A water soluble pillar[5]arene-based chemosensor for highly selective and sensitive fluorescence detection L-Methionine

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1. Experimental

1.1 Materials and instruments

All amino acid were purchased from Alfa Aesar and used as received. Other reagents used in the study were analytical grade. Fresh double distilled water was used throughout the experiment. All other reagents and solvents were commercially available at analytical grade and were used without further purification. ^{1}H NMR spectra were recorded on a Mercury−600BB spectrometer at 600 MHz and ^{13}C NMR spectra were recorded on a Mercury−600BB spectrometer at 150 MHz. Chemical shifts are reported in ppm downfield from tetramethylsilane (TMS, δ scale with solvent resonances as internal standards). Low-resolution mass spectra were recorded on a Bruker Esquire 6000 MS instrument. The infrared spectra were performed on a Digilab FTS-3000 Fourier transform-infrared spectrophotometer. Melting points were measured on an X-4 digital melting-point apparatus (uncorrected). Ultraviolet-visible (UV-vis) spectra were recorded on a Shimadzu UV-2550 spectrometer. Fluorescence spectra were recorded on a Shimadzu RF-5301PC spectrofluorophotometer.

1.2 General procedure for fluorescence experiments

Fluorescence spectroscopy was carried out keeping the host concentration constant in water solution on a Shimadzu RF-5301PC spectrofluorophotometer.

1.3 General procedure for ^{1}H NMR titrations

For ^{1}H NMR titrations, three stock solutions were prepared: one of them contained the host only in D_2O, the second one contained an appropriate concentration of guest in DMSO-*d6*. The third one contained an appropriate concentration of host and guest in D_2O. Aliquots of the two solutions were mixed directly in NMR tubes.

1.4 Synthesis and characterization of AWP5

The synthetic procedure of the cationic pillar[5]arene (**AWP5**) is shown in Scheme S1, which is based on a improved literature [1-3] methods.

1.4.1 Synthesis of compound 1

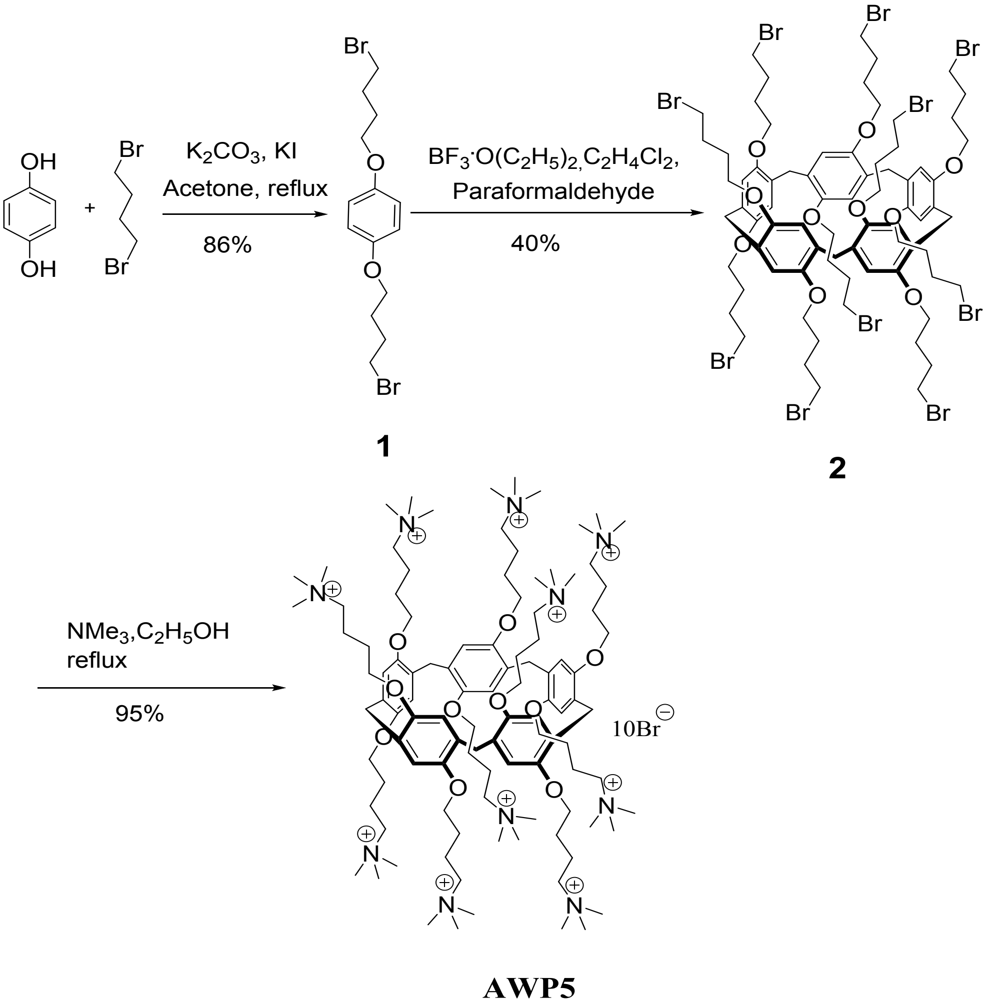
Hydroquinone (2.2 g, 20.0 mmol), K_2CO_3 (13.8 g, 100 mmol), KI (0.83 g, 5mmol), 1,4-Dibromobutane (17.28 g, 80.0mmol) and acetone (200.0 mL) were added in a 250 mL round–bottom flask. The reaction mixture was stirred at reflux for 5 days. Then 200 mL of cold water was added to the reaction mixture, where compound **1** precipitated as a white solid. The compound **1** was purified by column chromatography on silica gel with petroleumether/ethyl acetate (5:1v/v) as the eluent to get a white powder (6.5 g, 86 %). m.p. 86 °C. ^{1}H NMR (600 MHz, $CDCl_3$, Fig. S1) δ 6.79 (t, J = 6.0 Hz, 4H), 4.00 – 3.83 (m, 4H), 3.46 (t, J = 6.6 Hz, 4H), 2.12 – 1.81 (m, 8H). ^{13}C NMR (150 MHz, $CDCl_3$, Fig. S2) δ: 76.65 (s), 67.46 (s), 33.46 (s), 29.52 (s), 28.02 (s). MS: ESI (Fig. S3) m/z for **1** $C_{14}H_{21}Br_2O_2$, found: 380.9882, calcd: 380.9888.

1.4.2 Synthesis of compound 2

A solution of compound **1** (3.8 g, 10.0 mmol) in 1, 2-dichloroethane (200 mL), paraformaldehyde (0.686 g, 20.0 mmol) was added under nitrogen atmosphere. Then boron trifluoride diethyl etherate ($BF_3{\cdot}O(C_2H_5)_2$, 1.42 g, 10.0 mmol) was added to the solution and the mixture was stirred at room temperature for 4 h. A green solution was obtained. After the solvent was removed, the obtained solid was purified by column chromatography on silica gel with petroleummether/dichloromethane (1:1 v/v) as the eluent to get a white powder compound **2** (1.57 g, 40 %). m.p.124-126 °C. ^{1}H NMR (600 MHz, $CDCl_3$, Fig. S4) δ: 6.86 (s, 10H), 3.96 (s, 20H), 3.76 (d, J = 8.0 Hz, 10H), 3.50 (s, 10H), 3.29 (s, 10H), 2.12 (s, 20H), 1.99 (s, 20H).^{13}C NMR (150 MHz, $CDCl_3$, Fig. S5) δ: 149.55, 128.15, 67.33, 33.83, 32.09, 30.12 and 28.57. MS: ESI (Fig. S6) m/z for **2** $C_{75}H_{104}K_2Br_{10}O_{10}Na_6$, found: 2180.89, calcd : 2180.82.

1.4.3 Synthesis of AWP5

The compound **2** (1.00 g, 0.51 mmol) and trimethylamine (33 % in ethanol, 6.89 mL, 25.5 mmol) were added to ethanol (50 mL). The solution was refluxed over night. Then the solvent was removed by evaporation, deionized water (20 mL) was added. After filtration, a clear solution was obtained. Then the water was removed by evaporation to obtain **AWP5** as a white solid (1.28 g, 95 %). m.p.218-220 °C. ^{1}H NMR (600 MHz, D_2O, Fig. S7) δ 6.78 (s, 11H), 3.82 (d, J = 38.2 Hz, 31H), 3.25 (s, 21H), 2.97 (s, 90H), 1.78 (s, 41H). The ^{13}C NMR spectrum of **AWP5** is shown in Fig. S8 ^{13}C NMR (150 MHz, D_2O) δ: 150.12, 129.22, 116.81, 68.46, 65.87, 52.87, 25.78 and 19.46. HRESIMS (Fig. S9) m/z for **AWP5** [M-3Br+9Na+2NH$_4$]$^{3+}$ $C_{105}H_{198}Br_7N_{12}Na_9O_{10}$, found: 848.9418, calcd: 848.9554.



Scheme S1 Synthesis of **AWP5**.

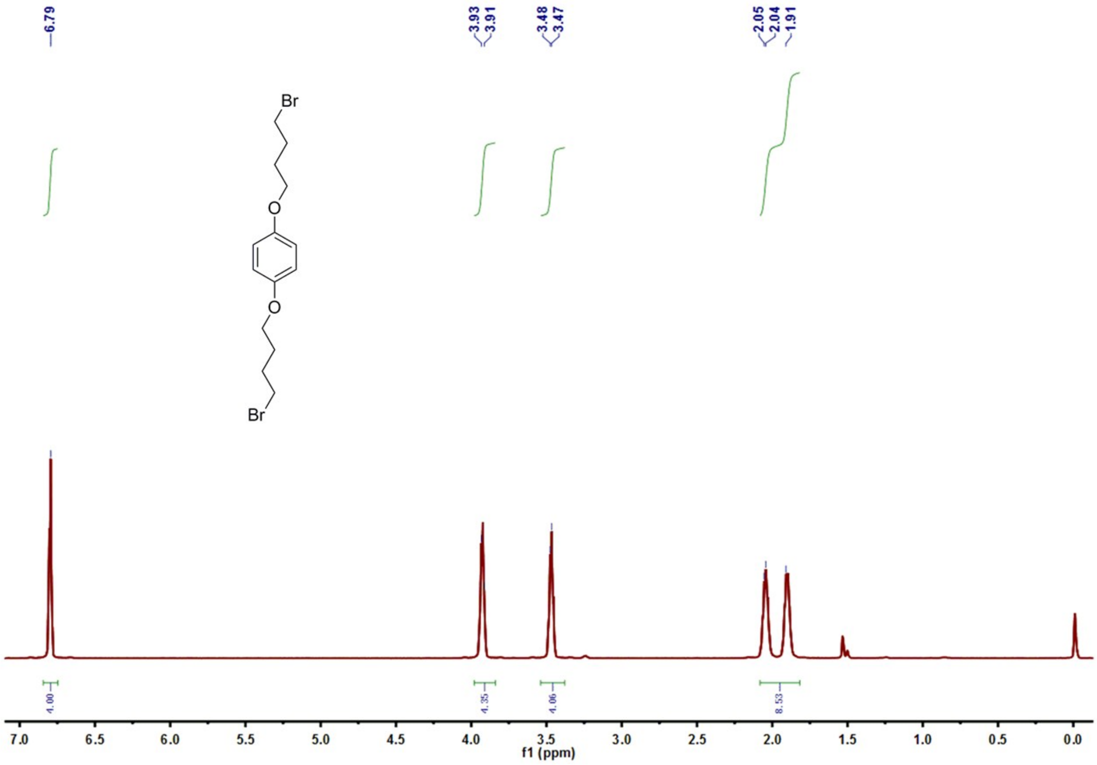


Fig. S1 ^{1}H NMR (600 MHz, 298 K) spectra of compound **1** in $CDCl_3$.

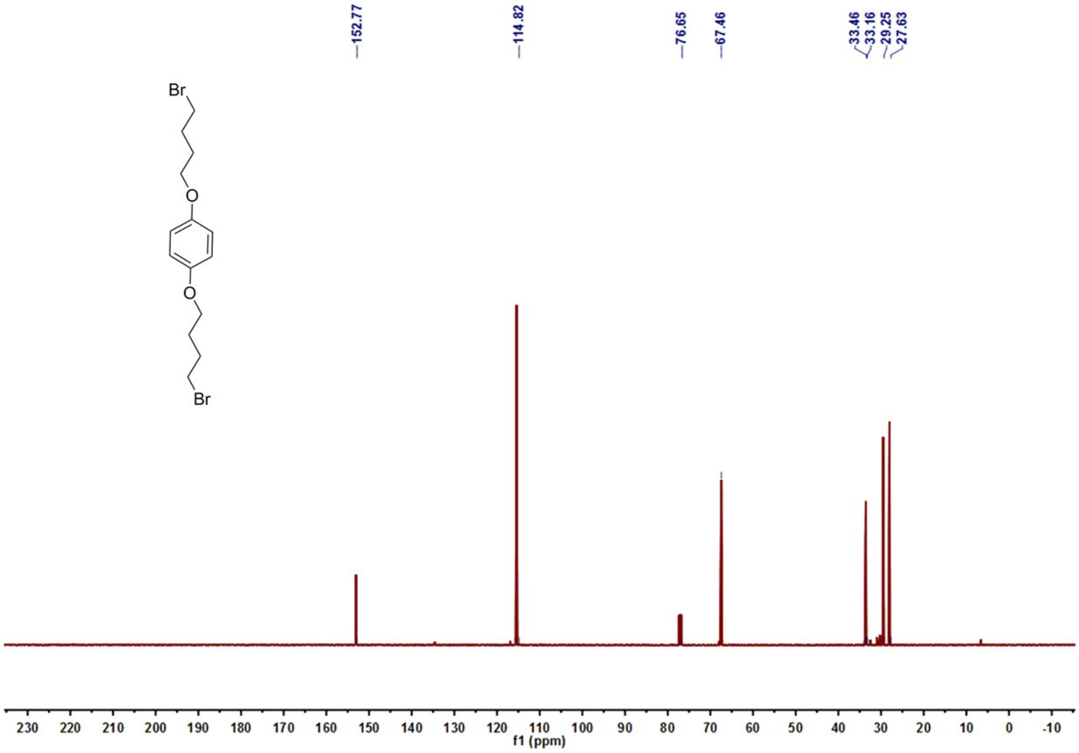


Fig. S2 ^{13}C NMR (150 MHz, 298K) spectra of compound **1** in $CDCl_3$.

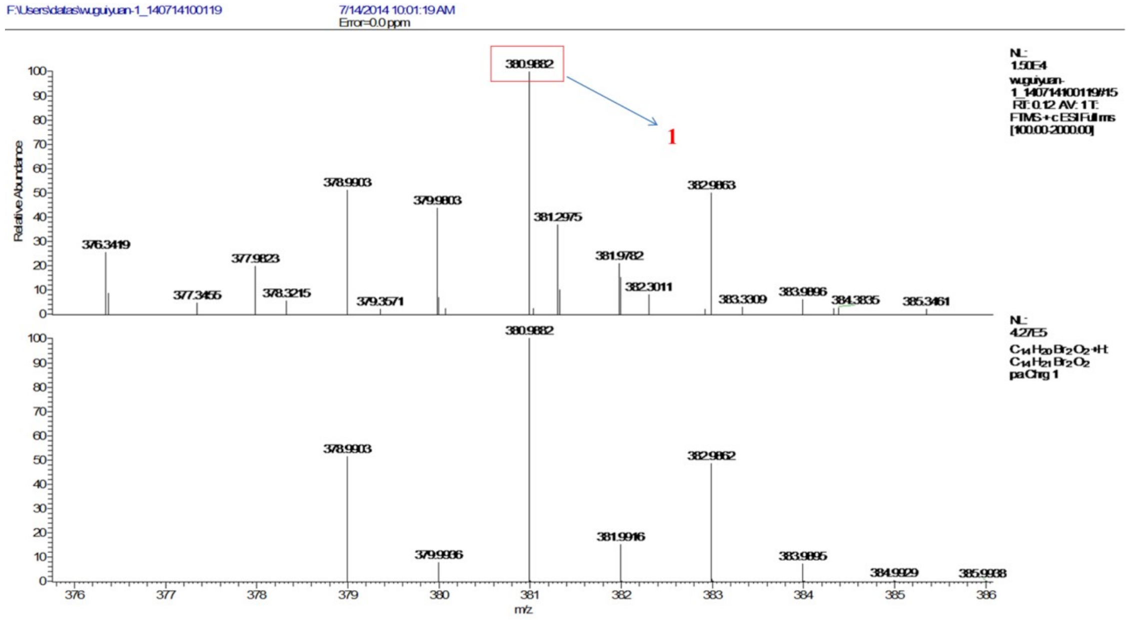


Fig. S3 Electrospray ionization mass spectrum of compound **1**.

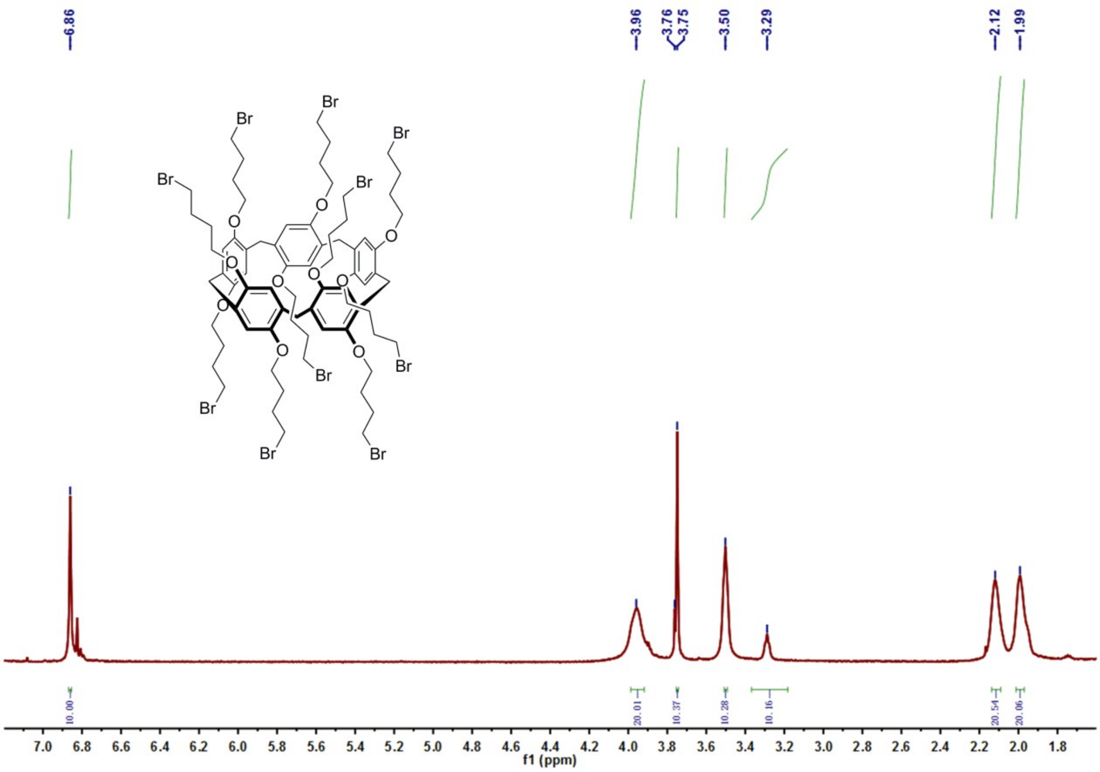


Fig. S4 ^{1}H NMR (600 MHz) spectra of product **2** in $CDCl_3$.

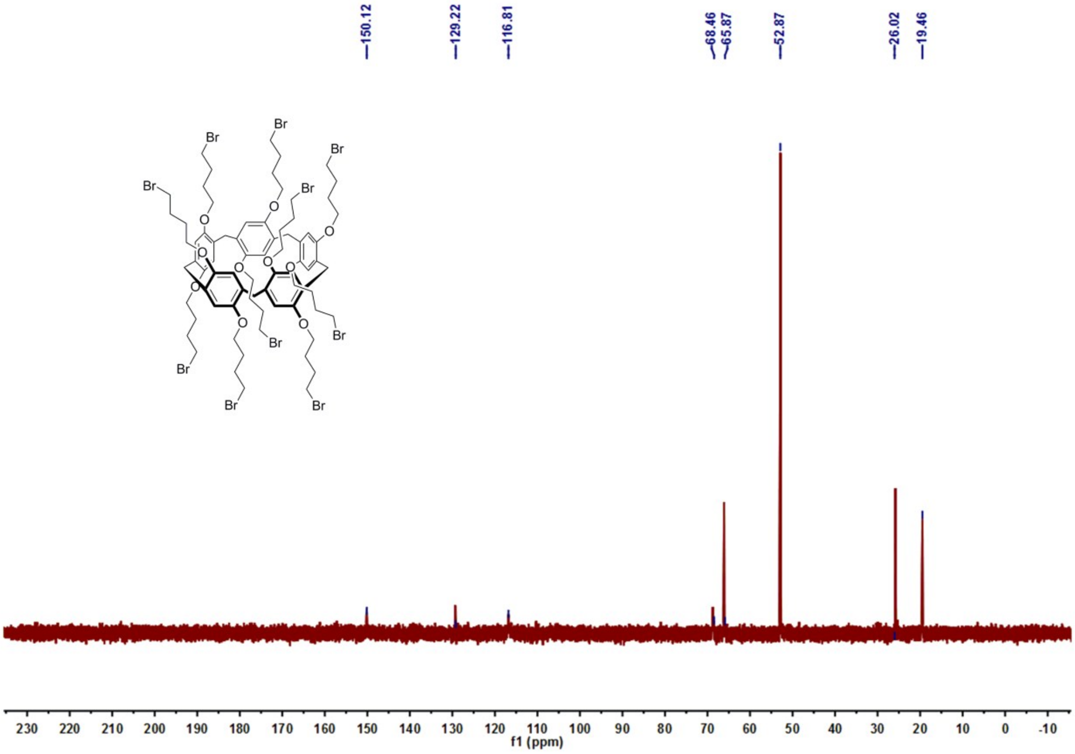


Fig. S5 ^{13}C NMR (150 MHz, 298K) spectra of product **2** in $CDCl_3$.

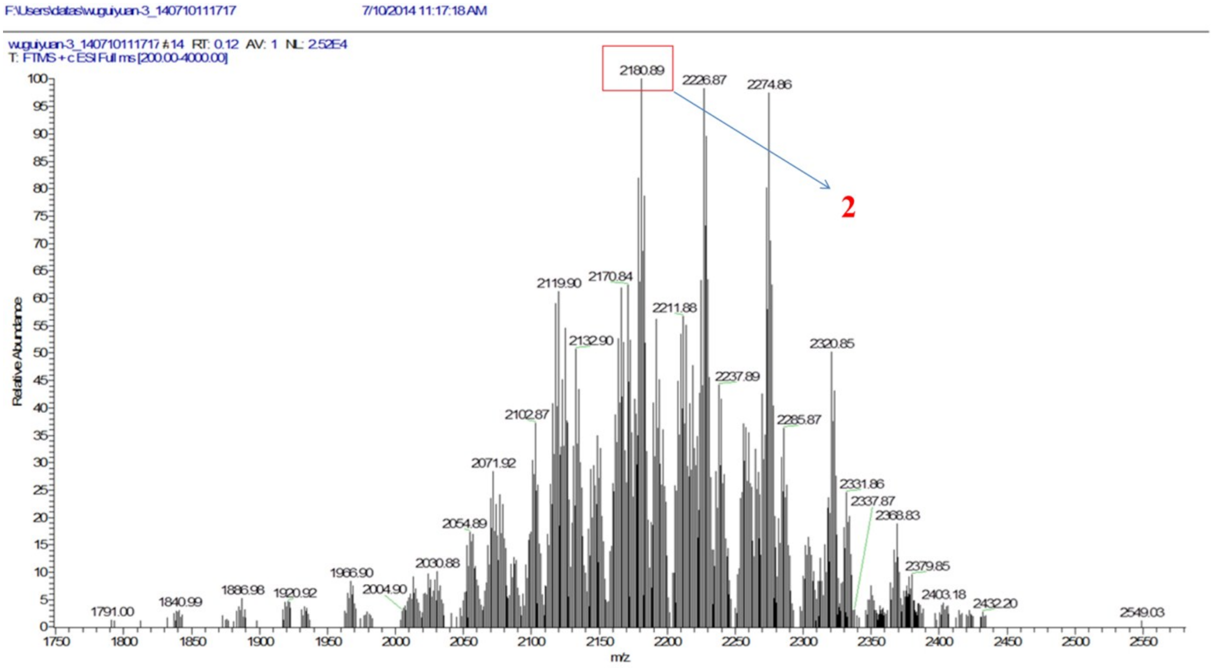


Fig. S6 Electrospray ionization mass spectrum of compound **2**.

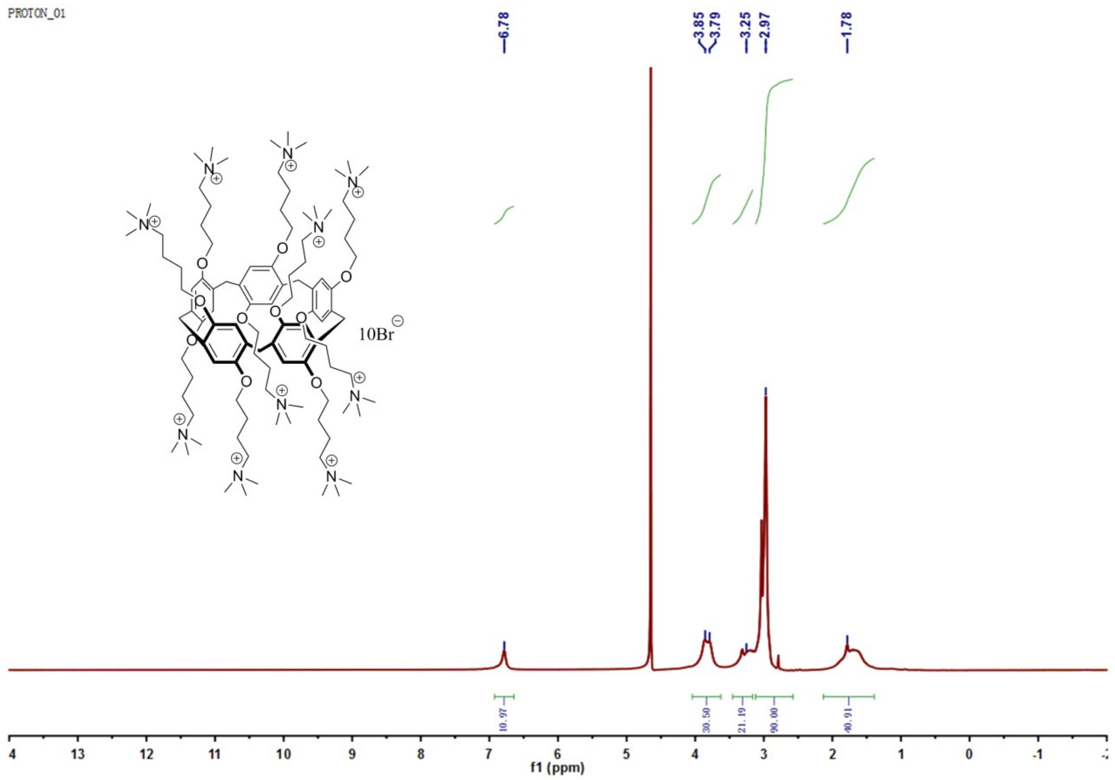


Fig. S7 ^{1}H NMR (600 MHz, 298K) spectra of product **AWP5** in D_2O.

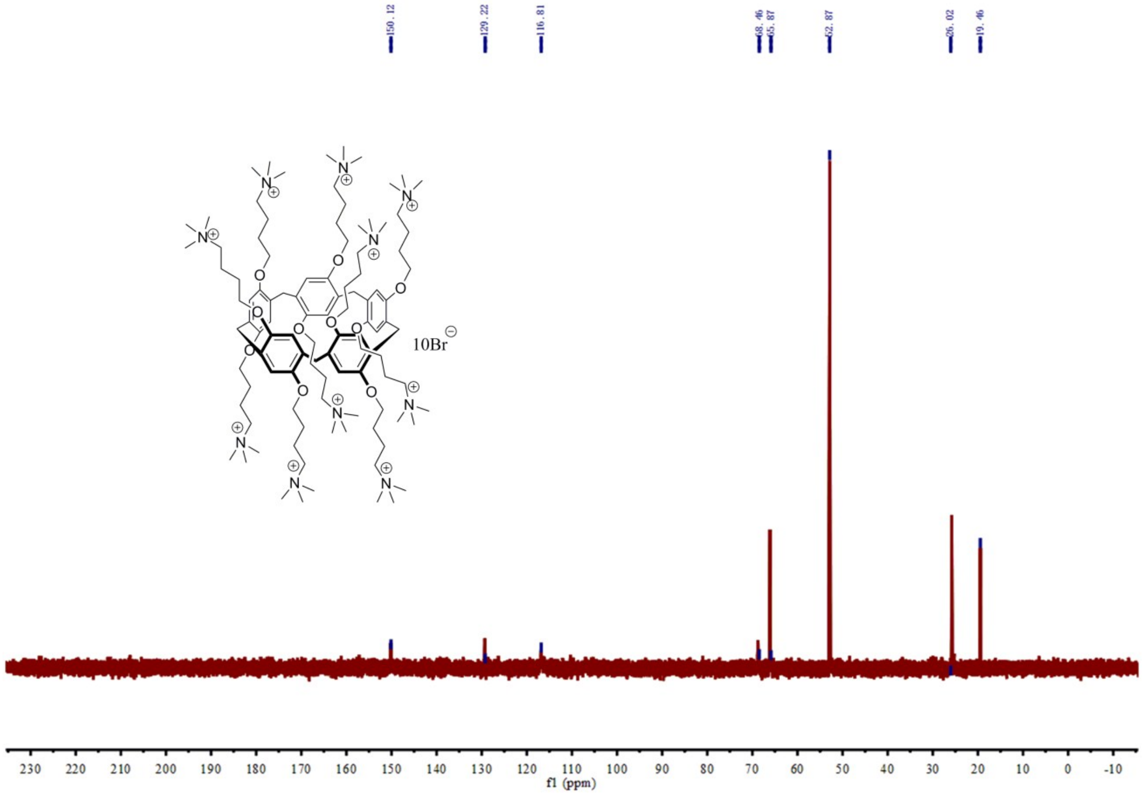


Fig. S8 ^{13}C NMR (150 MHz, 298K) spectra of product **AWP5** in D_2O.

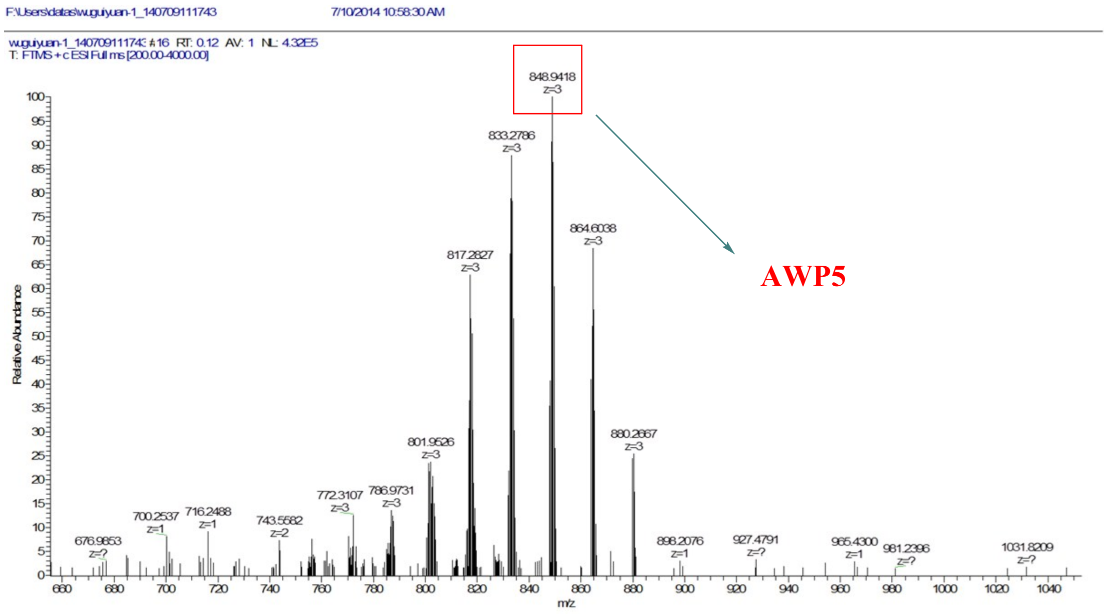


Fig. S9 Electrospray ionization mass spectrum of compound **AWP5**.

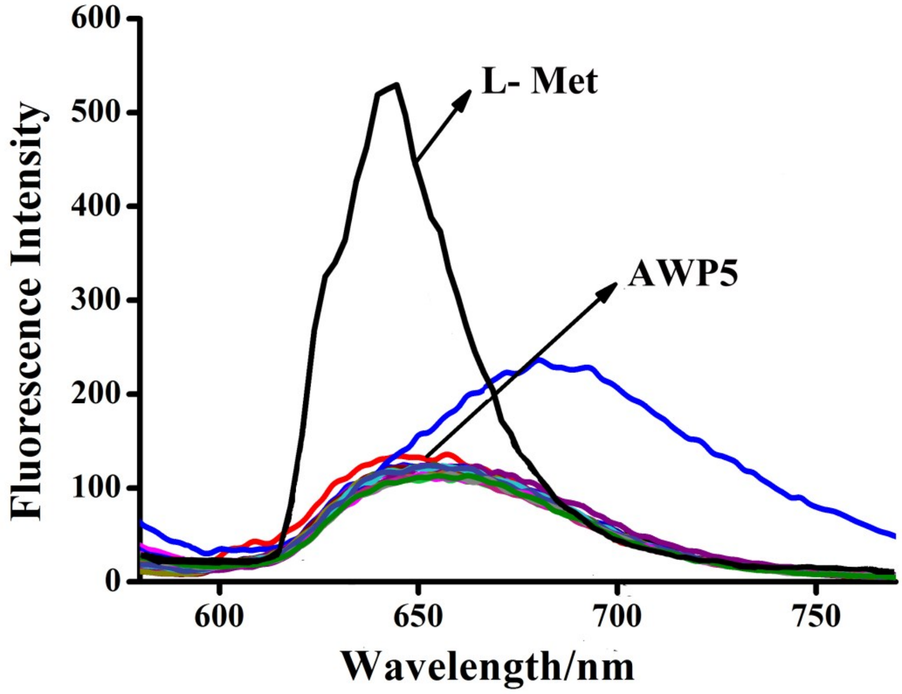
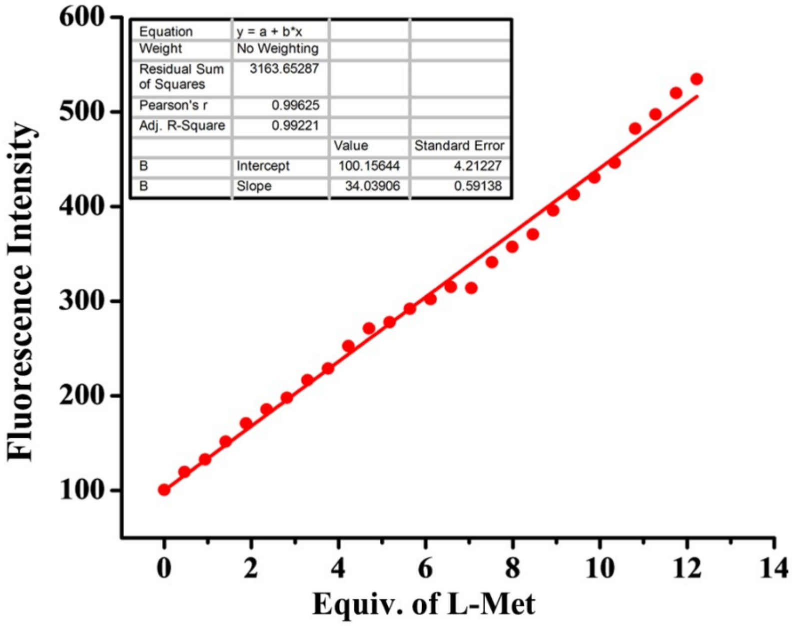


Fig. S10 Fluorescence spectra of supramolecular sensor **AWP5** in water solution (2 × 10^{-5} mol L^{-1}) upon addition of 10 equiv. of L-Ala, L-Arg, L-Asp, L-Cys, L-Gln, L-Glu, L-His, L-Ile, L-Gly, L-Asn, L-Leu, L-Lys, L-Met, L-Phe, L-Pro, L-Ser, L-Thr, L-Trp, L-Tyr, L-Val (λex = 520 nm).



Equation	y = a + b*x		
Weight	No Weighting		
Residual Sum of Squares	3163.65287		
Pearson's r	0.99625		
Adj. R-Square	0.99221		
		Value	Standard Error
B	Intercept	100.15644	4.21227
B	Slope	34.03906	0.59138

Fig. S11 The photograph of the linear range.

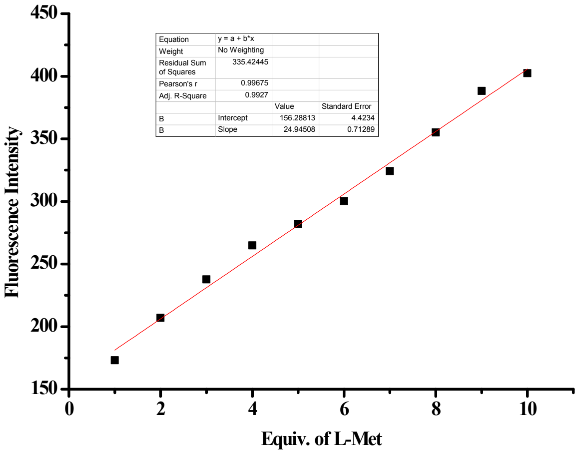
Linear Equation: Y= 34.03906X+100.15644

R^2=0.99625   S=3.403906×10^7

$$\delta = \sqrt{\frac{\Sigma(Fi - F0)^2}{N - 1}} \quad =6.20044$$

LOD =K × δ/S = 5.464 ×10^{-7} M
K=3

F_0 is the fluorescence intensity of **AWP5**; F_1 is the average of the $F_{0.}$



Equation	y = a + b*x		
Weight	No Weighting		
Residual Sum of Squares	335.42445		
Pearson's r	0.99675		
Adj. R-Square	0.9927		
		Value	Standard Error
B	Intercept	156.28813	4.4234
B	Slope	24.94508	0.71289

Fig. S12 The photograph of the linear range.
Linear Equation: Y= 24.94508X+156.288813

R^2=0.99675   S=2.494508×10^7

= 54.1539

LOD =K × δ/S = 2.0769 ×10^{-6} M
K=3

F_0 is the fluorescence intensity of AWP5; Fi is the average of the F_0.

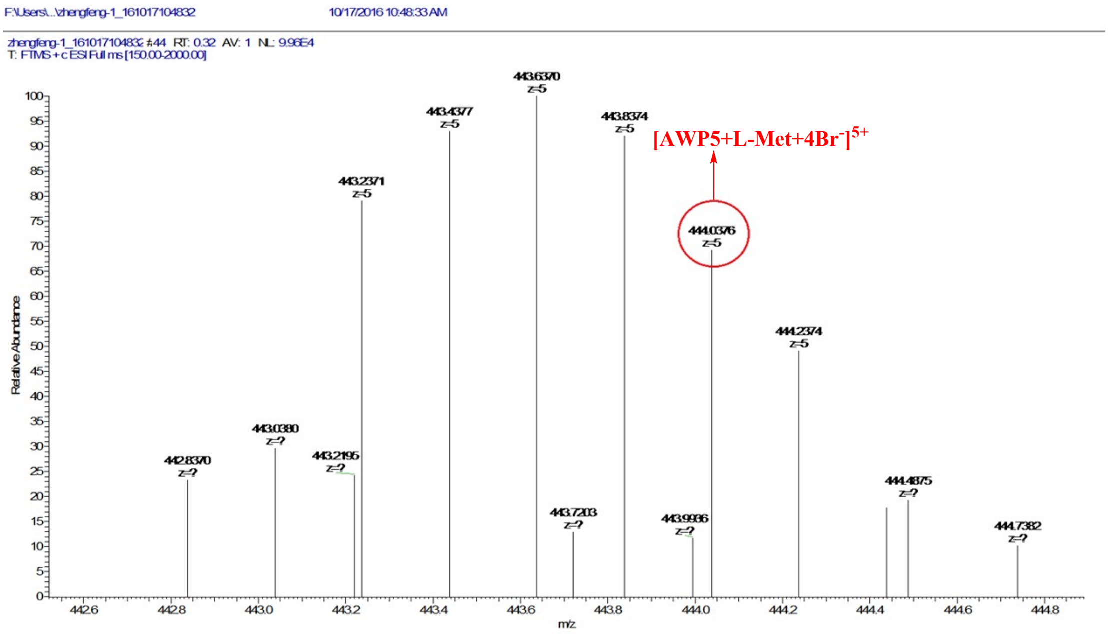


Fig. S13 High resolution electrospray ionization mass spectrum of **AWP5-L-Met**.

Reference

[1] G. Y. Wu, B. B. Shi, Q. Lin, H. Li, Y. M. Zhang, H. Yao, T. B. Wei, *RSC Adv.*, 2015, **5**, 4958.
[2] T. B. Wei, G. Y. Wu, Q. Lin, H. Yao, Y. M. Zhang, CN. Pat., 104447363 A, 2015.
[3] T. B. Wei, F. J. Chen, Y. M. Zhang, Q. Lin, H. Yao, CN. Pat., 105837527 A, 2016.