Electronic Supplementary Information

Acyclic phosphonate hosts for detection of antimicrobial medicines

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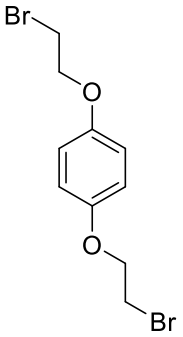
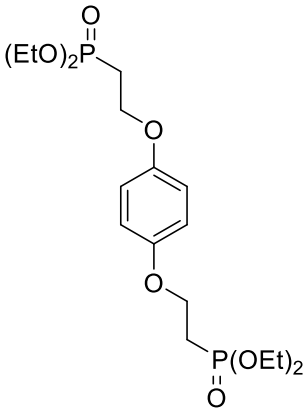
General experimental

Starting materials were purchased from commercial suppliers and were used without further purification. **CB1**, **CB2** and **CB4** were prepared according to literature procedures.[1-2] Melting points were uncorrected. NMR spectra were acquired with a Bruker BioSpin AV400 or JEOL JNM-ECZ400 instrument at 400 MHz in the indicated solvents. Chemical shifts were expressed in parts per million (δ) using residual solvent protons as internal standards. Maldi-TOF mass spectroscopy was performed on a Shimadazu Biotech AXIMA Performance spectrometer. UV-Vis experiments were performed on a Persee TU-1901 spectrometer. Fluorescence spectra were recorded on a Horiba FluoroMax-4 spectrofluorimeter. CD spectra were recorded on an applied photophysics chiralscan qCD spectrometer.

Synthetic Procedures and Characterization data

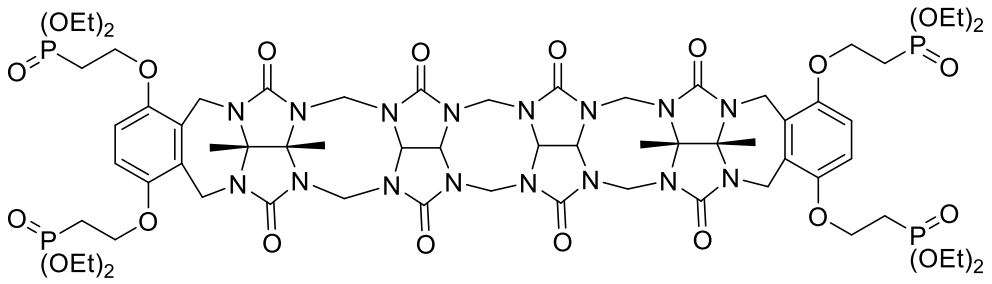


Compound P2C2. A solution of carbon tetrabromide (33.63 g, 101.41 mmol) in 50 mL of dry acetonitrile was added dropwise to a solution of 1,4-bis(2-hydroxyethoxy)benzene (8.45 g, 42.63 mmol) and triphenylphosphine (26.62 g, 101.49 mmol) in 160 mL of dry acetonitrile at 0 °C. The reaction mixture was allowed to warm to room temperature, and was stirred for another 4 h. Then 170 mL of water was poured into the reaction, and the white solid was formed. The precipitate was collected by filtration and was washed with methanol/water (3:2). The solid was recrystallized from methanol to give the 12.63 g of **P2C2** (91%) as white crystal. ^{1}H NMR (400 MHz, DMSO-d_6): δ 6.90 (s, 4H), 4.25 (t, 4H), 3.77 (t, 4H).

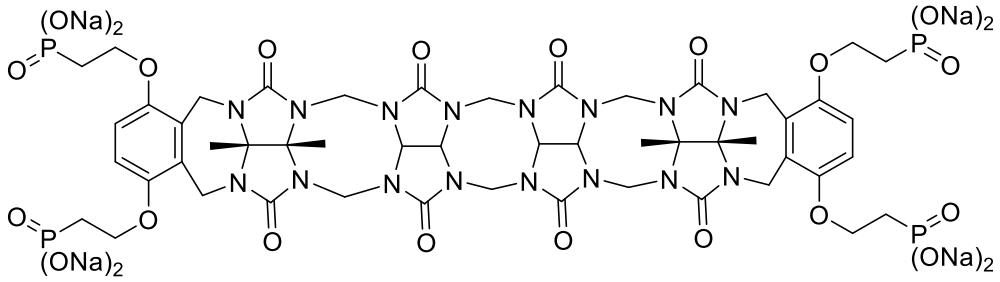


Compound P3C2. A mixture of compound **P2C2** (6.55 g, 20.22 mmol) and triethyl phosphite (33.59 g, 202.2 mmol) was refluxed in 66 mL of xylene for 72 h. The solvent and excess triethyl phosphite were removed by rotatory evaporation. The residue was purified by column

chromatography (dichloromethane/methanol, 100:1) to give the 8.69 g of **P3C2** (98%) as pale yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.83 (s , 4H), 4.16 (t, 4H), 4.13 (m, 8H), 2.28 (dt, 4H), 1.34 (t, 12H). ^{13}C NMR (400 MHz, $CDCl_3$): δ 152.1, 115.1, 62.1, 61.1, 26.7, 25.4, 15.8.

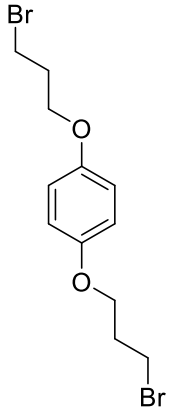


Compound P4C2. A mixture of compound **P3C2** (4.64 g, 10.5 mmol) and **CB4** (2.07 g, 2.65 mmol) in 14 mL of trifluoroacetic acid and 14 mL of acetic anhydride was stirred at 70 °C for 6 h. The mixture was poured into 150 mL of methanol. The solvent was removed by rotatory evaporation. Then 100 mL of ether was added and the solid was formed. The precipitate was collected by filtration, and dried under vacuum to give the 3.90 g of **P4C2** as pale yellow solid.

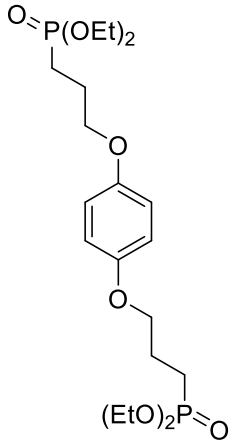


Compound P5C2. A solution of bromotrimethylsilane (7.37 g, 48.2 mmol) in 25 mL of dry dichloromethane was added dropwise to a solution of compound **P4C2** (3.90 g, 2.41 mmol) in 43 mL of dry dichloromethane at 0 °C. The reaction mixture was allowed to warm to room temperature, and was stirred for another 48 h. The mixture was poured into a large volume of iced water, and the solid was formed. The precipitate was collected by filtration, and was washed successively with methanol, dichloromethane and ether. The solid was dissolved with excess 1 N NaOH, and was filtered to remove the undissolved substances. The filtrate was washed with

dichloromethane, and the organic phase was removed. The resulting clear solution was acidified with 1 N HCl to neutral, and the solid was formed. The precipitate was filtered and washed with dichloromethane, and the obtained solid was dried under vacuum to give the **P5C2** (1.69 g, 43%) as white powder. The solid was dissolved quantitatively with 1 N NaOH to give the corresponding salt. The solvent was removed by rotary evaporation, and the obtained solid was dried further under vacuum. ^{1}H NMR (400 MHz, D_2O): δ 7.17 (s, 4H), 5.74 (d, 2H), 5.59 (d, 4H), 5.48 (q, 4H), 5.21 (d, 4H), 4.43 (d, 4H), 4.28 (m, 8H), 4.18 (m, 4H), 4.14 (d, 2H), 1.96 (m, 8H), 1.82 (s, 6H), 1.71 (s, 6H). ^{13}C NMR (400 MHz, D_2O): δ 157.1, 156.5, 150.5, 129.0, 118.4, 78.8, 77.7, 71.6, 70.2, 53.1, 48.6, 35.6, 30.4, 29.6, 16.2, 14.9. MS (ESI): m/z 1395.3 ($[M-H]^-$), 1417.3 ($[M-2H+Na]^-$). HRMS (ESI): calcd for $C_{50}H_{56}O_{24}N_{16}P_4$ 697.1542, found 697.1545.

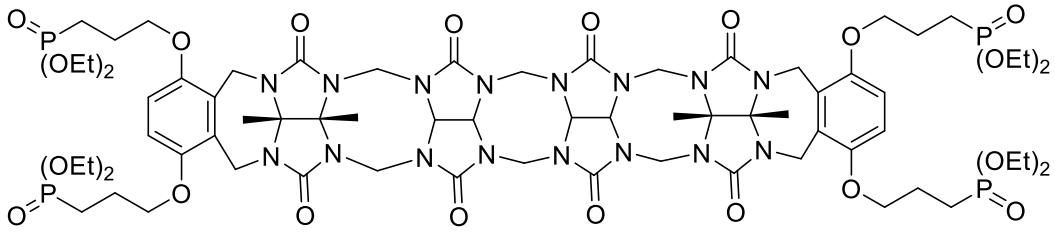


Compound P2C3. A mixture of hydroquinone (8.81 g, 0.08 mol), 1,3-dibromopropane (64.6 g, 0.32 mol), and anhydrous K_2CO_3 (66.3 g, 0.48 mol) in acetone (240 mL) was refluxed under nitrogen for 24 h. The mixture was filtered to remove the solid, and the filtrate was concentrated under vacuum. The residue was diluted with hexane, and the solid formed was removed by filtration. The filtrate was set aside overnight, and the solid was formed and crystallized with ethanol to obtain the **P2C3** (11.7 g, 42%) as yellow solid. ^{1}H NMR (400 MHz, DMSO-d6): δ 6.84 (s, 4H), 4.05 (t, 4H), 3.60 (t, 4H), 2.29 (m, 4H).

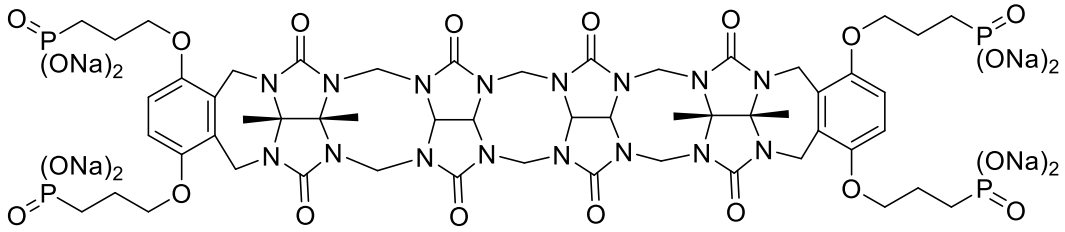


Compound P3C3. A mixture of compound **P2C3** (4.83 g, 13.7 mmol) and triethyl phosphite (19.3 g, 0.12 mol) was refluxed in 46 mL of xylene for 72 h. The solvent and excess triethyl phosphite were removed by rotatory evaporation. The residue was purified by column chromatography (dichloromethane/methanol, 100:1) to give the 5.01 g of **P3C3** (78%) as pale yellow oil. ^{1}H

NMR (400 MHz, $CDCl_3$): δ 6.76 (s, 4H), 4.06 (m, 8H), 3.91 (t, 4H), 2.03 (m, 4H), 1.88 (m, 4H), 1.27 (m, 12H). ^{13}C NMR (400 MHz, $CDCl_3$): δ 152.0, 114.4, 66.9, 60.5, 21.8, 20.7, 15.5.



Compound P4C3. A mixture of compound **P3C3** (7.20 g, 15.4 mmol) and **CB4** (3.01 g, 3.86 mmol) in 17 mL of trifluoroacetic acid and 17 mL of acetic anhydride was stirred at 70 °C for 6 h. The mixture was poured into 200 mL of methanol. The solvent was removed by rotatory evaporation. Then 150 mL of ether was added and the solid was formed. The precipitate was collected by filtration, and dried under vacuum to give the 6.07 g of **P4C3** as pale yellow solid.



Compound P5C3. A solution of bromotrimethylsilane (11.08 g, 72.4 mmol) in 40 mL of dry dichloromethane was added dropwise to a solution of compound **P4C3** (6.07 g, 3.62 mmol) in 50 mL of dry dichloromethane at 0 °C. The reaction mixture was allowed to warm to room temperature, and was stirred for another 48 h. The mixture was poured into a large volume of iced water, and the solid was formed. The precipitate was collected by filtration, and was washed successively with methanol, dichloromethane and ether. The solid was dissolved with excess 1 N NaOH, and was filtered to remove the undissolved substances. The resulting clear solution was acidified with 1 N HCl to neutral, and the solid was formed. The precipitate was filtered and washed with dichloromethane, and the obtained solid was dried under vacuum to give the **P5C3** (3.19 g, 62%) as white powder. The solid was dissolved

quantitatively with 1 N NaOH to give the corresponding salt. The solvent was removed by rotary evaporation, and the obtained solid was dried further under vacuum. ^{1}H NMR (400 MHz, D_2O): δ 7.02 (s, 4H), 5.68 (d, 2H), 5.56 (d, 4H), 5.46 (q, 4H), 5.37 (d, 4H), 4.29 (t, 8H), 4.15 (d, 2H), 4.05 (m, 8H), 1.95 (m, 8H), 1.79 (d, 12H), 1.54 (m, 8H). ^{13}C NMR (400 MHz, D_2O): δ 157.0, 156.5, 150.4, 128.4, 116.1, 78.9, 77.6, 72.8, 71.2, 52.6, 48.4, 35.3, 26.4, 25.5, 24.4, 16.2, 15.1. HRMS (MALDI): m/z 1497.3577 ($[M-H+2Na]^+$), 1519.3394 ($[M-2H+3Na]^+$). HRMS (MALDI): calcd for $C_{54}H_{72}O_{24}N_{16}NaP_4$ 1475.3748, found 1475.3756.

NMR and HRMS spectra of new compounds

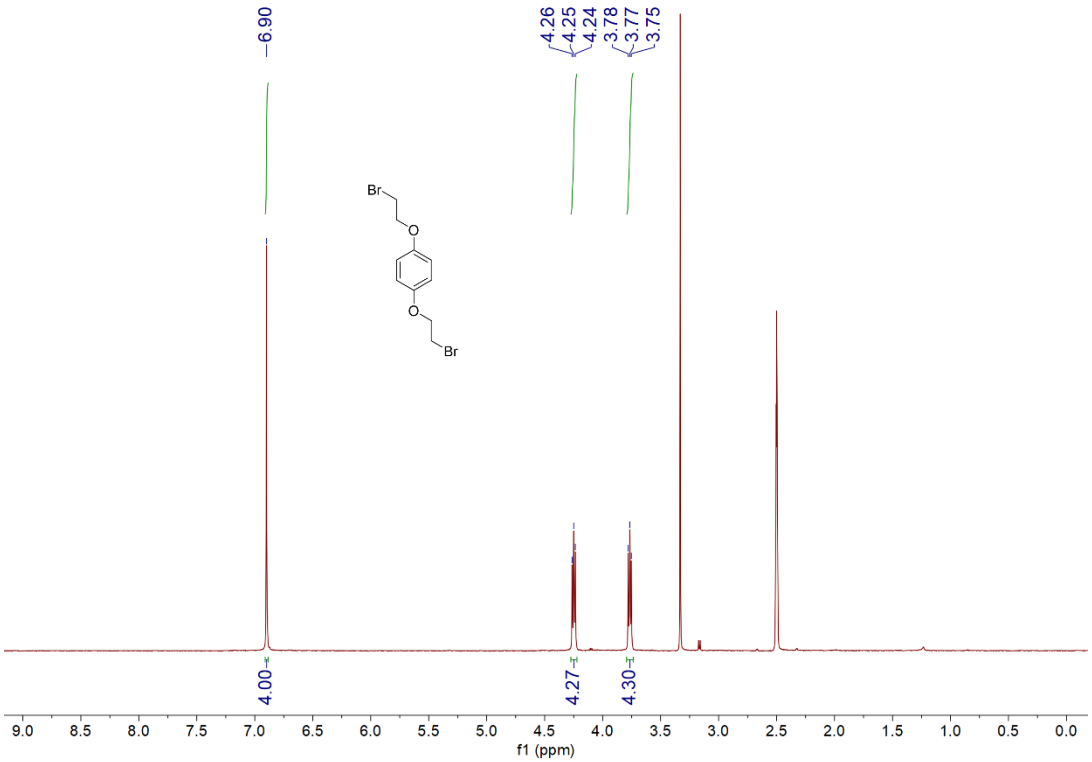


Figure S1. ^{1}H NMR spectra (400 MHz, DMSO-d_6) recorded for **P2C2**.

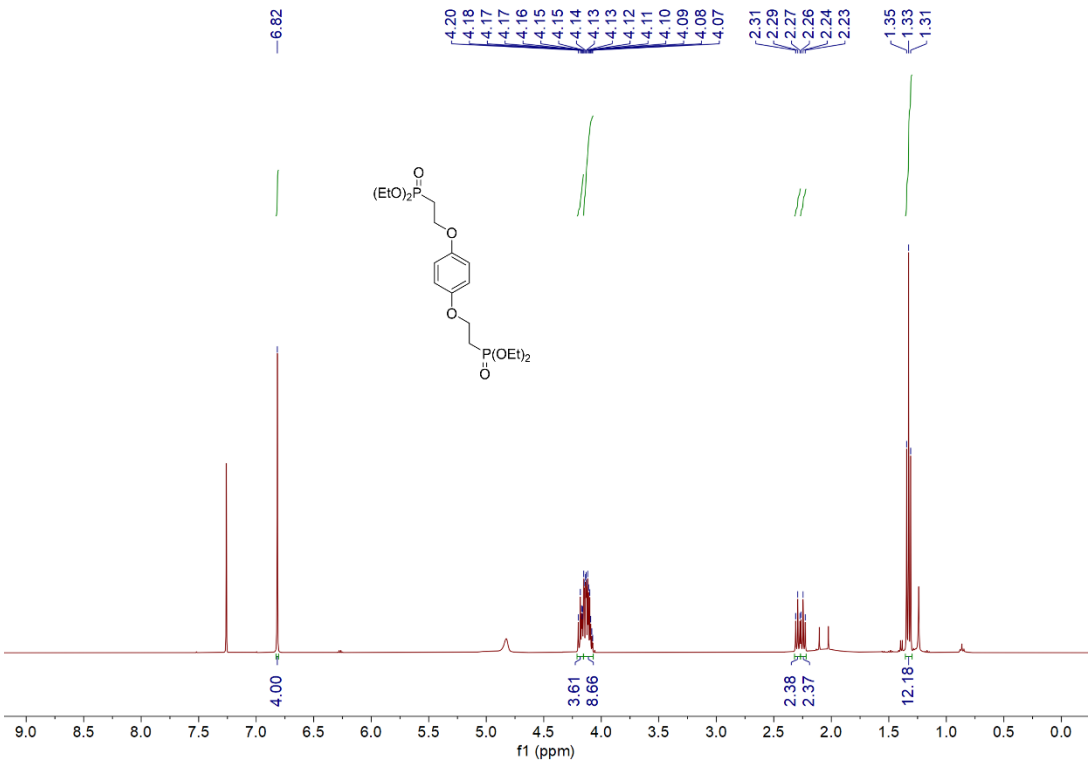


Figure S2. ^{1}H NMR spectra (400 MHz, $CDCl_3$) recorded for **P3C2**.

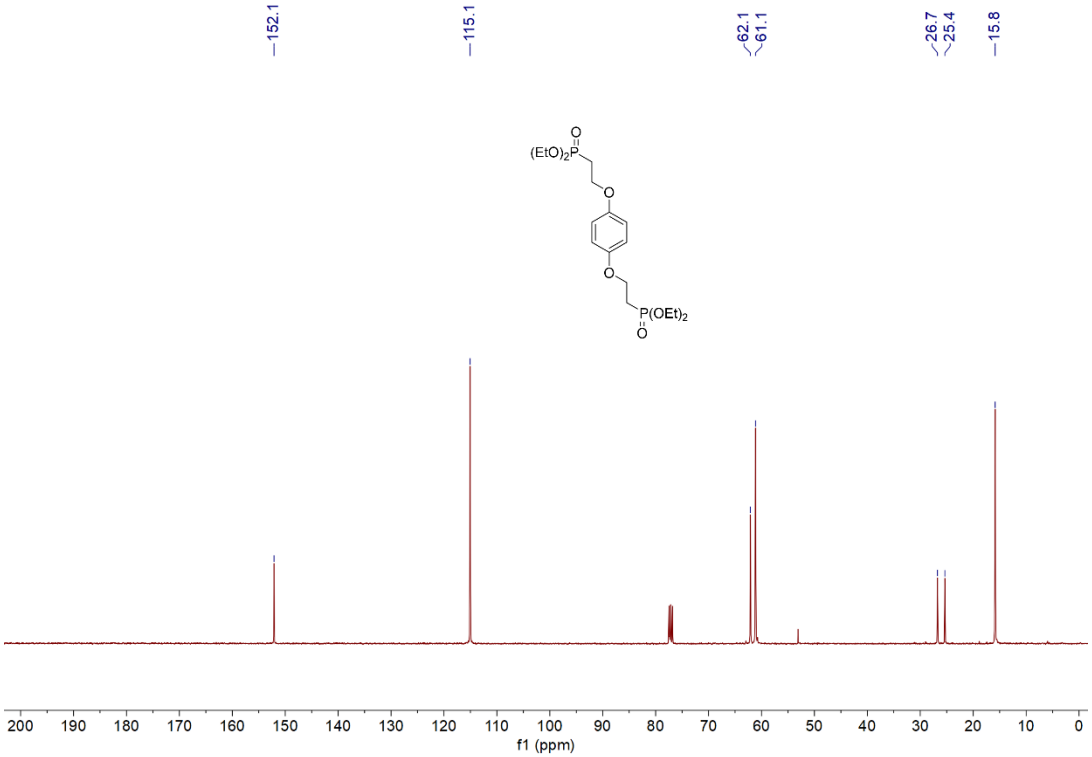


Figure S3. ^{13}C NMR spectra (400 MHz, $CDCl_3$) recorded for **P3C2**.

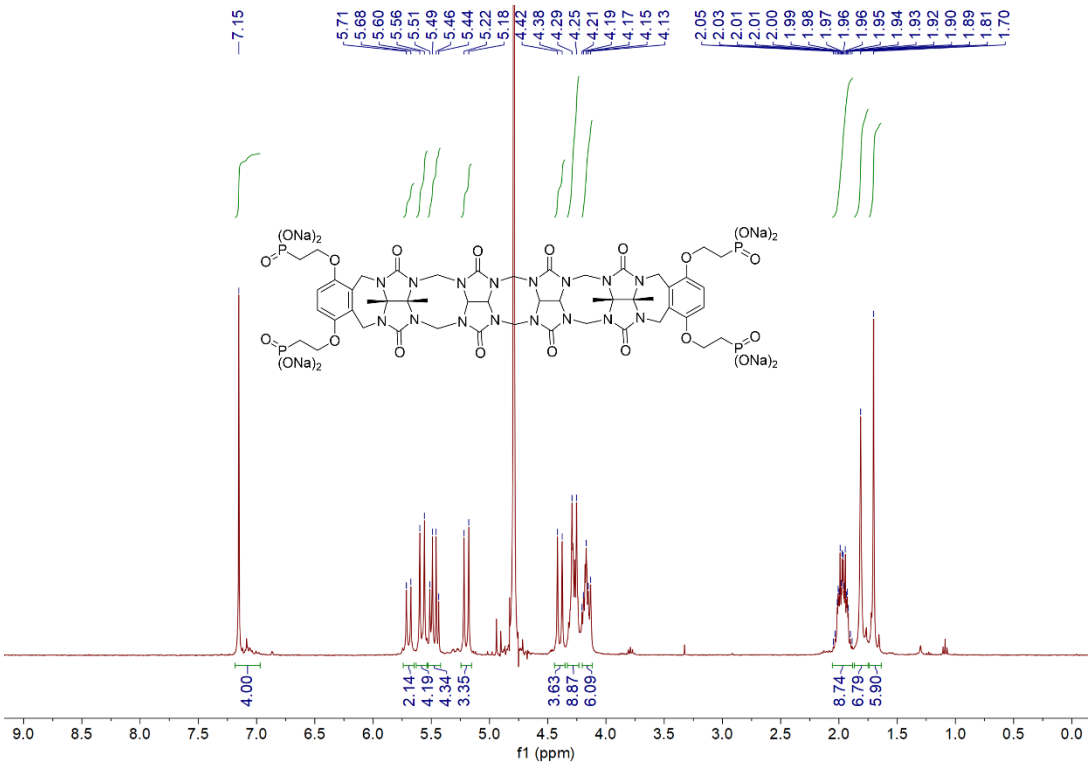


Figure S4. ^{1}H NMR spectra (400 MHz, D_2O) recorded for **P5C2**.

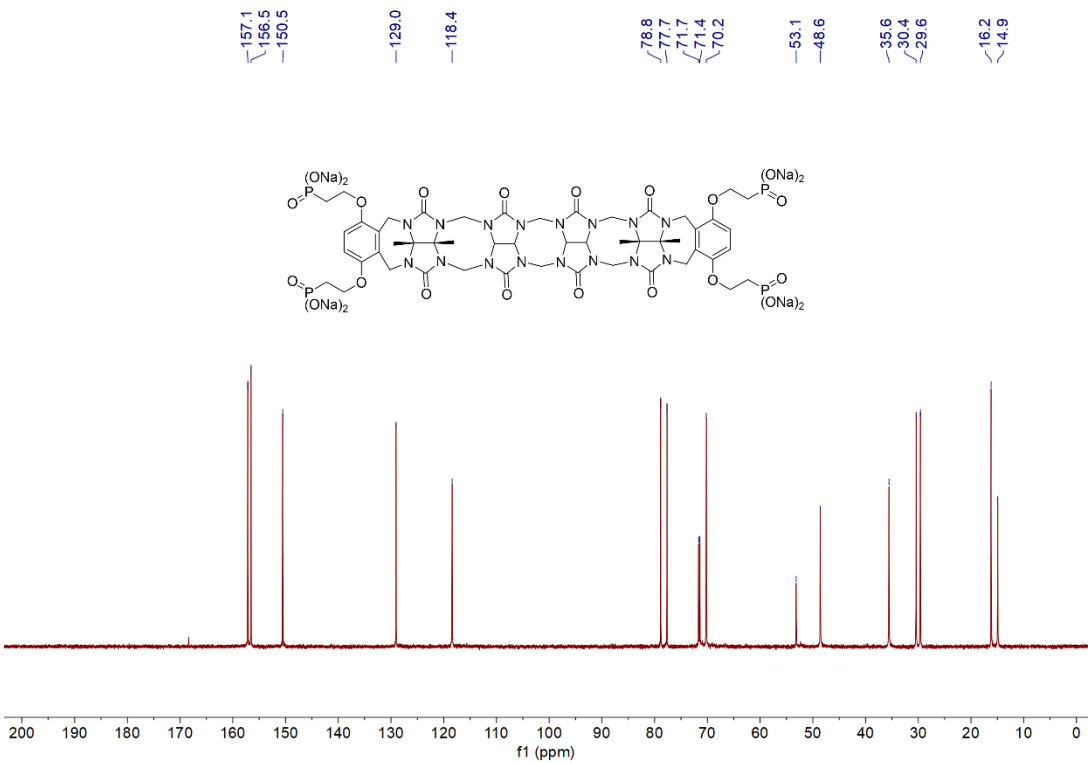


Figure S5. ^{13}C NMR spectra (400 MHz, D_2O) recorded for **P5C2**.

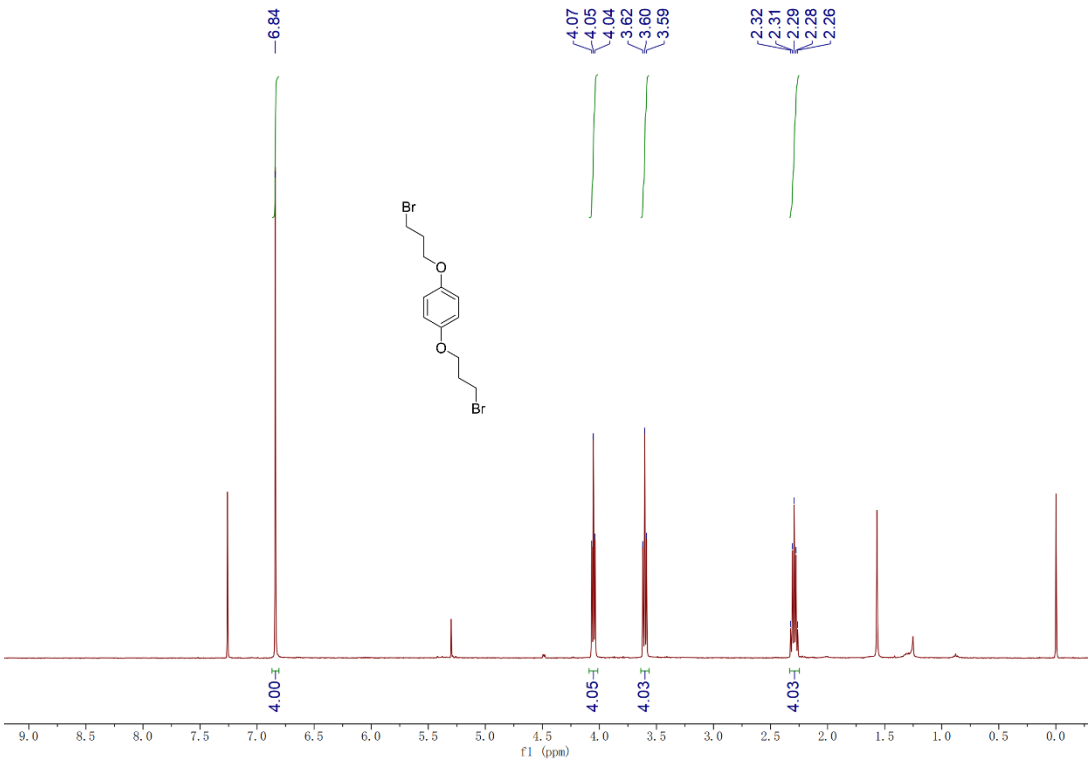


Figure S6. ^{1}H NMR spectra (400 MHz, $CDCl_3$) recorded for **P2C3**.

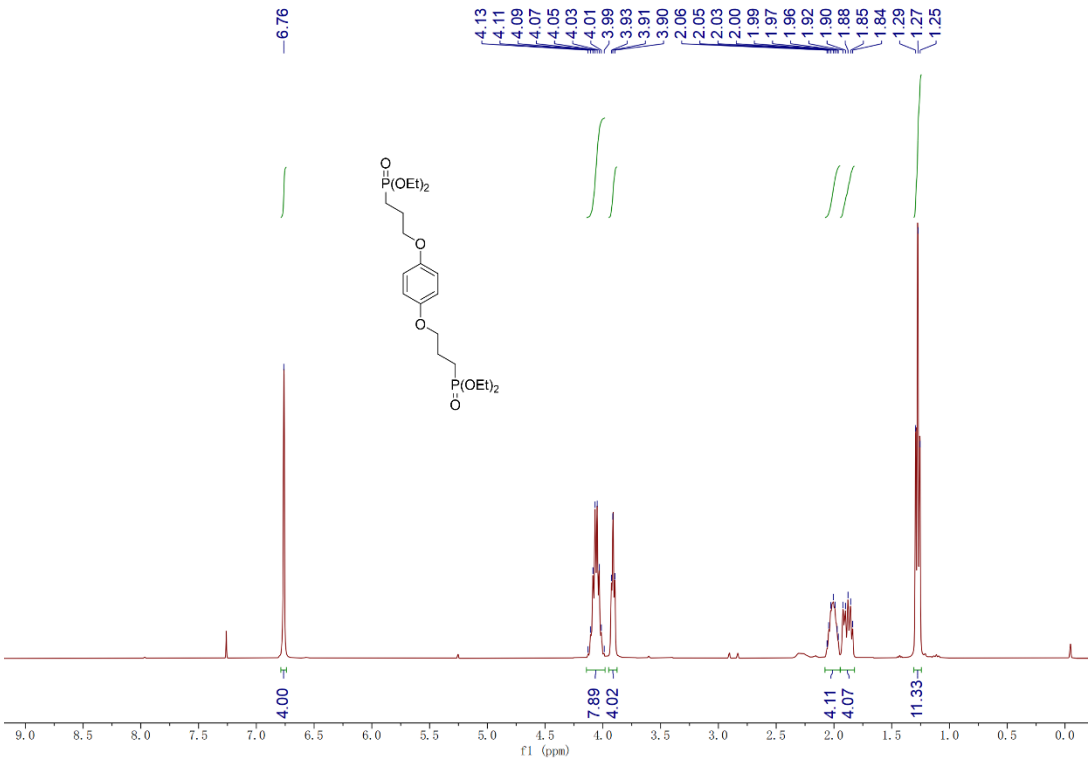


Figure S7. ^{1}H NMR spectra (400 MHz, $CDCl_3$) recorded for **P3C3**.

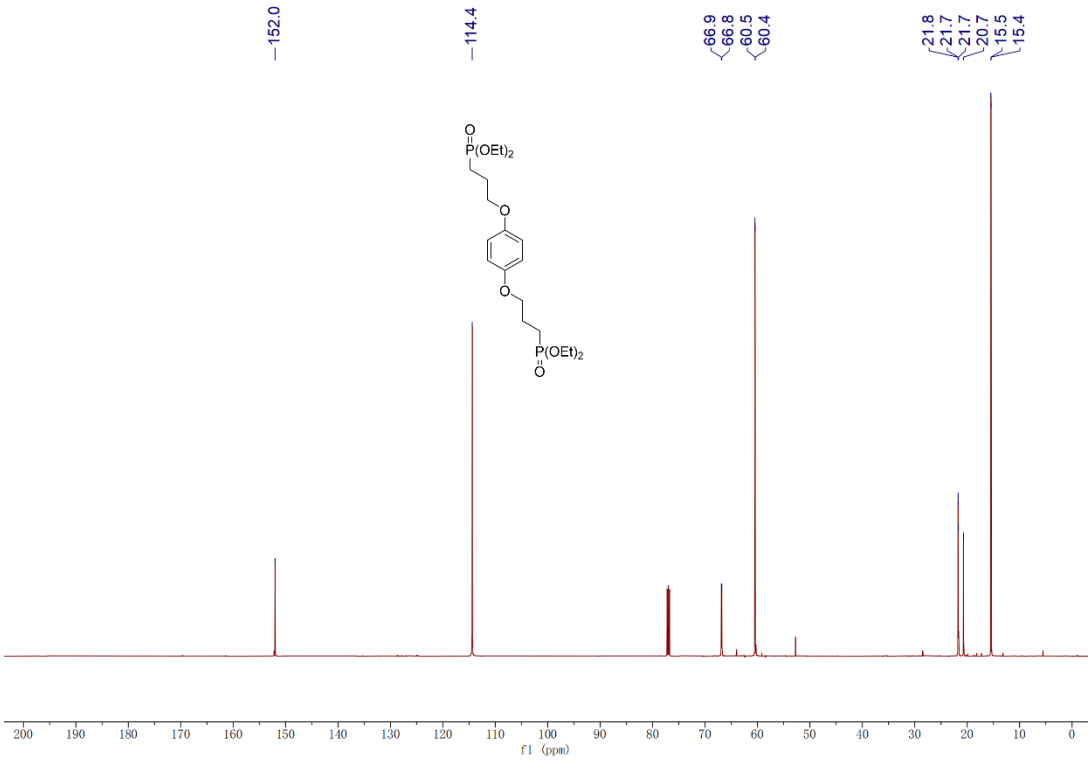


Figure S8. ^{13}C NMR spectra (400 MHz, $CDCl_3$) recorded for **P3C3**.

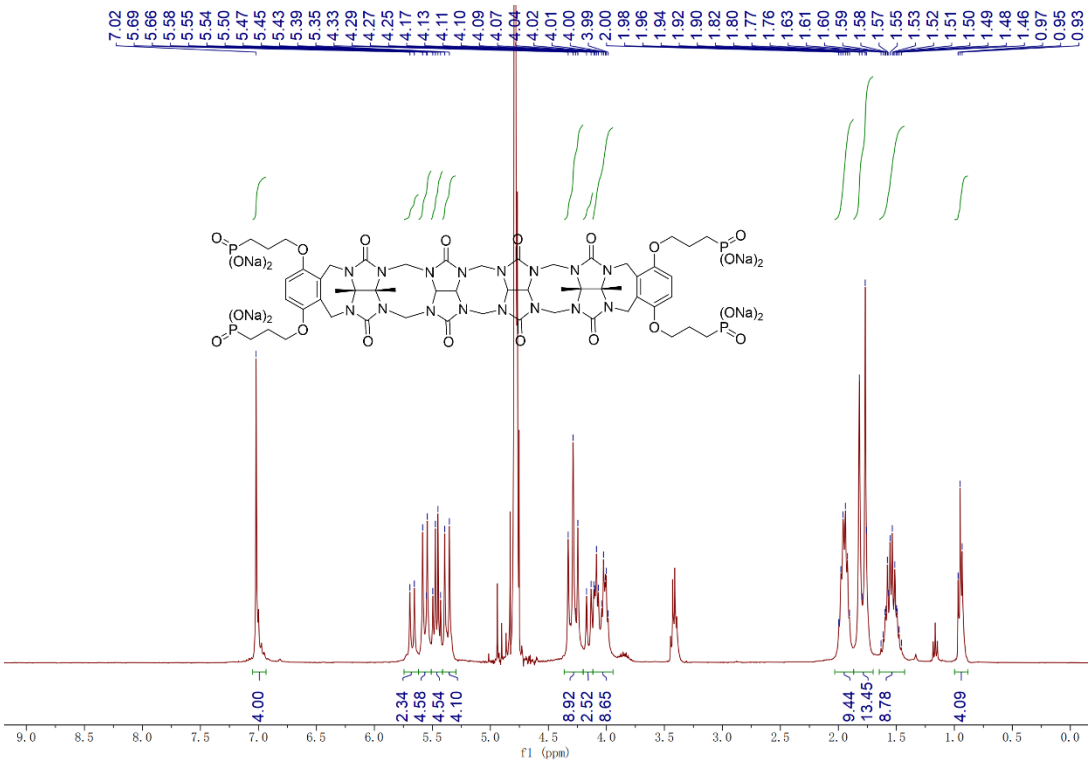


Figure S9. ^{1}H NMR spectra (400 MHz, D_2O) recorded for **P5C3**.

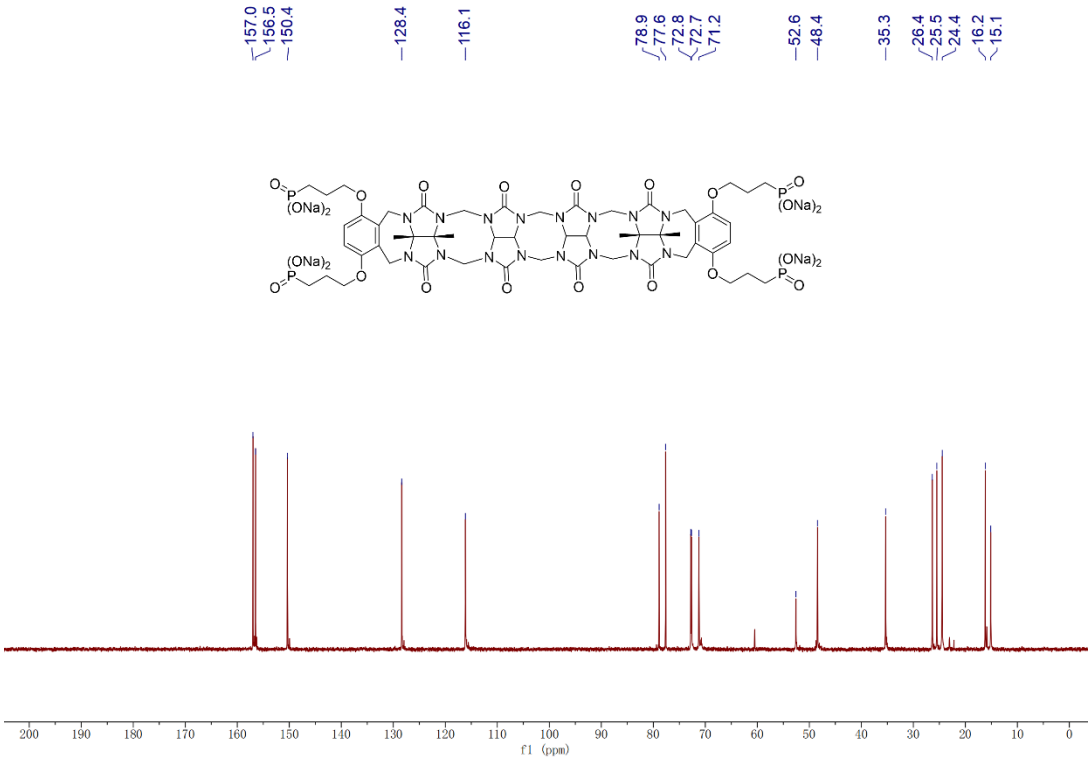
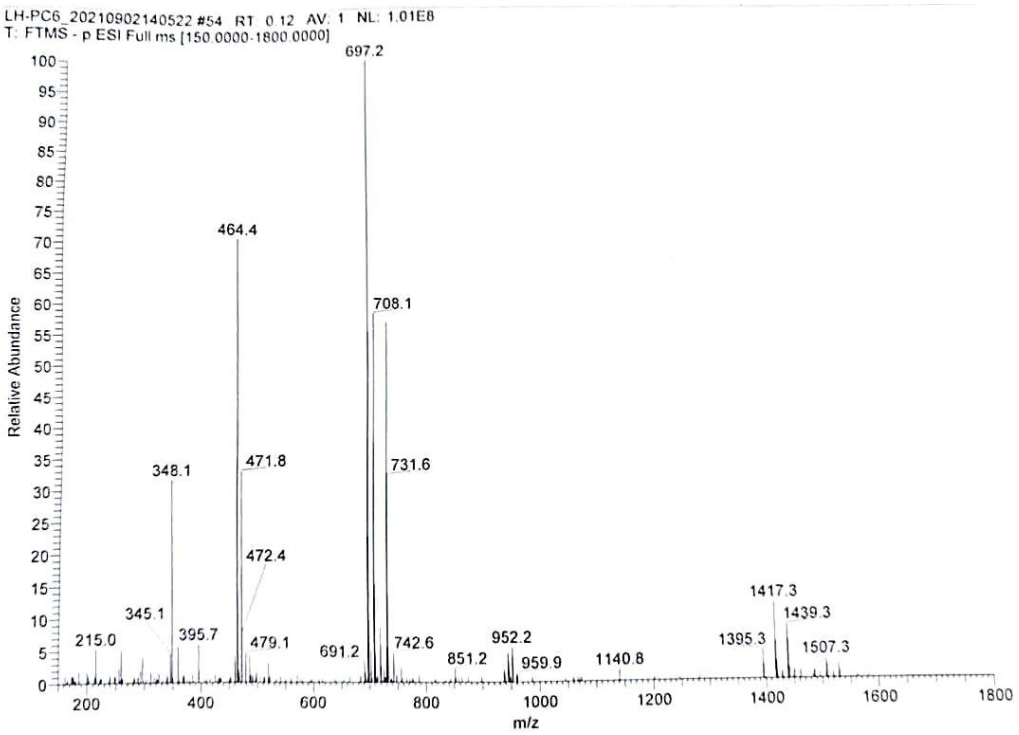


Figure S10. ^{13}C NMR spectra (400 MHz, D_2O) recorded for **P5C3**.



National Center for Organic Mass Spectrometry in Shanghai
Shanghai Institute of Organic Chemistry
Chinese Academic of Sciences
High Resolution ESI-MS REPORT

Instrument: Thermo Scientific Q Exactive HF Orbitrap-FTMS

Card Serial Number: E212237

Sample Serial Number: LH-PC6

Operator: Songw Date: 2021/09/02

Operation Mode: ESI Negative Ion Mode

Charge: z= -2

Elemental composition search on mass 697.1545

m/z= 692.1545-702.1545

m/z	Theo. Mass	Delta (ppm)	RDB equiv.	Composition
697.1545	697.1542	0.38	30.0	$C_{50}H_{62}O_{24}N_{16}P_4$

Figure S11. HRMS recorded for **P5C2**.

National Center for Organic Mass Spectrometry in Shanghai
Shanghai Institute of Organic Chemistry
Chinese Academic of Sciences
High Resolution AP-MALDI-MS REPORT

Instrument: Thermo Scientific Q Exactive HF Orbitrap-FTMS

Card Serial Number: 230295

Sample Serial Number: P5C3

Operator: Songw Date: 2023/02/06

Operation Mode: AP-MALDI Positive Ion Mode

Elemental composition search on mass 1475.3756

m/z= 1470.3756-1480.3756

	m/z	Theo. Mass	Delta (ppm)	RDB equiv.	Composition
1	1475.3756	1475.3748	0.56	28.5	$C_{54}H_{72}O_{24}N_{16}NaP_4$

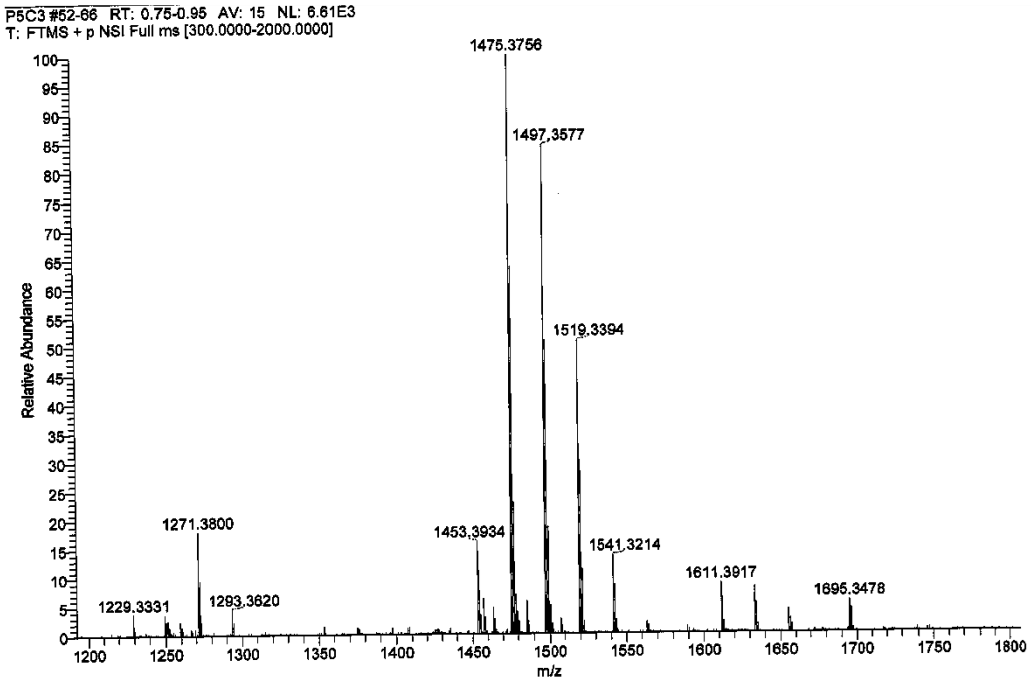


Figure S12. HRMS recorded for **P5C3**.

Self-association study

Prior to the host-guest interaction, the possibility of self-association of host **P5C2** or **P5C3** was investigated by ^{1}H NMR dilution experiments. ^{1}H NMR spectra were recorded in the concentration range from 3.12 mM to 400 mM. No changes in chemical shifts were observed for **P5C2**, which indicate the host do not undergo self-association. In contrast, the protons in the propylene sidechains of **P5C3** exhibited the upfield shifts of 0.09, 0.10, 0.17 ppm, respectively. The result was consistent with the previous literatures,[1-2] reflecting the self-inclusion of sidechains of **P5C3** in the cavity of host.

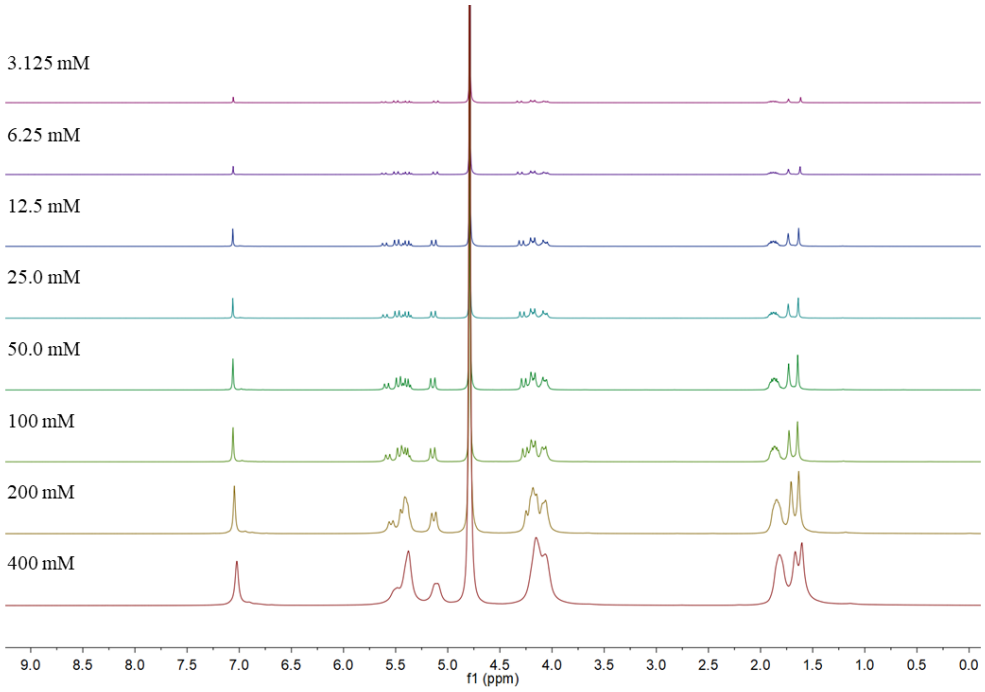


Figure S13. ^{1}H NMR recorded for **P5C2** at various concentration (400 MHz, D_2O).

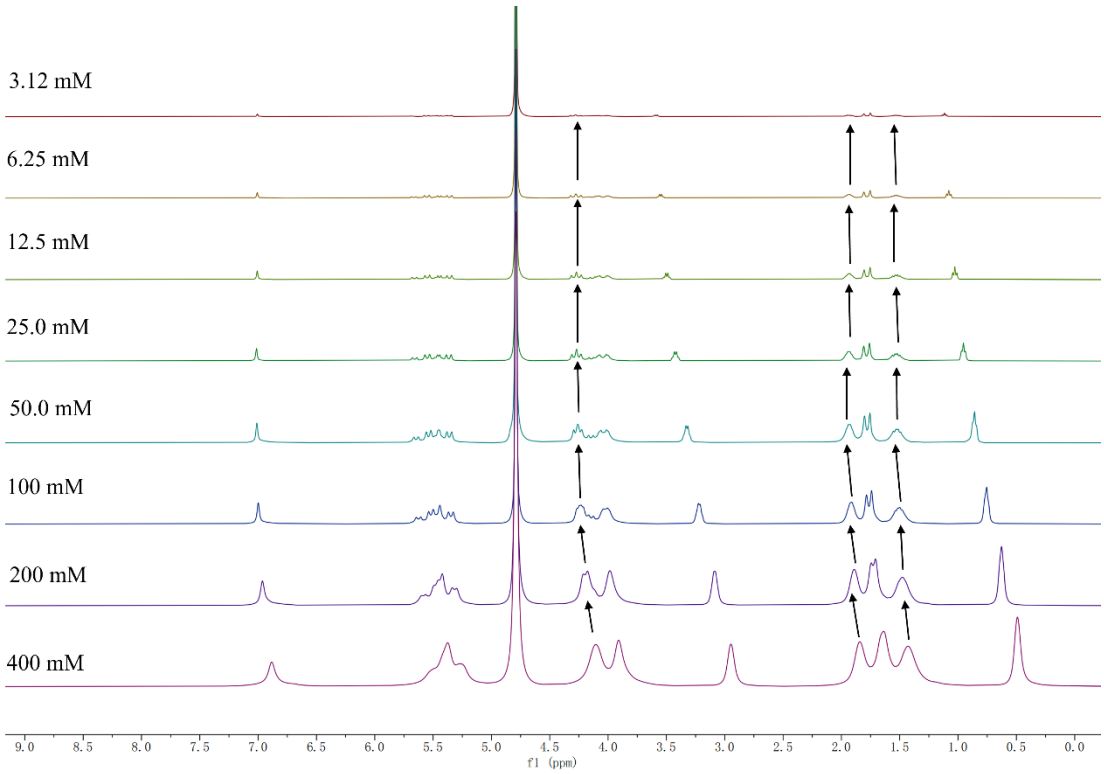


Figure S14. ^{1}H NMR recorded for **P5C3** at various concentration (400 MHz, D_2O).

Standard curve of P5C2 or P5C3

A UV-Vis spectrophotometer analysis method was established for **P5C2** or **P5C3**, drawing a standard curve of **P5C2** or **P5C3**. To determine the standard calibration curve, a series of diluted **P5C2** or **P5C3** solution in purified water or PBS buffer (pH 7.4) were prepared (0.50, 0.25, 0.125, 0.062, 0.031, 0.016 mM). The absorption at the wavelength of 291 nm was plotted as a function of the concentration of **P5C2** or **P5C3**, and the standard curve was obtained by linear regression analysis. A linear regression equation was determined ($r^2 > 0.99$), which was used to calculate the concentration of **P5C2** or **P5C3** in subsequent experiments.

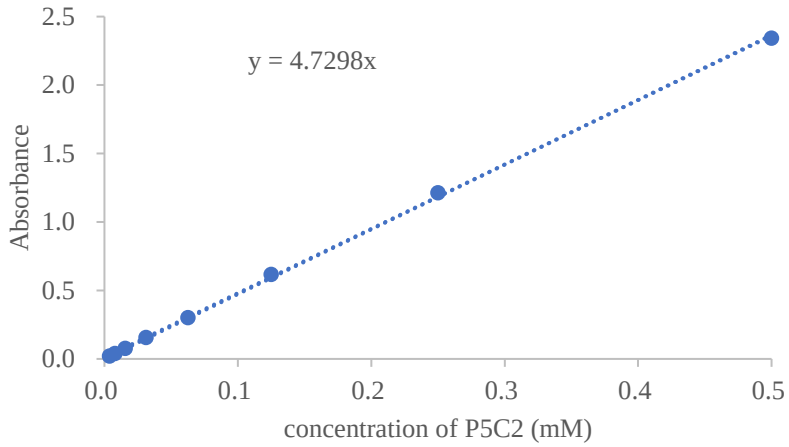


Figure S15. Standard curve of **P5C2** in 1 mM of PBS buffer (pH 7.4).

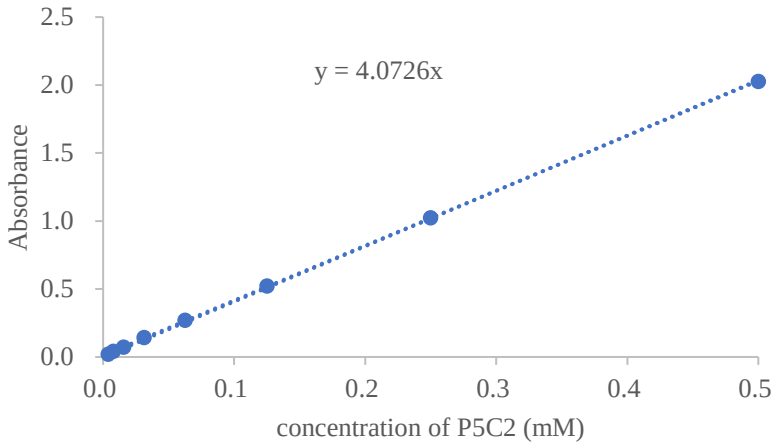


Figure S16. Standard curve of **P5C2** in water.

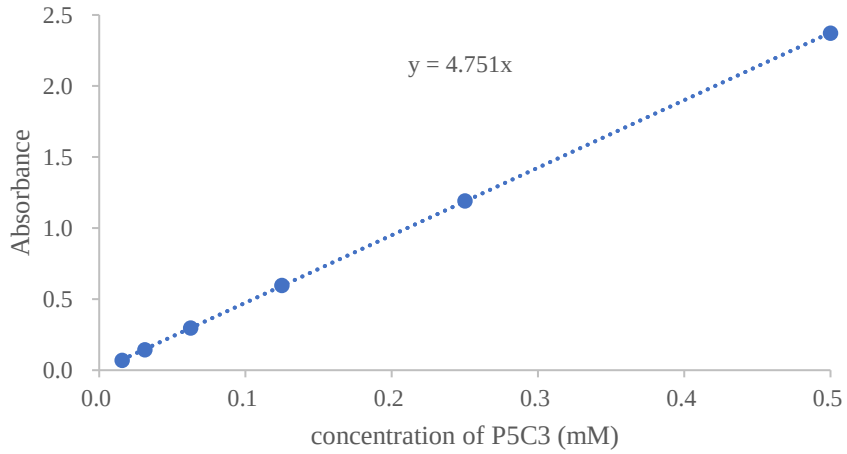


Figure S17. Standard curve of **P5C3** in 1 mM of PBS buffer (pH 7.4).

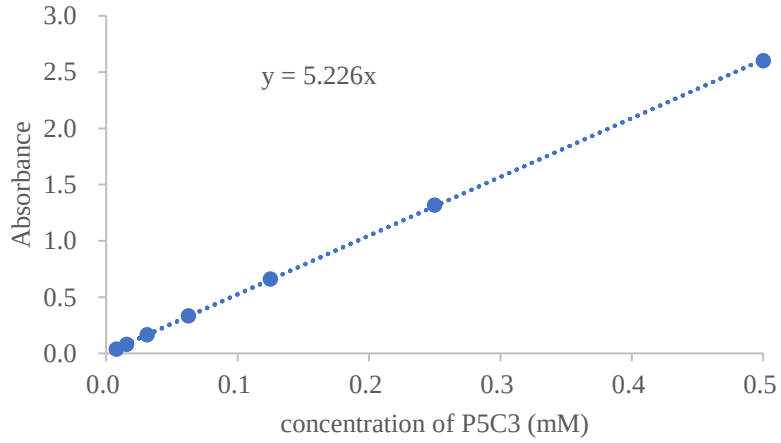


Figure S18. Standard curve of **P5C3** in water.

Determination of the solubility of P5C2 or P5C3 in water and neutral buffer.

1) by UV-Vis using the standard curve

An excess amount of **P5C2** was added into a glass vial containing 1 mL of purified water or PBS buffer (pH = 7.4). The vial was shaken on a horizontal rotary shaker at a speed of 50 rpm at 25 °C for 24 h. The suspension was filtered through a 0.8 μm hydrophilic disc filter to collect a clear solution. The concentration of **P5C2** in the solution was determined using a UV-Vis spectrometer.

Similar methods were used to determine the intrinsic solubility of **P5C3**.

2) by NMR using internal reference

An excess amount of **P5C2** was added into a glass vial containing 1 mL of deuterium oxide. The vial was shaken on a horizontal rotary shaker at a speed of 50 rpm at 25 °C for 24 h. The suspension was filtered through a 0.8 μm hydrophilic disc filter to collect a clear solution. The solution (10 μL) and 1,3,5-benzenetricarboxylic acid (20

μL of 120 mM in D_2O) were added into 0.5 mL of deuterium oxide. The concentration of **P5C2** was measured with ^1H NMR and calculated using 1,3,5-benzenetricarboxylic acid as internal reference.
Similar methods were used to determine the intrinsic solubility of **P5C3**.

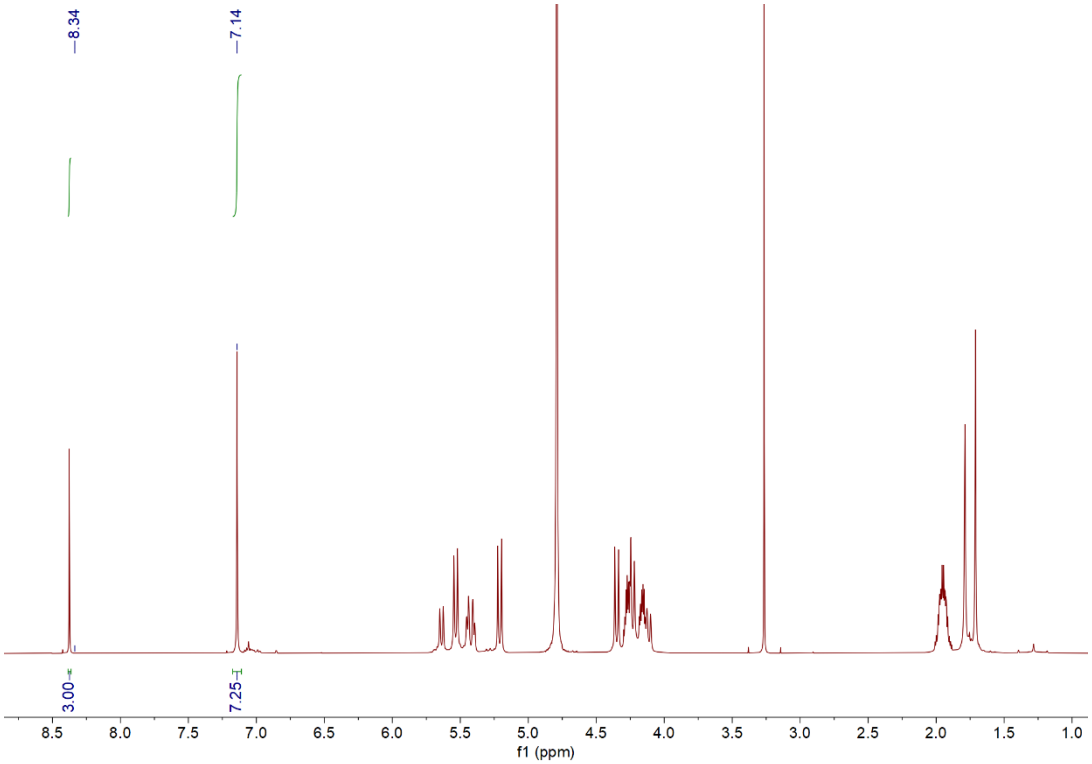


Figure S19. ^1H NMR spectra (400 MHz, D_2O) recorded for **P5C2** with 1,3,5-benzene tricarboxylic acid (120 mM) as internal reference. The solubility of **P5C2** in water is calculated to be 435 mM.

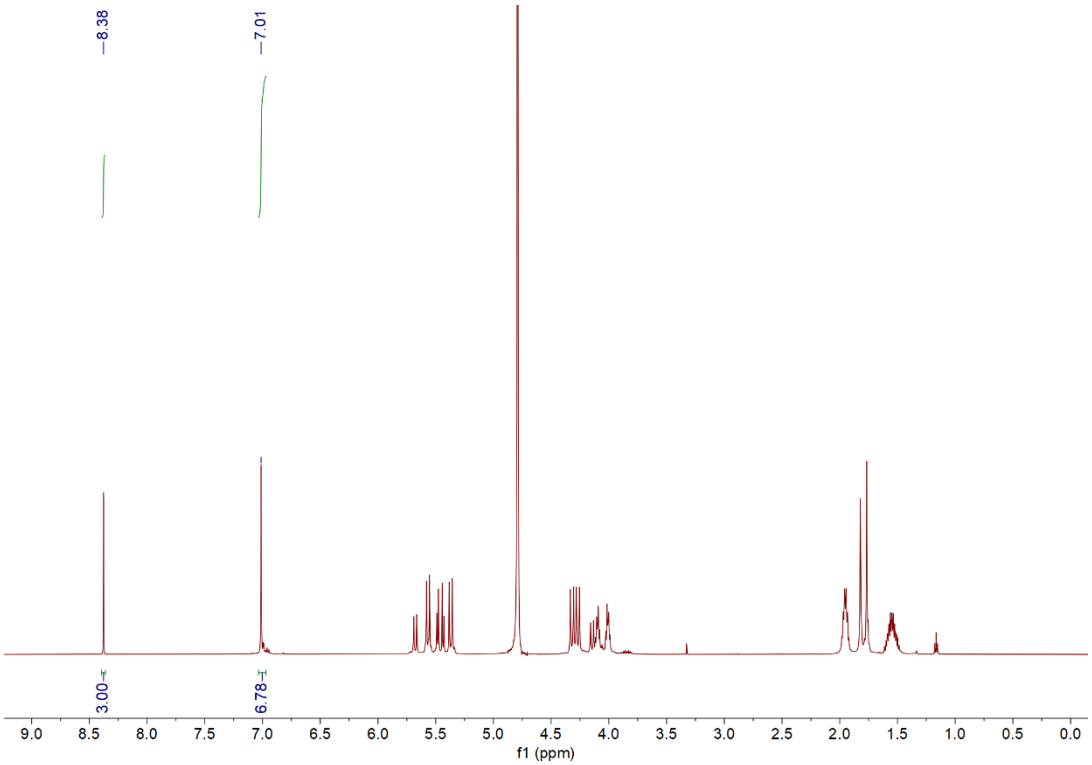


Figure S20. ^{1}H NMR spectra (400 MHz, D_2O) recorded for **P5C3** with 1,3,5-benzene tricarboxylic acid (120 mM) as internal reference. The solubility of **P5C3** in water is calculated to be 407 mM.

^{1}H NMR spectra of mixed solution

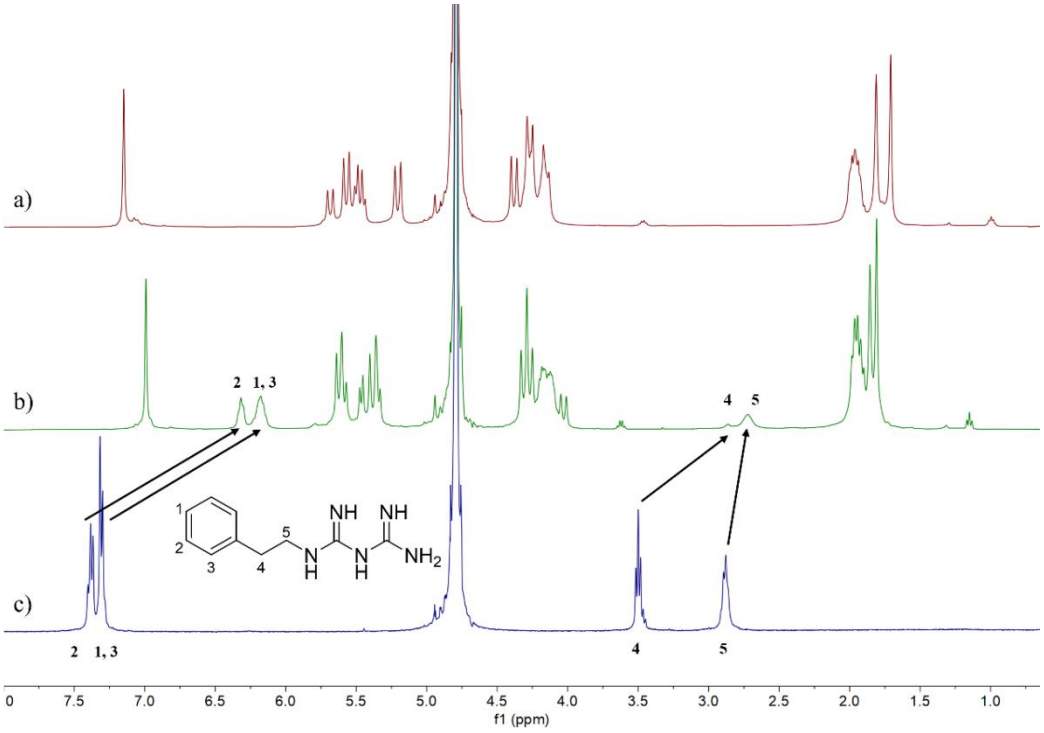


Figure S21. ^{1}H NMR spectra recorded (D_2O, 400MHz, RT) for: a) **P5C2** (25 mM), b) a mixture 1:1 of **P5C2** (25 mM) and **Phenformin** (25 mM), and c) **Phenformin** (25 mM).

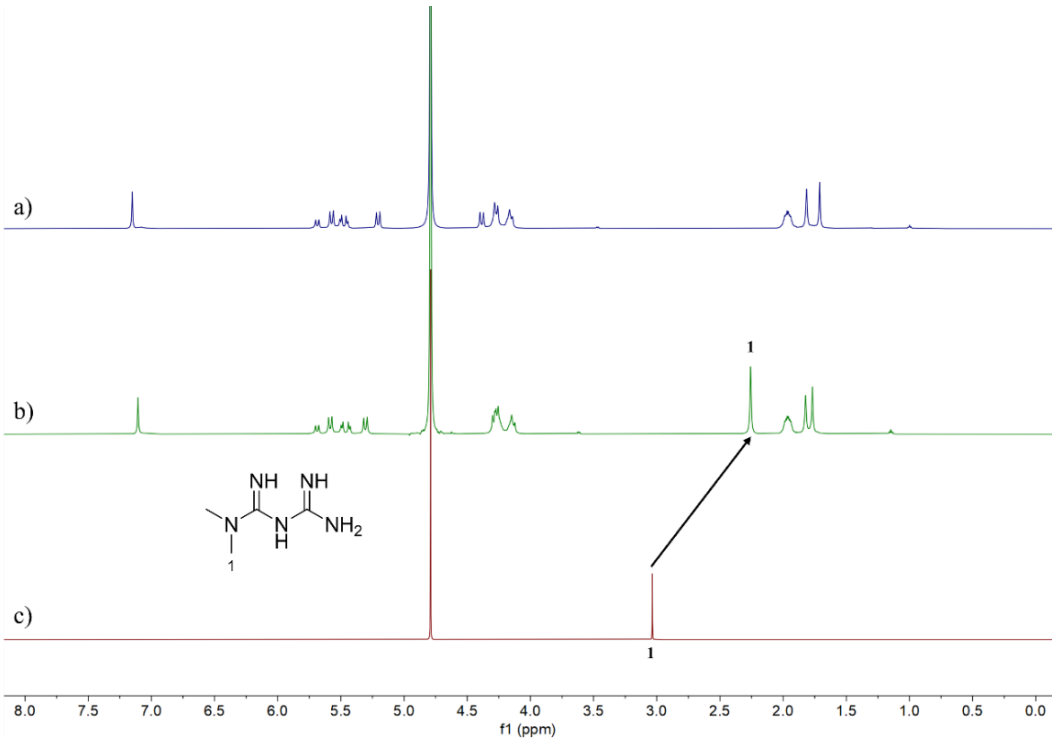


Figure S22. ^{1}H NMR spectra recorded (D_2O, 400MHz, RT) for: a) **P5C2** (25 mM), b) a mixture 1:1 of **P5C2** (25 mM) and **Metformin** (25 mM), and c) **Metformin** (25 mM).

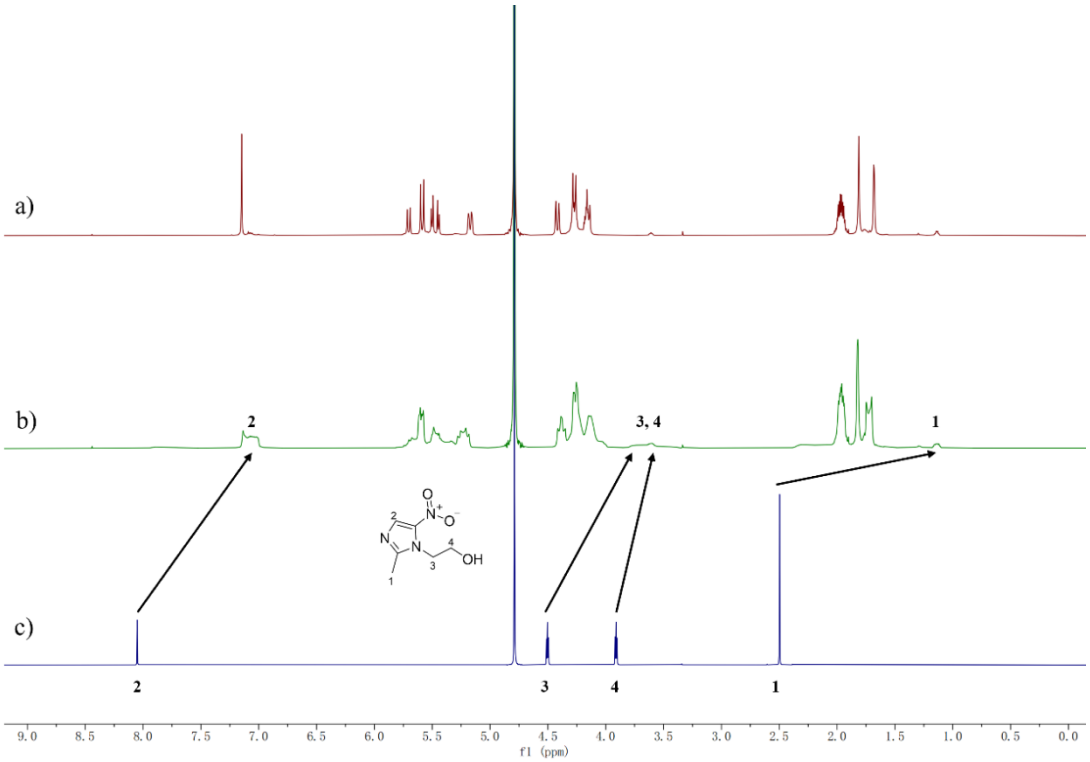


Figure S23. ^{1}H NMR spectra recorded (D_2O, 400MHz, RT) for: a) **P5C2** (10 mM), b) a mixture 1:1 of **P5C2** (10 mM) and **Metronidazole** (10 mM), and c) **Metronidazole** (10 mM).

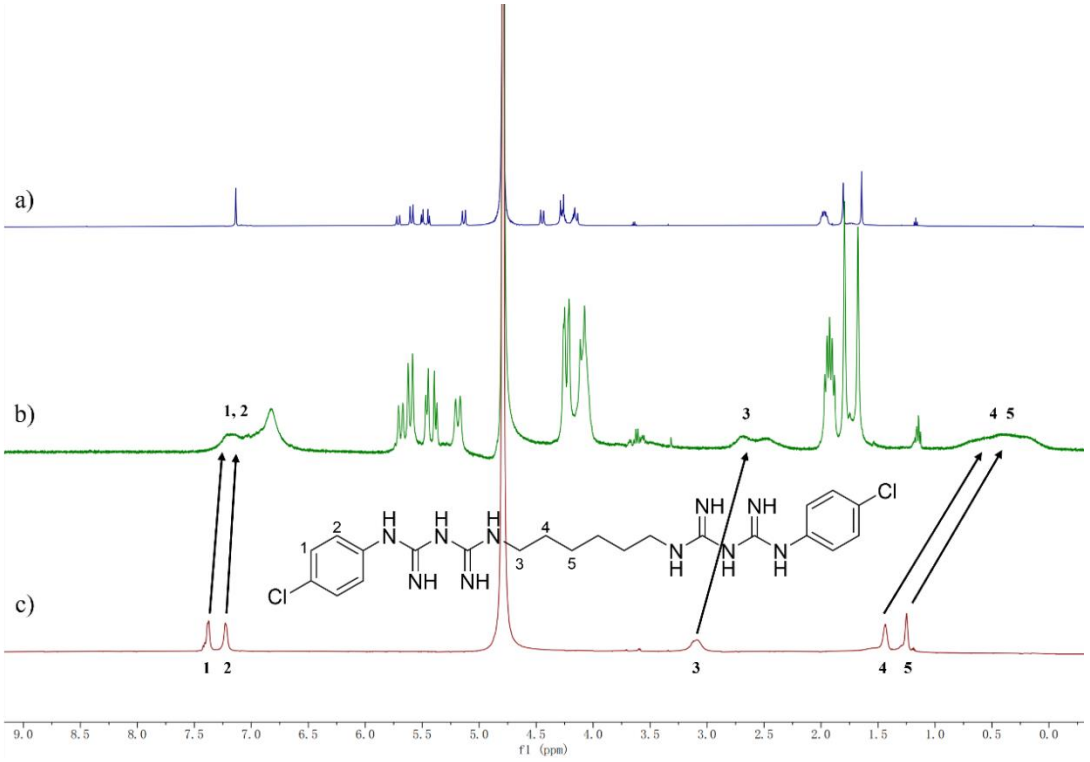


Figure S24. ^{1}H NMR spectra recorded (D_2O, 400MHz, RT) for: a) **P5C2** (5 mM), b) a mixture 1:1 of **P5C2** (5 mM) and **Chlorhexidine** (5 mM), and c) **Chlorhexidine** (0.1 mM).

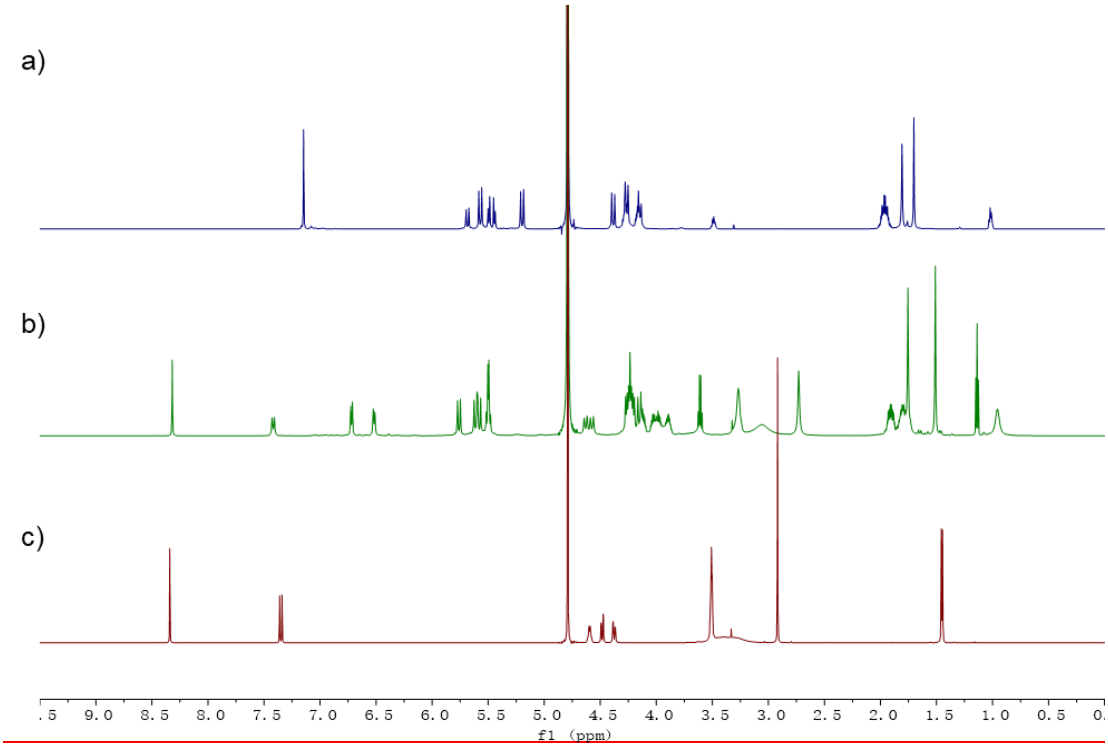


Figure S25. ^{1}H NMR spectra recorded (D_2O, 400MHz, RT) for: a) **P5C2** (25 mM), b) a mixture 1:1 of **P5C2** (25 mM) and **Levofloxacin** (25 mM), and c) **Levofloxacin** (25 mM).

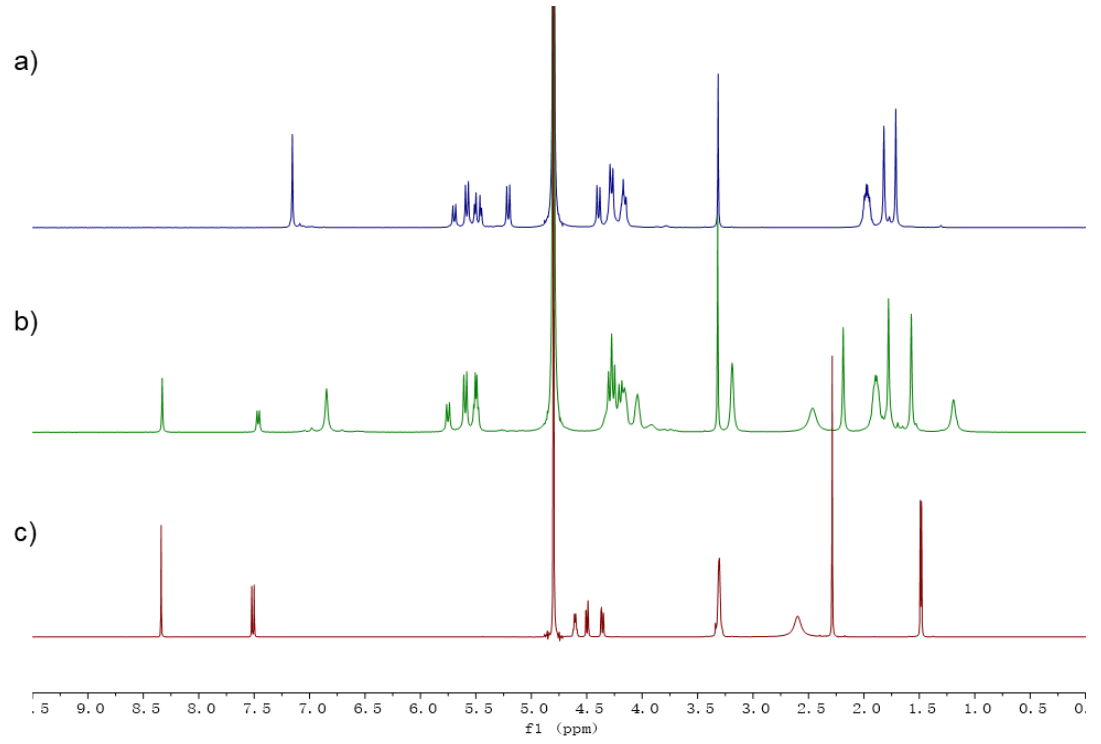


Figure S26. ^{1}H NMR spectra recorded (D_2O, 400MHz, RT) for: a) **P5C2** (25 mM), b) a mixture 1:1 of **P5C2** (25 mM) and **Ofloxacin** (25 mM), and c) **Ofloxacin** (25 mM).

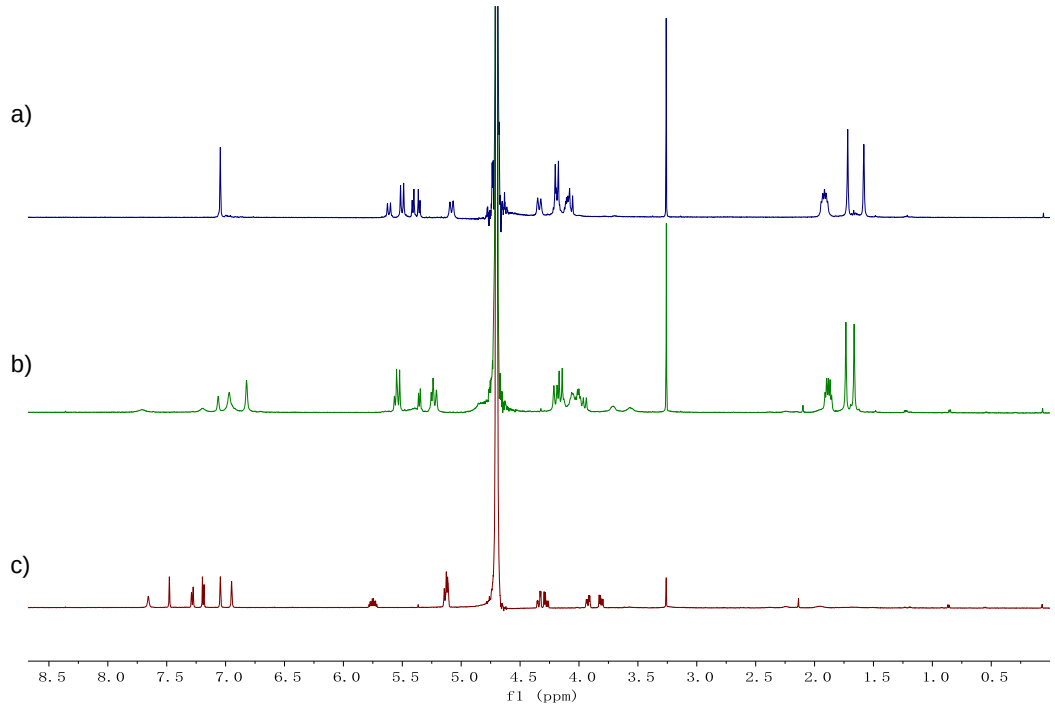


Figure S27. ^{1}H NMR spectra recorded (D_2O, 400MHz, RT) for: a) **P5C2** (0.6 mM), b) a mixture 1:1 of **P5C2** (0.6 mM) and **Enilconazole** (0.6 mM), and c) **Enilconazole** (0.6 mM).

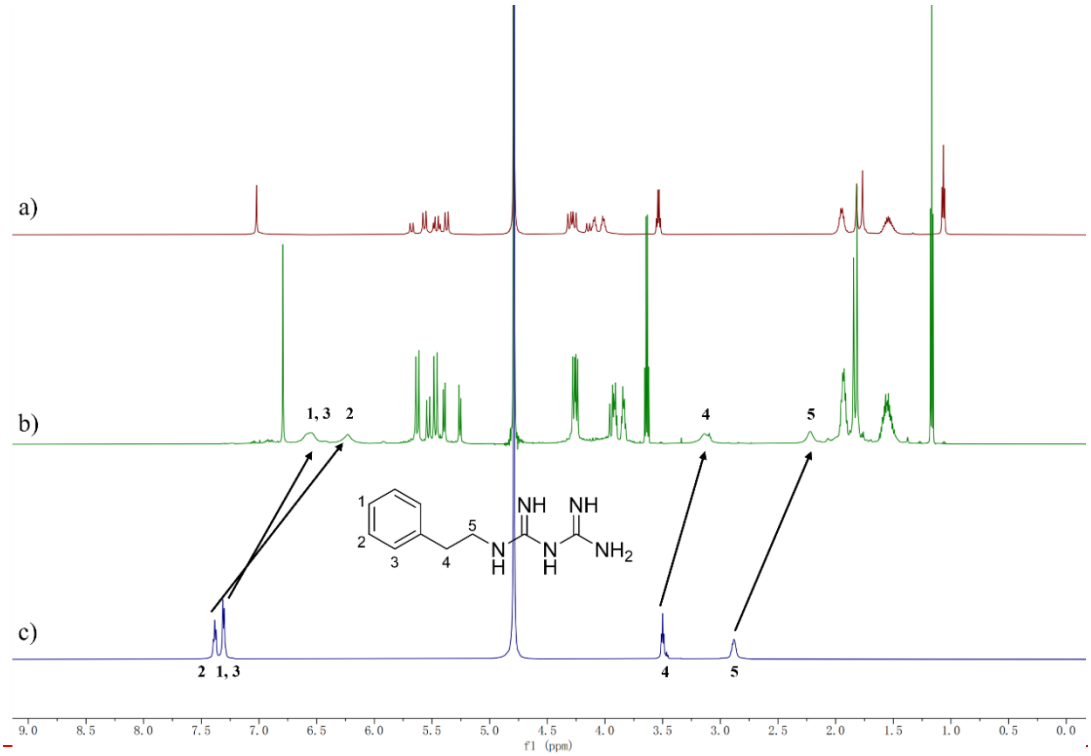


Figure S28. ^{1}H NMR spectra recorded (D_2O, 400MHz, RT) for: a) **P5C3** (25 mM), b) a mixture 1:1 of **P5C3** 2(5 mM) and **Phenformin** (25 mM), and c) **Phenformin** (25 mM).

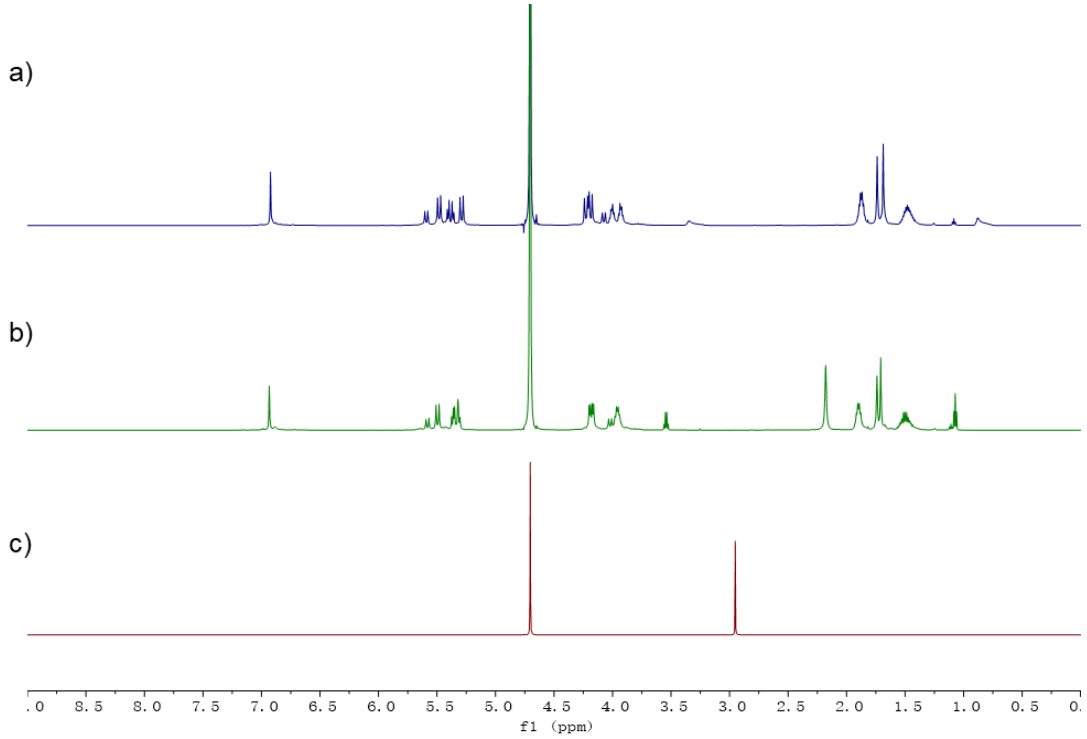


Figure S29. ^{1}H NMR spectra recorded (D_2O, 400MHz, RT) for: a) **P5C3** (25 mM), b) a mixture 1:1 of **P5C3** (25 mM) and **Metformin** (25 mM), and c) **Metformin** (25 mM).

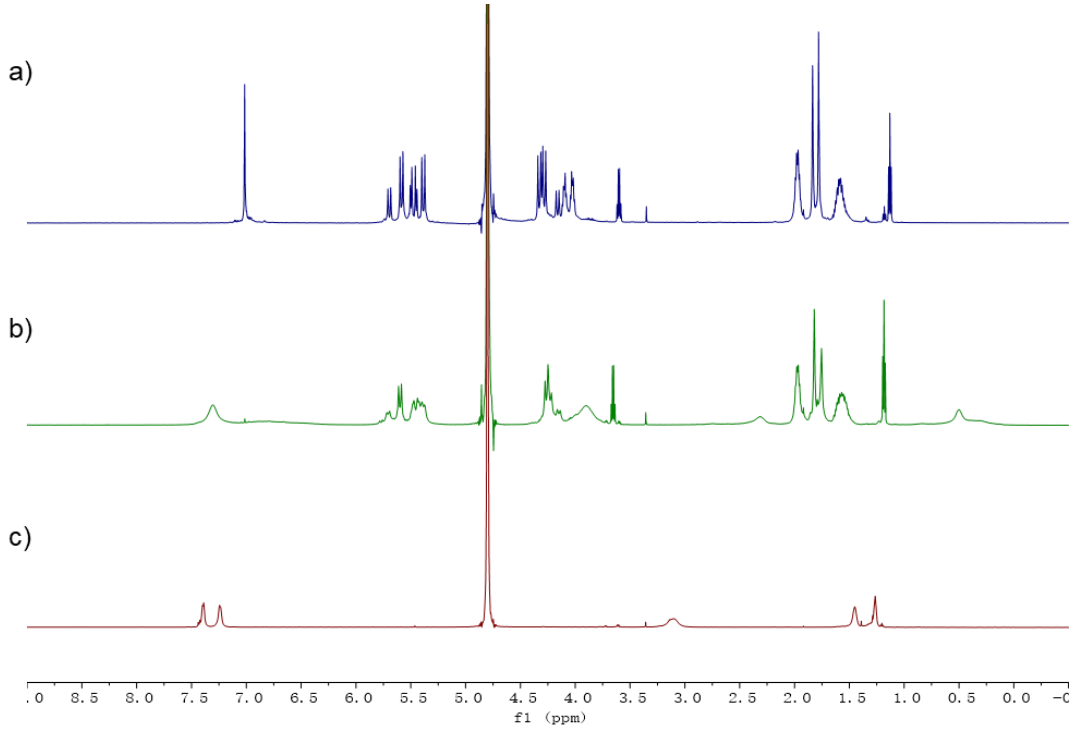


Figure S30. ^{1}H NMR spectra recorded (D_2O, 400MHz, RT) for: a) **P5C3** (5 mM), b) a mixture 1:1 of **P5C3** (5 mM) and **Chlorhexidine** (5 mM), and c) **Chlorhexidine** (0.1 mM).

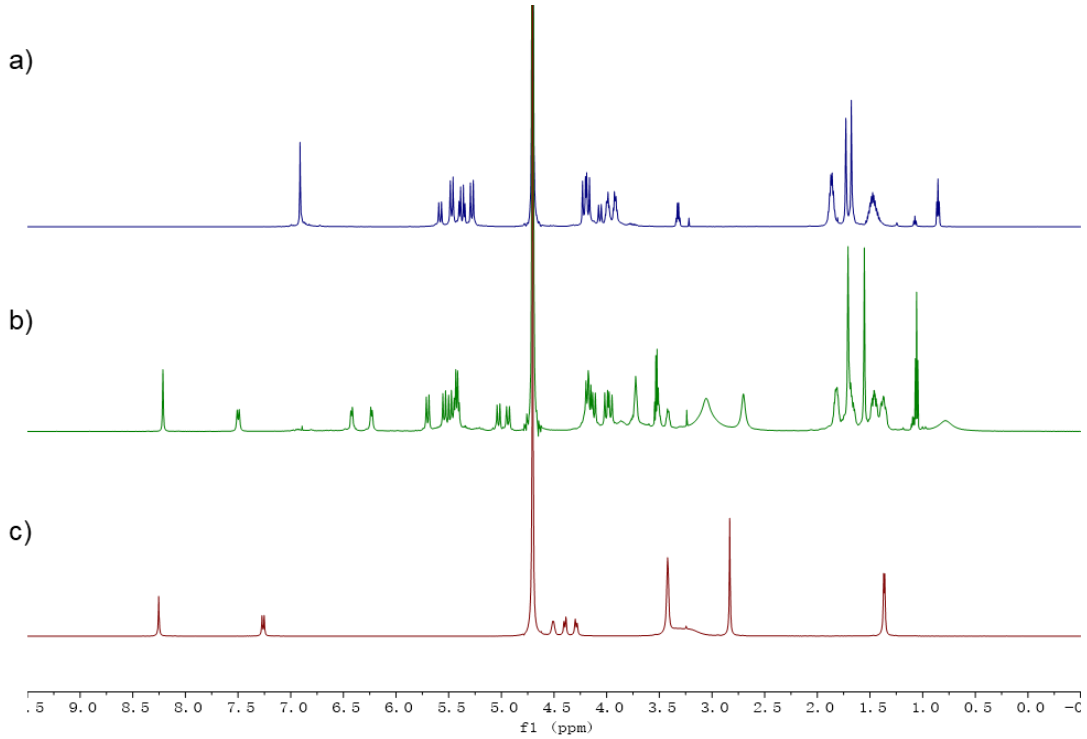


Figure S31. ^{1}H NMR spectra recorded (D_2O, 400MHz, RT) for: a) **P5C3** (25 mM), b) a mixture 1:1 of **P5C3** (25 mM) and **Levofloxacin** (25 mM), and c) **Levofloxacin** (25 mM).

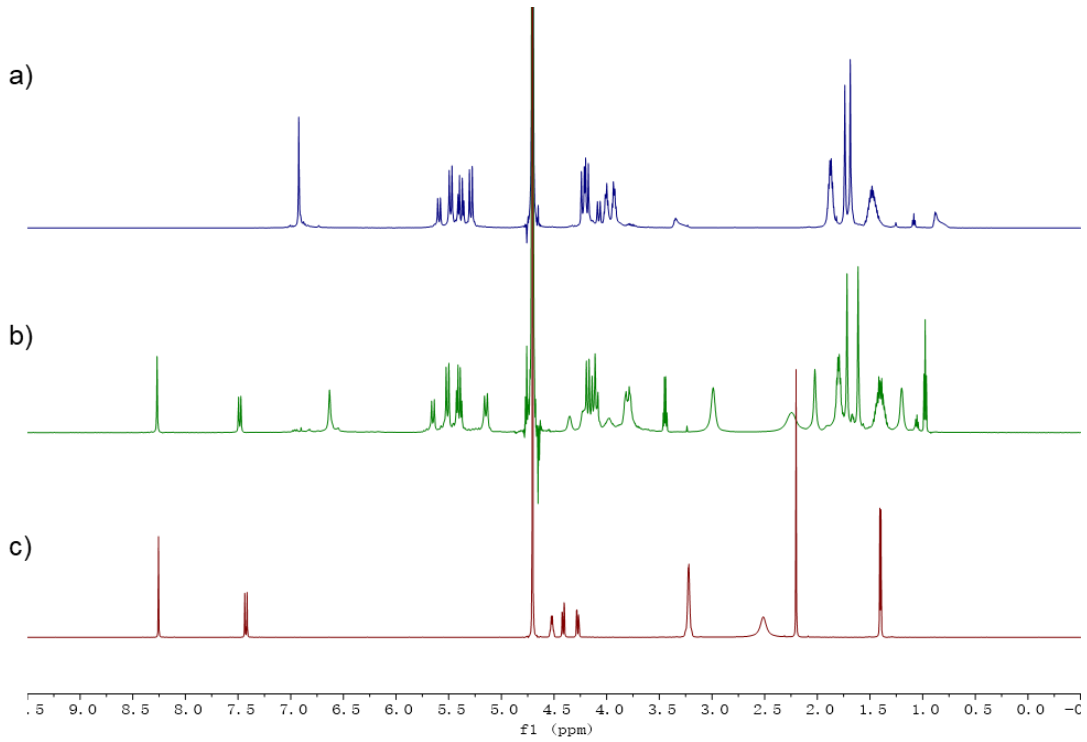


Figure S32. ^{1}H NMR spectra recorded (D_2O, 400MHz, RT) for: a) **P5C3** (25 mM), b) a mixture 1:1 of **P5C3** (25 mM) and O**floxacin** (25 mM), and c) **Ofloxacin** (25 mM).

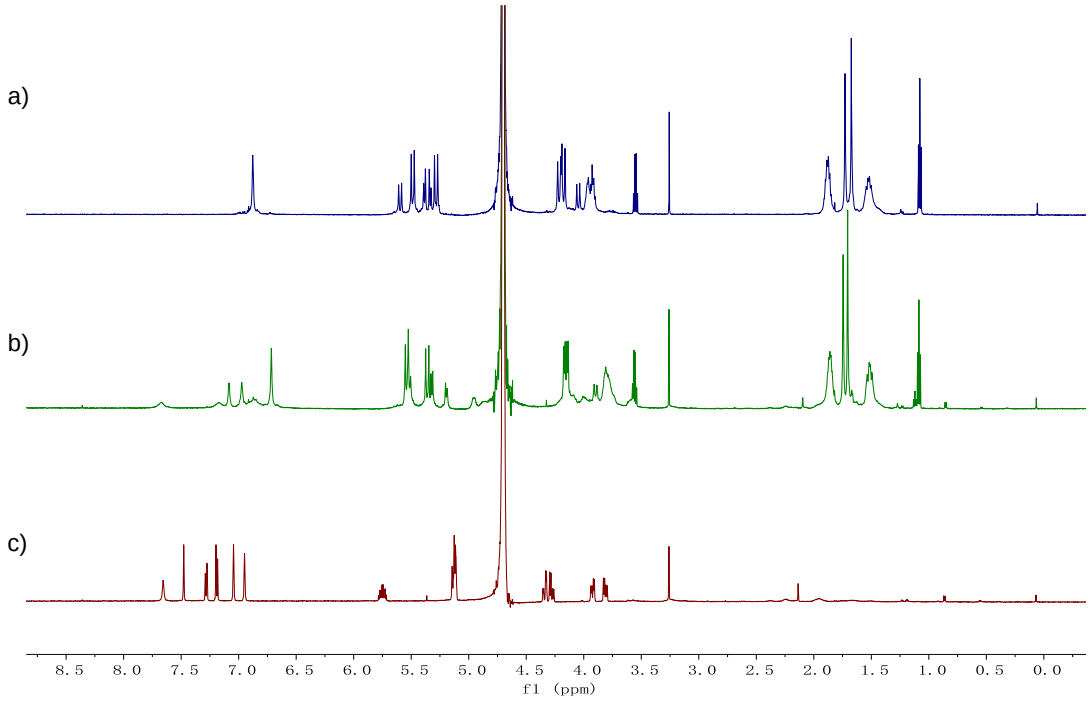


Figure S33. ^{1}H NMR spectra recorded (D_2O, 400MHz, RT) for: a) **P5C3** (0.6 mM), b) a mixture 1:1 of **P5C3** (0.6 mM) and **Enilconazole** (0.6 mM), and c) **Enilconazole** (0.6 mM).

Stoichiometry by Job's plot

The association ratio between host **P5C2** or **P5C3** and guest was determined by Job's plot method.[1] UV-Vis absorption spectra were investigated using a UV-Vis spectrometer. Equal molar concentrations of host and guest in aqueous solutions were mixed, in which the total molar concentration of host and guest was kept constant and the mole fraction was set between 0:10, 1:9, 2:8, 3:7, 4:6, 5:5, 6:4, 7:3, 8:2, 9:1, 10:0 of host and guest mixed solution (volume ratio). The absorbance values of a series of mixed solutions were measured. The value of the difference between the absorbance was plotted as a function of the mole fraction, and the turning point of the curve was regarded as the association ratio.

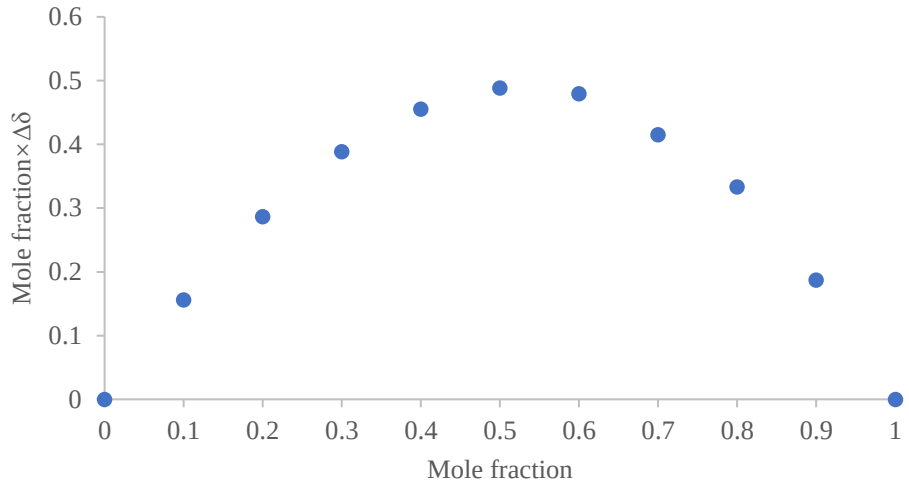


Figure S34. Job's plot constructed for **P5C2** and **Robenidine** (total concentration 20 μM, 1 mM PBS buffer, pH 7.4) by UV/Vis spectra at 527 nm.

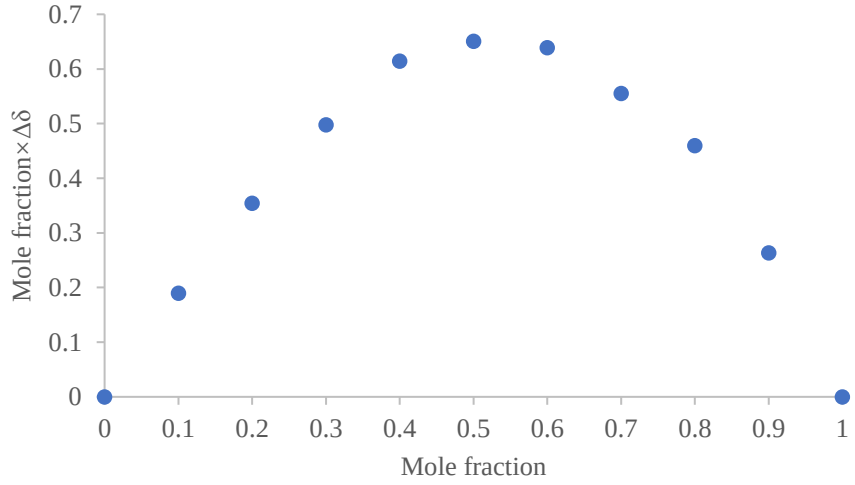


Figure S35. Job's plot constructed for **P5C2** and **Methylviologen** (total concentration 0.1 mM, pure water) by UV/Vis spectra at 252 nm.

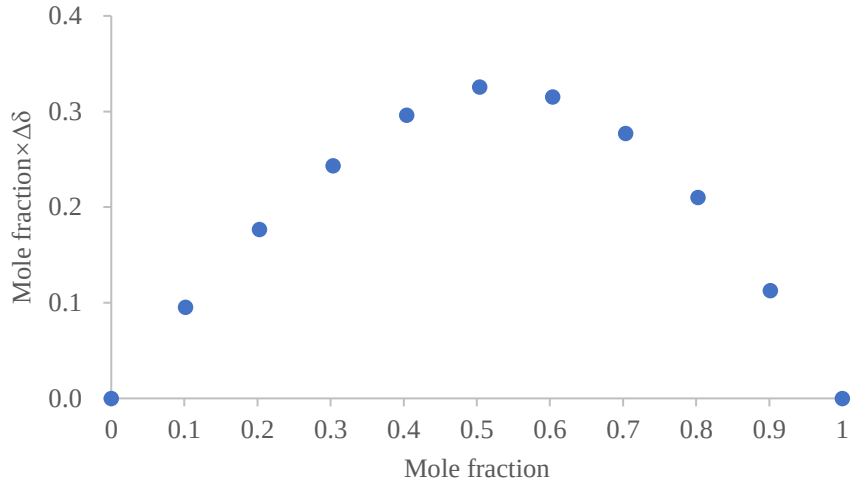


Figure S36. Job's plot constructed for **P5C2** and **Methylacridinium** (total concentration 50 μM, 1 mM PBS buffer, pH 7.4) by UV/Vis spectra at 357 nm.

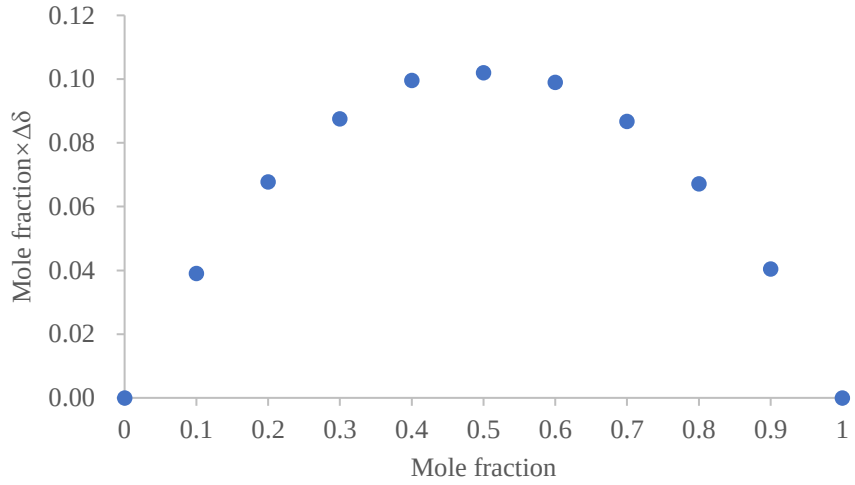


Figure S37. Job's plot constructed for **P5C2** and **Metformin** (total concentration 0.1 mM, pure water) by UV/Vis spectra at 291 nm.

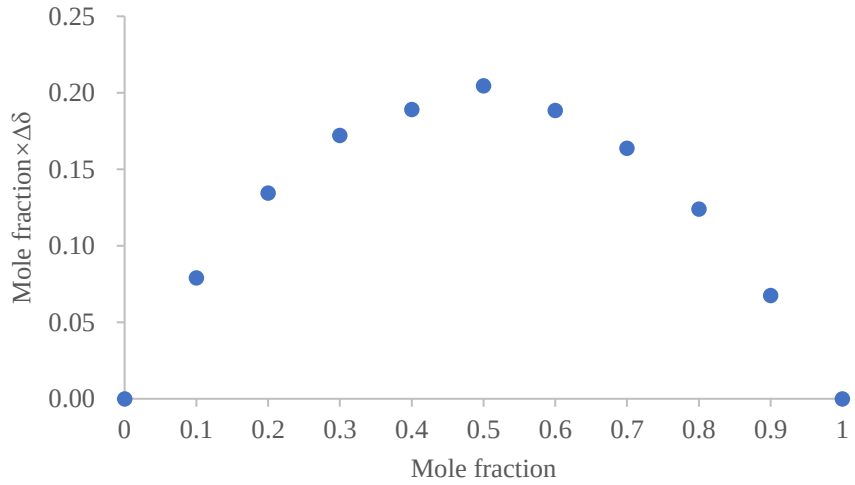


Figure S38. Job's plot constructed for **P5C2** and **Phenformin** (total concentration 0.1 mM, pure water) by UV/Vis spectra at 291 nm.

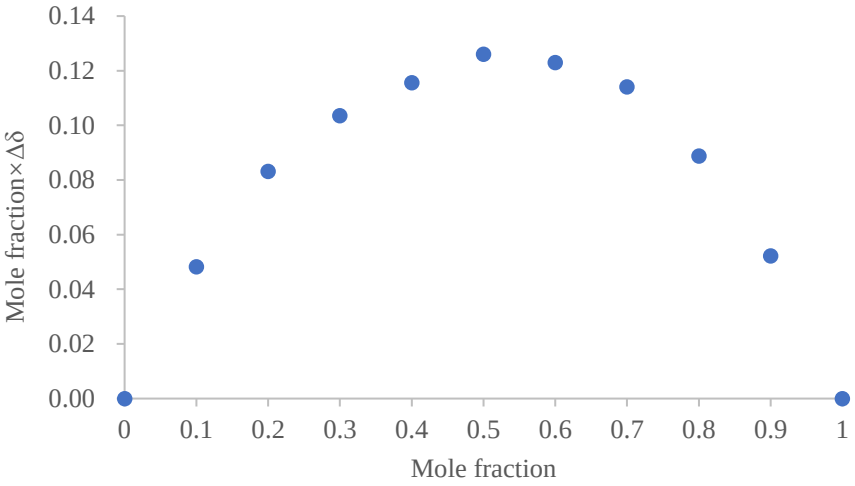


Figure S39. Job's plot constructed for **P5C2** and **Chlorhexidine** (total concentration 20 μM, pure water) by UV/Vis spectra at 252 nm.

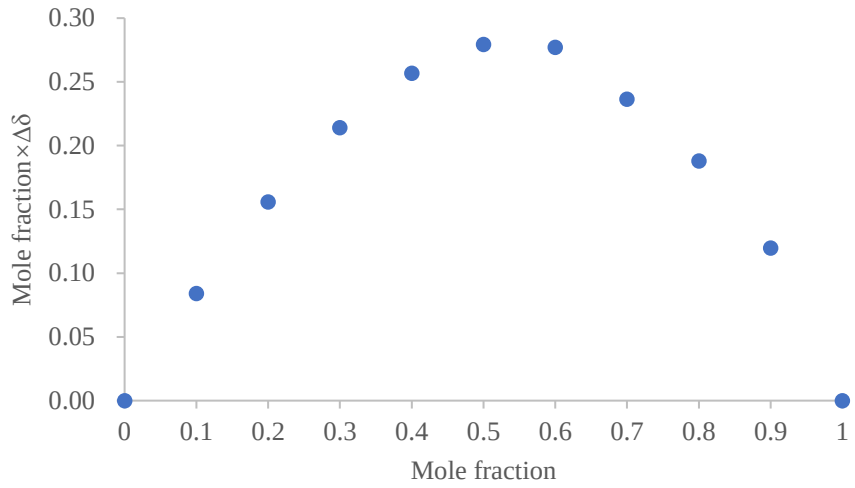


Figure S40. Job's plot constructed for **P5C3** and **Robenidine** (total concentration 10 μM, 1 mM PBS buffer, pH 7.4) by UV/Vis spectra at 527 nm.

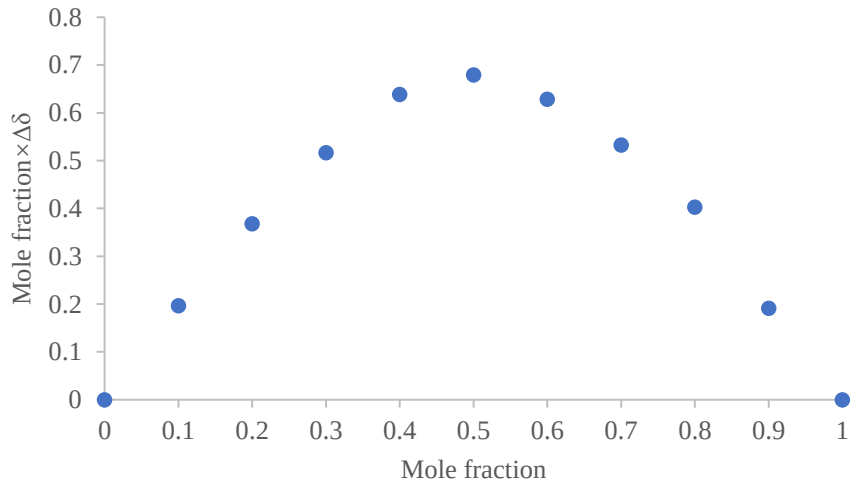


Figure S41. Job's plot constructed for **P5C3** and **Methylviologen** (total concentration 0.1 mM, pure water) by UV/Vis spectra at 253 nm.

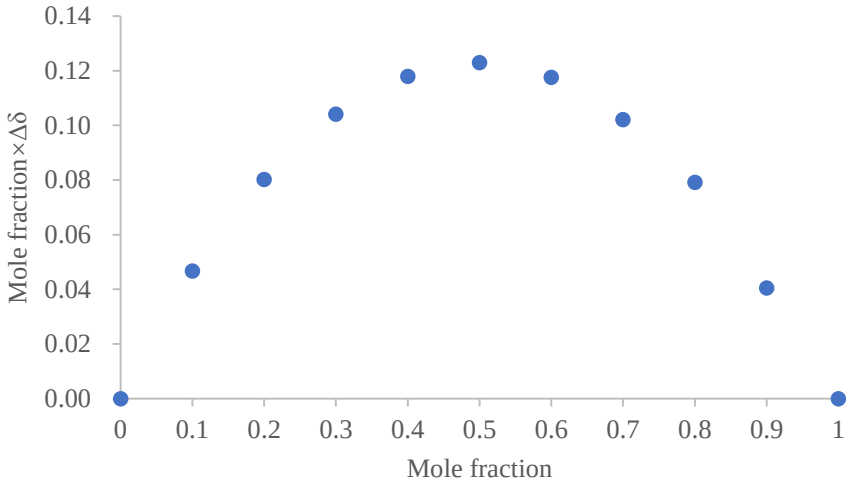


Figure S42. Job's plot constructed for **P5C3** and **Metformin** (total concentration 0.1 mM, pure water) by UV/Vis spectra at 294 nm.

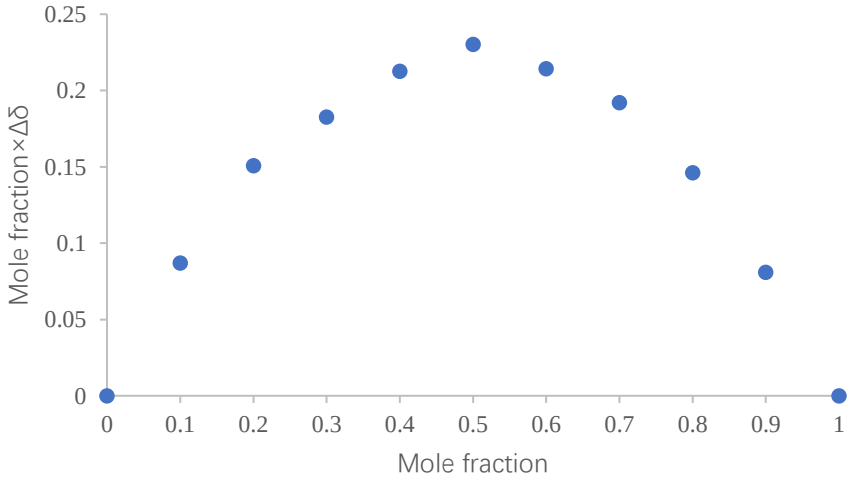


Figure S43. Job's plot constructed for **P5C3** and **Phenformin** (total concentration 0.1 mM, pure water) by UV/Vis spectra at 294 nm.

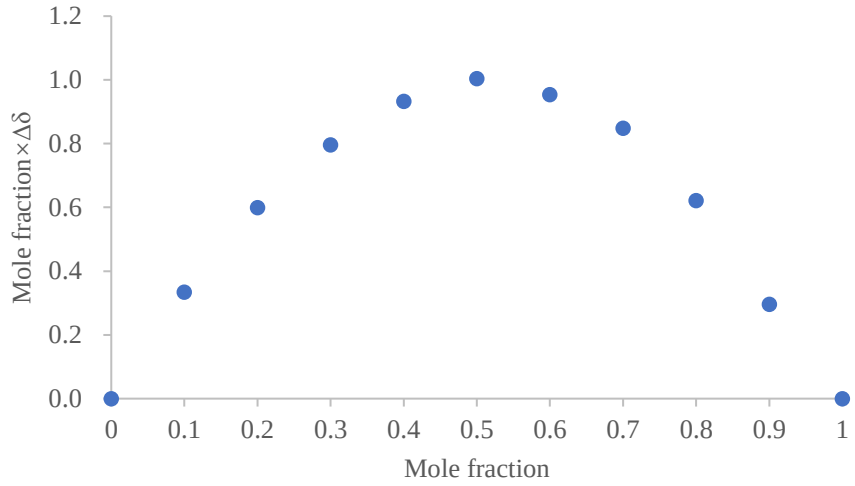


Figure S44. Job's plot constructed for **P5C3** and **Chlorhexidine** (total concentration 0.1 mM, pure water) by UV/Vis spectra at 253 nm.

Determination of binding constants[2,3]

Method for direct titration assay.

Binding constants K_a were calculated by nonlinear fitting with Origin® software based on 1:1 binding stoichiometry as the following equation:

$[H]_0$: initial host concentration; $[G]_0$: initial guest concentration; ΔI: change of fluorescence intensity; Δε: change of coefficiency; K_a: binding constant.

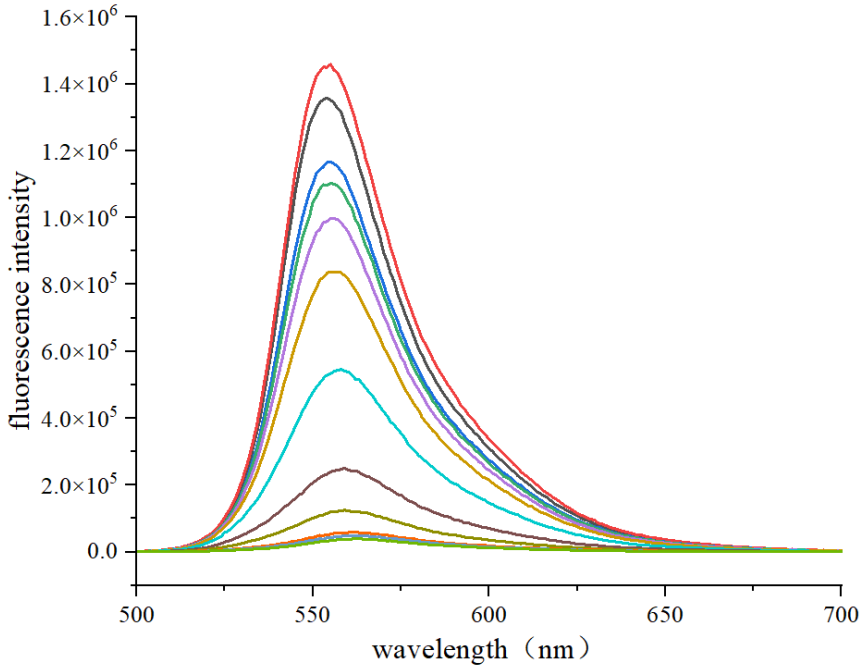
$$\Delta I = \Delta\varepsilon \cdot \{\frac{1}{2}([H]_0 + [G]_0 + \frac{1}{K_a}) - \sqrt{\frac{1}{4}([H]_0 + [G]_0 + \frac{1}{K_a})^2 - [H]_0 \cdot [G]_0}\}$$

Method for indicator displacement assay.

Binding constants K_a were measured with displacement assay and fitted with Scientist® software based on the following model.

// MicroMath Scientist Model File
IndVars: ConcAntot
DepVars: Absorb
Params: ConcHtot, ConcGtot, Khg, Kha, AbsorbMax, AbsorbMin
Khg = ConcHG / (ConcH * ConcG)
Kha = ConcHAn / (ConcH * ConcAn)
Absorb = AbsorbMin + (AbsorbMax-AbsorbMin)*(ConcHG/ConcGtot)
ConcHtot = ConcH + ConcHG + ConcHAn
ConcGtot = ConcHG + ConcG
ConcAntot = ConcAn + ConcHAn
0 < ConcHG < ConcHtot
0 < ConcH < ConcHtot
0 < ConcG < ConcGtot
0 < ConcAn < ConcAntot

(A)



(B)

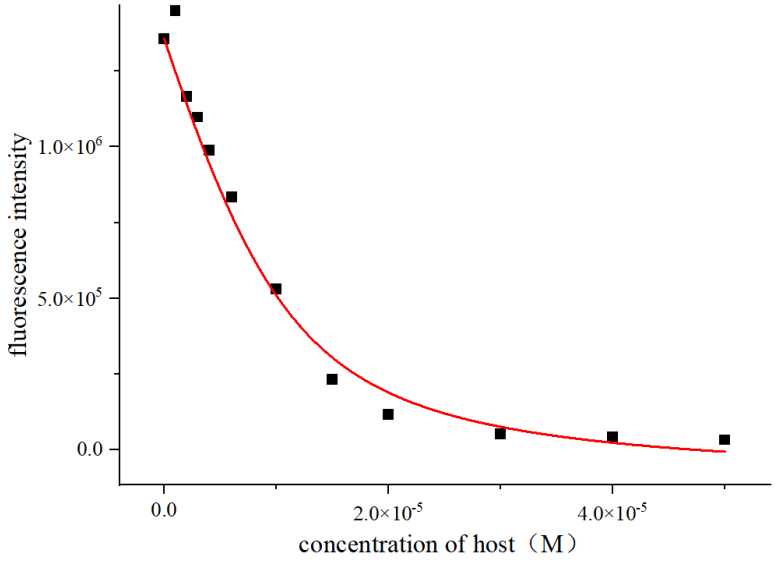
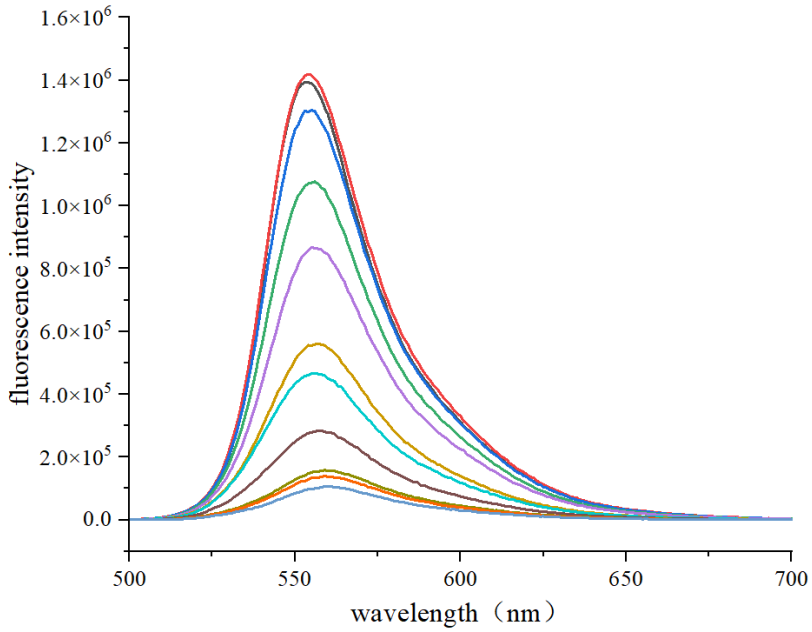


Figure S45. (A) Fluorescence spectra from the titration of **Rhodamine 6G** (10 μM) with **P5C2** (0 - 50 μM) in water, excited at 526 nm and emission at 554 nm; (B) Non-linear fitting plot of fluorescence intensity *versus* concentration for the direct titration of **Rhodamine 6G** with Origin. K_a was evaluated as 3.25×10^5 M^{-1}.

(A)



(B)

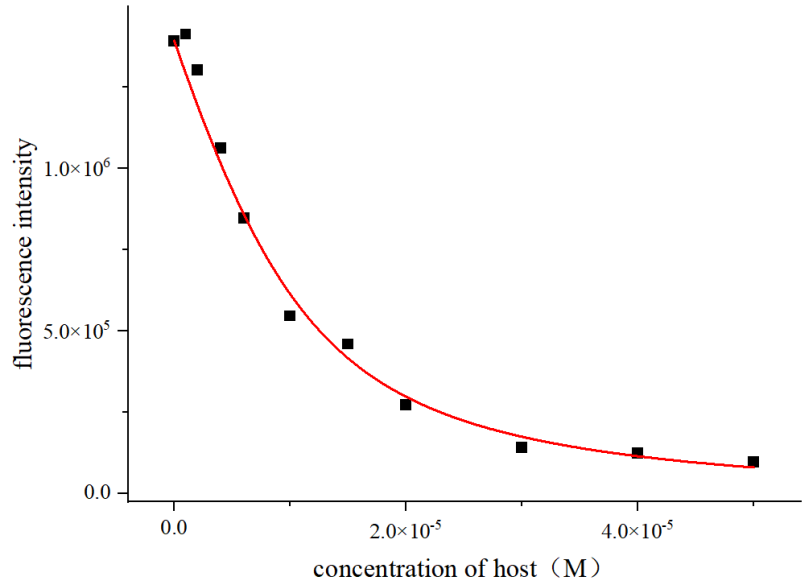
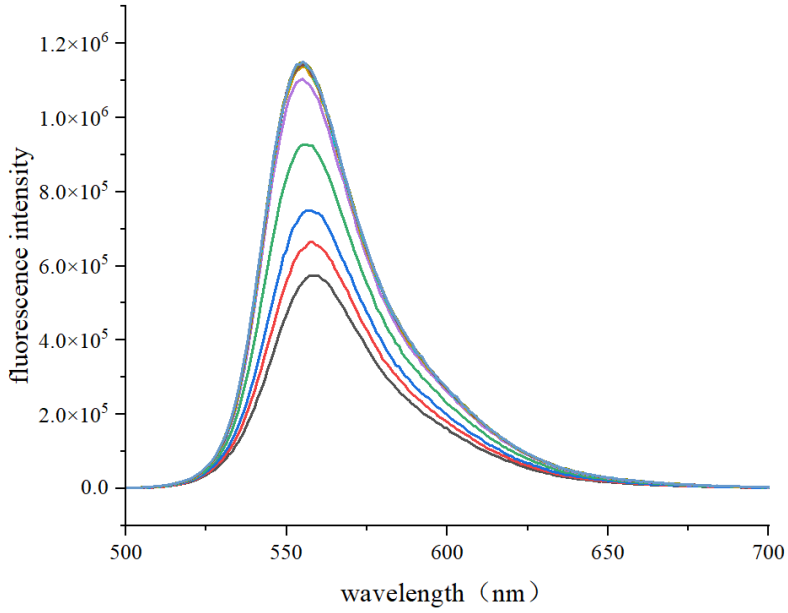


Figure S46. (A) Fluorescence spectra from the titration of **Rhodamine 6G** (10 μM) with **P5C2** (0 - 50 μM) in 1 mM PBS buffer (pH 7.4), excited at 526 nm and emission at 553 nm; (B) Non-linear fitting plot of fluorescence intensity *versus* concentration for the direct titration of **Rhodamine 6G** with Origin. K_a was evaluated as 2.59×10^5 M^{-1}.

(A)



(B)

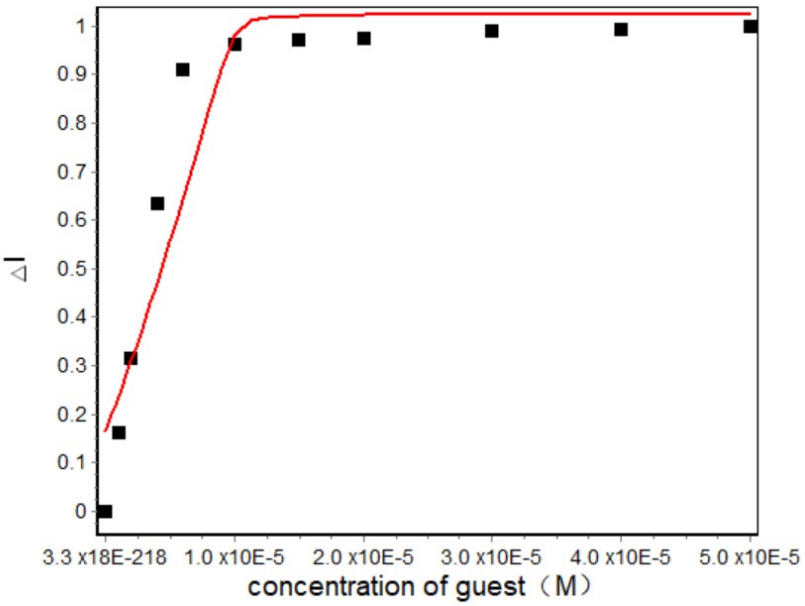
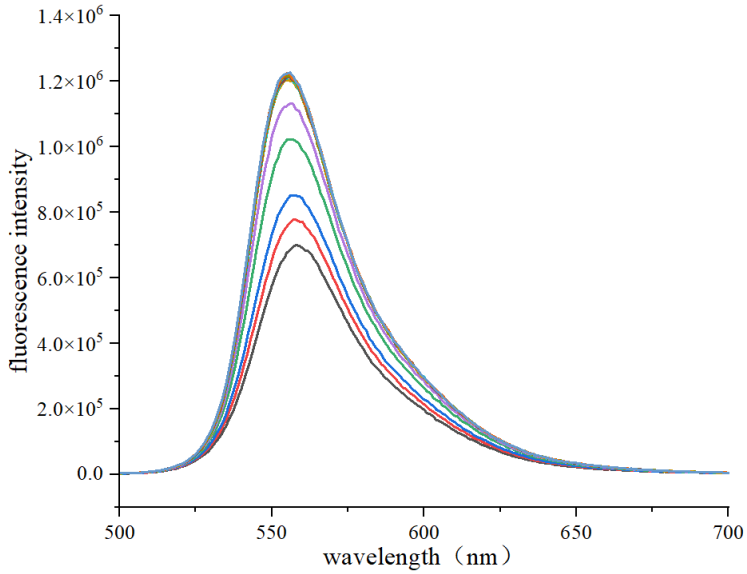


Figure S47. (A) Fluorescence spectra from the displacement titration of **P5C2** (10 μM) and **Rhodamine 6G** (15 μM) with **Methylviologen** (0 - 50 μM) in water, excited at 526 nm and emission at 558 nm; (B) Non-linear fitting plot of fluorescence intensity *versus* concentration for the displacement titration of **Methylviologen** with Scientist. K_a was evaluated as 2.90×10^8 M^{-1}.

(A)



(B)

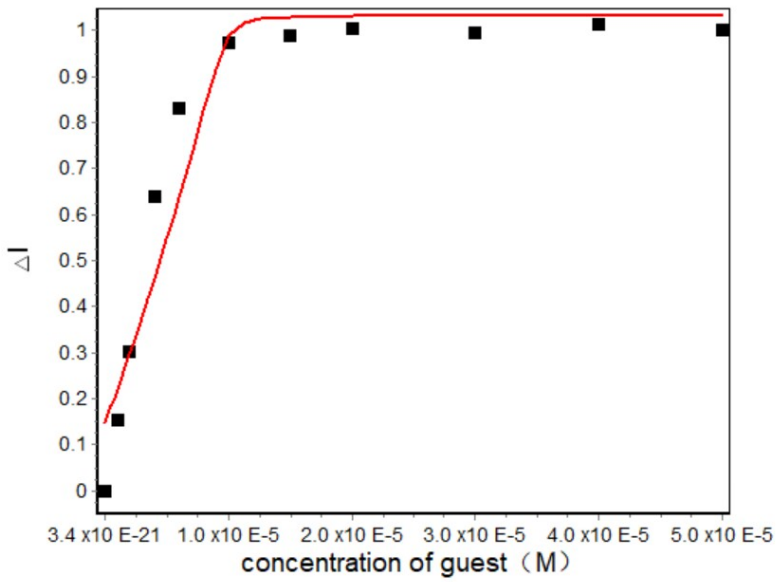
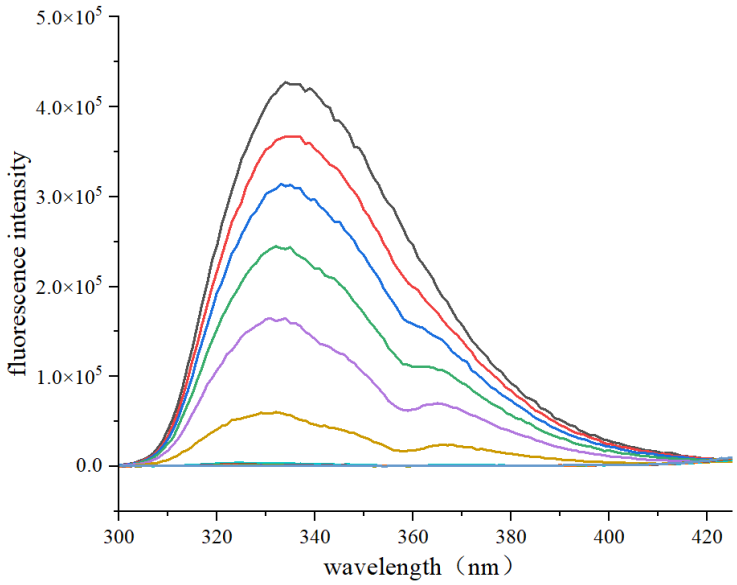


Figure S48. (A) Fluorescence spectra from the displacement titration of **P5C2** (10 μM) and **Rhodamine 6G** (15 μM) with **Methylviologen** (0 - 50 μM) in 1 mM PBS buffer (pH 7.4), excited at 526 nm and emission at 558 nm; (B) Non-linear fitting plot of fluorescence intensity *versus* concentration for the displacement titration of **Methylviologen** with Scientist. K_a was evaluated as 2.45×10^8 M^{-1}.

(A)



(B)

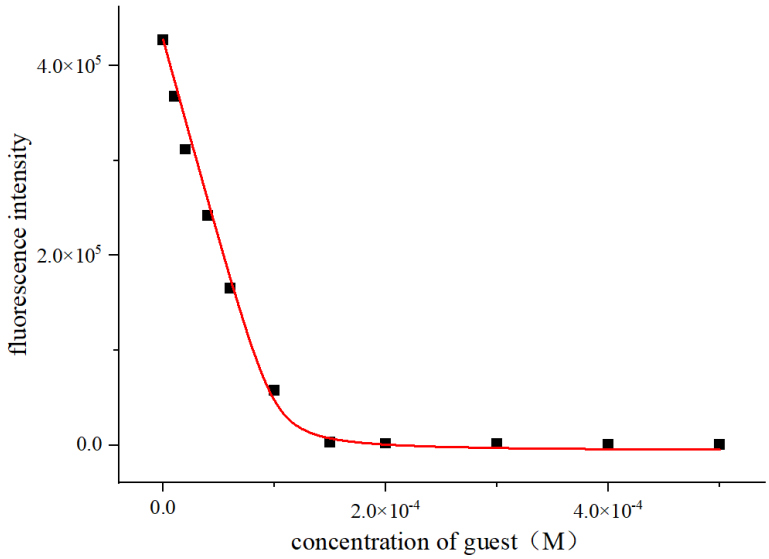
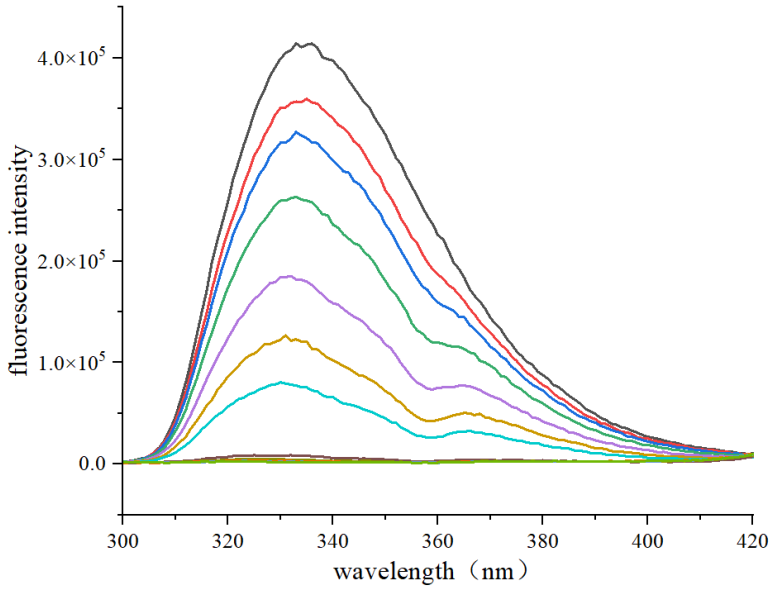


Figure S49. (A) Fluorescence spectra from the titration of **P5C2** (0.1 mM) with **Methylacridinium** (0 - 0.5 mM) in water, excited at 291 nm and emission at 334 nm; (B) Non-linear fitting plot of fluorescence intensity *versus* concentration for the direct titration of **Methylacridinium** with Origin. K_a was evaluated as 5.69×10^5 M^{-1}.

(A)



(B)

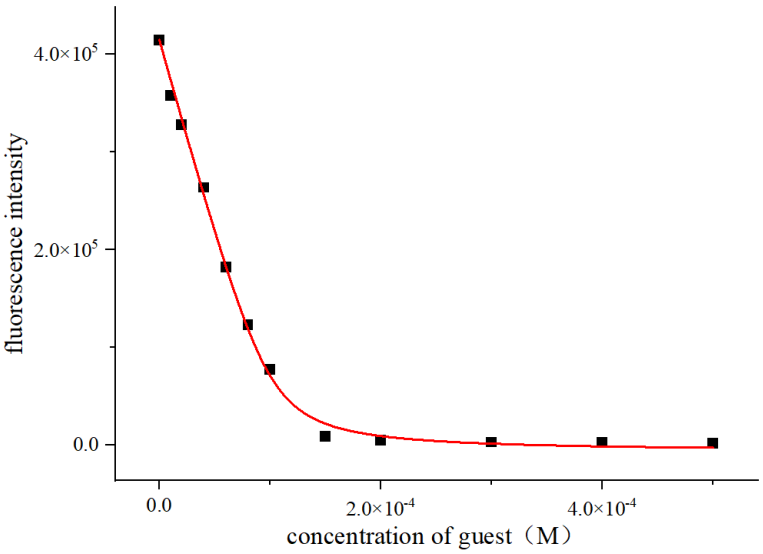
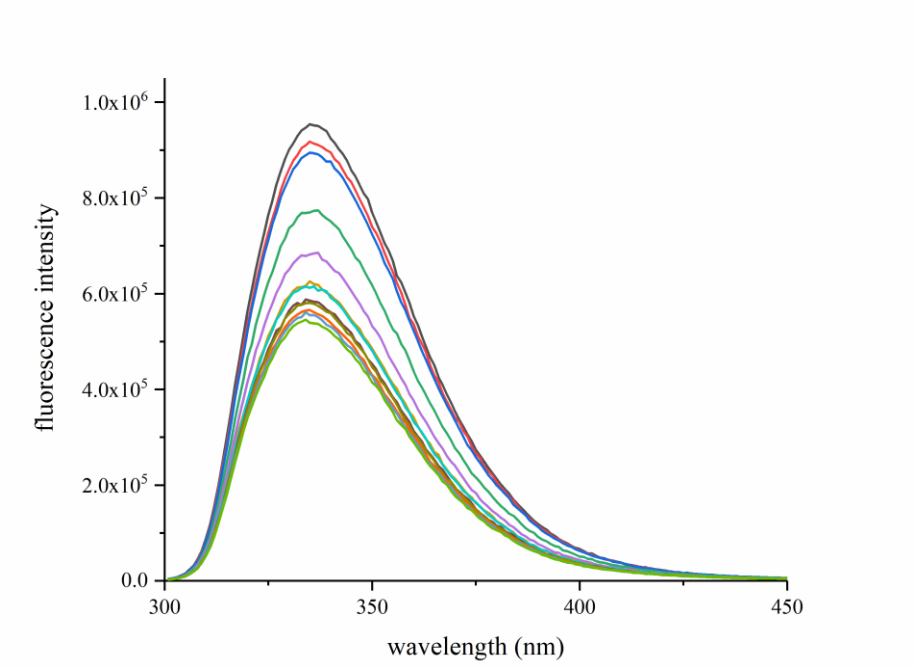


Figure S50. (A) Fluorescence spectra from the titration of **P5C2** (0.1 mM) with **Methylacridinium** (0 - 0.5 mM) in 1 mM PBS buffer (pH 7.4), excited at 291 nm and emission at 334 nm; (B) Non-linear fitting plot of fluorescence intensity *versus* concentration for the direct titration of **Methylacridinium** with Origin. K_a was evaluated as 2.38×10^5 M^{-1}.

(A)



(B)

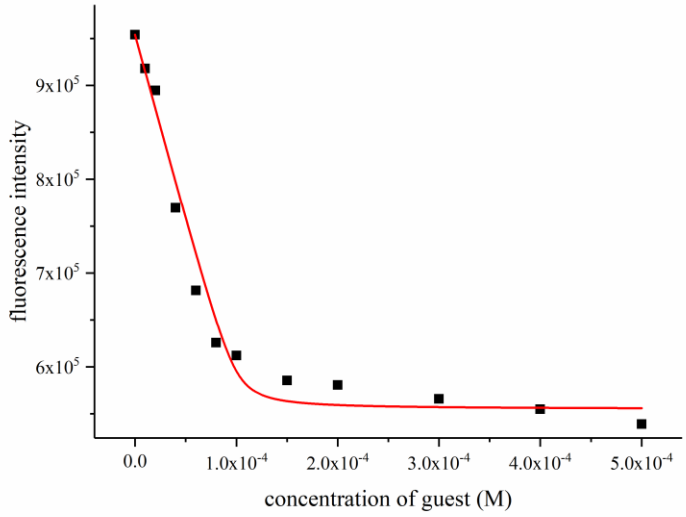


Figure S51. (A) Fluorescence spectra from the titration of **P5C2** (0.1 mM) with **Metformin** (0 - 0.5 mM) in water, excited at 291 nm and emission at 336 nm; (B) Non-linear fitting plot of fluorescence intensity *versus* concentration for the direct titration of **Metformin** with Origin. K_a was evaluated as 8.70×10^5 M^{-1}.

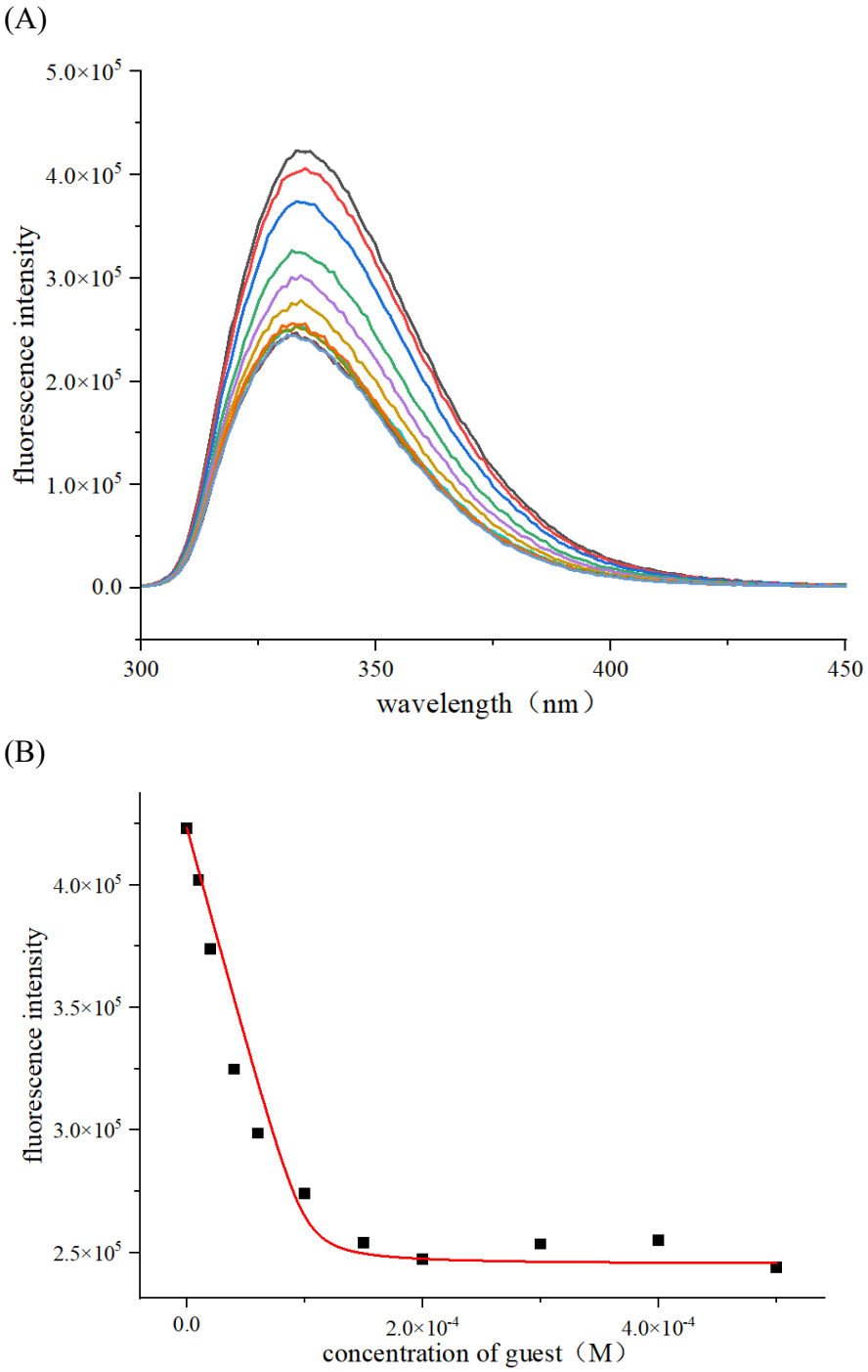
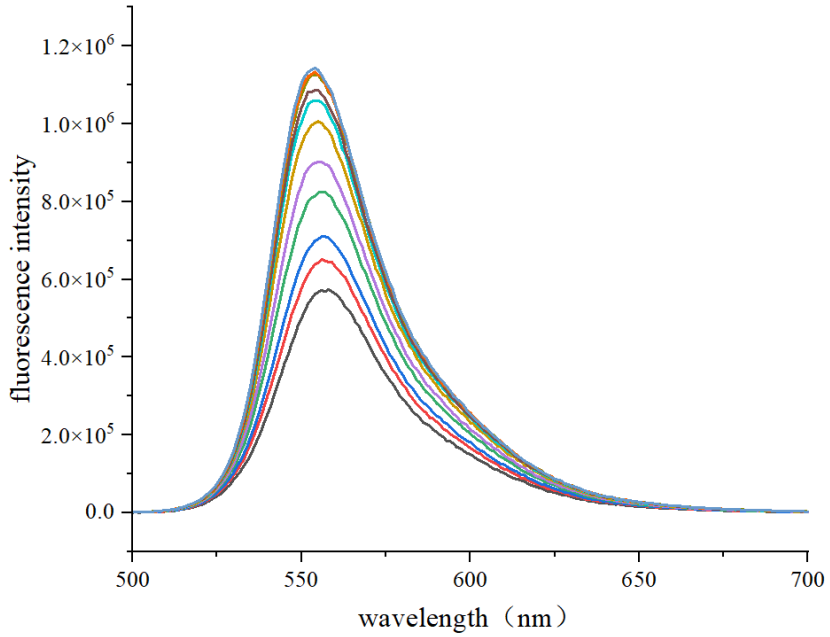


Figure S52. (A) Fluorescence spectra from the titration of **P5C2** (0.1 mM) with **Metformin** (0 - 0.5 mM) in 1 mM PBS buffer (pH 7.4), excited at 291 nm and emission at 333 nm; (B) Non-linear fitting plot of fluorescence intensity *versus* concentration for the direct titration of **Metformin** with Origin. K_a was evaluated as 7.26×10^5 M^{-1}.

(A)



(B)

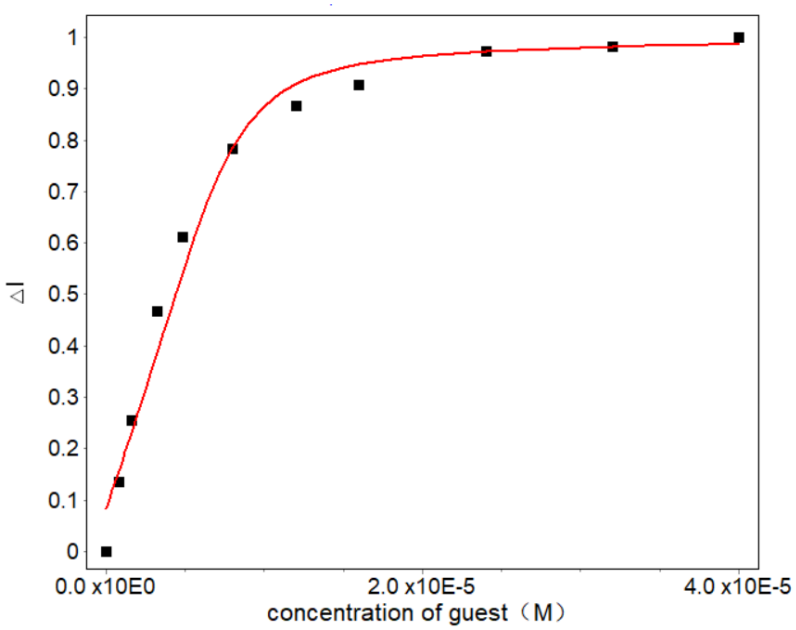
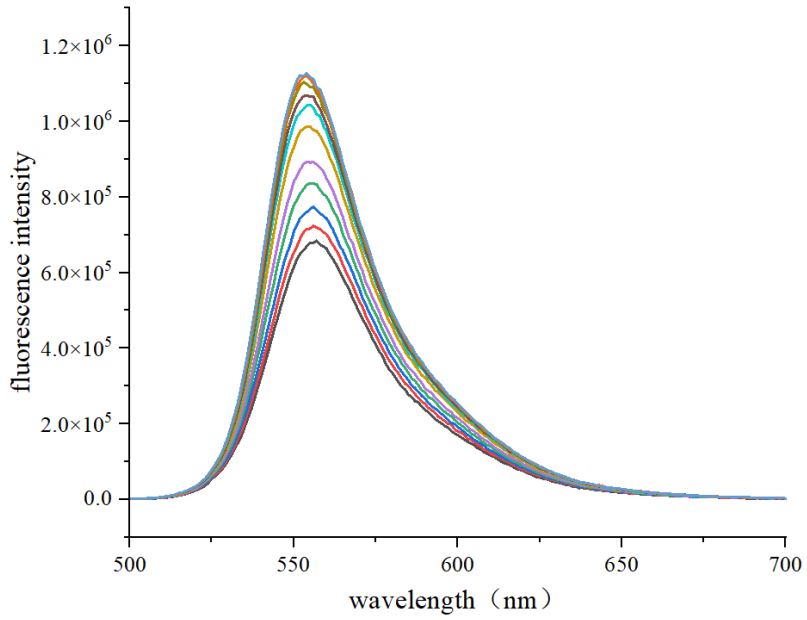


Figure S53. (A) Fluorescence spectra from the displacement titration of **P5C2** (8 μM) and **Rhodamine 6G** (12 μM) with **Phenformin** (0 - 40 μM) in water, excited at 526 nm and emission at 558 nm; (B) Non-linear fitting plot of fluorescence intensity *versus* concentration for the displacement titration of **Phenformin** with Scientist. K_a was evaluated as 1.04×10^7 M^{-1}.

(A)



(B)

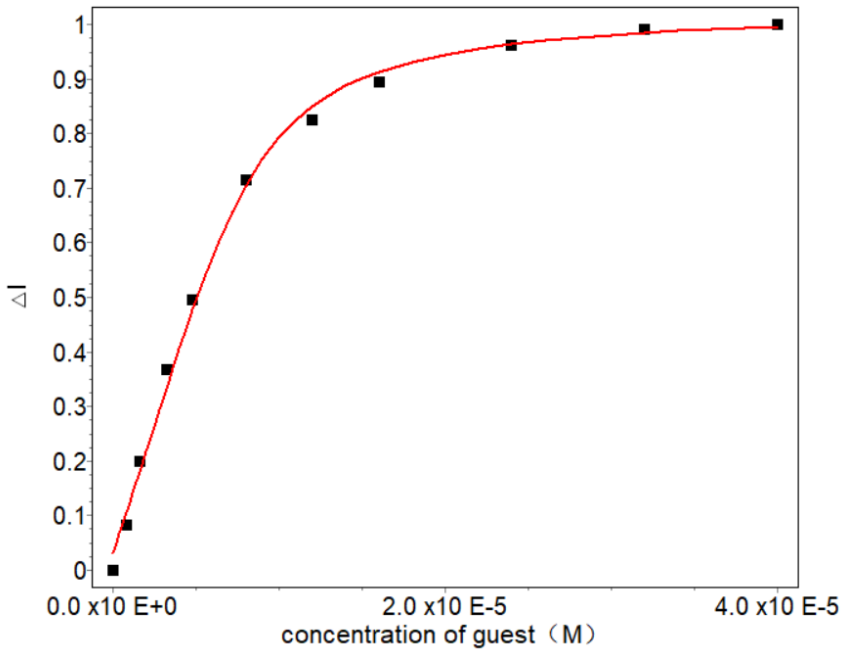
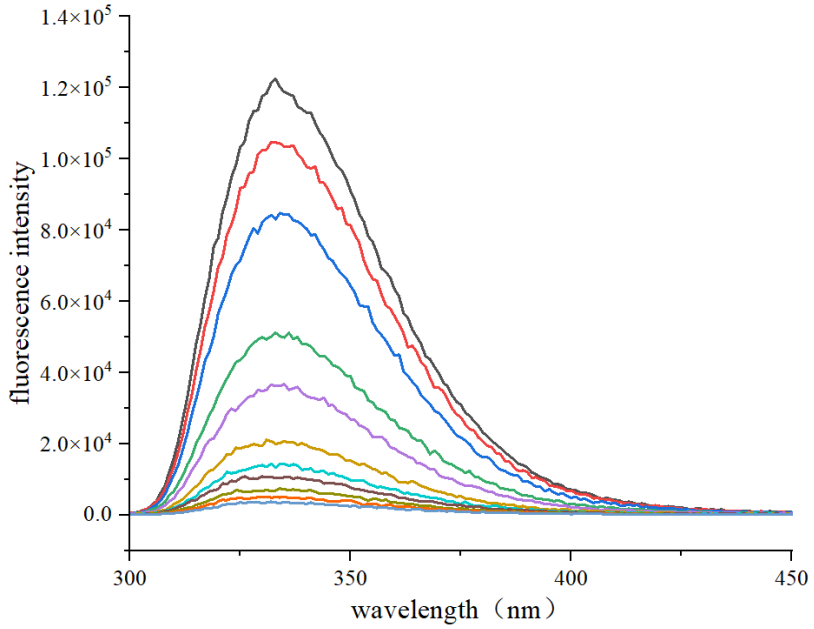


Figure S54. (A) Fluorescence spectra from the displacement titration of **P5C2** (8 μM) and **Rhodamine 6G** (12 μM) with **Phenformin** (0 - 40 μM) in 1 mM PBS buffer (pH 7.4), excited at 526 nm and emission at 558 nm; (B) Non-linear fitting plot of fluorescence intensity *versus* concentration for the displacement titration of **Phenformin** with Scientist. K_a was evaluated as 3.94×10^6 M^{-1}.

(A)



(B)

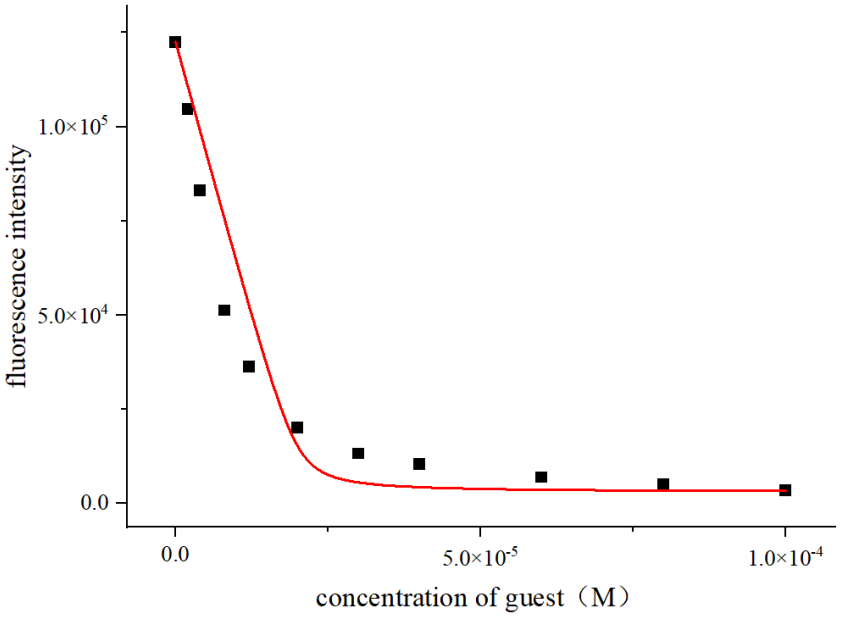
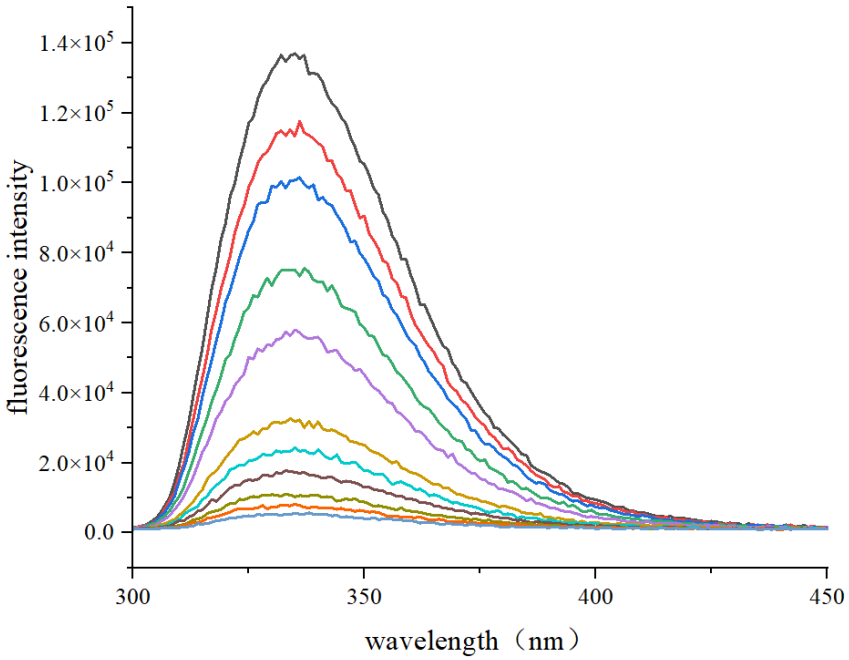


Figure S55. (A) Fluorescence spectra from the titration of **P5C2** (20 μM) with **Famotidine** (0 - 100 μM) in water, excited at 291 nm and emission at 333 nm; (B) Non-linear fitting plot of fluorescence intensity *versus* concentration for the direct titration of **Famotidine** with Origin. K_a was evaluated as 4.26 $\times 10^6$ M^{-1}.

(A)



(B)

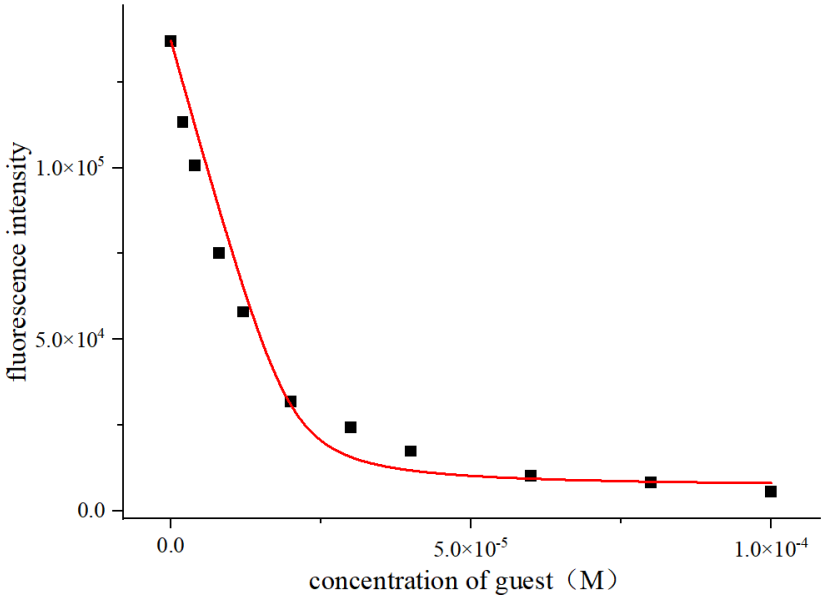
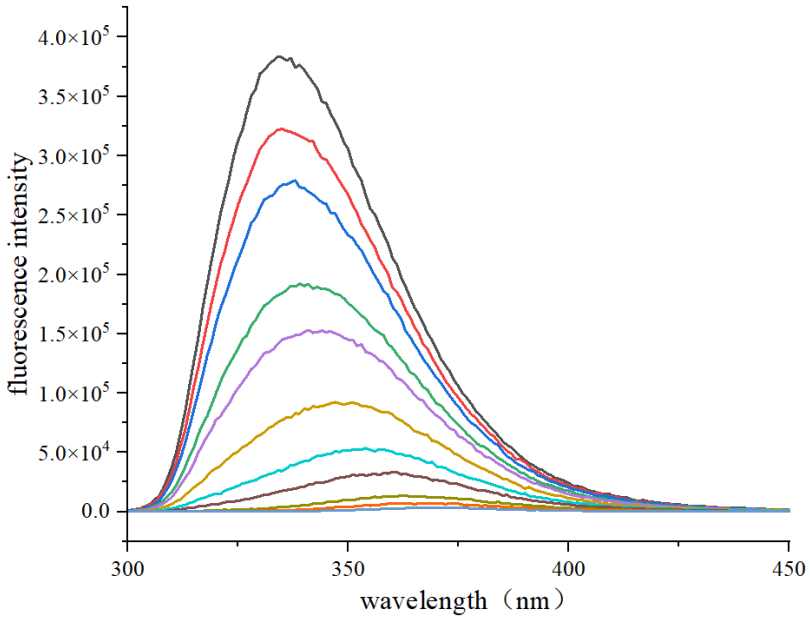


Figure S56. (A) Fluorescence spectra from the titration of **P5C2** (20 μM) with **Famotidine** (0 - 100 μM) in 1 mM PBS buffer (pH 7.4), excited at 291 nm and emission at 333 nm; (B) Non-linear fitting plot of fluorescence intensity *versus* concentration for the direct titration of **Famotidine** with Origin. K_a was evaluated as 1.19×10^6 M^{-1}.

(A)



(B)

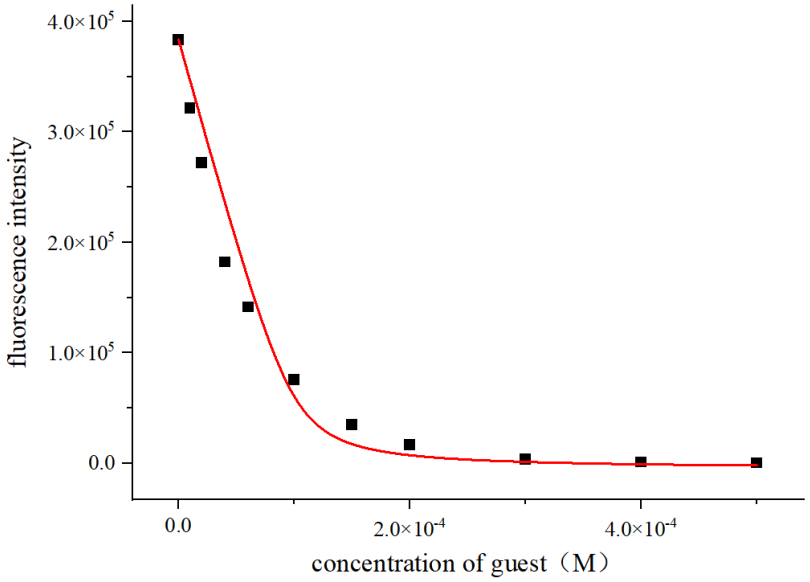
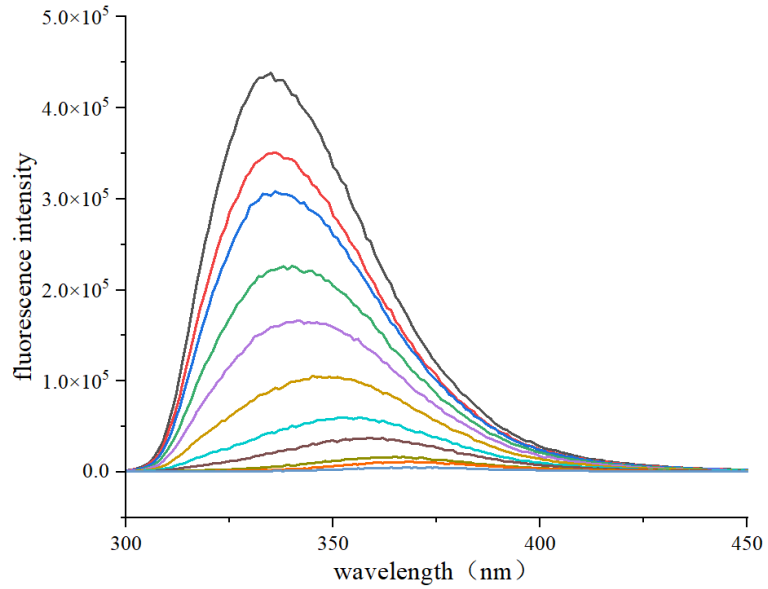


Figure S57. (A) Fluorescence spectra from the titration of **P5C2** (0.1 mM) with **Metronidazole** (0 - 0.5 mM) in water, excited at 291 nm and emission at 334 nm; (B) Non-linear fitting plot of fluorescence intensity *versus* concentration for the direct titration of **Metronidazole** with Origin. K_a was evaluated as 2.88×10^5 M^{-1}.

(A)



(B)

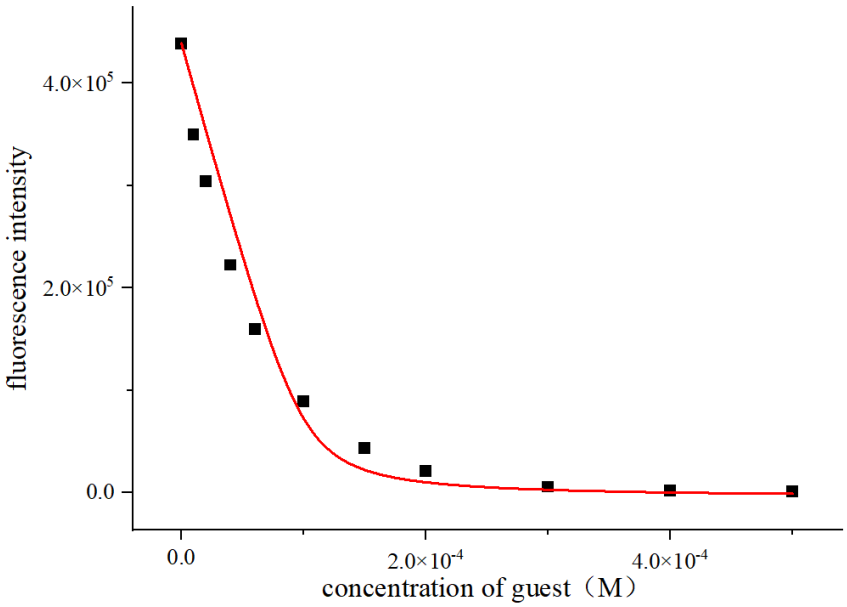
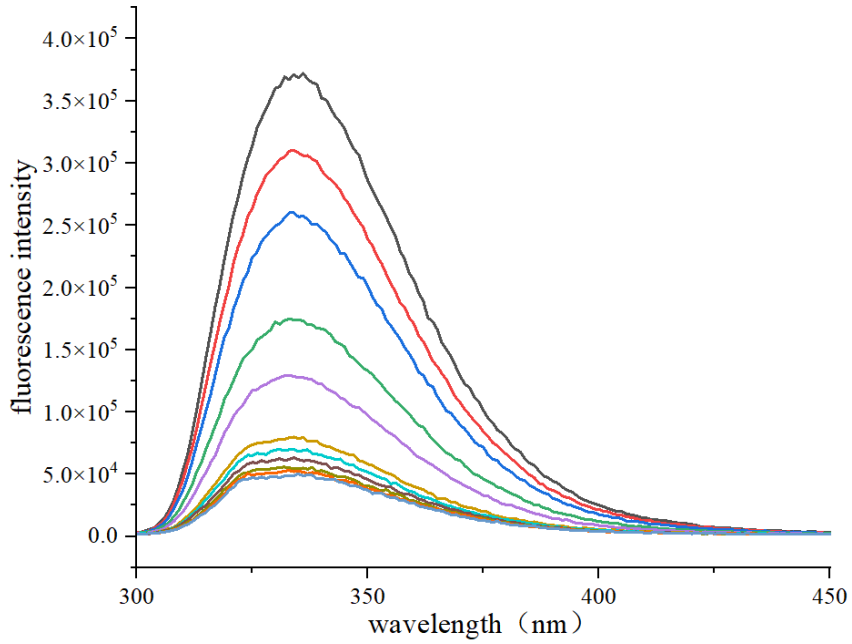


Figure S58. (A) Fluorescence spectra from the titration of **P5C2** (0.1 mM) with **Metronidazole** (0 - 0.5 mM) in 1 mM PBS buffer (pH 7.4), excited at 291 nm and emission at 334 nm; (B) Non-linear fitting plot of fluorescence intensity *versus* concentration for the direct titration of **Metronidazole** with Origin. K_a was evaluated as 2.70×10^5 M^{-1}.

(A)



(B)

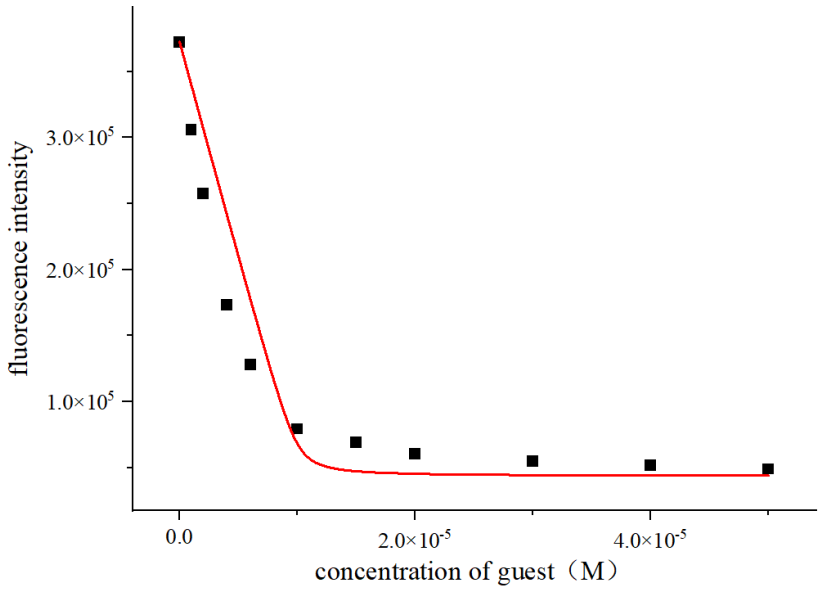
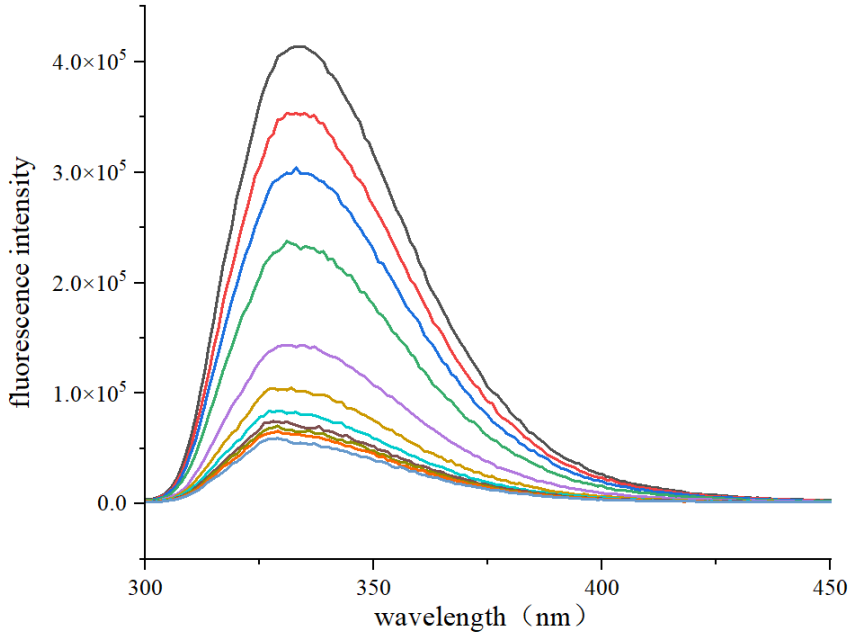


Figure S59. (A) Fluorescence spectra from the titration of **P5C2** (10 μM) with **Robenidine** (0 - 50 μM) in water, excited at 291 nm and emission at 336 nm; (B) Non-linear fitting plot of fluorescence intensity *versus* concentration for the direct titration of **Robenidine** with Origin. K_a was evaluated as 4.41×10^6 M^{-1}.

(A)



(B)

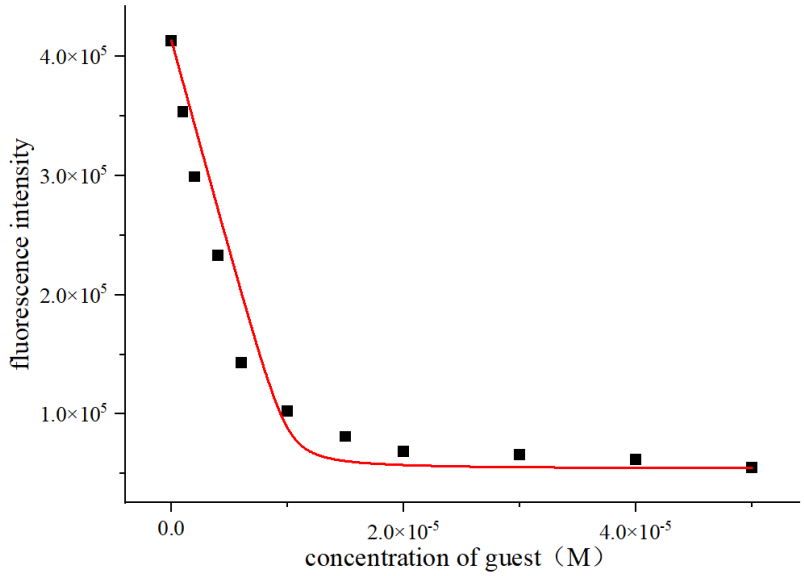
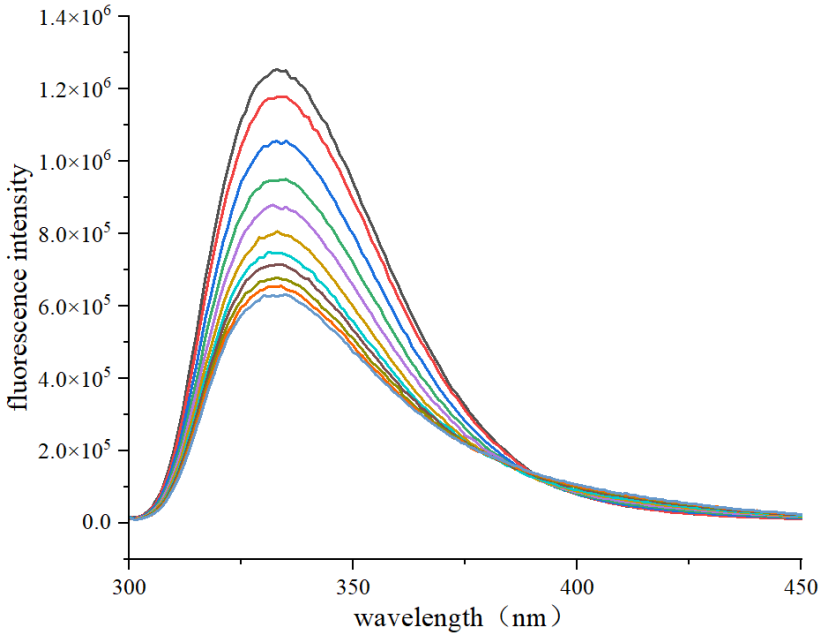


Figure S60. (A) Fluorescence spectra from the titration of **P5C2** (10 μM) with **Robenidine** (0 - 50 μM) in 1 mM PBS buffer (pH 7.4), excited at 291 nm and emission at 335 nm; (B) Non-linear fitting plot of fluorescence intensity *versus* concentration for the direct titration of **Robenidine** with Origin. K_a was evaluated as $1.84 \times 10^6\ M^{-1}$.

(A)



(B)

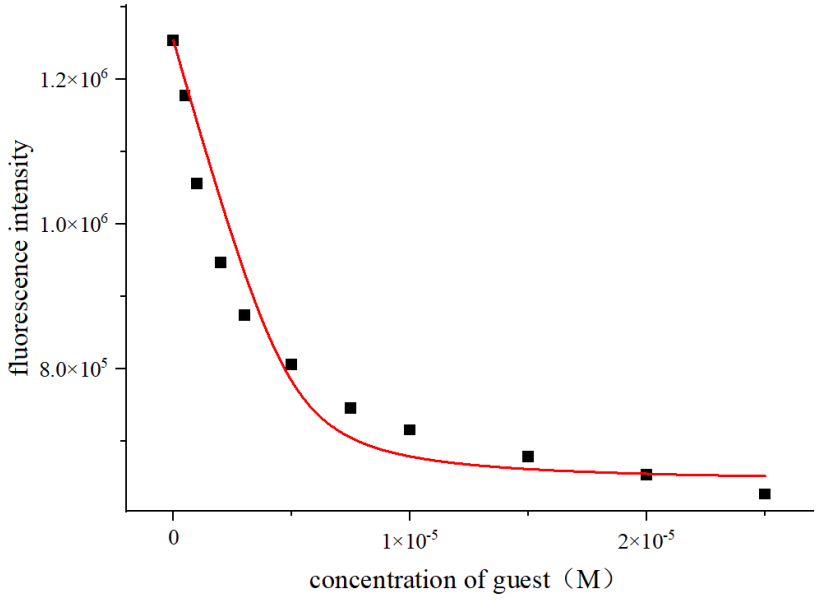
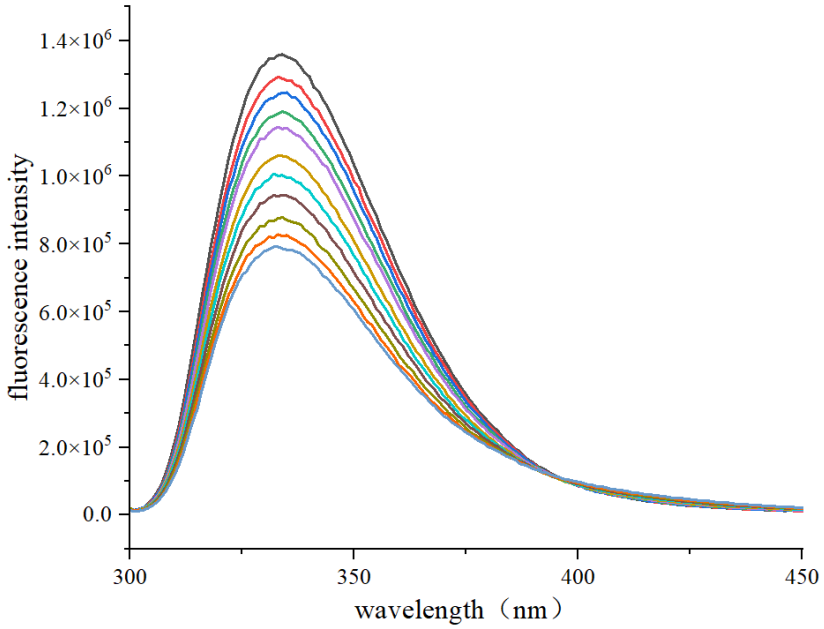


Figure S61. (A) Fluorescence spectra from the titration of **P5C2** (5 μM) with **Enilconazole** (0 - 25 μM) in water, excited at 291 nm and emission at 333 nm; (B) Non-linear fitting plot of fluorescence intensity *versus* concentration for the direct titration of **Enilconazole** with Origin. K_a was evaluated as 2.86×10^5 M^{-1}.

(A)



(B)

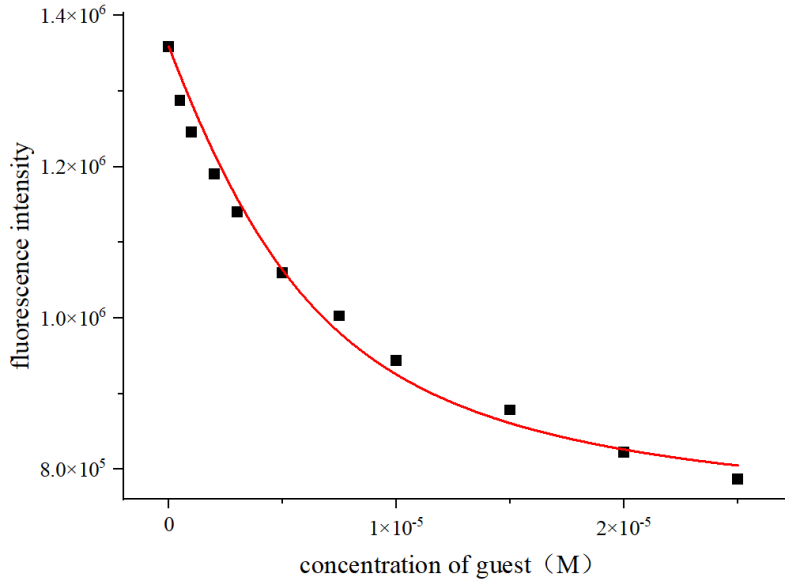
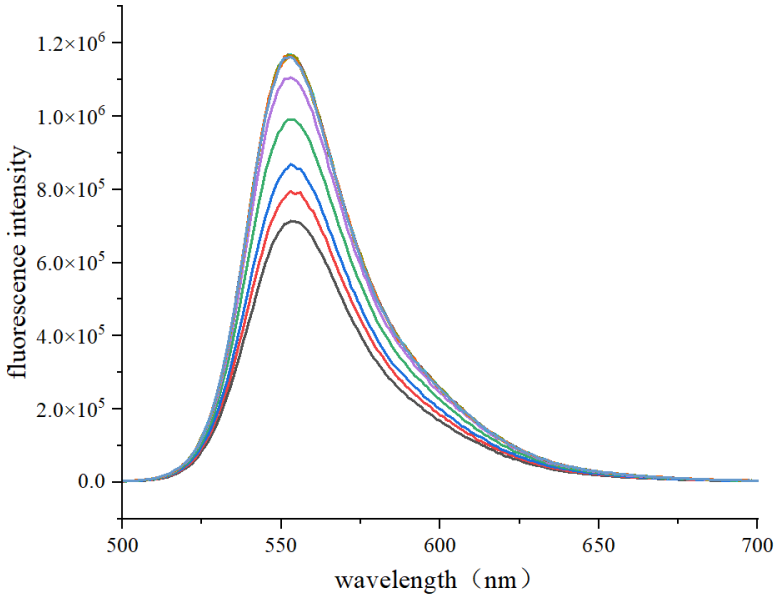


Figure S62. (A) Fluorescence spectra from the titration of **P5C2** (5 μM) with **Enilconazole** (0 - 25 μM) in 1 mM PBS buffer (pH 7.4), excited at 291 nm and emission at 335 nm; (B) Non-linear fitting plot of fluorescence intensity *versus* concentration for the direct titration of **Enilconazole** with Origin. K_a was evaluated as 3.23×10^5 M^{-1}.

(A)



(B)

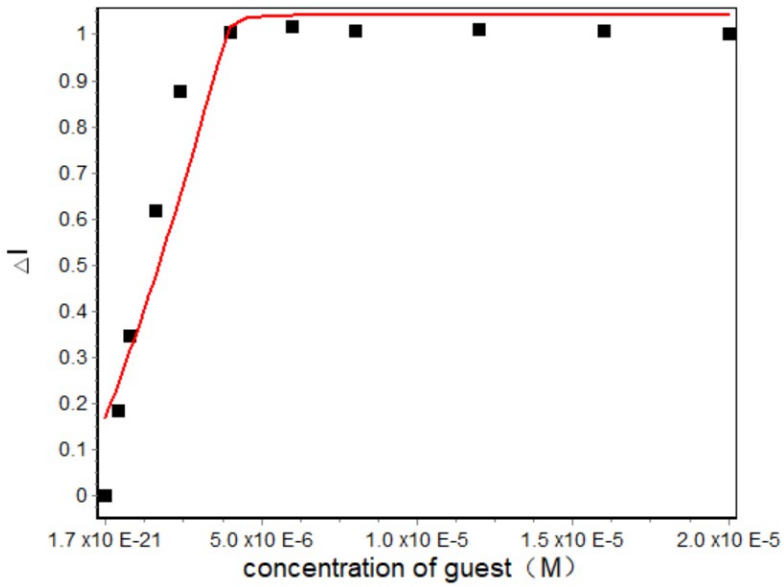
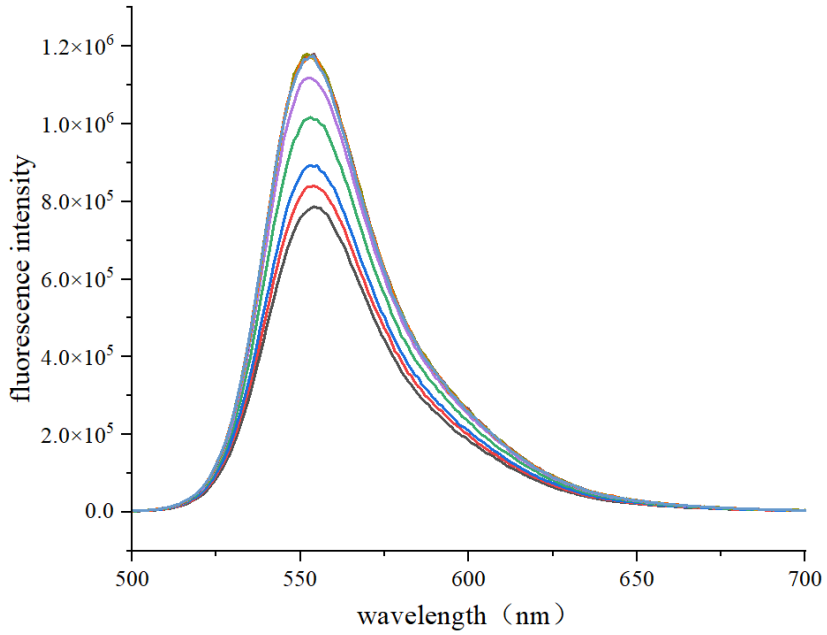


Figure S63. (A) Fluorescence spectra from the displacement titration of **P5C2** (4 μM) and **Rhodamine 6G** (6 μM) with **Chlorhexidine** (0 - 20 μM) in water, excited at 526 nm and emission at 553 nm; (B) Non-linear fitting plot of fluorescence intensity versus concentration for the displacement titration of **Chlorhexidine** with Scientist. K_a was evaluated as 1.10×10^9 M^{-1}.

(A)



(B)

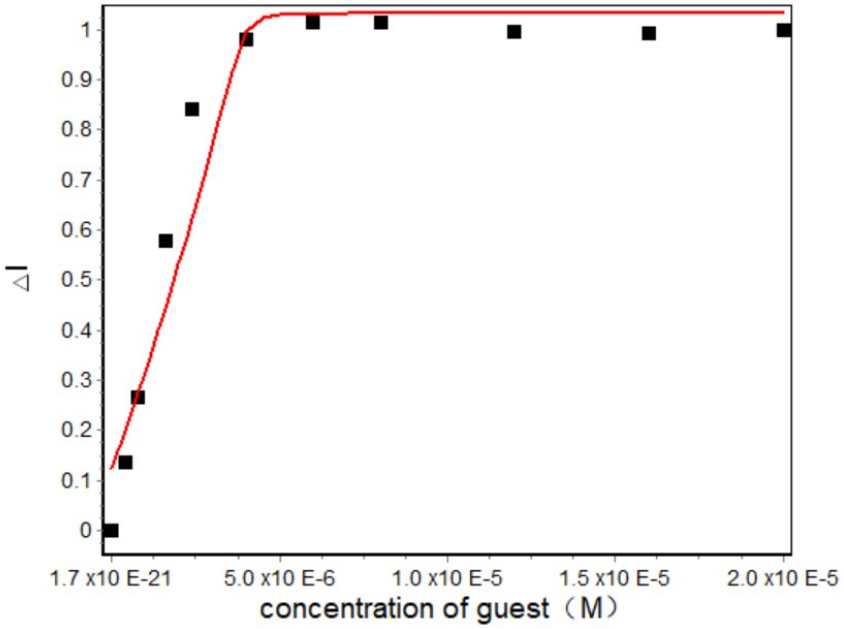


Figure S64. (A) Fluorescence spectra from the displacement titration of **P5C2** (4 μM) and **Rhodamine 6G** (6 μM) with **Chlorhexidine** (0 - 20 μM) in 1 mM PBS buffer (pH 7.4), excited at 526 nm and emission at 554 nm; (B) Non-linear fitting plot of fluorescence intensity versus concentration for the displacement titration of **Chlorhexidine** with Scientist. K_a was evaluated as 5.55×10^8 M^{-1}.

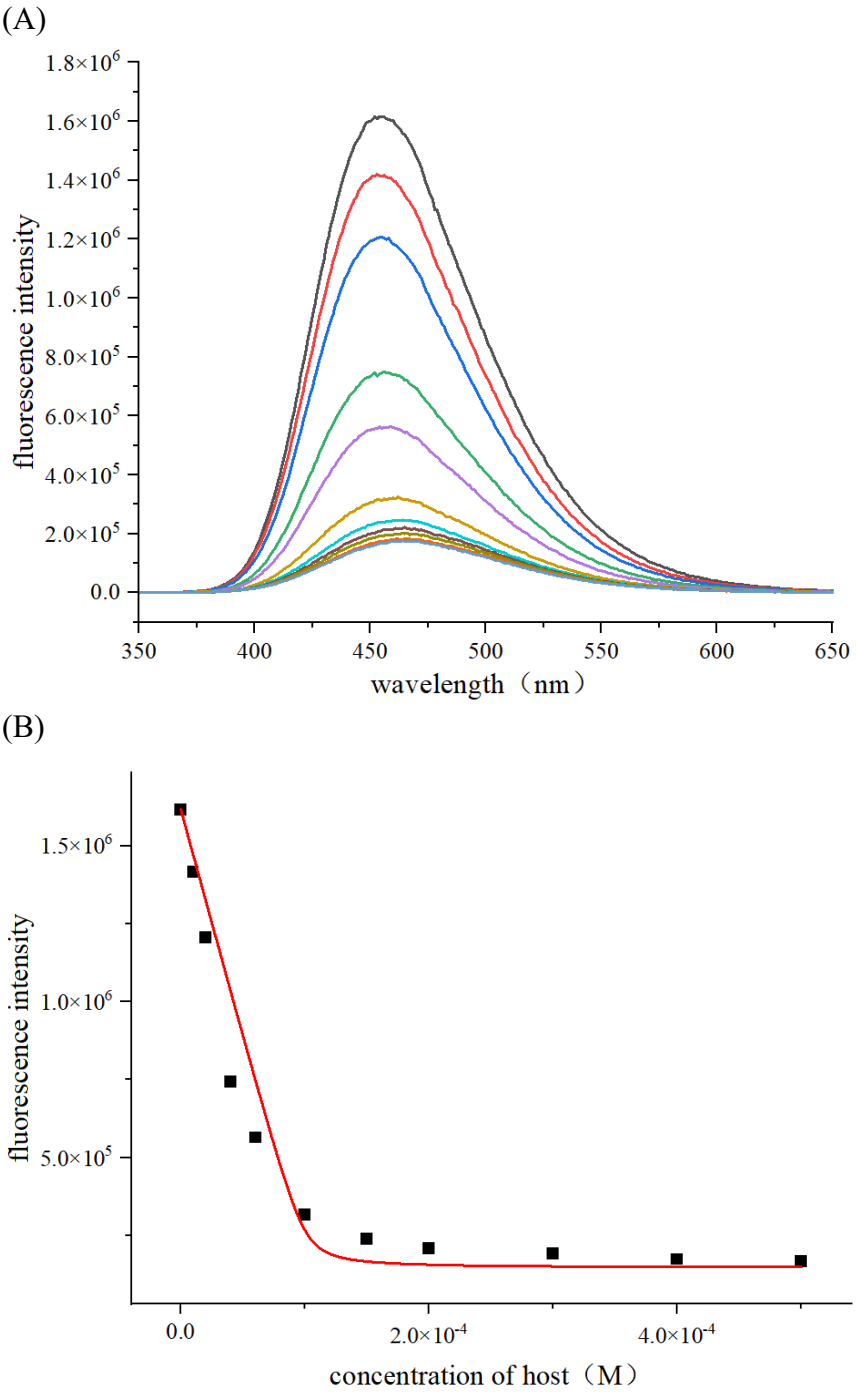
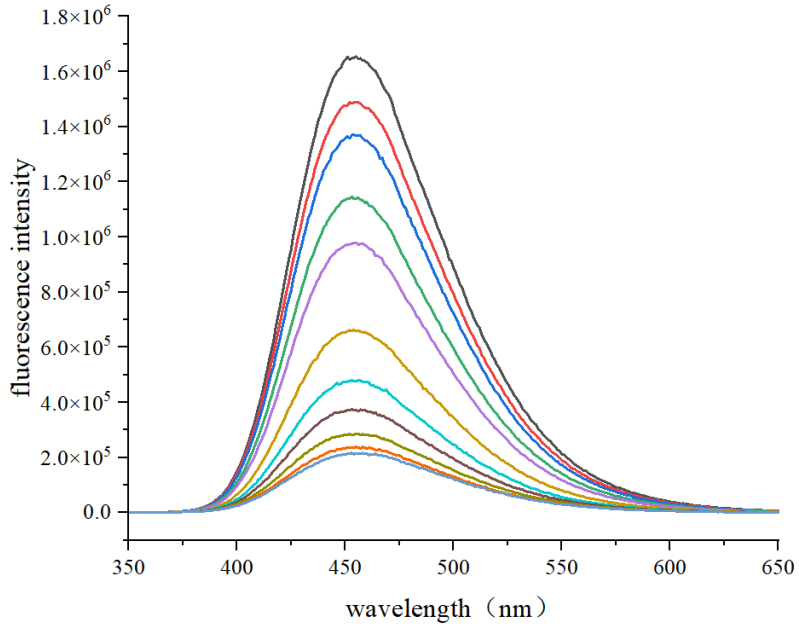


Figure S65. (A) Fluorescence spectra from the titration of **Levofloxacin** (10 μM) with **P5C2** (0 - 50 μM) in water, excited at 332 nm and emission at 454 nm; (B) Non-linear fitting plot of fluorescence intensity *versus* concentration for the direct titration of **Levofloxacin** with Origin. K_a was evaluated as 1.35×10^6 M^{-1}.

(A)



(B)

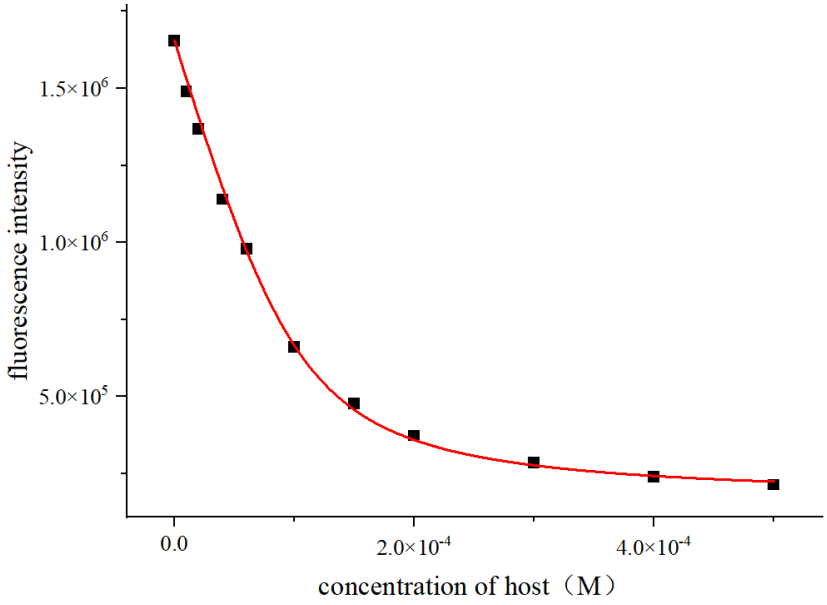
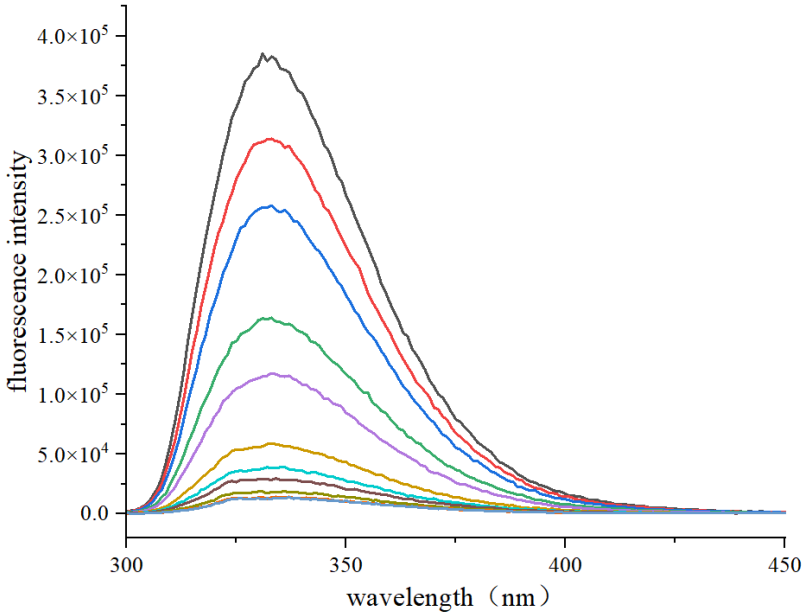


Figure S66. (A) Fluorescence spectra from the titration of **Levofloxacin** (10 μM) with **P5C2** (0 - 50 μM) in 1 mM PBS buffer (pH 7.4), excited at 332 nm and emission at 455 nm; (B) Non-linear fitting plot of fluorescence intensity *versus* concentration for the direct titration of **Levofloxacin** with Origin. K_a was evaluated as 2.58×10^4 M^{-1}.

(A)



(B)

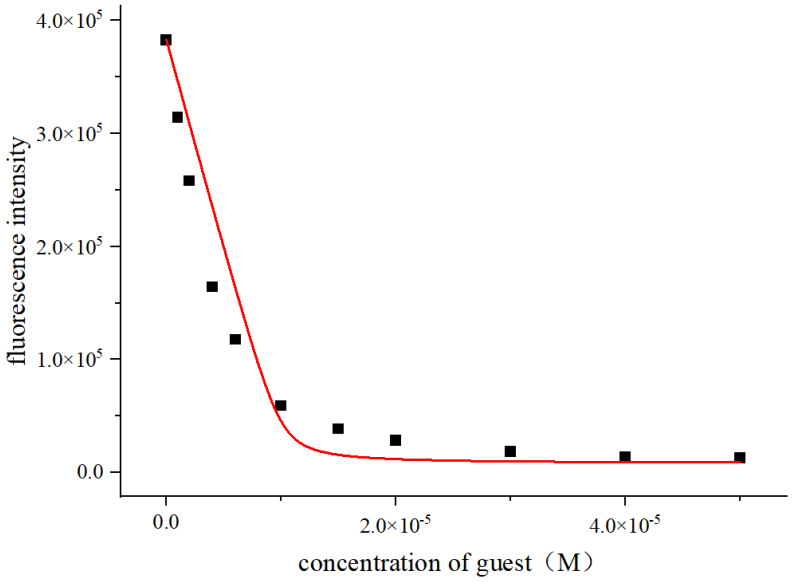
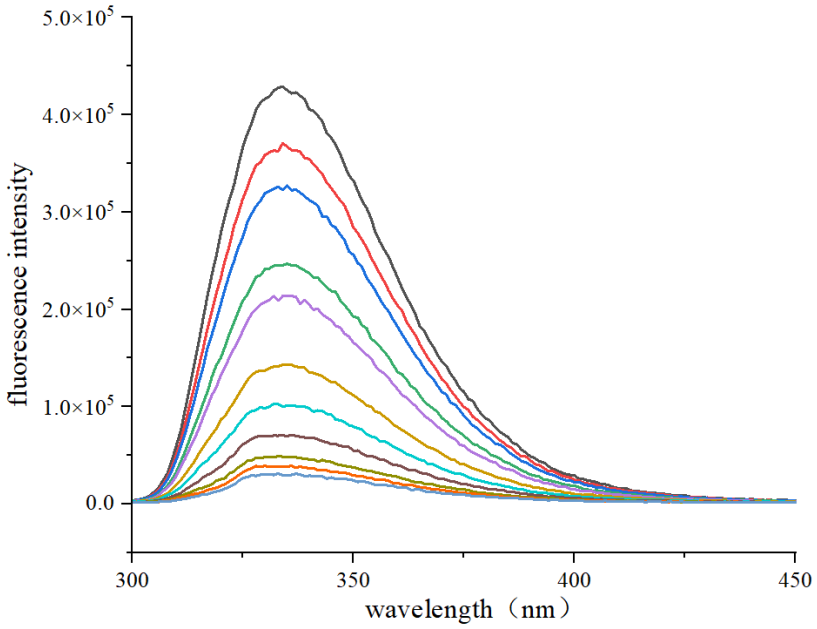


Figure S67. (A) Fluorescence spectra from the titration of **P5C2** (10 μM) with **Tizanidine** (0 - 50 μM) in water, excited at 291 nm and emission at 333 nm; (B) Non-linear fitting plot of fluorescence intensity *versus* concentration for the direct titration of **Tizanidine** with Origin. K_a was evaluated as 8.97×10^6 M^{-1}.

(A)



(B)

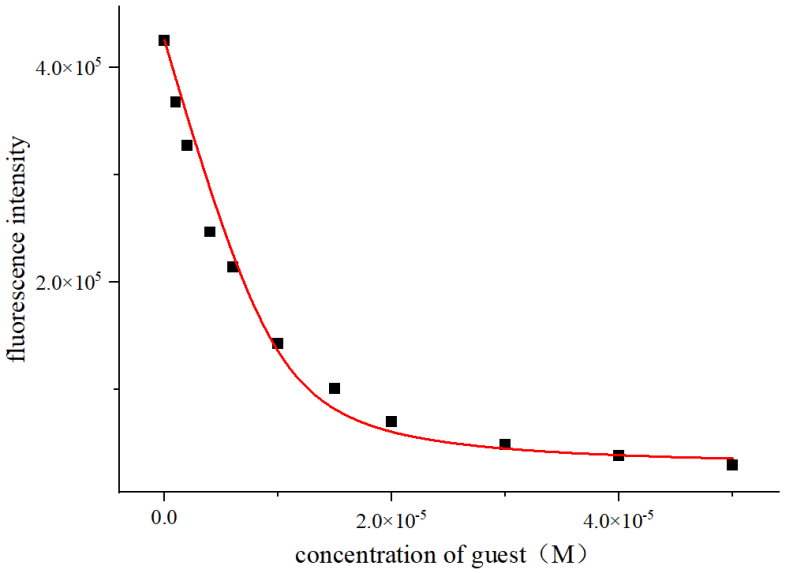
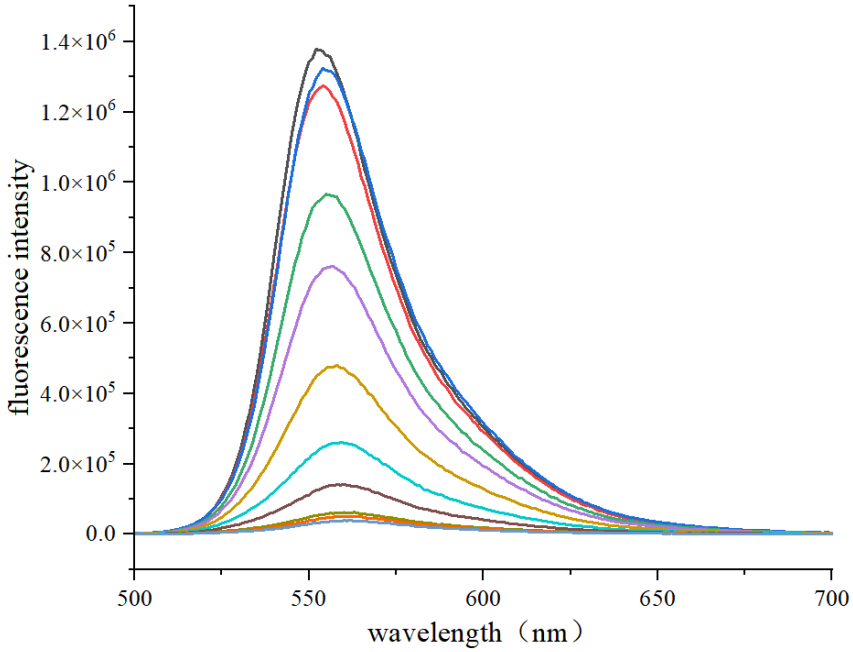


Figure S68. (A) Fluorescence spectra from the titration of **P5C2** (10 μM) with **Tizanidine** (0 - 50 μM) in 1 mM PBS buffer (pH 7.4), excited at 291 nm and emission at 335 nm; (B) Non-linear fitting plot of fluorescence intensity *versus* concentration for the direct titration of **Tizanidine** with Origin. K_a was evaluated as 6.68×10^6 M^{-1}.

(A)



(B)

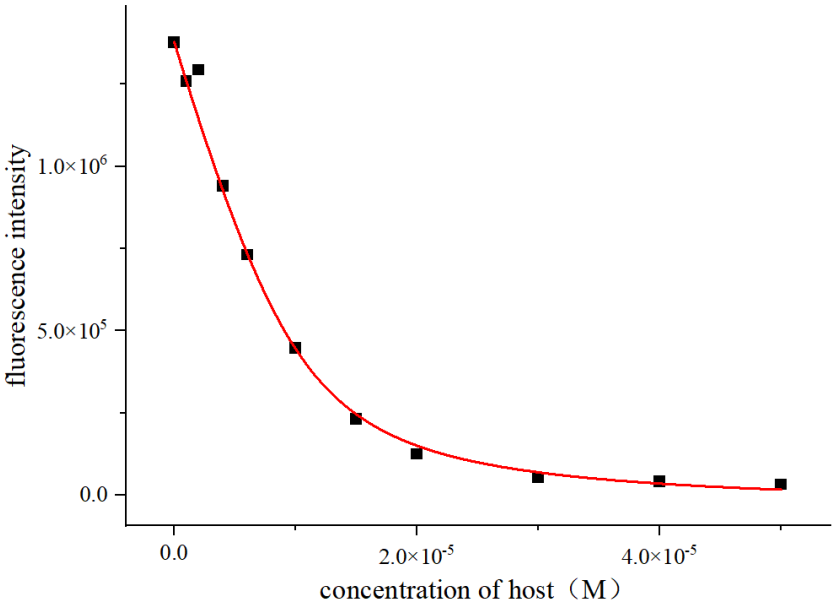
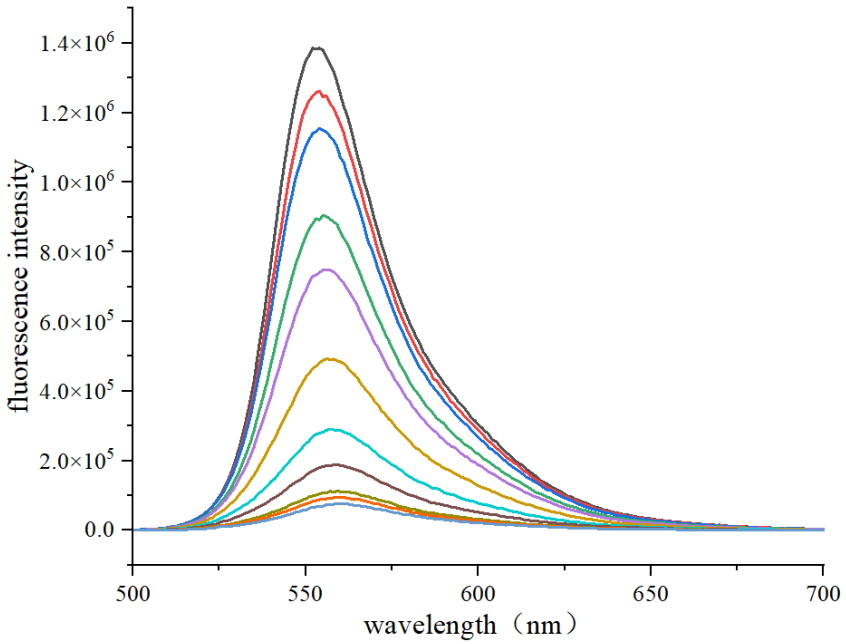


Figure S69. (A) Fluorescence spectra from the titration of **Rhodamine 6G** (10 μM) with **P5C3** (0 - 50 μM) in water, excited at 526 nm and emission at 552 nm; (B) Non-linear fitting plot of fluorescence intensity *versus* concentration for the direct titration of **Rhodamine 6G** with Origin. K_a was evaluated as 5.55×10^5 M^{-1}.

(A)



(B)

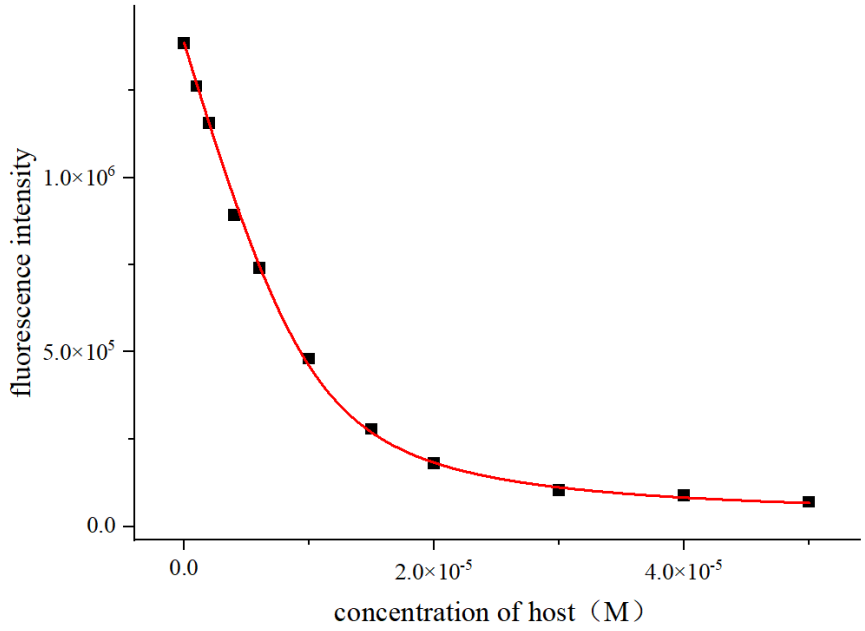


Figure S70. (A) Fluorescence spectra from the titration of **Rhodamine 6G** (10 μM) with **P5C3** (0 - 50 μM) in 1 mM PBS buffer (pH 7.4), excited at 526 nm and emission at 556 nm; (B) Non-linear fitting plot of fluorescence intensity *versus* concentration for the direct titration of **Rhodamine 6G** with Origin. K_a was evaluated as 3.44×10^5 M^{-1}.

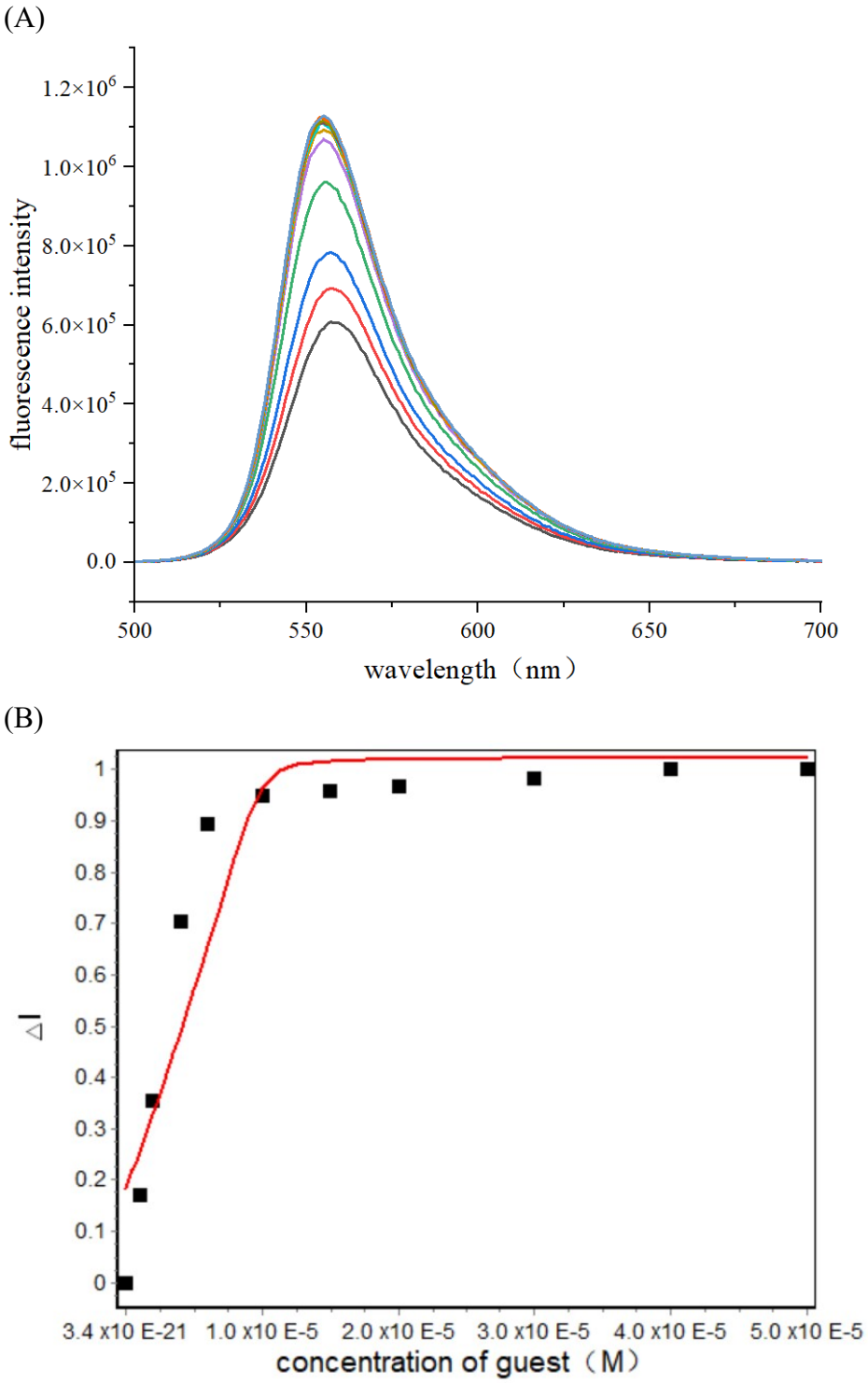
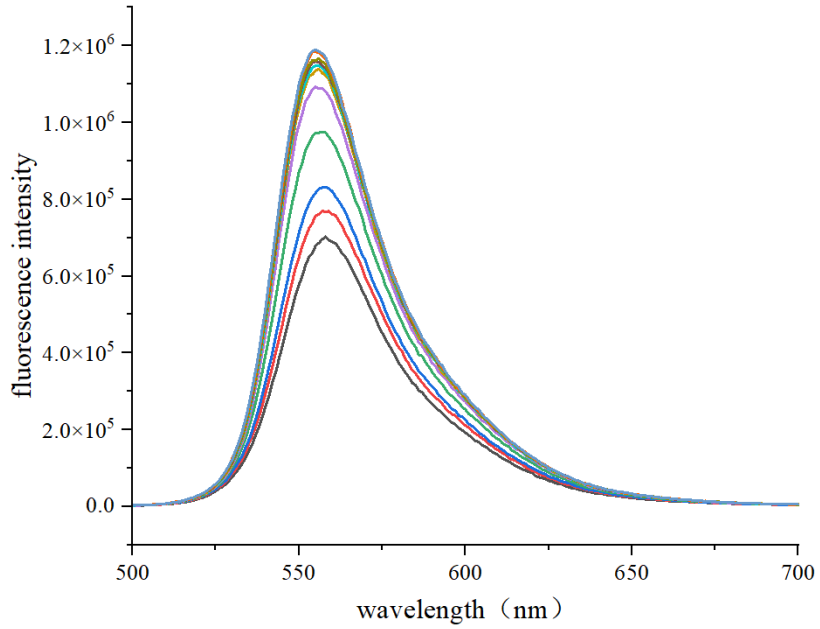


Figure S71. (A) Fluorescence spectra from the displacement titration of **P5C3** (10 μM) and **Rhodamine 6G** (15 μM) with **Methylviologen** (0 - 50 μM) in water, excited at 526 nm and emission at 559 nm; (B) Non-linear fitting plot of fluorescence intensity versus concentration for the displacement titration of **Methylviologen** with Scientist. K_a was evaluated as 2.20×10^8 M^{-1}.

(A)



(B)

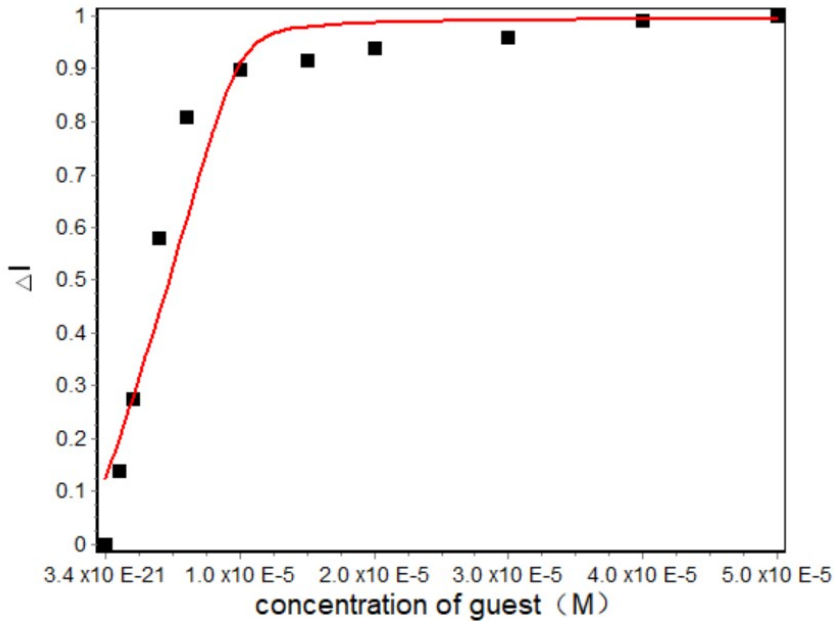
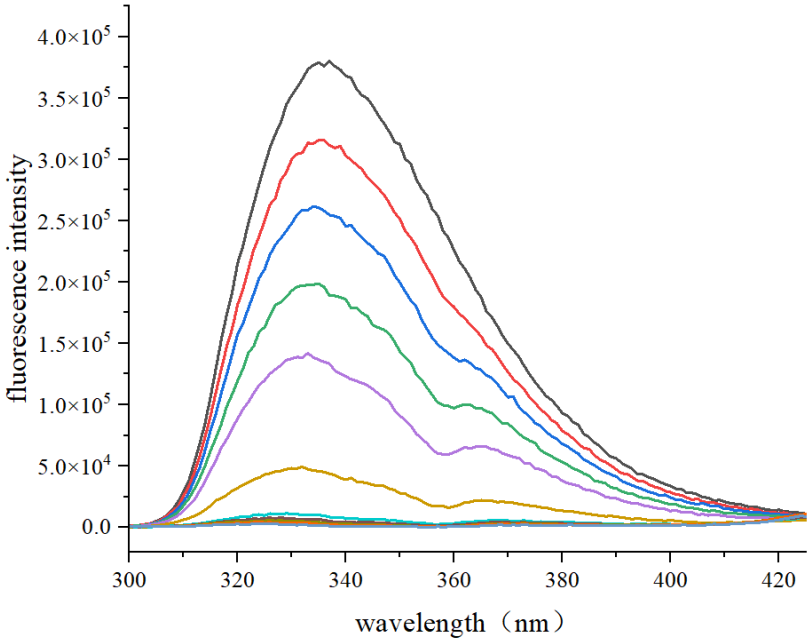


Figure S72. (A) Fluorescence spectra from the displacement titration of **P5C3** (10 μM) and **Rhodamine 6G** (15 μM) with **Methylviologen** (0 - 50 μM) in 1 mM PBS buffer (pH 7.4), excited at 526 nm and emission at 558 nm; (B) Non-linear fitting plot of fluorescence intensity versus concentration for the displacement titration of **Methylviologen** with Scientist. K_a was evaluated as 1.26×10^8 M^{-1}.

(A)



(B)

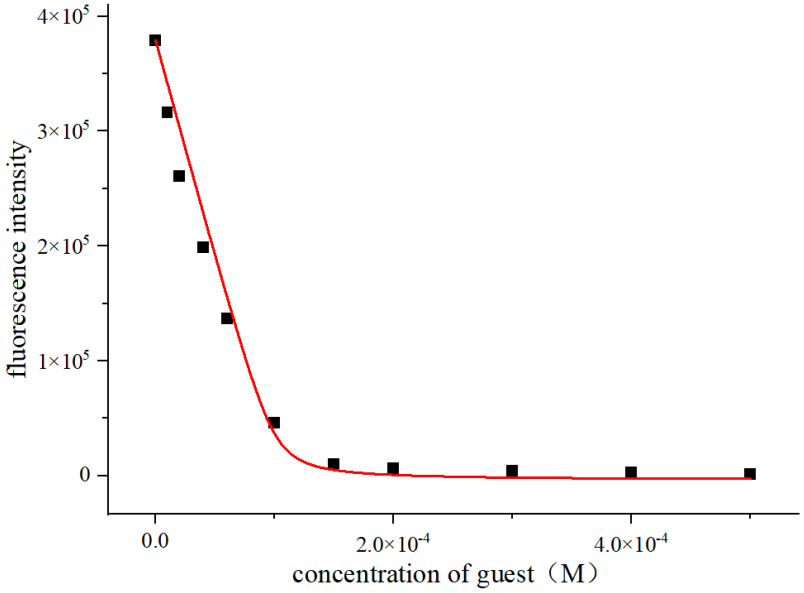
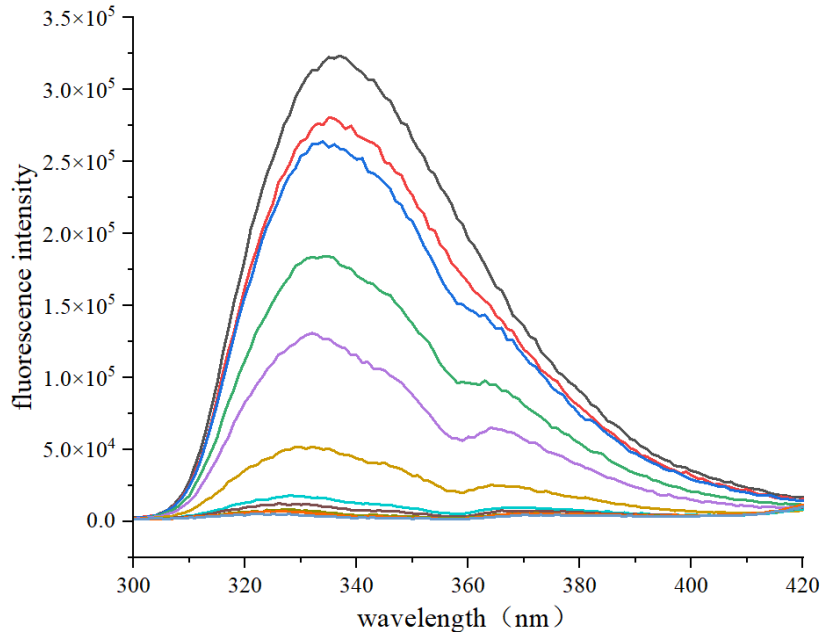


Figure S73. (A) Fluorescence spectra from the titration of **P5C3** (0.1 mM) with **Methylacridinium** (0 - 0.5 mM) in water, excited at 293 nm and emission at 335 nm; (B) Non-linear fitting plot of fluorescence intensity *versus* concentration for the direct titration of **Methylacridinium** with Origin. K_a was evaluated as 7.93×10^5 M^{-1}.

(A)



(B)

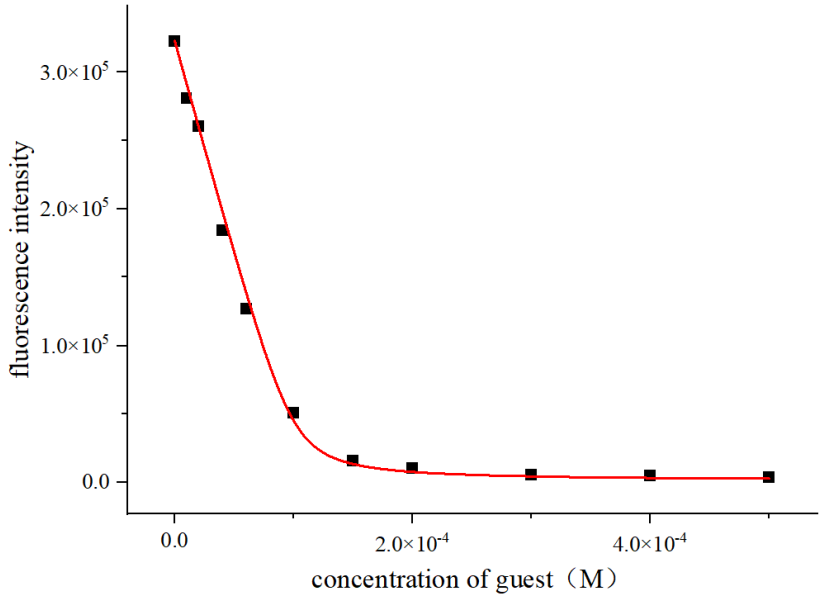


Figure S74. (A) Fluorescence spectra from the titration of **P5C3** (0.1 mM) with **Methylacridinium** (0 - 0.5 mM) in 1 mM PBS buffer (pH 7.4), excited at 293 nm and emission at 335 nm; (B) Non-linear fitting plot of fluorescence intensity *versus* concentration for the direct titration of **Methylacridinium** with Origin. K_a was evaluated as 4.60×10^5 M^{-1}.

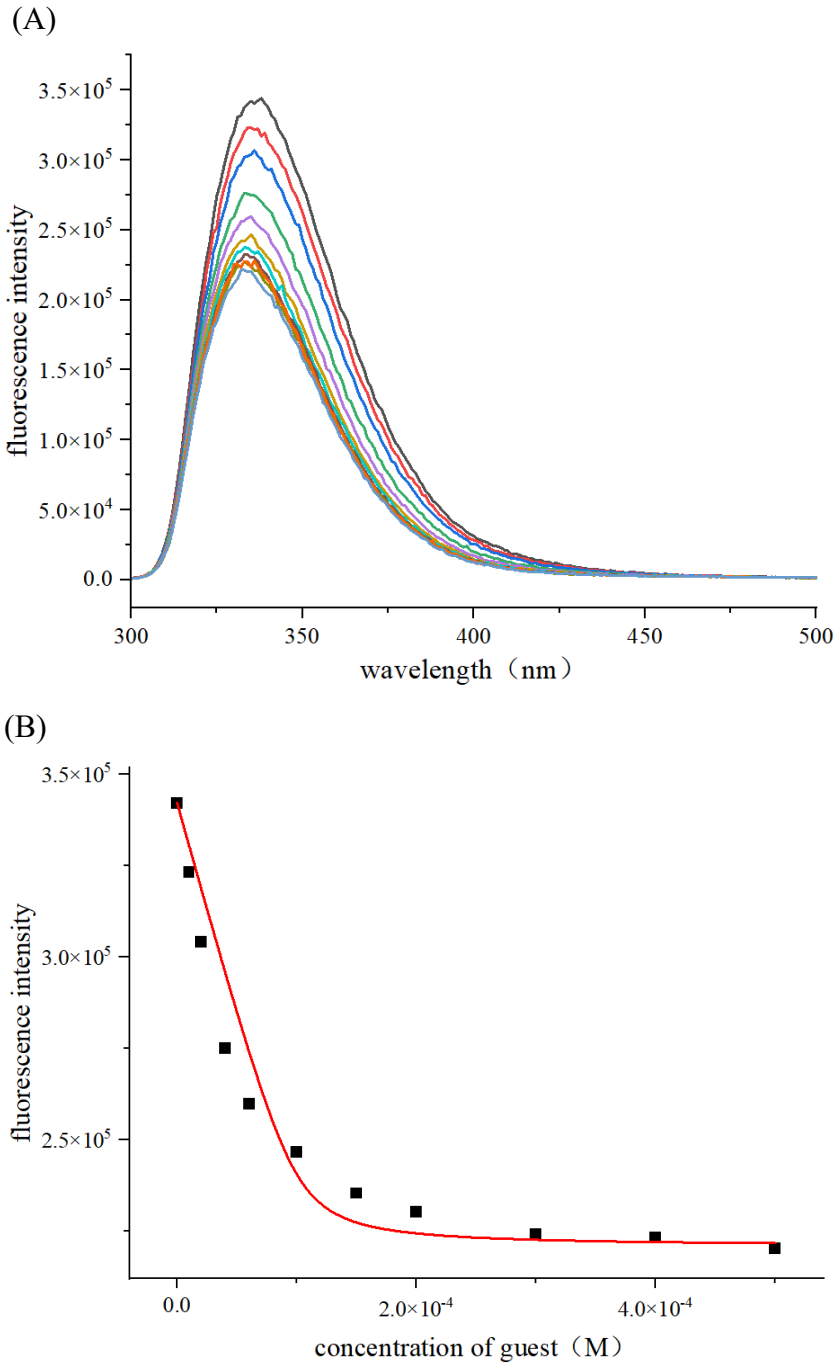
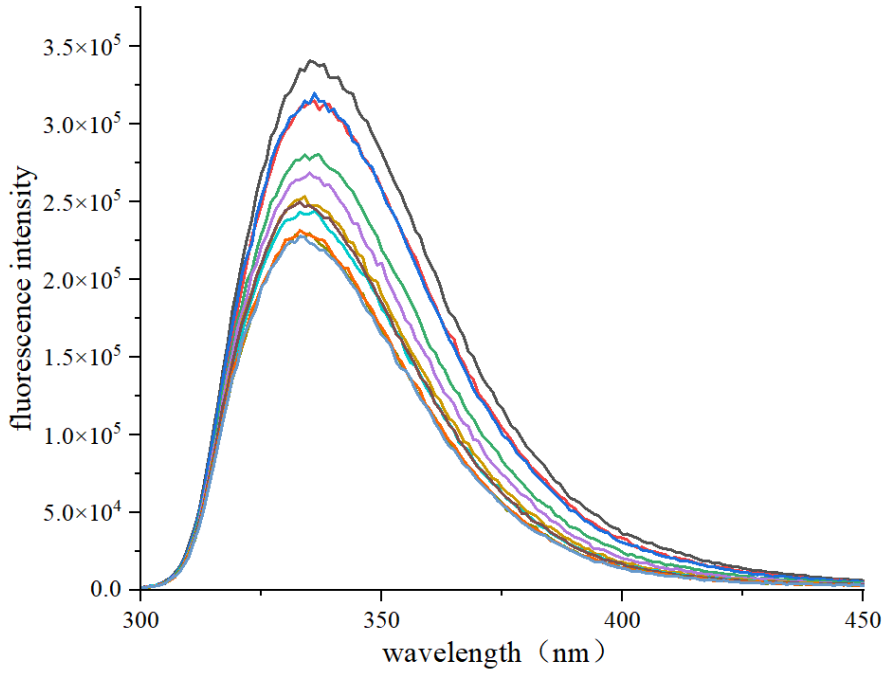


Figure S75. (A) Fluorescence spectra from the titration of **P5C3** (0.1 mM) with **Metformin** (0 - 0.5 mM) in water, excited at 293 nm and emission at 335 nm; (B) Non-linear fitting plot of fluorescence intensity *versus* concentration for the direct titration of **Metformin** with Origin. K_a was evaluated as 3.31×10^5 M^{-1}.

(A)



(B)

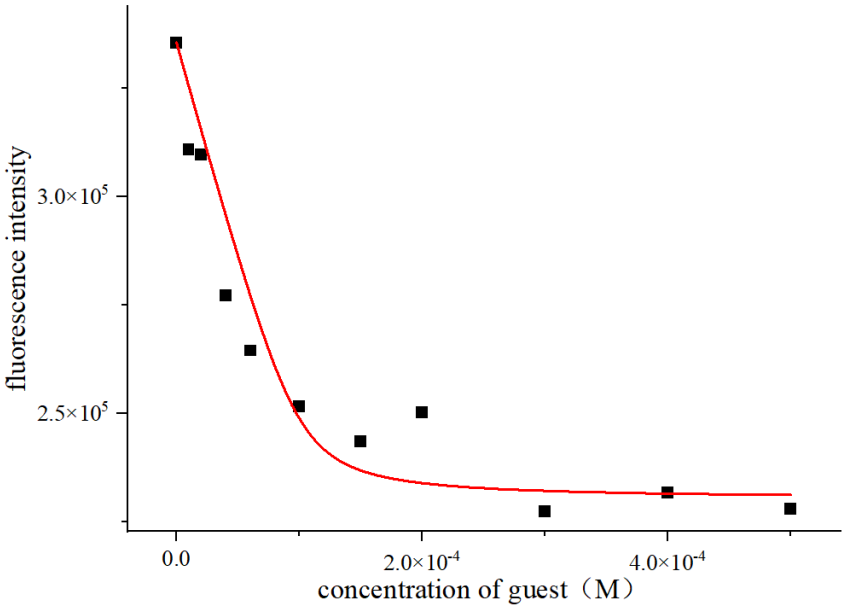
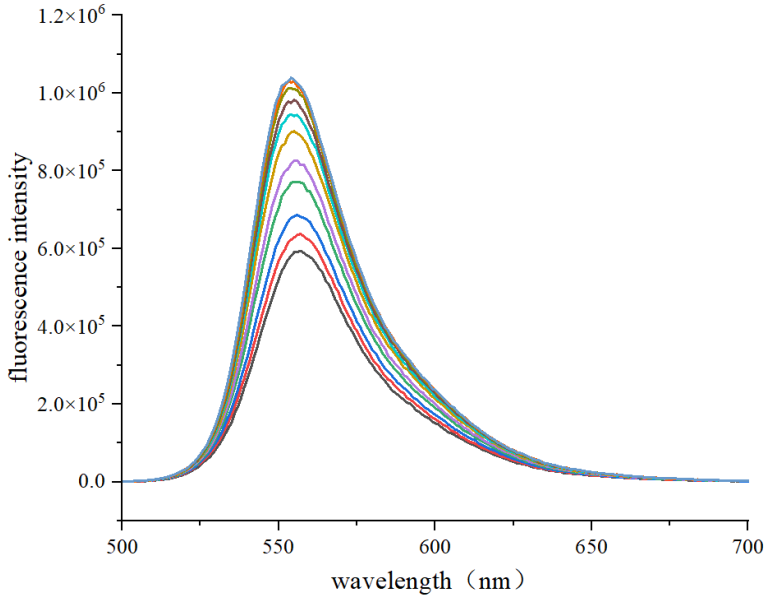


Figure S76. (A) Fluorescence spectra from the titration of **P5C3** (0.1 mM) with **Metformin** (0 - 0.5 mM) in 1 mM PBS buffer (pH 7.4), excited at 291 nm and emission at 333 nm; (B) Non-linear fitting plot of fluorescence intensity *versus* concentration for the direct titration of **Metformin** with Origin. K_a was evaluated as 2.63×10^5 M^{-1}.

(A)



(B)

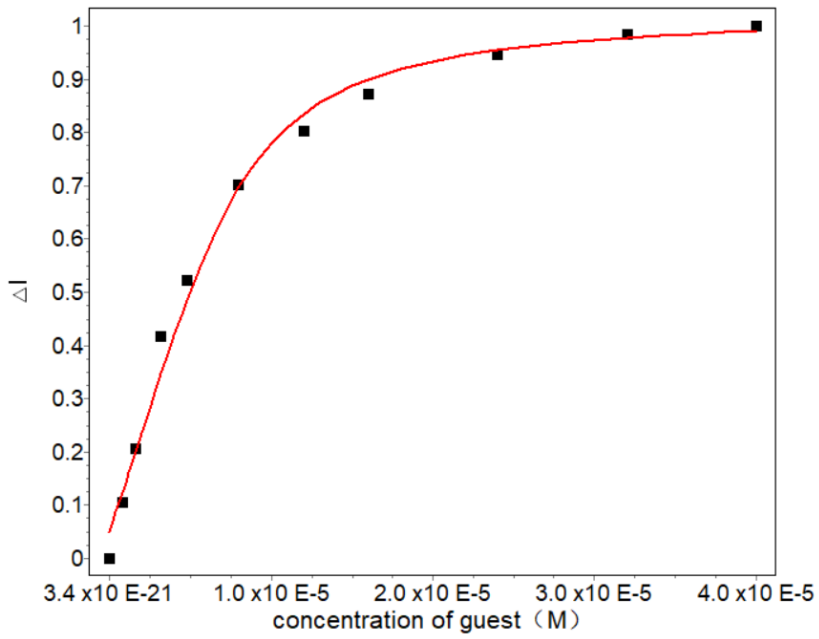
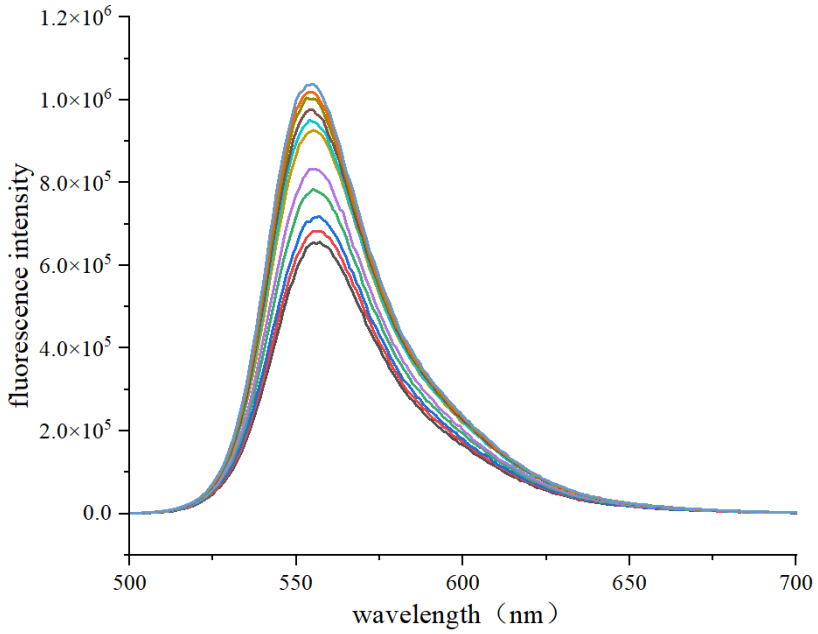


Figure S77. (A) Fluorescence spectra from the displacement titration of **P5C3** (8 μM) and **Rhodamine 6G** (12 μM) with **Phenformin** (0 - 40 μM) in water, excited at 526 nm and emission at 558 nm; (B) Non-linear fitting plot of fluorescence intensity versus concentration for the displacement titration of **Phenformin** with Scientist. K_a was evaluated as 5.81×10^6 M^{-1}.

(A)



(B)

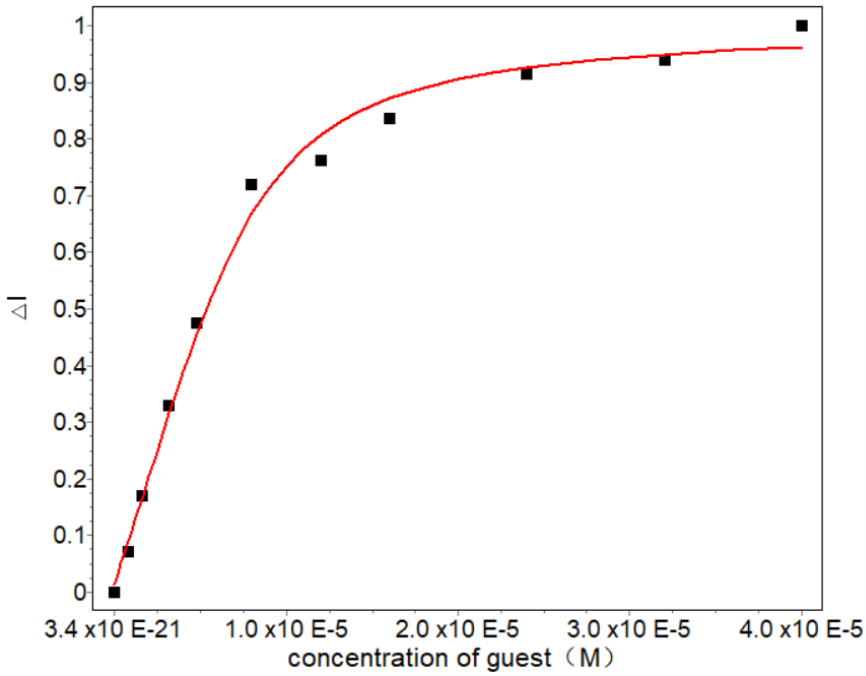
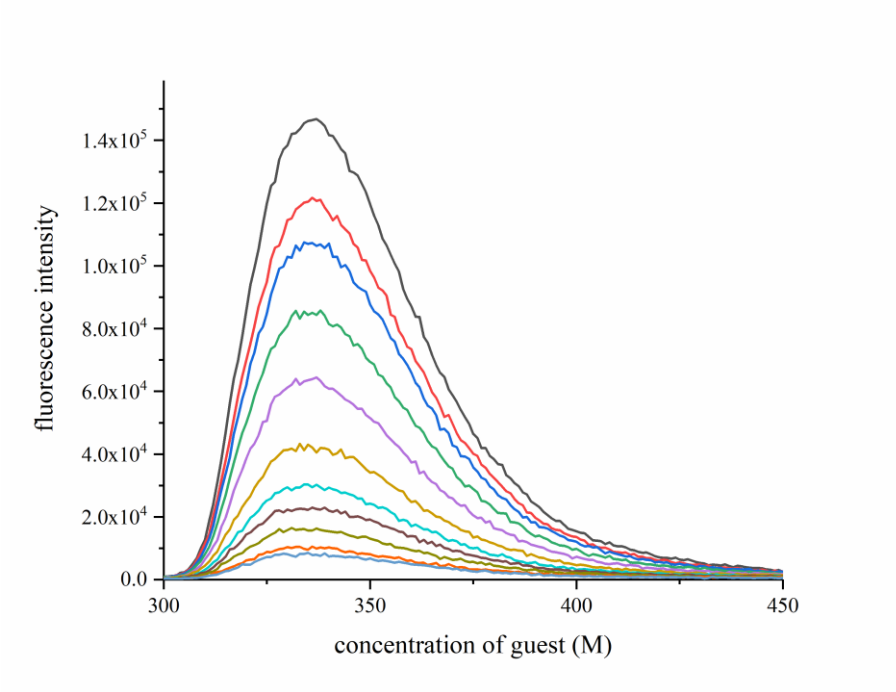


Figure S78. (A) Fluorescence spectra from the displacement titration of **P5C3** (8 μM) and **Rhodamine 6G** (12 μM) with **Phenformin** (0 - 40 μM) in 1 mM PBS buffer (pH 7.4), excited at 526 nm and emission at 558 nm; (B) Non-linear fitting plot of fluorescence intensity versus concentration for the displacement titration of **Phenformin** with Scientist. K_a was evaluated as 2.64×10^6 M^{-1}.

(A)



(B)

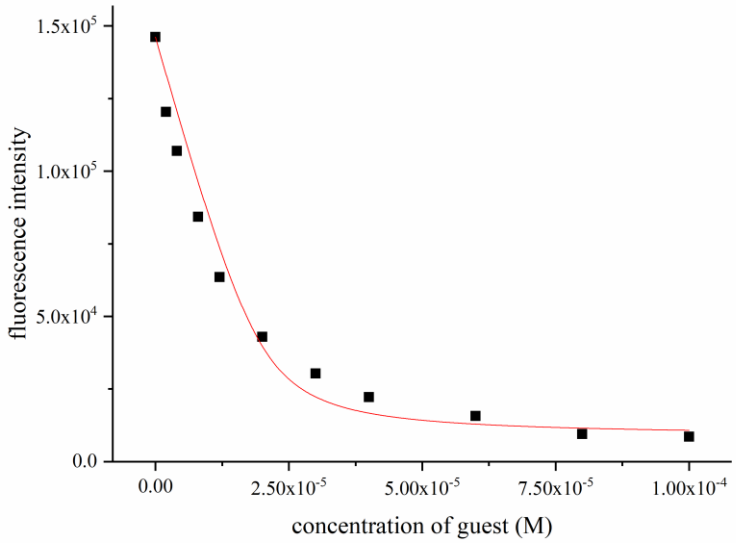
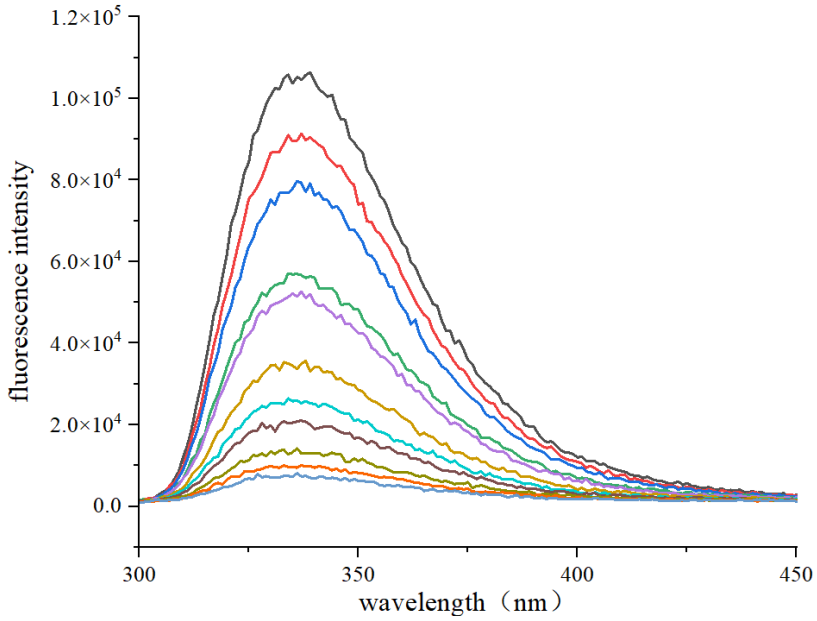


Figure S79. (A) Fluorescence spectra from the titration of **P5C3** (20 μM) with **Famotidine** (0 - 100 μM) in water, excited at 294 nm and emission at 335 nm; (B) Non-linear fitting plot of fluorescence intensity *versus* concentration for the direct titration of **Famotidine** with Origin. K_a was evaluated as 7.51×10^5 M^{-1}.

(A)



(B)

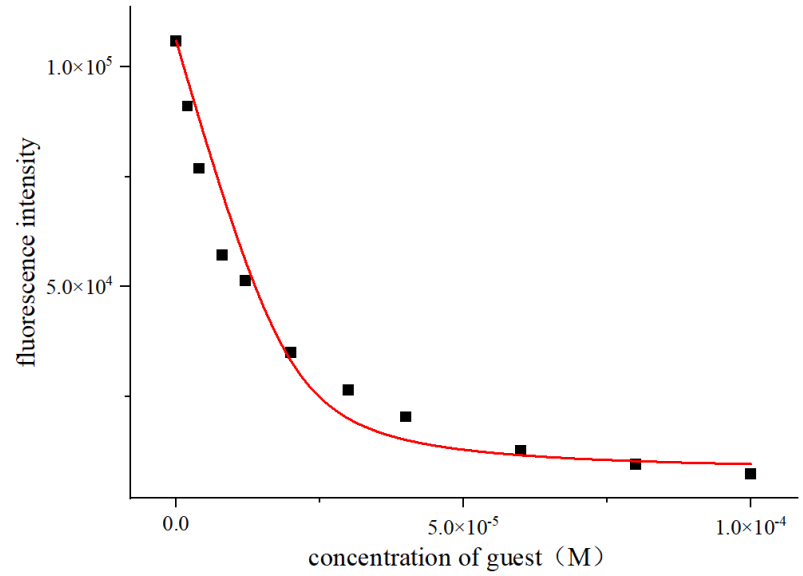
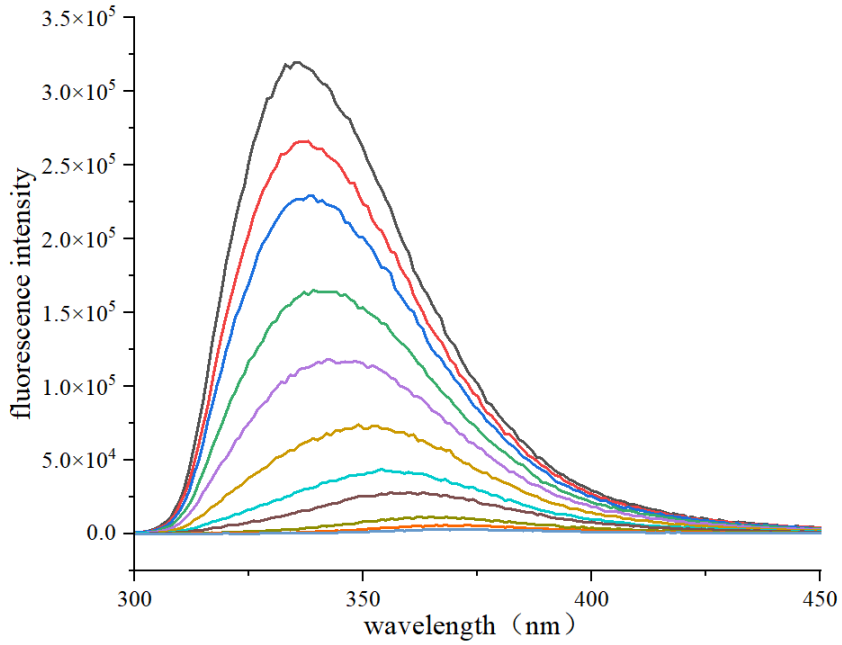


Figure S80. (A) Fluorescence spectra from the titration of **P5C3** (20 μM) with **Famotidine** (0 - 100 μM) in 1 mM PBS buffer (pH 7.4), excited at 291 nm and emission at 334 nm; (B) Non-linear fitting plot of fluorescence intensity *versus* concentration for the direct titration of **Famotidine** with Origin. K_a was evaluated as 5.46×10^5 M^{-1}.

(A)



(B)

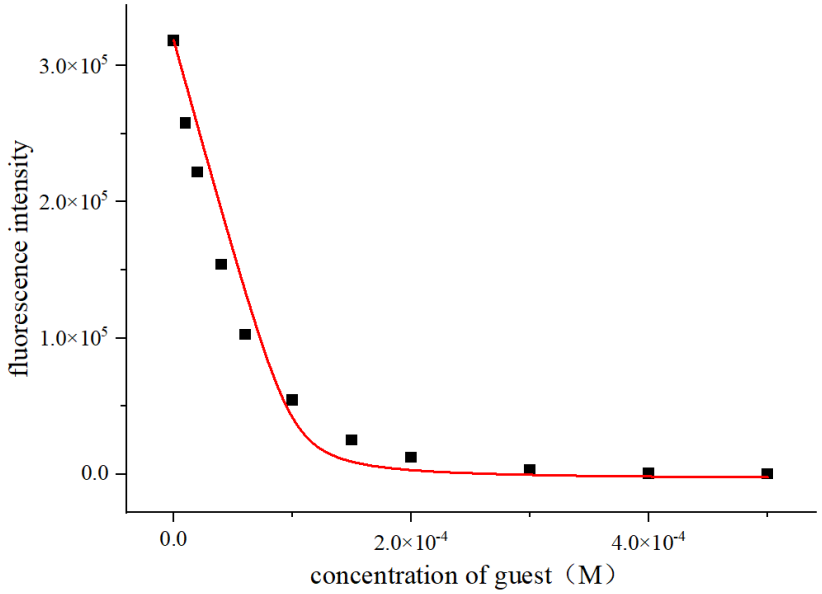
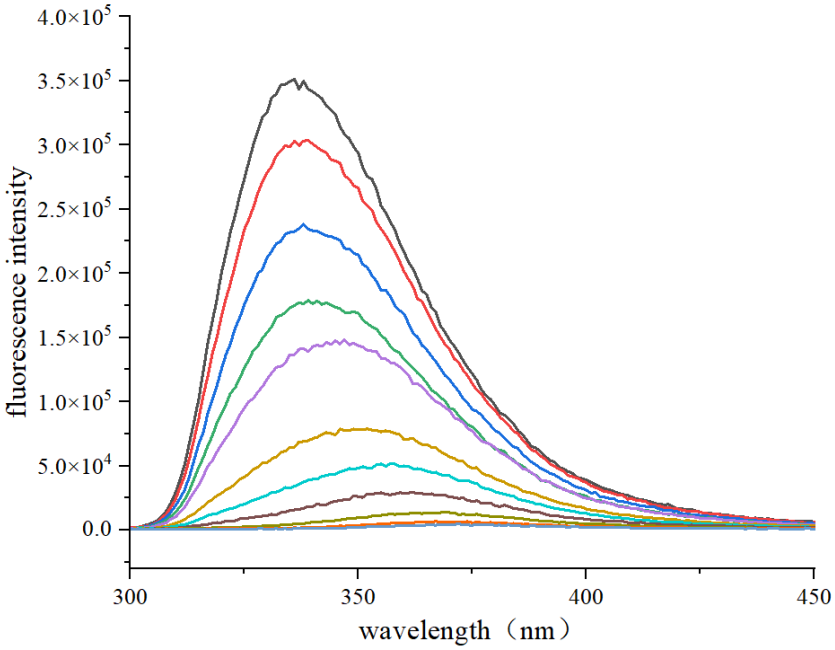


Figure S81. (A) Fluorescence spectra from the titration of **P5C3** (0.1 mM) with **Metronidazole** (0 – 0.5 mM) in water, excited at 293 nm and emission at 335 nm; (B) Non-linear fitting plot of fluorescence intensity *versus* concentration for the direct titration of **11** with Origin. K_a was evaluated as 4.28×10^5 M^{-1}.

(A)



(B)

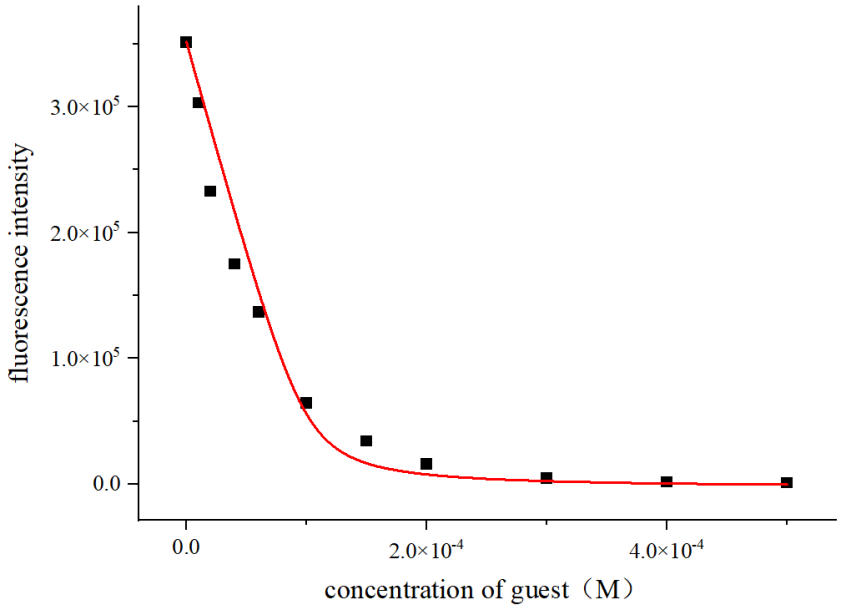
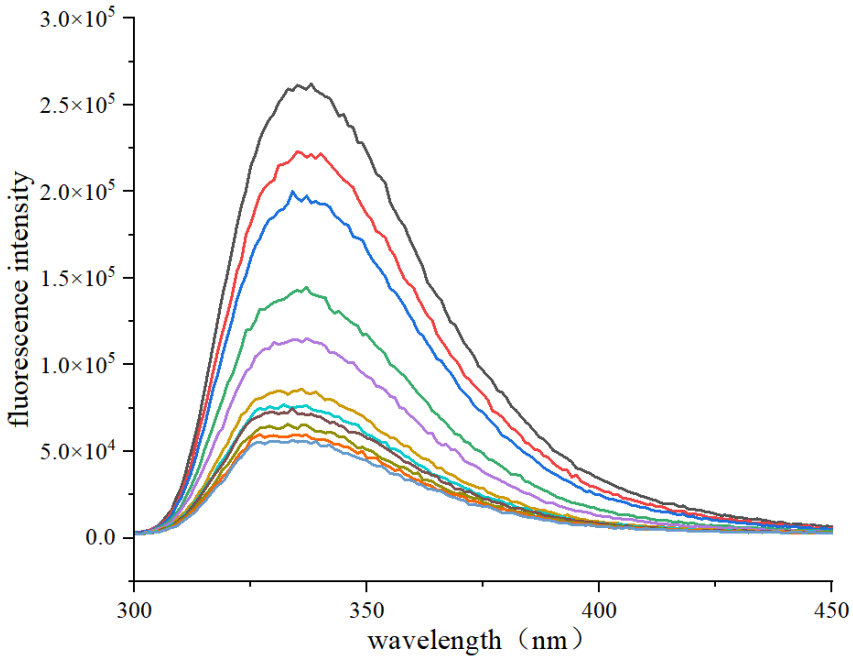


Figure S82. (A) Fluorescence spectra from the titration of **P5C3** (0.1 mM) with **Metronidazole** (0 - 0.5 mM) in 1 mM PBS buffer (pH 7.4), excited at 293 nm and emission at 336 nm; (B) Non-linear fitting plot of fluorescence intensity *versus* concentration for the direct titration of **Metronidazole** with Origin. K_a was evaluated as 3.01×10^5 M^{-1}.

(A)



(B)

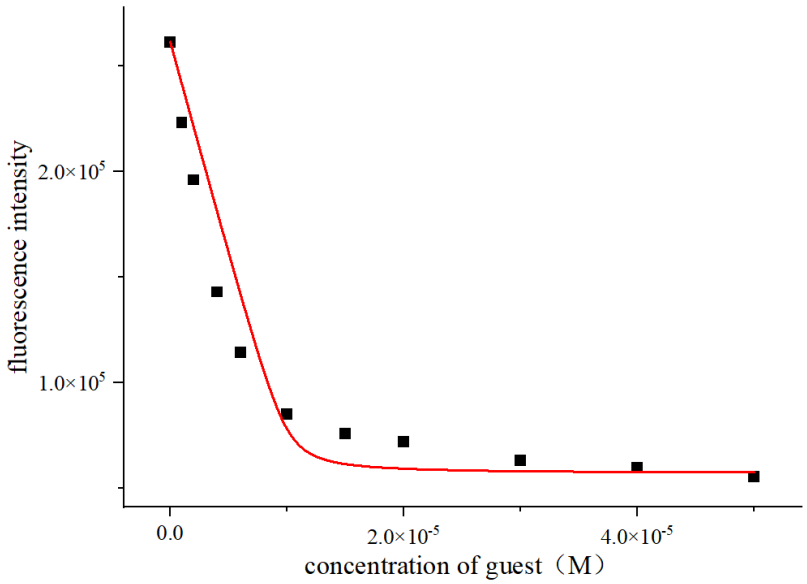
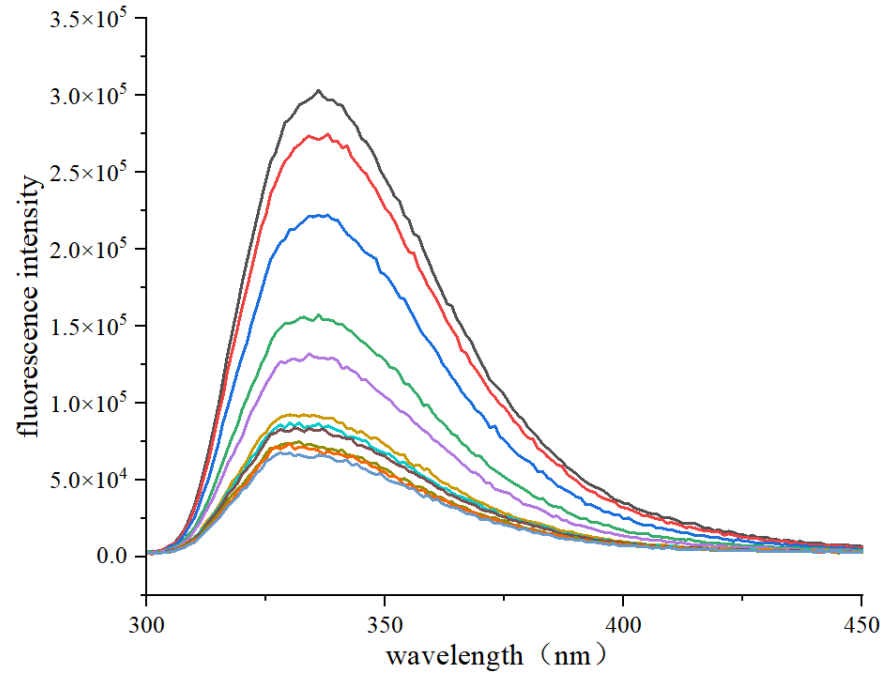


Figure S83. (A) Fluorescence spectra from the titration of **P5C3** (10 μM) with **Robenidine** (0 - 50 μM) in water, excited at 293 nm and emission at 335 nm; (B) Non-linear fitting plot of fluorescence intensity *versus* concentration for the direct titration of **Robenidine** with Origin. K_a was evaluated as 3.45×10^6 M^{-1}.

(A)



(B)

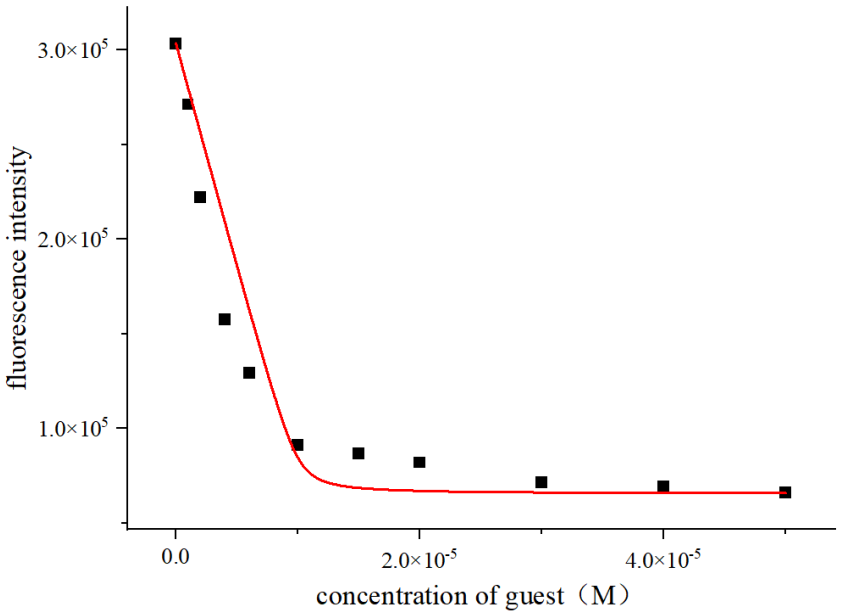
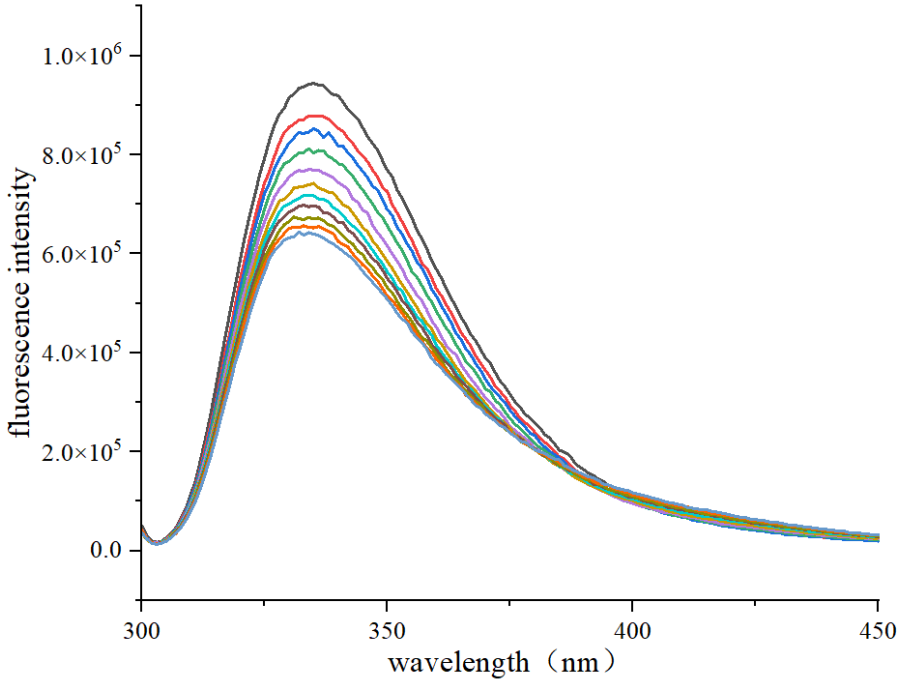


Figure S84. (A) Fluorescence spectra from the titration of **P5C3** (10 μM) with **Robenidine** (0 - 50 μM) in 1 mM PBS buffer (pH 7.4), excited at 293 nm and emission at 336 nm; (B) Non-linear fitting plot of fluorescence intensity *versus* concentration for the direct titration of **Robenidine** with Origin. K_a was evaluated as 1.15×10^6 M^{-1}.

(A)



(B)

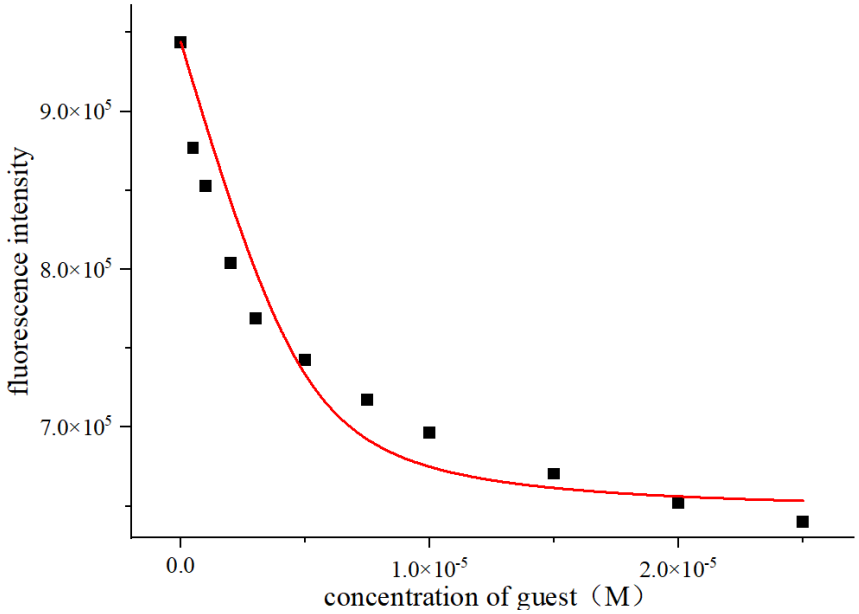
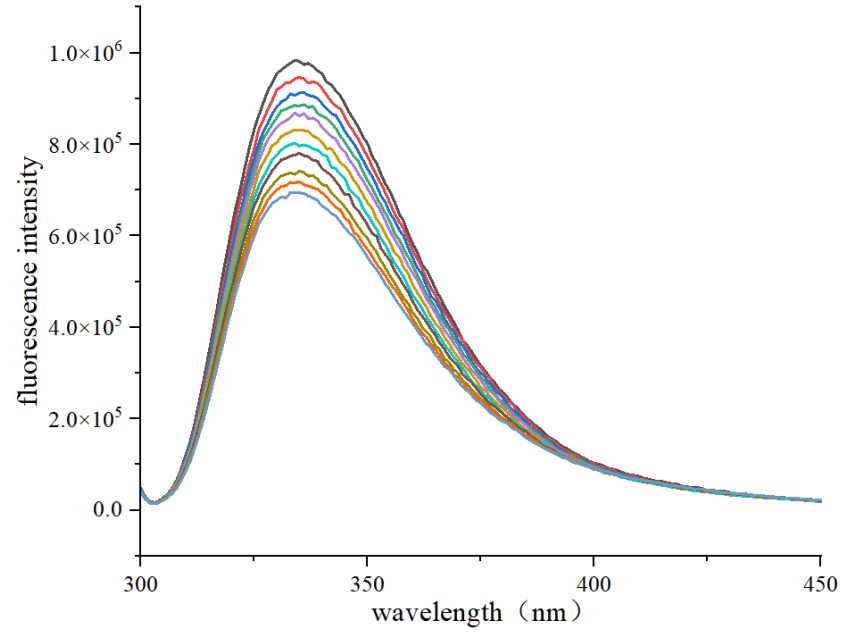


Figure S85. (A) Fluorescence spectra from the titration of **P5C3** (5 μM) with **Enilconazole** (0 - 25 μM) in water, excited at 293 nm and emission at 335 nm; (B) Non-linear fitting plot of fluorescence intensity *versus* concentration for the direct titration of **Enilconazole** with Origin. K_a was evaluated as 1.58×10^5 M^{-1}.

(A)



(B)

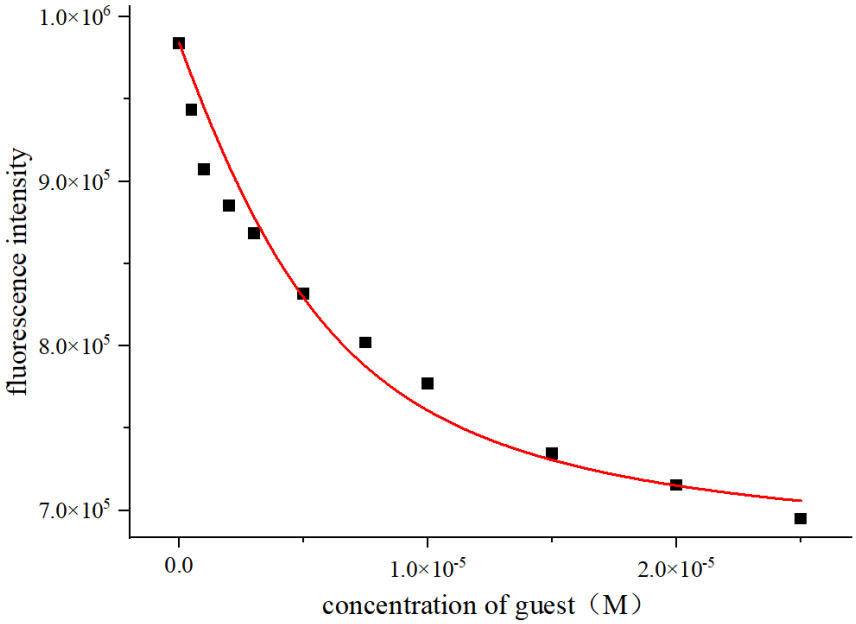
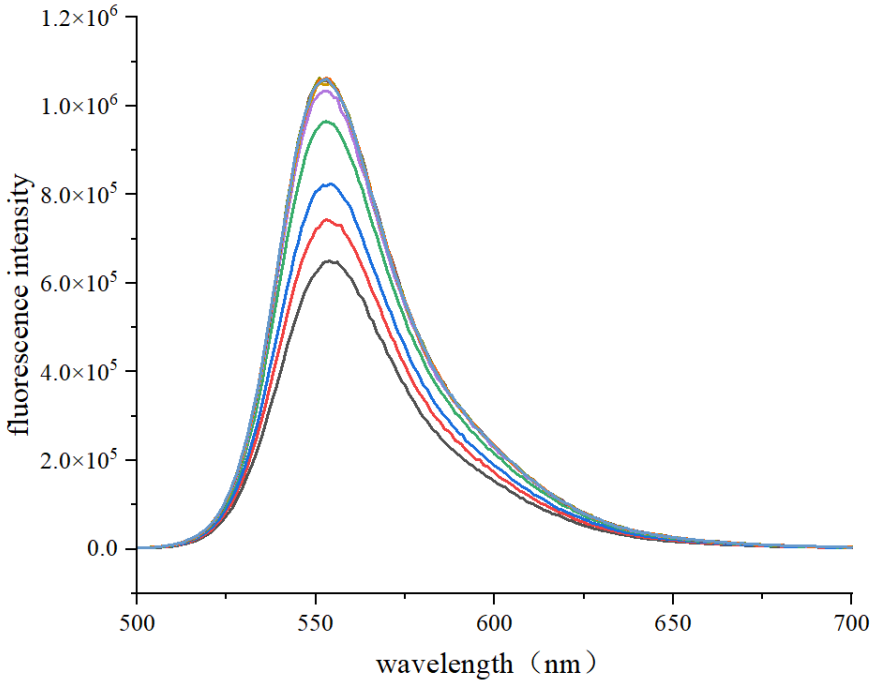


Figure S86. (A) Fluorescence spectra from the titration of **P5C3** (5 μM) with **Enilconazole** (0 - 25 μM) in 1 mM PBS buffer (pH 7.4), excited at 293 nm and emission at 335 nm; (B) Non-linear fitting plot of fluorescence intensity *versus* concentration for the direct titration of **Enilconazole** with Origin. K_a was evaluated as 3.86×10^5 M^{-1}.

(A)



(B)

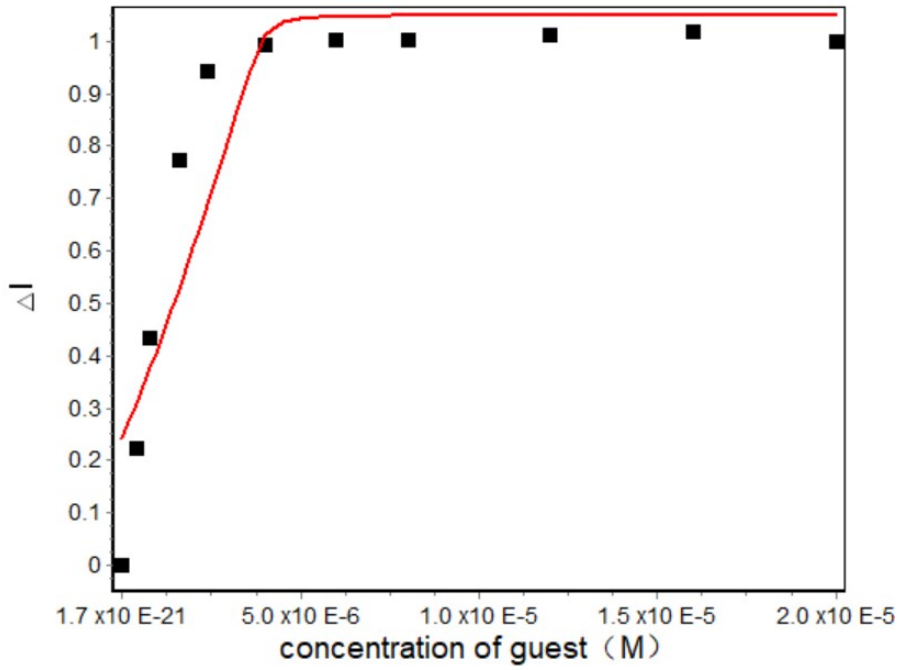
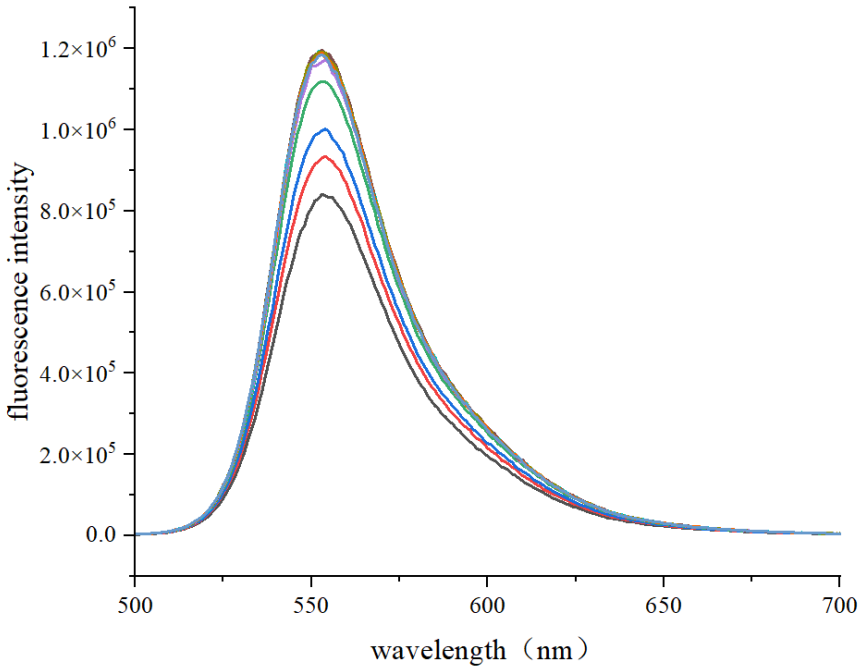


Figure S87. (A) Fluorescence spectra from the displacement titration of **P5C3** (4 μM) and **Rhodamine 6G** (6 μM) with **Chlorhexidine** (0 - 20 μM) in water, excited at 526 nm and emission at 554 nm; (B) Non-linear fitting plot of fluorescence intensity versus concentration for the displacement titration of **Chlorhexidine** with Scientist. K_a was evaluated as 6.24×10^8 M^{-1}.

(A)



(B)

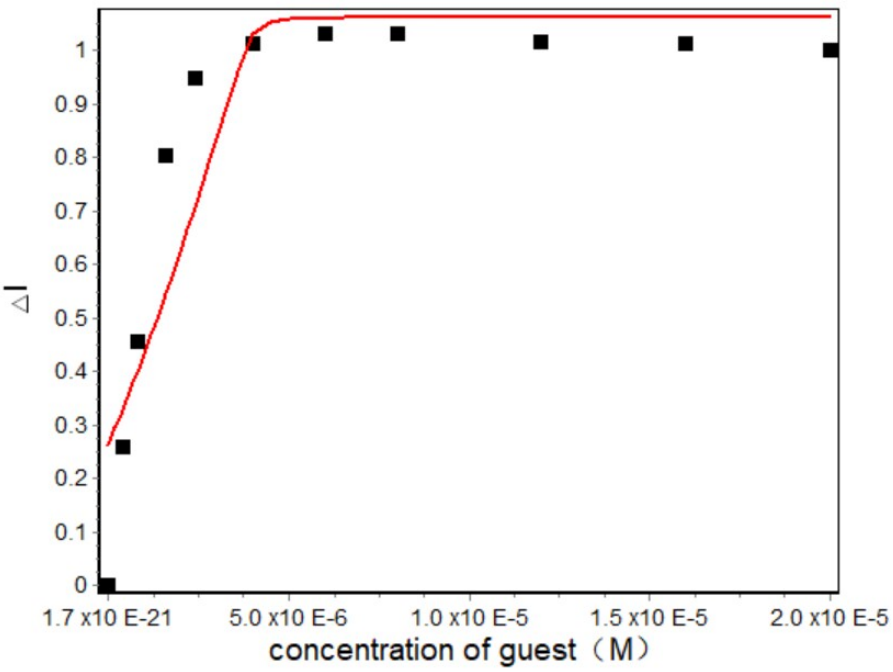
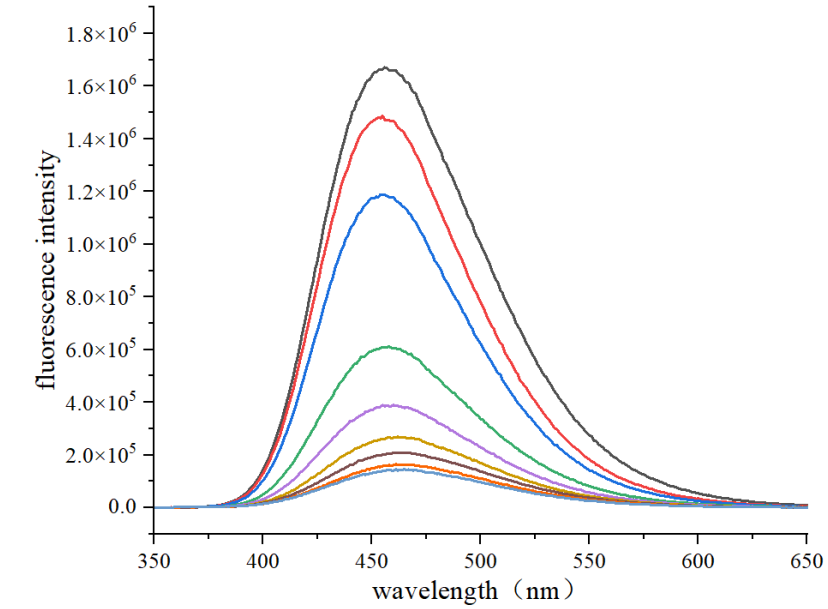


Figure S88. (A) Fluorescence spectra from the displacement titration of **P5C3** (4 μM) and **Rhodamine 6G** (6 μM) with **Chlorhexidine** (0 - 20 μM) in 1mM PBS buffer (pH 7.4), excited at 526 nm and emission at 553 nm; (B) Non-linear fitting plot of fluorescence intensity versus concentration for the displacement titration of **Chlorhexidine** with Scientist. K_a was evaluated as 2.88×10^8 M^{-1}.

(A)



(B)

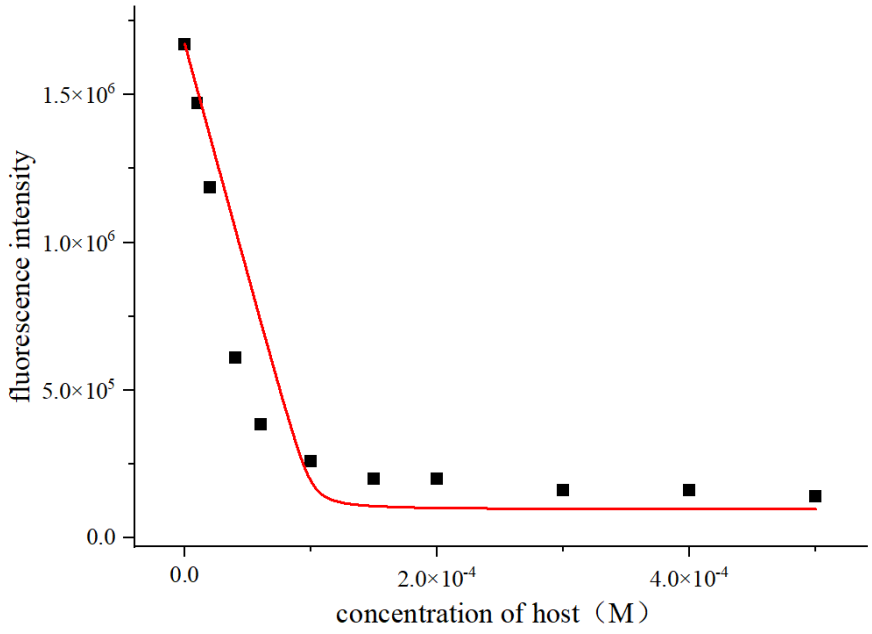
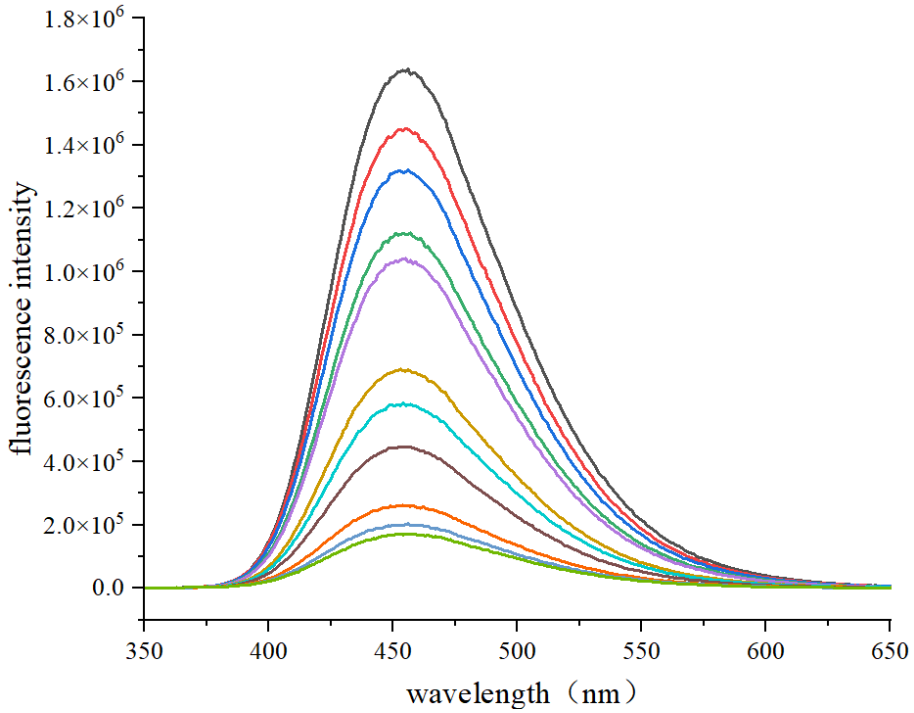


Figure S89. (A) Fluorescence spectra from the titration of **Levofloxacin** (10 μM) with **P5C3** (0 - 50 μM) in water, excited at 332 nm and emission at 454 nm; (B) Non-linear fitting plot of fluorescence intensity *versus* concentration for the direct titration of **Levofloxacin** with Origin. K_a was evaluated as 2.47×10^6 M^{-1}.

(A)



(B)

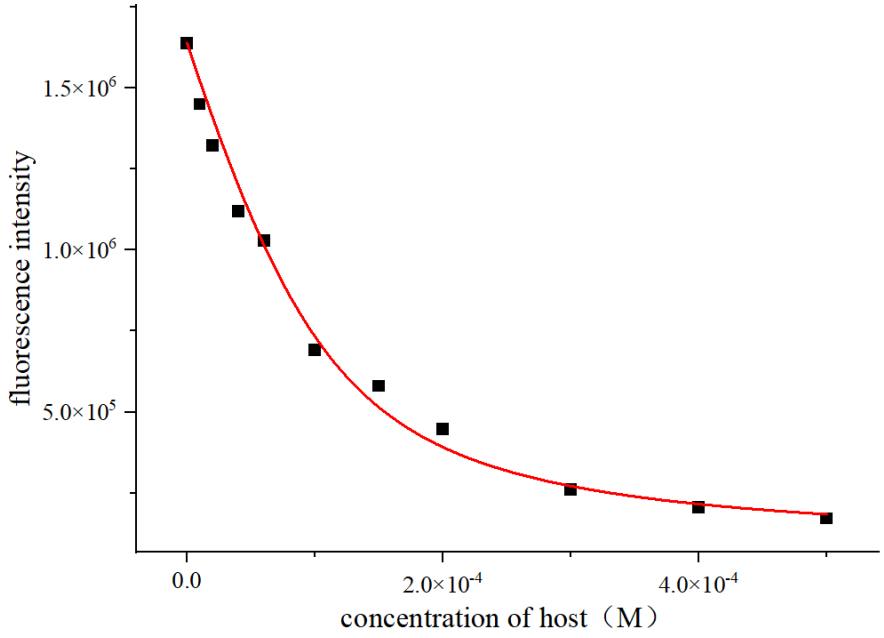


Figure S90. (A) Fluorescence spectra from the titration of **Levofloxacin** (10 μM) with **P5C3** (0 - 50 μM) in 1 mM PBS buffer (pH 7.4), excited at 332 nm and emission at 455 nm; (B) Non-linear fitting plot of fluorescence intensity *versus* concentration for the direct titration of **Levofloxacin** with Origin. K_a was evaluated as 3.28×10^4 M^{-1}.

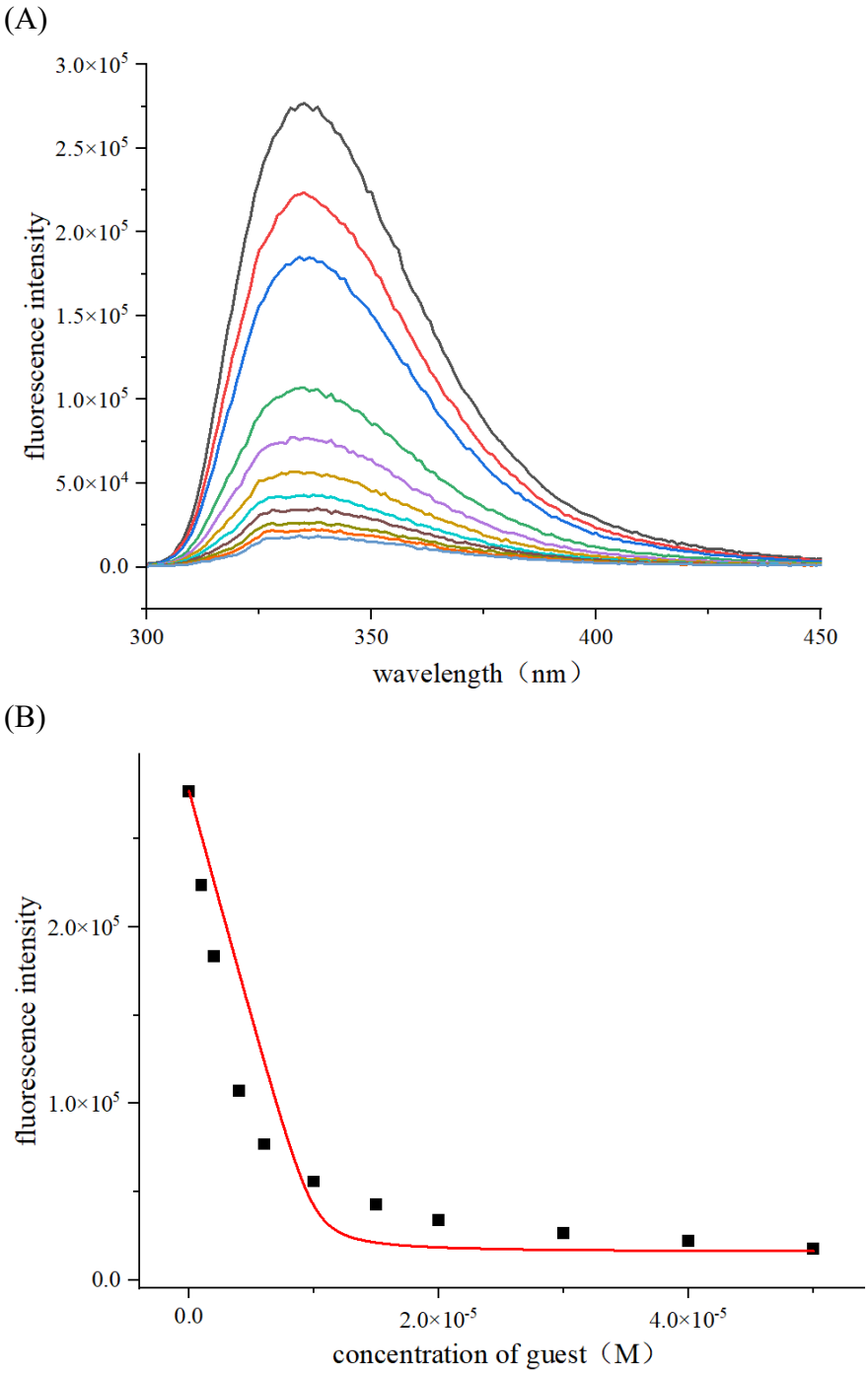


Figure S91. (A) Fluorescence spectra from the titration of **P5C3** (10 μM) with **Tizanidine** (0 - 50 μM) in water, excited at 293 nm and emission at 336 nm; (B) Non-linear fitting plot of fluorescence intensity *versus* concentration for the direct titration of **Tizanidine** with Origin. K_a was evaluated as 8.79×10^6 M^{-1}.

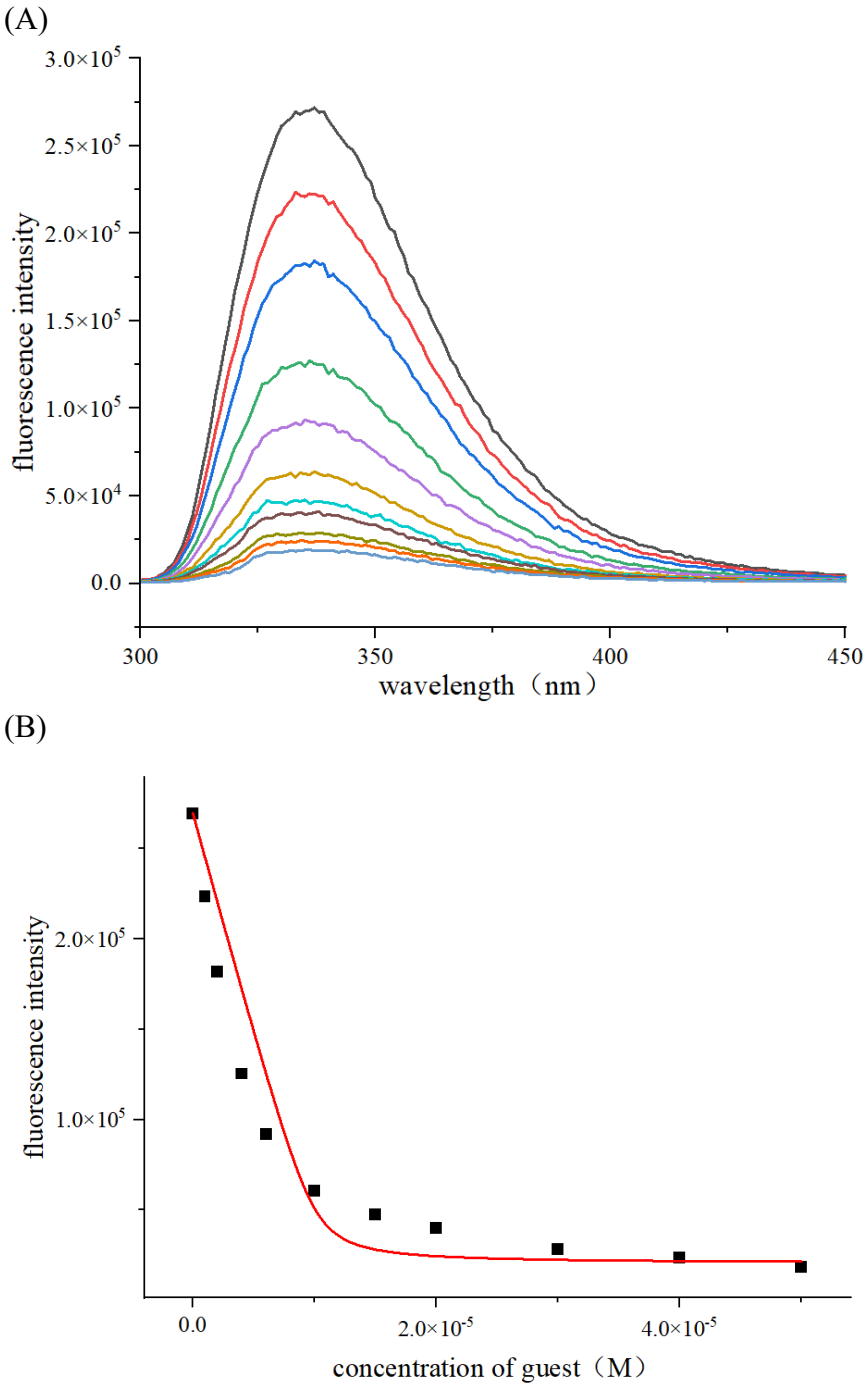


Figure S92. (A) Fluorescence spectra from the titration of **P5C3** (10 μM) with **Tizanidine** (0 - 50 μM) in 1 mM PBS buffer (pH 7.4), excited at 293 nm and emission at 335 nm; (B) Non-linear fitting plot of fluorescence intensity *versus* concentration for the direct titration of **Tizanidine** with Origin. K_a was evaluated as 5.84×10^6 M^{-1}.

All ITC experiments were conducted in the 950 μL working volume of the sample cell of the Nano ITC instrument at 25 °C. In a typical experiment, 10 μL guest solution with 300 seconds spacing was injected 25 times into the ITC cell. The binding data was fitted using the independent binding model or the competitive replacement model in Launch NanoAnalyze analysis software.

Table S1. Binding constant K_a (M^{-1}) obtained from ITC titration.

Guest	K_a (M^{-1})			
	P5C2		**P5C3**	
	Fluorescence	ITC	Fluorescence	ITC
Rhodamine 6G	3.25×10^5	7.23×10^5	5.55×10^5	7.04×10^5
Methylviologen	2.90×10^8	7.34×10^8	2.20×10^8	4.42×10^8
Chlorhexidine	1.10×10^9	8.95×10^7	6.24×10^8	5.27×10^7

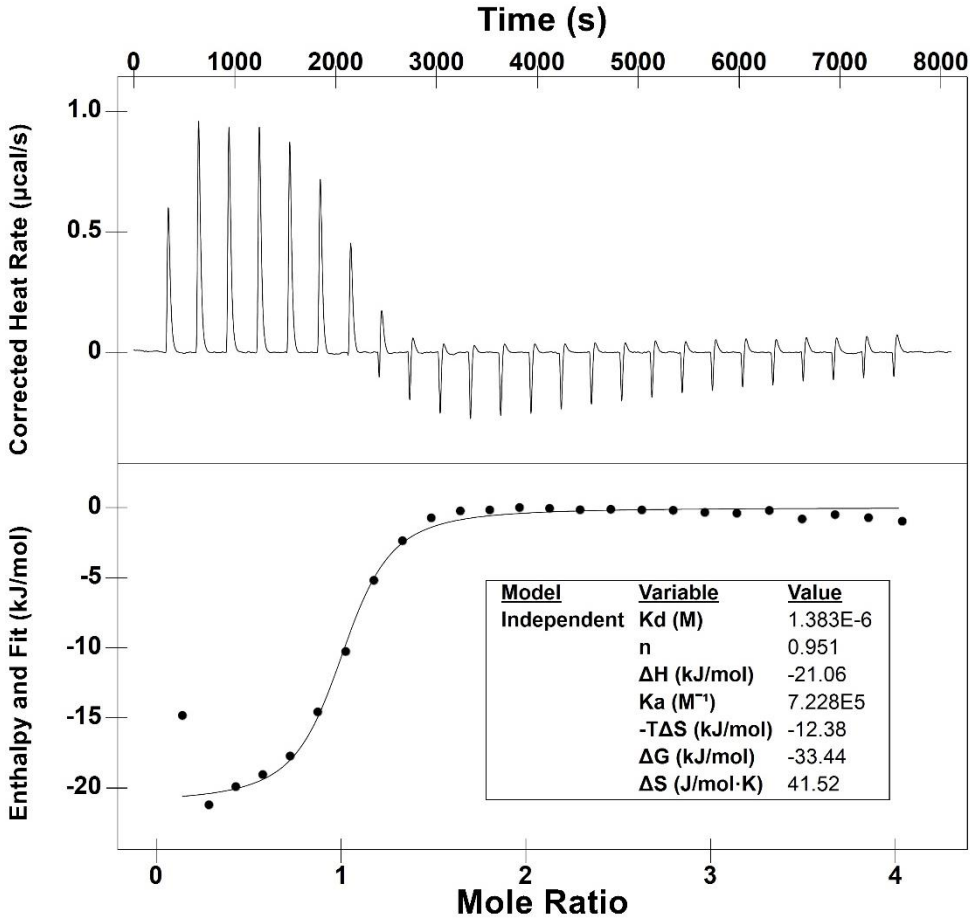


Figure S93. ITC isotherms from the titration of **Rhodamine 6G** (1 mM) into **P5C2** (75 μM) in water. The data was analyzed with the independent model. K_a was evaluated as 7.23×10^5 M^{-1}.

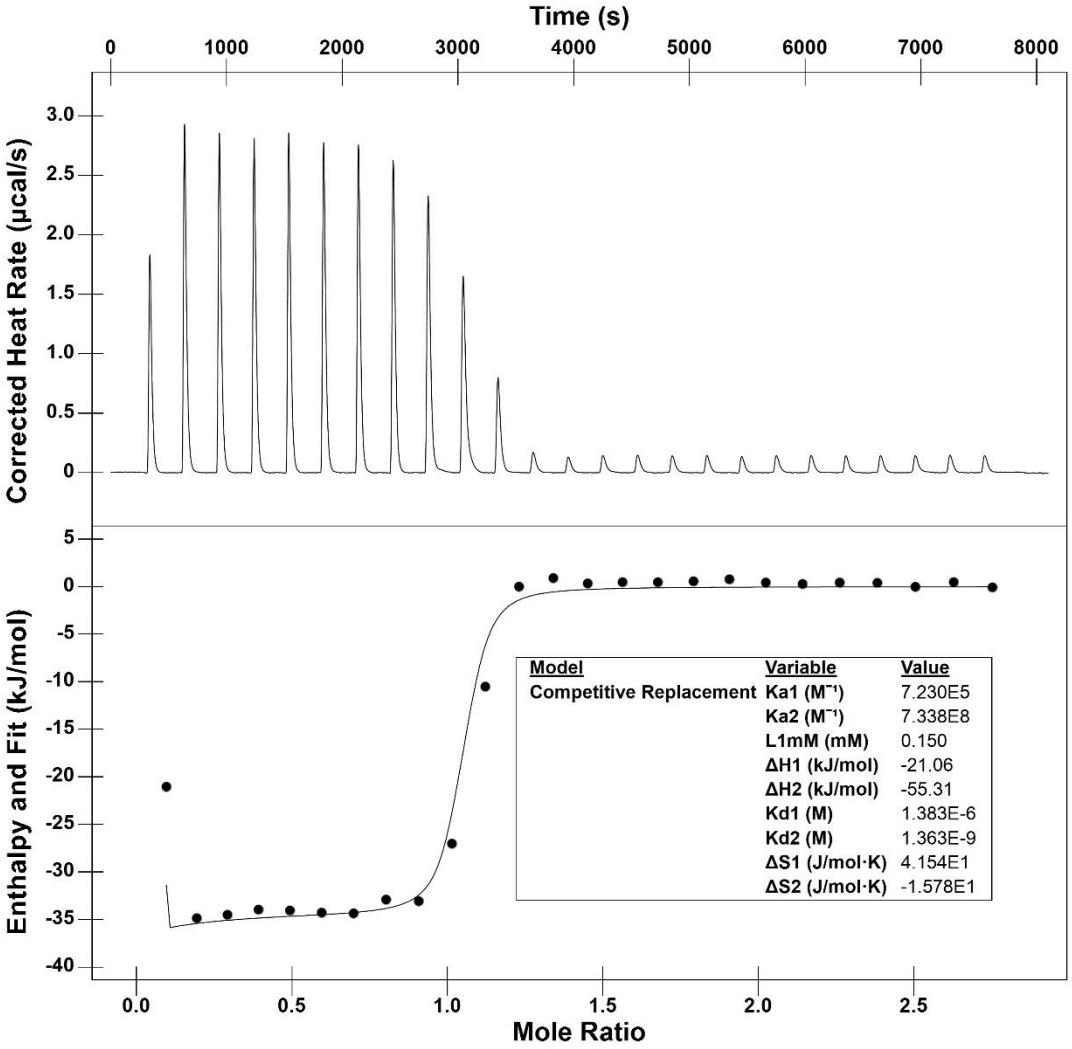


Figure S94. ITC isotherms from the titration of **Methylviologen** (1 mM) into **P5C2** (100 µM) and **Rhodamine 6G** (150 µM) in water. The data was analyzed with the competitive replacement model. K_a was evaluated as 7.34×10^8 M^{-1}.

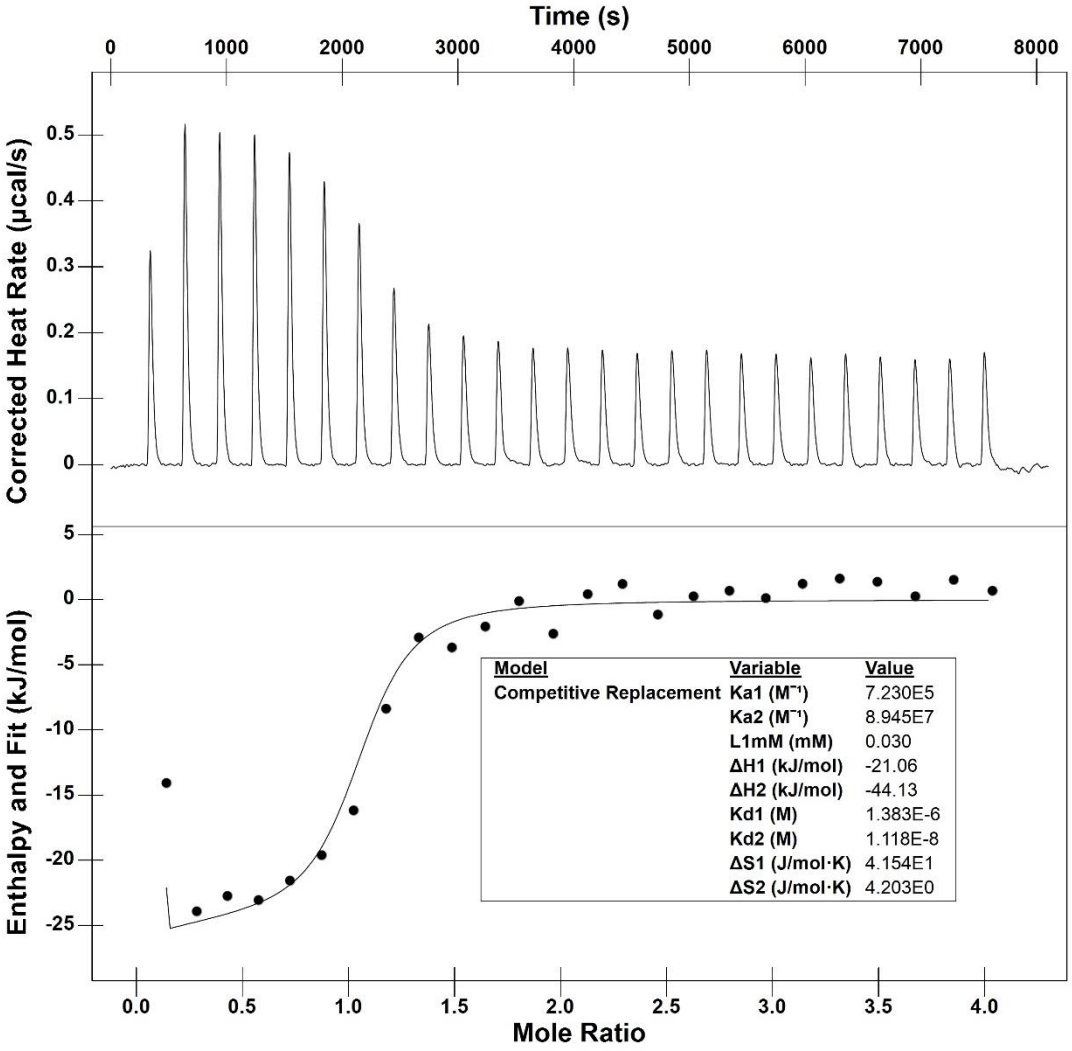


Figure S95. ITC isotherms from the titration of **Chlorhexidine** (200 µM) into **P5C2** (15 µM) and **Rhodamine 6G** (30 µM) in water. The data was analyzed with the competitive replacement model. K_a was evaluated as 8.95×10^7 M^{-1}.

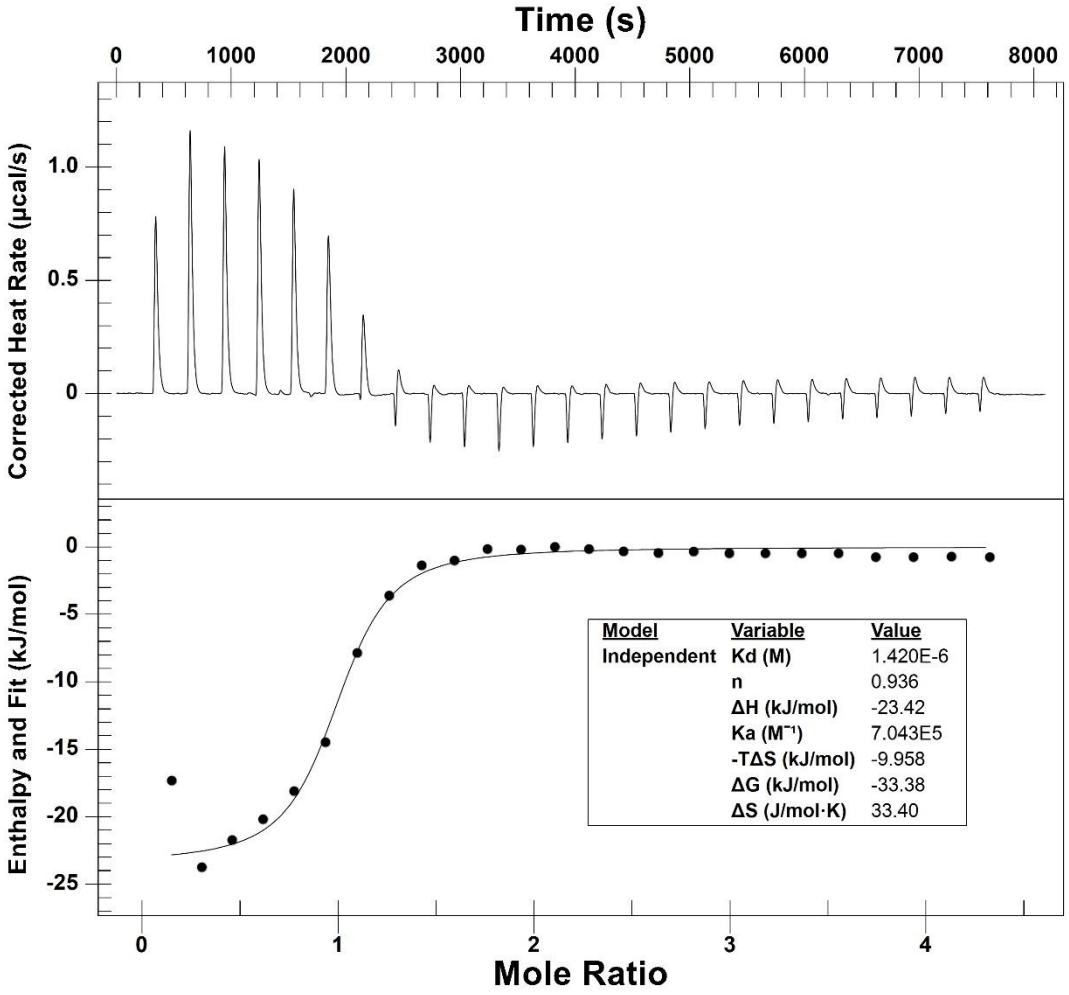


Figure S96. ITC isotherms from the titration of **Rhodamine 6G** (1 mM) into **P5C3** (70 μM) in water. The data was analyzed with the independent model. K_a was evaluated as 7.04×10^5 M^{-1}.

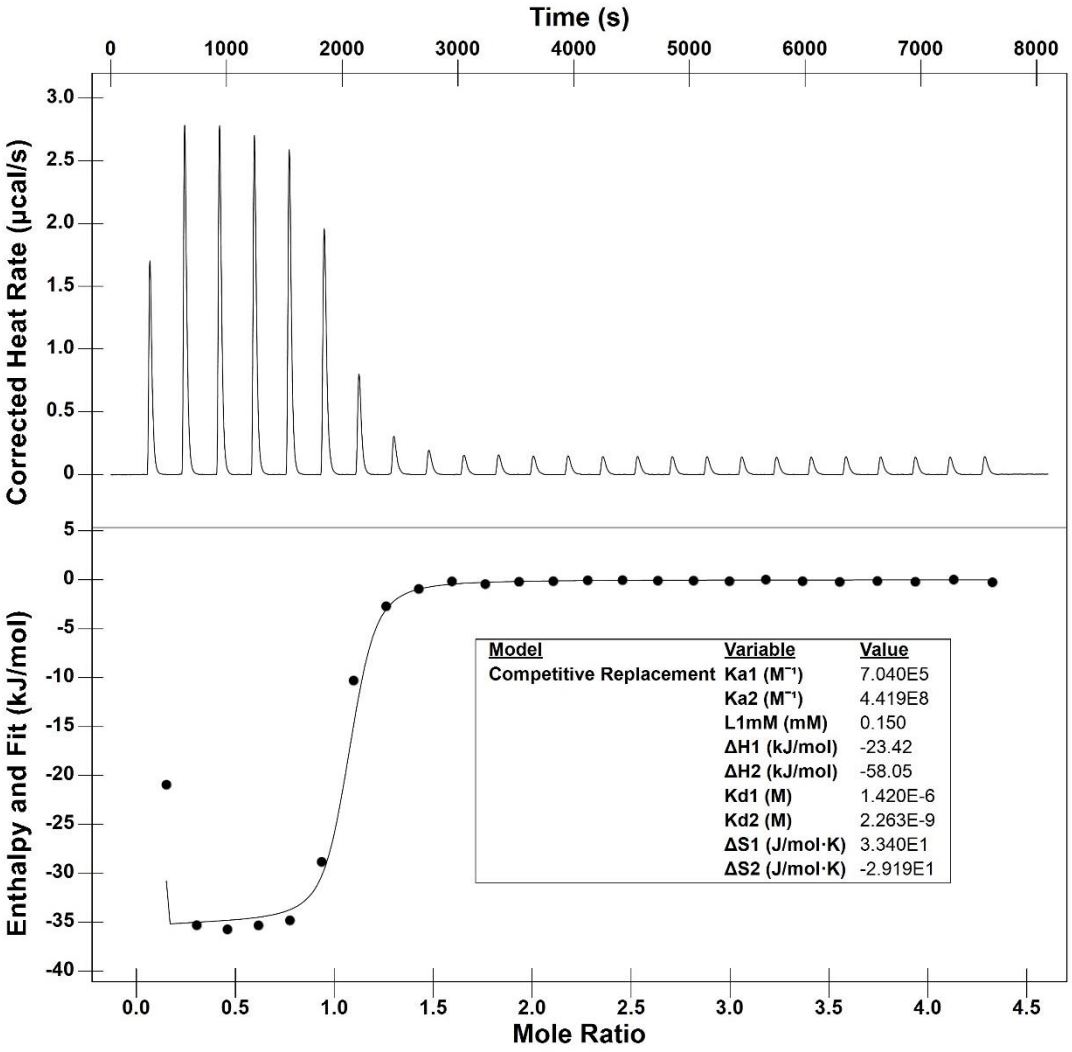


Figure S97. ITC isotherms from the titration of **Methylviologen** (1 mM) into **P5C3** (70 µM) and **Rhodamine 6G** (150 µM) in water. The data was analyzed with the competitive replacement model. K_a was evaluated as 4.42×10^8 M^{-1}.

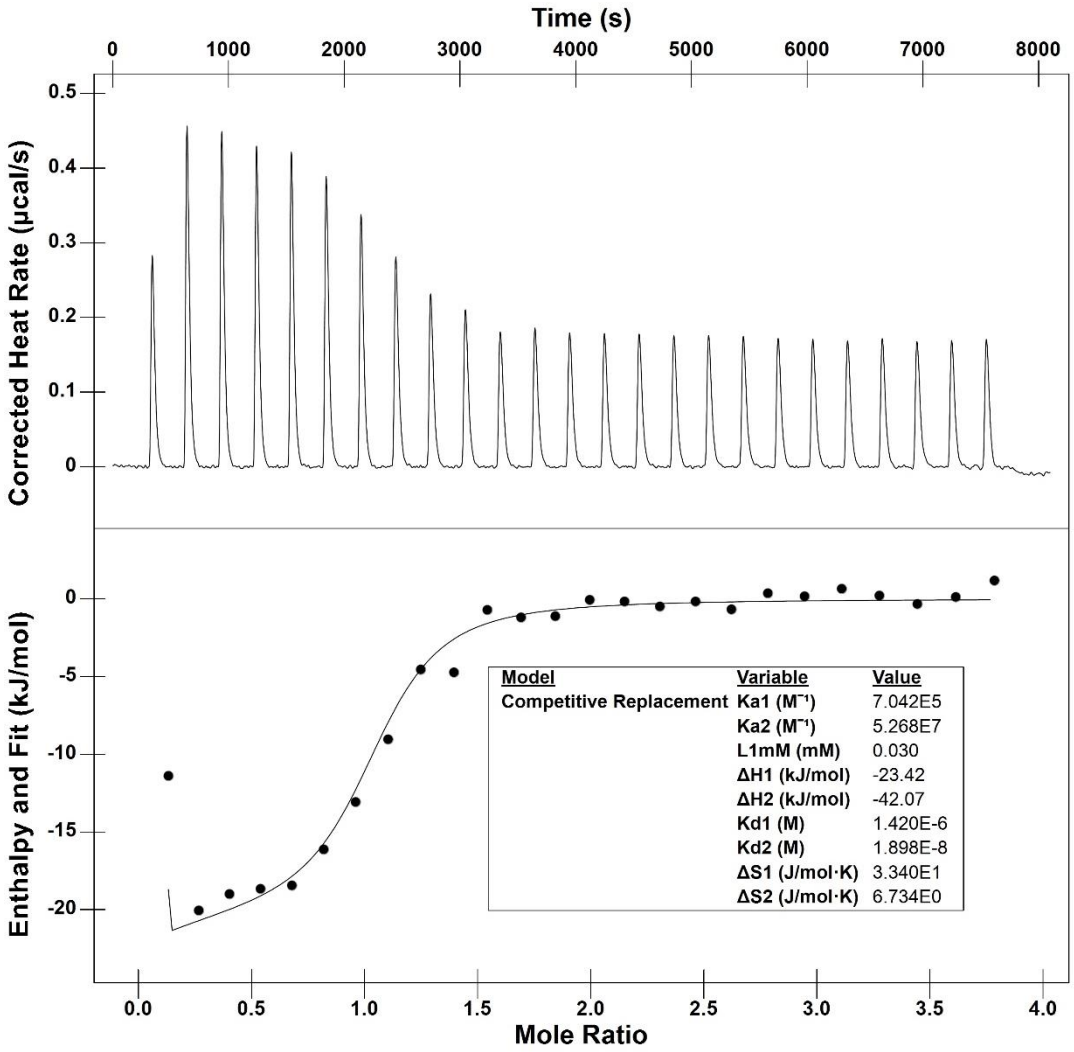


Figure S98. ITC isotherms from the titration of **Chlorhexidine** (200 µM) into **P5C3** (15 µM) and **Rhodamine 6G** (30 µM) in water. The data was analyzed with the competitive replacement model. K_a was evaluated as 5.27×10^7 M^{-1}.

Determination of LOD

The calculation is as follows: DL = 3×σ / S where S is the slope of the calibration curve and σ is the standard deviation of y-intercepts of regression lines.

Table S2. LOD (μM) of phosphonate hosts for pharmaceutical guests.

Guest	**P5C2**	**P5C3**
Chlorhexidine	0.044 μM	0.052 μM
Methylviologen	0.045 μM	0.027 μM
Robenidine	0.034 μM	0.057 μM
Levofloxacin	0.086 μM	0.082 μM

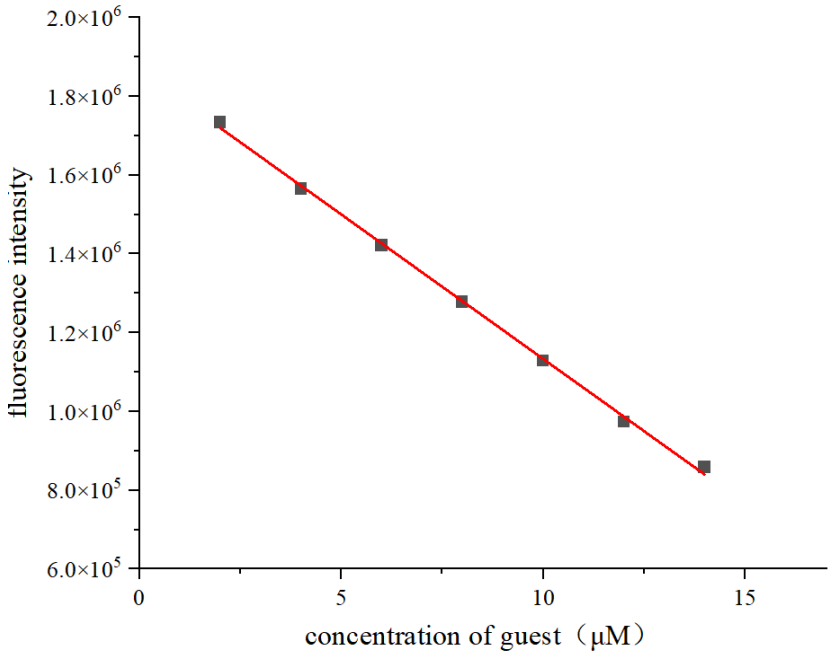


Figure S99. The linear relationship between the fluorescence intensity of **P5C2** and the concentrations of **Chlorhexidine**.

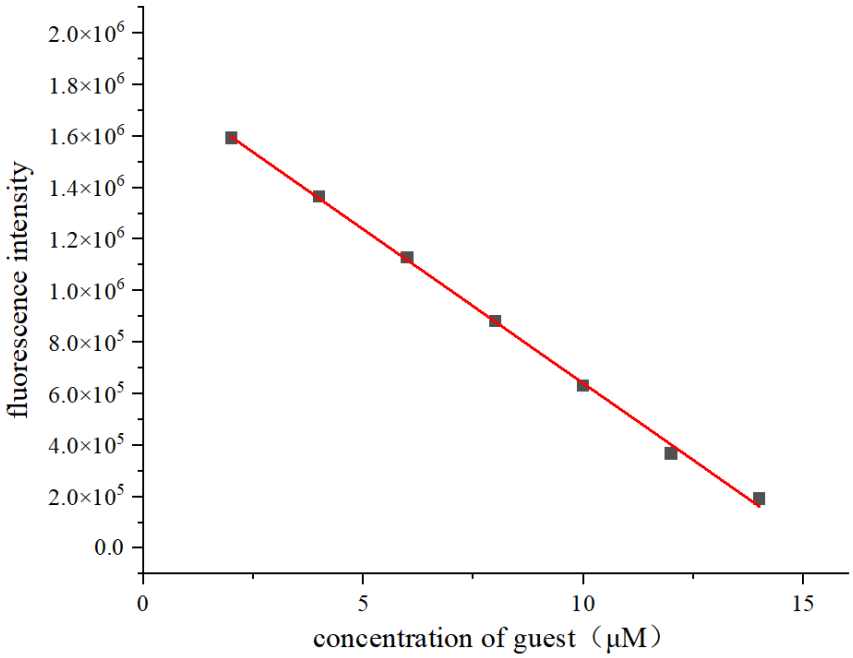


Figure S100. The linear relationship between the fluorescence intensity of **P5C2** and the concentrations of **Methylviologen**.

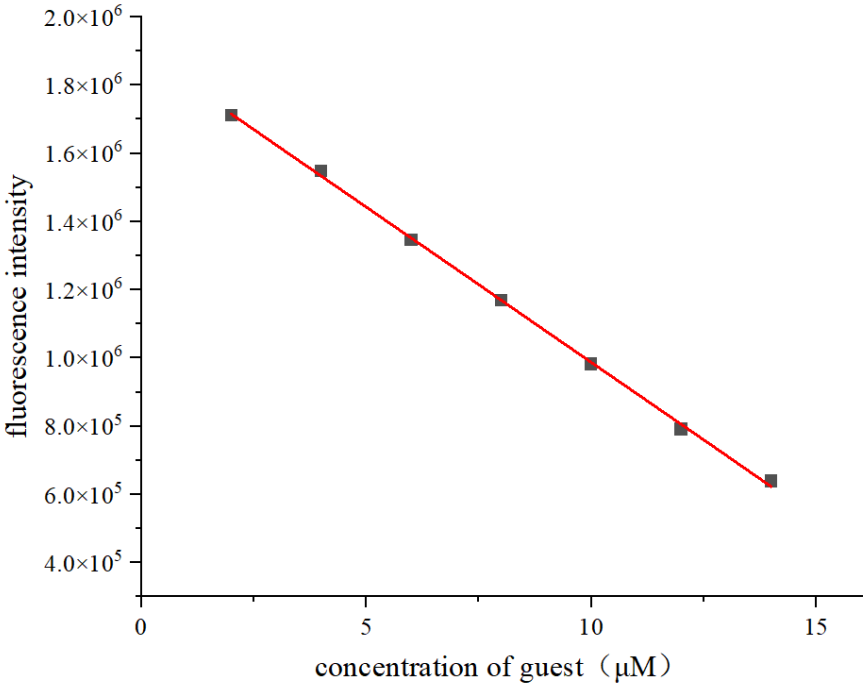


Figure S101. The linear relationship between the fluorescence intensity of **P5C2** and the concentrations of **Robenidine**.

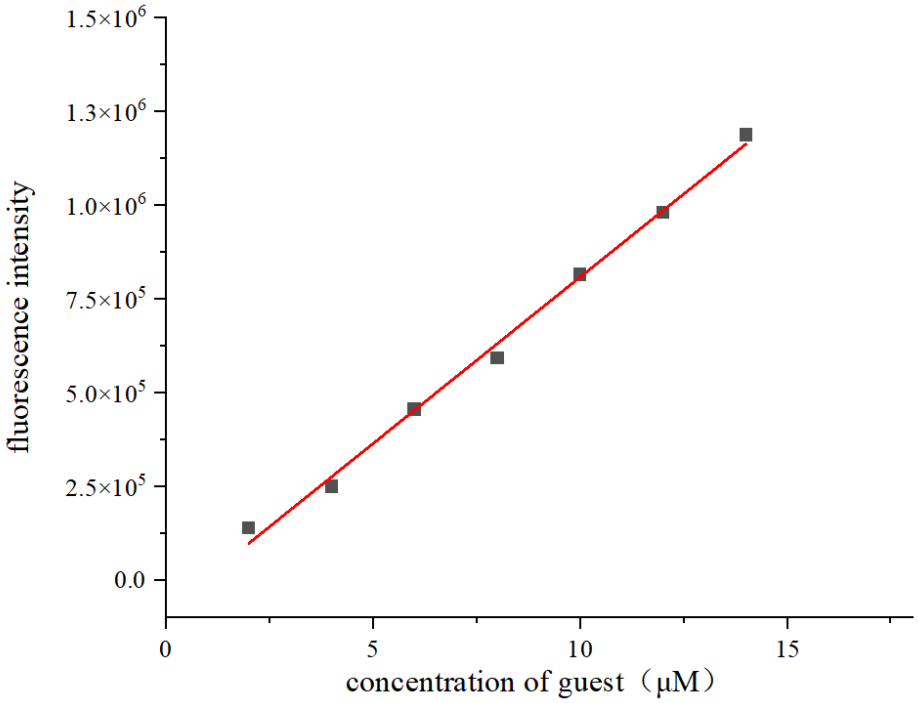


Figure S102. The linear relationship between the fluorescence intensity of **P5C2** and the concentrations of **Levofloxacin**.

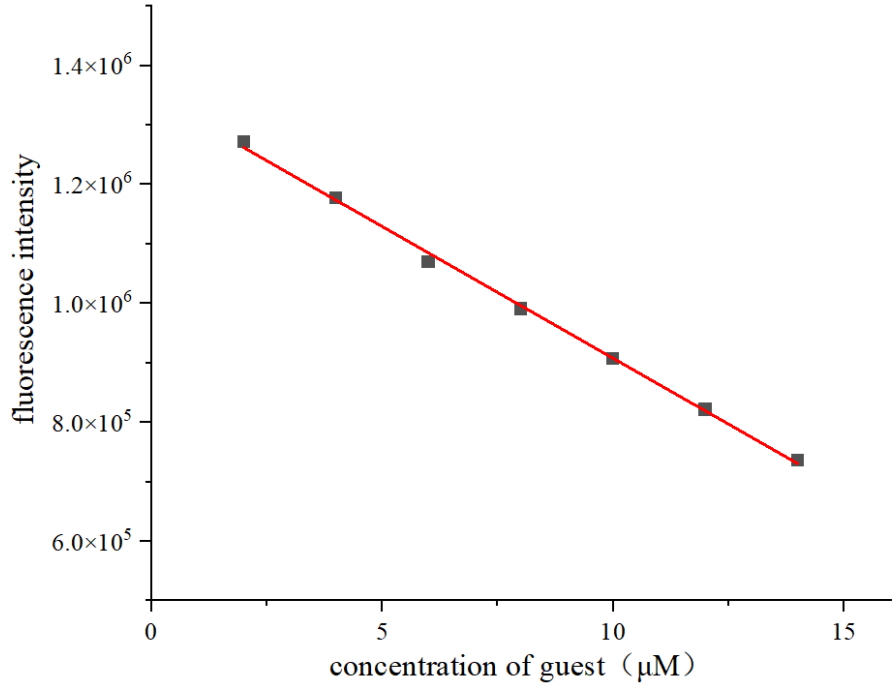


Figure S103. The linear relationship between the fluorescence intensity of **P5C3** and the concentrations of **Chlorhexidine**.

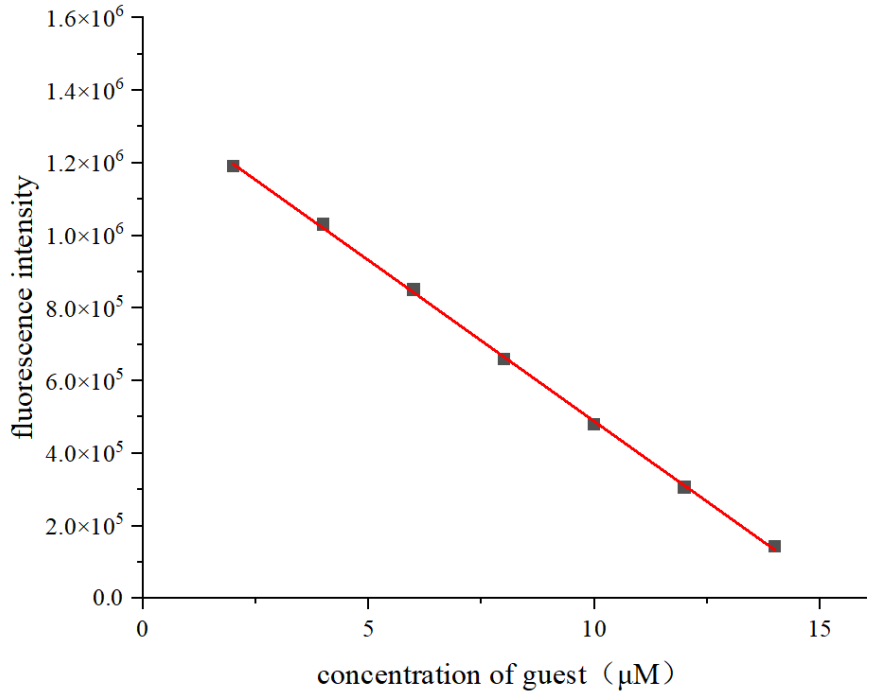


Figure S104. The linear relationship between the fluorescence intensity difference of **P5C3** and the concentrations of **Methylviologen**.

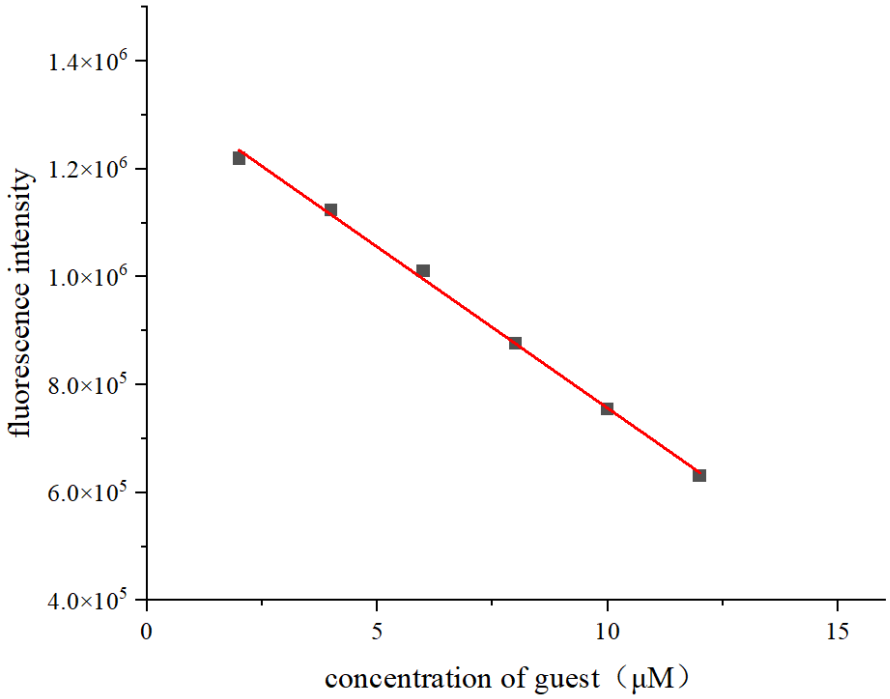


Figure S105. The linear relationship between the fluorescence intensity difference of **P5C3** and the concentrations of **Robenidine**.

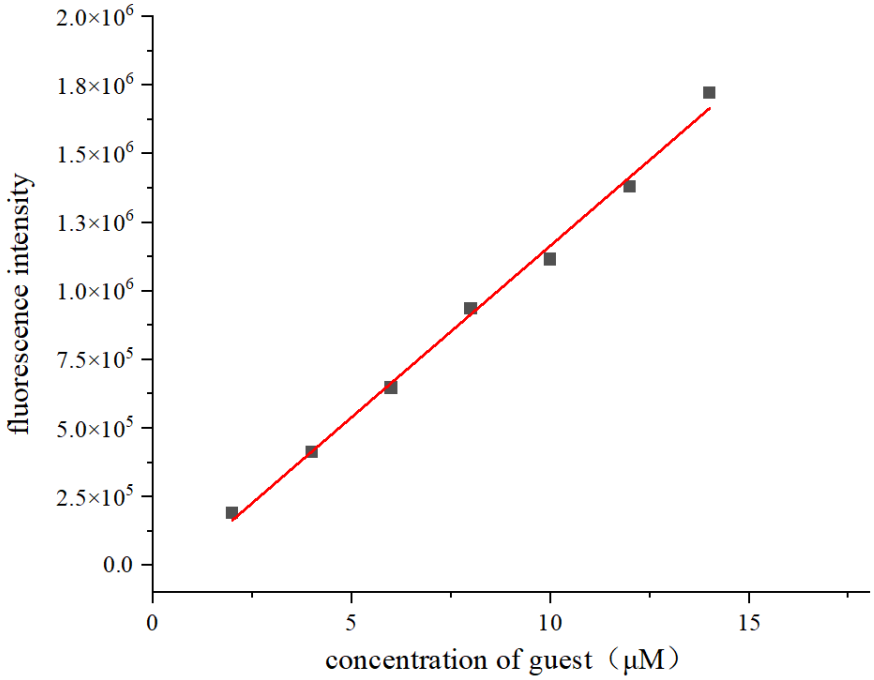


Figure S106. The linear relationship between the fluorescence intensity of **P5C3** and the concentrations of **Levofloxacin**.

Circular Dichroism

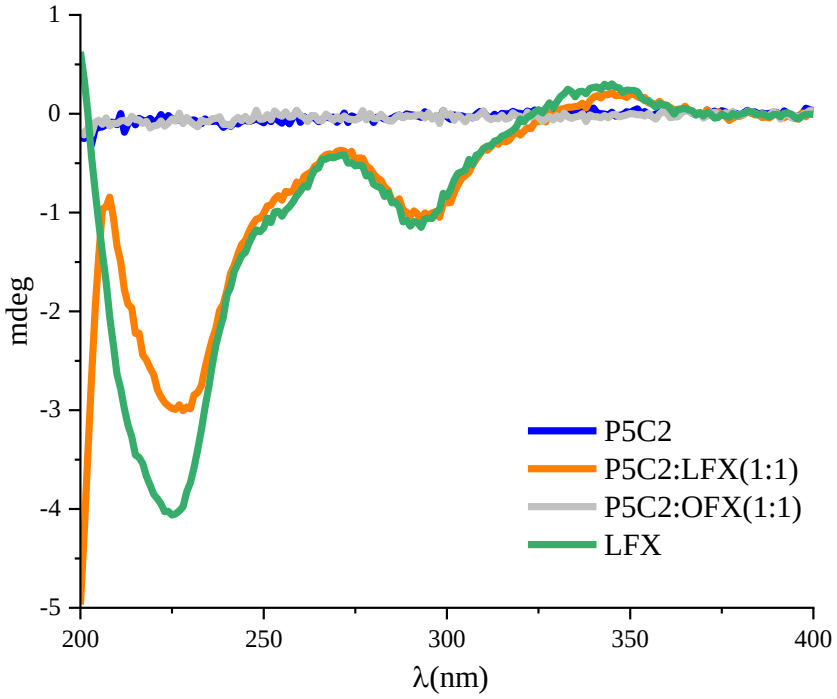


Figure S107. CD spectra of **P5C2** (100 μM), LFX (100 μM), 1:1 mixture of **P5C2** and LFX (100 μM), 1:1 mixture of **P5C2** and OFX (100 μM).

References

(1) Job, P. The Formation and Stability of Inorganic Complexes in Solution. *Ann. Chim.* **1928**, *9*, 113–203.

(2) Mao, W.; Mao, D.; Yang, F.; Ma, D. Thansformative Supramolecular Vesicles Based on Acid-Degradable Acyclic Cucurbit[n]uril and Prodrug for Promoted Tumoral-Cell Uptake. *Chem. Eur. J.* **2019**, *25*, 2272-2280.

(3) Thordarson, P. Determining Association Constants from Titration Experiments in Supramolecular Chemistry. *Chem. Soc. Rev.* **2011**, *40*, 1305-1323.