Supporting Information

Construction of Arene-Fused-Piperidine Motifs by Asymmetric Addition of 2-Trityloxymethylaryllithiums to Nitroalkenes: the Asymmetric Synthesis of A-86929

Mitsuaki Yamashita, Ken-ichi Yamada, and Kiyoshi Tomioka*

*Graduate School of Pharmaceutical Sciences, Kyoto University,
Yoshida, Sakyo-ku, Kyoto 606-8501, Japan*

General

All melting points are uncorrected. IR spectra were expressed in cm^{-1} . ^1H and ^{13}C NMR spectra were measured in CDCl_3 unless otherwise mentioned. Chemical shift values are expressed in ppm relative to internal tetramethylsilane. Abbreviations are as follows: s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet; br, broad. Column chromatography was carried out with silica gel.

Material

3,4-Dihydro-6,7-dimethoxy-1-nitronaphthalene (**3a**),¹ (*E*)-1-nitro-1-hexene (**10**),² 1-bromo-2-(trityloxymethyl)benzene,³ and 5-bromo-4-trimethylsilyl-1,3-benzodioxole,⁴ were prepared according to the reported procedures. 1-Nitrocyclohexene (**9**) and *trans*- β -nitrostyrene (**11**) were purchased from Aldrich Chemical Co., Inc.

3-Bromo-2-(trityloxymethyl)furan: to a solution of 3-bromofuran-2-methanol⁵ (177 mg, 1.0 mmol) and DBU (456 mg, 3.0 mmol) in DMF (1.0 mL) was added tritylchloride (695 mg, 2.5 mmol) at rt. After stirred for 16 h the reaction mixture was diluted with AcOEt. The organic layer was washed with 10% HCl, satd. NaHCO_3 , and brine, and then dried over Na_2SO_4 . Concentration, column chromatography (hexane/AcOEt = 100/1) and recrystallization (AcOEt) gave the titled product (250 mg, 60% yield) as colorless prisms of mp

¹ Michaelides, M. R.; Hong, Y.; DiDomenico, S.; Bayburt, E. K.; Asin, K. E.; Britton, D. R.; Lin, C. W.; Shiosaki, K. *J. Med. Chem.* **1997**, *40*, 1585–1599.

² Melton, J.; McMurry, J. E. *J. Org. Chem.* **1975**, *40*, 2138–2139.

³ Czernecki, S.; Perlat, M.-C. *J. Org. Chem.* **1991**, *56*, 6289–6292.

⁴ Mattson, R. J.; Sloan, C. P.; Lockhart, C. C.; Catt, J. D.; Gao, Q.; Huangl, S. *J. Org. Chem.* **1999**, *64*, 8004–8007.

⁵ Chan, K.-F.; Wong, H. N. C. *Org. Lett.* **2001**, *3*, 3991–3994.

125–126 °C: ^1H NMR: 4.08 (2H, s), 6.40 (1H, s), 7.25 (3H, t, $J = 7.3$ Hz), 7.32 (6H, dd, $J = 7.3, 8.0$ Hz), 7.39 (1H, d, $J = 1.9$ Hz), 7.50 (6H, d, $J = 7.3$ Hz). ^{13}C NMR: 13.6, 24.6, 32.2, 61.1, 87.3, 106.6, 126.5, 127.1, 127.9, 128.6, 133.9, 143.6, 145.1. IR (KBr): 1489, 1447, 1049, 744, 705. EIMS m/z : 244, 243, 233, 228, 215, 202, 165, 161, 159, 105, 77. Anal. Calcd. for $\text{C}_{24}\text{H}_{19}\text{BrO}_2$: C, 68.75; H, 4.57. Found: C, 68.83; H, 4.69.

3,5-Dibromothiophen-2-methanol: to a solution of 3,5-dibromothiophene-2-carbaldehyde⁶ (135 mg, 0.5 mmol) in MeOH (1.0 mL) was added NaBH_4 (19 mg, 0.5 mmol) at 0 °C. After stirred for 5 min the reaction mixture was quenched with satd. NH_4Cl and extracted with AcOEt. The organic layer was washed with brine and dried over Na_2SO_4 . Concentration and column chromatography (hexane/AcOEt = 10/1) gave the titled product (135mg, 99% yield) as a colorless oil: ^1H NMR: 2.01 (1H, s), 4.71 (2H, s), 6.91 (1H, s). ^{13}C NMR: 59.2, 107.8, 112.2, 132.1, 140.1. IR (neat): 3329, 1528, 1443, 995, 818. EIMS m/z : 274 ($\text{M}^+ + 2$), 272 (M^+), 270 ($\text{M}^+ - 2$), 275, 255, 253, 193, 191, 83. Anal. Calcd. for $\text{C}_5\text{H}_4\text{Br}_2\text{OS}$: C, 22.08; H, 1.48. Found: C, 22.02; H, 1.41.

3,5-Dibromo-2-trityloxymethylthiophene: to a solution of 3,5-dibromothiophen-2-methanol (14.2 g, 54 mmol) and DBU (28.7 g, 189 mmol) in DMF (54 mL) was added tritylchloride (45.0 g, 162 mmol) at rt. After stirred for 13 h the reaction mixture was diluted with AcOEt. The organic layer was washed with 10% HCl, satd. NaHCO_3 , and brine, and then dried over Na_2SO_4 . Concentration, column chromatography (hexane), and recrystallization (AcOEt) gave the titled product (25.2 g, 91% yield) as colorless prisms of mp 118.5–119.5 °C: ^1H NMR: 4.21 (2H, s), 6.88 (1H, s), 7.26 (3H, t, $J = 7.7$ Hz), 7.32 (6H, dd, $J = 7.7, 7.7$ Hz), 7.48 (6H, d, $J = 7.7$ Hz). ^{13}C NMR: 61.3, 87.6, 106.2, 111.5, 127.3, 128.0, 128.5, 131.7, 139.0, 143.3. IR (KBr): 1489, 1447, 1076. EIMS m/z : 257, 255, 253, 244, 243, 165, 105, 83, 77. Anal. Calcd. for $\text{C}_{24}\text{H}_{18}\text{Br}_2\text{OS}$: C, 56.05; H, 3.53. Found: C, 55.79; H, 3.38.

3-Bromo-5-propyl-2-trityloxymethylthiophene: to a solution of 3,5-dibromo-2-trityl-

⁶ Sauter, F.; Fröhlich, H.; Kalt, W. *Synthesis* **1989**, 771–773.

oxymethylthiophene (10.3 g, 20 mmol) in THF (30 mL) was added *t*-BuLi (23.5 mL, 1.7 M in pentane, 40 mmol) over 5 min at $-78\text{ }^{\circ}\text{C}$ and stirred for 10 min. Propyl bromide was then added over 2 min at $-78\text{ }^{\circ}\text{C}$, and the solution was stirred for 16 h at rt. The reaction was quenched with H_2O (50 mL), and the mixture was extracted with AcOEt. The organic layer was washed with brine and dried over Na_2SO_4 . Concentration, column chromatography (hexane), and recrystallization (toluene/EtOH) gave the titled product (5.93 g, 77% yield) as colorless prisms of mp $92\text{--}93\text{ }^{\circ}\text{C}$: ^1H NMR: 0.99 (3H, t, $J = 7.3\text{ Hz}$), 1.70 (6H, tq, $J = 7.3, 7.3\text{ Hz}$), 2.75 (2H, t, $J = 7.3\text{ Hz}$), 4.20 (2H, s), 6.60 (1H, s), 7.25 (3H, t, $J = 7.3\text{ Hz}$), 7.32 (6H, dd, $J = 7.3, 7.3\text{ Hz}$), 7.50 (6H, d, $J = 7.3\text{ Hz}$). ^{13}C NMR: 13.6, 24.6, 32.2, 61.1, 87.3, 106.6, 126.5, 127.1, 127.9, 128.6, 133.9, 143.6, 145.1. IR (KBr): 1489, 1447, 1080, 720. EIMS m/z : 244, 243, 235, 233, 217, 165, 105, 77. Anal. Calcd. for $\text{C}_{27}\text{H}_{25}\text{BrOS}$: C, 67.92; H, 5.28. Found: C, 67.79; H, 5.34.

1-Bromo-2-(1-trimethylsiloxyethenyl)benzene: prepared according to the reported procedure.⁷ To a solution of 1-(2-bromophenyl)ethanone (9.95 g, 50 mmol), TMSCl (7.87 mL, 62 mmol) Et_3N (8.64 mL, 62 mmol) was added NaI (9.30 g, 162 mmol) in CH_3CN (60 mL) over 0.5 h at rt. After stirring for 1 h the reaction mixture was diluted with hexane. The organic layer was washed with H_2O and then dried over Na_2SO_4 . Concentration and distillation ($120\text{ }^{\circ}\text{C}/5\text{ mmHg}$) gave the titled product (13.2 g, 97% yield) as a colorless oil. ^1H NMR: 0.22 (9H, s), 4.53 (1H, s), 4.60 (1H, s), 7.14 (1H, dd, $J = 7.6, 7.7\text{ Hz}$), 7.26 (1H, dd, $J = 7.1, 7.9\text{ Hz}$), 7.39 (1H, d, $J = 7.6\text{ Hz}$), 7.56 (1H, d, $J = 7.9\text{ Hz}$). ^{13}C NMR: 0.00, 96.0, 121.6, 127.0, 129.4, 130.6, 133.3, 140.1, 156.0. IR (neat): 1628, 1589, 1319, 1254, 1015, 849, 760. EIMS m/z : 257, 255, 215, 191, 177, 175, 147, 115, 102, 84, 75. Anal. Calcd. for $\text{C}_{11}\text{H}_{15}\text{BrOSi}$: C, 48.71; H, 5.57. Found: C, 48.59; H, 5.55.

1-(2-Bromophenyl)-3,3,3-triphenylpropan-1-one: prepared according to the reported procedure.⁸ To a solution of TrBF_4 (5.00 g, 4.5 mmol) and collidine (1.85 mL, 14 mmol) in CH_2Cl_2 (50 mL) was added 1-bromo-2-(1-trimethylsiloxyethenyl)benzene (3.44 g, 12.7 mmol) at rt. After stirred for 1 h the reaction mixture was quenched with H_2O . The mixture

⁷ Cazeau, P.; Duboudin, F.; Moulines, F.; Babot, O.; Dunogues, J. *Tetrahedron*, **1987**, 43, 2075–2088.

⁸ Jung, M. E.; Pan, Y. G. *J. Org. Chem.* **1977**, 42, 3961–3963.

was extracted with Et₂O. The organic layer was washed with satd. NaHCO₃ and brine, and then dried over Na₂SO₄. Concentration and recrystallization (AcOEt) gave the titled product (5.1 g, 91% yield) as colorless prisms of mp 97–99 °C: ¹H NMR: 4.42 (2H, s), 6.85 (1H, d, *J* = 6.4 Hz), 7.19–7.26 (17H, m), 7.51 (1H, d, *J* = 7.3 Hz). ¹³C NMR: 54.0, 56.2, 118.0, 126.2, 127.2, 127.8, 128.0, 129.3, 131.0, 133.2, 143.2, 146.7, 201.2. IR (KBr): 1697, 1493, 1423, 1342, 1211, 1022, 756, 702. EIMS *m/z*: 442, 440, 244, 243, 228, 165, 141, 103, 91, 77. Anal. Calcd. for C₂₄H₁₉BrO₂: C, 68.75; H, 4.57. Found: C, 68.83; H, 4.69.

1-Bromo-2-(3,3,3-triphenylpropyl)benzene: to a solution of 1-(2-bromophenyl)-3,3,3-triphenylpropan-1-one (5.00 g, 11.3 mmol) and triethylsilane (182 mL, 1.13 mol) was added trifluoroacetic acid (305 mL, 3.96 mol). The reaction mixture was stirred for 24 h at rt and then concentrated under reduced pressure. The residue was dissolved in AcOEt, and the solution was washed with satd. NaHCO₃ and brine, and then dried over Na₂SO₄. Concentration, column chromatography (hexane) and recrystallization (hexane/AcOEt) gave the titled product (1.01 g, 21% yield) as colorless cubes of mp 119–120 °C: ¹H NMR: 2.48–2.51 (2H, m), 2.82–2.86 (2H, m), 7.03 (1H, dd, *J* = 7.3, 8.0 Hz), 7.09 (1H, d, *J* = 7.7 Hz), 7.20 (4H, m), 7.29 (1H, dd, *J* = 7.7, 7.9 Hz), 7.37 (1H, d, *J* = 7.9 Hz), 7.49 (1H, d, *J* = 8.0 Hz). ¹³C NMR: 32.6, 40.8, 56.8, 124.3, 126.0, 127.6, 127.6, 127.9, 129.3, 130.4, 132.9, 142.3, 147.1. IR (KBr): 1493, 1470, 1038, 1011, 752, 702. EIMS *m/z*: 244, 243, 165, 103, 91, 77. Anal. Calcd. for C₂₇H₂₃Br: C, 75.88; H, 5.42. Found: C, 75.93; H, 5.51.

1-Bromo-2-triphenylmethoxybenzene: to a solution of 2-bromophenol (3.46 g, 20.0 mmol), Et₃N (3.64 mL, 30.0 mmol), and DMAP (122 mg, 1.0 mmol) in CH₂Cl₂ (1.0 mL) was added tritylchloride (6.68 g, 24 mmol) at 0 °C. After stirred for 2 h at rt the reaction mixture was quenched with H₂O. The mixture was extracted with Et₂O. The organic layer was washed with brine and then dried over Na₂SO₄. Concentration, column chromatography (hexane/AcOEt/Et₃N=50/1/1), and recrystallization (EtOH) gave the titled product (6.47 g, 78% yield) as colorless prisms of mp 94–95 °C: ¹H NMR: 6.51 (1H, d, *J* = 8.2 Hz), 6.64 (1H, dd, *J* = 7.4, 7.9 Hz), 6.77 (1H, dd, *J* = 7.4, 8.2 Hz), 7.22 (3H, t, *J* = 7.3 Hz), 7.27 (6H, dd, *J* = 7.3, 8.0 Hz), 7.41 (1H, d, *J* = 7.9 Hz), 7.52 (6H, d, *J* = 8.0 Hz). ¹³C NMR: 91.6, 115.8, 121.4, 122.3, 126.7, 127.3, 127.8, 128.8, 132.9, 143.8, 152.9. IR (KBr): 1466, 1443, 1227, 752, 702. EIMS *m/z*: 244, 243, 173, 171, 165, 115, 91, 63. Anal. Calcd. for C₂₅H₁₉BrO: C, 72.30; H, 4.61. Found: C, 72.49; H, 4.61.

General Procedure for External Chiral Ligand-Controlled Asymmetric Conjugate Addition of Aryllithium to Nitroalkene.

Table 1, entry 7. (1*S*,2*S*)- and (1*S*,2*R*)-1,2,3,4-Tetrahydro-6,7-dimethoxy-2-nitro-1-(2-trityloxymethylphenyl)naphthalene (*cis*- and *trans*-4c**):** under Ar atmosphere, to a solution of 1-bromo-2-trityloxymethylbenzene (321 mg, 0.75 mmol) and ligand **8** (364 mg, 1.1 mmol) in toluene (5.0 mL) was added *n*-BuLi (0.47 mL, 1.6 M in hexane, 0.75 mmol) at -78°C over 1 min and the mixture was stirred for 0.5 h. After the solution was cooled to -95°C , nitroalkene **3a** (118 mg, 0.5 mmol) in toluene (2.5 mL) was added over 2 min and the mixture was stirred for 0.5 h. The mixture was quenched with MeOH (0.1 mL) and then satd. NH_4Cl (20 mL). The mixture was extracted with AcOEt. The organic extracts were washed with 10% HCl, satd. NaHCO_3 , and brine, and then dried over Na_2SO_4 . Concentration and column chromatography (hexane/AcOEt = 20/1) gave **4c** (287 mg, 98% yield, *trans/cis* = 70/30) as pale yellow needles of mp $71\text{--}74^{\circ}\text{C}$: ^1H NMR: 2.00–2.04 (0.3H, m, *cis*), 2.27 (1.4H, m, *trans*), 2.46–2.50 (0.3H, m, *cis*), 2.80 (1.7H, m, *trans* and *cis*), 3.06–3.09 (0.3H, m, *cis*), 3.49 (0.9H, s, *cis*), 3.54 (2.1H, s, *trans*), 3.85 (2.1H, s, *trans*), 3.86 (0.9H, s, *cis*), 4.11–4.29 (2H, m, *trans* and *cis*), 4.70–4.85 (2H, m, *trans* and *cis*), 6.21 (0.7H, s, *trans*), 6.37 (0.3H, s, *cis*), 6.54 (0.7H, s, *trans*), 6.60, (0.3H, s, *cis*), 7.18–7.32 (12H, 3, *trans* and *cis*), 7.45–7.55 (7H, m, *trans* and *cis*). ^{13}C NMR: 23.0 (*cis*), 26.1 (*trans*), 26.2 (*cis*), 41.5 (*cis*), 55.7 (*trans*), 55.8 (*trans*), 55.9 (*cis*), 63.9 (*trans*), 64.0 (*cis*), 85.5 (*cis*), 87.5 (*trans*), 87.9 (*trans*), 110.5 (*trans*), 110.6 (*cis*), 112.4 (*trans*), 112.5 (*cis*), 126.4 (*trans*), 126.6 (*cis*), 126.7 (*cis*), 127.1 (*trans*), 127.4 (*cis*), 127.6 (*trans*), 127.7 (*trans*), 127.8 (*trans*), 127.9 (*cis*), 128.2 (*trans*), 128.6 (*trans*), 128.7 (*cis*), 129.8 (*trans*), 130.5 (*cis*), 130.8 (*cis*), 137.1 (*trans*), 138.8 (*cis*), 143.8 (*trans*), 143.8 (*cis*), 147.8 (*trans*), 147.8 (*cis*). IR (KBr): 1551, 1516, 1447, 1219, 1042, 756, 706. EIMS m/z : 586 (M^+), 539, 342, 296, 244, 243, 165, 105, 91, 77. Anal. Calcd. for $\text{C}_{38}\text{H}_{35}\text{NO}_5$: C, 77.93; H, 6.02; N, 2.39. Found: C, 77.76; H, 6.08; N, 2.34.

1-(*cis*-2-Nitrocyclohexyl)-2-trityloxymethylbenzene (*cis*-12c**):** separated from *trans*-**12c** by column chromatography (hexane/AcOEt/acetone = 80/1/1). Colorless needles of mp $59\text{--}61^{\circ}\text{C}$. $[\alpha]_{\text{D}}^{25} -72.0$ (c 1.0, CHCl_3) for 90% ee (the ee was determined after removal of

the Tr group). ^1H NMR: 1.22–1.27 (1H, m), 1.40–1.46 (1H, m), 1.54–1.59 (2H, m), 1.89–1.94 (2H, m), 2.04–2.07 (1H, m), 2.46 (1H, dddd, $J = 3.4, 12.8, 12.8, 12.8$ Hz), 3.01 (1H, ddd, $J = 3.4, 3.4, 12.8$ Hz), 4.04 (1H, d, $J = 10.4$ Hz), 4.09 (1H, d, $J = 10.4$ Hz), 4.89 (1H, m), 7.20 (1H, dd, $J = 1.5, 7.0$ Hz), 7.24–7.35 (12H, m), 7.50–7.52 (6H, d, $J = 7.3$ Hz). ^{13}C NMR: 19.6, 25.4, 25.6, 29.8, 40.9, 64.7, 86.3, 87.3, 127.0, 127.2, 127.2, 127.9, 128.6, 128.6, 130.4, 135.5, 140.4, 143.6. IR (KBr): 1543, 1447, 1045, 706. EIMS m/z : 244, 243, 234, 228, 215, 187, 165, 145, 105, 91, 77. Anal. Calcd. for $\text{C}_{32}\text{H}_{31}\text{NO}_3$: C, 80.47; H, 6.54; N, 2.93. Found: C, 80.46; H, 6.53; N, 2.63.

1-(*trans*-2-Nitrocyclohexyl)-2-trityloxymethylbenzene (*trans*-12c): colorless needles of mp 51–53 °C. $[\alpha]_D^{25} -23.3$ (c 0.83, CHCl_3) for 89% ee (the ee was determined after removal of the Tr group). ^1H NMR: 1.19–1.24 (1H, m), 1.37–1.42 (2H, m), 1.68–1.71 (2H, m), 1.88–1.90 (1H, m), 2.03–2.06 (1H, m), 2.27–2.29 (1H, m), 3.20 (1H, ddd, $J = 3.4, 11.6, 11.6$ Hz), 4.11 (1H, d, $J = 10.4$ Hz), 4.19 (1H, d, $J = 10.4$ Hz), 4.68 (1H, ddd, $J = 3.4, 11.6, 11.6$ Hz), 7.19 (1H, t, $J = 7.0$ Hz), 7.23–7.36 (12H, m), 7.52–7.53 (6H, d, $J = 7.4$ Hz). ^{13}C NMR: 24.5, 25.2, 32.4, 33.9, 42.4, 64.4, 87.2, 90.1, 126.9, 127.0, 127.8, 128.3, 128.3, 128.7, 130.3, 136.5, 140.5, 144.0. IR (KBr): 1547, 1447, 706. EIMS m/z : 244, 243, 234, 228, 215, 202, 187, 165, 154, 141, 129, 119, 105, 91, 77. Anal. Calcd. for $\text{C}_{32}\text{H}_{31}\text{NO}_3$: C, 80.47; H, 6.54; N, 2.93. Found: C, 80.44; H, 6.37; N, 2.64.

3-(*cis*-2-Nitrocyclohexyl)-5-propyl-2-trityloxymethylthiophene (*cis*-12d): separated from *trans*-12d by column chromatography (hexane/ $\text{Et}_2\text{O} = 40/1$). Colorless needles of mp 49–50 °C. $[\alpha]_D^{25} -47.3$ (c 1.1, CHCl_3) for 94% ee (the ee was determined after conversion to *trans*-12d). ^1H NMR: 0.95 (3H, t, $J = 7.3$ Hz), 1.20–1.29 (1H, m), 1.52–1.70 (5H, m), 1.75–1.90 (2H, m), 2.13–2.16 (1H, m), 2.35 (1H, dddd, $J = 4.0, 13, 13, 13$ Hz), 2.71 (3H, m), 4.02 (1H, d, $J = 12$ Hz), 4.15 (1H, d, $J = 12$ Hz), 4.77–4.79 (1H, m), 6.58 (1H, s), 7.26 (3H, t, $J = 7.9$ Hz), 7.33 (6H, dd, $J = 7.4, 7.9$ Hz), 7.51 (6H, d, $J = 7.4$ Hz). ^{13}C NMR: 13.6, 19.8, 24.7, 25.1, 26.1, 29.9, 32.2, 39.1, 58.4, 86.2, 87.1, 124.3, 127.2, 128.0, 128.6, 132.2, 138.9, 143.8, 144.3. IR (KBr): 1543, 1447, 1041, 705. EIMS m/z : 282, 244, 243, 165, 105, 91, 77. Anal. Calcd. for $\text{C}_{33}\text{H}_{35}\text{NO}_3\text{S}$: C, 75.40; H, 6.71; N, 2.66. Found: C, 75.65; H, 6.61; N, 2.51.

3-(*trans*-2-Nitrocyclohexyl)-5-propyl-2-trityloxymethylthiophene (*trans*-12d): a colorless oil. $[\alpha]_D^{25} +17.0$ (c 0.51, CHCl_3) for 95% ee (HPLC, Daicel Chiralcel OD-H, hexane/*i*-PrOH = 100/1, 1.0 mL/min, 254 nm, major 6.3 min and minor 7.4 min). ^1H NMR: 0.96 (3H, t, $J = 7.3$ Hz), 1.25–1.44 (3H, m), 1.63–1.78 (4H, m), 1.89 (2H, m), 2.23–2.26 (1H, m), 2.71 (2H, t, $J = 7.5$ Hz), 2.95 (1H, ddd, $J = 3.7, 12, 12$ Hz), 4.11 (1H, d, $J = 11.3$ Hz), 4.16 (1H, d, $J = 11.3$ Hz), 4.51 (1H, ddd, $J = 4.0, 12, 12$ Hz), 6.55 (1H, s), 7.26 (3H, t, $J = 7.4$ Hz), 7.33 (6H, dd, $J = 7.4, 7.6$ Hz), 7.52 (6H, d, $J = 7.6$ Hz). ^{13}C NMR: 13.6, 24.3, 24.6, 25.0, 32.1, 32.2, 32.5, 41.1, 58.6, 87.0, 90.2, 122.2, 127.1, 127.9, 128.7, 133.9, 137.4, 143.9, 144.9. IR (neat): 1547, 1045, 702. EIMS m/z : 282, 244, 243, 233, 165, 105, 91, 77. Anal. Calcd. for $\text{C}_{33}\text{H}_{35}\text{NO}_3\text{S}$: C, 75.40; H, 6.71; N, 2.66. Found: C, 75.10; H, 6.90; N, 2.56.

3-(*cis*-2-Nitrocyclohexyl)-2-trityloxymethylfuran (*cis*-12e): separated from *trans*-12e by column chromatography (hexane/ Et_2O = 30/1). Colorless cubes of mp 134–136 °C. $[\alpha]_D^{25} -40.6$ (c 0.51, CHCl_3) for 91% ee (HPLC, Daicel Chiralpak AD-H, hexane/*i*-PrOH = 50/1, 1.0 mL/min, 254 nm, minor 5.8 min and major 6.4 min). ^1H NMR: 1.30–1.38 (1H, m), 1.50–1.56 (1H, m), 1.60–1.70 (2H, m), 1.72–1.89 (2H, m), 2.17–2.30 (2H, m), 2.77–2.80 (1H, m), 3.99 (1H, d, $J = 11.9$ Hz), 4.11 (1H, d, $J = 11.9$ Hz), 4.63 (1H, m), 6.31 (1H, s), 7.26 (3H, t, $J = 7.2$ Hz), 7.31 (1H, s), 7.33 (6H, dd, $J = 7.2, 8.3$ Hz), 7.50 (6H, d, $J = 8.3$ Hz). ^{13}C NMR: 20.2, 24.2, 26.7, 29.2, 35.6, 56.7, 86.3, 86.9, 110.4, 122.5, 127.2, 128.0, 128.7, 141.9, 143.7, 148.2. IR (KBr): 1543, 1448, 1053, 708. EIMS m/z : 244, 243, 224, 165, 105, 91, 77. Anal. Calcd. for $\text{C}_{30}\text{H}_{29}\text{NO}_4$: C, 77.06; H, 6.25; N, 3.00. Found: C, 77.12; H, 6.32; N, 2.96.

3-(*trans*-2-Nitrocyclohexyl)-2-trityloxymethylfuran (*trans*-12e): colorless prisms of mp 48–50 °C. $[\alpha]_D^{25} +13.7$ (c 0.76, CHCl_3) for 91% ee (HPLC, Daicel Chiralcel OD-H, hexane/*i*-PrOH = 50/1, 1.0 mL/min, 254 nm, minor 6.1 min and major 7.0 min). ^1H NMR:

1.32–1.47 (3H, m), 1.75–1.83 (2H, m), 1.90–1.94 (2H, m), 2.25–2.27 (1H, m), 2.90 (1H, m), 4.03 (2H, s), 4.42 (1H, m), 6.26 (1H, s), 7.26 (3H, t, $J = 7.3$ Hz), 7.33 (6H, dd, $J = 7.5, 8.2$ Hz), 7.33 (1H, s), 7.52 (6H, d, $J = 8.2$ Hz). ^{13}C NMR: 24.2, 24.9, 31.9, 32.3, 38.0, 56.5, 86.9, 90.3, 108.7, 122.2, 127.1, 127.9, 128.8, 142.4, 143.9, 148.6. IR (KBr): 1549, 1447, 1366, 1053, 1028. EIMS m/z : 244, 243, 224, 165, 105, 91, 77. Anal. Calcd. for $\text{C}_{30}\text{H}_{29}\text{NO}_4$: C, 77.06; H, 6.25; N, 3.00. Found: C, 77.03; H, 6.22; N, 3.05.

1-(Nitromethyl)pentyl-2-trityloxymethylbenzene (13c): purified by column chromatography (hexane/ $\text{Et}_2\text{O} = 30/1$). A colorless oil. $[\alpha]_{\text{D}}^{25} +10.2$ (c 1.7, CHCl_3) for 85% ee (HPLC, Daicel Chiralcel OD-H, hexane/ i -PrOH = 100/1, 1.0 mL/min, 254 nm, major 6.2 min and minor 6.9 min). ^1H NMR: 0.73 (3H, t, $J = 7.3$ Hz), 0.92–0.99 (2H, m), 1.08–1.14 (2H, m), 1.58–1.66 (2H, m), 3.47–3.53 (1H, m), 4.12 (1H, d, $J = 11$ Hz), 4.15 (1H, d, $J = 11$ Hz), 4.40 (1H, dd, $J = 8.9, 12$ Hz), 4.47 (1H, dd, $J = 6.2, 12$ Hz), 7.18 (1H, d, $J = 7.4$ Hz), 7.24–7.34 (11H, m), 7.42 (1H, d, $J = 7.6$ Hz), 7.51–7.53 (6H, d, $J = 8.4$ Hz). ^{13}C NMR: 13.7, 22.4, 28.9, 32.6, 38.3, 64.3, 80.5, 87.5, 126.0, 127.1, 127.2, 127.9, 128.4, 128.7, 130.0, 137.0, 139.0, 143.9. IR (neat): 1551, 1492, 1450, 1377, 1219, 988, 768, 733, 706. EIMS m/z : 260, 244, 243, 233, 165, 159, 131, 117, 105, 91, 77. Anal. Calcd. for $\text{C}_{32}\text{H}_{33}\text{NO}_3$: C, 80.14; H, 6.94; N, 2.92. Found: C, 80.01; H, 6.94; N, 2.80.

1-[(R)-2-Nitro-1-phenylethyl]-2-trityloxymethylbenzene (14c): purified by column chromatography (hexane/acetone = 40/1). Colorless cubes of mp 61–62 °C. $[\alpha]_{\text{D}}^{25} +15.6$ (c 0.90, CHCl_3) for 91% ee (HPLC, Daicel Chiralpak AD, hexane/ i -PrOH = 100/1, 1.0 mL/min, 254 nm, major 11.4 min and minor 14.2 min). ^1H NMR: 4.08 (1H, d, $J = 11$ Hz), 4.18 (1H, d, $J = 11$ Hz), 4.85 (1H, dd, $J = 9.0, 13$ Hz), 4.91 (1H, dd, $J = 7.0, 13$ Hz), 5.00 (1H, dd, $J = 7.0, 9.0$ Hz), 6.90–6.92 (2H, m), 7.13–7.14 (3H, m), 7.25–7.33 (12H, m), 7.46–7.50 (7H, m). ^{13}C NMR: 44.0, 64.3, 78.9, 87.5, 126.6, 127.1, 127.2, 127.6, 127.7, 127.9, 128.2, 128.7, 128.7, 130.1, 136.8, 137.9, 138.8, 143.8. IR (KBr): 1547, 1489, 1447, 1049, 698. EIMS m/z : 244, 243, 228, 215, 193, 179, 165, 105, 91, 77. Anal. Calcd. for $\text{C}_{34}\text{H}_{29}\text{NO}_3$: C, 81.74; H, 5.85; N, 2.80. Found: C, 81.75; H, 6.05; N, 2.77.

Reaction of other organolithiums.

1-(*cis*-2-Nitrocyclohexyl)-2-(3,3,3-triphenylpropyl)benzene: separated from *trans*-isomer by column chromatography (hexane/AcOEt = 50/1). Colorless prisms of mp 140–141 °C. $[\alpha]_D^{25}$ –88.1 (c 1.0, CHCl₃), 85% ee (ee was determined after converting to *trans*-isomer). ¹H NMR: 1.20–1.29 (1H, m), 1.36–1.44 (1H, m), 1.54–1.57 (2H, m), 1.85–1.95 (2H, m), 2.04–2.07 (1H, m), 2.24 (1H, m), 2.37–2.61 (4H, m), 2.95 (1H, m), 4.32 (1H, s), 7.08 (1H, d, *J* = 7.7 Hz), 7.14 (1H, m), 7.20–7.23 (4H, m), 7.28–7.33 (7H, m), 7.39 (6H, d, *J* = 8.3 Hz). ¹³C NMR: 19.6, 25.1, 25.4, 28.2, 29.7, 40.6, 42.9, 56.8, 86.2, 126.1, 126.6, 126.9, 127.5, 128.1, 129.2, 129.7, 138.0, 139.8, 147.0. IR (KBr): 1543, 1493, 1447, 1369, 1354, 1331, 1011, 760, 706. EIMS *m/z*: 476 (M⁺), 429, 244, 243, 165, 129, 105, 91. Anal. Calcd. for C₃₃H₃₃NO₂: C, 83.33; H, 6.99; N, 2.94. Found: C, 83.08; H, 7.08; N, 3.05.

1-(*trans*-2-Nitrocyclohexyl)-2-(3,3,3-triphenylpropyl)benzene: colorless needles of mp 70–71 °C. $[\alpha]^{25}_{\text{D}} +29.3$ (c 0.30, CHCl_3), 85% ee (HPLC, Daicel Chiralpak AD-H, hexane/*i*-PrOH = 100/1, 1.0 mL/min, 254 nm, minor 9.7 min and major 10.7 min). ^1H NMR: 1.09–1.17 (1H, m), 1.24–1.42 (2H, m), 1.65–1.77 (3H, m), 1.90 (1H, m), 2.30–2.63 (4H, m), 2.85–2.97 (2H, m), 4.74 (1H, m), 7.14 (4H, m), 7.21 (3H, t, $J = 7.0$ Hz), 7.31 (6H, dd, $J = 7.0, 8.0$ Hz), 7.43 (6H, d, $J = 8.0$ Hz). ^{13}C NMR: 24.5, 25.1, 28.3, 32.4, 34.1, 42.1, 42.5, 56.8, 89.5, 125.1, 125.9, 126.6, 127.1, 128.0, 129.3, 130.3, 138.7, 140.7, 147.2. IR (KBr): 1547, 1493, 1447, 1373, 1242, 752, 706. EIMS m/z : 476 (M^+), 429, 244, 243, 165, 129, 105, 61, 77. Anal. Calcd. for $\text{C}_{33}\text{H}_{33}\text{NO}_2$: C, 83.33; H, 6.99; N, 2.94. Found: C, 83.28; H, 6.93; N, 2.71.

2-(*cis*-2-Nitrocyclohexyl)phenol: after quenching the reaction the mixture was extracted with AcOEt. The organic extracts were washed with brine and dried over Na_2SO_4 . The mixture was concentrated under reduced pressure. To a solution of resulting product in THF (3.0 mL) and MeOH (3.0 mL) was added 12 N HCl (1.0 mL). After stirred for 10 min the reaction mixture was diluted with AcOEt. The organic layer was washed with 10% HCl, satd. NaHCO_3 and brine, and then dried over Na_2SO_4 . Concentration and column chromatography (hexane/AcOEt=9/1) gave the titled product as colorless needles of mp 120–122 °C. $[\alpha]^{25}_{\text{D}} -124$ (c 0.98, CHCl_3), 61% ee (HPLC, Daicel Chiralcel OD-H, hexane/*i*-PrOH = 100/1, 1.0 mL/min, 254 nm, major 6.3 min and minor 7.4 min). ^1H NMR: 1.45–1.54 (1H, m), 4.67–1.74 (2H, m), 1.81–2.07 (3H, m), 2.34 (1H, m), 2.49 (1H, m), 3.39 (1H, m), 5.03–5.14 (1H, m), 5.24 (1H, s), 6.65 (1H, d, $J = 7.9$ Hz), 6.88 (1H, dd, $J = 7.4, 7.6$ Hz), 7.08 (1H, dd, $J = 7.4, 7.9$ Hz), 7.16 (1H, d, $J = 7.6$ Hz). ^{13}C NMR: 20.0, 24.0, 25.5, 30.0, 38.5, 84.6, 114.8, 121.1, 126.9, 128.1, 128.1, 152.8. IR (KBr): 3445, 1543, 1454, 1373, 1358, 1335, 1265, 1238, 756. EIMS m/z : 221 (M^+), 175, 173, 159, 145, 131, 107, 77. Anal. Calcd. for $\text{C}_{12}\text{H}_{15}\text{NO}_3$: C, 65.14; H, 6.83; N, 6.33. Found: C, 65.14; H, 6.78; N, 6.25.

5-(*cis*-2-Nitrocyclohexyl)-4-trimethylsilyl-1,3-benzodioxole: separated from *trans*-isomer by column chromatography (hexane/Et₂O = 30/1). Colorless prisms of mp 134–135 °C. $[\alpha]^{25}_{\text{D}} -105.9$ (c 0.98, CHCl₃), 76% ee (HPLC, Daicel Chiralpak AD-H, hexane/*i*-PrOH = 50/1, 1.0 mL/min, 254 nm, minor 4.8 min and major 5.7 min). ¹H NMR: 0.37 (9H, s), 1.38–1.46 (1H, m), 1.65–1.70 (2H, m), 1.78–1.86 (1H, m), 2.02–2.13 (2H, m), 2.28–2.30 (1H, m), 2.39–2.48 (1H, m), 3.14–3.18 (1H, m), 4.76 (1H, brs), 5.87 (1H, s), 5.88 (1H, s), 6.61 (1H, d, *J* = 8.3 Hz), 6.72 (1H, d, *J* = 8.3 Hz). ¹³C NMR: 1.49, 19.5, 25.7, 26.3, 29.9, 44.7, 87.7, 99.9, 109.3, 117.9, 119.8, 139.4, 145.3, 153.1. IR (KBr): 1543, 1420, 1261, 1250, 1209, 1051, 907, 843. EIMS *m/z*: 321 (M⁺), 276, 258, 233, 207, 84, 73, 58. Anal. Calcd. for C₁₆H₂₃NO₄Si: C, 59.78; H, 7.21; N, 4.36. Found: C, 59.63; H, 7.07; N, 4.35.

5-(*trans*-2-Nitrocyclohexyl)-4-trimethylsilyl-1,3-benzodioxole: colorless needles of mp 121–123 °C. $[\alpha]^{25}_{\text{D}} +39.9$ (c 0.99, CHCl₃), 76% ee (HPLC, Daicel Chiralpak AD-H, hexane/*i*-PrOH = 50/1, 1.0 mL/min, 254 nm, major 10.7 min and minor 11.2 min). ¹H NMR: 0.41 (9H, s), 1.35–1.51 (3H, m), 1.81–1.83 (1H, m), 1.89–1.98 (3H, m), 2.39–2.41 (1H, m), 3.39–3.44 (1H, m), 4.75–4.80 (1H, m), 5.85 (1H, s), 5.87 (1H, s), 6.73 (1H, d, *J* = 8.3 Hz), 6.76 (1H, d, *J* = 8.3 Hz). ¹³C NMR: 1.38, 24.5, 25.3, 32.7, 35.3, 46.0, 90.5, 99.9, 109.2, 118.5, 119.3, 139.5, 144.9, 153.1. IR (KBr): 1545, 1421, 1252, 1051, 847. EIMS *m/z*: 321 (M⁺), 276, 258, 207, 177, 83, 73, 58. Anal. Calcd. for C₁₆H₂₃NO₄Si: C, 59.78; H, 7.21; N, 4.36. Found: C, 59.54; H, 7.08; N, 4.34.

1-(2-Nitrocyclohexyl)benzene:⁹ purified by column chromatography (hexane/AcOEt = 40/1). 33% ee (HPLC, Daicel Chiralcel OD-H, hexane/*i*-PrOH = 9/1, 1.0 mL/min, 254 nm,

⁹ Hayashi, T.; Senda, T.; Ogasawara, M. *J. Am. Chem. Soc.* **2000**, *122*, 10716–10717.

cis-isomer: minor 15.3 min and major 16.2 min, *trans*-isomer: major 11.6 min and minor 12.7 min).

General Procedure for Isomerization of Nitro Compounds.

1-(*trans*-2-Nitrocyclohexyl)-2-trityloxymethylbenzene (*trans*-12c): a mixture of *cis*-12c (360 mg, 0.75 mmol) and sodium bicarbonate (633 mg, 7.5 mmol) in EtOH (7.5 mL) was heated under reflux for 6 h. The mixture was filtered and the filtrate was concentrated (*trans/cis* > 99/1). Purification by column chromatography (hexane/acetone = 30/1) gave *trans*-12c (349 mg, 97% yield).

General Procedure for the Removal of Tr Groups.

[2-(*cis*-2-Nitrocyclohexyl)phenyl]methanol: to a solution of *cis*-12c (75 mg, 0.16 mmol) in MeOH (3.0 mL) and THF (3.0 mL) was added 12 N HCl (1.0 mL, 12 mmol) at rt. After stirred for 12 h the reaction mixture was diluted with AcOEt. The organic layer was washed with satd. NaHCO₃ and brine, and then dried over Na₂SO₄. Concentration and column chromatography (hexane/AcOEt = 3/1) gave the titled product (37 mg, 99% yield) as a colorless oil. $[\alpha]_D^{25} -132$ (c 0.70, CHCl₃) for 90% ee (HPLC, Daicel Chiralcel OD-H, hexane/*i*-PrOH = 100/1, 1.0 mL/min, 254 nm, minor 6.0 min and major 6.7 min). ¹H NMR: 1.46–1.54 (1H, m), 1.67–1.70 (2H, m), 1.89–2.08 (4H, m), 2.30 (1H, m), 2.52 (1H, m), 3.38 (1H, m), 4.63 (1H, d, *J* = 12.2 Hz), 4.71 (1H, d, *J* = 12.2 Hz), 5.13 (1H, m), 7.21–7.29 (4H, m). ¹³C NMR: 19.7, 25.4, 25.5, 29.9, 41.1, 64.1, 86.8, 127.4, 127.4, 128.9, 129.6, 137.8, 140.0. IR (neat): 3387, 1543, 1447, 1373, 1042, 768. EIMS *m/z*: 187, 169, 141, 129, 115, 105, 91, 77. Anal. Calcd. for C₁₃H₁₇NO₃: C, 66.36; H, 7.28; N, 5.95. Found: C, 66.13; H, 7.14; N, 5.82.

[2-(*trans*-2-Nitrocyclohexyl)phenyl]methanol: a colorless oil. $[\alpha]_D^{25} +43.9$ (c 1.1,

CHCl₃) for 89% ee (HPLC, Daicel Chiralpak AD, hexane/*i*-PrOH = 5/1, 1.0 mL/min, 254 nm, minor 7.1 min and major 8.8 min). ¹H NMR: 1.50–1.51 (3H, m), 1.81–1.83 (2H, m), 1.96–2.02 (3H, m), 2.43–2.45 (1H, m), 3.60 (1H, ddd, *J* = 8.2, 8.3, 11.3 Hz), 4.71 (1H, d, *J* = 12.2 Hz), 4.79 (1H, d, *J* = 12.2 Hz), 4.84 (1H, ddd, *J* = 4.0, 11.3, 11.3 Hz), 7.21 (1H, ddd, *J* = 1.8, 7.0, 7.0 Hz), 7.26–7.32 (3H, m). ¹³C NMR: 24.6, 25.4, 32.6, 33.9, 42.4, 63.5, 90.3, 125.8, 127.3, 128.6, 129.6, 138.4, 139.7. IR (neat): 3383, 1543. EIMS *m/z*: 187, 169, 141, 129, 117, 105, 91, 77. Anal. Calcd. for C₁₃H₁₇NO₃: C, 66.36; H, 7.28; N, 5.95. Found: C, 66.49; H, 7.26; N, 5.94.

{2-[1-(Nitromethyl)pentyl]phenyl}methanol: a colorless oil. [α]_D²⁵ +24.0 (c 0.70, CHCl₃). ¹H NMR: 0.83 (3H, t, *J* = 7.2 Hz), 1.09–1.34 (4H, m), 1.72 (2H, m), 1.77 (1H, brs), 3.91 (1H, m), 4.59 (1H, m), 4.73 (1H, d, *J* = 12.2 Hz), 4.82 (1H, d, *J* = 12.2 Hz), 7.23–7.27 (2H, m), 7.33 (1H, d, *J* = 7.3 Hz), 7.37 (1H, d, *J* = 7.7 Hz). ¹³C NMR: 13.7, 22.5, 29.0, 33.0, 38.4, 63.3, 80.8, 126.0, 127.4, 128.7, 129.4, 138.5, 139.0. IR (neat): 3383, 1551, 1381. EIMS *m/z*: 189, 171, 143, 129, 117, 105, 91, 77. Anal. Calcd. for C₁₃H₁₉NO₃: C, 65.80; H, 8.07; N, 5.90. Found: C, 65.64; H, 8.12; N, 5.78.

{2-[(*R*)-2-Nitro-1-phenylethyl]phenyl}methanol: a colorless oil. [α]_D²⁵ –14.6 (c 0.70, CHCl₃). ¹H NMR: 1.68 (1H, brs), 4.67 (1H, d, *J* = 12.5 Hz), 4.81 (1H, d, *J* = 12.5 Hz), 4.96 (1H, dd, *J* = 8.0, 13 Hz), 5.05 (1H, dd, *J* = 8.3, 13 Hz), 5.35 (1H, dd, *J* = 8.0, 8.3 Hz), 7.24–7.39 (9H, m). ¹³C NMR: 43.9, 63.4, 79.1, 126.9, 127.6, 127.9, 128.6, 129.1, 129.7, 137.5, 138.6, 138.9. IR (neat): 3395, 1555. EIMS *m/z*: 210, 193, 178, 165, 115, 103, 91, 77. Anal. Calcd. for C₁₅H₁₅NO₃: C, 70.02; H, 5.88; N, 5.44. Found: C, 69.88; H, 5.73; N, 5.24.

{2-[(1*S*,2*R*)-1,2,3,4-Tetrahydro-6,7-dimethoxy-2-nitronaphthalen-1-yl]phenyl}-methanol (*trans*-4a): a colorless oil. [α]_D²⁵ –147 (c 0.99, CHCl₃) for 95% ee (HPLC, Daicel Chiralpak AD, hexane/*i*-PrOH = 4/1, 1.0 mL/min, 254 nm, major 12.8 min and minor 16.7 min). ¹H NMR: 1.89 (1H, brs), 2.41–2.51 (2H, m), 2.94–3.06 (2H, m), 3.58 (3H, s), 3.86 (3H, s), 4.77 (1H, s), 5.08–5.10 (1H, m), 6.20 (1H, s), 6.62 (1H, s), 6.96 (1H, d, *J* = 6.1 Hz), 7.23–7.40 (2H, m), 7.42 (1H, d, *J* = 7.4 Hz). ¹³C NMR: 26.3, 26.5, 44.6, 55.8,

63.3, 88.5, 110.8, 112.3, 126.7, 127.6, 127.7, 128.6, 129.6, 129.9, 138.8, 140.0, 147.9, 148.0. IR (neat): 3487, 1547, 1516, 1462, 1404, 1369, 1254, 1219, 1126, 1018, 756. EIMS m/z : 343 (M^+), 326, 296, 278, 265, 248, 178, 165, 151, 115, 91, 77. Anal. Calcd. for $C_{19}H_{21}NO_5$: C, 66.46; H, 6.16; N, 4.08. Found: C, 66.16; H, 6.17; N, 3.93.

Recrystallization from toluene afforded the enantiomerically pure titled product as colorless prisms of mp 52–53 °C: $[\alpha]^{25}_D -154$ (c 0.81, $CHCl_3$) for >99% ee (HPLC, Daicel Chiralpak AD, hexane/*i*-PrOH = 4/1, 1.0 mL/min, 254 nm, major 12.8 min and minor 16.3 min).

General Procedure for Conversion of Alcohols to Cyclic Amines.

***cis*-1,2,3,4,4a,5,6,10b-Octahydrophenanthridine (*cis*-16):** to a solution of [2-(*cis*-2-nitrocyclohexyl)phenyl]methanol (50 mg, 0.21 mmol) in EtOH (1.0 mL) was added Raney nickel catalyst rinsed with EtOH prior to use. The mixture was stirred for 1 h at rt under hydrogen atmosphere (80 atm). The mixture was filtered and filtrate was concentrated. The resulting amine was dissolved in 1,4-dioxane (3.0 mL) and 12 N HCl (1.8 mL), and the mixture was heated under reflux for 1 h. Removal of the solvent in vacuo gave the intermediate chloride, which was immediately dissolved in *t*-BuOH (2.5 mL), treated with K_2CO_3 (500 mg, 3.6 mmol), and heated under reflux for 0.5 h. The mixture was cooled to rt, poured into water, and extracted with $CHCl_3$. The organic layer was washed with brine and dried over K_2CO_3 . Concentration and column chromatography (AcOEt /MeOH = 100/1) gave *cis*-16 (27 mg, 68% yield) as a pale yellow oil: $[\alpha]^{25}_D -6.0$ (c 0.83, MeOH). ^1H NMR: 1.35–1.65 (4H, m), 1.70–1.77 (4H, m), 1.84–1.88 (1H, m), 2.60 (1H, m), 3.12 (1H, m), 4.08 (1H, d, $J = 16.2$ Hz), 4.13 (1H, d, $J = 16.2$ Hz), 7.01 (1H, d, $J = 6.7$ Hz), 7.07–7.15 (3H, m). ^{13}C NMR: 20.5, 25.9, 31.3, 31.9, 39.2, 48.9, 52.0, 125.7, 125.9, 126.0, 128.8, 135.0, 141.0. IR (neat): 3325, 1489, 1450, 756, 737. EIMS m/z : 187, 144, 130, 83. HRMS m/z : Calcd. for $C_{13}H_{17}N$, 187.1361(M^+); Found, 187.1364.

***trans*-1,2,3,4,4a,5,6,10b-Octahydrophenanthridine (*trans*-16):** colorless needles of mp 118–119 °C. $[\alpha]^{25}_D +126$ (c 0.50, MeOH). ^1H NMR: 1.16–1.48 (4H, m), 1.84–1.93 (3H, m), 2.36–2.49 (3H, m), 4.06 (1H, d, $J = 15.9$ Hz), 4.22 (1H, d, $J = 15.9$ Hz), 7.01 (1H, d, $J = 7.4$ Hz), 7.12–7.19 (2H, m), 7.29 (1H, d, $J = 7.3$ Hz). ^{13}C NMR: 25.3, 26.4, 29.3, 34.0,

43.9, 49.0, 59.0, 125.5, 125.7, 126.1, 135.6, 138.7. IR (neat): 3325, 1450, 756, 737. EIMS m/z : 187 (M^+), 144, 83. HRMS–EI (m/z): M^+ calcd for $C_{13}H_{17}N$, 187.1361; found, 187.1358.

4-Butyl-1,2,3,4-tetrahydroisoquinoline (17): a colorless oil. $[\alpha]^{25}_D +22.2$ (c 1.1, MeOH). ^1H NMR: 0.92 (3H, t, $J = 6.4$ Hz), 1.33–1.44 (4H, m), 1.60–1.71 (2H, m), 1.82 (1H, brs), 2.65–2.68 (1H, m), 3.01 (1H, dd, $J = 12.9, 4.6$ Hz), 3.13 (1H, dd, $J = 12.8, 4.6$ Hz), 3.99 (2H, s), 6.99 (1H, d, $J = 7.3$ Hz), 7.10–7.18 (3H, m). ^{13}C NMR: 14.0, 22.9, 29.5, 35.2, 37.1, 47.7, 48.6, 125.6, 126.0, 126.1, 128.8, 135.8, 139.6. IR (neat): 3410, 1647, 1454, 1408, 1385, 1038. EIMS m/z : 189 (M^+), 174, 160, 131, 104, 83. HRMS–EI (m/z): M^+ calcd for $C_{13}H_{19}N$, 189.1517; found, 189.1525.

(R)-1,2,3,4-Tetrahydro-4-phenylisoquinoline (18): a colorless oil. $[\alpha]^{25}_D +9.7$ (c 0.90, MeOH). ^1H NMR: 1.89 (1H, brs), 3.11 (1H, dd, $J = 6.4, 12.8$ Hz), 3.41 (1H, dd, $J = 5.2, 12.8$ Hz), 4.07–4.17 (3H, m), 6.91 (1H, d, $J = 7.7$ Hz), 7.08–7.35 (8H, m). ^{13}C NMR: 44.8, 48.5, 52.2, 125.9, 126.4, 126.4, 128.5, 128.9, 130.3, 136.3, 137.4, 145.0. IR (neat): 3414. EIMS m/z : 209, 179, 165, 83. HRMS–EI (m/z): M^+ calcd for $C_{15}H_{15}N$, 209.1204; found, 209.1203.

The absolute configuration was determined to be *R* by comparison of the specific rotation with that reported, $[\alpha]^{25}_D +11.1$ (c 3.5, MeOH) for >99% ee.¹⁰

(6aR,12bS)-5,6,6a,7,8,12b-Hexahydro-10,11-dimethoxybenzo[*a*]phenanthridine: to a solution of *trans*-**4a** (31 mg, 0.09 mmol) in EtOH (3.0 mL) and 6 N HCl (0.5 mL, 3.0 mmol) was added Zn (59 mg, 0.90 mmol). After stirred for 10 min at rt the mixture was filtered, and the filtrate was concentrated. The resulting amine was dissolved in 1,4-dioxane (1.3 mL) and 12 N HCl (0.8 mL), and the mixture was heated under reflux for 1 h. Removal of the solvent in vacuo gave the intermediate chloride, which was immediately dissolved in *t*-BuOH (2.5 mL). To the solution was added K_2CO_3 (500 mg, 3.6 mmol), and

¹⁰ Kihara, M.; Ikeuchi, M.; Adachi, S.; Nagao, N.; Moritoki, H.; Yamaguchi, M.; Taira, Z. *Chem. Pharm. Bull.* **1995**, 43, 1543–1546.

the mixture was heated under reflux for 0.5 h. The mixture was cooled to rt, poured into water, and extracted with CHCl₃. The organic layer was washed with brine and dried over K₂CO₃. Concentration and column chromatography (AcOEt/MeOH = 9/1) gave the titled product (23 mg, 86% yield) as colorless prisms of mp 155–156 °C (>99% ee): [α]_D²⁵ – 222 (c 1.1, CHCl₃). ¹H NMR: 1.69–1.75 (2H, m), 2.14–2.21 (1H, m), 2.71 (1H, ddd, *J* = 6.7, 10.7, 10.7 Hz), 2.78–2.84 (1H, m), 2.90–2.95 (1H, m), 3.77 (3H, s), 3.83 (1H, d, *J* = 10.7 Hz), 3.88 (3H, s), 4.03 (1H, d, *J* = 15.6 Hz), 4.11 (1H, d, *J* = 15.6 Hz), 6.74 (1H, s), 6.91 (1H, s), 7.16 (1H, d, *J* = 7.4 Hz), 7.21–7.29 (2H, m), 7.47 (1H, d, *J* = 7.4 Hz). ¹³C NMR: 27.4, 28.9, 44.6, 49.1, 56.0, 56.1, 58.8, 110.0, 111.9, 126.0, 126.1, 126.8, 128.5, 130.7, 130.9, 136.1, 137.7, 146.6, 147.1. IR (KBr): 3294, 1504. EIMS *m/z*: 295 (M⁺), 278, 263, 165, 130, 115, 102, 91, 77. The hydrochloride salt: colorless needles of mp >236 °C dec (>99% ee). [α]_D²⁵ +123 (c 0.75, EtOH) for >99% ee. Anal. Calcd. for C₁₉H₂₂ClNO₂: C, 68.77; H, 6.68; N, 4.22. Found: C, 68.53; H, 6.69; N, 4.16.

The absolute configuration was determined to be (6a*R*,12b*S*) by comparison of the specific rotation with that reported, [α]_D²⁵ +106 (c 0.75, EtOH) for >99% ee.¹¹

Synthesis of A-86929.

5-Propyl-3-[(1*S*,2*S*)- and (1*S*,2*R*)-1,2,3,4-tetrahydro-6,7-dimethoxy-2-nitronaphthalen-1-yl]-2-(trityloxymethyl)thiophene (*cis*- and *trans*-15**):** under Ar atmosphere, to a solution of 3-bromo-5-propyl-2-trityloxymethylthiophene (716 mg, 1.5 mmol) and ligand **8** (364 mg, 2.1 mmol) in toluene (12 mL) was added *n*-BuLi (0.94 mL, 1.6 M in hexane, 1.5 mmol) at –78 °C over 1 min, and the mixture was stirred for 0.5 h. After the solution was cooled to –95 °C, nitroalkene **3a** (118 mg, 0.5 mmol) in toluene (3.0 mL) was added over 2 min, and the mixture was stirred for 0.5 h. The mixture was quenched with MeOH (0.1 mL) and then satd. NH₄Cl (20 mL). The mixture was extracted with AcOEt. The organic extracts were washed with 10% HCl, satd. NaHCO₃, and brine, and then dried over Na₂SO₄. Concentration and column chromatography (hexane/AcOEt = 5/1) gave **15** (135 mg, 92% yield, *trans/cis* = 37/63) as pale yellow needles of mp 69–71 °C: ¹H NMR: 0.89–0.93 (3H, m, *trans* and *cis*), 1.57–1.68 (2H, m, *trans* and *cis*), 2.10–2.12 (0.63H, m, *cis*), 2.24–2.42

¹¹ Knoerzer, T. A.; Nichols, D. E.; Brewster, W. K.; Watts, V. J.; Mottola, D.; Mailman, R. B. *J. Med. Chem.* **1994**, 37, 2453–2460.

(1.37H, m, *trans* and *cis*), 2.63 (1.26H, t, $J = 7.3$ Hz, *cis*), 2.68 (0.74H, t, $J = 7.3$ Hz, *trans*), 2.79–2.84 (1.37H, m, *trans* and *cis*), 2.90–2.93 (0.63H, m, *cis*), 3.58 (1.11H, s, *trans*), 3.62 (1.89H, s, *cis*), 3.84 (1.89H, s, *cis*), 3.85 (1.11H, s, *trans*), 4.03 (0.63H, d, $J = 11.9$ Hz, *cis*), 4.08 (0.37H, d, $J = 11.6$ Hz, *trans*), 4.14 (0.37H, d, $J = 11.6$ Hz, *trans*), 4.20 (0.63H, d, $J = 11.9$ Hz, *cis*), 4.43–4.48 (1H, m, *trans* and *cis*), 4.75–4.79 (1H, m, *trans* and *cis*), 6.17 (0.63H, s, *cis*), 6.25 (0.37H, s, *trans*), 6.29 (0.37H, s, *trans*), 6.39 (0.63H, s, *cis*), 6.52 (0.37H, s, *trans*), 6.53 (0.63H, s, *cis*), 7.21–7.33 (9H, m, *trans* and *cis*), 7.46 (2.22H, d, $J = 7.3$ Hz, *trans*), 7.51 (3.78H, d, $J = 7.4$ Hz, *cis*). ^{13}C NMR: 13.5 (*cis*), 22.4 (*cis*), 24.6 (*cis*), 26.6 (*cis*), 26.8 (*trans*), 27.6 (*trans*), 32.0 (*cis*), 41.0 (*cis*), 42.1 (*trans*), 55.7 (*cis*), 55.8 (*cis*), 58.7 (*cis*), 85.0 (*cis*), 87.2 (*cis*), 88.2 (*trans*), 110.6 (*cis*), 111.8 (*trans*), 112.2 (*cis*), 124.7 (*trans*), 125.9 (*cis*), 126.0 (*cis*), 127.0 (*cis*), 127.6 (*cis*), 127.8 (*trans*), 127.8 (*cis*), 128.6 (*cis*), 128.6 (*trans*), 135.1 (*trans*), 135.3 (*cis*), 135.7 (*cis*), 137.4 (*trans*), 143.6 (*trans*), 143.7 (*cis*), 143.8 (*cis*), 145.0 (*trans*), 147.7 (*trans*), 147.7 (*cis*), 147.8 (*trans*), 148.0 (*cis*). IR (KBr): 1545, 1508, 1491, 1458, 706. EIMS m/z : 634 (M^+), 587, 390, 344, 243, 165. Anal. Calcd. for $\text{C}_{39}\text{H}_{39}\text{NO}_5\text{S}$: C, 73.91; H, 6.20; N, 2.21. Found: C, 73.85; H, 6.24; N, 2.02.

Isomerization of **15**.

The mixture of *cis*- and *trans*-**15** (265 mg, 0.42 mmol, *trans/cis* = 37/63) and sodium bicarbonate (351 mg, 4.2 mmol) in EtOH (4.0 mL) was heated under reflux for 1.5 h. The mixture was filtered, and the filtrate was concentrated. Purification by column chromatography (hexane/AcOEt = 5/1) gave **15** (263 mg, 99% yield, *trans/cis* = 96/4).

Determination of ee.

2-(Methoxymethyl)-5-propyl-3-[(1*S*,2*R*)-1,2,3,4-tetrahydro-6,7-dimethoxy-2-nitro-naphthalen-1-yl]thiophene: to a solution of **15** (25 mg, 20 mmol, *trans/cis* = 96/4) in THF (1.0 mL) and MeOH (2.0 mL) was added 12 N HCl (0.5 mL, 6.0 mmol) at rt. After stirred for 18 h the reaction mixture was diluted with AcOEt. The organic layer was washed with satd. NaHCO_3 and brine, and then dried over Na_2SO_4 . Concentration and column chromatography (hexane/AcOEt = 5/1) gave the titled product (14 mg, 88% yield) as a colorless oil: $[\alpha]_{\text{D}}^{25} -131$ (c 0.70, CHCl_3) for 97% ee (HPLC, Daicel Chiralpak AD-H,

hexane/*i*-PrOH = 100/1, 1.0 mL/min, 254 nm, major 11.7 min and minor 12.5 min). ¹H NMR: 0.88 (3H, t, *J* = 7.3 Hz), 1.60 (2H, tq, *J* = 7.3, 7.3 Hz), 2.43–2.46 (2H, m), 2.65 (2H, t, *J* = 7.3 Hz), 2.95–3.01 (2H, m), 3.39 (3H, s), 3.64 (3H, s), 3.86 (3H, s), 4.38 (2H, d, *J* = 12.5 Hz), 4.56 (2H, d, *J* = 12.5 Hz), 6.27 (1H, s), 6.34 (1H, s), 6.59 (1H, s). ¹³C NMR: 13.4, 24.6, 27.0, 27.8, 32.1, 42.2, 55.8, 55.8, 58.0, 66.7, 88.6, 110.6, 111.9, 124.7, 126.0, 127.2, 134.7, 138.3, 145.4, 147.8, 147.9. IR (neat): 1551, 1516, 1462, 1261, 1115, 1088. EIMS *m/z*: 405 (*M*⁺), 358, 327, 269, 139. HRMS–EI (*m/z*): *M*⁺ calcd for C₂₁H₂₇NO₅S, 405.1610; found, 405.1603.

(1*S*,2*S*)- and (1*S*,2*R*)-1,2,3,4-Tetrahydro-6,7-dimethoxy-1-[5-propyl-2-(trityloxy-methyl)thiophen-3-yl]naphthalen-2-amine: to a solution of **15** (240 mg, 0.38 mmol, *trans/cis* = 96/4) in THF (2.0 mL) and AcOH (3.0 mL) was added Zn (902 mg, 14 mmol). After stirred for 0.5 h at rt the mixture was filtered, and the filtrate was concentrated and partitioned between aqueous NaHCO₃ and AcOEt. The organic layer was washed with brine and dried over K₂CO₃. Concentration and column chromatography (AcOEt/MeOH = 30/1) gave the titled product (220 mg, 96% yield) as colorless needles of mp 54–56 °C: [α]_D²⁵ –38.9 (c 0.82, EtOH). The *trans*-amine: ¹H NMR: 0.93 (3H, t, *J* = 7.3 Hz), 1.65–1.69 (3H, m), 2.11–2.20 (1H, m), 2.67–2.85 (4H, m), 2.96–3.00 (1H, m), 3.43 (1H, m), 3.54 (3H, s), 3.83 (1H, m), 4.12 (1H, d, *J* = 11.6 Hz), 4.24 (1H, d, *J* = 11.6 Hz), 6.18 (1H, s), 6.29 (1H, s), 6.53 (1H, s), 7.21 (3H, t, *J* = 7.3 Hz), 7.28 (6H, dd, *J* = 7.3, 7.3 Hz), 7.48 (6H, d, *J* = 7.3 Hz). ¹³C NMR: 13.6, 24.7, 28.2, 31.0, 32.2, 48.6, 53.6, 55.8, 55.8, 58.9, 87.2, 110.8, 112.2, 124.9, 127.1, 127.8, 127.9, 128.6, 129.8, 134.7, 140.6, 143.7, 144.9, 147.1, 147.2. IR (KBr): 3368, 1597, 1512, 1450, 1254, 1034. EIMS *m/z*: 604 (*M*⁺), 360, 343, 243, 177, 165. Anal. Calcd. for C₃₉H₄₁NO₃S•1/2H₂O: C, 76.44; H, 6.91; N, 2.29. Found: C, 76.33; H, 6.83; N, 2.28.

3-[(1*S*,2*S*)- and (1*S*,2*R*)-2-Amino-1,2,3,4-tetrahydro-6,7-dimethoxynaphthalen-1-yl]-5-propylthiophen-2-methanol: to a solution of (1*S*,2*S*)- and (1*S*,2*R*)-1,2,3,4-Tetrahydro-6,7-dimethoxy-1-[5-propyl-2-(trityloxymethyl)thiophen-3-yl]naphthalen-2-amine (192 mg, 0.32

mmol, *trans/cis* = 96/4) in THF (6.0 mL) was added 12 N HCl (1.0 mL, 12 mmol) at rt. After stirred for 1 h the reaction mixture was diluted with AcOEt. The organic layer was washed with satd. NaHCO₃ and brine, and then dried over K₂CO₃. Concentration and column chromatography (CHCl₃/MeOH = 10/1) gave the titled product (114 mg, 99% yield) as colorless needles of mp 47–49 °C: [α]²⁵_D –36.4 (c 0.59, EtOH). The *trans*-amino alcohol: ¹H NMR: 0.89 (3H, t, *J* = 7.3 Hz), 1.61 (2H, m), 1.81–1.84 (1H, m), 2.05–2.08 (1H, m), 2.62–2.68 (3H, m), 2.86–2.99 (3H, m), 3.63 (3H, s), 3.86 (3H, s), 3.86 (1H, m), 4.47 (1H, d, *J* = 12.8 Hz), 4.89 (1H, d, *J* = 12.8 Hz), 6.20 (1H, s), 6.25 (1H, s), 6.60 (1H, s). ¹³C NMR: 13.4, 24.7, 28.8, 32.1, 32.9, 47.6, 53.3, 55.7, 55.8, 55.9, 110.7, 112.3, 124.7, 127.9, 130.0, 137.7, 141.3, 144.2, 147.2, 147.4. IR (KBr): 3348, 1589, 1515, 1254, 1119. EIMS *m/z*: 361 (M⁺), 343, 326, 300, 190, 178, 91. Anal. Calcd. for C₂₀H₂₇NO₃S•H₂O: C, 63.30; H, 7.70; N, 3.69. Found: C, 63.53; H, 7.41; N, 3.61.

(5aR,11bS)-4,5,5a,6,7,11b-Hexahydro-9,10-dimethoxy-2-propyl-3-thia-5-azacyclopenta[c]phenanthrene hydrochloride (19): to a solution of 3-[(1*S*,2*S*)- and (1*S*,2*R*)-2-amino-1,2,3,4-tetrahydro-6,7-dimethoxynaphthalen-1-yl]-5-propylthiophen-2-methanol (50 mg, 0.14 mmol, *trans/cis* = 96/4) in CH₂Cl₂ (5.0 mL) was added CBr₄ (154 mg, 0.46 mmol) and Ph₃P (145 mg, 0.56 mmol) over 4 h at rt, and the mixture was stirred for 0.5 h. The mixture was quenched with satd. NaHCO₃ (10 mL), and extracted with CHCl₃. The organic layer was washed with brine and dried over K₂CO₃. Concentration and column chromatograph (EtOAc/MeOH = 8/1) gave the free amine. The amine was dissolved in EtOH, and EtOH–HCl was then added. The solution was stirred for 0.5 h. Concentration and recrystallization (AcOEt/MeOH) afforded diastereomerically and enantiomerically pure **19** (35 mg, 67% yield) as colorless needles of mp >284 °C dec.: [α]²⁵_D –257 (c 0.55, MeOH). ¹H NMR: 1.00 (3H, t, *J* = 7.3 Hz), 1.64–1.76 (3H, m), 2.39 (1H, m), 2.62 (1H, m), 2.79 (1H, t, *J* = 7.3 Hz), 2.85–3.03 (2H, m), 3.19 (1H, m), 3.83 (3H, s), 3.88 (3H, s), 4.31–4.37 (2H, m), 4.56 (1H, d, *J* = 15.3 Hz), 6.69 (1H, s), 6.91 (1H, s), 6.99 (1H, s). ¹³C NMR: 13.6, 24.8, 25.0, 26.9, 32.1, 39.8, 42.8, 56.0, 56.1, 57.7, 109.9, 111.9, 123.7, 125.0, 127.6, 129.1, 134.6, 145.5, 147.3, 148.0. IR (KBr): 3425, 1512, 1408, 1211, 1099. EIMS *m/z*: 343 (M⁺), 300, 269, 190, 178. Anal. Calcd. for C₂₀H₂₆ClNO₂S•1/4H₂O: C, 62.48; H, 6.95; N, 3.64. Found: C, 62.69; H, 6.68; N, 3.62. The free amine: a pale-yellow solid of mp 90–91 °C. [α]²⁵_D –348 (c 0.43, MeOH) for >99% ee (HPLC, Daicel Chiralcel OD-H, hexane/*i*-PrOH = 10/1, 1.0 mL/min, 254 nm, major 10.1 min and minor 14.3 min).

The absolute configuration of hydrochloride **19** was determined to be (5a*R*,11b*S*) by

comparison of the specific rotation with that reported, $[\alpha]^{25}_{\text{D}} -263$ (c 3.31, MeOH).¹²

(5aR,11bS)-4,5,5a,6,7,11b-Hexahydro-2-propyl-3-thia-5-azacyclopenta[c]-phenanthrene-9,10-diol hydrobromide (20): to a suspension of **19** (20 mg, 0.05 mmol) in CH_2Cl_2 (3.0 mL) was added BBr_3 (0.21 mL, 1.0 M in hexane, 0.21 mmol) over 5 min at -78°C , and the mixture was stirred for 0.5 h and then at 0°C for an additional 0.5 h. The mixture was recooled to -78°C and carefully quenched with MeOH (0.5 mL). The cooling bath was removed, and the reaction mixture was stirred for 1.5 h. The mixture was concentrated under reduced pressure, and the product was triturated in $\text{CH}_2\text{Cl}_2/\text{MeOH}/\text{Et}_2\text{O}$ to give **20** (21 mg, 100% yield) as a tan solid of mp $>156^\circ\text{C}$ dec.: $[\alpha]^{25}_{\text{D}} -171$ (c 0.76, MeOH). ^1H NMR (CD_3OD): 1.02 (3H, t, $J = 7.3$ Hz), 1.75 (2H, tq, $J = 7.3, 7.5$ Hz), 1.91–1.98 (1H, m), 2.31–2.38 (1H, m), 2.86 (1H, t, $J = 7.5$ Hz), 2.80–3.00 (2H, m), 3.18–3.24 (1H, m), 4.02 (1H, d, $J = 11$ Hz), 4.46 (1H, d, $J = 15$ Hz), 4.48 (1H, d, $J = 15$ Hz), 6.67 (1H, s), 6.69 (1H, s), 7.01 (1H, s). ^{13}C NMR (CD_3OD): 13.9, 26.0, 26.2, 26.6, 33.0, 40.8, 44.4, 58.8, 113.6, 116.6, 125.9, 126.8, 128.8, 129.3, 134.8, 144.7, 145.5, 147.3. IR (KBr): 3398, 1620, 1512, 1458, 1300, 1223, 1177. EIMS m/z : 315 (M^+), 298, 282, 272, 243, 178, 154, 80. HRMS–EI (m/z): M^+ calcd for $\text{C}_{18}\text{H}_{21}\text{NO}_2\text{S}$, 315.1293; found, 315.1286.

¹² Ehrlich, P. P.; Ralston, J. W.; Michaelides, M. R. *J. Org. Chem.* **1997**, 62, 2782–2785.

***cis*-16**

***cis*-16**

trans-16

17

18