Supporting Information for:

Effect of Competing Metal Cations on Neutral Host's Anion Binding Ability

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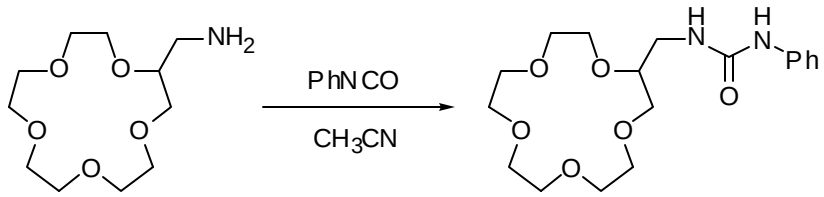
Synthesis

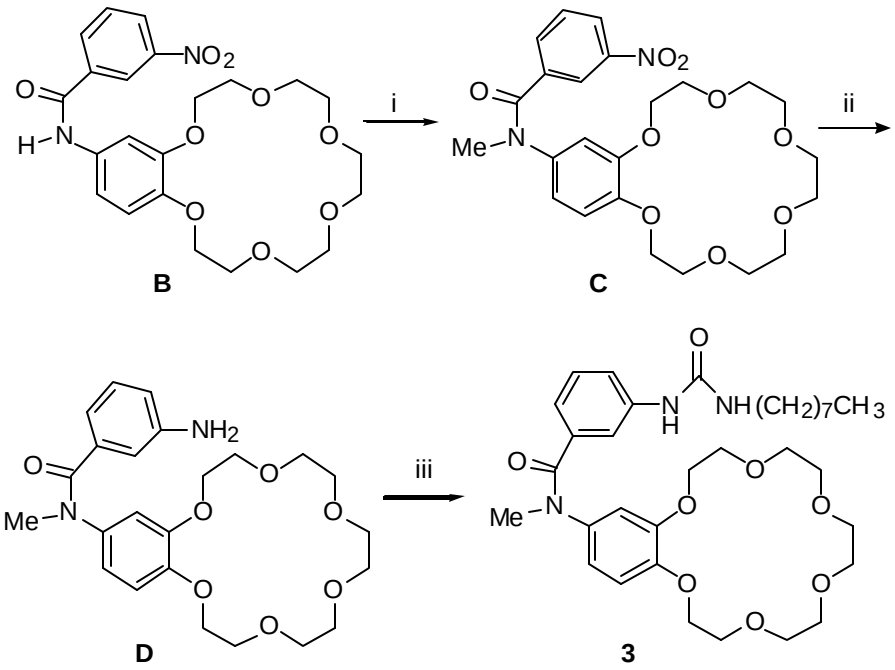
Host, 1 was prepared during a previous study; Hughes, M. P.; Smith, B. D. *J. Org. Chem.* **1997**, *62*, 4492-4501

Host, 2



A **2**

Phenyl isocyanate (0.057 g, 0.48 mmol) was added to a solution of 2-(aminomethyl)-15-crown-5, **A** (0.10 g, 0.4 mmol) in acetonitrile (8 mL) and the reaction heated to reflux temperature for 20 h. After removal of the solvent, the residue was purified by silica gel column chromatography with MeOH-$CHCl_3$ (1:9) as an eluent to give **2** as a viscous liquid (0.09 g, 61%). TLC R_f = 0.37 (methanol/chloroform 1:9); ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 8.19 (NH, s), 7.44 (2H, d, *J* = 8 Hz), 7.21 (2H, t, *J* = 8 Hz), 6.93 (1H, t, *J* = 8 Hz), 6.32 (1H, bs), 3.78–3.57 (19H, m), 3.55–3.36 (2H, m); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) 156.6, 140.0, 129.1, 122.5, 119.4, 77.6, 70.6, 70.6, 70.49, 70.2, 70.1, 70.0, 68.7, 41.3; HRMS (FAB) calcd for ($C_{18}H_{28}N_2O_6$+H) 369.2026, found 369.2025.



i) potassium tert-butoxide, MeI; ii) H_2/Pd; iii) $CH_3(CH_2)_7NCO$

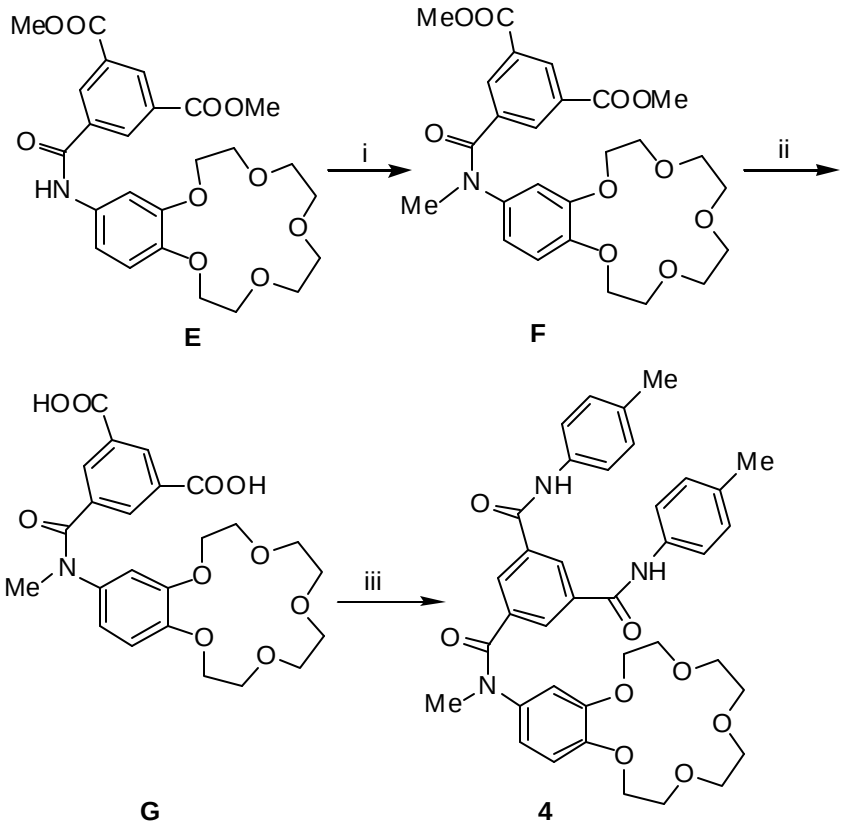
Intermediate B: 3-Aminobenzo-18-crown-6 (0.350 g, 1.06 mmol) and 4-(dimethylamino)pyridine (0.151 g, 1.2 mmol) were dissolved in THF (20 mL) and the solution cooled in an ice bath while stirring under nitrogen. After 10 minutes, 3-nitrobenzoyl chloride (0.230 g, 1.2 mmol) was added as solid and allowed to stir for 12 h. The reaction mixture was concentrated in vacuo, water added and the mixture extracted with chloroform. The organic layer was washed with 0.1 N HCl, satd. $NaHCO_3$ solution and subsequently with water, then dried over anhydrous $MgSO_4$. The solvent was evaporated to give **B** as a yellow solid (0.400 g, 79%) mp 128-131° C. ^{1}H NMR ($CDCl_3$, 300MHz): δ (ppm) 8.69 (s, 1H), 8.36 (d, 1H, *J* = 8.4 Hz), 8.24 (d, 1H, *J* = 8.4 Hz), 8.02 (s, br, 1H), 7.70 (m, 1H), 7.39 (s, 1H), 7.05 (d, 1H, *J* = 9.0 Hz), 6.81 (d, 1H, *J* = 9.0 Hz), 4.18 (m, 4H), 3.85 (m, 4H), 3.65 (m, 12H); ^{13}C NMR (75 MHz, $CDCl_3$): δ (ppm)163.3, 149.3, 148.4, 146.4, 136.8, 133.6, 131.44, 130.3, 126.4, 122.0, 114.4, 113.3, 107.6, 71.0, 70.9, 69.8, 69.7, 69.5, 69.1. MS (FAB) m/z 499 $[M+Na]^+$.

Intermediate C: Compound **B** (0.339 g, 0.71 mmol) was dissolved in THF (25 mL). Potassium *tert*-butoxide (0.823 g, .73 mmol) was added and the reaction was stirred for 10 minutes. Methyl iodide (1.041 g, 7.3 mmol) was added dropwise and stirring was continued for a further period of 6 h. The reaction was quenched with water and extracted with chloroform, washed with 0.1 N HCl and water, dried over $MgSO_4$ and evaporated to give **C** as a yellowish oil (0.300 g, 86 %). ^{1}H NMR ($CDCl_3$, 300MHz): δ (ppm), 8.18 (s, 1H), 8.05 (d, 1H, *J* = 7.2Hz), 7.53(d, 1H, *J* = 7.2 Hz), 7.32 (t, 1H, *J* = 8 Hz), 6.65 (d, 1H, *J* =9.3 Hz), 6.56 (m, 2H), 4.04 (m, 2H), 3.96 (m, 2H),3.81 (m,4H), 3.66 (m,12H), 3.42 (s, 3H);^{13}C NMR (75 MHz, $CDCl_3$): δ (ppm)168.1, 149.4, 148.3, 147.6, 137.8, 137.1, 134.2, 129.0, 124.3, 123.8, 120.1, 113.1, 70.9, 70.7, 69.4, 69.4, 69.3, 69.0, 68.0, 38.7. HRMS Calcd for $C_{24}H_{31}N_2O_9$ 491.2030, found 491.2047.

Intermediate D: Compound **C** (0.300 g, 0.61 mmol) was dissolved in methanol and a catalytic amount (0.030 g) of Pd/C (10% w/w) was added and stirred under H_2 at room temperature for 3h. After the reaction was complete, the solution was filtered and the solvent evaporated to give **D** (0.230 g, 82%) as a colorless oil. ^{1}H NMR ($CDCl_3$, 300MHz) : δ (ppm), 6.99 (t, 1H, *J* = 7.5 Hz), 6.86 (s, 1H), 6.83 (s, 1H), 6.74 (d, 1H, *J* =7.8 Hz), 6.66 (2H, m), 6.48 (d, 1H, *J* = 8 Hz) 4.07 (s, 2H), 3.98 (s, 2H), 3.82 (m, 4H), 3.64 (m, 6H), 3.62 (m, 6H), 3.38 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ (ppm) 170.1, 148.2, 146.8, 138.1, 137.4, 129.1, 121.5, 119.6, 119.2, 118.0, 112.8, 70.4, 70.4, 69.4, 69.1, 68.5, 38.7. HRMS Calcd for $C_{24}H_{33}N_2O_7$ 461.2288, found 461.2299.

Host 3: A mixture of **D** (0.230 g, 0.5 mmol) and octylisocyanate (0.077 g, 0.5 mmol) in chloroform was stirred at room temperature for 8h. The completed reaction was washed with

0.1N HCl, satd. Na_2CO_3 solution and water, dried over anhydrous $MgSO_4$ and the solvent removed under vacuum. The residual oil was purified by chromatography (SiO_2, CH_2Cl_2: MeOH, 20:1) to afford **3** (0.120 g, 39%) as a colorless oil. ^{1}H NMR ($CDCl_3$, 300MHz): δ (ppm), 7.64 (s, 1H), 7.58 (d, 1H, *J* =8.1 Hz), 7.01 (t, 1H, *J* = 7.5 Hz), 6.90 (s, 1H), 6.86 (d, 1H, *J* = 7.2 Hz), 6.60 (dd, 2H, *J* = 7.2 Hz), 6.48 (d, 1H, *J* = 8.1 Hz), 5.91 (t, 1H, br), 4.03 (s br, 4H), 3.79 (m, 4H), 3.65 (m, 6H), 3.62 (m, 6H), 3.38 (s, 3H), 3.10 (m, 2H), 1.42 (m, 2H), 1.22 (m, 10H), 0.84 (t, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) 170.8, 156.1, 148.6, 147.1, 139.9, 138.1, 136.3, 128.6, 121.9, 120.4, 119.7, 118.6, 112.9, 112.4, 70.6, 70.5, 69.4, 69.3, 68.6, 68.4, 40.1, 32.0, 30.5, 29.5, 29.4, 27.2, 22.8, 14.2. HRMS Calcd for $C_{33}H_{50}N_3O_8$ 616.3598, found 616.3605.



i) NaH, MeI; ii) KOH; iii) DMAP, EDC, HOAT, 4-toluidine

Intermediate E: 3,5-Dimethoxybenzoic acid (0.362 g, 1.5 mmol), 4-(dimethylamino)pyridine (0.185 g, 1.5 mmol), 1-[3-(dimethylamino)propyl]-3-ethylcarbodiimide hydrochloride (0.291 g, 1.5 mmol), 1-hydroxy-7-azabenzotriazole (0.189 g, 1.5 mmol) were suspended in acetonitrile (20 mL) and allowed to stir at 0-5 C for 30 mins. Aminobenzo-15-crown-5 (0.431 g, 1.5 mmol) dissolved in acetonitrile was slowly added with stirring. The reaction mixture was allowed to stir at room temperature for an additional 6 hrs. The resulting suspension was poured into water (50 mL) and extracted with methylene chloride. The organic layer was washed with 0.1 M HCl and subsequently with water, dried over anhydrous $MgSO_4$, then evaporated to give **E** as a white powder (0.450 g, 59%). ^{1}H NMR ($CDCl_3$, 300MHz): δ (ppm), 8.84 (t, 1H, *J* =1.9Hz), 8.72(d, 2H, *J*=1.2 Hz), 7.87 (s, 1H), 7.47 (m, 1H), 7.05 (m, 1H, J_1= 2.4, J_2 = 8.7 Hz), 6.88 (m, 1H *J* =

9.0 Hz), 4.18 (m, 4H), 3.99 (s, 6H), 3.93 (m, 4H), 3.91 (m, 8H). ^{13}C NMR (75 MHz, $CDCl_3$): δ (ppm), 165.6, 163.7, 149.6, 146.5, 136.0, 133.4, 132.3, 131.9, 131.4, 114.9, 113.3, 107.7, 71.3, 71.2, 70.8, 70.7, 69.9, 69.8, 69.7, 69.1, 52.9. HRMS (FAB) m/z 503.1776 $[M+1]^+$ calcd 503.1791.

Intermediate F: Intermediate **E** (0.450 g, 0.89 mmol was dissolved in 10 mL of THF:DMF (1:1. NaH (0.064 g, 2.6 mmol) was added and the reaction allowed to stir at room temperature for 10 mins. Iodomethane (0.634 g, 4.4 mmol) was added and the reaction mixture was heated to 100 C for 8 h. The solvent was evaporated and the reaction quenched with saturated ammonium chloride solution, extracted with dichloromethane, washed with 0.1M HCl and water, and dried over anhydrous magnesium sulfate. Removal of the solvent under vacuum yielded a colorless oil which was purified by chromatography (SiO_2 , eluent: 20:1 (CH_2Cl_2: MeOH) to afford the desired compound **F** (0.330 g, 71 %). ^{1}H NMR ($CDCl_3$, 300MHz): δ (ppm), 8.50 (t, 1H, *J* =1.1Hz), 8.15 (d, 2H, *J*=1.2 Hz), 6.60 (m, 3H), 4.18 (m, 4H), 3.95 (m, 4H), 3.89 (s, 6H), 3.81 (m, 4H), 3.65 (m, 8H), 3.41 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$), δ (ppm): 168.4, 165.1, 149.1, 147.9, 137.0, 137.0, 1333.1, 131.0, 130.0,119.9, 113.5, 113.1, 70.6, 70.0, 69.0, 68.8, 68.6, 52.2, 38.2. HRMS Calcd for $C_{26}H_{32}NO_{10}$ 518.2026, found 518.2018.

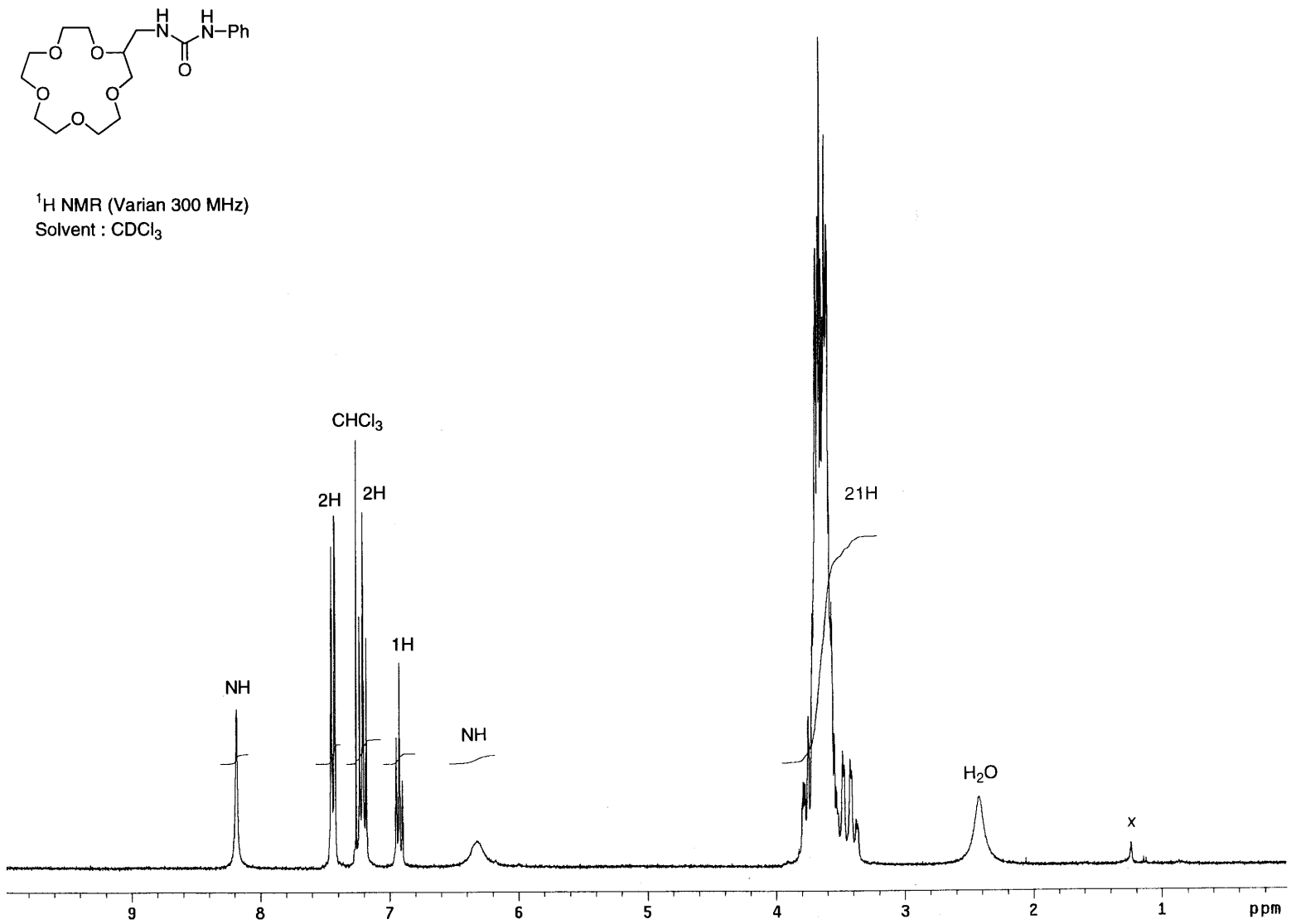
Intermediate G: To a solution of compound **F** (0.200 g, 0.38 mmol) in methanol (20 mL) was added KOH (0.042 g, 0.76 mmol) dissolved in water (2 mL) and the solution allowed to stir for 14h. The methanol was evaporated and another 5 mL of water was added. Upon acidification with dilute HCl, a white solid precipitated which was collected by filtration and washed with water and ethyl acetate. Recrystallization from methanol yielded 0.105 g of **G** (56%). ^{1}H NMR

(DMSO-d_6, 300MHz): δ (ppm), 8.32 (t, 1H, *J* =1.1Hz), 7.97 (d, 2H, *J*=1.2 Hz), 6.94 (d, 1H), 6.76 (m, 1H), 6.70 (m, 1H), 3.95 (m, 4H), 3.67 (m, 4H), 3.54 (m, 8H), 3.35 (s, 3H). HRMS Calcd for $C_{24}H_{27}NO_{10}$ 490.1713, found 490.1696.

Host 4: A solution of diacid **G** (0.050 g, 0.1 mmol), 4-(dimethylamino)pyridine (0.024 g, 0.2 mmol), 1-[3-(dimethylamino)propyl-3-ethyl]carbodiimide hydrochloride (0.039 g, 0.2 mmol), and 1-hydroxy-7-azabenzotriazole (0.027 g, 0.2 mmmol) in DMF (20 mL) was allowed to stir at ice bath temperature for 1h. *p*-Toluidine (0.021 g, 0. 2 mmol) was added and the solution allowed to warm to room temperature while stirring was continued for another 12 h. The DMF was evaporated and water (20 mL) was added and extracted with methylene chloride. The organic layer was washed with 0.1M HCl and water in succession, dried over $MgSO_4$. Removal of the solvent gave a yellowish solid which was chromatographed on silica using 25:1(CH_2Cl_2: MeOH) as eluent (0.030 g, 44 %). ^{1}H NMR ($CDCl_3$, 300MHz): δ (ppm), 8.29 (s, 2H), 8.13 (t, 1H, *J* = 1.1Hz) 7.82 (d, 2H, *J*=1.2 Hz), 7.55 (d, 4H, *J* = 8.4), 7.17 (d, 4H, *J* = 8.1Hz), 6.64 (d, 1H, *J* = 7.4), 6.59 (d, 1H, *J* = 7.4) 6.45 (s, 1H) , 4.01(m, 2H), 3.90 (m, 2H), 3.81 (m, 2H), 3.76 (m, 2H), 3.68 (m, 8H), 3.42 (s, 3H), 2.32 (s, 6H). HRMS Calcd for $C_{38}H_{42}N_3O_8$ 668.2972, found 668.2964.

^{1}H NMR Titrations. A solution of host compound (0.75 mL, 10 mM) in the absence and presence of one equiv. of alkali tetraphenylborate (or picrate) was titrated in NMR tubes with increasing amounts of guest stock solution (0.50 mL, 150 mM) as follows (in μL): 0, 12.5, 25, 37.5, 50, 75, 100, 150, 200, 250. The association constant K_a was calculated from the obtained curves (δ_{obs} vs $[G]_0/[H]_0$) using a nonlinear least squares regression analysis program (Hughes,

M. P.; Smith, B. D. *J. Org. Chem.* **1997**, *62*, 4492-4501), where δ_{obs} is the observed chemical shift of the host NH, $[H]_0$ and $[G]_0$ are the initial host and guest concentrations, respectively.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H
N–Ph
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O
O
O
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$CHCl_3$
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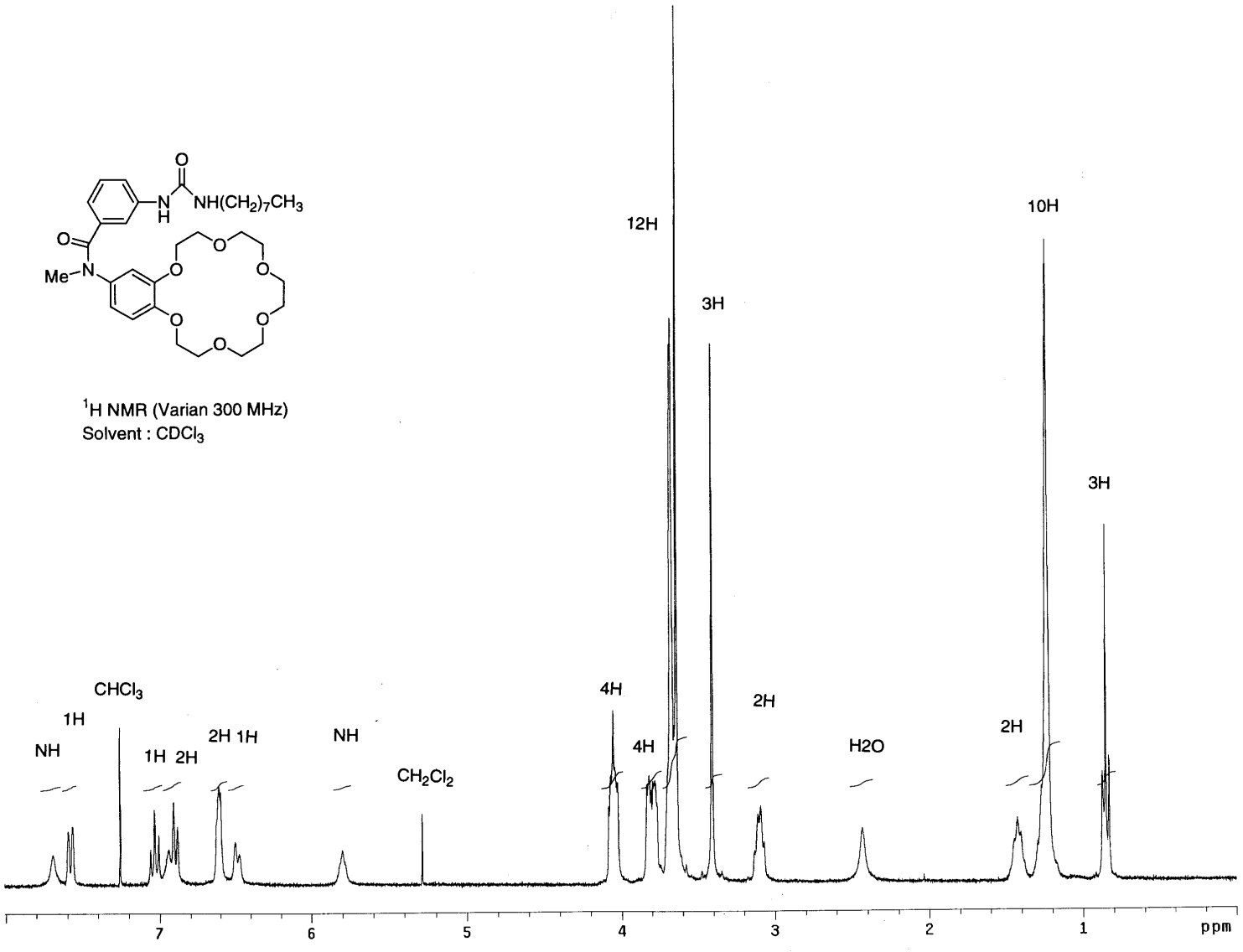
ppm


^{1}H NMR (Varian 300 MHz)
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2H
2H 1H
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4H
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10H
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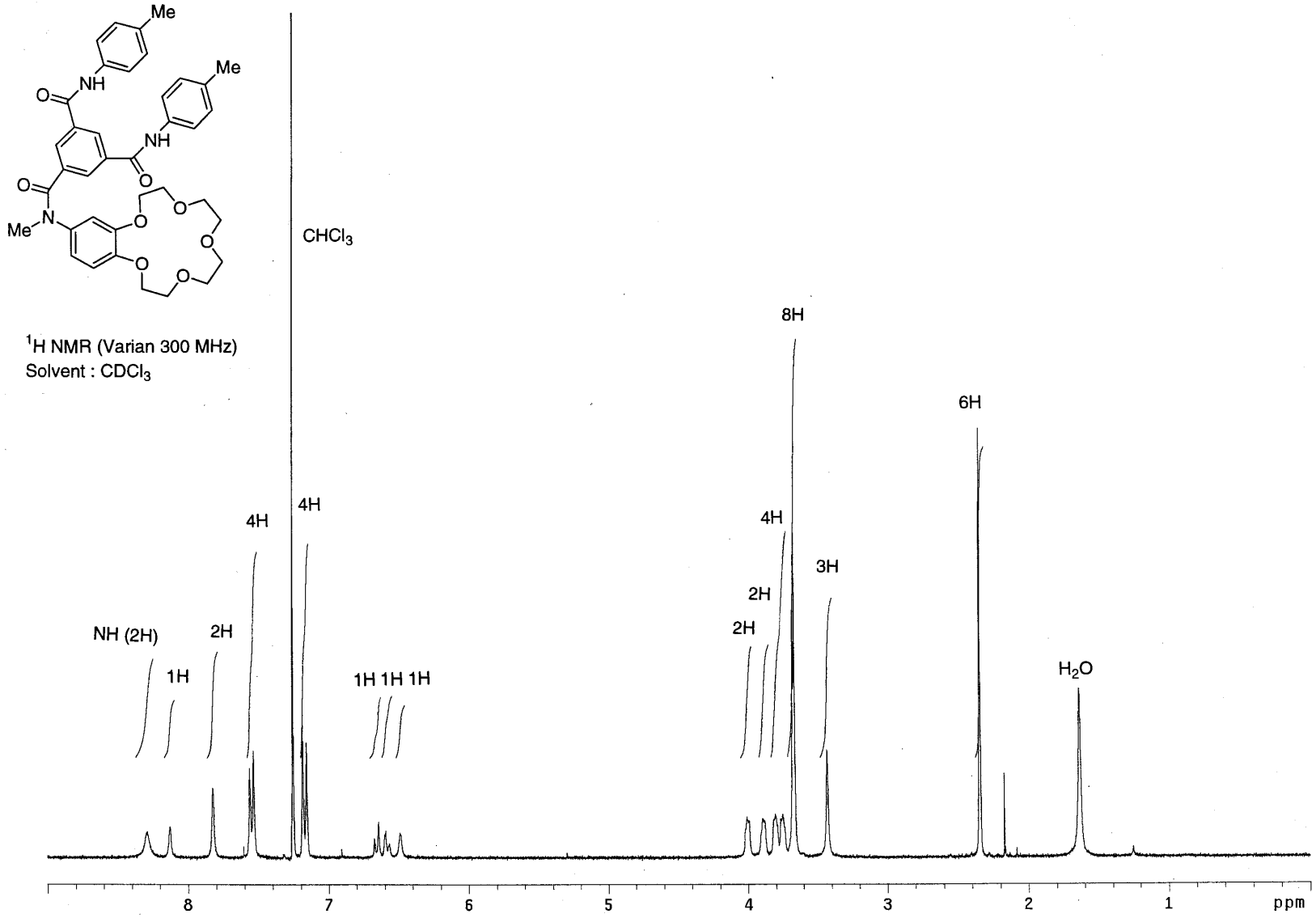
ppm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4H
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ppm