Supplementary Information

An Intramolecular Charge Transfer and Excited State Intramolecular Proton Transfer based Fluorescence Probe for Highly Selective Detection and Imaging of Formaldehyde in Living Cells

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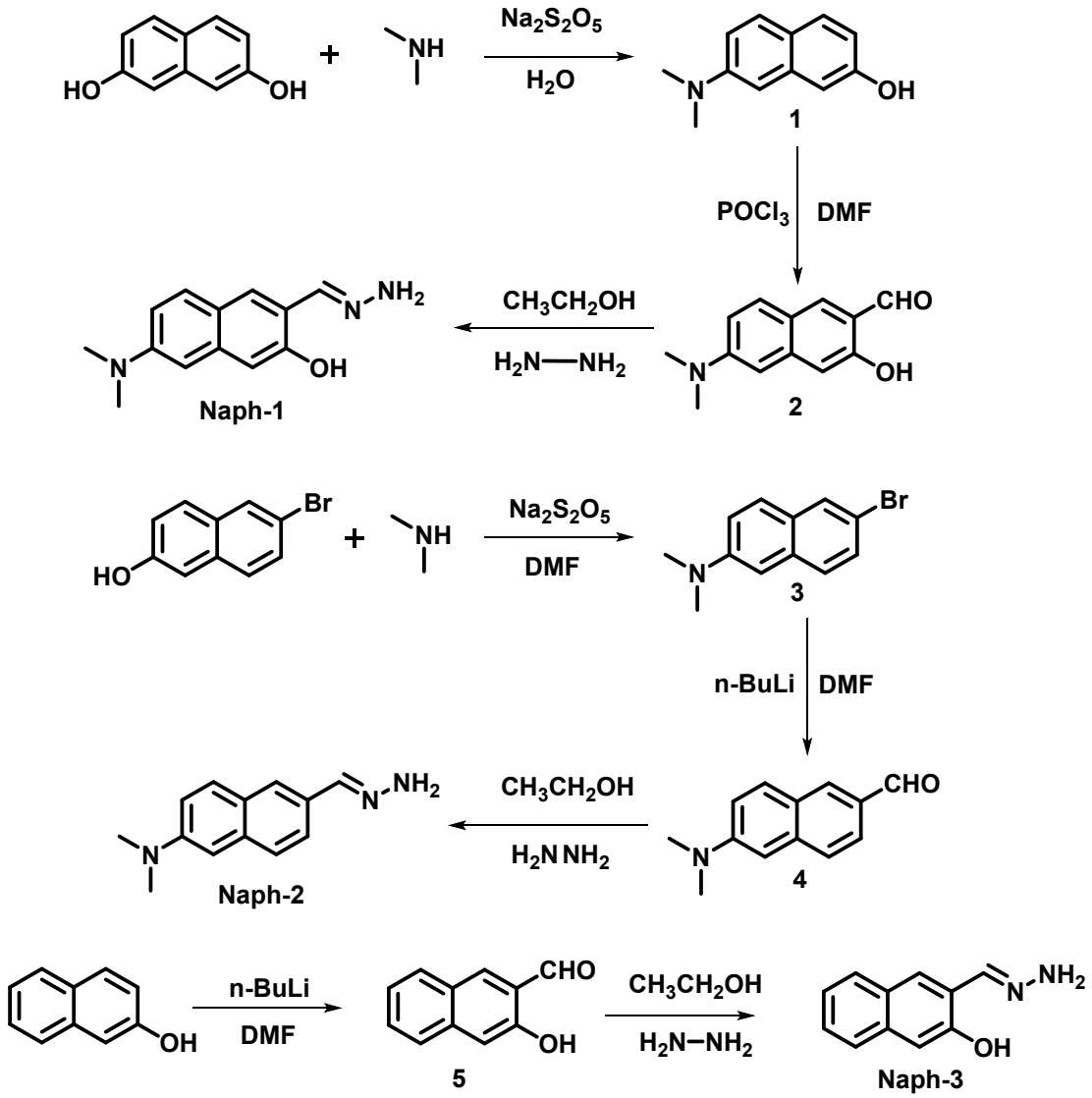
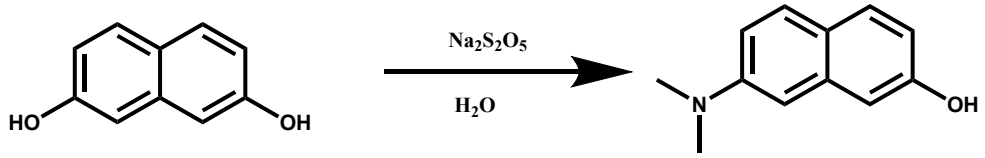
Synthesis of Naph-1, Naph-2 and Naph-3



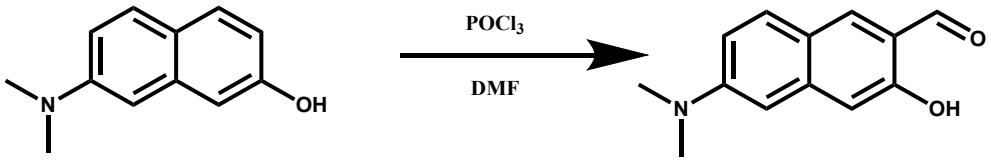
Scheme S1. Synthetic routes for Naph-1, Naph-2 and Naph-3.

Synthesis of Compound 1



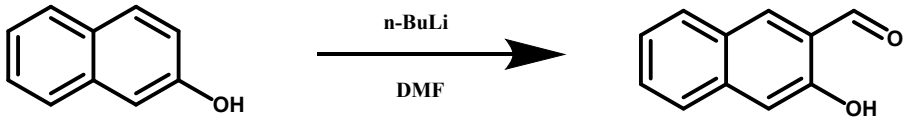
2,7-Dihydroxy naphthalene (0.36 g, 2.24 mM), dimethylamine (0.55 mL, 11.20 mM) and sodium metabisulfite (0.85 g, 4.48 mM) were mixed in 15 mL of water. The mixture was stirred at 140 °C for 20 h. After reaction, the mixture was filtered and washed with water. The residual was purified by silica-gel column chromatography using ethyl acetate/petroleum ether (1 : 10) as eluents to obtain Compound 1 as a yellow solid (0.35 g, yield: 82.3%). ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 2.96 (6H, s, 2 × -CH_3), 6.69 (1H, s, Ar-H), 6.74 (1H, d, J = 8.0 Hz, Ar-H), 6.89 (1H, s, Ar-H), 6.93 (1H, d, J = 8.0 Hz, Ar-H), 7.50-7.56 (1H, m, -CH_2). ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 40.12, 107.05, 113.06, 127.68, 128.35, 135.12, 153.00.

Synthesis of 6-(dimethylamino)-3-hydroxy-2-naphthaldehyde (Compound 2)



$POCl_3$ (0.7 mL) was first added into DMF (1.5 mL) at 0 °C under nitrogen atmosphere. The mixture was then heated to 50 °C for 30 min. Compound 2 (0.54 g, 2.50 mM) was then added and the mixture was reacted at 70 °C for 1.5 h. The reaction was stopped with ice water and the resulting precipitate was filtered to get a crude product. The coarse product was separated by the silica-gel column chromatography using ethyl acetate/petroleum ether (1 : 5) as eluents to obtain Compound 2 as a yellow solid (0.42g, yield 78.3%). ^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm): 3.06 (6H, s, 2 × -CH_3), 6.92 (1H, d, J =4.0 Hz, Ar-H), 7.16 (1H, d, J = 12.0 Hz, Ar-H), 7.67 (1H, d, J = 8.0 Hz, Ar-H), 7.88 (1H, d, J = 8.0 Hz, Ar-H), 8.49 (1H, s, Ar-H), 9.93 (1H, s, -CHO), 10.20 (1H, s, -OH). ^{13}C NMR (100MHz, DMSO-d_6) δ (ppm): 46.30, 106.49, 115.23, 115.26, 116.13, 123.09, 130.54, 134.08, 135.89, 159.12, 159.73, 191.06. MS (ESI) m/z: calcd for $C_{13}H_{13}O_2N$ $[M+H]^+$ m/z 215.09, found 216.1.

Synthesis of Compound 3



3

2-naphthol (0.144 g, 1.0 tendency) was dissolved in 3.0 mL anhydrous tetrahydrofuran (THF) and the mixture was stirred in an ice-salt bath under N_2 protection for 15 min. Then n-butyl lithium (n – BuLi, 760 μL) was added dropwise and the mixture was stirred for another 1 h before addition of DMF (50 μL). The mixture was then reacted at room temperature for ~3 h. Hydrochloric acid was added and the mixture was extracted with ethyl acetate (50 mL) for three times. The combined organic phase was washed twice with brine (50 mL) and dried over anhydrous sodium sulfate (Na_2SO_4). The mixture was then filtered and the filtrate was concentrated under reduced pressure. The crude product was purified by column chromatography using ethyl acetate/petroleum ether (1 : 20) as eluents to obtain a bright yellow solid (0.082 g, yield 47.6%). ^{1}H NMR (400 MHz, CDCl3) δ (ppm): 7.13 (1H, d, J = 8.0 Hz, Ar-H), 7.43 (1H, t, J = 8.0 Hz, Ar-H), 7.61 (1H, t, J = 8.0 Hz, Ar-H), 7.79 (1H, d, J = 8.0 Hz, Ar-H), 7.97 (1H, d, J = 8.0 Hz, Ar-H), 8.33 (1H, d, J = 8.0 Hz, Ar-H), 10.80 (1H, s, -OH), 13.16 (1H, s, -CHO). ^{13}C NMR (100MHz, CDCl3) δ (ppm): 111.30, 118.62, 119.21, 124.54, 127.82, 129.16, 129.52, 132.90, 139.20, 164.97, 193.32.

NMR spectra and HR-MS spectrum

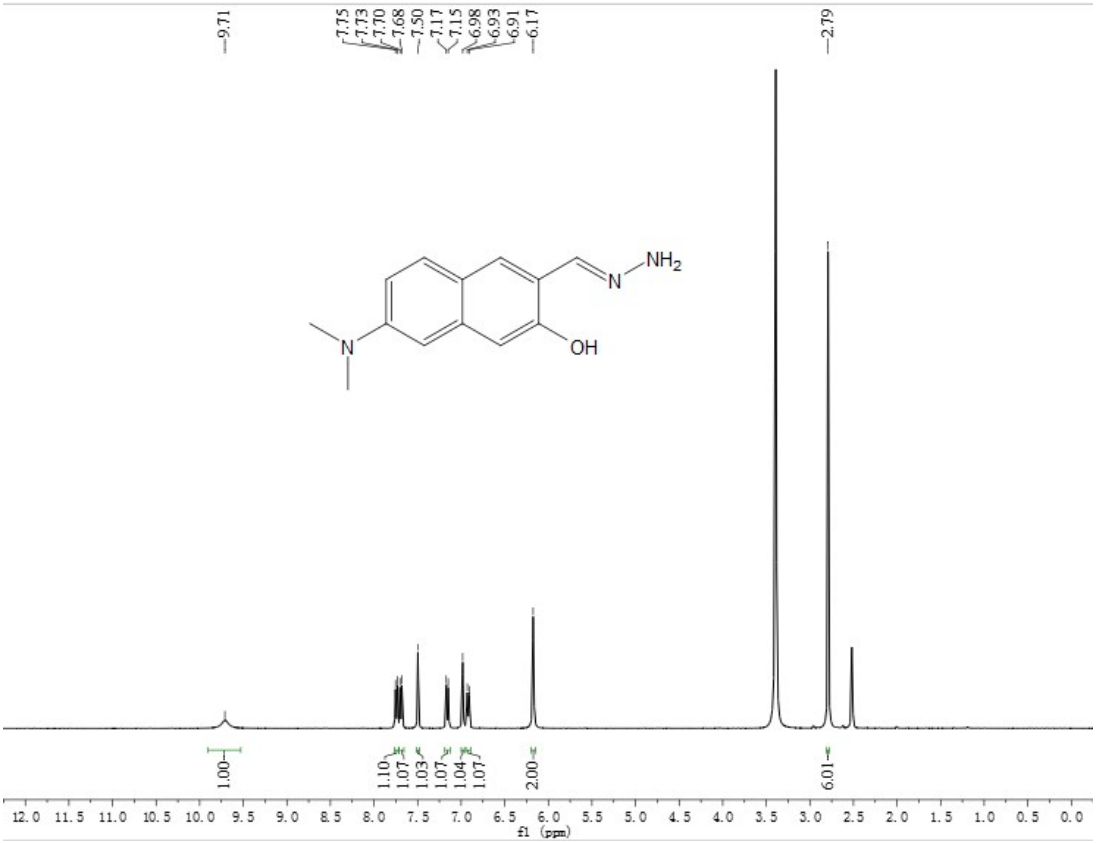


Fig.S1 ^{1}H NMR spectrum of Naph-1.

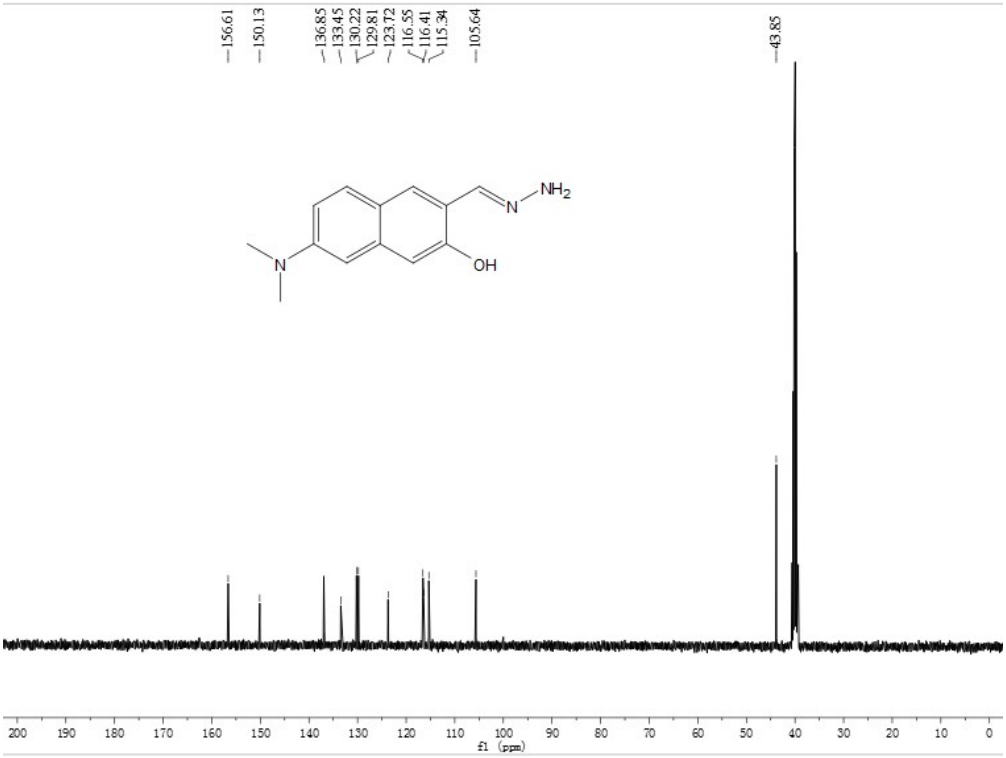
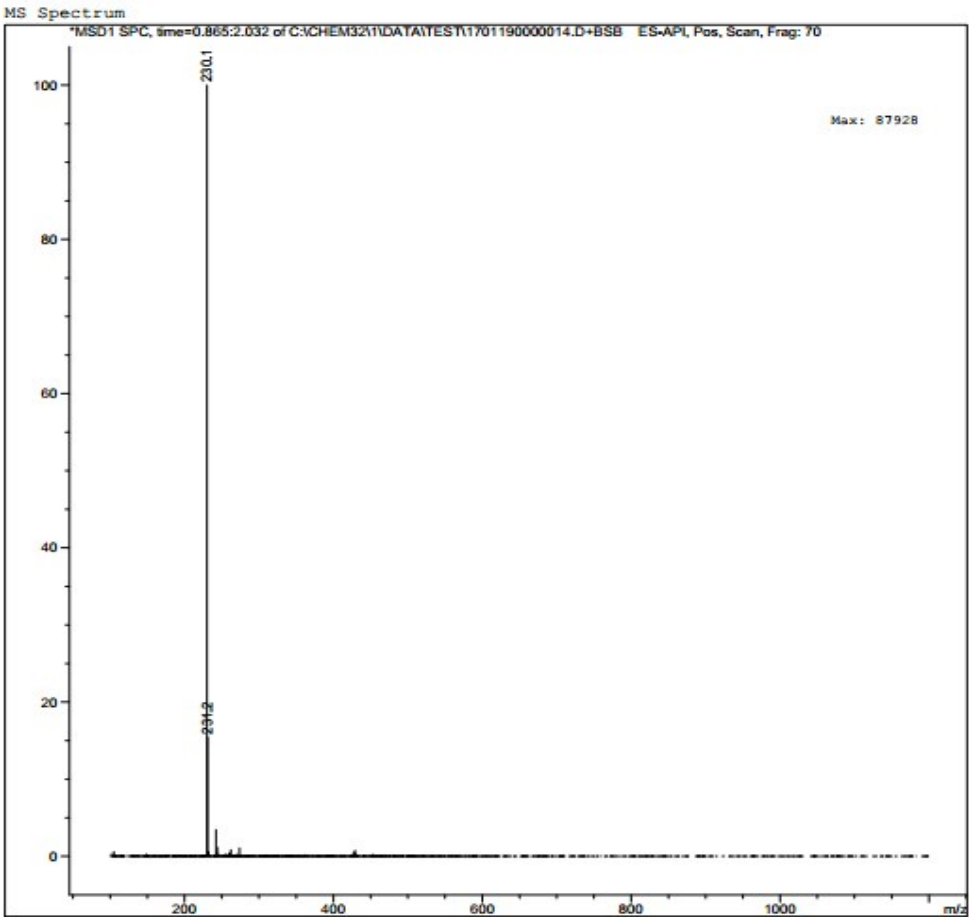


Fig.S2 ^{13}C-NMR spectrum of Naph-1.



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Scan No. 1 of 1

Mass	Relative Intensity	Theoretical Mass	Delta [ppm]	Delta [mmu]	Composition
229.121	125.8	229.1210	2.2	0.5	$C_{13}H_{15}O_1N_3$
		229.1335	-52.7	-12.1	$C_{14}H_{17}O_1N_2$
		229.1012	88.5	20.3	$C_{18}H_{13}$
		229.1461	-107.6	-24.7	$C_{15}H_{19}O_1N_1$
		229.0886	143.4	32.9	$C_{17}H_{11}N_1$

Fig.S3 HR-MS spectrum of Naph-1.

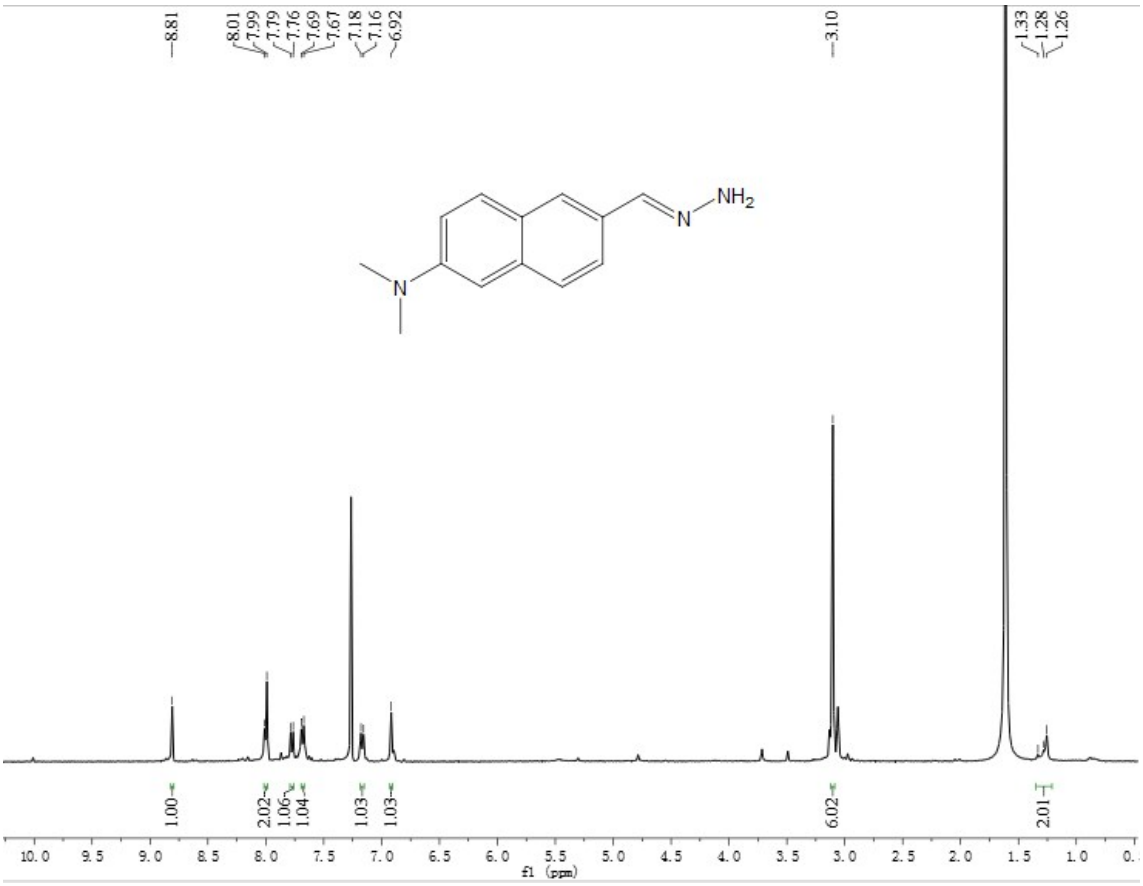


Fig.S4 ^{1}H-NMR spectrum of Naph-2.

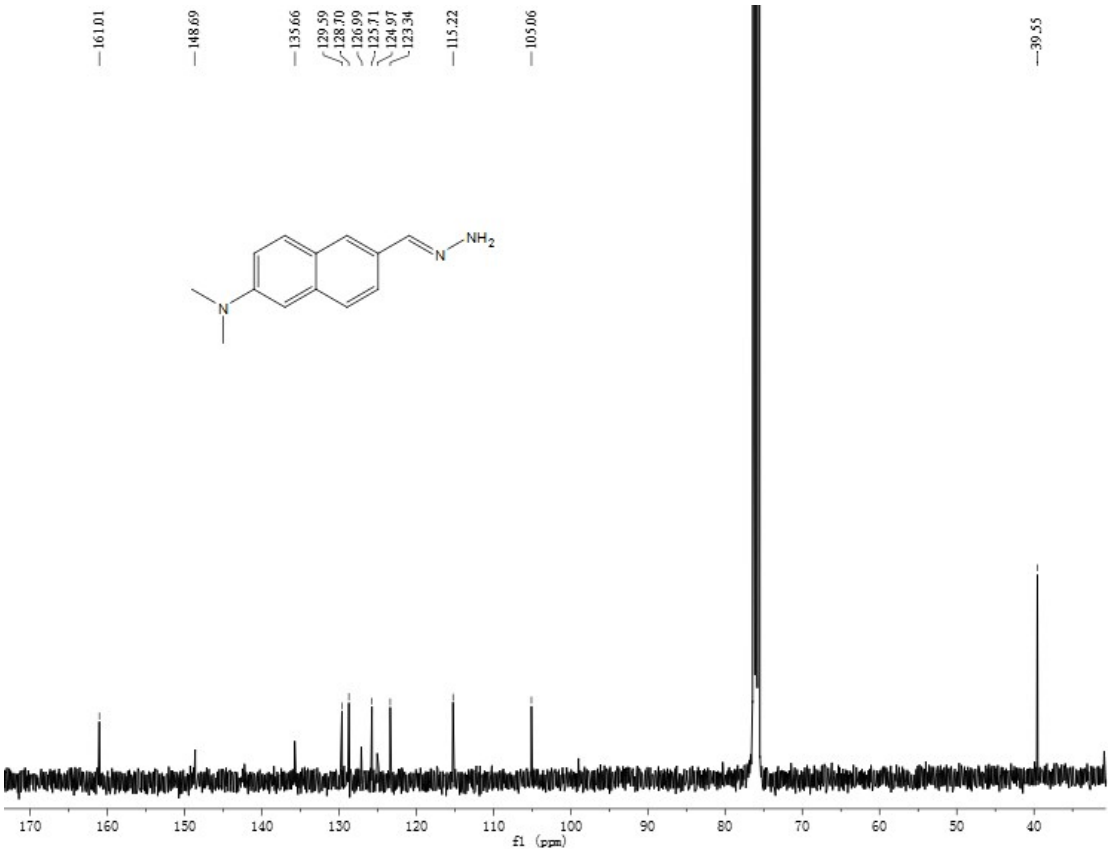
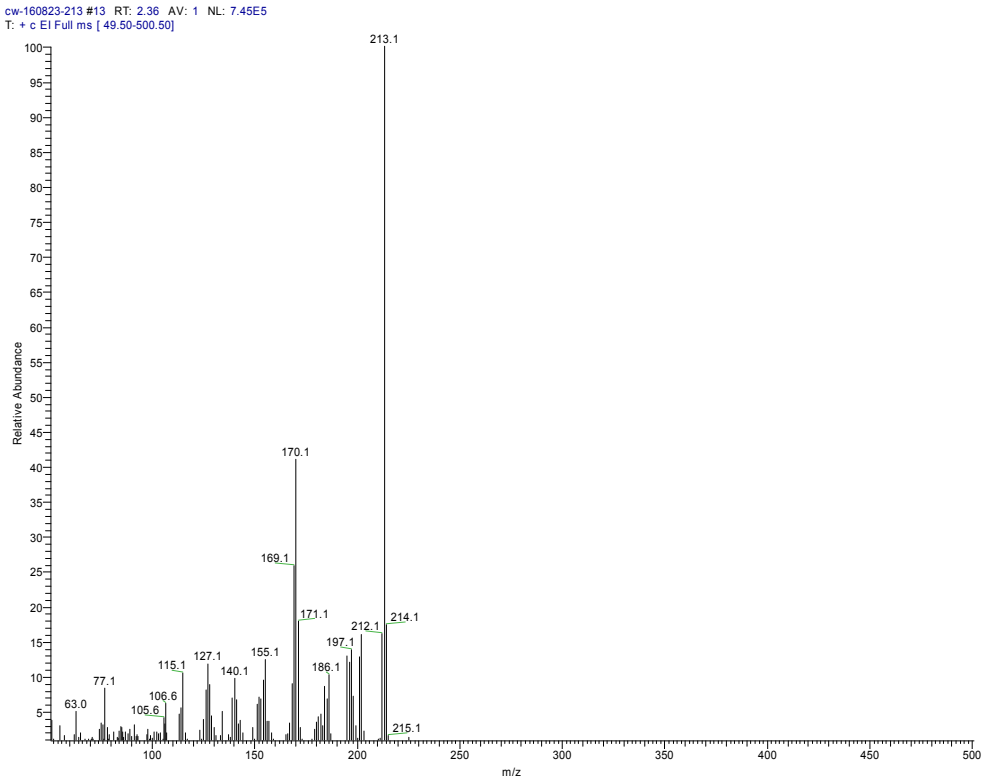


Fig.S5 ^{13}C-NMR spectrum of Naph-2.



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Scan No. 1 of 1

Mass	Relative Intensity	Theoretical Mass	Delta [ppm]	Delta [mmu]	Composition
213.126	100.0	213.1260	-2.3	-0.5	$C_{13}H_{15}N_3$
		213.1386	-61.3	-13.1	$C_{14}H_{17}N_2$
		213.1512	-120.3	-25.7	$C_{15}H_{19}N_1$
		213.1638	-179.3	-38.2	$C_{16}H_{21}$
		213.0699	261.3	55.7	$C_{17}H_9$

Fig.S6 HR-MS spectrum of Naph-2.

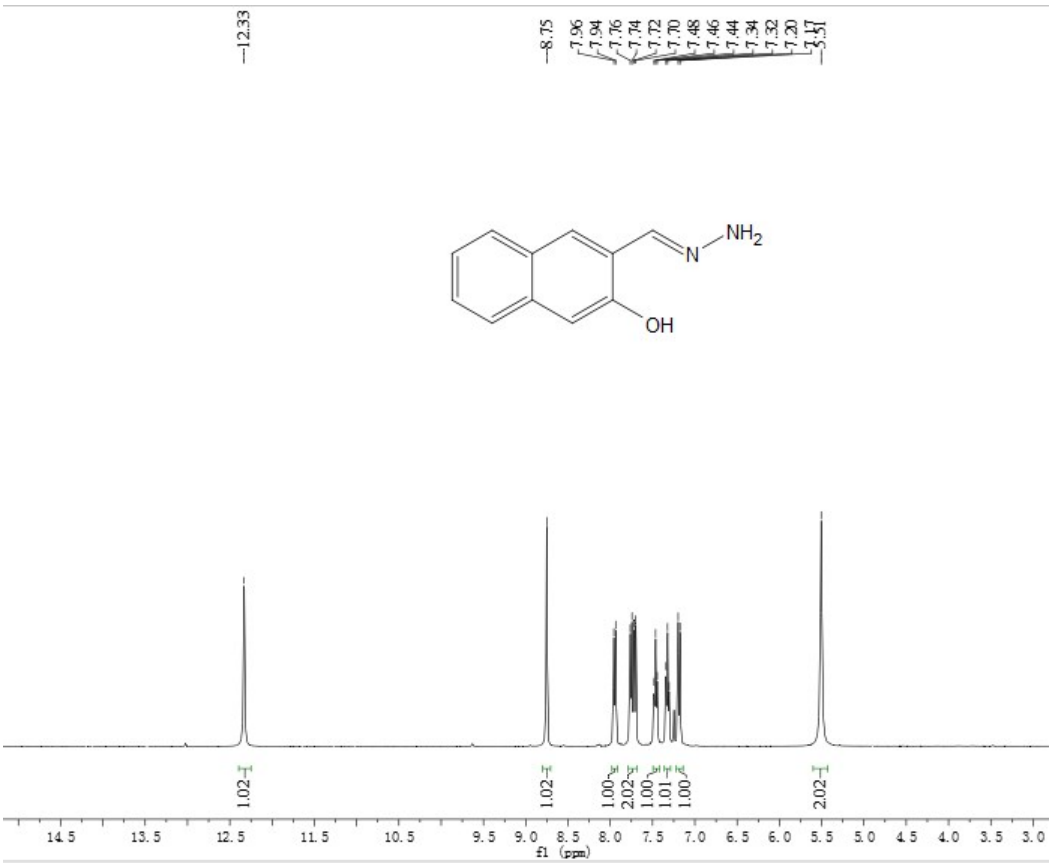


Fig.S7 ^{1}H-NMR spectrum of Naph-3.

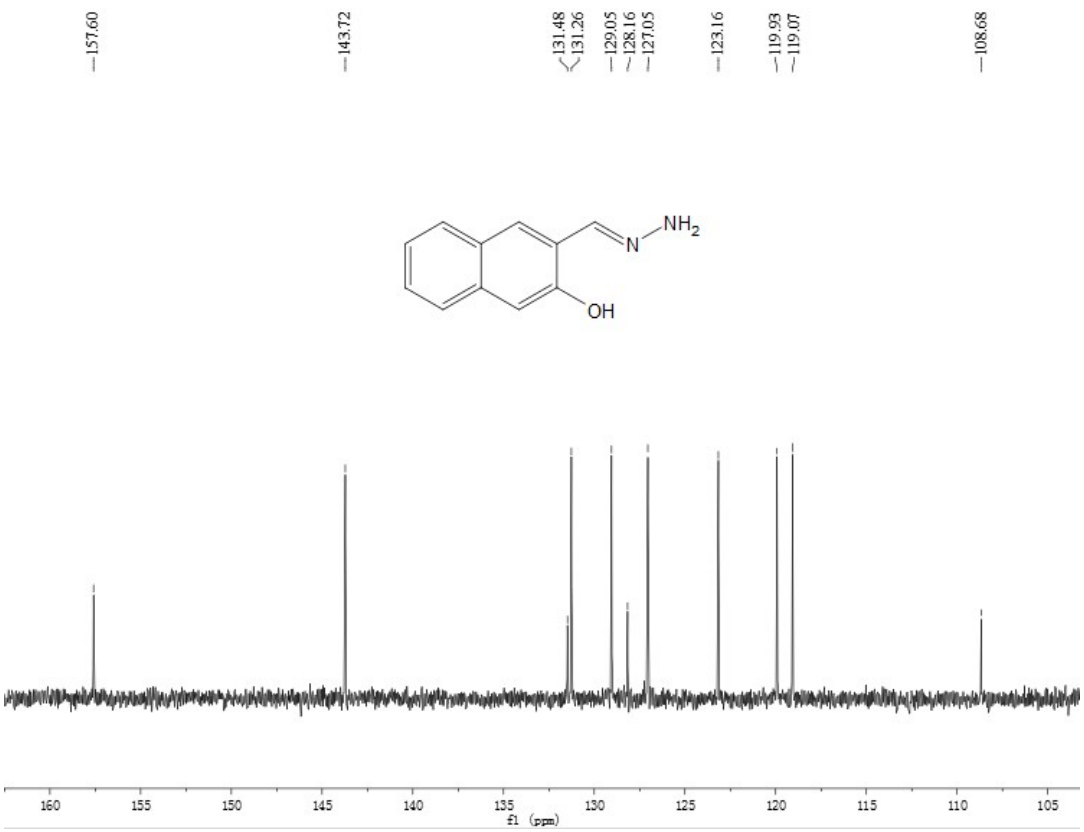
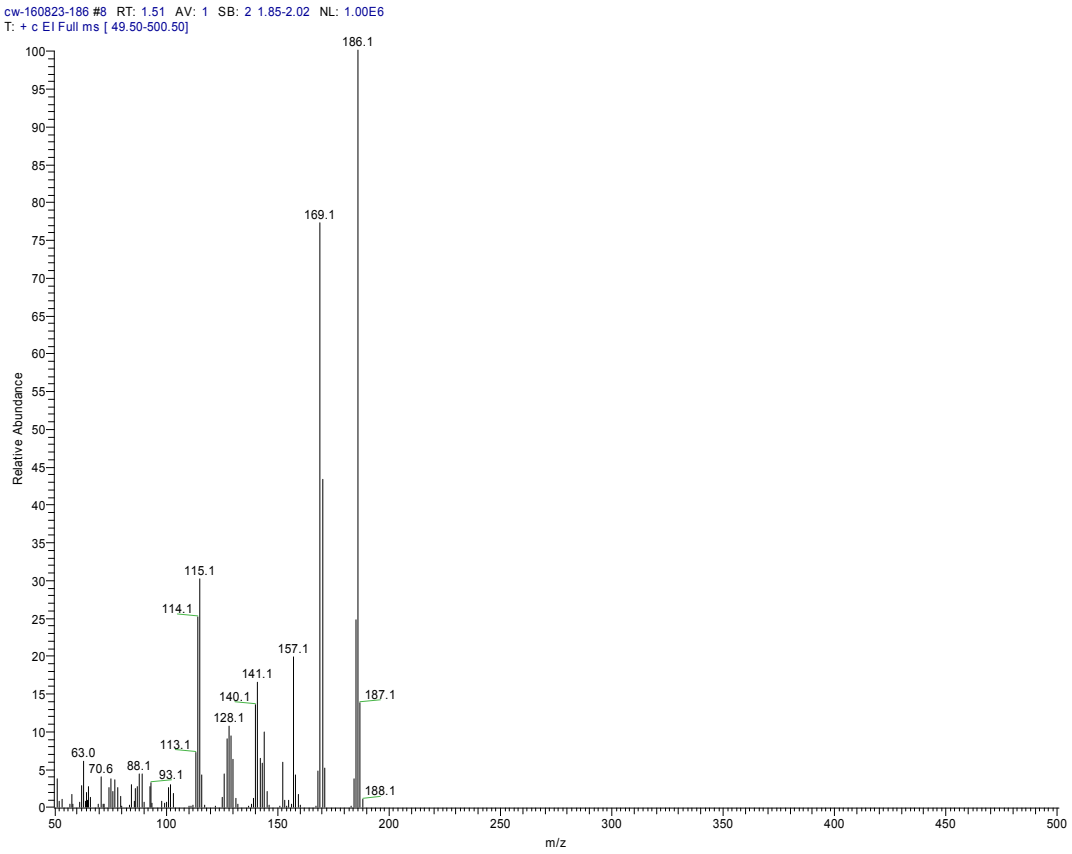


Fig.S8 ^{13}C-NMR spectrum of Naph-3.



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Scan No. 1 of 1

Mass	Relative Intensity	Theoretical Mass	Delta [ppm]	Delta [mmu]	Composition
186.079	100.3	186.0788	-0.3	-0.1	$C_{11}H_{10}O_1N_2$
		186.0662	67.3	12.5	$C_{10}H_8O_1N_3$
		186.0913	-67.9	-12.6	$C_{12}H_{12}O_1N_1$
		186.1026	-128.2	-23.9	$C_{11}H_{13}N_2$
		186.1039	-135.4	-25.2	$C_{13}H_{14}O_1$

Fig.S9 HR-MS spectrum of Naph-3.

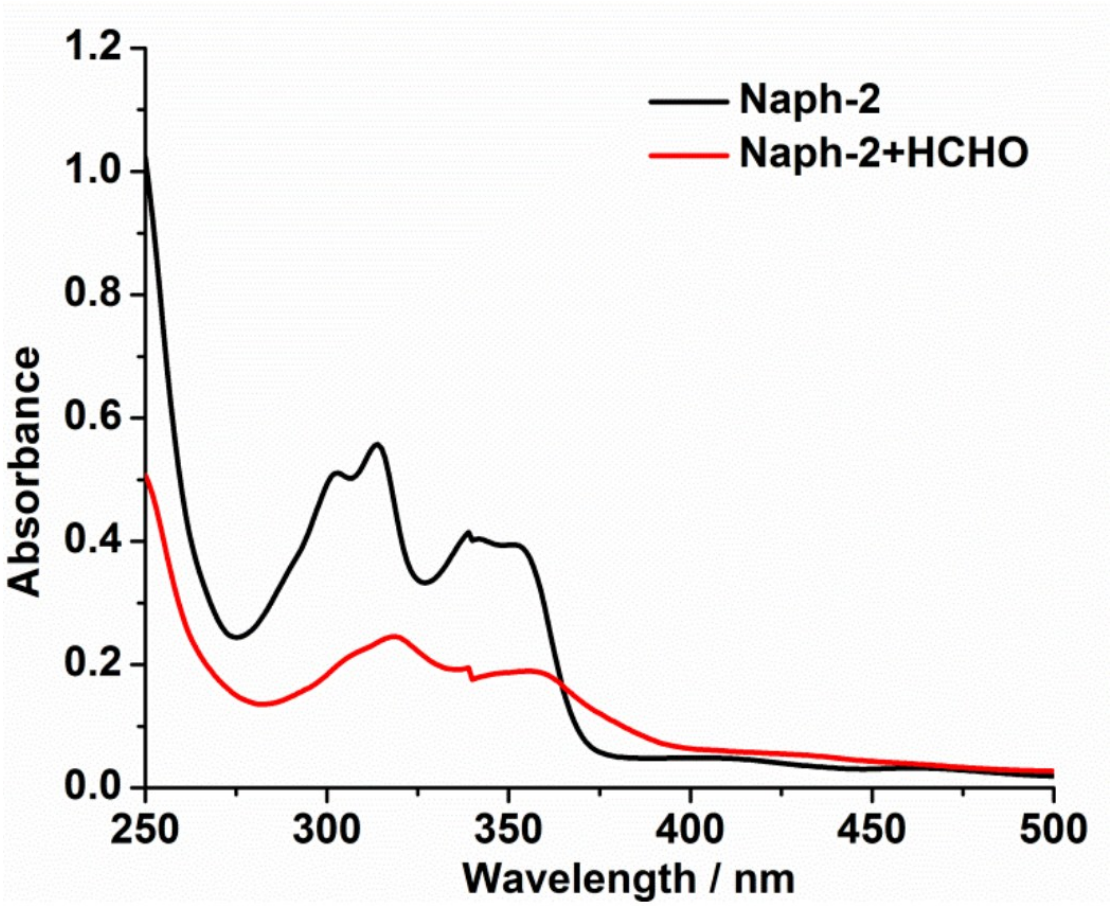

Fig. S10 Absorbance spectra of Naph-2 (10 μM) in the absence (black line) and presence (red line) of FA in PBS (10 mM, pH 7.4), containing 1% DMSO.

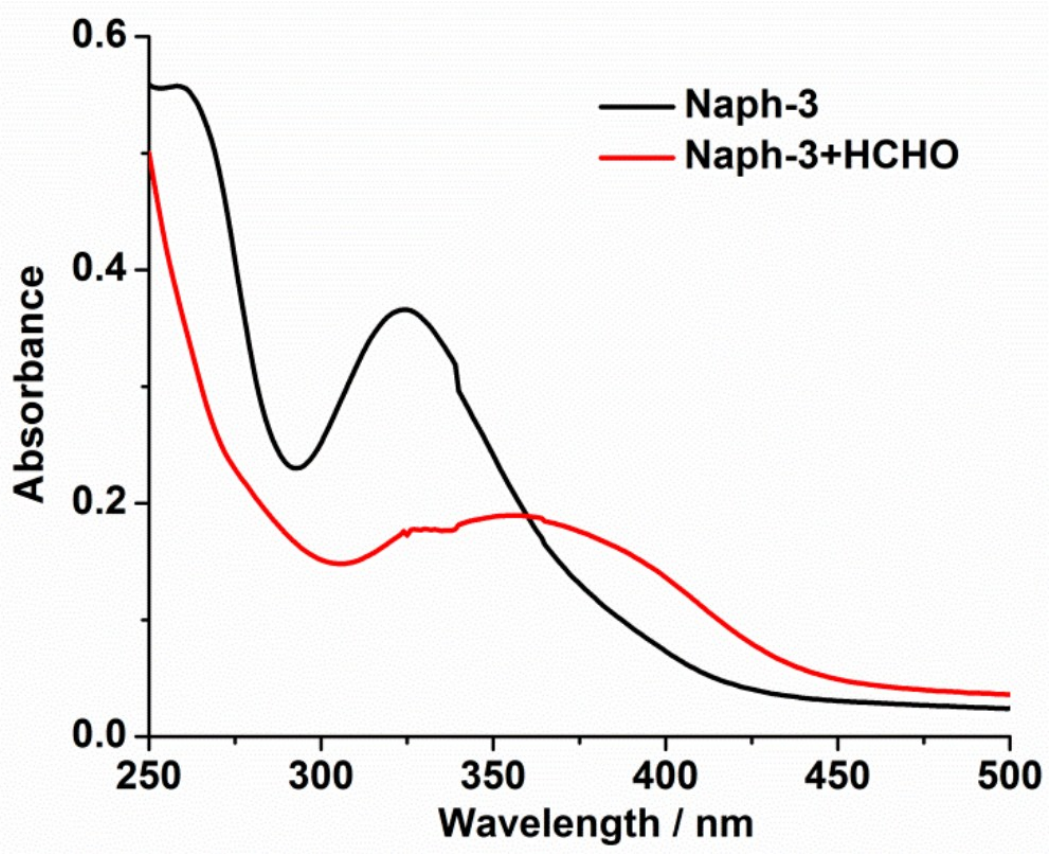

Fig. S11 Absorbance spectra of Naph-3 (10 μM) in the absence (black line) and presence (red line) of FA in PBS (10 mM, pH 7.4), containing 1% DMSO.

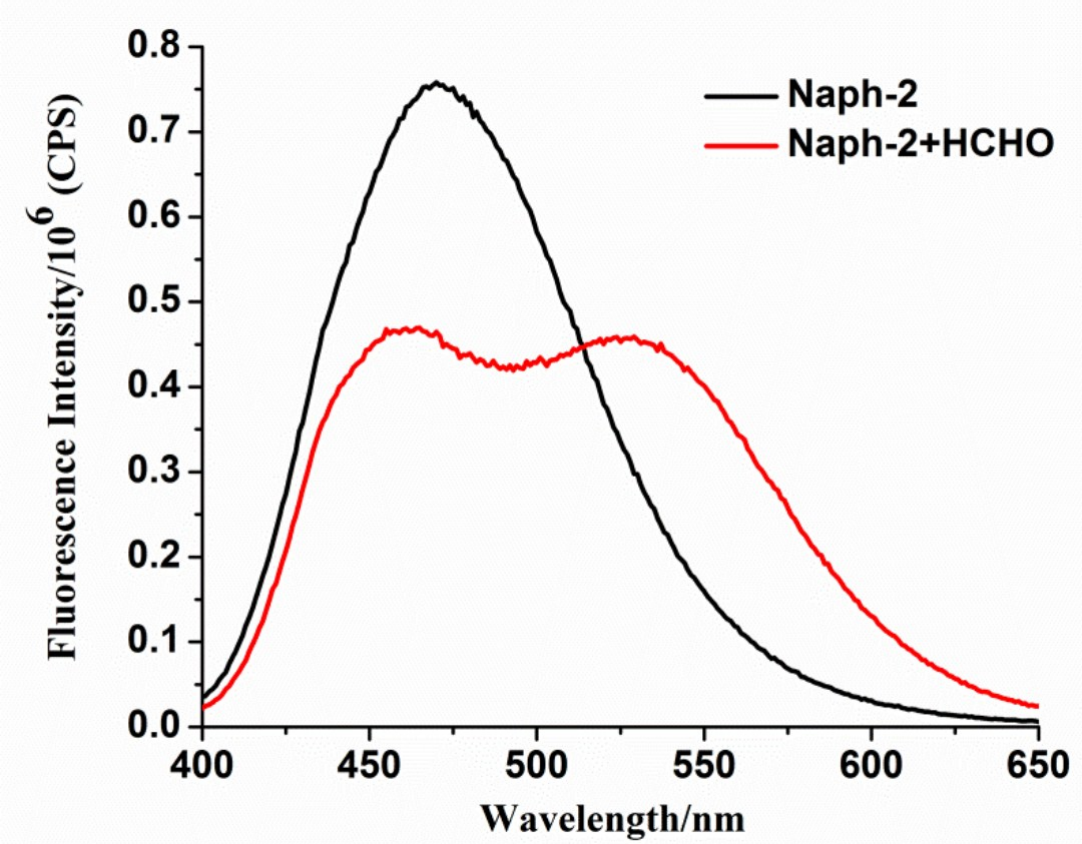

Fig. S12 Fluorescence emission spectra of Naph-2 (10 μM) in the absence (black line) and presence (red line) of FA in PBS buffer (10 mM, pH 7.4), containing 1% DMSO.

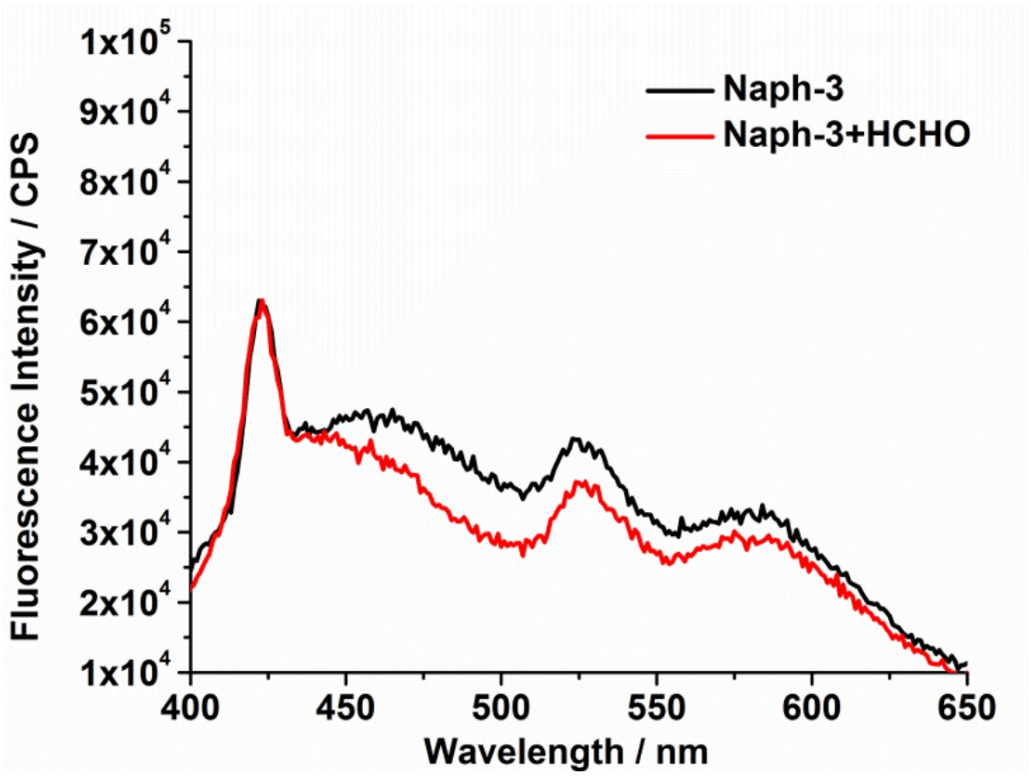

Fig. S13 Fluorescence emission spectra of Naph-3 (10 μM) in the absence (black line) and presence (red line) of FA in PBS buffer (10 mM, pH 7.4), containing 1% DMSO.

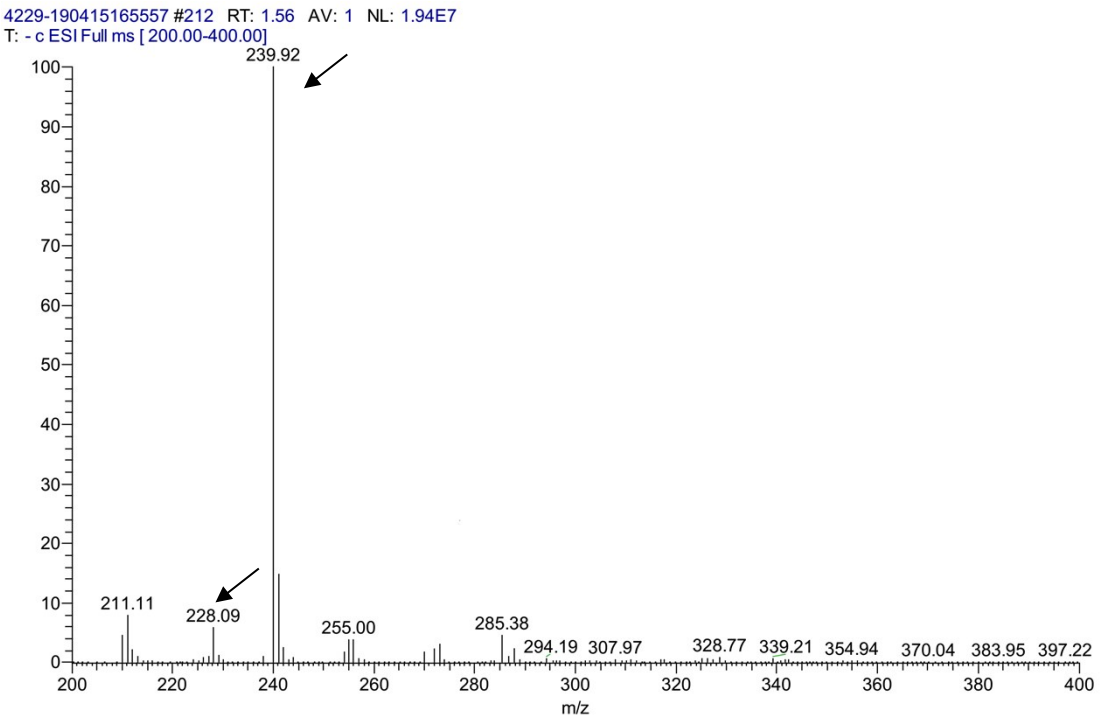

Fig. S14 Mass spectrum of the isolated products from the reaction mixture of Naph-1 and formaldehyde.

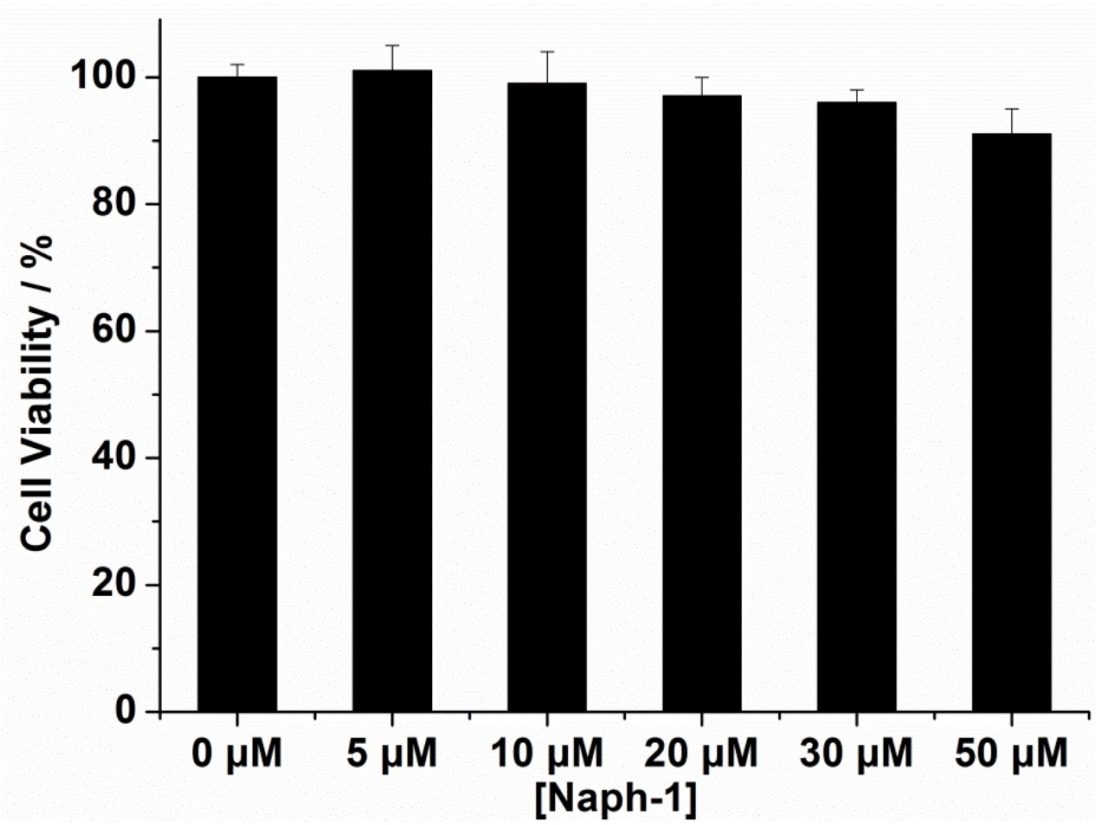

Fig. S15 Cell viability estimated by WST-1 assay. HeLa cells were incubated with different concentrations of Naph-1 (0 - 50 μM) for 24 h. The results were presented as means ± SD of three experiments

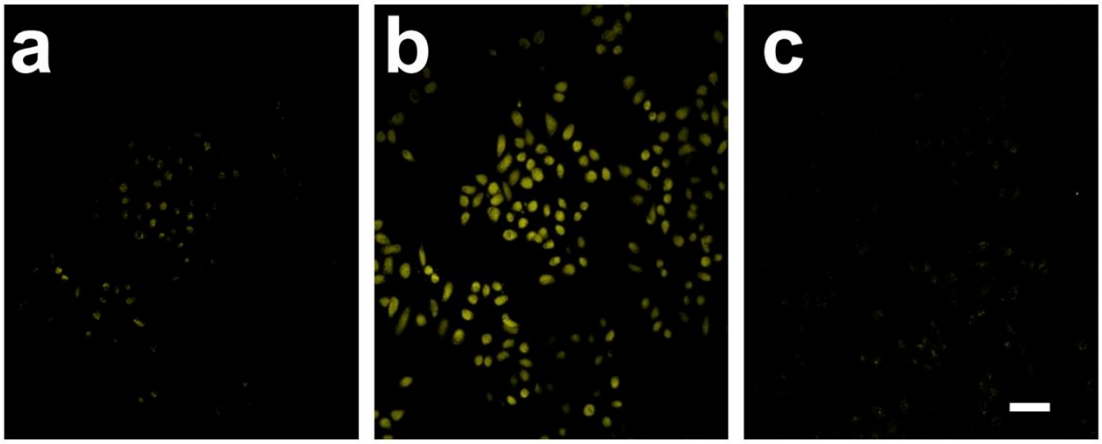

Fig. S16 Confocal microscopy images of cells with 20X objective lens. (a) HeLa cells incubated with 10 μM Naph-1 for 120 min; (b) HeLa cells incubated with 10 μM Naph-1 for 30 min followed by treatment with 20 μM formaldehyde for 2 h; (c) Hela cells pretreated with $NaHSO_3$ (200 μM) followed by treatment with 10 μM Naph-1 for 120 min. Scale bar = 20 μm

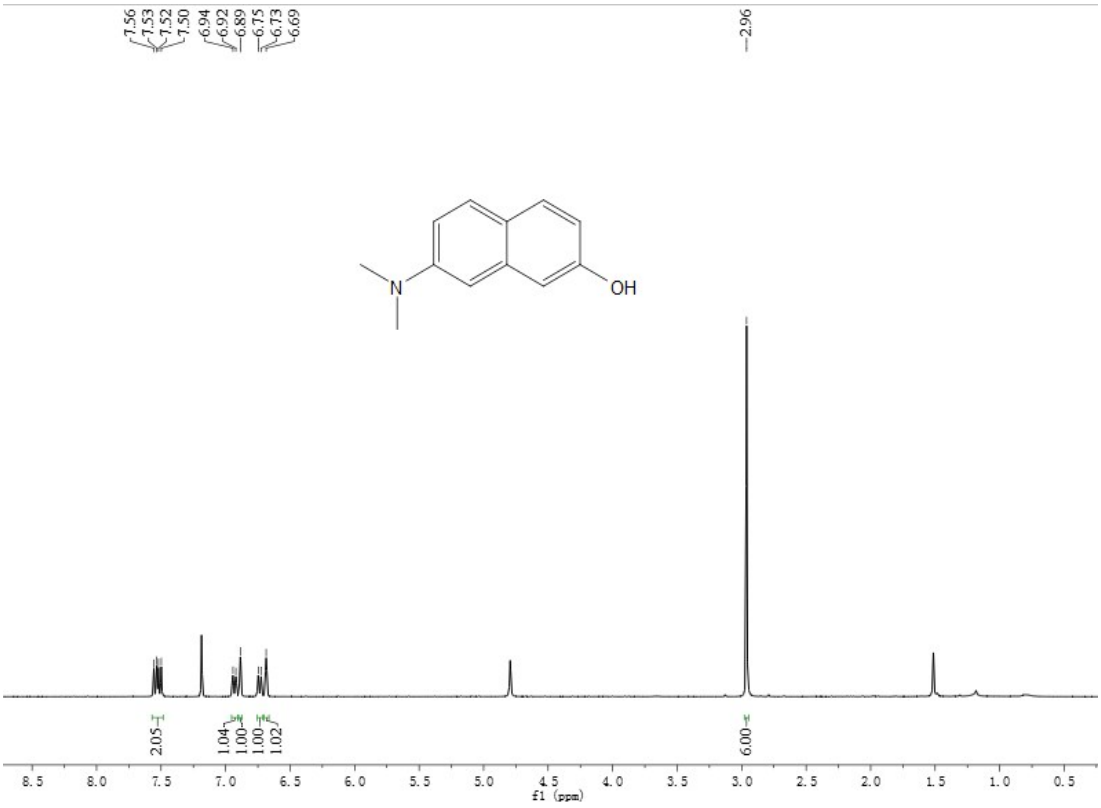

Fig.S17 ^{1}H NMR spectrum of Compound 1.

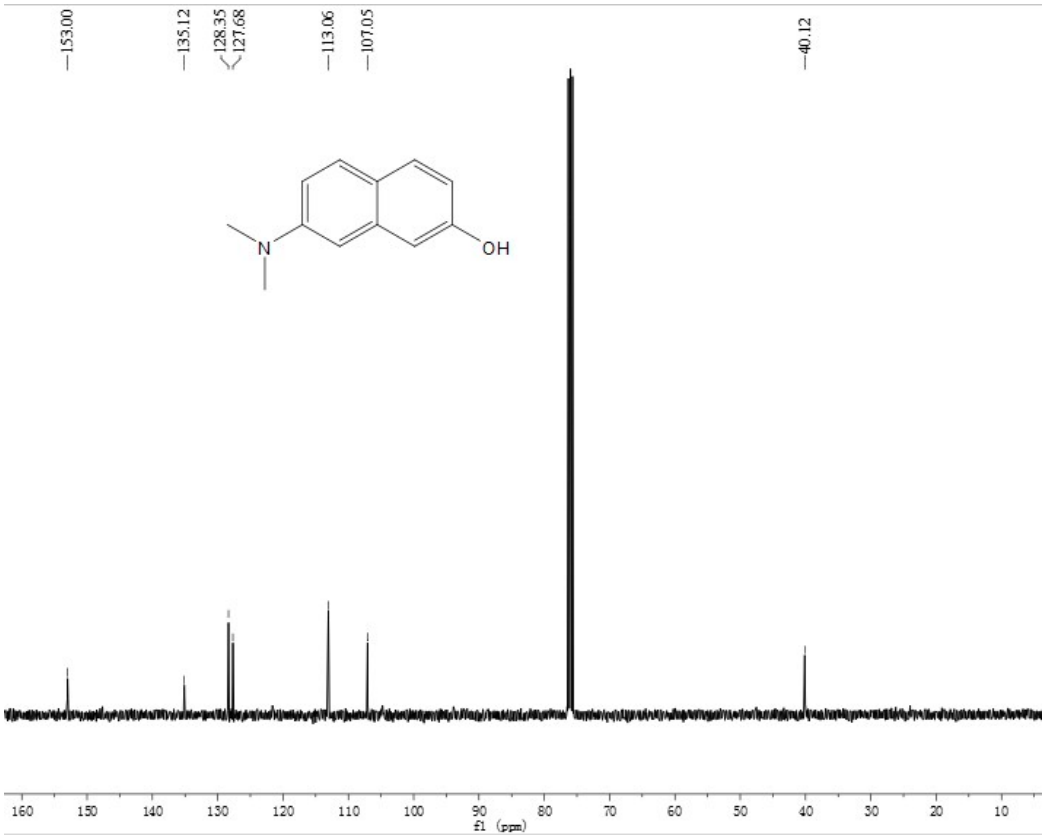

Fig.S18 ^{13}C-NMR spectrum of Compound 1.

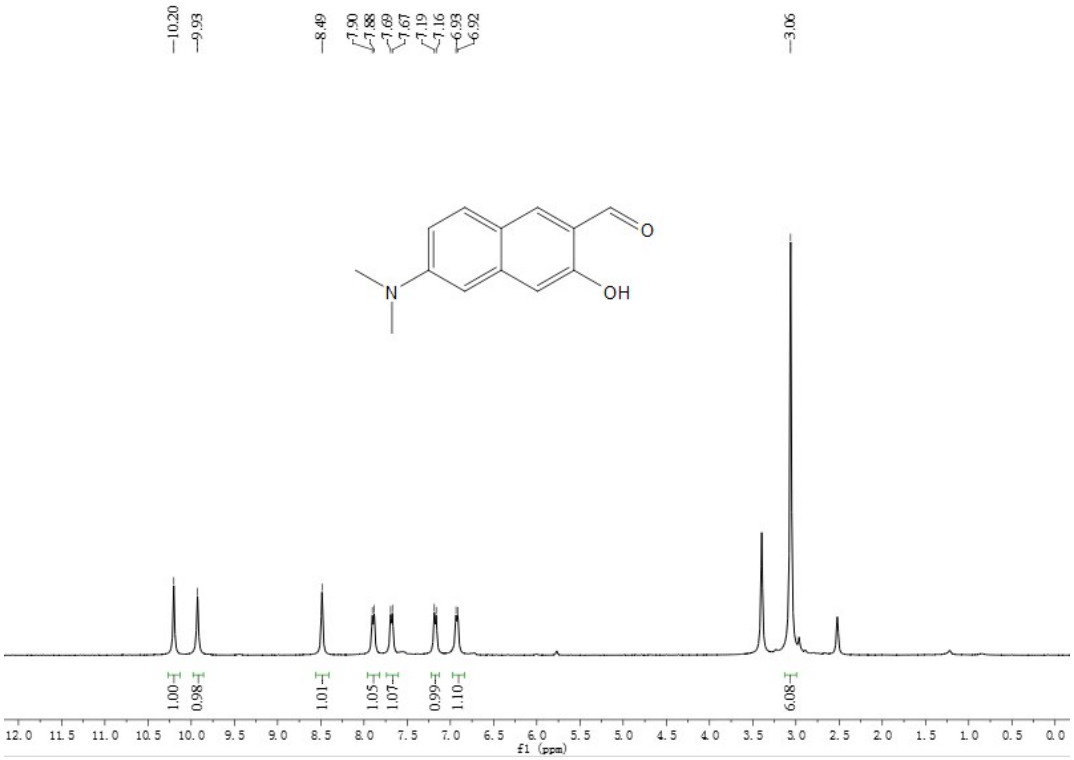

Fig.S19 ^{1}H NMR spectrum of Compound 2.

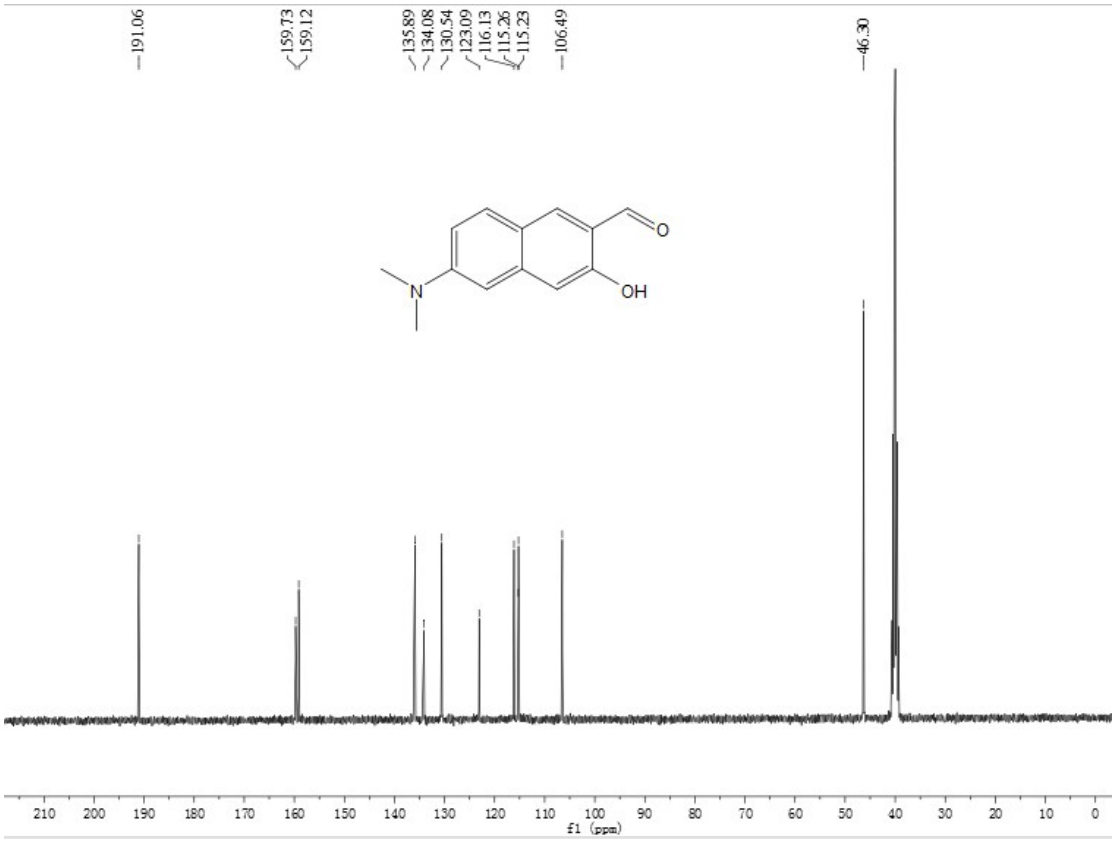

Fig.S20 ^{13}C-NMR spectrum of Compound 2.

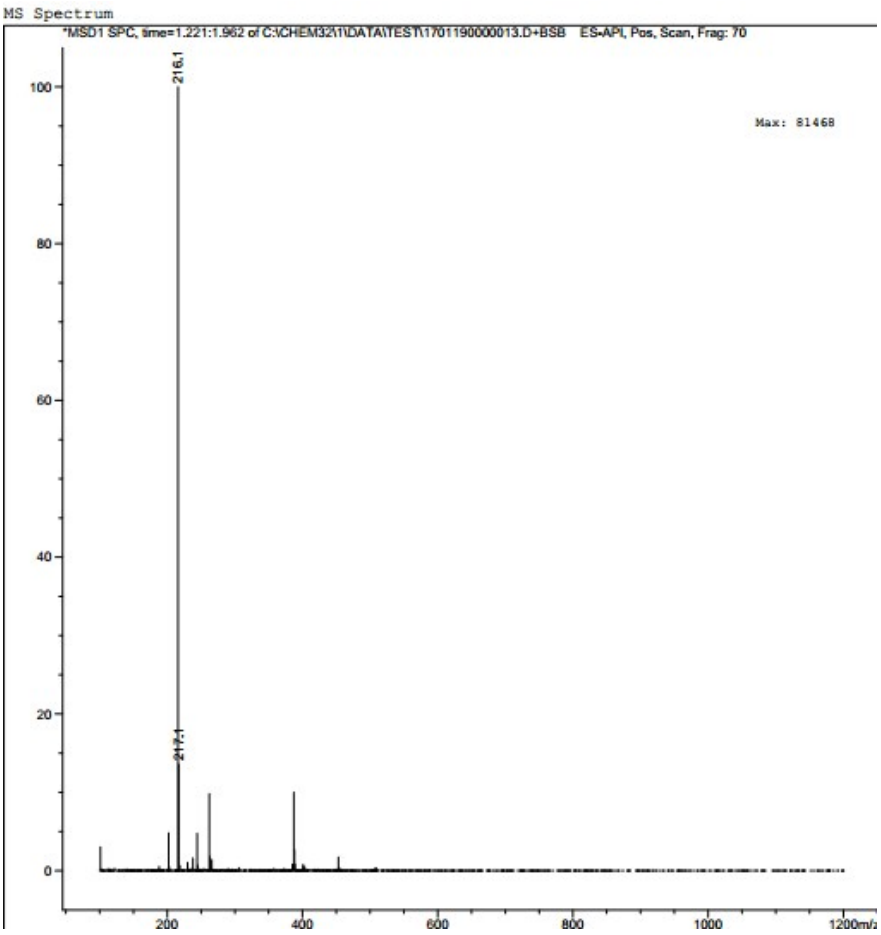

Fig.S21 MS spectrum of Compound 2.

Fig.S22 ^{1}H NMR spectrum of Compound 5.

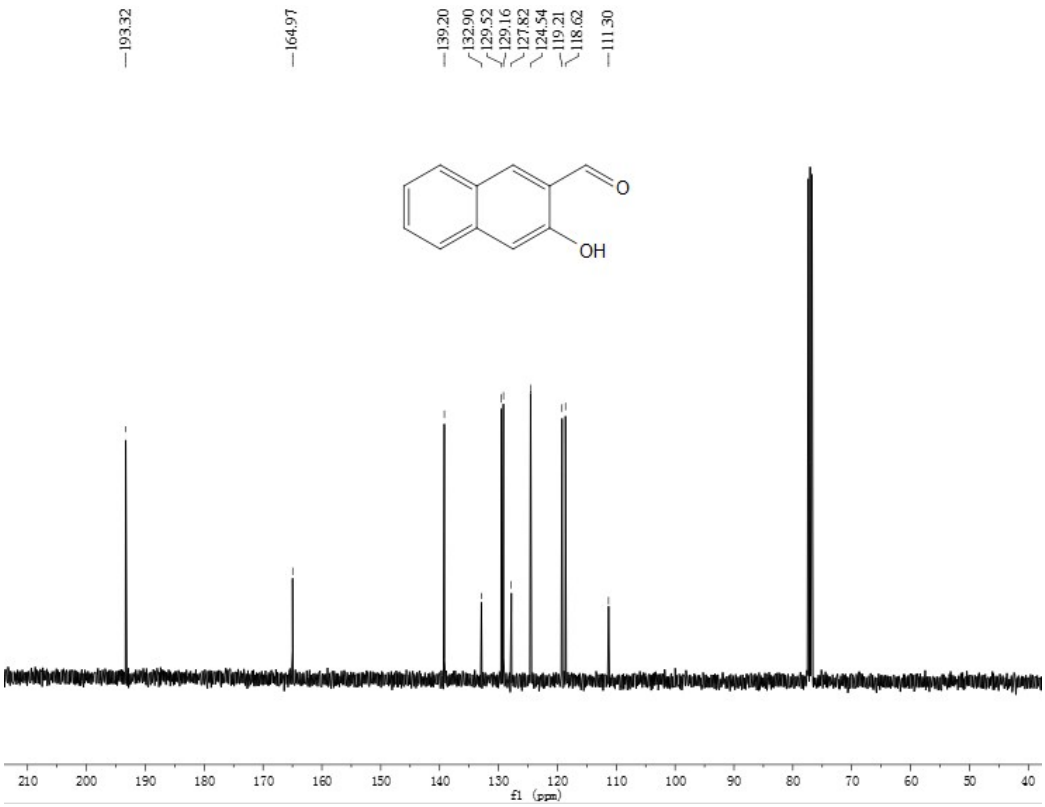

Fig.S23 ^{13}C-NMR spectrum of Compound 5.