Supporting Information

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Synthesis and Evaluation of Benzothiazole-triazole and Benzothiadiazole-triazole Scaffolds as Potential Molecular Probes for Amyloid-β Aggregation

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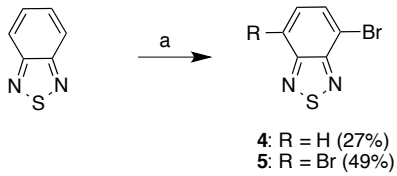


Scheme S1. Synthesis of compound **4** and **5**. Reagents and conditions: a) Br_2, 48% HBr, reflux, 1 h;

Synthesis of 4-bromobenzo[*c*][1,2,5]thiadiazole (4).[1] The title compound was synthesized as previously reported in the literature.[2] Br_2 (0.7 mL, 13.66 mmol) was added dropwise, during 20 min, to a stirred solution of 2,1,3-benzothiadiazole (**4**) (2.00 g, 14.76 mmol) and aqueous HBr (48%, 12 mL). The slurry was then refluxed setpoint: 120 ^{o}C) for 1 hour. After cooling, 200 mL of ice and 100 mL of saturated $NaHSO_3$ solution were poured into the reaction mixture. The slurry was filtered off and the solid was recrystallized from ethanol to give compound **5** as a beige powder (0.87 g, 27%). ^{1}H NMR ($CDCl_3$): 7.95-7.97 (dd, 1H), 7.82-7.84 (dd, 1H), 7.45-7.49 (dd, 1H).

Synthesis of 4,7-Dibromobenzo[*c*]-1,2,5-thiadiazole (5).[2-3] The title compound was synthesized as previous reported in the literature.[1,2] 2,1,3-Benzothiadiazole (**4**) (5.05 g, 36.91 mmol) was added to a stirred solution of aqueous HBr (48%, 30 mL). Br_2 (5.7 mL 110.73 mmol) was added slowly to the mixture and the reaction was refluxed for 2 hours at 130 °C. The final slurry was allowed to reach room temperature and was then poured into a solution of ice in saturated $NaHSO_3$. The resulting mixture was stirred for 10 minutes and the precipitation was filtered off. The crude product was recrystallized from water (35 mL, reflux for 30 min), filtered off, and washed with isopropanol (10 mL) to give a greenish/beige powder (5.28 g, 49%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.70 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 153.1, 132.5, 114.0. HRMS (EI+) $[M]^+$ Calcd for $C_6H_2Br_2N_2S$, 291.8305. Found, 291.8294.

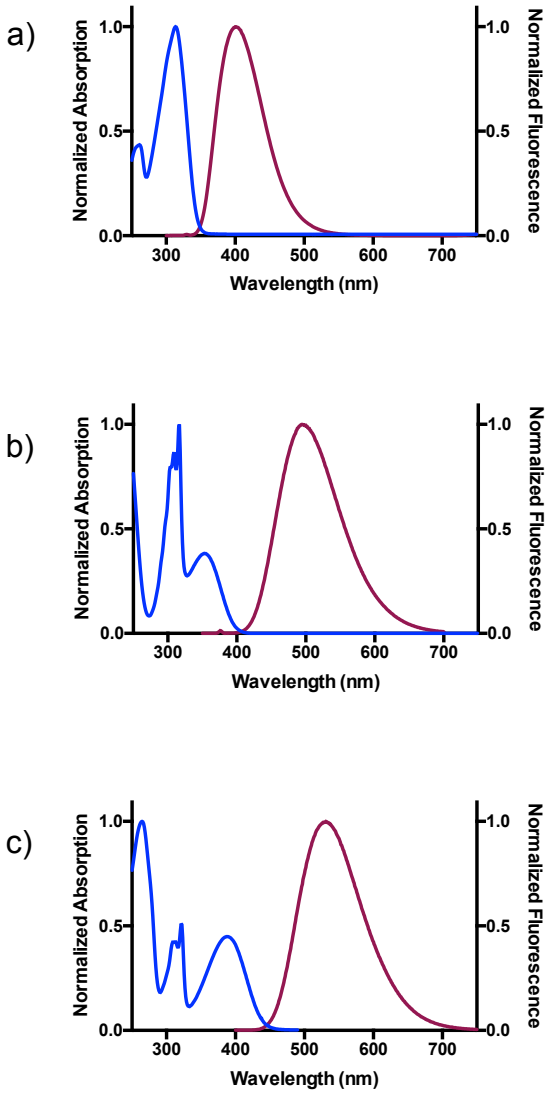


Figure S1. Absorption (blue line) and emission spectra (red line) for **L1** (a), **L2** (b) and **L3** (c) in 5% DMSO in phosphate buffered saline (PBS, 10 mM phosphate, 140 mM NaCl, 2.7 mM KCl, pH 7.4).

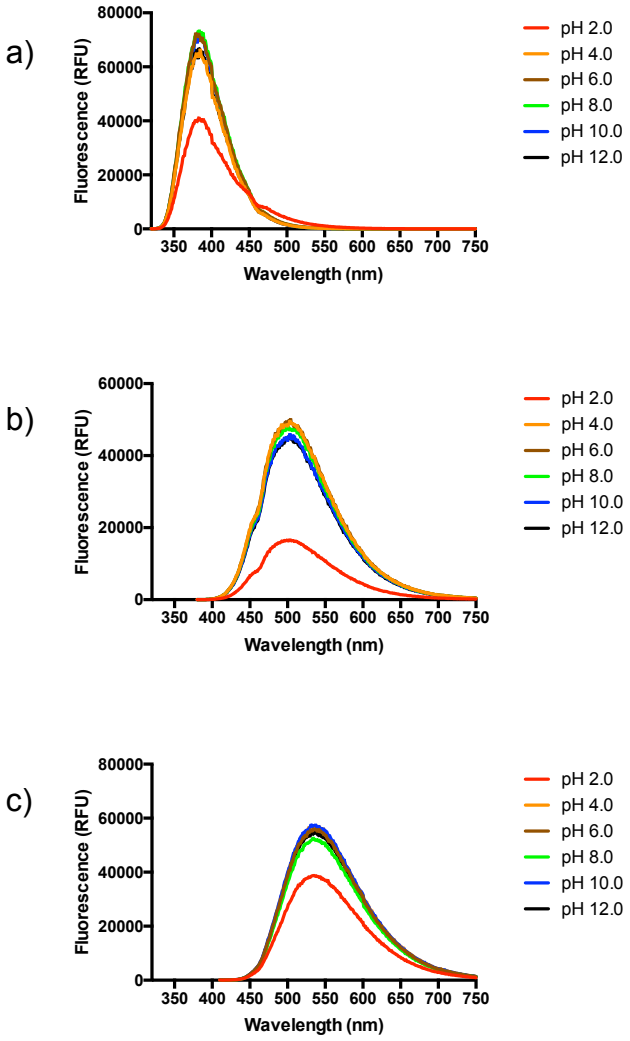


Figure S2. Emission spectra at 50 µM (5% DMSO in PBS buffer) for **L1** (a), **L2** (b) and **L3** (c) at different pH. pH 2 and 4: Glycine·HCl buffer (50 mM); pH 6 and 8: phosphate buffer (25 mM); and pH 10 and 12: Glycine·OH buffer (50 mM).

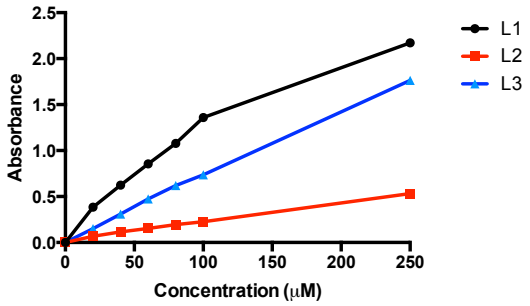


Figure S3. Concentration-absorbance curves for **L1**, **L2** and **L3** using known concentrations (20, 40, 60, 80, 100 and 250 μM) in 5% DMSO in PBS buffer, pH 7.4. Linear curve fitting (y = mx + b) afforded R^2 = 0.9335, 0.9955 and 0.9985 for **L1**, **L2** and **L3**, respectively.

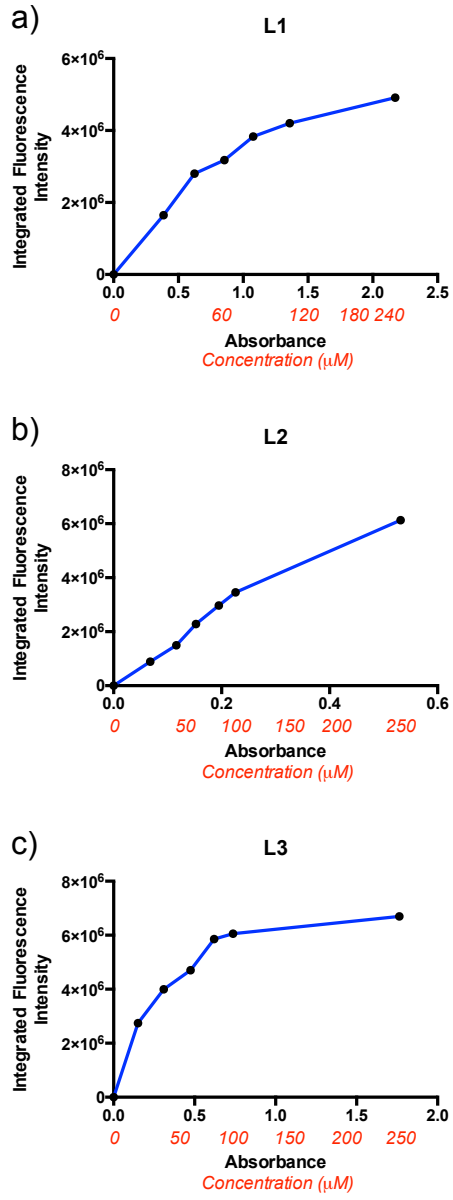


Figure S4. The absorbance-integrated fluorescence intensity relationship measured in 5% DMSO/PBS buffer, pH 7.4; a) **L1** (λ_{ex} = 310 nm), b) **L2** ((λ_{ex} = 350 nm), c) **L3** ((λ_{ex} = 400 nm).

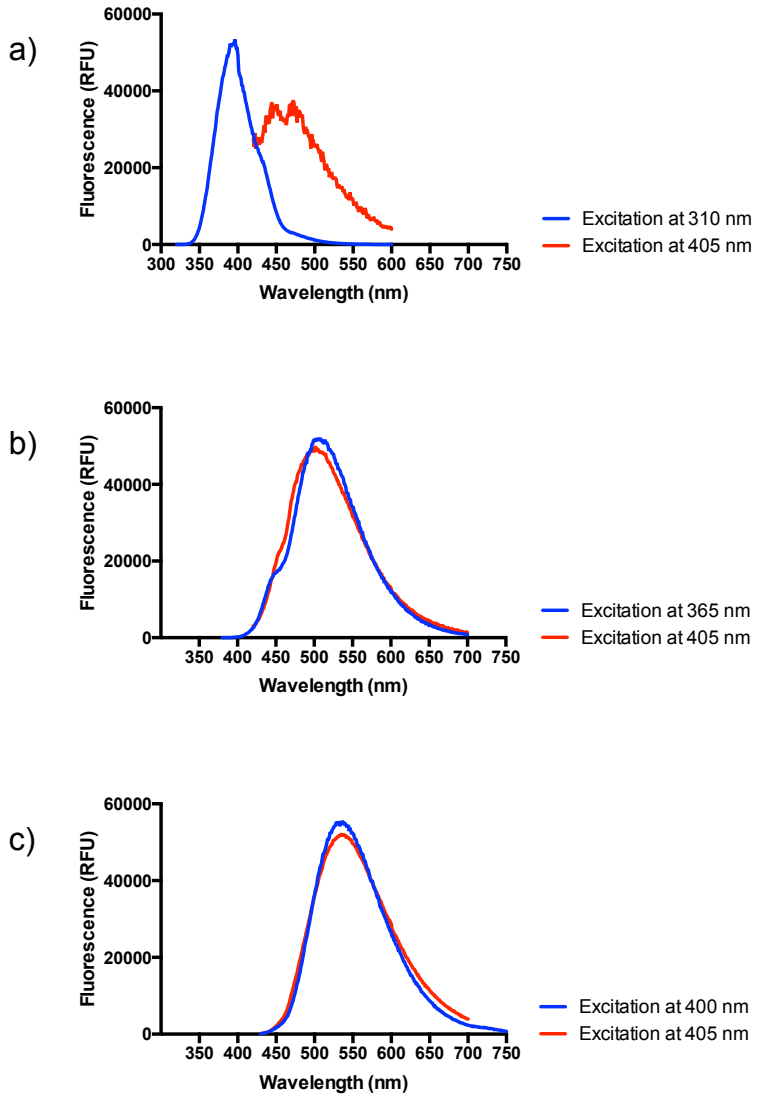


Figure S5. Emission spectra for **L1** (a), **L2** (b) and **L3** (c) at two different excitation wavelengths in 5% DMSO in phosphate buffered saline (PBS, 10 mM phosphate, 140 mM NaCl, 2.7 mM KCl, pH 7.4). Blue line represents the emission profile from excitation at a wavelength that is close to the absorption maxima for each compound, whereas the red line represents excitation at 405 nm, i.e. the excitation wavelength that were used in the fluorescent microscopy study.

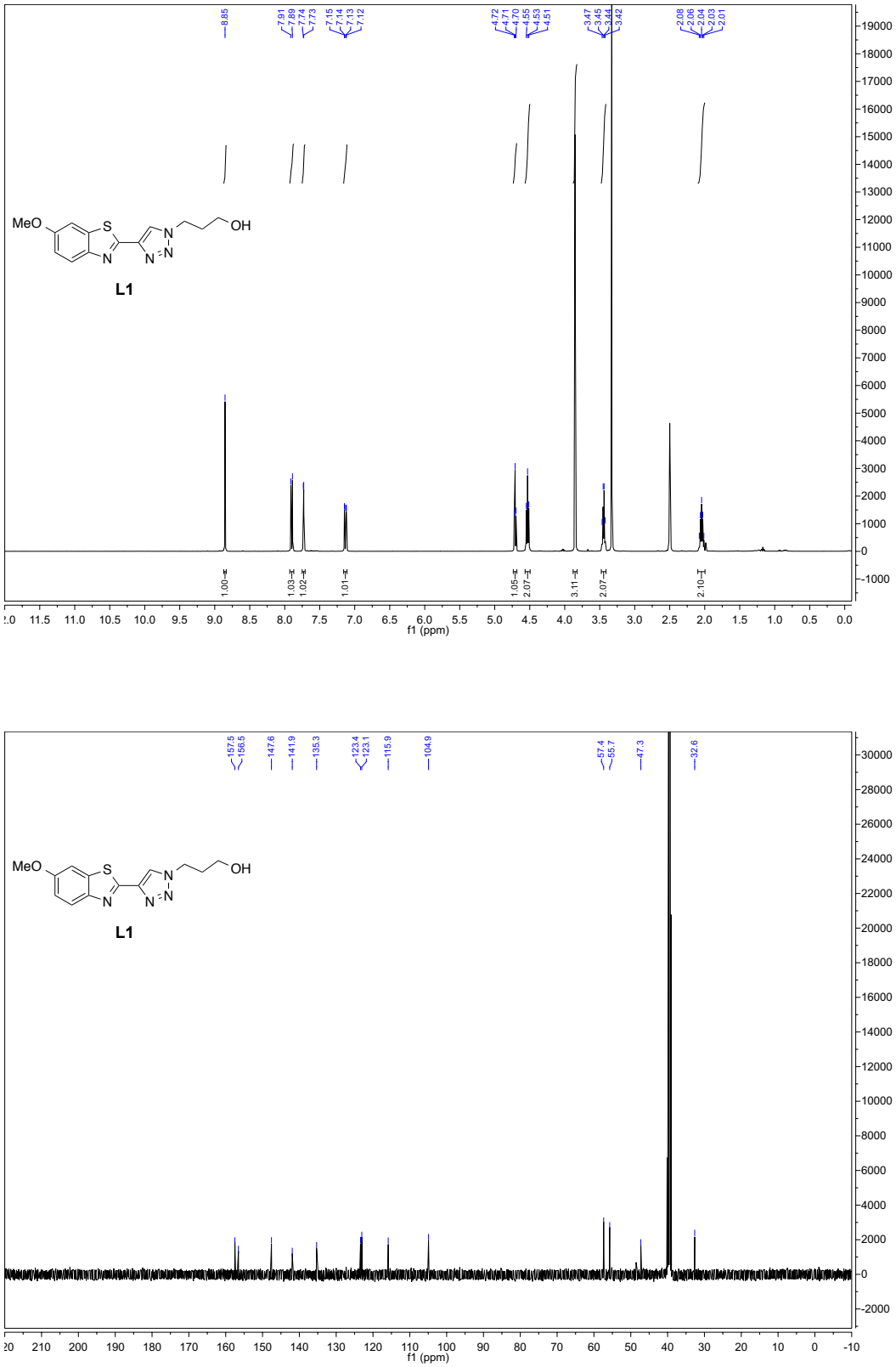


Figure S6. ^{1}H-NMR (top) and ^{13}C-NMR (bottom) spectra of **L1** in DMSO-d_6.

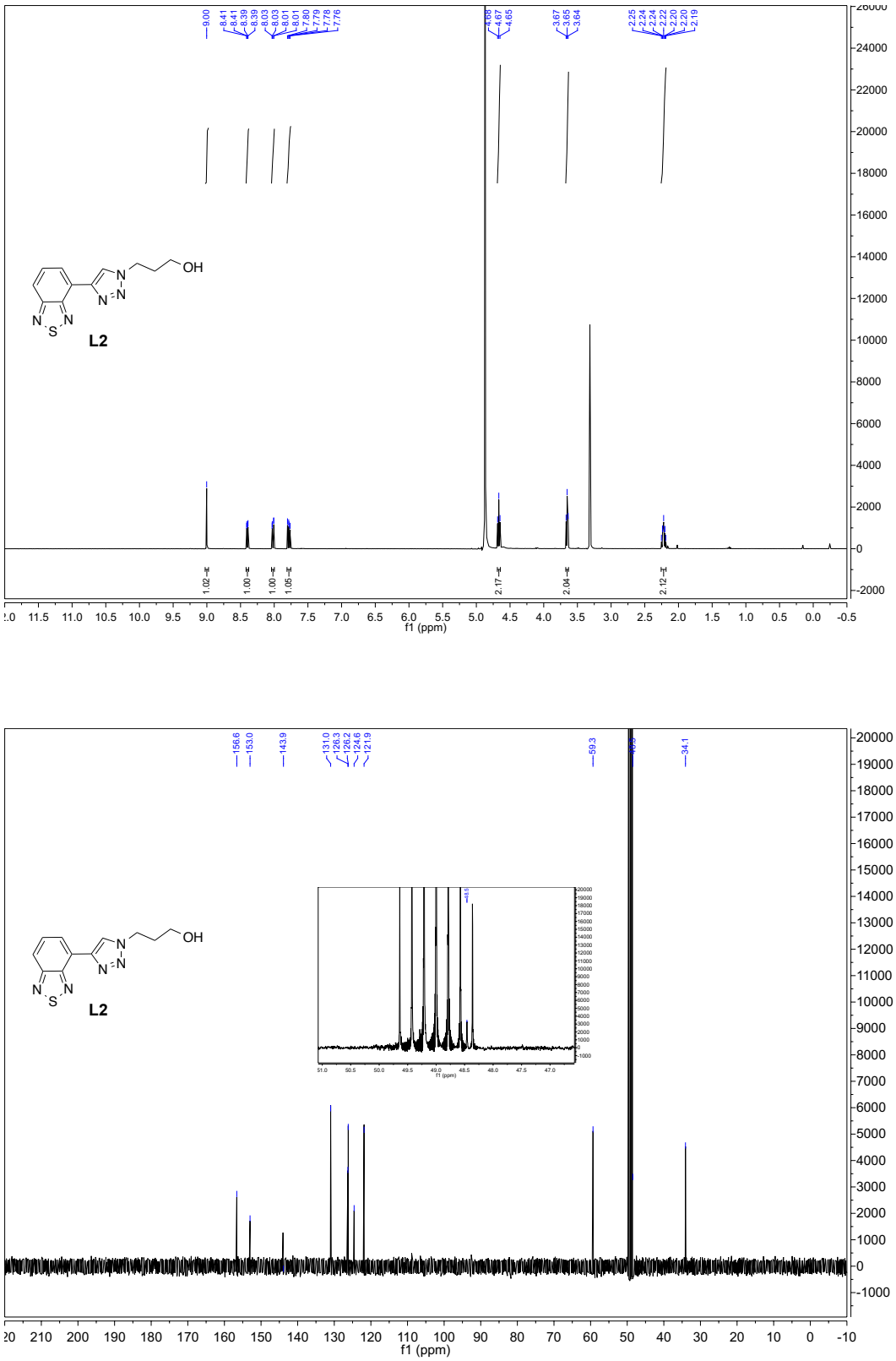
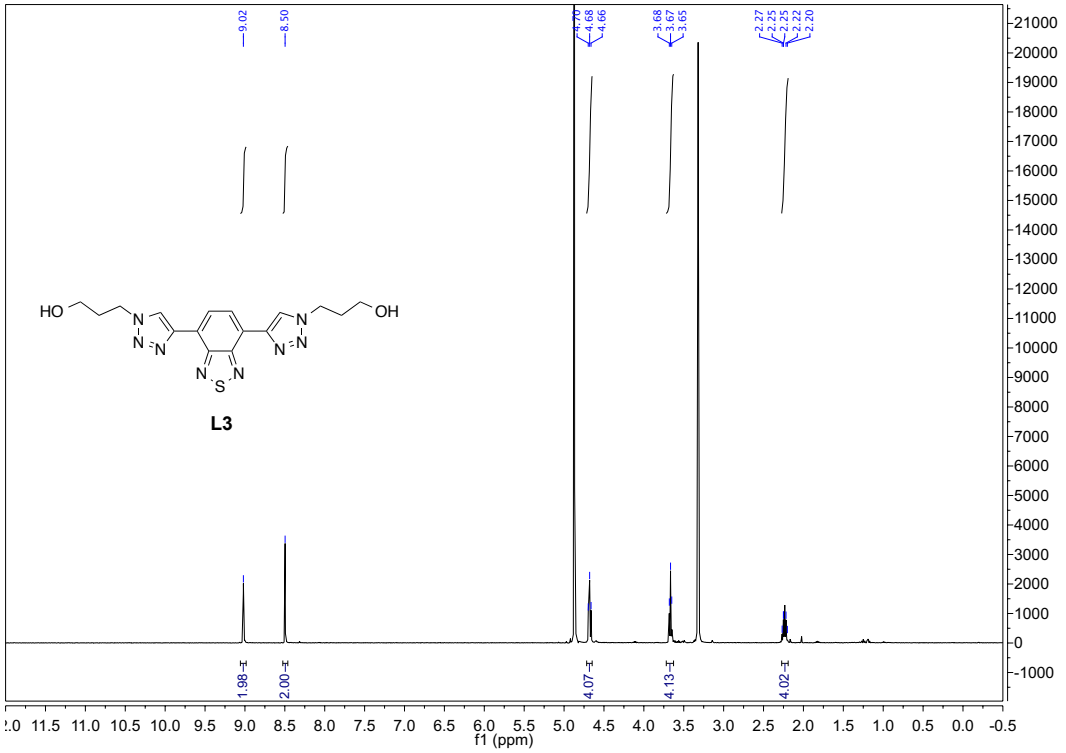


Figure S7. ^{1}H-NMR (top) and ^{13}C-NMR (bottom) spectra of **L2** in CD_3OD.



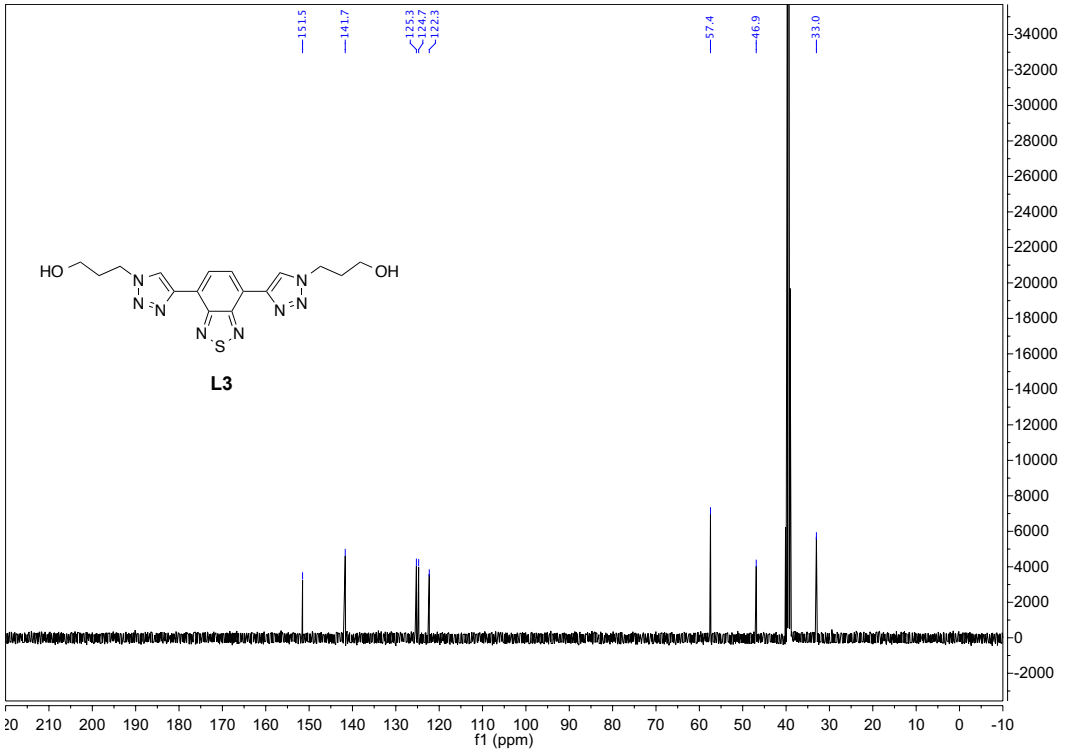


Figure S8. ^{1}H-NMR (top) and ^{13}C-NMR (bottom) spectra of **L3** in CD_3OD and DMSO-d_6, respectively.

References

1. R. C. Lirag; H. T. Le; O. S. Miljanic, *Chem. Commun.* 2013**, 49**, 4304.
2. B. A. Coombs; B. D. Lindner; R. M. Edkins; F. Rominger; A. Beeby; H. Uwe; F. Bunz, *New. J. Chem.* 2012**, 36**, 550.
3. B. Wang; S. W. Tsang; W. Zhang; Y. Tao; M. S. Wong, *Chem. Commun.* 2011**, 47**, 9471.