

Supporting Information

Rational Design of a Metallo-catalytic Cavitand for Regio-selective Hydration of Specific Alkynes

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1. General Information.

All reactions sensitive to air or moisture were carried out under an argon or an nitrogen atmosphere and anhydrous conditions unless otherwise noted. Dry solvents were purchased and used without further purification and dehydration. All reagents were purchased and used without further purification. Analytical thin layer chromatography was carried out on Merck silica 60F₂₅₄. Column chromatography was carried out with silica gel 60_N (Kanto Chemical Co.). LRMS were reported on the basis of DI (GC-2010 Plus; Shimadzu). HRMS were reported on the basis of TOF (time of flight)-MS (MADI-TOF or LCMS-IT-TOF; Shimadzu), and DART (Direct Analysis in Real Time)-MS. ¹H and ¹³C NMR spectra were recorded with a 5 mm QNP probe at 400 MHz and 100 MHz, respectively. Chemical shifts are reported in δ (ppm) with reference to residual solvent signals [¹H NMR: CHCl₃ (7.26), C₇H₈ (2.08), C₆H₆ (7.16), CH₂Cl₂ (5.32); ¹³C NMR: CDCl₃ (77.0)]. Signal patterns are indicated as s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet; br, broad.

2. Procedure for synthesis of **1** and **1**•AuCl (Scheme 1).

Phosphoramidate 1: Under an argon atmosphere, to the two-neck flask charged with a solution of the starting parent bis-phosphoramidite molecule in Scheme 1 (600 mg, 0.4 mmol) in dry toluene (16 mL) was added a solution of mCPBA (92 mg, 0.4 mmol) in toluene (8 mL) dropwise over 10 min at 0 °C. After 30 min at 0 °C, the reaction was quenched by addition of satd. aq. NaHCO₃ (8 mL) over 10 min. The organic layer was washed with water (20 mL x 3), brine (20 mL), and dried over Na₂SO₄, and concentrated in vacuo to give a crude of 585 mg as a white solid material. Purification by silica-gel column chromatography (toluene/EtOAc = 9/1 ~ 4/1) afforded **1** of 147 mg as yellowish white solid materials (24%). Further reprecipitation from CH₂Cl₂/CH₃OH (1/8) whitened **1** in 134 mg (22%). For data of **1**: ¹H NMR (400 MHz, CDCl₃) 7.83-7.78 (m, 4H), 7.51-7.50 (m, 4H),

7.41 (s, 2H), 7.33 (s, 2H), 7.22 (s, 2H), 7.14 (s, 2H), 5.72 (t, $J = 8.1$ Hz, 2H), 4.60-4.56 (m, 2H), 2.91 (d, $^3J_{\text{PH}} = 10.9$ Hz, 6H), 2.84 (d, $^3J_{\text{PH}} = 10.5$ Hz, 6H), 2.28-2.22 (m, 8H), 1.45-1.28 (m, 72H), 0.90-0.87 (m, 12H) ppm; ^1H NMR (400 MHz, CD_2Cl_2) 7.87 (m, 4H), 7.58 (dd, $J = 6.4, 3.4$ Hz, 4H), 7.39 (s, 2H), 7.30 (s, 2H), 7.27 (s, 2H), 7.25 (s, 2H), 5.68 (t, $J = 8.2$ Hz, 2H), 4.64-4.62 (m, 2H), 2.93 (d, $^3J_{\text{PH}} = 10.9$ Hz, 6H), 2.86 (d, $^3J_{\text{PH}} = 10.4$ Hz, 6H), 2.35-2.28 (m, 8H), 1.46-1.31 (m, 72H), 0.93-0.88 (m, 12H) ppm; ^{13}C NMR (100 MHz, CDCl_3) 153.2, 153.1, 152.6 (d, $J_{\text{CP}} = 1.4$ Hz), 152.4, 150.3 (d, $J_{\text{CP}} = 4.8$ Hz), 146.6 (d, $J_{\text{CP}} = 8.3$ Hz), 140.1 (two peaks are overlapped), 137.3 (d, $J_{\text{CP}} = 2.2$ Hz), 136.7 (d, $J_{\text{CP}} = 2.1$ Hz), 134.4 (d, $J_{\text{CP}} = 3.6$ Hz), 134.1, 129.7, 129.6, 128.5, 128.2, 123.2, 122.5, 117.7, 117.3 (d, $J_{\text{CP}} = 4.1$ Hz), 37.2 (d, $J_{\text{CP}} = 3.1$ Hz), 36.2, 36.0, 35.4 (d, $J_{\text{CP}} = 18.6$ Hz), 34.3, 32.3 (many peaks are overlapped), 32.0, 31.9, 31.4, 30.1 (many peaks are overlapped), 29.8 (many peaks are overlapped), 28.4, 28.3, 23.1 (many peaks are overlapped), 14.5 (many peaks are overlapped) ppm; ^{31}P NMR (162 MHz, CDCl_3) 140.6, -1.5 ppm; ^{31}P NMR (162 MHz, CD_2Cl_2) 140.2, -1.6 ppm; ^{31}P NMR (162 MHz, toluene- d_8) 137.7, -3.8 ppm; MS (MALDI-TOF) m/z : 1521 $[\text{M} + \text{H}_2]^+$. IR (neat): 2922, 2851, 1482, 1271, 1119, 1068, 868 cm^{-1} . HRMS (MALDI-TOF) calcd for $\text{C}_{92}\text{H}_{124}\text{N}_6\text{O}_9\text{P}_2\text{H}_2$: 1520.9056 $[\text{M} + \text{H}_2]^+$, Found : 1520.9120; Anal. Calcd for $\text{C}_{92}\text{H}_{124}\text{N}_6\text{O}_9\text{P}_2$: C, 72.70; H, 8.22; N, 5.53. Found: C, 72.66; H, 8.20; N, 5.44.

Au complex **1**•AuCl: Under an argon atmosphere, to a solution of **1** (148 mg, 0.1 mmol) in toluene (1 mL) at ambient temperature was added AuCl•S(CH₃)₂ (30 mg, 0.12 mmol) as a one portion of solid materials. After stirring for 2 h, the volatiles were evaporated off. The residue was purified through a short-plugged silica-gel column chromatography (eluent, hexane/EtOAc = 1/1) to yield white solid materials of 159 mg (93%). For data of **1**•AuCl: ^1H NMR (400 MHz, CDCl_3) 8.11 (d, $J = 8.4$ Hz, 2H), 7.90 (s, 2H), 7.86 (s, 2H), 7.62 (d, $J = 8.4$ Hz, 2H), 7.50 (s, 2H), 7.46 (s, 2H), 7.24 (dd, $J = 8.4, 8.4$ Hz, 2H), 6.04 (t, $J = 8.0$ Hz, 2H),

4.85 (t, $J = 7.8$ Hz, 1H), 4.74 (t, $J = 8.1$ Hz, 1H), 2.64 (d, $^3J_{\text{PH}} = 12.7$ Hz, 6H), 2.56 (d, $^3J_{\text{PH}} = 10.5$ Hz, 6H), 2.35-2.33 (m, 8H), 1.43-1.29 (m, 72H), 0.91-0.88 (m, 12H) ppm; ^1H NMR (400 MHz, toluene- d_8) 7.94 (dd, $J = 7.8, 1.9$ Hz, 2H), 7.82 (dd, $J = 7.8, 1.9$ Hz, 2H), 7.57-7.50 (m, 4H), 7.48 (s, 2H), 7.37 (s, 2H), 7.201 (s, 2H), 7.196 (s, 2H), 5.76 (t, $J = 8.1$ Hz, 2H), 4.60-4.56 (m, 1H), 4.56-4.52 (m, 1H), 3.11 (d, $^3J_{\text{PH}} = 12.9$ Hz, 6H), 2.90 (d, $^3J_{\text{PH}} = 10.9$ Hz, 6H), 2.31-2.24 (m, 8H), 1.42-1.27 (m, 72H), 0.92-0.87 (m, 12H) ppm; ^{13}C NMR (100 MHz, CDCl_3) 152.9 (d, $J_{\text{CP}} = 1.9$ Hz), 152.7 (d, $J_{\text{CP}} = 1.4$ Hz), 152.5, 152.4, 146.8 (d, $J_{\text{CP}} = 8.3$ Hz), 146.3 (d, $J_{\text{CP}} = 5.0$ Hz), 140.11, 140.09, 136.7, 135.9, 135.8 (d, $J_{\text{CP}} = 2.6$ Hz), 134.6 (d, $J_{\text{CP}} = 3.6$ Hz), 130.04, 130.01, 129.0, 128.2, 123.3, 122.6, 117.8 (d, $J_{\text{CP}} = 4.1$ Hz), 117.6 (d, $J_{\text{CP}} = 4.1$ Hz), 37.2 (d, $J_{\text{CP}} = 3.3$ Hz), 37.0 (d, $J_{\text{CP}} = 11.4$ Hz), 36.1, 35.8, 34.3, 32.3 (many peaks are overlapped), 32.2, 31.2, 30.7, 30.0 (many peaks are overlapped), 29.8, 29.7 (many peaks are overlapped), 28.3, 28.1, 23.0 (many peaks are overlapped), 14.5 (many peaks are overlapped) ppm; ^{31}P NMR (162 MHz, CDCl_3) 119.8, -2.8 ppm; ^{31}P NMR (162 MHz, toluene- d_8) 113.6, -1.5 ppm; MS (MALDI-TOF) m/z : 1774 [$\text{M} + \text{Na}$] $^+$; IR (neat): 2921, 2851, 1483, 1401, 1328, 1274, 1160, 1138, 1002 cm^{-1} ; HRMS (MALDI-TOF) calcd for $\text{C}_{92}\text{H}_{124}\text{AuClN}_6\text{O}_9\text{P}_2\text{Na}$: 1773.8151 [$\text{M} + \text{Na}$] $^+$, Found: 1773.8221.

3. Representative procedure for hydration reactions for Table 1, entry 1.

Under an argon atmosphere, to a solution of 1-phenyl-1-butyne (0.07 mL, 0.5 mmol) in toluene (1 mL) and H_2O (0.05 mL, 2.5 mmol) was added **1**•AuCl (18 mg, 0.01 mmol). The mixture was stirred at room temperature for 5 min, then AgOTf (3 mg, 0.012 mmol) was added, and the whole system was dipped in the 50 °C-preheated oil-bath. After stirred for 1 h, the reaction was allowed to cool to room temperature. Purification of the reaction mixture through a short-plugged silica-gel column chromatography (toluene only) and the following careful evaporation of the toluene eluent afforded yellow oil of mixtures that consisted of 1-phenyl-2-butanone **5a** (72.5 mg, 98% yield) and 1-phenyl-1-butanone **4a**

(1.5 mg, 2% yield). Data for **5a** was as follows, and that was identical to the commercially available authentic sample; ^1H NMR (400 MHz, CDCl_3) 7.35-7.20 (m, 5H), 3.69 (s, 2H), 2.48 (q, $J = 7.3$ Hz, 2H), 1.03 (t, $J = 7.3$ Hz, 3H) ppm. Data for **4a** was as follows, and that was identical to the commercially available sample; ^1H NMR (400 MHz, CDCl_3) 7.96 (d, $J = 7.8$ Hz, 2H), 7.55 (dd, $J = 7.8$ Hz, $J = 7.8$ Hz, 1H), 7.46 (dd, $J = 7.8$ Hz, $J = 7.8$ Hz, 2H), 2.95 (t, $J = 7.4$ Hz, 1H), 1.78 (qt, $J = 7.4$ Hz, $J = 7.4$ Hz, 2H), 0.99 (t, $J = 7.4$ Hz, 1H) ppm.

4. Representative procedure for hydration reactions for Table 3 (entry 2).

Under an argon atmosphere, to a solution of 2-octyne (0.07 mL, 0.5 mmol) in toluene (1 mL) and H_2O (0.05 mL, 2.5 mmol) was added **1**•AuCl (18 mg, 0.01 mmol). The mixture was stirred at room temperature for 5 min, then AgOTf (3 mg, 0.012 mmol) was added, and the whole system was dipped in the 50 °C-preheated oil-bath. After stirred for 1 h, the reaction was allowed to cool to room temperature. Purification of the reaction mixture through a short-plugged silica-gel column chromatography in which a Pasteur pipette and an eluent of toluene- d_8 were used gave a colorless C_7D_8 solution. The solution was analyzed by ^1H NMR to indicate production of 18% yield of 3-octanone **4h** and 82% yield of 2-octanone **5h**. The ^1H NMR data of **4h** and **5h** were identical to the commercially available authentic sample. The stack of those ^1H NMR spectra is as follows (Figure 1S).

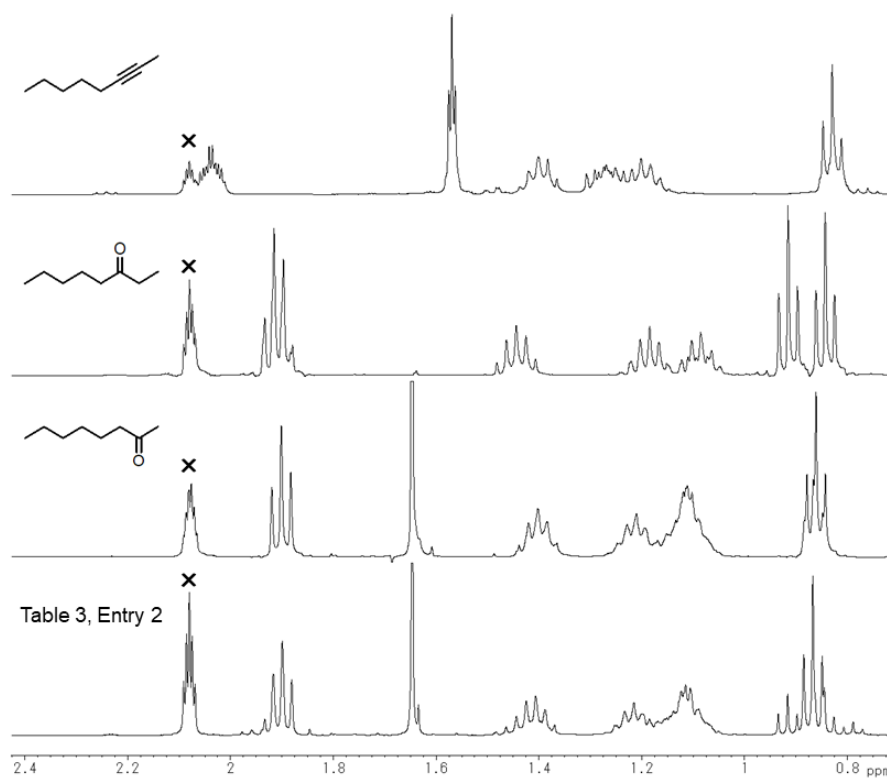
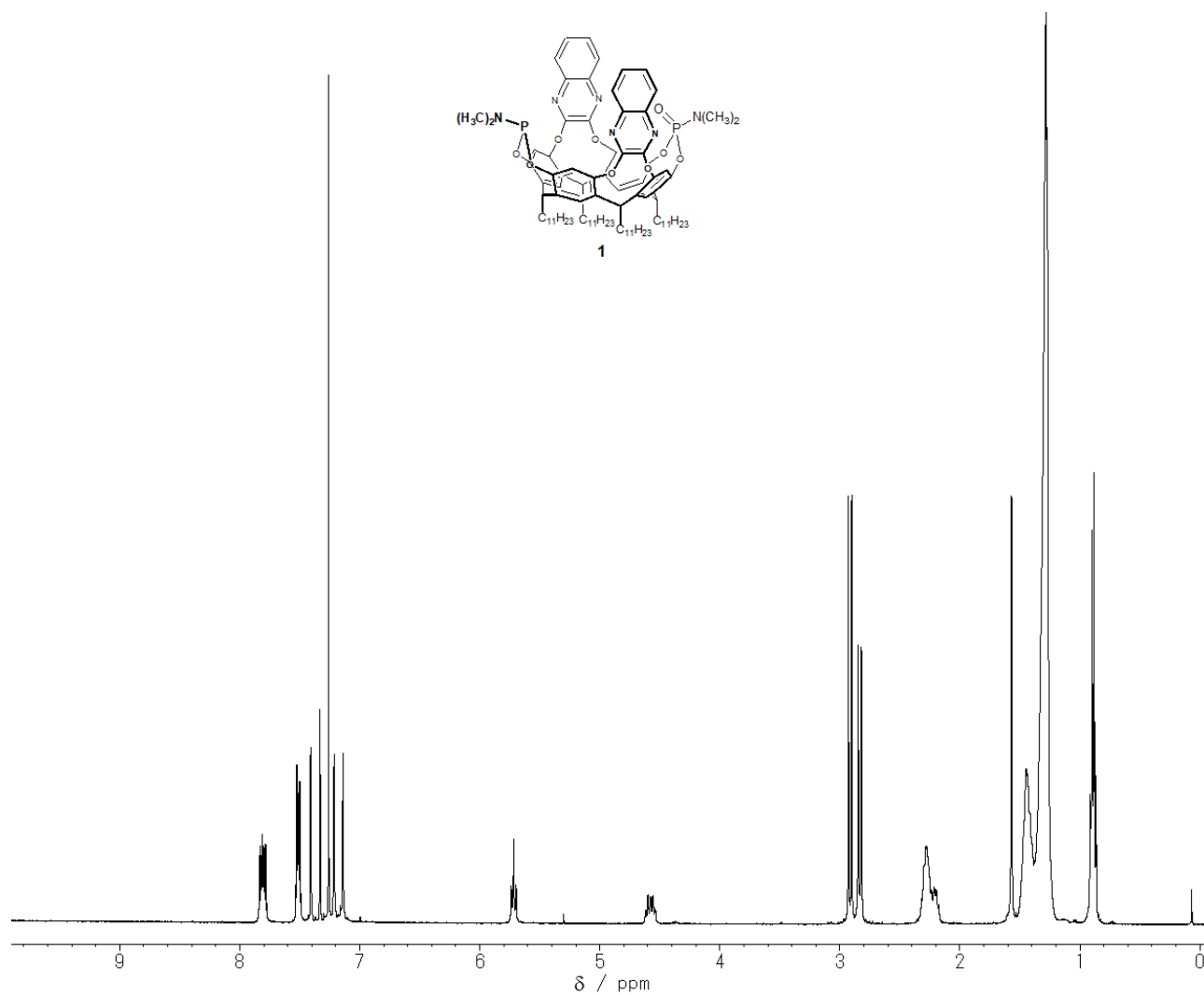


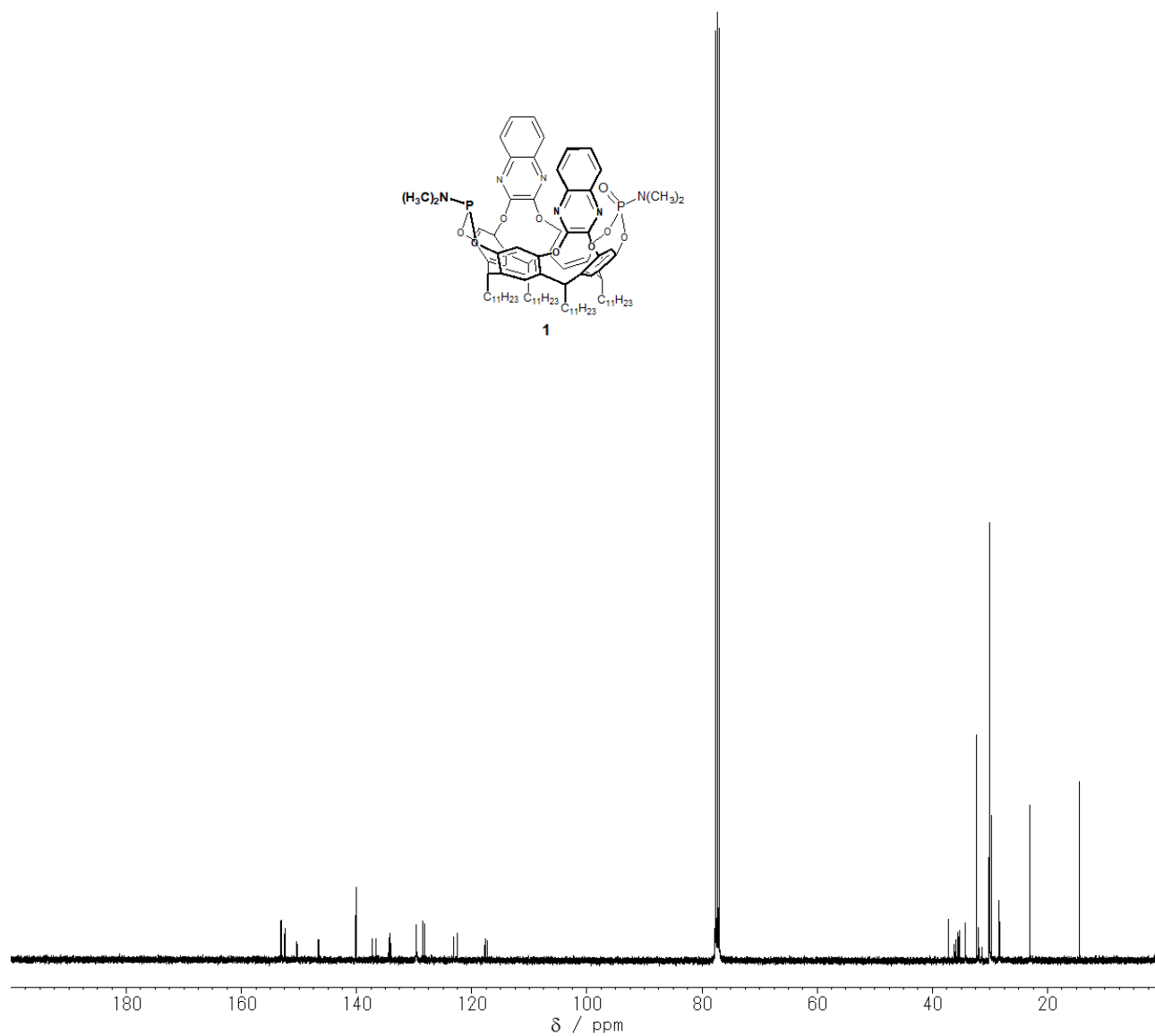
Figure 1S Portions of ^1H NMR spectra (400 MHz, $\text{toluene-}d_8$) for determination of NMR yields in Table 3, entry 2; the top, 2-octyne **3h**; and the second and third from the top, the commercially available authentic samples of 3-octanone **4h** and 2-octanone **5h**; the bottom the product in Table 3, entry 2. The peak labeled with x is a residual proton of $\text{toluene-}d_8$.

5. The ^1H and ^{13}C NMR spectra of all new compounds **1** and **1**•AuCl.

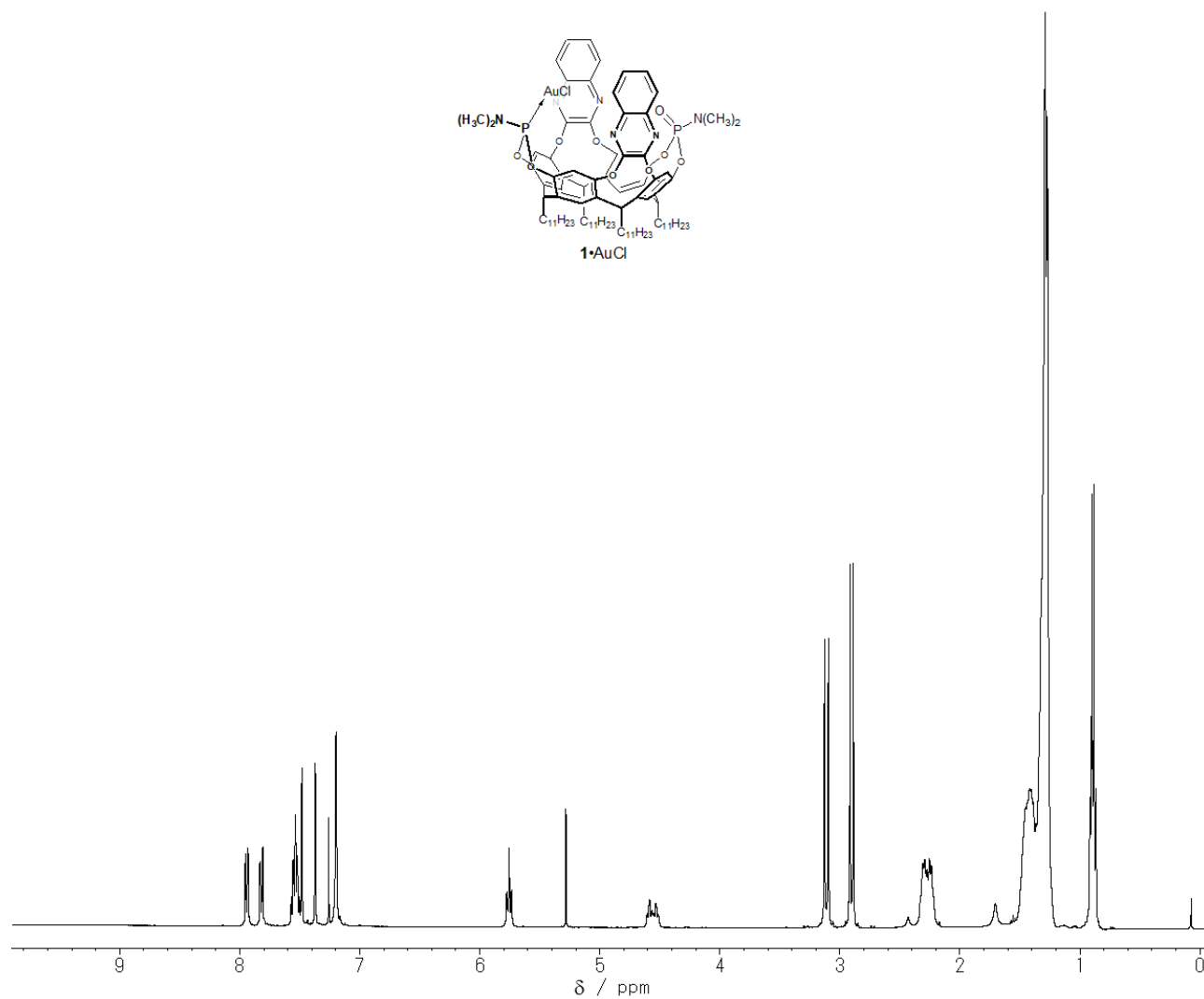
Compound **1** (^1H NMR spectrum in CDCl_3)



Compound **1** (^{13}C NMR spectrum in CDCl_3)



Compound **1**•AuCl (^1H NMR spectrum in CDCl_3)



Compound **1**•AuCl (^{13}C NMR spectrum in CDCl_3)

