Supplementary Material for:

Computation-Guided Improved One-Pot Synthesis of Macrocyclic Cation-Binding Aromatic Pyridone Pentamers†

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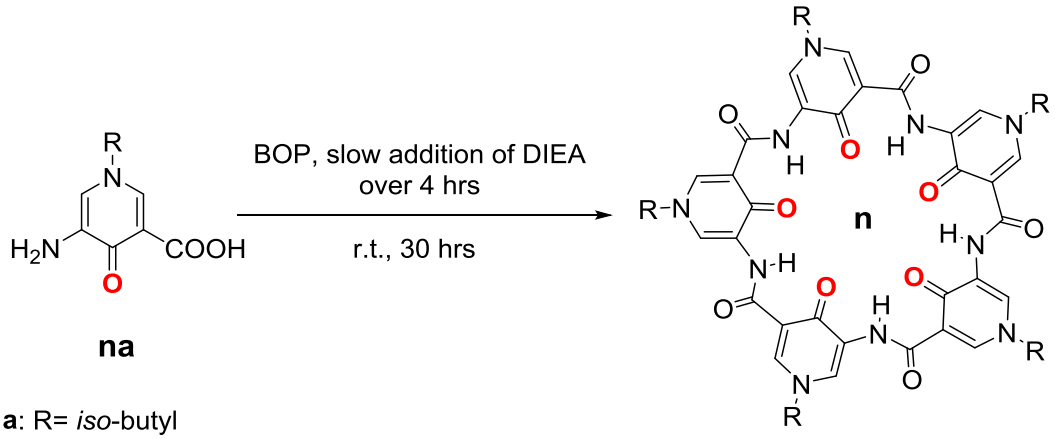
General Remarks

All the reagents were obtained from commercial suppliers and used as received unless otherwise noted. Aqueous solutions were prepared from distilled water. The organic solutions from liquid extractions were dried over anhydrous Na_2SO_4 for a minimum of 15 minutes before filtration. Reactions were monitored by thin-layer chromatography (TLC) on silica gel pre-coated glass plate (0.225 mm thickness, 60F-254, E. Merck). Flash column chromatography was performed using pre-coated 0.2 mm silica plates from Selecto Scientific. Chemical yields refer to pure isolated substances. Mass spectra were obtained using the Instrumentation includes Finnigan MAT95XL-T and Micromass VG7035. ^{1}H NMR spectra were recorded on Bruker ACF300 (300 MHz) and ACF500 (500 MHz) spectrometers. The solvent signal of $CDCl_3$ was referenced at δ = 7.26 ppm, and DMSO-d_6 at 2.50 ppm. Coupling constants (*J* values) are reported in Hertz (Hz). ^{1}H NMR data are recorded in the order: chemical shift value, multiplicity (s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet; br, broad), number of protons that gave rise to the signal and coupling constant, where applicable.

Scheme S1: One-pot synthesis of **1-6** from the corresponding monomers **1a-6a**.



1a: R= *iso*-butyl
2a: R= C_8H_{17}
3a: R= Bn= $CH_2C_6H_5$
4a: R= $CH_2CH_2OCH_2CH_3$
5a: R= $(CH_2CH_2O)_2CH_3$
6a: R= $(CH_2CH_2O)_3CH_3$

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2: R= C_8H_{17}
3: R= Bn= $CH_2C_6H_5$
4: R= $CH_2CH_2OCH_2CH_3$
5: R= $(CH_2CH_2O)_2CH_3$
6: R= $(CH_2CH_2O)_3CH_3$

For synthesis of **1a-6a**, see: Z. Y. Du, C. L. Ren, R. J. Ye, J. Shen, Y. J. Lu, J. Wang and H. Q. Zeng, *Chem. Commun.*, **2011**, *47*, 12488-12490.

Careful comparisons of our ^{1}H NMR data and spectra as well as the corresponding HR-MS with those published by Zeng and his co-workers (*Chem. Commun.*, **2011**, *47*, 12488-12490) suggest the successful synthesis of monomers **1a-6a** and high purity of pentamers **1-6**.

1a: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.11 (d, *J* = 2.1 Hz, 1H), 7.09 (d, *J* = 2.1 Hz, 1H), 3.71 (d, *J* = 7.5 Hz, 2H), 2.20 – 2.04 (m, 1H), 0.96 (s, 3H), 0.94 (s, 3H). HRMS-ESI: calculated for $[M+Na]^+$ ($C_{10}H_{14}O_3N_2Na$)： *m/z* 233.0902, found: *m/z* 233.0896.

2a: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.16 (d, *J* = 2.0 Hz, 1H), 7.12 (d, *J* = 2.2 Hz, 1H), 3.91 (t, *J* = 7.3 Hz, 2H), 1.83 (t, *J* = 7.1 Hz, 2H), 1.36 – 1.05 (m, 10H), (t, *J*= 6.9 Hz, 3H). HRMS-ESI: calculated for $[M+Na]^-$ ($C_{14}H_{22}O_3N_2$)： *m/z* 289.1528, found: *m/z* 289.1517.

3a: ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.50 (d, *J* = 2.1 Hz, 1H), 7.47 – 7.27 (m, 6H), 5.49 (s, 2H), 5.34 (s, 2H). HRMS-ESI: calculated for $[M+Na]^-$ ($C_{13}H_{12}O_3N_2Na$)： *m/z* 267.0746, found: *m/z* 267.0738.

4a:^{1}H NMR (400 MHz, $CDCl_3$) δ 8.21 (d, *J* = 2.2 Hz, 1H), 7.16 (d, *J* = 2.2 Hz, 1H), 4.08 – 4.03 (m, 2H), 3.75 – 3.71 (m, 2H), 3.48 (q, *J* = 7.0 Hz, 2H), 1.16 (t, *J* = 7.0 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 170.71, 167.43, 139.17, 138.85, 120.06, 111.89, 68.66, 67.09, 58.94, 14.88. HRMS-ESI: calculated for $[M-H]^-$ ($C_{10}H_{13}O_4N_2$)： *m/z* 225.085, found: *m/z* 225.0932.

5a: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.21 (d, *J* = 2.2 Hz, 1H), 7.21 (d, *J* = 2.2 Hz, 1H), 4.10 – 4.05 (m, 2H), 3.84 – 3.80 (m, 2H), 3.62 – 3.58 (m, 2H), 3.51 – 3.48 (m, 2H), 3.35 (s, 3H). HRMS-ESI: calculated for $[M-H]^-$ ($C_{11}H_{15}O_5N_2$)： *m/z* 255.0981, found: *m/z* 255.0987.

6a: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.19 (d, *J* = 2.1 Hz, 1H), 7.42 (d, *J* = 2.1 Hz, 1H), 4.11 – 4.07 (m, 2H), 3.85 – 3.81 (m, 2H), 3.64 – 3.56 (m, 8H), 3.38 (s, 3H). HRMS-ESI: calculated for $[M-H]^-$ ($C_{11}H_{15}O_5N_2$)：*m/z* 299.1243, found: *m/z* 299.1252.

1: ^{1}H NMR (500 MHz, DMSO-d_6, 55℃) δ 13.48 (s, 5H), 8.99 (d, *J* = 2.3 Hz, 5H), 8.51 (d, *J* = 2.4 Hz, 5H), 4.05 (d, *J* = 7.2 Hz, 10H), 2.14 (td, *J* = 13.8, 6.9 Hz, 5H), 0.87 (d, *J* = 6.6 Hz, 30H). HRMS-ESI: calculated for $[M+K]^+$ ($C_{50}H_{60}O_{10}N_{10}K$)：*m/z* 999.4131, found: *m/z* 999.4125.

2: ^{1}H NMR (500 MHz, $CDCl_3$/DMSO-d_6=1/2, 55℃) δ 13.55 (s, 5H), 8.89 (d, *J* = 2.3 Hz, 5H), 8.34 (d, *J* = 2.3 Hz, 5H), 4.05 (t, *J* = 7.2 Hz, 10H), 1.82 (s, 10H), 1.47 – 1.03 (m, 50H), 0.79 (t, *J* = 6.6 Hz, 15H). HRMS-ESI: calculated for $[M+K]^+$($C_{70}H_{100}O_{10}N_{10}K$)：*m/z* 1279.7261, found: *m/z* 1279.7255.

3: ^{1}H NMR (500 MHz, DMSO-d_6, 55℃) δ 13.42 (s, 5H), 8.99 (s, 5H), 8.68 (s, 5H), 7.54 – 7.31 (m, 25H), 5.42 (s, 10H). HRMS-ESI: calculated for $[M+K]^+$ ($C_{65}H_{50}O_{10}N_{10}K$)： *m/z* 1169.3348, found: *m/z* 1169.3341.

4: ^{1}H NMR (500 MHz, $CDCl_3$/DMSO-d_6=1/9, 110℃) δ 13.21 (s, 5H), 8.90 (d, *J* = 1.5 Hz, 5H), 8.38 (d, *J* = 1.8 Hz, 5H), 4.35 (t, *J* = 5.0 Hz, 10H), 3.86 (t, *J* = 5.0 Hz, 10H), 3.56 (q, *J* = 6.9 Hz, 10H), 1.17 (t, *J* = 6.9 Hz, 15H). HRMS-ESI: calculated for $[M+K]^+$ ($C_{50}H_{60}O_{15}N_{10}K$)：*m/z* 1079.3877, found: *m/z* 1079.3920.

5: ^{1}H NMR (500 MHz, $CDCl_3$/DMSO-d_6=1/9, 110℃) δ 13.29 (s, 5H), 8.94 (s, 5H), 8.42 (s, 5H), 4.37 (t, *J* = 4.7 Hz, 10H), 3.90 (t, *J* = 4.8 Hz, 10H), 3.62 (t, *J* = 4.8 Hz, 10H), 3.48 (t, *J* = 4.8 Hz, 10H), 3.27 (s, 15H). HRMS-ESI: calculated for $[M+K]^+$ ($C_{55}H_{70}O_{20}N_{10}K$)：*m/z* 1229.4405, found: *m/z* 1229.4423.

6: ^{1}H NMR (500 MHz, $CDCl_3$/DMSO-d_6=1/9, 110℃) δ 13.09 (s, 5H), 8.77 (s, 5H), 8.26 (s, 5H), 4.31 (d, *J* = 4.6 Hz, 10H), 4.00 – 3.96 (m, 10H), 3.72 – 3.57 (m, 30H), 3.50 – 3.43 (m, 10H), 3.28 (s, 15H). HRMS-ESI: calculated for $[M+K]^+$ ($C_{65}H_{90}O_{25}N_{10}K$)：*m/z* 1449.5716, found: *m/z* 1449.5730.

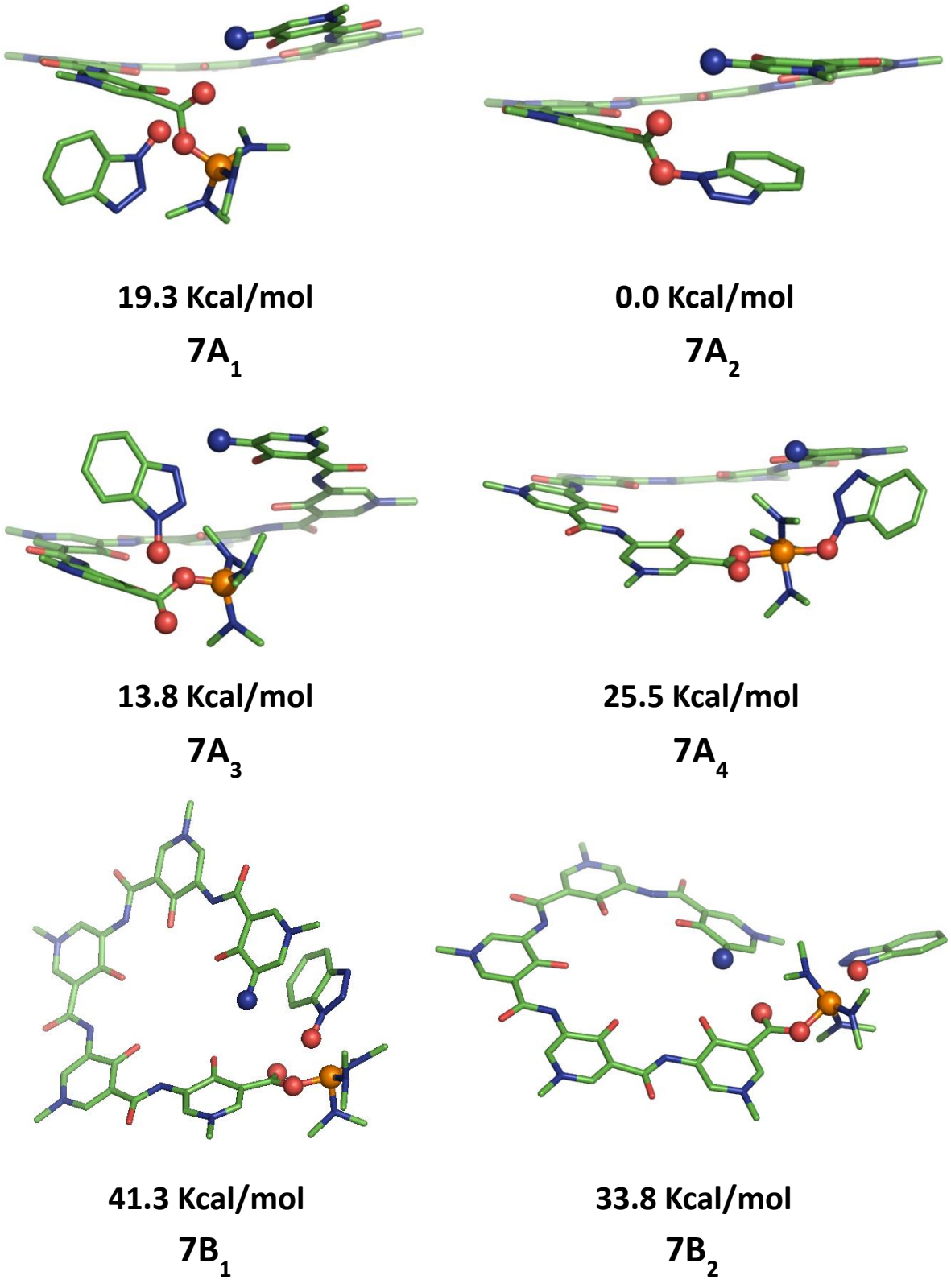


Figure S1 Computed structures for **7-BOP** conjugates **$7A_1$-$7B_2$** with relative energies. All the structures were optimzied at the B3LYP/6-31G(d,p) level with single point energy calculation performed at the 6-311+G(2d, p) level.

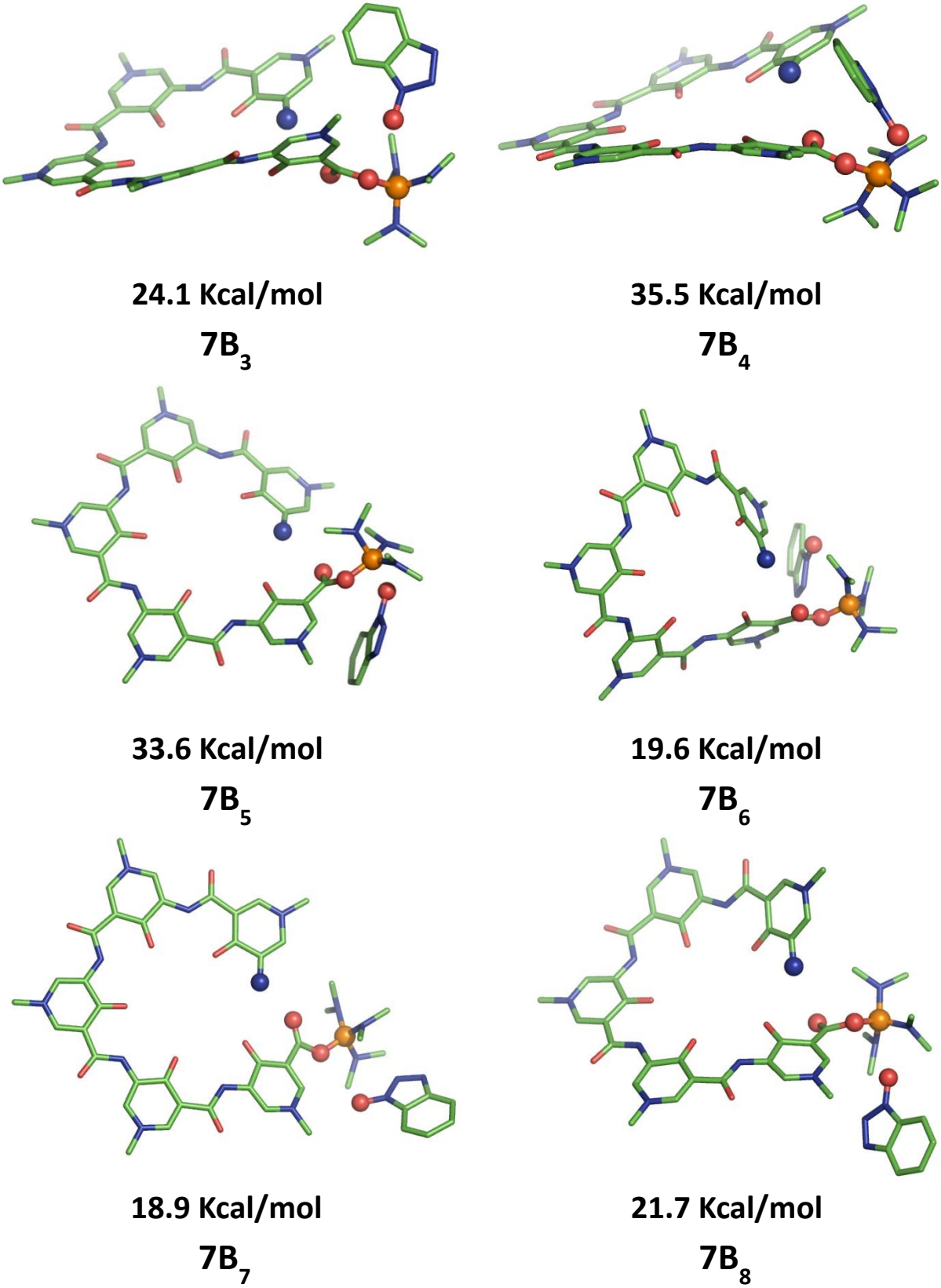


Figure S2 Computed structures for **7-BOP** conjugates **$7B_3$-$7B_8$** with relative energies. All the structures were optimzied at the B3LYP/6-31G(d,p) level with single point energy calculation performed at the 6-311+G(2d, p) level.

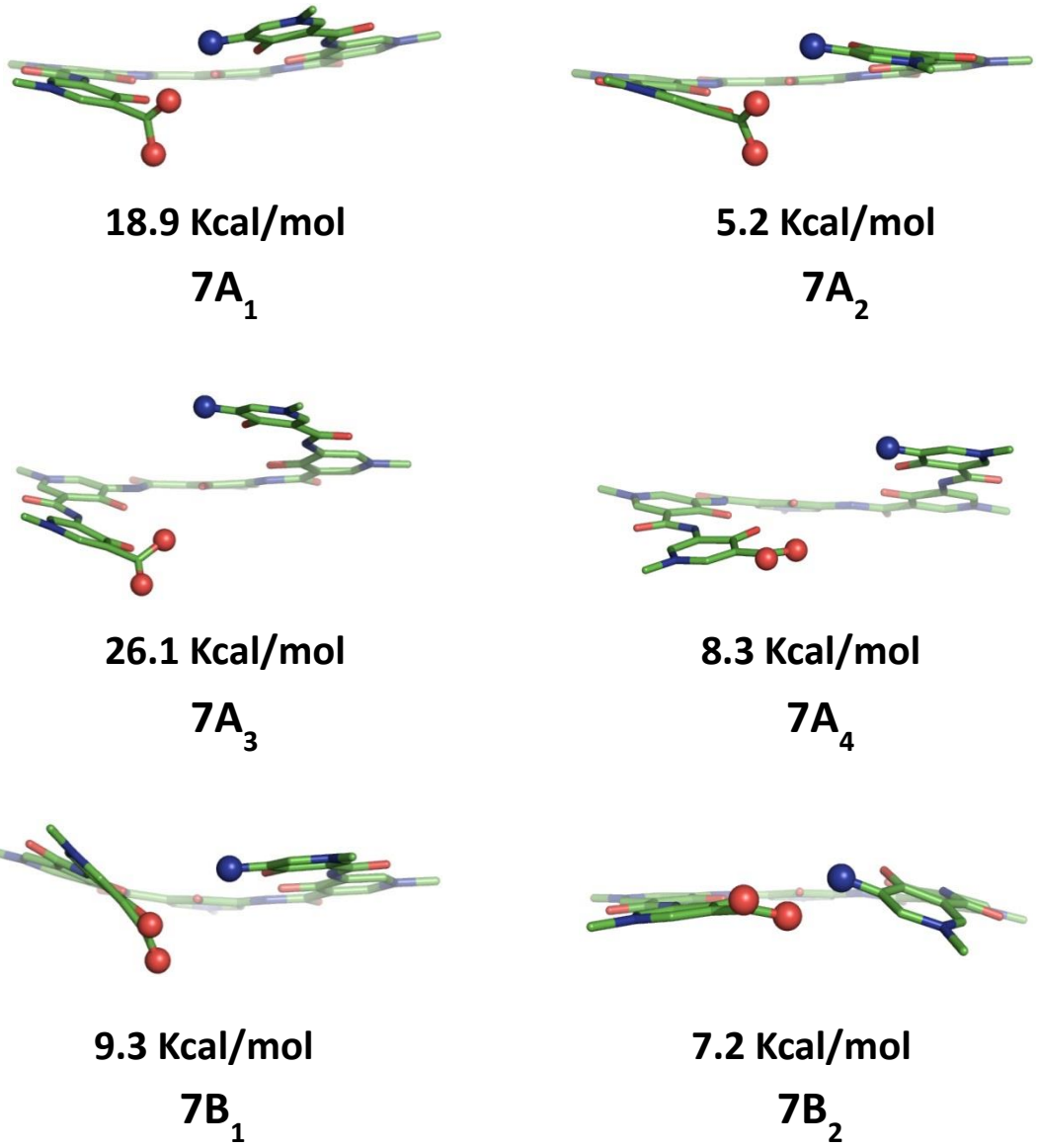


Figure S3 Computed structures for **7** in **$7A_1$-$7B_2$** with relative energies. All the structures were optimzied at the B3LYP/6-31G(d,p) level with single point energy calculation performed at the 6-311+G(2d, p) level.

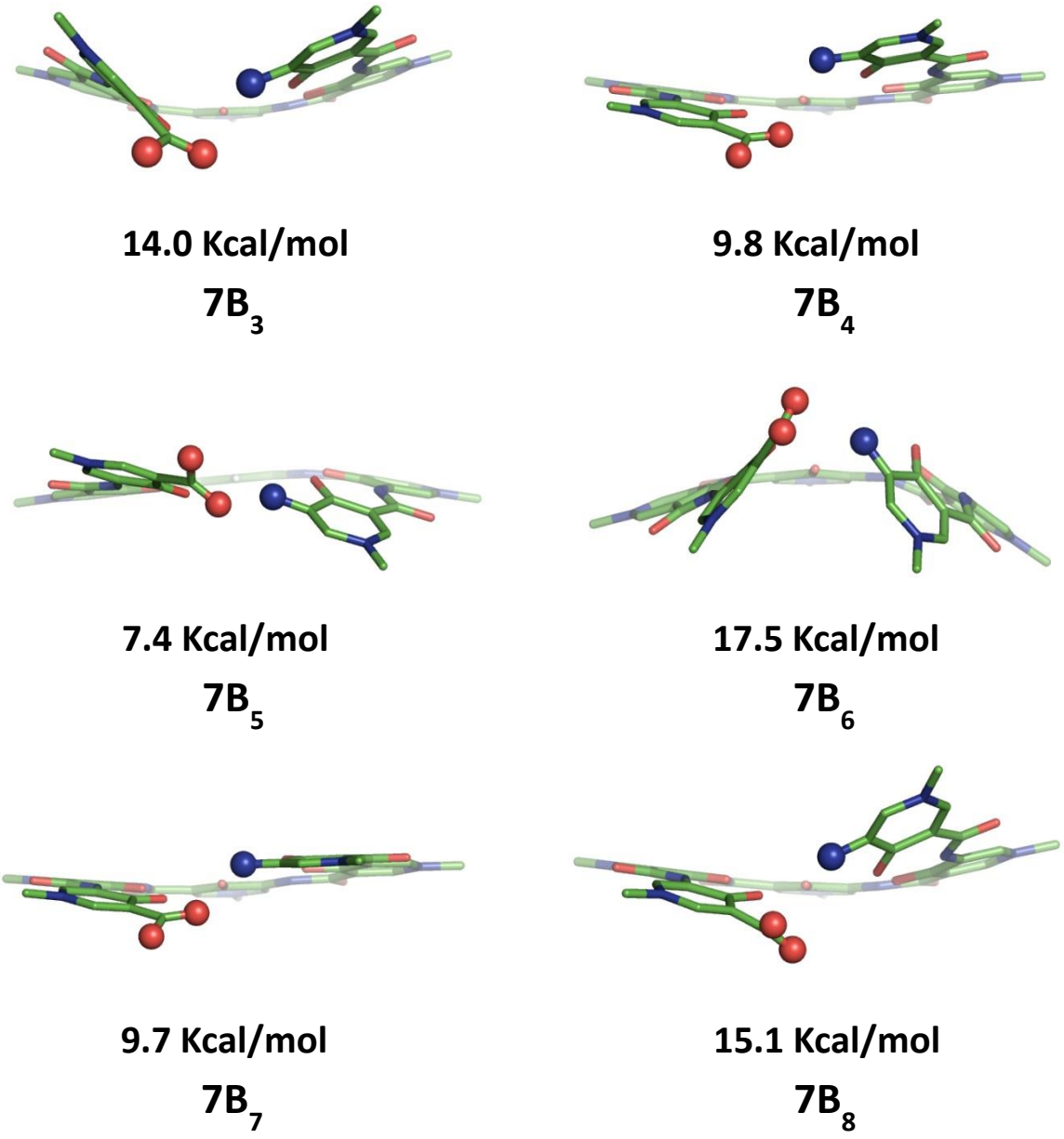
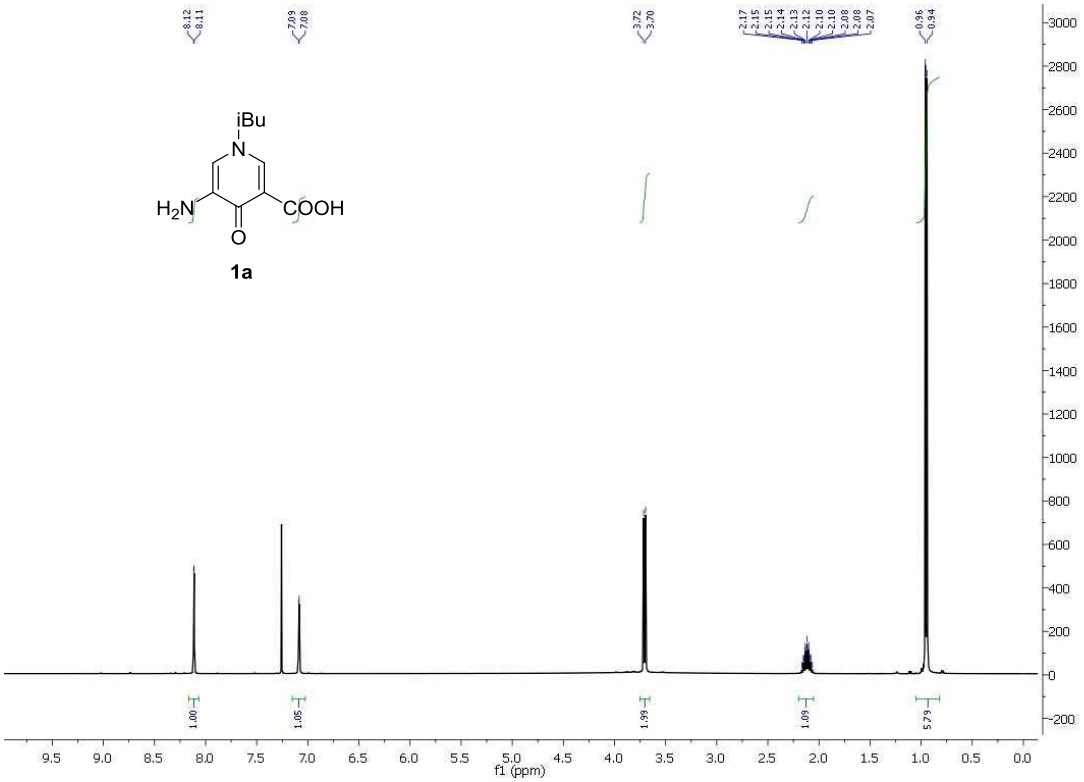
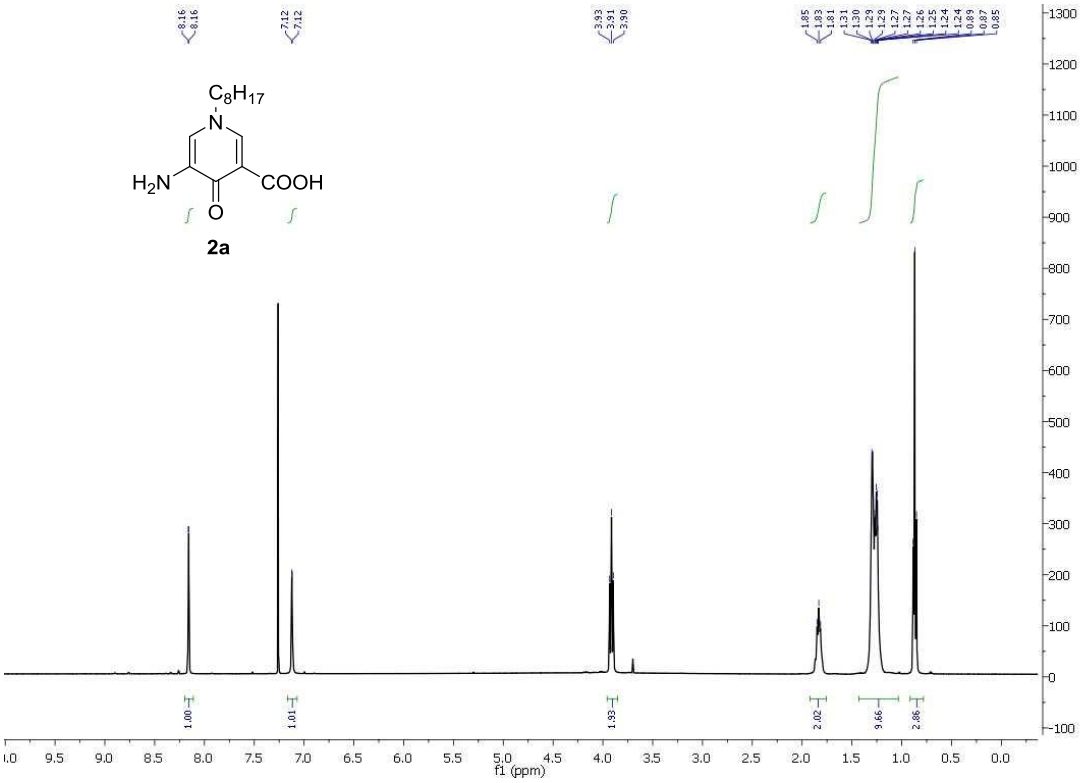
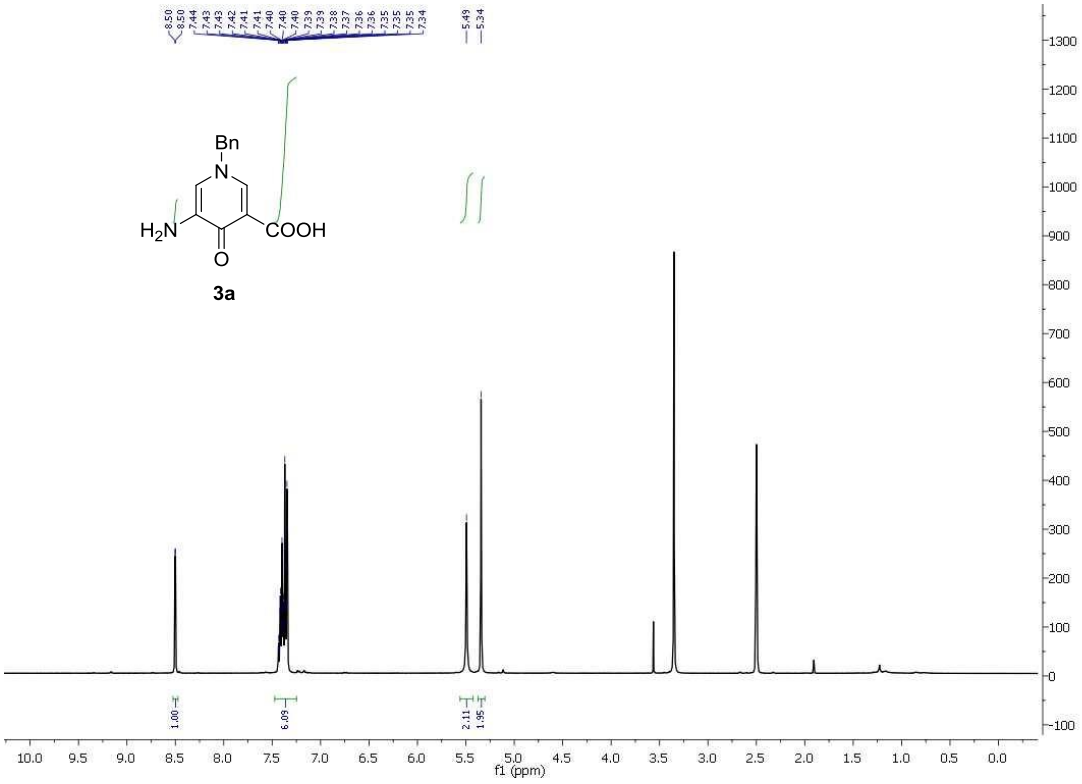


Figure S4 Computed structures for **7** in **7B$_3$-7B$_8$** with relative energies. All the structures were optimzied at the B3LYP/6-31G(d,p) level with single point energy calculation performed at the 6-311+G(2d, p) level.

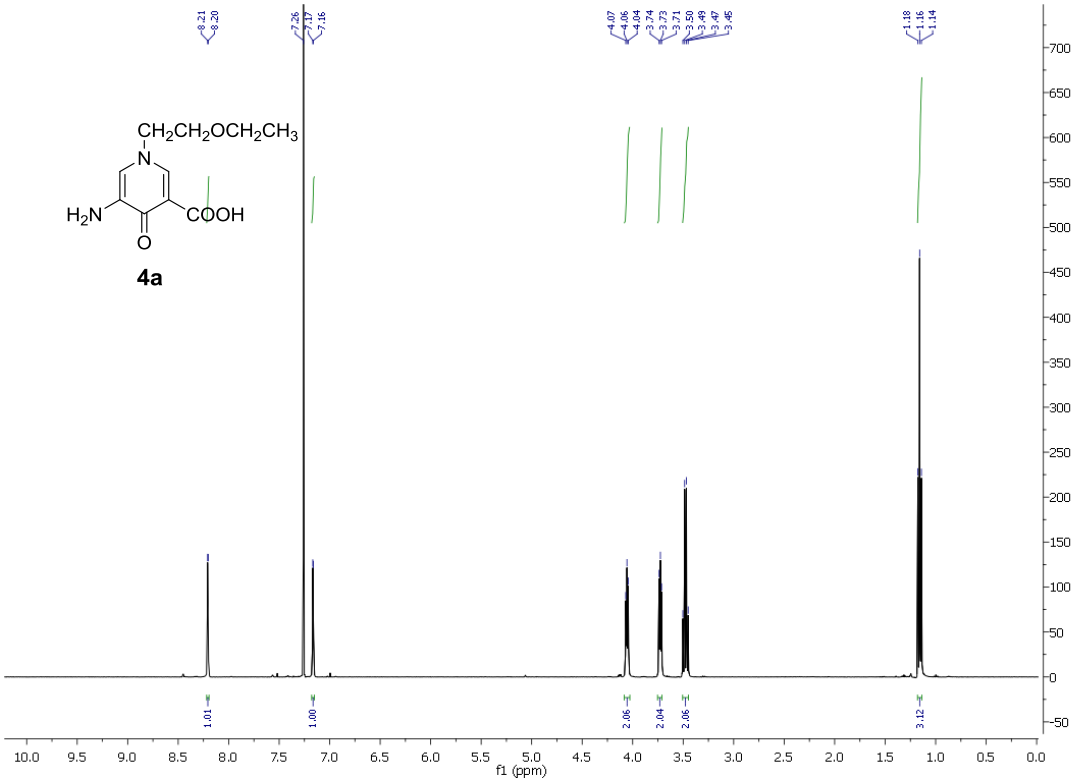
^{1}H NMR Spectra for **1a-6a** and **1-6**



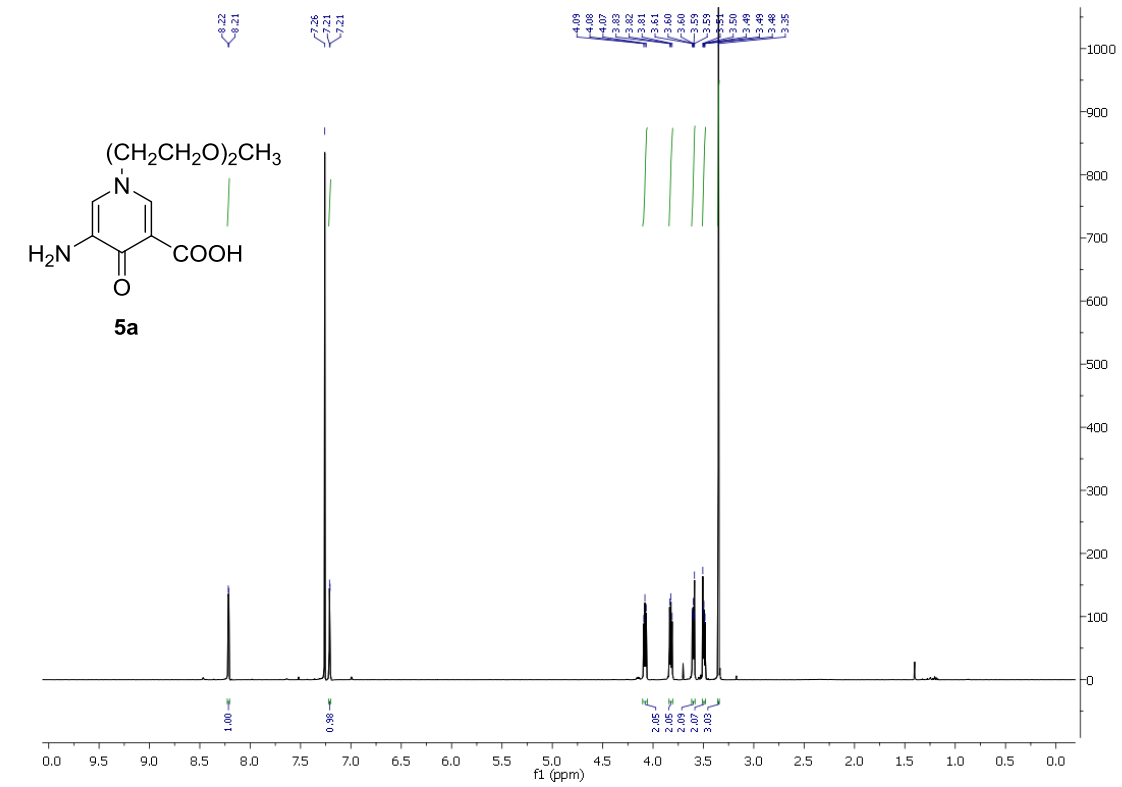




3a



4a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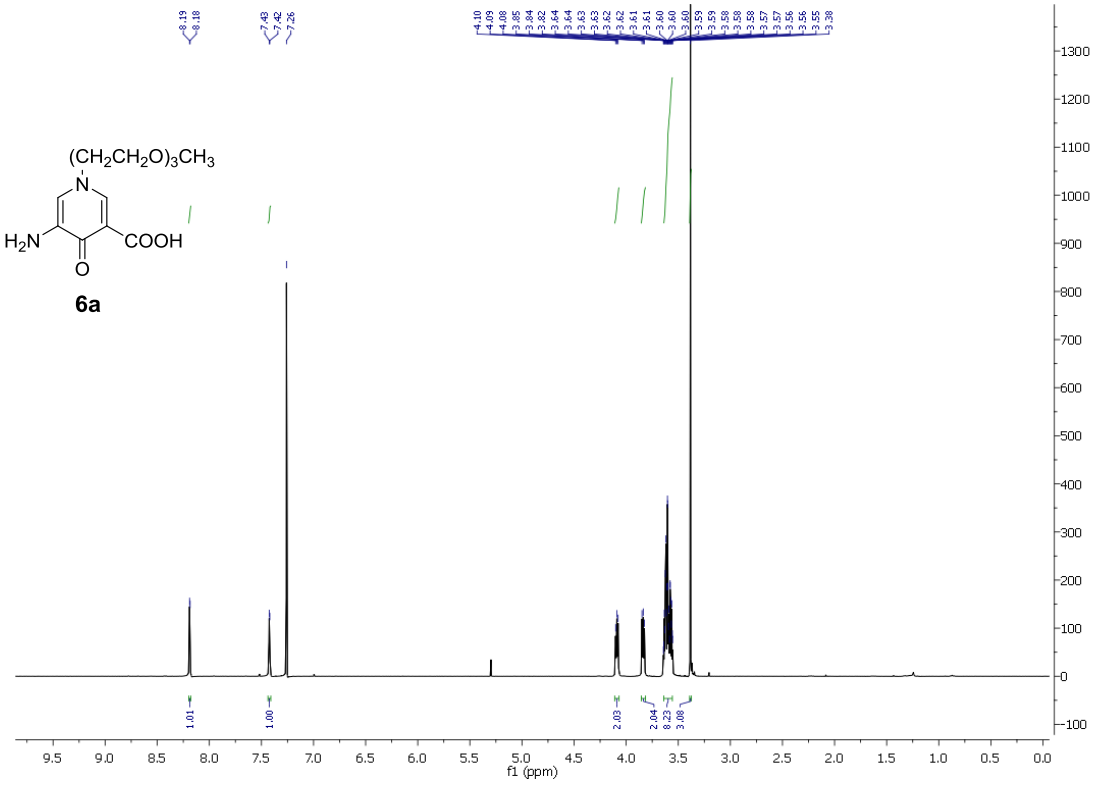
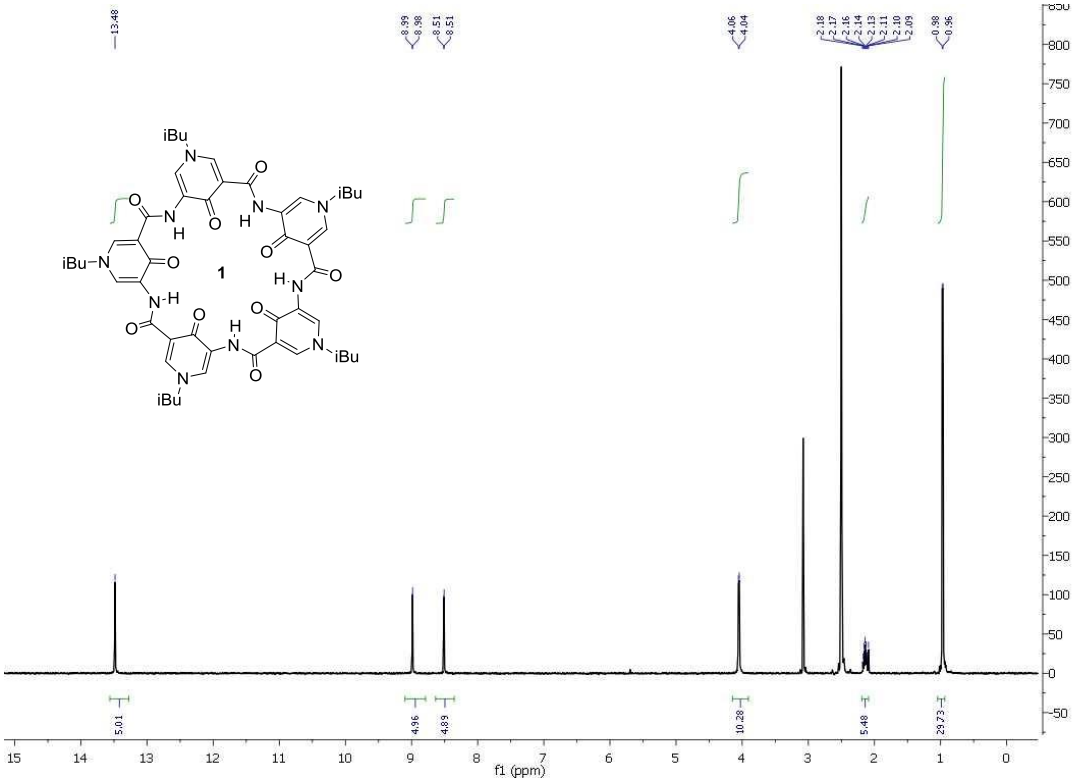
N
H2N
COOH
O
f1 (ppm)

5a


(CH2CH2O)3CH3
N
H2N
COOH
O
f1 (ppm)

6a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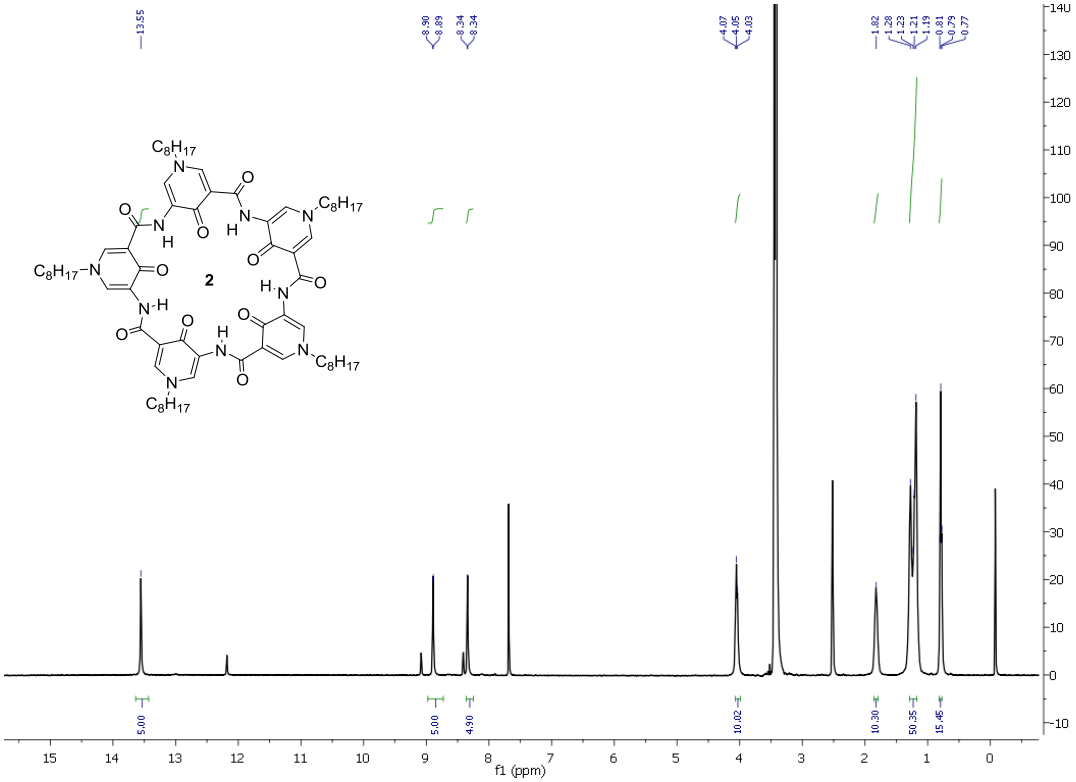
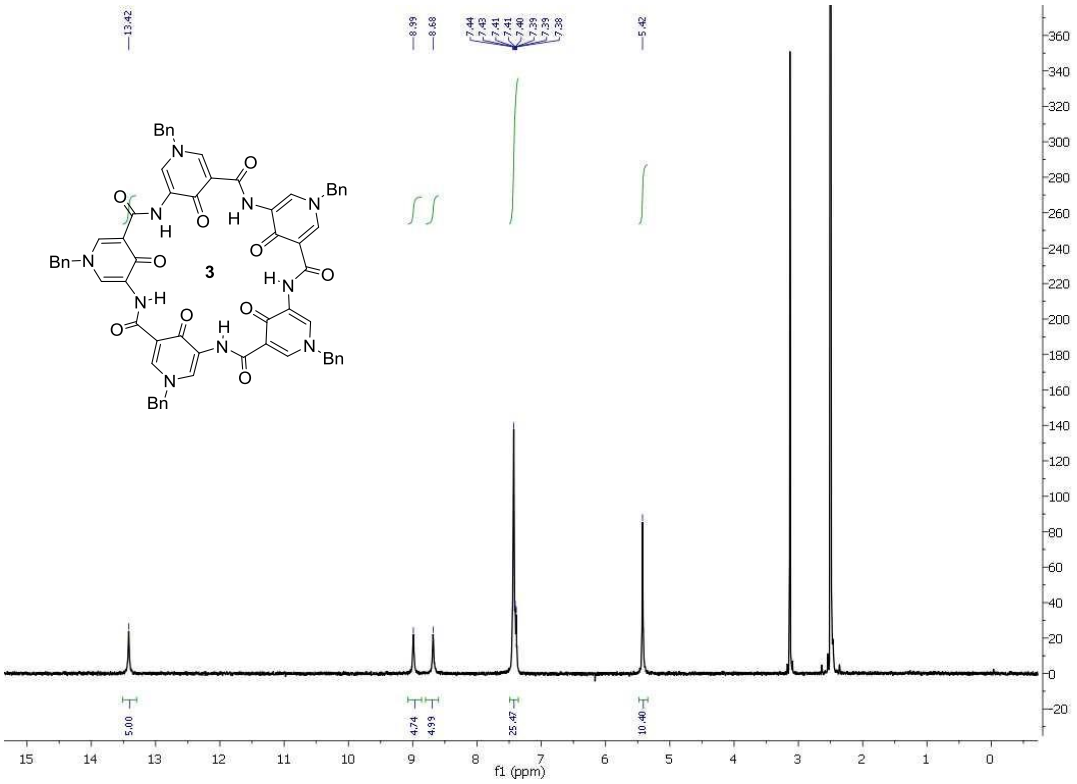
iBu
iBu
iBu
iBu
1
f1 (ppm)


C8H17
C8H17
C8H17
C8H17
C8H17
2
f1 (ppm)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8.68
7.44
7.43
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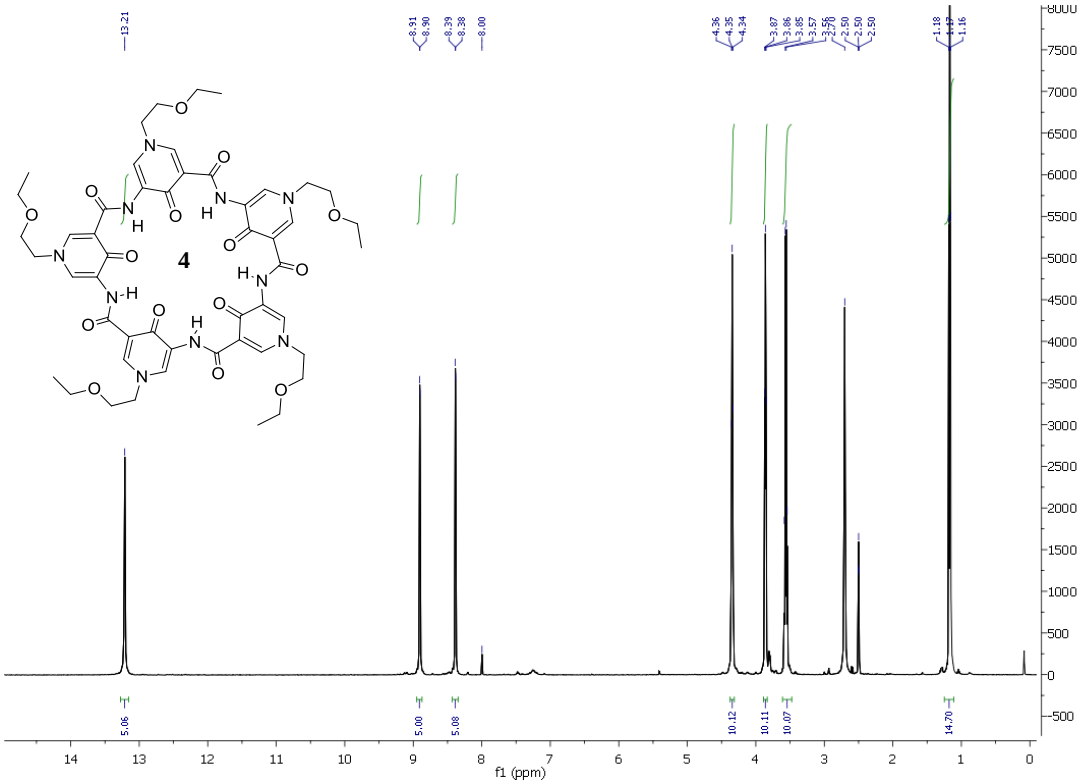
7.41
7.40
7.39
7.39
7.38
5.42
Bn
Bn
Bn
Bn
Bn
Bn
3
5.00
4.74
4.99
25.47
10.40
f1 (ppm)


13.21
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8.00
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4.35
4.34
3.87
3.86
3.85
3.57
3.56
2.76
2.50
2.50
2.50
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1.17
1.16
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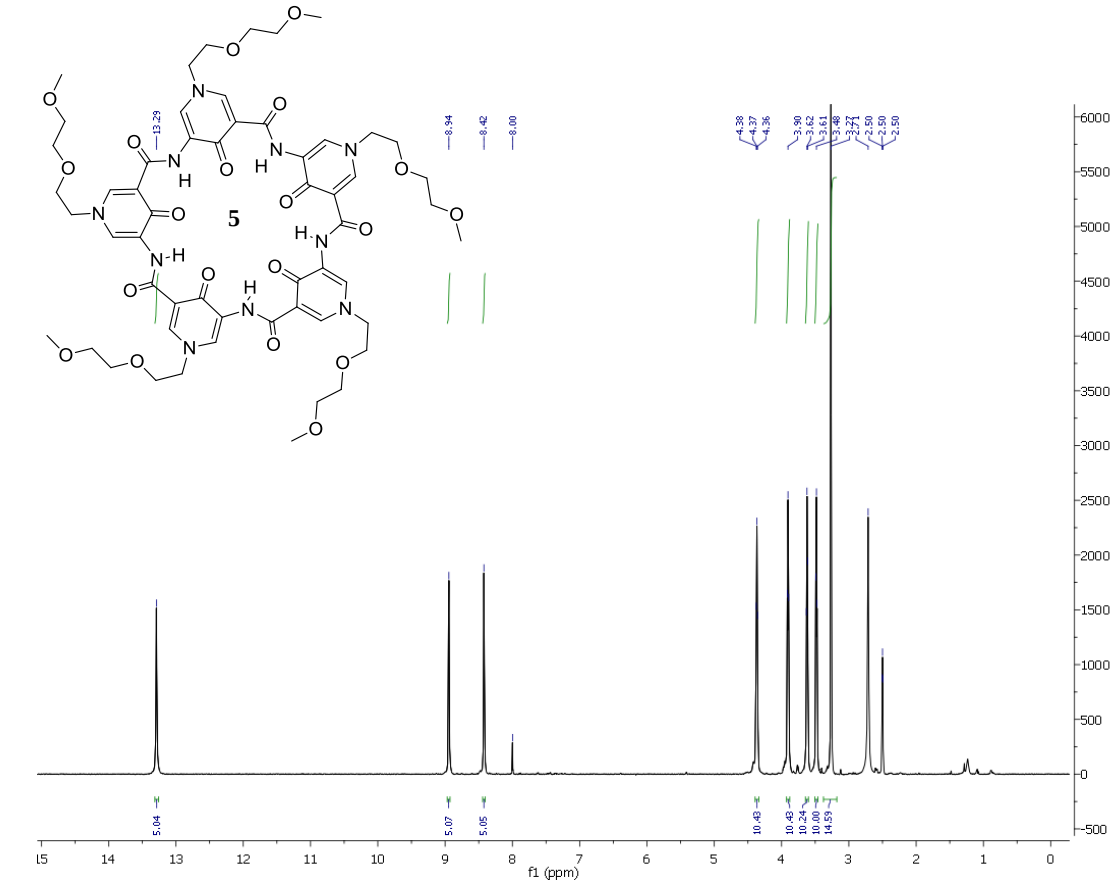
5.00
5.08
10.12
10.11
10.07
14.70
f1 (ppm)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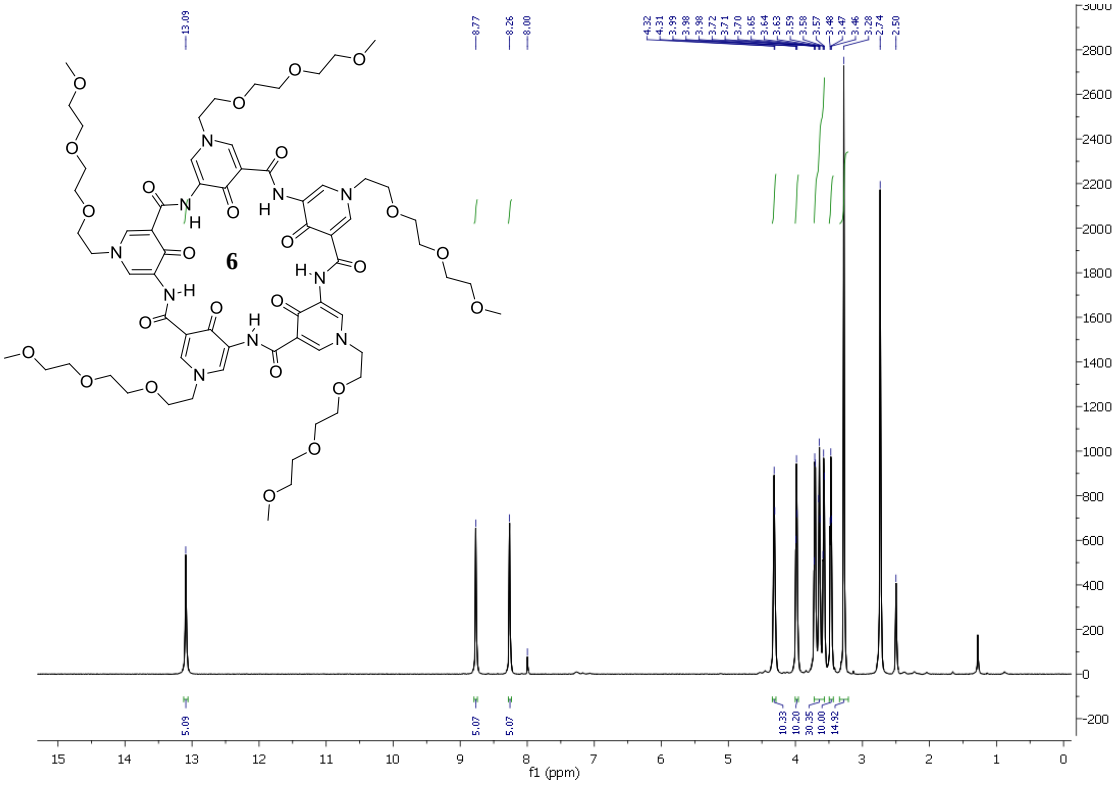
f1 (ppm)


6
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4.31
3.99
3.98
3.98
3.72
3.71
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3.65
3.64
3.63
3.59
3.58
3.57
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3.47
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3.28
2.74
2.50
5.09
5.07
5.07
10.33
10.20
30.35
10.00
14.92
f1 (ppm)