

Supporting Information

Water tuned nano/micro-structures in redox-responsive supramolecular gel

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1. Instruments

^1H and ^{13}C NMR spectra were recorded on a JOEL JNM-ECA 300 or 400 spectrometer; Electrospray ionization mass spectrometry (ESI-MS) was obtained on Bruker ESQUIRE-LC spectrometer; High-resolution mass spectrometry (HRMS) was measured using quadrupole time-of-flight (Q-ToF) as mass analyzer in positive mode; Scanning electron microscopy (SEM) was performed on LEO-1530 instrument operating at accelerating voltages of 10 kV; Samples were placed on the glass and coated with gold before the measurement; Atomic Force Microscope (AFM) was recorded on a SPM-9600 (Shimadzu) in tapping mode; Samples were placed on the mica plate and dried in air before test; Transmission Electron Microscope (TEM) was acquired on Hitachi H-7650B instrument; The samples were prepared by drop-casting the hot solution of gel on the copper grid, and then dried in air; IR spectra were measured as KBr pellets with a Nicolet 360 FT-IR spectrometer; UV-Vis and fluorescence spectra were obtained on TU-1901 and Perkin Elmer LS55 Luminescence spectrometer, respectively; Circular dichroism (CD) spectra were carried on a Pistar π -180 instrument (Applied Photophysics Ltd) with a 150 w xenon lamp as the light source; X-ray diffraction (XRD) was performed on a Rigaku D/max 2500v X-ray diffractometer with CuK α radiation ($\lambda=1.5406 \text{ \AA}$), operating at 45 kV, 100 mA; Rheological measurements were characterized with a TA-AR2000ex rheometer with a 8 mm diameter parallel plate geometry at 25 °C.

2.

entry	solvent	state ^a
1	CHCl ₃	S
2	CH ₃ OH	I
3	CH ₃ CN	P
4	acetone	P
5	isopropanol	I
6	dioxane	P
7	toluene	S
8	o-dichlorobenzene	S
9	THF	S
10	DMSO	PG
11	DMF	S
12	DMF/H ₂ O	G

^a S = soluble; I= insoluble; P =precipitate; PG = partical gel; G = stable gel.

Table S1 The gelation behavior of **1** in various organic solvents.

3.

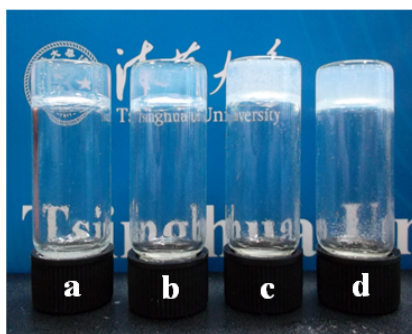


Figure S1 Optical images of gels formed by **1** (10 mg/mL) in different DMF/H₂O (v/v) ratio: (a) 20:1; (b) 10:1; (c) 6:1; (d) 5:1.

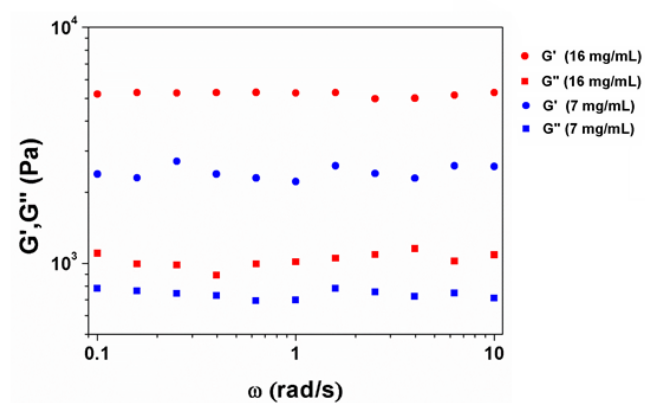


Figure S2 Evolution of G' and G'' as functions of the angle frequency of **1** in DMF/H₂O (10:1, v/v) under different concentration

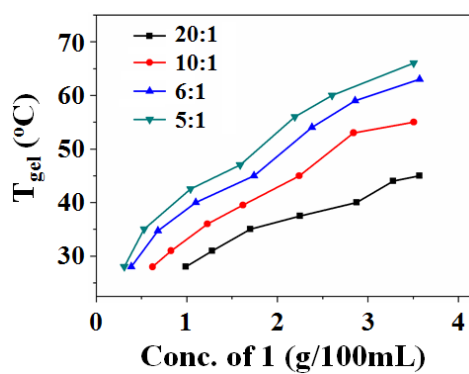


Figure S3 Plots of T_{gel} against the concentration of **1** in different DMF/H₂O (v/v) ratio.

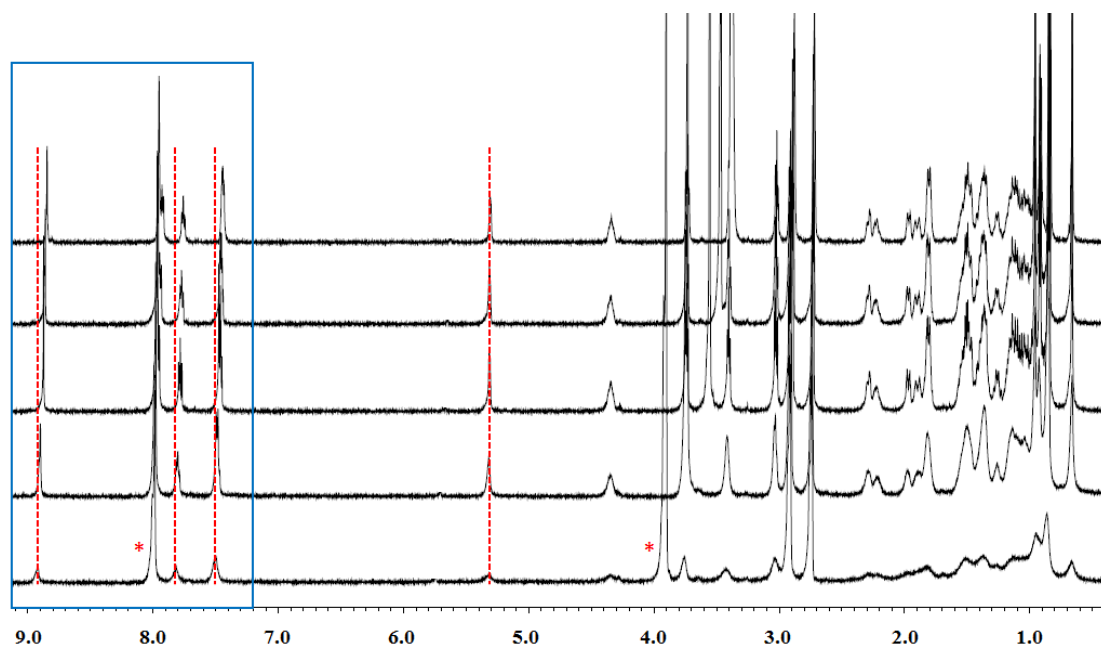


Figure S4 Temperature-dependent ^1H NMR (600MHz) of **1** (10 mg/mL) in DMF- d_7 /D $_2$ O (10:1, v/v), * indicates the signal of solvents.

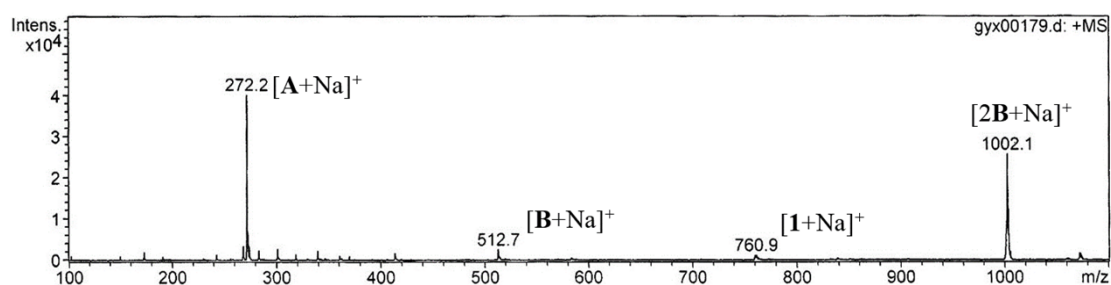
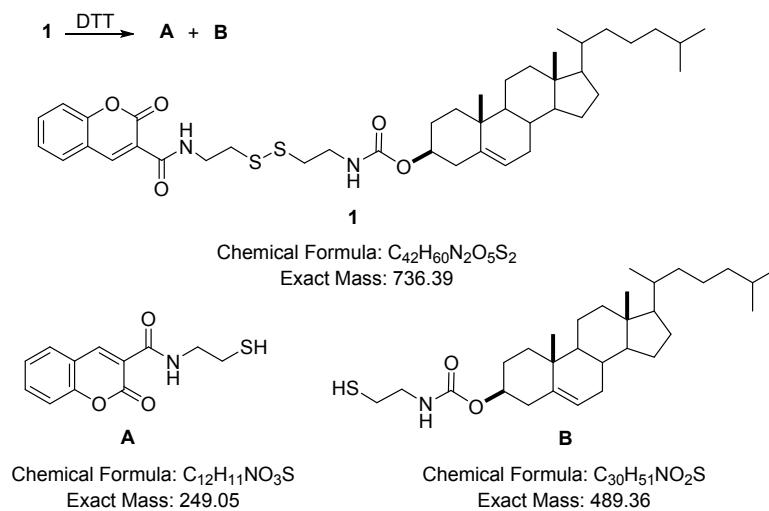


Figure S5 ESI-MS spectrum of the gel from **1** in DMF/H $_2$ O (10:1, v/v) after DTT reduction. The disulfide bond of compound **1** was cleaved by DTT to form two sulfhydryl compounds A and B. Structures are provided below:

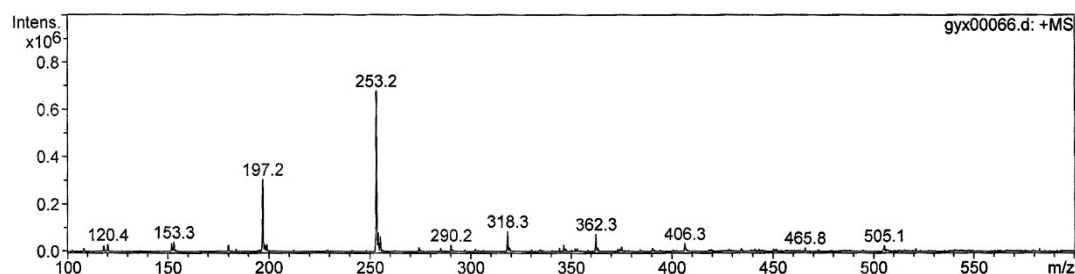


4. Synthesis and structure characterization of gelator 1

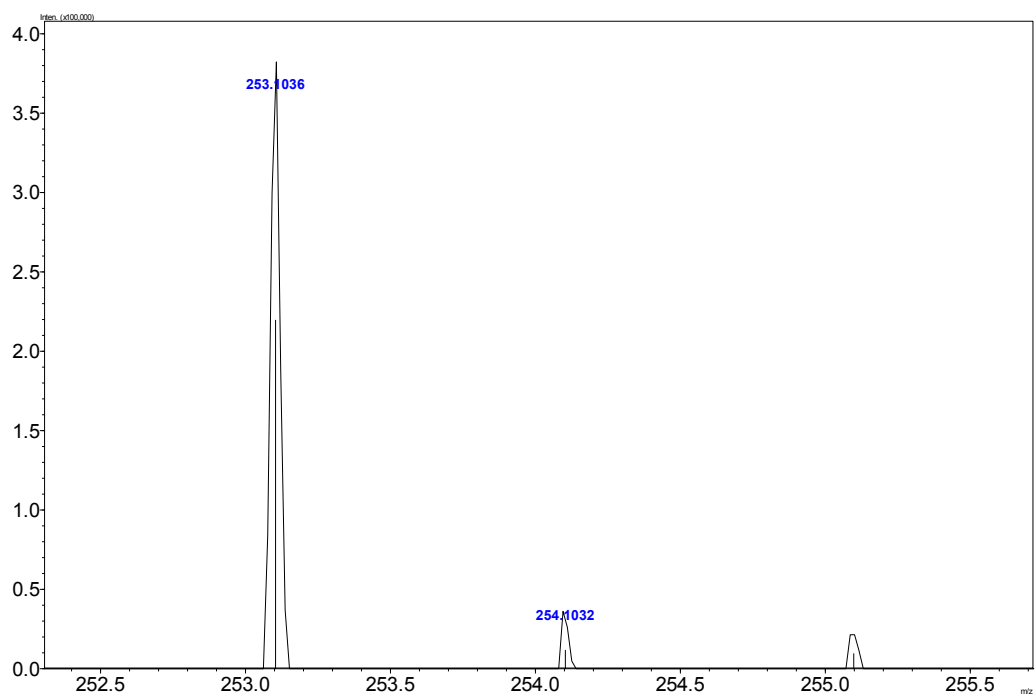
Compound 2

The solution of Boc₂O (2.18 g, 10 mmol) in CH₃OH (10 mL) was added dropwise to a solution of triethylamine (4.5 mL, 31 mmol) and cystamine dihydrochloride (2.25 g, 10 mmol) in CH₃OH (25 mL) in 20 minutes.¹ The reaction mixture was stirred at room temperature for 5 h, and then the solvent was evaporated. The residue was dissolved in 25 mL KH₂PO₄ (1 mol/L) to make pH 4.27, then washed by ether (3×30 mL). The water phase was regulated with NaOH aqueous (1 mol/L) until the pH reached 9, and then extracted with ethyl acetate (3×30 mL). The organic layer was combined and dried over anhydrous sodium sulfate. After the filtration and evaporation, a yellow oily liquid was obtained (951mg, yield 38 %). ESI-MS (+): 253.2 [M+H]⁺; HRMS (ESI): m/z [M+H]⁺ calcd. for C₉H₂₀N₂O₂S₂: 253.1039, found 253.1036 [M+H]⁺; ¹H NMR (400 MHz, CDCl₃): 5.42 (broad, H, NH₂Boc), 3.27 (d, 2H, -CH₂-NH₂Boc, *J* = 5.5 Hz), 2.86 (t, 2H, NH₂-CH₂, *J* = 6.4 Hz), 2.64, 2.63, 2.61 (t, 4H, 2×S-CH₂, *J* = 6.4 Hz), 1.95 (broad, 2H, -CH₂-NH₂), 1.27 (s, 9H, 3×-CH₃); ¹³C NMR (100 MHz, CDCl₃): 155.87 (O=C-NH), 77.69 (-C(CH₃)₃), 41.91 (NH₂Boc-CH₂), 40.34 (NH₂-CH₂-CH₂-S-), 39.35 (NH₂Boc-CH₂-CH₂), 38.29 (NH₂-CH₂), 28.40 (-CH₃).

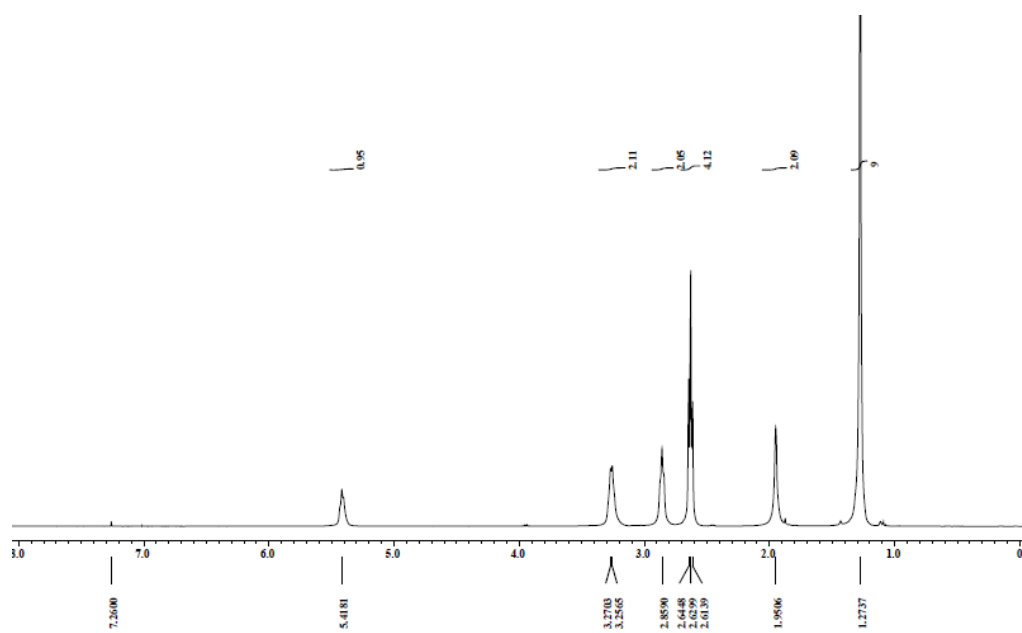
(1) ESI-MS (+) spectrum of compound 2



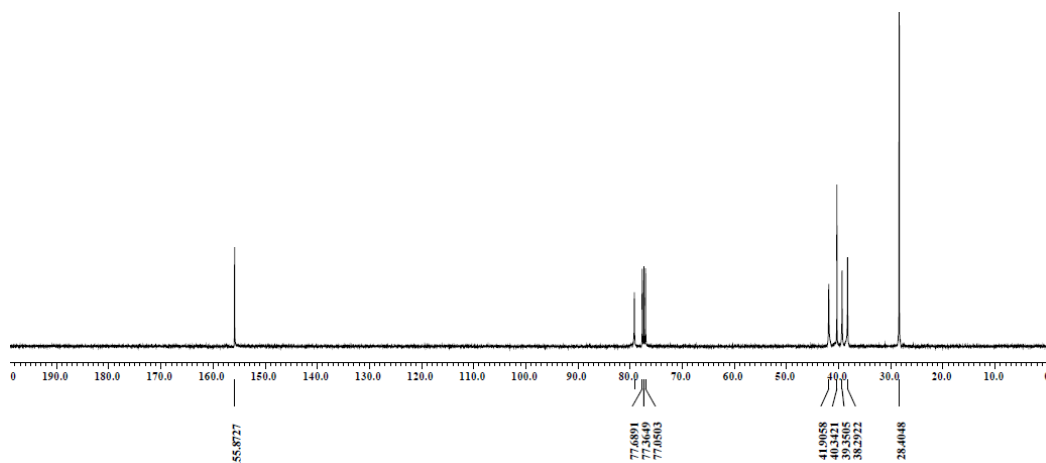
(2) HRMS (ESI) spectrum of compound 2



(3) ^1H NMR spectrum of compound **2** (400 MHz, CDCl_3)



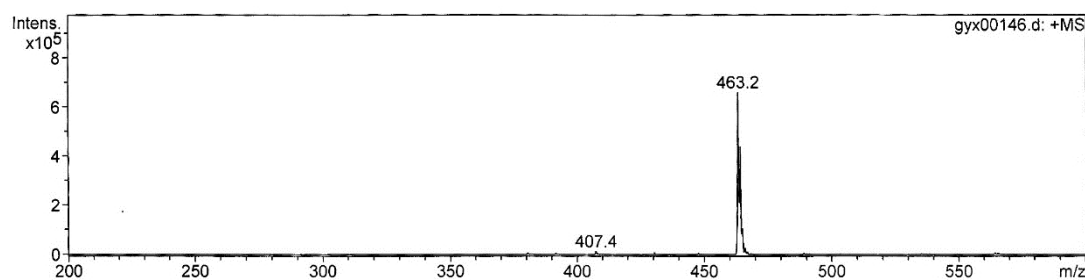
(4) ^{13}C NMR spectrum of compound **2** (100 MHz, CDCl_3)



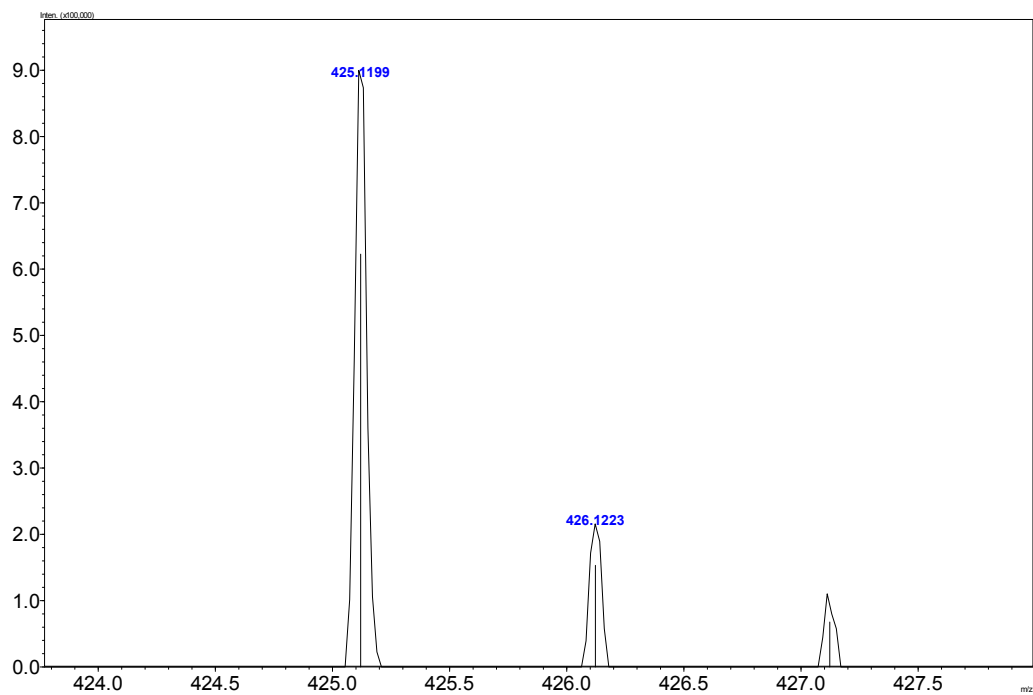
Compound 3

Thionyl chloride (1 mL, 13.8 mmol) was added to a solution of coumarin-3-carboxylic acid (285 mg, 1.50 mmol) in CH_2Cl_2 , then the mixture refluxed at 40 °C for 8 h. Acyl chloride (light yellow solid) was obtained after evaporating the solvent and unreacted thionyl chloride. Triethylamine (0.5 mL, 3.4 mmol) was added to a solution of **2** (378 mg, 1.50 mmol) in dry CH_2Cl_2 , then the dilution solution of acyl chloride in 10 mL CH_2Cl_2 was added dropwise at 0°C. The mixture was stirred at room temperature for 12 h, then washed with water and brine water, the organic layer was dried over anhydrous sodium sulfate. After filtration and evaporation, the crude product was purified by chromatography (CH_2Cl_2 : CH_3OH =100:1) to give compound **3** as a white solid (550 mg, 87 %). ESI-MS (+): 463.2 $[\text{M}+\text{K}]^+$; HRMS (ESI): m/z $[\text{M}+\text{H}]^+$ calcd. for $\text{C}_{19}\text{H}_{24}\text{N}_2\text{O}_5\text{S}_2$: 425.1199, found 425.1199 $[\text{M}+\text{H}]^+$; ^1H NMR (300 MHz, CDCl_3): 9.06 (broad, H, $\text{NH}(\text{Boc})$), 8.87 (s, H, Coumarin-4- CH), 7.65, 7.38 (t, t, 4H, Ar-H), 5.13 (broad, H, Coumarin-3-CO-NH), 3.75 (q, 2H, Coumarin-3-CO-NH- CH_2 , $J = 6.5$ Hz), 3.42 (q, 2H, $\text{NH}(\text{Boc})$ - CH_2 , $J = 6.2$ Hz), 2.90 (t, 2H, Coumarin-3-CO-NH- CH_2 - CH_2 -S-, $J = 6.5$ Hz), 2.80 (t, 2H, -S- CH_2 - CH_2 - $\text{NH}(\text{Boc})$, $J = 6.2$ Hz), 1.40 (s, 9H, $3 \times$ - CH_3); ^{13}C NMR (75 MHz, CDCl_3): 161.83 (Coumarin-2- $\text{C}=\text{O}$), 161.43 (Coumarin-3- CO -NH-), 155.88 ($\text{C}(\text{CH}_3)_3$ -O- $\text{C}=\text{O}$), 154.51, 148.57, 134.26, 129.92, 125.42, 118.33 (Ar- C -), 118.66 (Coumarin-4- CH), 116.73 (Coumarin-3- C), 79.46 ($\text{C}(\text{CH}_3)_3$), 39.38, 38.89, 38.72, 37.44 ($4 \times$ - CH_2), 28.48 (- CH_3).

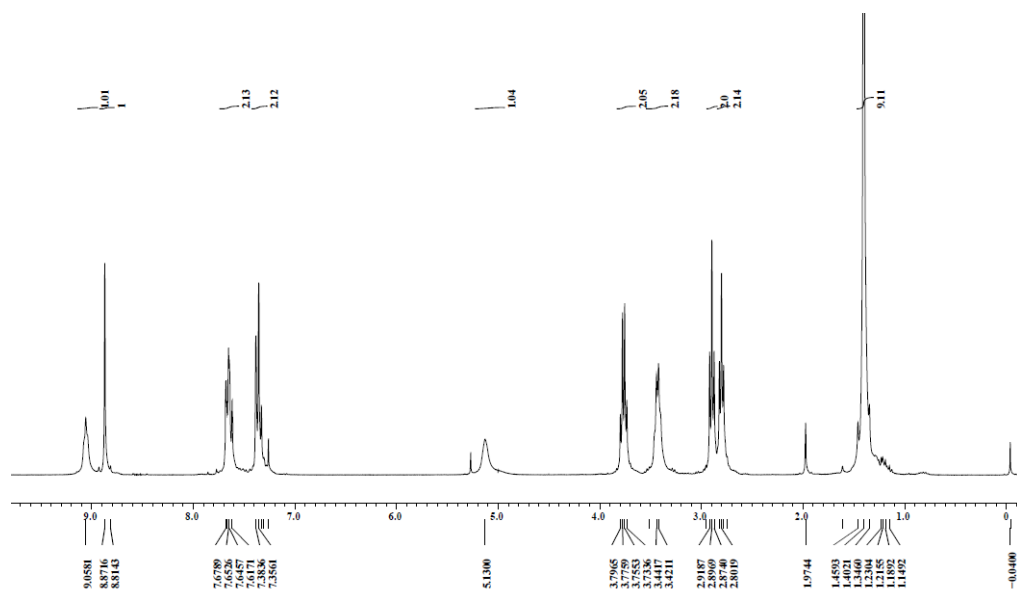
(1) ESI-MS (+) spectrum of compound 3



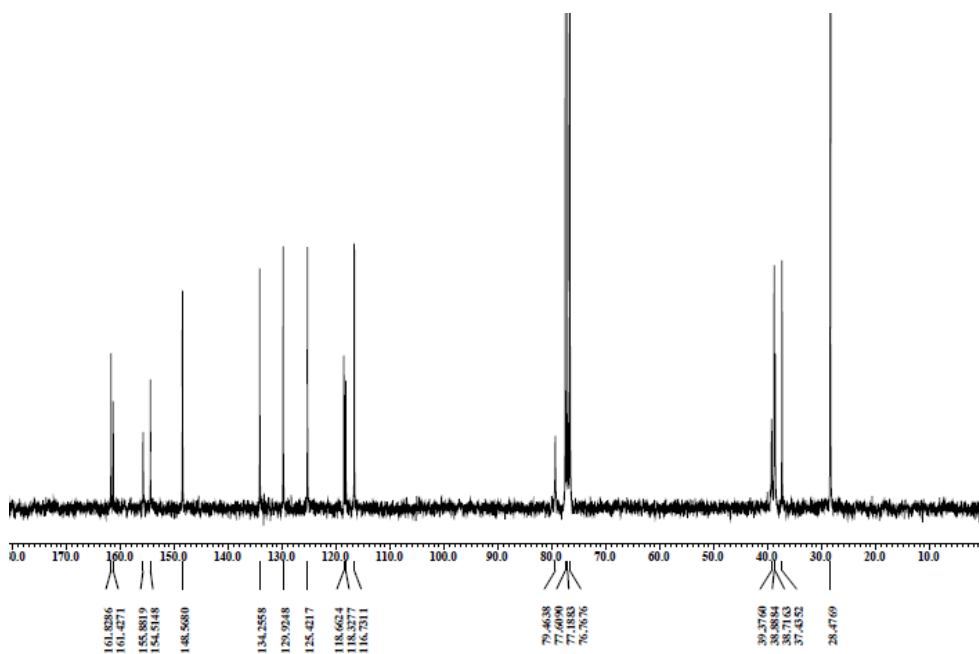
(2) HRMS (ESI) spectrum of compound **3**



(3) ^1H NMR spectrum of compound **3** (300 MHz, CDCl_3)



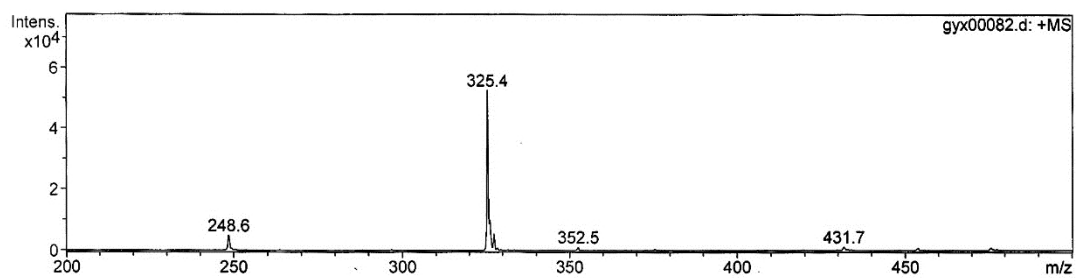
(4) ^{13}C NMR spectrum of compound **3** (75 MHz, CDCl_3)



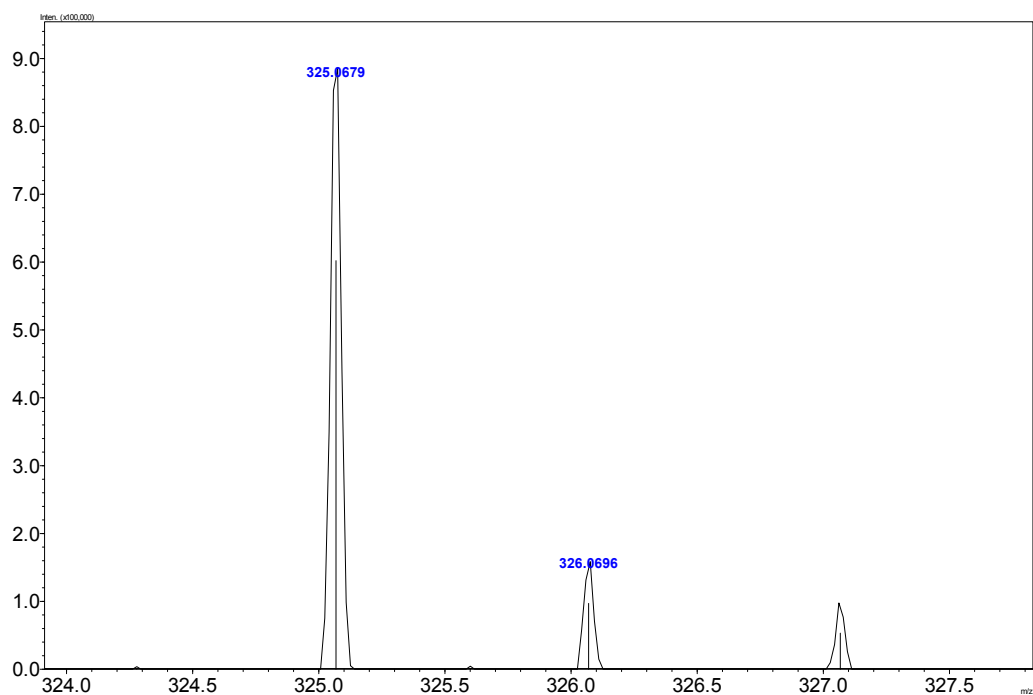
Compound 4

Trifluoroacetic acid (TFA) was added dropwise to a solution of **3** (840 mg, 1.98 mmol) in 10 mL CH_2Cl_2 at 0°C , the mixture was stirred at room temperature for 10 h. Evaporation was used to remove the unreacted TFA and solvent. The residue was dissolved in CH_2Cl_2 and washed with NaHCO_3 for twice, then washed with water and brine water. The organic layer was dried over the anhydrous sodium sulfate and evaporated to give the crude product. The chromatography (CH_2Cl_2 : CH_3OH =100:1 to 10:1) was employed to purify the crude product and compound **4** was gained as a white solid (580 mg, 90%). ESI-MS (+): 325.4 $[\text{M}+\text{H}]^+$; HRMS (ESI): m/z $[\text{M}+\text{H}]^+$ calcd. for $\text{C}_{14}\text{H}_{16}\text{N}_2\text{O}_3\text{S}_2$: 325.0675, found 325.0679 $[\text{M}+\text{H}]^+$; ^1H NMR (300 MHz, CDCl_3): 9.00 (broad, H, $\text{NH}-\text{C}=\text{O}$), 8.82 (s, H, Coumarin-4- CH), 7.62, 7.33 (t, t, 4H, Ar-H), 3.75 (q, 2H, Coumarin-3- $\text{CO}-\text{NH}-\text{CH}_2$, $J = 6.5$ Hz), 2.95 (q, 2H, NH_2-CH_2 , $J = 6.2$ Hz), 2.85 (q, 2H, Coumarin-3- $\text{CO}-\text{NH}-\text{CH}_2-\text{CH}_2-\text{S}$, $J = 6.5$ Hz), 2.75 (q, 2H, $-\text{S}-\text{CH}_2-\text{CH}_2-\text{NH}_2$, $J = 6.2$ Hz), 1.36 (broad, 2H, NH_2); ^{13}C NMR (75 MHz, CDCl_3): 161.70 (Coumarin-2- $\text{C}=\text{O}$), 161.36 (Coumarin-3- $\text{CO}-\text{NH}$), 154.46, 148.47, 134.21, 129.90, 118.61, 118.30 (Ar- C), 125.37 (Coumarin-4- CH), 116.66 (Coumarin-3- C), 42.71, 40.73, 38.87, 37.62 ($4\times-\text{CH}_2$).

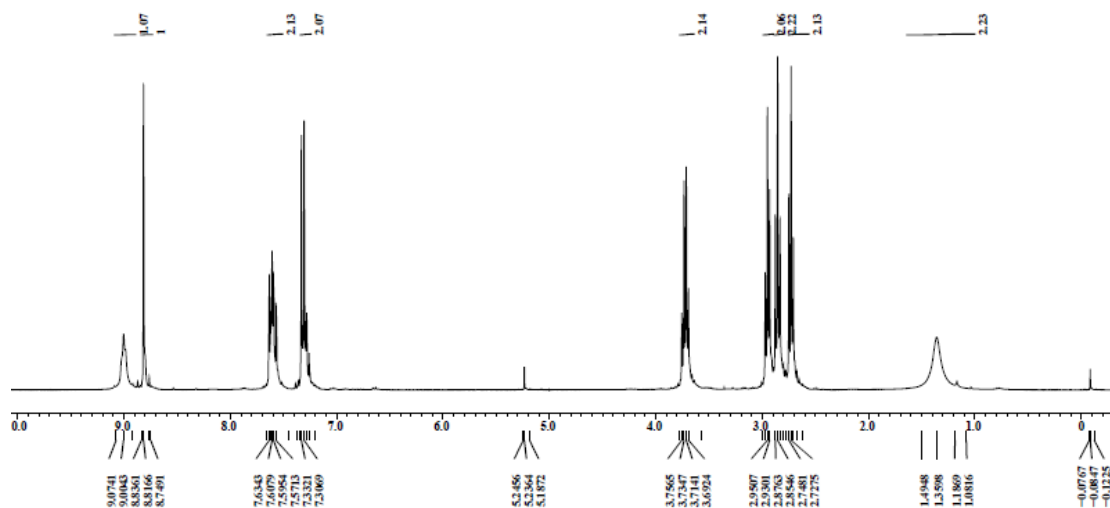
(1) ESI-MS (+) spectrum of compound 4



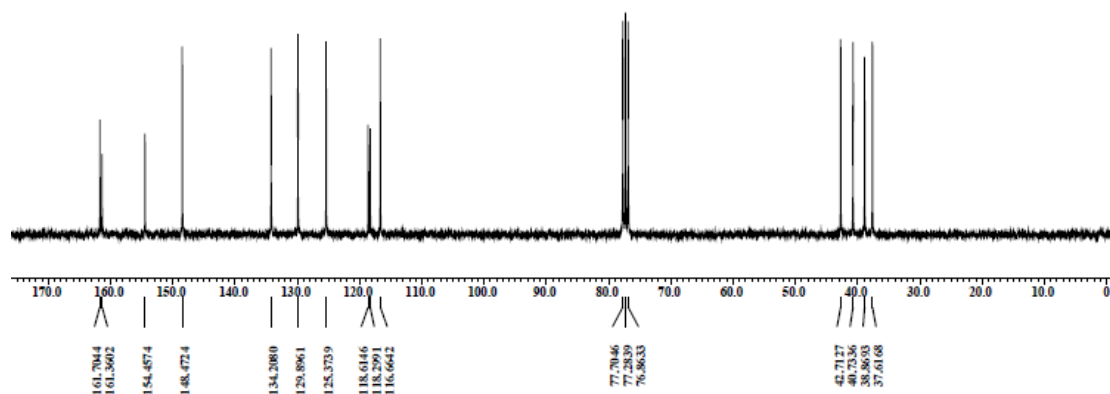
(2) HRMS (ESI) spectrum of compound 4



(3) ¹H NMR spectrum of compound 4 (300 MHz, CDCl₃)



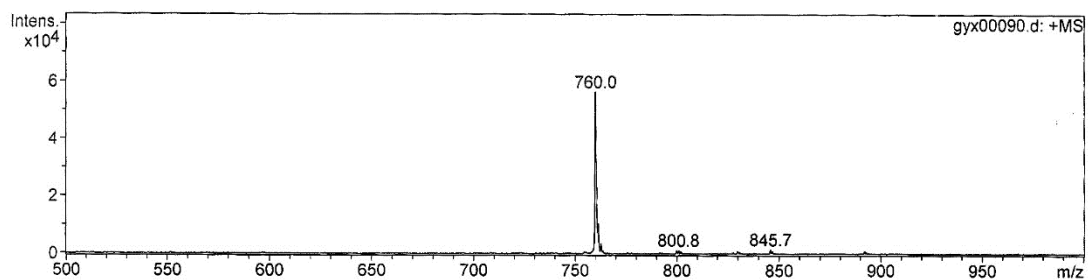
(4) ^{13}C NMR spectrum of compound **4** (75 MHz, CDCl_3)



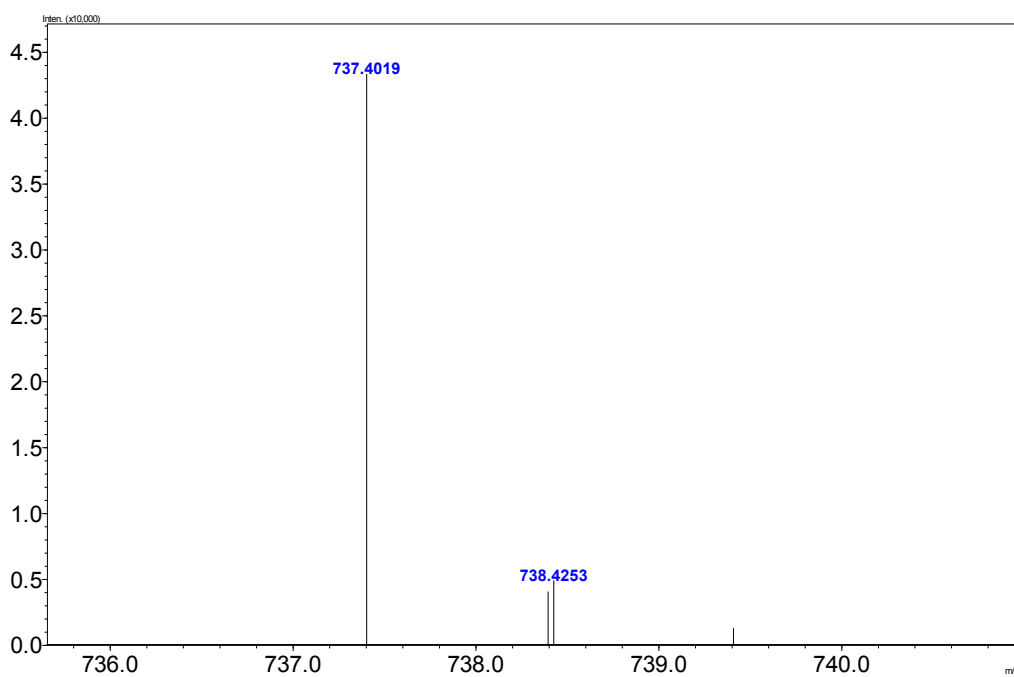
Compound **1**

To a solution of compound **4** (564mg, 1.74mmol) and triethylamine (0.5 mL, 3.4 mmol) in 15 mL CH_2Cl_2 , cholesteryl chloroformate (780mg, 1.74mmol) was added at 0 °C, then the mixture was stirred at room temperature for 12 h. The reaction mixture was washed with water (30 mL \times 2) and brine water (30 mL), organic layer was dried and evaporated to give the crude product. The target compound **1** (657 mg, 53%) was obtained by further silica column chromatography (CH_2Cl_2 : CH_3OH =150:1) as a white solid. m.p. 153-154 °C; ESI-MS (+):760.0 $[\text{M}+\text{Na}]^+$; HRMS (ESI): m/z $[\text{M}+\text{H}]^+$ calcd. for $\text{C}_{42}\text{H}_{60}\text{N}_2\text{O}_5\text{S}_2$: 737.4016, found 737.4019 $[\text{M}+\text{H}]^+$; ^1H NMR (300 MHz, CDCl_3): 9.06 (broad, H, NH), 8.87 (s, H, Coumarin-4- CH), 7.65, 7.38 (t, t, 4H, Ar-H), 5.30 (broad, H, NH), 5.21 (s, H, Cholesterol-6- CH), 4.45 (m, H, Cholesterol-3- CH), 3.78 (q, 2H, Coumarin-3-CO-NH- CH_2 , $J = 6.5$ Hz), 3.49 (q, 2H, CH_2 -NH-COO, $J = 6.2$ Hz), 2.90 (q, 2H, Coumarin-3-CO-NH CH_2 - CH_2 -S-, $J = 6.5$ Hz), 2.83 (q, 2H, -S- CH_2 - CH_2 -NH-COO, $J = 6.2$ Hz), 0.94, 0.84, 0.82, 0.63 (4 \times s, 4 \times 3H, - CH_3); ^{13}C NMR (75 MHz, CDCl_3): 161.82 (Coumarin-2- $\text{C}=\text{O}$), 161.40 (Coumarin-3- CO -NH-), 156.15 (NH- COO), 154.53, 148.55, 134.24, 129.92, 118.68, 118.37 (Ar- C -), 139.85 (Cholesterol-5- C), 125.40 (Cholesterol-6- CH), 122.52 (Coumarin-4- CH), 116.73 (Coumarin-3- C), 74.46 (Cholesterol-3- CH), 56.75, 56.21, 53.54, 50.06, 42.37, 39.81, 39.58, 38.93, 38.63, 37.48, 36.59, 36.26, 35.86, 31.92, 28.30, 28.24, 28.07, 24.35, 23.91, 22.91, 22.65, 21.11, 19.38, 18.80, 11.94.

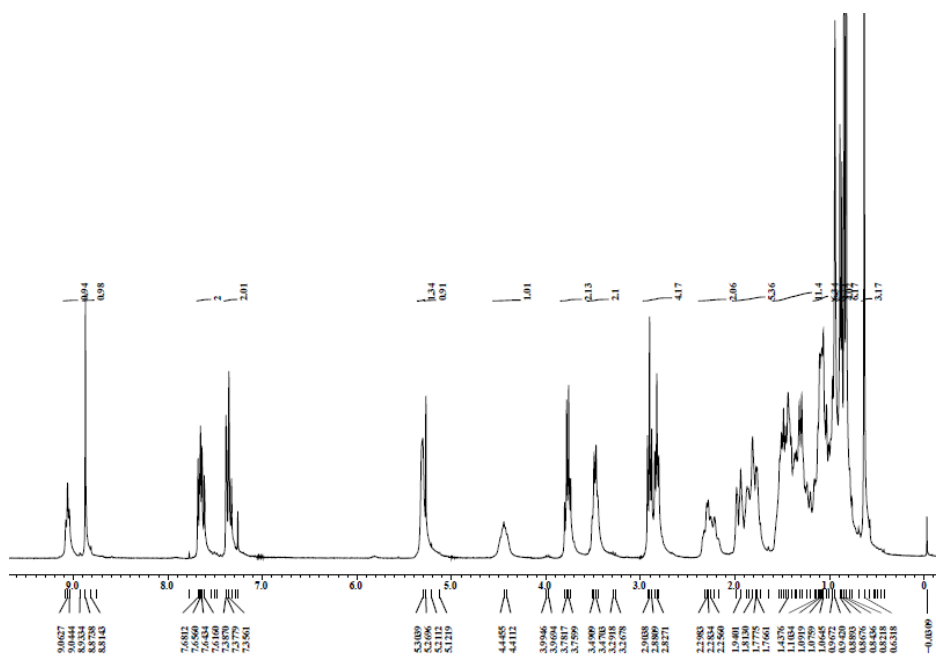
(1) ESI-MS (+) spectrum of compound **1**



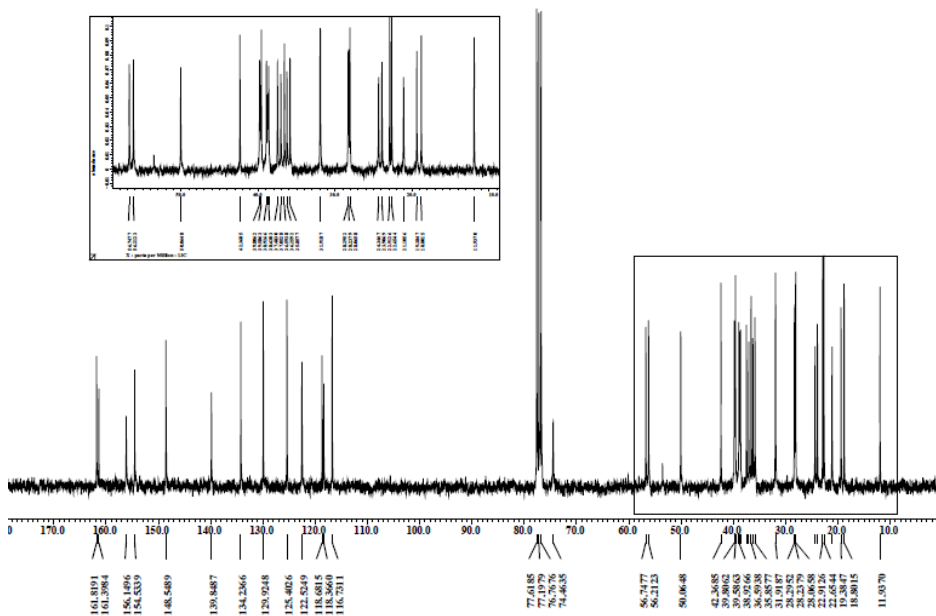
(2) HRMS (ESI) spectrum of compound **1**



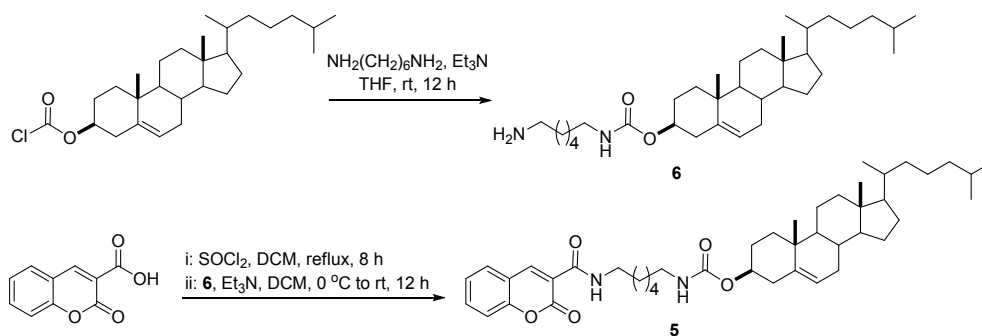
(3) ¹H NMR spectrum of compound **1** (300 MHz, CDCl₃)



(4) ^{13}C NMR spectrum of compound **1** (75 MHz, CDCl_3)



5. Synthesis and structure characterization of the control molecule 5

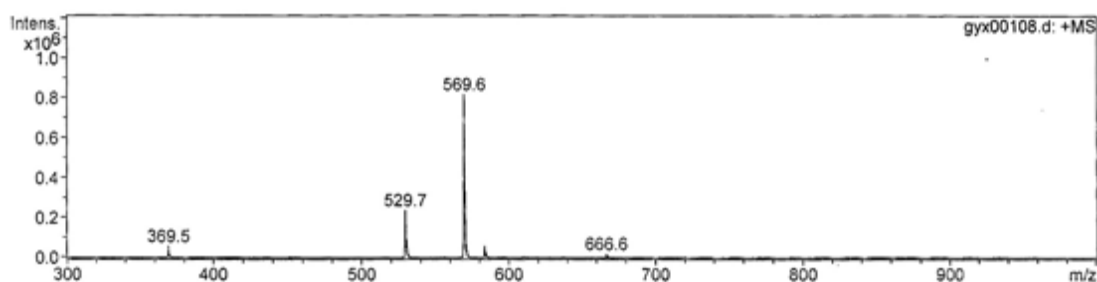


Scheme. S1 The synthetic route of compound 5

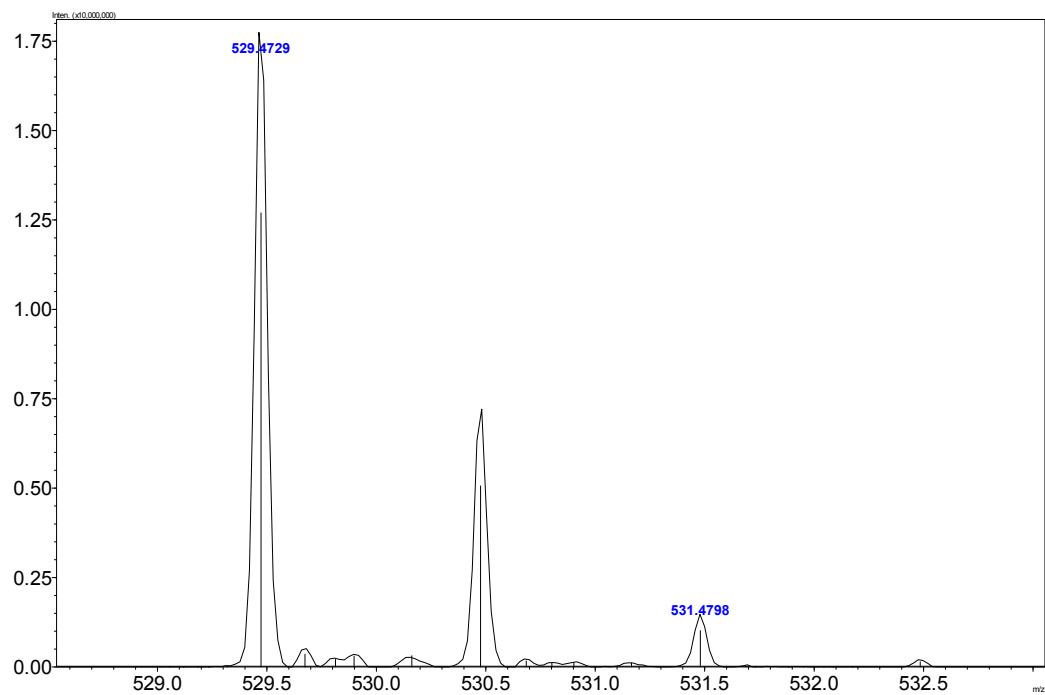
Compound 6

1,6-hexanediamine (4.68 mL, 35.6 mmol) and triethylamine (0.25 mL, 1.7 mmol) were dissolved in dry THF (20 mL). To the solution, 10 mL THF solution of cholesteryl chloroformate (800 mg, 1.78 mmol) was added dropwise at 0 °C (ice bath), then the mixture was stirred at room temperature for 12 h. The reaction mixture was filtered and the filtrate was evaporated. Then the residue was dissolved in CH_2Cl_2 and washed with water (30 mL \times 2) and brine water (30 mL). The organic layer was separated and dried by anhydrous sodium sulfate, finally evaporated to dryness. The crude product was further purified by chromatography (CH_2Cl_2 : CH_3OH = 50:1) to give compound 6 as a white solid (477 mg, 51 %). ESI-MS (+): 529.7 $[\text{M}+\text{H}]^+$, 569.6 $[\text{M}+\text{Na}+\text{H}_2\text{O}]^+$; HRMS (ESI): m/z $[\text{M}+\text{H}]^+$ calcd. for $\text{C}_{34}\text{H}_{60}\text{N}_2\text{O}_2$: 529.4728, found 529.4729 $[\text{M}+\text{H}]^+$; ^1H NMR (300 MHz, CDCl_3): 5.29 (s, H, Cholesterol-6- $\underline{\text{CH}}$), 4.89 (broad, H, $\text{O}=\text{C}-\underline{\text{NH}}$ -), 4.40 (m, H, Cholesterol-3- $\underline{\text{CH}}$), 3.09 (d, 2H, $\text{NH}-\underline{\text{CH}_2}$ -, $J = 6.2$ Hz), 2.62 (t, 2H, $\text{H}_2\text{N}-\underline{\text{CH}_2}$ -, $J = 7.9$ Hz), 0.94, 0.81, 0.79, 0.61 (4 \times s, 4 \times 3H, $-\text{CH}_3$); ^{13}C NMR (75 MHz, CDCl_3): 156.25 ($\text{NH}-\underline{\text{C}}\text{OO}$), 139.89 (Cholesterol-5- $\underline{\text{C}}$), 122.46 (Cholesterol-6- $\underline{\text{CH}}$), 74.07 (Cholesterol-3- $\underline{\text{CH}}$), 56.72, 56.17, 50.03, 42.33, 42.07, 40.83, 39.78, 39.57, 38.66, 37.05, 36.58, 36.23, 35.86, 33.53, 31.90, 30.06, 28.26, 28.05, 26.65, 26.58, 24.34, 23.90, 22.90, 22.64, 21.09, 19.39, 18.77, 11.91.

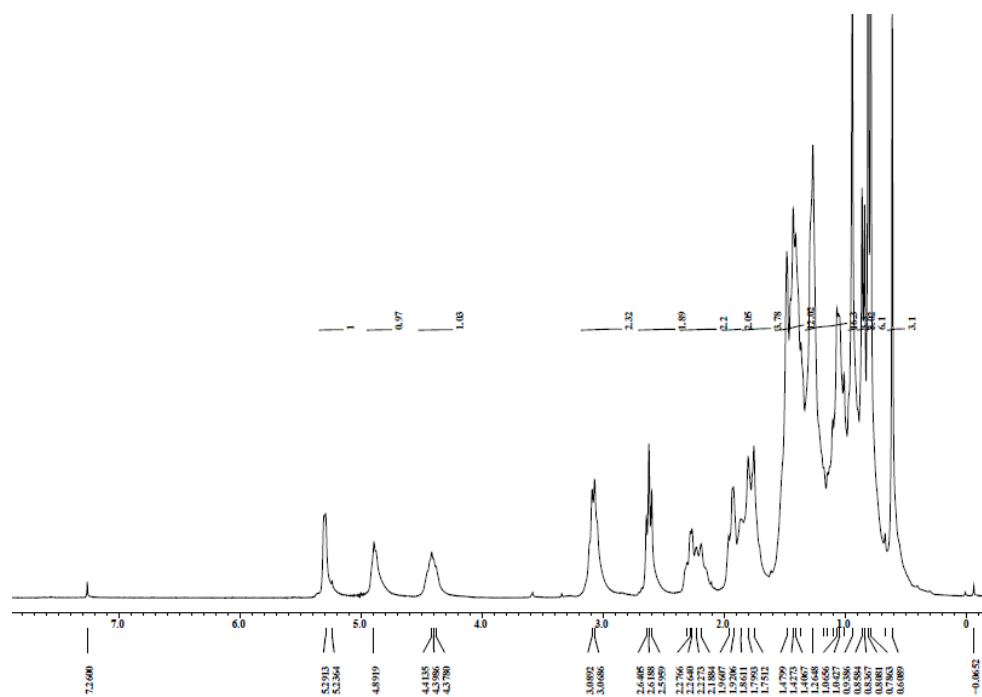
(1) ESI-MS (+) spectrum of compound 6



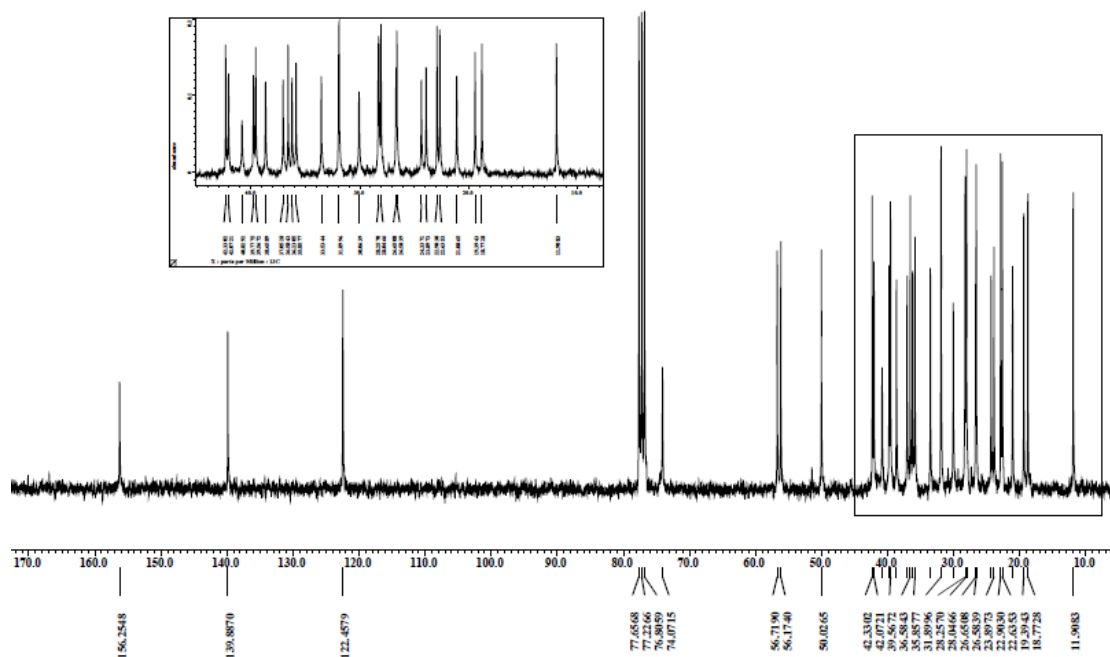
(2) HRMS (ESI) spectrum of compound **6**



(3) ^1H NMR spectrum of compound **6** (300 MHz, CDCl_3)



(4) ^{13}C NMR spectrum of compound **6** (75 MHz, CDCl_3)

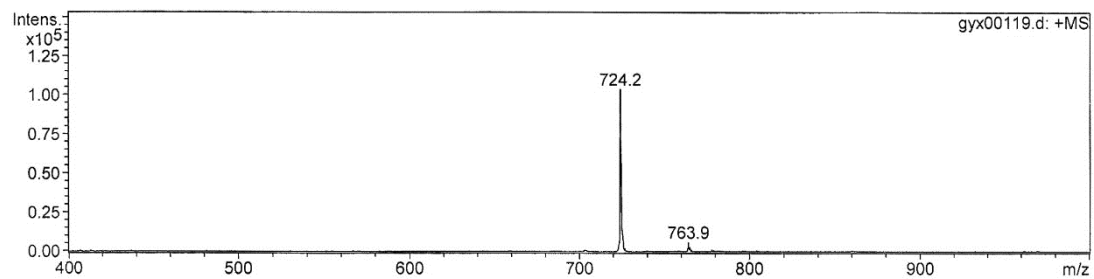


Compound 5

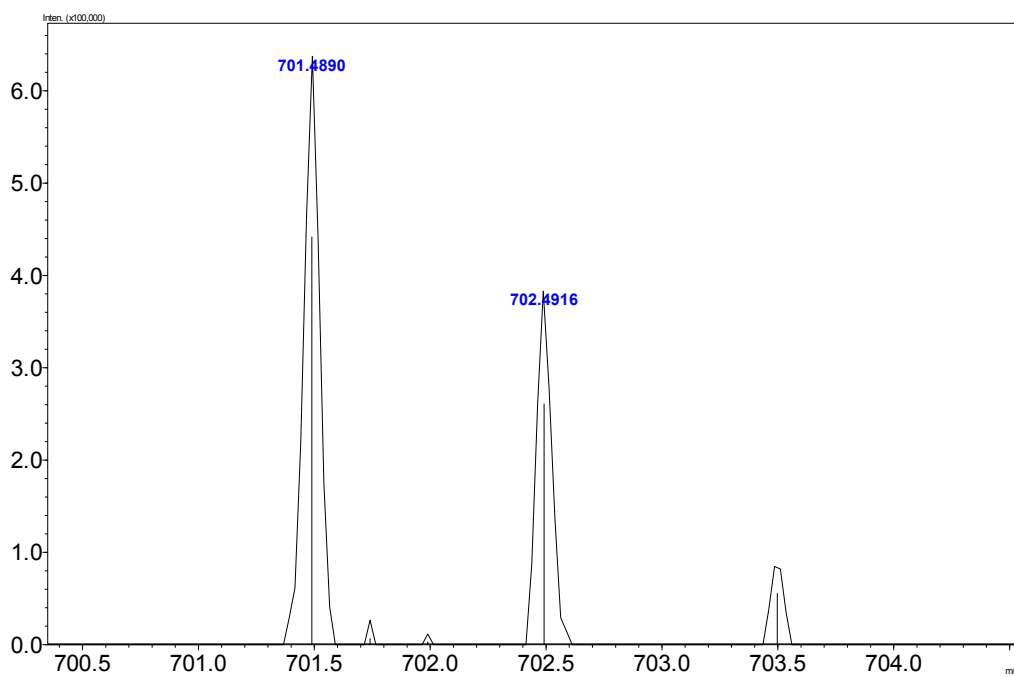
The coumarin-3-carboxylic acid (171 mg, 0.90 mmol) was first transformed to thionyl chloride, similar synthesis procedure was used as the synthesis of compound 4. Triethylamine (0.2 mL, 1.36 mmol) was added to a solution of **6** (477 mg, 0.90 mmol) in dry CH₂Cl₂, then 10 mL CH₂Cl₂ solution of acyl chloride was added dropwise at 0 °C. After addition, the mixture was stirred at room temperature for 20 h, then washed with water and brine water respectively. The organic phase was dried and filtered, then evaporated to dryness. The control molecule **5** (490 mg, 78%) was obtained as a white solid by chromatography (CH₂Cl₂ : CH₃OH=100:1). m.p. 166-168 °C; ESI-MS (+): 724.2 [M+Na]⁺; HRMS (ESI): m/z [M+H]⁺ calcd. for C₄₄H₆₄N₂O₅: 701.4888, found 701.4890 [M+H]⁺; ¹H NMR (400 MHz, CDCl₃): 8.85 (s, H, Coumarin-4-CH), 8.76 (broad, H, NH), 7.63, 7.34 (t, t, 4H, Ar-H), 5.30 (s, H, Cholesterol-6-CH), 4.70 (broad, H, NH), 4.42 (m, H, Cholesterol-3-CH), 3.41 (s, 2H, Coumarin-3-CO-HN-CH₂), 3.11 (s, 2H, CH₂-NH-COO), 0.93, 0.86, 0.81, 0.61 (4×s, 4×3H, -CH₃); ¹³C NMR (100 MHz, CDCl₃): 161.53 (Coumarin-2-C=O), 161.46 (Coumarin-3-CO-NH-), 156.22 (NH-COO), 154.43, 148.27, 134.02, 129.84, 118.72, 118.59 (Ar-C-), 139.91 (Cholesterol-5-C), 125.33 (Cholesterol-6-CH), 122.44 (Coumarin-4-CH), 116.66 (Coumarin-3-C), 74.13 (Cholesterol-3-CH), 56.71, 56.16, 50.03, 42.34, 40.81, 39.78, 39.57, 38.65, 37.05,

36.59, 36.23, 35.85, 31.90, 29.37, 28.30, 28.24, 28.06, 26.68, 26.43, 24.34, 23.90, 22.91, 22.65, 21.08, 19.39, 18.77, 11.92.

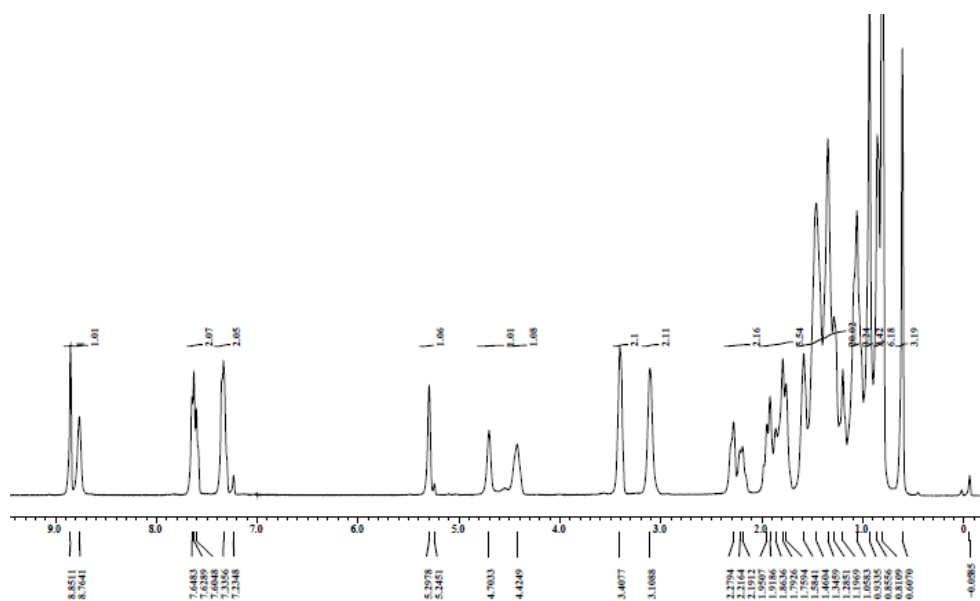
(1) ESI-MS (+) spectrum of compound **5**



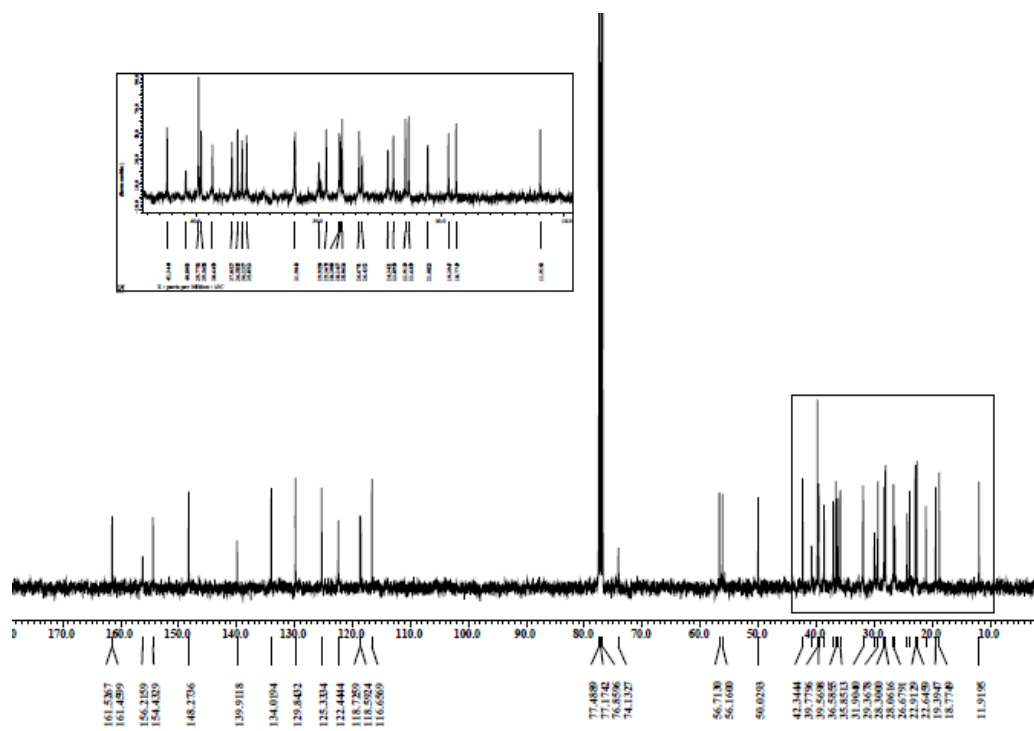
(2) HRMS (ESI) spectrum of compound **5**



(3) ¹H NMR spectrum of compound **5** (400 MHz, CDCl₃)



(4) ^{13}C NMR spectrum of compound **5** (75 MHz, CDCl_3)



6. Reference

1. J. Niu, Z. H. Liu, L. Fu, F. Shi, H. W. Ma, Y. Ozaki and X. Zhang, *Langmuir*, 2008, **24**, 11988.