.03 (3H, t, *J* = 7.3 Hz, CH₃), 1.86-1.95 (2H, m, CH₂), 4.38 (1H, d, *J* = 6.1 Hz, H-3), 6.24 (1H, d, *J* = 6.1 Hz, H-4). ¹³C NMR δ -5.3, -5.2, -3.8, and -3.1 (SiMe₂), 8.4 (CH₃), 18.3 and 18.3 (CMe₃), 25.7 and 25.7 (CMe₃), 36.3 (CH₂), 69.7 (C-2), 110.1 (C-3), 121.1 (CN), 140.8 (C-4). HRMS calcd for C₁₆H₃₂NO₂Si₂, (M⁺ - CH₂CH₃), 326.1972, found 326.1929.

(E)-27 (R = *i*-Pr):

For separation of *E/Z* isomers, MPLC (elution with hexane:Et₂O = 80:1) was used. a colorless oil, *R_f* = 0.40 (hexane:Et₂O = 30:1). IR (film) 1661, 1471, 1258, 1210, 1079 cm⁻¹. ¹H NMR δ 0.13 and 0.22 (each 3H, s, SiMe₂), 0.18 (6H, s, SiMe₂), 0.89 and 0.93 (each 9H, s, *t*-Bu), 0.97 and 1.06 (each 3H, d, *J* = 6.6 Hz, CH₃), 1.89 (1H, sep, *J* = 6.6 Hz, H-1'), 4.96 (1H, d, *J* = 12.0 Hz, H-3), 6.77 (1H, d, *J* = 12.0 Hz, H-4). ¹³C NMR δ -5.0, -5.0, -3.8, and -2.7 (SiMe₂), 17.1 and 17.4 (CH₃), 18.4 (CMe₃), 25.7 (CMe₃), 40.2 (C-1'), 75.8 (C-2), 111.0 (C-3), 119.8 (CN), 144.7 (C-4). HRMS calcd for C₁₆H₃₂NO₂Si₂, (M⁺ - CH(CH₃)₂), 326.1972, found 326.1929.

(Z)-27 (R = *i*-Pr):

For separation of *E/Z* isomers, MPLC (elution with hexane:CH₂Cl₂ = 10:1) was used. a colorless oil, *R_f* = 0.40 (hexane:Et₂O = 30:1). IR (film) 1658, 1471, 1257, 1112, 1080 cm⁻¹. ¹H NMR δ 0.16, 0.17, 0.19 and 0.25 (each 3H, s, SiMe₂), 0.89 and 0.96 (each 9H, s, *t*-Bu), 1.02 (6H, d, *J* = 6.8 Hz, (CH₃)₂), 2.06 (1H, sep, *J* = 6.8 Hz, H-1'), 4.30 (1H, d, *J* = 6.4 Hz, H-3), 6.27 (1H, d, *J* = 6.4 Hz, H-4). ¹³C NMR δ -5.3 and -5.2 and -4.0 and -3.1 (SiMe₂), 16.6 and 17.3 (CH₃), 18.3 and 18.4 (CMe₃), 25.7 and 25.8 (CMe₃), 39.7 (C-1'), 72.9 (C-2), 109.2 (C-3), 120.5 (CN), 140.7 (C-4). HRMS calcd for C₁₆H₃₂NO₂Si₂, (M⁺ - CH(CH₃)₂), 326.1972, found 326.1929.

(E)-27 (R = CH₂CH=CH₂):

For separation of *E/Z* isomers, MPLC (elution with hexane:CH₂Cl₂ = 10:1) was used. a colorless oil, *R_f* = 0.41 (hexane:Et₂O = 30:1). IR (film) 1662, 1471, 1257, 1203, 1089 cm⁻¹. ¹H NMR δ 0.14 and 0.22 (each 3H, s, SiMe₂), 0.18 (6H, s, SiMe₂), 0.88 and 0.92 (each 9H, s, *t*-Bu), 2.49 and 2.57 (each 1H, dd, *J* = 13.9, 7.3 Hz, H-1'), 5.02 (1H, d, *J* = 12.0 Hz, H-3), 5.20 (1H, dd, *J* = 17.6, 1.2 Hz, H-3'), 5.22 (1H, dd, *J* = 9.2, 1.2 Hz, H-3'), 5.82 (1H, dddd, *J* = 17.6, 9.2, 7.3, 7.3 Hz, H-2'), 6.79 (1H, d, *J* = 12.0 Hz, H-4). ¹³C NMR δ -5.1 and -5.0 and -3.6 and -2.8 (SiMe₂), 18.3 and 18.4 (CMe₃), 25.7 and 25.7 (CMe₃), 48.7 (C-1'), 71.2 (C-2), 111.9 (C-3), 120.1 (CN), 120.4 (C-3'), 131.2 (C-2'), 144.6 (C-4). HRMS calcd for C₁₆H₃₂NO₂Si₂, (M⁺ - CH₂CH=CH₂), 326.1972, found 326.1929.

(Z)-27 (R = CH₂CH=CH₂):

For separation of *E/Z* isomers, MPLC (elution with hexane:CH₂Cl₂ = 8:1) was used. a colorless oil, *R_f* = 0.41 (hexane:Et₂O = 30:1). IR (film) 1657, 1471, 1257, 1114, 1091 cm⁻¹. ¹H NMR δ 0.20 and 0.24 (each 3H, s, SiMe₂), 0.18 (6H, s, SiMe₂), 0.88 and 0.96 (each 9H, s, *t*-Bu), 2.65 (2H, d, *J* = 7.1 Hz, H-1'), 4.42 (1H, d, *J* = 6.4 Hz, H-3), 5.17 (1H, d, *J* = 17.2 Hz, H-3'), 5.18 (1H, d, *J* = 10.4 Hz, H-3'),

5.86 (1H, ddt, $J = 17.2, 10.4, 7.1$ Hz, H-2'), 6.25 (1H, d, $J = 6.4$ Hz, H-4). ^{13}C NMR δ -5.3, -5.2, -3.8, and -3.2 (SiMe_2), 18.3 and 18.3 (CMe_3), 25.7 and 25.7 (CMe_3), 47.3 (C-1'), 68.8 (C-2), 109.9 (C-3), 119.7 (C-3'), 120.8 (CN), 131.9 (C-2'), 141.0 (C-4). HRMS calcd for $\text{C}_{16}\text{H}_{32}\text{NO}_2\text{Si}_2$, ($\text{M}^+ - \text{CH}_2\text{CH}=\text{CH}_2$), 326.1972, found 326.1929.

(E)-27 (R = CH_2Ph_2):

For separation of *E/Z* isomers, MPLC (elution with hexane: Et_2O = 40:1) was used. a colorless oil, $R_f = 0.38$ (hexane: Et_2O = 30:1). IR (film) 1661, 1472, 1258, 1184, 1086 cm^{-1} . ^1H NMR δ 0.07 and 0.10 (each 3H, s, SiMe_2), 0.16 (6H, s, SiMe_2), 0.86 and 0.91 (each 9H, s, *t*-Bu), 3.04 and 3.08 (each 1H, d, $J = 13.4$ Hz, H-1'), 5.04 (1H, d, $J = 12.0$ Hz, H-3), 6.74 (1H, d, $J = 12.0$ Hz, H-4), 7.27-7.31 (5H, m, Ph). ^{13}C NMR δ -5.1, -5.0, -3.9, and -2.9 (SiMe_2), 18.3 and 18.4 (CMe_3), 25.7 and 25.8 (CMe_3), 50.6 (H-1'), 71.9 (C-2), 112.0 (C-3), 120.1 (CN), 127.5, 128.1, 130.0 and 134.4 (Ph), 144.5 (C-4). HRMS calcd for $\text{C}_{16}\text{H}_{32}\text{NO}_2\text{Si}_2$, ($\text{M}^+ - \text{CH}_2\text{CH}=\text{CH}_2$), 326.1972, found 326.1929.

(Z)-27 (R = CH_2Ph_2):

For separation of *E/Z* isomers, MPLC (elution with hexane: CH_2Cl_2 = 10:1) was used. a colorless oil, $R_f = 0.38$ (hexane: Et_2O = 30:1). IR (film). ^1H NMR δ 0.02, 0.09, 0.16, and 0.19 (each 3H, s, SiMe_2), 0.86 and 0.99 (each 9H, s, *t*-Bu), 3.09 and 3.21 (each 1H, d, $J = 13.4$ Hz, H-1'), 4.38 (1H, d, $J = 6.1$ Hz, H-3), 6.23 (1H, d, $J = 6.1$ Hz, H-4), 7.23-7.27 (5H, m, Ph). ^{13}C NMR δ -5.3, -5.1, -4.1, and -3.3 (SiMe_2), 18.2 and 18.3 (CMe_3), 25.7 and 25.8 (CMe_3), 48.3 (H-1'), 69.5 (C-2), 110.6 (C-3), 120.6 (CN), 127.2, 127.9, 131.4 and 135.1 (Ph), 140.7 (C-4). HRMS calcd for $\text{C}_{16}\text{H}_{32}\text{NO}_2\text{Si}_2$, ($\text{M}^+ - \text{CH}_2\text{CH}=\text{CH}_2$), 326.1972, found 326.1929.

(2*R,3*R**)-3-(*tert*-butyldiphenylsilyl)-2,3-epoxypropanal**

To a cooled (-80 °C) solution of 3-(1-ethoxyethoxy)-1-propyne (4.5 g, 35.1 mmol) in THF (62 mL) was added *n*-BuLi (2.30 M in hexane, 16.0 mL, 36.9 mmol) over 10 min. The solution was stirred at the same temperature for 15 min before addition of *t*-butyldiphenylsilyl chloride (9.6 mL, 36.9 mmol). After being stirred at the same temperature for 1 hr, the cooling bath was removed and stirring was continued for 12 hr. The mixture was diluted with saturated aqueous NaHCO_3 solution (100 mL), and then extracted with Et_2O (50 mL x 3). The combined organic phases were washed with saturated brine (100 mL), dried, and concentrated to give crude silylated compound (14.66 g). The product was used in the following step without further purification.

To a solution of the above compound in acetone- H_2O (70:30, 100 mL) was added *p*-toluenesulfonic acid monohydrate (1.01 g, 5.3 mmol). After being refluxed for 3 hr, the reaction mixture was diluted with saturated aqueous NaHCO_3 solution (50 mL) and extracted with Et_2O (50 mL x 3). The combined organic phases were washed with saturated brine, dried, and concentrated to give crude 3-(*t*-butyldiphenylsilyl)-2-propyn-1-ol (11.89 g). The product was used in the following step without further purification.

To a cooled (ice-water) solution of Red-Al® (65% in toluene, 16.4 g, 52.6 mmol) in Et_2O (40 mL) was added dropwise a solution of the above compound in Et_2O (20 mL) over 15 min. After stirring at the same temperature for 10 min, the cooling bath was removed, and stirring was continued for 1 hr. After addition of 3% aqueous H_2SO_4 solution (100 mL), the mixture was filtered through a pad of Celite. The filtrate was separated, and the lower phase was extracted with Et_2O (50 mL x 3). Combined organic phases were successively washed with water (100 mL) and saturated brine (100 mL), dried, and

concentrated to give curde 3-(*tert*-butyldiphenylsilyl)-2,3-propene-1-ol (12.34 g). The product was used in the following step without further purification.

To a cooled (ice-water) solution the above compound and $\text{Na}_2\text{HPO}_4 \cdot \text{H}_2\text{O}$ (15.1 g, 42.1 mmol) in CH_2Cl_2 (70 mL) was added mCPBA (77% purity, 9.6 g, 42.1 mmol). After the cooling bath was removed, the reaction mixture was stirred at room temperature for 3 days. The mixture was diluted with saturated aqueous NaHCO_3 solution (100 mL), separated, and the aqueous phase was extracted with CH_2Cl_2 (70 mL x 3). Combined organic phases were washed with saturated brine (100 mL), dried, and concentrated. The residual oil was subjected to column chromatography (silica gel 350 g, elution with hexane:AcOE = 3:1) to give (*tert*-Butyldiphenylsilyl)-2,3-epoxypropanol (6.03 g, 55%), plates (hexane), mp 74.0-75.0 °C, R_f = 0.31 (hexane:AcOEt = 2:1). IR (film) 3305 cm^{-1} . ^1H NMR δ 1.19(9H, s, *t*-Bu), 1.86 (1H, br, CH_2OH), 2.90 (2H, m, H-2, H-3), 3.68 (1H, dd, J = 11.9, 3.4 Hz, H-1), 3.99 (1H, dd, J = 11.9, 2.3 Hz, H-1), 7.33-7.46 (6H, m, Ph), 7.59-7.63 (4H, m, Ph). ^{13}C NMR δ 18.8 (CMe_3), 28.0 (CMe_3), 45.2 (C-3), 55.8 (C-2), 62.9 (C-1), 127.9, 128.1, 129.8, 128.9, 132.1, 132.4, 136.1, 136.2 (Ph).

To a cooled (ice-water) solution of 3-(*tert*-butyldiphenylsilyl)-2,3-epoxypropanol (1.31 g, 4.19 mmol), DMSO (6.0 mL, 83.8 mmol), and NEt_3 (4.67 mL, 33.5 mmol) in CH_2Cl_2 (10 mL) was added $\text{SO}_3 \cdot \text{pyridine}$ (98%, 1.64 g, 10.1 mmol). After stirring at the same temperature for 1 hr, the cooling bath was removed and stirring was continued for 1.5 hr. The mixture was diluted with hexane- Et_2O (1:1, 20 mL). Phases were separated, and the lower phase was extracted with Et_2O -hexane (1:1, 20 mL x 3). Combined organic phases were successively washed with 1M hydrochloric acid (30 mL) and saturated brine (30 mL), dried, and concentrated. The residual oil was subjected to column chromatography (silica gel 50 g, elution with hexane:AcOEt = 7:1) to give the title compound (1.13 g, 87%), a pale yellow oil. R_f = 0.34 (hexane:AcOEt = 6:1). IR (film) 1728 cm^{-1} . ^1H NMR δ 1.21 (9H, s, *t*-Bu), 3.03 (1H, dd, J = 6.4, 3.4 Hz, H-2), 3.08 (1H, d, J = 3.4 Hz, H-3), 7.34-7.47 (6H, m, Ph), 7.56-7.58 (4H, m, Ph), 8.95 (1H, d, J = 6.4 Hz, CHO). ^{13}C NMR δ 18.9 (CMe_3), 27.9 (CMe_3), 45.8 (C-3), 56.5 (C-2), 128.1, 128.3, 130.3, 130.4, 131.0, 131.2, 136.0, 136.2 (Ph), 198.8 (CHO). HRMS calcd for $\text{C}_{15}\text{H}_{13}\text{O}_2\text{Si}$, ($\text{M}^+ - \text{C}_4\text{H}_9$), 253.0685 found 255.0680.

(2*R,3*S**,4*S** and 2*R**,3*R**,4*R**)-2-(*tert*-butyldimethylsiloxy)-4-(*tert*-butyldiphenylsilyl)-3,4-epoxybutanenitriles (33a,b)**

To a cooled (ice-water) solution of 3-(*tert*-butyldiphenylsilyl)-2,3-epoxypropanol (2.00 g, 6.44 mmol) in CH_2Cl_2 (12.8 mL) was added KCN (20 mg, 0.31 mmol), *n*- Bu_4PBr (55 mg, 0.16 mmol), and TBSCN (97%, 954 mg, 6.56 mmol). After stirring at the same temperature for 10 min, the cooling bath was removed and

stirring was continued for 2 hr. The mixture was diluted with hexane, filtrated through a plug of Al_2O_3 and concentrated. The residue was purified by column chromatography (silica gel 70 g, elution with hexane: Et_2O = 15:1) to give **33** (2.50 g, 86%, **33a**:**33b** = 1.00:1.24). For separation of diastereomers, MPLC (elution with hexane:ether = 25:1) was used. The relative stereochemistry in **33a** and **33b** was determined on the basis of X-ray analysis of **33b**. **33a**: plates (hexane), mp 70.0-71.0 °C, R_f = 0.38 (hexane: Et_2O = 10:1). IR (KBr) 1250, 1117, 852, 841 cm^{-1} . ^1H NMR δ 0.13 and 0.18 (each 3H, s, SiMe_2Bu), 0.91(9H, s, *t*-Bu), 1.20 (9H, s, *t*-Bu), 2.90 (1H, d, J = 3.2 Hz, H-4), 2.96 (1H, dd, J = 5.3, 3.2 Hz, H-3), 4.44 (1H, d, J = 5.3 Hz, H-2), 7.33-7.46 (6H, m, Ph), 7.57-7.59 (2H, m, Ph), 7.63-7.65 (2H, m, Ph). ^{13}C NMR δ -5.1 and -5.0 (SiMe_2), 18.3 (CMe_3), 18.7 (OSiCMe_3), 25.7 (CMe_3), 28.0 (OSiCMe_3), 46.1 (C-4), 56.3 (C-3), 66.7 (C-2), 117.2 (CN), 128.0, 128.2, 130.0, 130.2, 131.6, 131.7, 136.2, 136.2(Ph). MS (APCI-LC/MS) 451 (M^+). Anal Calcd for $\text{C}_{26}\text{H}_{37}\text{NO}_2\text{Si}_2$ C, 69.13; H, 8.26; N, 3.10. found C, 68.78; H, 8.45; N, 3.29. **33b**: plates (hexane), mp 76.5-77.0 °C. R_f = 0.36 (hexane: Et_2O = 10:1). IR (KBr) 1268, 1259, 1114, 1096, 851, 841 cm^{-1} . ^1H NMR δ 0.15 and 0.18 (each 3H, s,

SiMe₂Bu), 0.92(9H, s, *t*-Bu), 1.20 (9H, s, *t*-Bu), 2.92 (1H, d, *J* = 3.2 Hz, H-4), 2.99 (1H, dd, *J* = 4.1, 3.2 Hz, H-3), 4.47 (1H, d, *J* = 4.1 Hz, H-2), 7.33-7.47 (6H, m, Ph), 7.56-7.58 (2H, m, Ph), 7.62-7.64 (2H, m, Ph). ¹³C NMR δ -5.1 (SiMe₂), 18.3 (CMe₃), 18.8 (OSiCMe₃), 25.7 (CMe₃), 28.0 (OSiCMe₃), 46.6 (C-4), 56.0 (C-3), 64.6 (C-2), 117.7 (CN), 128.0, 128.2, 130.1, 130.2, 131.6, 131.7, 136.1, 136.2(Ph). HRMS calcd for C₂₆H₃₇NO₂Si₂, 451.2363 found 451.2371.

General Procedure for methylation of **33**: Reaction of **33b** with NHMDS

To a cooled (-80 °C) solution of **33b** (83 mg, 0.184 mmol) and MeI (6.0M in THF, 37 μL, 0.221 mmol) in THF (0.49 mL) was added a solution of NHMDS (0.95 M in THF, 0.21 mL, 0.202 mmol). After stirring at the same temperature for 5 min, the mixture was diluted with saturated aqueous NH₄Cl solution (10 mL), and extracted with Et₂O (5 mL x 3). Combined organic phases were washed with saturated brine (10 mL), dried, concentrated. The residual oil was subjected to column chromatography (silica gel 10 g, elution with hexane: Et₂O = 30:1) to give (*E*)-**34** (79.3 mg, 93%).

(*E*)-**34**:

a colorless clear oil. *R_f* = 0.30 (hexane: Et₂O = 30:1). IR (film) 1662, 1469, 1113 cm⁻¹. ¹H NMR δ 0.08 and 0.12 (each 3H, s, SiMe₂), 0.80 (9H, s, *t*-Bu), 1.09 (9H, s, *t*-Bu), 1.56 (3H, s, CH₃), 5.18 (1H, d, *J* = 11.9 Hz, H-3), 6.78 (1H, d, *J* = 11.9 Hz, H-4), 7.38-7.47 (6H, m, Ph), 7.65-7.67 (4H, m, Ph). ¹³C NMR δ -3.5 and -3.1 (SiMe₂), 18.1(SiMe₂CMe₃), 19.4 (SiPh₂CMe₃), 25.6 and 26.7 (CMe₃), 31.7 (CH₃), 67.5 (C-2), 114.1 (C-3), 121.2 (CN), 128.1, 128.2, 130.4, 132.2, 135.6, 135.6, (Ph), 144.2 (C-4). HRMS calcd for C₂₃H₃₀NO₂Si₂, 408.1815 (M⁺ - C₄H₉), found 408.1778.

(*E*)-**35**:

To a cooled (-80 °C) solution of **21b** (460 mg, 1.40 mmol) in THF (3.98 mL) was added a solution of NHMDS (0.95 M in THF, 1.62 mL, 1.54 mmol) The solution was stirred at the same temperature for 5 min before addition of CH₃COOH (1.0M in THF, 1.68 mL, 1.68 mmol). After being stirred at the same temperature for 5 min, the reaction mixture was diluted with saturated aqueous NH₄Cl solution (10 mL), and extracted with Et₂O (5 mL x 3). Combined organic phases were washed with saturated brine (10 mL), dried, concentrated. The residual oil was subjected to column chromatography (silica gel 20 g, elution with hexane: Et₂O = 20:1) to give (*E*)-**35** (391.3 mg, 85%), a colorless clear oil. *R_f* = 0.25 (hexane:Et₂O = 30:1). IR (film) 1662, 1469, 1258, 1200, 1072 cm⁻¹. ¹H NMR δ 0.14 and 0.16 (each 3H, s, SiMe₂Bu), 0.16 (6H, s, SiMe₂Bu), 0.90 and 0.91 (each 9H, s, *t*-Bu), 4.86 (1H, d, *J* = 7.8 Hz, H-2), 5.14 (1H, dd, *J* = 7.8, 11.9Hz, H-3), 6.63 (1H, d, *J* = 11.9 Hz, H-4). ¹³C NMR δ -5.2, -5.2 and -4.8 (OSiMe₂), 18.2 and 18.3 (OSiCMe₃), 25.6 and 25.6 (OSiCMe₃), 60.2 (C-2), 107.6 (C-3), 119.2 (CN). 146.2 (C-4). HRMS calcd for C₁₆H₃₃NO₂Si₂, 327.2050 found 327.2035.

(*Z*)-**35**:

To a cooled (-20 °C) solution of **21a** (703 mg, 2.14 mmol) in Et₂O (2.79 mL) was added a solution of KHMDS (0.44 M in toluene, 5.34 mL, 2.35 mmol) The solution was stirred at the same temperature for 9 min before addition of CH₃COOH (1.0M in Et₂O, 2.57 mL, 2.57 mmol). After being stirred at -40 °C for 5 min, the reaction mixture was diluted with saturated aqueous NH₄Cl solution (10 mL), and extracted with Et₂O (5 mL x 3). Combined organic phases were washed with saturated brine (10 mL), dried, concentrated. The residual oil was subjected to column chromatography (silica gel 70 g, elution with hexane: Et₂O = 30:1) to give **35** (468 mg, 67%, *E/Z* = 0.46). Separation of *E/Z* isomers, MPLC (elution with hexane:ether = 40:1) was used. a colorless clear oil *R_f* = 0.25 (hexane:Et₂O = 30:1). IR (film) 1654, 1472, 1257, 1237, 1084 cm⁻¹. ¹H NMR δ 0.13, 0.16, 0.16 and 0.18 (each 3H, s, SiMe₂Bu), 0.90 and 0.93 (each 9H, s, *t*-Bu), 4.75 (1H, dd, *J* = 5.7, 8.9 Hz, H-3), 5.48 (1H, d, *J* = 8.9 Hz, H-2),

6.35 (1H, d, $J = 5.7$ Hz, H-4). ^{13}C NMR δ -5.3, -5.2, -5.0 and -4.8 (OSiMe_2), 18.3 and 18.3 (OSiCMe_3), 25.7 and 25.7 (OSiCMe_3), 55.6 (C-3), 106.6 (C-2), 119.9 (CN), 142.9 (C-4). HRMS calcd for $\text{C}_{16}\text{H}_{33}\text{NO}_2\text{Si}_2$, 327.2050 found 327.2035.

Isomerization of (*E,Z*)-**35**

To a cooled (-80°C) solution of (*E*)-**35** (50 mg, 0.153 mmol) and MeI (6.0M in THF, 31 μL , 0.184 mmol) in THF (0.404 mL) was added a solution of NHMDS (0.95 M in THF, 0.117 mL, 0.168 mmol). After stirring at the same temperature for 5 min, the mixture was diluted with saturated aqueous NH_4Cl solution (10 mL), and extracted with Et_2O (5 mL x 3). Combined organic phases were washed with saturated brine (10 mL), dried, and concentrated. The residual oil was subjected to column chromatography (silica gel 5 g, elution with hexane: $\text{Et}_2\text{O} = 40:1$) to give (*E*)-**27** ($\text{R} = \text{Me}$) (48.4 mg, 93%).

Competitive Methylation Reaction of **21a** and **21b** with LDA/MeI.

To a cooled (-80°C) solution of **21a** and **21b** (**21a:21b** = 1.00:1.04, 121 mg, 0.369 mmol) and MeI (11.5 μL , 0.184 mmol) in THF (1.17 mL) was added a solution of LDA (0.30 mL, 0.184 mmol) prepared from diisopropylamine (269 μL , 1.92 mmol) and *n*-BuLi (2.05 M in hexane, 898 μL , 1.84 mmol) in THF (1.84 μL). After stirring at the same temperature for 5 min, the mixture was diluted with saturated aqueous NH_4Cl solution (10 mL), and extracted with Et_2O (10 mL x 3). Combined organic phases were washed with saturated brine (10 mL), dried, and concentrated. The residual oil was subjected to column chromatography (silica gel 12 g, elution with hexane: $\text{Et}_2\text{O} = 30:1$) to give **27** ($\text{R} = \text{Me}$) (44.6 mg, 35%) and **21** (48.4 mg, 40%, **21a:21b** = 1.00:0.70).

(**2R***,**3S***)-3-*tert*-butyldimethylsilyl-2,3-epoxypropanal

To a cooled (ice-water) solution of DIBAL (0.93M in hexane, 45.6 mL, 42.4 mmol), which was concentrated in vacuo, in Et_2O (3 mL) was added dropwise a solution of 3-(*tert*-butyldimethylsilyl)-2-propyn-1-ol (1.72 g, 10.2 mmol) in Et_2O (4 mL) over 10 min. The reaction mixture was stirred at same temperature for 10 min and then at reflux for 3 hr. The mixture was cooled to -80°C , $\text{MeOH}/\text{Et}_2\text{O}$ (1:10, 50 mL) was added. The mixture was allowed to warm to 0°C , H_2O (100 mL) and 10% H_2SO_4 was added until the evolution of H_2 ceased completely. The mixture was separated, and the aqueous phase was extracted with Et_2O (100 mL x 3). Combined organic phases were washed with saturated brine (100 mL), dried, and concentrated. The residual oil was subjected to column chromatography (silica gel 40 g, elution with hexane: $\text{Et}_2\text{O} = 2:1$) to give (*Z*)-3-(*tert*-butyldimethylsilyl)-2,3-propene-1-ol (1.47 g, 84%), a colorless clear oil. ^1H NMR δ 0.10 (6H, s, SiMe_2), 0.88 (9H, s, *t*-Bu), 4.19 (1H, dd, $J = 6.5, 1.4$ Hz, H-1), 5.70 (1H, dt, $J = 14.4, 1.4$ Hz, H-3), 6.52 (1H, dt, $J = 14.4, 6.5$ Hz, H-2). ^{13}C NMR δ -4.0 (SiMe_2), 16.9 (CMe_3), 26.5 (CMe_3), 63.5 (C-1), 129.7 (C-3), 147.6 (C-2).

To a cooled (ice-water) solution of the above compound (1.47 g, 8.53 mmol) and $\text{Na}_2\text{HPO}_4 \cdot 12\text{H}_2\text{O}$ (3.93 g, 10.2 mmol) in CH_2Cl_2 (17 mL) was added mCPBA (77% purity, 2.32 g, 10.2 mmol). After the cooling bath was removed, the reaction mixture was stirred at room temperature for 3 h. The mixture was diluted with saturated aqueous NaHCO_3 solution (100 mL), separated, and the aqueous phase was extracted with CH_2Cl_2 (50 mL x 3). Combined organic phases were washed with saturated brine (100 mL), dried, and concentrated. The residual oil was subjected to column chromatography (silica gel 150 g, elution with hexane:AcOEt = 3:1) to give the title compound (1.42 g, 88%), a colorless oil. $R_f = 0.27$ (hexane:AcOEt = 2:1). IR (film) 3429, 1254 cm^{-1} . ^1H NMR δ -0.01 and 0.07 (each 3H, s, SiMe_2), 0.95

(9H, s, *t*-Bu), 2.41 (1H, d, $J = 5.3$ Hz, H-3), 3.36 (1H, ddd, $J = 7.8, 5.3, 2.7$ Hz, H-2), 3.48 (1H, dd, $J = 12.1, 7.8$ Hz, H-1), 3.86 (1H, dd, $J = 12.1, 2.7$ Hz, H-1). ^{13}C NMR δ -6.1, 5.9 (SiMe_2), 16.9 (CMe_3), 26.5 (CMe_3), 48.0 (C-3), 57.8 (C-2), 64.0 (C-1).

To a cooled (ice-water) solution of 3-(*tert*-butyldimethylsilyl)-2,3-epoxypropanol (1.37 g, 7.27 mmol), DMSO (10.3 mL, 145 mmol), and NEt_3 (8.1 mL, 58.2 mol) in CH_2Cl_2 (18 mL) was added $\text{SO}_3 \cdot \text{pyridine}$ (98%, 2.83 g, 17.4 mmol). After 90 min, the cooling bath was removed, and the reaction mixture was stirred at room temperature for 2 hr. the mixture was diluted with hexane-Et₂O (1:1, 70 mL). The organic phase was successively washed with 1M hydrochloric acid (100 mL) and saturated aqueous NaHCO_3 solution (100 mL), dried, and concentrated. The residual oil was subjected to column chromatography (silica gel 70 g, elution with hexane: AcOEt = 10:1) to give the title compound (1.14 g, 84%), a color less oil. $R_f = 0.41$ (hexane:AcOEt = 6:1). IR (film) 1727, 1256 cm^{-1} . ^1H NMR δ 0.03 and 0.14 (each 3H, s, SiMe_2), 0.98 (9H, s, *t*-Bu), 2.66 (1H, d, $J = 6.0$ Hz, H-3), 3.48 (1H, dd, $J = 6.4, 6.0$ Hz, H-2), 9.21 (1H, d, $J = 6.4$ Hz, CHO). ^{13}C NMR δ -5.9 and -5.8 (SiMe_2), 17.0 (CMe_3), 26.5 (CMe_3), 50.2 (C-3), 58.6 (C-2), 200.2 (CHO). HRMS calcd for $\text{C}_9\text{H}_{17}\text{O}_2\text{Si}$ ($\text{M}^+ - \text{H}$) 185.0998, found 185.0980.

(2*R,3*S**,4*R** and 2*R**,3*R**,4*S**)-2-(*tert*-butyldimethylsiloxy)-4-(*tert*-butyldimethylsilyl)-3,4-epoxybutanenitriles (37a,b)**

To a solution of 3-(*tert*-butyldimethylsilyl)-2,3-epoxypropanal (885 mg, 4.75 mmol) in CH_2Cl_2 (11.4 mL) was added KCN (62 mg, 0.95 mmol), *n*-Bu₄PBr (322 mg, 0.95 mmol), and TBSCN (97%, 830 mg, 5.70 mmol). After stirring at room temperature for 2 h, the mixture was diluted with saturated aqueous NaHCO_3 solution (20 mL), separated, and the aqueous phase was extracted with CH_2Cl_2 (10 mL x 3). Combined organic phases were washed with saturated brine (20 mL), dried, and concentrated. The residual oil was subjected to column chromatography (silica gel 200 g, elution with hexane: Et₂O = 20:1) to give **37a** (945 mg, 61%) and **37b** (344 mg, 22%). The relative stereochemistry in **37a** and **37b** was determined on the basis of X-ray analysis of **37a**. **37a**: plates (hexane), mp 34.0 °C. $R_f = 0.50$ (hexane:Et₂O = 10:1). IR (KBr) 1257 cm^{-1} . ^1H NMR δ 0.09 and 0.14 (each 3H, s, SiMe_2Bu), 0.17 (6H, s, SiMe_2Bu), 0.94 (9H, s, *t*-Bu), 1.00 (9H, s, *t*-Bu), 2.48 (1H, d, $J = 5.3$ Hz, H-4), 3.48 (1H, dd, $J = 7.8, 5.3$ Hz, H-3), 4.02 (1H, d, $J = 7.8$ Hz, H-2). ^{13}C NMR δ -6.2 and -6.0 (SiMe_2), -5.0 and -4.8 (OSiMe_2), 17.0 (CMe_3), 18.3 (OSiCMe_3), 25.7 (CMe_3), 26.6 (OSiCMe_3), 47.8 (C-4), 59.4 (C-3), 64.8 (C-2), 117.6 (CN). HRMS calcd for $\text{C}_{12}\text{H}_{24}\text{NO}_2\text{Si}_2$, ($\text{M}^+ - \text{C}_4\text{H}_9$), 270.1346, found 270.1361. **37b**: colorless clear oil, $R_f = 0.42$ (hexane:Et₂O = 10:1). IR (film) 1256 cm^{-1} . ^1H NMR δ 0.08 and 0.09 (each 3H, s, SiMe_2Bu), 0.20 and 0.28 (each 3H, s, SiMe_2Bu), 0.92 (9H, s, *t*-Bu), 0.98 (9H, s, *t*-Bu), 2.48 (1H, d, $J = 4.6$ Hz, H-4), 3.40 (1H, dd, $J = 7.8, 4.6$ Hz, H-3), 4.11 (1H, d, $J = 7.8$ Hz, H-2). ^{13}C NMR δ -6.4 and -6.3 (SiMe_2), -4.5 and -4.2 (OSiMe_2), 17.0 (CMe_3), 18.2 (OSiCMe_3), 25.7 (CMe_3), 26.5 (OSiCMe_3), 50.6 (C-4), 57.8 (C-3), 63.1 (C-2), 118.4 (CN). Anal Calcd for $\text{C}_{16}\text{H}_{33}\text{NO}_2\text{Si}_2$ C, 58.66; H, 10.15; N, 4.28. found C, 58.30; H, 10.40; N, 4.17.

Competitive Methylation Reaction of 21b and 33b with base/Mel

To a cooled (-80 °C) solution of **21b** and **33b** (**21b**:**33b** = 1.00:1.00, 79.8 mg, 0.205 mmol) and MeI (9.0 μL , 0.144 mmol) in THF (1.75 mL) was added a solution of LDA (0.5M, 288 μL , prepared from diisopropylamine (147 μL , 1.05 mmol) and *n*-BuLi (2.30 M in hexane, 435 μL , 1.00 mmol) in THF (1.42 mL). After stirring at the same temperature for 5 min, the mixture was diluted with saturated aqueous NH_4Cl solution (10 mL), and extracted with Et₂O (10 mL x 3). Combined organic phases were washed with saturated brine (10 mL), dried, and concentrated. The residual oil was subjected to column chromatography (silica gel 12 g, elution with hexane: Et₂O = 25:1) to give a mixture (70.3 mg) of (*E*)-**27**(22%), (*E*)-**34**(7%), **21b**(18%) and **33b** (40%).

(3*R,4*R**)-4-(*tert*-Butyldimethylsilyl)-2,3-epoxybutanenitrile (38)**

To a cooled (ice-water) solution of pyridine (1.12 mL, 13.9 mmol) in CH_2Cl_2 (29 mL) was added dropwise trifluoromethanesulfonic anhydride (2.34 mL, 13.9 mmol) over 10 min. The reaction mixture was stirred at the same temperature for 10 min before dropwise addition of (2*R**,3*R**)-3-(*tert*-butyldimethylsilyl)-2,3-epoxypropanol (2.50 g, 13.3 mmol) in CH_2Cl_2 (59 mL). The mixture was allowed to warm to room temperature over 30 min, and diluted with water (100 mL), extracted with CH_2Cl_2 (30 mL x 3). Combined organic phases were washed with saturated brine (50 mL), dried, and concentrated. To a cooled (ice-water) solution of the residual oil (4.00 g) in CH_2Cl_2 (31 mL) was added tetrabutylphosphonium bromide (1.05 g, 3.10 mmol) and KCN (1.22 g, 18.7 mmol). The mixture was stirred at the same temperature for 10 min and at room temperature for 3 h before addition of saturated aqueous sodium bicarbonate solution (30 mL), and extracted with Et_2O (30 mL x 3). Combined organic phases were washed with saturated brine (30 mL), dried, and concentrated. The residual oil was subjected to column chromatography (silica gel 50 g, elution with hexane: CH_2Cl_2 = 5:6) to give the title compound (1.22 g, 48%), a pale yellow oil. R_f = 0.13 (hexane:AcOEt = 10:1). IR (film) 2255, 1468, 1254 cm^{-1} . ^1H NMR δ -0.08 and -0.02 (each 3H, s, SiMe_2), 0.93 (9H, s, *t*-Bu), 2.23 (1H, d, J = 3.4 Hz, H-4), 2.66 (1H, dd, J = 17.1, 4.9 Hz, H-2), 2.75 (1H, dd, J = 17.1, 4.5 Hz, H-2), 3.00 (1H, m, H-3). ^{13}C NMR δ -8.3, -8.16 (SiMe_2), 16.7 (CMe_3), 22.8 (C-2), 26.6 (CMe_3), 49.9 and 50.3 (C-3, C-4), 116.0 (C-1). HRMS calcd for $\text{C}_6\text{H}_{10}\text{ONSi}$, ($\text{M}^+ - \text{C}_4\text{H}_9$), 140.0531, found 140.0503.

Methylation of 38

To a cooled solution of **38** (100 mg, 0.507 mmol) and MeI (0.103 mL, 0.608 mmol) in THF (1.37 mL) was added dropwise NHMDS (0.91 M in THF, 0.557 mL, 0.507 mmol). After stirring at the same temperature for 5 min, the mixture was diluted with saturated aqueous NH_4Cl solution (10 mL), and extracted with Et_2O (10 mL x 3). Combined organic phases were washed with saturated brine (10 mL), dried, and concentrated. The residual oil was subjected to column chromatography (silica gel 10 g, elution with hexane: AcOEt = 10:1) to give a mixture (74 mg) of **40**, **41**, and **42**, which were separated by MPLC (elution with hexane:AcOEt = 20:1).

(*E*)-40:

a colorless oil, R_f = 0.28 (hexane:AcOEt = 10:1). IR (film) 2240, 1664 cm^{-1} . ^1H NMR δ 0.15 (6H, s, SiMe_2), 0.91 (9H, s, *t*-Bu), 1.38 (3H, d, J = 7.1 Hz, 2- CH_3), 3.21 (1H, dq, J = 7.1, 7.2 Hz, H-2), 4.94 (1H, dd, J = 12.0, 7.2 Hz, H-3), 6.52 (1H, dd, J = 12.0, 1.0 Hz, H-4). ^{13}C NMR δ -5.15 (SiMe_2), 18.4 (CMe_3), 20.3 (C-2), 24.2 (CH_3), 25.6 (CMe_3), 107.4 (C-3), 121.8 (C-1), 143.6 (C-4). HRMS calcd for $\text{C}_7\text{H}_{12}\text{ONSi}$, ($\text{M}^+ - \text{C}_4\text{H}_9$), 154.0688, found 154.0662.

(*Z*)-40:

a colorless oil, R_f = 0.32 (hexane:AcOEt = 10:1). IR (film) 2242, 1656 cm^{-1} . ^1H NMR δ 0.15 and 0.16 (each 3H, s, SiMe_2), 0.92 (9H, s, *t*-Bu), 1.35 (3H, d, J = 7.1 Hz, 2- CH_3), 3.73 (1H, m, H-2), 4.48 (1H, dd, J = 8.5, 5.6 Hz, H-3), 6.29 (1H, dd, J = 5.6, 1.0 Hz, H-4). ^{13}C NMR δ -5.3 and -5.2 (SiMe_2), 18.3 (CMe_3), 19.1 (CH_3), 20.3 (C-2), 25.6 (CMe_3), 105.7 (C-3), 122.5 (C-1), 141.7 (C-4). HRMS calcd for $\text{C}_7\text{H}_{12}\text{ONSi}$, ($\text{M}^+ - \text{C}_4\text{H}_9$), 154.0688, found 154.0656.

(*E*)-41, (*Z*)-41:

a colorless oil, R_f = 0.28 (hexane:AcOEt = 10:1). IR (film) 2236, 1659, 1468 cm^{-1} . ^1H NMR (*E*)-**41**: δ 0.16 (6H, s, SiMe_2), 0.92 (9H, s, *t*-Bu), 1.43 (6H, s, CH_3), 4.96 (1H, d, J = 12.0 Hz, H-3), 6.61 (1H, d, J = 12.0 Hz, H-4). (*Z*)-**41**: δ 0.18 (6H, s, SiMe_2), 0.97 (9H, s, *t*-Bu), 1.49 (6H, s, CH_3), 4.32 (1H, d, J = 5.9 Hz, H-3), 6.24 (1H, J = 5.9 Hz, H-4). ^{13}C NMR δ -5.3, -5.1 (SiMe_2), 18.3 and 18.5

(CMe₃), 25.7 and 25.8 (CH₃), 28.0 and 28.8 (CMe₃), 29.6 and 31.3 (C-2), 110.1 and 114.0 (C-3), 124.0 (CN), 141.7 and 142.0 (C-4). HRMS calcd for C₈H₁₄ONSi, (M⁺-C₄H₉), 168.0844, found 168.0835.

(E)-42:

a colorless oil, R_f = 0.26 (hexane:AcOEt = 10:1). IR (film) 2251, 1668 cm⁻¹. ¹H NMR δ 0.15 (6H, s, SiMe₂), 0.91 (9H, s, *t*-Bu), 2.97 (2H, dd, J = 6.6, 1.5 Hz, H-2), 4.92 (1H, dt, J = 12.0, 6.6 Hz, H-3), 6.49 (1H, dt, J = 11.7, 1.5 Hz, H-4). ¹³C NMR δ -5.1 (SiMe₂), 16.1 (C-2), 18.4 (CMe₃), 25.7 (CMe₃), 99.2 (C-3), 118.4 (C-1), 145.0 (C-4). HRMS calcd for C₆H₁₀ONSi, (M⁺-C₄H₉), 140.0531, found 140.0503.

(Z)-42:

a colorless oil, R_f = 0.33 (hexane:AcOEt = 10:1). IR (film) 2251, 1660, 1259, 1121 cm⁻¹. ¹H NMR δ 0.16 (6H, s, SiMe₂), 0.93 (9H, s, *t*-Bu), 3.12 (2H, dd, J = 7.1, 1.5 Hz, H-2), 4.51 (1H, dt, J = 7.1, 5.6 Hz, H-3), 6.37 (1H, dt, J = 5.6, 1.5 Hz, H-4). ¹³C NMR δ -5.2 (SiMe₂), 12.4 (C-2), 18.3 (CMe₃), 25.7 (CMe₃), 97.5 (C-3), 118.9 (C-1), 143.2 (C-4). HRMS calcd for C₆H₁₀ONSi, (M⁺-C₄H₉), 140.0531, found 140.0503.

5-(tert-Butyldimethylsilyl)-4,5-epoxy-(E)-2-pentenal

A solution of epoxy aldehyde **22** (317 mg, 1.70 mmol) and (triphenylphosphoranylidene)acetaldehyde (97 %, 801 mg, 2.55 mmol) in CH₃CN (3.2 mL) was refluxed for 25 min before concentration. The residue was filtered using Et₂O and the filtrate was concentrated. The residual oil was

subjected to column chromatography (silica gel, 12 g; elution with hexane:CH₂Cl₂ = 1:1) to give the title compound (345 mg, 95 %). a colorless oil, R_f = 0.35 (hexane:AcOEt = 6:1). IR (film) 1693, 1469, 1254, 1095 cm⁻¹. ¹H NMR δ -0.02 and 0.04 (each 3H, s, SiMe₂), 0.96 (9H, s, *t*-Bu), 2.34 (1H, d, J = 3.4 Hz, H-5), 3.37 (1H, dd, J = 6.6, 3.4 Hz, H-4), 6.40 (1H, dd, J = 15.6, 7.1 Hz, H-2), 6.47 (1H, dd, J = 15.6, 6.6 Hz, H-3), 9.55 (1H, d, J = 7.1 Hz, H-1). ¹³C NMR δ -8.3 and -8.1 (SiMe₂), 16.9 (CMe₃), 26.6 (CMe₃), 53.0 (C-5), 53.6 (C-4), 133.6 (C-3), 155.6 (C-2), 192.7 (CHO). HRMS calcd for C₁₁H₁₉O₂Si (M⁺ - H) 211.1154, found 211.1135.

2-(tert-butyldimethylsiloxy)-6-(tert-butyldimethylsilyl)-5,6-epoxy-(E)-3-hexenenitrile (39)

To a cooled (ice-water) solution of 5-(tert-butyldimethylsilyl)-4,5-epoxy-(E)-2-pentenal (345 mg, 1.62 mmol), KCN (21 mg, 0.325 mmol), and tetrabutylphosphonium bromide (110 mg, 0.325 mmol) in CH₂Cl₂ (3.5 mL) was added TBSCN (97 %, 284 mg, 1.95 mmol). The reaction mixture was

allowed to warm to room temperature and stirred for 20 min, and then quenched by saturated aqueous NaHCO₃ solution (20 mL). The phases were separated, and the aqueous phase was extracted with Et₂O (5 mL x 2). The combined organic phases were washed with saturated aqueous NaHCO₃ solution (20 mL), dried, and concentrated. The residual oil was subjected to column chromatography (silica gel, 40 g; elution with hexane:AcOEt = 10:1) to give **39** (541 mg, 94 %) as a 1:1 mixture of diastereomers. colorless plates (hexane) as a mixture of diastereomers ; mp 41-43 °C, R_f = 0.33 (hexane:AcOEt = 15:1). IR (film) 1469, 1255, 1105 cm⁻¹. ¹H NMR δ -0.04, -0.03, 0.01 and 0.018 (each 3H, s, SiMe₂), 0.15, 0.15, 0.18 and 0.18 (each 3H, s, SiMe₂), 0.91 and 0.91 (each 9H, s, *t*-Bu), 0.96 and 0.96 (each 9H, s, *t*-Bu), 2.22 and 2.23 (each 1H, d, J = 3.4 Hz, H-6), 3.20 and 3.20 (each 1H, dd, J = 3.4, 7.3 Hz, H-5), 4.97 and 4.99 (each 1H, d, J = 5.4 Hz, H-2), 5.70 and 5.72 (each 1H, dd, J = 7.3, 15.4 Hz, H-4), 5.92 and 5.92 (each 1H, dd, J = 5.4, 15.4 Hz, H-3). ¹³C NMR δ -8.3, -8.2, -8.2, -8.1, -5.0, -4.9, -4.9 and -4.9 (SiMe₂), 16.8 and 16.8 (CMe₃), 18.3 and 18.3 (OSiCMe₃), 25.7, 25.7, 26.7 and 26.7 (CMe₃), 52.0 and 52.1 (C-6), 54.1 and 54.1 (C-5), 61.8 and 62.1 (C-2), 118.2 and 118.3 (CN), 128.2 and 128.4 (C-3), 134.4 and 134.6 (C-4). Anal. Calcd for C₁₈H₃₅NO₂Si₂: C, 61.13; H, 9.98; N, 3.96. Found: C, 61.25; H, 9.89; N, 3.83.

General Procedure for methylation of 39: Reaction with NHMDS

To a cooled (-80 °C) solution of **39** (112 mg, 0.317 mmol) and MeI (24 μ L, 0.380 mmol) in THF (1.58 mL) was added a solution of NHMDS (0.88 M in THF, 396 μ L, 0.348 mmol). After stirring at the same temperature for 5 min, the mixture was diluted with saturated aqueous NH_4Cl solution (10 mL), and extracted with Et_2O (5 mL x 2). Combined organic phases were washed with saturated brine (10 mL), dried, and concentrated. The residual oil was subjected to column chromatography (silica gel, 10 g; elution with hexane:AcOEt = 20:1) to give **43** (113 mg, 97%). For separation of *E/Z* isomers, MPLC (elution with hexane: CH_2Cl_2 = 6:1) was used.

(E)-43:

a colorless oil, R_f = 0.37 (hexane:AcOEt = 20:1). IR (film) 1655, 1620, 1469, 1301, 1257, 1204, 1109 cm^{-1} . ^1H NMR δ 0.13 and 0.20 (each 3H, s, SiMe_2), 0.18 (6H, s, SiMe_2), 0.88 (9H, s, *t*-Bu), 0.92 (9H, s, *t*-Bu), 1.63 (3H, s, CH_3), 5.38 (1H, d, J = 15.1 Hz, H-3), 5.67 (1H, dd, J = 11.7, 11.2 Hz, H-5), 6.39 (1H, dd, J = 15.1, 11.2 Hz, H-4), 6.66 (1H, d, J = 11.7 Hz, H-6). ^{13}C NMR δ -5.1, -5.0, -3.4 and -2.9 (SiMe_2), 18.1 and 18.4 (CMe_3), 25.7 (CMe_3), 31.1 (CH_3), 70.3 (C-2), 111.3 (C-5), 121.3 (CN), 127.5 (C-3), 128.3 (C-4), 147.8 (C-6). HRMS calcd for $\text{C}_{19}\text{H}_{37}\text{NO}_2\text{Si}_2$ 367.2363, found 367.2383.

(Z)-43:

a colorless oil, R_f = 0.37 (hexane:AcOEt = 20:1). IR (film) 1652, 1611, 1469, 1411, 1259, 1103, 1061 cm^{-1} . ^1H NMR δ 0.17 and 0.22 (each 3H, s, SiMe_2), 0.17 (6H, s, SiMe_2), 0.90 (9H, s, *t*-Bu), 0.94 (9H, s, *t*-Bu), 1.65 (3H, s, CH_3), 5.16 (1H, dd, J = 10.7, 5.6 Hz, H-5), 5.50 (1H, d, J = 15.6 Hz, H-3), 6.31 (1H, d, J = 5.6 Hz, H-6), 6.93 (1H, dd, J = 10.7, 15.6 Hz, H-4). ^{13}C NMR δ -5.3, -5.2, -3.4 and -3.1 (SiMe_2), 18.2 and 18.5 (CMe_3), 25.7 and 25.8 (CMe_3), 30.9 (CH_3), 69.9 (C-2), 108.4 (C-5), 121.3 (CN), 124.3 (C-4), 128.8 (C-3), 143.0 (C-6). HRMS calcd for $\text{C}_{18}\text{H}_{34}\text{NO}_2\text{Si}_2$ ($\text{M}^+ - \text{CH}_3$) 352.2128, found 352.2147.

21a

(Z)-27 (R = Me)

(Z)-27 (R = CH₂CH=CH₂)

TM-II-302B

TM-II-302E