Electronic Supplementary Material (ESI) for Organic Chemistry Frontiers.

Supporting Information

Enantioselective Determination of Chiral Acids and Amino Acids by Chiral Receptor with Aggregation-induced Emission

Mingyu Chen,[a†] Chunxuan Qi,[a†] Yu-Ting Yin,[a] Panpan Lv,[a] Song Xiang,[a] Jingjing Tian,[a] Jing Feng Zhao,[c] Hai-Tao Feng*[a] and Ben Zhong Tang*[b]

a *AIE Research Center, Shaanxi Key Laboratory of Phytochemistry, College of Chemistry and Chemical Engineering, Baoji University of Arts and Sciences, Baoji 721013, China.*

b *School of Science and Engineering, Shenzhen Institute of Aggregate Science and Technology, The Chinese University of Hong Kong, Shenzhen, Guangdong 518172, China.*

c *Department of Chemistry, School of Pharmacy, The Fourth Military Medical University, Xi'an 710032, China.*

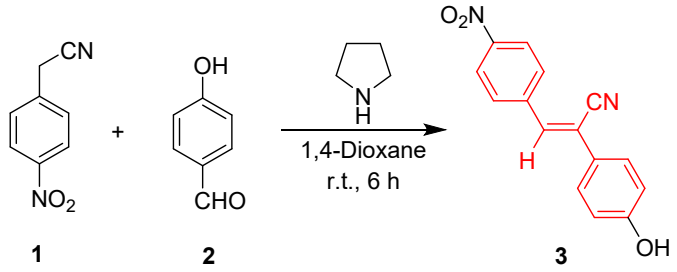
*Corresponding authors (email: haitaofeng907@163.com; tangbenz@ust.hk

1. General information

Materials: All reagents and solvents were chemical pure (CP) grade or analytical reagent (AR) grade and were used as received unless otherwise indicated.

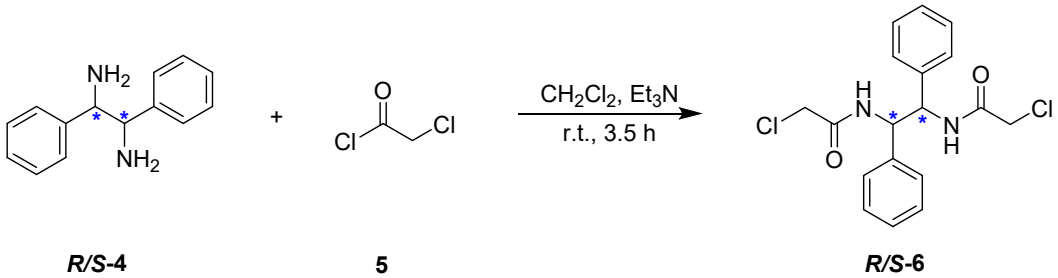
Measurements: ^{1}H NMR and ^{13}C NMR spectra were obtained by an Agilent NMR Systems 400 MHz NMR Spectrometer at 298 K in DMSO-d_6. Absorption spectra were recorded on a Shimadzu UV-2550 UV-Vis spectrophotometer. High-resolution mass spectra (HRMS) were measured by an AB SCIEX 4600 mass spectrometer. Fluorescence spectra were collected on a HORIBA FLOUROMAX-4 fluorophotometer at 298 K. The surface morphologies of the samples were analyzed using field emission scanning electron microscopy (FE-SEM, SU8010, Hitachi).

2. Synthesis



Scheme S1. Synthetic procedure of compound **3**.

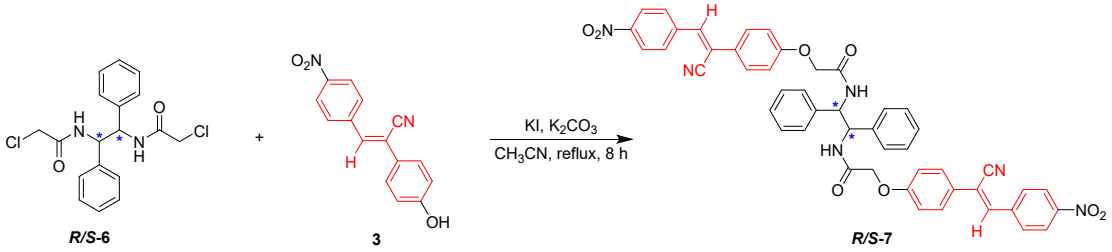
Synthesis of 3: The synthesis method of compound **3** refers to the known literature.[1] *p*-Nitrophenylacetonitrile (4 g, 25 mmol) and *p*-Hydroxybenzaldehyde (3.01 g, 25 mmol), pyrrolidine (3 mL, 36 mmol) were dissolved in 60 mL of 1, 4-Dioxane. After stirring at room temperature for 4 h, the reaction solution was concentrated under reduced pressure. The residue was washed with 1,4-dioxane to afford compound **3** as light yellow solid (5.51 g, 85%). The ^{1}H NMR spectrum of compound **3** was shown in Figure S1. ^{1}H NMR (DMSO-d_6, 298 K, 400 MHz), δ (ppm): 10.45 (s, 1H), 8.32-8.28 (m, 2H), 8.13 (s, 1H), 7.98-7.91 (m, 4H), 6.94 (d, J=8.8 Hz, 2H). ^{13}C NMR (DMSO-d_6, 298 K, 100 MHz), δ (ppm): 160.97, 146.76, 146.28, 140.83, 132.19, 126.34, 126.30, 124.25, 118.00, 116.05 and 103.55.



Scheme S2. Synthetic procedure of chiral compound ***R*/*S*-6**.

Synthesis of *R*-6: The synthesis method of compound ***R*-6** refers to the known literature.[1] 700 mg (3 mmol) of compound (1*R*, 2*R*)-4 and 0.92 mL (7 mmol) of triethylamine were dissolved in 20 mL of dichloromethane. Dropping 0.53 mL (7 mmol) chloroacetyl chloride dissolved in 10 mL dichloromethane to the solution in 0.5 h under the ice bath and then further stirring 3 h at room temperature. After completion, the solution was washed with water, and dried with anhydrous sodium sulfate. The raw product was recrystallized by anhydrous ether to give a white solid (1.09 g, 92%). The ^{1}H NMR spectrum of compound ***R*-6** was shown in Figure S3. ^{1}H NMR (DMSO-d_6, 298 K, 400 MHz), δ (ppm): 8.86 (d, *J*=8.84 Hz, 2H), 7.21-7.11 (m, 10H), 5.19 (d, *J*=8.52 Hz, 2H), 4.05 (d, *J*=1.64 Hz, 4H). The ^{13}C NMR spectrum of compound ***R*-6** was shown in Figure S4. ^{13}C NMR (DMSO-d_6, 298 K, 100 MHz), δ (ppm): 165.50, 139.50, 127.94, 127.41, 127.08, 57.41 and 42.61.

Synthesis of *S*-6: The synthesis method of compound ***S*-6** refers to the known literature.[1] The procedure was similar to that of ***R*-6**. ***S*-6** prepared from compound **(*1S*, *2S*)-4** was obtained as a white solid (1.52 g, 88%). The ^{1}H NMR spectrum of compound ***S*-6** was shown in Figure S5. ^{1}H NMR (DMSO-d_6, 298 K, 400 MHz), δ (ppm): 8.85 (d, *J*=8.64 Hz, 2H), 7.21-7.12(m, 10H), 5.19 (d, *J*=8.52 Hz, 2H), 4.05 (d, *J*=1.72 Hz, 4H). The ^{13}C NMR spectrum of compound ***S*-6** was shown in Figure S6. ^{13}C NMR (DMSO-d_6, 298 K, 100 MHz), δ (ppm): 165.51, 139.50, 127.95, 127.41, 127.09, 57.41 and 42.62.



***R*/*S*-6** + **3** → ***R*/*S*-7**

Scheme S3. Synthetic procedure of chiral AIEgens ***R*-7** and ***S*- 7**.

Synthesis of *R*-7: 365 mg (1 mmol) compound ***R*-6**, 533 mg (2 mmol) compound **3**, 691 mg (5 mmol) K_2CO_3 and 166 mg (1 mmol) KI were dissolve in 60 mL of acetonitrile. TLC monitored the reaction (EA:PE=1:4). After the reaction is completed, the solution was extracted with EA and saturated aqueous sodium chloride solution and dried with anhydrous sodium sulfate. The residue was washed with methanol to give a yellow solid powder (717.6 mg, 87%). The ^{1}H NMR spectrum of ***R*-7** was shown in Figure S7. ^{1}H NMR (DMSO-d_6, 298 K, 400 MHz), δ (ppm): 8.80 (d, *J*=6.4 Hz, 2H), 8.25 (d, *J*=8.68 Hz, 4H), 8.03 (s, 2H), 7.90 (d, *J*=2.64 Hz, 4H), 7.88 (d, *J*=2.68 Hz, 4H), 7.24-7.14 (m, 10H), 6.97 (d, *J*=8.56 Hz, 4H), 5.36 (d, *J*=8.36 Hz, 2H), 4.54 (d, *J*=5.16 Hz, 4H). The ^{13}C NMR spectrum of ***R*-7** was shown in Figure S8. ^{13}C NMR (DMSO-d_6, 298 K, 100 MHz), δ (ppm): 167.08, 160.29, 146.81, 145.48, 140.33, 139.77, 131.67, 127.92, 127.46, 127.02, 126.36, 126.16, 124.17, 117.59, 115.21, 104.97, 66.87 and 56.92. Figure S11 was shown the HRMS m/z calcd for $C_{48}H_{36}N_6O_8$ 823.2595 [M-H], found 823.2564 [M-H].

Synthesis of *S*-7: The procedure was similar to that of ***R*-7**. ***S*-7** prepared from compound ***S*-6** was obtained as a white solid (765.8 mg, 93%). The ^{1}H NMR spectrum of ***S*-7** was shown in Figure S9. ^{1}H NMR (DMSO-d_6, 298 K, 400 MHz), δ (ppm): 8.85 (d, *J*=28.7 Hz, 2H), 8.25 (d, *J*=8.92 Hz, 4H), 8.03(s, 2H), 7.90 (d, *J*=3 Hz, 4H), 7.88 (d, *J*=3 Hz, 4H), 7.24-7.14 (m, 10H), 6.97(d, *J*=8.96

Hz, 4H), 5.36 (d, *J*=8.4 Hz, 2H), 4.55(d, *J*=4.56 Hz, 4H). The ^{13}C NMR spectrum of ***S*-7** was shown in Figure S10. ^{13}C NMR (DMSO-d_6, 298 K, 100 MHz), δ (ppm): 167.08, 160.29, 146.82, 145.49, 140.34, 139.78, 131.67, 127.93, 127.46, 126.37, 126.16, 124.18, 117.60, 115.22, 104.98, 66.86 and 56.92. Figure S12 was shown the HRMS m/z calcd for $C_{48}H_{36}N_6O_8$ 823.2595 [M-H], found 823.2530 [M-H].

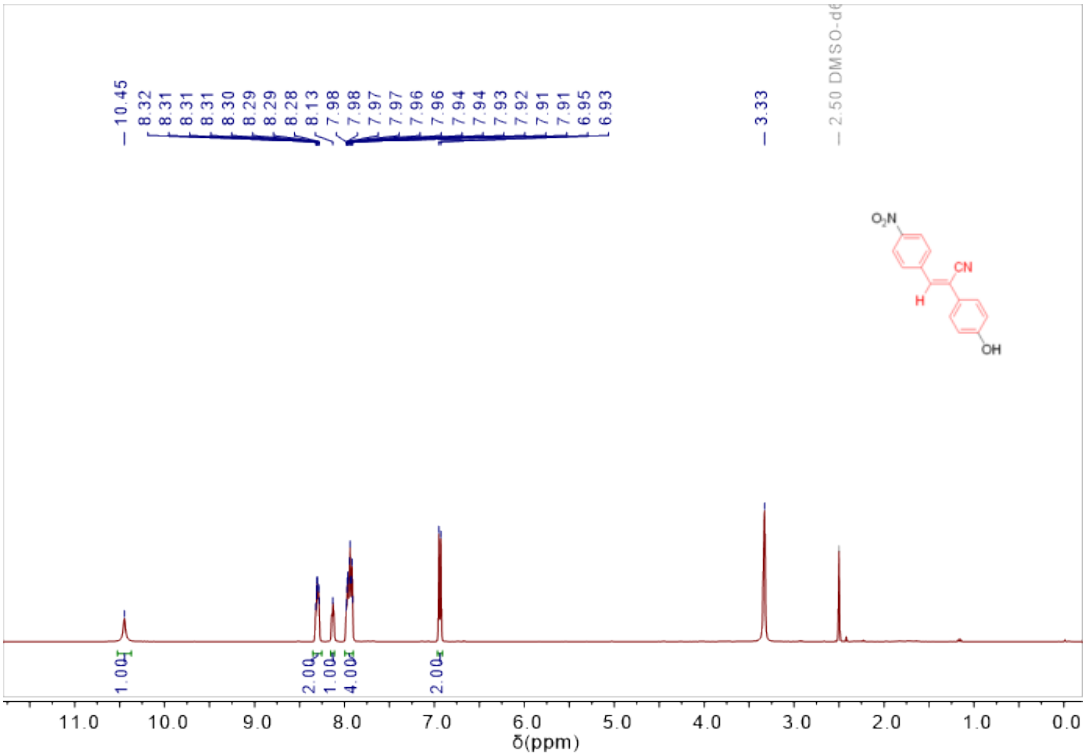


Figure S1. ^{1}H NMR spectrum of compound **3** in DMSO-d_6.

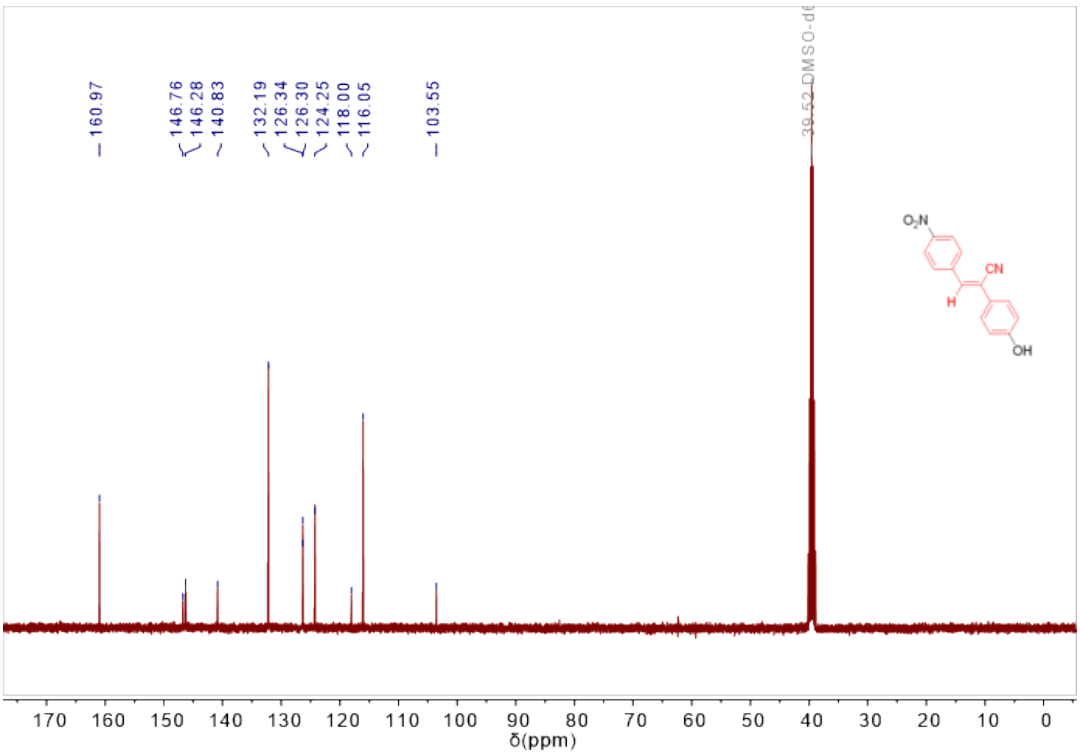


Figure S2. ^{13}C NMR spectrum of compound **3** in DMSO-d_6.

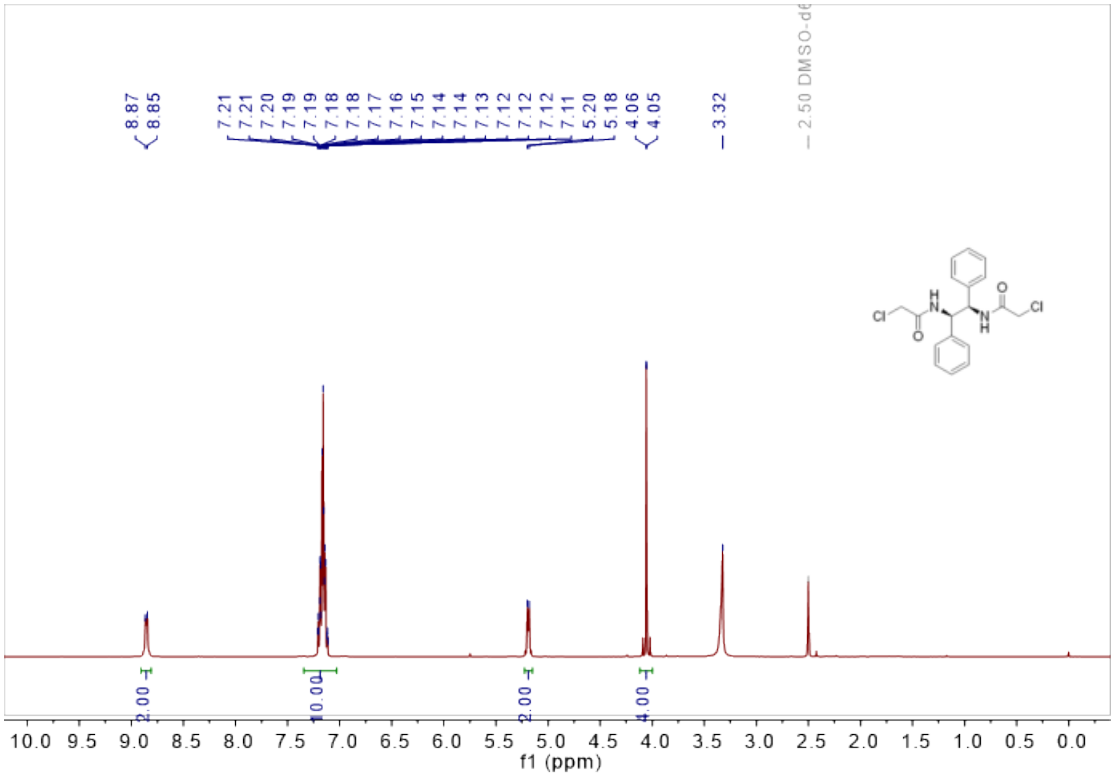


Figure S3. ^{1}H NMR spectrum of compound ***R*-6** in DMSO-d_6.

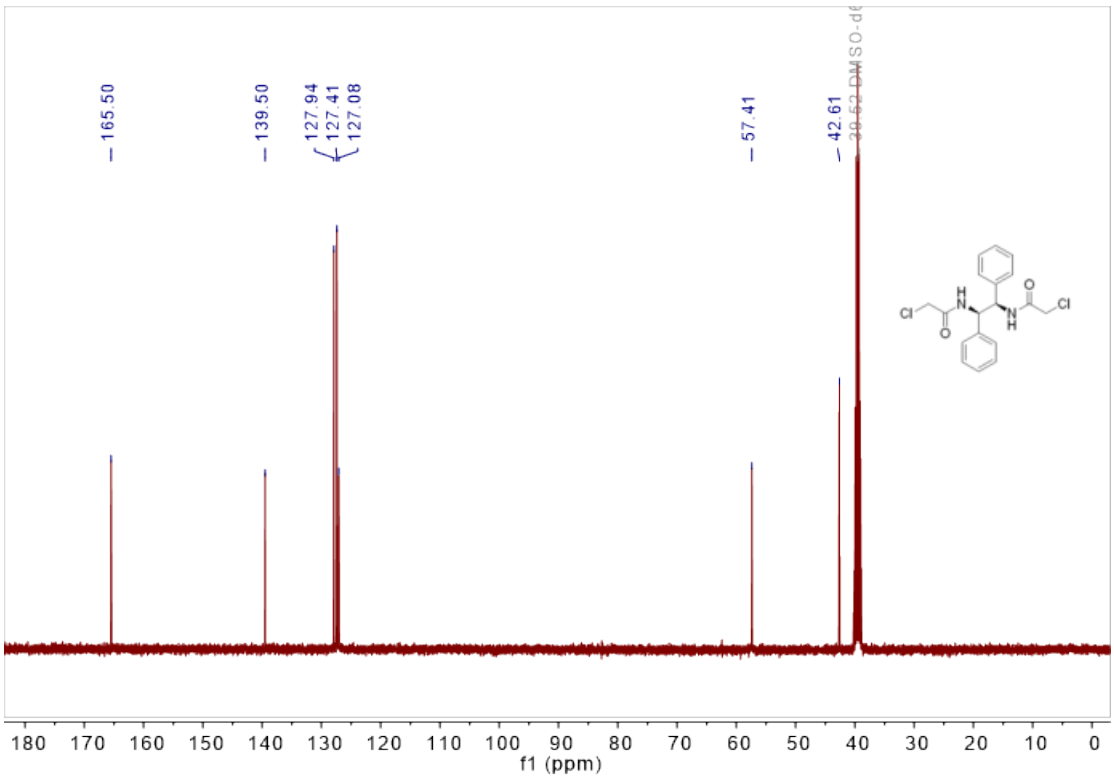


Figure S4. ^{13}C NMR spectrum of compound ***R*-6** in DMSO-d_6.

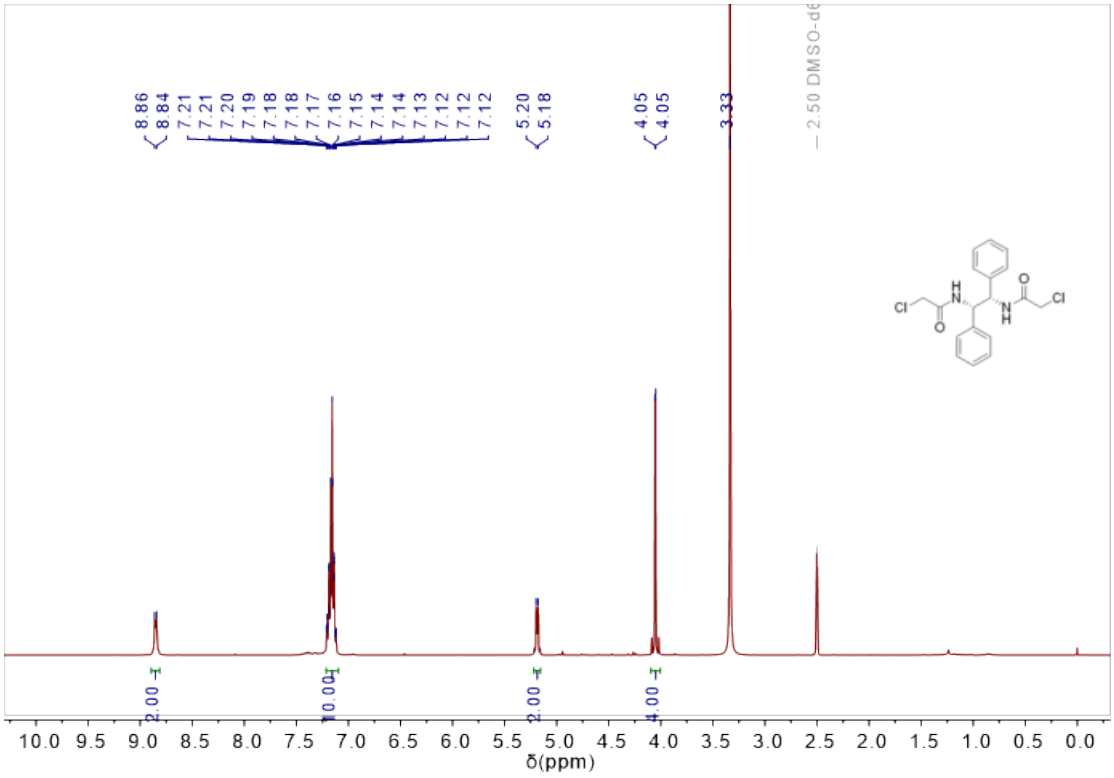


Figure S5. ^{1}H NMR spectrum of compound ***S*-6** in DMSO-d_6.

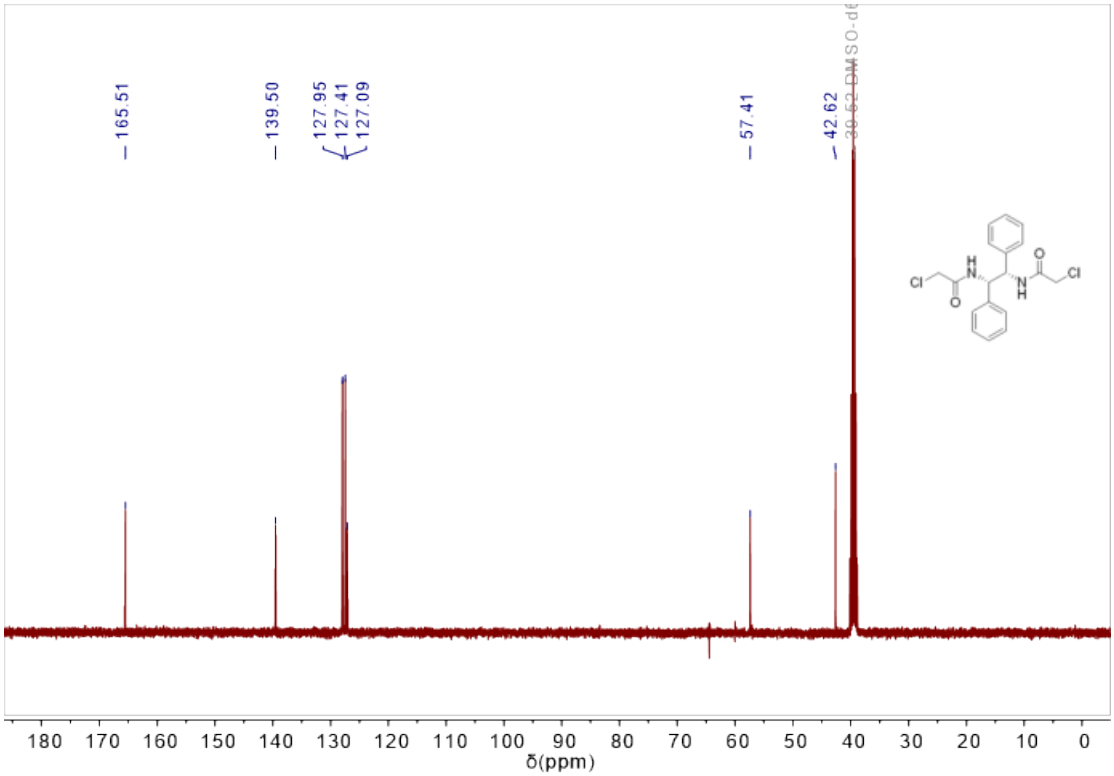


Figure S6. ^{13}C NMR spectrum of compound ***S*-6** in DMSO-d_6.

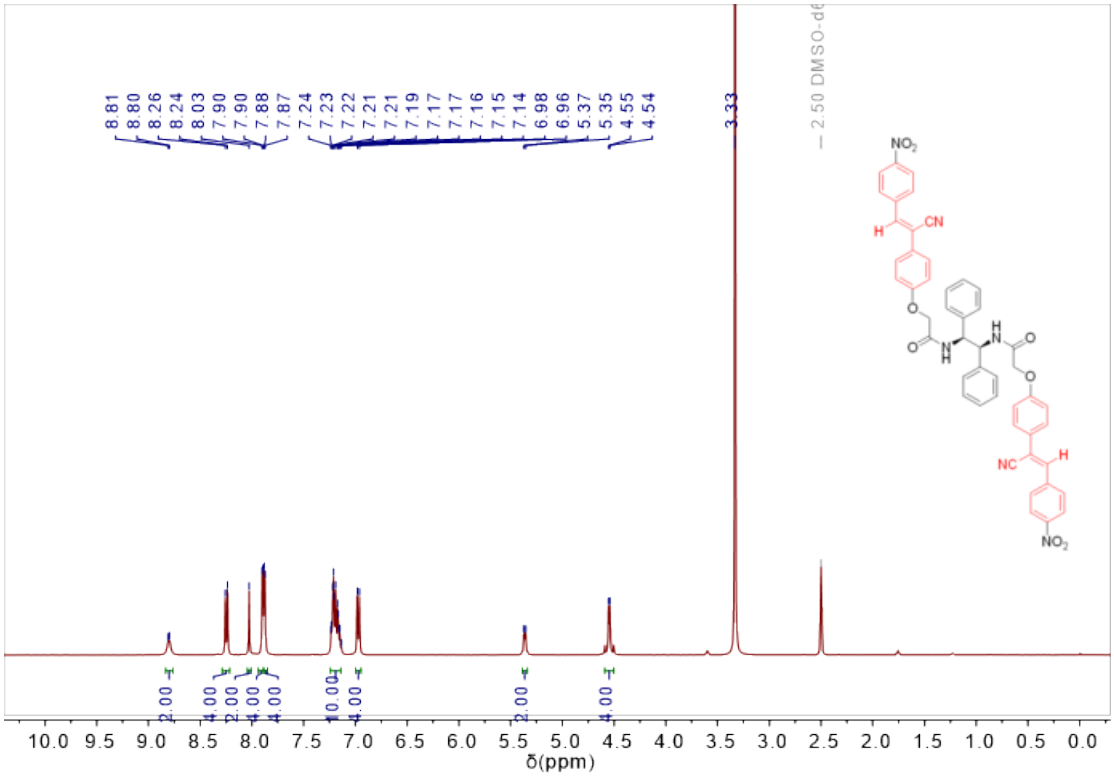


Figure S7. ^{1}H NMR spectrum of ***R*-7** in DMSO-d_6.

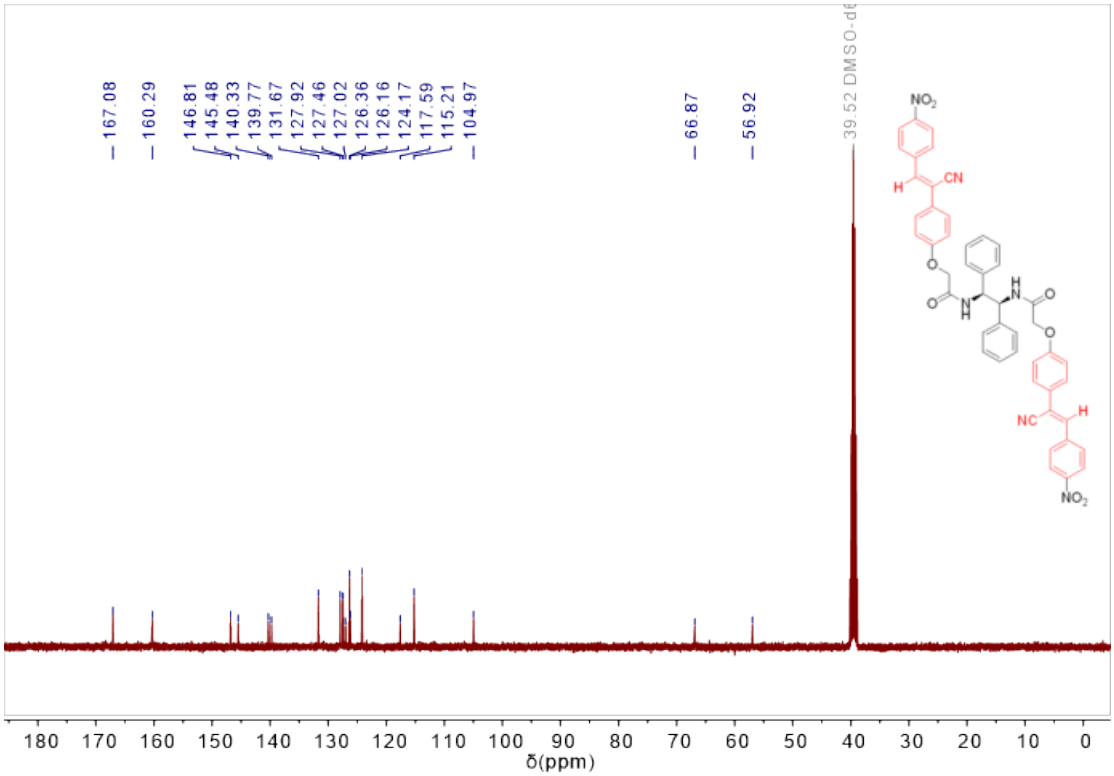


Figure S8. ^{13}C NMR spectrum of ***R*-7** in DMSO-d_6.

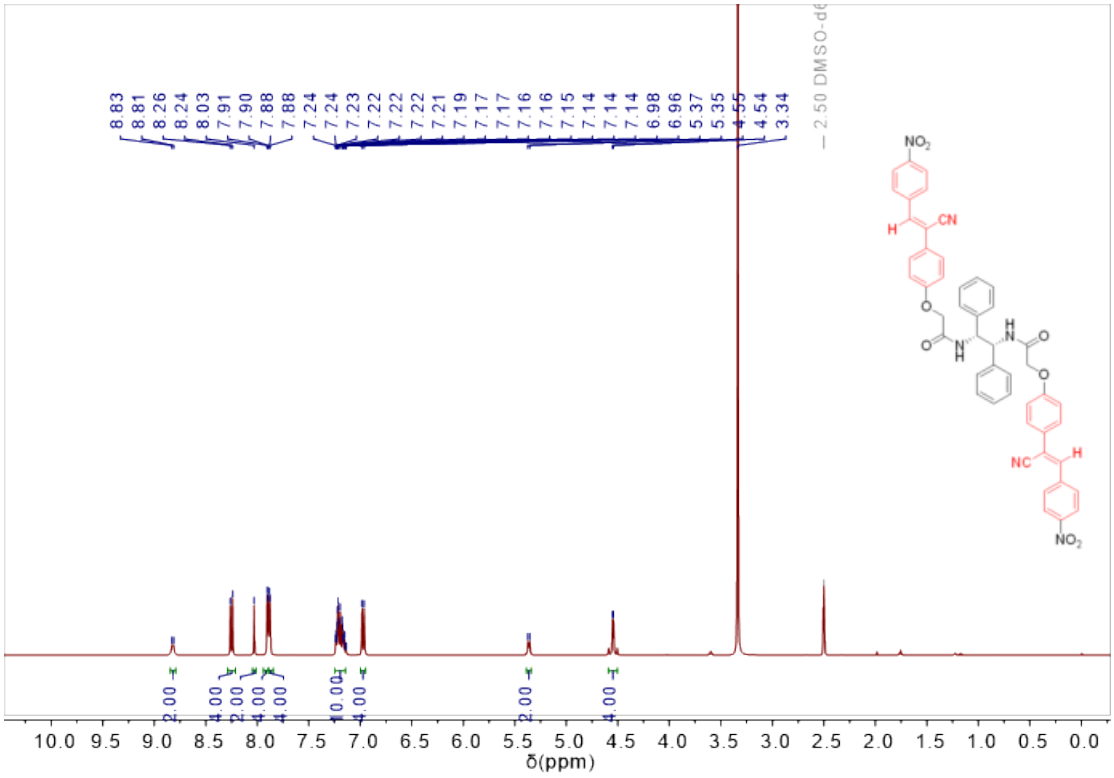


Figure S9. ^{1}H NMR spectrum of ***S*-7** in DMSO-d_6.

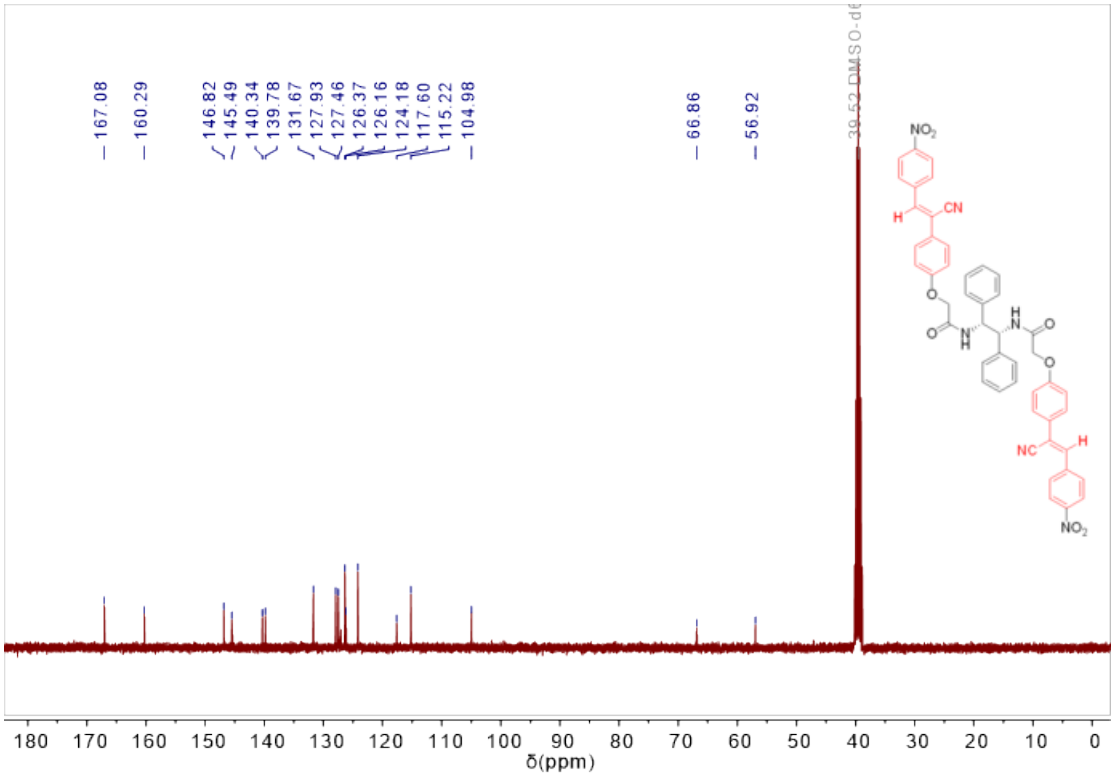


Figure S10. ^{13}C NMR spectrum of ***S*-7** in DMSO-d_6.

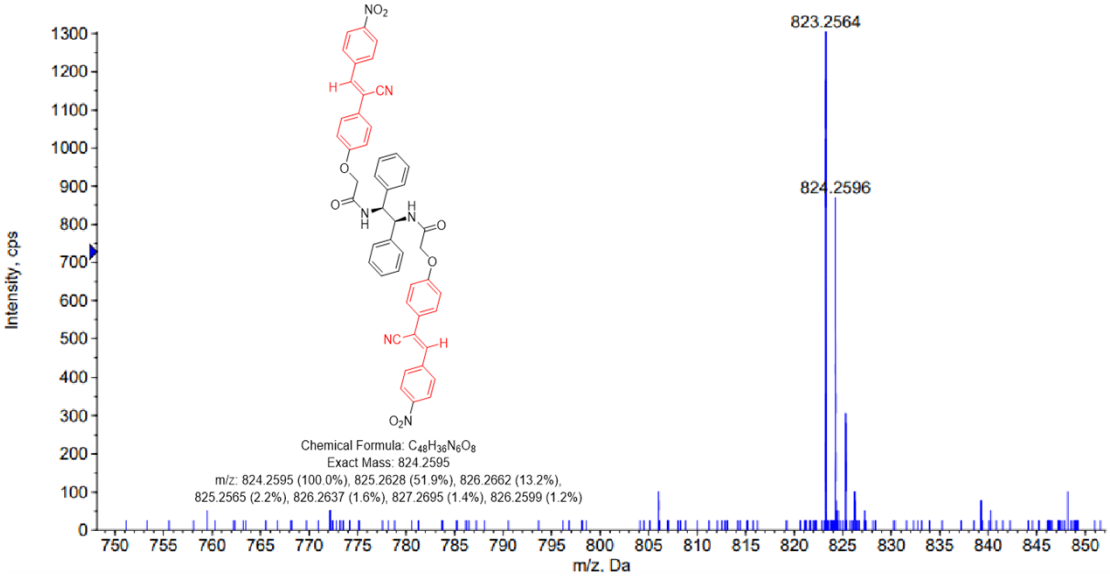


Figure S11. HRMS spectrum of ***R*-7**.

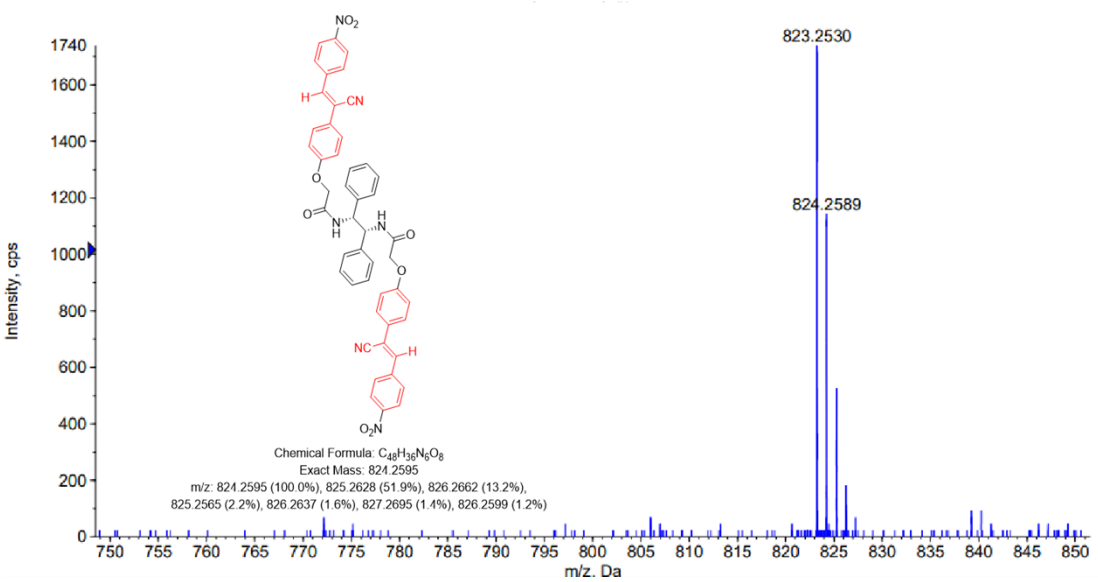


Figure S12. HRMS spectrum of ***S*-7**.

3. Photophysical properties of *R*-7 and *S*-7.

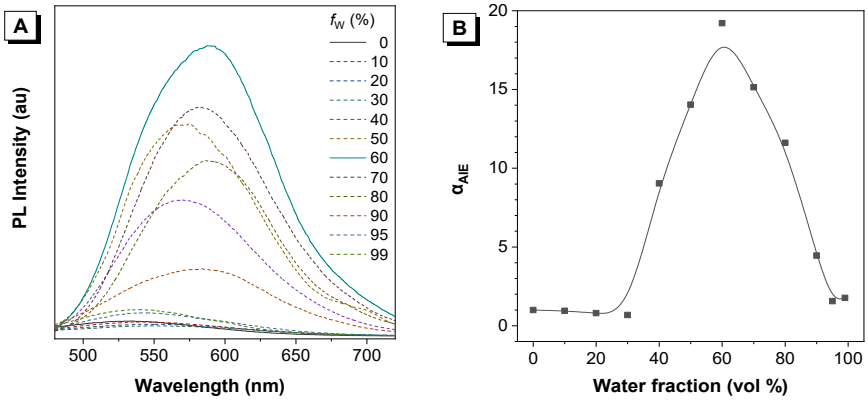


Figure S13. (A) PL spectra of ***R*-7** in DMF/water mixture with different water fraction. Excitation wavelength: 369 nm, [***R*-7**] = 1.0 × 10^{-5} M. (B) Fluorescence intensity ratio of α_{AIE} in different DMF/water mixture.

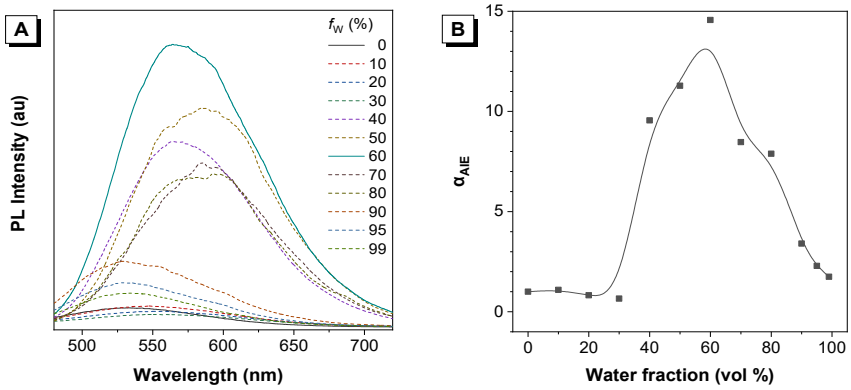
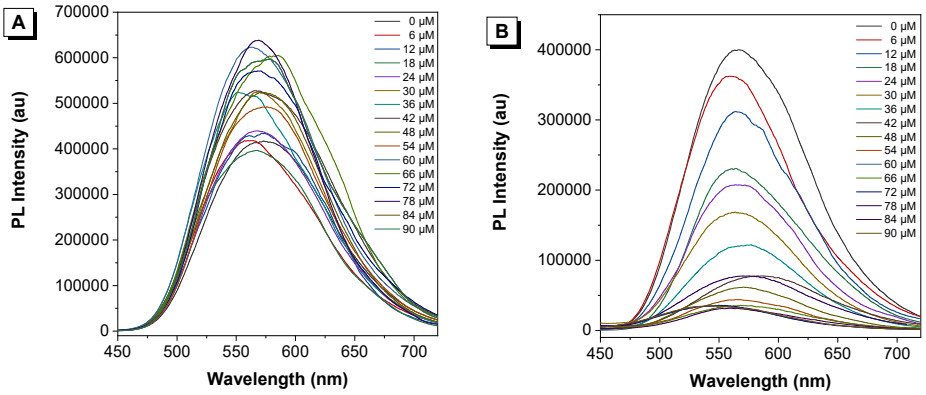


Figure S14. (A) PL spectra of ***S*-7** in DMF/water mixture with different water fraction. Excitation wavelength: 369 nm, [***S*-7**] = 1.0 × 10^{-5} M. (B) Fluorescence intensity ratio of α_{AIE} in different DMF/water mixture.



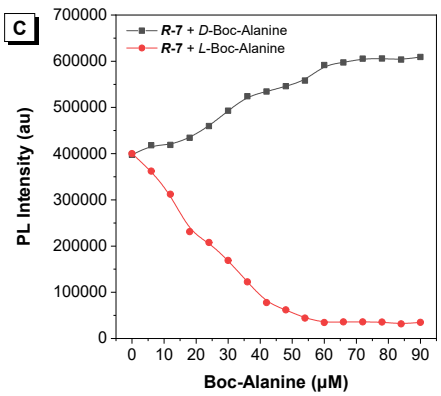


Figure S15. (A) PL titration of ***R*-7** (1.0×10^{-5} M) in the presence of 0 to 90 μM of *D*-Boc-Alanine in DMF/H_2O (60/40); (B) PL titration of ***R*-7** in the presence of 0 to 90 μM of *L*-Boc-Alanine in DMF/H_2O (60/40); (C) Curve of PL intensity versus concentration of Boc-Alanine.

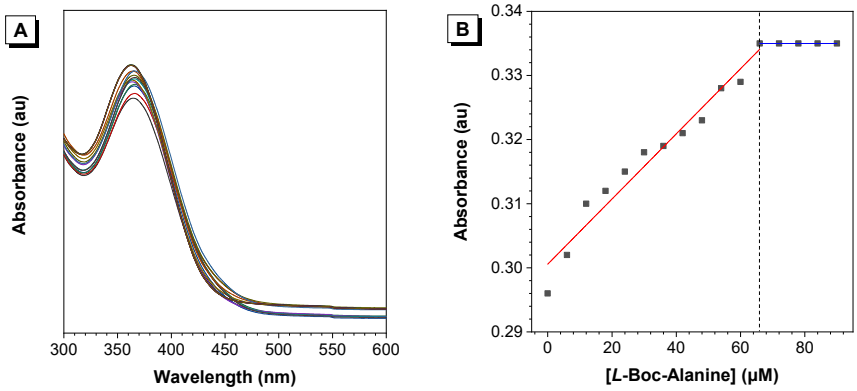


Figure S16. (A) UV-vis titration of ***R*-7** (1.0×10^{-5} M) in the presence of 0 to 90 μM of *L*-Boc-Alanine in DMF/H_2O (60/40). (B) Curve of absorbance versus concentration of *L*-Boc-Alanine. [***R*-7**] = 30 μM.

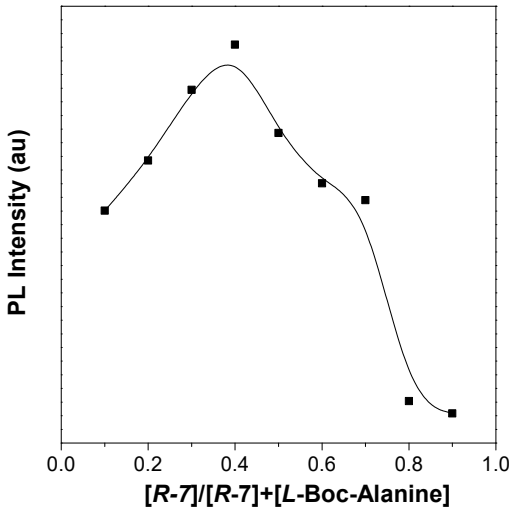


Figure S17. Job's plots for PL titration of *L*-Boc-Alanine with ***R*-7** in DMF/H_2O (60/40).

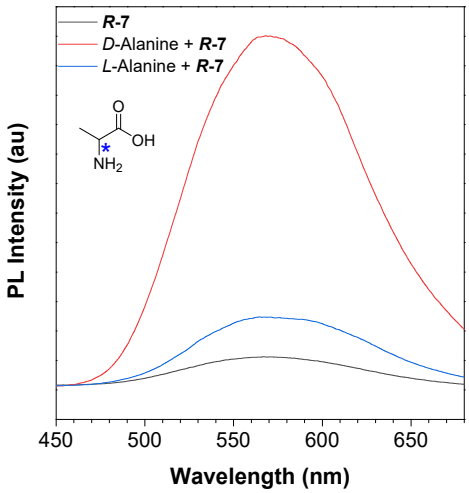
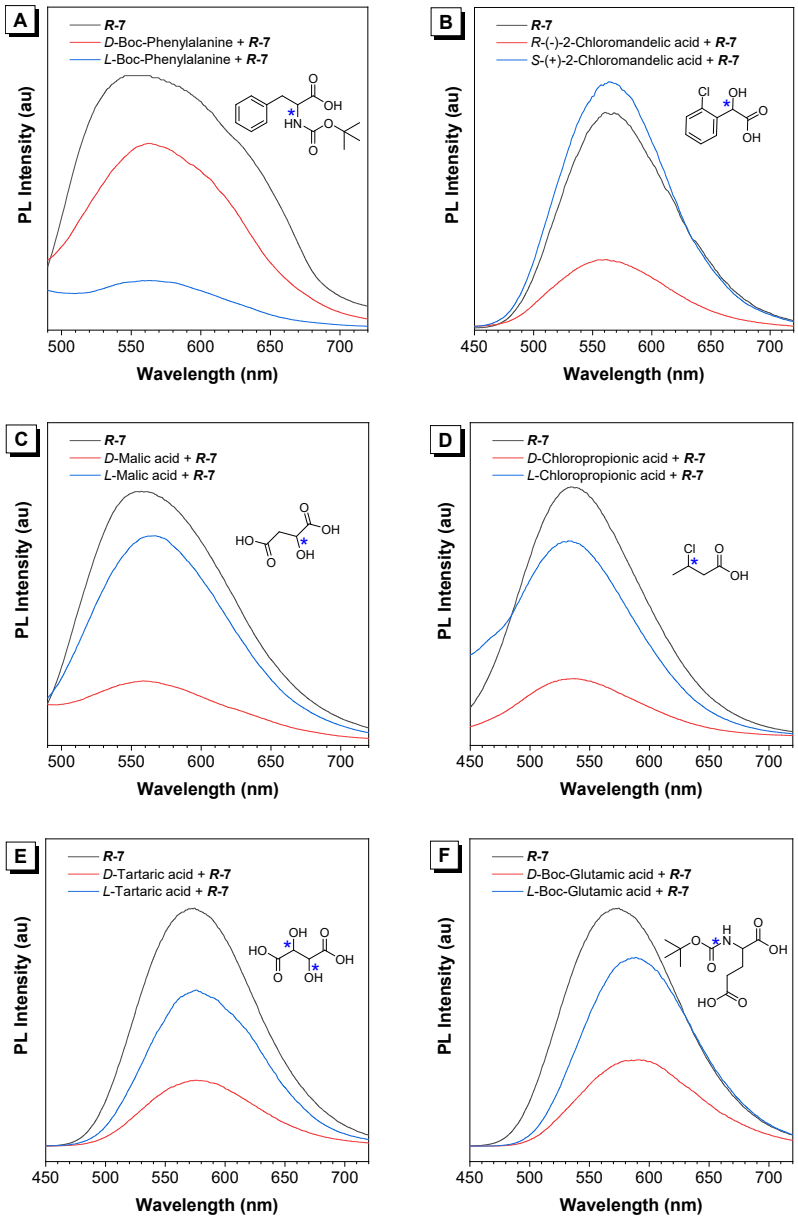
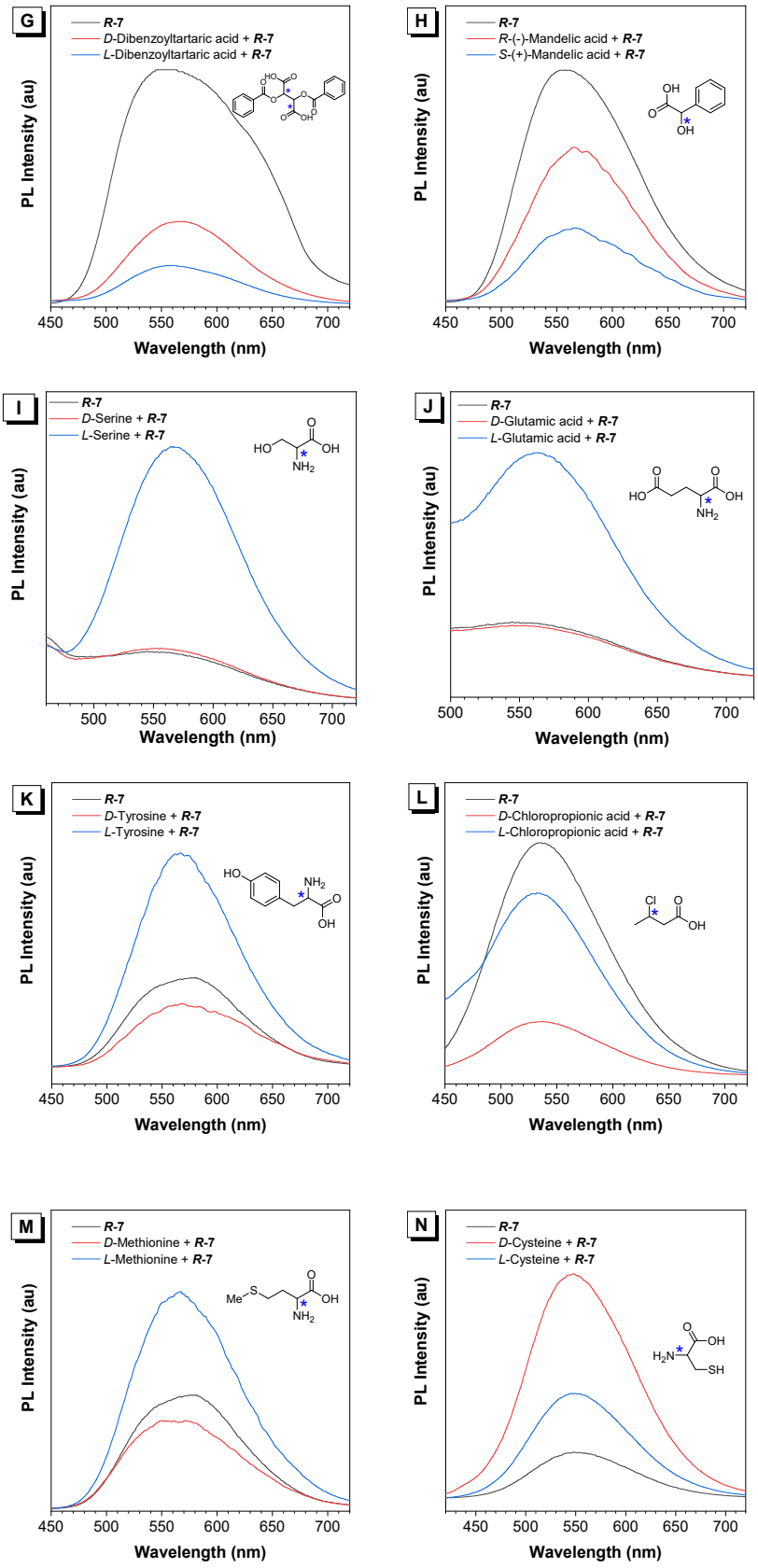


Figure S18 PL spectra of a mixture of ***R*-7** and enantiomers of Alanine in DMSO/H_2O (v/v, 3/2). [***R*-7**] = 1/2[analyte] = 1.0×10^{-5} M, λ_{ex} = 369 nm. I_D/I_L = 4.86.




G
R-7
D-Dibenzoyltartaric acid + R-7
L-Dibenzoyltartaric acid + R-7
PL Intensity (au)
Wavelength (nm)
H
R-7
R-(-)-Mandelic acid + R-7
S-(+)-Mandelic acid + R-7
PL Intensity (au)
Wavelength (nm)
I
R-7
D-Serine + R-7
L-Serine + R-7
PL Intensity (au)
Wavelength (nm)
J
R-7
D-Glutamic acid + R-7
L-Glutamic acid + R-7
PL Intensity (au)
Wavelength (nm)
K
R-7
D-Tyrosine + R-7
L-Tyrosine + R-7
PL Intensity (au)
Wavelength (nm)
L
R-7
D-Chloropropionic acid + R-7
L-Chloropropionic acid + R-7
PL Intensity (au)
Wavelength (nm)
M
R-7
D-Methionine + R-7
L-Methionine + R-7
PL Intensity (au)
Wavelength (nm)
N
R-7
D-Cysteine + R-7
L-Cysteine + R-7
PL Intensity (au)
Wavelength (nm)

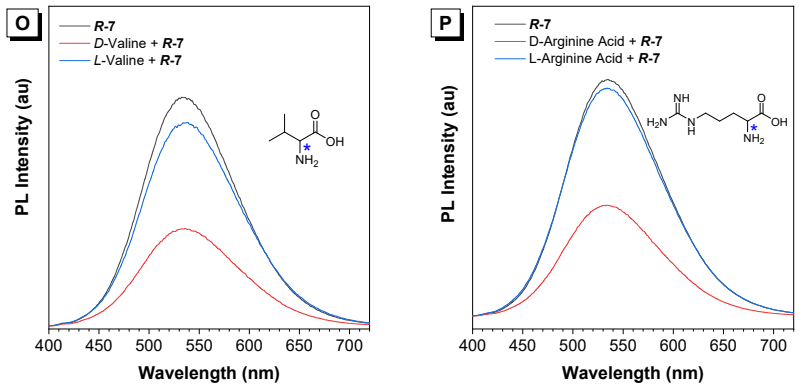


Figure S19. PL spectra of a mixture of ***R*-7** and enantiomers of *D* /*L*-Boc-Phenylalanine (A), *D*/*L*-2-Chloromandelic acid (B), *D*/*L*-Malic acid (C), *D*/*L*-Chloropropionic acid (D), *D*/*L*-Tartaric acid (E), *D*/*L*-Boc-Glutamic acid (F), *D*/*L*-Dibenzoyltartaric acid (G), *R*/*S*-(+)-Mandelic acid (H), *D*/*L*-Serine (I), *D*/*L*-Glutamic acid (J), *D*/*L*-Tyrosine (K), *D*/*L*-Chloropropionic acid (L), *D*/*L*-Methionine/*D*-Methionine (M), *D*/*L*-Cysteine (N), *D*/*L*-Valine (O), *D*/*L*-Arginine Acid (P).

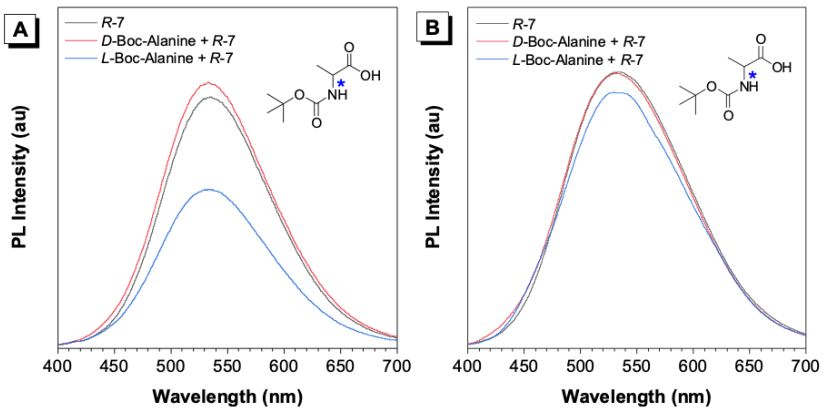


Figure S20. PL spectra of a mixture of ***R*-7** and enantiomers of Boc-Alanine in DMF(A) and DMSO(B) [***R*-7**] = 1/2[analyte] = 1.0×10^{-5} M, λ_{ex} = 369 nm.

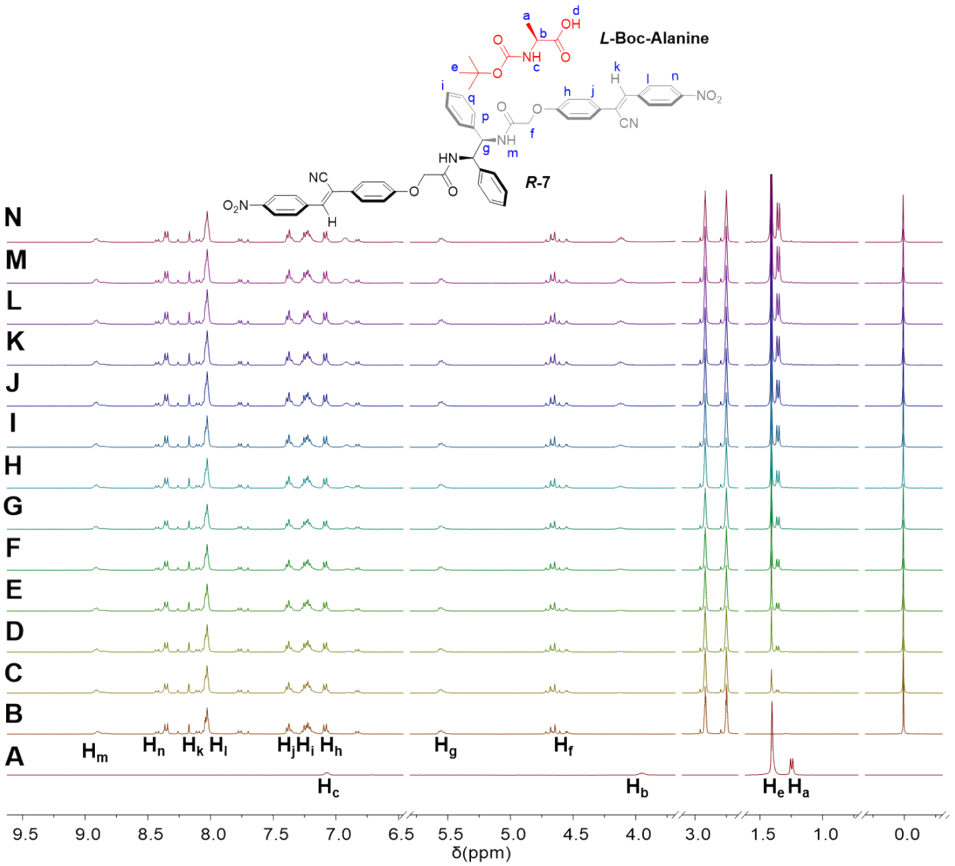


Figure S21. ^{1}H NMR titration of the ***R*-7** and *L*-Boc-alanine system in DMF-d_7 at 298 K. (A) Resonance signals for the free *L*-Boc-alanine (4.0 mM). (B) Resonance signals for the free ***R*-7** (4.0 mM). (C–N) Changes in resonance signals of *L*-Boc-alanine in the presence of 0.2 to 3.0 equivalents of ***R*-7**.

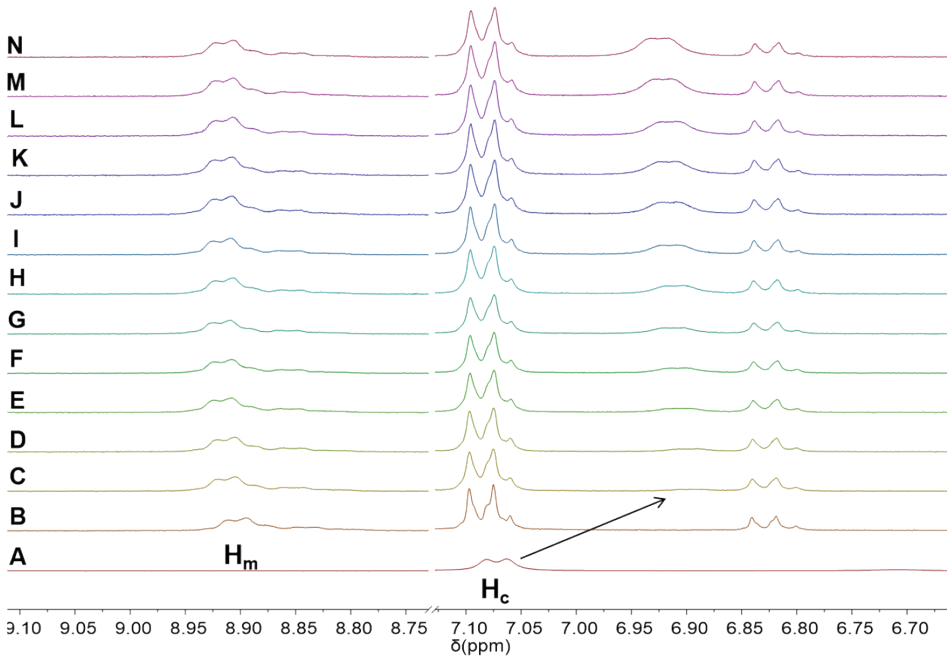


Figure S22. Change of chemical shifts of protons H_c and H_m upon titration with *L*-Boc-Alanine in the presence of ***R*-7** (4.0 mM).

Table S1. Changes of chemical shift of ***R*-7** during ^{1}H NMR titration.

Chemical shift	H_a	H_b	H_c	H_f	H_g	H_i	H_j	H_k	H_m	H_n
From	1.3513	4.1213	6.9236	4.6475	5.5461	7.2201	7.3709	8.1684	8.3406	8.9060
To	1.3439	4.1179	6.8973	4.6466	5.5518	7.2237	7.3758	8.1713	8.3426	8.9037
△δ/ppm	0.0074	0.0034	0.0263	0.0009	-0.0057	-0.0036	-0.0049	-0.0029	-0.002	0.0023

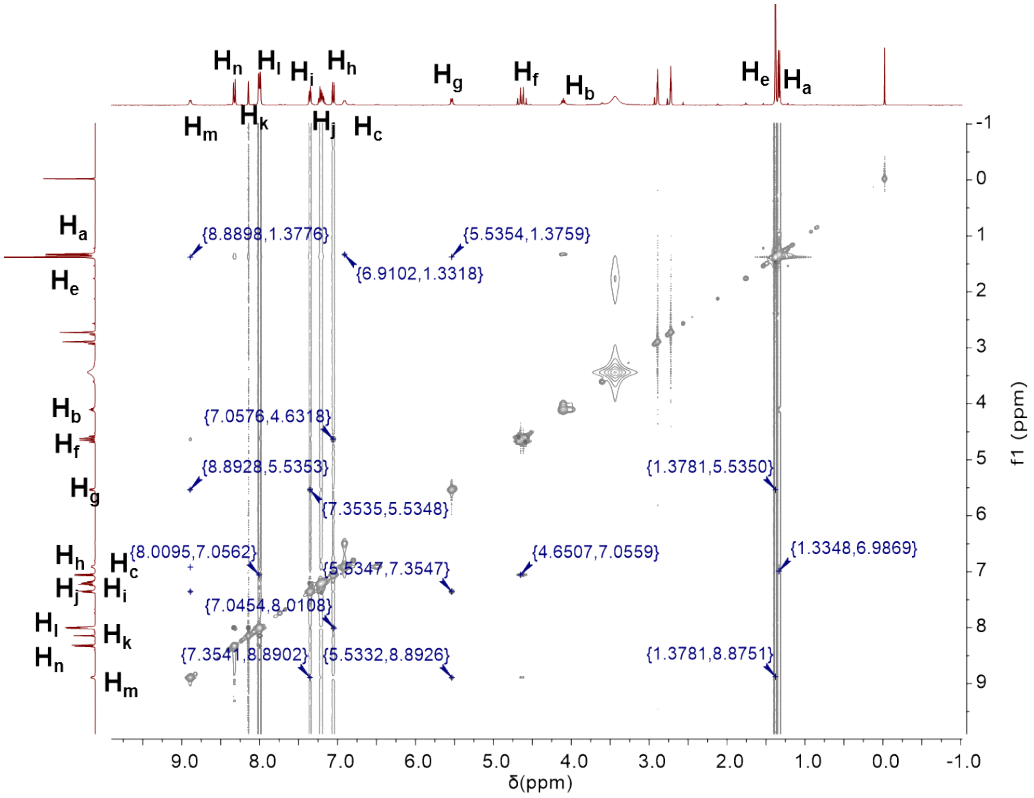


Figure S23. 2D NOESY spectrum of ***R*-7** and Arginine (measured by a 400 MHz instrument over 18 h, ***R*-7** = 10 mM and *L*-Boc-Alanine =20 mM in DMF-d_7 at 298 K).

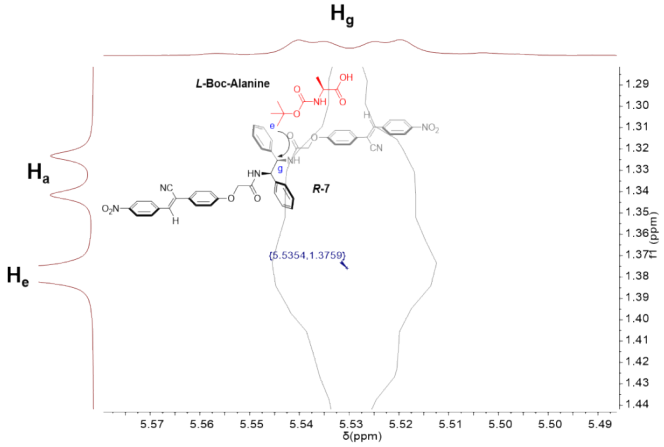


Figure S24. Partial 2D NOESY spectra of ***R*-7** (10 mM) and ***L*-Boc-Alanine** (20 mM).The NOE effect between H_e and H_g.

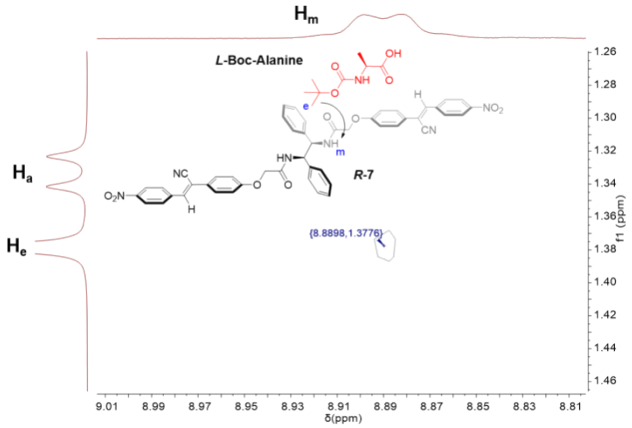


Figure S25. Partial 2D NOESY spectra of ***R*-7** (10 mM) and ***L*-Boc-Alanine** (20 mM). The NOE effect between H_e and H_m.

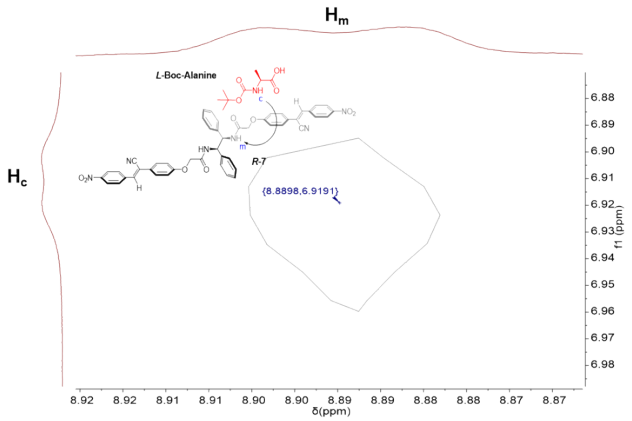


Figure S26. Partial 2D NOESY spectra of ***R*-7** (10 mM) and ***L*-Boc-Alanine** (20 mM). The NOE effect between H_m and H_c.

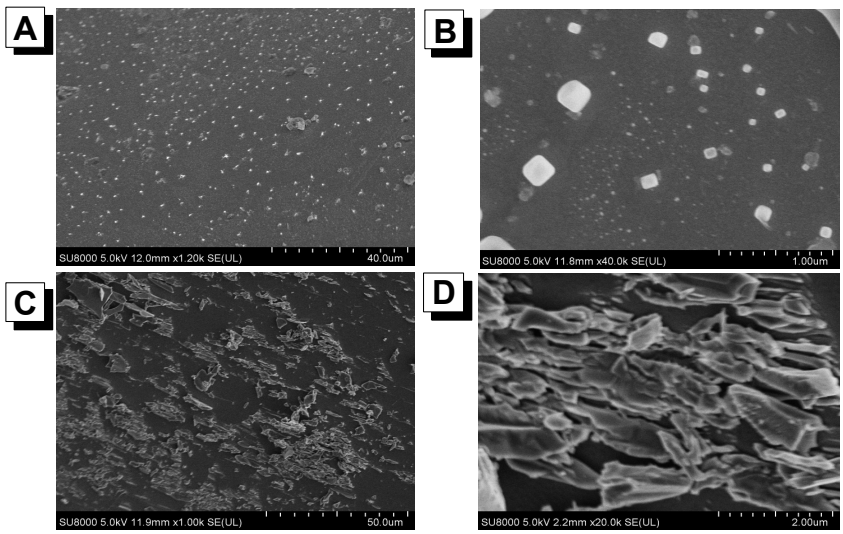


Figure S27. SEM images of the mixture (A and B: D-Boc-Alanine + ***R*-7**, C and D: L-Boc-Alanine + ***R*-7**) in DMF/Water (v/v, 60/40), [***R*-7**] = 1.0×10^{-5} M.

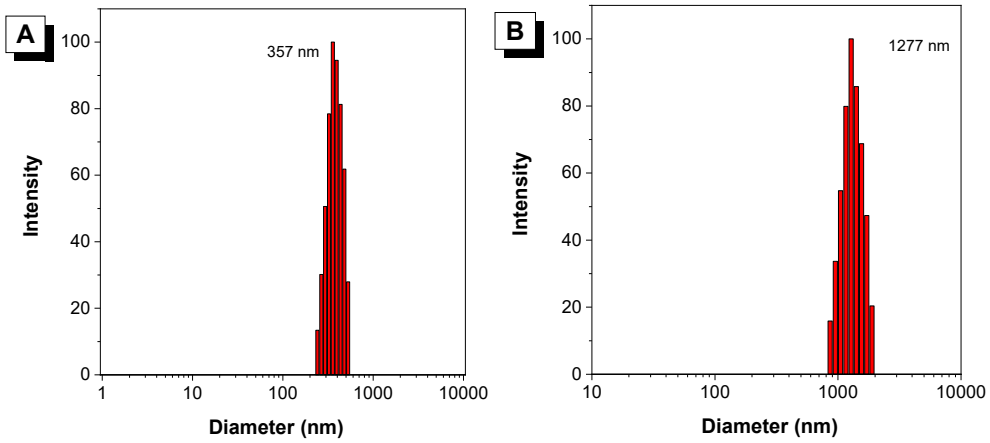


Figure S28. Dynamic light scattering diagram of Boc-*D*-Alanine + ***R*-7** (A) and Boc-*L*-Alanine + ***R*-7** (B) in DMF/H_2O (60/40), respectively.

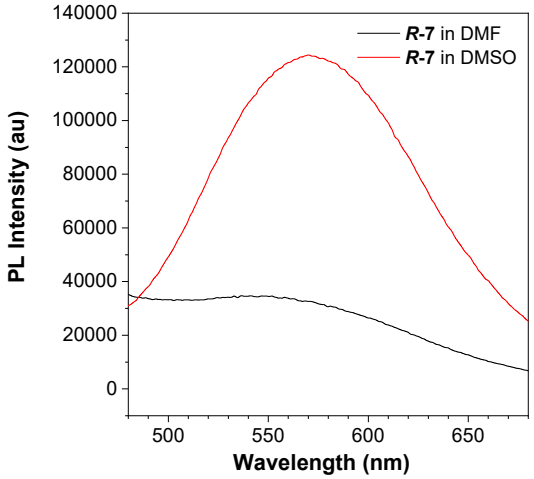


Figure S29. PL spetrum of ***R*-7** in pure DMF and pure DMSO.

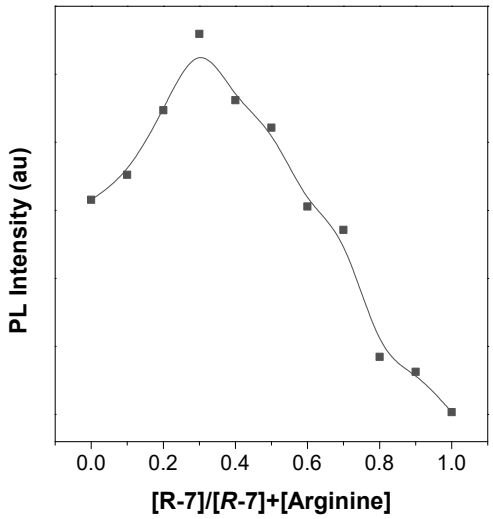


Figure S30. Job's plot for PL titration of Arginine with ***R*-7** in DMSO.

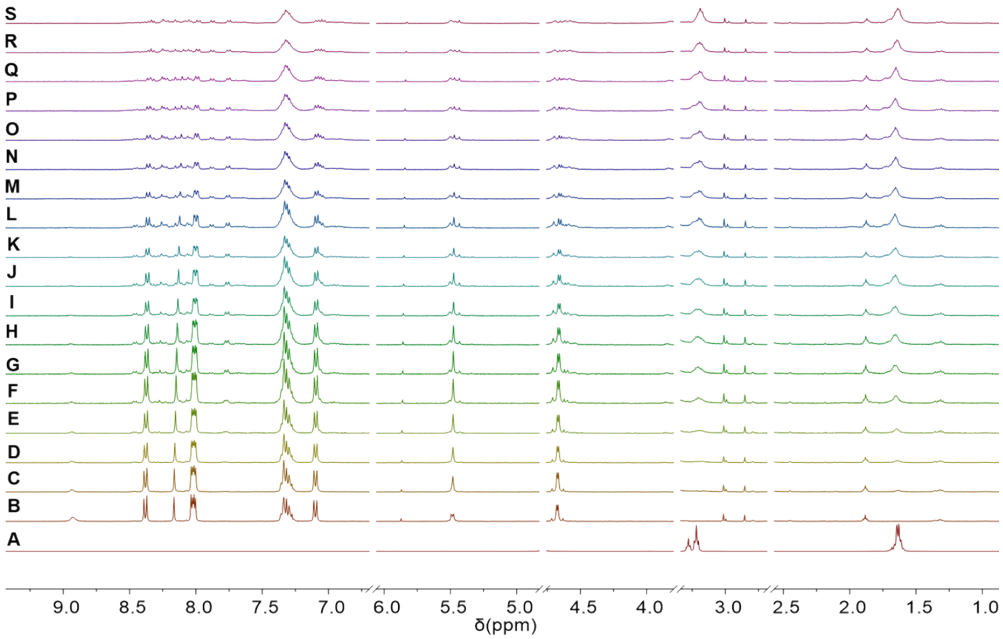


Figure S31. ^{1}H NMR titration of the ***R*-7** and Arginine system in d_6-DMSO at 298 K. (A) Resonance signals for the free Arginine (5.0 mM). (B) Resonance signals for the free ***R*-7** (5.0 mM). (C−S) Changes in resonance signals of Arginine in the presence of 0.2 to 4.0 equivalents of ***R*-7**.

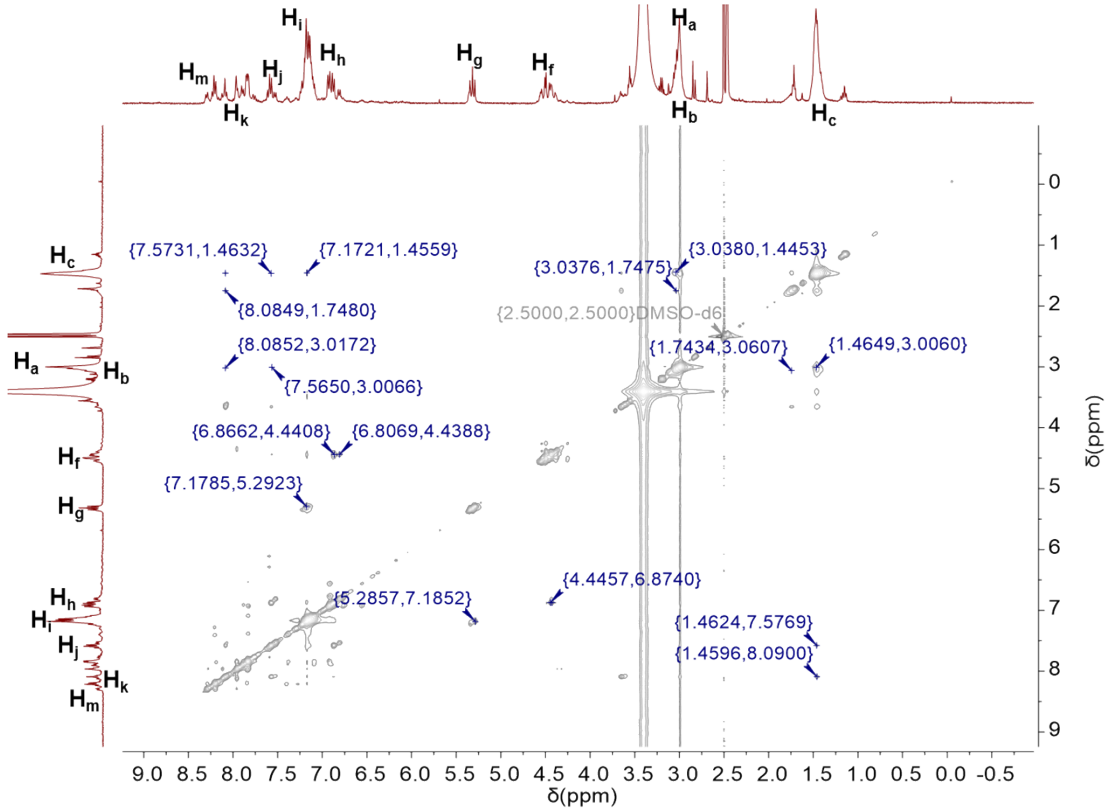


Figure S32. 2D NOESY spectrum of ***R*-7** and Arginine (measured by a 400 MHz instrument over 18 h, ***R*-7** = 10 mM and Arginine =20 mM in DMSO-d_6 at 298 K).

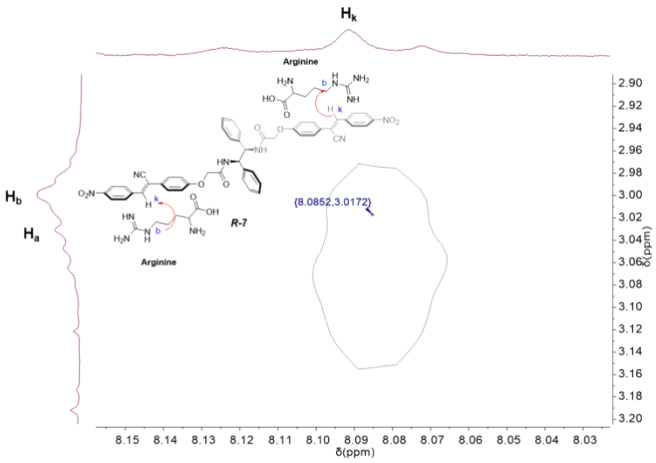


Figure S33. 2D NOESY spectra of ***R*-7** (10 mM) and Arginine (20 mM). The NOE effect between H_b and H_k.

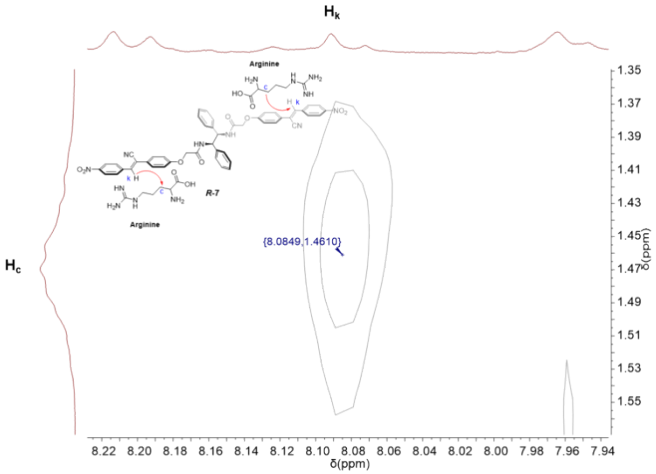


Figure S34. 2D NOESY spectra of ***R*-7** (10 mM) and Arginine (20 mM). The NOE effect between H_c and H_k.

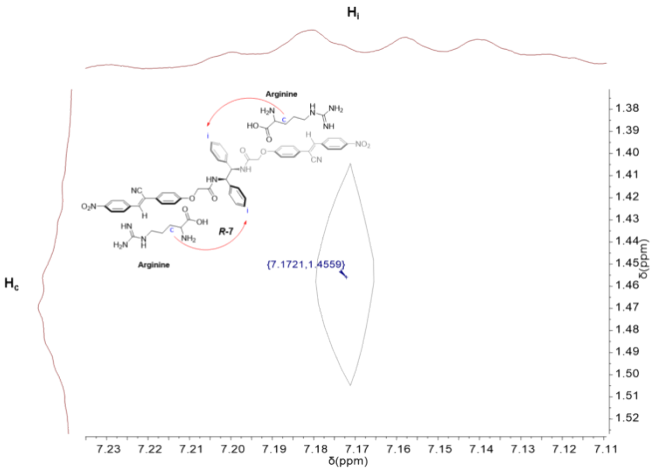


Figure S35. 2D NOESY spectra of ***R*-7** (10 mM) and Arginine (20 mM). The NOE effect between H_c and H_i.

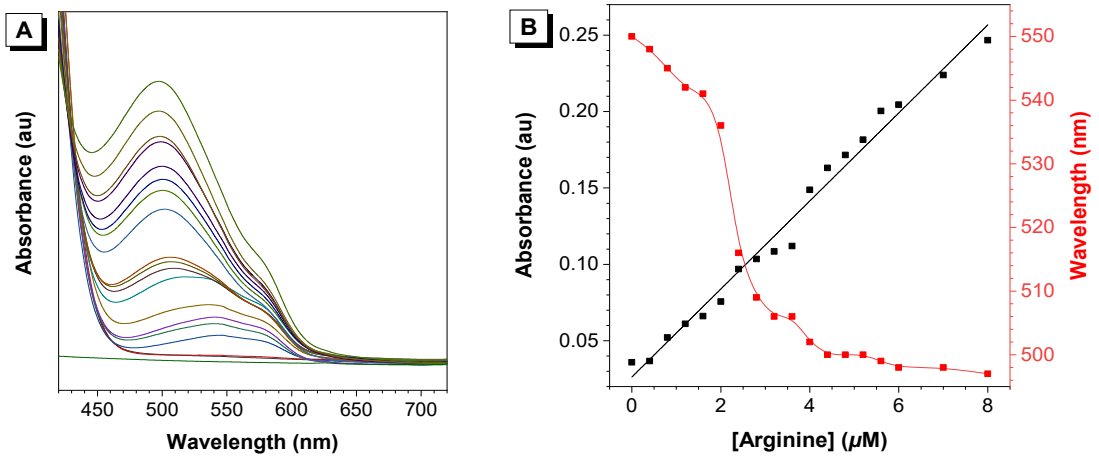


Figure S36. (A) The absorbance curve of Arginine at 0 × 10^{-6} M to 8 × 10^{-5} M + ***R*-7** (2 × 10^{-5} M), in DMSO. (B) Plot of absorbance intensity in different concentrations. Acordding to LOD = 3δ/s [2, 3] the limit of detection is 2.38 10^{-7} M.

References

1. D.-M. Li, Y.-S. Zheng, *Chem. Commun.*, 2011, **47**, 10139–10141.
2. J. Xiong, Z. Li, J. Tan, S. Ji, J. Sun, X. Li, Y. Huo, *Analyst*, 2018, **143**, 4870-4886.
3. H.-T. Feng, S. Song; Y.-C. Chen; C.-H. Shen; Y.-S. Zheng, *J. Mater. Chem. C*, 2014, **2**, 2353-2359.