Electronic Supplementary Material (ESI) for RSC Advances.

A Hybrid Macrocyclic Anion Receptor Exploiting the Pyrrole-2,5-diacetamide Unit

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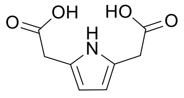
Supporting Information

Synthesis

Pyrrole-2,5-diacetic acid (9)



9

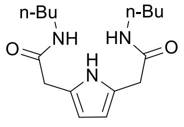
Pyrrole-2,5-diacetic acid methyl ester (3.4 g, 16 mmol) was dissolved in ethanol (8 ml) and KOH (7 g) in water (8 ml) was added. The mixture was refluxed for 1 h. Then additional water (10 ml) was added and pH was adjusted to 1 with HCl. Product was extracted with chloroform (3x50 ml) and diethyl ether (3x50 ml), combined organic layers were dried with $MgSO_4$ and evaporated. Crude product was crystalized from pentane/diethyl ether mixture, yielding 2.3 g (13 mmol, 80%) of **8**.

mp. 120-122˚C.

^{1}H NMR (200 MHz, DMSO) δ = 12.22 (bs, 2H), 10.47 (bs, 1H), 5.72 (d, 2H, J_1 = 2.4 Hz), 3.44 (s, 4H, CH_2).

^{13}C NMR (50 MHz, DMSO) δ = 172.5, 124.0, 107.0, 33.9.

Pyrrole-2,5-diacetic butyl diamide (8a)



8a

Pyrrole-2,5-diacetic methyl diester (0.7 g, 3 mmol) was dissolved in butylamine (4 ml) under Ar. Sealed flask was heated to 60 deg C and the reaction mixture was stirred overnight. 1 M HCl (20 ml) was then added, and product was extracted with $CHCl_3$ (4x15 ml). Combined organic layers were dried with $MgSO_4$, solvent was evaporated and the residue was purified with gel chromatography using CH_2Cl_2:MeOH 100:3. Yield 0.75 g (2.6 mmol, 87%). Product **8a** was recrystallized in ethyl acetate:hexanes 4:6.

mp. 165-167˚C.

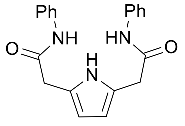
^{1}H NMR (200 MHz, DMSO) δ = 9.63 (s, 1H), 6.02 (t, 2H, J_1 = 5.4 Hz), 5.94 (d, 2H, J_1 = 2.4 Hz), 3.19 (s, 4H), 3.19 (dt, 4H, J_1 = 7.0 Hz, J_2 = 6.8 Hz), 1.41 (m, 4H), 1.29 (m, 4H), 0.88 (t, 6H, J_1 = 7.2 Hz).

^{13}C NMR (50 MHz, DMSO) δ = 170.47, 125.09, 107.88, 39.39, 35.84, 31.44, 19.96, 13.68.

HRMS (ESI TOF) calcd for $C_{16}H_{27}N_3O_2Na$ [M+Na]+: 316,1995 found: 316,2001.

Elemental Analysis calcd for $C_{16}H_{27}N_3O_2$: C 65.53, H 9.22, N 14.33, found: C 65.54, H 9.11, N 14.35.

Pyrrole-2,5-diacetic phenyl diamide (8b)


8b

Diacid 8 (1 g, 5.8 mmol) was stirred with aniline (2.1 ml, 23 mmol) in dry THF (25 ml) under Ar. Diisopropylcarbodiimide (2 ml, 12.8 mmol) was dropped into the reaction mixture, and was stirred overnight. Solvent was then evaporated, residue was suspended in $CHCl_3$ (100 ml) and sonicated. The resulting precipitate was dissolved in CH_2Cl_2:MeOH 1:1, 1M HCl was added, and layers were separated. Solid precipitated from the organic layer, which was then filtered of and recrystallized from ethanol, yielding with 1 g (3 mmol, 51%) of **4b** as a colorless needles.

mp. 186-192˚C.

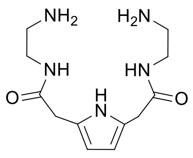
^{1}H NMR (200 MHz, DMSO) δ = 10.52 (s, 1H), 10.00 (s, 2H), 7.60 (d, 4H, J_1 = 8.6 Hz), 7.30 (dd, 4H, J_1 = 8.4 Hz J_2 = 8.4 Hz), 7.03 (t, 2H), 5.79 (s, 2H), 3.56 (s, 4H).

^{13}C NMR (50 MHz, DMSO) δ = 169.01, 139.75, 129.18, 125.03, 123.60, 119.51, 106.84, 36.64.

HRMS (ESI TOF) calcd for $C_{20}H_{19}N_3O_2Na$ [M+Na]+: 356,1369 found: 356,1381.

Elemental Analysis calcd for $C_{20}H_{19}N_3O_2$: C 72.07, H 5.70, N 12.61, found: C 71.84, H 5.60, N 12.65.

Pyrrole-2,5-diacetic 2-aminoethyl diamide (6)


6

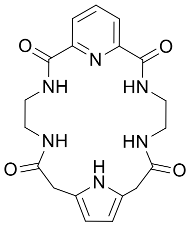
Pyrrole-2,5-diacetic methyl diester (1 g, 4.7 mmol) was dissolved in ethylenediamine (6 ml) under Ar. Sealed flask was heated to 60˚C and the reaction mixture was stirred overnight. Ethylenediamine was evaporated under reduced pressure, the residue was washed with CH_2Cl_2 and purified using gel chromatography in gradient of MeOH:$NH_3 \cdot H_2O$ 100:3 (200ml), 100:5 (400ml), 100:10 (200ml). Yield 0.8 g (3.1 mmol, 66%).

^{1}H NMR (200 MHz DMSO) δ = 10.38 (bs, 1H), 7.79 (t, 2H, J_1 = 6.2 Hz), 5.66 (d, 2H, J_1 = 2.2 Hz), 3.3 (s, 4H), 3.02 (dt, 4H, J_1 = 6.2 Hz, J_2 = 6.0 Hz), 2.52 (t, 4H, J_1 = 6.0 Hz), 2.27 (bs, 4H).

^{13}C NMR (125 MHz, DMSO) δ =170.2, 125.3, 106.5, 42.8, 41.7, 35.6.

HRMS (ESI TOF) calcd for $C_{12}H_{21}N_5O_2$ M^+: 267.16953, found: 267.16852.

Macrocycle 4



4

Amine **6** (0.8 g, 3 mmol) and dipicolic acid methyl diester **7** (0.6 g, 3 mmol) were dissolved in methanol (50 ml). DBU (0.3 ml) was added and the mixture was left for 14 days. Next, oligomeric side products were filtered off and the filtrate was purified by gel chromatography, using isocratic 3-5% gradient of MeOH:CH_2Cl_2, yielding 180 mg of macrocycle **1** (0.45mmol, 15%).

mp. 282˚C (decomposition).

^{1}H NMR (200 MHz, DMSO) δ = 10.03 (bs, 1H), 9.04 (t, 2H, J_1 = 4.6 Hz), 8.20 (m, 3H), 7.27 (bs, 2H, J_1 = 5.0 Hz), 5.65 (d, 2H, J_1 = 2.6 Hz), 3.36 (m, 12H).

^{13}C NMR (50 MHz, DMSO) δ = 170.8, 163.9, 149.1, 139.9, 124.9, 124.6, 107.3, 41.2, 35.8.

HRMS (ESI TOF) calcd for $C_{19}H_{22}N_6O_4Na$ $[M+Na]^+$: 421.1600, found: 421.1592.

Elemental Analysis calcd for $C_{19}H_{22}N_6O_4$: C 57.28, H 5.57, N 21.09, found: C 57.01, H 5.63, N 21.22.

Crystalographic data: Monocrystal was obtained by slow evaporation of THF from the solution of the receptor. $C_{20}H_{19}N_3O_2$, M = 333.38, monoclinic, *Cc*, a = 11.6197(3) Å, b = 9.4493(4) Å, c = 30.4715(10) Å, α = 90º, β = 92.932(2)º, γ = 90º, V = 3341.3(2) Å^3, T=100(2) K, Z = 8, μ(Mo-K_α) = 0.088 mm^{-1}, 17472 collected reflexes, 3471 unique (R_{int}= 0.0421). Final R indices [I>2σ(I)]: $R1(F^2)$= 0.0549 i $wR2(F^2)$= 0.1479, R indices (all data): $R1(F^2)$= 0.0576 i $wR2(F^2)$= 0.1512. All heavy atoms were refined anisotropically. All hydrogen atoms were located geometrically.

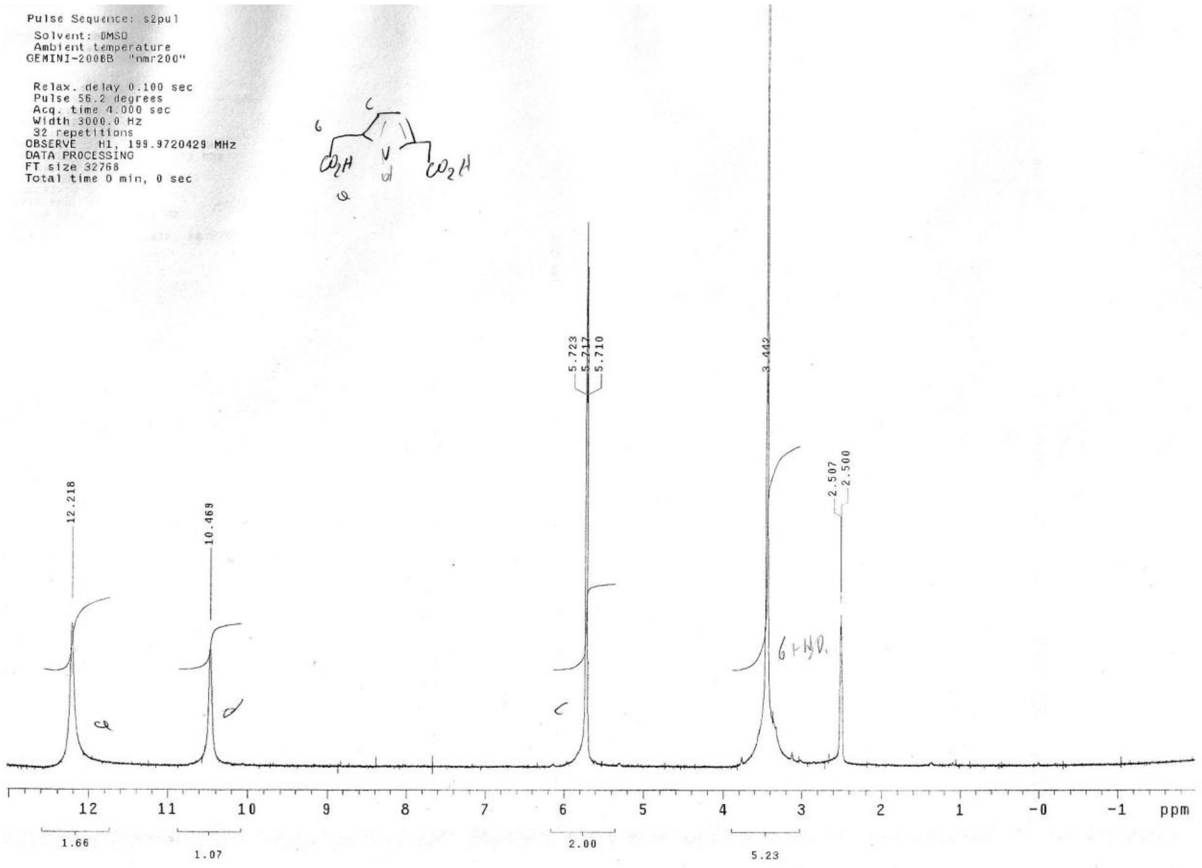


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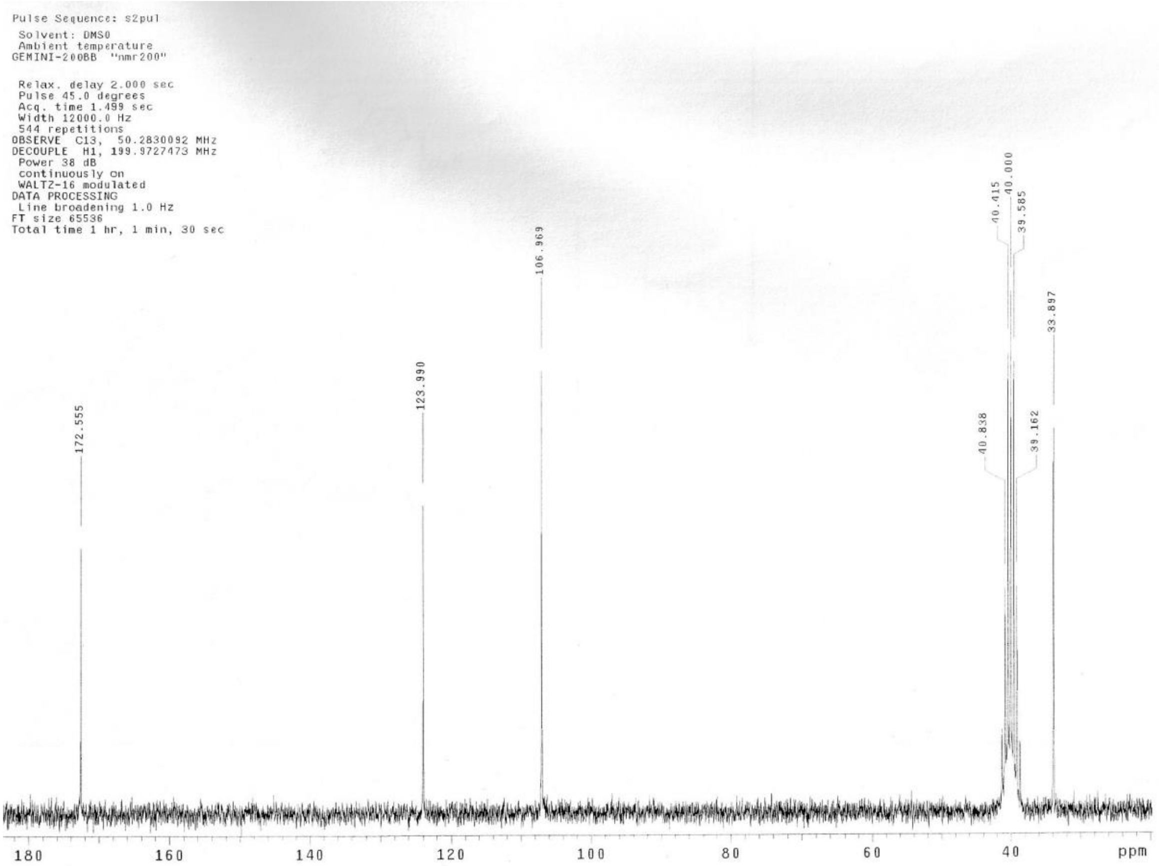
Figure S1. ^{1}H NMR spectrum of diacid **9**.



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 544 repetitions
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DECOUPLE  H1, 199.9727473 MHz
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DATA PROCESSING
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Figure S2. ^{13}C NMR spectrum of diacid **9**.

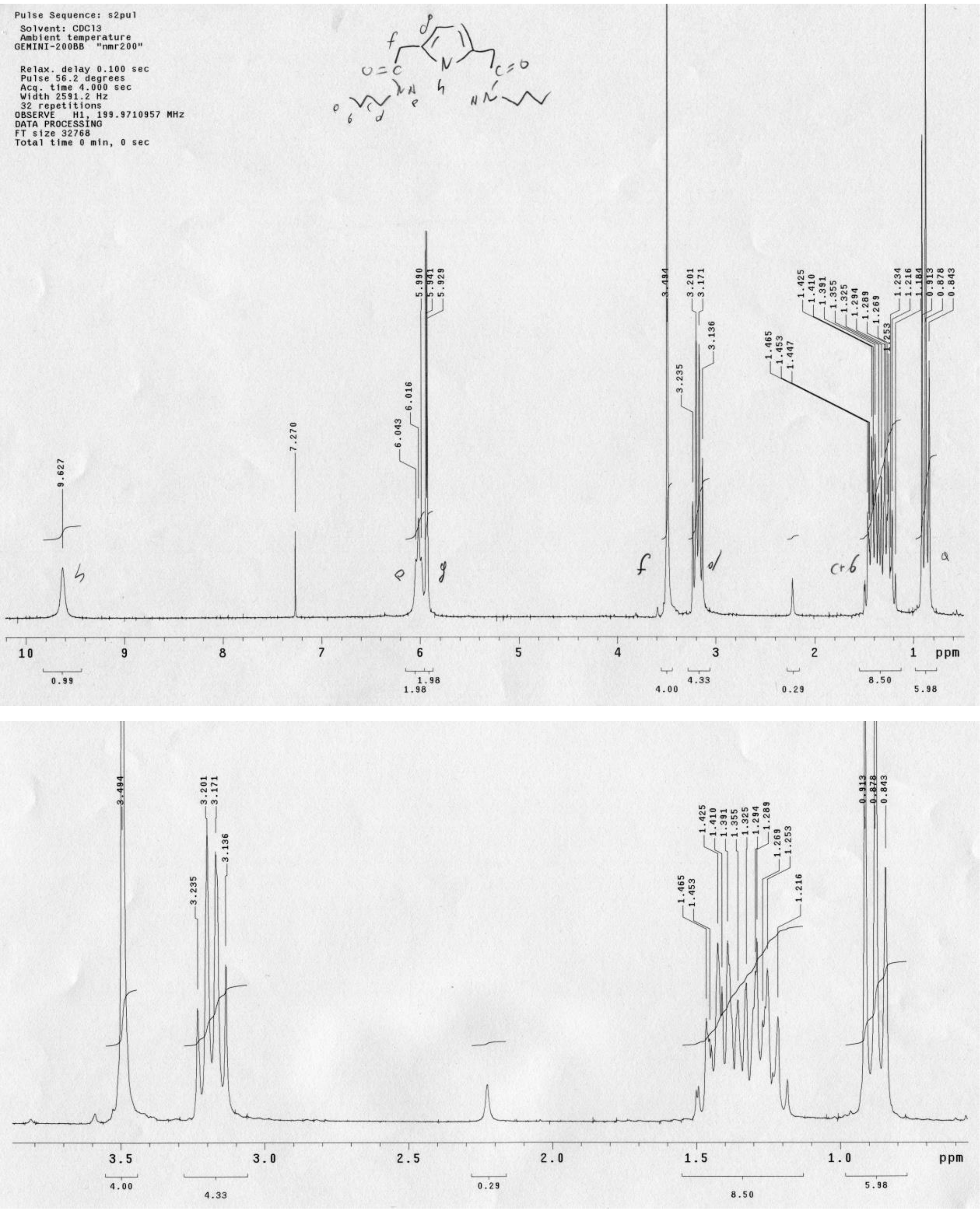
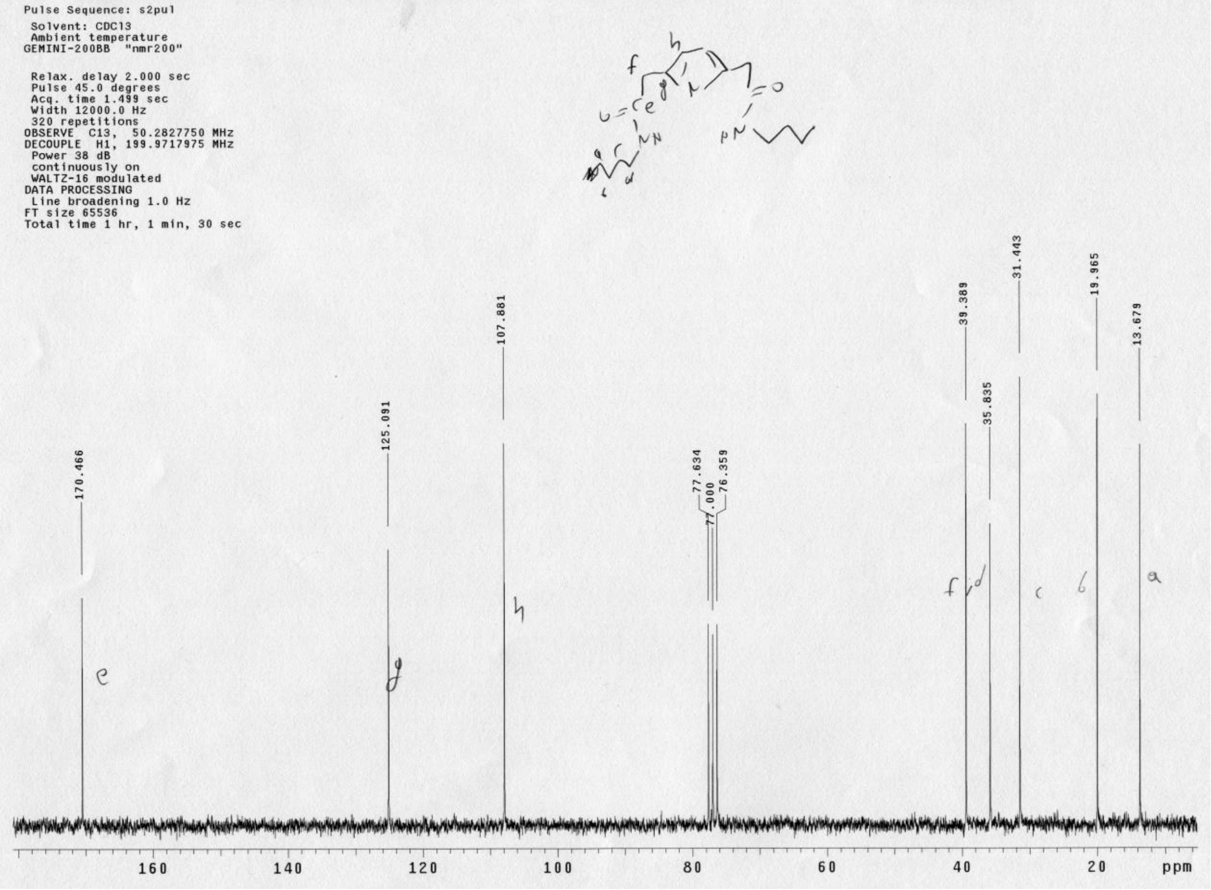


Figure S3. ^{1}H NMR spectra of diamide **8a**.



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DECOUPLE  H1, 199.9717975 MHz
 Power 38 dB
 continuously on
 WALTZ-16 modulated
DATA PROCESSING
 Line broadening 1.0 Hz
FT size 65536
Total time 1 hr, 1 min, 30 sec
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Figure S4. ^{13}C NMR spectrum of diamide **8a**.

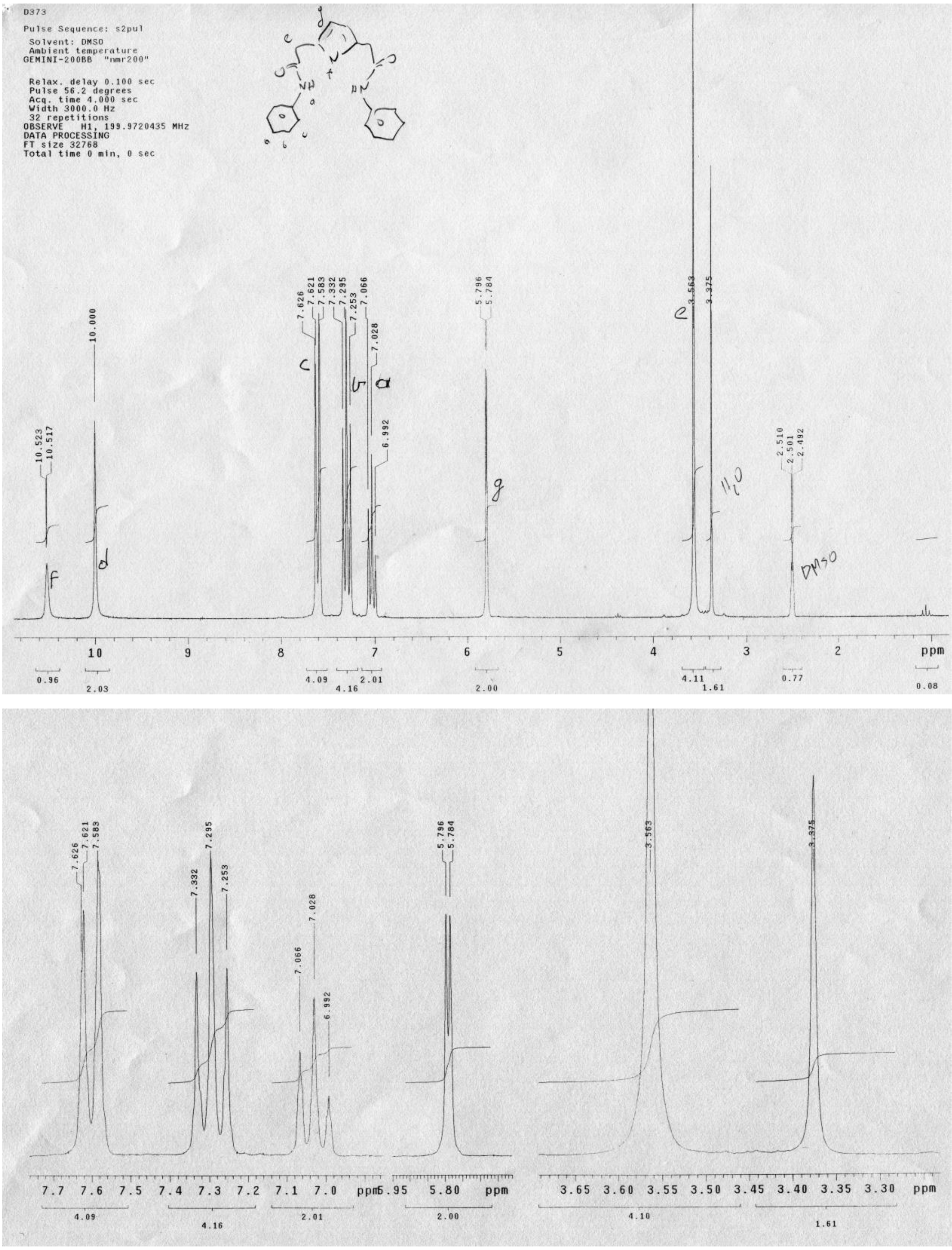
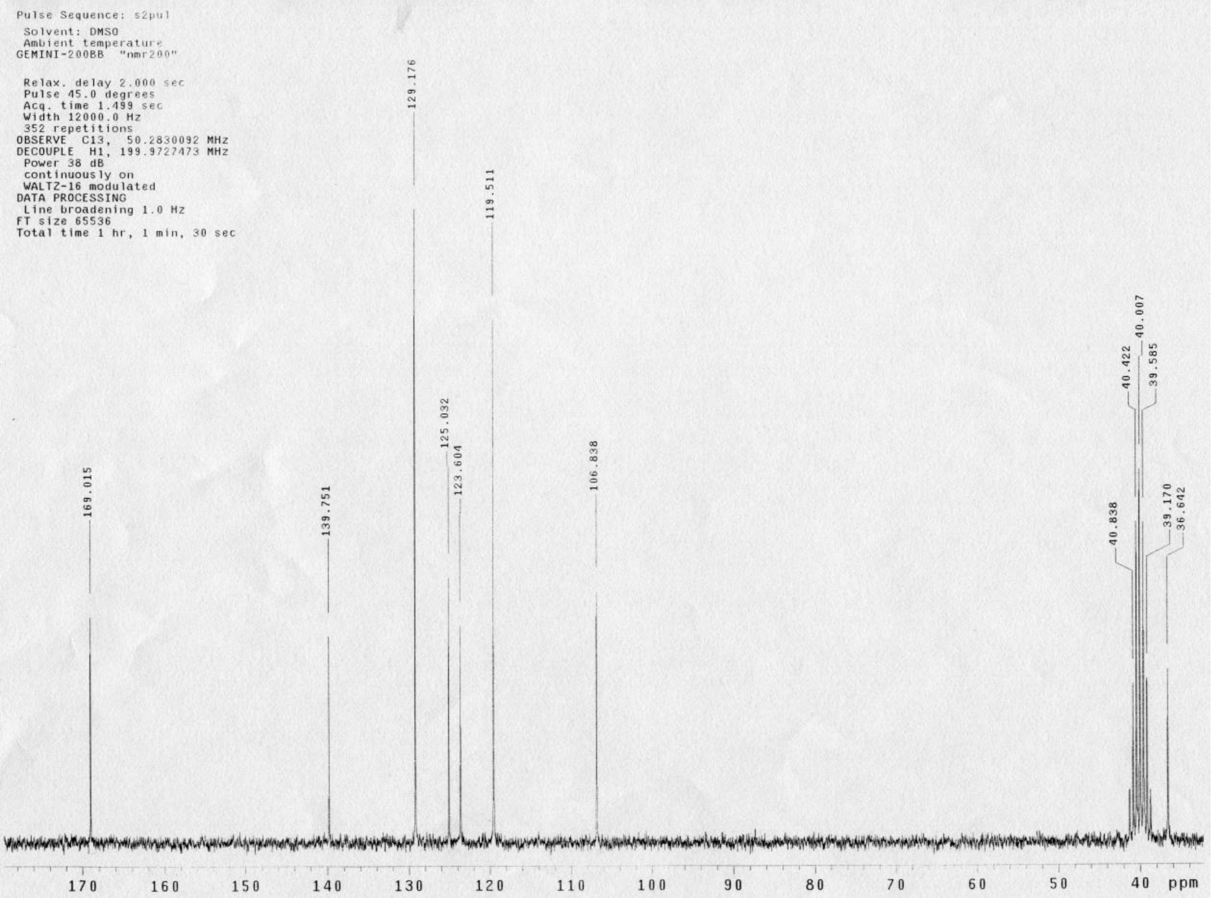


Figure S5. ^{1}H NMR spectra of diamide **8b**.



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 Width 12000.0 Hz
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OBSERVE  C13,  50.2830092 MHz
DECOUPLE  H1, 199.9727473 MHz
 Power 38 dB
 continuously on
 WALTZ-16 modulated
DATA PROCESSING
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FT size 65536
Total time 1 hr, 1 min, 30 sec
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Figure S6. ^{13}C NMR spectrum of diamide **8b**.

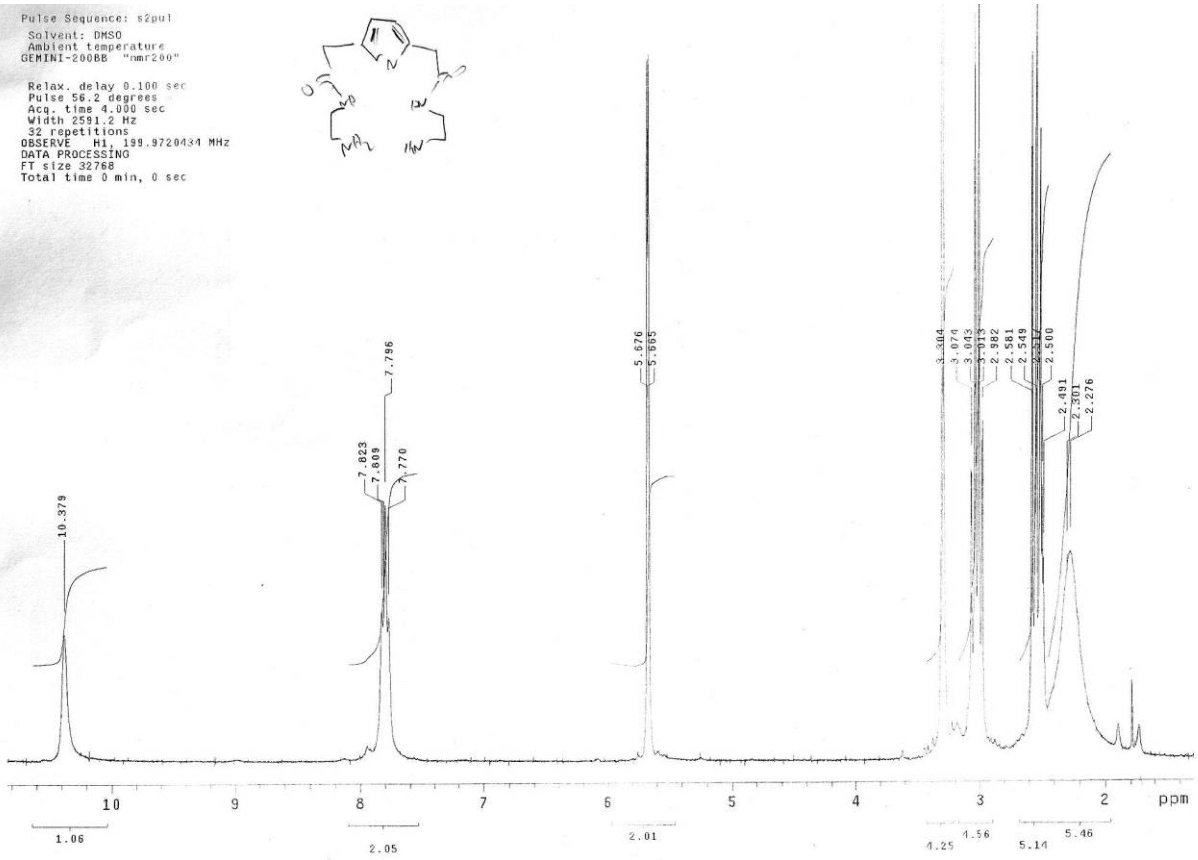

Figure S7. ^{1}H NMR spectrum of diamine **6**.

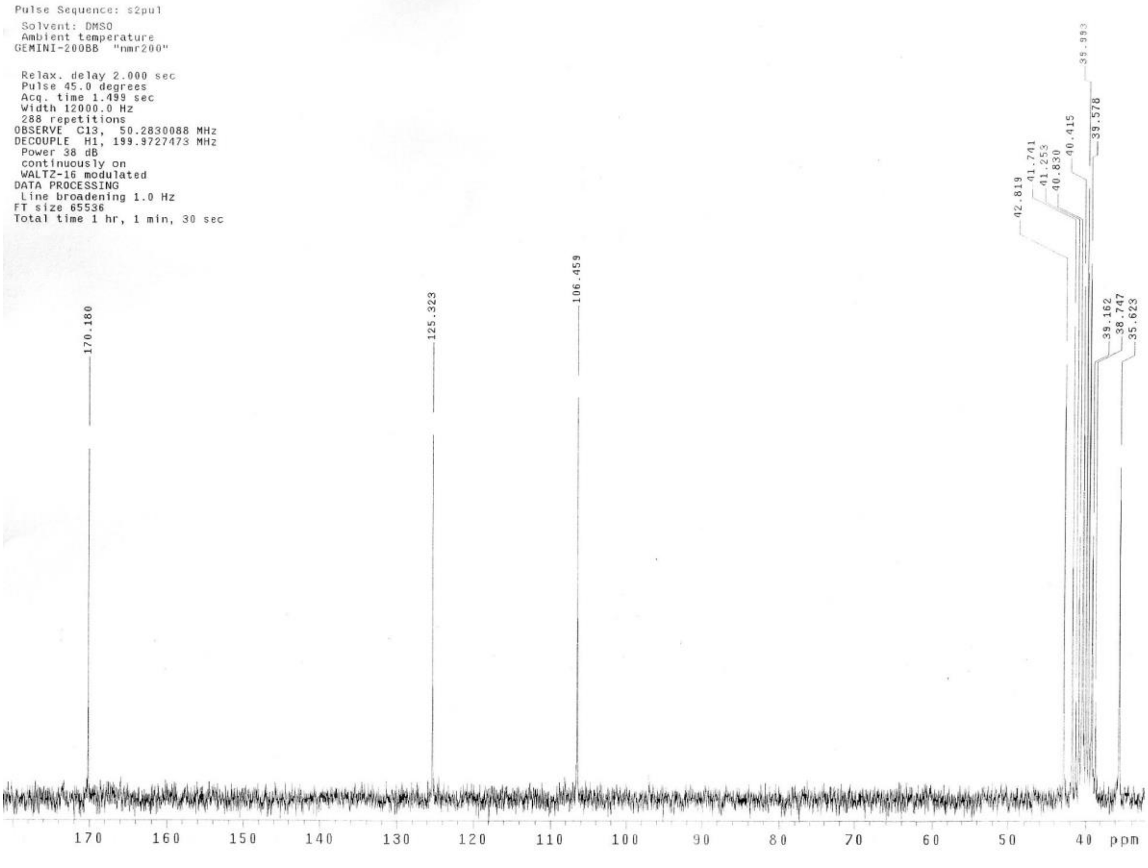

Figure S8. ^{13}C NMR spectrum of diamine **6**.

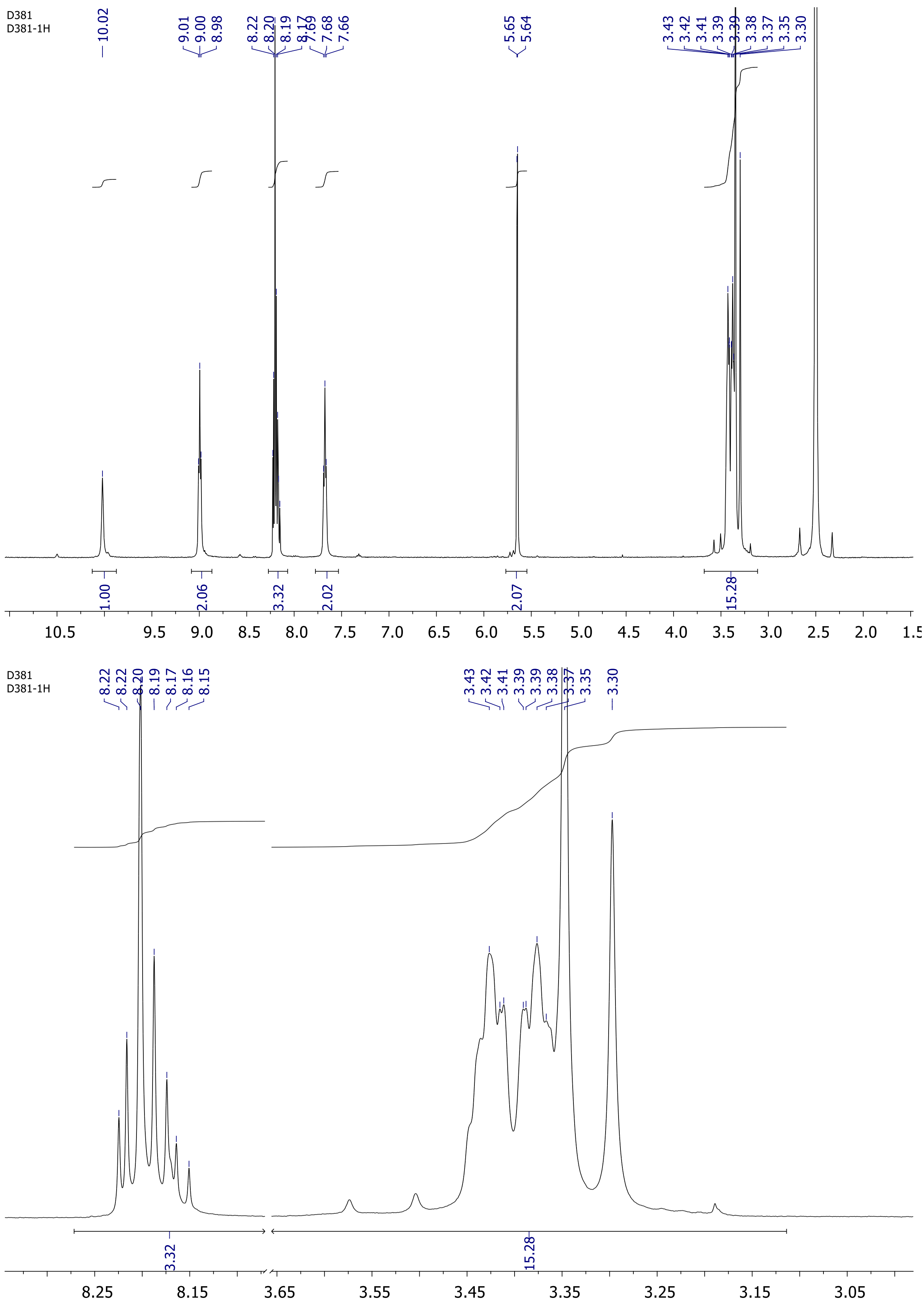

Figure S9. ^{1}H NMR spectra of macrocycle **4**.

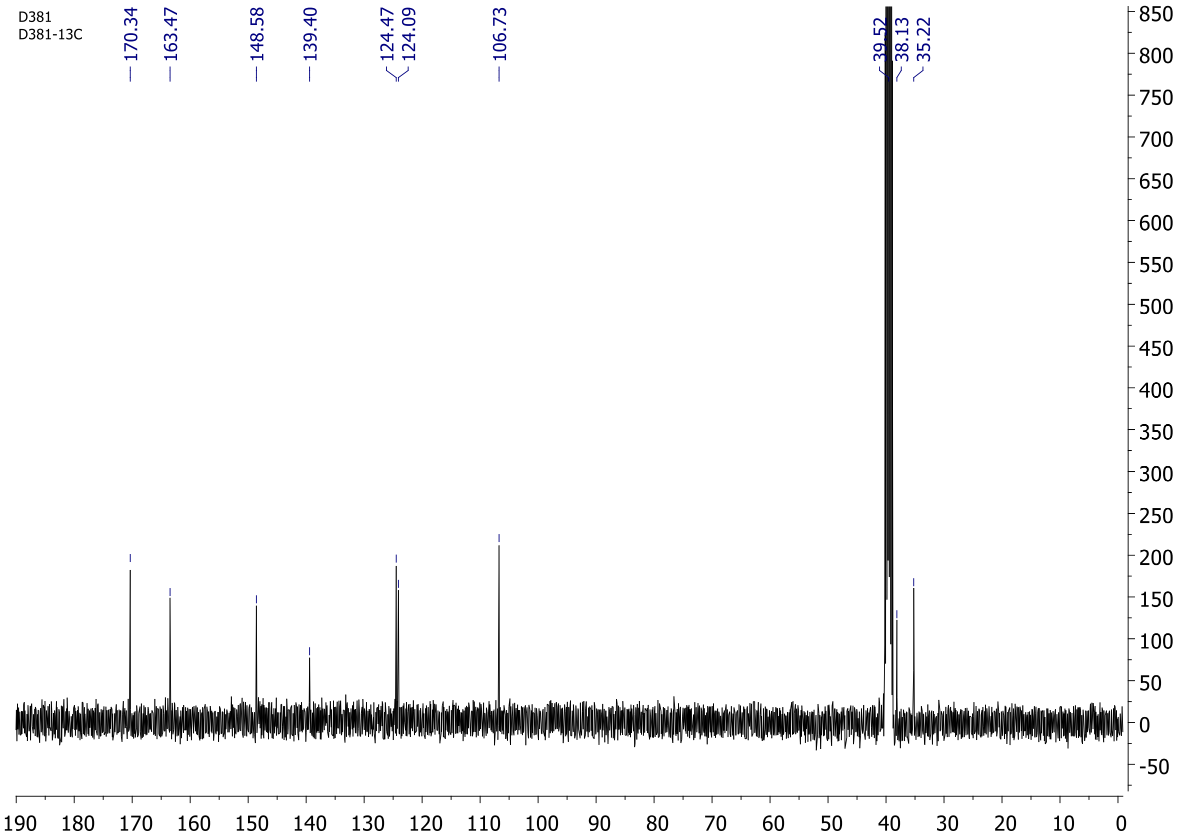

Figure S10. ^{13}C NMR spectrum of macrocycle **4**.