Supplementary Material (ESI) for Organic and Biomolecular Chemistry

Supporting Information

Novel Asymmetrically Functionalized Bis-Dipicolylamine Metal Complexes: Peripheral Decoration of a Potent Anion Recognition Scaffold

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Supporting Information

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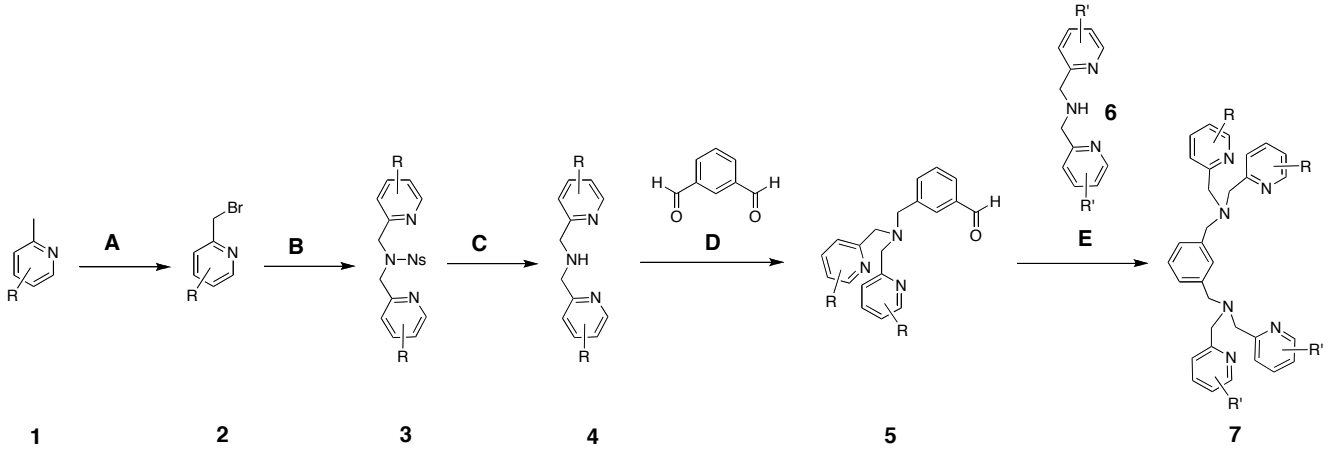
Chemistry: General Methods. Anhydrous solvents methanol, DMSO, CH_2Cl_2, THF and DMF were purchased from Sigma Aldrich and used directly from Sure-Seal bottles. Molecular sieves were used after heating under vacuum for several minutes. All reactions were performed under an atmosphere of dry nitrogen in oven-dried glassware and were monitored for completeness by thin-layer chromatography (TLC) using silica gel (visualized by UV light, or developed by treatment with $KMnO_4$ stain or phosphomolybdic acid stain). ^1H and ^{13}C NMR spectra were recorded on Bruker 400 MHz in $CDCl_3$. Chemical shifts (δ) are reported in parts per million after calibration to residual isotopic solvent. Coupling constants (*J*) are reported in Hz.

Isothermal Titration Calorimetry Binding Experiments. Isothermal titration calorimetry (ITC) experiments were used to measure the binding of our metal complexes to various substrates, and were performed at 25 ºC (298 K) using Microcal VP-ITC titration microcalorimeter. In order to minimize mixing heat effects caused by differences in solution composition, the substrates and receptor were both dissolved in freshly prepared HEPES buffer (± 5% DMSO) (50 mM, pH = 7.2) before each titration experiment. All solutions prior to experiments were degassed before being added to the calorimeter cell. The substrates, at a concentration of approximately 2.0 mM, were injected in 10μL increments into the reaction cell (cell volume 1.49 mL) containing complex at a concentration of *ca* 0.1 mM, until there occurred a saturation of binding sites. A 250 μL injection syringe with 310–400 rpm stirring was used to give a series of 10 μL injections at 3.5-minute intervals. Control experiments for heats of mixing and dilution were performed under identical conditions and used for data correction in subsequent analysis. Data acquisition and subsequent non-linear regression analysis were done in terms of a simple binding model using the Microcal ORIGIN software package.

Supporting Information

Synthetic Protocols

General Procedures



General Procedure A – Methyl bromination of 2-methylpyridine-R[1] derivatives with NBS. To a solution of the picoline (1 eq) and NBS (1.1 eq) stirred in anhydrous CCl_4 (0.1 M) was added catalytic benzoyl peroxide. The solution was then heated to 75 °C and the reaction allowed to stir at room temperature overnight. When TLC indicated the reaction was complete, the solution was diluted with CH_2Cl_2, and washed twice with small portions of saturated sodium bicarbonate solution. The organic layer was then dried over Na_2SO_4 and concentrated *in vacuo*.

General Procedure B - Alkylation of 2-nitrobenzene-sulphonamide with 2-(bromomethyl)pyridine derivatives. To a stirred solution of bromide **2** (2.1 eq) and K_2CO_3 (2.5 eq) in DMF (0.1M), 2-nitrobenzene-sulfonamide (1 eq) was added in one portion. The solution was then heated to 60 °C and allowed to stir for several hours. When TLC confirmed that the reaction was complete, the solution was allowed to cool to room temperature. The solution was then decanted into a saturated sodium bicarbonate solution, and the product was extracted into ethyl acetate. The organic fractions were then combined, washed several times with small portions of 50 % saturated bicarbonate solution, dried over Na_2SO_4 and concentrated *in vacuo.*

General Procedure C – Thiophenol mediated deprotection of nosyl protected secondary amines. To a stirred solution of nosyl protected amine **3** (1 eq) and K_2CO_3 (1.5 eq) in DMF (0.1 M) was added thiophenol (1.1 eq). The solution was then allowed to stir at room temperature until TLC confirmed that the reaction was complete. The solution was then decanted into saturated sodium bicarbonate solution, and the product was extracted several times into ethyl acetate. The organic fractions were then combined and washed thoroughly with small portions of half-saturated bicarbonate solution, dried over Na_2SO_4 and concentrated *in vacuo.*

Supporting Information

General Procedure D – Mono-substitution of isophthalaldehyde via reductive amination with functionalized dipicolylamine derivatives. To a stirred solution of isophalaldehyde (3 eq) and 4 Å molecular sieves in 1,2-dichloroethane (0.1 M) was added $NaBH(OAc)_3$ (1.3 eq) in one portion at room temperature under an atmosphere of nitrogen. Amine **4** (1 eq) was then added dropwise over a 10 minute period, and the solution was allowed to stir overnight. When TLC confirmed that the reaction was complete, the 1,2-dichloroethane solution was diluted with dichloromethane, and washed twice with saturated sodium bicarbonate solution. The organic layer was then dried over Na_2SO_4 and concentrated *in vacuo*.

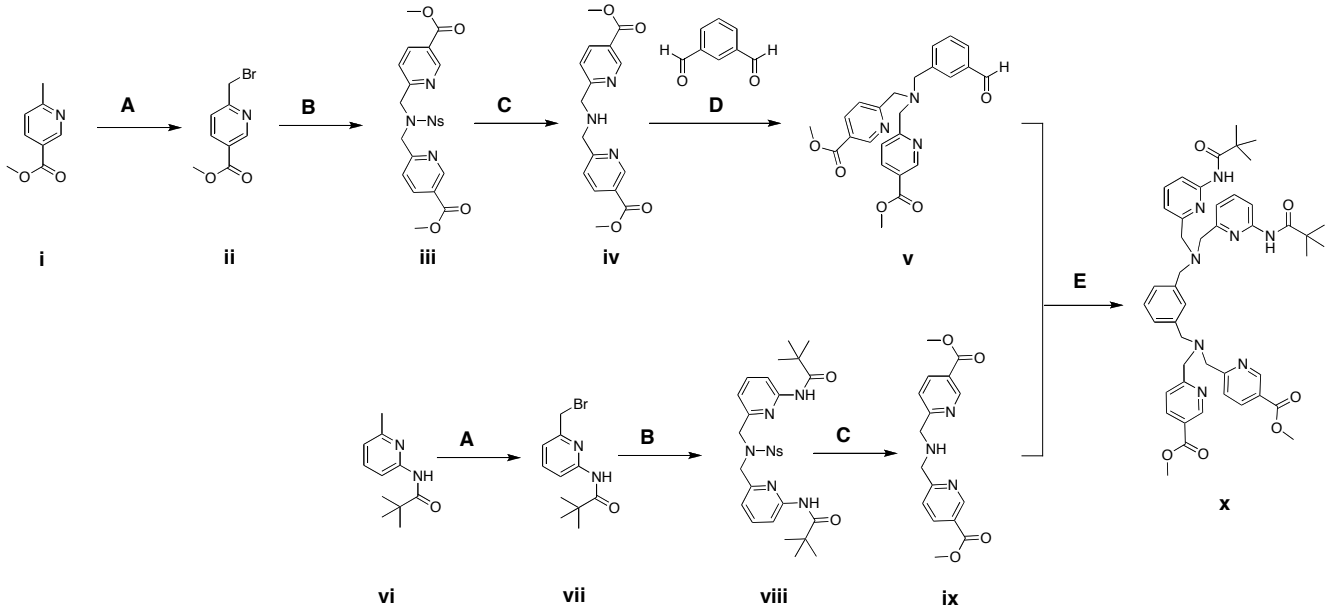
General Procedure E – Second substitution of mono-substituted isophthalaldehyde via reductive amination with functionalized dipicolylamine derivatives. To a stirred solution of aldehyde **5** (1 eq), amine **6** (1 eq) and 4 Å molecular sieves in 1,2-dichloroethane (0.1 M), was added $NaBH(OAc)_3$ (1.3 eq) at room temperature. The solution was then allowed to react under N_2 overnight. When TLC confirmed that the reaction was complete, the 1,2-dichloroethane solution was diluted with dichloromethane, and washed twice with small equivalents of saturated sodium bicarbonate solution. The organic layer was then dried over Na_2SO_4 and concentrated *in vacuo*.

General Procedure for Metallation of Functionalized Scaffolds. Following purification by silica gel chromatography the final scaffolds were dissolved in anhydrous methanol, zinc triflate (2.05 eq) was added in one portion, and the solution was allowed to stir overnight at room temperature. The methanol was then removed *in vacuo* and the resulting solid was washed twice with ether to remove unreacted scaffold. The solid was then re-dissolved in a small volume of methanol and filtered through National Scientific Target Syringe Filters (Cellulose Acetate Membrane) 4mm, 0.20 μm. Finally, the filtrate was diluted in distilled water and lyophilized to dryness.

Supporting Information

REPRESENTATIVE SYNTHESIS

(1) Dimethyl 6,6'-(3-((bis((5-hydroxypyridin-2-yl)methyl)amino)methyl)benzylazanediyl) bis(methylene)dinicotinate.



Methyl 6-(bromomethyl)nicotinate (ii). Methyl 6-methylnicotinate (**i**) was brominated with NBS on a 13.23 mmol scale *via* General Procedure **A,** purified via silica gel chromatography (4:1 Hexanes:EtOAc), to furnish **ii** (2.04 g, 67 %): δ_H (400 MHz, $CDCl_3$) 3.88 (s, 3H, -OCH_3), 4.50 (s, 2H, -CH_2Br), 7.46 (d, J = 8.7 Hz, 1H, CH (Ar)), 8.21 (dd, J = 8.2 and 2.0 Hz, 1H, CH (Ar)), 9.1 (s (br), 1H, CH (Ar)); δ_C (400 MHz, $CDCl_3$) 32.6, 52.3, 122.8, 125.0, 137.0, 150.5, 160.7, 165.0; LRMS (ES+) m/z = 230.0 [M+]; IR (KBr, cm^{-1}) 3072, 2959, 1728, 1712, 1638, 1617, 1597, 1435.

Dimethyl 6,6'-(2-nitrophenylsulfonylazanediyl)bis(methylene)dinicotinate (iii). Methyl 6-(bromomethyl)nicotinate **(ii)** was protected with 2-nitrobenzenesulfonamide and K_2CO_3 on a 3.159 mmol scale *via* General Procedure **B,** purified via silica gel chromatography (2:5 Hexanes:EtOAc), to furnish **iii** (679 mg, 90%): δ_H (400 MHz, $CDCl_3$) 3.88 (s, 6H, 2 x -OC<u>H</u>$_3$), 4.76 (s, 4H, 2 x -NC<u>H</u>$_2$Ar), 7.34 (d, J = 8.3 Hz, 2H, 2 CH (Ar)), 7.61 (m, 3H, 3 CH (Ar)), 8.02 (dd, J = 7.9 and 1.1 Hz, 1H, CH (Ar)), 8.12 (dd, J = 8.2 and 2.2 Hz, 2H, 2 CH (Ar)), 8.91 (d, J = 1.5 Hz, 2H, CH (Ar)); δ_C (400 MHz, $CDCl_3$) 52.2, 52.9, 121.7, 124.0, 124.7, 131.0, 131.5, 133.3, 133.6, 137.6, 147.7, 150.2, 159.9, 165.2; LRMS (ES+) m/z = 501.06 [M+H]; IR (KBr, cm^{-1}) 3417, 3050, 3010, 2921, 2865, 1608, 1590, 1571, 1506, 1469, 1426.

Supporting Information

Dimethyl 6,6'-azanediylbis(methylene)dinicotinate (iv). Dimethyl 6,6'-(2-nitrophenylsulfonyl-azanediyl)bis(methylene)dinicotinate (**iii**) was deprotected with thiophenol on a 1.46 mmol scale *via* General Procedure **C,** purified via silica gel chromatography (98% DCM, 1.75% MeOH, 0.25% NH_4OH), to furnish **iv** (420 mg, 91%): δ_H (400 MHz, $CDCl_3$) 2.60, (s (br), 1H, NH), 3.90 (s, 6H, 2 -OC$\underline{H}_3$), 4.0 (s, 4H, NC$\underline{H}_2$Pyr), 7.41 (d, J = 8.1 Hz, 2H, 2 CH (Ar)), 8.20 (dd, J = 8.3 and 2.2 Hz, 2H, 2 CH (Ar)), 9.10 (d, J = 2.0 Hz, 2H, 2 CH (Ar)); δ_C (400 MHz,$CDCl_3$) 52.1, 54.4, 121.5, 124.2, 137.3, 150.4, 163.9, 165.5; LRMS (ES+) *m/z* = 316.16 [M+H]; IR (KBr, cm^{-1}) 3419, 3291, 3082, 3063, 3017, 2962, 2916, 2860, 2819, 1721, 1601, 1571, 1485, 1462, 1439.

Dimethyl 6,6'-(3-formylbenzylazanediyl)bis(methylene)dinicotinate (v). Dimethyl 6,6'-azanediylbis(methylene)dinicotinate (**iv**) was coupled to isophthalaldehyde via reductive amination on a 0.630 mmol scale (relative to amine) *via* General Procedure **D**, purified via silica gel chromatography (98% DCM, 1.75% MeOH, 0.25% NH_4OH), to furnish **v** (235 mg, 86 %): δ_H (400 MHz, $CDCl_3$) 3.66 (s, 2H, -NC$\underline{H}_2$Ph), 3.84 (s, 4H, -NC$\underline{H}_2$Pyr), 3.87 (s, 6H, 2 -OC$\underline{H}_3$), 7.44 (t, J = 7.6 Hz, 1H, CH (Ar)), 7.58 (d, J = 8.8 Hz, 2H, 2 CH (Ar)), 7.63 (d, J = 8 Hz, 1H, CH (Ar)), 7.70 (d, J = 7.6 Hz, 1H, CH (Ar)), 7.85 (s (br), 1H, CH (Ar)), 8.21 (dd, J = 8.2 and 2.2 Hz, 2H, 2 CH (Ar)), 9.07 (d, J = 2.1 Hz, 2H, 2 CH (Ar)), 9.95 (s, 1H, -CHO); δ_C (400 MHz, $CDCl_3$) 52.2, 58.0, 59.7, 122.2, 124.5, 128.9, 129.0, 129.5, 134.8, 136.4, 137.4, 139.5, 150.2, 163.4, 165.5, 192.0; LRMS (ES+) *m/z* = 434.09 [M+H]; IR (KBr, cm^{-1}) 3414, 2953, 2846, 1727, 1638, 1598, 1542, 1483, 1436.

N-(6-(bromomethyl)pyridin-2-yl)pivalamide (vii). N-(6-methylpyridin-2-yl)pivalamide (**vi**) was brominated with NBS and BPO on a 17 mmol scale *via* General Procedure **A**, purified via silica gel chromatography (3:2 Hexanes:EtOAc), to furnish **vii** (2.5 g, 54 %): δ_H (400 MHz, $CDCl_3$) 1.31 (s, 9H, -C(C$\underline{H}_3$)$_3$), 4.38 (s, 2H, -C$\underline{H}_2$Br), 7.10 (d, J = 7.6 Hz, 1H, CH (Ar)), 7.65 (t, J = 8.0 Hz, 1H, CH (Ar)), 7.97 (s (br), 1H, NH), 8.15 (d, J = 8.5 Hz, 1H, CH (Ar)); δ_C (400 MHz, $CDCl_3$); 27.3, 33.2, 39.7, 113.2, 119.0, 139.2, 151.2, 154.7, 177.0; LRMS (ES+) *m/z* = 271.1 [M]; IR (KBr, cm^{-1}) 3066, 2968, 2872, 2548, 1691, 1639, 1599, 1579, 1520, 1455, 1401.

N,N'-(6,6'-(2-nitrophenylsulfonylazanediyl)bis(methylene)bis(pyridine-6,2-diyl))bis(2,2-dimethylpropanamide) (viii). N-(6-(bromomethyl)pyridin-2-yl)pivalamide **(vii)** was protected with 2-nitrobenzenesulfonamide and K_2CO_3 on a 4.3 mmol scale *via* General Procedure **B,** purified via silica gel chromatography (1.25:1 Hexanes:EtOAc), to furnish **viii** (2.69 g, 96%): δ_H (400 MHz, $CDCl_3$) 1.31

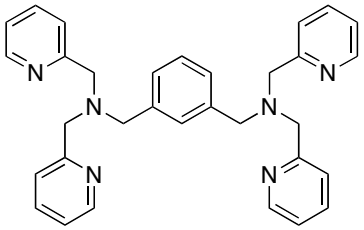
(s, 18H, -C(C$\underline{H}_3$)$_3$), 4.60 (s, 4H, -NC$\underline{H}_2$Pyr), 6.95 (d, *J* = 7.7 Hz, 2H, CH (Ar)), 7.59 (m, 5H, CH (Ar)), 7.84 (s (br), 2H, 2 NH), 7.96 (dd, *J* = 8.0 and 1.1 Hz, 1H, CH (Ar)), 8.05 (d, *J* = 8.4 Hz, 2H, 2 CH (Ar)); δ_C (400 MHz, $CDCl_3$) 27.3, 39.6, 52.5, 112.4, 117.7, 123.9 131.3, 131.6, 133.2, 134.1, 135.8 138.9, 151.0, 153.6, 176.9; LRMS (ES+) *m/z* = 583.22 [M+H]; IR (KBr, cm^{-1}) 3424, 2967, 2872, 1687, 1636, 1599, 1580, 1543, 1519, 1455, 1404.

N,N'-(6,6'-azanediylbis(methylene)bis(pyridine-6,2-diyl))bis(2,2-dimethylpropanamide) (ix). N,N'-(6,6'-(2-nitrophenylsulfonylazanediyl)bis(methylene)bis(pyridine-6,2-diyl))bis(2,2-dimethyl propanamide) **(viii)** was deprotected with thiophenol on a 4.05 mmol scale *via* General Procedure **C**, purified via silica gel chromatography (98.4% DCM, 1.4% MeOH, 0.2% NH_4OH), to furnish **ix** (1.81 g, 92%): δ_H (400 MHz, $CDCl_3$); 1.31 (s, 18H, -C(C$\underline{H}_3$)$_3$), 3.86 (s, 4H, -NC$\underline{H}_2$Pyr), 7.03 (d, *J* = 7.9 Hz, 2H, 2 CH (Ar)), 7.64 (t, *J* = 7.9 Hz, 2H, 2 CH (Ar)), 7.99 (s (br), 2H, 2 NH), 8.11 (d, *J* = 7.9 Hz, 2H, 2 CH (Ar)); δ_C (400 MHz, $CDCl_3$) 27.4, 39.6, 54.1, 111.9, 117.9, 138.6, 151.1, 157.5, 176.9; LRMS (ES+) *m/z* = 398.46 [M+H]; IR (KBr, cm^{-1}) 3425, 2966, 2925, 1685, 1601, 1581, 1518, 1453, 1402.

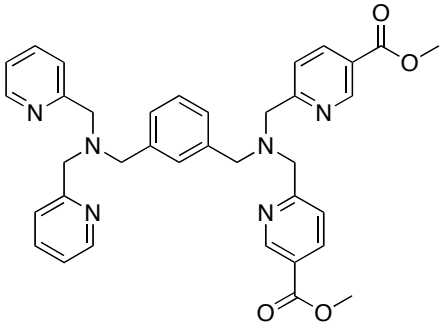
Dimethyl 6,6'-(3-((bis((6-pivalamidopyridin-2-yl)methyl)amino)methyl)benzylazanediyl) bis(methylene) dinicotinate (x). Dimethyl 6,6'-(3-formylbenzylazanediyl)bis(methylene)dinicotinate (**v**) was coupled to N,N'-(6,6'-azanediylbis(methylene)bis(pyridine-6,2-diyl))bis(2,2-dimethylpropanamide) (**ix**) via reductive amination on a 0.32 mmol scale *via* General Procedure **E**, purified via silica gel chromatography (98% DCM, 1.75% MeOH, 0.25% NH_4OH) to furnish **x** (257 mg, 89 %): δ_H (400 MHz, $CDCl_3$) 1.29 (s, 18H, -C(C$\underline{H}_3$)$_3$), 3.64 (s, 4H, –NC$\underline{H}_2$Pyr), 3.65 (s, 2H, PhC$\underline{H}_2$N-), 3.85 (s, 4H, –NC$\underline{H}_2$Pyr), 3.91 (s, 6H, 2 x -OCH_3), 7.28 (m, 4H, 4 CH (Ar)), 7.39 (s (br), 1H, CH (Ar)), 7.62 (m, 4H, 4 CH (Ar)), 7.92 (s (br), 2H, 2 NH), 8.07 (d, *J* = 8.9 Hz, 2H, 2 CH (Ar)), 8.20 (dd, *J* = 8.2 and 2.3 Hz, 2H, 2 CH (Ar)), 9.09 (d, *J* = 2.2 Hz, 2H, 2 CH (Ar)); δ_C (400 MHz,$CDCl_3$) 27.3, 39.6, 52.17, 58.3, 58.6, 59.4, 59.7, 111.7, 118.1, 112.1, 124.4, 127.6, 127.7, 128.3, 129.2, 137.3, 138.2, 138.6, 150.2, 150.7, 157.9, 164.0, 165.6, 176.8; HRMS (ES+) calcd for [$C_{46}H_{54}N_8O_6$ + 2H] 408.2155, found 408.2175; IR (KBr, cm^{-1}) 3550, 3414, 2956, 2359, 1728, 1687, 1637, 1616, 1598, 1578, 1520, 1454, 1402.

Supporting Information

FINAL LIGAND & METAL COMPLEX CHARACTERIZATION.

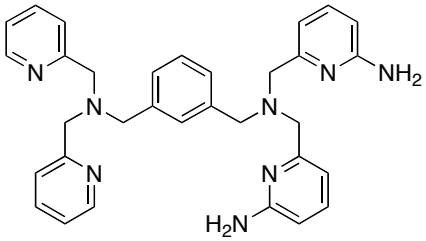


N,N'-(1,3-phenylenebis(methylene))bis(1-(pyridin-2-yl)-N-(pyridin-2-ylmethyl)methanamine). δ_H (400 MHz, $CDCl_3$) 3.66 (s, 4H, PhC$\underline{H_2}$N-), 3.79 (s, 8H, -NC$\underline{H_2}$Pyr), 7.10 (m, 4H, 4 CH (Ar)), 7.26 (m, 4H, 4 CH (Ar)), 7.58 (m, 8H, 8 CH (Ar)), 8.47 (m, 4H, 4 CH (Ar)); δ_C (400 MHz, $CDCl_3$) 121.7, 122.6, 127.4, 128.1, 129.0, 136.3, 138.9, 148.8, 159.6; HRMS (ES+) *m/z* calcd for $C_{32}H_{32}N_6$ 500.2688. Found 500.2689; IR (KBr, cm^{-1}) 3421, 3058, 3012, 2921, 2824, 2360, 2342, 1636, 1593, 1569, 1541, 1475, 1434. **Zn_2-L** (**1**): MS (ESI+) *m/z* calcd for [$C_{32}H_{32}N_6Zn_2$ + H] 632.1, found 632.1; mp = 167-178 °C; UV/Vis (d_2O, 10 mM HEPES, pH = 7.5) λ 260, 267; IR (KBr, cm^{-1}) 3502, 1608, 1487, 1446.

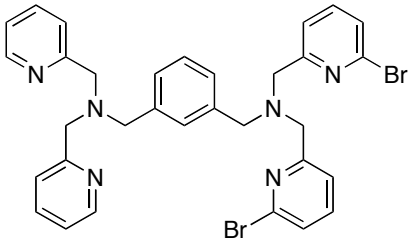


Dimethyl 6,6'-(3-((bis(pyridin-2-ylmethyl)amino)methyl)benzylazanediyl)bis(methylene) dinicotinate. δ_H (400 MHz, $CDCl_3$) 3.68 (s, 2H, PhC$\underline{H_2}$N-), 3.69 (s, 2H, PhC$\underline{H_2}$N-), 3.80 (s, 4H, -NC$\underline{H_2}$Pyr), 3.85 (s, 4H, -NC$\underline{H_2}$Pyr), 3.92 (s, 6H, 2 –OC$\underline{H_3}$), 7.14 (t, *J* = 6.1 Hz, 2H, 2 CH (Ar)), 7.27 (m, 3H, 3 CH (Ar)), 7.45 (s, 1H, CH (Ar)), 7.61 (m, 6H, 6 CH (Ar)), 8.20 (dd, *J* = 8.2 and 2.2 Hz, 2H, 2 CH (Ar)), 8.51 (d, *J* = 4.6 Hz, 2H, 2 CH (Ar)), 9.10 (d, *J* = 1.8 Hz, 2H, 2 CH (Ar)); δ_C (400 MHz, $CDCl_3$) 52.2, 58.3, 58.6, 59.7, 59.8, 121.83, 122.1, 122.6, 124.4, 127.5, 127.8, 128.3, 129.2, 136.3, 137.4, 138.2, 139.0, 148.8, 150.2, 164.1, 165.6, 169.5; HRMS (ES+) calcd for $C_{36}H_{36}N_6O_4$ [M+H] 617.2870. Found 617.2841; IR (KBr, cm^{-1}) 3412, 2951, 2360, 1725, 1637, 1616, 1597, 1567, 1475, 1435. **Zn_2-L** (**2**): MS (ESI+) *m/z* calcd for [$C_{36}H_{36}N_6O_4Zn_2$ + 2Na] 793.51, found 793.51; mp = 107-120 °C, UV/Vis (d_2O, 10 mM HEPES, pH = 7.5) λ 221, 261; IR (KBr, cm^{-1}) 3504, 1728, 1610, 1575, 1488, 1442.

Supporting Information

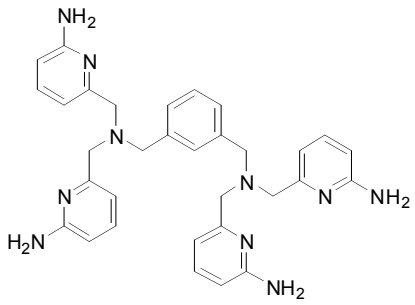


6-((((6-aminopyridin-2-yl)methyl)(3-((bis(pyridin-2-ylmethyl)amino)methyl)benzyl)amino) methyl)pyridin-2-amine. δ_H (400 MHz, $CDCl_3$) 3.64 (s, 4H, -NC<u>H</u>$_2$Pyr), 3.65 (s, 2H, PhC<u>H</u>$_2$N-), 3.67 (s, 2H, PhC<u>H</u>$_2$N-), 3.78 (s, 4H, 2 -NC<u>H</u>$_2$Pyr), 5.33 (s (br), 4H, 2 -NH_2), 6.48 (d, J = 8.3 Hz, 2H, 2 CH (Ar)), 6.85 (d, J = 7.6 Hz, 2H, 2 CH (Ar)), 7.12 (t, J = 6.1 Hz, 2H, 2 CH (Ar)), 7.25 (m, 3H, 3 CH (Ar)), 7.37 (t, J = 7.9 Hz, 2H, 2 CH (Ar)), 7.44 (s, 1H, CH (Ar)), 7.60 (m, 4H, 4 CH (Ar)), 8.49 (d, J = 4.5 Hz, 2H, 2 CH (Ar)); δ_C (400 MHz, $CDCl_3$) 58.3, 58.5, 59.6, 59.9, 106.3, 112.2, 121.7, 122.6, 127.2, 127.4, 128.0, 128.9, 136.2, 138.0, 138.8, 139.2, 148.7, 157.7, 158.4, 159.8; HRMS (ES+) calcd for $C_{32}H_{34}N_8$ [M+H] 531.2979. Found 531.2953; IR (KBr, cm^{-1}) 3410, 2924, 2851, 2360, 1618, 1570, 1468. **Zn_2-L (3):** MS (ESI+) *m/z* calcd for [$C_{32}H_{34}N_8Zn_2$ + Na] 681.14. Found 681.3; UV/Vis (d_2O, 10 mM HEPES, pH = 7.5) λ 228, 256, 296; mp = 75-80 °C; IR (KBr, cm^{-1}) 3438, 2925, 1630, 1575, 1483, 1446.

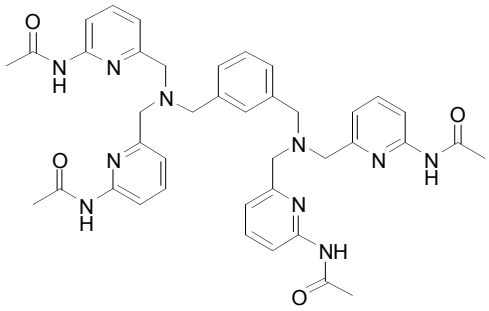


N-(3-((bis((6-bromopyridin-2-yl)methyl)amino)methyl)benzyl)-1-(pyridin-2-yl)-N-(pyridin-2-ylmethyl)methanamine. δ_H (400 MHz, $CDCl_3$) 3.67 (s, 2H, PhC<u>H</u>$_2$N-), 3.68 (s, 2H, PhC<u>H</u>$_2$N-), 3.77 (s, 4H, 2 -NC<u>H</u>$_2$Pyr), 3.78 (s, 4H, 2 -NC<u>H</u>$_2$Pyr), 7.12 (t, J = 5.9 Hz, 2H, 2 CH (Ar)), 7.27 (m, 5H, 5 CH (Ar)), 7.53 (m, 9H, 9 CH (Ar)), 8.49 (d, J = 5.0 Hz, 2H, 2 CH (Ar)); δ_C (400 MHz, $CDCl_3$) 58.3, 58.4, 59.1, 59.9, 121.2, 121.8, 122.6, 126.1, 127.4, 127.7, 128.2, 129.1, 136.3, 138.4, 138.6, 139.0, 141.1, 148.8, 159.6, 161.2; HRMS (ES+) calcd for $C_{32}H_{30}N_6Br_2$ [M+H] 657.0971. Found 657.0965; IR (KBr, cm^{-1}) 3473, 3411, 2360, 1637, 1617, 1557. **Zn_2-L (4)**: MS (ESI+) *m/z* calcd for [$C_{32}H_{30}Br_2N_6Zn_2$ + NH_4OAc] 866.33. Found 867.1 [M+H]; UV/Vis (d_2O, 10 mM HEPES, pH = 7.5) λ 262; mp = 122-137 °C; IR (KBr, cm^{-1}) 3504, 2926, 1610, 1560, 1487, 1441.

Supporting Information

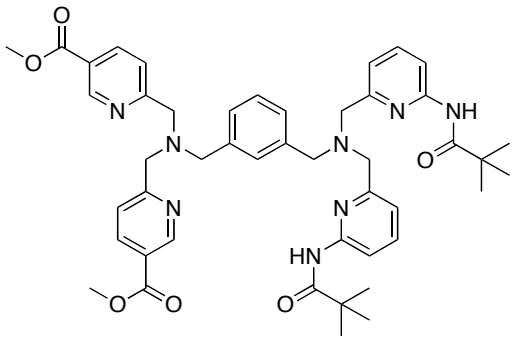


Tetra-amino 6,6',6'',6'''-(1,3-phenylenebis(methylene))bis(azanetriyl)tetrakis(methylene) tetranicotinate. δ_H (400 MHz, MeOD) 3.52 (s, 8H, -NC<u>H</u>$_2$Pyr), 3.62 (s, 4H, 2 -NC<u>H</u>$_2$Pyr), 6.41 (d, J = 8.4 Hz, 4H, 4 CH (Ar)), 6.91 (d, J = 7.2 Hz, 4H, 4 CH (Ar)), 7.22 (m, 3H, 3 CH (Ar)), 7.39 (t, J = 7.8 Hz, 4H, 4 CH (Ar)), 7.57 (s, 1H, CH (Ar)); δ_C (400 MHz, MeOD) 59.7, 60.6, 108.3, 112.5, 128.7, 139.7, 140.5, 158.7, 160.4, 168.1, 176.4; HRMS (ES+) calcd for [$C_{32}H_{38}N_{10}$ + 2H] 562.3286, found 562.3268; IR (KBr, cm^{-1}) 3466, 3312, 3175, 2921, 2797, 1623, 1573, 1467. **Zn_2-L** (**5**): UV/Vis (d_2O, 10 mM HEPES, pH = 7.5) λ 231, 297; mp = 63-75 °C; IR (KBr, cm^{-1}) 3444, 2921, 1637, 1574, 1480, 1445.

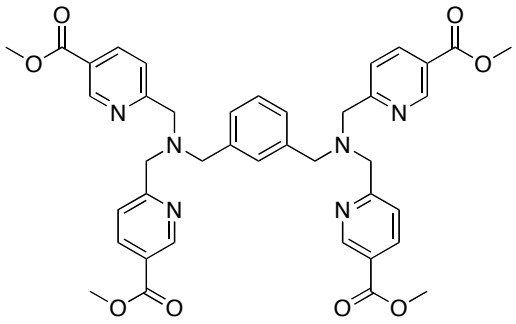


N,N',N'',N'''-(6,6',6'',6'''-(1,3-phenylenebis(methylene))bis(azanetriyl)tetrakis(methylene) tetrakis(pyridine-6,2-diyl))tetraacetamide. δ_H (400 MHz, $CDCl_3$) 2.02 (s, 12H, 4 -COC<u>H</u>$_3$), 3.56 (s, 4H, 2 PhC<u>H</u>$_2$N-), 3.64 (s, 8H, -NC<u>H</u>$_2$Pyr), 7.19 (m, 7H, CH (Ar)), 7.63 (m, 5H, CH (Ar)), 8.10 (d, J = 8.0 Hz, 4H, 4 CH (Ar)), 9.26 (s (br), 4H, 4 NH); δ_C (400 MHz, $CDCl_3$) 23.4, 57.0, 58.2, 111.7, 117.9, 127.0, 127.1, 128.8, 137.4, 138.4, 150.4, 156.7, 168.2; HRMS (ES+) calcd for [$C_{40}H_{46}N_{10}O_4$ + 2H] 730.3674, found 730.3692; IR (KBr, cm^{-1}) 3412, 3055, 2925, 1682, 1601, 1578, 1539, 1455, 1407. **Zn_2-L (6)**: MS (ESI+) *m/z* calcd for [$C_{40}H_{46}N_{10}O_4Zn_2$ + Na] 879.20. Found 879.3 [M+Na]; UV/Vis (d_2O, 10 mM HEPES, pH = 7.5) λ 233, 281; mp = 150-165 °C; IR (KBr, cm^{-1}) 3526, 2934, 1716, 1621, 1581, 1540, 1471, 1416.

Supporting Information



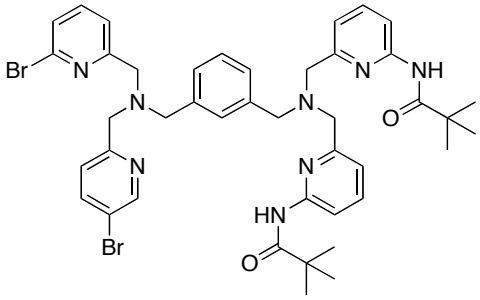
Dimethyl-6,6'-(3-((bis((6-pivalamidopyridin-2-yl)methyl)amino)methyl)benzylazanediyl) bis(methylene)dinicotinate. δ_H (400 MHz, $CDCl_3$) 1.29 (s, 18H, -C(C<u>H</u>$_3$)$_3$), 3.64 (s, 4H, –NC<u>H</u>$_2$Pyr), 3.65 (s, 2H, -PhC<u>H</u>$_2$NR$_2$), 3.85 (s, 4H, 2 –NC<u>H</u>$_2$Pyr), 3.91 (s, 6H, 2 -OC<u>H</u>$_3$), 7.28 (m, 4H, 4 CH (Ar)), 7.39 (s (br), 1H, CH (Ar)), 7.62 (m, 4H, 4 CH (Ar)), 7.92 (s (br), 2H, 2 NH), 8.07 (d, *J* = 8.9 Hz, 2H, 2 CH (Ar)), 8.20 (dd, *J* = 8.2 and 2.3 Hz, 2H, 2 CH (Ar)), 9.09 (d, *J* = 2.2 Hz, 2H, 2 CH (Ar)); δ_C (400 MHz,$CDCl_3$) 27.3, 39.6, 52.17, 58.3, 58.6, 59.4, 59.7, 111.7, 118.1, 112.1, 124.4, 127.6, 127.7, 128.3, 129.2, 137.3, 138.2, 138.6, 150.2, 150.7, 157.9, 164.0, 165.6, 176.8; HRMS (ES+) calcd for [$C_{46}H_{54}N_8O_6$ + 2H] 816.4344, found 816.431; IR (KBr, cm^{-1}) 3550, 3414, 2956, 2359, 1728, 1687, 1637, 1616, 1598, 1578, 1520, 1454, 1402. **Zn_2-L** (**7**): MS (ESI+) *m/z* calcd for [$C_{46}H_{54}N_8O_6Zn_2$] 942.27. Found 943.3 [M+H]; UV/Vis (d_2O, 10 mM HEPES, pH = 7.5) λ 226, 272; Mp = 110-119 °C; IR (KBr, cm^{-1}) 3525, 2967, 1730, 1621, 1578, 1527, 1466.



Tetramethyl 6,6',6'',6'''-(1,3-phenylenebis(methylene))bis(azanetriyl)tetrakis(methylene) tetranicotinate. δ_H (400 MHz, $CDCl_3$) 3.67 (s, 4H, 2 PhC<u>H</u>$_2$N-), 3.84 (s, 8H, 4 -NC<u>H</u>$_2$Pyr), 3.91 (s, 12H, 4 -OCH_3), 7.27 (s, 1H, CH (Ar)), 7.43 (s (br), 1H, CH (Ar)), 7.64 (m, 5H, 5 CH (Ar)), 8.20 (m, 5H, 5 CH (Ar)), 9.08 (d, *J* = 2.1 Hz, 4H, 4 CH (Ar)); δ_C (400 MHz, $CDCl_3$) 52.2, 58.4, 59.7, 122.1, 124.4, 127.8, 128.4, 129.2, 137.4, 138.3, 150.2, 164.0, 165.5; HRMS (ES+) calcd for $C_{40}H_{41}N_6O_8$ [M+H] 733.2980. Found 733.2948; IR (KBr, cm^{-1}) 3413, 2952, 2359, 1722, 1635, 1597, 1541, 1435. **Zn_2-L (8)**: MS (ESI+) *m/z* calcd for [$C_{40}H_{40}N_6O_8Zn_2$ + Na] 883.14. Found 883.2 [M+Na]; UV/Vis

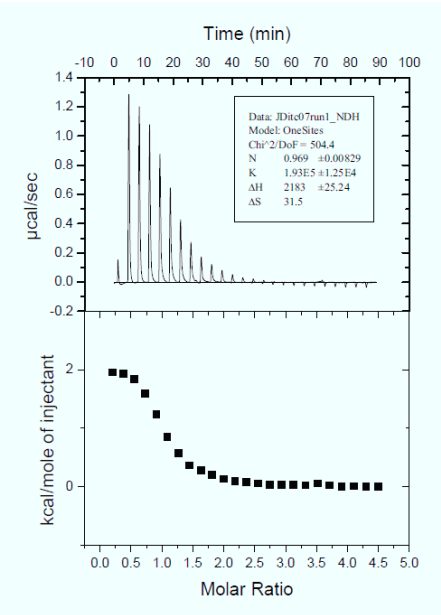
Supporting Information

(d_2O, 10 mM HEPES, pH = 7.5) λ 221, 265; Mp = 75-90 °C; IR (KBr, cm^{-1}) 3529, 2955, 2919, 1728, 1613, 1541, 1492, 1438, 1407.

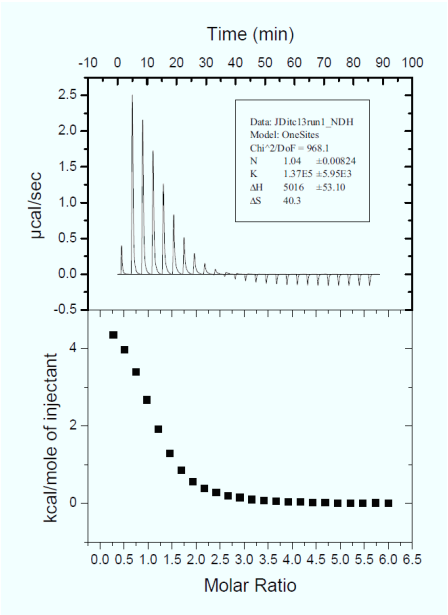


Dimethyl 6,6'-(3-((bis((5-aminopyridin-2-yl)methyl)amino)methyl)benzylazanediyl) bis (methylene)dinicotinate. δ_H (400 MHz, $CDCl_3$) 1.27 (s, 18H, -C($C\underline{H}_3$)$_3$), 3.63 (s, 4H, 2 -NC$\underline{H}_2$Pyr), 3.65 (s, 2H, PhC$\underline{H}_2$N-), 3.74 (s, 2H, PhC$\underline{H}_2$N-), 3.89 (s, 4H, 2 -NC$\underline{H}_2$Pyr), 7.29 (m, 6H, 6 CH (Ar)), 7.54 (m, 6H, 6 CH (Ar)), 7.62 (t, J = 7.8 Hz, 2H, 2 CH (Ar)), 7.90 (s (br), 2H, 2 NH), 8.06 (d, J = 8.63 Hz, 2H, 2 CH (Ar)); δ_C (400 MHz, $CDCl_3$) 27.4, 39.6, 58.3, 58.4, 59.1, 59.3, 111.7, 118.2, 120.9, 121.2, 126.1, 126.2, 127.5, 127.7, 128.3, 129.1, 138.4, 138.5, 138.6, 141.2, 150.7, 161.1, 176.8; HRMS (ES+) calcd for $C_{42}H_{48}N_8O_2$ [M+2H] 428.1206. Found 428.1214; IR (KBr, cm^{-1}) 3415, 2923, 1686, 1635, 1579, 1556, 1518, 1453, 1404.

Representative ITC Traces

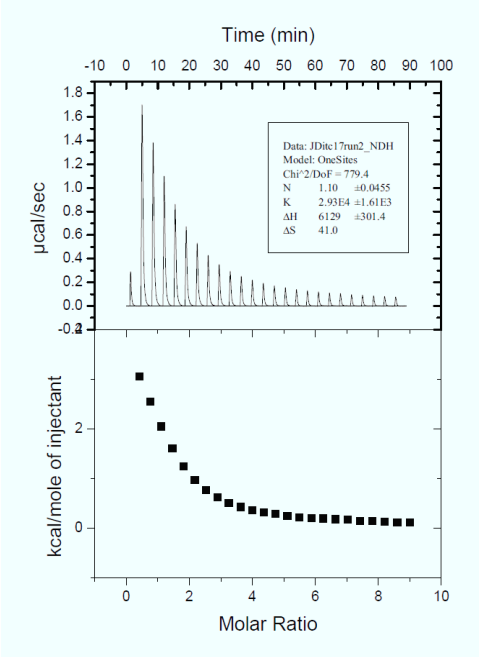


1 binding to **NaH_2PO_4**

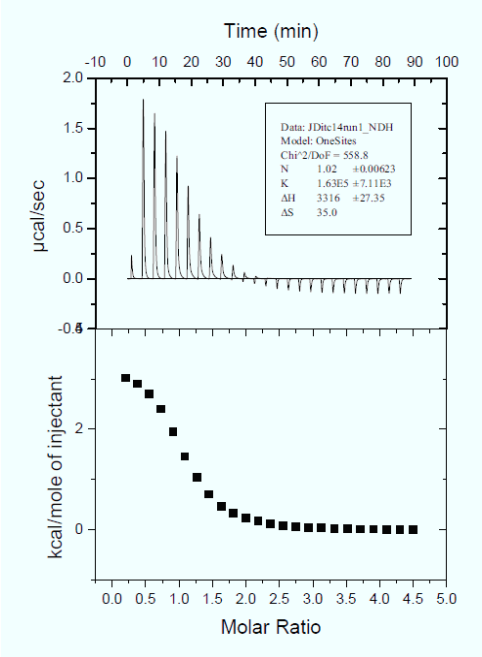


3 binding to **AMP**

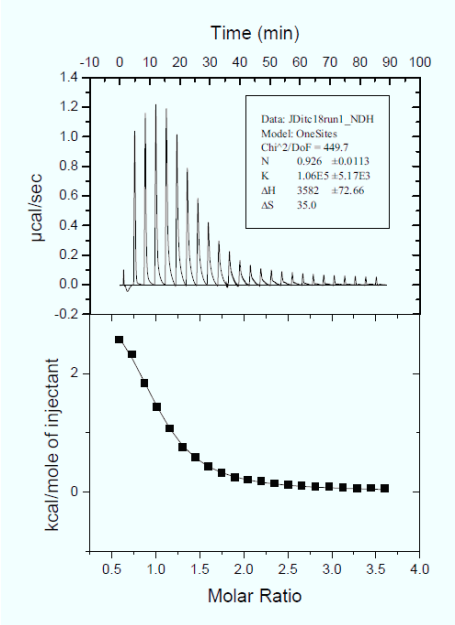
Supporting Information



2 binding to **β-GP**



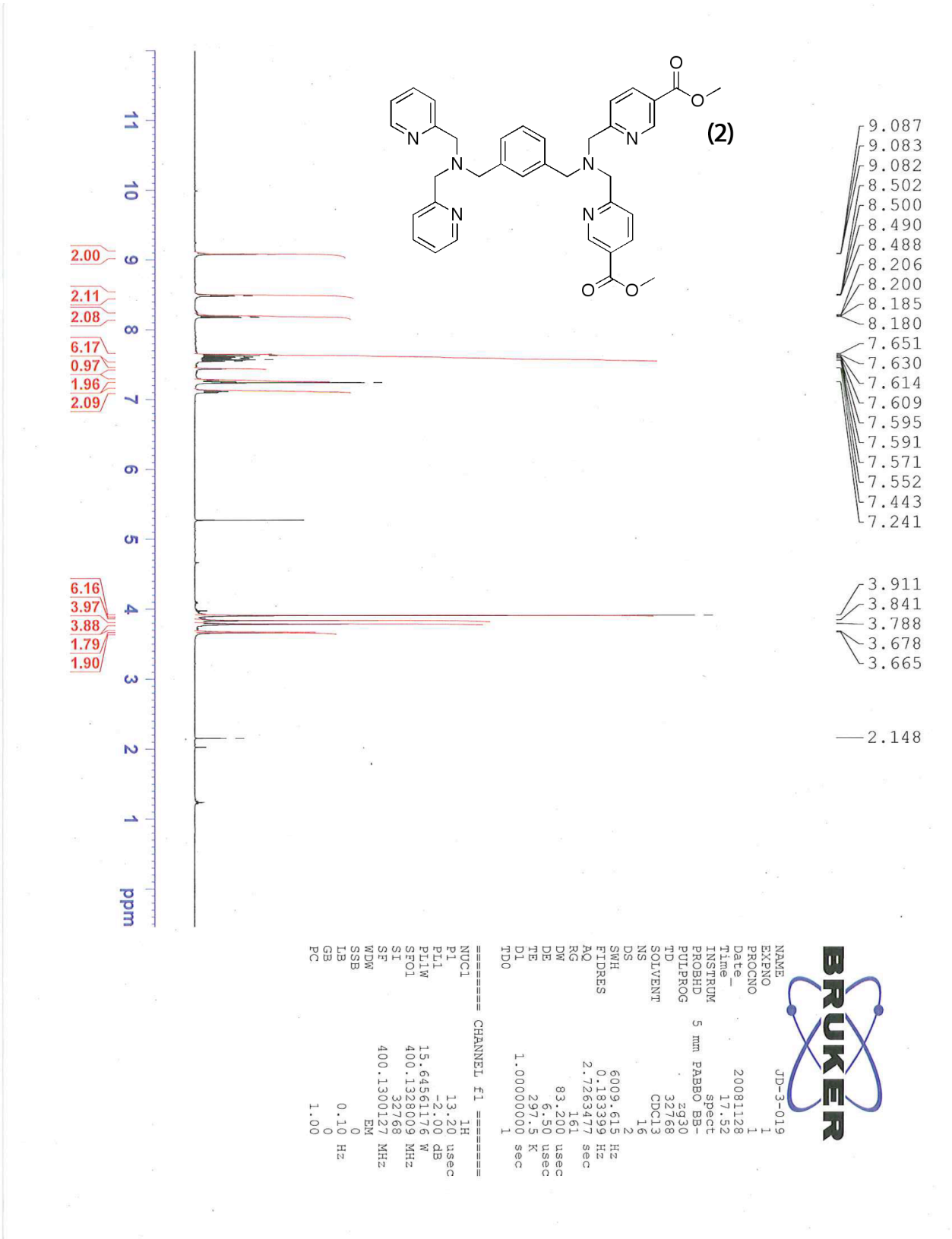
1 binding to **AMP**



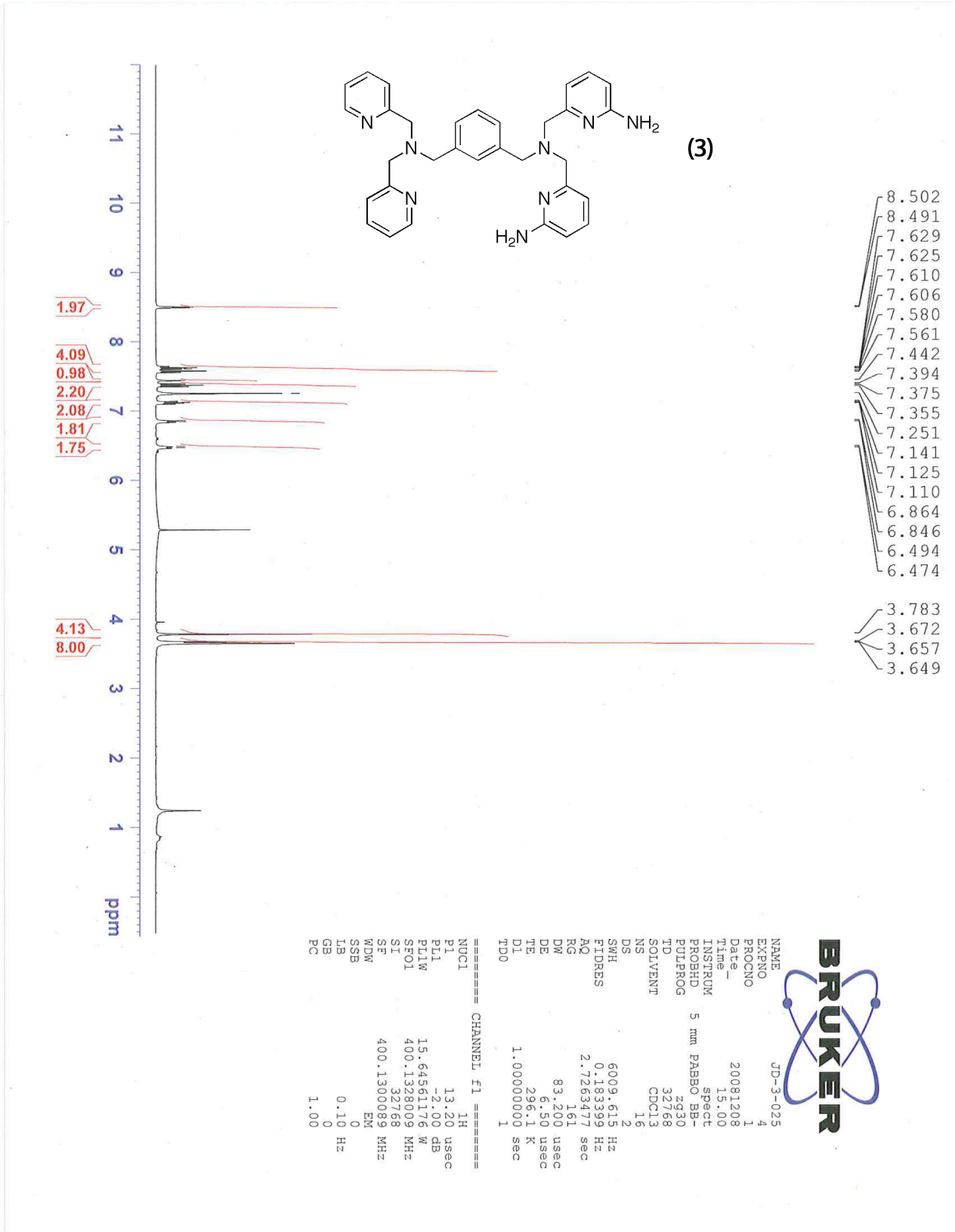
4 binding to **NaH_2PO_4**

Supporting Information

Representative ^{1}H NMR



Supporting Information



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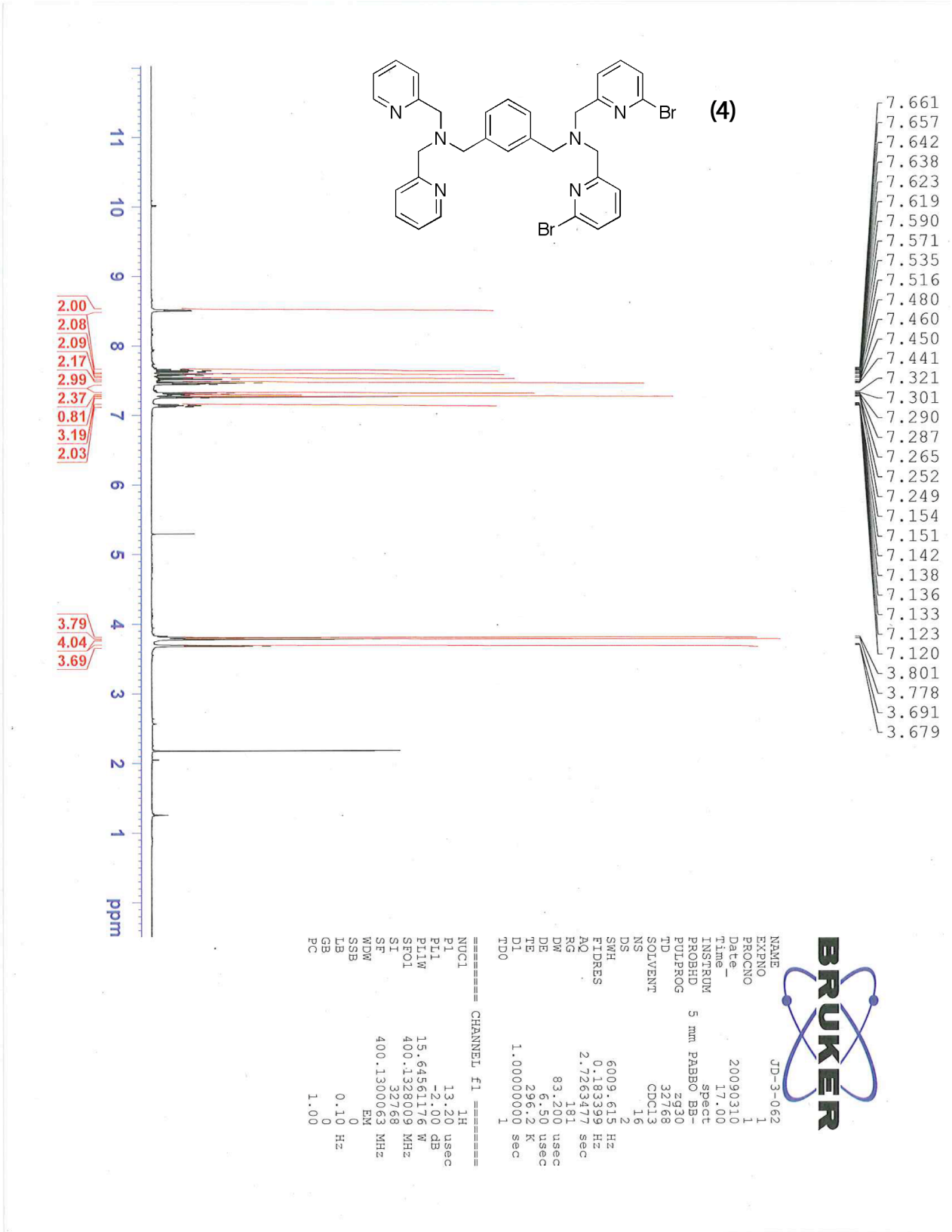

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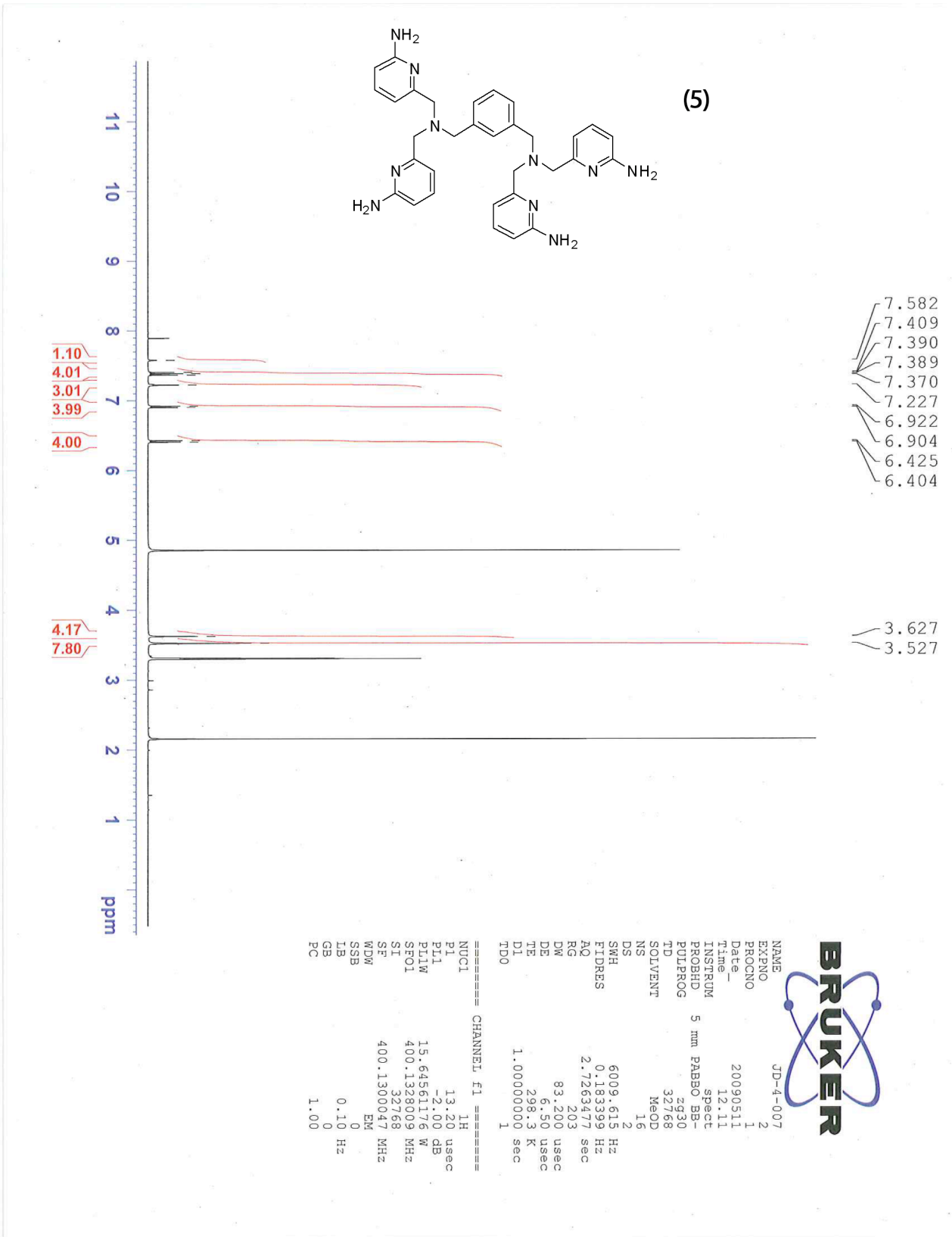

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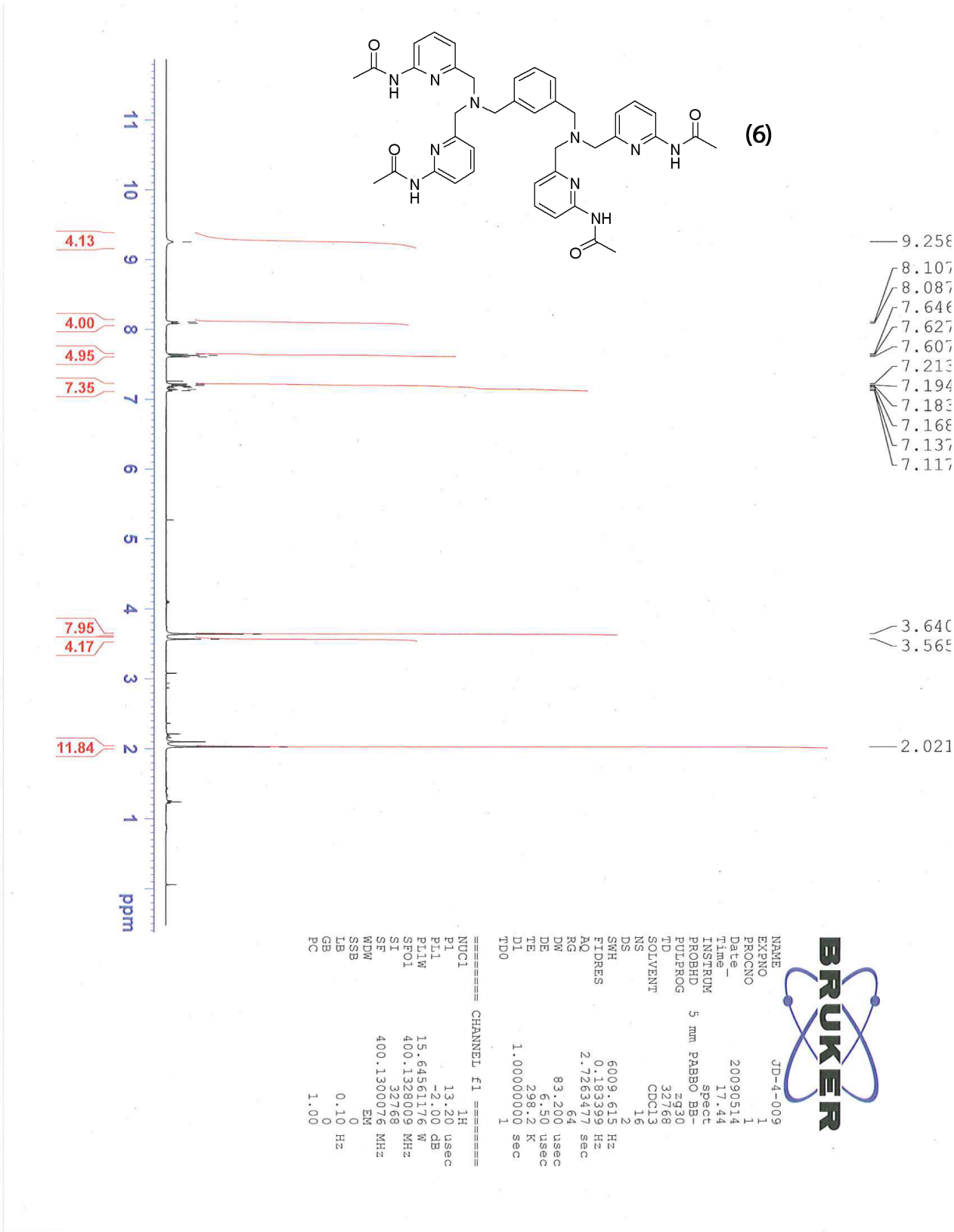

Supporting Information

Supporting Information