Enantioselective Synthesis of C_2 -Symmetric Spirobipyridine Ligands through Cationic Rh(I)/Modified-BINAP-Catalyzed Double [2 + 2 + 2] Cycloaddition

Azusa Wada, Keiichi Noguchi, Masao Hirano, and Ken Tanaka*

Department of Applied Chemistry, Graduate School of Engineering, and Instrumentation Analysis Center, Tokyo University of Agriculture and Technology, Koganei, Tokyo 184-8588, Japan

I. General

Anhydrous CH_2Cl_2 (No. 27,099-7) was obtained from Aldrich and used as received. (*R*)-Segphos and (*R*)- H_8 -BINAP were obtained from Takasago International Corporation. All other reagents were obtained from commercial sources and used as received. All reactions were carried out under an atmosphere of argon or nitrogen in oven-dried glassware with magnetic stirring.

II. Synthesis of Bis-alkynenitrile

2,2-Dipent-3-ynylmalononitrile (**4**, Scheme 2).

KOH (4.72 g, 84.0 mmol) was added to a stirred solution of 3-pentyn-1-ol (883 mg, 10.5 mmol) and *p*-toluenesulfonyl chloride (2.20 g, 11.6 mmol) in THF (10 mL) at -40°C , and the resulting mixture was stirred at -40°C for 1 h. The reaction was quenched with saturated aqueous NH_4Cl and extracted with Et_2O . The organic layer was washed with brine, dried over Na_2SO_4 , and concentrated. To a stirred DMF (10 mL) solution of the residue was added Na_2CO_3 (1.12 g, 10.5 mmol), malononitrile (301 mg, 4.56 mmol), and KI (1.70 mg, 10.5 mmol), and the resulting mixture was stirred at 50°C for 1 h and then at rt for 1 h. The reaction was quenched with water and extracted with Et_2O . The organic layer was dried over Na_2SO_4 , concentrated, and purified by silica gel column chromatography (hexane:ethyl acetate = 10:1), which furnished 2,2-dipent-3-ynylmalononitrile (**4**, 660 mg, 3.33 mmol, 73% yield) as a colorless oil.

IR (neat) 2920, 2856, 2247, 1734, 1449 cm^{-1} ; ^1H NMR (CDCl_3 , 300 MHz) δ 2.52 (dt, $J = 7.8, 2.4$ Hz, 4H), 2.17 (t, $J = 7.8$ Hz, 4H), 1.78 (t, $J = 2.4$ Hz, 6H); ^{13}C NMR (CDCl_3 , 75 MHz) δ 114.5, 78.6, 74.8, 36.6, 36.1, 15.6, 3.32; $\text{C}_{13}\text{H}_{14}\text{N}_2$ $[\text{M}]^+$ 198.1157, found 198.1015.

III. Synthesis of Bis-diynenitriles

Representative Procedure for the synthesis of bis-diynenitriles: 2,2-Bis[5-(3-phenylprop-2-ynyloxy)pent-3-ynyl]malononitrile (9a, Scheme 3).

To a stirred suspension of sodium hydride (634 mg, 13.2 mmol) in THF (30 ml) was added a THF (5.0 mL) solution of 5-(*t*-butyldimethylsilyloxy)pent-2-yn-1-ol¹ (**7**, 2.21 g, 11.01 mmol) and (3-bromoprop-1-ynyl)benzene (2.58 g, 13.2 mmol) at 0 °C, and the resulting mixture was stirred at rt for 6 h. The reaction was quenched with saturated aqueous NH₄Cl and extracted with Et₂O. The organic layer was washed with brine, dried over Na₂SO₄, and concentrated. The residue was dissolved in THF (11 ml) and tetrabutylammonium fluoride (1.0 M in THF, 11 mL, 11.0 mmol) was added. The resulting mixture was stirred at rt for 1 h and the reaction was quenched with water. The mixture was extracted with ether, dried over Na₂SO₄, and concentrated. The residue was purified by silica gel column chromatography (hexane:ethyl acetate = 5:1), which furnished 5-(3-phenylprop-2-ynyloxy)pent-3-yn-1-ol (**8**, 1.50 g, 10.9 mmol, 98% yield) as a colorless oil.

KOH (1.26 g, 22.4 mmol) was added to a stirred solution of **8** (600 mg, 2.80 mmol) and *p*-toluenesulfonyl chloride (587 mg, 3.08 mmol) in THF (20 mL) at −40 °C, and the resulting mixture was stirred at −40 °C for 2 h. The reaction was quenched with saturated aqueous NH₄Cl and extracted with Et₂O. The organic layer was washed with brine, dried over Na₂SO₄, and concentrated. To a stirred DMF (20 mL) solution of the residue was added K₂CO₃ (387 mg, 2.80 mmol), tetrabutylammonium hydrogensulfate (3 mg, 0.009 mmol), malononitrile (84 mg, 1.27 mmol), and KI (465 mg, 2.80 mmol), and the resulting mixture was stirred at 40 °C for 2 h and stirred at rt for 1 h. The reaction was quenched with water and extracted with Et₂O. The organic layer was dried over Na₂SO₄, concentrated, and purified by silica gel column chromatography (hexane:ethyl acetate = 10:1), which furnished 2,2-bis[5-(3-phenylprop-2-ynyloxy)pent-3-ynyl]malononitrile (**9a**, 477 mg, 1.04 mmol, 82% yield) as a pale yellow oil.

IR (neat) 3058, 2852, 2238, 1722, 1489, 1443, 1350, 1258, 1074, 757, 692 cm^{−1}; ¹H NMR (CDCl₃, 300 MHz) δ 7.49–7.40 (m, 4H), 7.36–7.27 (m, 6H), 4.46 (s, 4H), 4.30 (t, *J* = 1.8 Hz, 4H), 2.65 (tt, *J* = 7.2, 1.8 Hz, 4H), 2.21 (t, *J* = 7.2 Hz, 4H); ¹³C NMR (CDCl₃, 75 MHz) δ 131.7, 128.5, 128.3, 122.4, 114.2, 86.8, 84.2, 82.7, 78.3, 57.5, 57.0, 36.3, 36.1, 15.7; HRMS (EI) calcd for C₃₁H₂₆N₂O₂ [M]⁺ 458.1994, found 458.2029.

2,2-Bis{5-[3-(4-chlorophenyl)prop-2-ynyloxy]pent-3-ynyl}malononitrile (9b).

Pale yellow oil; IR (neat) 2852, 2244, 1733, 1488, 1350, 1244, 1075, 830, 753 cm^{-1} ; ^1H NMR (CDCl_3 , 300 MHz) δ 7.41–7.34 (m, 4H), 7.33–7.26 (m, 4H), 4.44 (s, 4H), 4.29 (t, J = 1.8 Hz, 4H), 2.67 (tt, J = 7.5, 1.8 Hz, 4H), 2.22 (t, J = 7.5 Hz, 4H); ^{13}C NMR (CDCl_3 , 75 MHz) δ 134.6, 132.9, 128.6, 120.1, 114.1, 85.6, 85.2, 82.8, 78.2, 57.3, 57.0, 36.2, 36.1, 15.7; HRMS (ESI) calcd for $\text{C}_{31}\text{H}_{24}\text{Cl}_2\text{N}_2\text{NaO}_2$ $[\text{M}+\text{Na}]^+$ 549.1113, found 549.1115.

2,2-Bis[5-[3-(4-methoxyphenyl)prop-2-ynyloxy]pent-3-ynyl]malononitrile (9c).

Pale yellow oil; IR (neat) 2840, 2237, 1606, 1507, 1446, 1350, 1246, 1076, 835, 734 cm^{-1} ; ^1H NMR (CDCl_3 , 300 MHz) δ 7.42–7.34 (m, 4H), 6.88–6.80 (m, 4H), 4.44 (s, 4H), 4.29 (t, J = 2.1 Hz, 4H), 3.81 (s, 6H), 2.66 (tt, J = 7.5, 2.1 Hz, 4H), 2.21 (t, J = 7.5 Hz, 4H); ^{13}C NMR (CDCl_3 , 75 MHz) δ 159.8, 133.3, 114.5, 114.2, 114.0, 86.8, 82.8, 82.6, 78.4, 57.6, 56.9, 55.3, 36.3, 36.2, 15.7; HRMS (ESI) calcd for $\text{C}_{33}\text{H}_{30}\text{N}_2\text{NaO}_4$ $[\text{M}+\text{Na}]^+$ 541.2103, found 541.2128.

2,2-Bis[5-(but-2-ynyloxy)pent-3-ynyl]malononitrile (9d).

Pale yellow oil; IR (neat) 2855, 2226, 1733, 1447, 1350, 1246, 1073, 893, 773 cm^{-1} ; ^1H NMR (CDCl_3 , 300 MHz) δ 4.21 (t, J = 2.1 Hz, 4H), 4.18 (q, J = 2.1 Hz, 4H), 2.65 (tt, J = 7.5, 2.1 Hz, 4H), 2.22 (t, J = 7.5 Hz, 4H), 1.99 (t, J = 2.1 Hz, 6H); ^{13}C NMR (CDCl_3 , 75 MHz) δ 114.2, 83.2, 82.4, 78.4, 74.2, 57.2, 56.6, 36.3, 36.2, 15.7, 3.6; HRMS (EI) calcd for $\text{C}_{21}\text{H}_{22}\text{N}_2\text{O}_2$ $[\text{M}]^+$ 334.1681, found 334.1691.

2,2-Bis[5-(prop-2-ynyloxy)pent-3-ynyl]malononitrile (9e).

Pale yellow oil; IR (neat) 3289, 2857, 2250, 2116, 1445, 1347, 1139, 1078, 933, 886 cm^{-1} ; ^1H NMR (CDCl_3 , 300 MHz) δ 4.27–4.22 (m, 8H), 2.66 (tt, $J = 6.6, 2.4$ Hz, 4H), 2.22 (t, $J = 2.4$ Hz, 2H), 2.23 (t, $J = 6.6$ Hz, 4H); ^{13}C NMR (CDCl_3 , 75 MHz) δ 114.1, 82.7, 78.8, 78.0, 75.0, 56.8, 56.5, 36.2, 36.1, 15.6; HRMS (EI) calcd for $\text{C}_{19}\text{H}_{18}\text{N}_2\text{O}_2$ $[\text{M}]^+$ 306.1368, found 306.1388.

2,2-Bis[6-(3-phenylprop-2-ynyloxy)hex-4-ynyl]malononitrile (9f).

Pale yellow oil; IR (neat) 3056, 2852, 2239, 1489, 1442, 1349, 1073, 758, 692 cm^{-1} ; ^1H NMR (CDCl_3 , 300 MHz) δ 7.48–7.40 (m, 4H), 7.39–7.28 (m, 6H), 4.46 (s, 4H), 4.30 (t, $J = 2.4$ Hz, 4H), 2.40 (tt, $J = 6.6, 2.4$ Hz, 4H), 2.02–2.12 (m, 4H), 1.94–1.84 (m, 4H); ^{13}C NMR (CDCl_3 , 75 MHz) δ 131.8, 128.6, 128.3, 122.4, 115.2, 86.8, 85.0, 84.2, 77.1, 57.3, 57.1, 37.2, 36.8, 24.4, 18.1; HRMS (ESI) calcd for $\text{C}_{33}\text{H}_{30}\text{N}_2\text{NaO}_2$ $[\text{M}+\text{Na}]^+$ 509.2205, found 509.2198.

2,2-Bis[6-(but-2-ynyloxy)hex-4-ynyl]malononitrile (9g).

Pale yellow oil; IR (neat) 2855, 2291, 2224, 1443, 1349, 1135, 1072, 923, 892, 773 cm^{-1} ; ^1H NMR (CDCl_3 , 300 MHz) δ 4.22 (t, $J = 2.1$ Hz, 4H), 4.19 (q, $J = 2.4$ Hz, 4H), 2.40 (tt, $J = 6.6, 2.1$ Hz, 4H), 2.12–2.04 (m, 4H), 1.96–1.87 (m, 4H), 1.87 (t, $J = 2.4$ Hz, 6H); ^{13}C NMR (CDCl_3 , 75 MHz) δ 115.2, 84.6, 83.1, 77.2, 74.3, 57.1, 56.8, 37.2, 36.8, 24.4, 18.1, 3.6; HRMS (EI) calcd for $\text{C}_{23}\text{H}_{26}\text{N}_2\text{O}_2$ $[\text{M}]^+$ 362.1994, found 362.1965.

2,2-Bis{2-[3-(3-phenylprop-2-ynyloxy)prop-1-ynyl]benzyl}malononitrile (9h).

To a solution of 2-iodobenzaldehyde (22.6 mmol, 4.18 g) and (3-prop-2-ynyloxyprop-1-ynyl)benzene² (16.5 mmol, 2.80 g) in Et₃N (35 ml) was added PdCl₂(PPh₃)₂ (145.0 mg, 0.206 mmol). The mixture was stirred at rt for 5 min and CuI (20 mg, 0.105 mmol) was added. The resulting mixture was stirred at 50 °C for 6 h and then at rt for 1 h. The resulting mixture was filtered, concentrated, and purified by silica gel column chromatography (hexane:ethyl acetate = 20:1), which furnished 2-[3-(3-phenylprop-2-ynyloxy)prop-1-ynyl]benzaldehyde (3.69 g, 13.4 mmol, 81% yield) as a pale yellow oil.

To a stirred suspension of sodium borohydride (380 mg, 10.1 mmol) in EtOH (20 ml) was added a EtOH (5.0 ml) solution of 2-[3-(3-phenylprop-2-ynyloxy)prop-1-ynyl]benzaldehyde (3.69 g, 13.4 mmol) at 0 °C, and the resulting mixture was stirred at 0 °C for 1 h. The reaction was quenched with water (10.0 mL), stirred for 10 min, and extracted with CH₂Cl₂. The organic layer was concentrated and the residue was purified by silica gel column chromatography (hexane:ethyl acetate = 10:1), which furnished {2-[3-(3-phenylprop-2-ynyloxy)prop-1-ynyl]phenyl}methanol (3.22 g, 11.7 mmol, 87% yield) as a colorless oil.

KOH (5.25 g, 93.6 mmol) was added to a stirred solution of {2-[3-(3-phenylprop-2-ynyloxy)prop-1-ynyl]phenyl}methanol (3.22 g, 11.7 mmol) and *p*-toluenesulfonyl chloride (2.45 g, 12.9 mmol) in THF (30 ml) at -40 °C, and the resulting mixture was stirred at -40 °C for 10 h. The reaction was quenched with saturated aqueous NH₄Cl and extracted with Et₂O. The organic layer was washed with brine, dried over Na₂SO₄, and concentrated. To a stirred DMF (20 ml) solution of the residue was added K₂CO₃ (2.31 g, 16.7 mmol), tetrabutylammonium hydrogensulfate (3 mg, 0.009 mmol), malononitrile (367 mg, 5.57 mmol), and KI (2.77 g, 16.7 mmol), and the resulting mixture was stirred at 40 °C for 3 h and then at rt for 2 h. The reaction was quenched with water, extracted with Et₂O, dried over Na₂SO₄, and concentrated. The residue was purified by silica gel column chromatography (hexane:ethyl acetate = 10:1), which furnished 2,2-bis{2-[3-(3-phenylprop-2-ynyloxy)prop-1-ynyl]benzyl}malononitrile (**9h**, 2.56 g, 4.39 mmol, 78% yield) as a pale orange oil.

IR (neat) 2849, 2238, 1733, 1488, 1442, 1348, 1243, 1079, 756, 692 cm⁻¹; ¹H NMR (CDCl₃, 300 MHz) δ 7.57–7.48 (m, 4H), 7.48–7.40 (m, 4H), 7.40–7.27 (m, 10H), 4.51 (s, 4H), 4.48 (s, 4H), 3.59 (s, 4H); ¹³C NMR (CDCl₃, 75 MHz) δ 134.0, 133.1, 131.7, 130.4, 129.1, 128.5, 128.2, 123.8, 122.3, 114.8, 90.1, 86.9, 84.5, 84.2, 57.6, 57.2, 40.3, 40.0; HRMS (ESI) calcd for C₄₁H₃₀N₂NaO₂ [M+Na]⁺ 605.2205, found 605.2194.

IV. Enantioselective Synthesis of C₂-Symmetric Spirobipyridine Ligands (Table 1)

General Procedure (Table 1, entry 1). (*R*)-Segphos (6.1 mg, 0.01 mmol) and [Rh(cod)₂]₂BF₄ (4.1 mg, 0.01 mmol) were dissolved in CH₂Cl₂ (1.0 mL) and the mixture was stirred at rt for 5 min. H₂ was introduced to the resulting solution in a Schlenk tube. After stirring at rt for 0.5 h, the resulting solution was concentrated and dissolved in CH₂Cl₂ (0.5 mL). To this solution was added a solution of **9a** (45.8 mg, 0.10 mmol) in CH₂Cl₂ (0.25 mL) at rt and washed the remaining substrate away by using CH₂Cl₂ (0.25 mL). The mixture was stirred at rt for 16 h. The mixture was concentrated and purified by silica gel column chromatography (CH₂Cl₂:ethyl acetate = 100 : 3), which furnished bipyridine (–)-**10a** (45.4 mg, 0.099 mmol, 99% yield, 64% ee) as a colorless solid.

Bipyridine (–)-10a (entry 1, 99% yield, 64% ee).

Mp 212.5–213.5 °C; [α]_D²⁵ –200.7° (*c* 1.06, CHCl₃, 64% ee); IR (neat); 3000, 2848, 1568, 1436, 1100, 784, 710 cm^{–1}; ¹H NMR (CDCl₃, 300 MHz) δ 7.68–7.60 (m, 4H), 7.43–7.27 (m, 6H), 5.35–5.23 (m, 4H), 5.12 (s, 4H), 3.48–3.28 (m, 2H), 3.00–2.80 (m, 4H), 2.45–2.30 (m, 2H); ¹³C NMR (CDCl₃, 75 MHz) δ 168.8, 150.0, 145.7, 139.6, 130.7, 128.5, 128.4, 128.3, 127.6, 73.4, 72.1, 59.5, 38.1, 27.5 HRMS (EI) calcd for C₃₁H₂₆N₂O₂ [M]⁺ 458.5503, found 458.2029.; CHIRALPAK OD-H, hexane:2-PrOH = 70:30, 0.9 mL/min, retention times: 9.5 min (major isomer) and 12.9 min (minor isomer).

Bipyridine (*S*)-(–)-10b (entry 2, 89% yield, 71% ee).

Reaction Time 24 h (catalyst 5 mol %); colorless solid; Mp >250 °C; [α]_D²⁵ –275.5° (*c* 0.668, CHCl₃, 71% ee); IR (neat) 2940, 2850, 1489, 1398, 1088, 1052, 835, 755 cm^{–1}; ¹H NMR (CDCl₃, 300 MHz) δ 7.58–7.53 (m, 4H), 7.38–7.32 (m, 4H), 5.30–5.20 (m, 4H), 5.12

(s, 4H), 3.45–3.30 (m, 2H), 3.05–2.75 (m, 4H), 2.40–2.30 (m, 2H); ^{13}C NMR (CDCl_3 , 75 MHz) δ 168.8, 148.8, 146.0, 137.9, 134.3, 130.7, 128.9, 128.8, 128.6, 73.2, 72.0, 59.4, 38.1, 27.5; HRMS (ESI) calcd for $\text{C}_{31}\text{H}_{24}\text{Cl}_2\text{N}_2\text{NaO}_2$ $[\text{M}+\text{Na}]^+$ 549.1113, found 549.1065; CHIRALPAK AD, hexane:2-PrOH = 75:25, 1.0 mL/min, retention times: 6.6 min (major isomer) and 8.4 min (minor isomer).

Bipyridine (–)-10c (entry 2, 85% yield, 62% ee).

Reaction Time 24 h (catalyst 5 mol %); colorless solid; Mp 170.0–171.0 °C; $[\alpha]_D^{25}$ –199.0° (*c* 0.680, CHCl_3 , 62% ee); IR (neat) 2940, 2830, 1606, 1513, 1405, 1250, 1034, 837, 754 cm^{-1} ; ^1H NMR (CDCl_3 , 300 MHz) δ 7.60 (d, *J* = 8.7 Hz, 4H), 6.92 (d, *J* = 8.7 Hz, 4H), 5.34–5.20 (m, 4H), 5.11 (s, 4H), 3.82 (s, 6H), 3.45–3.32 (m, 2H), 3.00–2.80 (m, 4H), 2.40–2.30 (m, 2H); ^{13}C NMR (CDCl_3 , 75 MHz) δ 168.7, 159.8, 149.7, 145.6, 132.3, 129.9, 128.9, 127.7, 113.8, 73.5, 72.1, 59.5, 55.3, 38.1, 27.5; HRMS (ESI) calcd for $\text{C}_{33}\text{H}_{30}\text{N}_2\text{NaO}_4$ $[\text{M}+\text{Na}]^+$ 541.2103, found 541.2117; CHIRALPAK OD-H, hexane:2-PrOH = 70:30, 0.8 mL/min, retention times: 13.7 min (major isomer) and 33.5 min (minor isomer).

Bipyridine (–)-10d (entry 4, 98% yield, 49% ee).

Reaction Time 16 h; colorless solid; Mp 188.0–189.0 °C; $[\alpha]_D^{25}$ –8.5° (*c* 0.434, CHCl_3 , 49% ee); IR (neat) 2980, 2848, 1591, 1408, 1100, 1049, 898, 754 cm^{-1} ; ^1H NMR (CDCl_3 , 300 MHz) δ 5.13–5.00 (m, 4H), 5.06 (s, 4H), 3.52–3.02 (m, 2H), 2.90–2.75 (m, 2H), 2.58–2.43 (m, 2H), 2.33 (s, 6H), 2.58–2.43 (m, 2H); ^{13}C NMR (CDCl_3 , 75 MHz) δ 167.9, 149.9, 144.2, 131.3, 127.4, 72.7, 72.6, 59.7, 38.0, 26.9, 22.2; HRMS (EI) calcd for $\text{C}_{21}\text{H}_{22}\text{N}_2\text{O}_2$ $[\text{M}]^+$ 334.1681, found 334.1658; CHIRALPAK AD-H, hexane:2-PrOH = 97:3, 1.0 mL/min, retention times: 15.8 min (major isomer) and 13.2 min (minor isomer).

Bipyridine (+)-10e (entry 5, 70% yield, 47% ee).

Reaction Time 24 h; colorless solid; Mp 160.5–161.5 °C; $[\alpha]_D^{25} +33.9^\circ$ (*c* 0.112, CHCl₃, 47% ee); IR (neat) 2980, 2850, 1559, 1457, 1048, 896, 753 cm⁻¹; ¹H NMR (CDCl₃, 300 MHz) δ 8.28 (s, 2H), 5.16–5.08 (m, 4H), 5.01 (s, 4H), 3.23–3.07 (m, 2H), 3.05–2.85 (m, 2H), 2.71–2.58 (m, 2H), 2.43–2.23 (m, 2H); ¹³C NMR (CDCl₃, 75 MHz) δ 168.0, 145.1, 141.4, 133.6, 130.0, 72.1, 72.0, 59.6, 38.1, 27.2; HRMS (EI) calcd for C₁₉H₁₈N₂O₂ [M]⁺ 306.1368, found 306.1365; CHIRALPAK AD-H, hexane:2-PrOH = 90:10, 1.0 mL/min, retention times: 21.2 min (major isomer) and 20.2 min (minor isomer).

Bipyridine (–)-10f (entry 6, 90% yield, 45% ee).

Reaction Time 24 h; colorless solid; Mp 193.5–194.5 °C; $[\alpha]_D^{25} -73.9^\circ$ (*c* 0.214, CHCl₃, 45% ee); IR (neat) 2930, 2840, 1559, 1416, 1055, 911, 756 cm⁻¹; ¹H NMR (CDCl₃, 300 MHz) δ 7.62–7.46 (m, 4H), 7.36–7.26 (m, 6H), 5.33 (s, 4H), 5.10 (s, 4H), 2.98–2.77 (m, 2H), 2.76–2.65 (m, 4H), 2.24–2.05 (m, 4H), 2.04–1.82 (m, 2H); ¹³C NMR (CDCl₃, 75 MHz) δ 162.5, 148.1, 147.4, 139.7, 128.7, 128.3, 128.1, 127.5, 125.0, 73.9, 72.4, 46.6, 36.7, 26.5, 18.5; HRMS (ESI) calcd for C₃₃H₃₀N₂NaO₂ [M+Na]⁺ 509.2205, found 509.2198; CHIRALPAK AD-H, hexane:2-PrOH = 97:3, 1.0 mL/min, retention times: 12.0 min (major isomer) and 14.2 min (minor isomer).

Bipyridine (+)-10g (entry 7, 98% yield, 40% ee).

Reaction Time 24 h; colorless amorphous; $[\alpha]_D^{25} +15.6^\circ$ (*c* 0.674, CHCl₃, 40% ee); IR (neat) 2945, 2846, 1589, 1441, 1422, 1042, 900, 754 cm⁻¹; ¹H NMR (CDCl₃, 300 MHz) δ 5.05 (s, 8H), 2.84–2.74 (m, 2H), 2.64–2.38 (m, 4H), 2.20 (s, 6H), 2.06–1.78 (m, 6H); ¹³C NMR (CDCl₃, 75 MHz) δ 162.2, 147.4, 136.4, 129.5, 123.4, 73.1, 72.9, 46.3, 36.9, 26.4, 22.2, 18.4; HRMS (EI) calcd for C₂₃H₂₆N₂O₂ [M]⁺ 362.1994, found 362.1992; CHIRALPAK AD-H and CHIRALCEL OD-H, hexane:2-PrOH = 97:3, 1.0 mL/min,

retention times: 12.0 min (major isomer) and 14.2 min (minor isomer).

Bipyridine (+)-10h (entry 8, 99% yield, 18% ee).

Reaction Time 24 h; colorless solid; Mp >250 °C; $[\alpha]_D^{25} +19.2^\circ$ (c 0.534, CHCl₃, 18% ee); IR (neat) 3024, 2960, 2840, 1559, 1403, 1057, 754, 696 cm⁻¹; ¹H NMR (CDCl₃, 300 MHz) δ 7.54–7.47 (m, 4H), 7.38–7.26 (m, 10H), 7.27–7.18 (m, 4H), 5.48 (s, 4H), 5.40 (d, J = 12.3 Hz, 2H), 5.24 (d, J = 12.3 Hz, 2H), 3.98 (d, J = 15.6 Hz, 2H), 3.13 (d, J = 15.6 Hz, 2H); ¹³C NMR (CDCl₃, 75 MHz) δ 158.7, 147.8, 145.8, 139.0, 136.2, 133.0, 131.4, 129.0, 128.4, 128.3, 128.1, 127.7, 126.9, 125.5, 124.3, 73.8, 72.8, 45.8, 39.7; HRMS (ESI) calcd for C₄₁H₃₀N₂O₂ [M]⁺ 605.2205, found 605.2251; CHIRALPAK AD-H, hexane:2-PrOH = 85:15, 1.0 mL/min, retention times: 9.6 min (major isomer) and 10.9 min (minor isomer).

V. References

- 1) Pettus, T. R. R.; Schlessinger, R. H. *Synth. Commun.* **2002**, 32, 3019.
- 2) Bonaga, L. V. R.; Zhang, H.-C.; Maryanoff, B. E. *Chem. Commun.* **2004**, 21, 2394.

2,2-Dipent-3-ynylmalononitrile (4)

2,2-Bis[5-(3-phenylprop-2-ynyloxy)pent-3-ynyl]malononitrile (9a)

2,2-Bis{5-[3-(4-chlorophenyl)prop-2-ynoxy]pent-3-ynyl}malononitrile (9b)

2,2-Bis{5-[3-(4-methoxyphenyl)prop-2-ynyl]pent-3-ynyl}malononitrile (9c)

2,2-Bis[5-(but-2-ynyloxy)pent-3-ynyl]malononitrile (9d)

2,2-Bis[5-(prop-2-ynyloxy)pent-3-ynyl]malononitrile (9e)

2,2-Bis[6-(3-phenylprop-2-ynyloxy)hex-4-ynyl]malononitrile (9f)

2,2-Bis[6-(but-2-ynyloxy)hex-4-ynyl]malononitrile (9g)

2,2-Bis{2-[3-(3-phenylprop-2-ynyloxy)prop-1-ynyl]benzyl}malononitrile (9h)

Bipyridine (–)-10a

Bipyridine (S)-(-)-10b

Bipyridine (–)-10c

Bipyridine (–)-10d

Bipyridine (+)-10e

Bipyridine (–)-10f

Bipyridine (+)-10g

Bipyridine (+)-10h