Peripherally "tertiary butyl ester" functionalized bipyridine cored dendrons: From Synthesis, Characterization to Molecular Dynamic Simulation study

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Synthesis

Carbon tetrabromide, 18-crown-6, 3,5-dihydroxy benzyl alcohol, triphenyl phosphine, *tert*-butyl bromoacetate, silica gel (100-200 and 60-120 mesh) for column chromatography, silica gel G-type for TLC (Avra) were used as received. Molecular sieves 4Å (Avra) was used after activating by heating in an oven at 120°C for 8h. Calcium chloride (anhydrous) and sodium sulphate anhydrous (Merck) were used as such for drying solvents. Double distilled water obtained by distilling pre-distilled water over alkaline potassium permanganate was used throughout the study. 99.5% acetone (SRL), acetonitrile (VETEC), chloroform (SRL), 99.5% dichloromethane (SRL), ethanol, 99.5% ethyl acetate (SRL), 99% hexane (SRL), and methanol (NICE) were used as obtained. 4,4'-bromomethyl 2,2'-bipyridine was prepared from the previously published literature.[1]

Instrumentations

^{1}H-NMR spectra were recorded on a Bruker 400MHz and 500MHz spectrometer in $CDCl_3$ solvent, ^{13}C-NMR was recorded on 100MHz Bruker spectrometer in $CDCl_3$, HRMS and ESI-MS mass spectrometry was recorded using XEVO-G2 XS QTOF mass spectrometer in positive mode. The DLS measurements were recorded using a dynamic light scattering (DLS) instrument (Zetasizer ZS, Nano series ZEN 3600, Malvern Instruments Ltd, U.K.) The contact angle measurements were performed by employing a Hol-marc HO-IOD-CAN-018 equipment at ambient temperature.

1. Synthesis of 3,5-bis(2'-(*tert*-butoxy)-2-oxoethoxy)benzyl bromide (G0-Br)

The product was obtained as a white solid, 70% yield. ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.47 (d, 2H), 6.34 (t, 1H), 4.41 (s, 4H), 4.31 (s, 2H), 1.42 (s, 18H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 168.84, 159.02, 139.94, 108.33, 102.08, 82.55, 65.29, 27.81.

2. Synthesis of 3,5-bis[3',5'-bis(2-(*tert*-butoxy)-2-oxoethoxy)benzyloxy]benzyl bromide (G1-Br)

The product was obtained as white solid, with 54% yield. ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.59-6.58 (m, 6H), 6.47 (t, *J* = 2.3 Hz, 1H), 6.44 (t, *J* = 2.0 Hz, 2H), 4.41 (s, 4H), 4.47 (s, 8H), 4.38 (s, 2H), 1.47 (s, 36H). ^{13}C NMR (100 MHz, $CDCl_3$): δ167.83, 160.26, 159.57, 140.01, 139.47, 108.55, 106.81, 102.52, 101.89, 82.47, 70.11, 66.16, 33.41, 28.20.

3. Synthesis of 3, 5 - bis [3', 5'-bis (2-(*tert*-butoxy)-2-oxoethoxy)benzyloxy]benzyl alcohol (G1-OH)

The crude product was purified by chromatography with hexane/ethyl acetate (2:1.5) as the eluent to yield a colorless oil, 90% yield. ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.57-6.52 (m, 6H), 6.39 (t, *J* = 2.3 Hz, 1H), 6.36 (t, *J* = 2.3 Hz, 2H), 4.87 (s, 4H), 4.54 (s, 2H), 4.41 (s, 8H), 1.41 (s, 36H). ^{13}C NMR (100 MHz, $CDCl_3$): δ167.80, 159.92, 159.20, 139.52, 106.92, 101.36, 82.46, 69.69, 65.72, 65.37, 28.03 HR-MS Chemical Formula $C_{45}H_{60}O_{15}$ $[M+H]^+$ m/z : 841.4019 Exact Mass: 840.393u

4. Synthesis of 3,5-bis[3',5'-bis [3'', 5''-bis(2-(*tert*-butoxy)-2-oxoethoxy)benzyloxy] benzyloxyl] benzyl alcohol (G2-OH)

The crude product was purified by chromatography with hexane/ethyl acetate (2:1.5) as the eluent to yield a colorless oil (Yield 90%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.63 (d, *J* = 2.3 Hz, 4H), 6.59 (d, *J* =2.5 Hz, 10H), 6.51 (t, *J* = 2.3 Hz, 1H), 6.49 (t, *J* = 2.3 Hz, 2H), 6.43 (t, *J* = 2.3 Hz, 4H), 4.94 (s, 12H), 4.47 (s, 2H), 4.48 (s, 16), 1.47 (s, 72H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 167.77, 160.17, 160.11, 139.54, 106.68, 106.54, 105.97, 101.79, 101.68, 82.36, 66.01, 28.05 HRMS Chemical Formula $C_{97}H_{124}O_{31}$ $[M+H]^+$ m/z: 1785.816 Exact Mass: 1784.813u

5. Synthesis of 4,4'-bis [3'',5''-bis(2-(*tert*-butoxy)-2-oxoethoxy)benzyloxy]2,2'-bipyridine (G0-bpy)

The product was obtained as a reddish oil liquid, yield of 98% ^{1}H-NMR $CDCl_3$- δ 1.48 (36H-CH_3), δ 4.47 (4H-CH_2), δ 4.59 (4H- CH_2-O), δ 6.39 (2H, Ar-H) , δ 6.52 (4H Ar-H) , δ 7.28 (2 H, Ar-H (bpy), δ 8.43(4 H Ar-H (bpy)) ^{13}C-NMR $CDCl_3$ δ 27.88 CH_3 ,5.703 CH_2, δ 77.32 CH_2, δ 82.44 (t-*butyl*-C), δ 100.87 (Ar-C), δ 106.14(Ar-C), δ 121.11(Ar-C(Bpy)), δ 123.89 (Ar-C-(bpy)), δ143.79 (Ar-C), δ 147.43 (Ar-C-(bpy)), δ 149.63 (Ar-C-(bpy)), δ159.35 (Ar-C-O), δ

167.89 (C=O). ESI MS Chemical Formula: $C_{50}H_{64}N_2O_{14}$ m/z $[M]^+$ 916.44 Exact Mass: 916.44u

6. **Synthesis of 4,4'- [3'',5''-bis[3''',5'''-bis(2-(*tert*-butoxy)-2-oxoethoxy)benzyloxy] benzyloxyl] 2,2'-bipyridine G1-bpy**

The product was obtained as a red oily liquid with a yield of 96.9%. ^{1}H NMR $CDCl_3$: δ 1.33 (72H, s), 4.43-4.46 (20H, 4.43 (s), 4.46 (s)), 4.61 (4H, s), 4.90 (8H, s), 6.30 (6H), 6.52 (12H), 7.38 (2H), 8.41 (2H), 8.55 (2H, d). ^{13}C NMR $CDCl_3$: δ 28.98 (24C, s), 65.45 (8C, s), 69.27 (8C, s), 81.32 (8C, s), 100.32-100.82 (6C,s), 120.72 (4C, s), 140.6-140.8 (6C,s), 146.7 (2C, s), 149.9 (4C, s), 159.50 (12C,)167.1 (8C, s). HRMS Chemical Formula: $C_{102}H_{128}N_2O_{30}$ m/z: $[M+H]^+$ 1861.8585 Exact Mass: 1860.8552 u

7. Synthesis of 4,4'-bis [3'',5''-bis [3''',5'''-bis [3'''',5''''-bis (2-(*tert*-butoxy)-2-oxoethoxy)benzyloxy] benzyloxy] benzyloxyl] 2,2'- bipyridine G2-bpy

The product was obtained as a red oily liquid with a yield of 69.7%. ^{1}H NMR $CDCl_3$: δ 1.47 (144H, s), 4.48-4.62 (40H, (s)), 4.95 (24H,(s)), 6.42-6.59 (14H), 6.59 (28H), 7.27 (2H, ddd,), 7.34 (2H, dd,), 8.35-8.64 (4H, ddd) ^{13}C NMR $CDCl_3$: δ 28.05, 65.80, 69.81, 77.05, 82.43, 101.18-100.57, 106.51, 139.46, 159.46, 160.00, 160.05, 167.78. HRMS Chemical Formula: $C_{206}H_{256}N_2O_{62}$ m/z $[M+1]^+$ 3750.70.43 Exact Mass: 3749.6941u

Dynamic light scattering analysis

Sample Preparation: Each dendrons stock solution was made as 1mg/mL in DMSO. Then the DLS analysis of the dendrons solutions (100 μL from stock) were carried out in DMSO-Water Mixture as given in the **Table S1**

Table S1. DLS measurement parameters

Solvent ratios (DMSO : Water) in 5mL	Refractive index	Viscosity cP	Dielectric constant
100 % of DMSO	1.4768	1.99	46.68
75 % of DMSO	1.4457.	3.68	55.00
50% of DMSO	1.4071	2.83	64.67
25% of DMSO	1.3677	1.50	72.88
100 % of Water	1.3225	0.89	78.4

Table S2. Models and simulation details. First an NPT simulation is performed, followed by an NVT simulation.

System	Initial simulation box size (Å×Å×Å)	Number of polymer molecules	Solvent	Number of solvent molecules	Conc. (mg/ml)	Simulation time (NPT) (ns)	Simulation box size after the NPT simulation ($Å^3$)	Final conc. (mg/ml)	Simulation time (NVT) (ns)
G0-bpy	50×50×50	1	Water	4181	12.19	10	53.20^3	10.12	40
G1-bpy	63×63×63	1	Water	8362	12.37	20	67.89^3	9.89	50
G2-bpy	80×80×80	1	Water	17124	12.17	30	84.20^3	10.44	65
G0-bpy	50×50×50	1	DMSO	1054	12.19	10	55.90^3	8.72	40
G1-bpy	63×63×63	1	DMSO	2118	12.37	20	65.90^3	10.81	50
G2-bpy	80×80×80	1	DMSO	4337	12.17	30	85.40^3	10.00	65

^{1}HNMR and ^{13}C-NMR and Mass spectral analysis

1. *t*-butyl iodoacetate

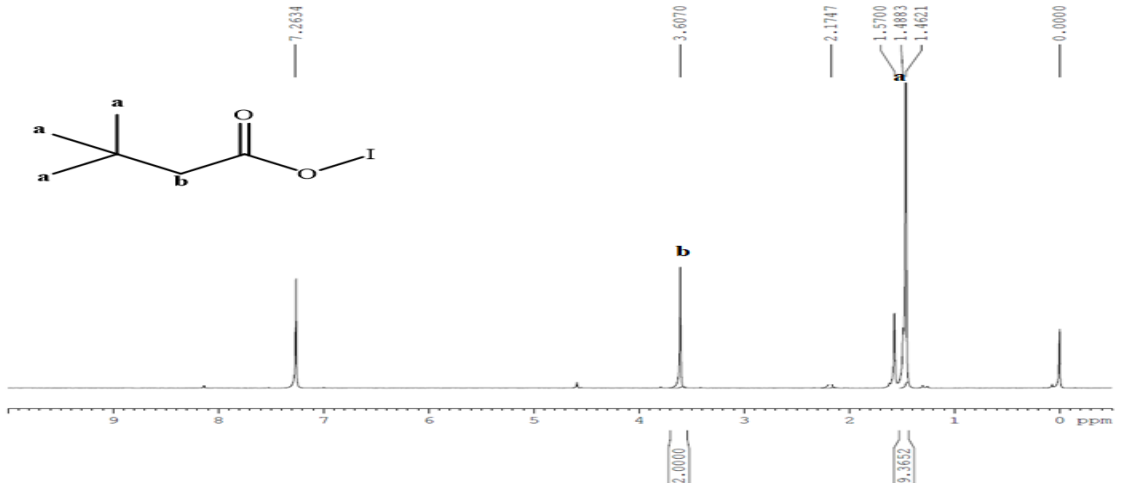

Figure S1. ^{1}H-NMR $CDCl_3$ spectra of *t*-butyl iodoacetate

2. 3,5-bis(2'-(tert-butoxy)-2-'oxoethoxy)benzyl alcohol (G0-OH)

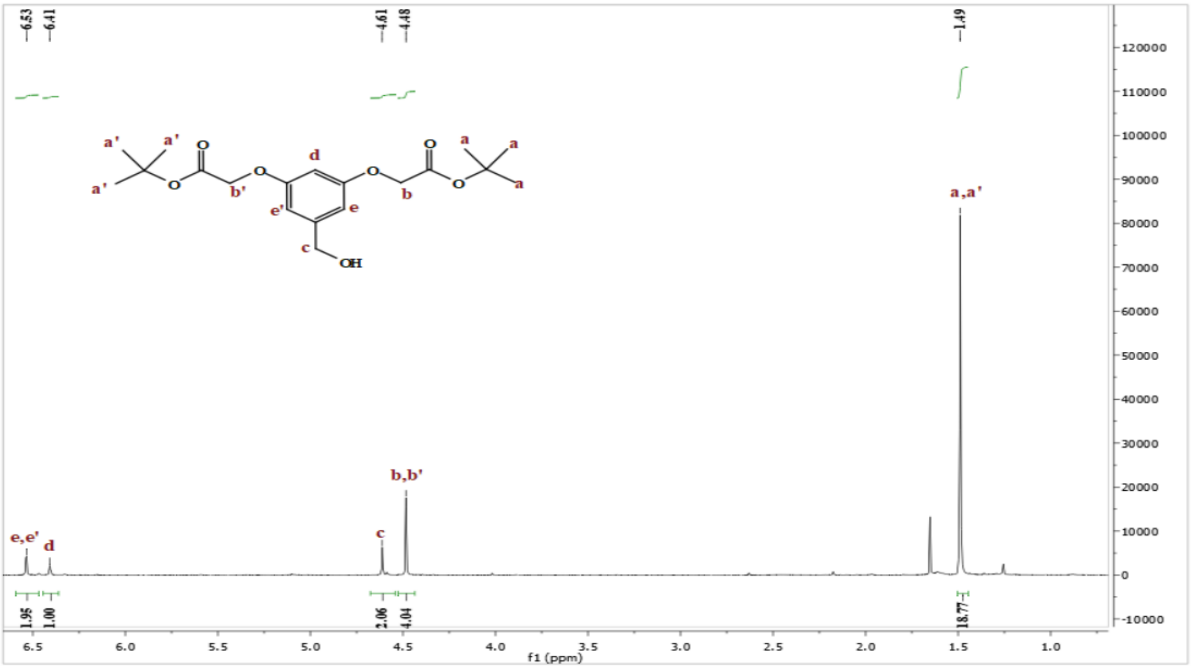

Figure S2. ^{1}HNMR $CDCl_3$ of **3,5-bis(2'-(tert-butoxy)-2-'oxoethoxy)benzyl alcohol (G0-OH)**

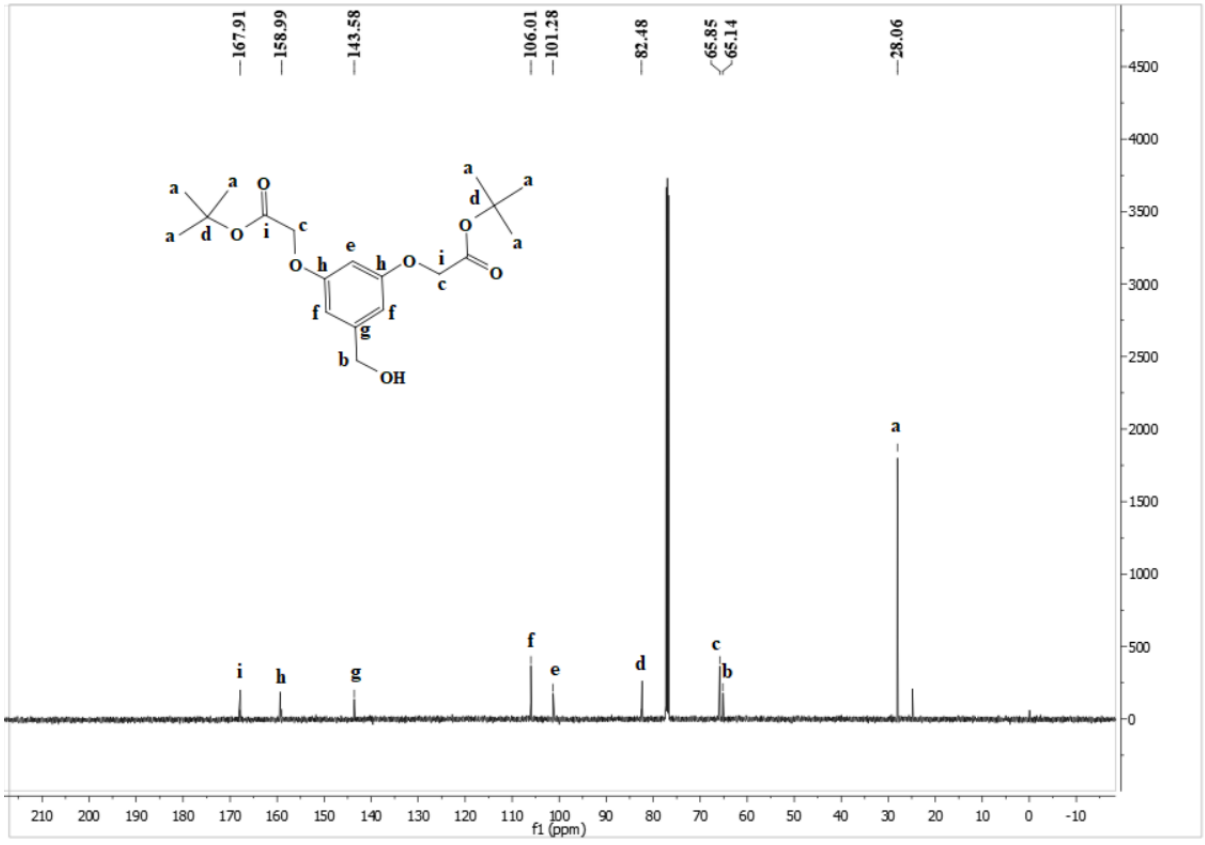

Figure S3. ^{13}C-NMR $CDCl_3$ of **3,5-bis(2'-(tert-butoxy)-2-'oxoethoxy)benzyl alcohol (G0-OH)**

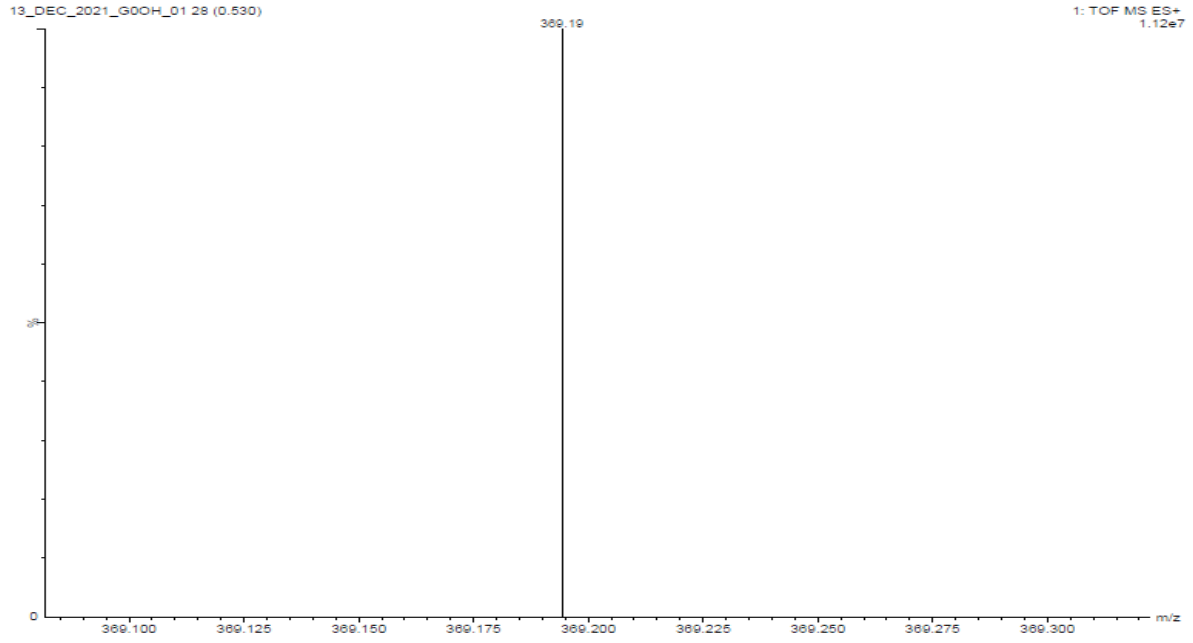

Figure S4. ESI MS spectra of **3,5-bis(2'-(tert-butoxy)-2-'oxoethoxy)benzyl alcohol (G0-OH)**

3. 3,5-bis(2'-(tert-butoxy)-2-oxoethoxy)benzyl bromide (G0-Br)

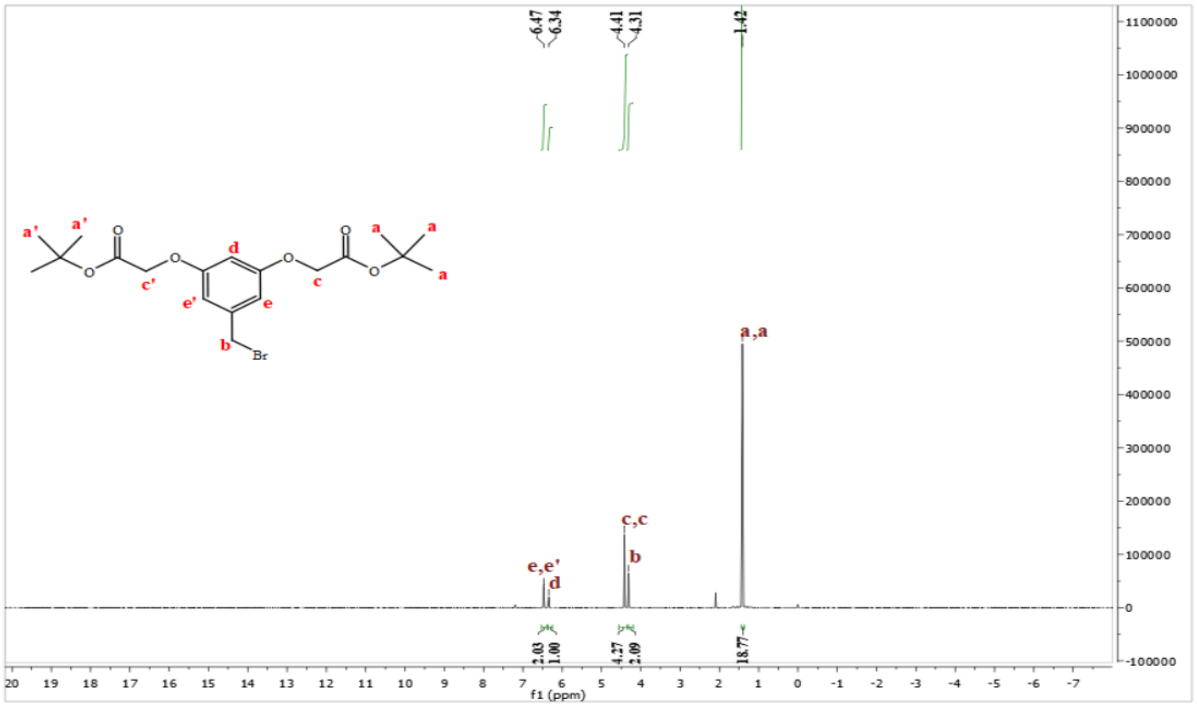

Figure S5. ^{1}HNMR $CDCl_3$ spectra of 3,5-bis(2'-(tert-butoxy)-2-oxoethoxy)benzyl bromide (G0-Br)

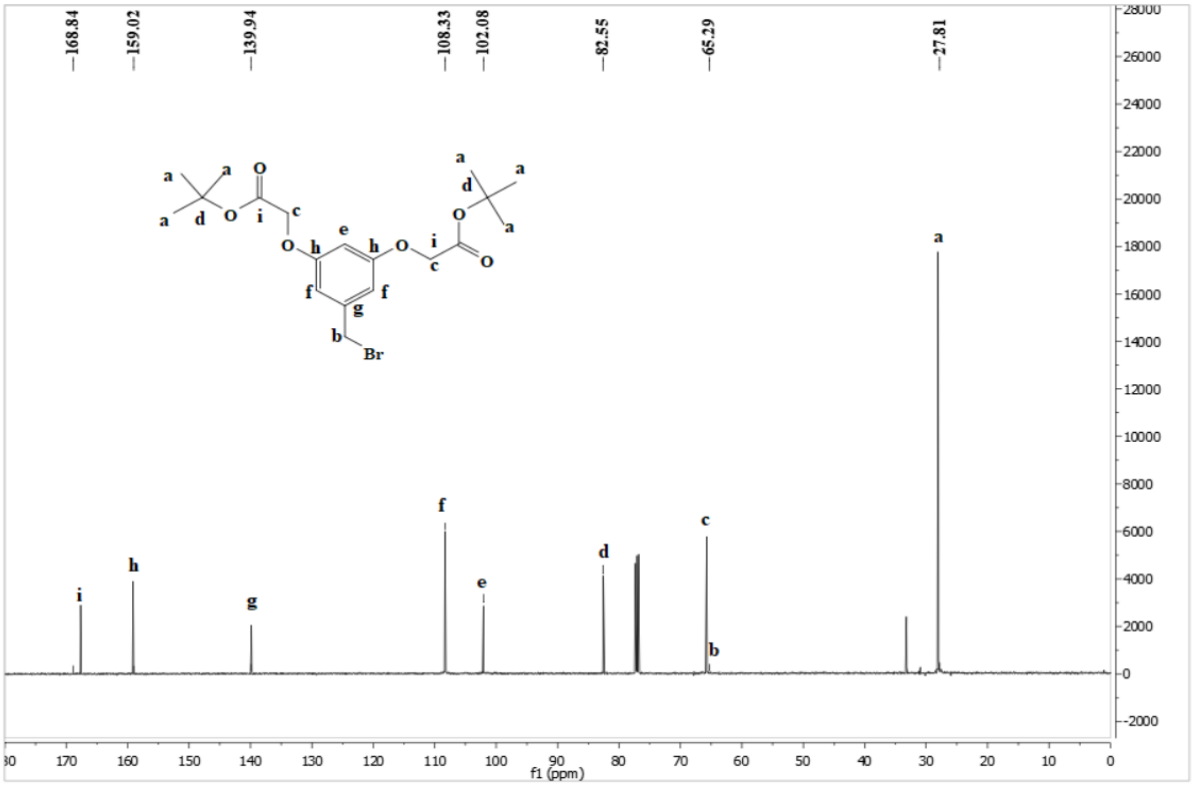

Figure S6. ^{13}CNMR $CDCl_3$ spectra of 3,5-bis(2'-(tert-butoxy)-2-oxoethoxy)benzyl bromide (G0-Br)

4. 3, 5 - bis [3', 5'-bis (2-(tert-butoxy)-2-oxoethoxy)benzyloxy]benzyl alcohol G1-OH

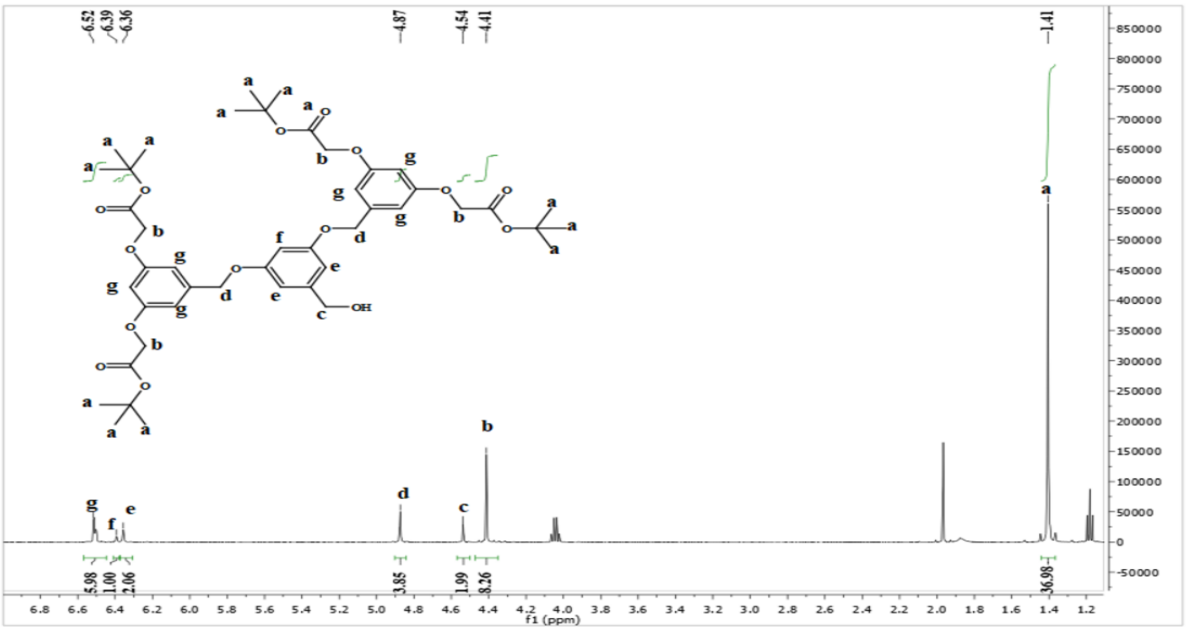

Figure S7. ^{1}HNMR $CDCl_3$ spectra of 3, 5 - bis [3', 5'-bis (2-(tert-butoxy)-2-oxoethoxy)benzyloxy]benzyl alcohol **G1-OH**

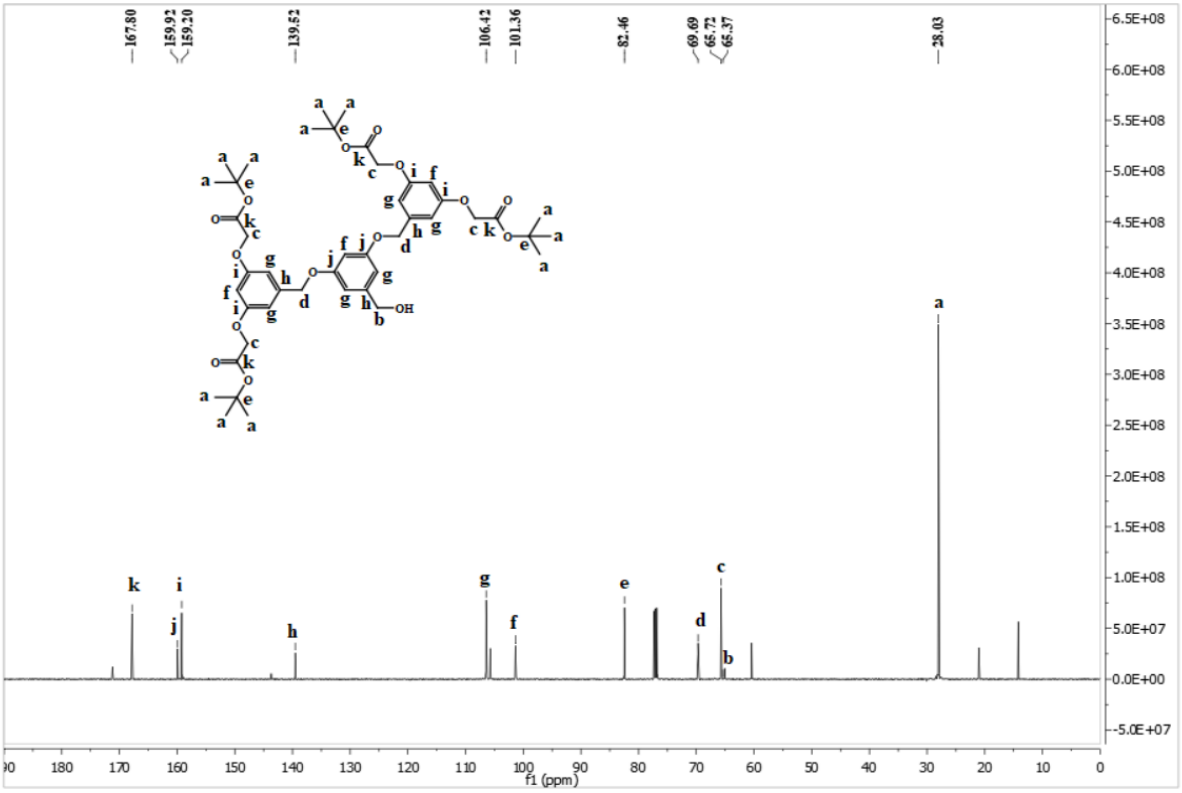

Figure S8. ^{13}C-NMR $CDCl_3$ spectra of 3, 5 - bis [3', 5'-bis (2-(tert-butoxy)-2-oxoethoxy)benzyloxy]benzyl alcohol **G1-OH**

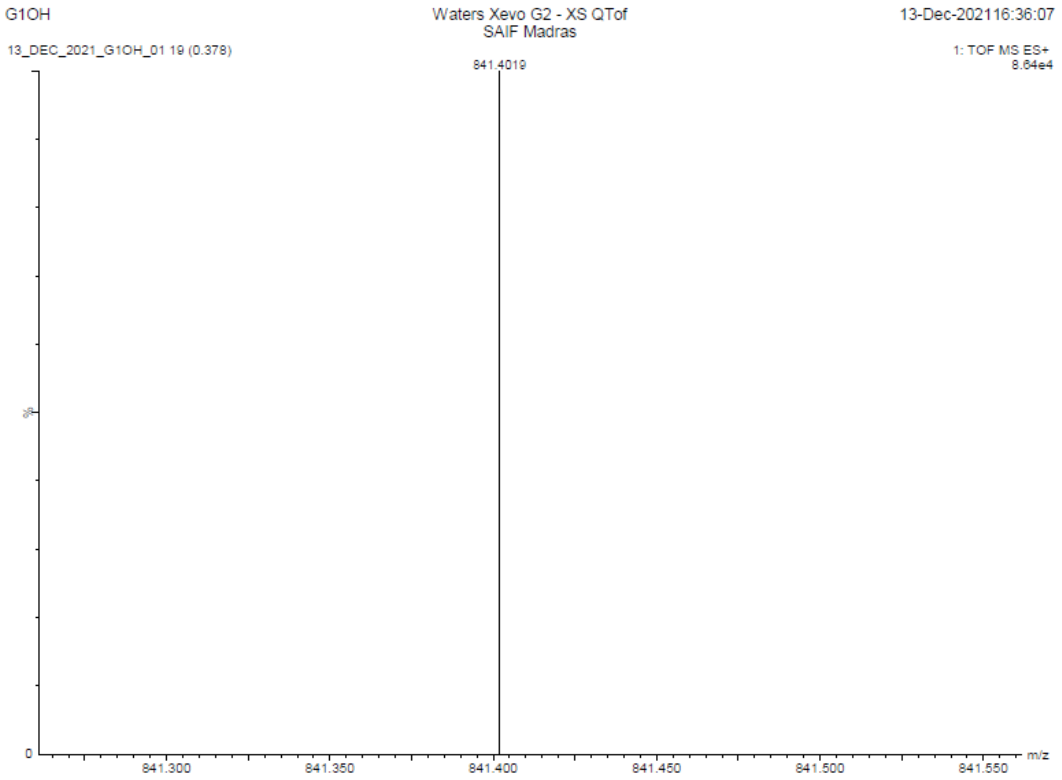

Figure S9. HRMS spectra of 3, 5 - bis [3', 5'-bis (2-(tert-butoxy)-2-oxoethoxy)benzyloxy]benzyl alcohol **G1-OH**

5. 3,5-bis[3',5'-bis(2-(tert-butoxy)-2-oxoethoxy)benzyloxy]benzyl bromide (G1-Br)

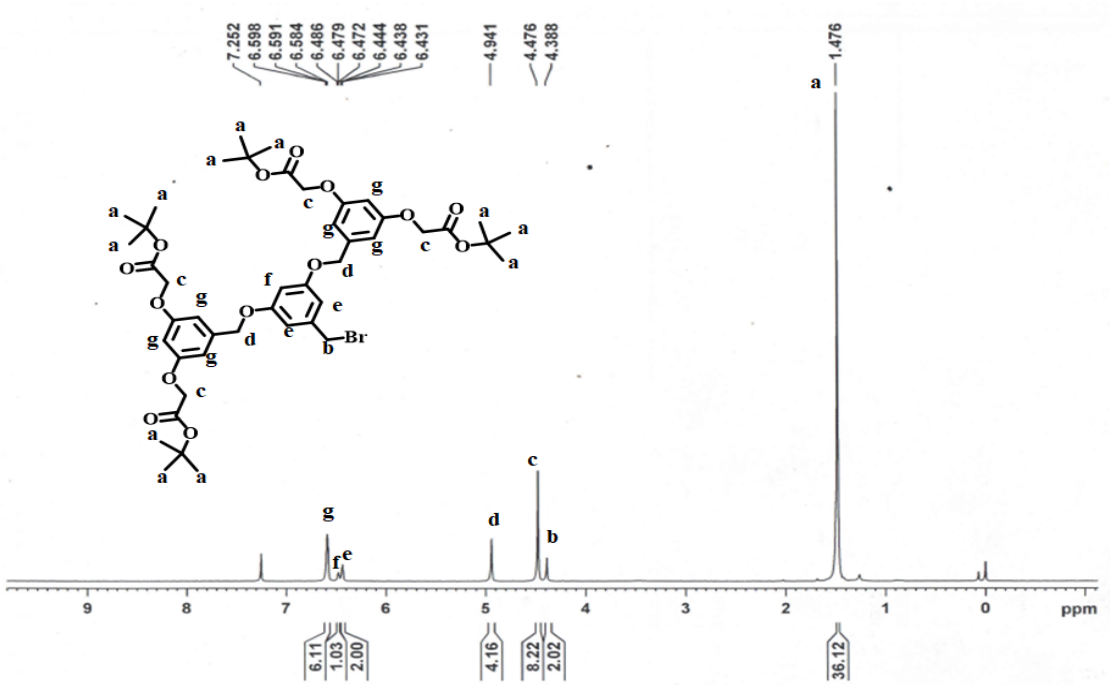

Figure S10. ^{1}HNMR $CDCl_3$ spectra of 3,5-bis[3',5'-bis(2-(tert-butoxy)-2-oxoethoxy)benzyloxy]benzyl bromide (**G1-Br**)

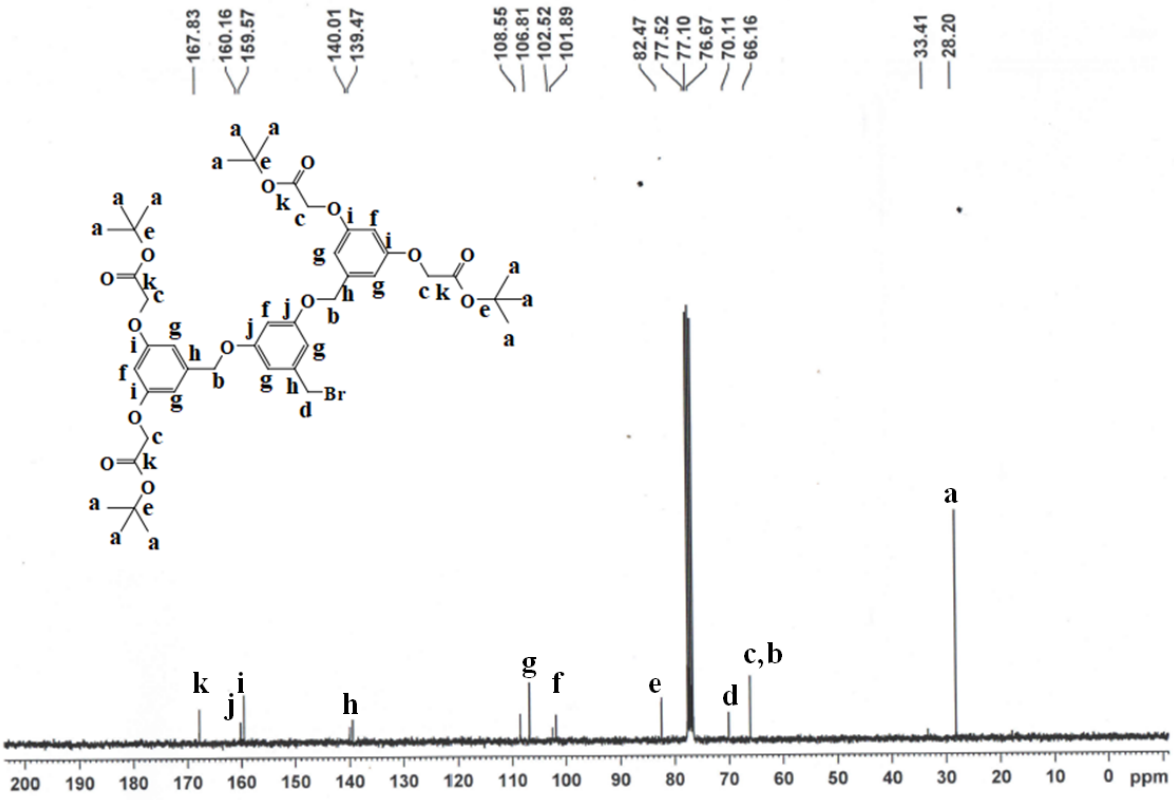

Figure S11. ^{13}C-NMR $CDCl_3$ spectra of 3,5-bis[3',5'-bis(2-(tert-butoxy)-2-oxoethoxy)benzyloxy]benzyl bromide (**G1-Br**)

6. 3,5-bis[3',5'-bis [3'', 5''-bis(2-(tert-butoxy)-2-oxoethoxy)benzyloxy] benzyloxyl] benzyl alcohol G2-OH

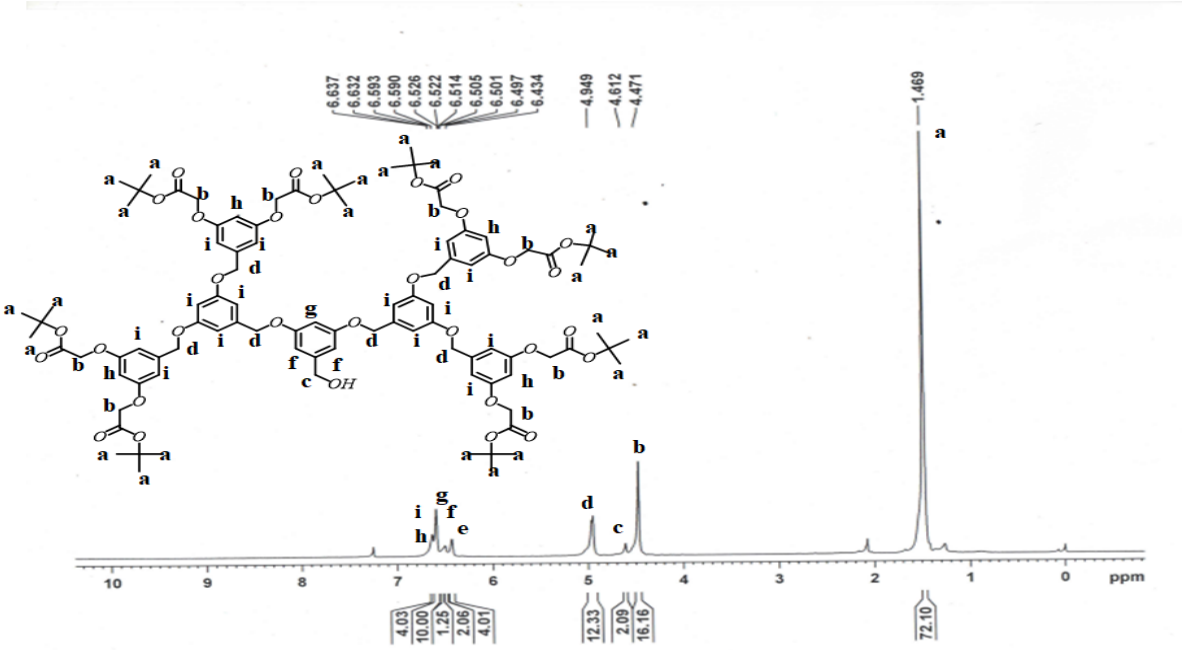

Figure S12. ^{1}H-NMR $CDCl_3$ spectra of 3,5-bis[3',5'-bis [3'', 5''-bis(2-(tert-butoxy)-2-oxoethoxy)benzyloxy] benzyloxyl] benzyl alcohol G2-OH

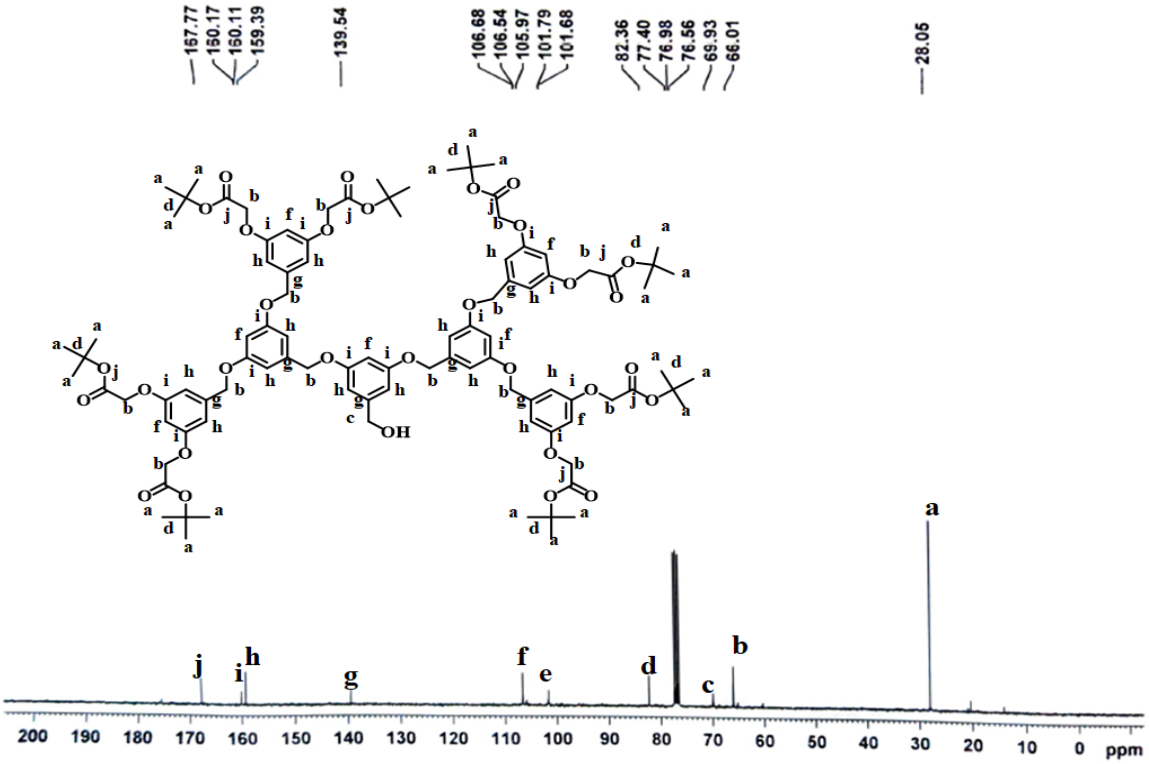

Figure S13. ^{13}C-NMR $CDCl_3$ spectra of 3,5-bis[3',5'-bis [3", 5"-bis(2-(tert-butoxy)-2-oxoethoxy)benzyloxy] benzyloxyl] benzyl alcohol **G2-OH**

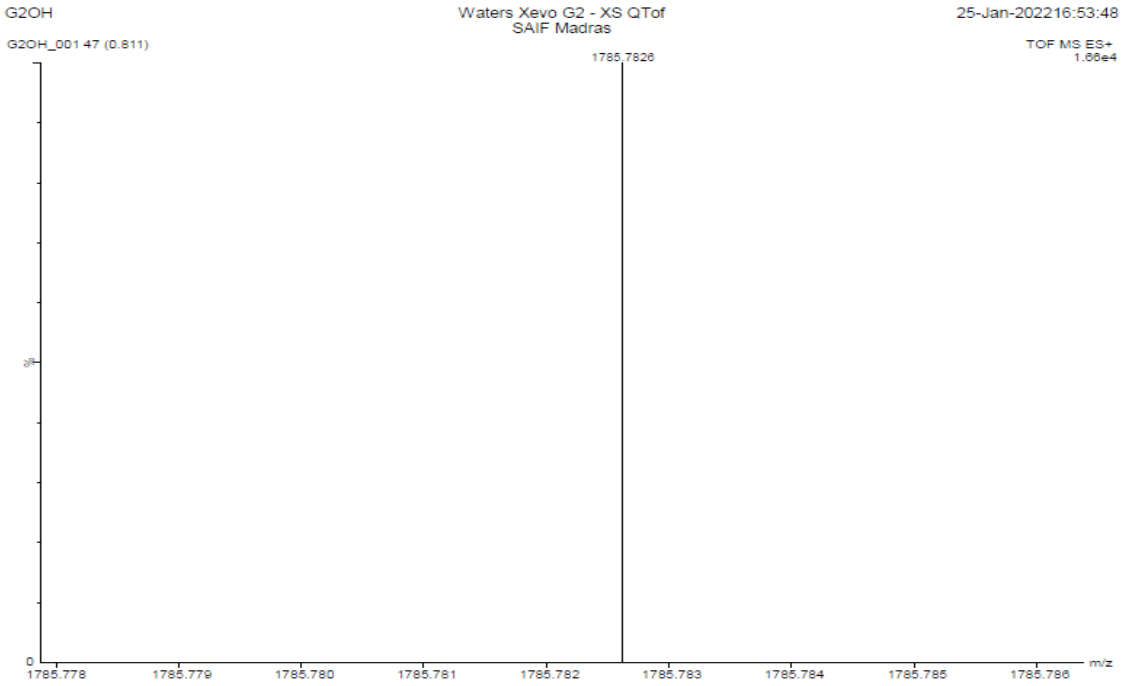

Figure S14. HRMS spectra of 3,5-bis[3',5'-bis [3", 5"-bis(2-(tert-butoxy)-2-oxoethoxy)benzyloxy] benzyloxyl] benzyl alcohol **G2-OH**

7. 4,4'-bis [3'',5''-bis(2-(tert-butoxy)-2-oxoethoxy)benzyloxy]2,2'-bipyridine G0-bpy

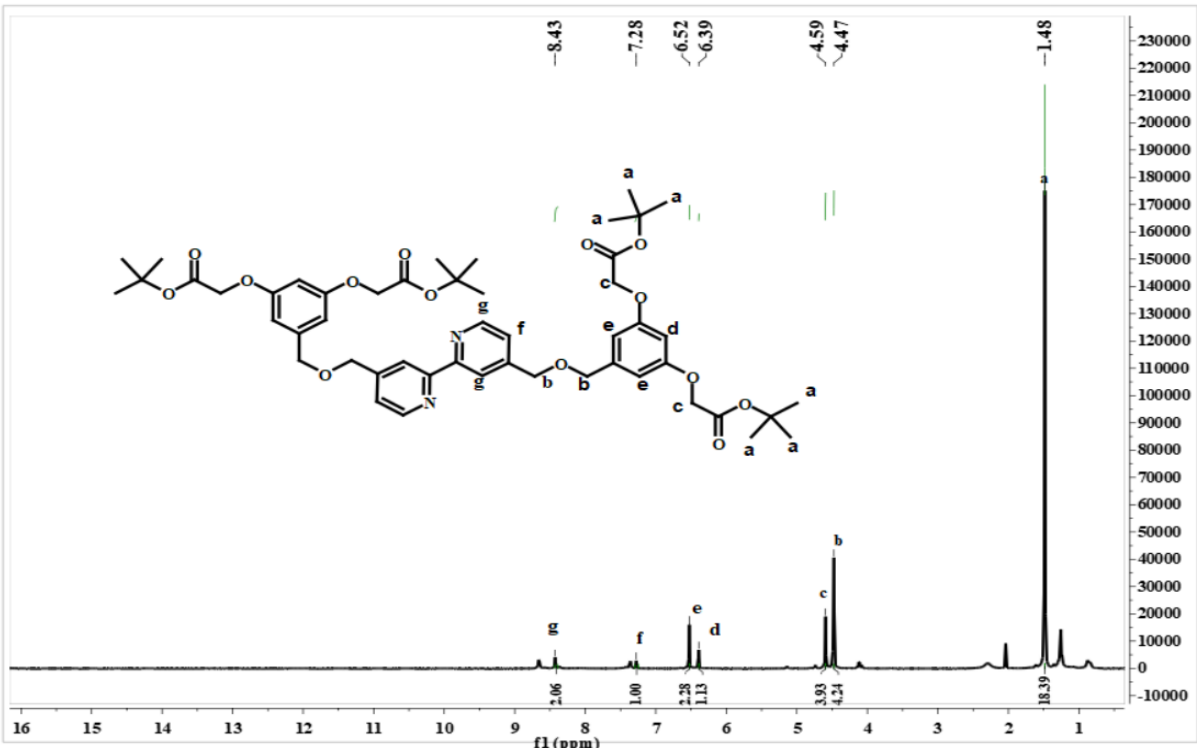

Figure S15. ^{1}HNMR $CDCl_3$ spectra of 4,4'-bis [3'',5''-bis(2-(tert-butoxy)-2-oxoethoxy)benzyloxy]2,2'-bipyridine **G0-bpy**

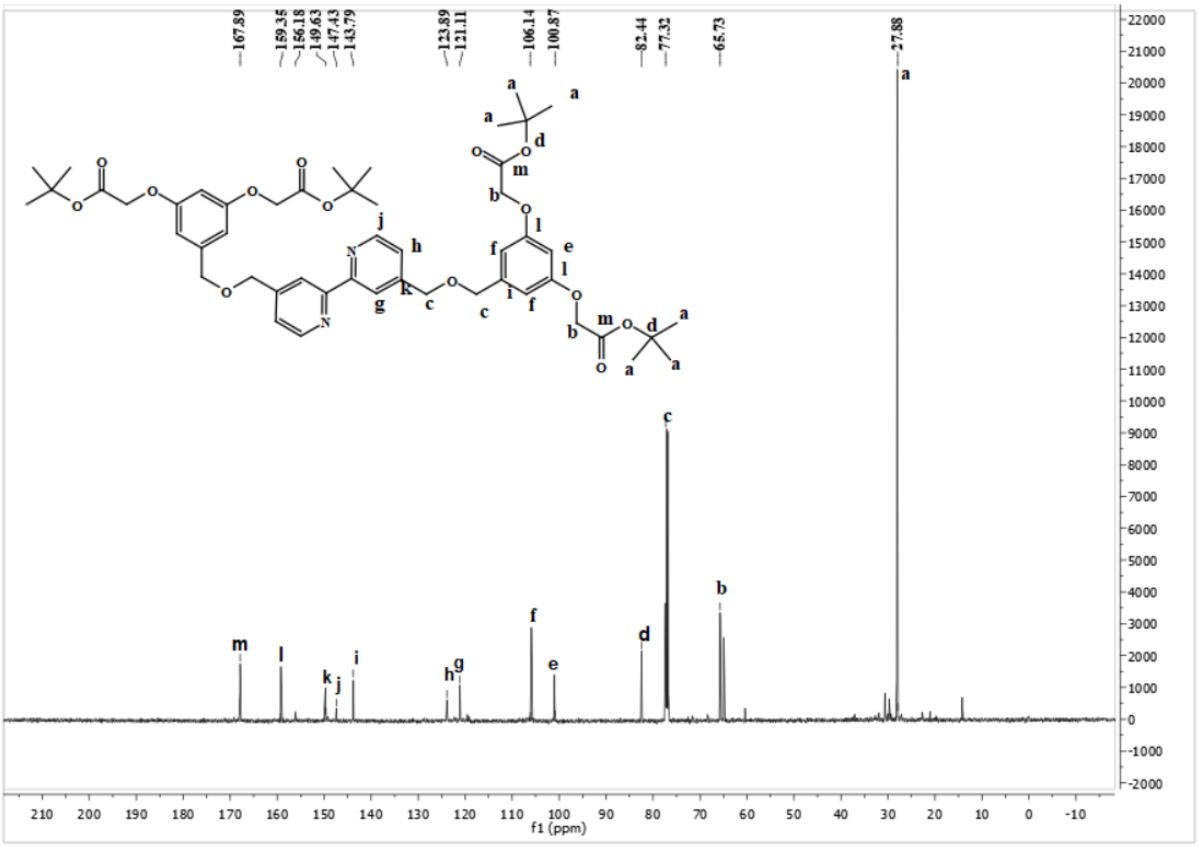

Figure S16. ^{13}C NMR $CDCl_3$ spectra of 4,4'-bis [3",5"-bis(2-(tert-butoxy)-2-oxoethoxy)benzyloxy]2,2'-bipyridine **G0-bpy**

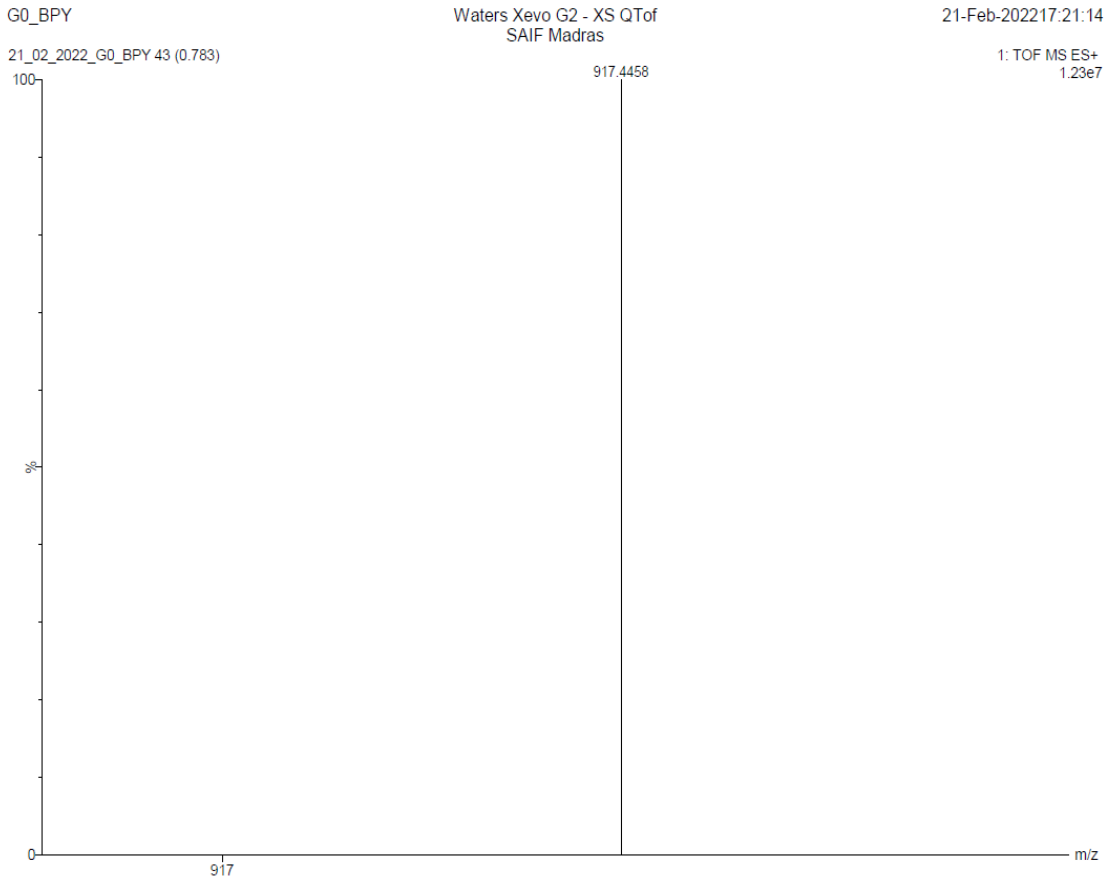

Figure S17. HRMS spectra of 4,4'-bis [3",5"-bis(2-(tert-butoxy)-2-oxoethoxy)benzyloxy]2,2'-bipyridine **G0-bpy**

8. **4,4'- [3'',5''-bis[3''',5'''-bis(2-(tert-butoxy)-2-oxoethoxy)benzyloxy] benzyloxyl] 2,2'-bipyridine G1-bpy**

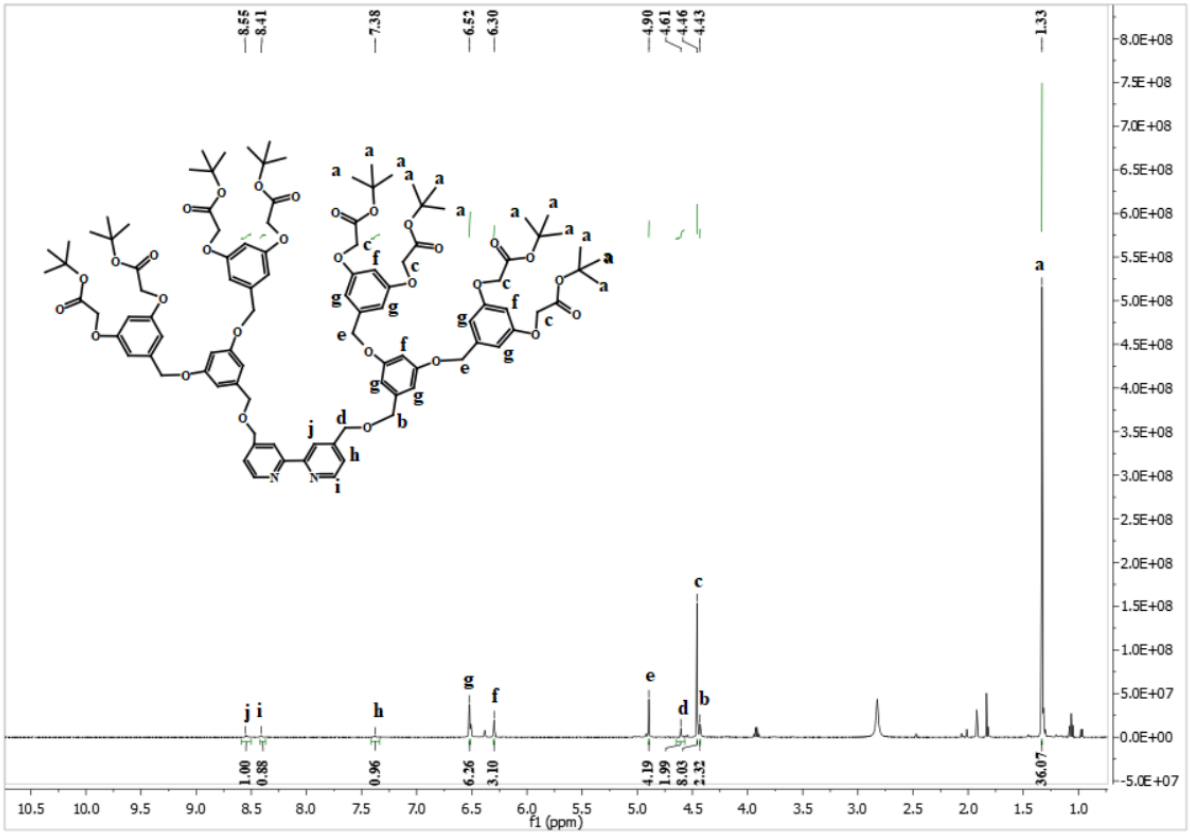

Figure S18. ^{1}HNMR $CDCl_3$ spectra of 4,4'- [3'',5''-bis[3''',5'''-bis(2-(tert-butoxy)-2-oxoethoxy)benzyloxy] benzyloxyl] 2,2'-bipyridine **G1-bpy**

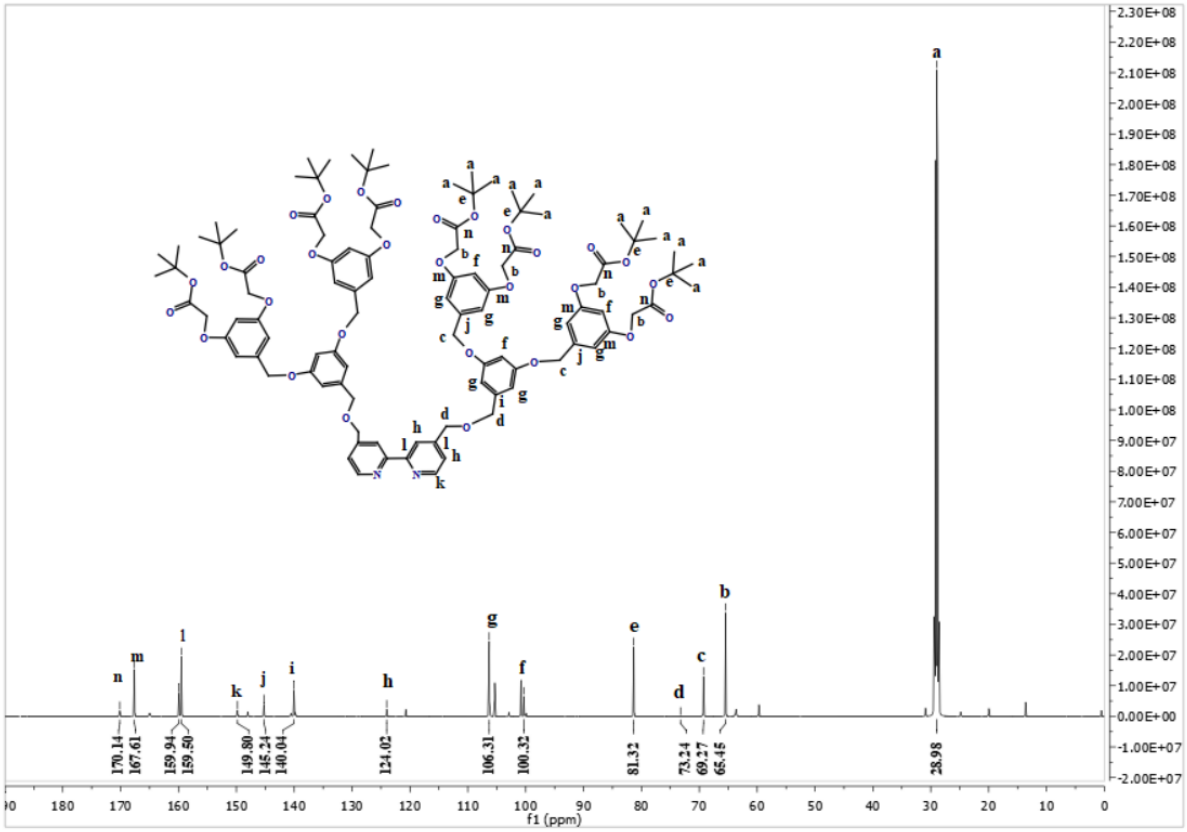

Figure S19. ^{13}C-NMR $CDCl_3$ spectra of 4,4'- [3'',5''-bis[3''',5'''-bis(2-(tert-butoxy)-2-oxoethoxy)benzyloxy] benzyloxyl] 2,2'-bipyridine **G1-bpy**

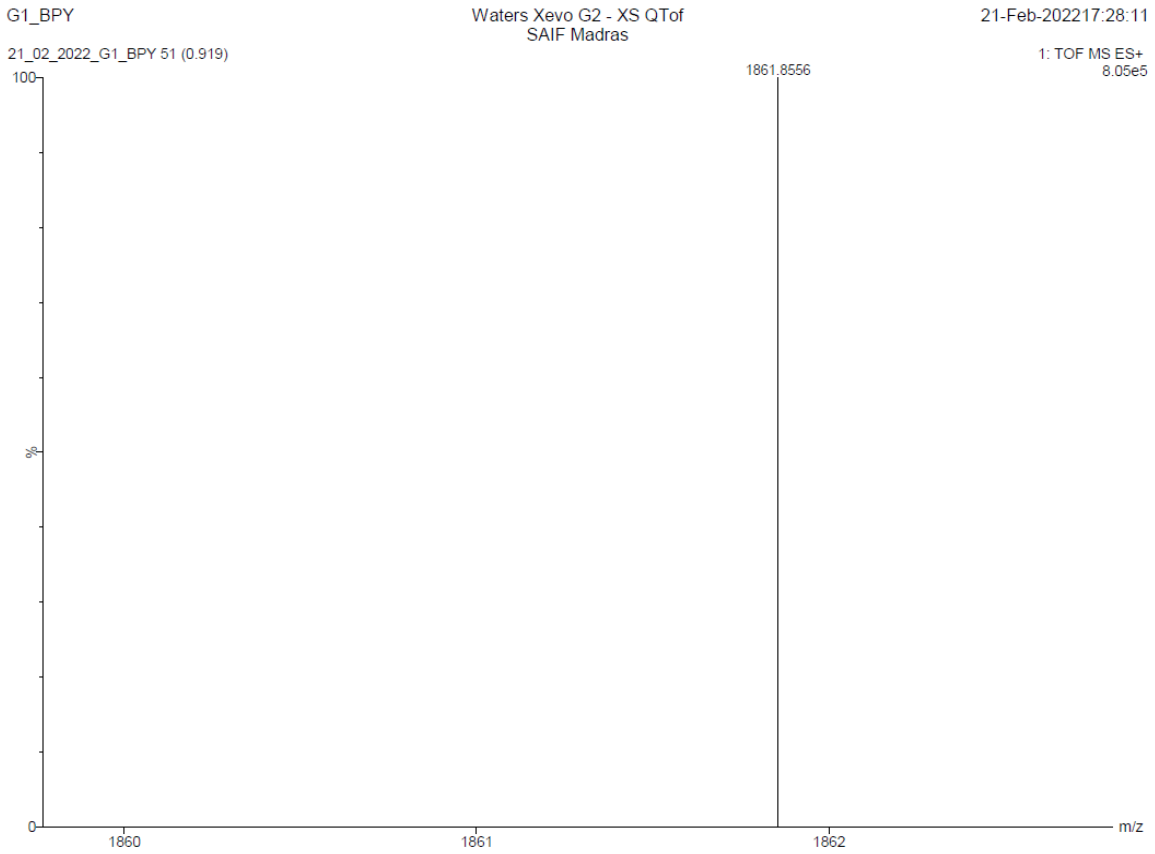

Figure S20. HRMS $CDCl_3$ spectra of 4,4'- [3'',5''-bis[3''',5'''-bis(2-(tert-butoxy)-2-oxoethoxy)benzyloxy] benzyloxyl] 2,2'-bipyridine **G1-bpy**

9. **4,4’-bis [3'',5''-bis [3''',5'''-bis [3'''',5''''-bis (2-(tert-butoxy)-2-oxoethoxy)benzyloxy] benzyloxy] benzyloxyl] 2,2'- bipyridine G2-bpy**

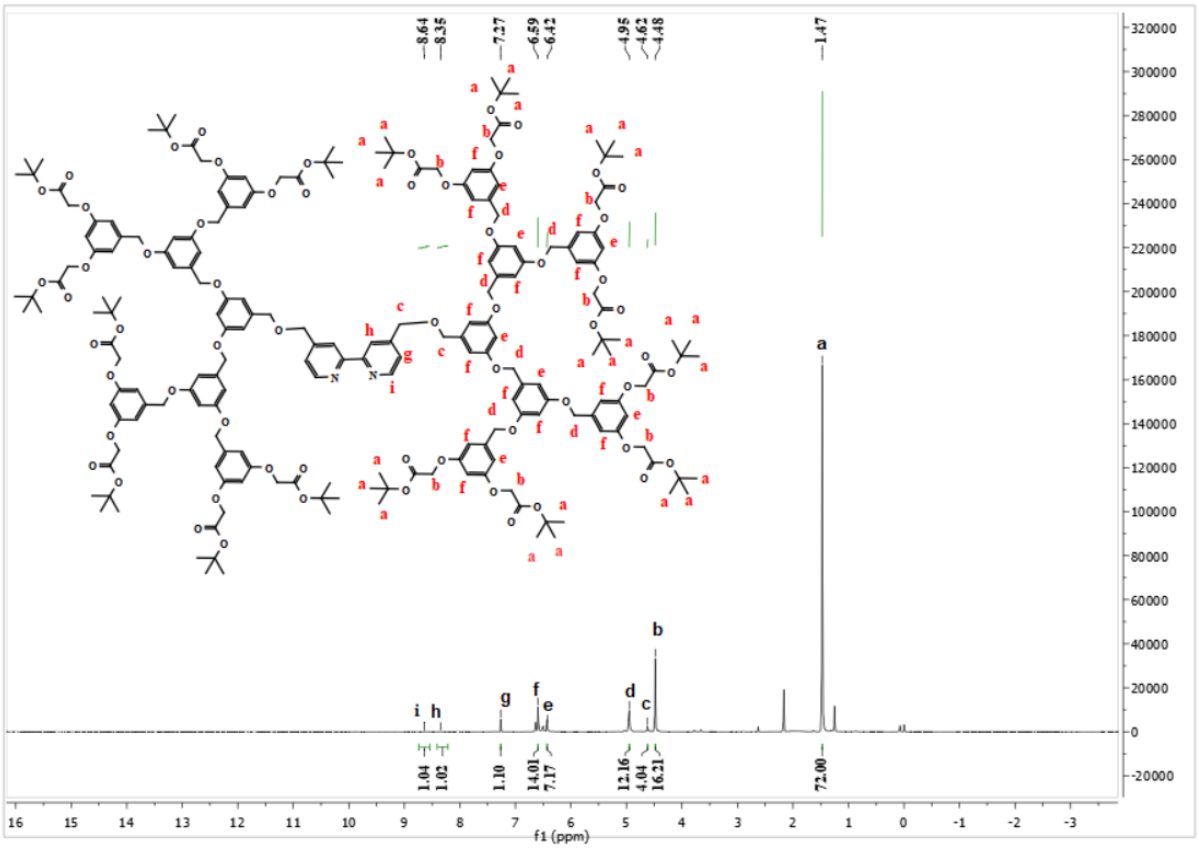

Figure S21. ^{1}HNMR $CDCl_3$ spectra of 4,4’-bis [3'',5''-bis [3''',5'''-bis [3'''',5''''-bis (2-(tert-butoxy)-2-oxoethoxy)benzyloxy] benzyloxy] benzyloxyl] 2,2'- bipyridine **G2-bpy**

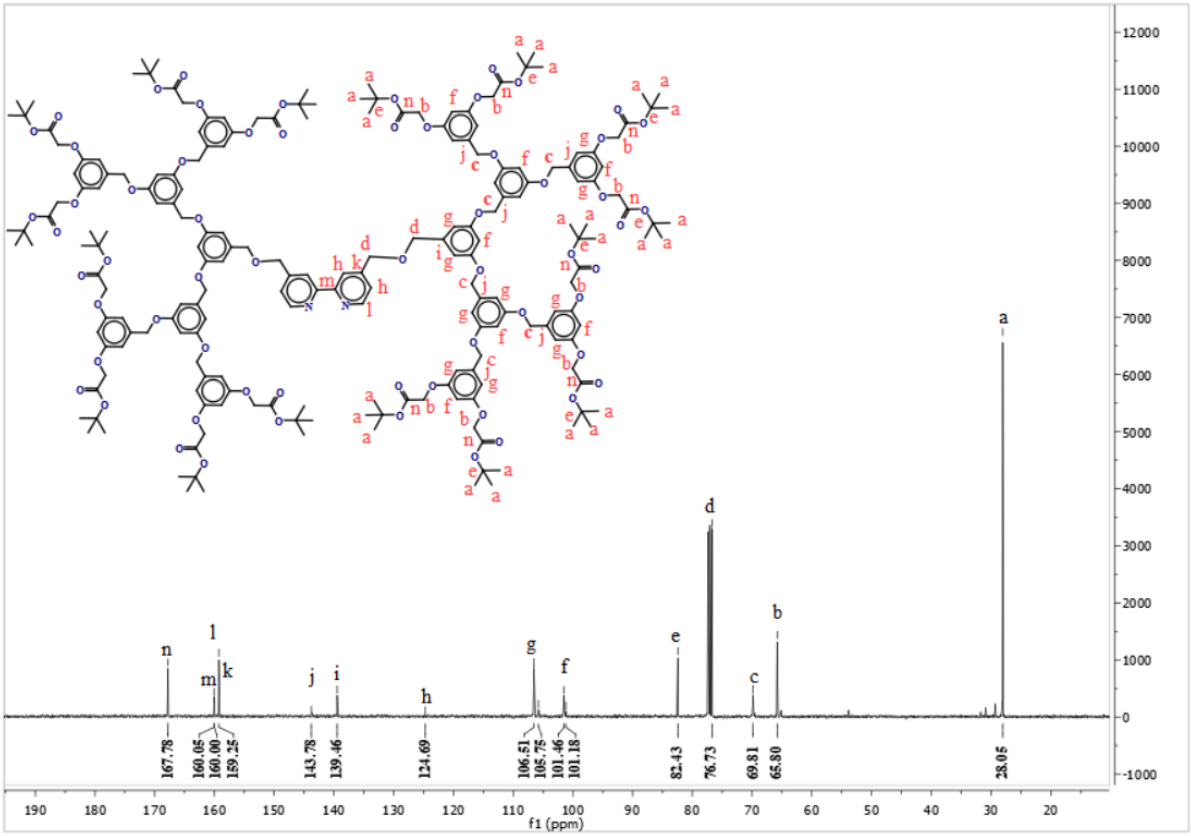

Figure S22. ^{13}C-NMR $CDCl_3$ spectra of 4,4'-bis [3",5"-bis [3"',5"'-bis [3"",5""-bis (2-(tert-butoxy)-2-oxoethoxy)benzyloxy] benzyloxy] benzyloxyl] 2,2'- bipyridine **G2-bpy**

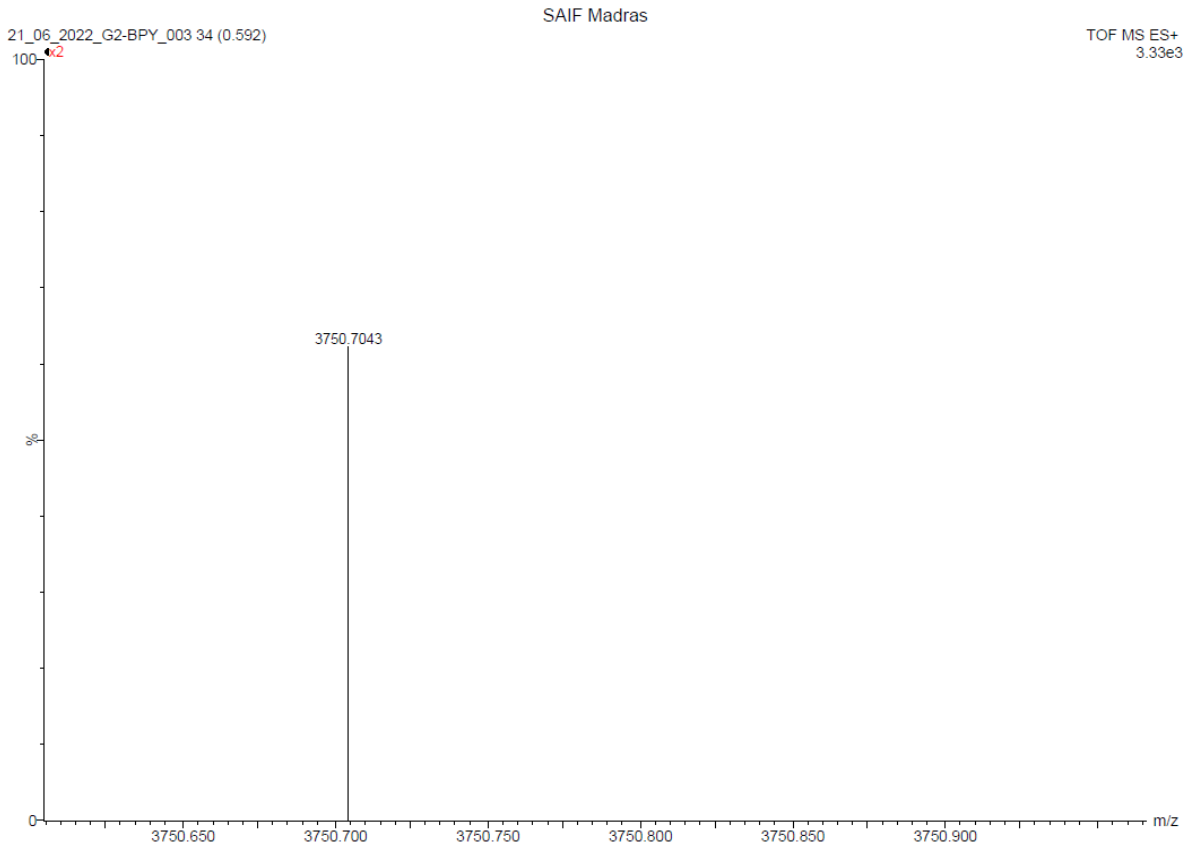

Figure S23. HRMS spectra of 4,4’-bis [3",5"-bis [3"',5"'-bis [3"",5""-bis (2-(tert-butoxy)-2-oxoethoxy)benzyloxy] benzyloxy] benzyloxyl] 2,2'- bipyridine **G2-bpy**

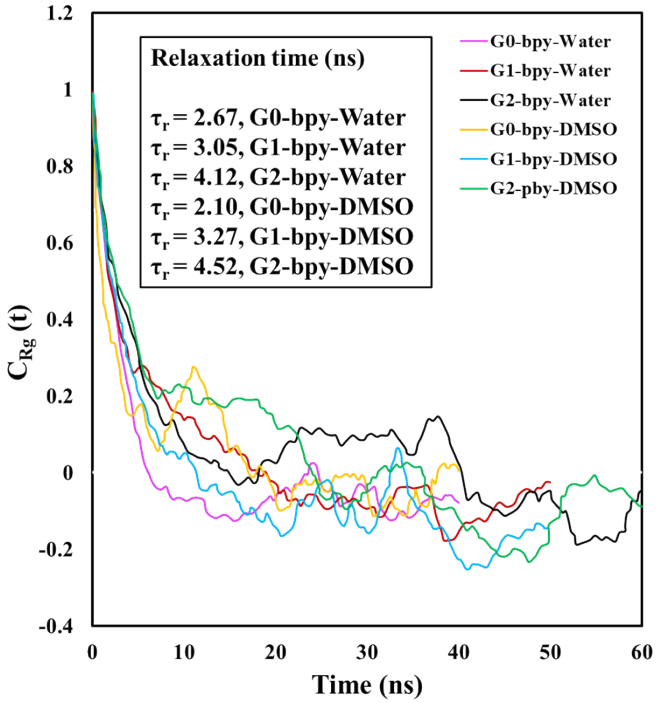

Figure S24. Autocorrelation function of the radius of gyration as a function of time $C_{Rg}(t)$ for G0, G1, and G2 dendrons in water and DMSO. The values in the graph are the calculated relaxation times (τ_r).

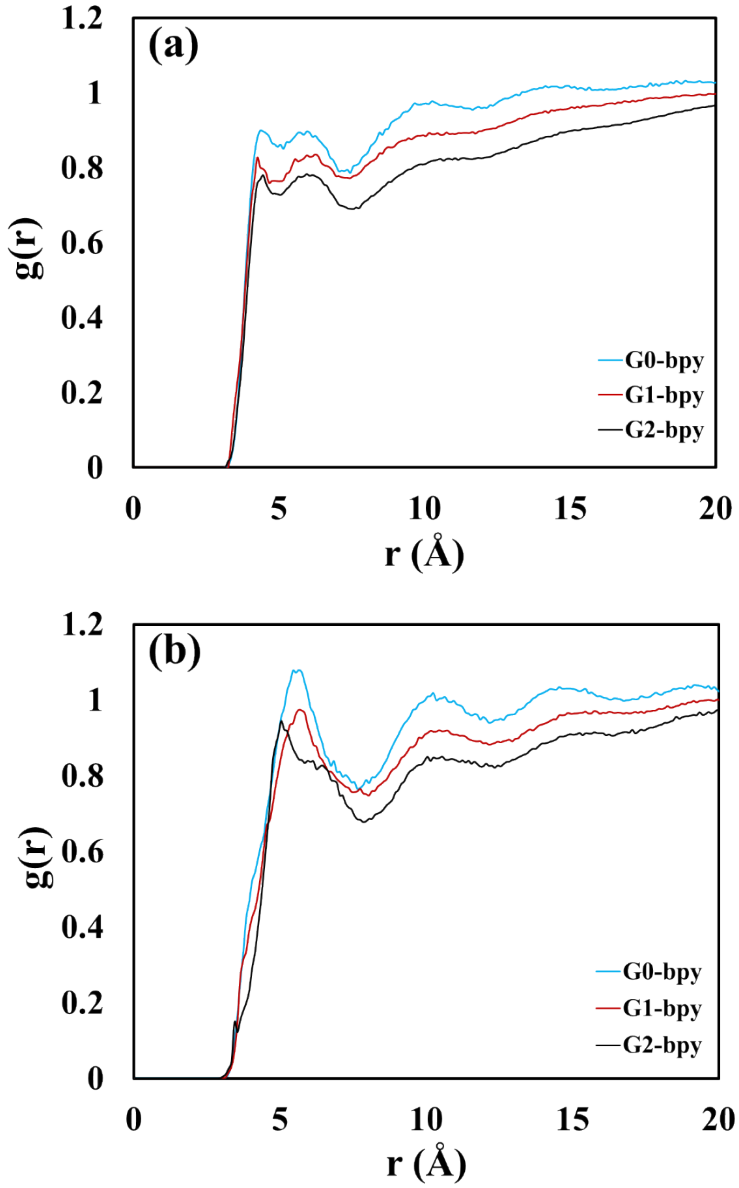

Figure S25. Radial distribution function between (a) the carbon atoms from dendron and DMSO, and (b) the oxygen from dendrons and sulphur atoms from DMSO. g(r) data analysis is based on the last 10 ns of the simulations.

Reference

(1) Ciana, L. D.; Dressick, W. J.; Von Zelewsky, A. Synthesis of 4,4′-Divinyl-2,2′-Bipyridine. *Journal of Heterocyclic Chemistry* **1990**, *27* (2), 163–165. https://doi.org/10.1002/jhet.5570270209.