Rational Design of Click-Assembled Chiral Dendrimers: Anticancer Activity and Molecular Dynamics Study

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Compound 6

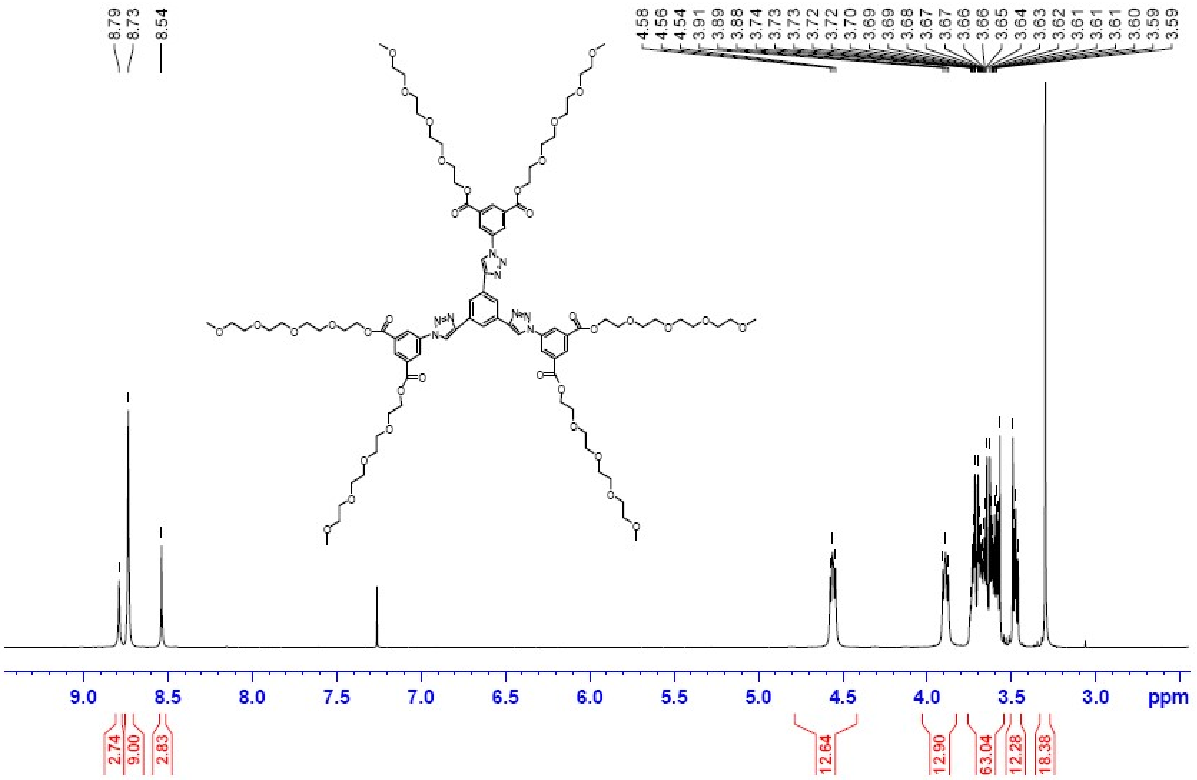

Figure S1. ^{1}H NMR spectrum of compound **6** (400 MHz, $CDCl_3$, 25 °C)

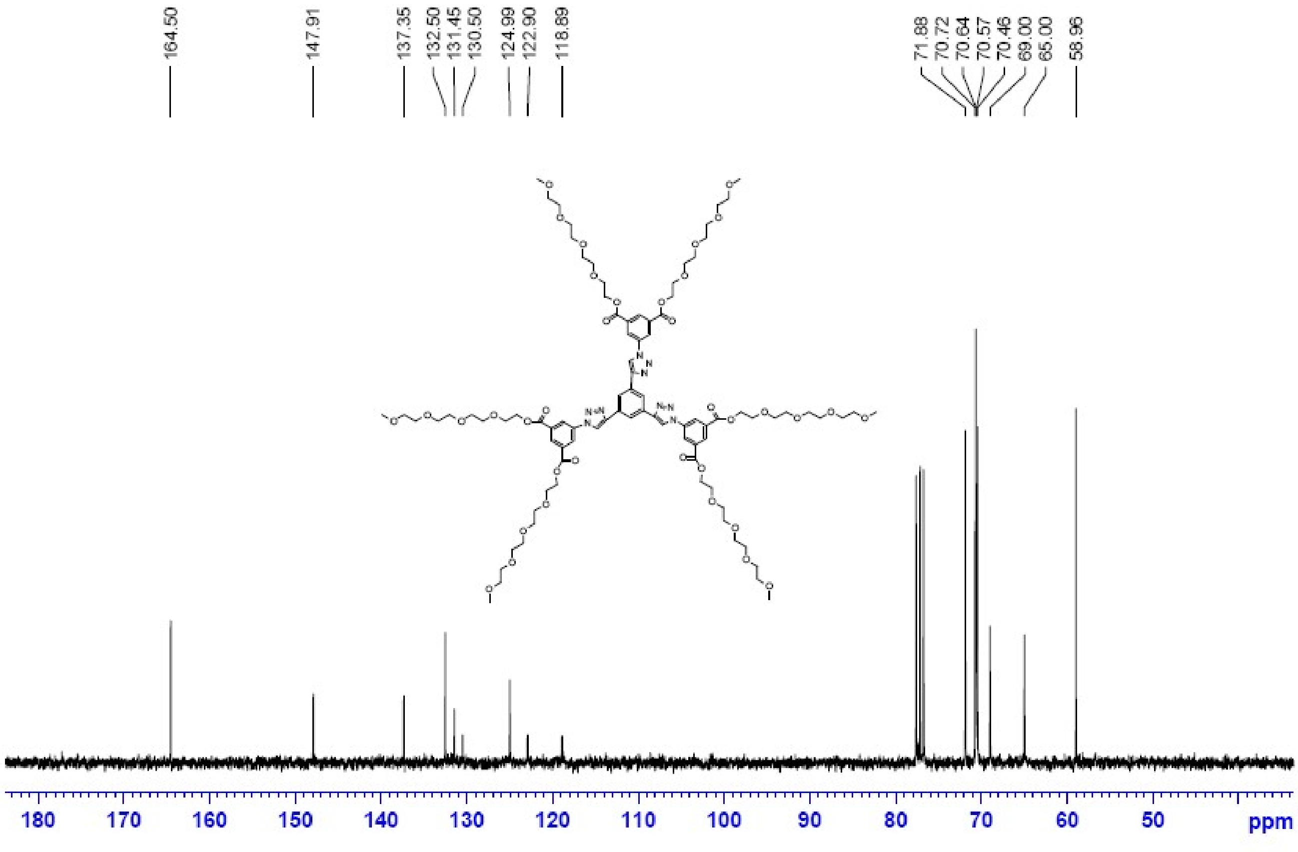

Figure S2. ^{13}C NMR spectrum of compound **6** (100 MHz, $CDCl_3$, 25 °C)

Compound 3

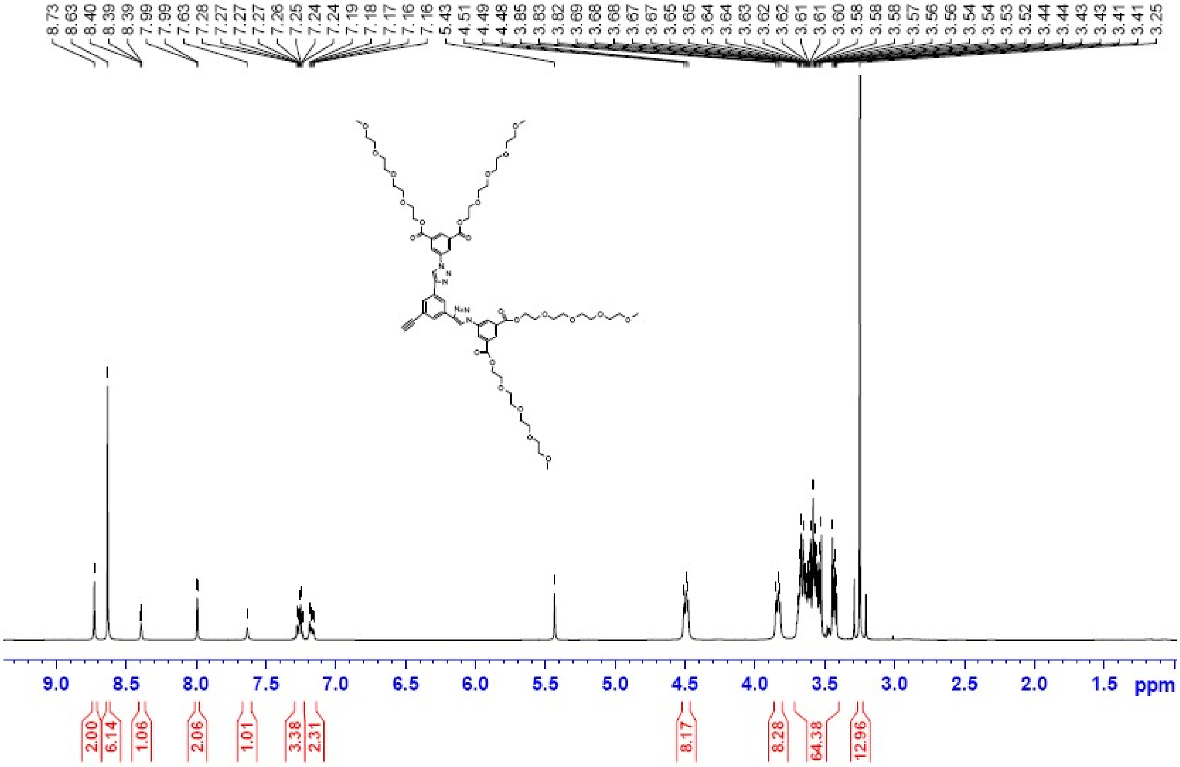

Figure S3. ^{1}H NMR spectrum of compound **3** (400 MHz, $CDCl_3$, 25 °C)

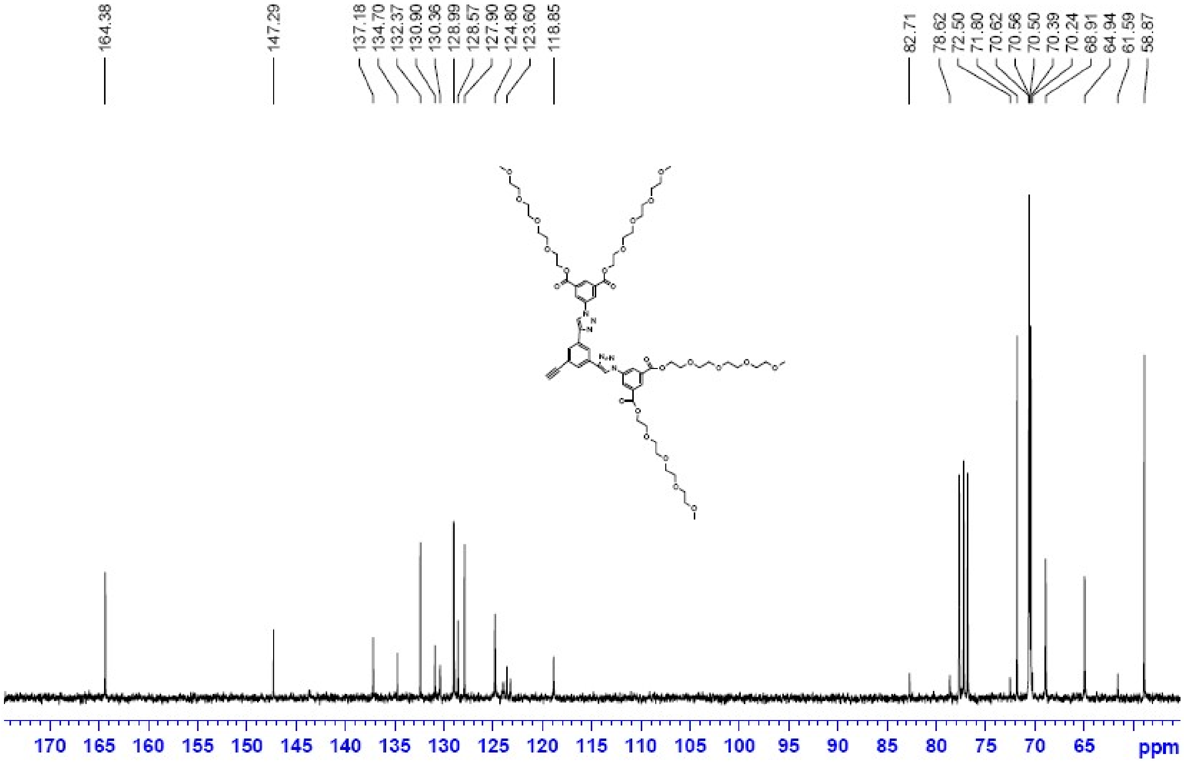

Figure S4. ^{13}C NMR spectrum of compound **3** (100 MHz, $CDCl_3$, 25 °C)

Compound 7

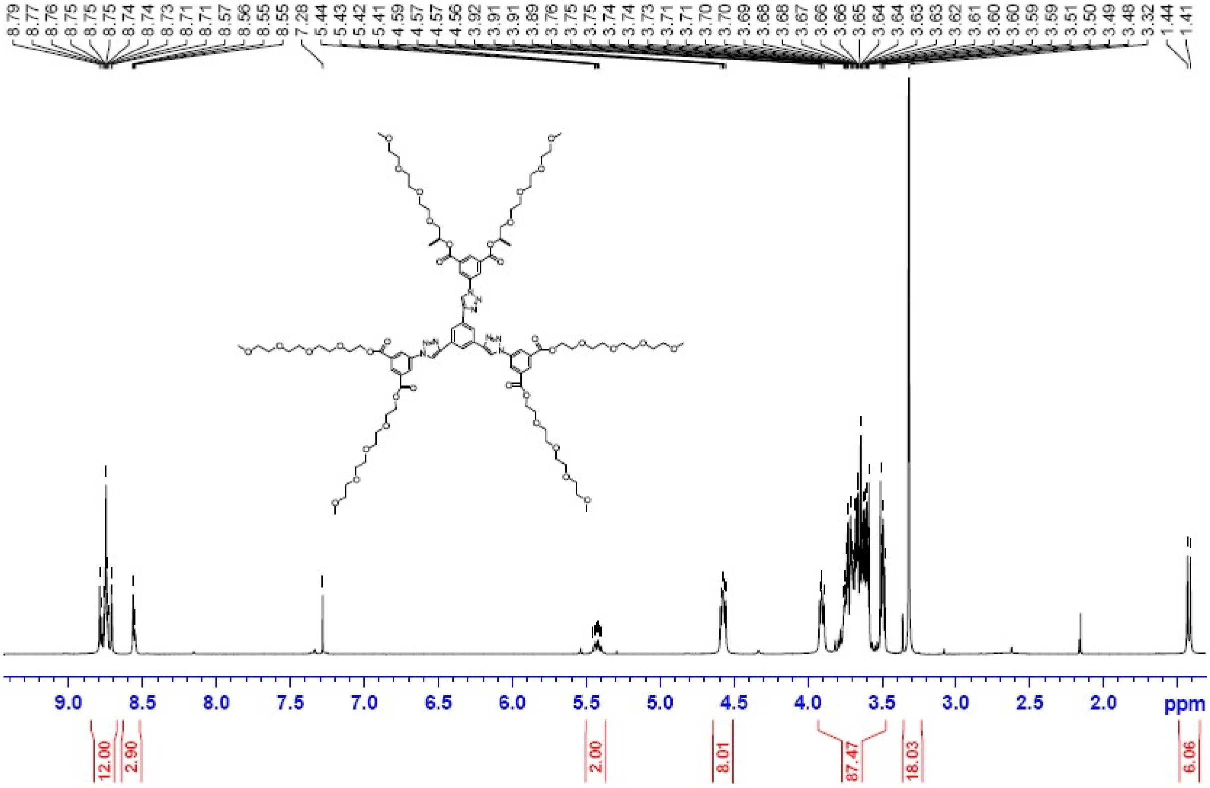

Figure S5. ^{1}H NMR spectrum of compound **7** (400 MHz, CDCl$_3$, 25 °C)

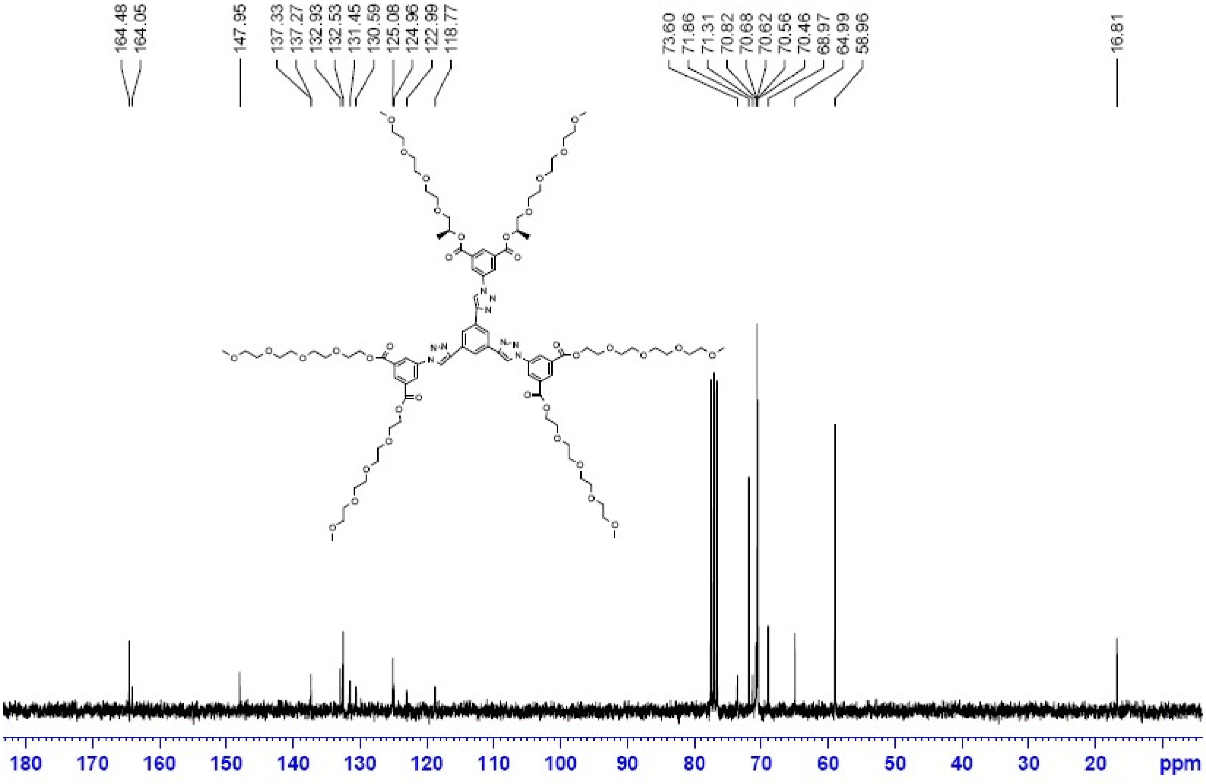

Figure S6. ^{13}C NMR spectrum of compound **7** (100 MHz, CDCl$_3$, 25 °C)

Compound 5

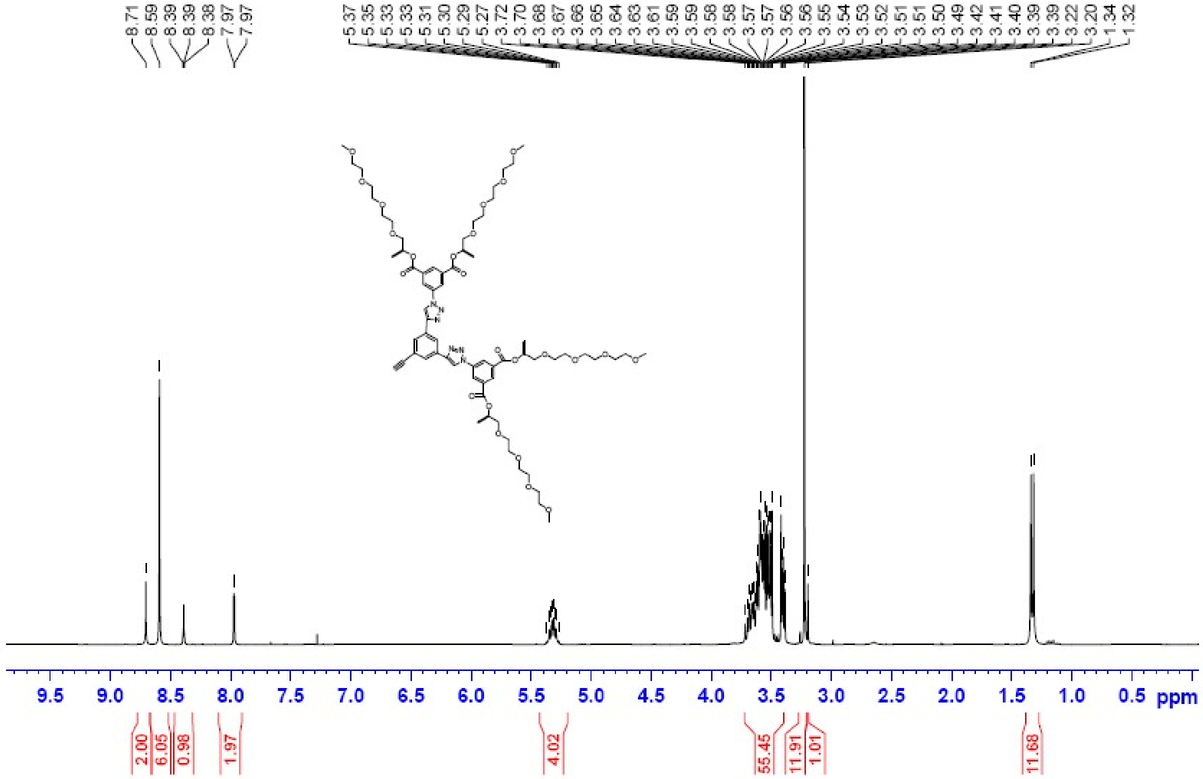

Figure S7. ^{1}H NMR spectrum of compound **5** (400 MHz, CDCl$_3$, 25 °C)

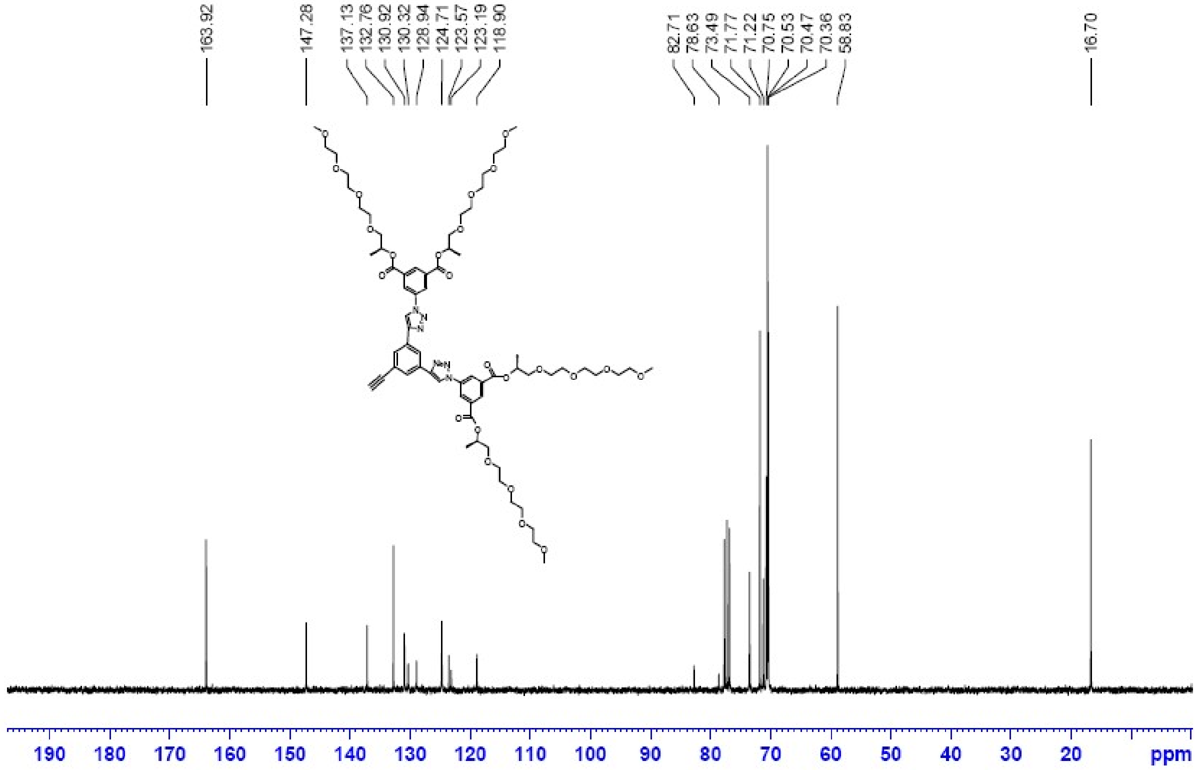

Figure S8. ^{13}C NMR spectrum of compound **5** (100 MHz, CDCl$_3$, 25 °C)

Compound 8

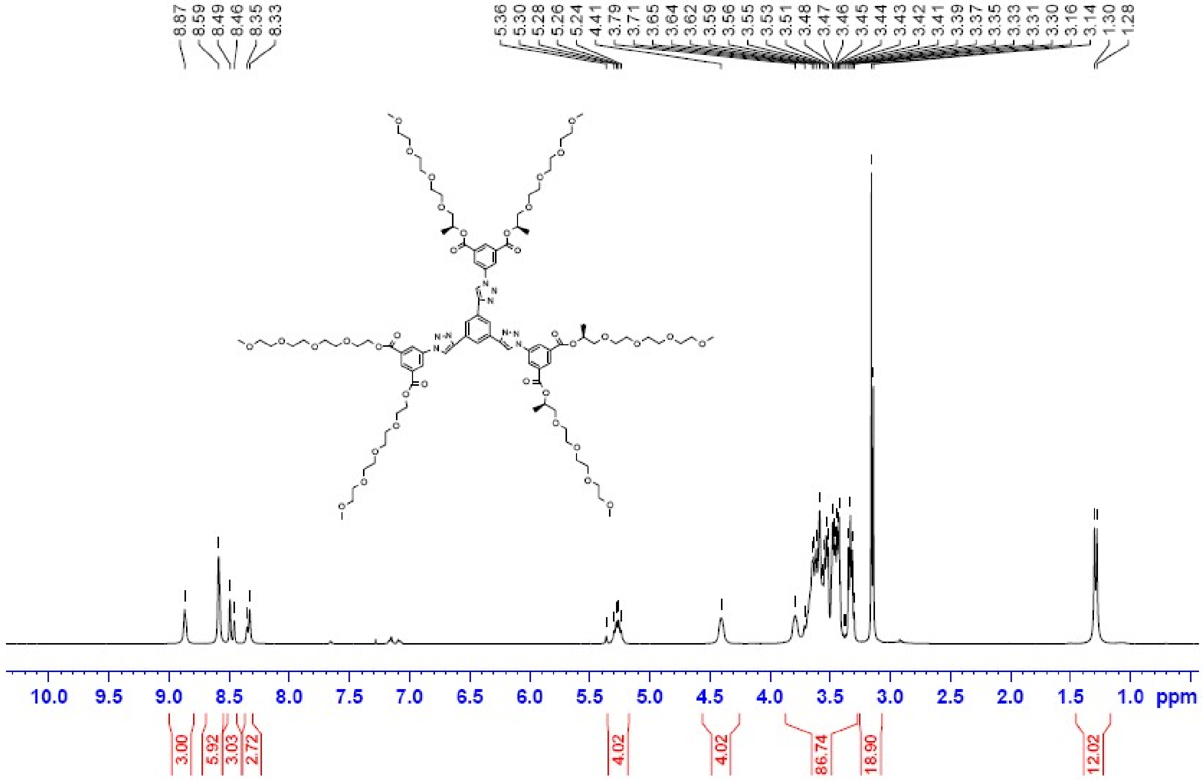

Figure S9. ^{1}H NMR spectrum of compound **8** (400 MHz, $CDCl_3$, 25 °C)

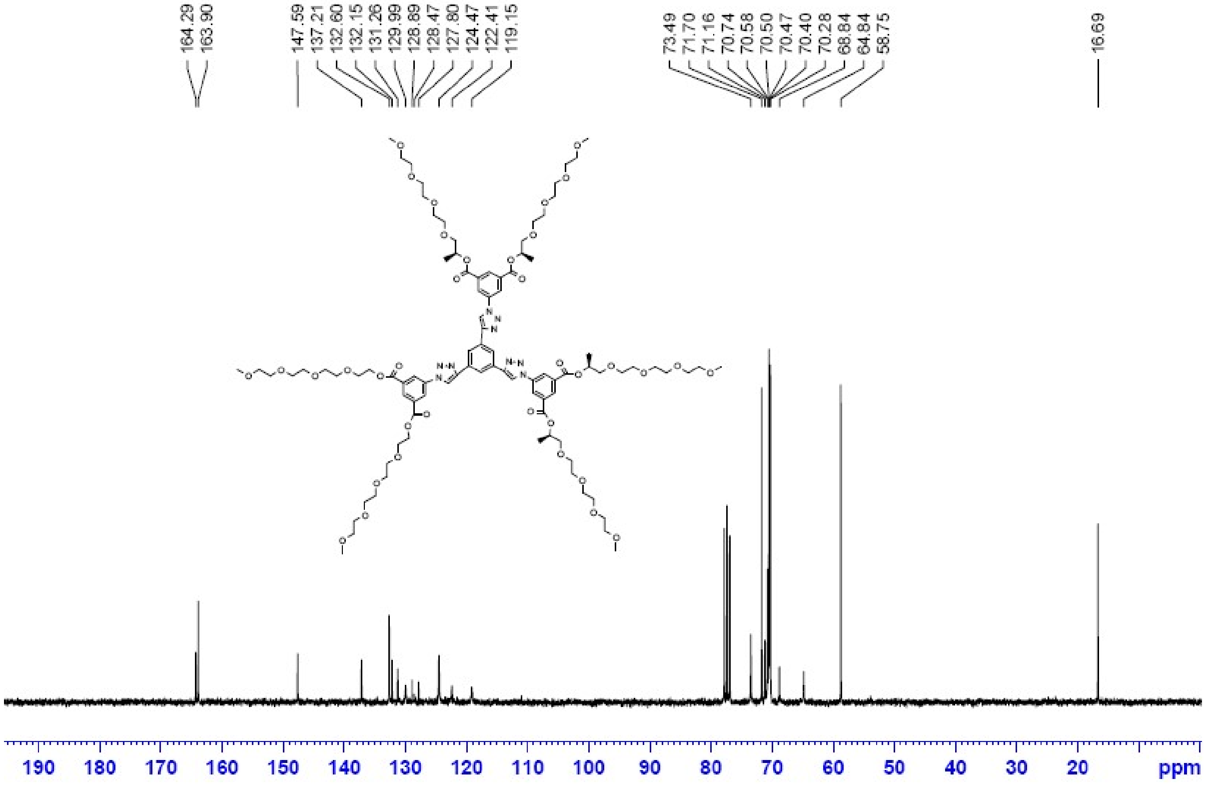

Figure S10. ^{13}C NMR spectrum of compound **8** (100 MHz, $CDCl_3$, 25 °C)

Supplementary Table S1. Per-residue binding free energy contributions (kcal/mol) of key amino acids to the binding of dendrimer 9 with the ERα receptor (AMBER system numbering).

Residue (AMBER No.)	**ΔG Contribution (kcal/mol)**	**Putative Corresponding Residue in PDB 3ERT[1]**	**Interaction Type[2]**
Asp 6	-6.50 ± 0.5	Asp 311	Electrostatic / H-bond
Val 63	-5.87 ± 0.4	Val368	Hydrophobic
Leu 65	-5.24 ± 0.4	Leu 370	Hydrophobic
Thr 66	-6.89 ± 0.5	Thr 371	H-bond / Polar
Leu 67	-10.14 ± 0.7	Leu 372	Hydrophobic
Asp 69	-4.24 ± 0.3	Asp 374	Electrostatic
Gln 70	-7.61 ± 0.5	Gln 375	H-bond / Polar
Val 71	-5.49 ± 0.4	Val 376	Hydrophobic
Ser 163	-6.53 ± 0.5	Ser 450	H-bond / Polar
Glu 165	-5.27 ± 0.4	Glu 452	Electrostatic
Lys 167	-8.76 ± 0.6	Lys 454	Electrostatic / Cation-π
Arg 243	-6.47 ± 0.5	Arg 548	H-bond / Electrostatic
Leu 244	-6.14 ± 0.5	Leu 549	Hydrophobic
Pro 247	-7.24 ± 0.5	Pro 552	Hydrophobic

Footnotes for Supplementary Table S1:

[1] **Putative Corresponding Residue in PDB 3ERT:** Due to the automated preprocessing and solvation box setup in AMBER tleap, the residue numbering in the simulation system differs from the canonical PDB (3ERT) numbering. A full residue mapping table between the AMBER system and PDB 3ERT is available from the authors upon request.

[2] **Interaction Type:** Suggested primary non-covalent interaction based on residue chemistry and decomposed energy terms (van der Waals vs. electrostatic). Specific interactions are detailed in the main text (Figure 5, ligand-residue interaction profiles).