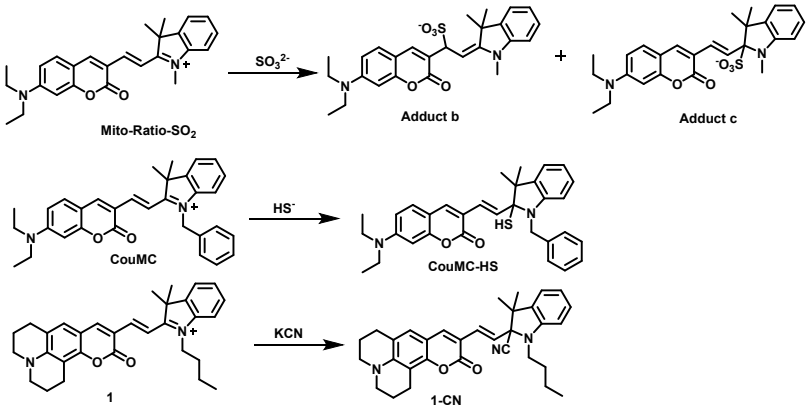
Electronic Supplementary Material (ESI) for New Journal of Chemistry.

Supporting Information

Tuning lipophilicity for optimizing H_2S sensing performance of coumarin-merocyanine derivatives

Hongbao Fang, Yuncong Chen*, Xiangchao Shi, Yang Bai, Zhongyan Chen, Zhong Han, Yuming Zhang, Weijiang He* and Zijian Guo

State Key Laboratory of Coordination Chemistry, School of Chemistry and Chemical Engineering, Nanjing University, Nanjing, Jiangsu 210023, China.



Scheme S1 Three example compounds based on the nucleophilic addition

Synthesis and characterizations

Synthetic procedures

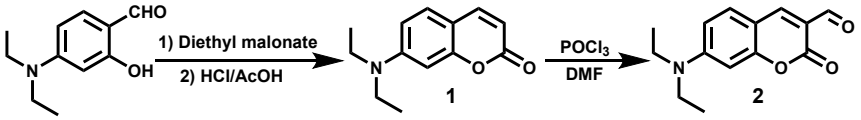
Compounds **1** and **2** were synthesized following by the previously reported literatures. [1]

Synthesis of 7-diethylaminocoumarin (1)

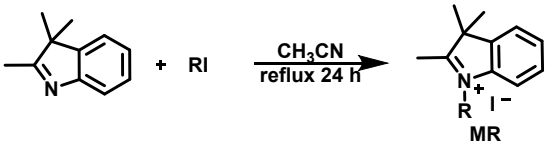
3.3 g diethyl malonate (20 mmol) and 1 mL piperidine (10 mmol) were mixed and added to the solution of 1.93 g 4-(Diethylamino)-salicylaldehyde (10 mmol) dissolved in 30 mL absolute ethanol. After stirring and heating to reflux for 6 hours, the solvent was removed by rotate evaporating. And then 20.0 mL concentrated HCl and 20.0 mL acetic acid were added for hydrolysis and stirred thoroughly for another 6 hours. After the mixture cooled down to room temperature, 100 mL ice water were poured into the solution and then 40% NaOH solution was added dropwise to adjust pH to ~5, and pale precipitate was produced immediately. After stirring for another 30 min, the mixture was filtered, washed with water and then recrystallized with toluene, dried by vacuum drying oven to give **1**(1.63 g, 7.5 mmol) in 75% yield.

Synthesis of 7-diethylaminocoumarin-3-aldehyde (2)

2 mL dry DMF was added dropwise to 2 mL $POCl_3$ at ice bath with N_2 atmosphere and stirred for 30 minutes at 50 °C to yield a red solution. And then **1** (1.50 g, 6.91 mmol) dissolved in 10 mL DMF was added to the solution to yield a scarlet suspension. The mixture was stirred and heated to 60 °C for 12 h, then added to 100 mL ice water. 20% NaOH solution was added to adjust the pH of the mixture to yield a large amount of precipitate. The mixture was filtered, washed with water for 3 times, recrystallized in absolute ethanol and dried by vacuum drying oven to give **2** (1.11 g, 4.52 mmol) in 65.5% yield. ^{1}H NMR (300 MHz, Chloroform-*d*) δ 10.13 (s, 1H), 8.26 (s, 1H), 7.41 (d, J = 9.0 Hz, 1H), 6.64 (dd, J = 9.0, 2.5 Hz, 1H), 6.49 (d, J = 2.3 Hz, 1H), 3.48 (q, J = 7.1 Hz, 4H), 1.26 (t, J = 7.1 Hz, 6H).



Scheme S2 The synthesis of 7-diethylaminocoumarin-3-aldehyde (**2**)



MC_1: R=CH_3 MC_4: R=C_4H_9 MC_5: R=C_5H_{11} MC_6: R=C_6H_{13}

Scheme S3 The synthesis of the indole derivatives (**MR**)

CM-NC$_1$, 56%. ^{1}H NMR (300 MHz, Chloroform-*d*) δ 10.05 (s, 1H), 8.59 (d, *J* = 15.9 Hz, 1H), 8.11 (d, *J* = 9.1 Hz, 1H), 8.01 (d, *J* = 15.9 Hz, 1H), 7.69 – 7.37 (m, 4H), 6.71 (dd, *J* = 9.1, 2.4 Hz, 1H), 6.47 (d, *J* = 2.2 Hz, 1H), 4.31 (s, 3H), 3.52 (q, *J* = 7.1 Hz, 4H), 1.84 (s, 7H), 1.29 (t, *J* = 7.1 Hz, 6H). ^{13}C NMR (75 MHz, Chloroform-*d*) δ 181.17, 160.99, 158.75, 154.48, 150.66, 149.39, 142.64, 141.50, 134.38, 129.25, 128.63, 122.49, 113.26, 112.48, 110.96, 108.92, 96.77, 77.37, 76.95, 76.52, 51.58, 45.58, 35.94, 27.41, 12.53. HRMS (positive mode, *m/z*): Calcd. 401.2224, found 401. 2226 for $[M]^+$.

CM-NC$_4$, 48.9%. ^{1}H NMR (300 MHz, DMSO-d_6) δ 8.80 (d, *J* = 4.3 Hz, 1H), 8.30 (d, *J* = 15.7 Hz, 1H), 8.11 – 7.74 (m, 3H), 7.59 (dd, *J* = 9.7, 4.0 Hz, 3H), 6.92 (dd, *J* = 9.1, 2.2 Hz, 1H), 6.71 (d, *J* = 1.9 Hz, 1H), 4.45 (t, *J* = 7.2 Hz, 2H), 3.58 (q, *J* = 7.0 Hz, 4H), 1.93 – 1.71 (m, 6H), 1.44 (dd, *J* = 15.2, 7.4 Hz, 2H), 1.19 (t, *J* = 7.0 Hz, 6H), 0.96 (t, *J* = 7.3 Hz, 3H). ^{13}C NMR (75 MHz, DMSO-d_6) δ 181.08, 159.69, 158.01, 154.43, 151.11, 150.54, 143.60, 141.32, 132.81, 129.39, 128.95, 123.34, 114.90, 112.61, 111.73, 110.03, 109.84, 96.90, 51.79, 46.40, 45.23, 40.72, 40.44, 40.16, 39.88, 39.60, 39.33, 39.05, 30.13, 26.55, 19.90, 13.94, 12.86. HRMS (positive mode, *m/z*): Calcd. 443.2693, found 443. 2695 for $[M]^+$.

CM-NC$_5$, 58.3%. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 10.15 (s, 1H), 8.63 (d, *J* = 15.8 Hz, 1H), 8.14 (d, *J* = 9.0 Hz, 1H), 8.06 (d, *J* = 15.8 Hz, 1H), 7.59 – 7.47 (m, 3H), 7.44 – 7.39 (m, 1H), 6.69 (dd, *J* = 9.1, 2.5 Hz, 1H), 6.45 (d, *J* = 2.4 Hz, 1H), 4.75 (s, 1H), 3.52 (q, *J* = 7.1 Hz, 4H), 2.02 – 1.90 (m, 2H), 1.88 (s, 6H), 1.60 – 1.47 (m, 2H), 1.45 – 1.35 (m, 2H), 1.28 (t, *J* = 7.1 Hz, 6H), 0.91 (t, *J* = 7.3 Hz, 3H).^{13}C NMR (101 MHz, Chloroform-*d*) δ 180.99, 161.10, 158.77, 154.55, 151.22, 143.31, 140.88, 134.50, 129.22, 128.62, 122.79, 113.36, 112.58, 111.05, 110.92, 108.95, 96.72, 51.75, 47.28, 45.62, 28.79, 28.30, 27.75, 22.39, 13.84, 12.62. HRMS (positive mode, *m/z*): Calcd. 457.2850, found 457.2854 for $[M]^+$.

CM-NC$_6$, 42.1%. ^{1}H NMR (300 MHz, Chloroform-*d*) δ 10.10 (s, 1H), 8.63 (d, *J* = 15.8 Hz, 1H), 8.20 – 8.01 (m, 2H), 7.65 – 7.48 (m, 3H), 7.47 – 7.35 (m, 1H) 6.69 (dd, *J* = 9.1, 2.2 Hz, 1H), 6.45

(d, J = 2.2 Hz, 1H), 3.52 (q, J = 7.1 Hz, 4H), 2.06 – 1.90 (m, 2H), 1.88 (s, 6H), 1.61 – 1.48 (m, 2H), 1.38 – 1.20 (m, 10 H), 0.86 (t, J = 6.9 Hz, 3H). ^{13}C NMR (75 MHz, Chloroform-*d*) δ 180.94, 160.96, 158.64, 154.45, 151.17, 150.50, 143.21, 140.78, 134.36, 129.15, 128.55, 122.70, 113.32, 112.53, 110.92, 110.83, 108.95, 96.62, 77.40, 77.18, 76.97, 76.55, 51.65, 47.17, 45.52, 31.27, 28.43, 27.63, 26.32, 22.26, 13.87, 12.52. HRMS (positive mode, *m/z*): Calcd. 471.3006,found 471.3008 for $[M]^+$.

Supporting figures

Fluorescence and UV/vis response time for H_2S

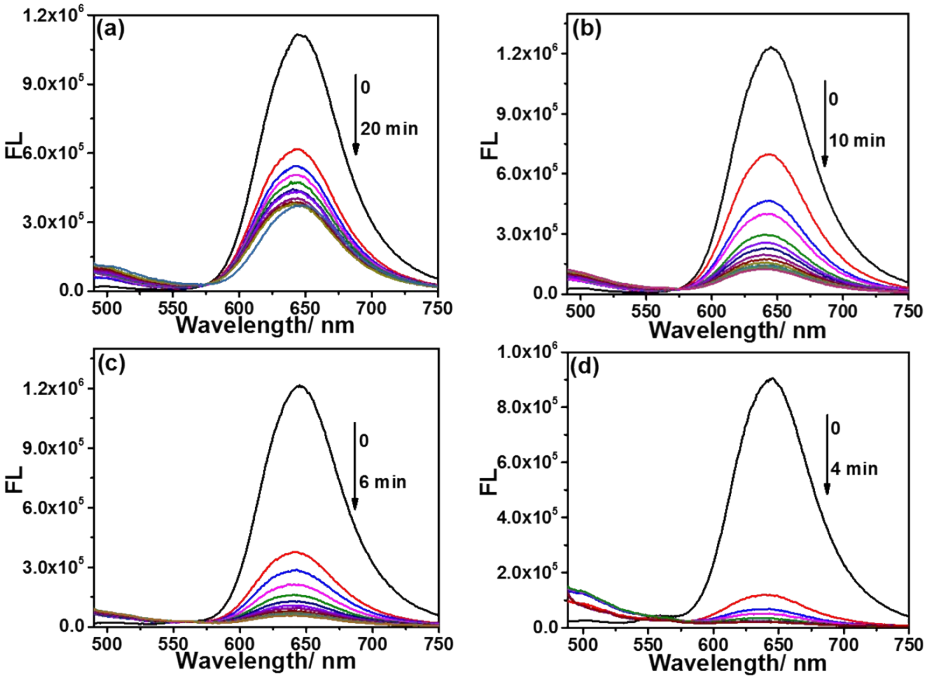


Figure S1 (a-d) Fluorescence spectra changes of **CM-NC$_1$** (a), **CM-NC$_4$**(b), **CM-NC$_5$**(c) and **CM-NC$_6$** (d) (10 μM) in PBS solution (20 mM, pH 7.40, 2% DMSO, v/v) with the addition of 200 μM NaHS over time, λ_{ex}=475 nm.

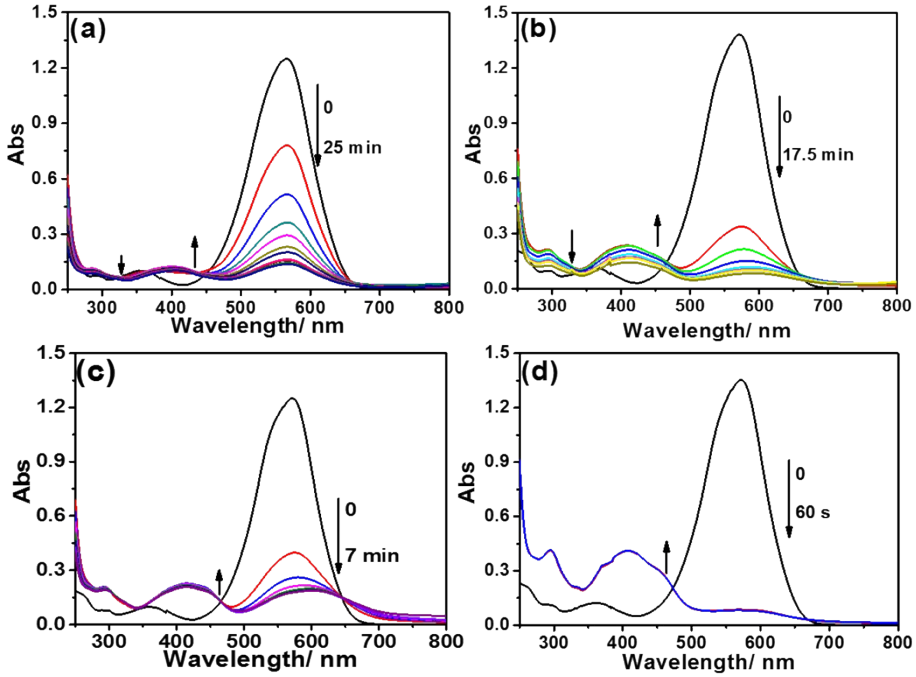


Figure S2 (a-d) Absorption spectra changes of **CM-NC$_1$**(a), **CM-NC$_4$**(b), **CM-NC$_5$**(c) and **CM-NC$_6$**(d) (20 μM) in PBS solution (20 mM, pH 7.40, 2% DMSO, v/v) with the addition of 400 μM NaHS over time.

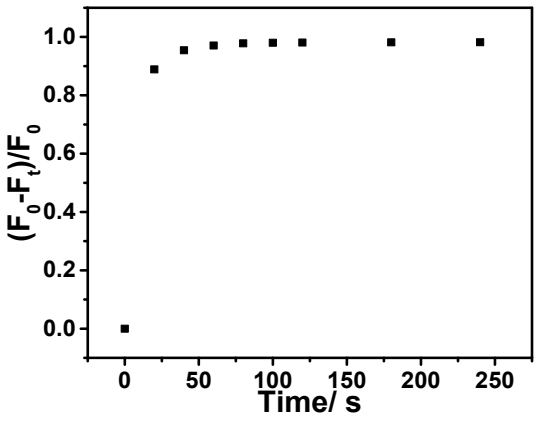


Figure S3 Fluorescence change rate curve at 650 nm $(F_0-F_t)/F_0$ of 10 μM **CM-NC$_6$** in PBS buffer (20 mM, pH=7.4, 2% DMSO, v/v) in the presence of 200 μM NaHS, λ_{ex}= 475 nm.

Detection Limit of Probe CM-NC$_6$ for HS$^-$

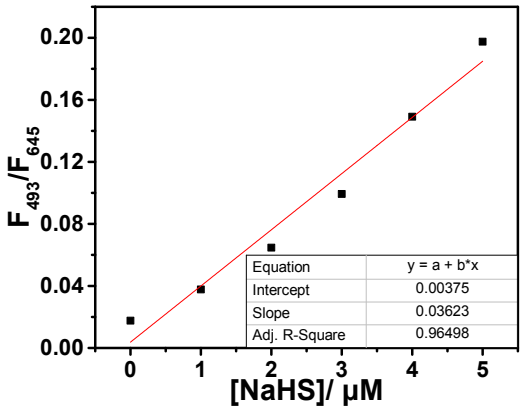


Figure S4 Fluorescence intensity ratio at 493 nm and 645 nm (F_{493}/F_{645}) of 10 μM **CM-NC$_6$** as a function of the different NaHS concentration. λ_{ex}= 475 nm.

MCF-7 cell imaging

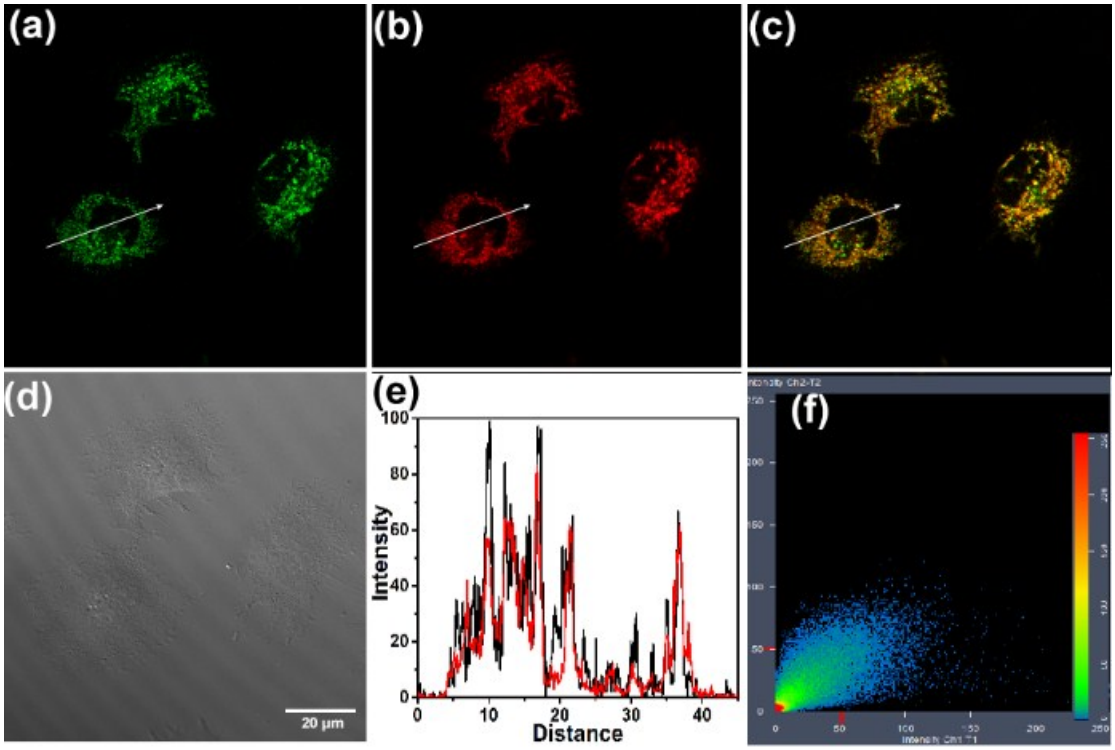


Figure S5 (a-c) Confocal images of MCF-7 cells incubated with **CM-NC$_1$** (5 μM, 15 min) and Mitotracker Deep Red 633 (1 μM, 15 min). (a) The green channel image obtained with 488 nm excitation; (b) The red channel image of Mitotracker Deep Red 633 colllected with 633 nm excitation; (c) overlay of (a) and (b); (d) Bright-field image of MCF-7 cells; (e) the intensity profile of the linear region of the interest (white arrow) across the MCF-7 cells co-incubated with Mitotracker Deep Red 633 and **CM-NC$_1$**; and (f) correlation plot of **CM-NC$_1$** and Mitotracker Deep Red 633 intensities. Scale bar = 20 μm.

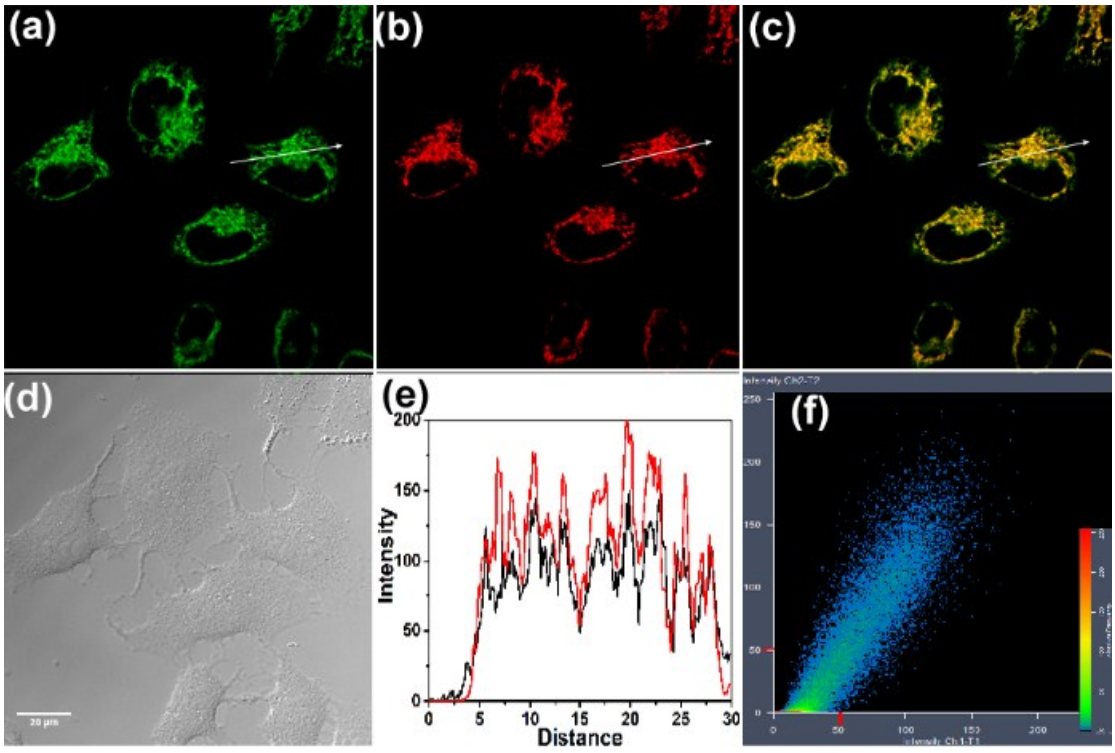


Figure S6 (a-c) Confocal images of MCF-7 cells incubatied with **CM-NC$_4$** (5 μM, 15 min) and Mitotracker Deep Red 633 (1 μM, 15 min). (a) The green channel image obtained with 488 nm excitation; (b) The red channel image of Mitotracker Deep Red 633 colllected with 633 nm excitation; (c) overlay of (a) and (b); (d) Bright-field image of MCF-7 cells; (e) the intensity profile of the linear region of the interest (white arrow) across the MCF-7 cells co-incubated with Mitotracker Deep Red 633 and **CM-NC$_4$**; and (f) correlation plot of **CM-NC$_4$** and Mitotracker Deep Red 633 intensities. Scale bar = 20 μm.

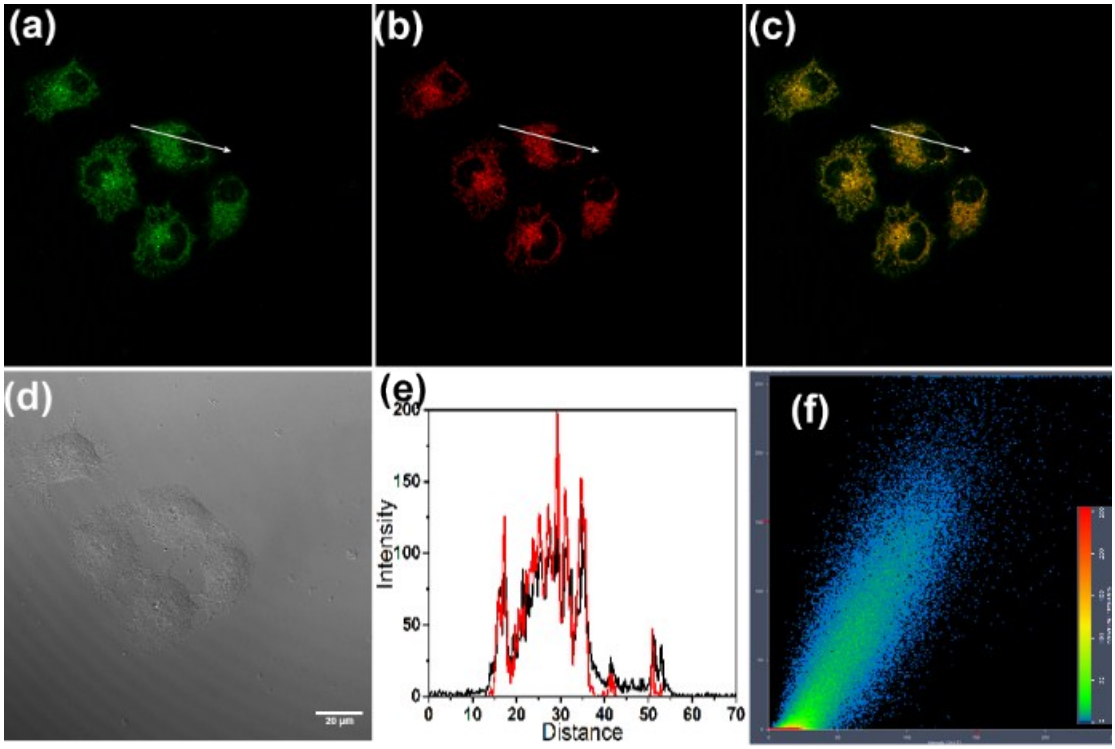


Figure S7 (a-c) Confocal fluorescence images of MCF-7 cells incubated with **CM-NC$_5$** (5 μM, 15 min) and Mitotracker Deep Red 633 (1 μM, 15 min). (a) The green channel image obtained with 488 nm excitation; (b) The red channel image of Mitotracker Deep Red 633 colllected with 633 nm excitation; (c) overlay of (a) and (b); (d) Bright-field image of MCF-7 cells; (e) the intensity profile of the linear region of the interest (white arrow) across the MCF-7 cells co-incubated with Mitotracker Deep Red 633 and **CM-NC$_5$**; and (f) correlation plot of **CM-NC$_5$** and Mito-marker Deep Red 633 intensities. Scale bar = 20 μm.

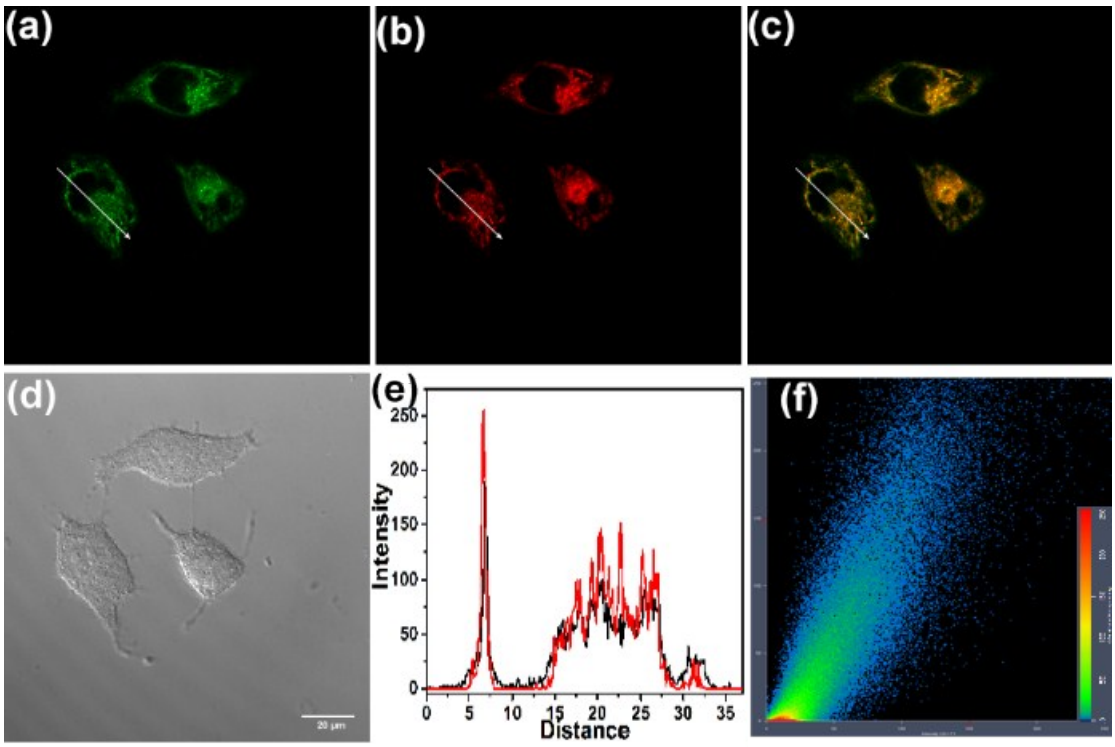


Figure S8 (a-c) Confocal images of MCF-7 cells incubated with **CM-NC$_6$** (5 μM, 15 min) and Mitotracker Deep Red 633 (1 μM, 15 min). (a) The green channel image obtained with 488 nm excitation; (b) The red channel image of Mitotracker Deep Red 633 colllected with 633 nm excitation; (c) Overlay of (a) and (b); (d) Bright-field image of MCF-7 cells; (e) The intensity profile of the linear region of the interest (white arrow) across the MCF-7 cells co-incubated with Mitotracker Deep Red 633 and **CM-NC$_6$**; and (f) correlation plot of **CM-NC$_6$** and Mitotracker Deep Red 633 intensities. Scale bar = 20 μm.

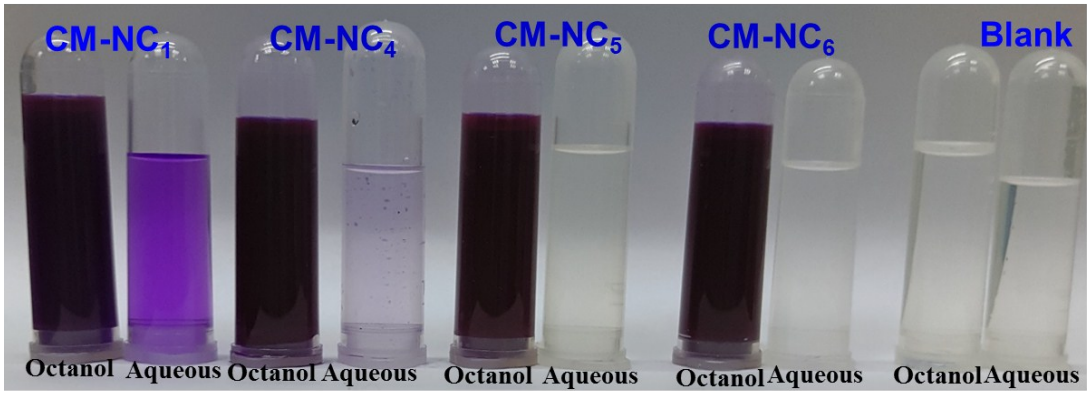


Figure S9 Photograph of **CMC** Octanol-aqueous buffer partition

^{1}H and ^{13}C NMR spectra

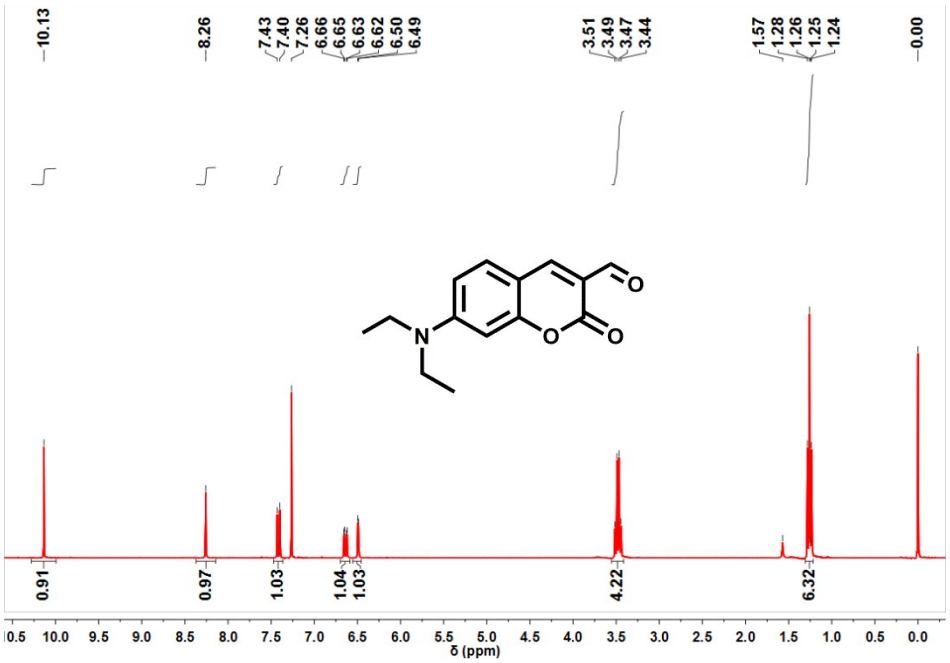


Figure S10 ^{1}H NMR spectrum of **2** (Chloroform-*d*, 300 MHz)

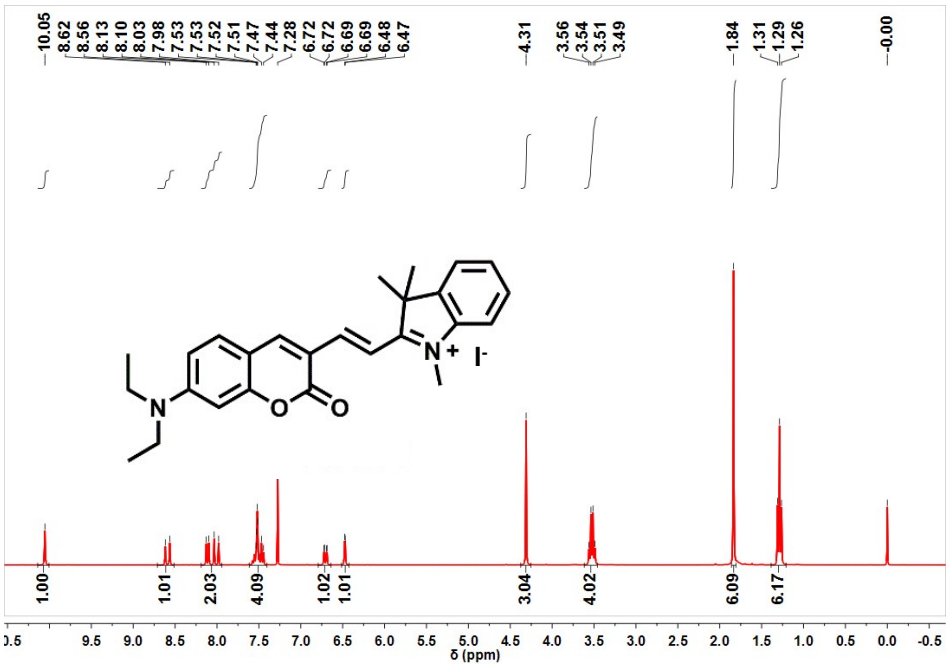


Figure S11 ^{1}H NMR spectrum of **CM-NC$_1$** (Chloroform-*d*, 300 MHz)

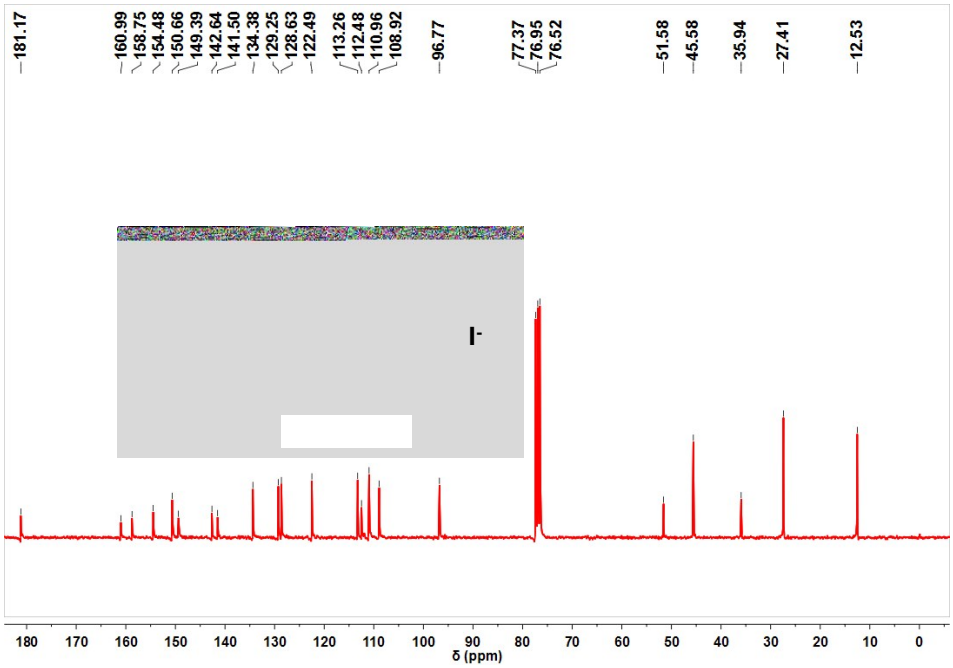


Figure S12 ^{13}C NMR spectrum of **CM-NC$_1$** (Chloroform-*d*, 75 MHz)

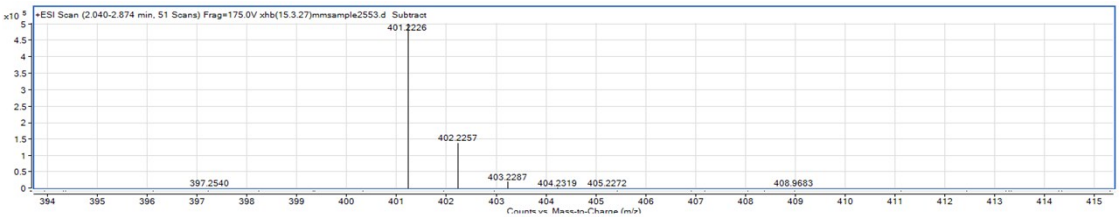


Figure S13HRMS Spectrum of **CM-NC$_1$**

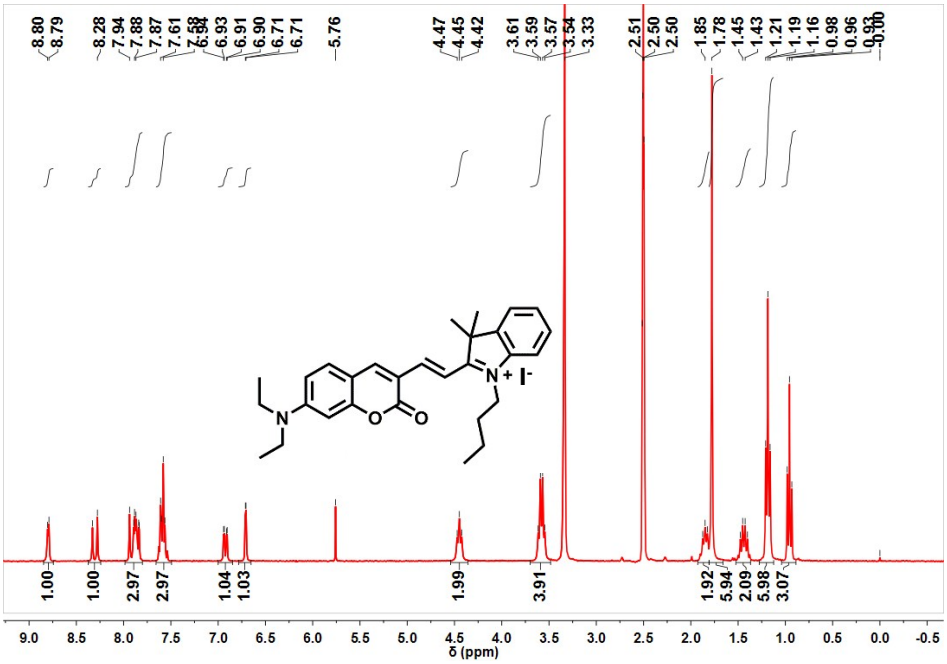


Figure S14 ^{1}H NMR spectrum of **CM-NC$_4$** (DMSO-d_6, 300 MHz)

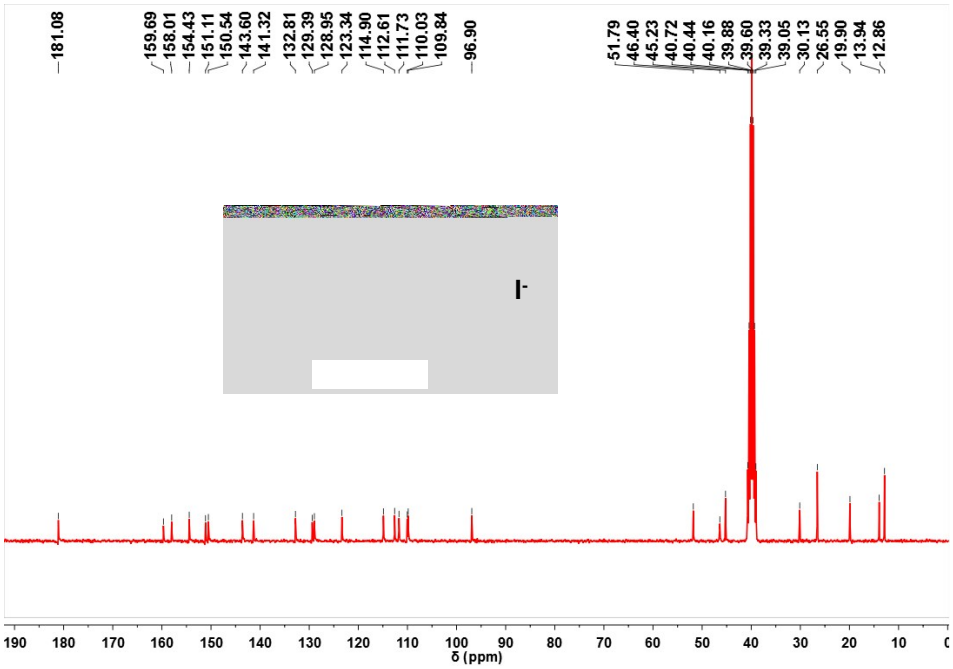


Figure S15 ^{13}C NMR of **CM-NC$_4$** (DMSO-d_6, 75 MHz)

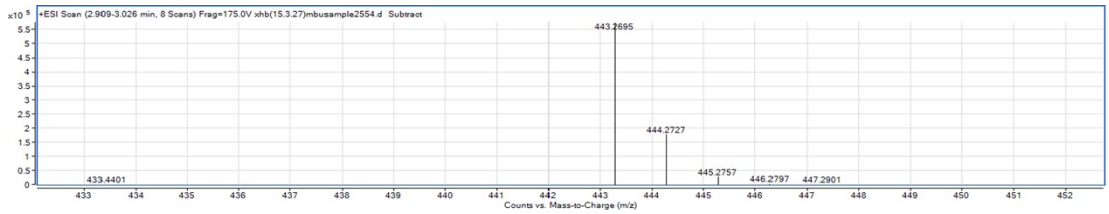


Figure S16 HRMS Spectrum of **CM-NC$_4$**

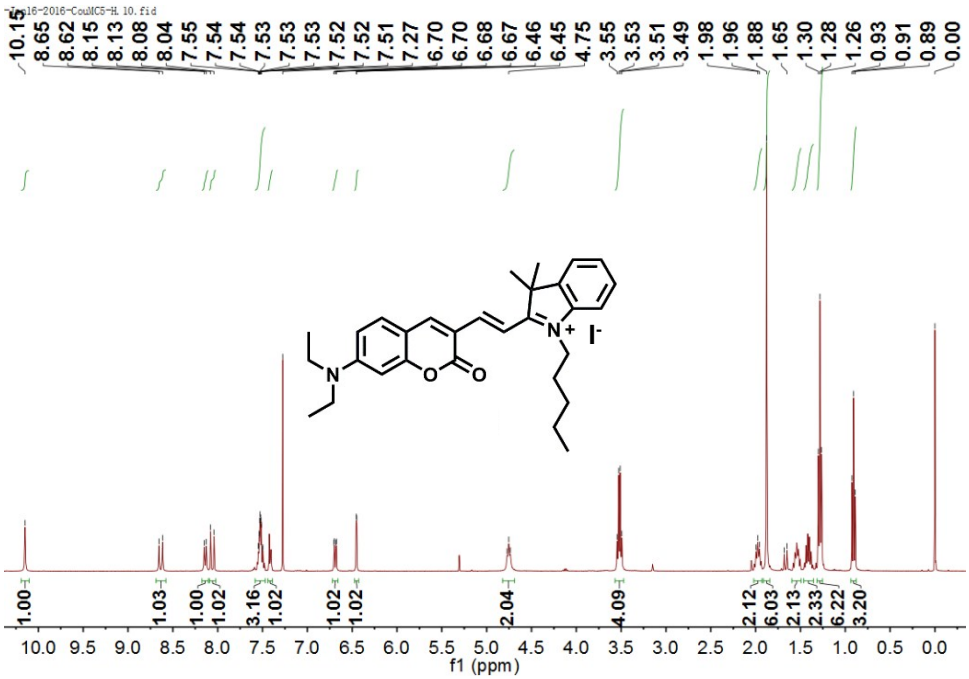


Figure S17 ^{1}H NMR spectrum of **CM-NC$_5$** (Chloroform-*d*, 400 MHz)

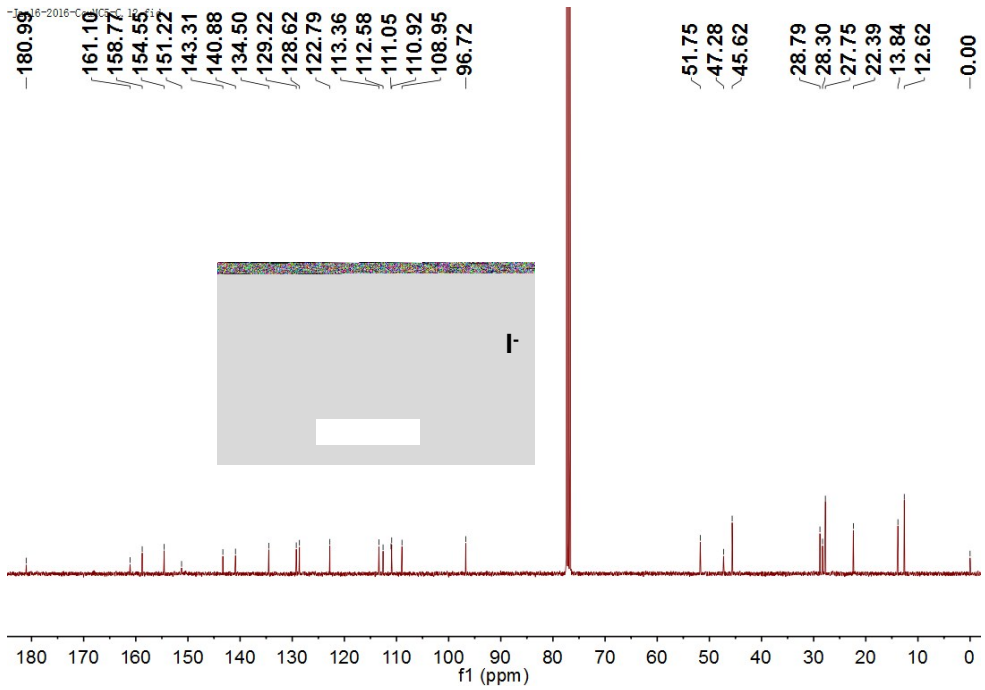


Figure S18 ^{13}C NMR spectrum of **CM-NC$_5$** (Chloroform-*d*, 101 MHz)

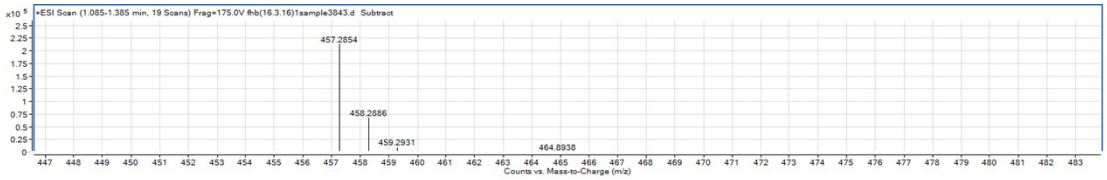


Figure S19 HRMS of **CM-NC$_5$**

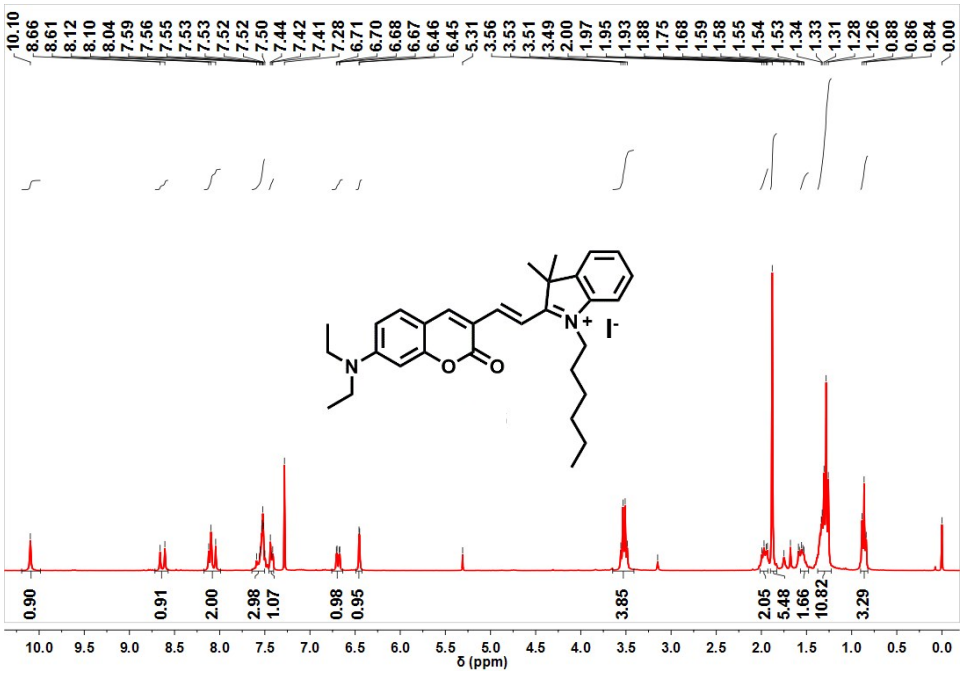


Figure S20 ^{1}H NMR spectrum of **CM-NC$_6$** (Chloroform-*d*, 300 MHz)

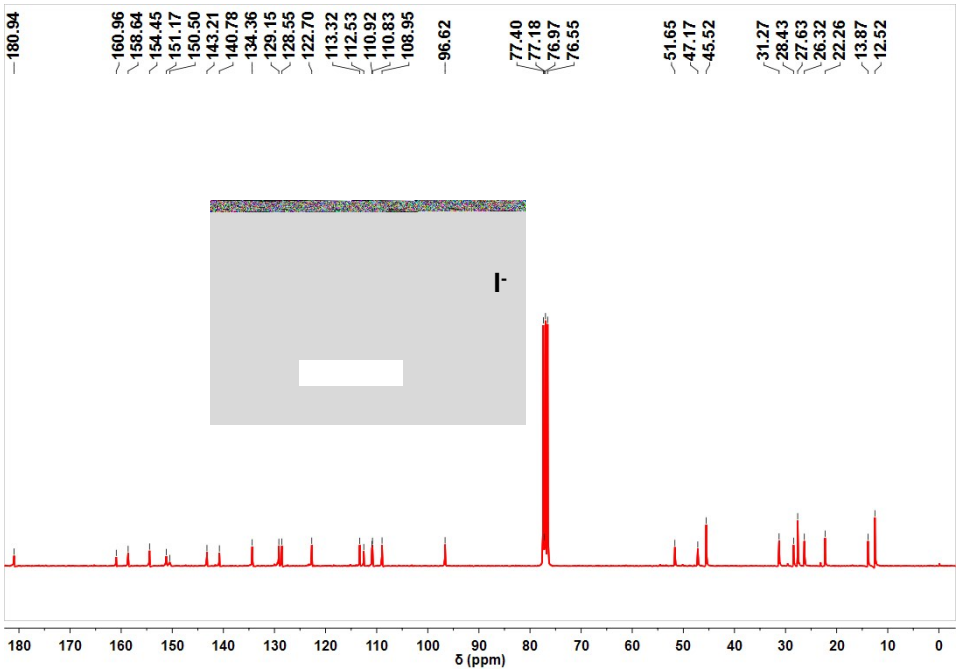


Figure S21 ^{13}C NMR spectrum of **CM-NC$_6$** (Chloroform-*d*, 75 MHz)

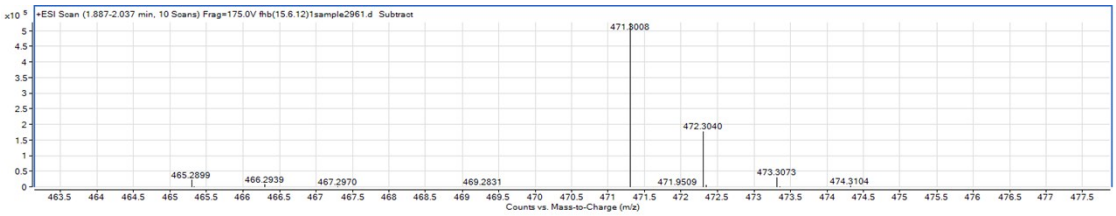


Figure S22 HRMS of **CM-NC$_6$**

Reference

1 J. Wu, W. Liu, X. Zhuang, F. Wang, P. Wang, S. Tao, X. Zhang, Wu S., S. Lee, Org. Lett. 2007, **9**, 33.