

## Supporting Information

### Metallopeptoids as Efficient Biomimetic Catalysts

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**Materials.** Rink Amide resin was supplied by Novabiochem; (S)-1-phenylethylamine (spe) and benzylamine (pm) were supplied by Acros organics, Israel; [Cu(MeCN)<sub>4</sub>]OTf, 4-aminoTEMPO (tempo), 1,10 phenanthroline-5-amine (phen), Amylamine (aa), t-butylmethlamine (tbm), 2-methoxyethyl amine (me), 1-Naphthalenemethylamine (nm), bromoacetic acid and N,N'-diisopropylcarbodiimide (DIC) were supplied by Sigma Aldrich. Other reagents and solvents were obtained from commercial sources and used without additional purification.

**Instrumentation.** Peptoid oligomers were analyzed by reversed-phase HPLC (analytical C18 column, 5  $\mu$ m, 100 Å, 2.0x50 mm) on a Jasco UV-2075 instrument. A linear gradient of 5–95% ACN in water (0.1% TFA) over 10 min was used at a flow rate of 0.7 mL/min. Preparative HPLC was performed using a phenomenex C18 column (15 $\mu$ m, 100 Å 21.20x100mm) on a Jasco UV-2075 instrument. Peaks were eluted with a linear gradient of 5–95% ACN in water (0.1% TFA) over 50 min at a flow rate of 5 mL/min. Mass spectrometry was performed on an Waters LCT Premier mass and Advion expression mass under electrospray ionization (ESI), direct probe ACN:H<sub>2</sub>O (70:30). Reactions were monitored and analyzed by A Varian 3800 Gas Chromatograph using CP-Sil-8 column. CD measurements were performed using a JASCO circular dichroism

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spectropolarimeter Model J-810-150S. The  $^1\text{H}$  NMR spectra were recorded on a Bruker 400 MHz instrument. Coupling constants are given in Hz. The following abbreviations are used to indicate the multiplicity: s, singlet; d, doublet; m, multiplet; bs, broad signal.

### **Preparation of the peptoid oligomers:**

Peptoids were synthesized manually on Rink amide resin using the submonomer approach [1]. All peptoid oligomers were synthesized at room temperature. Typically, 100 mg of resin was swollen in DCM for 40 minutes before initiating oligomer synthesis. Multiple washing steps using DMF were performed between each step described below. De-protection of resin was performed by addition of 20% piperidine solution (1.5 ml in DMF) and the reaction was allowed to shake at room temperature for 20 min. Following the reaction, piperidine was washed from the resin using DMF (10 mL  $\text{g}^{-1}$  resin) (3 x 1 min). Bromoacetylation was completed by adding 20 eq. bromoacetic acid (1.2 M in DMF, 8.5 mL  $\text{g}^{-1}$  resin) and 24 eq. of diisopropylcarbodiimide (2 mL  $\text{g}^{-1}$  resin); this reaction was allowed to shake at room temperature for 20 min. Following the reaction, the bromoacetylation reagents were washed from the resin using DMF (10 mL  $\text{g}^{-1}$  resin) (3 x 1 min) and 20 eq. of submonomer amine (1.0 M in DMF, 10 mL  $\text{g}^{-1}$  resin) were added. The amine displacement reaction was allowed to shake at room temperature for 20 min and was followed by multiple washing steps (DMF, 10 mL  $\text{g}^{-1}$  resin) (3 x 1 min). This two-step addition cycle was modified as follows: the last amine displacement with 1,10-Phenanthroline-5-amine (20 equivalents, 0.4 M in DMF, 10 mL  $\text{g}^{-1}$  resin) was performed for 24 hr. Bromoacetylations and amine displacement steps were repeated until the peptoids were obtained. To cleave the peptoid oligomers from solid support for analysis, approximately 5 mg of resin was treated with 95% TFA in water (40 mL  $\text{g}^{-1}$  resin) for 10 minutes. The cleavage cocktail was evaporated under nitrogen gas and the peptoid oligomers were re-suspended in 0.5 mL HPLC solvent (1:1 HPLC grade acetonitrile:HPLC grade water). To cleave the peptoid oligomers from solid support for preparative HPLC the beads were treated with 5ml of 95% TFA in water for 30 minutes. The cleavage cocktail was evaporated under low pressure, re-suspended in 2 mL HPLC solvent and lyophilized overnight.

### Characterization of the peptoid oligomers:

Peptoid **Helix i+3**, **Helix i+1** and **Nonhelix i+3** were characterized by analytical HPLC using a C18 column. The peptoids **DI**, **BT**, **MT**, **RBT**, **PT**, **TT** and **NT** were characterized by preparative HPLC using a C18 column and <sup>1</sup>H NMR. Analysis with analytical C18 column was done using a solvent gradient conducted from 5% to 95% solvent B (0.1% TFA in HPLC grade acetonitrile) over solvent A (0.1% TFA in HPLC grade water) in 10 minutes with a flow rate of 0.7 mL min<sup>-1</sup>. Analysis with preparative C18 column was done using a solvent gradient conducted from 5% to 95% solvent B (0.1% TFA in HPLC grade acetonitrile) over solvent A (0.1% TFA in HPLC grade water) in 50 minutes with a flow rate of 5 mL min<sup>-1</sup>. Additional characterization was conducted by ESI MS. The peptoids were further purified to >95% by RP-HPLC and lyophilized overnight. HPLC traces of the pure peptoid oligomers are depicted in Figures S1-S9. All peptoids were subjected again to ESI MS characterization. MS spectra of the pure peptoid oligomers are depicted in Figures S10-S19. The two helical peptoids **Helix i+3** and **Helix i+1** were also characterized by CD spectroscopy (Figure S35 and S36). The peptoids **DI**, **BT**, **MT**, **RBT**, **PT**, **TT** and **NT** were characterized further by <sup>1</sup>H NMR (S38-S44).

### Catalysis experiments:

In a typical catalytic procedure acetonitrile was distilled over calcium hydride until a water content of 0.05% (w/w) in the solvent was reached. [Cu(MeCN)<sub>4</sub>]OTf (0.617 mg, 1.65 μmol) and the peptoid catalysts (1mg, 1.65 μmol) were placed in a dry vial, which was then capped with a septum. Dry acetonitrile (0.1 mL) and 1-methyl imidazole (1.8 μL, 3.3 μmol) were added, and the mixture was stirred for 5 minutes at rt following the exposure of the solution mixture to air. Benzyl alcohol (34 μL, 330 μmol) was then added, and the resulting mixture was stirred for 3hrs under air.

### ESI-MS analysis of intermediates 1-6:

Peptoid catalyst **BT** (1.65 μmol) and [Cu(MeCN)<sub>4</sub>]OTf (1.65 μmol) were placed in a dry vial, which was then capped with a septum and purged with N<sub>2</sub> for 3-4 minutes. Dry acetonitrile 100 μl was then add as the solvent, followed by these steps (i) a sample was diluted with dry acetonitrile and subjected to MS analysis, (ii) under these conditions,

MMI (3.3  $\mu\text{mol}$ ) was added, stirred and a sample was similarly analyzed. Thereafter, the system was exposed to air, followed by an immediate analysis of a sample by ESI-MS (S32). (iii) Finally, benzyl alcohol (330  $\mu\text{mol}$ ) was added to the mixture, stirred for 10 minutes, and a sample was analyzed by ESI-MS (Fig. S20-S25 respectively). Similar analysis was done with **DI** peptoid catalyst except the stirring time was increased to 30 min upon adding NMI and benzyl alcohol (S26-S31).

## References

1. R. N. Zuckermann, J. M. Kerr, S. B. W. Kent, W. H. Moos, *J. Am. Chem. Soc.* **1992**, *114*, 10646.

**Table S1.** Peptoid oligomer sequences and their corresponding molecular weights.

Peptoid	Oligomer sequence	Oligomer length	Molecular weight Calculated: Found
<b>Helix i+3</b>	<i>Nphen(Nspe)<sub>2</sub>Ntempo(Nspe)<sub>3</sub></i>	7mer	1269.5:1270.1
<b>Nonhelix i+3</b>	<i>Nphen(Nme)<sub>2</sub>Ntempo(Nme)<sub>3</sub></i>	7mer	1039.2:1040.0
<b>Helix i+1</b>	<i>NphenNtempo(Nspe)<sub>5</sub></i>	7mer	1269.5:1269.7
<b>DI</b>	<i>NphenNtempo</i>	2mer	463.5: 465.2
<b>BT</b>	<i>NphenNtempoNpm</i>	3mer	610.7: 612.0
<b>MT</b>	<i>NphenNtempoNme</i>	3mer	578.6: 580.0
<b>RBT</b>	<i>NphenNpmNtempo</i>	3mer	610.7: 611.8
<b>PT</b>	<i>NphenNtempoNaa</i>	3mer	590.7:592.6
<b>TT</b>	<i>NphenNtempoNtbm</i>	3mer	590.7:592.4
<b>NT</b>	<i>NphenNtempoNnm</i>	3mer	660.8:662.5

## **<sup>1</sup>H NMR Data**

**DI** (400 MHz, CD<sub>3</sub>OD):  $\delta$  1.36 (s, 6H), 1.40 (s, 6H), 1.93-1.96 (m, 2H), 2.09-2.16 (m, 2H), 3.20 (s, 4H), 4.23 (s, 3H), 4.92-4.98 (m, 1H), 6.89 (s, 1H), 7.88-7.94 (m, 2H), 8.64 (d, 1H,  $J = 5.2$  Hz), 8.70 (d, 1H,  $J = 8.3$  Hz), 8.77 (d, 1H,  $J = 8.4$  Hz), 9.09 (d, 1H,  $J = 3.8$  Hz).

**BT** (400 MHz, CD<sub>3</sub>OD):  $\delta$  1.22-1.34 (m, 12H), 1.78-1.88 (m, 2H), 1.97-2.04 (m, 2H), 4.08-4.11 (m, 4H), 4.29-4.33 (m, 1H), 4.48-4.49 (m, 2H), 4.59 (bs, 2H), 6.82-6.89 (m, 1H), 7.13-7.19 (m, 2H), 7.22-7.33 (m, 3H), 7.77-7.83 (m, 2H), 8.47-8.52 (m, 1H), 8.47-8.52 (m, 1H), 8.62 (d, 1H,  $J = 4.8$  Hz), 8.70-8.73 (m, 1H), 9.04-9.05 (bs, 1H).

**MT** (400 MHz, CD<sub>3</sub>OD):  $\delta$  1.44-1.49 (m, 12H), 1.95-2.05 (m, 2H), 2.13-2.16 (m, 2H), 3.39-3.47 (m, 3H), 3.55-3.75 (m, 5H), 4.21-4.23 (bs, 2H), 4.35-4.36 (bs, 1H), 4.49-4.54 (bs, 2H), 4.68-4.72 (bs, 3H), 6.96-7.05 (m, 1H), 7.98-7.99 (m, 2H), 8.74-8.86 (m, 3H), 9.12-9.18 (bs, 1H).

**RBT** (400 MHz, CD<sub>3</sub>CN):  $\delta$  1.36 (s, 6H), 1.47 (s, 6H), 2.08-2.11 (m, 4H), 3.96-4.03 (m, 2H), 4.17-4.25 (m, 3H), 4.34 (bs, 1H), 4.69-4.79 (m, 3H), 6.71 (bs, 2H), 7.00 (s, 1H), 7.34-7.47 (m, 5H), 7.78-7.93 (m, 2H), 8.57-8.67 (m, 2H), 8.80-8.81 (bs, 1H), 9.07-9.08 (bs, 1H), 12.66 (bs, 1H).

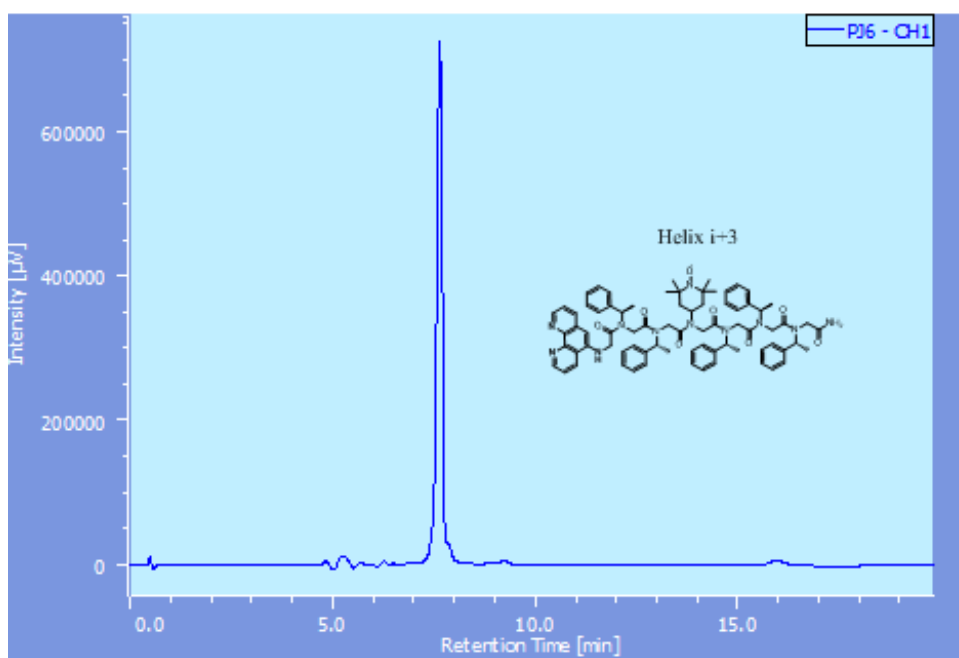
**PT** (400 MHz, CD<sub>3</sub>OD):  $\delta$  0.83-0.86 (m, 3H), 1.33-1.34 (m, 4H), 1.42-1.66 (m, 14H), 1.42-1.60 (m, 2H), 1.74-1.76 (m, 1H), 2.02-2.90 (m, 2H), 2.13-2.16 (m, 2H), 3.45-3.53 (m, 2H), 4.18-4.28 (m, 4H), 4.53-4.59 (m, 2H), 6.97-7.02 (bs, 1H), 7.94-7.98 (m, 2H), 8.70-8.75 (m, 2H), 8.82-8.85 (m, 1H), 9.16-9.17 (bs, 1H).

**TT** (400 MHz, CD<sub>3</sub>OD):  $\delta$  0.80-0.81 (m, 9H), 1.23-1.30 (m, 12H), 1.79-1.82 (m, 2H), 1.99-2.01 (m, 2H), 3.12-3.13 (m, 4H), 4.01-4.02 (bs, 2H), 4.16-4.18 (bs, 2H), 4.35-4.36 (bs, 2H), 6.76-6.78 (bs, 1H), 7.75-7.78 (m, 2H), 8.52-8.54 (m, 2H), 8.61-8.65 (m, 1H), 8.95 (bs, 1H).

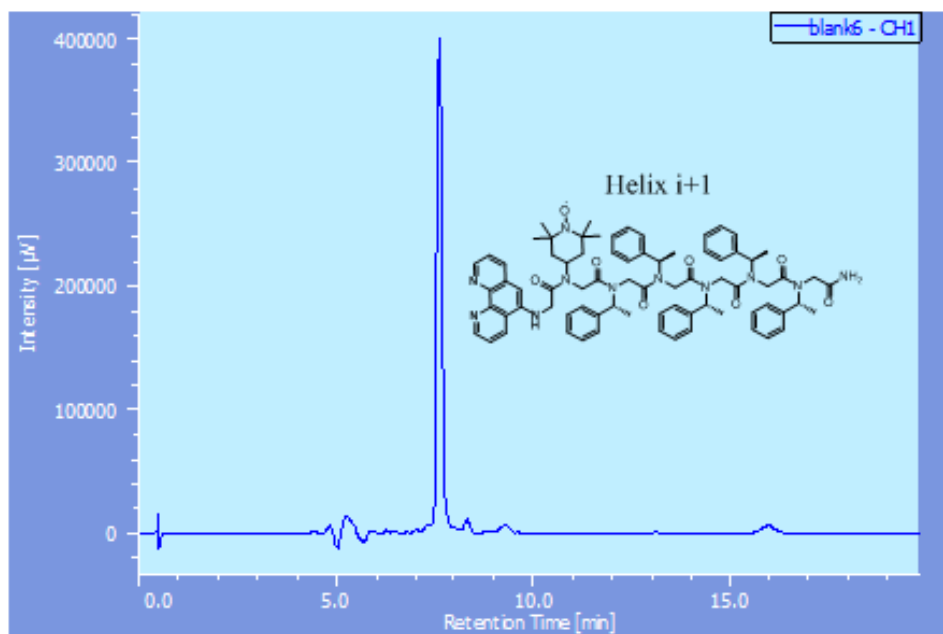
NT(400 MHz, CD<sub>3</sub>CN):  $\delta$ 1.29 (s, 6H), 1.42 (s, 6H), 2.05 (d, 4H,  $J = 7.6$  Hz), 3.96 (d, 4H,  $J = 5.2$  Hz), 4.29 (s, 2H), 4.86-4.94 (m, 1H), 5.01 (s, 2H), 6.20 (s, 1H), 6.49 (s, 1H), 6.79 (s, 1H), 7.21-7.26 (m, 3H), 7.40 (d, 1H,  $J = 7.9$  Hz), 7.45 (d, 1H,  $J = 6.6$  Hz), 7.73-7.82 (m, 4H), 8.04 (d, 1H,  $J = 8.1$  Hz), 8.33 (d, 1H,  $J = 8.2$  Hz), 8.59 (d, 1H,  $J = 8.3$  Hz), 8.70 (d, 1H,  $J = 4.6$  Hz), 8.98 (d, 1H,  $J = 3.6$  Hz), 12.58 (bs, 1H).

## HPLC

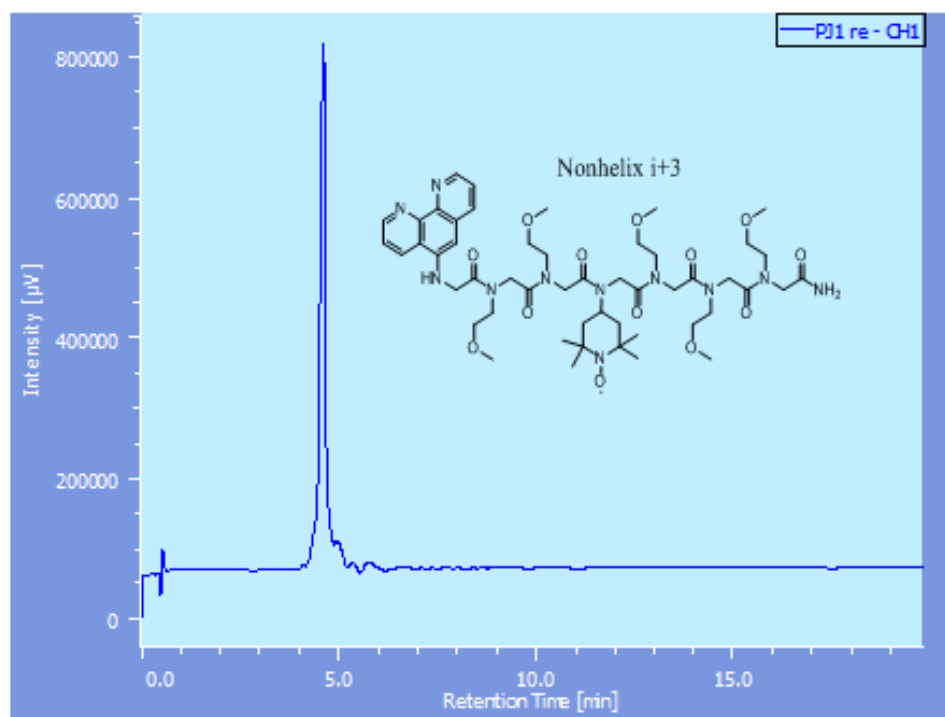
HPLC solvent A: (0.1 % TFA in water), HPLC solvent B: (0.1 % TFA in acetonitrile)



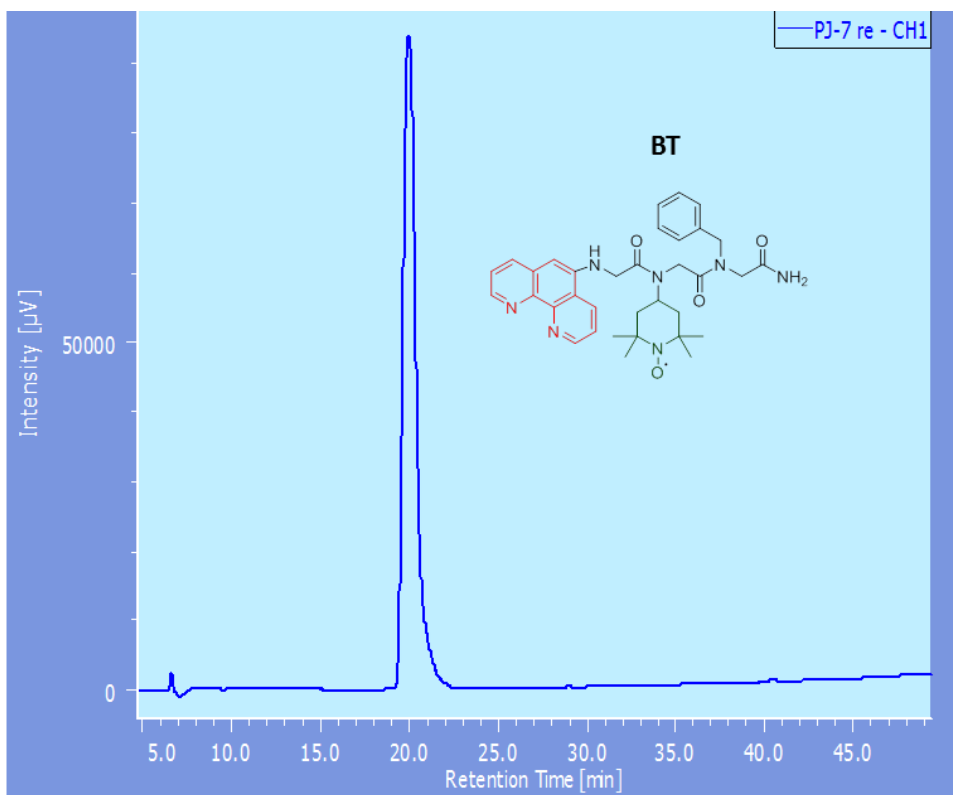
**Figure S1.** HPLC trace of peptoid **Helix i+3**



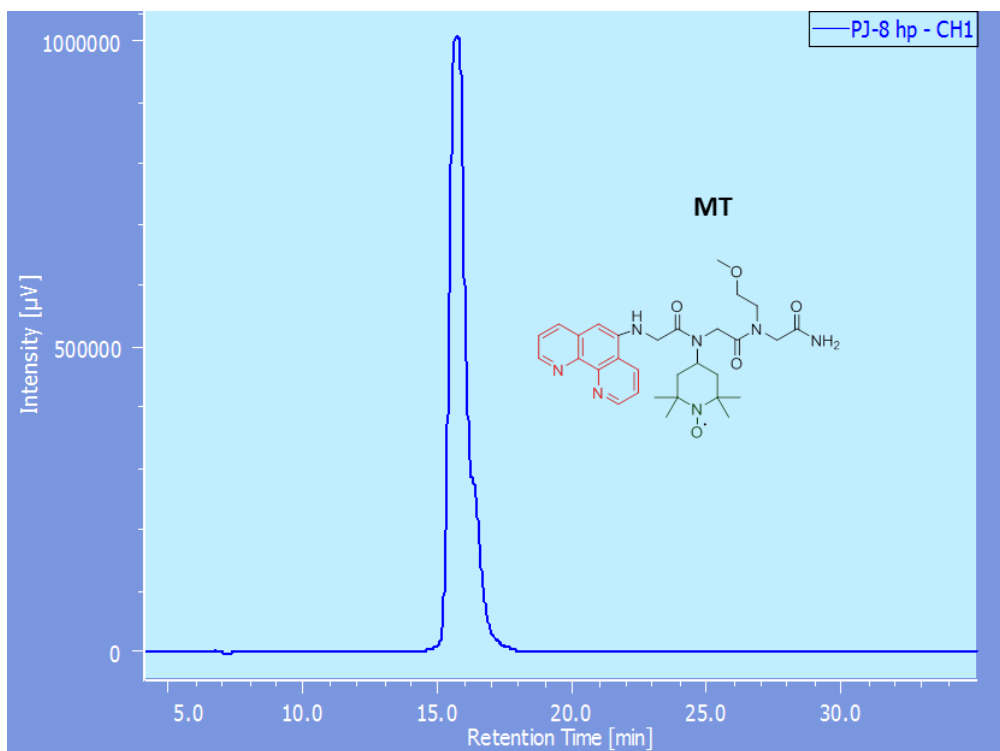
**Figure S2.** HPLC trace of peptoid **Helix i+1**



**Figure S3.** HPLC trace of peptoid **Nonhelix i+3**

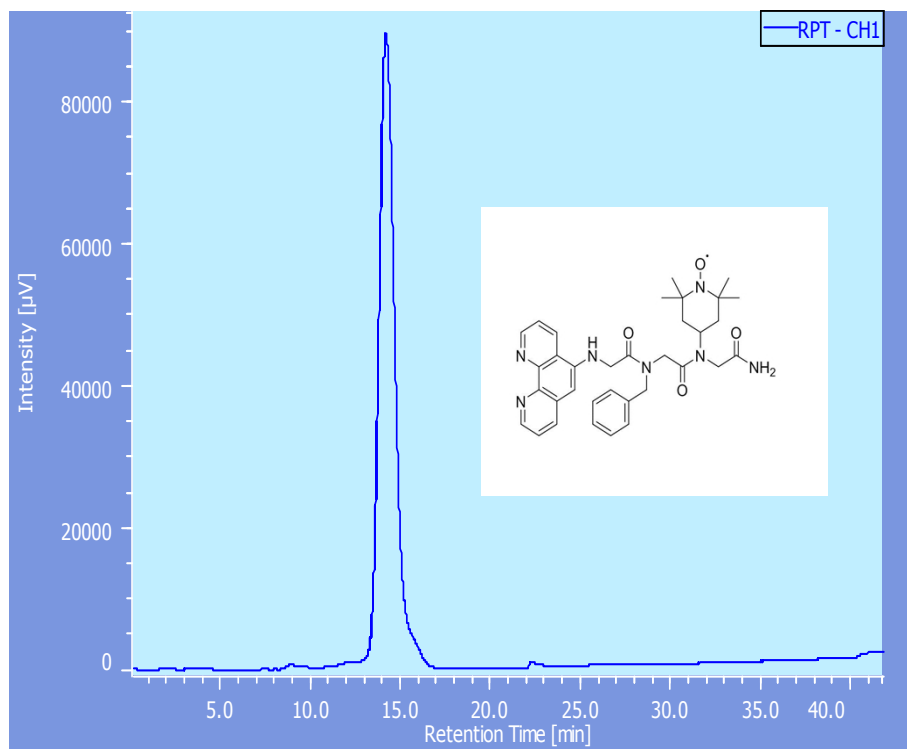


**Figure S4.** HPLC trace of peptoid **BT**

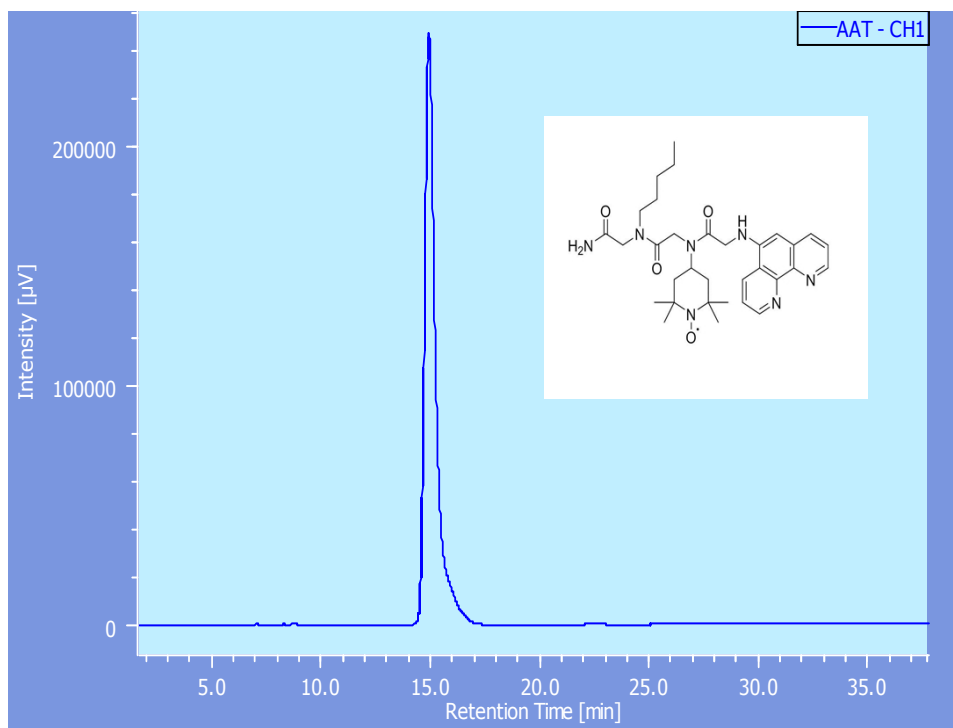


**Figure S5.** HPLC trace of peptoid **MT**

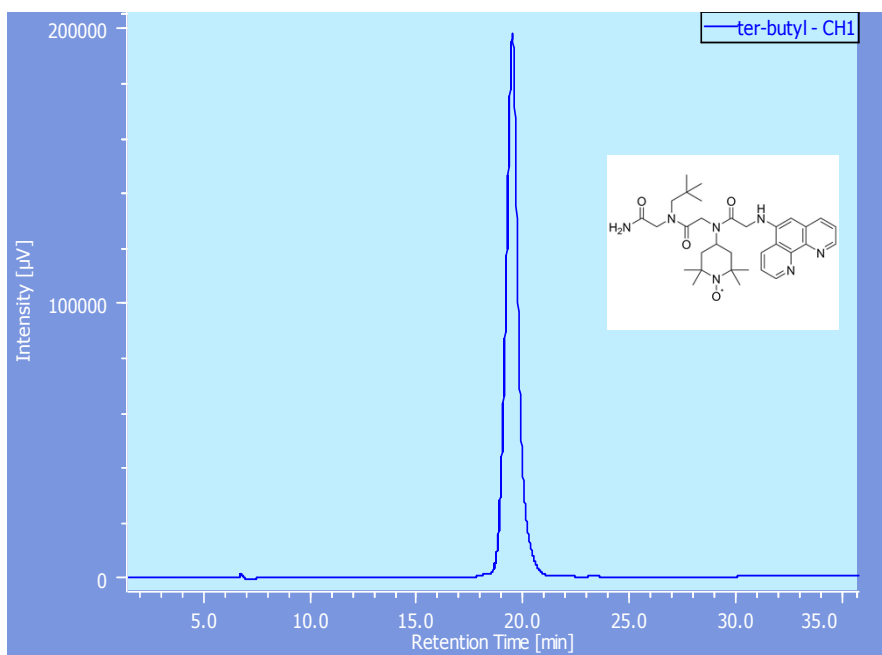




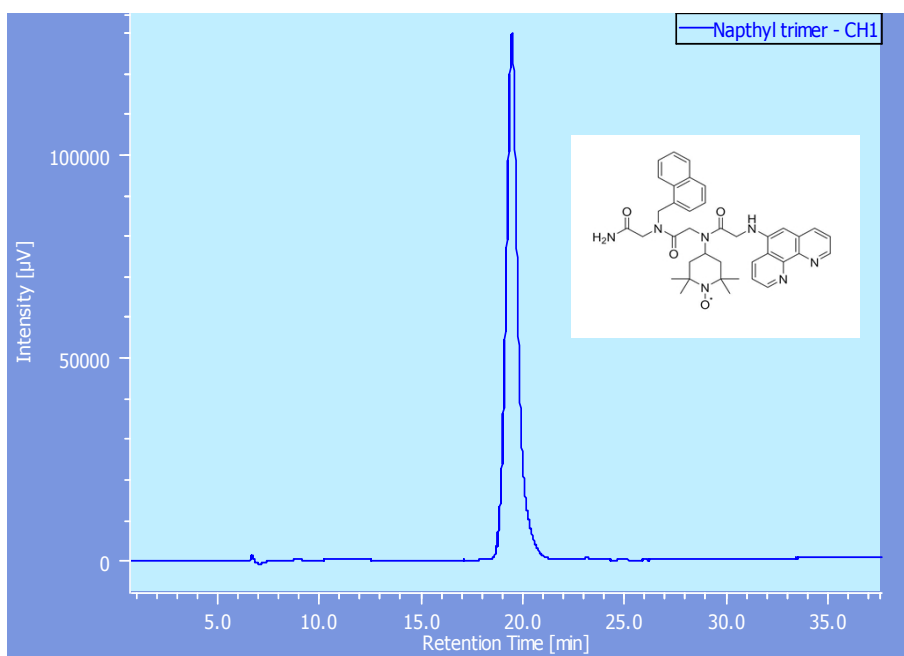
**Figure S6.** HPLC trace of peptoid **RBT**



**Figure S7.** HPLC trace of peptoid **PT**

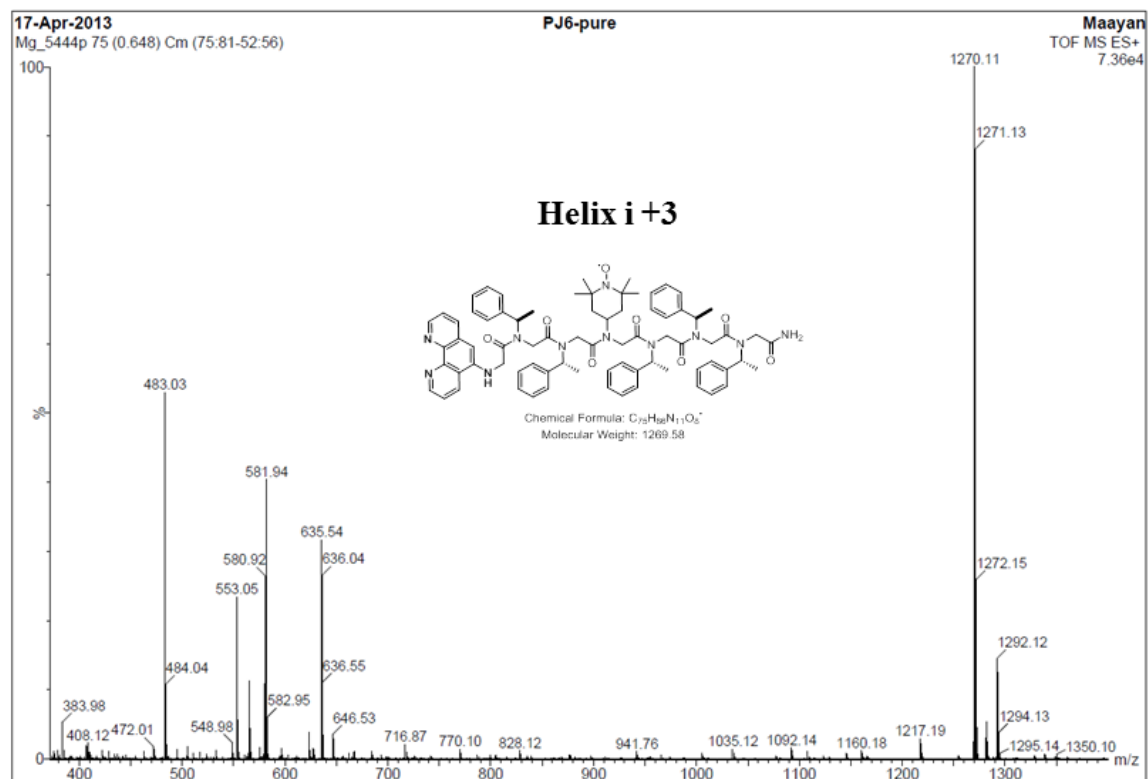


**Figure S8.** HPLC trace of peptoid **TT**

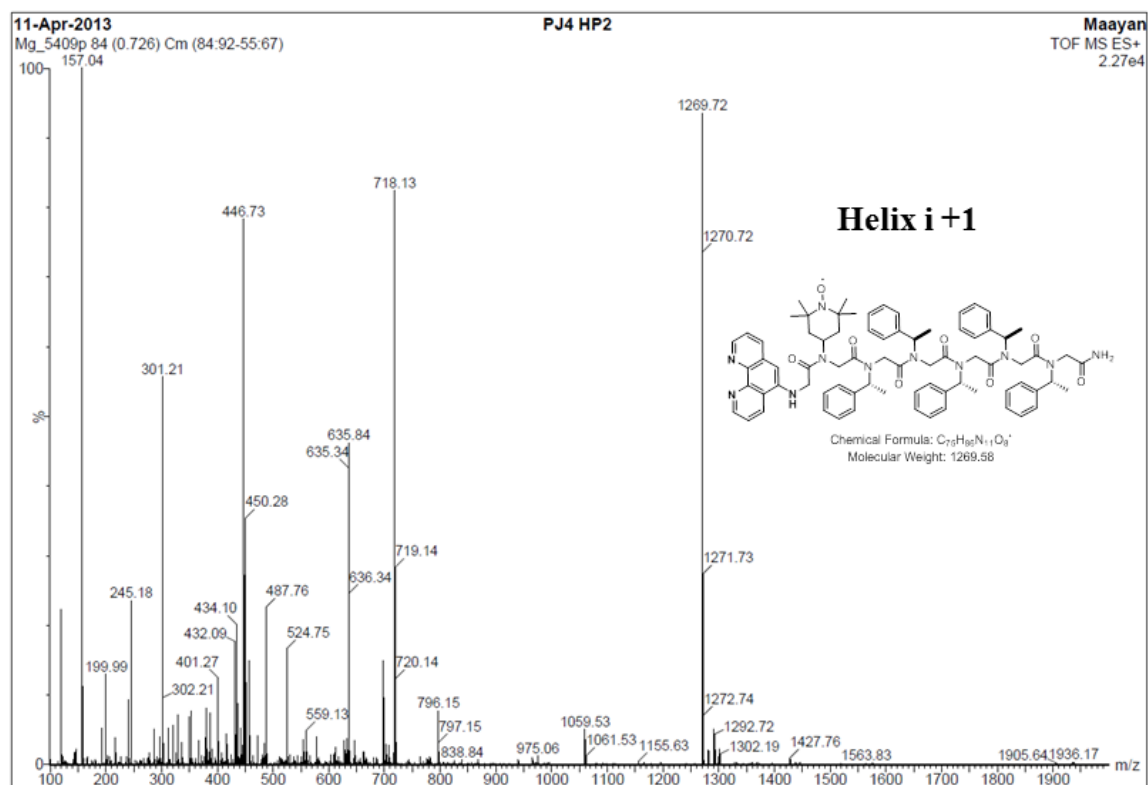


**Figure S9.** HPLC trace of peptoid **NT**

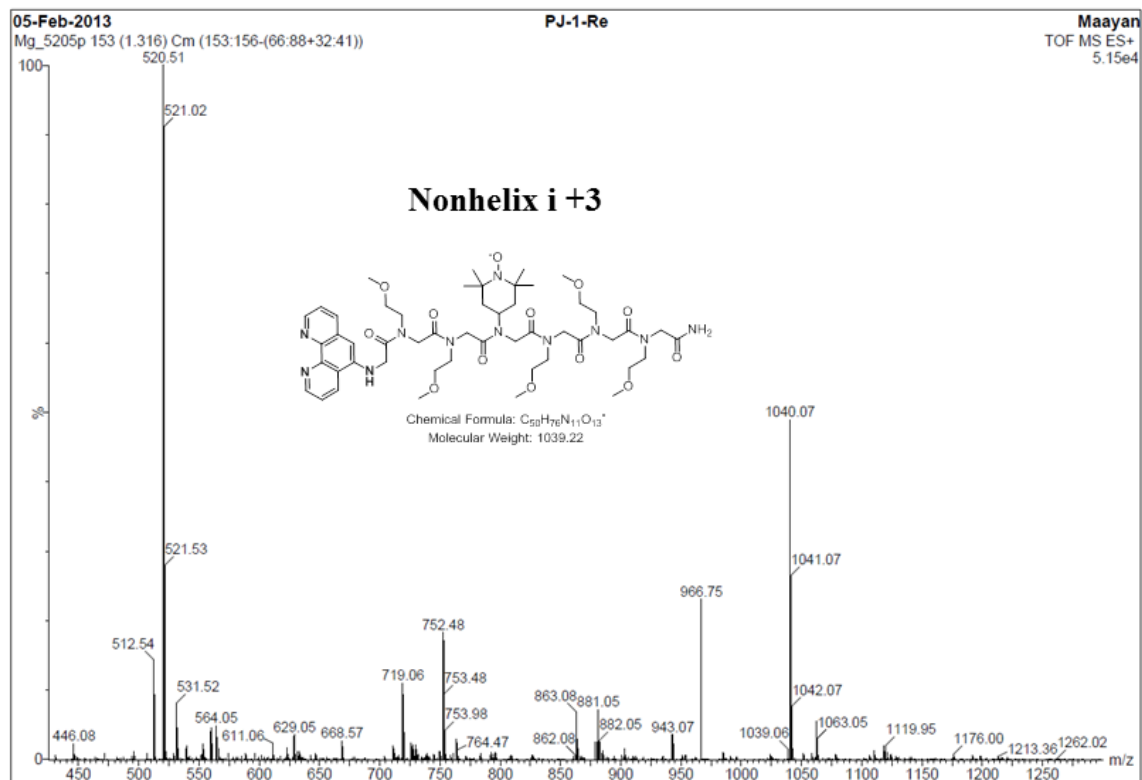
## ESI MS of peptoid oligomers



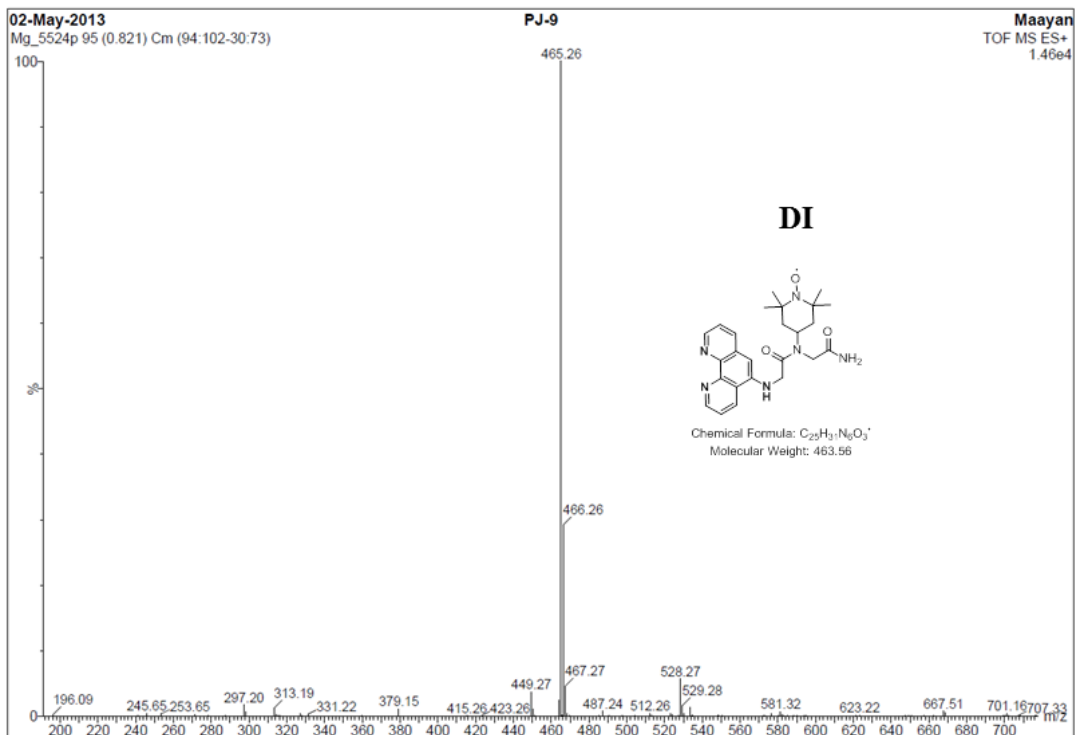
**Figure S10.** ESI MS of peptoid **Helix i+3**



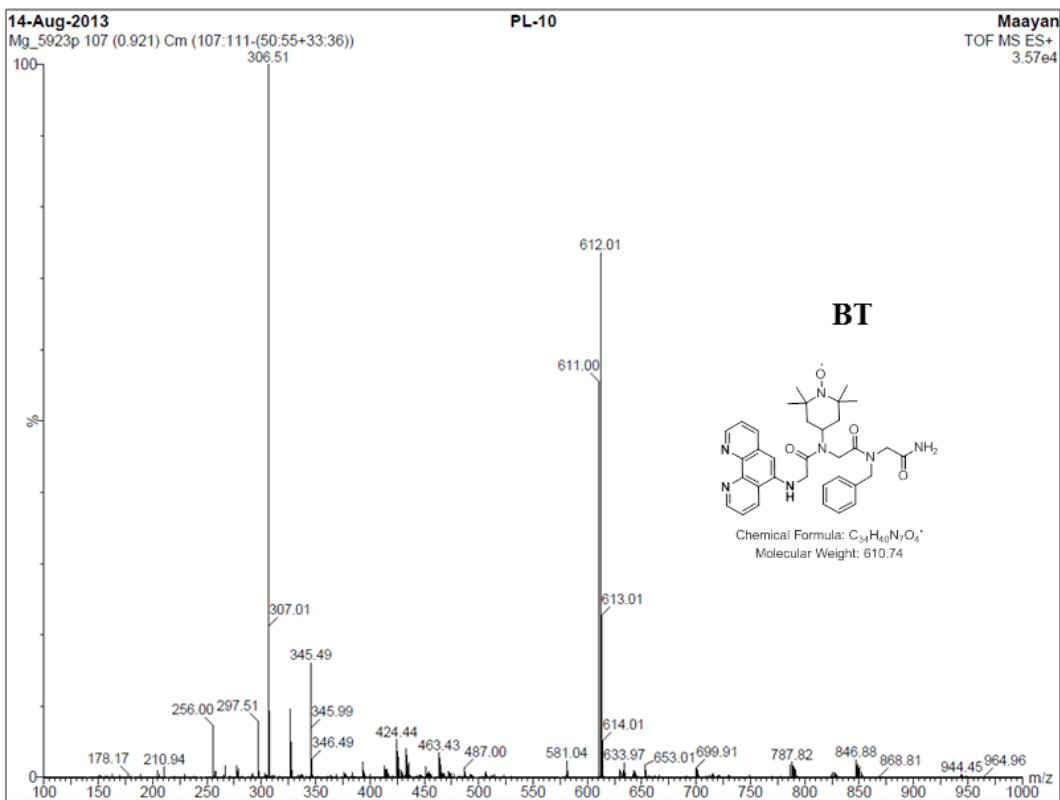
**Figure S11.** ESI MS of peptoid **Helix i+1**



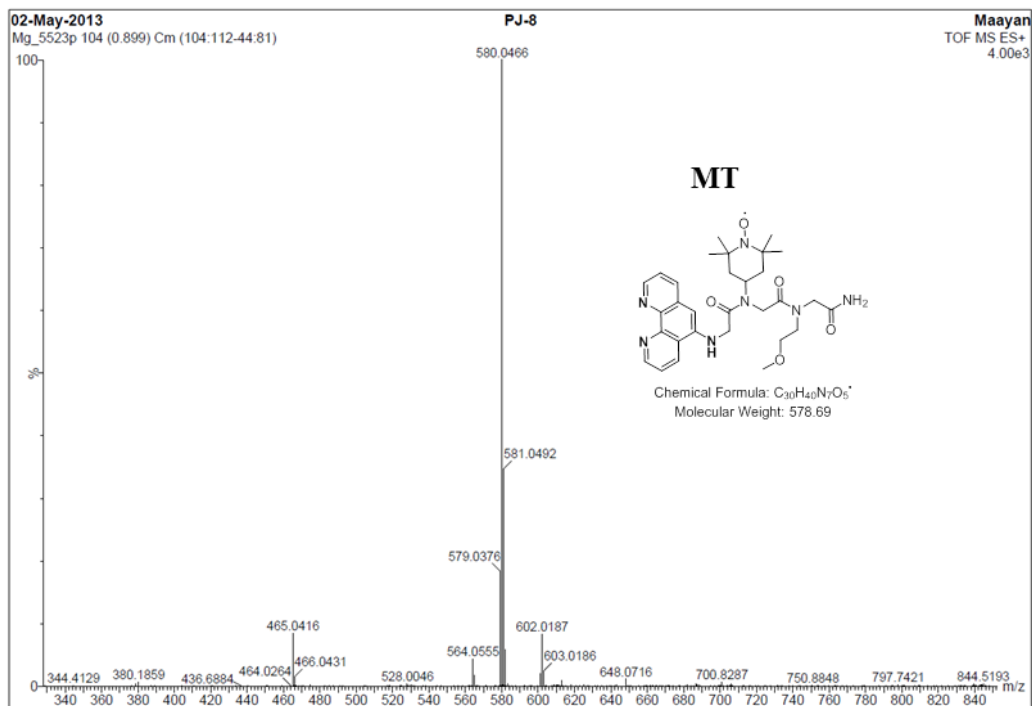
**Figure S12.** ESI MS of peptoid Nonhelix i+3



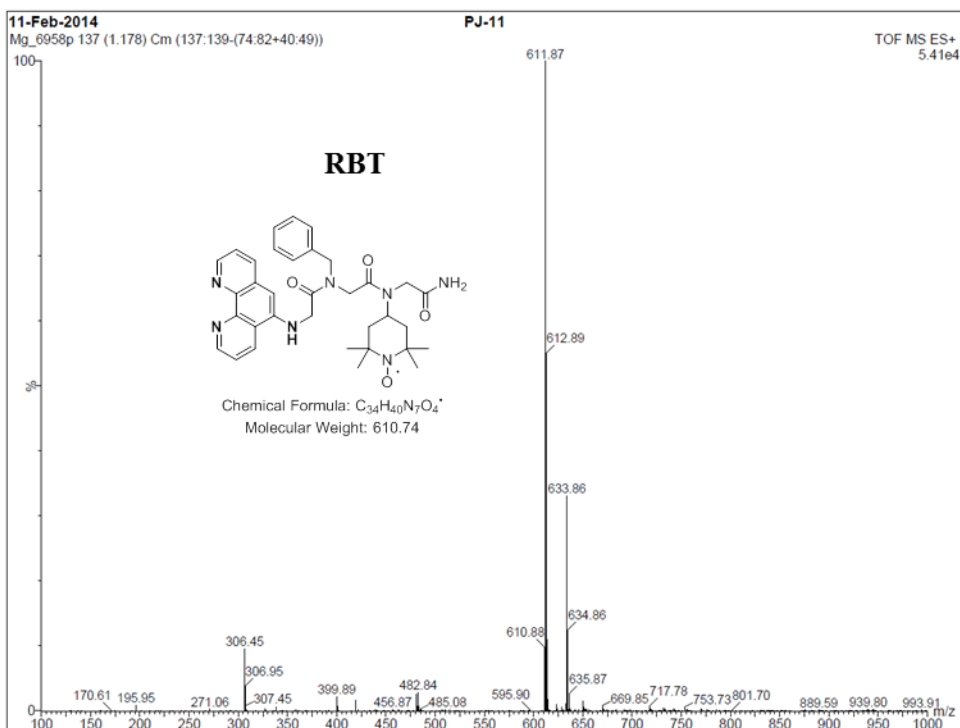
**Figure S13.** ESI MS of peptoid **DI**



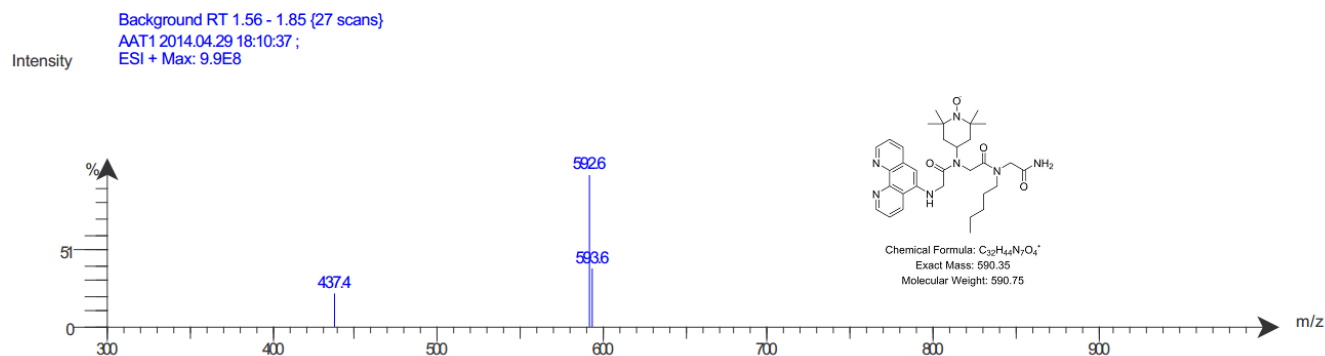
**Figure S14.** ESI MS of peptoid **BT**



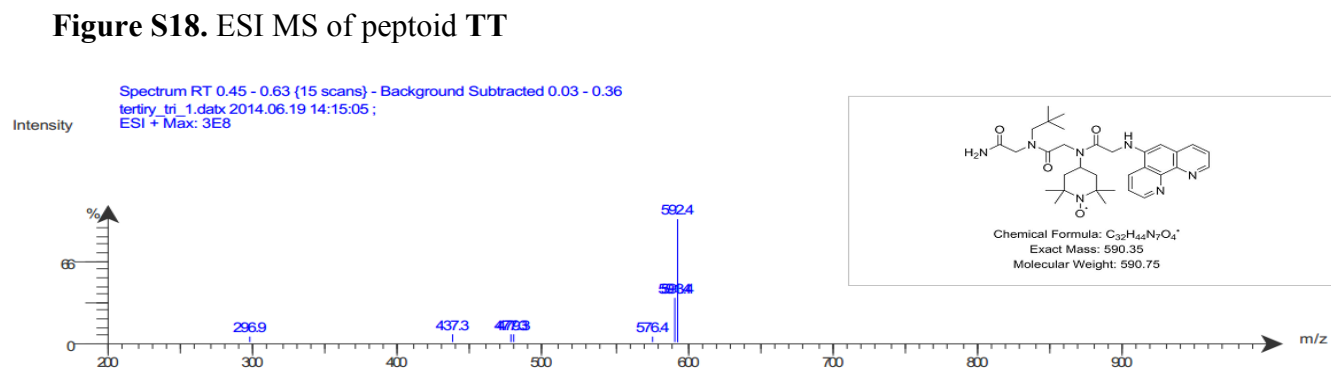
**Figure S15.** ESI MS of peptoid **MT**



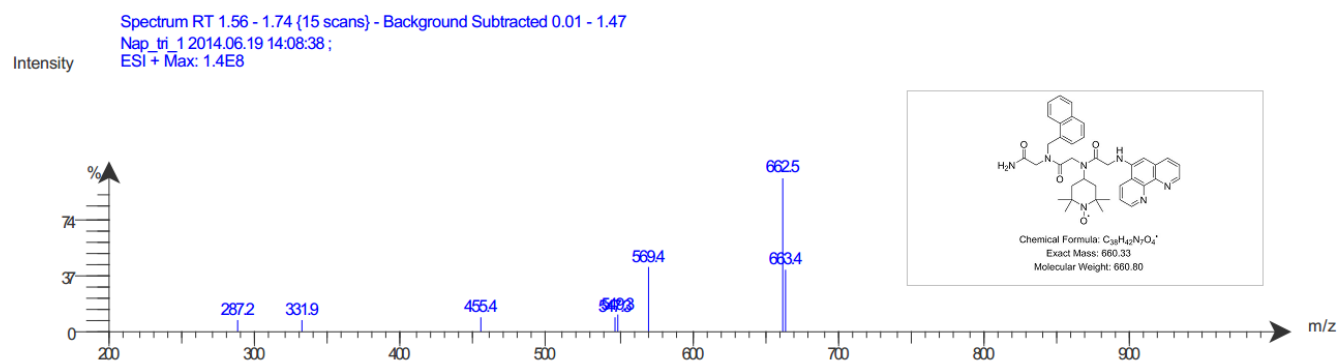
**Figure S16.** ESI MS of peptoid **RBT**



**Figure S17.** ESI MS of peptoid PT



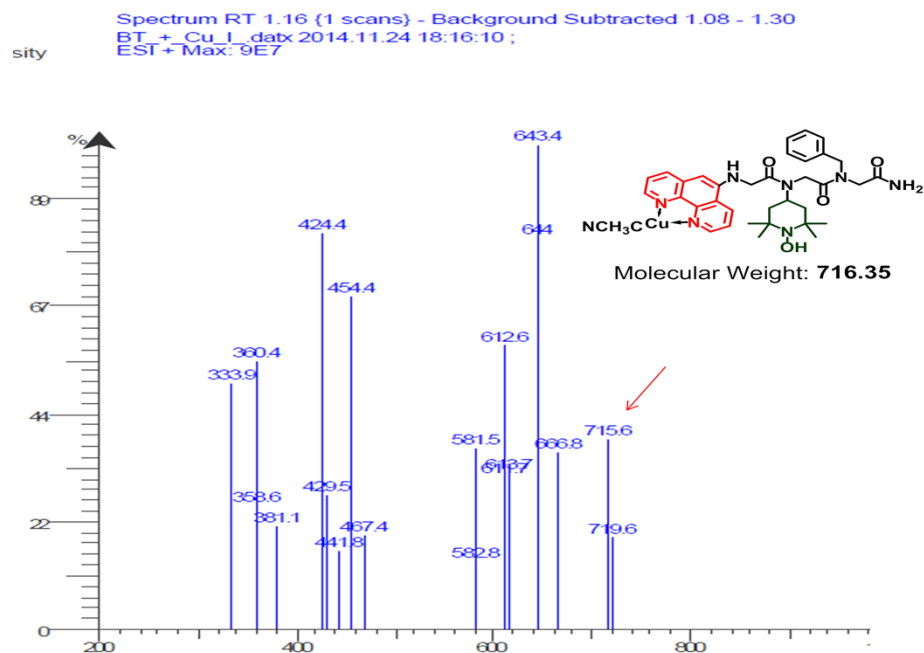
**Figure S18.** ESI MS of peptoid TT



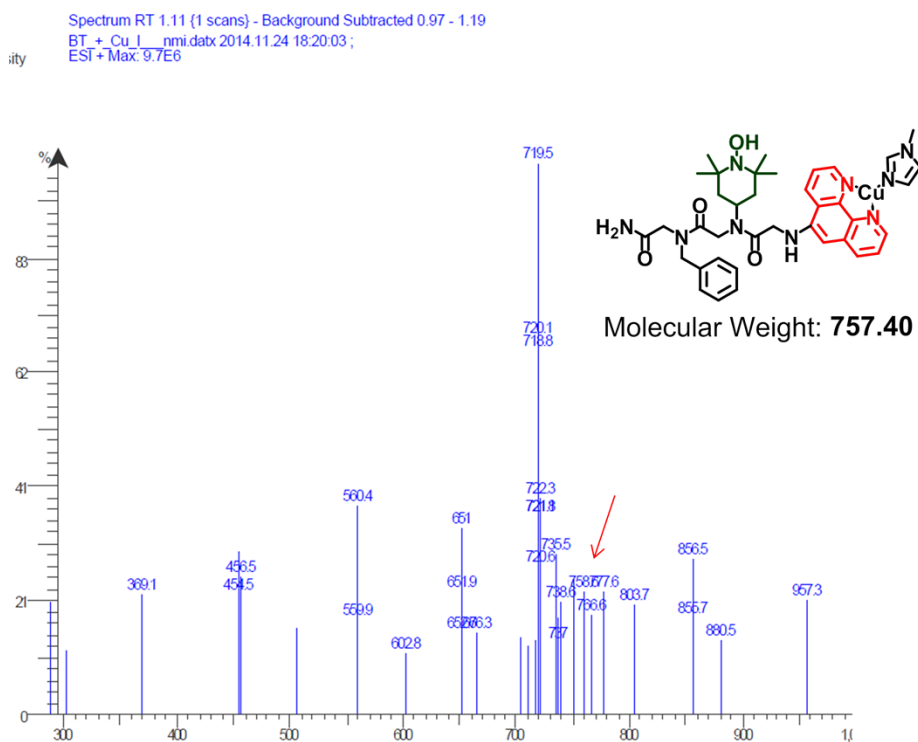
**Figure S19.** ESI MS of peptoid NT

**ESI MS of catalysis intermediates**

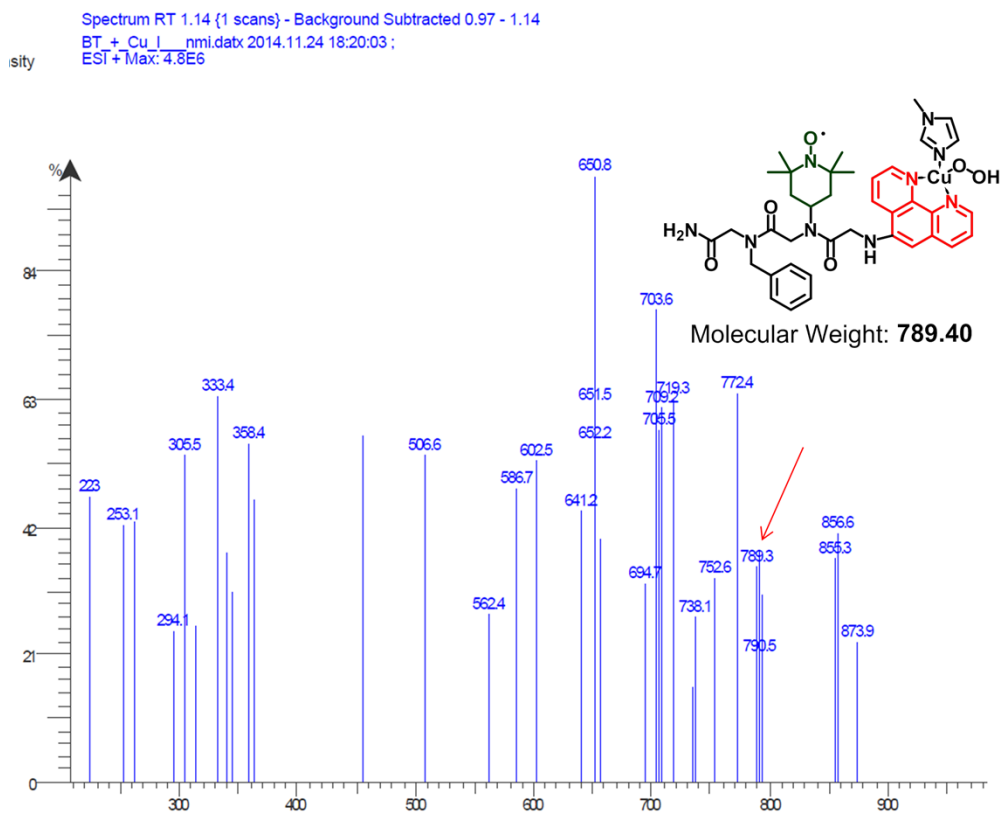




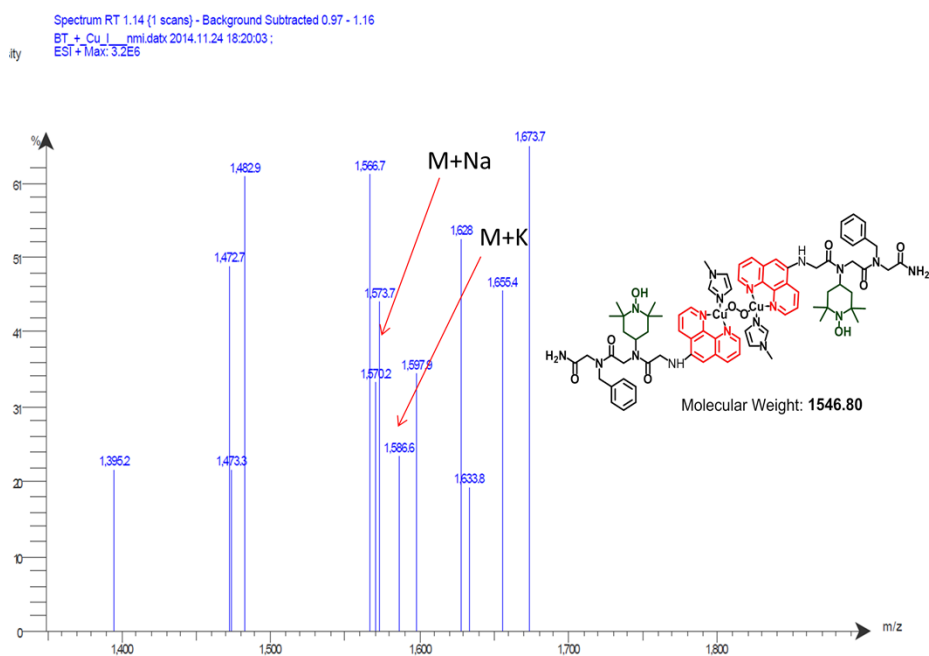
**Figure S20.** ESI MS of reaction intermediate 1 of BT



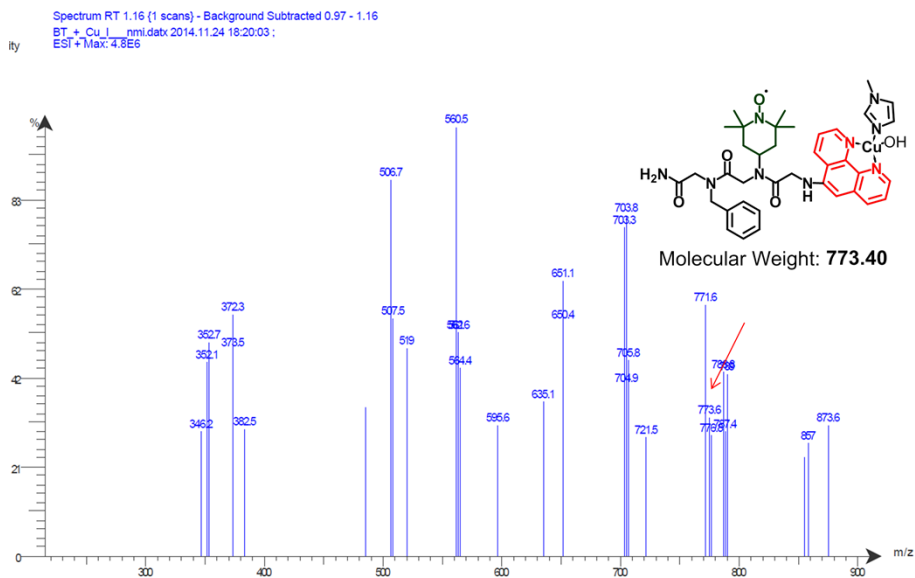
**Figure S21.** ESI MS of reaction intermediate 2 of BT



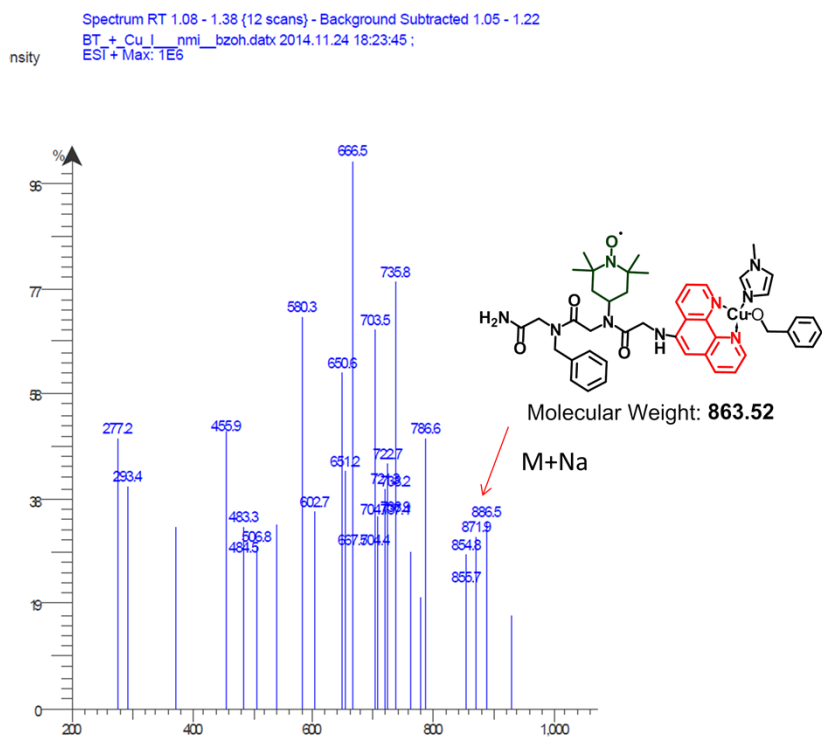
**Figure S22.** ESI MS of reaction intermediate 4 of BT



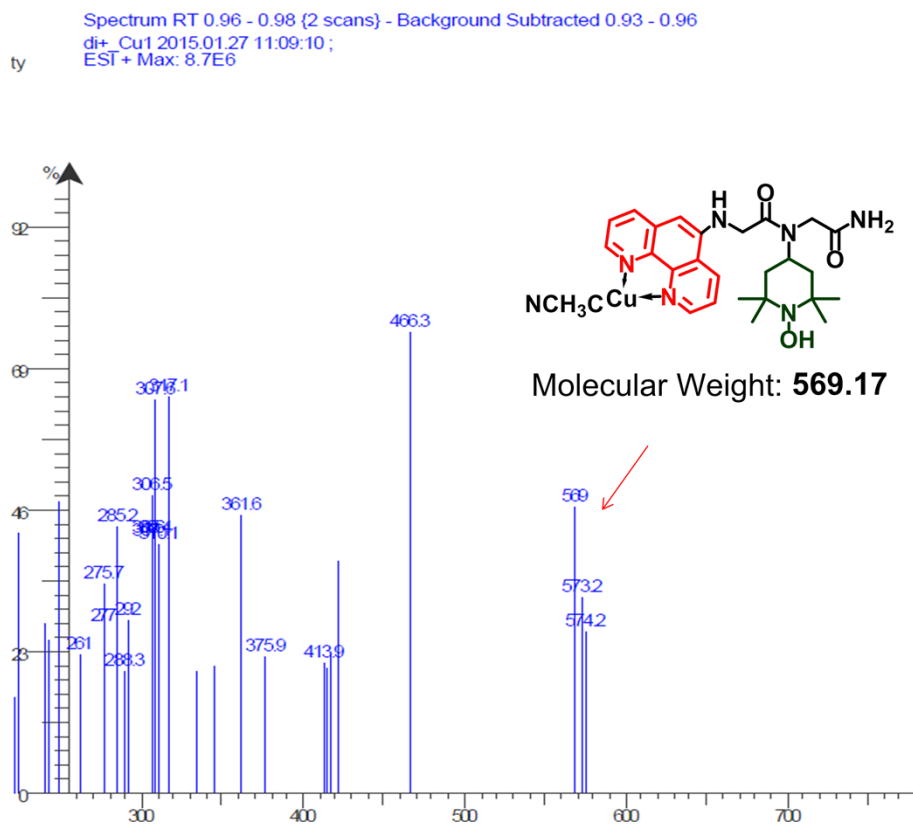
**Figure S23.** ESI MS of reaction intermediate 3 of BT



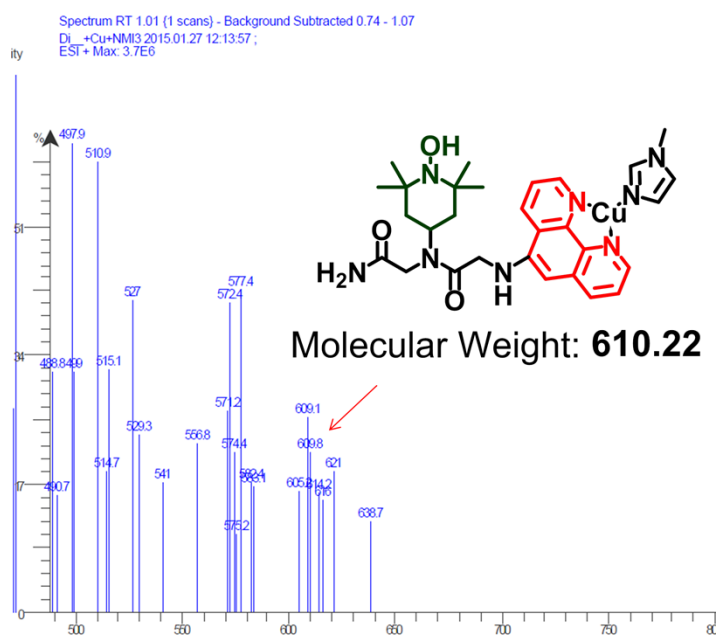
**Figure S24.** ESI MS of reaction intermediate **5** of **BT**



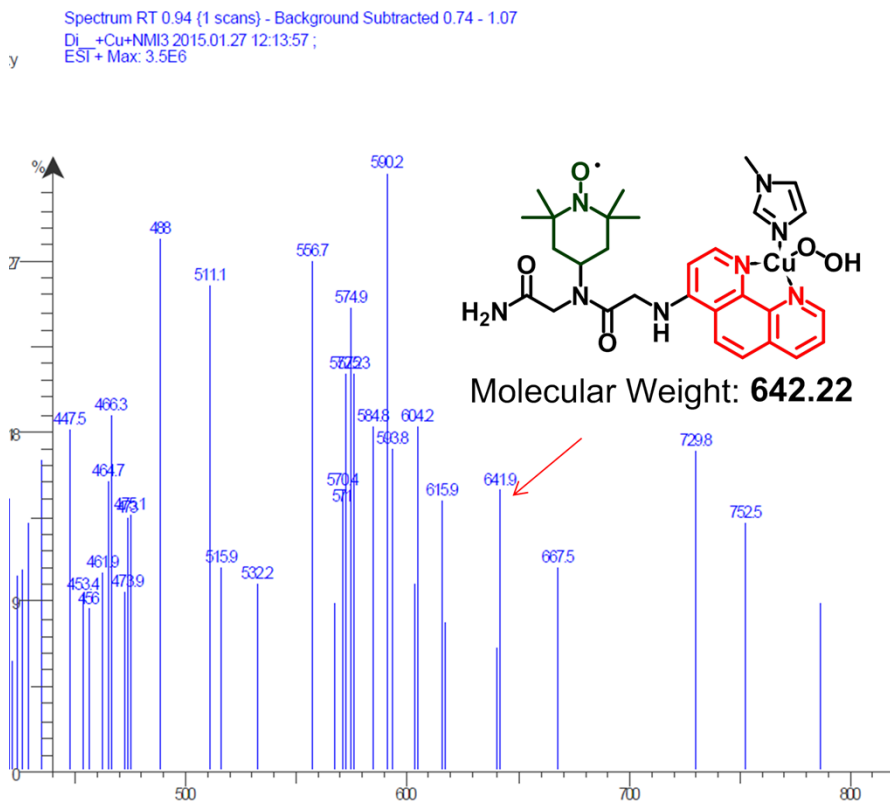
**Figure S25.** ESI MS of reaction intermediate **6** of **BT**



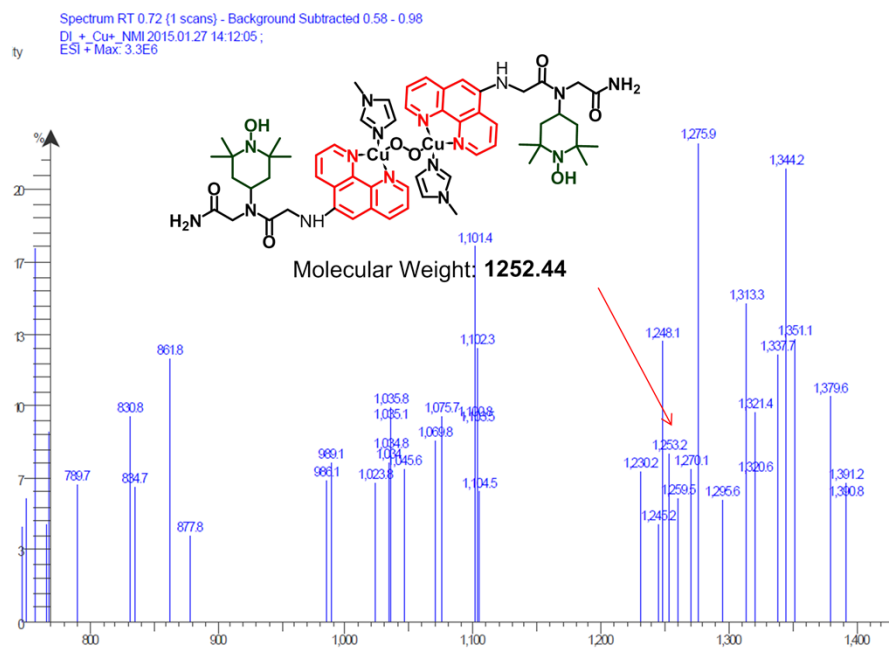
**Figure S26.** ESI MS of reaction intermediate 1 of DI



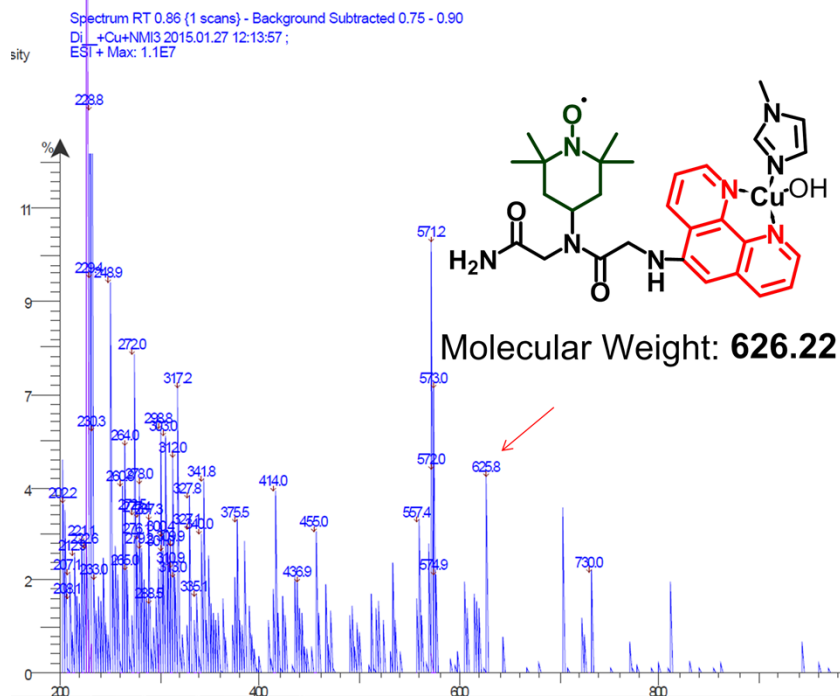
**Figure S27.** ESI MS of reaction intermediate 2 of DI



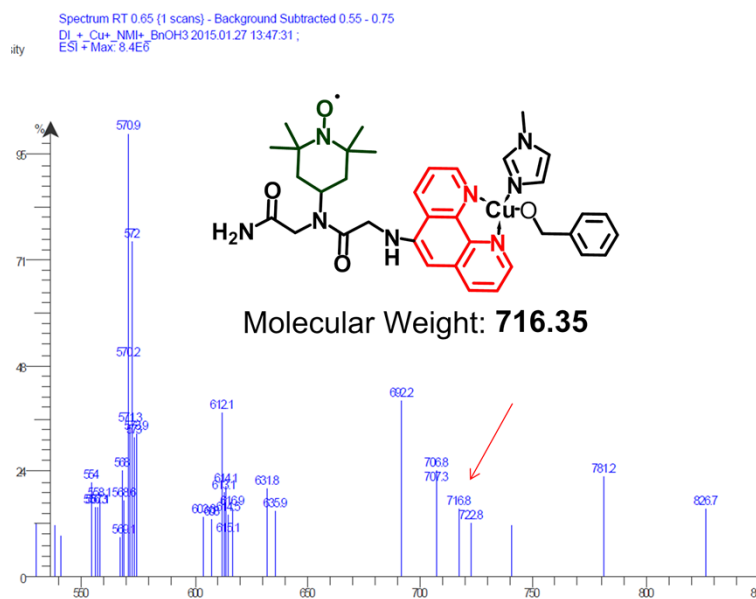
**Figure S28.** ESI MS of reaction intermediate 4 of DI



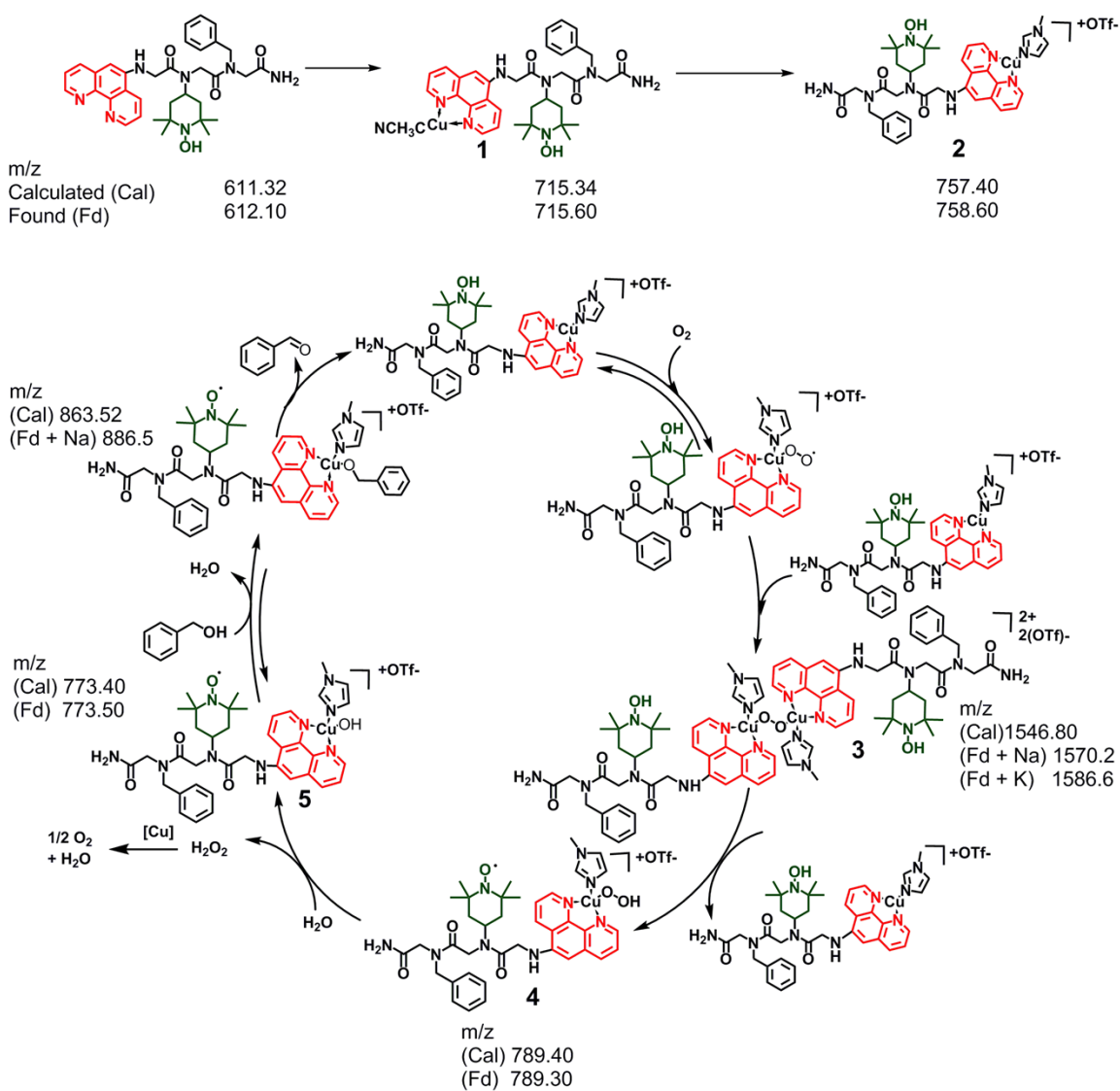
**Figure S29.** ESI MS of reaction intermediate 3 of DI



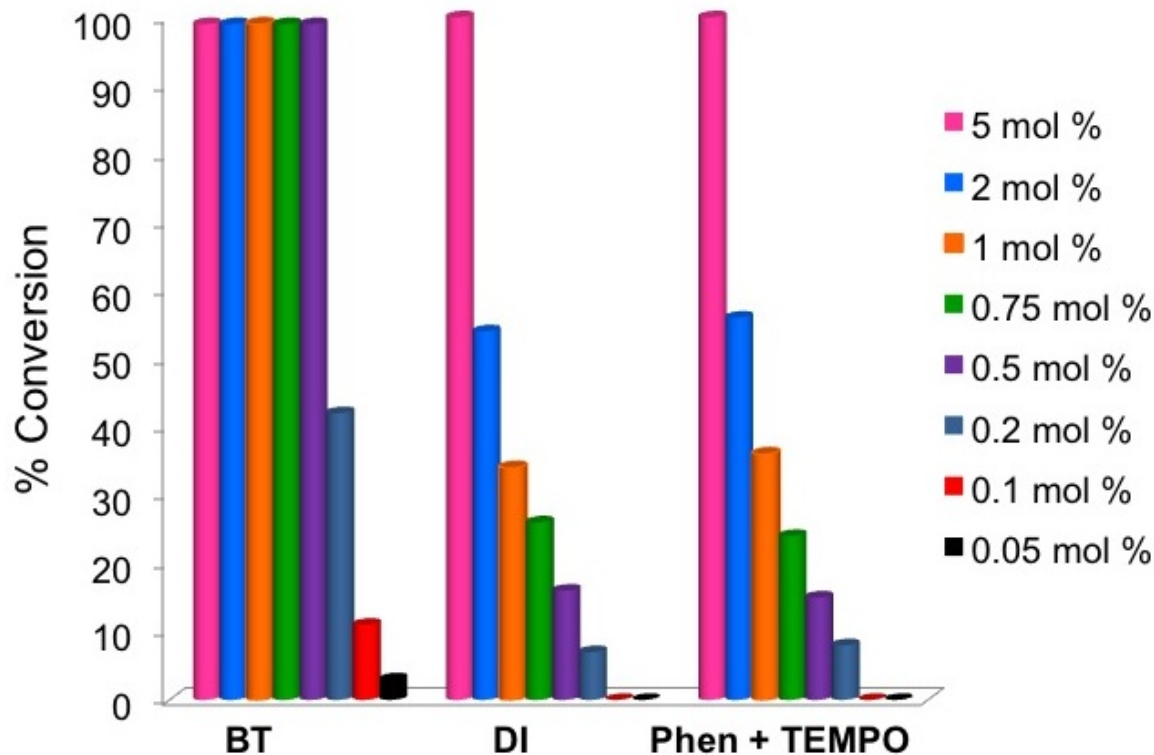
**Figure S30.** ESI MS of reaction intermediate **5** of **DI**



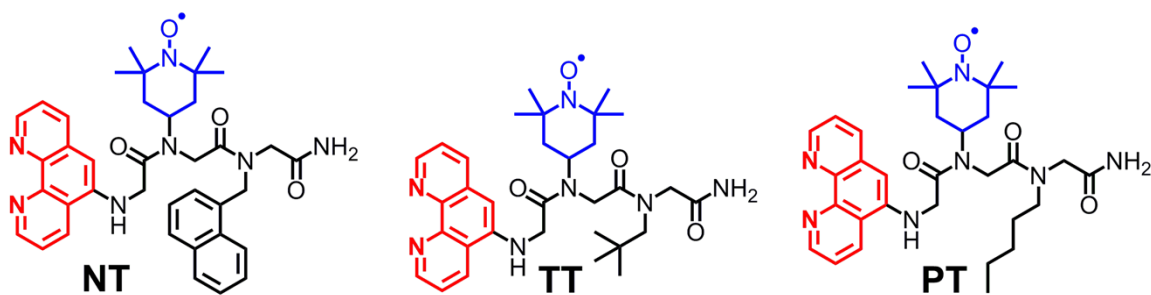
**Figure S31.** ESI MS of reaction intermediate **6** of **DI**



**Figure S32.** ESI-MS analysis of our reaction intermediates as a support for the proposed mechanism suggested by Sthal et al. Reaction conditions: dry acetonitrile (0.1 mL) at room temperature with 330  $\mu\text{mol}$  benzyl alcohol, 0.5 mol % catalyst(s), 0.5 mol %  $[\text{Cu}(\text{MeCN})_4]\text{OTf}$  and 1 mol % NMI.



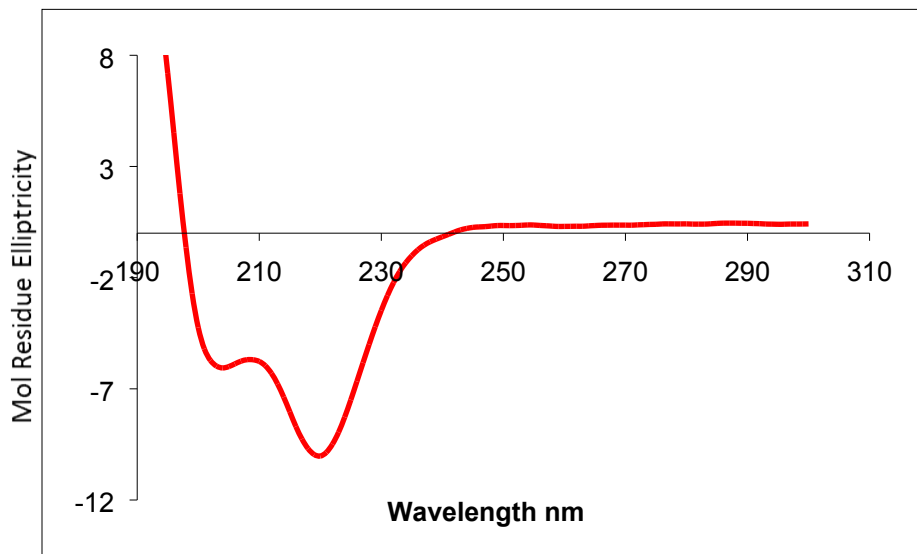
**Figure S33.** Oxidation of benzyl alcohol with three different catalytic systems in concentrations varied from 5 mol% to 0.05 mol%. All of the reactions were performed in dry acetonitrile (0.1 mL) at room temperature for 3 hrs. with 330  $\mu$ mol benzyl alcohol, 1 equiv.  $[\text{Cu}(\text{MeCN})_4]\text{OTf}$  and 2 equiv. NMI for each equiv. of catalyst(s). Conversions were determined by gas chromatography



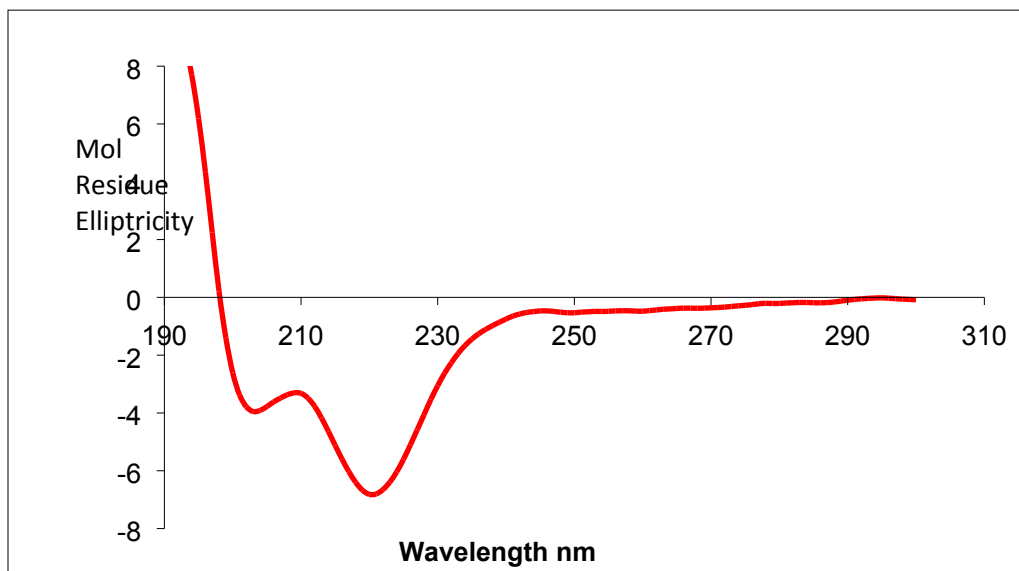
**Figure S34.** The third set of peptoid sequences that were used to evaluate intramolecular cooperative catalysis in the oxidation of benzyl alcohol.



## CD



**Figure S35.** CD spectrum of peptoid **Helix i+1**. The spectrum was recorded at room temperature, in a MeOH/H<sub>2</sub>O (4:1) and peptoid concentration of 5mM.



**Figure S36.** CD spectrum of peptoid **Helix i+3**. The spectrum was recorded at room temperature, in a MeOH/H<sub>2</sub>O (4:1) and peptoid concentration of 5mM.

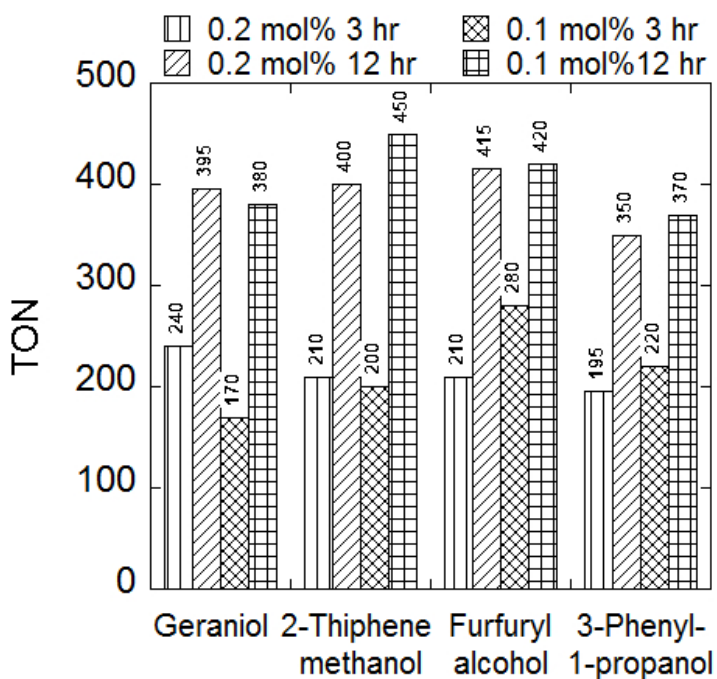
## Catalysis

**Table S2.**Efficiency of the peptoid catalysts **BT** and **DI** compared to the intermolecular control system in the oxidation of benzyl alcohol, with different catalysts loadings

Entry	Catalyst loading (mol %)	% Conversion (TON) <sup>[a]</sup>				
		<b>BT</b>	<b>NT</b>	<b>TT</b>	<b>DI</b>	<b>Phen+TEMPO</b>
1	0.5	99 (198)	98 (196)	97 (194)	10 (20)	16(32)
2	0.2	41 (205)	nd	nd	2 (4)	2 (4)
3 <sup>[b]</sup>	0.2	66 (330)	nd	nd	6 (30)	7 (35)
4	0.1	11 (110)	nd	nd	nd	nd
5 <sup>[b]</sup>	0.1	49 (490)	49 (490)	46 (460)	3 (30)	3 (30)

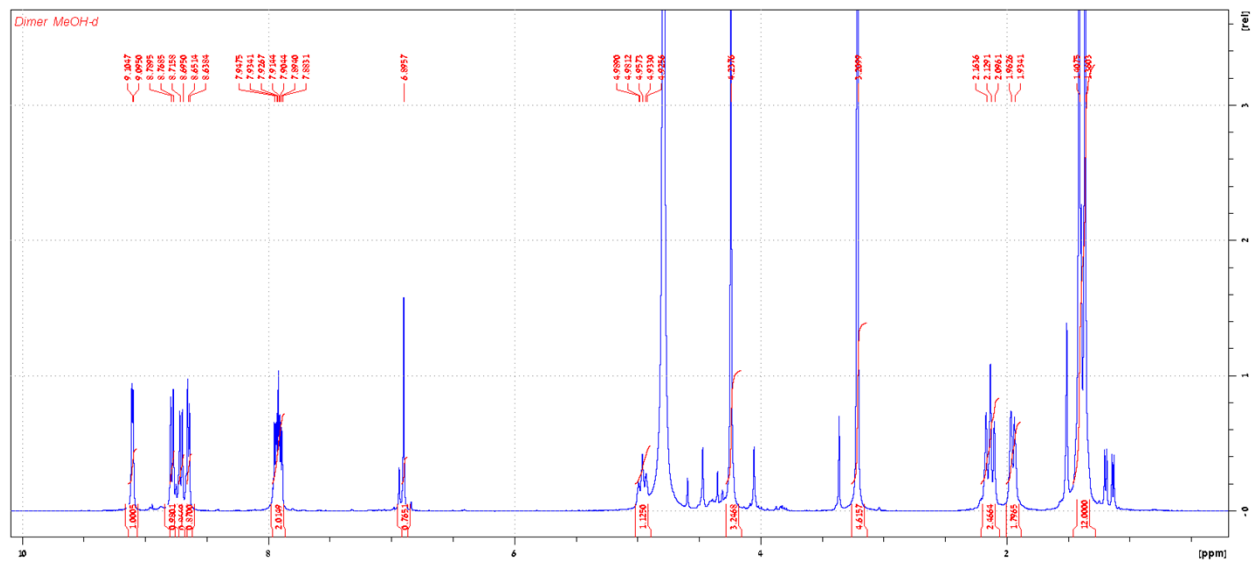
All of the reactions were conducted in dry acetonitrile as the solvent (0.1ml) at room temperature for 3hrs., using 0.5mol% catalyst,0.5mol% [Cu(MeCN<sub>4</sub>)OTf and 1mol% NMI. [a]As determined by gas chromatography.[b] Reaction time was 12 hours.

nd = not detected

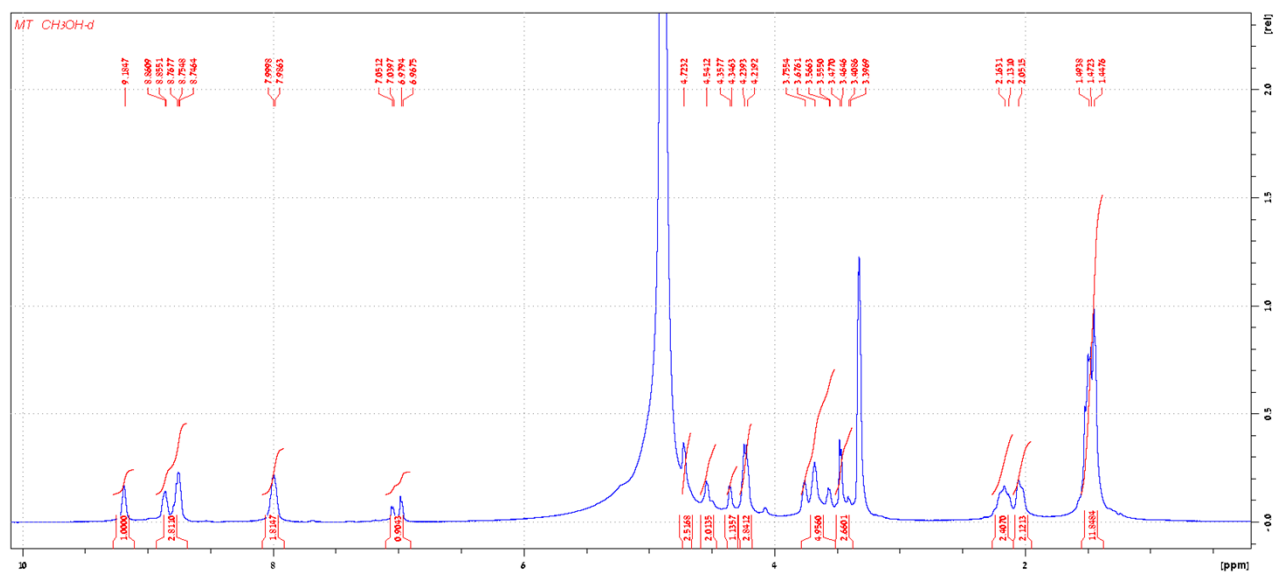


**Figure S37.** Oxidation of aromatic alcohols catalyzed by **BT** at low catalyst loadings.

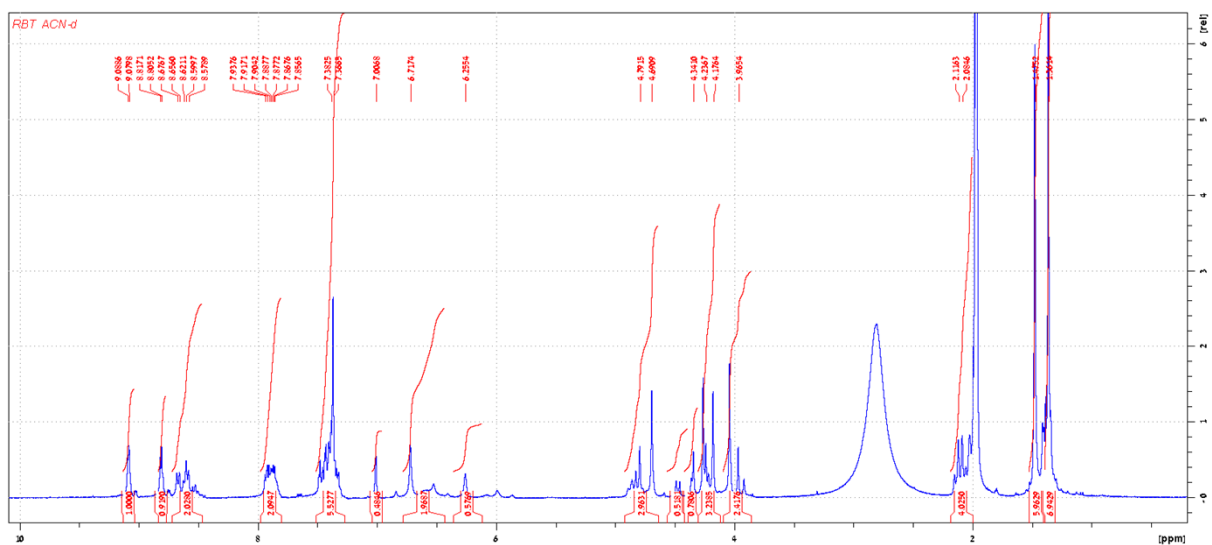
## **<sup>1</sup>H NMR Spectra**



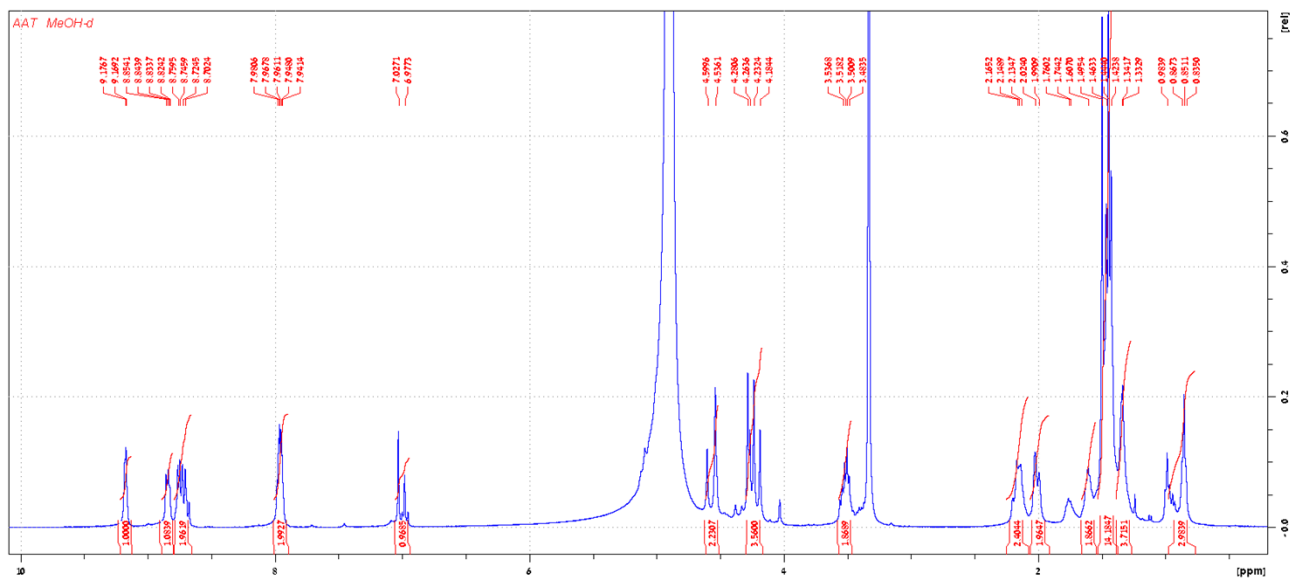
**Figure S38.** <sup>1</sup>H NMR spectra of **DI** in CD<sub>3</sub>OD



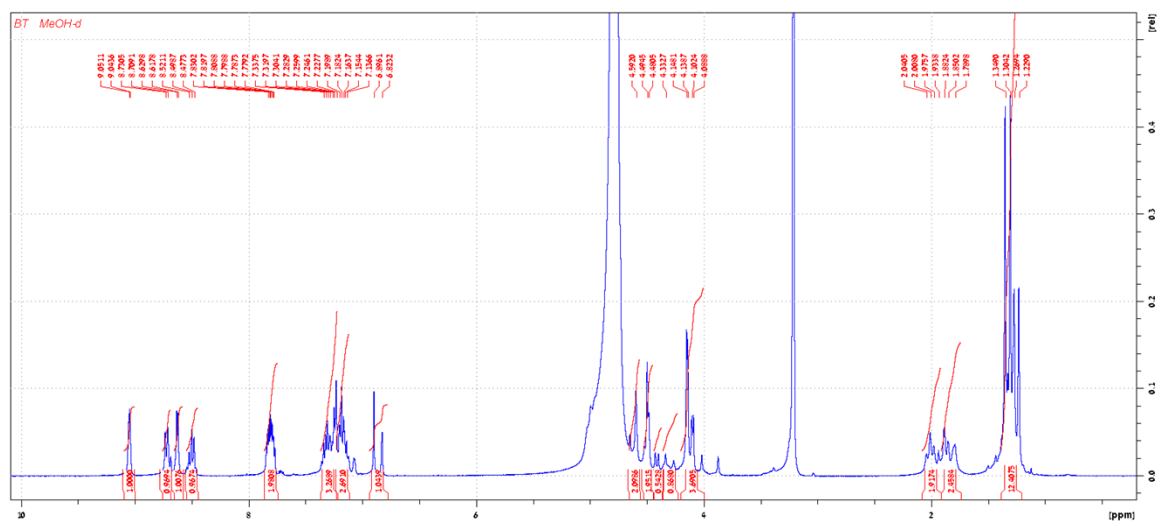
**Figure S39.** <sup>1</sup>H NMR spectra of **MT** in CD<sub>3</sub>OD



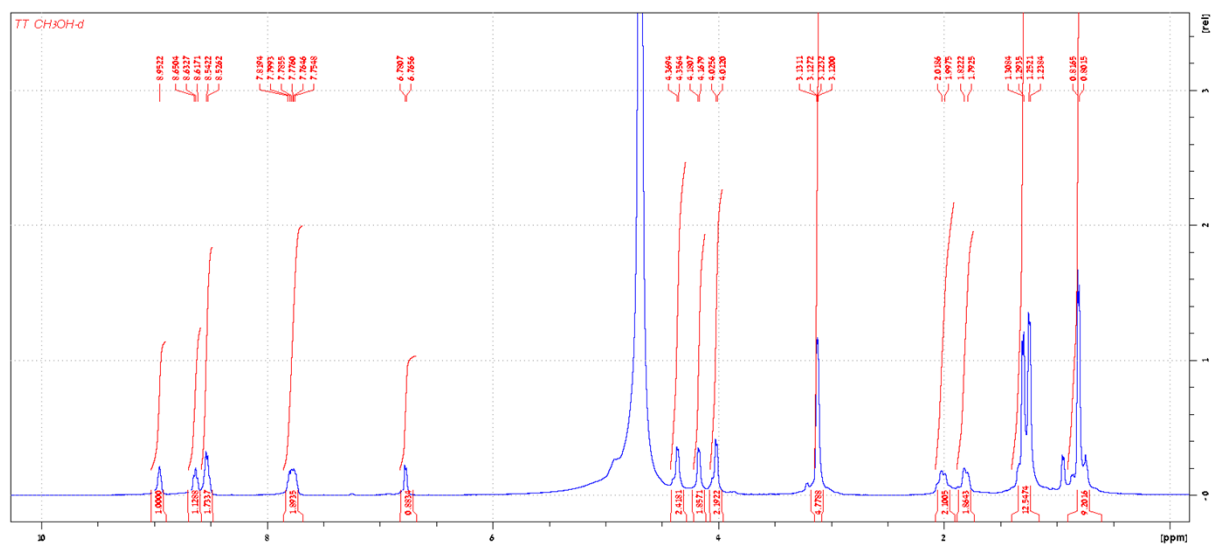
**Figure S40.**  $^1\text{H}$  NMR spectra of **RBT** in  $\text{CD}_3\text{OD}$



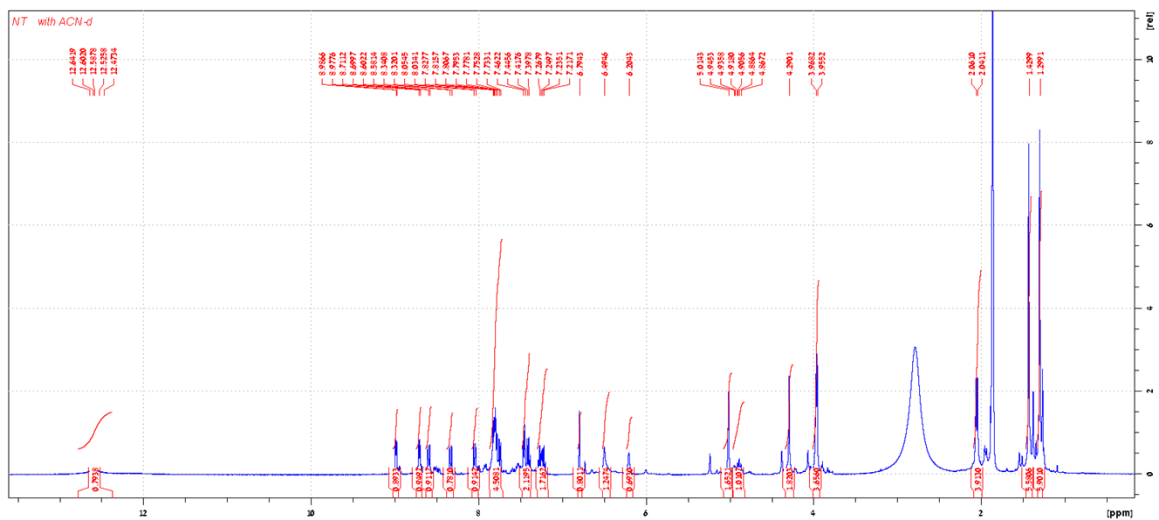
**Figure S14.**  $^1\text{H}$  NMR spectra of **PT** in  $\text{CD}_3\text{CN}$



**Figure S42.**  $^1\text{H}$  NMR spectra of **BT** in  $\text{CD}_3\text{OD}$



**Figure S43.**  $^1\text{H}$  NMR spectra of TT in  $\text{CD}_3\text{OD}$



**Figure S44.**  $^1\text{H}$  NMR spectra of NT in  $\text{CD}_3\text{CN}$