Supporting Information

One-pot Parallel Synthesis of Unclosed Cryptands – Searching for Selective Anion Receptors *via* Static Combinatorial Chemistry Techniques

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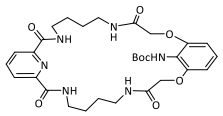
1. Synthetic Procedures and Structural Analysis

1.1. General Remarks

All solvents were of reagent grade quality. All reagents were purchased from Sigma-Aldrich and TCI Chemicals and used without further purification. Column chromatography was carried out using Merck Kieselgel 60 (63–100 µm mesh size), TLC was carried out on Merck Kieselgel F254 plates. Melting points were determined using a Boëtius M HMK hot-stage apparatus and were uncorrected. The NMR spectra were recorded on a Bruker Mercury 400 instrument. Chemical shifts are reported in ppm and are set to solvent residue peak. The splitting pattern of multiplets is described by abbreviations (s – singlet, d – doublet, t – triplet, q – quartet, dd – doublet of doublets, m – multiplet, c – covered signal, b – broad peak). *J* coupling constants values are reported in Hz. Mass spectral analyses were performed with the ESI-TOF technique on a Mariner mass spectrometer from PerSeptive Biosystem.

1.2. Substance Analysis

*tert-Butyl N-{4,11,17,24-Tetraoxo-2,26-dioxa-5,10,18,23,32-pentaazatricyclo[25.3.1.1^{12,16}]dotriaconta-1(31),12,14,16-(32),27,29-hexaen-31-yl}carbamate (**1**)*



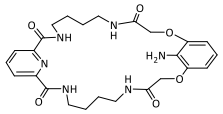
M_w = 612.68 g/mol

The product **1** was obtained as previously described.[1]

^{1}H NMR (400 MHz, DMSO-d_6) δ 9.34 (t, *J* = 5.5 Hz, 2H), 8.70 (s, 1H), 8.19 – 8.10 (m, *J* = 8.9, 2.7 Hz, 3H), 8.07 (t, *J* = 4.7 Hz, 2H), 7.11 (t, *J* = 8.4 Hz, 1H), 6.64 (d, *J* = 8.5 Hz, 2H), 4.54 (s, 4H), 3.30 – 3.25 (m, 4H), 3.20 (dd, *J* = 11.6, 5.8 Hz, 4H), 1.61 (dd, *J* = 14.6, 8.2 Hz, 4H), 1.56 – 1.46 (m, 4H), 1.16 (s, 9H).

^{13}C NMR (100 MHz, DMSO-d_6) δ 167.4, 162.9, 154.1, 152.5, 148.7, 139.1, 126.6, 123.9, 115.1, 105.0, 78.9, 66.7, 38.1, 27.9, 26.7, 26.2.

*31-amino-2,26-dioxa-5,10,18,23,32-pentaazatricyclo[25.3.1.1^{12,16}]dotriaconta-1(31),12,14,16(32),27,29-hexaene-4,11,17,24-tetrone (**2**)*



M_w = 512.57 g/mol

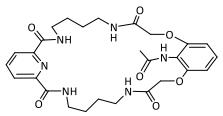
The macrocyclic compound **1** (2.5 g, 4.0 mmol) was suspended in anhydrous DCM (20 mL) and cooled to 0 °C. Then 4M HCl in dioxane (5 mL) was added dropwise and the mixture was stirred for 2 h in room temperature. Subsequently the mixture was cooled to 0 °C and *N,N*-diisopropylethylamine (4.9 mL) was added. So obtained mixture was stirred further 30 min and the solvent was evaporated under a vacuum. The residue was dissolved in a small amount of methanol and the sonicated in water. The product **2** (1.97 g, 3.84 mmol, **96%**) was obtained in a form of colorless solid (mp 228-229 °C).

^{1}H NMR (400 MHz, DMSO-d_6) δ 9.46 (bs, 2H), 8.33 (bs, 2H), 8.19-8.15 (m, 3H), 6.59 (d, *J* = 7.8, 2H), 6.48 (t, *J* = 8.1 Hz, 1H), 5.22 (bs, 2H), 4.43 (s, 4H), 3.26 (bs, 8H), 1.60 (bs, 4H), 1.51 (bs, 4H).

^{13}C NMR (100 MHz, DMSO-d_6) δ 167.5, 162.9, 148.8, 145.1, 139.3, 124.2, 114.9, 106.9, 68.2, 39.0, 37.9, 30.6, 27.7, 27.3.

HRMS ESI (m/z) Calcd for $C_{25}H_{32}N_6O_6Na$ $[M + Na]^+$: 535.2281; found: 535.2277.

*N-{4,11,17,24-tetraoxo-2,26-dioxa-5,10,18,23,32-pentaazatricyclo[25.3.1.1^{12,16}]dotriaconta-1(31),12,14,16(32),27,29-hexaen-31-yl}acetamide (**3**)*



M_w = 554.60 g/mol

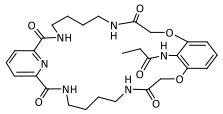
Following General Procedure **A** and using acetyl chloride (20 µL, 0.28 mmol) the product ***3*** (0.106 g, 0.19 mmol, **83%**) was obtained as a colorless solid (mp > 300 °C)

^{1}H NMR (400 MHz, DMSO-d_6) δ 9.52 (s, 1H), 9.37 (t, *J* = 6.0 Hz, 2H), 8.25 (t, *J* = 5.3 Hz, 2H), 8.22 – 8.10 (m, 3H), 7.15 (t, *J* = 8.4 Hz, 1H), 6.69 (d, *J* = 8.5 Hz, 2H), 4.51 (s, 4H), 3.30 (d, *J* = 7.0 Hz, 4H), 3.21 (dd, *J* = 10.9, 5.3 Hz, 4H), 1.95 (s, 3H), 1.68 (d, *J* = 6.2 Hz, 4H), 1.52 (d, *J* = 3.9 Hz, 4H).

^{13}C NMR (100 MHz, DMSO-d_6) δ 169.0, 167.2, 163.0, 152.3, 148.9, 139.2, 127.1, 124.0, 114.8, 105.3, 66.9, 39.0, 37.9, 26.8, 26.3, 22.6.

*N-{4,11,17,24-tetraoxo-2,26-dioxa-5,10,18,23,32-pentaazatricyclo[25.3.1.1^{12,16}]dotriaconta-1(31),12,14,16(32),27,29-hexaen-31-yl}propanamide (**4**)*

Following General Procedure **A** and using propionyl chloride (24 µL, 0.28 mmol) the product ***4*** (0.122 g, 0.21 mmol, **93%**) was obtained as a colorless solid (mp 261-262 °C)



M_w = 568.63 g/mol

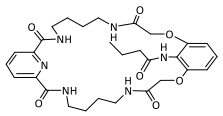
^{1}H NMR (400 MHz, DMSO-d_6) δ 9.42 (s, 1H), 9.36 (t, *J* = 5.1 Hz, 2H), 8.35 (t, *J* = 4.9 Hz, 2H), 8.20 – 8.10 (m, 3H), 7.15 (t, *J* = 8.3 Hz, 1H), 6.67 (d, *J* = 8.4 Hz, 2H), 4.53 (s, 4H), 3.31 – 3.26 (m, 4H), 3.20 (dd, *J* = 10.5, 5.6 Hz, 4H), 2.28 (dd, *J* = 14.7, 7.2 Hz, 2H), 1.73 – 1.62 (m, 4H), 1.56 – 1.45 (m, 4H), 0.59 (t, *J* = 7.4 Hz, 3H).

^{13}C NMR (100 MHz, DMSO-d_6) δ 172.5, 167.3, 162.9, 152.3, 148.8, 139.1, 127.1, 123.9, 114.7, 105.1, 66.7, 39.0, 38.0, 28.2, 26.7, 26.2, 9.3.

HRMS ESI (m/z) Calcd for $C_{28}H_{36}N_6O_7Na$ [M + Na]$^+$: 591.2543; found: 591.2546.

*N-{4,11,17,24-tetraoxo-2,26-dioxa-5,10,18,23,32-pentaazatricyclo[25.3.1.1^{12,16}]dotriaconta-1(31),12,14,16(32),27,29-hexaen-31-yl}butanamide (**5**)*

Following General Procedure **A** and using butyryl chloride (29 µL, 0.28 mmol) the product ***5*** (0.128 g, 0.23 mmol, **98%**) was obtained as a colorless solid (mp 235-236 °C)



M_w = 582.66 g/mol

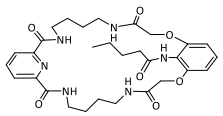
^{1}H NMR (400 MHz, DMSO-d_6) δ 9.45 (s, 1H), 9.38 (t, *J* = 5.2 Hz, 2H), 8.39 (t, *J* = 4.8 Hz, 2H), 8.22 – 8.08 (m, 3H), 7.15 (t, *J* = 8.3 Hz, 1H), 6.68 (d, *J* = 8.4 Hz, 2H), 4.53 (s, 4H), 3.29 (d, *J* = 6.1 Hz, 4H), 3.20 (d, *J* = 4.6 Hz, 4H), 2.23 (t, *J* = 7.3 Hz, 2H), 1.69 (s, 4H), 1.51 (s, 4H), 1.23 – 1.12 (m, 2H), 0.36 (t, *J* = 7.2 Hz, 3H).

^{13}C NMR (100 MHz, DMSO-d_6) δ 171.8, 167.2, 162.9, 152.2, 148.9, 139.1, 127.1, 123.9, 114.6, 104.9, 66.6, 38.9, 37.9, 37.0, 26.6, 26.2, 18.5, 12.9.

HRMS ESI (m/z) Calcd for $C_{29}H_{38}N_6O_7Na$ [M + Na]$^+$: 605.2700; found: 605.2697.

*N-{4,11,17,24-tetraoxo-2,26-dioxa-5,10,18,23,32-pentaazatricyclo[25.3.1.1^{12,16}]dotriaconta-1(31),12,14,16(32),27,29-hexaen-31-yl}pentanamide (**6**)*

Following General Procedure **A** and using valeroyl chloride (33 µL, 0.28 mmol) the product ***6*** (0.115 g, 0.19 mmol, **84%**) was obtained as a colorless solid (mp 247-248 °C)



M_w = 596.69 g/mol

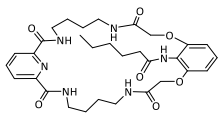
^{1}H NMR (400 MHz, DMSO-d_6) δ 9.46 (s, 1H), 9.39 (t, *J* = 5.1 Hz, 2H), 8.39 (bs, 2H), 8.22 – 8.10 (m, 3H), 7.15 (t, *J* = 8.3 Hz, 1H), 6.68 (d, *J* = 8.4 Hz, 2H), 4.53 (s, 4H), 3.31 – 3.26 (m, 4H), 3.23 – 3.18 (m, 4H), 2.26 (t, *J* = 7.4 Hz, 2H), 1.70 (bs, 4H), 1.51 (bs, 4H), 1.21 – 1.11 (m, 2H), 0.85 – 0.75 (m, 2H), 0.41 (t, *J* = 7.2 Hz, 3H).

^{13}C NMR (100 MHz, DMSO-d_6) δ 171.9, 167.2, 162.9, 152.3, 148.9, 139.1, 127.1, 123.9, 114.6, 104.9, 66.6, 38.9, 37.9, 34.8, 27.0, 26.6, 26.2, 21.3, 13.2.

HRMS ESI (m/z) Calcd for $C_{30}H_{40}N_6O_7Na$ [M + Na]$^+$: 619.2856; found: 619.2861.

*N-{4,11,17,24-tetraoxo-2,26-dioxa-5,10,18,23,32-pentaazatricyclo[25.3.1.1^{12,16}]dotriaconta-1(31),12,14,16(32),27,29-hexaen-31-yl}hexanamide (**7**)*

Following General Procedure **A** and using caproyl chloride (39 µL, 0.28 mmol) the product **7** (0.117 g, 0.19 mmol, **83%**) was obtained as a colorless solid (mp 202-203 °C)



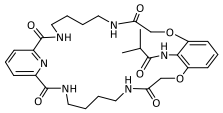
M_w = 610.71 g/mol

^{1}H NMR (400 MHz, DMSO-d_6) δ 9.46 (s, 1H), 9.39 (bs, 2H), 8.39 (bs, 2H), 8.23 – 8.10 (m, 3H), 7.15 (t, *J* = 7.2 Hz, 1H), 6.68 (d, *J* = 7.3 Hz, 2H), 4.52 (s, 4H), 3.31 – 3.28 (m, 4H), 3.23 – 3.18 (m, 4H), 2.25 (t, *J* = 5.2 Hz, 2H), 1.74 – 1.66 (m, 4H), 1.56 – 1.48 (m, 4H), 1.16 (bs, 2H), 0.82 – 0.73 (m, 4H), 0.52 (t, *J* = 6.0 Hz, 3H).

^{13}C NMR (100 MHz, DMSO-d_6) δ 172.0, 167.2, 162.9, 152.3, 148.9, 139.1, 127.1, 123.9, 114.6, 104.9, 66.6, 37.8, 35.2, 30.4, 26.6, 26.2, 24.9, 21.4, 13.6.

HRMS ESI (m/z) Calcd for $C_{31}H_{42}N_6O_7Na$ [M + Na]$^+$: 633.3013; found: 633.3008.

*2-methyl-N-{4,11,17,24-tetraoxo-2,26-dioxa-5,10,18,23,32-pentaazatricyclo[25.3.1.1^{12,16}]dotriaconta-1(31),12,14,16(32),27,29-hexaen-31-yl}propanamide (**8**)*



M_w = 582.66 g/mol

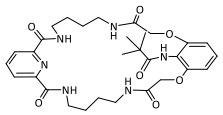
Following General Procedure **A** and using isopropyl chloride (22 mg, 0.28 mmol) the product ***8*** (0.130 g, 0.22 mmol, **97%**) was obtained as a colorless solid (mp 220-221 ^oC)

^{1}H NMR (400 MHz, DMSO-d_6) δ 9.37 – 9.31 (m, 3H), 8.28 (t, *J* = 4.7 Hz, 2H), 8.20 – 8.09 (m, 3H), 7.15 (t, *J* = 8.3 Hz, 1H), 6.67 (d, *J* = 8.5 Hz, 2H), 4.54 (s, 4H), 3.32 – 3.26 (m, 4H), 3.23 – 3.17 (m, 4H), 1.72 – 1.61 (m, 4H), 1.55 – 1.46 (m, 4H), 1.17 (s, 1H), 0.81 (d, *J* = 6.7 Hz, 6H).

^{13}C NMR (100 MHz, DMSO-d_6) δ 175.8, 167.3, 162.9, 152.4, 148.8, 139.1, 127.0, 123.8, 114.7, 105.0, 66.7, 38.1, 33.5, 27.9, 26.7, 26.2, 19.4.

HRMS ESI (m/z) Calcd for $C_{29}H_{38}N_6O_7Na$ $[M + Na]^+$: 605.2700; found: 605.2697.

*2,2-dimethyl-N-{4,11,17,24-tetraoxo-2,26-dioxa-5,10,18,23,32-pentaazatricyclo[25.3.1.1^{12,16}]dotriaconta-1(31),12,14,16(32),27,29-hexaen-31-yl}propanamide (**9**)*



M_w = 596.69 g/mol

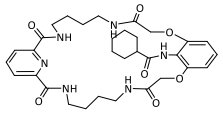
Following General Procedure **A** and using pivaloyl chloride (35 µL, 0.28 mmol) the product ***9*** (0.108 g, 0.18 mmol, **79%**) was obtained as a colorless solid (mp 161-162 ^oC)

^{1}H NMR (400 MHz, DMSO-d_6) δ 9.32 (bs, 2H), 8.94 (s, 1H), 8.22 – 8.09 (m, 3H), 7.94 (s, 2H), 7.16 (d, *J* = 7.6 Hz, 1H), 6.68 (d, *J* = 6.6 Hz, 2H), 4.54 (s, 4H), 3.29 (bs, 4H), 3.18 (bs, 4H), 1.64 (bs, 4H), 1.49 (bs, 4H), 0.97 (s, 9H).

^{13}C NMR (100 MHz, DMSO-d_6) δ 177.5, 167.4, 163.0, 153.2, 148.8, 127.4, 123.9, 115.2, 105.3, 66.8, 38.4, 38.2, 27.2, 26.9, 26.3.

HRMS ESI (m/z) Calcd for $C_{30}H_{40}N_6O_7Na$ $[M + Na]^+$: 619.2856; found: 619.2845.

*N-{4,11,17,24-tetraoxo-2,26-dioxa-5,10,18,23,32-pentaazatricyclo[25.3.1.1^{12,16}]dotriaconta-1(31),12,14,16(32),27,29-hexaen-31-yl}cyclohexanecarboxamide (**10**)*



M_w = 622.72 g/mol

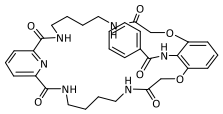
Following General Procedure **A** and using cyclohexanecarbonyl chloride (37 µL, 0.28 mmol) the product ***10*** (0.125 g, 0.20 mmol, **87%**) was obtained as a colorless solid (mp 268-269 ^oC)

^{1}H NMR (400 MHz, DMSO-d_6) δ 9.44 – 9.27 (m, 3H), 8.36 (s, 2H), 8.22 – 8.07 (m, 3H), 7.15 (t, *J* = 7.3 Hz, 1H), 6.66 (d, *J* = 7.5 Hz, 2H), 4.53 (s, 4H), 3.30 – 3.16 (m, 8H), 2.37 (t, *J* = 11.0 Hz, 1H), 1.71 (bs, 6H), 1.50 (bs, 4H), 1.25 – 1.05 (m, 6H), 0.99 – 0.85 (m, 2H).

^{13}C NMR (100 MHz, DMSO-d_6) δ 174.8, 167.3, 162.8, 152.2, 148.8, 139.0, 126.9, 123.8, 114.6, 104.8, 66.6, 43.4, 37.9, 29.2, 26.5, 26.2, 24.9, 24.9.

HRMS ESI (m/z) Calcd for $C_{32}H_{42}N_6O_7Na$ $[M + Na]^+$: 645.3013; found: 645.3008.

*N-{4,11,17,24-tetraoxo-2,26-dioxa-5,10,18,23,32-pentaazatricyclo[25.3.1.1^{12,16}]dotriaconta-1(31),12,14,16(32),27,29-hexaen-31-yl}benzamide (**11**)*



M_w = 616.68 g/mol

Following General Procedure **A** and using benzoyl chloride (33 µL, 0.28 mmol) the product ***11*** (0.136 g, 0.22 mmol, **96%**) was obtained as a colorless solid (mp 283-284 ^oC)

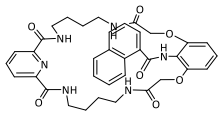
^{1}H NMR (400 MHz, DMSO-d_6) δ 9.99 (s, 1H), 9.33 (t, *J* = 6.1 Hz, 2H), 8.26 – 8.16 (m, 3H), 8.08 (t, *J* = 5.4 Hz, 2H), 7.90 (d, *J* = 7.5 Hz, 2H), 7.30 (t, *J* = 7.4 Hz, 1H), 7.23 (t, *J* = 8.4 Hz, 1H), 6.89 (t, *J* = 7.8 Hz, 2H), 6.72 (d, *J* = 8.5 Hz, 2H), 4.57 (s, 4H), 3.19 (d, *J* = 5.8 Hz, 4H), 3.12 (d, *J* = 4.8 Hz, 4H), 1.41 (s, 8H).

^{13}C NMR (100 MHz, DMSO-d_6) δ 167.3, 166.1, 162.8, 152.9, 149.0, 139.3, 133.6, 131.4, 128.0, 127.7, 127.6, 124.0, 114.9, 105.3, 66.8, 38.8, 37.8, 26.1.

HRMS ESI (m/z) Calcd for $C_{32}H_{36}N_6O_7Na$ $[M + Na]^+$: 639.2543; found: 639.2542.

*N-{4,11,17,24-tetraoxo-2,26-dioxa-5,10,18,23,32-pentaazatricyclo[25.3.1.1^{12,16}]dotriaconta-1(31),12,14,16(32),27,29-hexaen-31-yl}naphthalene-1-carboxamide (**12**)*

Following General Procedure **A** and using 1-naphthoyl chloride (42 µL, 0.28 mmol) the product ***12*** (0.152 g, 0.23 mmol, **99%**) was obtained as a colorless solid (mp 164-165 °C)



M_w = 666.74 g/mol

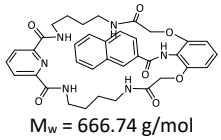
^{1}H NMR (400 MHz, DMSO-d_6) δ 10.18 (s, 1H), 9.44 (t, *J* = 5.3 Hz, 2H), 8.41 (d, *J* = 7.8 Hz, 1H), 8.29 (t, *J* = 5.3 Hz, 2H), 8.22 – 8.11 (m, 3H), 7.87 (dd, *J* = 13.1, 8.2 Hz, 2H), 7.73 (d, *J* = 6.6 Hz, 1H), 7.53 – 7.44 (m, 2H), 7.24 (t, *J* = 8.3 Hz, 1H), 6.98 (t, *J* = 7.5 Hz, 1H), 6.75 (d, *J* = 8.4 Hz, 2H), 4.64 (s, 4H), 3.30 – 3.24 (m, 4H), 3.18 – 3.09 (m, 4H), 1.58 (bs, 4H), 1.45 (bs, 4H).

^{13}C NMR (100 MHz, DMSO-d_6) δ 167.8, 167.3, 163.0, 152.6, 148.9, 139.2, 134.7, 132.8, 129.9, 129.8, 128.1, 127.5, 126.8, 126.1, 125.8, 125.3, 124.3, 124.0, 114.6, 105.2, 67.0, 38.9, 37.8, 26.6, 26.2.

HRMS ESI (m/z) Calcd for $C_{36}H_{38}N_6O_7Na$ $[M + Na]^+$: 689.2700; found: 689.2693.

*N-{4,11,17,24-tetraoxo-2,26-dioxa-5,10,18,23,32-pentaazatricyclo[25.3.1.1^{12,16}]dotriaconta-1(31),12,14,16(32),27,29-hexaen-31-yl}naphthalene-2-carboxamide (**13**)*

Following General Procedure **A** and using 2-naphthoyl chloride (54 mg, 0.28 mmol) the product ***13*** (0.149 g, 0.22 mmol, **97%**) was obtained as a colorless solid (mp 158-159 °C)



M_w = 666.74 g/mol

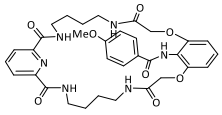
^{1}H NMR (400 MHz, DMSO-d_6) δ 10.18 (s, 1H), 9.31 (bs, 2H), 8.59 (s, 1H), 8.21 (s, 3H), 8.16 (s, 2H), 7.94 (d, *J* = 8.2 Hz, 1H), 7.69 (t, *J* = 8.2 Hz, 2H), 7.53 (t, *J* = 7.3 Hz, 1H), 7.42 (t, *J* = 7.2 Hz, 1H), 7.25 (t, *J* = 8.3 Hz, 1H), 7.16 (d, *J* = 8.3 Hz, 1H), 6.75 (d, *J* = 8.4 Hz, 2H), 4.60 (s, 4H), 3.14 (bs, 8H), 1.40 (bs, 8H).

^{13}C NMR (100 MHz, DMSO-d_6) δ 167.4, 166.1, 162.8, 152.9, 148.9, 139.2, 134.1, 131.7, 130.1, 128.5, 128.4, 127.7 (x2), 127.4, 127.2, 126.5, 124.7, 124.0, 115.0, 105.3, 66.9, 38.7, 37.7, 26.1 (x2).

HRMS ESI (m/z) Calcd for $C_{36}H_{38}N_6O_7Na$ $[M + Na]^+$: 689.2700; found: 689.2694.

*4-methoxy-N-{4,11,17,24-tetraoxo-2,26-dioxa-5,10,18,23,32-pentaazatricyclo[25.3.1.1^{12,16}]dotriaconta-1(31),12,14,16(32),27,29-hexaen-31-yl}benzamide (**14**)*

Following General Procedure **A** and using 4-anisoyl chloride (36 µL, 0.28 mmol) the product ***14*** (0.140 g, 0.22 mmol, **94%**) was obtained as a colorless solid (mp 233-234 °C)



M_w = 646.70 g/mol

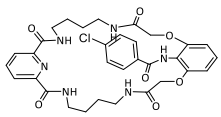
^{1}H NMR (400 MHz, DMSO-d_6) δ 9.83 (s, 1H), 9.34 (t, *J* = 6.1 Hz, 2H), 8.28 – 8.15 (m, 3H), 8.08 (t, *J* = 5.4 Hz, 2H), 7.88 (d, *J* = 8.8 Hz, 2H), 7.22 (t, *J* = 8.4 Hz, 1H), 6.72 (d, *J* = 8.5 Hz, 2H), 6.35 (d, *J* = 8.8 Hz, 2H), 4.56 (s, 4H), 3.59 (s, 3H), 3.22 – 3.18 (m, 4H), 3.12 (d, *J* = 5.0 Hz, 4H), 1.41 (s, 8H).

^{13}C NMR (100 MHz, DMSO-d_6) δ 167.4, 165.6, 162.8, 161.7, 152.9, 149.0, 139.3, 129.9, 127.6, 125.7, 124.0, 115.1, 112.8, 105.3, 66.8, 55.0, 38.8, 37.8, 26.1, 26.0.

HRMS ESI (m/z) Calcd for $C_{33}H_{38}N_6O_8Na$ $[M + Na]^+$: 669.2649; found: 669.2646.

*4-chloro-N-{4,11,17,24-tetraoxo-2,26-dioxa-5,10,18,23,32-pentaazatricyclo[25.3.1.1^{12,16}]dotriaconta-1(31),12,14,16(32),27,29-hexaen-31-yl}benzamide (**15**)*

Following General Procedure **A** and using 2-naphthoyl chloride (36 µL, 0.28 mmol) the product ***15*** (0.133 g, 0.20 mmol, **89%**) was obtained as a colorless solid (mp 255-256 °C)



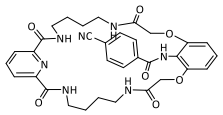
M_w = 651.12 g/mol

^{1}H NMR (400 MHz, DMSO-d_6) δ 10.08 (s, 1H), 9.31 (t, *J* = 5.6 Hz, 2H), 8.27 – 8.18 (m, 3H), 8.10 (t, *J* = 5.6 Hz, 2H), 7.92 (d, *J* = 8.2 Hz, 2H), 7.24 (t, *J* = 8.4 Hz, 1H), 6.87 (d, *J* = 8.2 Hz, 2H), 6.73 (d, *J* = 8.5 Hz, 2H), 4.58 (s, 4H), 3.20 (bs, 4H), 3.15 (bs, 4H), 1.43 (bs, 8H).

^{13}C NMR (100 MHz, DMSO-d_6) δ 167.3, 164.9, 162.7, 152.8, 148.9, 139.3, 136.3, 132.2, 129.8, 127.8, 127.7, 124.1, 114.6, 105.3, 66.8, 38.8, 37.8, 26.2, 26.1.

HRMS ESI (m/z) Calcd for $C_{32}H_{35}N_6O_7ClNa$ $[M + Na]^+$: 673.2153; found: 673.2153.

*4-cyano-N-{4,11,17,24-tetraoxo-2,26-dioxa-5,10,18,23,32-pentaazatricyclo[25.3.1.1^{12,16}]dotriaconta-1(31),12,14,16(32),27,29-hexaen-31-yl}benzamide (**16**)*



M_w = 641.69 g/mol

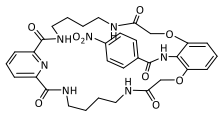
Following General Procedure **A** and using 4-cyanobenzoyl chloride (46 mg, 0.28 mmol) the product ***16*** (0.137 g, 0.21 mmol, **93%**) was obtained as a colorless solid (mp 276-277 ^{o}C (decomposition))

^{1}H NMR (400 MHz, DMSO-d_6) δ 10.26 (s, 1H), 9.26 (t, *J* = 5.7 Hz, 2H), 8.27 – 8.18 (m, 3H), 8.10 (t, *J* = 4.8 Hz, 2H), 8.04 (d, *J* = 8.0 Hz, 2H), 7.33 – 7.22 (m, 3H), 6.74 (d, *J* = 8.5 Hz, 2H), 4.58 (s, 4H), 3.17 (bs, 8H), 1.44 (bs, 8H).

^{13}C NMR (100 MHz, DMSO-d_6) δ 167.3, 164.3, 162.7, 152.8, 148.9, 139.3, 137.4, 131.6, 128.7, 128.1, 124.1, 118.0, 114.2, 109.5, 105.3, 66.8, 38.8, 37.8, 26.3, 26.0.

HRMS ESI (m/z) Calcd for $C_{33}H_{35}N_7O_7Na$ [M + Na]$^+$: 664.2496; found: 664.2496.

*4-nitro-N-{4,11,17,24-tetraoxo-2,26-dioxa-5,10,18,23,32-pentaazatricyclo[25.3.1.1^{12,16}]dotriaconta-1(31),12,14,16(32),27,29-hexaen-31-yl}benzamide (**17**)*



M_w = 661.67 g/mol

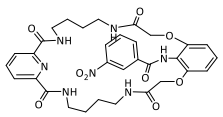
Following General Procedure **A** and using 4-nitrobenzoyl chloride (52 mg, 0.28 mmol) the product ***17*** (0.145 g, 0.22 mmol, **95%**) was obtained as an yellow solid (mp 168-169 ^{o}C)

^{1}H NMR (400 MHz, DMSO-d_6) δ 10.36 (s, 1H), 9.30 (t, *J* = 6.0 Hz, 2H), 8.21 (s, 3H), 8.16-8.09 (m, 4H), 7.65 (d, *J* = 8.7 Hz, 2H), 7.27 (t, *J* = 8.4 Hz, 1H), 6.75 (d, *J* = 8.5 Hz, 2H), 4.59 (s, 4H), 3.18 (dd, *J* = 13.6, 5.0 Hz, 8H), 1.44 (bs, 8H).

^{13}C NMR (100 MHz, DMSO-d_6) δ 167.3, 164.1, 162.7, 152.7, 148.9, 148.8, 139.3, 139.1, 129.4, 128.1, 124.1, 122.7, 114.1, 105.3, 66.8, 38.8, 37.8, 26.3, 26.1.

HRMS ESI (m/z) Calcd for $C_{32}H_{35}N_7O_9Na$ [M + Na]$^+$: 684.2389; found: 684.2412.

*3-nitro-N-{4,11,17,24-tetraoxo-2,26-dioxa-5,10,18,23,32-pentaazatricyclo[25.3.1.1^{12,16}]dotriaconta-1(31),12,14,16(32),27,29-hexaen-31-yl}benzamide (**18**)*



M_w = 661.67 g/mol

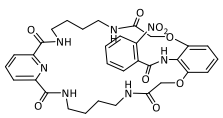
Following General Procedure **A** and using 3-nitrobenzoyl chloride (52 mg, 0.28 mmol) the product ***18*** (0.146 g, 0.22 mmol, **96%**) was obtained as an yellowish solid (mp 192-193 ^{o}C)

^{1}H NMR (400 MHz, DMSO-d_6) δ 10.39 (s, 1H), 9.18 (t, *J* = 5.7 Hz, 2H), 8.80 (s, 1H), 8.32 (d, *J* = 7.5 Hz, 1H), 8.22 – 8.13 (m, 6H), 7.27 (t, *J* = 8.4 Hz, 1H), 7.04 (t, *J* = 7.9 Hz, 1H), 6.75 (d, *J* = 8.5 Hz, 2H), 4.60 (s, 4H), 3.17 (bs, 8H), 1.46 (bs, 8H).

^{13}C NMR (100 MHz, DMSO-d_6) δ 167.3, 163.5, 162.8, 152.8, 148.8, 147.2, 139.1, 134.8, 134.2, 129.3, 128.1, 126.1, 124.0, 122.7, 114.0, 105.2, 66.8, 38.7, 37.6, 26.1, 26.0.

HRMS ESI (m/z) Calcd for $C_{32}H_{35}N_7O_9Na$ [M + Na]$^+$: 684.2389; found: 684.2394.

*2-nitro-N-{4,11,17,24-tetraoxo-2,26-dioxa-5,10,18,23,32-pentaazatricyclo[25.3.1.1^{12,16}]dotriaconta-1(31),12,14,16(32),27,29-hexaen-31-yl}benzamide (**19**)*



M_w = 661.67 g/mol

Following General Procedure **A** and using 2-nitrobenzoyl chloride (37 µL, 0.28 mmol) the product ***19*** (0.145 g, 0.22 mmol, **95%**) was obtained as an yellowish solid (mp 167-168 ^{o}C)

^{1}H NMR (400 MHz, DMSO-d_6) δ 10.22 (s, 1H), 9.17 (bt, *J* = 5.8 Hz, 2H), 8.18 – 8.08 (m, 3H), 8.02 (bt, *J* = 5.1 Hz, 2H), 7.88 (d, *J* = 7.7 Hz, 1H), 7.78 (d, *J* = 6.9 Hz, 1H), 7.59 – 7.49 (m, 2H), 7.22 (t, *J* = 8.4 Hz, 1H), 6.72 (d, *J* = 8.5 Hz, 2H), 4.59 (s, 4H), 3.28 – 3.21 (m, 4H), 3.20 – 3.15 (m, 4H), 1.58 – 1.49 (m, 4H), 1.45 (bs, 4H).

^{13}C NMR (100 MHz, DMSO-d_6) δ 167.3, 164.5, 162.9, 153.0, 148.8, 147.0, 139.1, 133.1, 131.6, 131.0, 129.6, 127.9, 124.0, 123.8, 113.8, 105.3, 67.0, 38.8, 37.9, 26.8, 26.4.

HRMS ESI (m/z) Calcd for $C_{32}H_{35}N_7O_9Na$ [M + Na]$^+$: 684.2389; found: 684.2388.

1.3. Conversions observed in combinatorial experiments

Table S1. Conversions of macrocyclic compound **2** in combinatorial experiments[a]

Entry	Compound	Template	Conversion [%]															
			A	**B**	**C**	**D**	**E**	**F**	**G**	**H**	**I**	**J**	**K**	**L**	**M**	**N**	**O**	**P**	**Q**
1	**A**	Untemplated		81	73	77	71	78	90	70	75	82	73	77	73	77	77	78	76
		TBA-H_2PO_4		71	73	82	77	81	80	75	77	74	76	78	77	74	71	72	71
2	**B**	Untemplated	81		80	75	85	92	96	95	98	100	97	99	98	100	100	98	100
		TBA-H_2PO_4	71		73	79	68	55	73	80	38	75	55	84	20	32	15	14	19
3	**C**	Untemplated	73	80		77	91	-[b]	99	91	100	100	98	97	100	-[b]	97	99	-[b]
		TBA-H_2PO_4	73	73		48	55		81	77	39	43	76	84	19		17	13	
4	**D**	Untemplated	77	75	77		93	97	-[b]	99	99	95	97	-[b]	100	99	-[b]	98	94
		TBA-H_2PO_4	82	79	48		77	79		81	83	81	81		82	81		81	81
5	**E**	Untemplated	71	85	91	93		100	97	-[b]	100	-[b]	1008	99	99	98	100	98	99
		TBA-H_2PO_4	77	68	55	77		68	59		53		2	93	36	55	25	20	34
6	**F**	Untemplated	78	92	-[b]	97	100		100	99	99	98	99	96	100	-[b]	99	99	-[b]
		TBA-H_2PO_4	81	55		79	68		49	55	34	56	62	85	22		17	13	
7	**G**	Untemplated	90	96	99	-[b]	97	100		100	-[b]	96	99	-[b]	98	95	-[b]	100	98
		TBA-H_2PO_4	80	73	81		59	49		61		76	59		49	61		50	55
8	**H**	Untemplated	70	95	91	99	-[b]	99	100		95	-[b]	97	100	91	95	99	100	98
		TBA-H_2PO_4	75	80	77	81		55	61		34		65	83	17	11	23	10	15
9	**I**	Untemplated	75	98	100	99	100	99	-[b]	95		95	97	95	98	98	-[b]	-[b]	100
		TBA-H_2PO_4	77	38	39	83	53	34		34		80	80	86	76	78			77
10	**J**	Untemplated	82	100	100	95	-[b]	98	96	-[b]	95		99	98	100	97	96	99	98
		TBA-H_2PO_4	74	75	43	81		56	76		80		83	88	81	78	74	73	74
11	**K**	Untemplated	73	97	98	97	100	99	99	97	97	99		100	96	99	97	97	94
		TBA-H_2PO_4	76	55	76	81	82	62	59	65	80	83		91	83	82	77	76	78
12	**L**	Untemplated	77	99	97	-[b]	99	96	-[b]	100	95	98	100		98	99	-[b]	99	100
		TBA-H_2PO_4	78	84	84		93	85		83	86	88	91		89	90		83	87
13	**M**	Untemplated	73	98	100	100	99	100	98	91	98	100	96	98		97	99	99	96
		TBA-H_2PO_4	77	20	19	82	36	22	49	17	76	81	83	89		82	74	73	74
14	**N**	Untemplated	77	100	-[b]	99	98	-[b]	95	95	98	97	99	99	97		97	94	-[b]
		TBA-H_2PO_4	74	32		81	55		61	11	78	78	82	90	82		71	73	
15	**O**	Untemplated	77	100	97	-[b]	100	99	-[b]	99	-[b]	96	97	-[b]	99	97		100	99
		TBA-H_2PO_4	71	15	17		25	17		23		74	77		74	71		68	72
16	**P**	Untemplated	78	98	99	98	98	99	100	100	-[b]	99	97	99	99	94	100		99
		TBA-H_2PO_4	72	14	13	81	20	13	50	10		73	76	83	73	73	68		65
17	**Q**	Untemplated	76	100	-[b]	94	99	-[b]	98	98	100	98	94	100	96	-[b]	99	99	
		TBA-H_2PO_4	71	19		81	34		55	15	77	74	78	87	74		72	65	

[a] Determined using HPLC analysis, [b] Impossible to determine due to overlapping signals

2. Copies of ^{1}H and ^{13}C NMR spectra

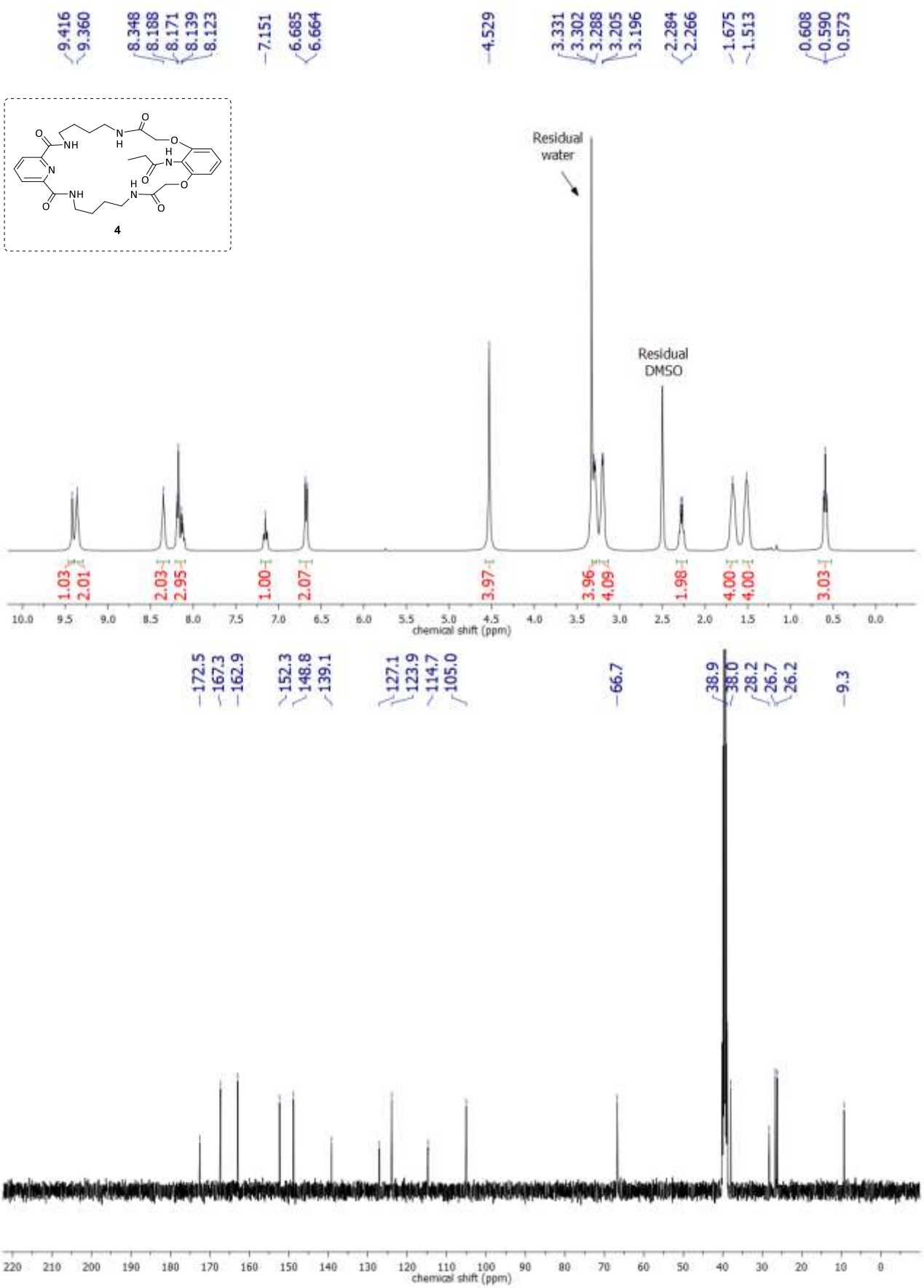
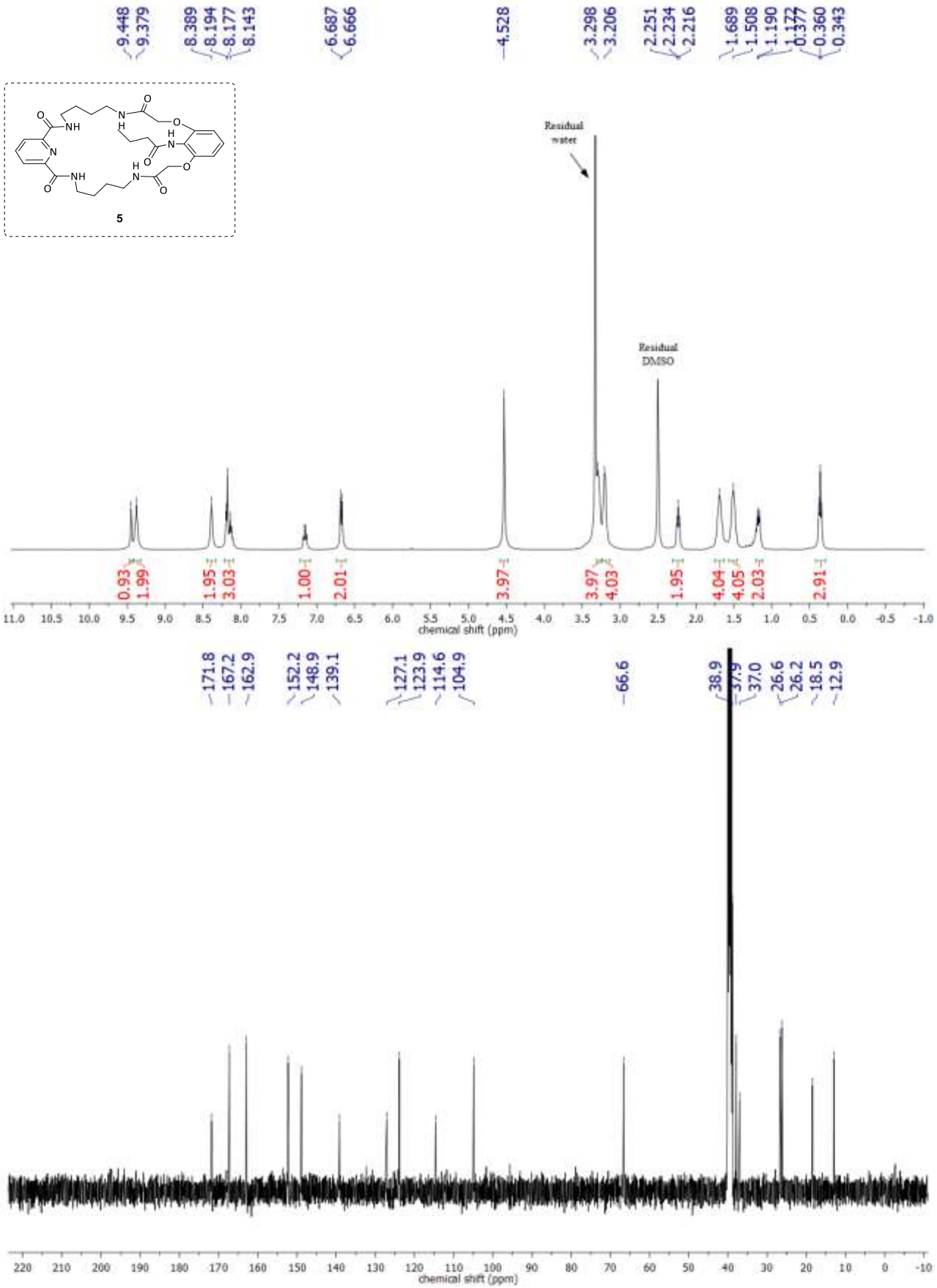
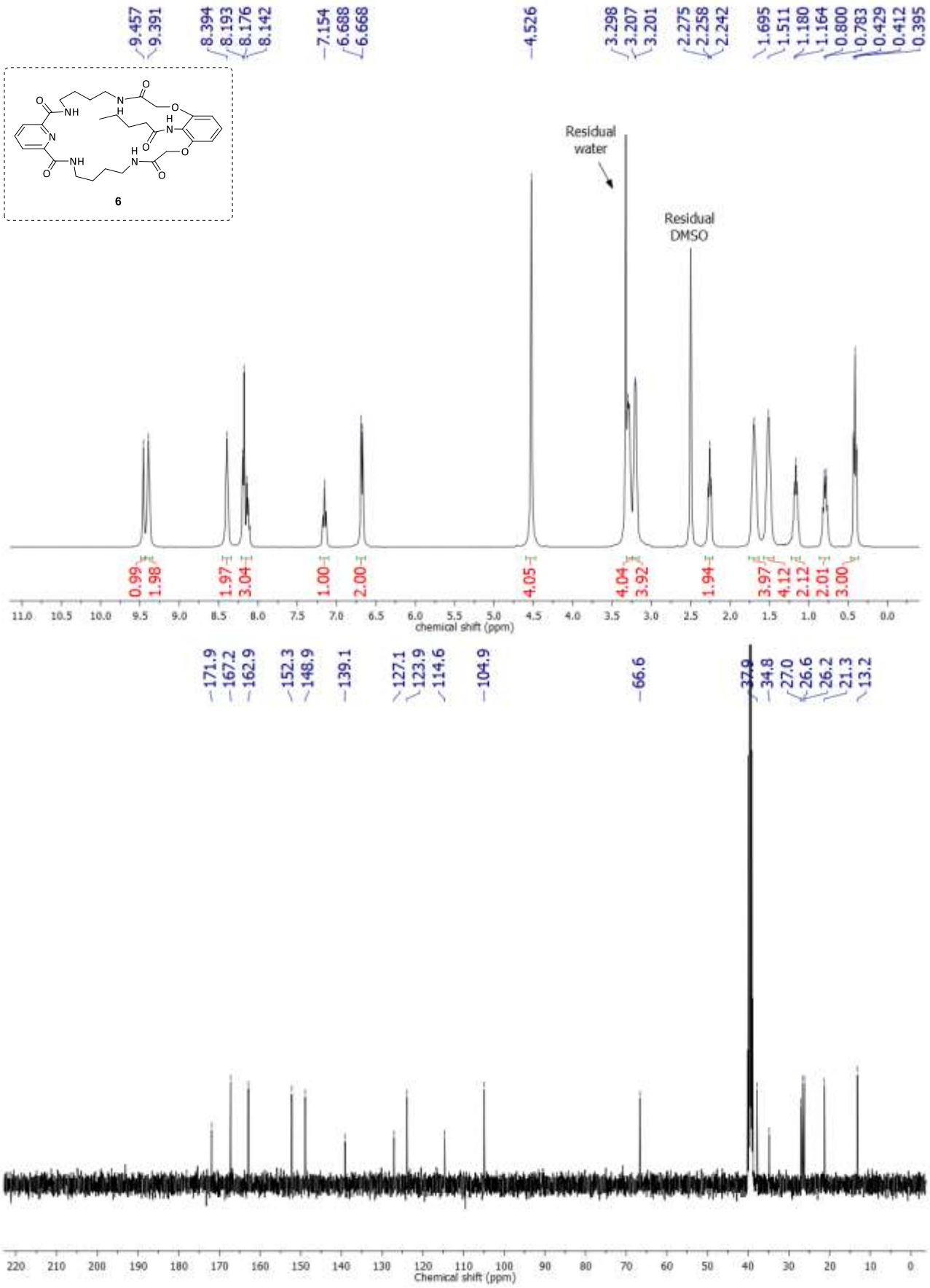


Figure S1. ^{1}H NMR (400 MHz) and ^{13}C NMR (100 MHz) spectra of compound **4** in DMSO-d_6.



5

Figure S2. ^{1}H NMR (400 MHz) and ^{13}C NMR (100 MHz) spectra of compound **5** in DMSO-d_6.



6

Figure S3. ^{1}H NMR (400 MHz) and ^{13}C NMR (100 MHz) spectra of compound **6** in DMSO-d_6.

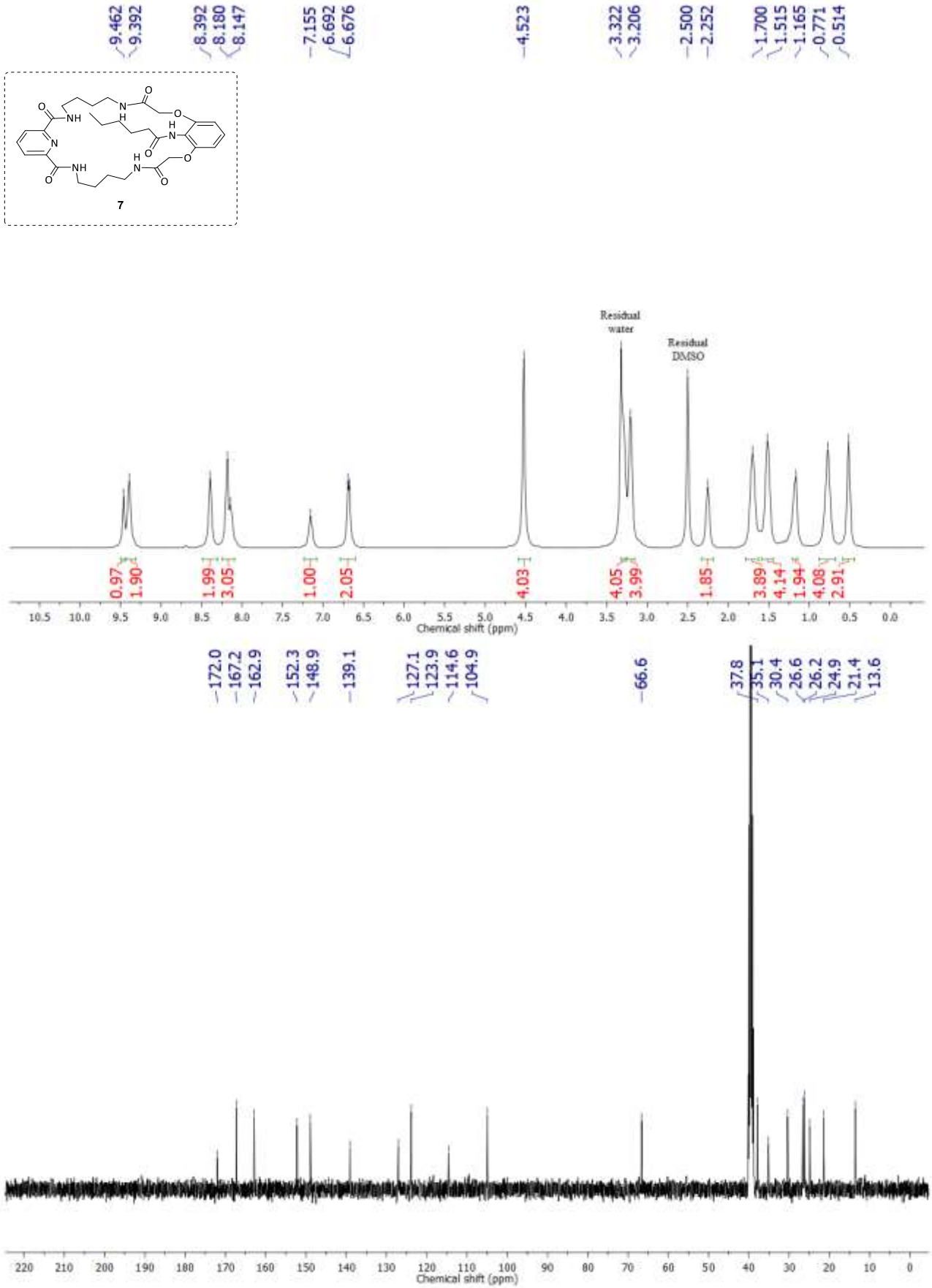


Figure S4. ^{1}H NMR (400 MHz) and ^{13}C NMR (100 MHz) spectra of compound **7** in DMSO-d_6.

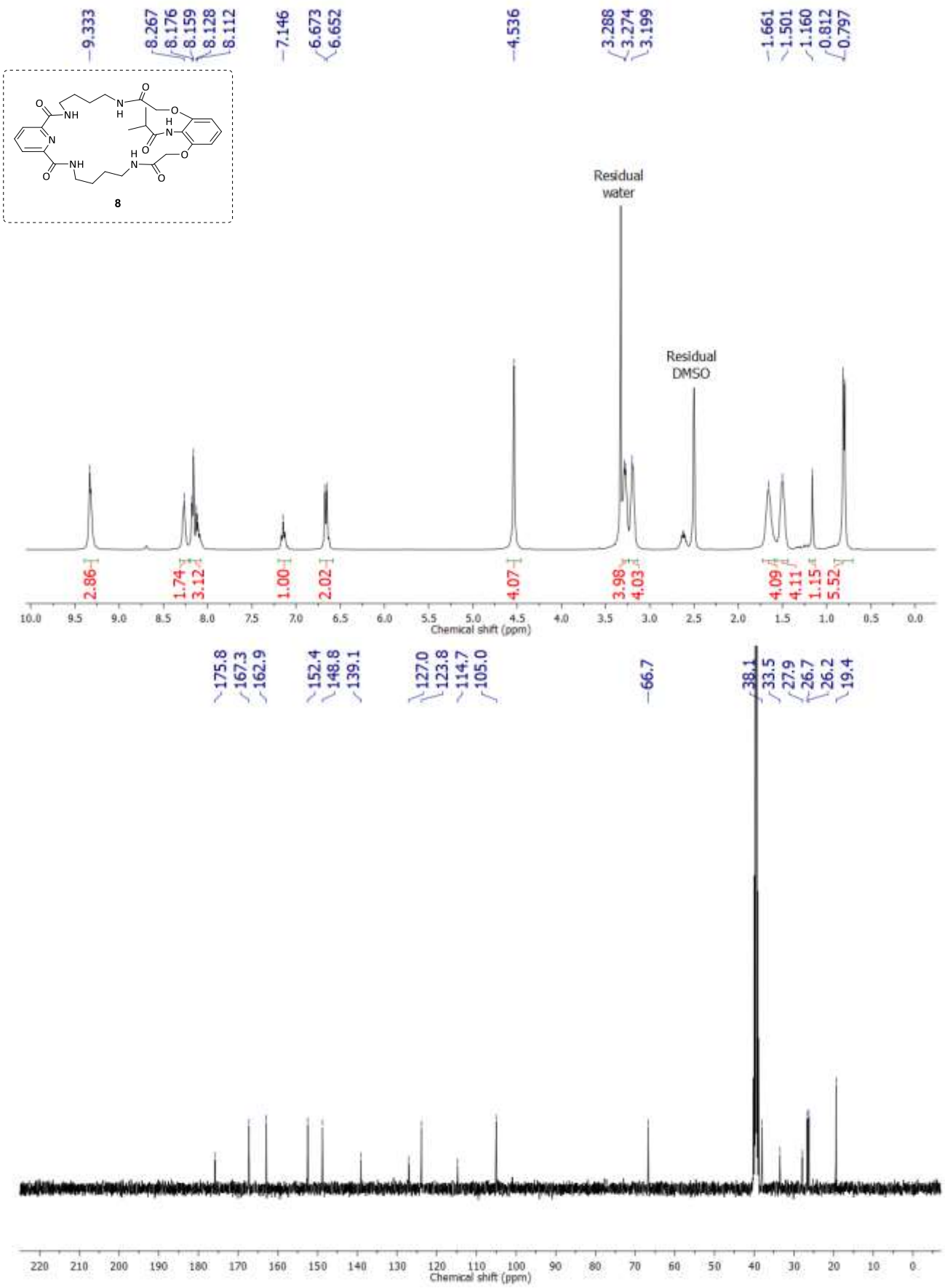


Figure S5. ^{1}H NMR (400 MHz) and ^{13}C NMR (100 MHz) spectra of compound **8** in DMSO-d_6.

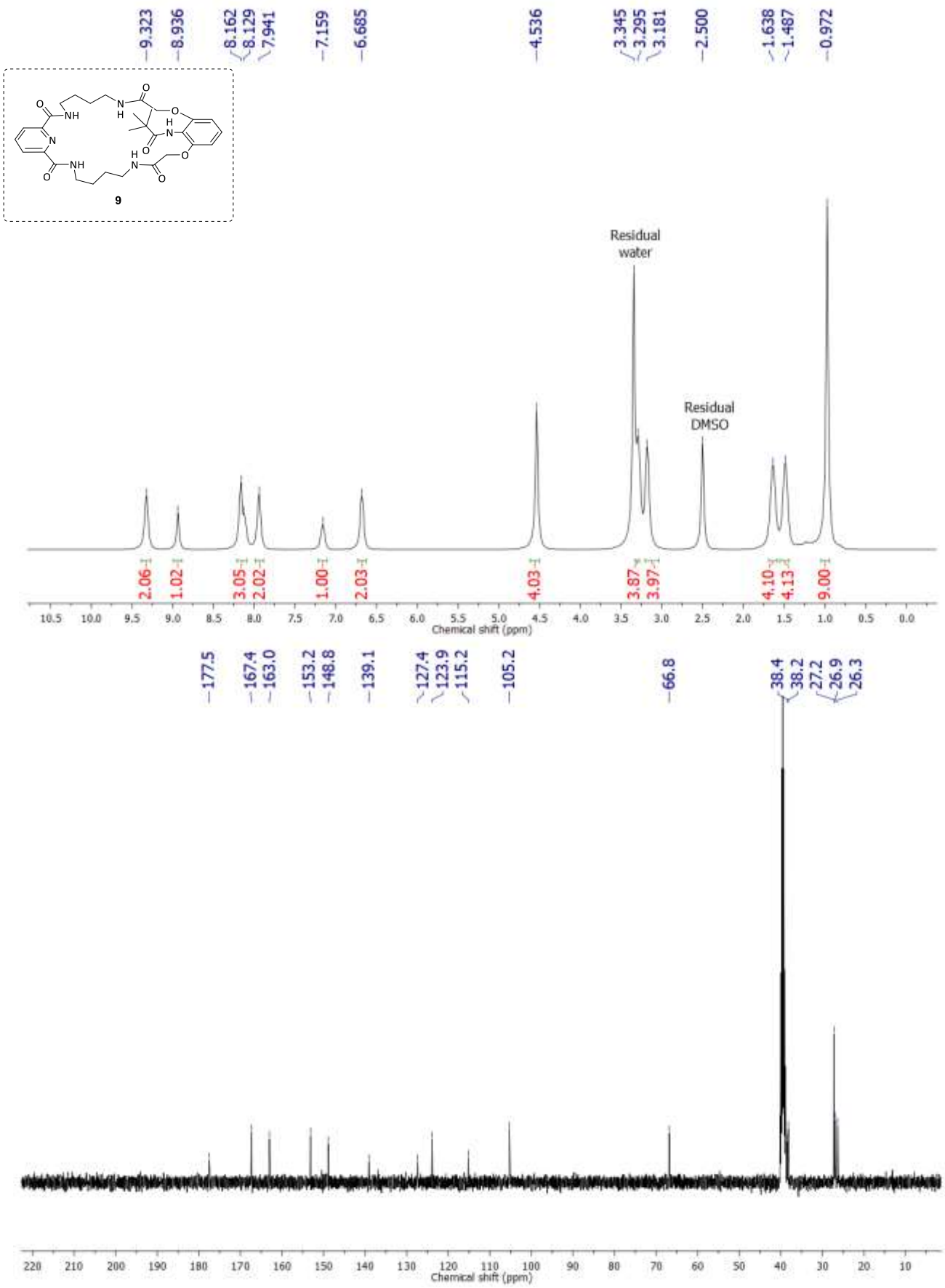


Figure S6. ^{1}H NMR (400 MHz) and ^{13}C NMR (100 MHz) spectra of compound **9** in DMSO-d_6.

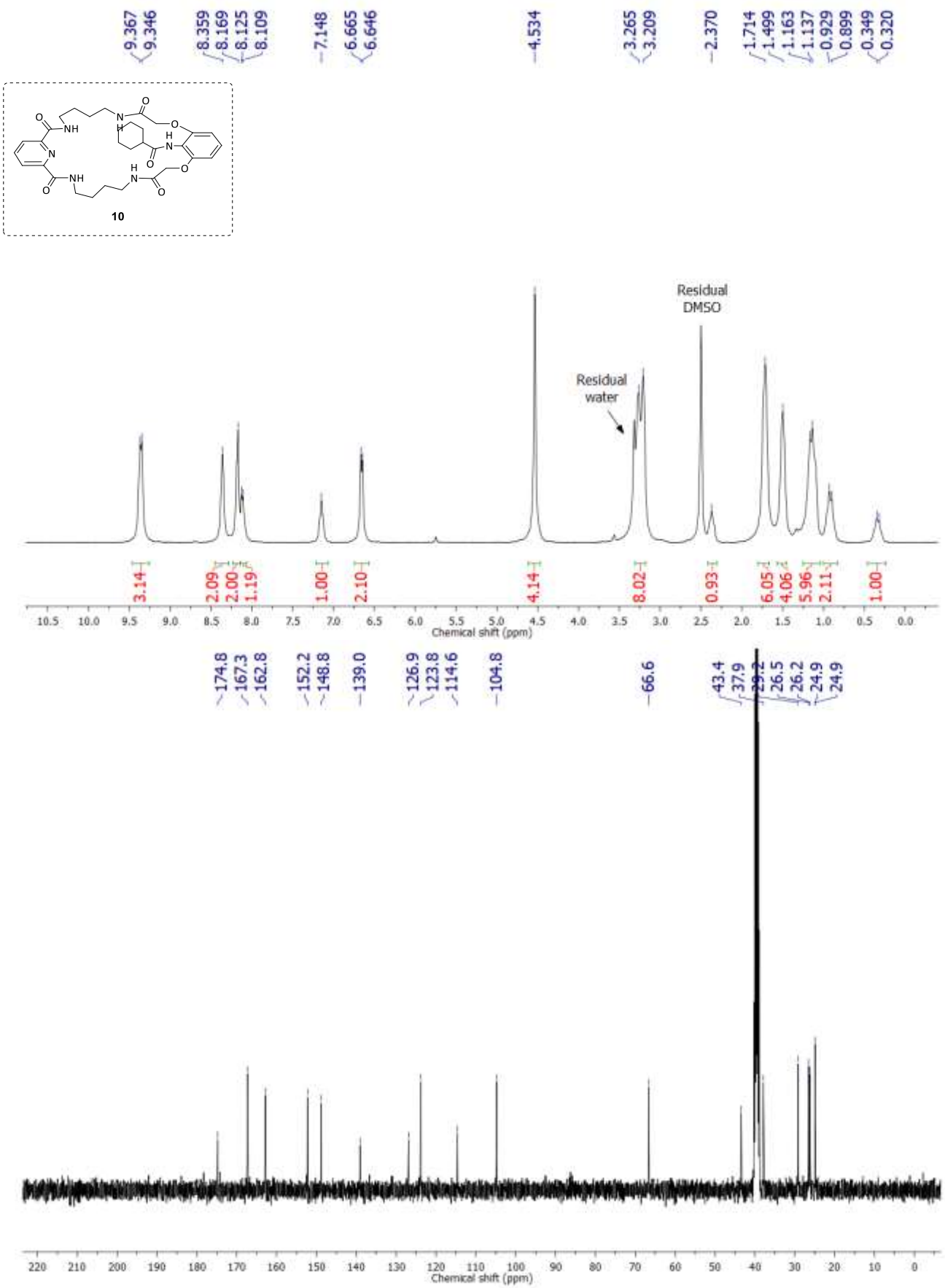


Figure S7. ^{1}H NMR (400 MHz) and ^{13}C NMR (100 MHz) spectra of compound **10** in DMSO-d_6.

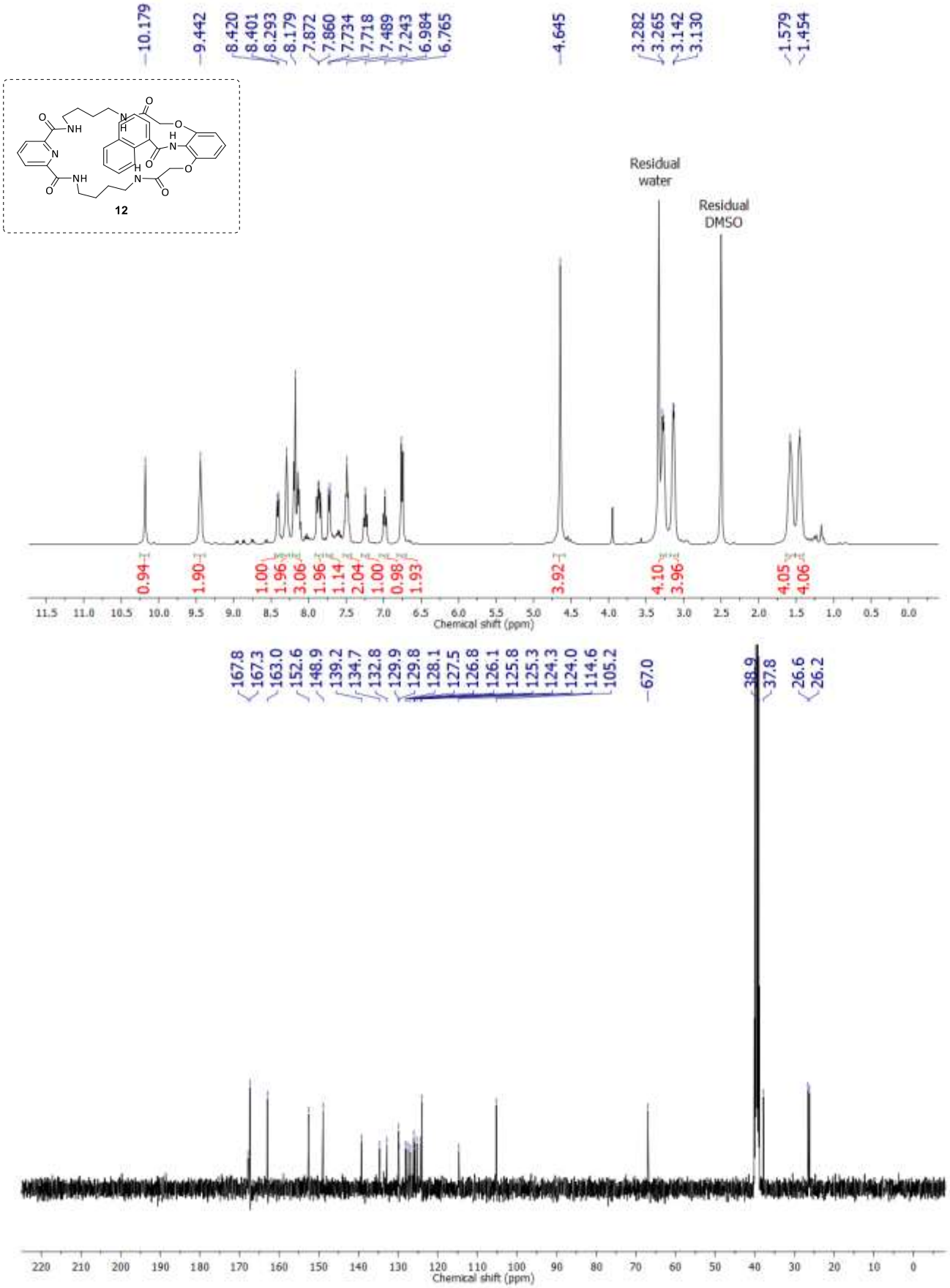


Figure S8. ^{1}H NMR (400 MHz) and ^{13}C NMR (100 MHz) spectra of compound **12** in DMSO-d_6.

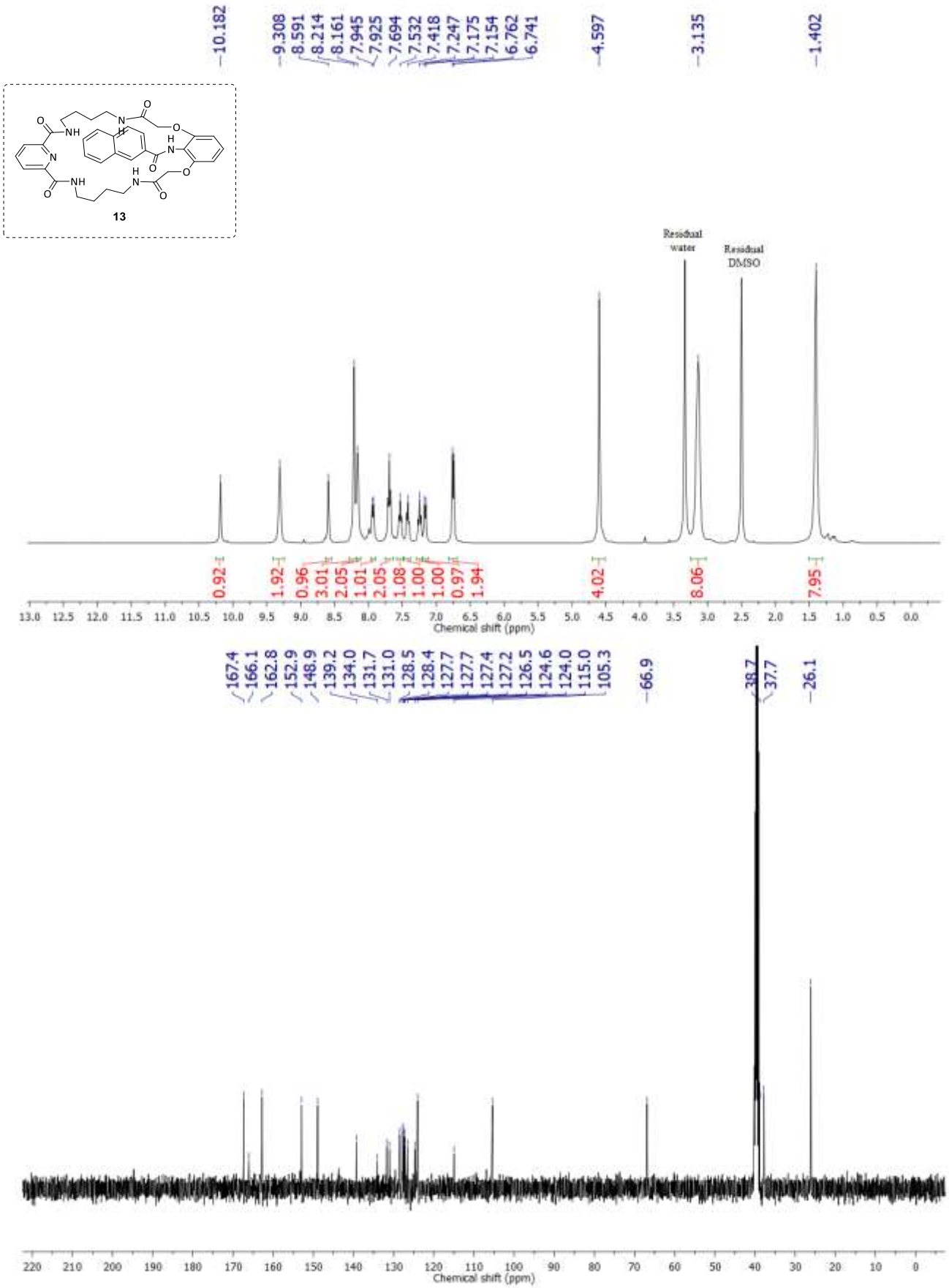


Figure S9. ^{1}H NMR (400 MHz) and ^{13}C NMR (100 MHz) spectra of compound **13** in DMSO-d_6.

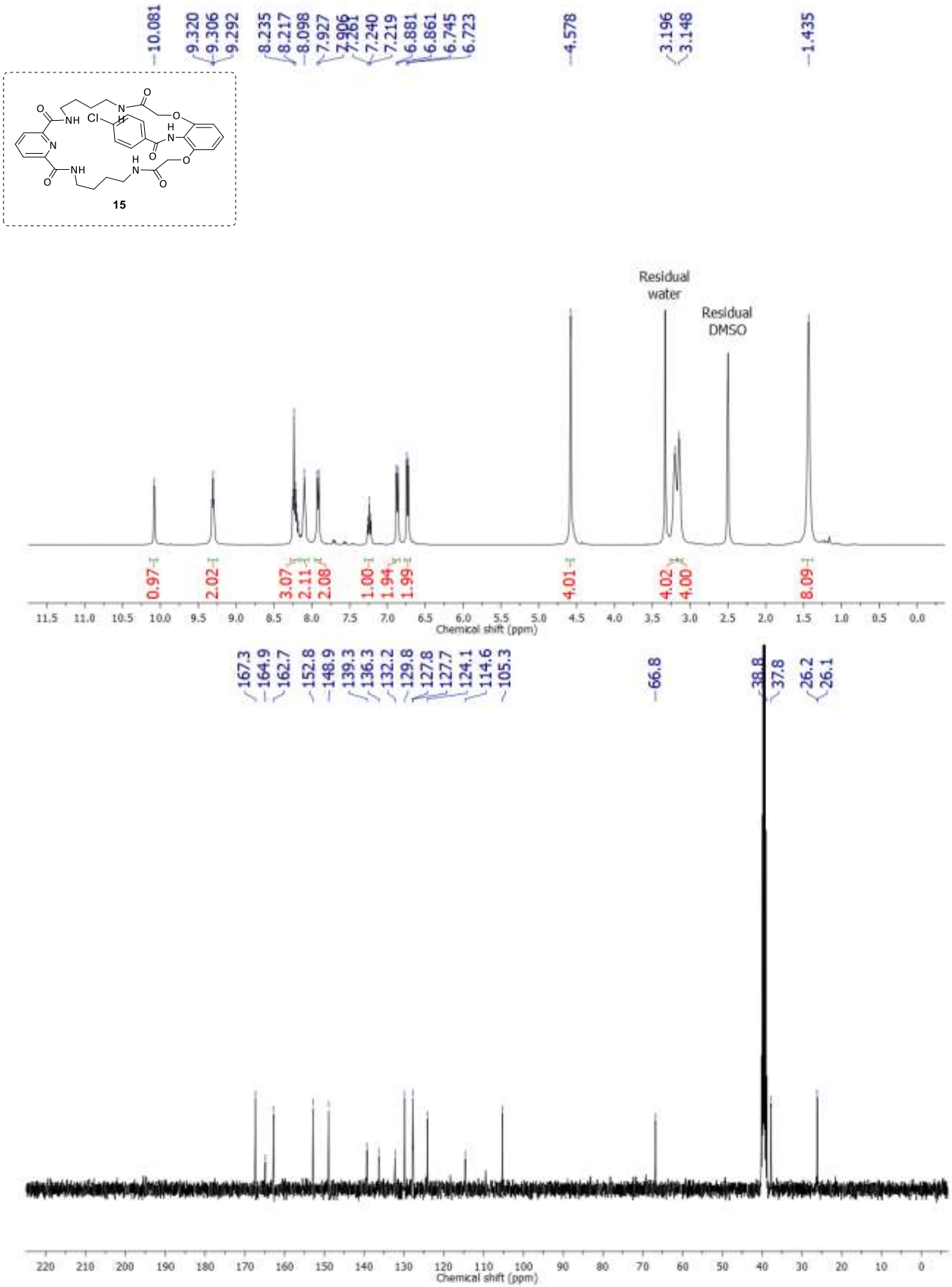


Figure S10. ^{1}H NMR (400 MHz) and ^{13}C NMR (100 MHz) spectra of compound **15** in DMSO-d_6.

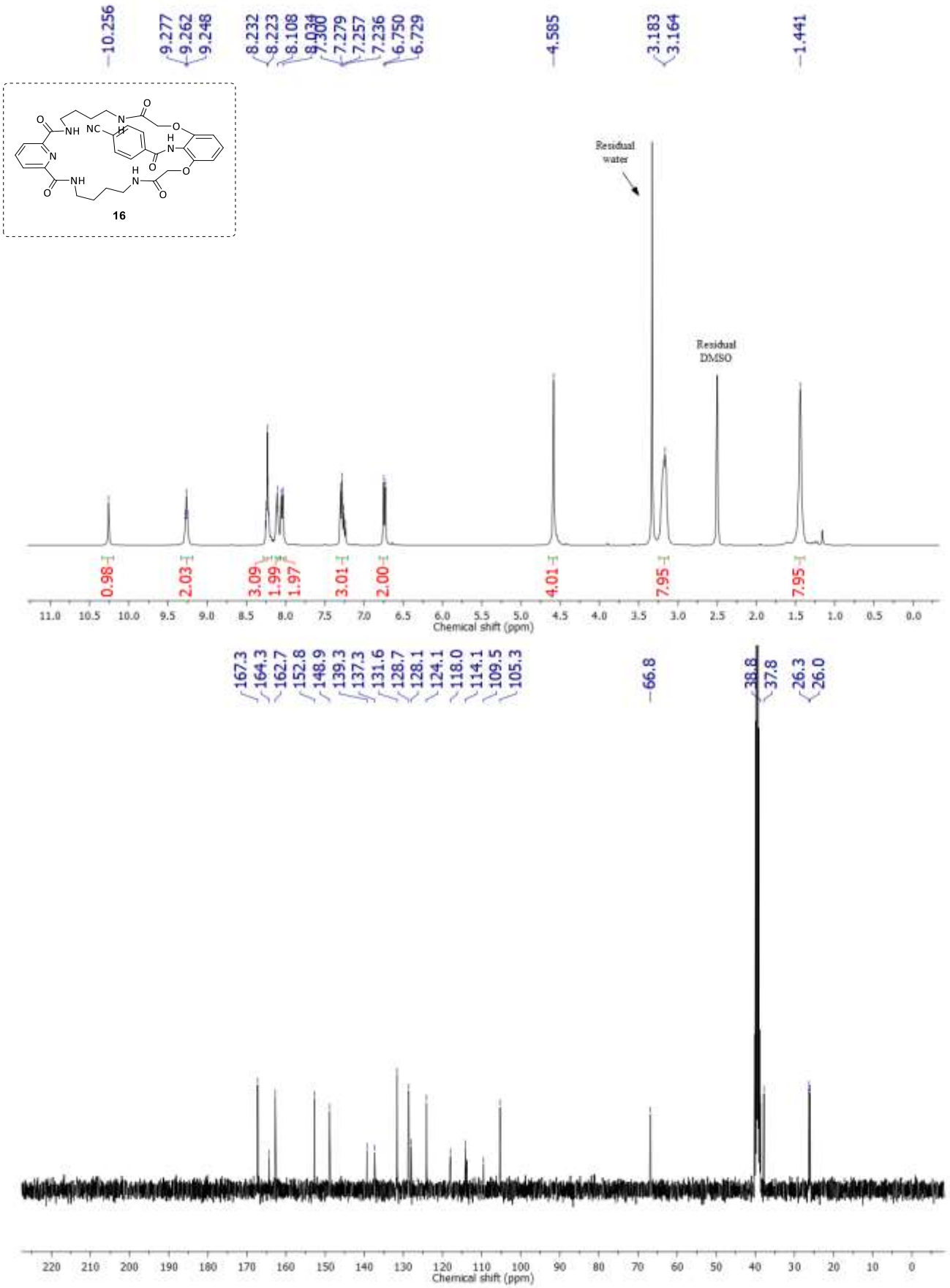


Figure S11. ^{1}H NMR (400 MHz) and ^{13}C NMR (100 MHz) spectra of compound **16** in DMSO-d_6.

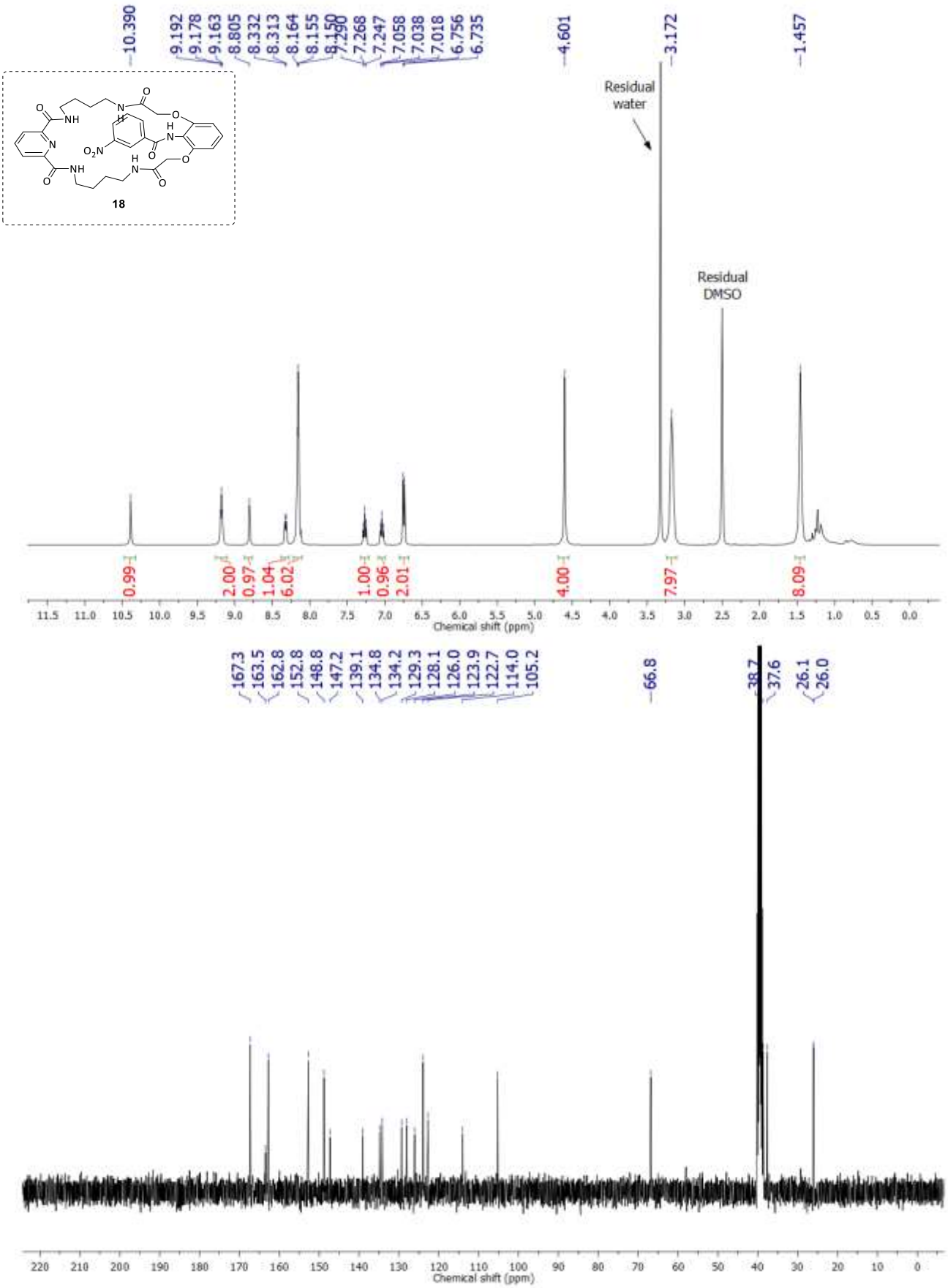


Figure S12. ^{1}H NMR (400 MHz) and ^{13}C NMR (100 MHz) spectra of compound **18** in DMSO-d_6.

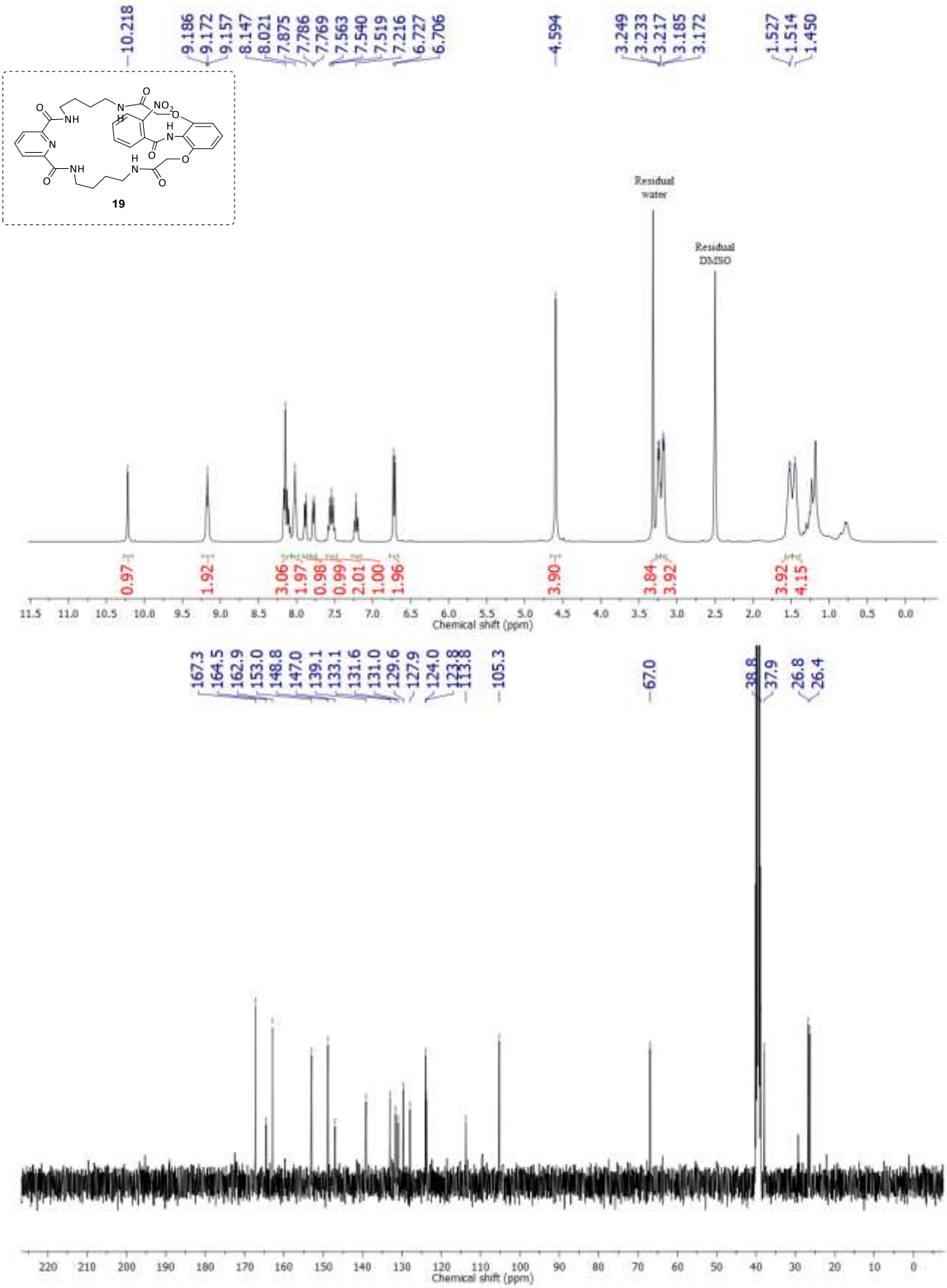


Figure S13. ^{1}H NMR (400 MHz) and ^{13}C NMR (100 MHz) spectra of compound **19** in DMSO-d_6.

3. Titration experiments

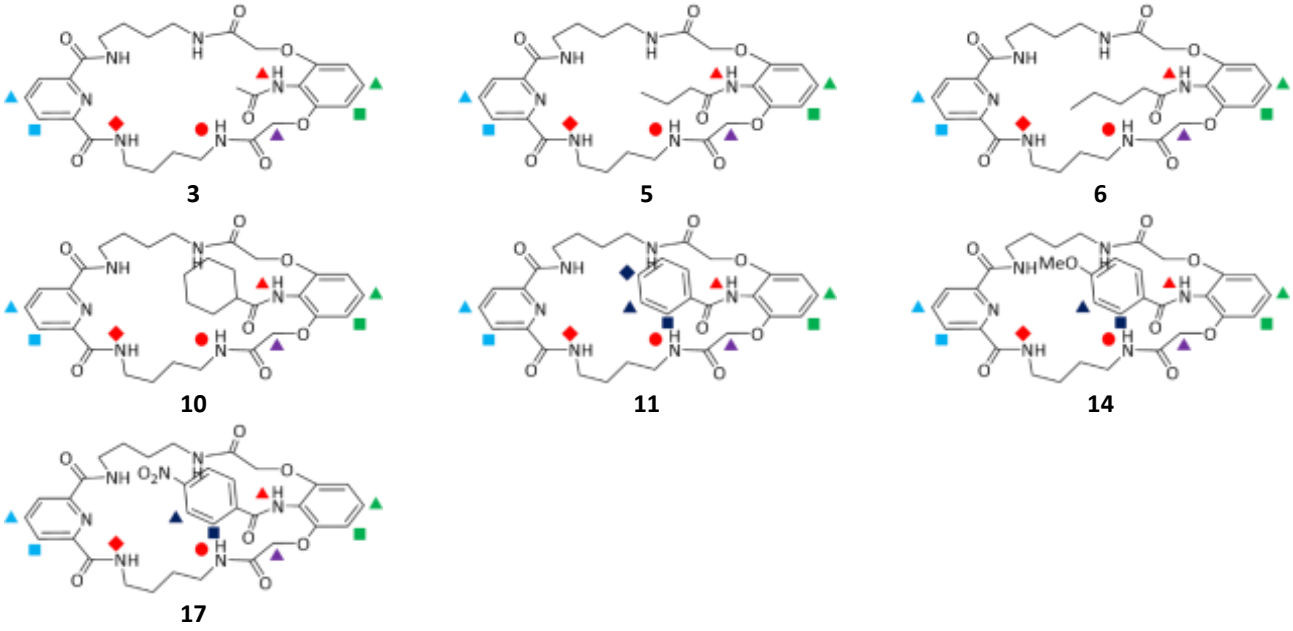
As the source of anion, commercially available tetrabutylammonium salt was used. HPLC grade water was added to the commercially available DMSO-d_6 of 99.9% isotopic purity to obtain the appropriate water concentration. The host solution was titrated in a NMR tube with the solution of the TBA salt in receptor aliquots (details are given in Table S1). The binding constants were calculated from the changes in chemical shifts of ligand protons which were shifted during titration. Nonlinear curve fitting was carried out with HypNMR 2008[2] (Version 4.0.71) program with fitting to the appropriate global binding model (see Table S1).

Table. S2. Titration details, global stability constants K_a (M^{-1}), and selected maximum signal shifts ($\Delta\delta_{max}$) of amide protons for Receptors **3**, **5**, **6**, **10**, **11**, **14**, and **17** with $H_2PO_4^-$ in DMSO-d_6 + 0.5% H_2O[a]

Entry	Receptor	C_{Host} [M]	C_{Guest} [M]	K_a [M^{-1}] (H:G)	$\Delta\delta_{max}$ [ppm] NH◆	NH●	CH▲	CH■
1	**3**	0.01558	0.09008	8600 (1:1) 210 (1:2)	1.42	0.18	-0.06	-0.04
2	**5**	0.01440	0.08960	40 (1:1) 100 (2:1)	1.05	0.10	-0.08	-0.07
3	**6**	0.01494	0.08859	1520 (1:1) 6 (1:2)	1.52	0.06	-0.05	-0.02
4	**10**	0.01401	0.08802	1620 (1:1) 20 (1:2)	1.75	0.10	-0.04	-0.01
5	**11**	0.01518	0.06653	1700 (1:1) 290 (2:1)	1.47	0.31	-0.07	-0.01
6	**14**	0.01439	0.08763	1020 (1:1) 210 (2:1)	1.75	0.27	-0.01	-
7	**17**	0.01033	0.05327	3770 (1:1) 40 (1:2)	1.72	0.27	-0.10	-0.08

[a] Values determined by ^{1}H NMR titration experiments at T = 298 K using HypNMR 2008 software,[2] errors < 10%, TBA salt as the source of anion.

Figure S14. Labeling of the selected proton peaks of the receptors **3**, **5**, **6**, **10**, **11**, **14**, and **17**



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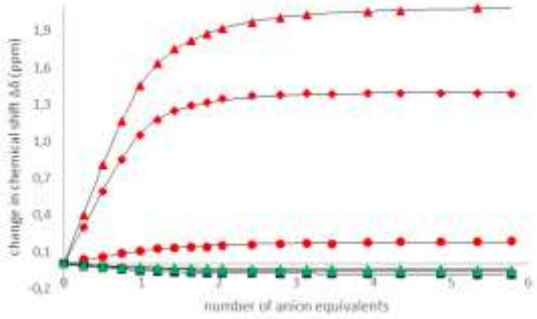
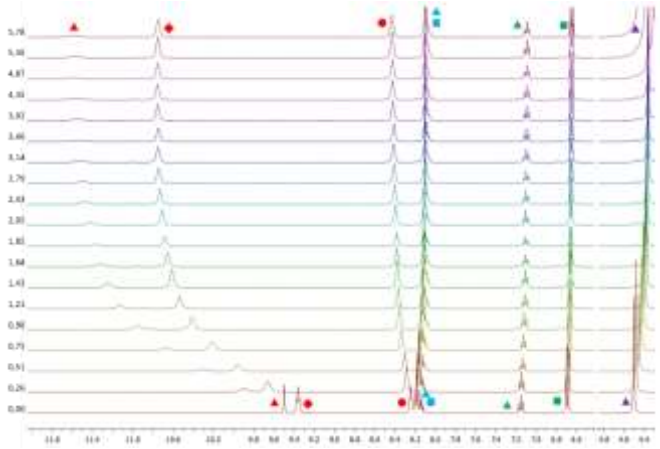

change in chemical shift Δδ (ppm)
number of anion equivalents



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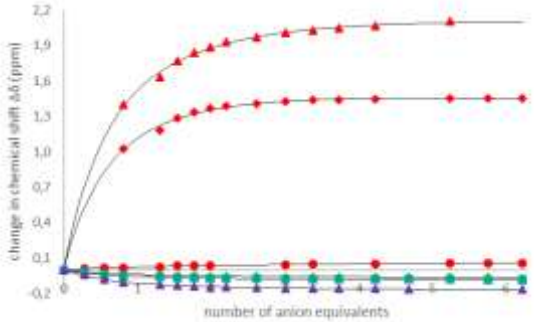
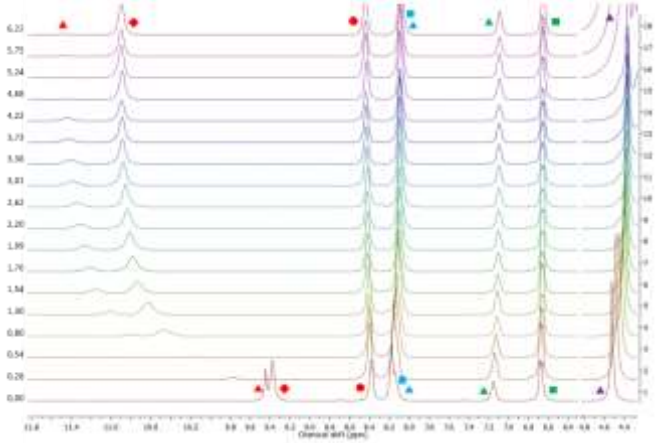

change in chemical shift Δδ (ppm)
number of anion equivalents



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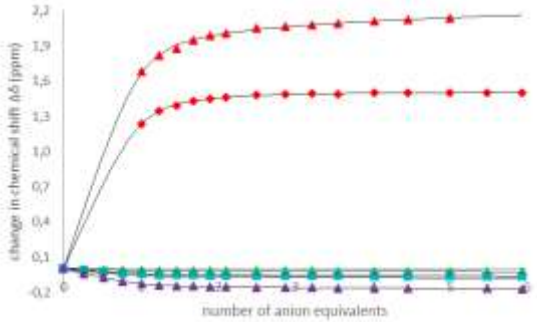
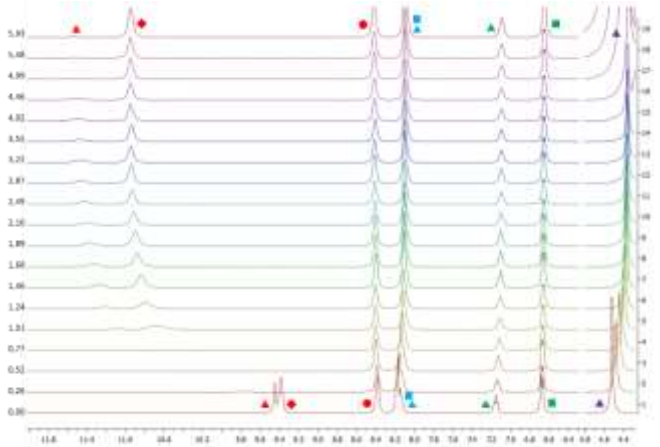

change in chemical shift Δδ (ppm)
number of anion equivalents



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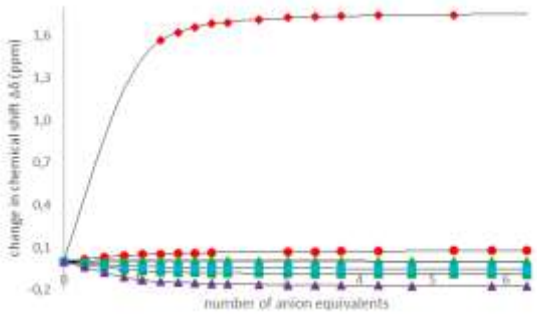
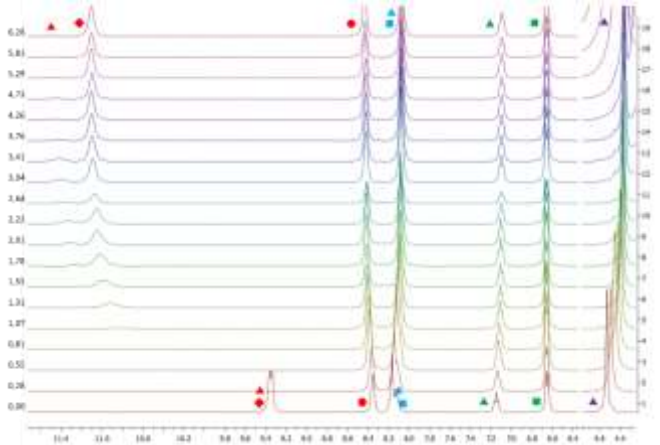

change in chemical shift Δδ (ppm)
number of anion equivalents



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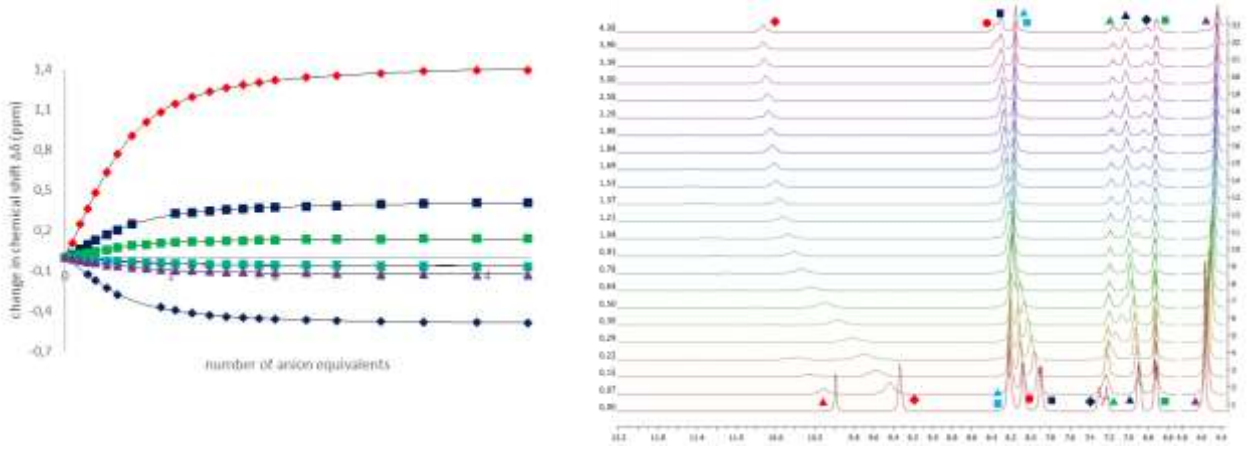

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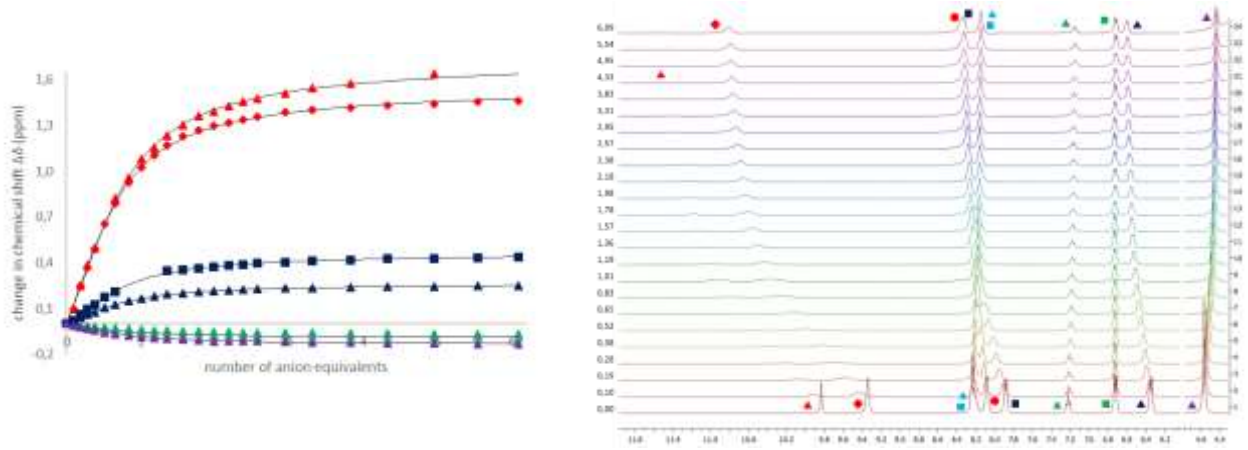

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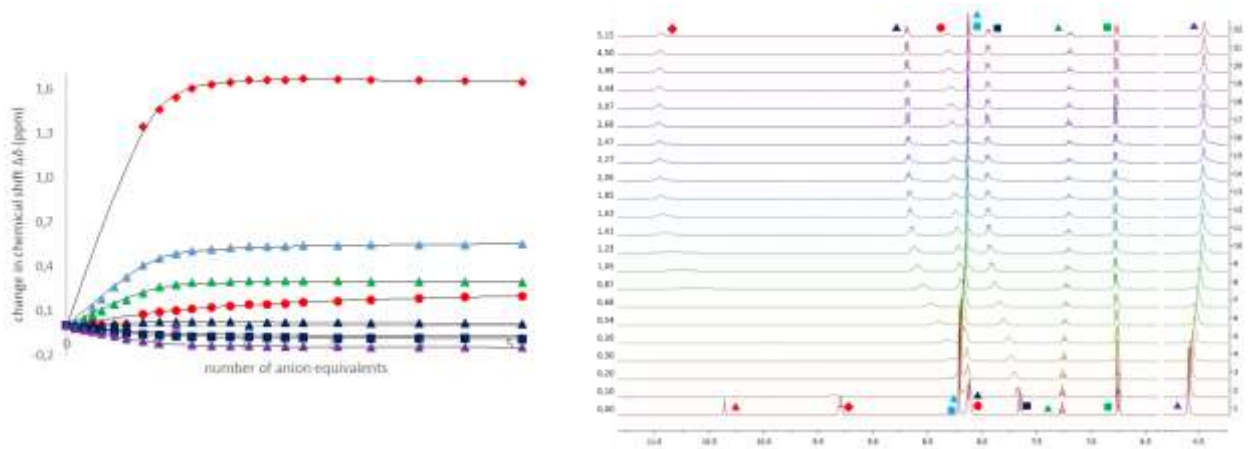

Figure S15. Corresponding experimental chemical shift changes (symbols) and calculated binding isotherms (lines) (left); Stacked plots from ^{1}H NMR titrations of Receptors **3**, **5**, **6**, **10**, **11**, **14**, and **17** with increasing amount of *n*-$Bu_4NH_2PO_4$ in DMSO-d_6 + 0.5% H_2O (v/v) (right).

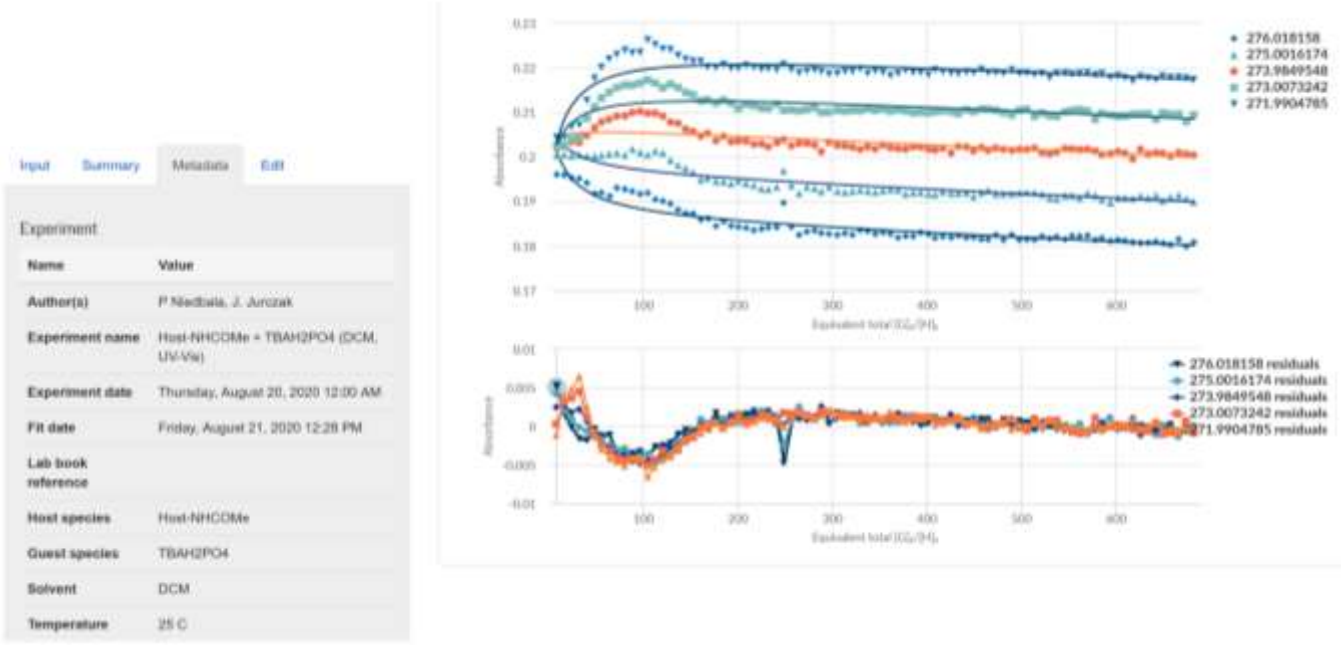

Figure S16. Calculated binding isotherms of UV-Vis titration of Receptor **3** with increasing amount of *n*-$Bu_4NH_2PO_4$ in DCM.

4. References

[1] Dabrowa, K.; Niedbała, P.; Majdecki, M.; Duszewski, P.; Jurczak, J. A General Method for Synthesis of Unclosed Cryptands *via* H-Bond Templated Macrocyclization and Subsequent Mild Postfunctionalization. *Org. Lett.* **2015,** *17,* 4774-4777.

[2] Rodríguez-Barrientos, D.; Rojas-Hernández, A.; Gutiérrez, A.; Moya-Hernández, R.; Gómez-Balderas, R.; Ramírez-Silva, M. T. Determination of pKa values of tenoxicam from 1H NMR chemical shifts and of oxicams from electrophoretic mobilities (CZE) with the aid of programs SQUAD and HYPNMR. *Talanta* **2009**, *80*, 754-762.