

Electronic supplementary information

SYNTHETIC APPROACHES TO 18-TRIAZACROWN-6 ETHER AND A LEAD COMPLEX OF ITS BIPYRIDYL DERIVATIVE

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1. Materials and methods

All commercially available reagents and solvents were used without further purification. Reaction progress was followed by TLC using aluminum oxide (Merck, 60 F254, neutral). The ^1H and ^{13}C NMR spectra were recorded on Varian Inova 400 or Bruker Avance 400 spectrometers at 25 °C. The chemical shifts are reported in parts per million (δ) relative to the deuterated solvent signal used as an internal reference (CDCl_3 δ = 7.27 ppm). The coupling constants (J) are given in Hertz. The spectral assignments were partially based on the results of 2D NMR experiments (COSY, NOESY, HSQC, and HMBC). The numbering scheme of the hydrogen and carbon nuclei used to describe the NMR spectra is given in Figures in the Electronic supplementary information (ESI). Electrospray ionization mass spectrometry (ESI-MS) analysis was performed using a Shimadzu LCMS-2020 High Performance Liquid Chromatograph Mass Spectrometer with a single quadrupole detector, desolvation line/heat block temperature 250/400 °C, and an ionization voltage of 4.5 kV. The electrospray full scan spectra were obtained by infusion at 0.4 mL/min of MeCN solution of the compound. The elemental analysis was conducted on a Carlo Erba 1108 elemental analyzer in the Laboratory of Microanalysis of INEOS RAS.

2. Synthesis of compounds

Compounds **1**, **4** [1], **5** [2], **6** [3], and **8** [4] were prepared according to the published procedures.

6,9,12-Trioxa-3,15-diaza-1(2,6)-pyridinecyclohexadecaphane-2,16-dione (2). A solution of dimethyl pyridine-2,6-dicarboxylate **1** (54 mg, 0.277 mmol) in anhydrous methanol (9 mL) and a solution of 1,11-diamino-3,6,9-trioxaundecane (53 mg, 0.277 mmol) in anhydrous methanol (9 mL) were simultaneously added dropwise to a solution of methanol (9 mL) containing potassium carbonate (77 mg, 0.558 mmol) upon vigorous stirring. The reaction mixture was stirred at room temperature for 7 days. The solvent was evaporated under vacuum, and the resulting residue was dissolved in water and extracted with dichloromethane. The organic solvent was removed under vacuum to yield the target product as a white solid. Yield: 42 mg (47%). ^1H NMR (CDCl_3 , 400 MHz): 3.65–3.69 (m, 12H, H(6–8)), 3.80 (q, 4H, H(5), J = 4.8), 8.02 (t, 1H, H(1), J = 7.6), 8.35 (d, 2H, H(2), J = 7.7), 8.84 (br. s, 2H, NH). The data obtained correspond to the literature data [5].

Synthesis of 6,9,12-trioxa-3,15-diaza-1(2,6)-pyridinecyclohexadecaphane (3)

Method A. 1M $\text{BH}_3 \cdot \text{THF}$ (5.57 mL, 5.57 mmol) was added to compound **2** (30 mg, 0.093 mmol) in an argon atmosphere at 0 °C. The mixture was stirred at 0 °C for 4 days. Then MeOH (5 mL) was added and the mixture was stirred for 15 min. The solvent was evaporated under vacuum, and then 0.5 M HCl (4 mL) was added and the mixture refluxed for 24 h. After cooling, the reaction mixture was washed with CHCl_3 , adjusted to pH = 10 by adding KOH, and the target product was extracted with CHCl_3 . After solvent evaporation, compound **3** was obtained as a yellow oil.

Method B. A solution of 2,6-bis(chloromethyl)pyridine **5** (27 mg, 0.153 mmol) in anhydrous MeCN (10 mL) and a solution of 1,11-diamino-3,6,9-trioxaundecane (29 mg, 0.153 mmol) in anhydrous MeCN (10 mL) were simultaneously added dropwise to a MeCN solution (50 mL) containing potassium carbonate (85 mg, 0.614 mmol) upon vigorous stirring. The reaction mixture was stirred at room temperature for 7 days. The solvent was evaporated under vacuum, and the residue was dissolved in water and extracted with dichloromethane. The organic solvent was removed under vacuum to give the target product as a yellow oil.

Method C. A solution of 2,2'-[2,2'-oxybis(ethane-2,1-diyl)bis(oxy)]diethanamine (417 mg, 2.172 mmol) in MeOH (50 mL) was added dropwise to a solution of 2,6-pyridinedicarbaldehyde **6** (294 mg, 2.172 mmol) and CaCl_2 (242 mg, 2.172 mmol) in MeOH (95 mL) over 2 h under an argon atmosphere. The reaction mixture was refluxed for 2 h. The solution was cooled to 5 °C, then NaBH_4 (1096 mg, 29.326 mmol) was added dropwise over 1 h and the mixture was stirred at room temperature overnight. To remove the template, H_2O (57 mL) was added, and stirring was continued for 4 h. The solvent was

evaporated, and the product was extracted with dichloromethane. The solvent was evaporated under vacuum to give the target product as a yellow oil. Yield: 590 mg (92%).

^1H NMR (CDCl_3 , 400 MHz): 2.84 (t, 4H, H(5), $J = 4.7$), 3.60–3.68 (m, 12H, H(6,7,8)), 3.86 (s, 4H, H(4)), 7.01 (d, 2H, H(2), $J = 7.8$), 7.54 (t, 1H, H(1), $J = 7.6$). The data obtained correspond to the literature data [6].

3,15-Bis(pyridin-2-ylmethyl)-6,9,12-trioxa-3,15-diaza-1(2,6)-pyridinecyclohexadecaphane (PADPy). A solution of 2-chloromethylpyridine **8** (87 mg, 0.528 mmol) in acetonitrile (6 mL) was added to a mixture of **3** (78 mg, 0.264 mmol) and potassium carbonate (146 mg, 1.056 mmol) in acetonitrile (6 mL). The reaction mixture was refluxed for 24 h. Acetonitrile was evaporated under vacuum, and the product was extracted with chloroform. The solvent was evaporated under vacuum, and the product was purified by flash chromatography (Al_2O_3 basic, $\text{CHCl}_3/\text{MeOH}$ (10:1)). The product was obtained as a brown oil. Yield: 102 mg (71%). ^1H NMR (CDCl_3 , 300 MHz): 2.77 (t, 4H, H(5), $J = 5.9$), 3.46 (br. s, 8H, H(7,8)), 3.54 (t, 4H, H(6), $J = 5.9$), 3.86 (s, 8H, H(4), H(9)), 7.08 (t, 2H, H(13), $J = 5.3$), 7.20 (d, 2H, H(2), $J = 7.5$), 7.50–7.55 (m, 3H, H(1,11)), 7.60 (t, 2H, H(12), $J = 7.3$), 8.45 (d, 2H, H(14), $J = 4.8$). ^{13}C NMR (CDCl_3 , 400 MHz): 52.68 (C-5), 60.18 (C-4), 61.43 (C-9), 68.94 (C-6), 70.04 (C-7), 70.44 (C-8), 121.17 (C-2), 121.71 (C-13), 122.77 (C-11), 136.23 (C-1, C-12), 148.77 (C-14), 158.41 (C-3), 159.58 (C-10). MS (ESI), m/z : calcd for $\text{C}_{27}\text{H}_{35}\text{N}_5\text{O}_3 + \text{H}^+$: 478.3 $[\text{M} + \text{H}]^+$; found: 478.3; calcd for $\text{C}_{27}\text{H}_{35}\text{N}_5\text{O}_3 + \text{Na}^+$: 500.3 $[\text{M} + \text{Na}]^+$; found: 500.3; calcd for $\text{C}_{27}\text{H}_{35}\text{N}_5\text{O}_3 + 2\text{H}^+$: 239.6 $[\text{M} + 2\text{H}]^{2+}$; found: 239.8. Anal. Calcd for $\text{C}_{27}\text{H}_{35}\text{N}_5\text{O}_3 \cdot 2\text{MeOH}$: C, 64.30; H, 8.00; N, 12.93. Found: C, 64.29; H, 7.85; N, 12.81%.

3. ESI MS experiment

The sample of the Pb^{2+} complex for ESI MS experiment was prepared by mixing a solution of the corresponding ligand (0.05 μmol) in MeCN (50 μL) with a solution of $\text{Pb}(\text{ClO}_4)_2$ (0.05 μmol) in MeCN (50 μL) and diluting to 1000 μL . The resulting solution was studied by ESI mass spectrometry.

4. NMR study

The sample of the Pb^{2+} complex for the NMR measurement was prepared by dissolving the ligand ($c_L = 0.02$ M) and 5 eq. $\text{Pb}(\text{ClO}_4)_2$ in CD_3CN .

5. NMR spectra and ESI MS

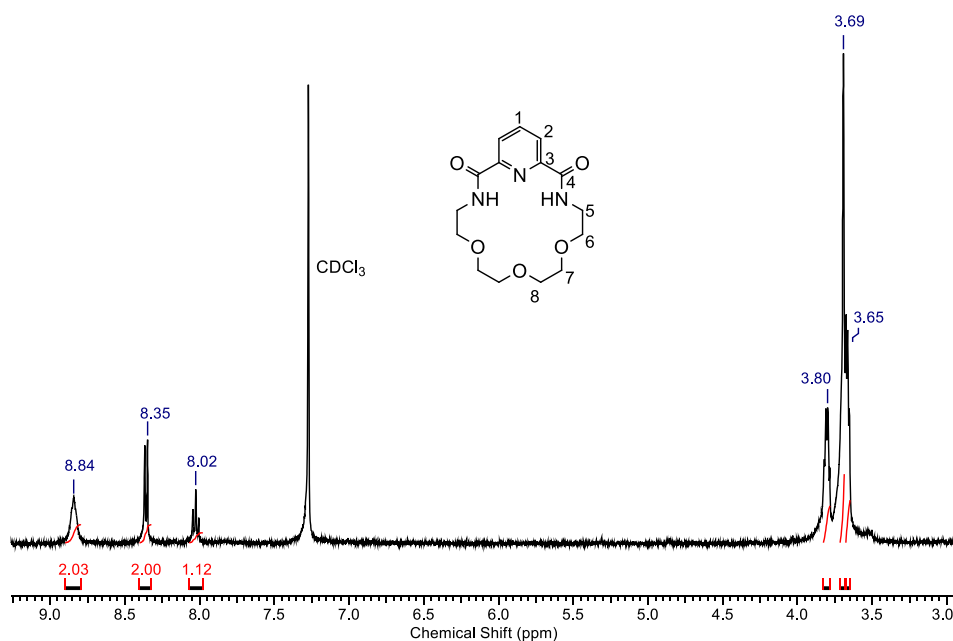


Figure S1. ^1H NMR spectrum of **2** in CDCl_3 .

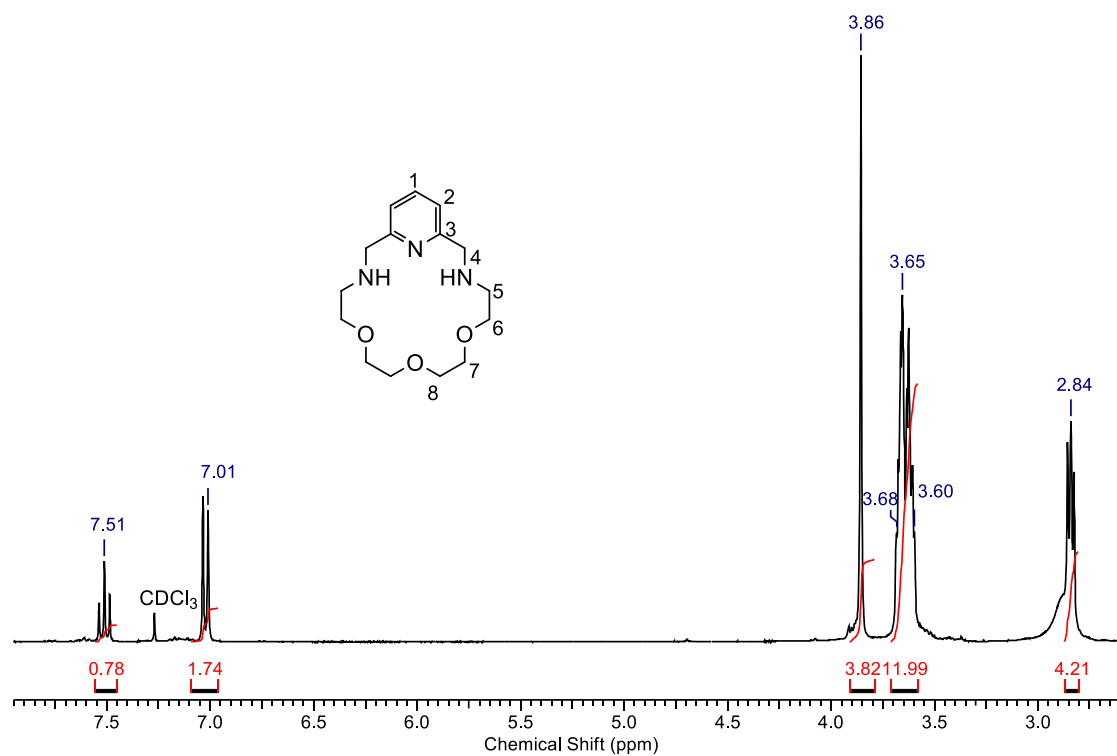


Figure S2. ¹H NMR spectrum of **3** in CDCl₃.

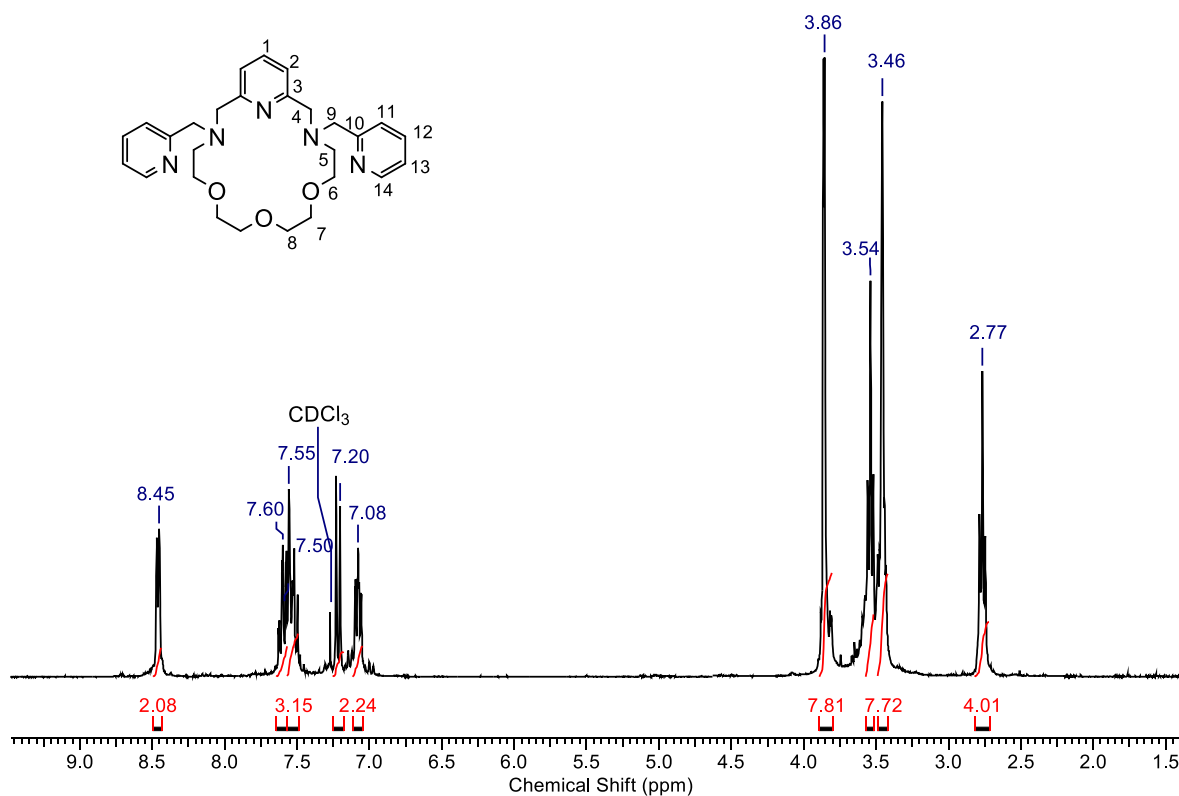


Figure S3. ¹H NMR spectrum of **PADPy** in CDCl₃.

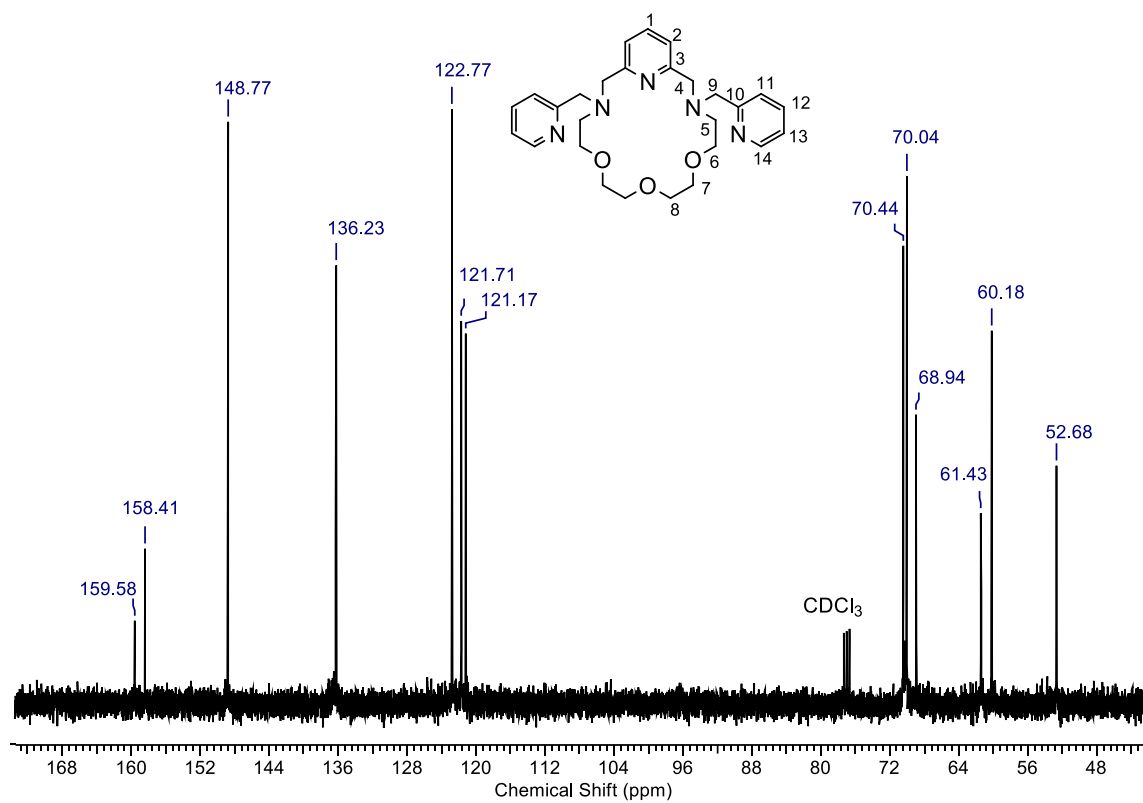


Figure S4. ¹³C NMR spectrum of PADPy in CDCl₃.

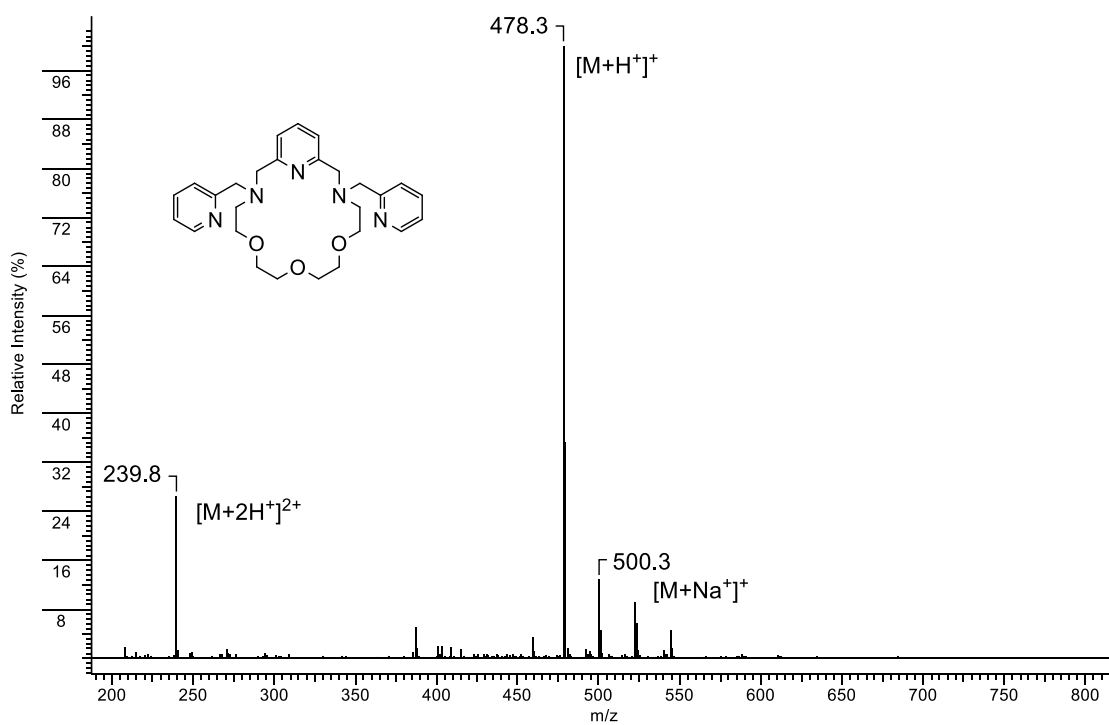


Figure S5. ESI MS of PADPy.

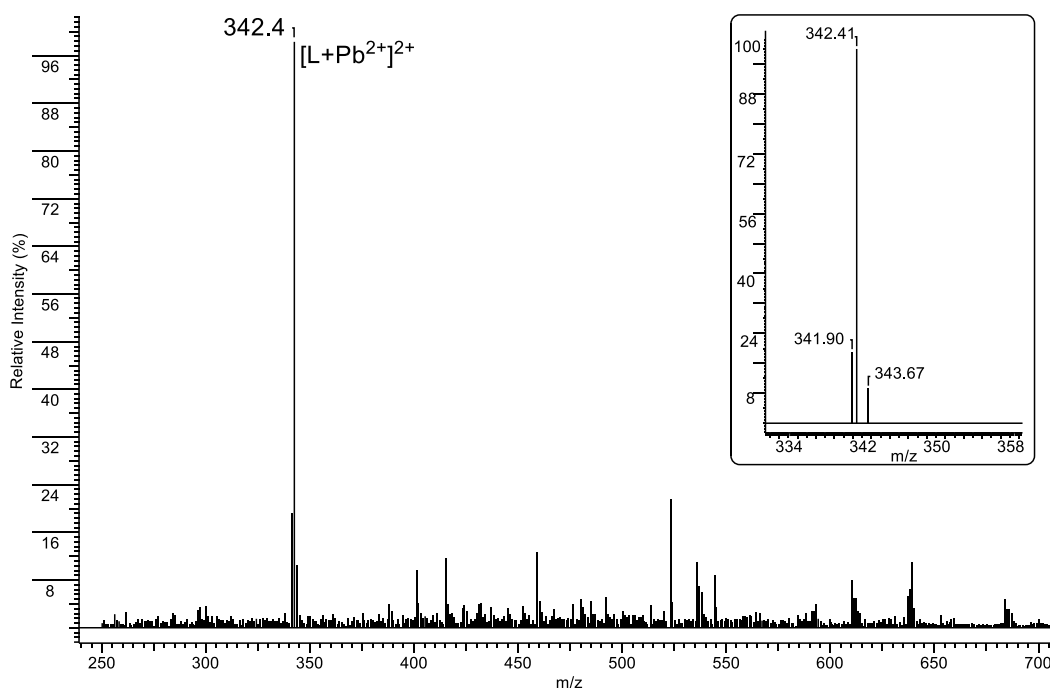


Figure S6. ESI MS of Pb-PADPy.

6. References

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