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Supporting Information

Targeting the Transmembrane Domain 5 of Latent Membrane Protein 1 Using Small Molecule Modulators

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Supplementary figures

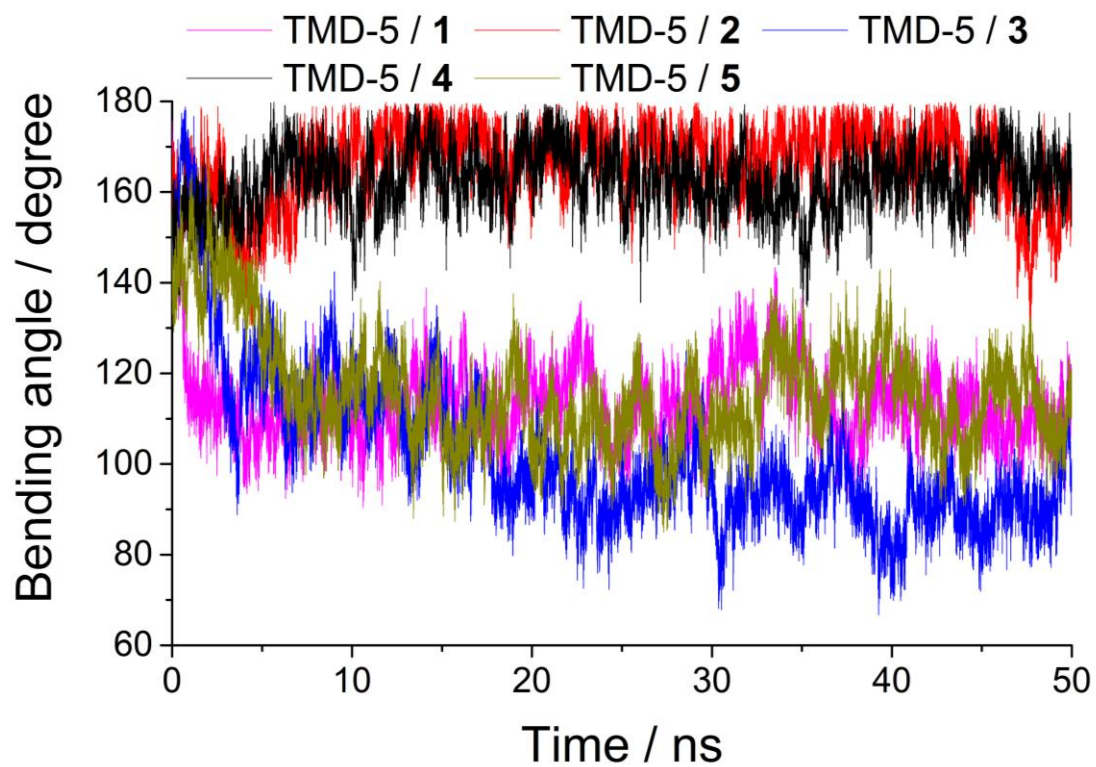
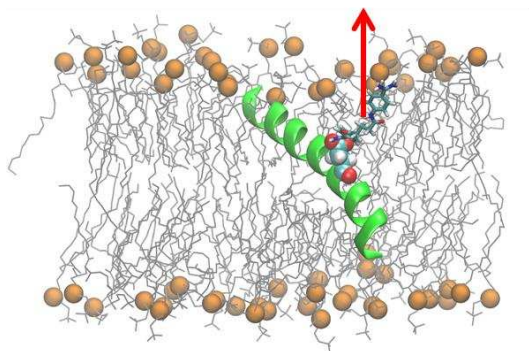


Figure S1. Bending angle of TMD-5 during molecular dynamics simulations with the influence of compound **1 – 5**.

TMD-5 / 2



TMD-5 / 4

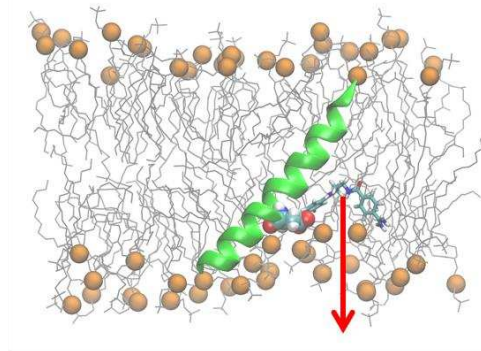


Figure S2. Definition of reaction coordinates for compound binding to TMD5. The reaction coordinate for TMD-5/2 is Z_{COM} of non-hydrogen atoms of compound - $Z_{\text{carbon atom of carboxyl group of D150}}$ and the reaction coordinate for TMD5/4 is $Z_{\text{carbon atom of carboxyl group of D150}}$ - Z_{COM} of non-hydrogen atoms of compound.

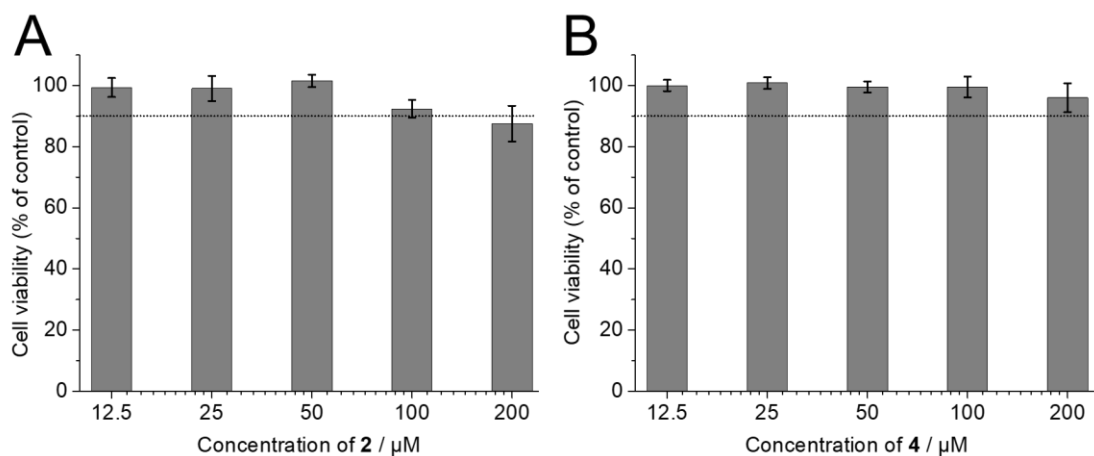


Figure S3. Cell viability measured by the MTT assay. The MTT assay indicated that compounds **2** and **4** were nontoxic to the MDCK cells at the concentration of 100 μM .

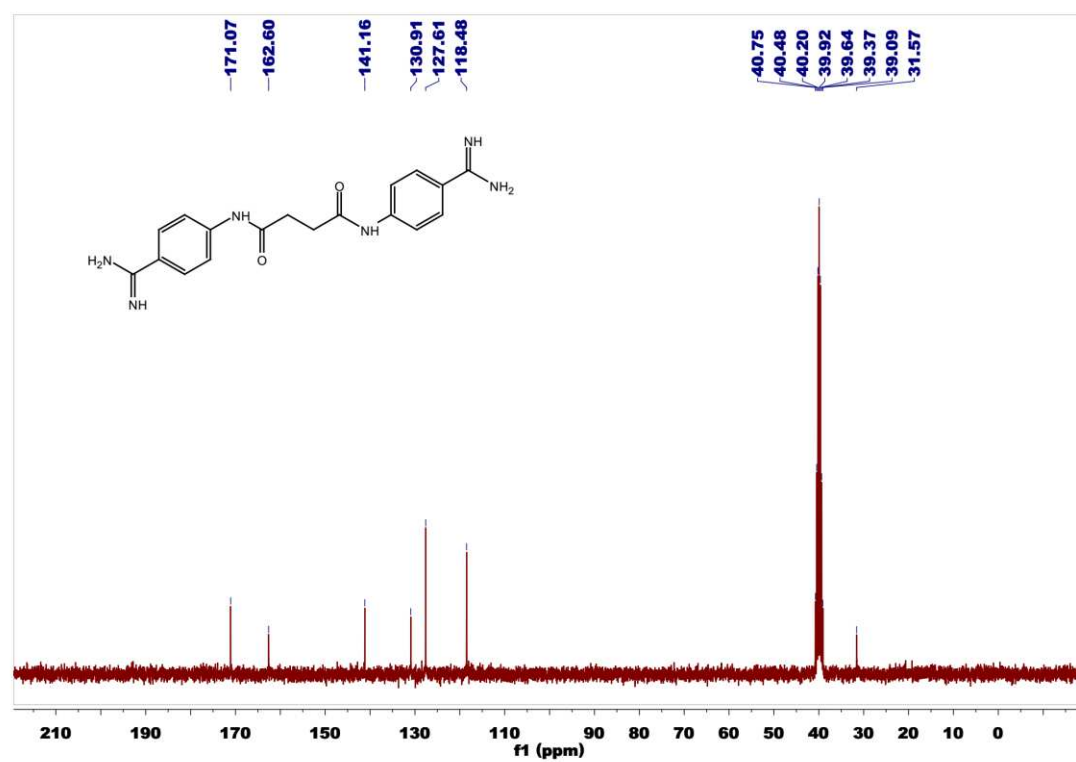
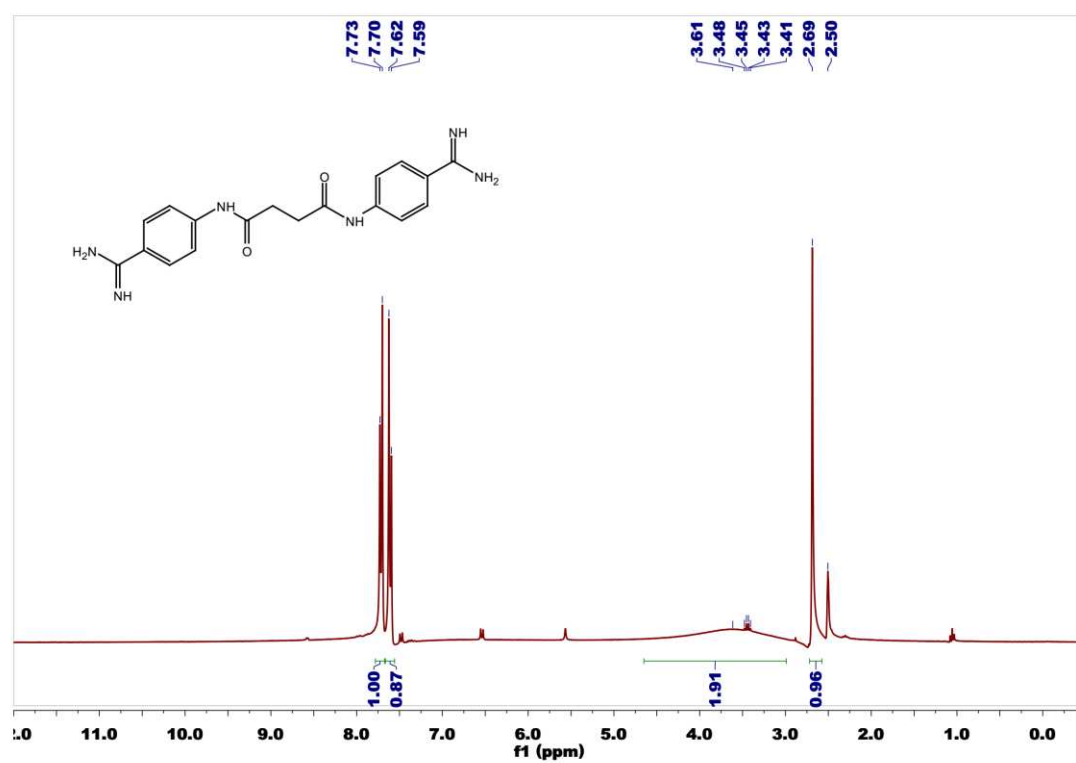


Figure S4. NMR spectra of compound 1.

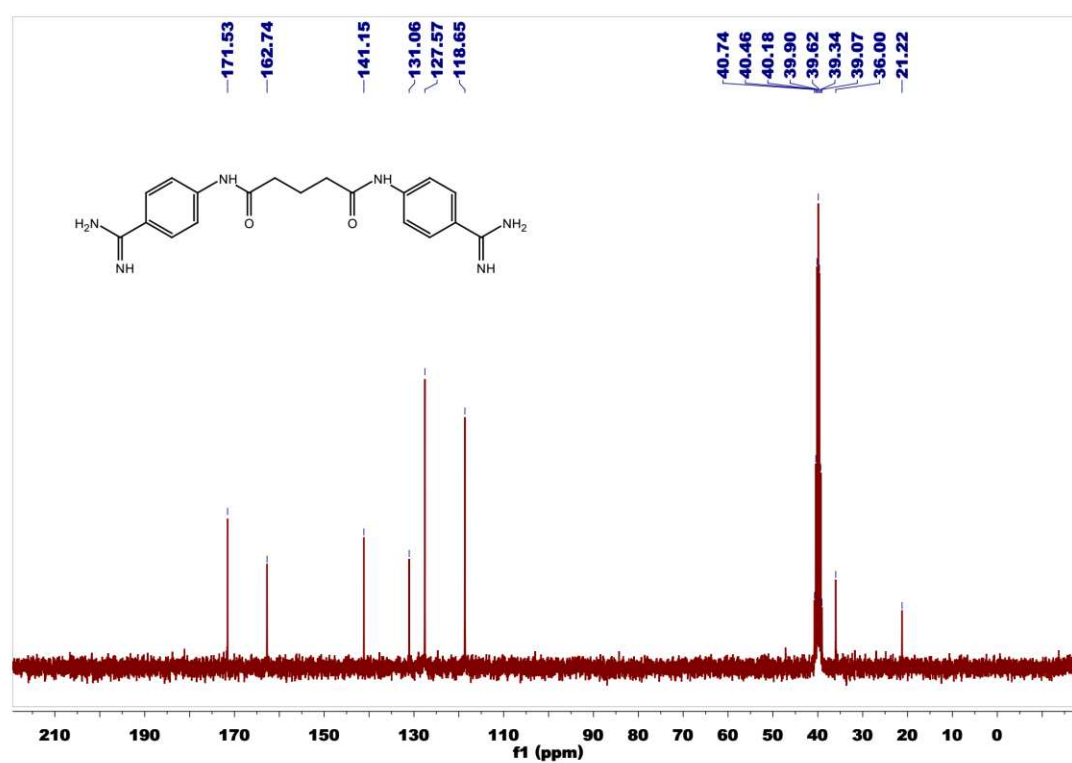
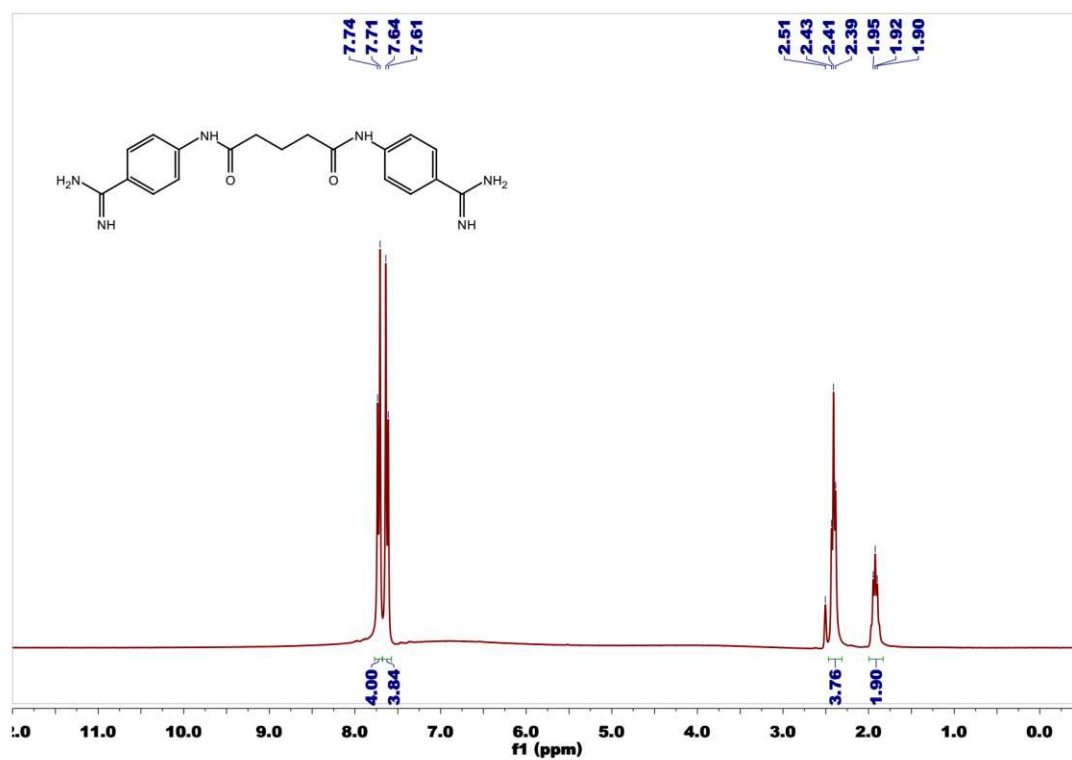


Figure S5. NMR spectra of compound 2.

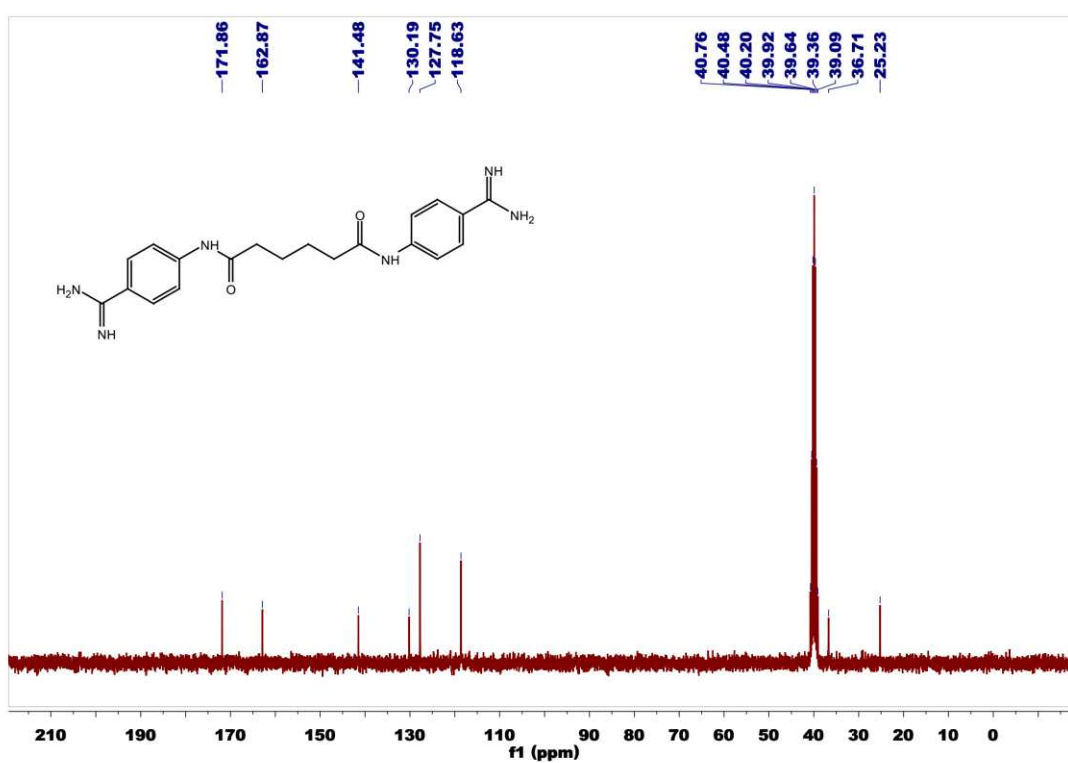
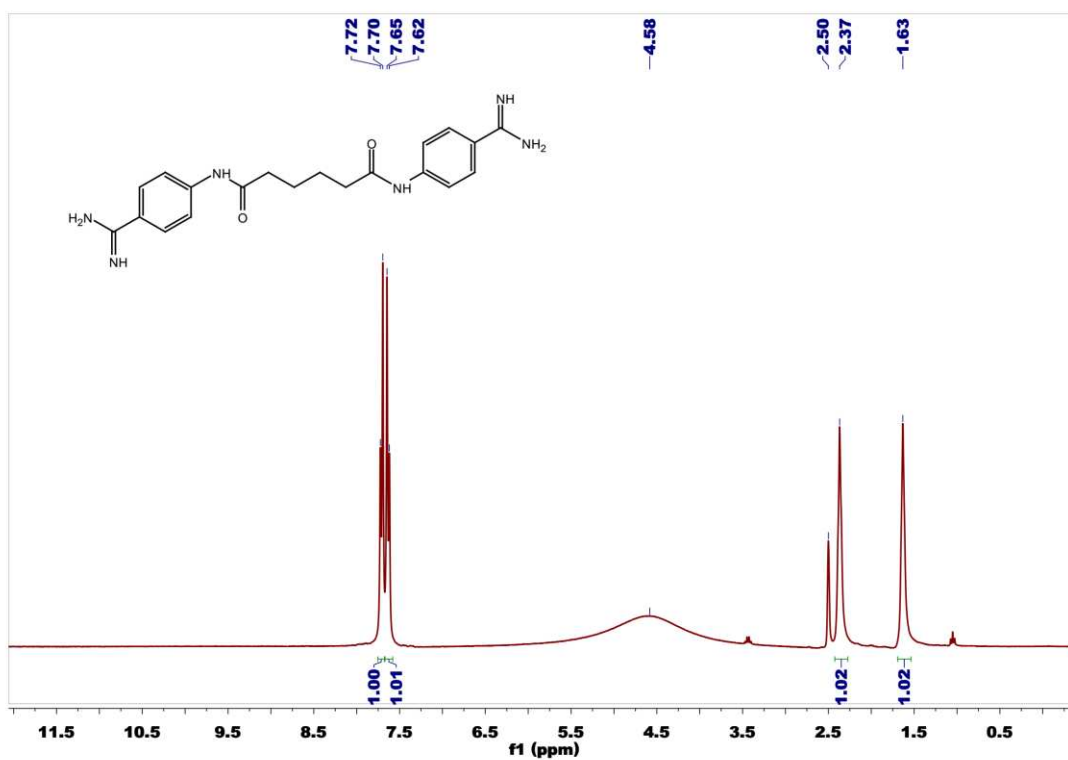


Figure S6. NMR spectra of compound 3.

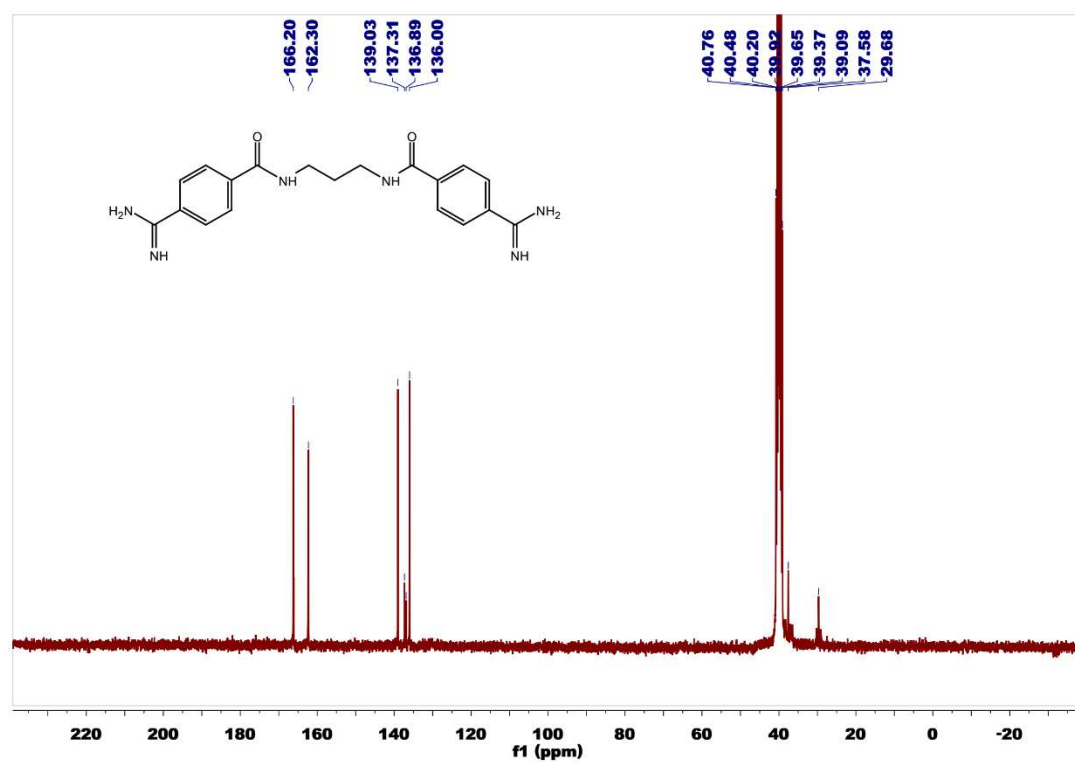
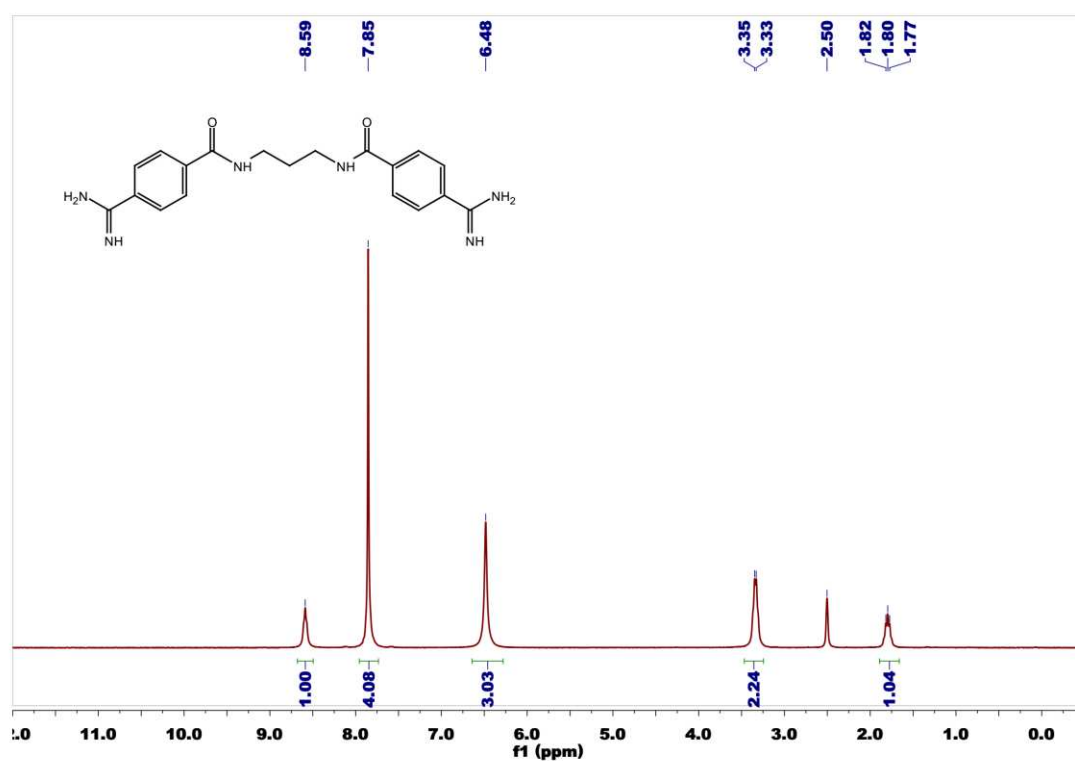


Figure S7. NMR spectra of compound 4.

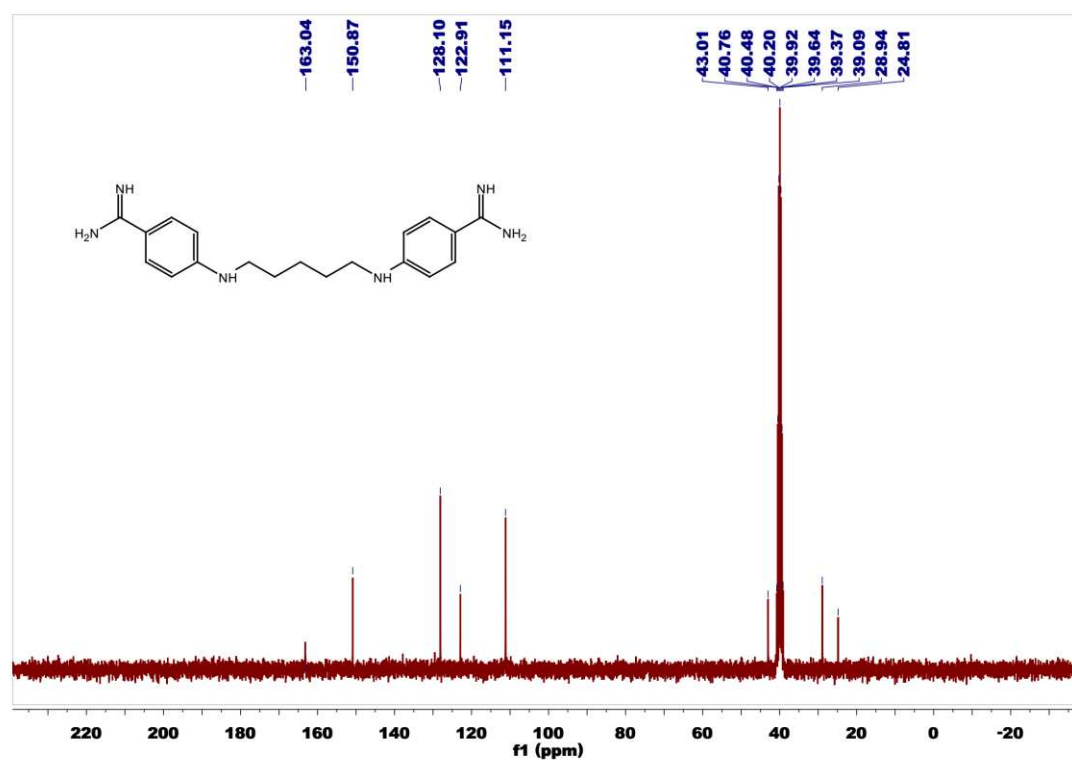
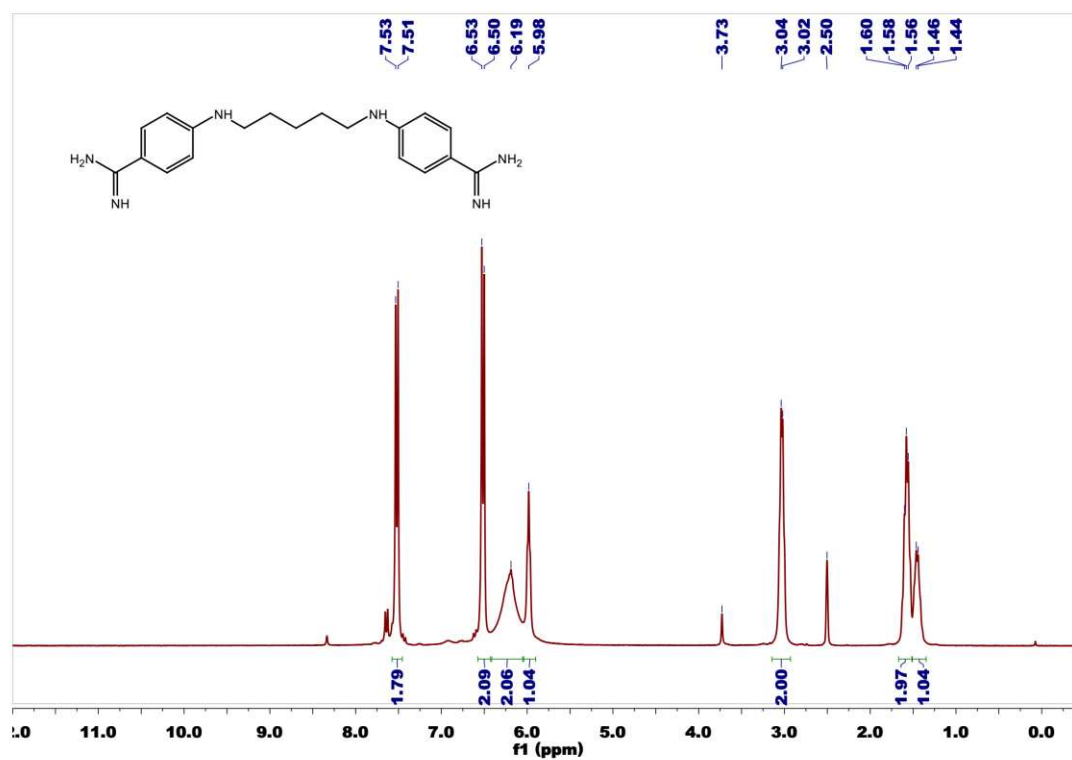


Figure S8. NMR spectra of compound 5.

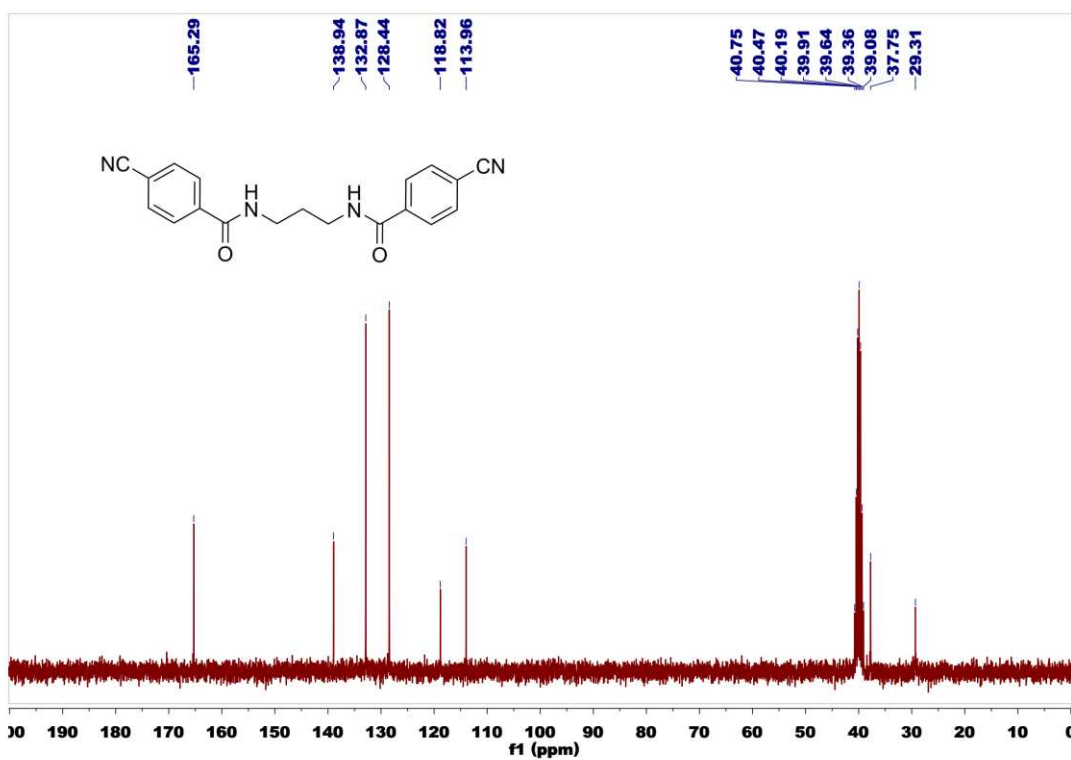
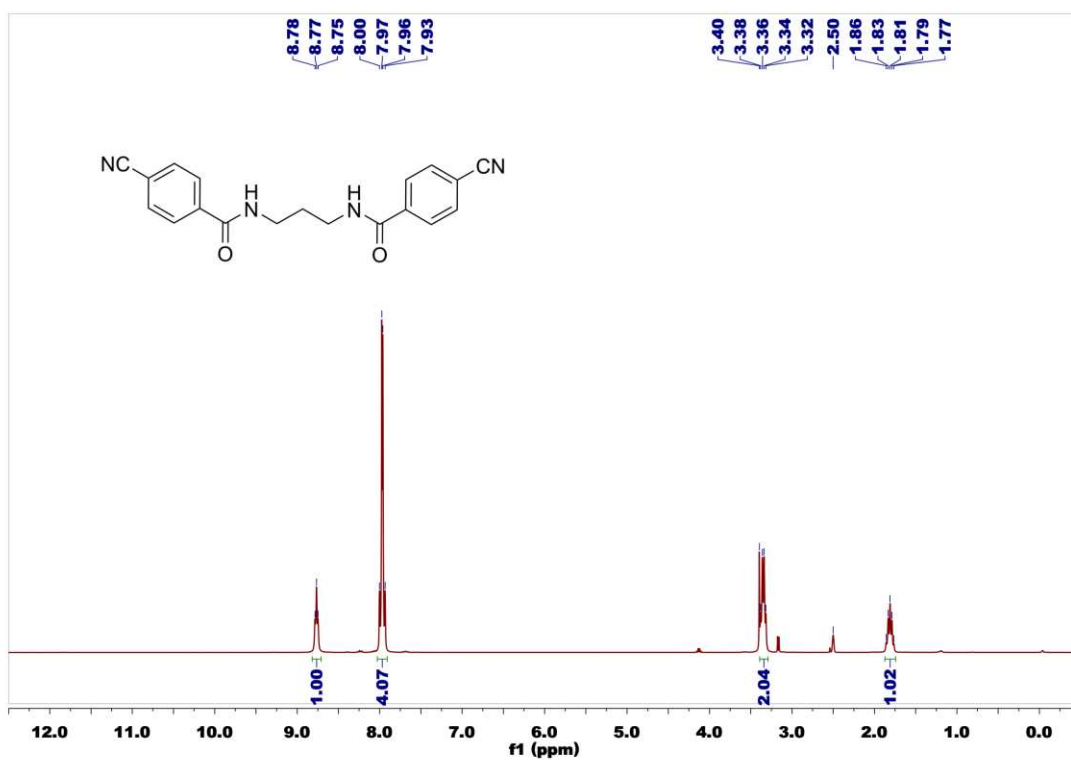


Figure S9. NMR spectra of compound 9.

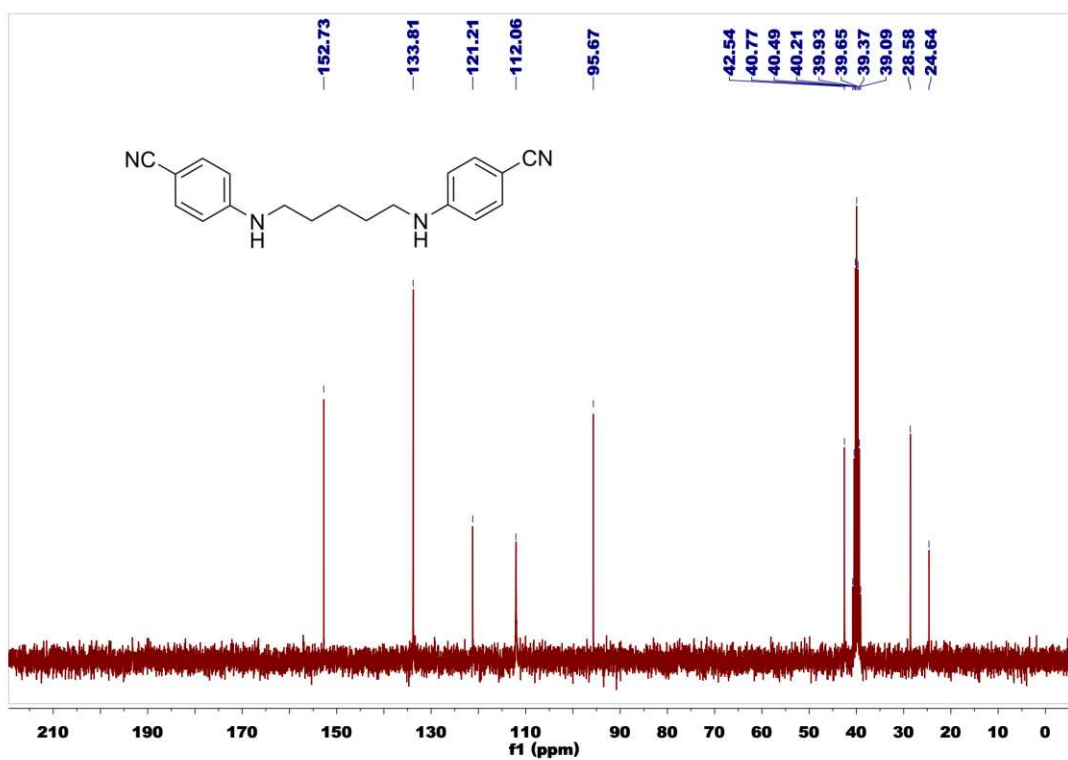
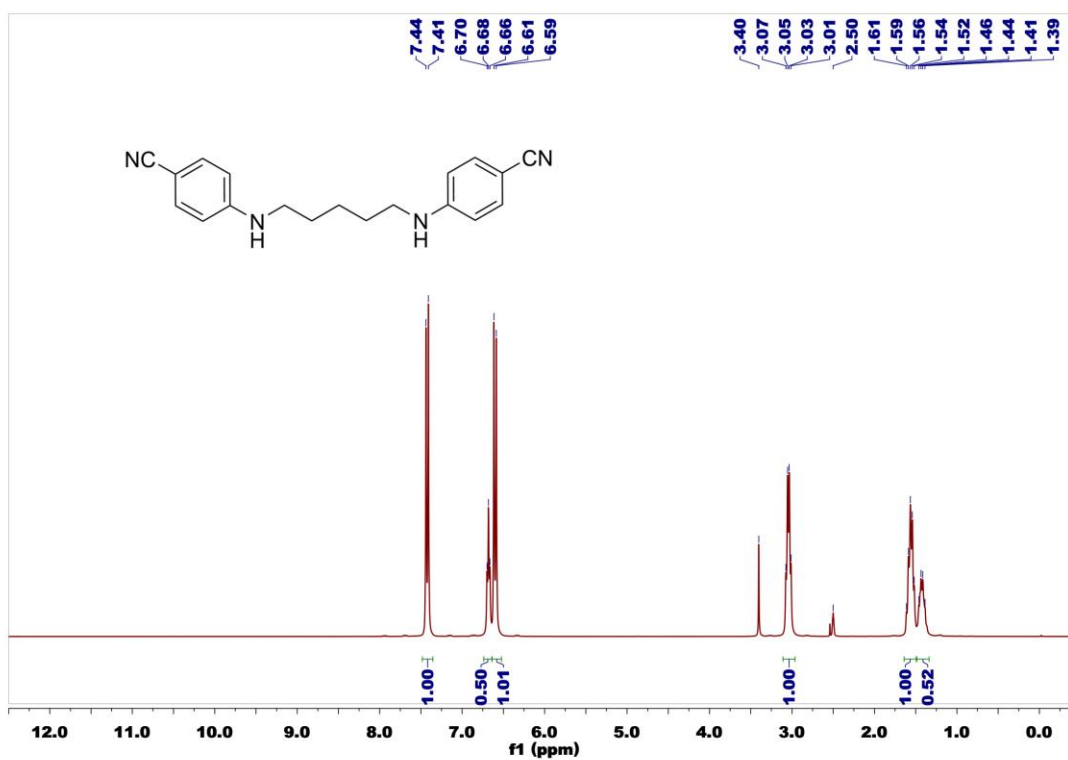


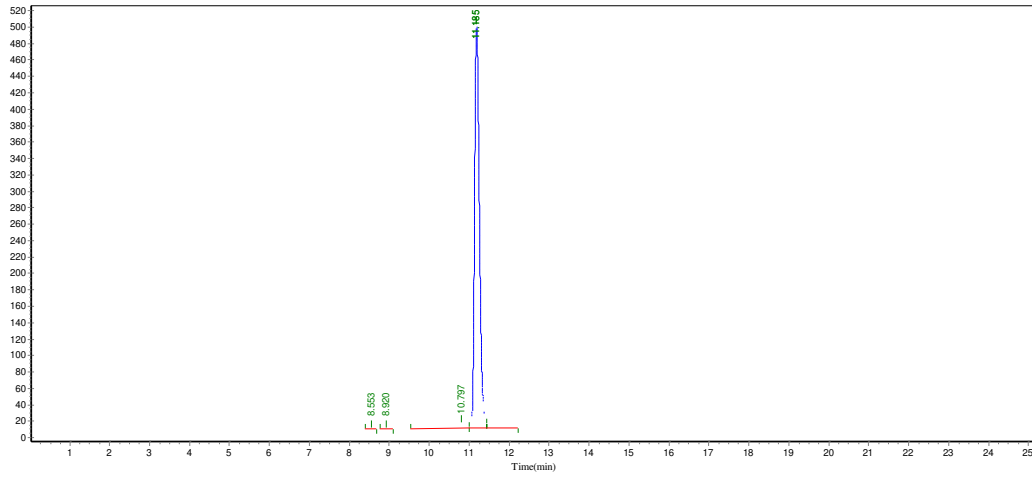
Figure S10. NMR spectra of compound 11.

Figure S11. HPLC Report for TMD-5

Structure : TMD-5
 Column : 4.6×250mm, Venusil MP C18-5
 Solvent A : 0.1% trifluoroacetic in 100% acetonitrile
 Solvent B : 0.1% trifluoroacetic in 100% water
 Gradient :

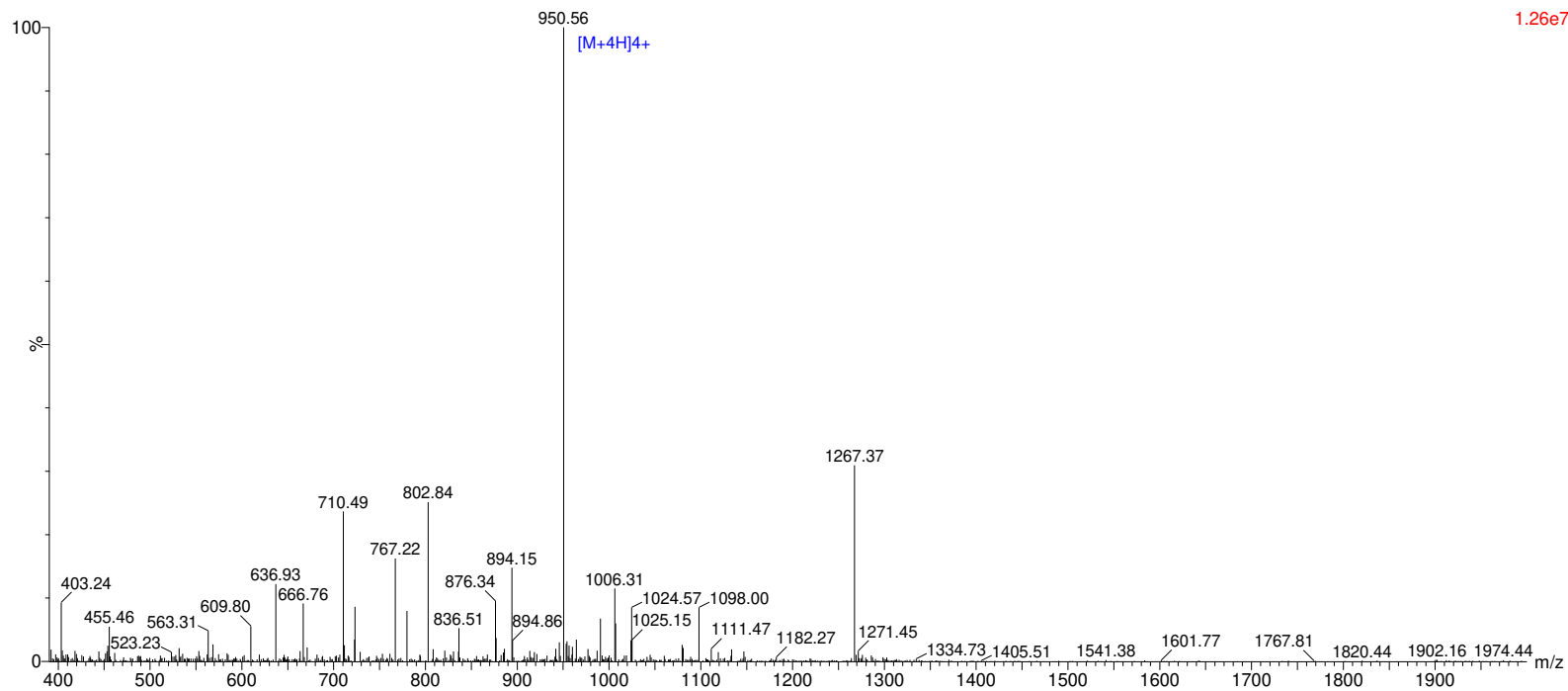
| | A | B |
|---------|------|-----|
| 0.01min | 55% | 45% |
| 25min | 100% | 0% |
| 25.1min | 100% | 0% |
| 30min | STOP | |

Flow rate : 1.0 mL/min
 Wavelength : 220nm
 Volume : 5ul



| Peak No. | Ret Time | Height | Area | Conc.. |
|----------|----------|------------|-------------|----------|
| 1 | 8.553 | 335.982 | 2560.503 | 0.0601 |
| 2 | 8.920 | 1142.773 | 8896.888 | 0.2089 |
| 3 | 10.797 | 7004.221 | 75740.398 | 1.7785 |
| 4 | 11.185 | 490966.563 | 4109966.750 | 96.5070 |
| 5 | 11.185 | 5274.425 | 61557.281 | 1.4454 |
| Total | | | | 100.0000 |

Figure S12. Mass Spectrometry Report for TMD-5



1.26e7

Sample Description

Analyzed date: 2016-11-15
 Analyst: YU
 Sample: TMD-5
 M.W.: 3795.91
 Lot. No.: P161111-SY545400

Instrument

Probe:
 Nebulizer Gas Flow:
 CDL:
 CDL Temp.:
 Block Temp.:

Waters ZQ2000

ESI
 1.5L/min
 -20.0v
 250 °C
 200 °C
 Probe Bias: +4.5kv
 Detector: 1.5kv
 T.Flow: 0.2ml/min
 B. Conc.: 50%H2O/50%ACN