Supporting Information

Rhodium-Catalyzed [2 + 2 + 2] Cyclotrimerization in an Aqueous–Organic Biphasic System

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Instrumentation and Materials

^1H NMR (300 MHz) and ^{13}C NMR (75.3 MHz) spectra were taken on Varian GEMINI 300 and Mercury 300 spectrometers. ^1H NMR and ^{13}C NMR spectra were obtained in CDCl_3 with tetramethylsilane as an internal standard. IR spectra were recorded on JASCO IR-810 and SHIMADZU FTIR-8200PC spectrometers. Mass spectra were determined on a JEOL Mstation 700 spectrometer. Silica gel (Wakogel 200 mesh) was used for column chromatography. The analyses were carried out at the Elemental Analysis Center of Kyoto University. Pure water was obtained with Millipore Direct-Q system. Degassed water was used for macrocyclization. Pure water was degassed by bubbling of N_2 with sonication for 30 min before use. Unless otherwise noted, materials obtained from commercial suppliers were used without further purification.

General Procedure

Macrocyclization of triynes

In a 100-mL flask, $[\text{RhCl}(\text{cod})]_2$ (6.2 mg, 0.0125 mmol) and trisodium salt of tris(*m*-sulfonatophenyl)phosphine (tppts, 45.5 mg, 0.08 mmol) were placed under argon atmosphere. Degassed pure water (10 mL) was introduced, and the mixture was stirred vigorously at 75 °C for about an hour until the solution was homogeneous. The solution was cooled to room temperature and then diluted with 40 mL of pure water. Without stirring, diethyl ether (5 mL) was added gently. The system became biphasic. A solution of 4,10-dioxatrideca-1,6,12-triyne (**1b**, 88.1 mg, 0.5 mmol) in ether (5 mL) was added via a syringe to the diethyl ether phase. After stirring vigorously for 10 h, the mixture was extracted with hexane/ethyl acetate (1 : 1). The organic extracts were dried through a short pad of silica gel on Na_2SO_3 layer. Concentration followed by purification of the residual oil afforded 1,3,6,8,9-pentahydro-2,7-dioxacyclohexa[*e*]indene (**2b**, 81.8 mg, 0.47 mmol) in 93% yield.

Selective Cross-Annulation

In a 30-mL flask, $[\text{RhCl}(\text{cod})]_2$ (6.2 mg, 0.0125 mmol) and tppts (45.5 mg, 0.08 mmol) were placed under argon atmosphere. Pure water (9 mL) was introduced, and the mixture was stirred vigorously at 75 °C for an hour. A yellow clear solution was obtained. The solution was cooled to room temperature and then NaCl (58.4 mg, 1.0 mmol) and HCl aq. (1 mL, 1.0 M) were introduced. Propargyl alcohol (0.09 mL, 1.5 mmol) was dropped, and the mixture was stirred for 5 min. Without stirring, diethyl ether (10 mL) was introduced gently and the system became biphasic. Dipropargyl ether (0.1 mL, 1.0 mmol) was added with a syringe to the diethyl ether phase. After stirring vigorously for 24 h, the mixture was extracted with ethyl acetate. The organic extracts were dried through a short pad of silica gel on Na_2SO_3 layer. Concentration followed by silica gel column purification provided 5-hydroxymethyl-1,3-dihydroisobenzofuran (**4a**, 120 mg, 0.80 mmol) in 80% yield as a white solid.

Compound Data

1,3,6,8,9,10-Hexahydro-2,7-dioxacyclohepta[*e*]indene (**2c**):

White solid, Mp 84 °C, IR (nujol) 2853, 1364, 1103, 1084, 1057, 1030 cm^{-1} ; ^1H NMR (CDCl_3) δ 1.80–1.88 (m, 2H), 2.83–2.87 (m, 2H), 4.04–4.07 (m, 2H), 4.67 (s, 2H), 5.13 (s, 4H), 7.00 (d, $J = 7.5$ Hz, 1H), 7.09 (d, $J = 7.5$ Hz, 1H); ^{13}C NMR (CDCl_3) δ 29.65, 31.23, 72.99, 74.15, 74.37, 75.45, 118.22, 128.17, 135.80, 138.01, 138.64, 139.49. Found: C, 75.47; H, 7.40 %. Calcd for $\text{C}_{12}\text{H}_{14}\text{O}_2$: C, 75.76; H, 7.42%.

1,3,6,8,9,10,11-Heptahydro-2,7-dioxacycloocta[*e*]indene (**2d**):

White solid, Mp 50 °C, IR (nujol) 2856, 1366, 1277, 1234, 1163, 1092, 1049, 1032, 903, 878 cm⁻¹; ¹H NMR (CDCl₃) δ 1.59–1.66 (m, 2H), 1.69–1.78 (m, 2H), 2.88–2.92 (m, 2H), 3.69–3.72 (m, 2H), 4.75 (s, 2H), 5.14 (s, 4H), 7.05 (d, *J* = 7.5 Hz, 1H), 7.11 (d, *J* = 7.5 Hz, 1H); ¹³C NMR (CDCl₃) δ 27.18, 27.47, 28.41, 69.48, 70.14, 72.96, 74.15, 118.56, 128.36, 134.19, 136.64, 138.47, 138.61. Found: C, 76.30; H, 7.90%. Calcd for C₁₃H₁₆O₂: C, 76.44; H, 8.00%.

1,3,6,8,9,10,11,12-Octahydro-2,7-dioxacyclonona[*e*]indene (2e):

IR (neat) 2918, 2856, 1443, 1358, 1086, 1057, 908, 816 cm⁻¹; ¹H NMR (CDCl₃) δ 1.29–1.37 (m, 2H), 1.47–1.55 (m, 2H), 1.74–1.82 (m, 2H), 2.91 (t, *J* = 6.6 Hz, 2H), 3.60 (t, *J* = 5.4 Hz, 2H), 4.70 (s, 2H), 5.12 (s, 4H), 7.00 (d, *J* = 7.5 Hz, 1H), 7.05 (d, *J* = 7.5 Hz, 1H); ¹³C NMR (CDCl₃) δ 24.51, 27.25, 28.85, 30.08, 70.05, 72.72, 73.00, 73.75, 117.87, 128.84, 135.75, 137.05, 139.04, 139.21. Found: C, 76.73; H, 8.34%. Calcd for C₁₄H₁₈O₂: C, 77.03; H, 8.31%.

1,3,6,8,9,10,11,12,13-Nonahydro-2,7-dioxacyclodeca[*e*]indene (2f):

White solid, Mp 44 °C, IR (nujol) 2855, 1352, 1101, 1055, 907, 810 cm⁻¹; ¹H NMR (CDCl₃) δ 1.35–1.43 (m, 2H), 1.52–1.78 (m, 6H), 2.70 (t, *J* = 6.9 Hz, 2H), 3.64 (t, *J* = 5.3 Hz, 2H), 4.60 (s, 2H), 5.11 (s, 2H), 5.15 (s, 2H), 7.01 (d, *J* = 7.5 Hz, 1H), 7.12 (d, *J* = 7.5 Hz, 1H); ¹³C NMR (CDCl₃) δ 24.70, 24.89, 27.51, 27.82, 28.12, 70.53, 72.83, 73.09, 73.70, 117.71, 129.24, 135.98, 136.75, 139.00, 139.15. Found: C, 77.27; H, 8.52%. Calcd for C₁₅H₂₀O₂: C, 77.55; H, 8.68%.

1-Methyl-3,6,8,9,10-pentahydro-2,7-dioxacyclohepta[*e*]indene (2g):

IR (neat) 2855, 1356, 1084, 1067, 1011, 860 cm⁻¹; ¹H NMR (CDCl₃) δ 1.45 (d, *J* = 6.3 Hz, 3H),

1.80–1.87 (m, 2H), 2.91–2.95 (m, 2H), 3.99–4.13 (m, 2H), 4.67 (sd, $J = 1.5$ Hz, 2H), 5.01 (d, $J = 12.4$ Hz, 1H), 5.16 (dd, $J = 12.4$ Hz, 2.1 Hz, 1H), 5.46 (qd, $J = 6.2$ Hz, 2.1 Hz, 1H), 6.98 (d, $J = 7.6$ Hz, 1H), 7.10 (d, $J = 7.6$ Hz, 1H); ^{13}C NMR (CDCl_3) δ 22.01, 29.67, 30.44, 72.03, 74.41, 75.38, 79.75, 118.33, 128.38, 135.94, 138.62, 139.74, 142.10. Found: C, 76.17; H, 7.69%. Calcd for $\text{C}_{13}\text{H}_{16}\text{O}_2$: C, 76.44; H, 7.90%.

1,3,6,8,9,10,11,12,13,14-Decahydro-2,7-dioxacycloundeca[*e*]indene (2h):

White solid, Mp 100 °C, IR (nujol) 2855, 1352, 1107, 1076, 1053, 903 cm^{-1} ; ^1H NMR (CDCl_3) 1.40–1.50 (m, 6H), 1.62–1.73 (m, 4H), 2.53 (t, $J = 7.5$ Hz, 2H) 3.56 (t, $J = 5.6$ Hz, 2H), 4.46 (s, 2H), 5.11 (s, 2H), 5.16 (s, 2H), 7.00 (d, $J = 7.5$ Hz, 1H), 7.15 (d, $J = 7.5$ Hz, 1H); ^{13}C NMR (CDCl_3) 20.30, 21.75, 25.82, 26.10, 26.50, 27.24, 68.29, 72.72, 72.82, 73.76, 117.76, 129.77, 134.75, 137.85, 138.96, 139.42. HRMS (m/z) Found: 246.1615. Calcd for $\text{C}_{16}\text{H}_{22}\text{O}_2$: 246.1620.

3,14-Dioxatricyclo[9.6.1.0^{12,16}]octadeca-1(18),11,16-triene (3h):

IR (neat) 2856, 1769, 1601, 1454, 1356, 1111, 1084, 1049, 905 cm^{-1} ; ^1H NMR (CDCl_3) δ 0.74–0.84 (m, 2H), 1.34–1.62 (m, 6H), 1.78–1.87 (m, 2H), 2.62–2.66 (m, 2H), 3.23 (t, $J = 5.6$ Hz, 2H), 4.56 (s, 2H), 5.11 (dd, $J = 7.8$ Hz, 1.8 Hz, 4H), 6.88 (s, 1H), 7.55 (s, 1H); ^{13}C NMR (CDCl_3) 22.85, 23.30, 24.86, 28.40, 29.21, 33.13, 64.47, 71.96, 72.75, 73.94, 118.22, 126.16, 136.19, 137.05, 138.45, 139.19. HRMS (m/z) Found: 246.1615. Calcd for $\text{C}_{16}\text{H}_{22}\text{O}_2$: 246.1620.

1,3,6,8,9,10,11,12,13,15-Decahydro-2,7,14-trioxacyclododeca[*e*]indene (2i):

White solid, Mp 81–82 °C, IR (nujol) 2849, 1362, 1244, 1103, 1065, 1026, 935, 899, 826 cm^{-1} ; ^1H

NMR (CDCl₃) δ 1.43–1.53 (m, 4H), 1.55–1.65 (m, 4H), 3.54–3.61 (m, 4H), 4.51 (s, 2H), 4.56 (s, 2H), 5.12 (s, 2H), 5.21 (s, 2H), 7.14 (d, J = 7.8 Hz, 1H), 7.22 (d, J = 7.8 Hz, 1H); ¹³C NMR (CDCl₃) δ 22.25, 22.34, 27.70, 27.91, 67.94, 68.54, 68.69, 71.28, 72.89, 73.70, 120.21, 130.25, 131.12, 136.03, 139.30, 140.18. HRMS (m/z) Found: 262.1574. Calcd for C₁₆H₂₂O₃: 262.1569.

3,10,15-Trioxatricyclo[10.6.1.0^{13,17}]nonadeca-1(19),12,17-triene (3i):

White solid, Mp 96–98 °C, IR (nujol) 2858, 1365, 1105, 876 cm⁻¹; ¹H NMR (CDCl₃) δ 1.43–1.66 (m, 8H), 3.58 (t, J = 5.1 Hz, 2H), 3.64 (t, J = 5.1 Hz, 2H), 4.48 (s, 2H), 4.58 (s, 2H), 5.06 (s, 2H), 5.10 (s, 2H), 6.95 (s, 1H), 7.61 (s, 1H); ¹³C NMR (CDCl₃) δ 23.70, 23.80, 29.53, 68.51, 68.55, 69.03, 71.68, 72.01, 73.56, 118.24, 123.85, 133.35, 135.51, 139.08, 139.78. HRMS (m/z) Found: 262.1560. Calcd for C₁₆H₂₂O₃: 262.1569.

5-(2-Hydroxyethyl)-1,3-dihydroisobenzofuran (4b):

IR (neat) 3600–3100, 3018, 2858, 1902, 1763, 1622, 1587, 1435, 1367, 1047, 899, 820 cm⁻¹; ¹H NMR (CDCl₃) δ 1.57 (bs, 1H), 2.89 (t, J = 6.6 Hz, 2H), 3.87 (t, J = 6.6 Hz, 2H), 5.09 (s, 4H), 7.10–7.21(m, 3H); ¹³C NMR (CDCl₃) δ 39.03, 63.74, 73.38, 73.41, 121.00, 121.40, 127.97, 137.18, 137.63, 139.49. Found: C, 73.38; H, 7.57%. Calcd for C₁₀H₁₂O₂: C, 73.15; H, 7.37%.

5-(3-Hydroxypropyl)-1,3-dihydroisobenzofuran (4c):

IR (neat) 3600–3100, 2858, 1622, 1587, 1493, 1433, 1367, 1321, 1267, 1140, 1042, 901 cm⁻¹; ¹H NMR (CDCl₃) δ 1.33 (bs, 1H), 1.85–1.94 (m, 2H), 2.74 (t, J = 7.8 Hz, 2H), 3.69 (t, J = 6.3 Hz, 2H), 5.09 (s, 4H), 7.08–7.17 (m, 3H); ¹³C NMR (CDCl₃) δ 31.98, 34.52, 62.19, 73.41, 73.46, 120.72, 120.77,

127.40, 136.56, 139.32, 140.95. Found: C, 74.08; H, 7.93%. Calcd for $C_{11}H_{14}O_2$: C, 74.13; H, 7.92%.

5-Hydroxymethyl-2-(*p*-toluenesulfonyl)-1,3-dihydroisoindole (4d):

White solid, Mp 140–142 °C, IR (nujol) 3500–3000, 2855, 1342, 1159, 1101, 1018, 818 cm^{-1} ; 1H NMR ($CDCl_3$) δ 1.99 (bs, 1H), 2.40 (s, 3H), 4.57 (s, 4H), 4.65 (s, 2H), 7.13 (d, $J = 7.5$ Hz, 1H), 7.19 (s, 1H), 7.22 (d, $J = 7.5$ Hz, 1H), 7.31 (d, $J = 8.1$ Hz, 2H), 7.75 (d, $J = 8.1$ Hz, 2H); ^{13}C NMR ($CDCl_3$) 21.60, 53.52, 53.61, 64.83, 121.02, 122.49, 126.40, 127.40, 129.67, 133.38, 135.18, 136.28, 140.69, 143.54. Found: C, 62.96; H, 5.66%. Calcd for $C_{16}H_{17}SO_3N$: C, 63.35; H, 5.65%.