Supporting information：

Design, Synthesis, Anticancer Activity and Molecular Docking of Quinoline-based Dihydrazone Derivatives

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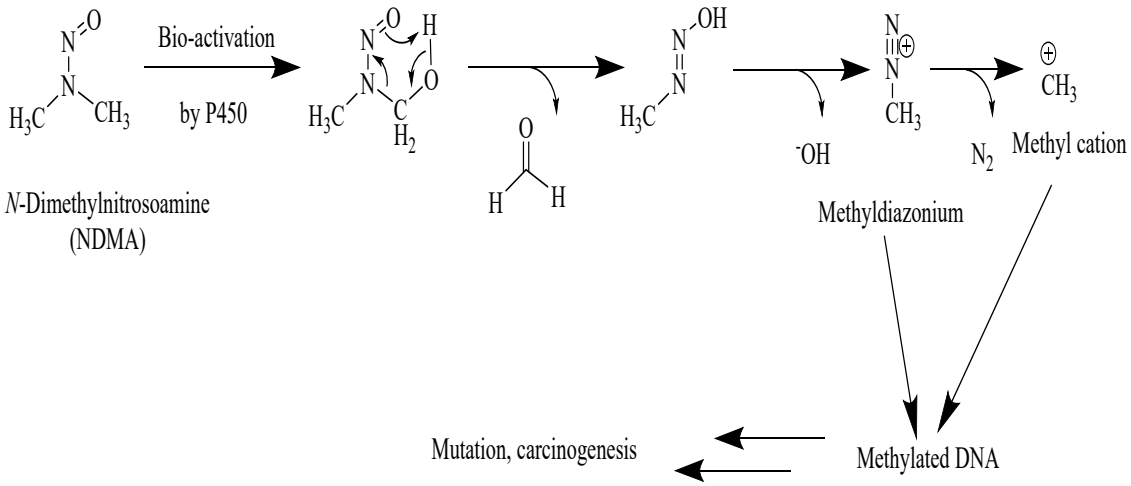
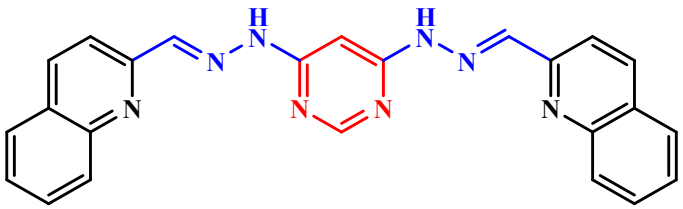


Scheme S1. Mechanism of NDMA bio-activation leading to its mutagenesis and carcinogenicity.



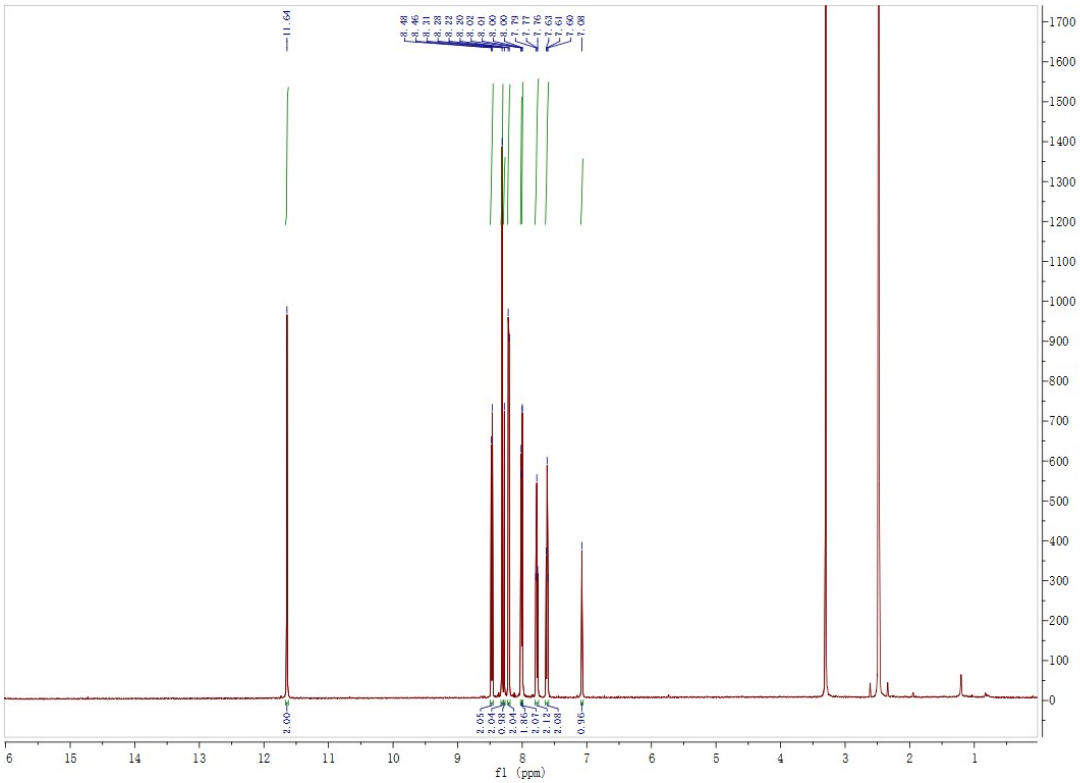


Figure S1 ^{1}H NMR spectrum of **3a** in DMSO-d6.

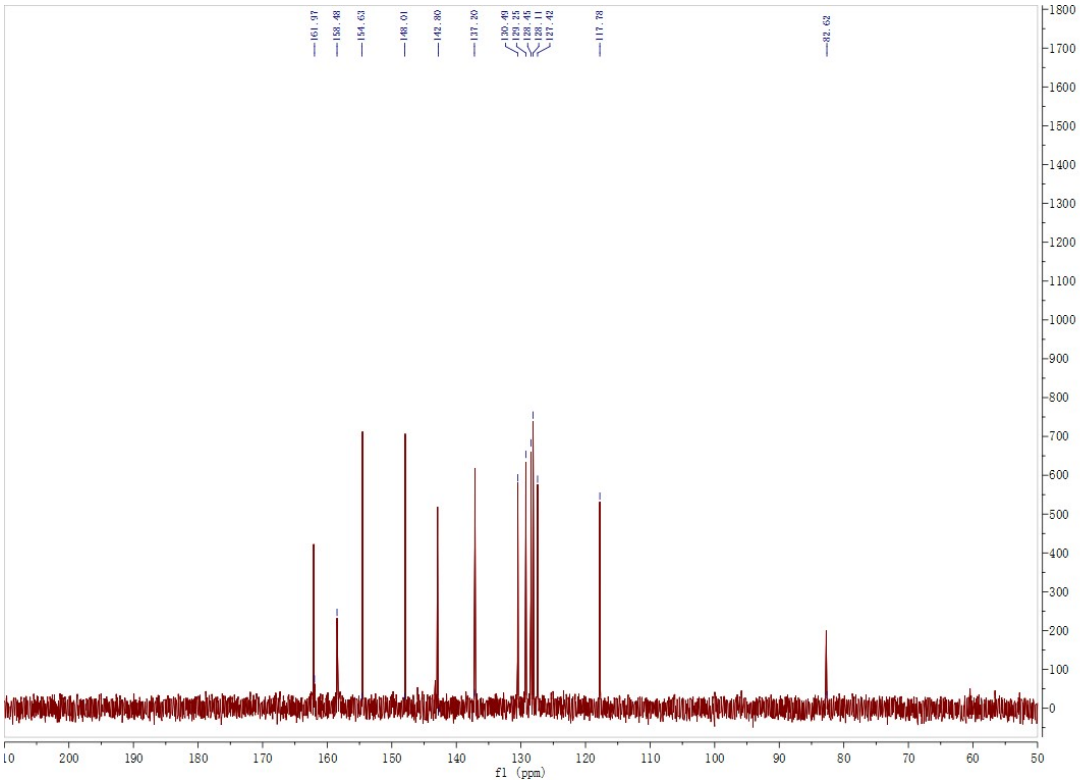


Figure S2 ^{13}C NMR spectrum of **3a** in DMSO-d6.

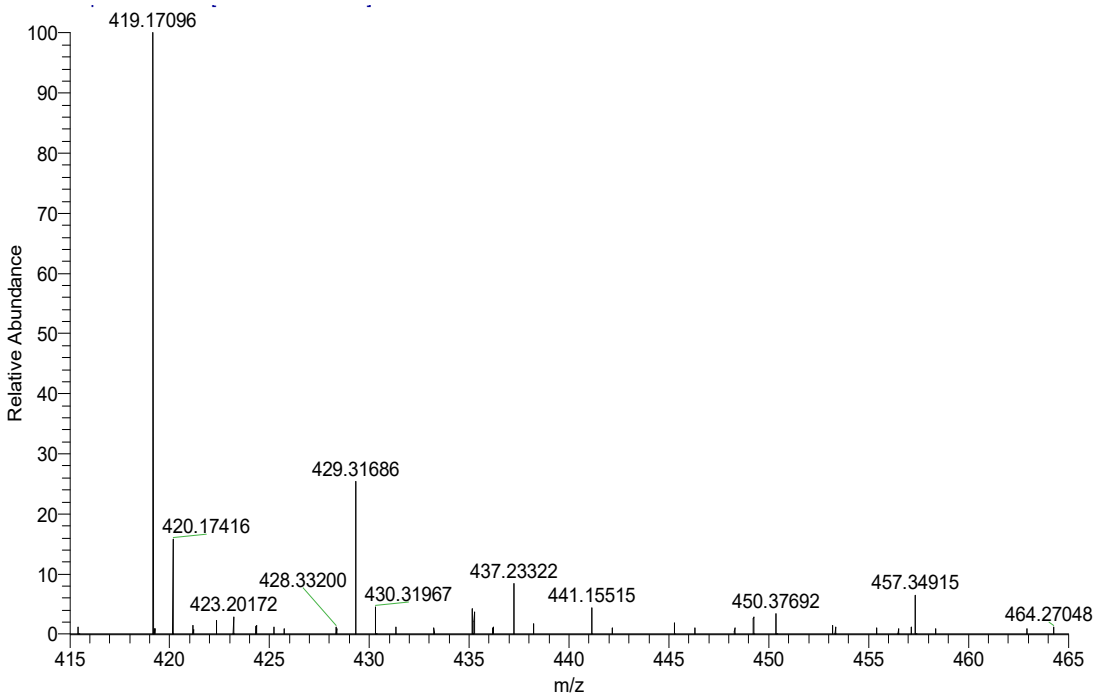
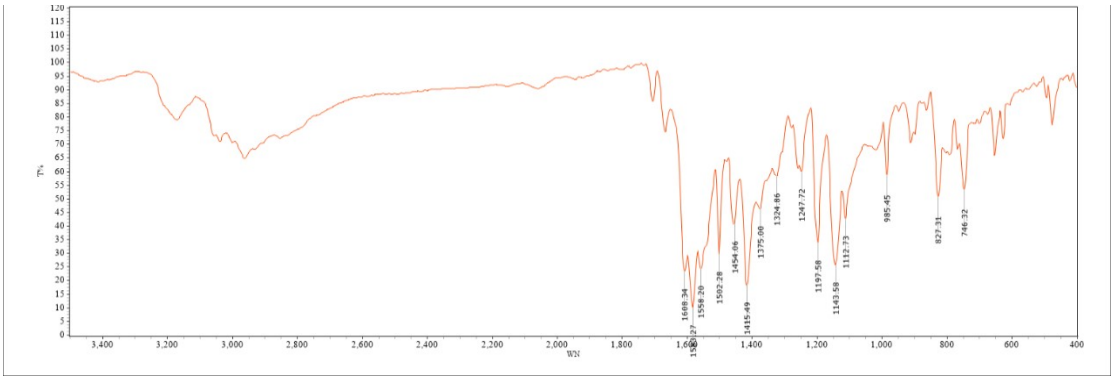


Figure S3 ESI-HRMS of **3a** at m/z 419.17096 for $C_{24}H_{18}N_8$ $[M+H]^+$.



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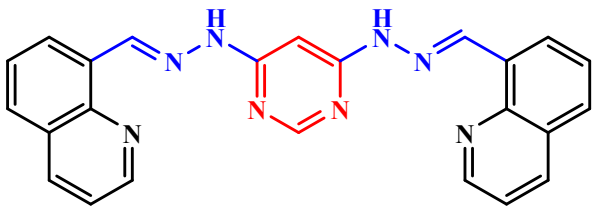


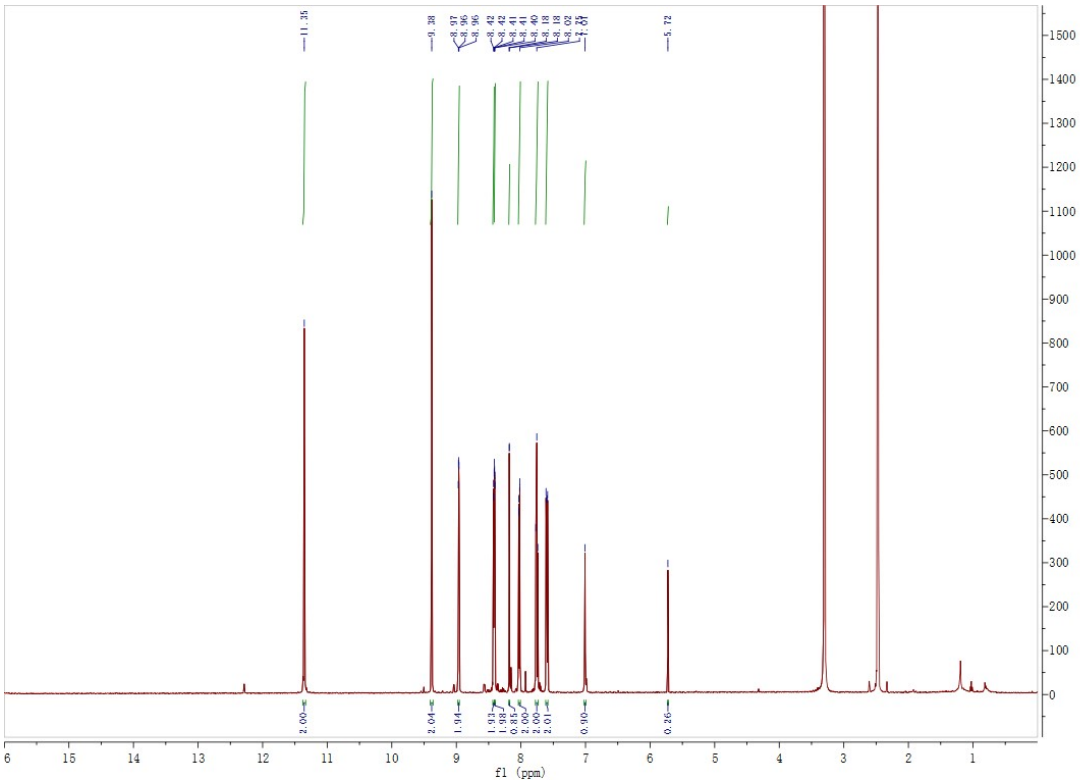


Figure S5 ^{1}H NMR spectrum of **3b** in DMSO-d6.

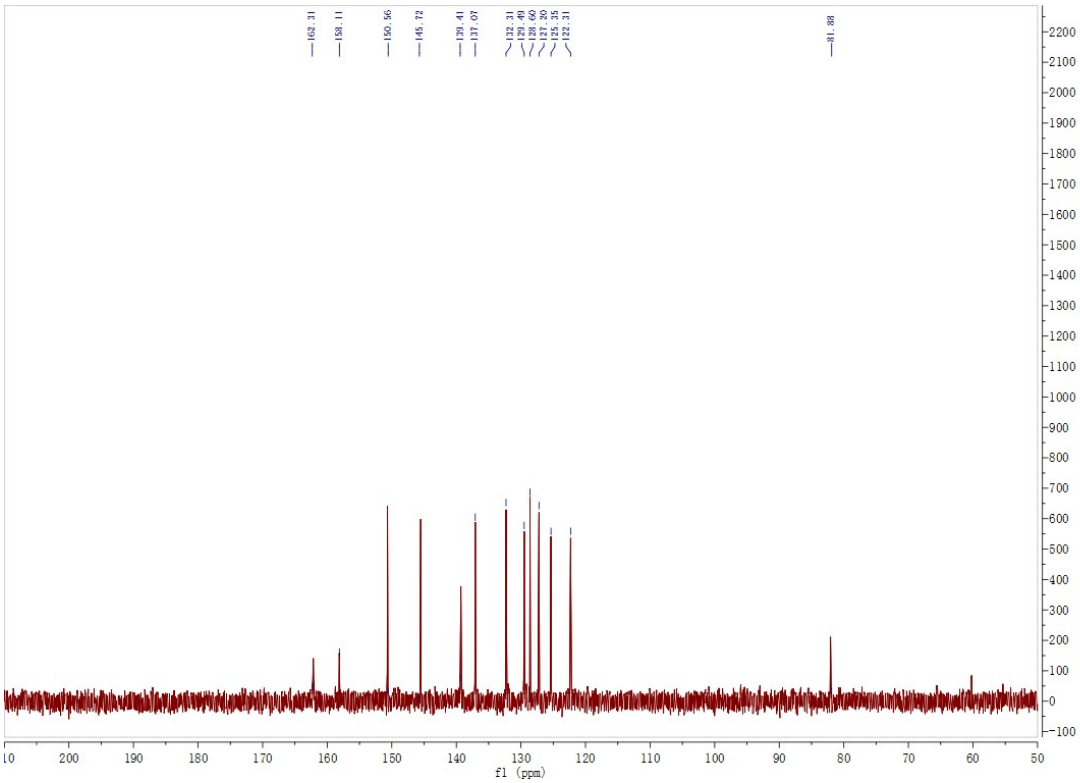


Figure S6 ^{13}C NMR spectrum of **3b** in DMSO-d6.

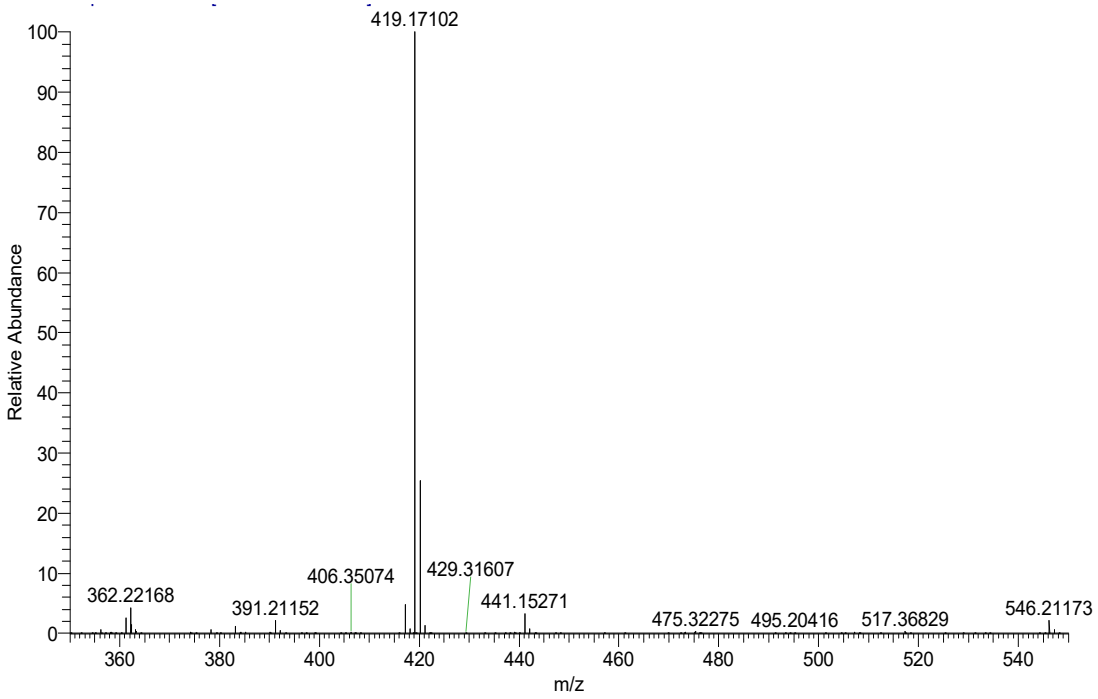


Figure S7 ESI-HRMS of **3b** at m/z 419.17102 for $C_{24}H_{18}N_8$ $[M+H]^+$.

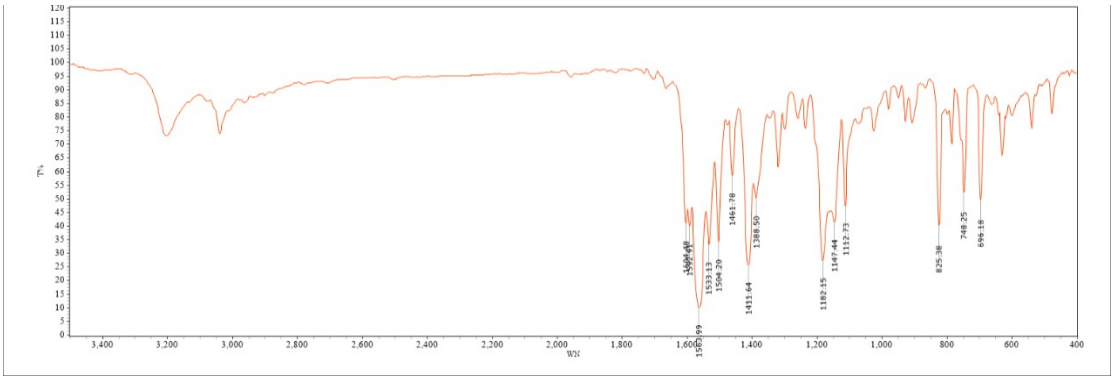
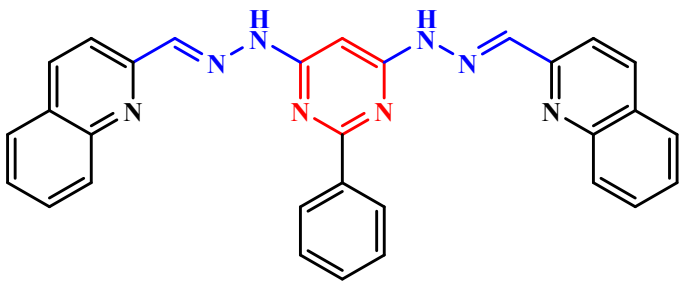


Figure S8 IR spectrum of **3b**.



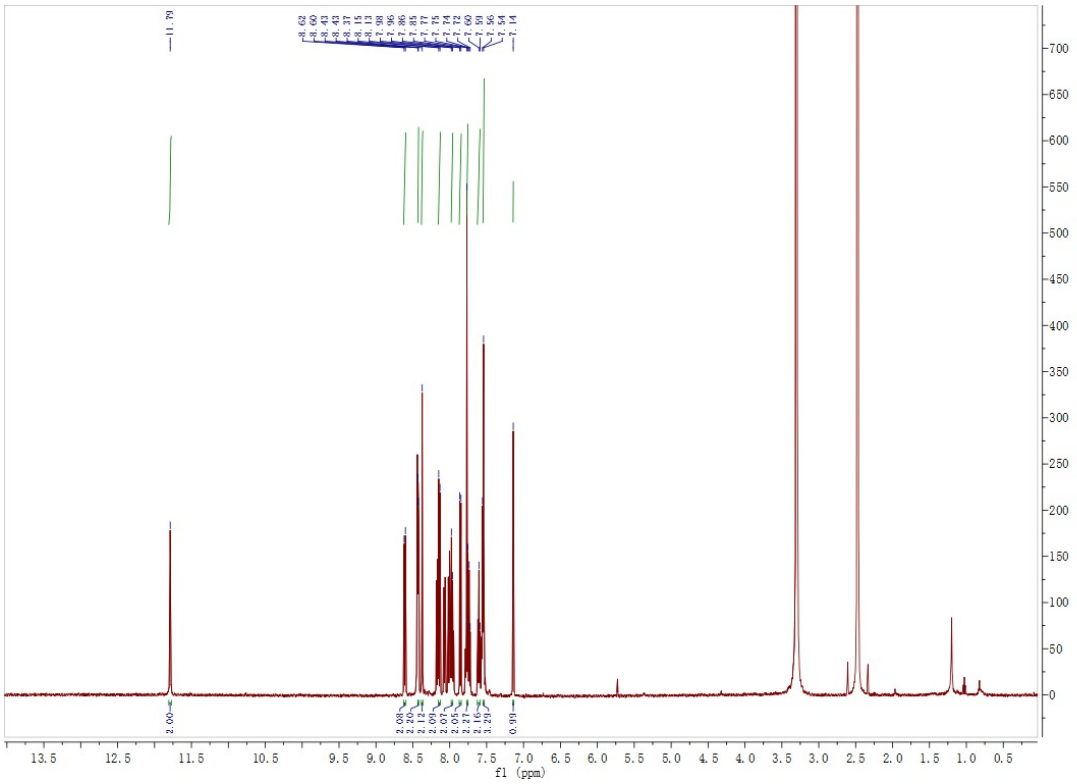


Figure S9 ^{1}H NMR spectrum of **3c** in DMSO-d6.

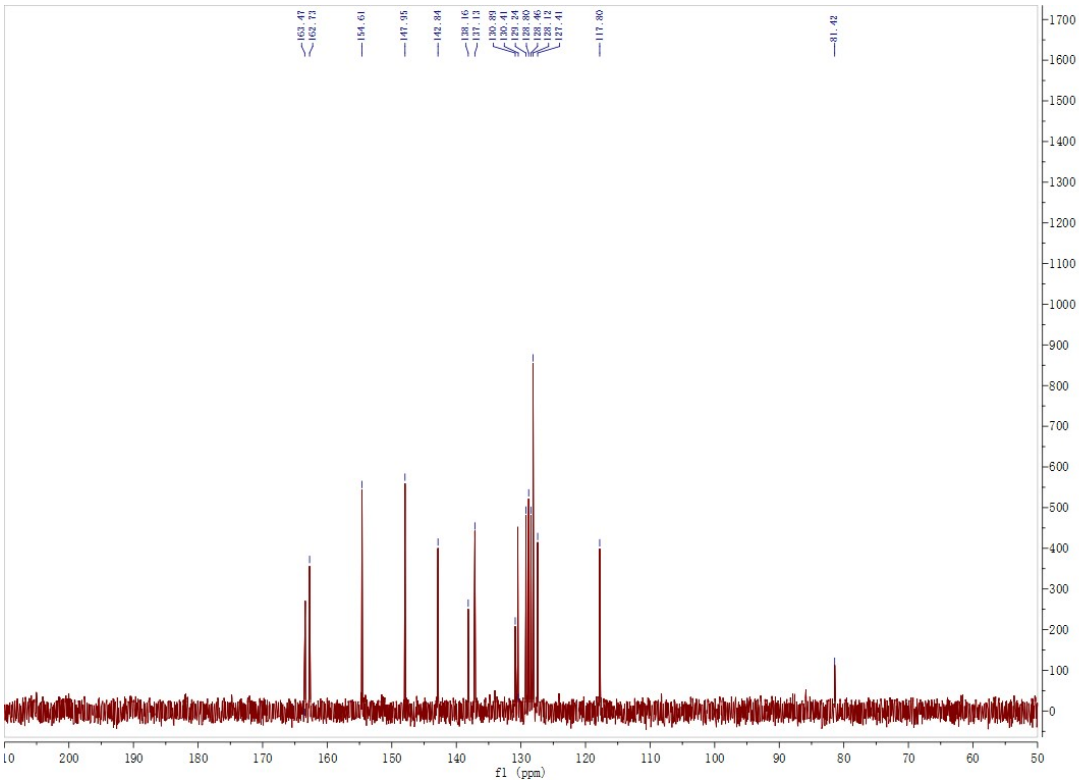


Figure S10 ^{13}C NMR spectrum of **3c** in DMSO-d6.

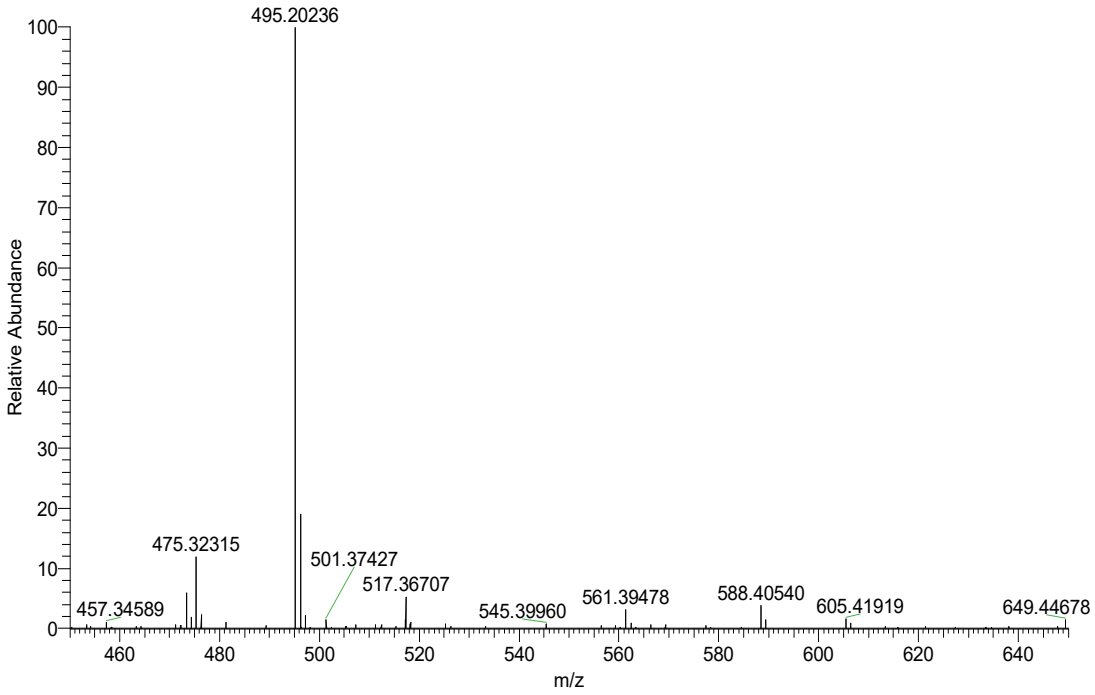


Figure S11 ESI-HRMS of **3c** at m/z 495.20236 for $C_{30}H_{22}N_8$ $[M+H]^+$.

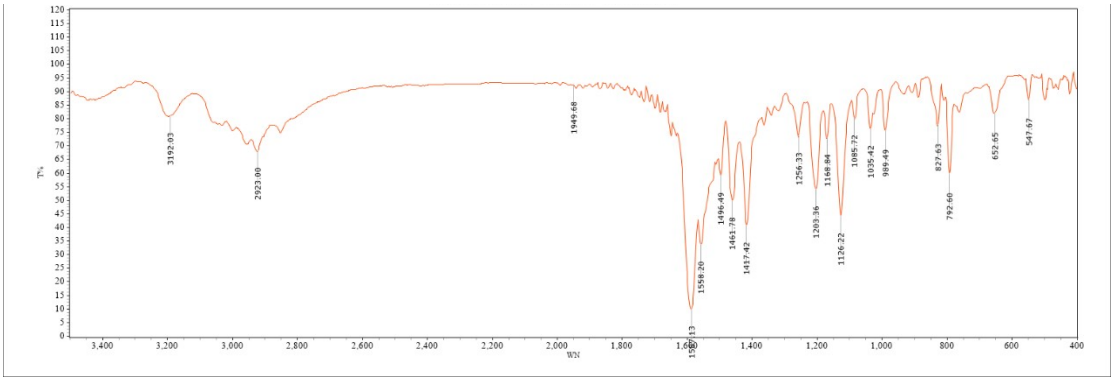
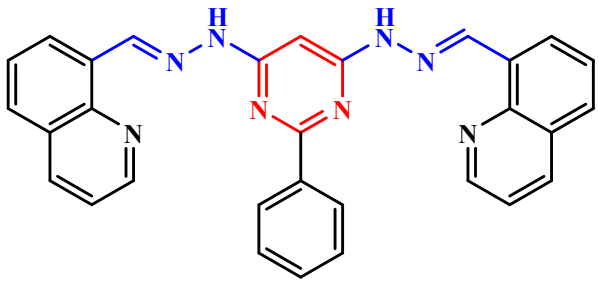


Figure S12 IR spectrum of **3c**.



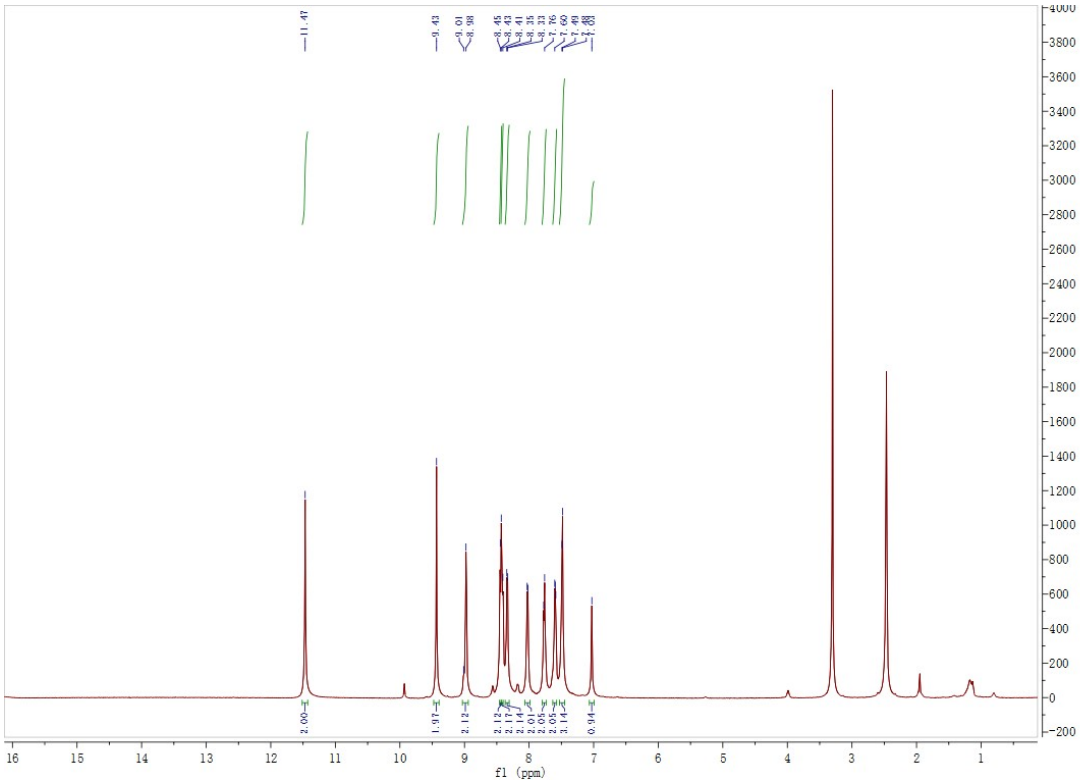


Figure S13 ^{1}H NMR spectrum of **3d** in DMSO-d6

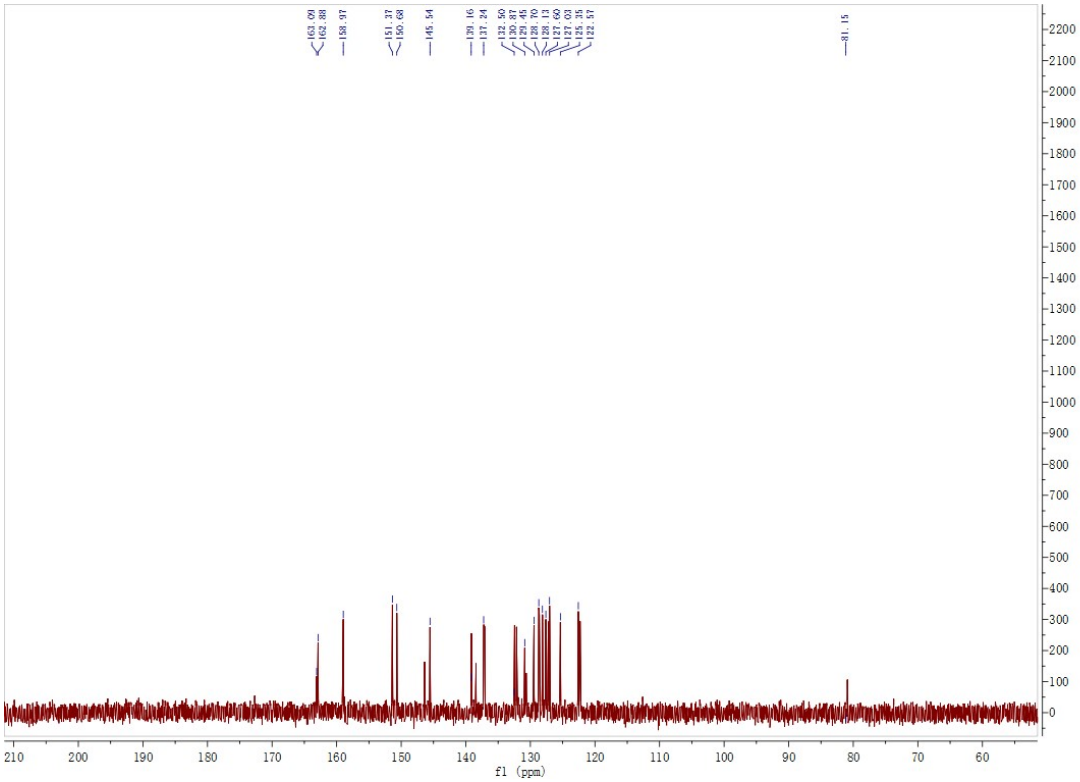


Figure S14 ^{13}C NMR spectrum of **3d** in DMSO-d6.

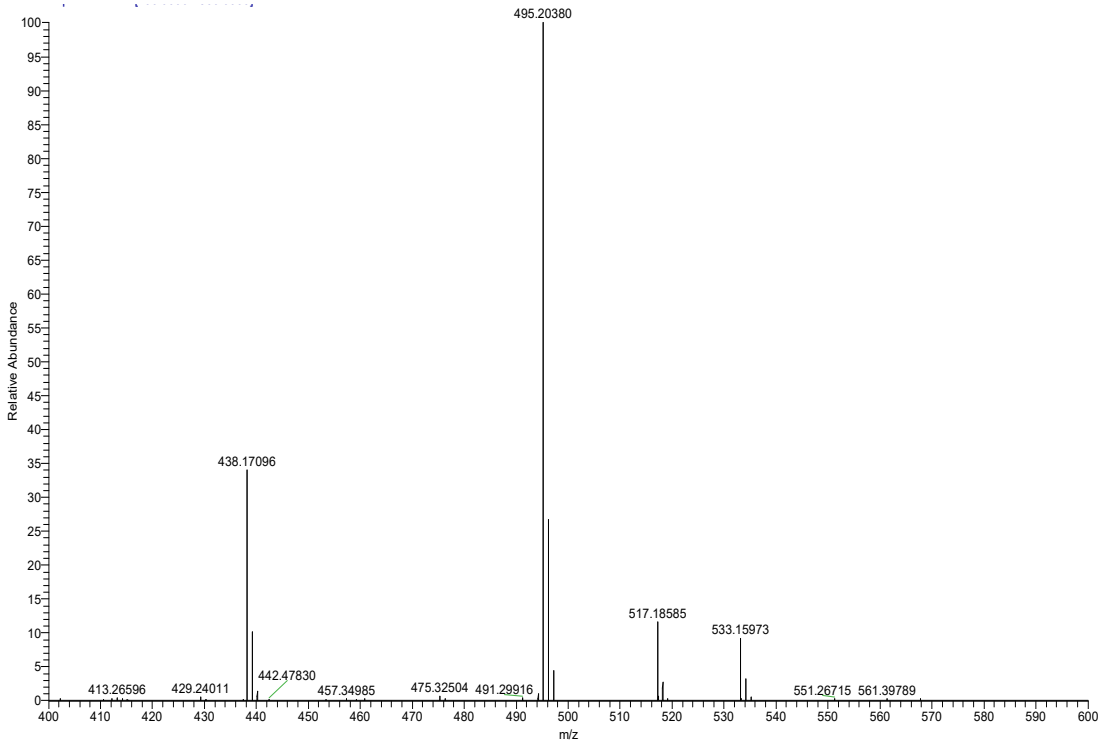


Figure S15 ESI-HRMS of **3d** atm/z 495.20380 for $C_{30}H_{22}N_8$ $[M+H]^+$.

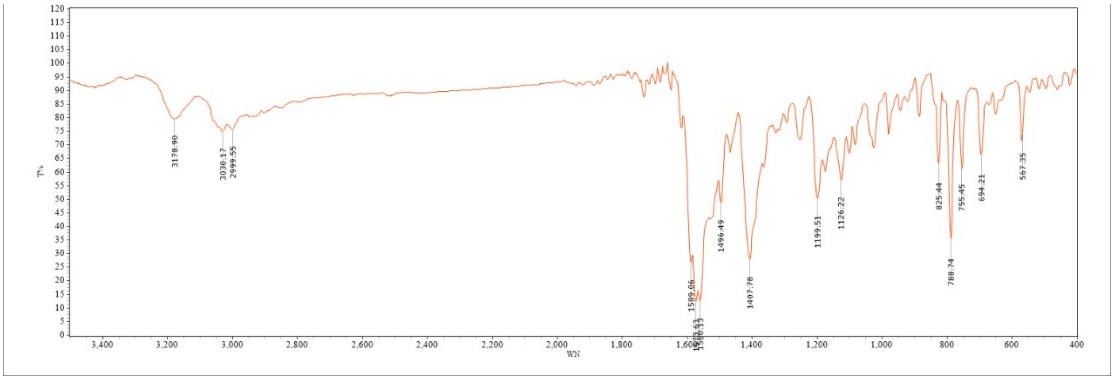


Figure S16 IR spectrum of **3d**.

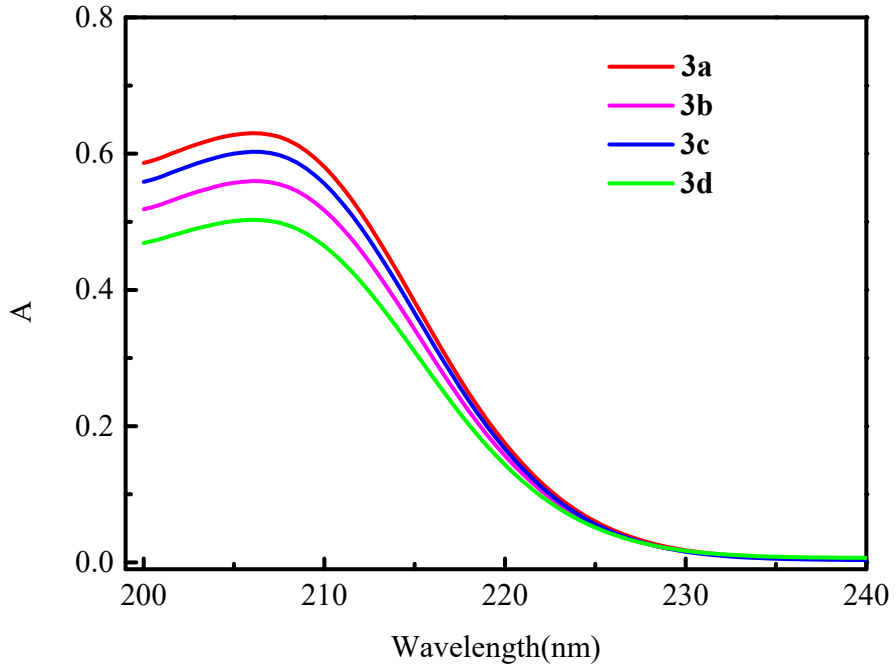


Figure S17 UV-vis spectra of **3a-3d**.

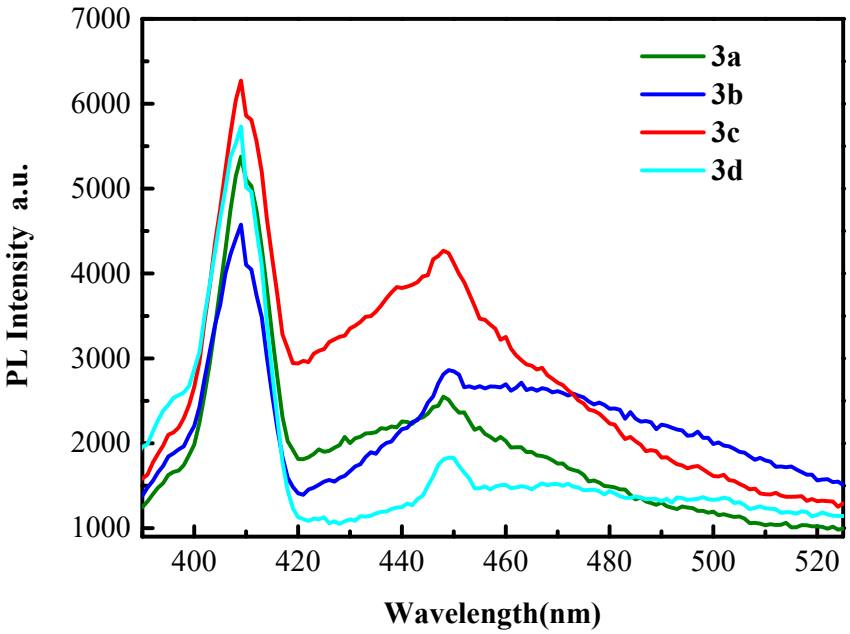


Figure S18 Fluorescence spectra of **3a-3d**.

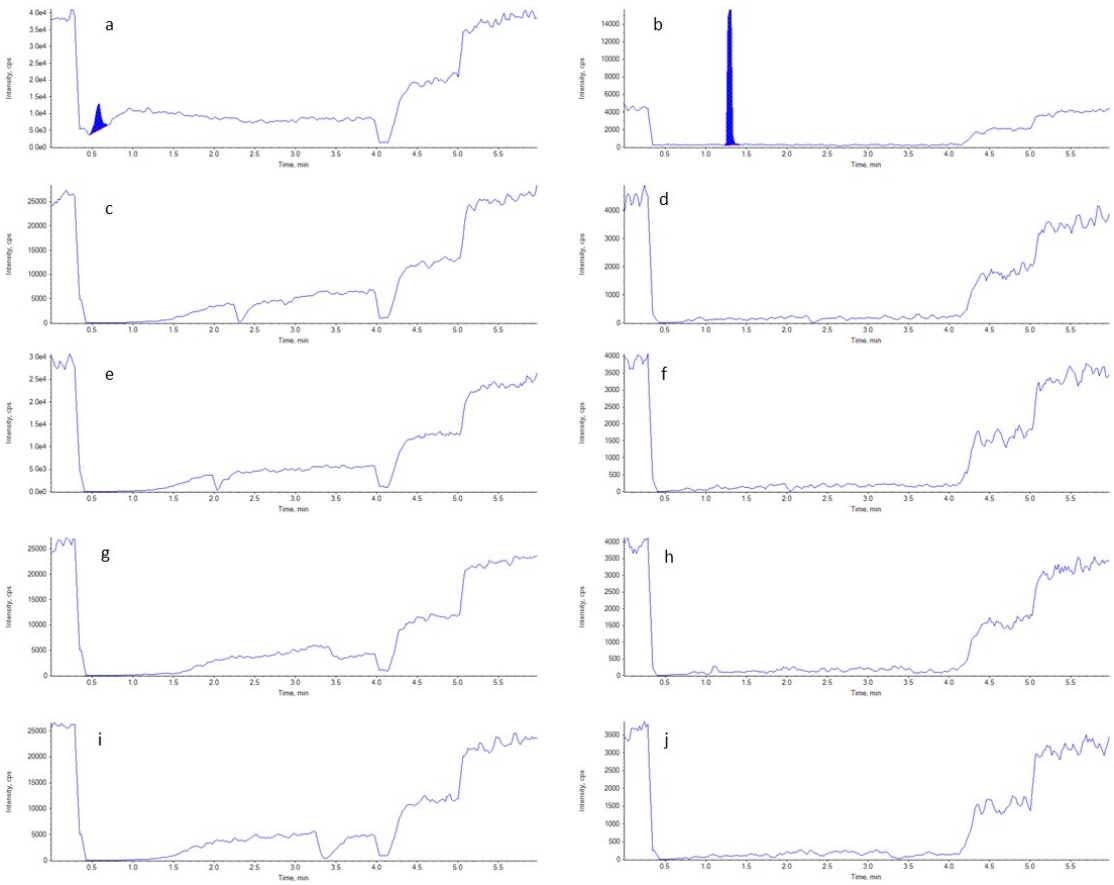


Figure S19. NDMA (a) and NDEA (b) represent the peaks on the chromatogram, as well as compound **3a** (c-d), **3b** (e-f), **3c** (g-h), **3d**(i-j) detection chromatograms. (NDMA: a, c, e, g, i; NDEA: b, d, f, h, j).

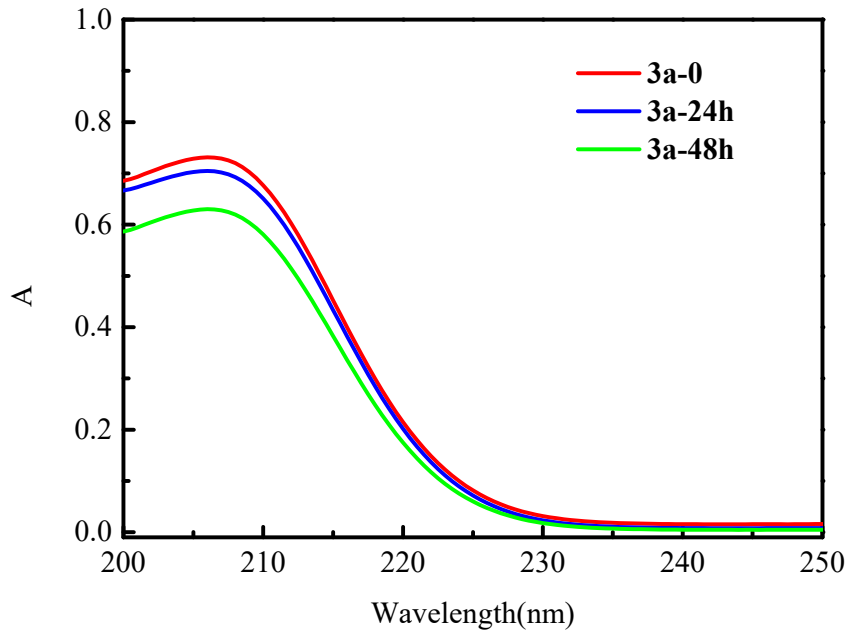


Figure S20 The UV-vis spectra of **3a** within 48 h in Tris-HCl buffer (pH 7.4).

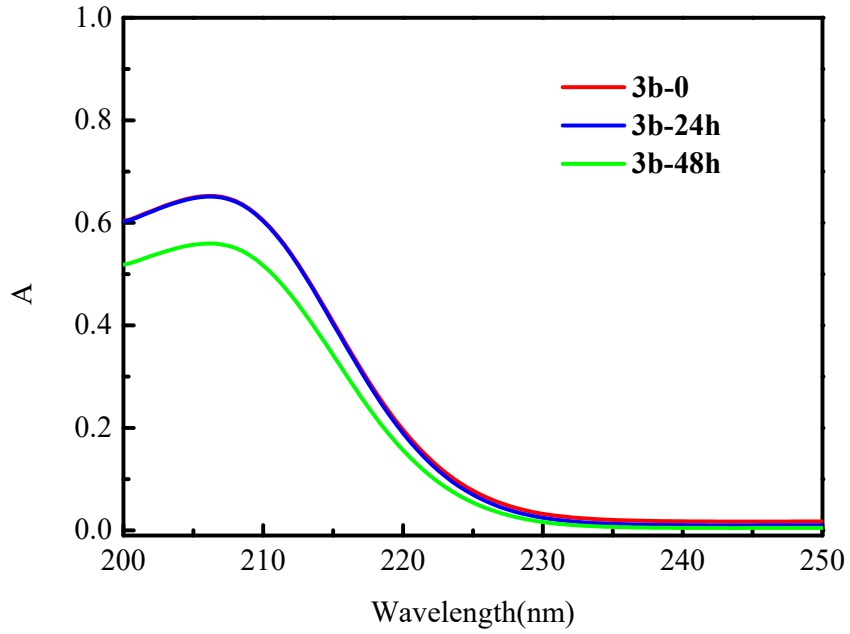


Figure S21 The UV-vis spectra of **3b** within 48 h in Tris-HCl buffer (pH 7.4).

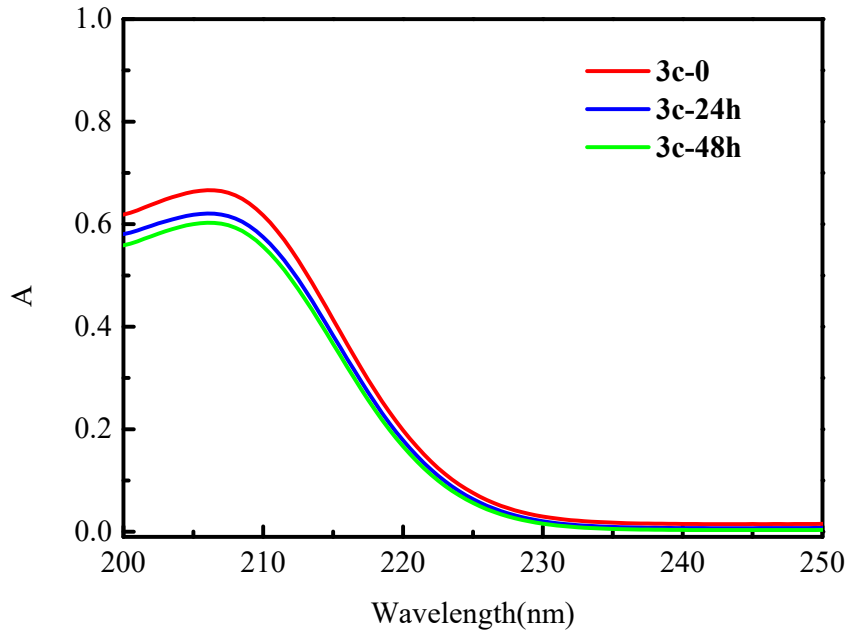


Figure S22 The UV-vis spectra of **3c** within 48 h in Tris-HCl buffer (pH 7.4).

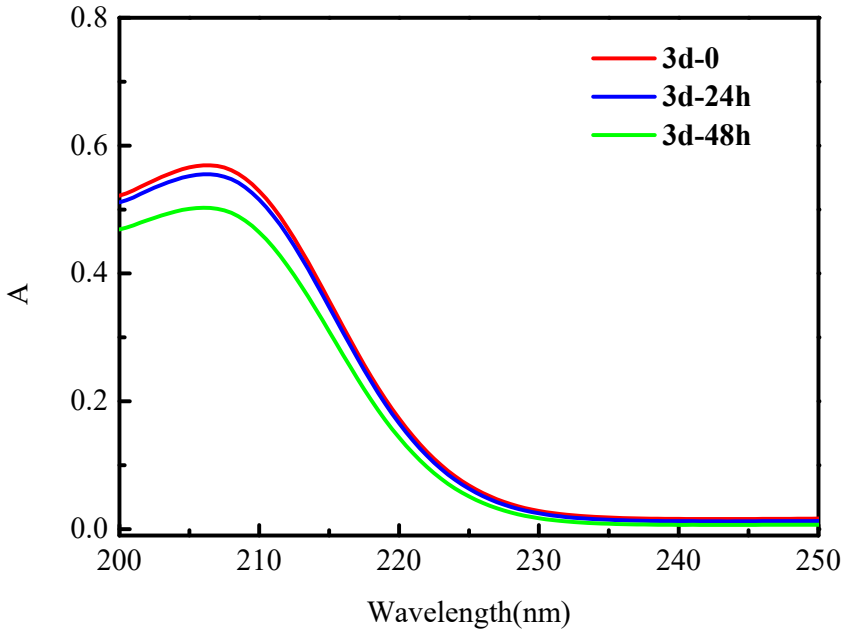


Figure S23 The UV-vis spectra of **3d** within 48 h in Tris-HCl buffer (pH 7.4).

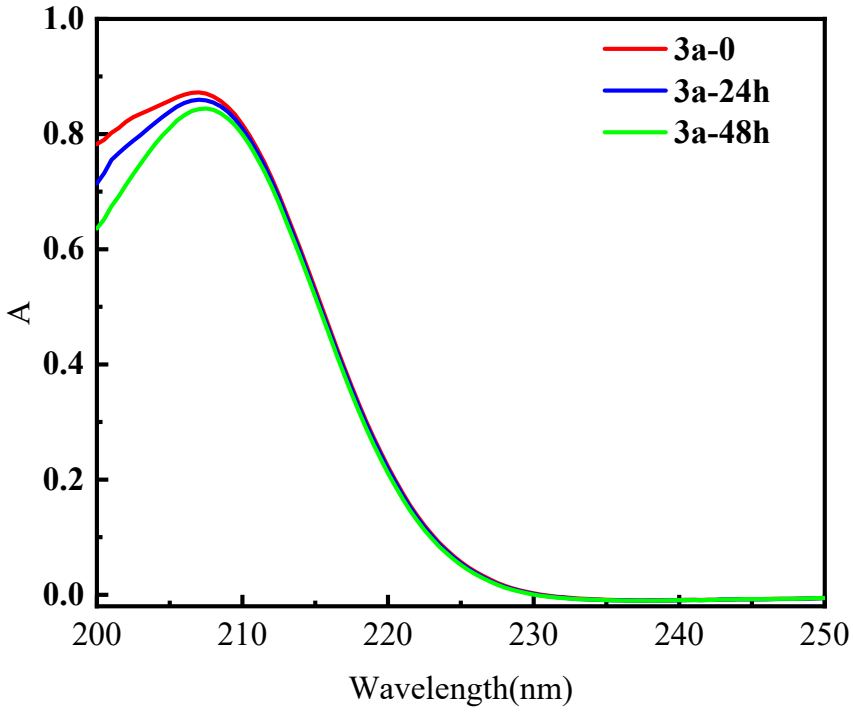


Figure S24 The UV-vis spectra of **3a** within 48 h in PBS buffer (pH 7.4).

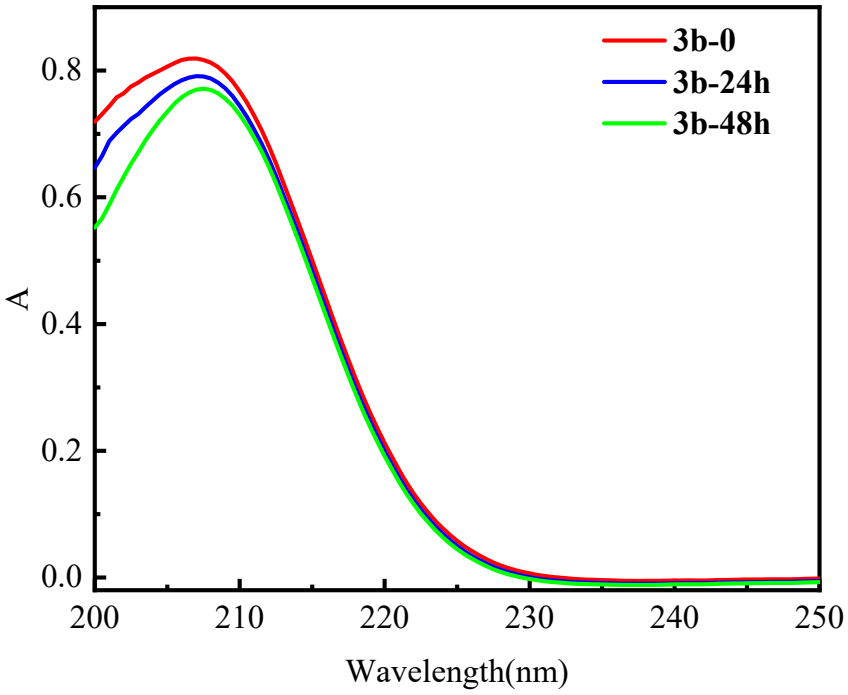


Figure S25 The UV-vis spectra of **3b** within 48 h in PBS buffer (pH 7.4).

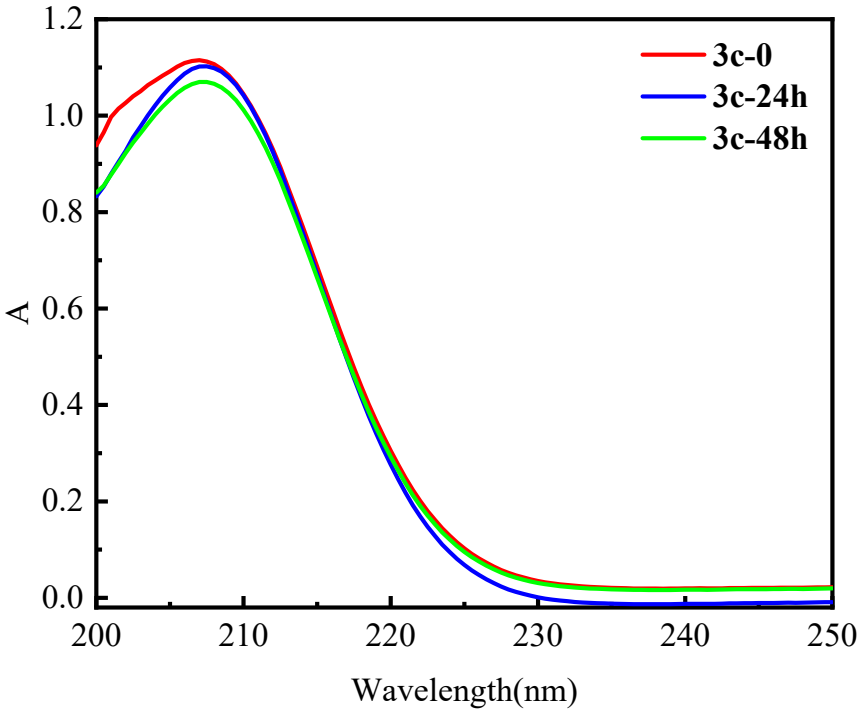


Figure S26 The UV-vis spectra of **3c** within 48 h in PBS buffer (pH 7.4).

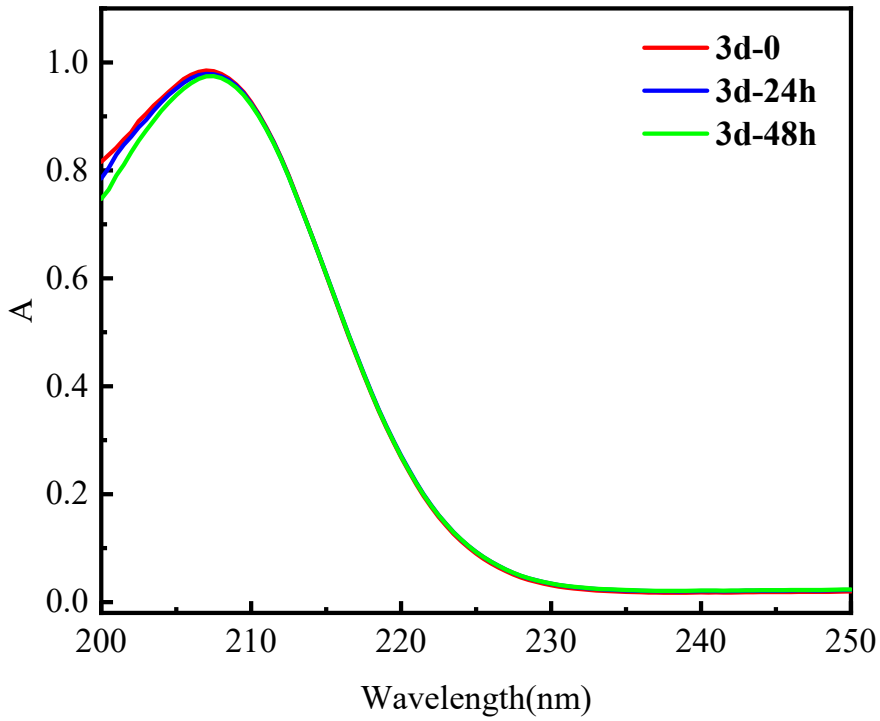


Figure S27 The UV-vis spectra of **3d** within 48 h in PBS buffer (pH 7.4).

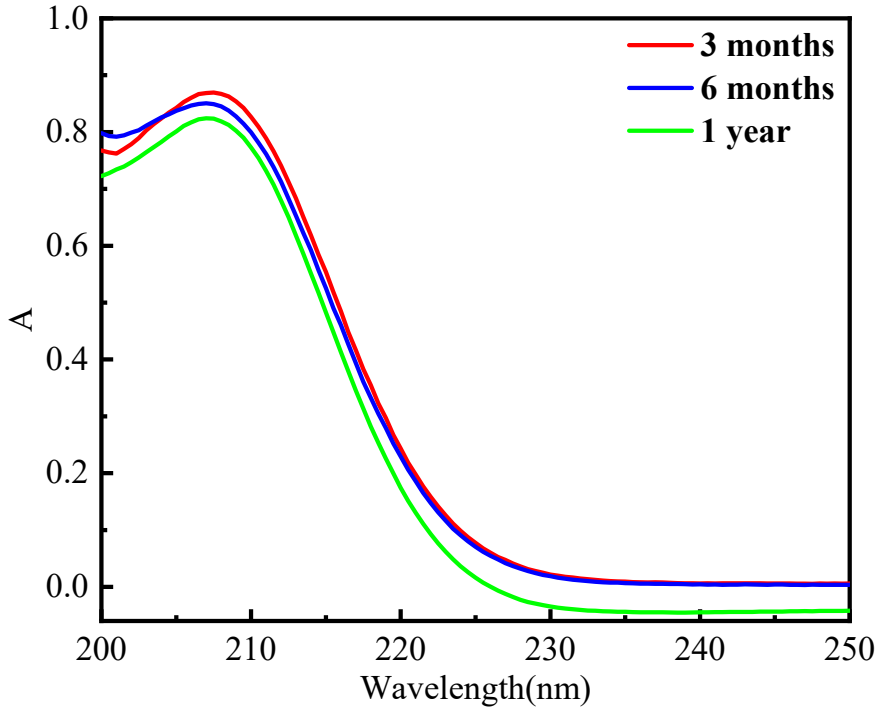


Figure S28 The UV-Vis spectra of **3a** in PBS buffer (pH 7.4) at 4°C

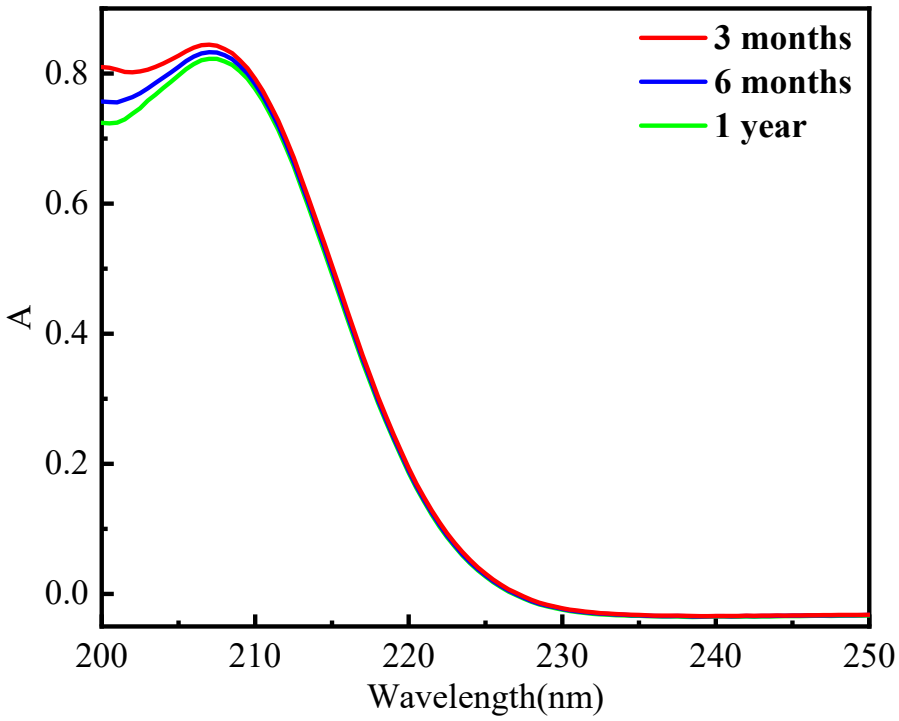


Figure S29 The UV-Vis spectra of **3b** in PBS buffer (pH 7.4) at 4°C

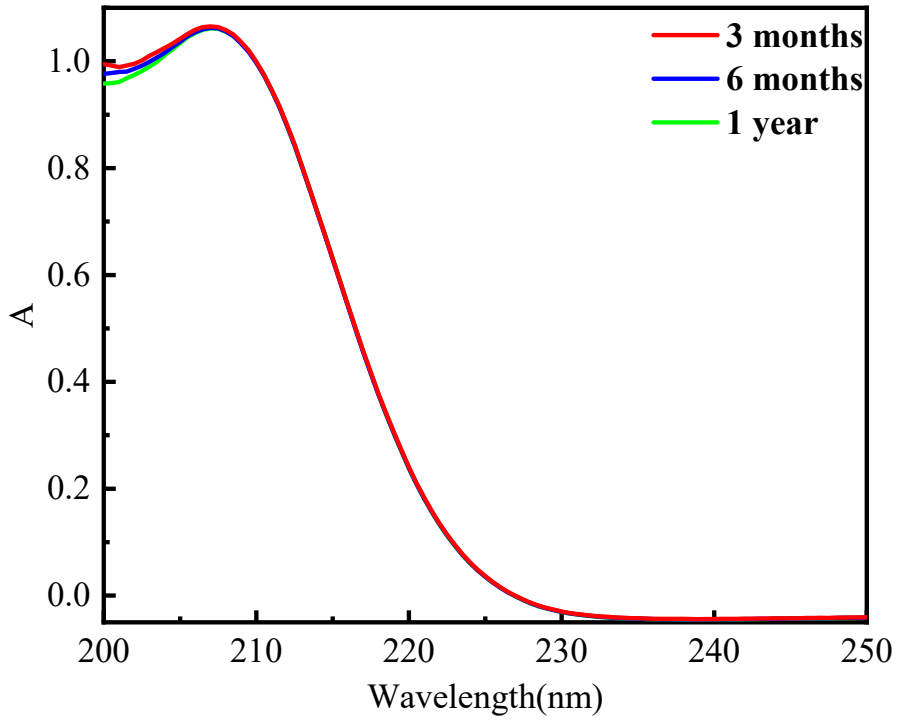


Figure S30 The UV-Vis spectra of **3c** in PBS buffer (pH 7.4) at 4°C

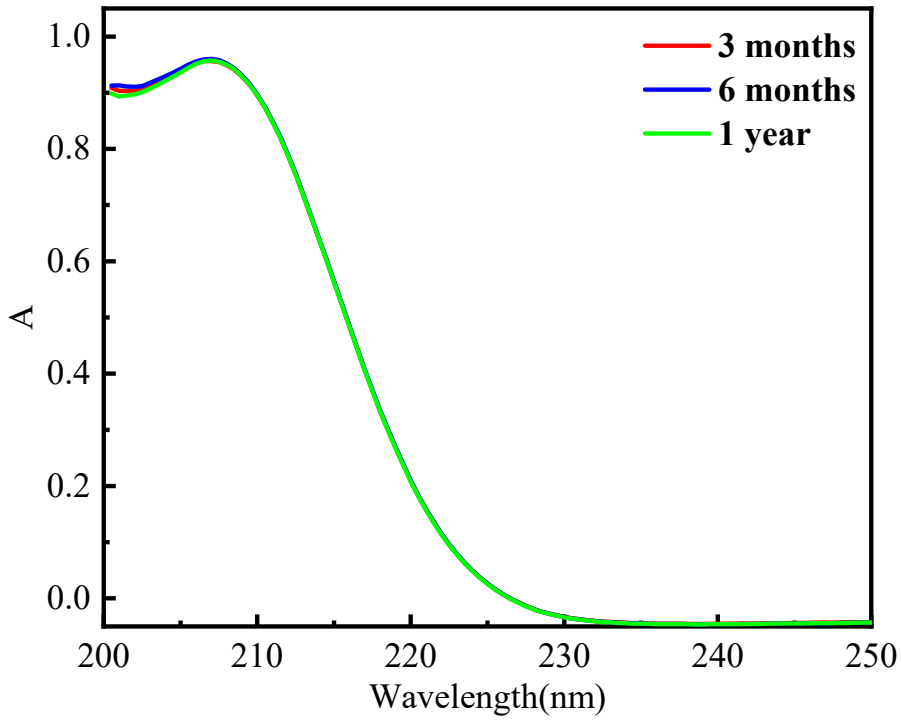


Figure S31 The UV-Vis spectra of **3d** in PBS buffer (pH 7.4) at 4°C

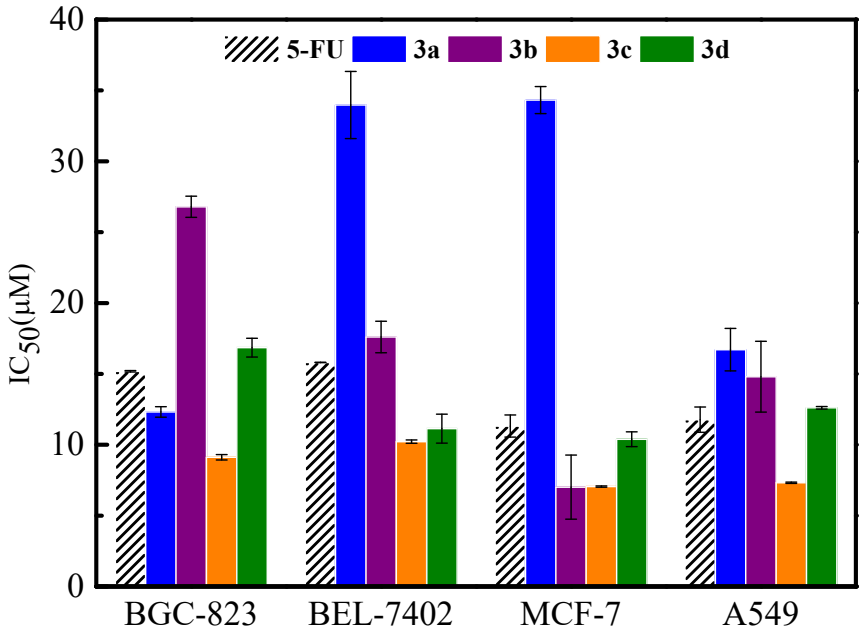
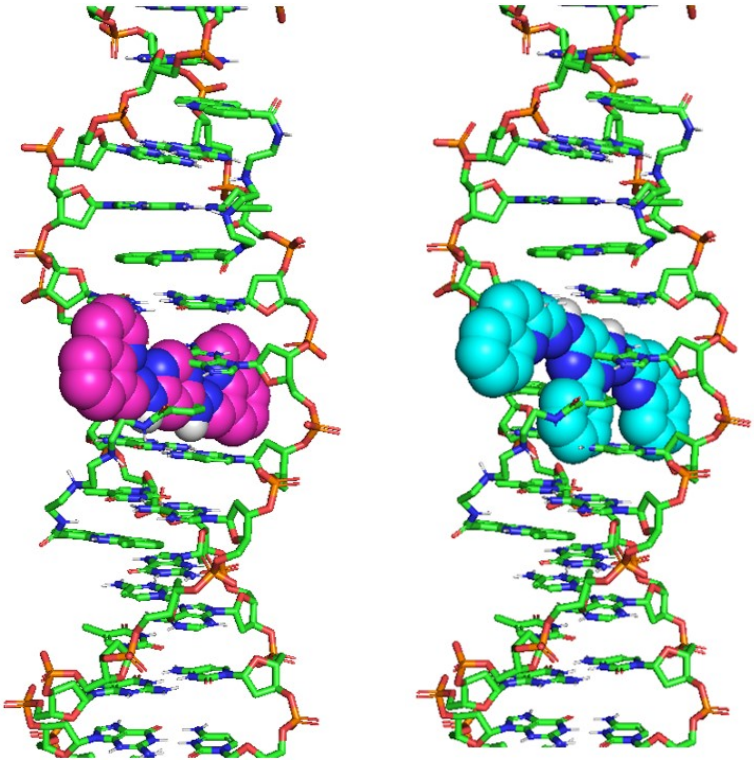


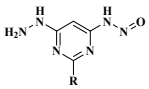
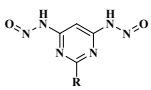
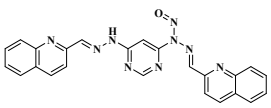
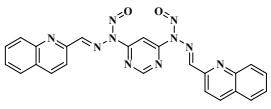
Figure S32 IC_{50} values of **3a-3d** against BGC-823, BEL-7402, A549 and MCF-7 cells for 48 h.



(a) **(b)**

Figure S33 Stacking-based visualizations of **(a) 3b** and **(b) 3c** docking with DNA (PDB ID: 2MG8).

Table S1. Summary of Potential Nitrosamine Impurities Risk Assessment in API.

Number	Impurity Name	Impurity structure	Recommended Daily Allowance(AI Value)	Validation testing (Yes or no)
1	NDMA		96 ng/day	Yes
2	NDEA		26.5 ng/day	Yes
3	N-Nitrosodimethylamine **2a** and **2b**		1500 ng/day	No
4	Dual N-nitrosyl **2a** and **2b**		1500 ng/day	No
5	N-Nitrosamine **3a**		1500 ng/day	No
6	Dual N-nitrosyl **3a**		1500 ng/day	No

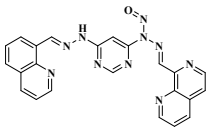
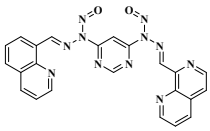
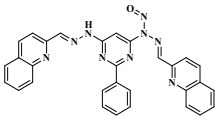
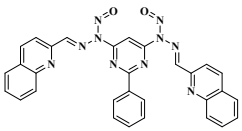
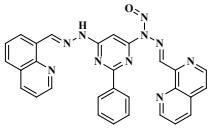
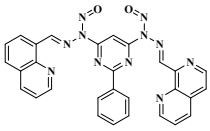
7	N-Nitrosamine **3b**		1500 ng/day	No
8	Dual N-nitrosyl **3b**		1500 ng/day	No
9	N-Nitrosamine **3c**		1500 ng/day	No
10	Dual N-nitrosyl **3c**		1500 ng/day	No
11	N-Nitrosamine **3d**		1500 ng/day	No
12	Dual N-nitrosyl **3d**		1500 ng/day	No

Table S2. The ΔG_b^θ of **3a-3d** interacting with CDK2 (PDB ID: 4BGH).

Compound	ΔG_b^θ (kcal/mol)
3a	−8.0
3b	−8.6
3c	−8.4
3d	−8.3

Table S3. The ΔG_b^θ of **3b and 3c** interacting with CDK1 (PDB ID: 6GU7).

Compound	ΔG_b^θ (kcal/mol)
3b	−9.2
3c	−9.6

Table S4. The ΔG_b^θ of **3b and 3c** interacting with CDK4 (PDB ID: 2W9Z).

Compound	ΔG_b^θ (kcal/mol)
3b	−7.3
3c	−7.8

Table S5. The ΔG_b^{θ} of **3b and 3c** interacting with CDK8 (PDB ID: 5I5Z).

Compound	ΔG_b^{θ} (kcal/mol)
3b	−9.6
3c	−10.9