Electronic Supporting Information

Ligand-Assisted Nickel-Catalysed sp^3-sp^3 Homocoupling of Unactivated Alkyl Bromides and its Application to the Active Template Synthesis of Rotaxanes

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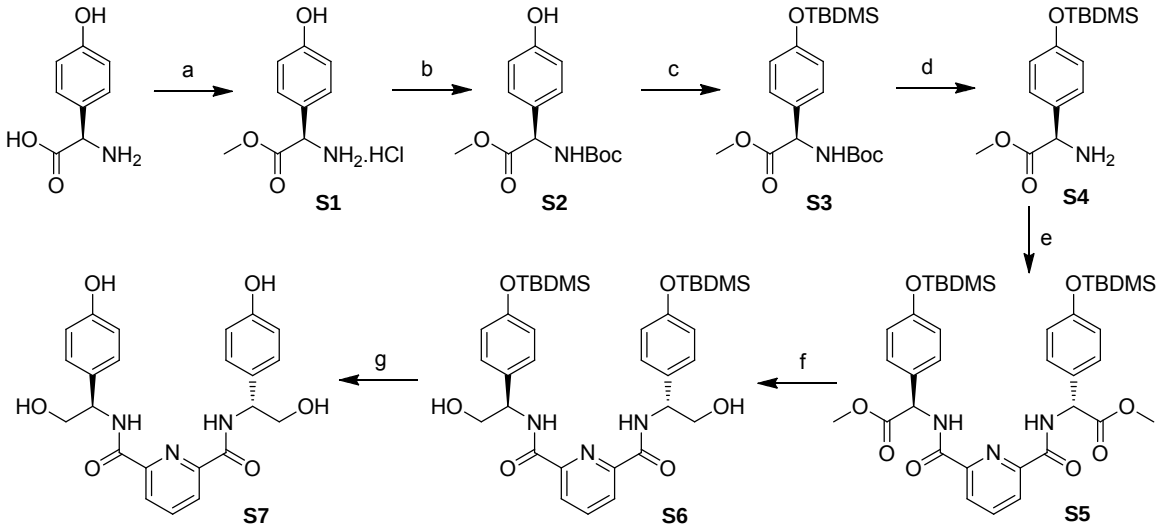
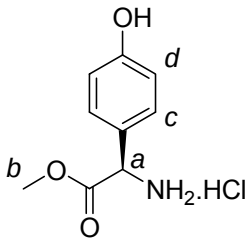
General Experimental Section

Unless stated otherwise, all reagents and solvents were purchased from Aldrich Chemicals and used without further purification, tetrahydrofuran, dichloromethane, and acetonitrile were dried using a solvent purification system manufactured by Innovative Technology, Newburyport, MA, USA. Stoppered alkyl bromide **2**[1], *N*,*N*'-*di*-boc-decamethylendiamine[2] and 1-(1-bromoethyl)-4-methylbenzene[12] were prepared according to a literature procedures. Unless stated otherwise, all reactions were carried out under an atmosphere of nitrogen. Column chromatography was carried out using Silica 60A (particle size 35-70 μm, Fisher, UK) as the stationary phase, and TLC was performed on precoated silica gel plates (0.25 mm thick, 60 F254, Merck, Germany) and observed under UV light. All ^{1}H and ^{13}C NMR spectra were recorded on a Bruker AV 400 instrument. Chemical shifts are reported in parts per million (ppm) from low to high frequency and referenced to the residual solvent resonance. Coupling constants (*J*) are reported in hertz (Hz). Standard abbreviations indicating multiplicity were used as follows: s = singlet, d = doublet, t = triplet, q = quartet, qt = quintet, m = multiplet, br = broad. Melting points (M.p.) were determined using a Sanyo Gallenkamp apparatus and are reported uncorrected. Mass spectrometry data was obtained from the EPSRC National Mass Spectrometry Service Centre (Swansea, U.K.) and the services at The University of Edinburgh.

Synthesis and Experimental Section



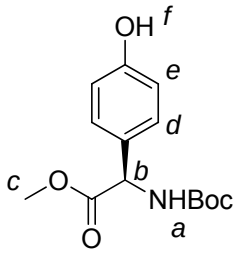
Scheme S1: Synthesis of **S7** from (*R*)-4-hydroxyphenylglycine. Reagents and conditions: (a) $SOCl_2$, MeOH, 0 °C to RT, 18 h, 99%; (b) Boc_2O, Et_3N, THF, reflux, 18 h, 99%; (c) TBDMSCl, imidazole, DMF, 0 °C to RT, 18 h, 99%; (d) TFA, CH_2Cl_2, 18 h, 83%; (e) 2,6-pyridinedicarbonyl dichloride, Et_3N, THF, 0 °C to RT, 18 h; (f) $NaBH_4$, THF, MeOH, 70%; (g) AcCl, MeOH, 48 h, 92%.



(*R*)-4-Hydroxyphenylglycine methyl ester hydrochloride – S1[3]

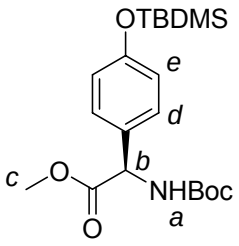
To a suspension of (*R*)-4-hydroxyphenylglycine methyl ester hydrochloride (19.3 g, 115 mmol) in MeOH (120 mL) at 0 °C was added dropwise $SOCl_2$ (10.9 mL, 150 mmol). The solution was allowed to warm to room temperature and stirred for 18 h. The solvent was removed under reduced pressure to yield the title compound as a colorless solid (25.1 g, >99%). The product was used without further purification. M.p. 180 ºC (dec.); ^{1}H NMR (400 MHz, CD_3OD): δ = 3.80 (s, 3H, H_b), 5.08 (s, 1H, H_a), 6.85 (d, 2H, J = 8.6, H_d), 7.28 (d, 2H, J = 8.6, H_c); ^{13}C NMR

(100 MHz, CD_3OD): δ = 52.4, 55.7, 115.7, 122.2, 129.2, 158.9, 169.0; LRFAB-MS (3-NOBA matrix): *m/z* = 182 $[M\text{-}Cl]^+$.



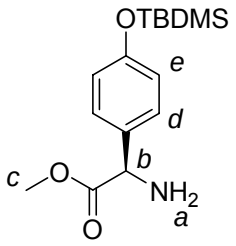
(*R*)-*N*-(*t*Butoxycarbonyl)-4-hydroxyphenylglycine methyl ester –S2[4]

A solution of **S1** (33.0 g, 0.152 mol), Boc_2O (33.1 g, 0.152 mol) and Et_3N (25.6 mL, 0.182 mol) in THF (150 mL) was heated at reflux for 18 h. The solvent was removed under reduced pressure and the crude residue was redissolved in $CHCl_3$ (300 ml). The organic layer was washed with 1 M HCl (2 x 150 mL), water (100 mL), dried ($MgSO_4$), filtered and concentrated under reduced pressure to yield the title compound as a colorless solid (43.0 g, >99%). The product was used without further purification. M.p. 139 ºC; $[\alpha]_D^{20}$ = -159.6º (*c* = 1.01, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.35 (s, 9H, H_{Boc}), 3.70 (s, 3H, H_c), 5.22 (1H, d, *J* = 7.1, H_c), 5.59 (d, 1H, *J* = 7.1, H_a), 6.07 (s, 1H, H_f), 6.72 (d, 2H, *J* = 8.5, H_e), 7.16 (d, 2H, *J* = 8.5, H_d); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 28.3, 52.8, 57.0, 80.5, 115.8, 128.3, 151.0, 155.1, 156.2, 172.0. LRFAB-MS (3-NOBA matrix): *m/z* = 282 $[MH]^+$; HRFAB-MS (3-NOBA matrix): *m/z* = 282.1347 (calcd. for $C_{14}H_{20}NO_5$, 282.1341).



(*R*)-*N*-(*t* Butoxycarbonyl)-4-(*t*-butyldimethylsiloxyphenyl)glycine methyl ester – S3[3]

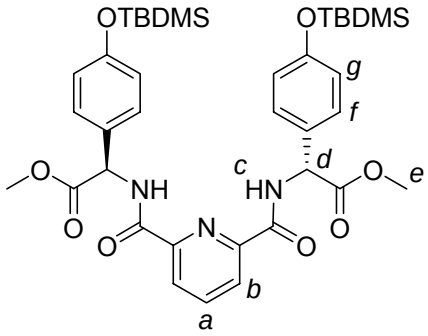
To a solution of **S2** (8.64 g, 30.7 mmol) in DMF (20 mL) at 0 ºC was added imidazole (4.180 g, 61.4 mmol) and TBDMSCl (5.09 g, 33.8 mmol). The solution was allowed to warm to room temperature and stirred for 18 h. The solvent was removed under reduced pressure and the resultant oil was redissolved in CH_2Cl_2 (150 mL), washed with 1 M HCl (100 mL), saturated aqueous $NaHCO_3$ (100 mL) and water (100 mL). The organic layer was dried ($MgSO_4$), filtered and concentrated under reduced pressure to yield the title compound as a yellow oil (12.4 g, >99%). The product was used without further purification. $[\alpha]_D^{21}$ = -4.8º (*c* = 2.5, $CHCl_3$) ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.19 (s, 6H, H_{silyl}), 0.98 (s, 9H, H_{silyl}), 1.44 (s, 9H, H_{Boc}), 3.72 (s, 3H, H_c), 5.24 (d, 1H, *J* = 7.1, H_b), 5.45 (d, 1H, *J* = 7.1, H_a), 6.80 (d, 2H, *J* = 8.5, H_e), 7.21 (d, 2H, *J* = 8.5, H_d); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 25.6, 28.3, 36.5, 52.6, 57.0, 120.4, 128.3, 130.1, 137.2, 138.6, 145.4, 155.9, 164.5; LRFAB-MS (3-NOBA matrix): *m/z* = 396 $[MH]^+$; HRFAB-MS (THIOG matrix): *m/z* = 396.2206 (calcd. for $C_{20}H_{34}NO_5Si$, 396.2206).



(*R*)-4-(*t*-Butyldimethylsiloxy)phenylglycine methyl ester – S4

To a solution of **S3** in CH_2Cl_2 (180 mL) was added TFA (20 mL), the solution was stirred for 18 h. The reaction was diluted with CH_2Cl_2 (70 mL) and washed with saturated aqueous $NaHCO_3$ (2 x 200 mL) and brine (200 mL). The organic layer was dried ($MgSO_4$), filtered and concentrated under reduced pressure to yield the title compound as a yellow oil (4.49 g, 83%). The compound was used without further purification. $[\alpha]_D^{21}$ = -3.1º (*c* = 2.65, $CHCl_3$); ^{1}H NMR (400 MHz,

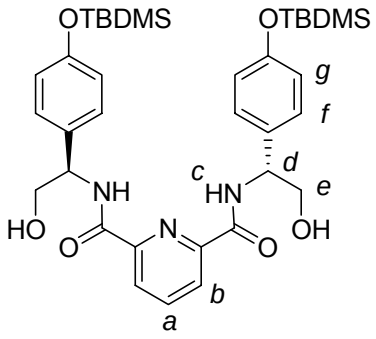
$CDCl_3$): δ = 0.19 (s, 6H, H_{silyl}), 0.98 (s, 9H, H_{silyl}), 2.00 (br, 2H, H_a), 3.70 (s, 3H, H_c), 4.56 (s, 1H, H_b), 6.81 (d, 2H, J = 8.6, H_e), 7.23 (d, 2H, J = 8.6, H_d); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 18.1, 25.6, 52.4, 55.7, 120.2, 128.0, 132.8, 155.5, 166.9, 174.7. LRFAB-MS (3-NOBA matrix): m/z = 294 $[M\text{-}H]^+$; HRFAB-MS (THIOG matrix): m/z = 294.1525 (calcd. for $C_{15}H_{24}NO_3{}^{28}Si$, 294.1525).



S5

To a solution of **S4** (4.49 g, 15.2 mmol) and Et_3N (2.9 mL, 20.7 mmol) in THF (150 mL) at -78 ºC was added dropwise a solution of 2,6-pyridinedicarbonyl dichloride (1.407 g, 6.9 mmol) in THF (20 mL) over a period of 1 h. The solution was allowed to warm to room temperature and stirred for 18 h. The resulting suspension was filtered and concentrated under reduced pressure. The crude residue was purified by column chromatography (30:70 EtOAc:Pet Ether) to yield the title compound as a yellow oil (4.73 g, 95%). $[\alpha]_D^{20}$ = +6.9º (c = 1.15, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.20 (s, 12H, H_{silyl}), 0.98 (s, 18H, H_{silyl}), 3.79 (s, 6H, H_e), 5.69 (d, 2H, J = 7.2, H_d), 6.87 (d, 4H, J = 8.6, H_g), 7.38 (d, 4H, J = 8.6, H_f), 8.01 (t, 1H, J = 7.8, H_a), 8.32 (d, 2H, J = 7.8, H_b), 8.76 (d, 2H, J = 7.2, H_c); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 18.1, 23.4, 25.6, 52.9, 56.1, 120.5, 125.3, 128.4, 128.8, 139.1, 148.3, 156.0, 157.5, 162.6; LRFAB-MS (3-NOBA matrix):

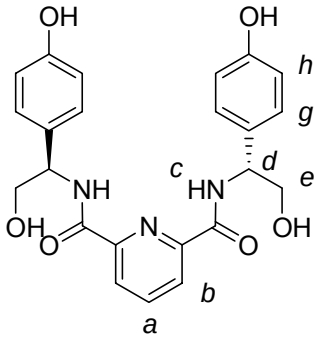
m/z = 722 [M*H*]$^+$; HRFAB-MS (THIOG matrix): *m/z* = 722.3290 (calcd. for $C_{37}H_{52}N_3O_8Si_2$, 722.3292).



R,R-**S6**

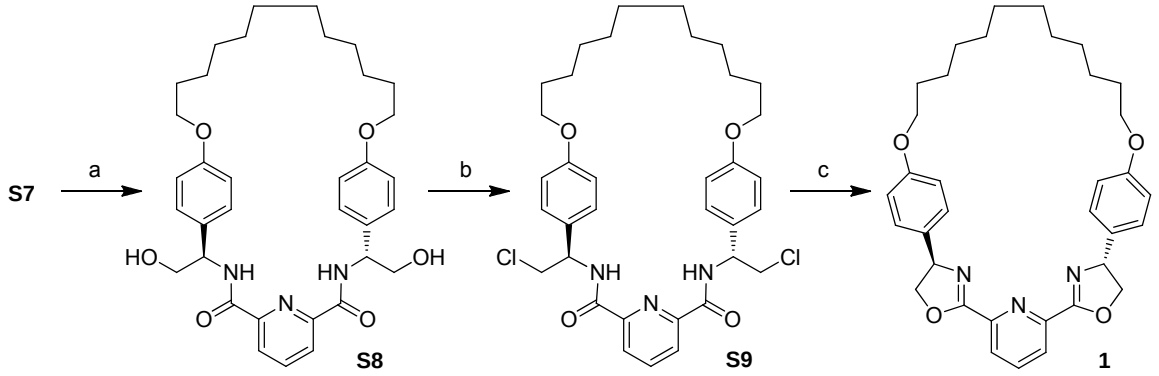
To a solution of **S5** (3.41, 4.7 mmol) in THF (42 mL) and MeOH (7 mL) was added $NaBH_4$ (0.428 g, 11.3 mmol). After 75 min, TFA (1 mL) was added and the solvent was removed under reduced pressure. The crude residue was redissolved in EtOAc (300 mL), washed with 1 M HCl (50 mL), saturated aqueous $NaHCO_3$ (50 mL) and brine (50 mL). The organic layer was dried ($MgSO_4$), filtered, concentrated under reduced pressure and purified by column chromatography (60:40 EtOAc:Pet Ether). Two diastereoisomers were isolated. The major diastereoisomer, *R,R*-**S6**, was obtained as a colorless solid (2.19 g, 70%) and used for subsequent reactions. Analytical data for *R,R*-**S6**: R_f = 0.22 (EtOAc): $[\alpha]_D^{20}$ = +50.4º (*c* = 1.11, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.20 (s, 12H, H_{silyl}), 0.98 (s, 18H, H_{silyl}), 3.98 (br, 4H, H_e), 5.21 (q, 2H, *J* = 7.2 Hz, H_d), 6.86 (d, 4H, *J* = 8.5, H_g), 7.26 (d, 4H, *J* = 8.5, H_f), 8.06 (t, 1H, *J* = 7.7, H_a), 8.35 (d, 2H, *J* = 7.7, H_b), 8.48 (d, 2H, *J* = 7.2, H_c); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 1.0, 18.1, 25.6, 54.9, 66.0, 120.3, 125.1, 127.8, 131.5, 139.0, 148.5, 155.3, 163.6. LRFAB-MS (3-NOBA matrix): *m/z* = 664 [M-*H*]$^+$; HRFAB-MS (THIOG matrix): *m/z* = 664.3238 (calcd. for $C_{35}H_{50}N_3O_6{}^{28}Si_2$, 664.3238).

Minor diastereoisomer, *meso*-**S6**: R_f = 0.08 (EtOAc); M.p. 174 ºC; $[\alpha]_D^{20}$ = 0.0º (*c* = 0.71, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.16 (s, 12H, H_{silyl}), 0.96 (s, 18H, H_{silyl}), 3.89 (d, 4H, *J* = 5.2, H_e), 5.25 (dt, 2H, *J* = 5.2, 8.3, H_d), 6.78 (d, 4H, *J* = 8.5, H_g), 7.21 (d, 4H, *J* = 8.5, H_f), 7.86 (t, 1H, *J* = 7.8, H_a), 8.16 (d, 2H, *J* = 7.8, H_b), 8.80 (d, 2H, *J* = 8.3, H_c); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 18.1, 25.6, 31.0, 55.1, 66.5, 120.4, 125.1, 127.8, 131.3, 139.2, 148.5, 155.4, 163.4; LRFAB-MS (3-NOBA matrix): *m/z* = 688 [M*Na*]$^+$; HRFAB-MS (3-NOBA matrix): *m/z* = 688.3235 (calcd. for $C_{35}H_{51}N_3O_6NaSi_2$, 688.3208).

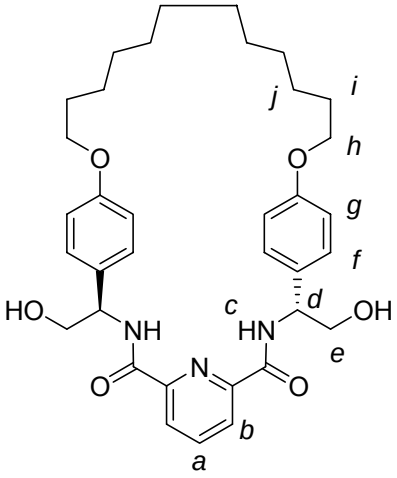


S7

R,*R*-**S6** (4.675 g, 7.02 mmol) was dissolved in MeOH (70 mL) and AcCl (0.12 mL, 2.1 mmol) was added. The solution was stirred for 48 h. The resultant suspension was filtered to yield the title compound as a white solid (2.822 g, 92%) The product was used without further purification. M.p. 241 ºC; $[\alpha]_D^{21}$ = 73.1º (*c* = 0.52, MeOH); ^{1}H NMR (400 MHz, CD_3OD): δ = 3.93 (t, 4H, *J* = 5.9, H_e), 5.20 (t, 2H, *J* = 5.9, H_d), 6.78 (d, 4H, *J* = 8.6, H_h), 7.28 (d, 4H, *J* = 8.6, H_g), 8.14 (t, 1H, *J* = 7.4, H_a), 8.28 (d, 2H, *J* = 7.4, H_b); ^{13}C NMR (100 MHz, CD_3OD): δ = 53.2, 58.0, 116.7, 126.4, 127.8, 130.1, 140.6, 150.0, 159.1, 165.5; LR-FABMS (3-NOBA matrix): *m/z* = 438 [M*H*]$^+$; HR-FABMS (3-NOBA matrix): *m/z* = 438.1652 (calcd. for $C_{23}H_{24}N_3O_6$, 438.1659).



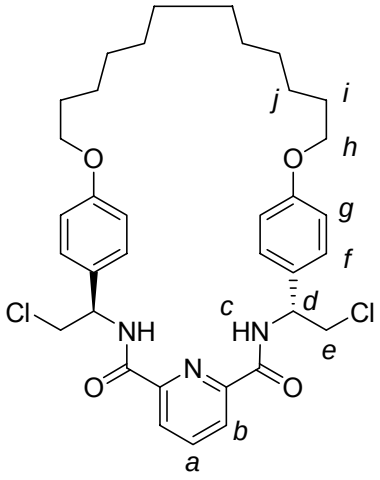
Scheme S2: Synthesis of pybox macrocycle **1**. Reagents and conditions: (a) 1,12-dibromododecane, K_2CO_3, DMF, 100 ºC, 22%; (b) $SOCl_2$, $CHCl_3$, reflux, 8 h, 70%, (c) TBAF, THF, 4 h, 79%.



S8

To a solution of **S7** (1.50 g, 3.4 mmol) and 1,12-dibromododecane (1.116 g, 3.4 mmol) in DMF (1 L) was added K_2CO_3 (19.0 g, 13.7 mmol). The suspension was stirred at 100 ºC for 48 h. The solvent was removed under reduced pressure, and the crude residue was redissolved in water (100 mL) and extracted into CH_2Cl_2 (3 x 300 mL). The combined organic layers were dried ($MgSO_4$), filtered, concentrated under reduced pressure and purified by column chromatography (1:99 MeOH:EtOAc) to yield the title compound as a colorless solid (0.450 g, 22%). M.p. 91 ºC;

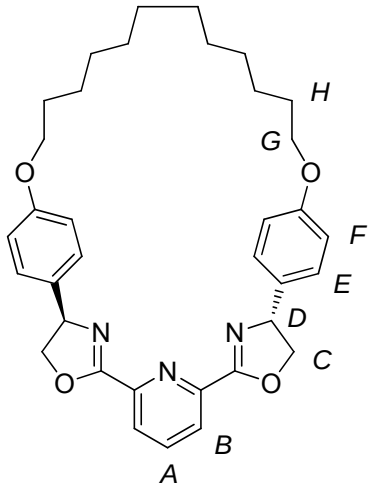
$[\alpha]_D^{22}$ = +13.9º (*c* = 1.01, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.32 (br, 12H, H_{alkyl}), 1.50 (m, 4H, H_j), 1.81 (m, 4H, H_i), 3.96 (m, 4H, H_e), 3.99 (m, 4H, H_h), 5.17 (m, 2H, H_d), 6.95 (d, 4H, *J* = 8.6, H_f), 7.27 (d, 4H, *J* = 8.6, H_g), 8.07 (t, 1H, *J* = 7.8, H_a), 8.10 (d, 2H, *J* = 5.6 Hz, H_c), 8.83 (d, 2H, *J* = 7.8, H_b); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 25.4, 27.9, 28.4, 28.8, 28.9, 56.6, 66.6, 68.0, 115.1, 125.2, 127.9, 130.3, 139.2, 148.2, 159.1, 163.9; LR-FABMS (3-NOBA matrix): *m/z* = 604 $[MH]^+$; HR-FABMS (3-NOBA matrix): *m/z* = 604.3398 (calcd. for $C_{35}H_{46}N_3O_6$, 604.3381).



S9

To a solution of **S8** (0.450 g, 0.75 mmol) in $CHCl_3$ was added $SOCl_2$ (0.54 mL, 7.5 mmol). The solution was heated at a reflux for 8 h. The solvent was removed under reduced pressure and the crude residue was purified by column chromatography (1:19 EtOAc:CH_2Cl_2) to yield the title compound as a colorless solid (0.336 g, 70%). M.p. 92 ºC; $[\alpha]_D^{20}$ = 4.35º (*c* = 0.46, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.31 (br, 12H, H_{alkyl}), 1.50 (m, 4H, H_j), 1.81 (m, 4H, H_i), 3.95 (m, 4H, H_e), 4.01 (m, 4H, H_h), 5.41 (q, 2H, H_d), 6.96 (d, 4H, *J* = 8.7, H_g), 7.34 (d, 4H, *J* = 8.7, H_f), 8.09 (d, 2H, *J* = 7.8, H_c), 8.10 (t, 1H, *J* = 7.8, H_a), 8.39 (d, 2H, *J* = 7.8, H_b); ^{13}C NMR (100 MHz,

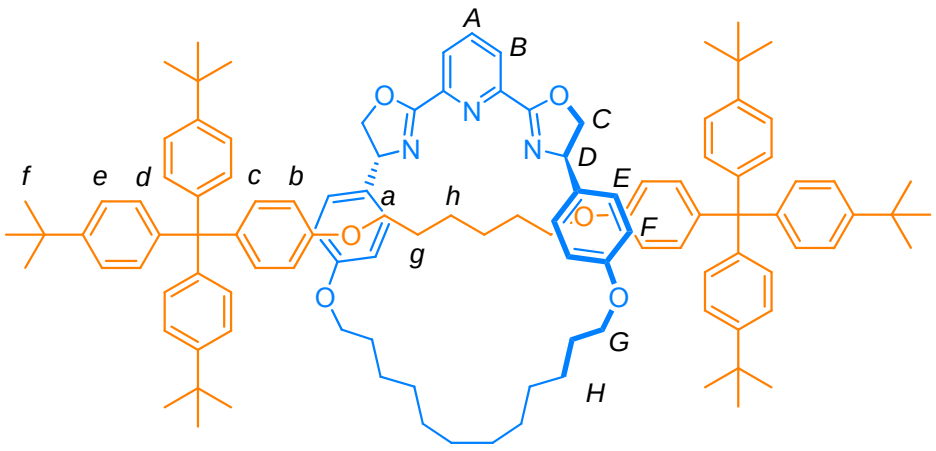
$CDCl_3$): δ = 25.4, 27.9, 28.0, 28.5, 28.7, 47.4, 53.8, 67.9, 115.0, 125.4, 127.9, 129.7, 139.4, 148.4, 159.3, 162.8; LR-FABMS (3-NOBA matrix): *m/z* = 640 $[MH]^+$; HR-FABMS (3-NOBA matrix): *m/z* = 640.2719 (calcd. for $C_{35}H_{44}N_3O_4Cl_2$, 640.2703). Cl isotope



Pybox Macrocycle - **1**

To a solution of **S9** (1.765 g, 2.76 mmol) in THF (30 mL) was added TBAF (1M in THF, 11.0 mL, 11.0 mmol) the solution was stirred for 4 h, after which time the solvent was removed under reduced pressure. The crude residue was redissolved in CH_2Cl_2 (50 mL) and Et_2) (50 mL) and washed with trisodium citrate (3 x 50 mL), the organic layer was washed with brine (50 mL), dried ($MgSO_4$) and concentrated under reduced pressure to yield the title compound as a colorless solid (1.239 g, 79%). m.p. 81 ºC; $[\alpha]_D^{22}$ = +38.7º (*c* = 1.24, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.22 (br, 12H, $H_{J,K,L}$), 1.36 (m, 4H, H_I), 1.69 (m, 4H, H_H), 4.01 (t, *J* = 6.9 Hz, 4H, H_G), 4.51 (dd, *J* = 6.1, 8.6, 2H, $H_{C'}$), 4.75 (dd, *J* = 8.6, 9.8, 2H, H_D), 5.38 (dd, *J* = 6.1, 9.8, 2H, H_C), 6.84 (d, *J* = 8.7, 4H, H_F), 7.20 (d, *J* = 8.7, 4H, H_E), 7.91 (t, *J* = 7.8, 1H, H_A), 8.11 (d, *J* = 7.8, 2H, H_B); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 23.8, 26.5, 27.2, 27.8, 28.0, 65.9, 67.5, 73.3,

113.3, 123.5, 126.0, 132.1, 135.5, 145.1, 156.3, 160.8; LR-FABMS (3-NOBA matrix): *m/z* = 568 $[MH]^+$; HR-FABMS (3-NOBA matrix): *m/z* = 568.3169 (calcd. for $C_{35}H_{42}N_3O_4$, 568.3169).



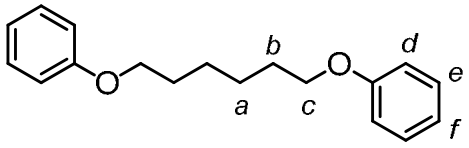
Rotaxane - **3**

To a solution of pybox macrocycle **1** (28 mg, 49 µmol) and $NiCl_2$•diglyme (10 mg, 45 µmol) in THF (1 mL) under an inert atmosphere of nitrogen was added activated zinc (12 mg, 180 µmol) and NMP (1 mL) and the resulting suspension sonicated for 5 min giving color change green/yellow to deep purple. To this was added stoppered bromide **2** (69 mg, 110 µmol) and the resulting mixture stirred at rt for 2.5 h. The reaction mixture was diluted with EtOAc (40 mL) and extracted with 17.5% $NH_{3(aq)}$ saturated with EDTA (2 × 40 mL portions), H_2O (3 × 40 mL) and brine (40 mL). The organic layer was dried ($MgSO_4$) and the solvent removed under reduced pressure. The residue was diluted with hexane (40 mL) and extracted with acetonitrile (3 × 20 mL). The hexane layer was isolated and concentrated, purification of the resulting residue on a short plug of C_{18} end capped reversed-phase silica (gradient elution: MeOH-THF 1. 9:1 2. 4:1) gave rotaxane **3** (42 mg, 46%). m.p 140 – 143 °C; $[\alpha]_D^{22}$ = -113.3 (*c* = 0.3, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$:CD_3OD 1:1): δ = 1.23 (br, 74H, H_f + H_h + H_{alkyl}), 1.37 (m, 4H, H_g), 1.62 (m, 4H, H_H), 3.53 (m, 4H, H_a), 3.77 (t, 4H, *J* = 6.5, H_G), 4.34 (dd, 1H, *J* = 5.3, 8.5, $H_{C'}$), 4.60 (t, 1H,

J_t = 9.1, H_D), 5.28 (dd, 1H, J = 5.3, 9.4, H_C), 6.56 (m, 8H, H_b + H_F), 6.92 (m, 8H, H_c + H_E), 7.04 (d, 12H, J = 8.5, H_d), 7.19 (d, 12H, J = 8.5, H_e), 7.54 (t, 1H, J = 7.8, H_A), 7.92 (d, 2H, J = 7.8, H_B); ^{13}C NMR (400 MHz, $CDCl_3$): δ = 14.1, 22.6, 25.6, 25.7, 31.3, 34.2, 62.9, 67.3, 67.7, 69.2, 74.9, 112.9, 114.7, 123.9, 127.6, 130.6, 131.8, 132.4, 133.9, 139.0, 144.2, 146.6, 148.0, 156.8, 158.1, 162.3; LRFAB-MS (3-NOBA matrix): *m/z* = 1660 $[MH]^+$; HRFAB-MS (3-NOBA matrix): *m/z* = 1660.077 $[MH]^+$ (calcd. for $C_{114}H_{140}{}^{13}CO_6N_3$, 1660.077).

General Procedure for sp^3-sp^3 Homocoupling Reactions of Unactivated Bromides

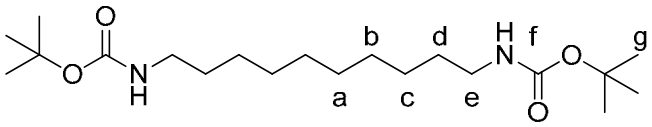
To a solution of 2,6-bis[(*4S*)-4-phenyl-2-oxazolinyl]pyridine (Ph-pybox) or 2,2':6',2''-terpyridine (terpy) (50 μmol) and $NiCl_2$•$6H_2O$, $Ni(cod)_2$ (bis(cyclooctadiene)nickel(0)) or $NiCl_2$•DME (50 μmol) in DMF (2 mL) under an inert atmosphere of nitrogen was added activated Zn (70 mg, 1 mmol) followed by the unactivated bromide (1 mmol). Upon stirring the suspension turned from light green/blue (pybox/terpy) to deep purple and was stirred at room temperature for 4 h. The reaction mixture was diluted with EtOAc (40 mL) and extracted with 17.5% $NH_{3(aq)}$ saturated with EDTA (2 × 40 mL portions), 1M $HCl_{(aq)}$ (2 x 40 mL), H_2O (3 × 40 mL) and brine (40 mL). The organic layer was dried ($MgSO_4$) and the solvent and volatile impurities removed under reduced pressure to give the homocoupled product which required no further purification.



1,6-Dipenoxyhexane – 6

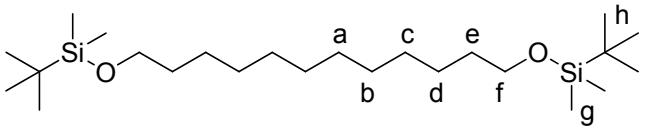
Following the general procedure with terpy (11.8 mg, 50 μmol), $NiCl_2$•$6H_2O$ (12.8 mg, 50 μmol), activated Zn (70 mg, 1 mmol) and (3-bromo-propoxy)-benzene (0.17 mL, 1 mmol) in

DMF (2 mL) afforded 1,6-dipenoxyhexane **6** (137 mg, 95%) as a colourless solid. Melting point was consistent with published data.[5] M.p. 80 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.59-1.53 (m, 4H, H_a), 1.88-1.80 (m, 4H, H_b), 3.98 (t, 4H, J = 6.5, H_c), 6.97-6.90 (m, 6H, H_d and H_f), 7.33-7.27 (m, 4H, H_e); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 25.8, 29.2, 67.6, 114.4, 120.4, 129.3, 159.0; LRAPCI-MS: *m/z* = 271.2 [M*H*]$^+$; HRAPCI-MS: *m/z* = 270.1610 [M]$^+$ (calcd. for $C_{18}H_{22}O_2$, 270.1614).



N,N'-di-boc-decamethylendiamin – S10

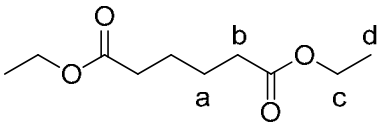
Following the general procedure with terpy (11.8 mg, 50 µmol), $NiCl_2$•$6H_2O$ (12.8 mg, 50 µmol), activated Zn (70 mg, 1 mmol) and (5-Bromo-pentyl)-carbamic acid tert-butyl ester (287 mg, 1 mmol) in DMF (2 mL) afforded *N*,*N*'-*di*-boc-decamethylendiamine **S10 (**195 mg, 97%) as a colorless solid. M.p. 107 °C;[6] ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.12-1.29 (m, 12H, H_a, H_b and H_c), 1.38-1.48 (m, 22H, H_d and H_g), 3.02-3.13 (m, 4H, H_e), 4.54 (br, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 28.3, 29.1, 29.3, 29.6, 29.9, 40.5, 78.9, 155.9. LRAPCI-MS: *m/z* = 373.3 [M*H*]$^+$; HRESI-MS: *m/z* = 373.3058 [M*H*]$^+$ (calcd. for $C_{20}H_{41}O_4N_2$, 373.3068).



1,12-Bis-(*tert*-butyl-dimethyl-silanyloxy)-dodecane – S11

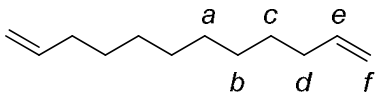
Following the general procedure with terpy (11.8 mg, 50 µmol), $NiCl_2$•$6H_2O$ (12.8 mg, 50 µmol), activated Zn (70 mg, 1 mmol) and (6-bromohexyloxy)-*tert*-butyldimethylsilane (303 µL,

1 mmol) in DMF (2 mL) afforded 1,12-bis-(*tert*-butyl-dimethyl-silanyloxy)-dodecane **S11 (**223 mg, 96%) as a yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.04 (s, 12H, H_g), 0.89 (s, 18H, H_h), 1.23-1.33 (m, 16H, H_a, H_b, H_c and H_d), 1. 46-1.56 (m, 4H, H_e), 3.59 (t, 4H, J = 6.7, H_f); ^{13}C NMR (100 MHz, $CDCl_3$): δ = -5.2, 18.3, 25.7, 25.9, 29.4, 29.5, 29.6, 32.8, 63.3; LRAPCI-MS: *m/z* = 431.4 [M*H*]$^+$; HRESI-MS: *m/z* = 431.3736 [M*H*]$^+$ (calcd. for $C_{24}H_{55}O_2Si_2$, 431.3735).



Hexanedioic acid diethyl ester – S12

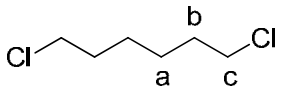
Following the general procedure with terpy (11.8 mg, 50 µmol), $NiCl_2$•$6H_2O$ (12.8 mg, 50 µmol), activated Zn (70 mg, 1 mmol) and ethyl 3-bromopropionoate (138 µL, 1 mmol) in DMF (2 mL) afforded hexanedioic acid diethyl ester **S12 (**85 mg, 78%) as a colorless solid. ^{1}H NMR was consistent with published data.[9] ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.21 (t, 6H, J = 7.1, H_d), 1.65-1.58 (m, 4H, H_a), 2.31-2.24 (m, 4H, H_b), 4.08 (q, 4H, J = 7.1, H_c); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.2, 24.4, 33.9, 60.3, 173.4.



Dodeca-1,11-diene – S13

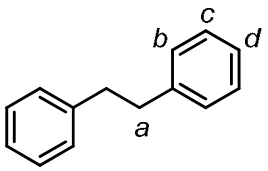
Following the general procedure with terpy (11.8 mg, 50 µmol), $NiCl_2$•$6H_2O$ (12.8 mg, 50 µmol), activated Zn (70 mg, 1 mmol) and bromohexene (144 µL, 1 mmol) in DMF (2 mL) afforded dodeca-1,11-diene **S13 (**89 mg, >99%) as a colorless oil. ^{1}H NMR and ^{13}C NMR were consistent with published data.[11] ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.31-1.25 (m, 8H, H_a and H_b),

1.33-1.41 (m, 4H, H_c), 2.00-2.07 (m, 4H, H_d), 4.90-4.95 (m, 2H, H_f), 4.95-5.02 (m, 2H, $H_{f'}$), 5.81 (tdd, 2H, J = 6.7, 10.2, 16.9, H_e); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 28.9, 29.1, 29.4, 33.8, 114.0, 139.2.



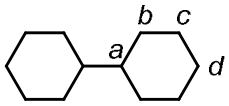
1,6-Dichlorohexane – S14

Following the general procedure with terpy (11.8 mg, 50 µmol), $NiCl_2$•$6H_2O$ (12.8 mg, 50 µmol), activated Zn (70 mg, 1 mmol) and 1-bromo-3-chloropropane (106 µL, 1 mmol) in DMF (2 mL) afforded 1,6-dichlorohexane **S14 (**96 mg, >99%) as a yellow oil. ^{1}H NMR and ^{13}C NMR were consistent with published data.[7] ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.44-1.49 (m, 4H, H_a), 1.75-1.83 (m, 4H, H_b), 3.54 (t, 4H, J = 6.6, H_c); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 21.0, 32.3, 44.9.



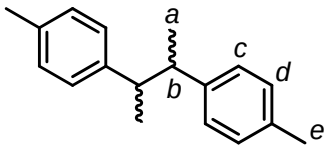
1,2-Diphenylethane – S15

Following the general procedure with terpy (11.8 mg, 50 µmol), $NiCl_2$•$6H_2O$ (12.8 mg, 50 µmol), activated Zn (70 mg, 1 mmol) and benzyl bromide (128 µL, 1 mmol) in DMF (2 mL) afforded 1,2-diphenylethane **S15 (**76 mg, 95%) as a yellow oil which solidified on standing. ^{1}H NMR and ^{13}C NMR were consistent with published data.[10] ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.93 (s, 4H, H_a), 7.17-7.23 (m, 6H, H_b and H_d), 7. 26-7.32 (m, 4H, H_c); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 38.0, 126.0, 128.4, 128.5, 141.9.



Bicyclohexyl – S16

Following the general procedure with terpy (11.8 mg, 50 µmol), $NiCl_2 \cdot 6H_2O$ (12.8 mg, 50 µmol), activated Zn (70 mg, 1 mmol) and bromo-cyclohexane (133 µL, 1 mmol) in DMF (2 mL) afforded bicyclohexyl **S16 (**89 mg, >99%) as a colorless oil. ^{1}H NMR and ^{13}C NMR were consistent with published data.[8] ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.88-1.29 (m, 12H), 1.58-1.75 (m, 10H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 26.9 (2xC), 30.2, 43.5.

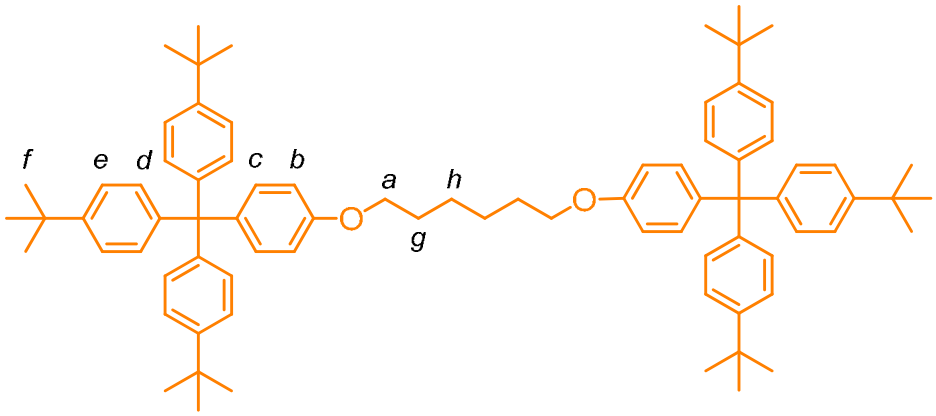


2,3-Di-*p*-toluyl-butane – S17

Following the general procedure with terpy (11.8 mg, 50 µmol), $NiCl_2 \cdot 6H_2O$ (12.8 mg, 50 µmol), activated Zn (70 mg, 1 mmol) and 1-(1-bromoethyl)-4-methylbenzene (133 µL, 1 mmol) in DMF (2 mL) afforded 2,3-di-*p*-toluyl-butane **S17 (**103 mg, 80%) as a pale yellow solid in a 1:1 mixture of the chiral and meso diastereoisomers as judged by ^{1}H NMR.[13]

meso-**S17** – ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.96 – 1.03 (m, 6H, H_a), 2.27 (s, 6H, H_e) , 2.68 – 2.79 (m, 2H, H_b), 7.12 (s, 8H, H_c + H_d).

chiral-**S17** – ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.21 – 1.24 (m, 6H, H_a), 2.34 (s, 6H, H_e), 2.87 – 2.97 (m, 2H, H_b), 6.91 – 6.95 (m, 4H, H_c), 7.00 (d, J = 7.9, 4H, H_d).



Thread **– S18**

Following the general procedure with terpy (0.46 mg, 2 µmol), $NiCl_2$•$6H_2O$ (0.48 mg, 2 µmol), activated Zn (2.6 mg, 40 µmol) and stoppered bromide **2** (25 mg, 40 µmol) in DMF (0.5 mL) and THF (0.5 mL) afforded thread **S18 (**22 mg, >99%) as a colorless solid. M.p >310 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.26-1.32 (m, 54H, H_f), 1.49-1.54 (m, 4H, H_h), 1.75-1.83 (m, 4H, H_g), 3.93 (t, 4H, J = 6.5, H_a), 6.77-6.73 (m, 4H, H_b), 7.04-7.10 (m, 16H, H_c and H_d), 7.19-7.25 (m, 12H, H_e); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 25.9, 29.3, 31.3, 34.2, 63.0, 67.6, 112.9, 124.0, 130.7, 132.2, 139.3, 144.1, 148.2, 156.8; LREI-MS: *m/z* = 1091.5 $[MH]^+$; HREI-MS: *m/z* = 1090.755 $[M]^+$ (calcd. for $C_{80}H_{98}O_2$, 1090.756).

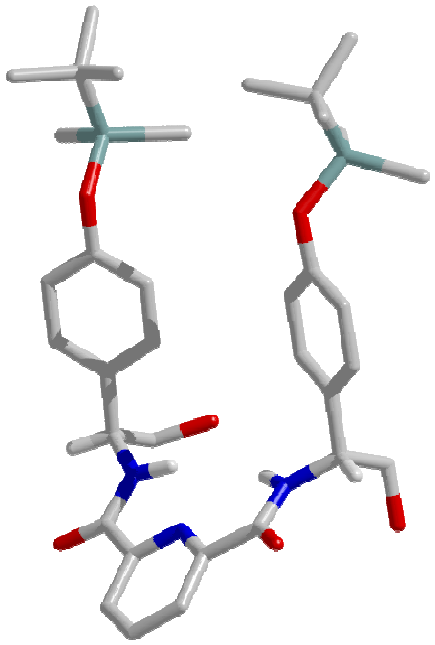


Figure S1: Crystal structure of the *meso* enantiomer of **S6**. Carbon atoms are shown in light grey, nitrogen atoms blue, oxygen red, silicon green/grey, selected hydrogen atoms are shown in white.

Table S1: Crystal data and structure refinement for *meso*-**S6**.

Identification code	*meso*-**S6**	
Empirical formula	$C_{35}H_{52}N_{3O6.50}Si_2$	
Formula weight	674.98	
Temperature	93(2) K	
Wavelength	0.71073 Å	
Crystal system	Triclinic	
Space group	P-1	
Unit cell dimensions	a = 10.1290(6) Å	α = 75.478(3)°.
	b = 18.6652(11) Å	β = 88.638(3)°.
	c = 21.5360(13) Å	γ = 78.940(3)°.
Volume	3867.0(4) $Å^3$	
Z	4	
Density (calculated)	1.159 Mg/m^3	
Absorption coefficient	0.137 mm^{-1}	
F(000)	1452	
Crystal size	0.100 x 0.100 x 0.050 mm^3	
Theta range for data collection	2.25 to 25.35°.	

Index ranges	-12≤h≤12, -19≤k≤22, -25≤l≤25
Reflections collected	35807
Independent reflections	13692 [R(int) = 0.0510]
Completeness to theta = 25.00°	97.8 %
Absorption correction	Multiscan
Max. and min. transmission	1.0000 and 0.4884
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	13692 / 8 / 892
Goodness-of-fit on F^2	1.051
Final R indices [I>2sigma(I)]	R1 = 0.0503, wR2 = 0.1215
R indices (all data)	R1 = 0.0591, wR2 = 0.1284
Extinction coefficient	0.0039(10)
Largest diff. peak and hole	0.822 and -0.695 e.$Å^{-3}$

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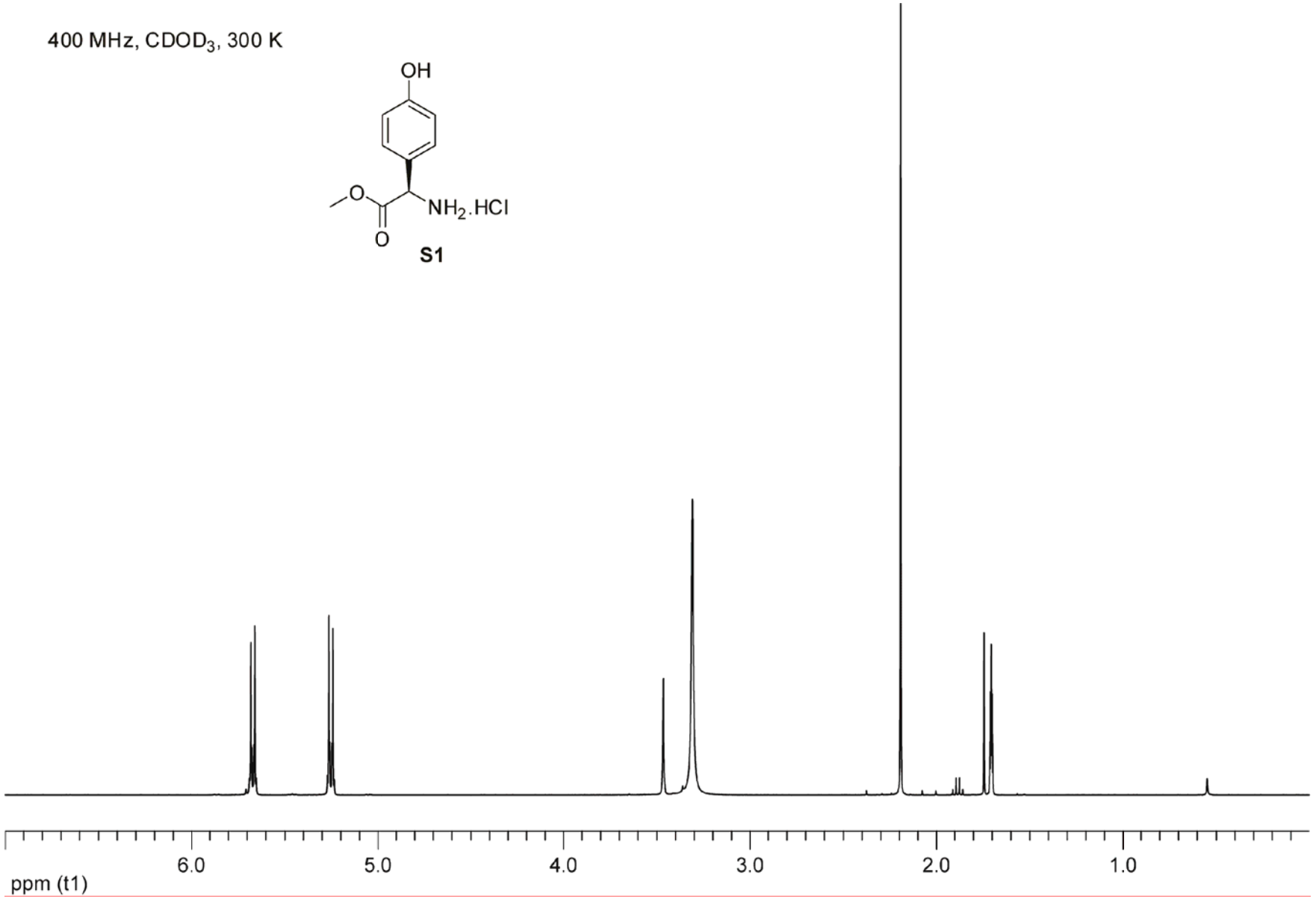
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NH2.HCl
O
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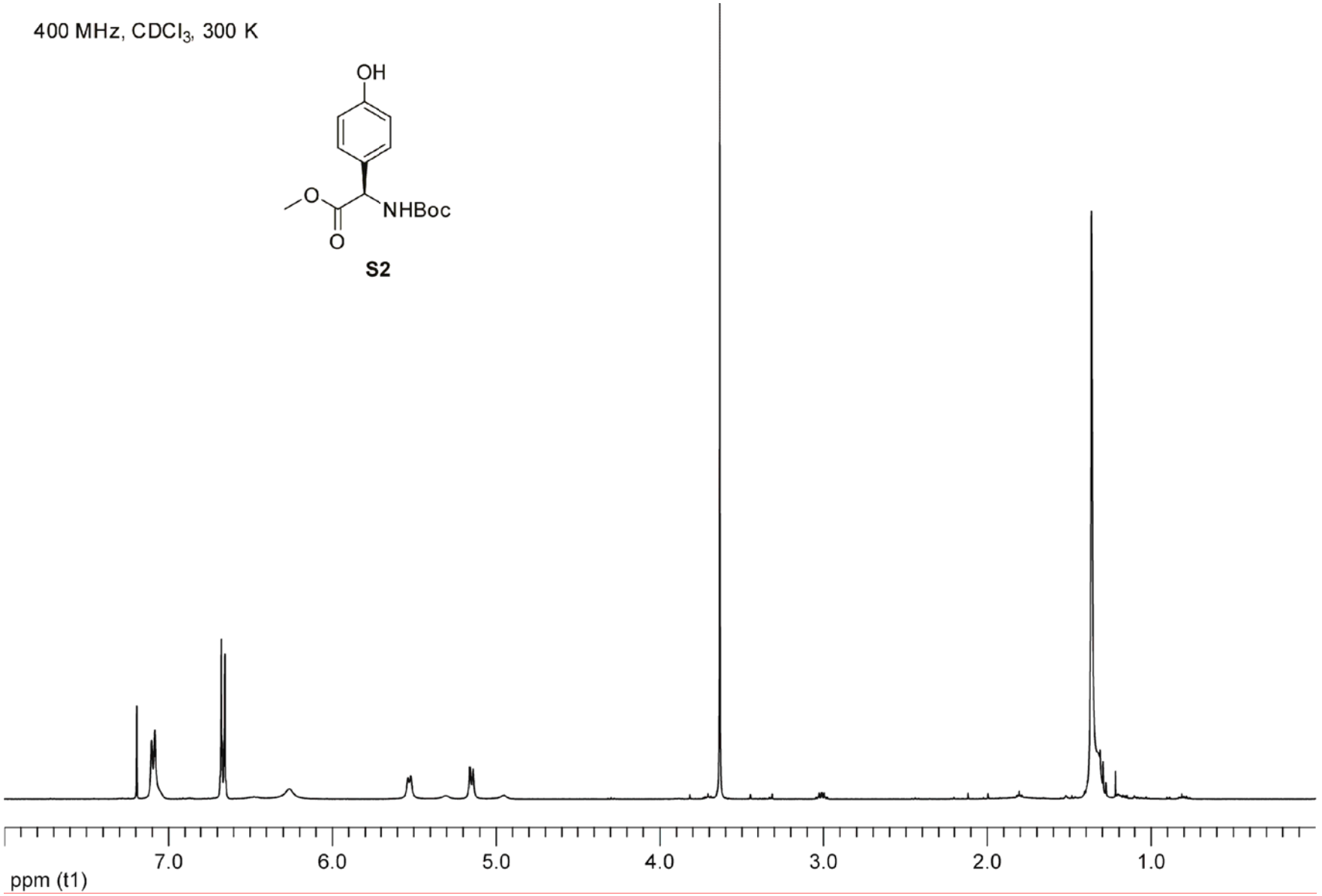
5.0
4.0
3.0
2.0
1.0
ppm (t1)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O
NHBoc
O
S2
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6.0
5.0
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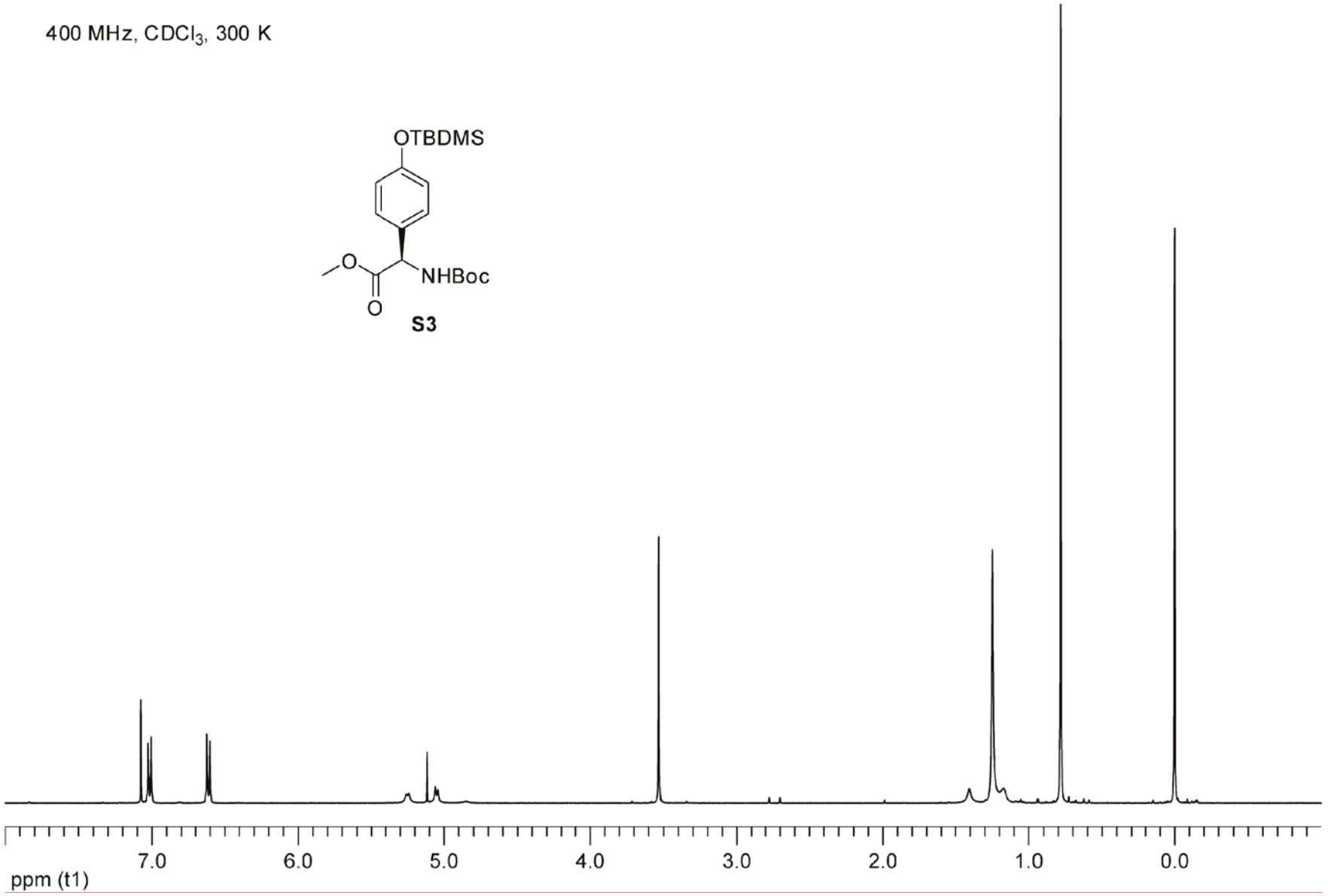
1.0
ppm (t1)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OTBDMS
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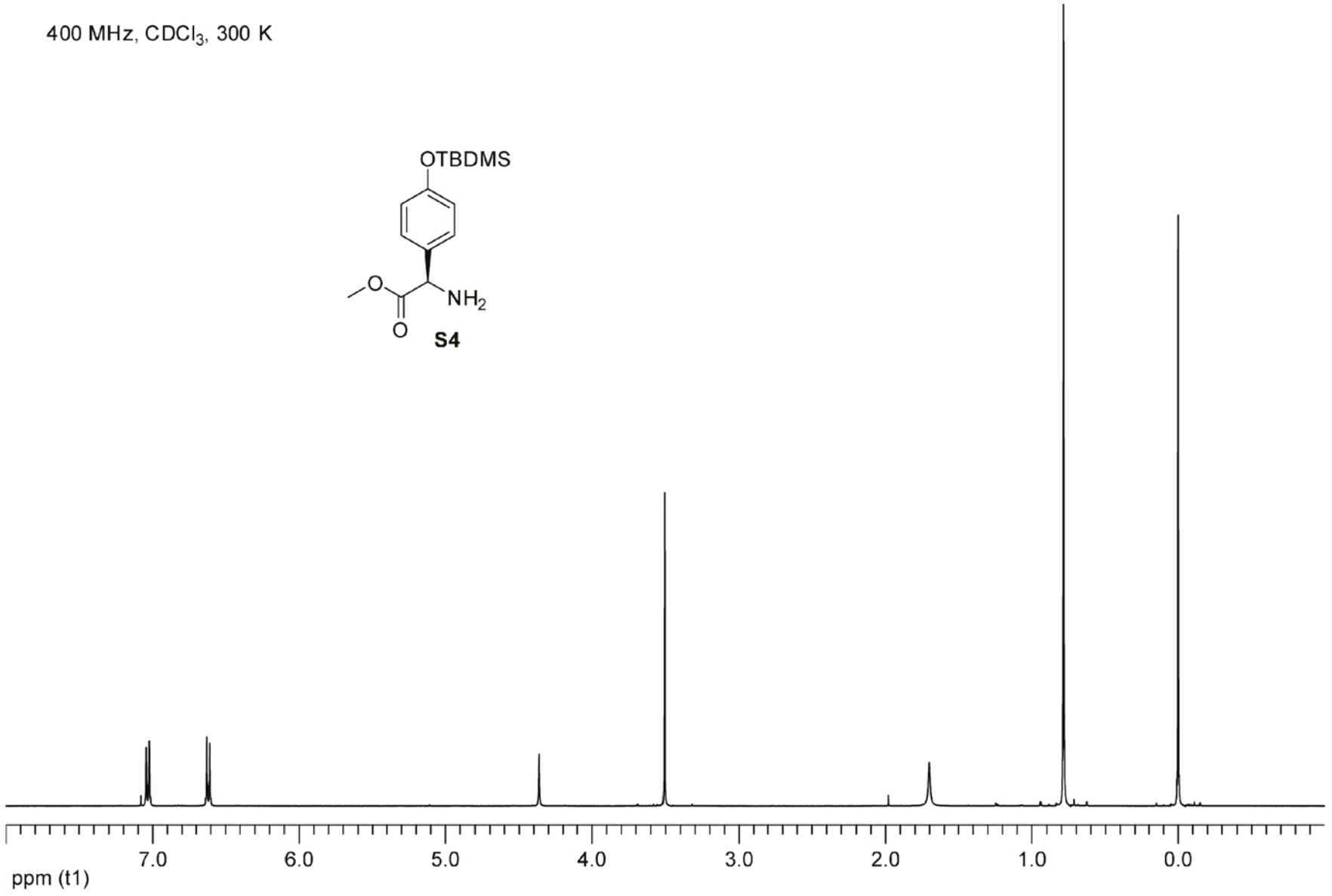
ppm (t1)


400 MHz, CDCl3, 300 K
OTBDMS
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NH2
O
S4
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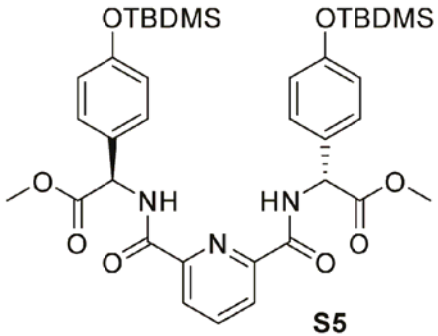
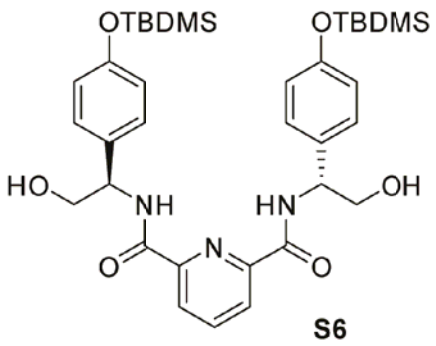
5.0
4.0
3.0
2.0
1.0
0.0
ppm (t1)

400 MHz, $CDCl_3$, 300 K

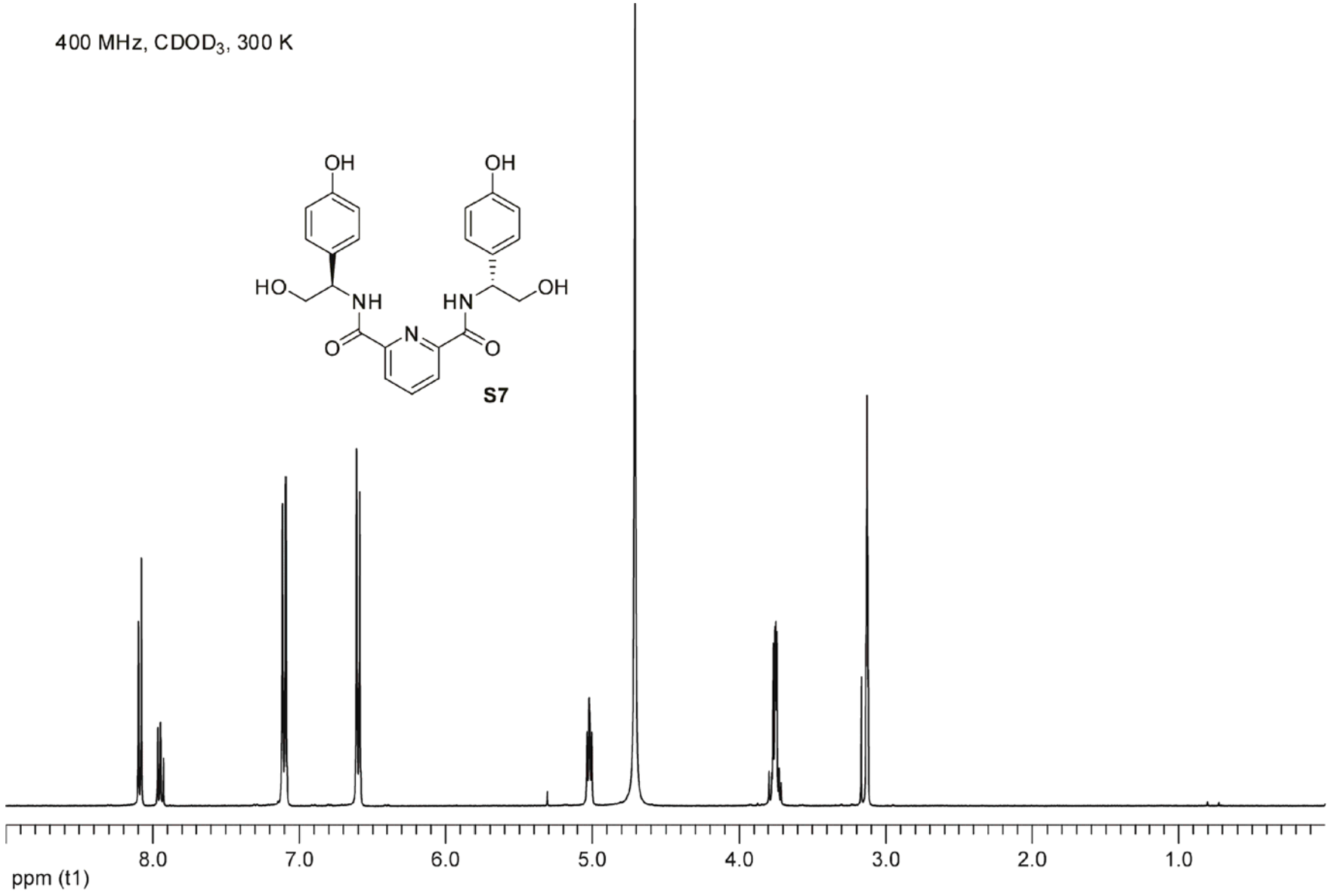


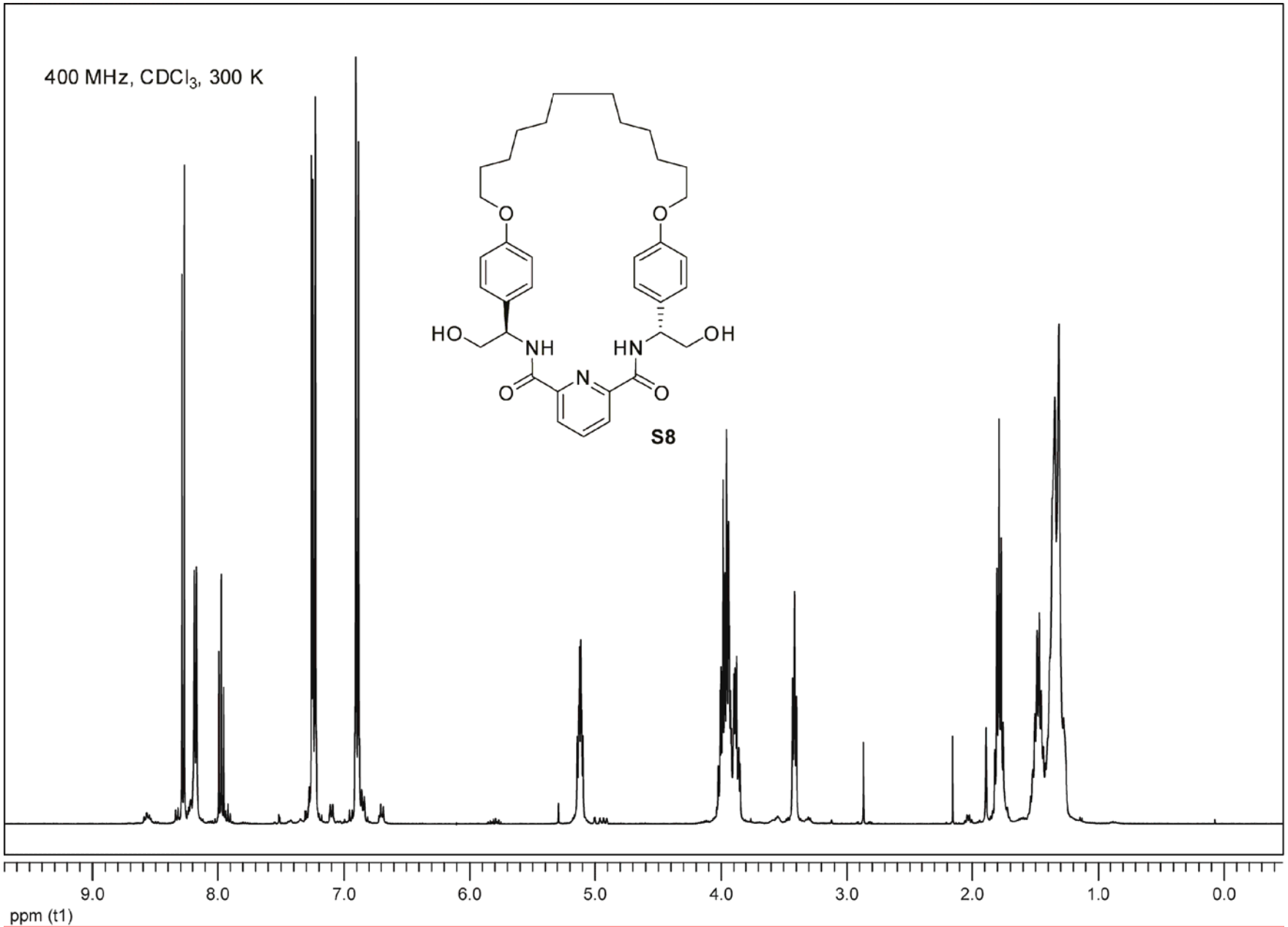
S5

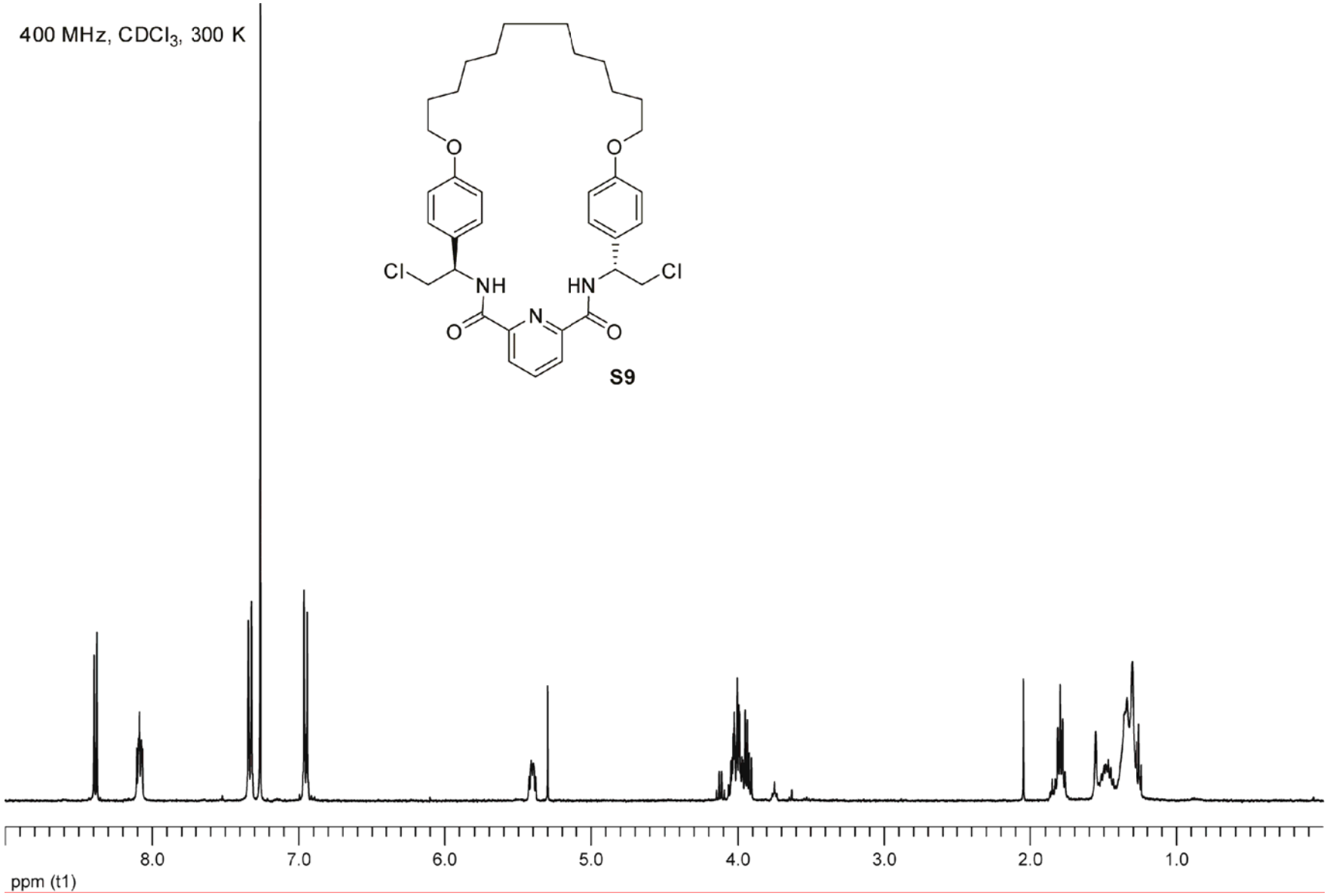
400 MHz, $CDCl_3$, 300 K



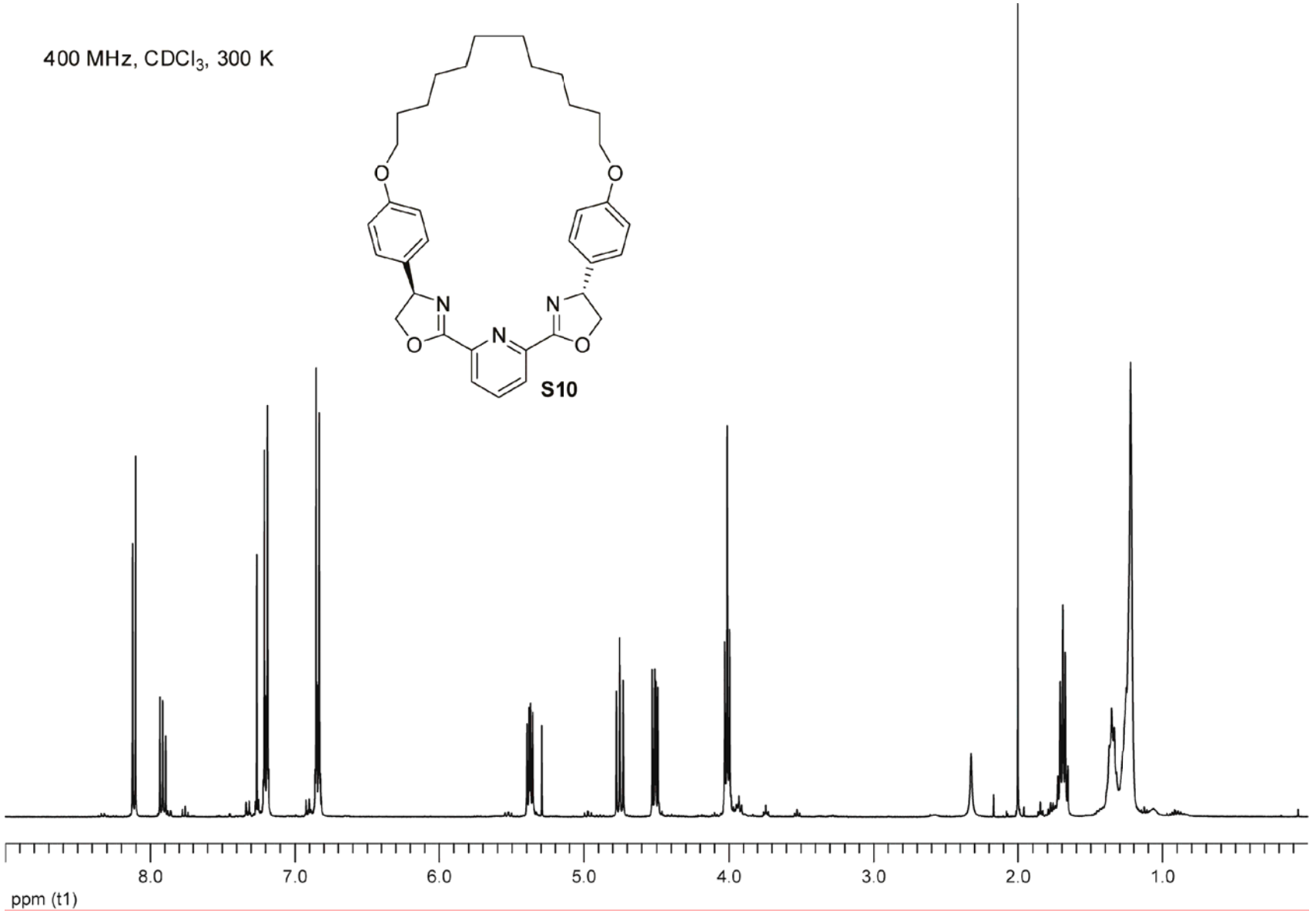
S6

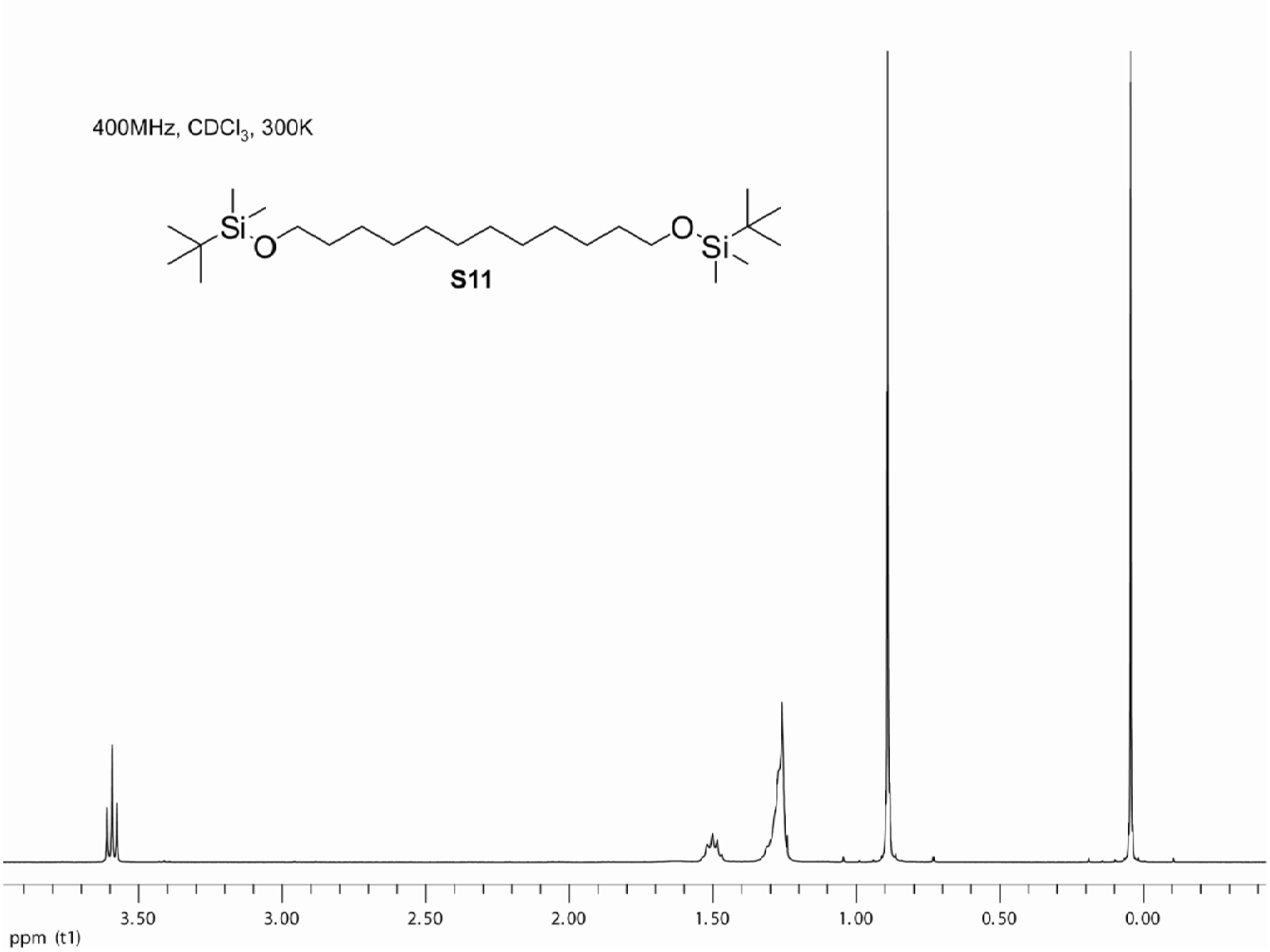

400 MHz, CDOD3, 300 K
OH
OH
HO
NH
HN
OH
N
O
O
S7
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
ppm (t1)

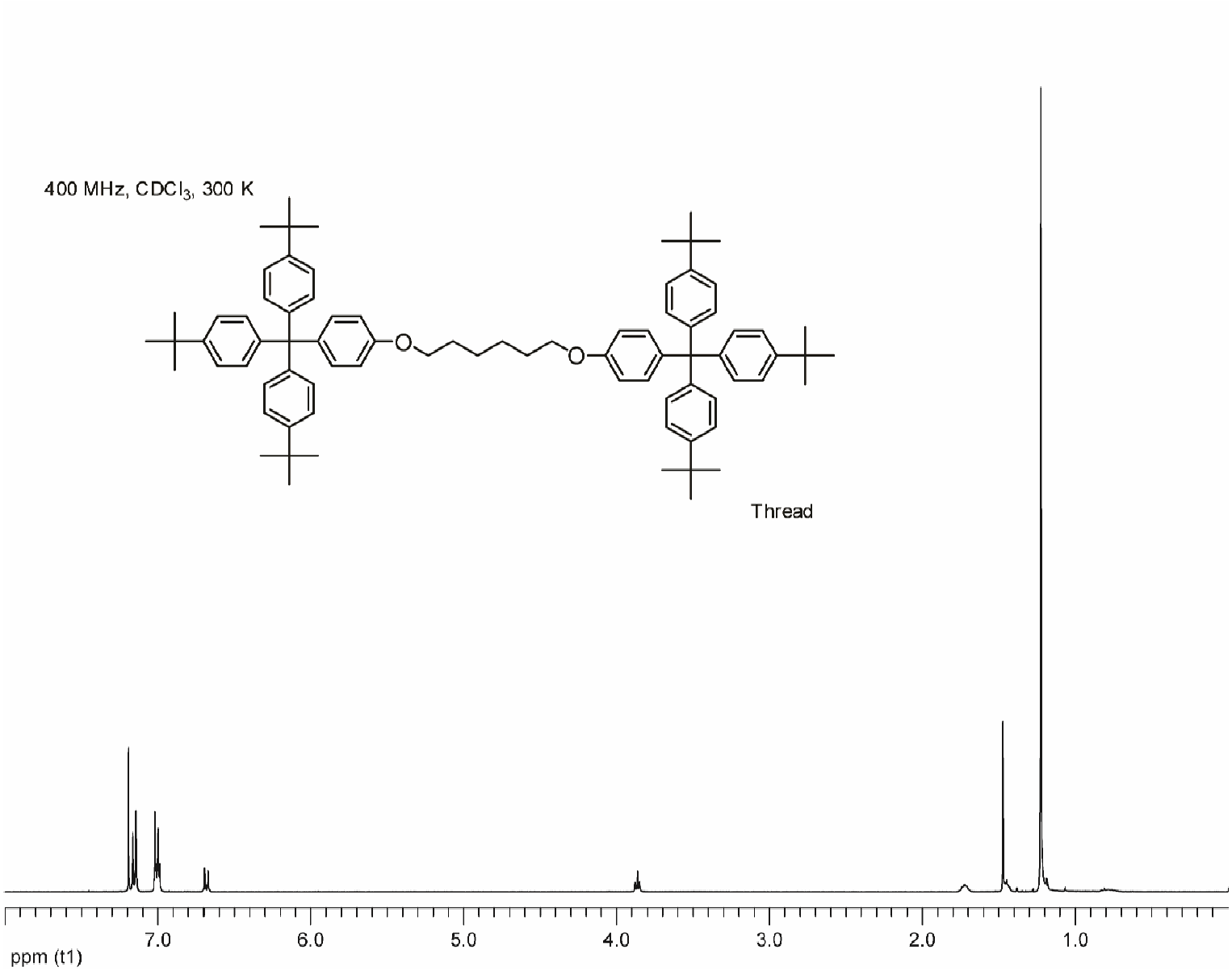

400 MHz, CDCl3, 300 K
HO
NH
HN
OH
O
O
N
O
O
S8
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
ppm (t1)



S9


400 MHz, CDCl3, 300 K
O
O
N
N
N
O
O
S10
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
ppm (t1)


400MHz, CDCl3, 300K
Si
O
O
Si
S11
3.50
3.00
2.50
2.00
1.50
1.00
0.50
0.00
ppm (t1)


400 MHz, CDCl3, 300 K
Thread
7.0
6.0
5.0
4.0
3.0
2.0
1.0
ppm (t1)