A system for artificial light signal transduction via molecular translocation in a lipid membrane

Huiting Yang,[a] Shengjie Du,[a] Zhicheng Ye,[a] Xuebin Wang,[a] Zexin Yan,[a] Cheng Lian,*[a] Chunyan Bao,*[ab] Linyong Zhu[ab]

[a]Key Laboratory for Advanced Materials and Joint International Research Laboratory of Precision Chemistry and Molecular Engineering, Feringa Nobel Prize Scientist Joint Research Center, Frontiers Science Center for Materiobiology and Dynamic Chemistry, Institute of Fine Chemicals, School of Chemistry and Molecular Engineering, East China University of Science and Technology, Shanghai 200237, China

[b]Shanghai Frontiers Science Center of Optogenetic Techniques for Cell Metabolism, East China University of Science and Technology, Shanghai 200237, China

1. General materials

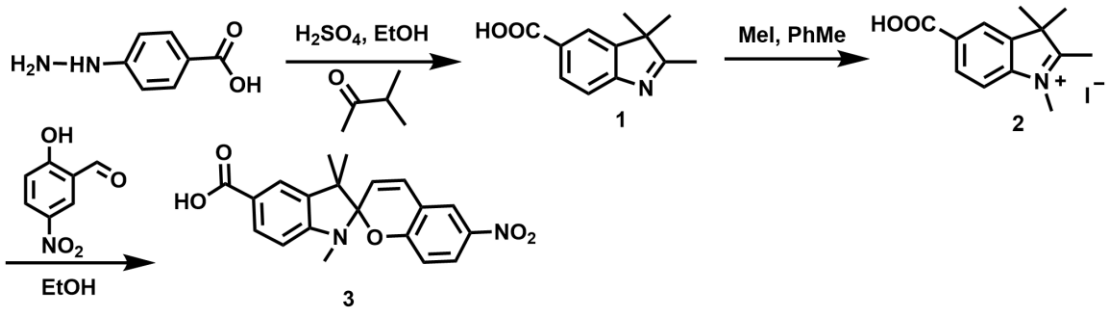
Materials: All synthetic manipulations were performed under standard air-free conditions with magnetic stirring unless otherwise mentioned. Flash chromatography was performed using silica gel (200–300 mesh) as the stationary phase. All reactants and solvents were purchased from commercial suppliers and used without further purification, unless otherwise noted. Dry dichloromethane (DCM) was distilled from calcium hydride; triethylamine (TEA) was redistilled and stored over KOH pellets prior to use. Egg yolk phosphatidylcholine (EYPC) was obtained from Avanti Polar lipids as a solution in chloroform (25 mg·mL^{-1}) and stored at -20 ºC prior to use.

Characterizations: Proton and carbon magnetic resonance spectra (^{1}H, ^{13}C NMR) were recorded on a Bruker Avance 400/600 MHz spectrometer. Chemical shifts were reported in parts per million (ppm) downfield from the Me_4Si resonance which was used as the internal standard when recording ^{1}H NMR spectra. The electronic spray ionization (ESI) mass spectra were obtained on a LCT Premier XE mass spectrometer. Absorption spectra were recorded on a Shimadzu UV-2550 UV-Vis spectrometer.

Fluorescence measurements were performed on a Varian Cary Eclipses fluorescence spectrometer equipped with a stirrer and a temperature controller (kept at 25 °C unless otherwise noted). Confocal luminescence imaging was performed with an A1R Nikon confocal microscope with 10× or 40× objective lens. A Mini-Extruder used for the preparation of large unilamellar vesicles (LUVs) was purchased from Avanti Polar lipids. The size of EYPC vesicles was determined using a Delsa™ Nano Submicron Particle Size and Zeta Potential Particle Analyzer (Beckman Coulter Inc., USA).

2. Synthesis of compounds

Synthesis of 3:



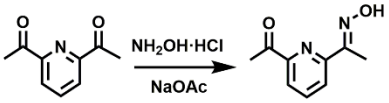
Compound **1**: To a solution of 4-hydrazino benzoic acid (10.0 g, 33.0 mmol) and 3-methyl-2-butanone (7.8 mL, 36.0 mmol) in ethanol (150 mL) was added 2.0 mL conc. H_2SO_4, and the obtained solution were stirred at 100 ºC for 18 h. After cooling to room temperature and filtrating the precipitate, the resulting solution was extracted with DCM (3 × 100 mL). The obtained organic layers were dried over anhydrous Na_2SO_4, filtered and concentrated. The solvent was removed under vacuum. The product was purified by silica gel flash column chromatography (DCM/MeOH = 100:2) to afford compound **1** as a brownish solid (11.7 g, 88% yield). ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.81 (s, 1H), 8.01 (s, 1H), 7.94 (d, J = 8.2 Hz, 1H), 7.53 (d, J = 8.1 Hz, 1H), 2.27 (s, 3H), 1.29 (s, 6H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 192.14, 167.96, 157.87, 146.57, 130.08, 127.75, 123.18, 119.57, 53.93, 22.73, 15.81. MS(ESI): m/z calcd. for $C_{12}H_{13}NO_2$[M+Na]$^+$: 226.1; found: 226.1.

Compound **2**: To a solution of compound **1** (9.0 g 30.0 mmol) in PhMe (200 mL) was added MeI (4.14 mL, 36.0 mmol), the solution was stirred at 130 ºC for 24 h. After

cooling to room temperature, the obtained precipitation was filtered. The solid was washed with ethyl acetate to afford pink solid compound **2** without further purification (12.5 g, 82% yield). ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.81 (s, 1H), 8.38 (s, 1H), 8.19 (d, J = 8.4 Hz, 1H), 8.04 (d, J = 8.4 Hz, 1H), 4.02 (s, 3H), 2.84 (s, 3H), 1.58 (s, 6H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 199.48, 166.95, 145.73, 142.42, 132.04, 130.83, 124.67, 115.86, 54.73, 35.57, 21.97, 15.18. MS(ESI): m/z calcd. for $C_{13}H_{16}INO_2[M+Na]^+$: 368.0; found: 368.0.

Compound **3**: To a solution of compound **2** (10.0 g 24.0 mmol) in ethanol (200 mL) was added 5-Nitro-2-hydroxybenzaldehyde (5.8 g, 28.8 mmol). The obtained mixture was stirred at 100 ºC for 12 h. Then, the mixture was cooled to room temperature and the solvent was removed under vacuum. The product was purified by silica gel flash column chromatography (DCM/MeOH = 100:1) to afford compound **3** as a yellow solid (7.6 g, 72% yield). ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.37 (s, 1H), 8.25 (d, J = 2.9 Hz, 1H), 8.02 (dd, J = 9.0, 2.8 Hz, 1H), 7.82 (dd, J = 8.2, 1.8 Hz, 1H), 7.68 (d, J = 1.7 Hz, 1H), 7.27 (d, J = 10.3 Hz, 1H), 6.93 (d, J = 8.9 Hz, 1H), 6.71 (d, J = 8.2 Hz, 1H), 6.03 (d, J = 10.4 Hz, 1H), 2.77 (s, 3H), 1.25 (s, 3H), 1.14 (s, 3H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 167.85, 159.42, 151.66, 141.18, 136.34, 131.30, 128.97, 126.27, 123.41, 123.35, 122.08, 121.35, 119.24, 115.93, 106.73, 106.37, 52.02, 28.86, 25.94, 19.99. MS(ESI): m/z calcd. for $C_{20}H_{18}N_2O_5[M+Na]^+$: 389.1; found: 389.1.

Synthesis of 4:

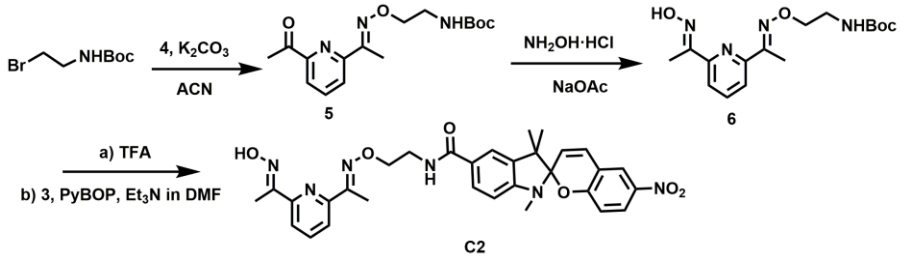


4

Compound **4**: A solution of 2,6-diacetylpyridine (10.0 g, 24.0 mmol), hydroxylamine hydrochloride (3.55 g, 20.0 mmol) and sodium acetate (0.55 g, 2.6 mmol) in water (10.0 mL) was refluxed for 3 h and then stirred at room temperature for 15 h. The resultant solid was filtered, washed with water and purified by silica gel flash column chromatography (EA/PE = 6:1) to afford compound **4** as a white solid (7.7 g, 85% yield). ^{1}H NMR (400 MHz, DMSO-d_6). ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.70 (s, 1H), 8.10

(dd, J = 7.9, 1.2 Hz, 1H), 7.99 (t, J = 7.7 Hz, 1H), 7.92 (dd, J = 7.6, 1.2 Hz, 1H), 2.68 (s, 3H), 2.30 (s, 3H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 199.68, 154.37, 154.32, 152.51, 138.20, 123.69, 121.19, 25.88, 10.48. MS(ESI): m/z calcd. for $C_9H_{10}N_2O_2$ $[M+Na]^+$: 201.1; found:201.1.

Synthesis of compound C2:



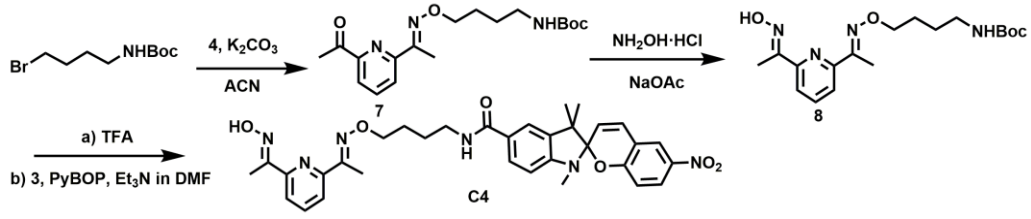
Compound **5**: To a solution of compound **4** (1.0 g, 10.0 mmol) in ACN (100 mL) was added K_2CO_3 (3.01 g, 40.0 mmol), and the mixture was stirred at room temperature for 15 min. Then (2-Bromoethyl) carbamic acid tert-butyl ester (1.7 g, 12.0 mmol) was added and stirred at 90 °C for 12 h. After cooling to room temperature and filtrating, the solution was concentrated under vacuum. The obtained crude was purified by silica gel flash column chromatography (DCM/MeOH = 200:1) to afford white solid compound **5** (1.7 g, 94% yield). ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.11 (dd, J = 7.8, 1.3 Hz, 1H), 8.02 (t, J = 7.7 Hz, 1H), 7.96 (dd, J = 7.6, 1.3 Hz, 1H), 6.94 (t, J = 5.9 Hz, 1H), 4.19 (t, J = 5.7 Hz, 2H), 3.29 (t, J = 5.8 Hz, 2H), 2.67 (s, 3H), 2.33 (s, 3H), 1.37 (s, 9H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 199.54, 156.04, 154.74, 153.41, 152.59, 138.37, 124.02, 121.60, 77.70, 74.47, 64.59, 28.59, 26.50, 11.13. MS(ESI): m/z calcd. for $C_{16}H_{23}N_3O_4$[M+H]$^+$: 322.2; found: 322.2.

Compound **6**: To a solution of compound **5** (1.0 g, 5.0 mmol) in 1:1 $CHCl_3$/ethanol (20 mL) was added a solution of hydroxylamine hydrochloride (0.27 g, 6.25 mmol) and sodium acetate (0.319 g, 6.25 mmol) in H_2O (2.0 mL), and the reaction was heated at 60 °C for 12 h. The reaction was diluted with $CHCl_3$ (10 mL), and washed with water (3 × 5 mL). Then, the organic layer was dried over Na_2SO_4, and the solvent was removed under vacuum. The product was purified by silica gel flash column chromatography (DCM/MeOH = 100:1) to afford compound **6** as a white solid (0.96 g,

92% yield). ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.56 (s, 1H), 7.88 – 7.78 (m, 3H), 6.93 (t, J = 5.8 Hz, 1H), 4.16 (t, J = 5.8 Hz, 2H), 3.26 (q, J = 5.8 Hz, 2H), 2.28 (s, 3H), 2.25 (s, 3H), 1.37 (s, 9H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 160.03, 156.12, 155.83, 154.63, 154.06, 152.91, 137.38, 120.11, 78.08, 73.27, 64.59, 28.66, 11.41, 10.57. MS(ESI): m/z calcd. for $C_{16}H_{24}N_4O_4$[M+Na]$^+$: 359.2; found: 359.2.

Compound **C2**: To a solution of compound **6** (0.56 g, 1.95 mmol) in dichloromethane (25 mL) was added trifluoroacetic acid (2.5 mL), and the obtained solution was stirred at room temperature for 1 h. After removing the solvent under vacuum, the residue was dissolved in 25 mL DMF and compound **3** (0.6 g, 1.95 mmol), PyBop (1.3 g, 2.93 mmol) and TEA (0.46 mL, 3.9 mmol) were added successively. The reaction was kept at room temperature overnight. After removing the solvent, the obtained crude was dissolved in 100 mL dichloromethane and washed with brine (3 × 60 mL). The organic layer was dried over Na_2SO_4 and concentrated under vacuum. The crude was purified by silica gel flash column chromatography (DCM/MeOH = 100:1) to afford compound **C2** as a yellow solid (0.76 g, 79% yield). ^{1}H NMR (600 MHz, DMSO-d_6) δ 11.56 (s, 1H), 8.35 (t, J = 5.7 Hz, 1H), 8.24 (d, J = 2.9 Hz, 1H), 8.02 (dd, J = 9.0, 2.8 Hz, 1H), 7.86 (dd, J = 7.4, 1.5 Hz, 1H), 7.83 – 7.78 (m, 2H), 7.74 (dd, J = 8.2, 1.8 Hz, 1H), 7.66 (d, J = 1.8 Hz, 1H), 7.26 (d, J = 10.3 Hz, 1H), 6.90 (d, J = 9.0 Hz, 1H), 6.67 (d, J = 8.2 Hz, 1H), 6.02 (d, J = 10.3 Hz, 1H), 4.32 (t, J = 5.9 Hz, 2H), 3.60 (q, J = 5.9 Hz, 2H), 2.74 (s, 3H), 2.31 (s, 3H), 2.25 (s, 3H), 1.24 (s, 3H), 1.12 (s, 3H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 166.94, 162.78, 159.55, 155.93, 154.64, 154.07, 152.88, 150.31, 141.11, 137.40, 136.11, 128.92, 128.52, 126.26, 126.14, 123.32, 121.47, 121.43, 120.11, 119.29, 115.87, 106.57, 106.51, 72.93, 52.12, 36.24, 31.23, 26.41, 26.33, 11.50, 10.58. MS(HR-ESI): m/z calcd. for $C_{31}H_{32}N_6O_6$[M+H]$^+$: 585.2464; found: 585.2464.

Synthesis of compound C4:

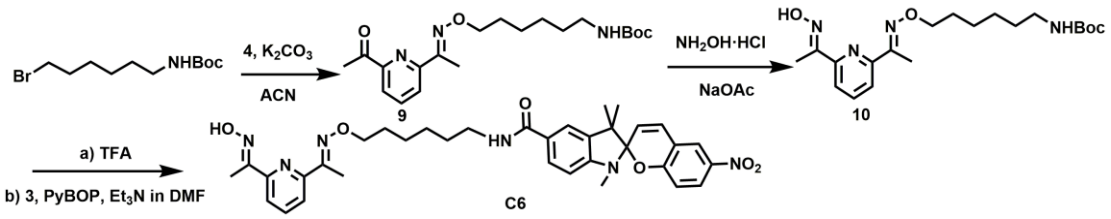


Compound **7**: Compound **7** was prepared using a similar method to that described for compound **5** (1.82 g, 93% yield). ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.10 (dd, J = 7.9, 1.2 Hz, 1H), 8.01 (t, J = 7.7 Hz, 1H), 7.95 (dd, J = 7.6, 1.2 Hz, 1H), 6.84 (t, J = 5.8 Hz, 1H), 4.21 (t, J = 6.5 Hz, 2H), 2.96 (q, J = 6.6 Hz, 2H), 2.67 (s, 3H), 2.32 (s, 3H), 1.72 – 1.62 (m, 2H), 1.50 (q, J = 7.1 Hz, 2H), 1.36 (s, 9H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 199.53, 156.05, 154.80, 153.41, 152.60, 138.36, 124.04, 121.61, 77.77, 74.32, 28.69, 28.63, 26.66, 26.49, 25.86, 11.14. MS(ESI): m/z calcd. for $C_{18}H_{27}N_3O_4[M+H]^+$: 350.2; found: 350.2.

Compound **8**: Compound **8** was prepared using a similar method to that described for compound **6** (0.92 g, 89% yield). ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.55 (s, 1H), 7.87 – 7.78 (m, 3H), 6.83 (t, J = 5.8 Hz, 1H), 4.18 (t, J = 6.5 Hz, 2H), 2.96 (q, J = 6.6 Hz, 2H), 2.28 (s, 3H), 2.25 (s, 3H), 1.66 (p, J = 6.7 Hz, 2H), 1.49 (h, J = 7.0 Hz, 2H), 1.36 (s, 9H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 156.06, 155.26, 154.63, 154.05, 152.95, 137.37, 120.03, 119.98, 77.78, 74.12, 28.71, 28.58, 26.68, 26.51, 11.28, 10.56. MS(ESI): m/z calcd. for $C_{18}H_{28}N_4O_4[M+Na]^+$: 387.2; found: 387.2.

Compound **C4**: Compound **C4** was prepared using a similar method to that described for compound **C2** (0.58 g, 76% yield). ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.55 (s, 1H), 8.23 (dd, J = 8.6, 4.2 Hz, 2H), 8.02 (dd, J = 9.0, 2.9 Hz, 1H), 7.82 (ddd, J = 11.4, 8.4, 6.4 Hz, 3H), 7.72 (dd, J = 8.2, 1.7 Hz, 1H), 7.65 (d, J = 1.8 Hz, 1H), 7.26 (d, J = 10.4 Hz, 1H), 6.90 (d, J = 9.0 Hz, 1H), 6.65 (d, J = 8.2 Hz, 1H), 6.02 (d, J = 10.4 Hz, 1H), 4.23 (t, J = 6.5 Hz, 2H), 3.16 – 3.04 (m, 2H), 2.73 (s, 3H), 2.29 (s, 3H), 2.24 (s, 3H), 1.75 (p, J = 6.7 Hz, 2H), 1.64 (q, J = 7.4 Hz, 2H), 1.24 (d, J = 3.1 Hz, 3H), 1.13 (s, 3H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 166.56, 162.76, 159.57, 155.29, 154.64, 154.05, 152.94, 150.18, 141.11, 137.40, 136.07, 128.91, 128.39, 126.42, 126.24, 123.32, 121.49, 121.38, 120.04, 119.99, 119.30, 115.86, 106.53, 74.20, 52.15, 46.23, 36.23, 31.22, 28.91, 26.89, 20.07, 10.58, 9.10. MS(HR-ESI): m/z calcd. for $C_{33}H_{36}N_6O_6[M+H]^+$: 613.2776; found: 613.2776.

Synthesis of compound C6:



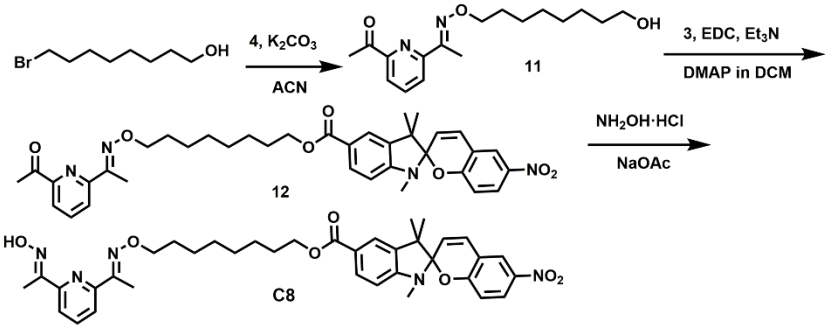
Compound **9**: Compound **9** was prepared using a similar method to that described for compound **5** (1.89 g, 89% yield). ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.10 (dd, J = 7.8, 1.2 Hz, 1H), 8.01 (t, J = 7.7 Hz, 1H), 7.95 (dd, J = 7.6, 1.2 Hz, 1H), 6.77 (t, J = 5.7 Hz, 1H), 4.21 (t, J = 6.6 Hz, 2H), 2.90 (q, J = 6.5 Hz, 2H), 2.67 (s, 3H), 2.32 (s, 3H), 1.69 (p, J = 6.8 Hz, 2H), 1.39 (d, J = 7.2 Hz, 2H), 1.36 (s, 9H), 1.35 – 1.20 (m, 4H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 199.54, 156.03, 154.73, 153.41, 152.59, 138.37, 124.01, 121.60, 77.70, 74.57, 29.87, 29.16, 28.70, 28.59, 26.54, 25.87, 25.60, 11.13. MS(ESI): m/z calcd. for $C_{20}H_{31}N_3O_4[M+H]^+$: 378.2; found: 378.2.

Compound **10**: Compound **10** was prepared using a similar method to that described for compound **6** (0.9 g, 87% yield). ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.55 (s, 1H), 7.88 – 7.74 (m, 3H), 6.77 (t, J = 5.8 Hz, 1H), 4.18 (t, J = 6.6 Hz, 2H), 2.90 (q, J = 6.5 Hz, 2H), 2.28 (s, 3H), 2.25 (s, 3H), 1.67 (p, J = 6.8 Hz, 2H), 1.39 (d, J = 6.9 Hz, 2H), 1.36 (s, 9H), 1.35 – 1.21 (m, 4H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 158.46, 156.09, 155.44, 154.63, 154.05, 152.93, 137.37, 120.08, 77.78, 74.12, 29.87, 29.16, 28.71, 28.58, 25.86, 25.60, 11.38, 10.56. MS(ESI): m/z calcd. for $C_{20}H_{32}N_4O_4[M+Na]^+$: 415.2; found: 415.2.

Compound **C6**: Compound **C6** was prepared using a similar method to that described for compound **C2** (0.78 g, 81% yield). ^{1}H NMR (600 MHz, DMSO-d_6) δ 11.55 (s, 1H), 8.24 (d, J = 2.8 Hz, 1H), 8.18 (t, J = 5.7 Hz, 1H), 8.01 (dd, J = 8.9, 2.9 Hz, 1H), 7.84 (dd, J = 7.4, 1.5 Hz, 1H), 7.83 – 7.81 (m, 1H), 7.81 – 7.77 (m, 1H), 7.72 (dd, J = 8.1, 1.8 Hz, 1H), 7.65 (d, J = 1.8 Hz, 1H), 7.25 (d, J = 10.4 Hz, 1H), 6.89 (d, J = 9.0 Hz, 1H), 6.66 (d, J = 8.2 Hz, 1H), 6.02 (d, J = 10.4 Hz, 1H), 4.19 (t, J = 6.6 Hz, 2H), 3.25 (dt, J = 8.8, 6.8 Hz, 2H), 2.73 (s, 3H), 2.28 (s, 3H), 2.25 (s, 3H), 1.71 (p, J = 6.8 Hz, 2H), 1.54 (p, J = 7.3 Hz, 2H), 1.43 – 1.36 (m, 4H), 1.25 (s, 3H), 1.13 (s, 3H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 166.50, 159.58, 155.20, 154.63, 154.05, 152.96, 150.15,

141.10, 137.40, 136.05, 128.90, 128.37, 126.49, 126.24, 123.32, 121.49, 121.37, 120.02, 119.97, 119.30, 115.85, 106.54, 74.42, 52.14, 46.23, 39.56, 29.76, 29.20, 28.90, 26.83, 25.74, 20.07, 11.28, 10.57. MS(HR-ESI): m/z calcd. for $C_{35}H_{40}N_6O_6[M+H]^+$: 641.3087; found: 641.3087 .

Synthesis of compound C8:



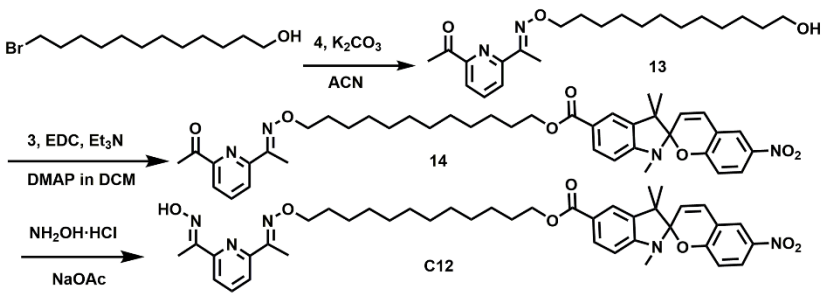
Compound **11**: Compound **11** was prepared using a similar method to that described for compound **5** (2.96 g, 86% yield). ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.09 (d, J = 7.7 Hz, 1H), 8.00 (t, J = 7.7 Hz, 1H), 7.94 (d, J = 7.5 Hz, 1H), 4.35 (s, 1H), 4.20 (t, J = 6.6 Hz, 2H), 3.39 (d, J = 6.5 Hz, 2H), 2.67 (s, 3H), 2.32 (s, 3H), 1.69 (p, J = 6.8 Hz, 2H), 1.46 – 1.27 (m, 10H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 199.49, 154.66, 153.40, 152.57, 138.32, 123.97, 121.57, 74.64, 61.18, 33.00, 29.38, 29.37, 29.20, 25.93, 25.87, 25.83, 11.07. MS(ESI): m/z calcd. for $C_{17}H_{26}N_2O_3[M+Na]^+$: 329.2; found: 329.2.

Compound **12**: To a mixture of compound **11** (1.2 g, 8.1 mmol) and compound **3** (1.4 g, 9.7 mmol) in dry DCM (20 mL) was added DMAP (0.2 g, 4.05 mmol) and EDC (1.88 g, 24.3 mmol), and the resulting solution was stirred at room temperature for 24 h. The product was dissolved by 100 mL dichloromethane. The combined organics was washed with brine (3 × 60 mL) and dried over Na_2SO_4. The solvent was removed under vacuum. The product was purified by silica gel flash column chromatography (DCM/MeOH = 200:1) to afford compound **12** as a yellow solid (1.37 g, 64% yield). ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.25 (d, J = 2.9 Hz, 1H), 8.09 (dd, J = 7.8, 1.3 Hz, 1H), 8.01 (dd, J = 5.3, 3.6 Hz, 1H), 7.98 (d, J = 7.8 Hz, 1H), 7.94 (dd, J = 7.6, 1.3 Hz, 1H), 7.83 (dd, J = 8.3, 1.7 Hz, 1H), 7.67 (d, J = 1.7 Hz, 1H), 7.26 (d, J = 10.4 Hz, 1H), 6.90 (d, J = 9.0 Hz, 1H), 6.72 (d, J = 8.3 Hz, 1H), 6.02 (d, J = 10.3 Hz, 1H), 4.24 – 4.21 (m, 2H), 4.05 – 4.00 (m, 2H), 2.76 (s, 3H), 2.66 (s, 3H), 2.31 (s, 3H), 1.99 (s, 3H), 1.36

(s, 8H), 1.24 (d, J = 4.2 Hz, 4H), 1.13 (s, 3H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 199.57, 169.99, 159.61, 154.73, 153.43, 152.61, 152.53, 138.24, 136.92, 136.19, 129.10, 128.88, 127.92, 127.57, 126.30, 126.20, 125.38, 123.72, 123.30, 121.21, 119.30, 119.23, 115.91, 74.65, 61.18, 52.26, 35.63, 33.00, 29.37, 29.36, 29.20, 28.64, 27.98, 25.93, 25.89, 25.86, 11.16. MS(ESI): m/z calcd. for $C_{37}H_{42}N_4O_7[M+Na]^+$: 677.3; found: 677.3.

Compound **C8**: To a solution of compound **12** (0.68 g, 3.9 mmol) in 1:1 $CHCl_3$/ethanol (20 mL) was added a solution of hydroxylamine hydrochloride (0.108 g, 5.85 mmol) and sodium acetate (0.128 g, 5.9 mmol) in H_2O (2.0 mL), and the resulting solution was stirred at room temperature for 48 h. The reaction was diluted with $CHCl_3$ (50 mL), and washed with water (3 × 50 mL). The organic layer was dried over Na_2SO_4 and the solvent was removed under vacuum. The product was purified by silica gel flash column chromatography (DCM/MeOH = 200:1) to afford compound **C8** as a yellow solid (0.36 g, 52% yield). ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.55 (s, 1H), 8.24 (d, J = 2.9 Hz, 1H), 8.01 (dd, J = 8.9, 2.9 Hz, 1H), 7.89 – 7.74 (m, 4H), 7.67 (d, J = 1.8 Hz, 1H), 7.26 (d, J = 10.4 Hz, 1H), 6.90 (d, J = 9.0 Hz, 1H), 6.71 (d, J = 8.3 Hz, 1H), 6.01 (d, J = 10.4 Hz, 1H), 4.22 (tt, J = 6.4, 3.2 Hz, 2H), 4.17 (t, J = 6.6 Hz, 2H), 2.77 (s, 3H), 2.27 (s, 3H), 2.24 (s, 3H), 1.69 (dp, J = 11.2, 6.5 Hz, 4H), 1.38 (dq, J = 22.9, 6.1 Hz, 8H), 1.25 (s, 3H), 1.13 (s, 3H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 165.48, 159.35, 155.15, 154.61, 154.04, 152.95, 151.89, 137.36, 136.49, 134.20, 131.17, 129.92, 129.02, 126.26, 123.35, 123.08, 121.22, 120.00, 119.91, 119.22, 115.90, 106.83, 106.29, 74.42, 64.47, 52.00, 30.38, 29.17, 28.84, 27.94, 25.92, 25.82, 23.87, 22.86, 19.94, 11.35, 10.54. MS(HR-ESI): m/z calcd. for $C_{37}H_{43}N_5O_7[M+H]^+$: 670.3243; found: 670.3243.

Synthesis of compound C12:



Compound **13**: Compound **13** was prepared using a similar method to that described

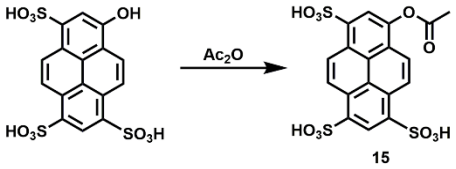
for compound **5** (3.42 g, 84% yield). ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.09 (dd, J = 7.8, 1.2 Hz, 1H), 8.01 (t, J = 7.7 Hz, 1H), 7.95 (dd, J = 7.7, 1.2 Hz, 1H), 4.32 (t, J = 5.1 Hz, 1H), 4.21 (t, J = 6.6 Hz, 2H), 3.37 (t, J = 5.7 Hz, 2H), 2.67 (s, 3H), 2.32 (s, 3H), 1.68 (q, J = 6.9 Hz, 2H), 1.40 – 1.23 (m, 18H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 199.51, 154.67, 153.41, 152.59, 138.35, 123.98, 121.60, 74.63, 61.18, 33.02, 29.60, 29.50, 29.45, 29.28, 29.17, 25.99, 25.85, 11.09. MS(ESI): m/z calcd. for $C_{21}H_{34}N_2O_3$[M+Na]$^+$: 385.2; found: 385.2.

Compound **14**: Compound **14** was prepared using a similar method to that described for compound **12** (2.4 g, 62% yield). ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.24 (d, J = 2.8 Hz, 1H), 8.08 (dd, J = 7.8, 1.2 Hz, 1H), 8.04 – 7.97 (m, 2H), 7.94 (dd, J = 7.7, 1.2 Hz, 1H), 7.83 (dd, J = 8.2, 1.7 Hz, 1H), 7.67 (d, J = 1.6 Hz, 1H), 7.26 (d, J = 10.4 Hz, 1H), 6.90 (d, J = 9.0 Hz, 1H), 6.72 (d, J = 8.3 Hz, 1H), 6.02 (d, J = 10.4 Hz, 1H), 4.20 (q, J = 6.6 Hz, 4H), 2.77 (s, 3H), 2.66 (s, 3H), 2.31 (s, 3H), 1.67 (p, J = 6.8 Hz, 4H), 1.34 – 1.22 (m, 19H), 1.13 (s, 3H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 199.49, 166.20, 159.33, 154.66, 153.39, 152.57, 151.87, 141.18, 138.32, 136.46, 131.16, 129.02, 126.22, 123.95, 123.34, 123.06, 121.58, 121.22, 121.19, 119.20, 115.85, 106.80, 106.28, 74.61, 64.44, 51.98, 29.41, 29.39, 29.24, 29.14, 29.11, 28.82, 28.74, 25.96, 25.87, 25.83, 19.92, 11.07. MS(ESI): m/z calcd. for $C_{41}H_{50}N_4O_7$[M+Na]$^+$: 733.4; found: 733.4.

Compound **C12**: Compound **C12** was prepared using a similar method to that described for compound **C8** (0.45 g, 44% yield). ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.54 (s, 1H), 8.24 (d, J = 2.9 Hz, 1H), 8.01 (dd, J = 9.0, 2.8 Hz, 1H), 7.86 – 7.74 (m, 4H), 7.67 (d, J = 1.7 Hz, 1H), 7.26 (d, J = 10.3 Hz, 1H), 6.90 (d, J = 8.9 Hz, 1H), 6.71 (d, J = 8.3 Hz, 1H), 6.01 (d, J = 10.3 Hz, 1H), 4.20 (tt, J = 6.7, 3.4 Hz, 2H), 4.16 (t, J = 6.6 Hz, 2H), 2.77 (s, 3H), 2.26 (s, 3H), 2.24 (s, 3H), 1.70 – 1.62 (m, 4H), 1.39 – 1.33 (m, 4H), 1.32 – 1.28 (m, 4H), 1.25 (s, 11H), 1.13 (s, 3H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 166.22, 159.35, 155.13, 154.60, 154.04, 152.95, 151.89, 141.20, 137.35, 136.48, 131.17, 129.02, 126.25, 123.35, 123.07, 122.95, 121.22, 120.00, 119.90, 119.22, 115.89, 106.83, 106.29, 74.41, 64.47, 52.00, 29.38, 29.24, 29.16, 29.10, 28.83, 28.73, 25.96, 25.85, 25.75, 19.94, 11.22, 10.54. MS(HR-ESI): m/z calcd. for $C_{41}H_{51}N_5O_7$[M+H]$^+$:

726.3868; found: 726.3868.

Synthesis of compound 15:



15

Compound **15:** 8-hydroxypyrene-1,3,6-trisulfonate trisodium salt (1.3 g, 2.5 mmol) and sodium acetate (25.0 mg, 0.3 mmol) were dissolved in acetic anhydride (15 mL), and the mixture was stirred at reflux for 48 h. Then the mixture was cooled to room temperature and diluted with tetrahydrofuran containing 10% (v/v) of acetic acid (15 mL). The solid was collected by vacuum filtration and washed with cold acetone (3 × 15 mL) and diethylether (2 × 15 mL) to afford compound **15** as a pale brown solid (1.2 g, 84%). ^{1}H NMR (400 MHz, D_2O) δ 9.17 (s, 1H), 9.14 (d, J = 9.8 Hz, 1H), 9.07 (d, J = 9.8 Hz, 1H), 9.03 (d, J = 9.5 Hz, 1H), 8.44 (s, 1H), 8.37 (d, J = 9.5 Hz, 1H), 2.56 (s, 3H). ^{13}C NMR (101 MHz, D_2O) δ 170.98, 141.59, 135.81, 133.67, 127.14, 126.48, 124.78, 123.96, 122.84, 122.74, 122.70, 122.58, 122.53, 122.26, 121.88, 120.78, 117.78, 18.20. MS(ESI): m/z calcd. for $C_{18}H_{12}O_{11}S_3[M+Na]^+$: 522.9; found: 522.9.

3. Geometry optimized molecular structures of transducers

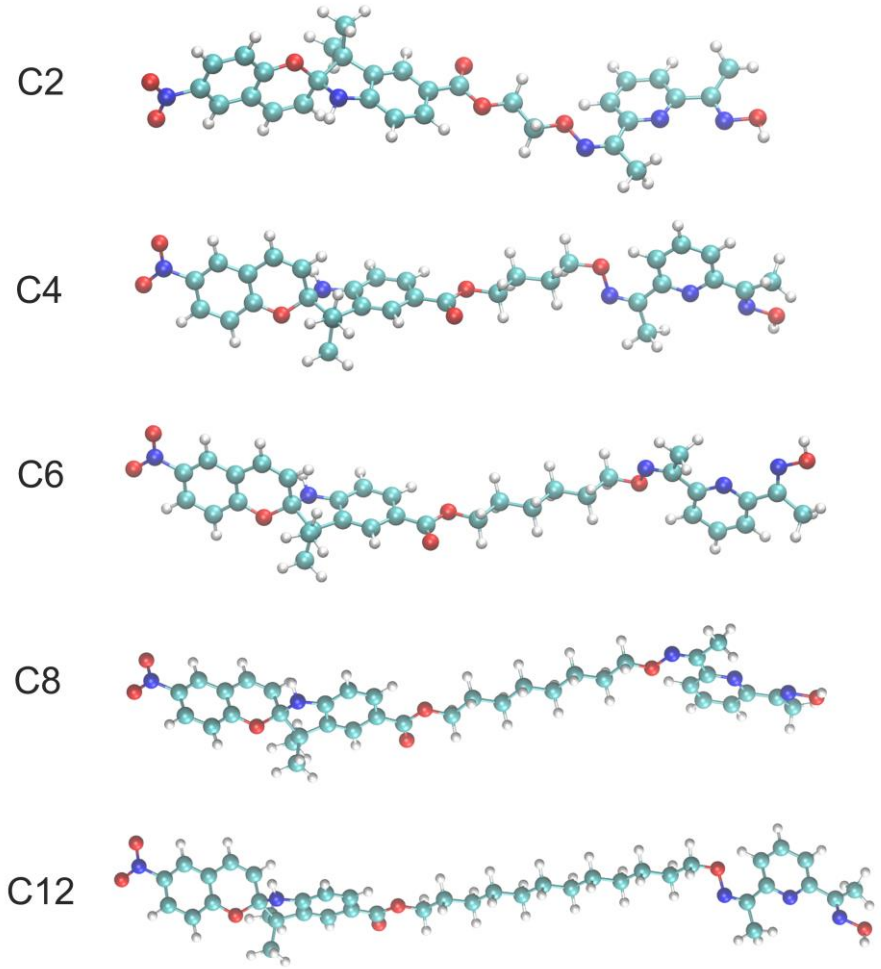


Figure S1. The optimized structures of transducers, which show molecular lengths of 2.59 nm (**C2**), 2.77 nm (**C4**), 3.01 nm (**C6**), 3.26 nm (**C8**) and 3.71 nm (**C12**). Here the white, cyan, blue and red balls represent H, C, N and O atoms, respectively. The molecules are shown in CPK model.

4. Photoisomerization of transducers

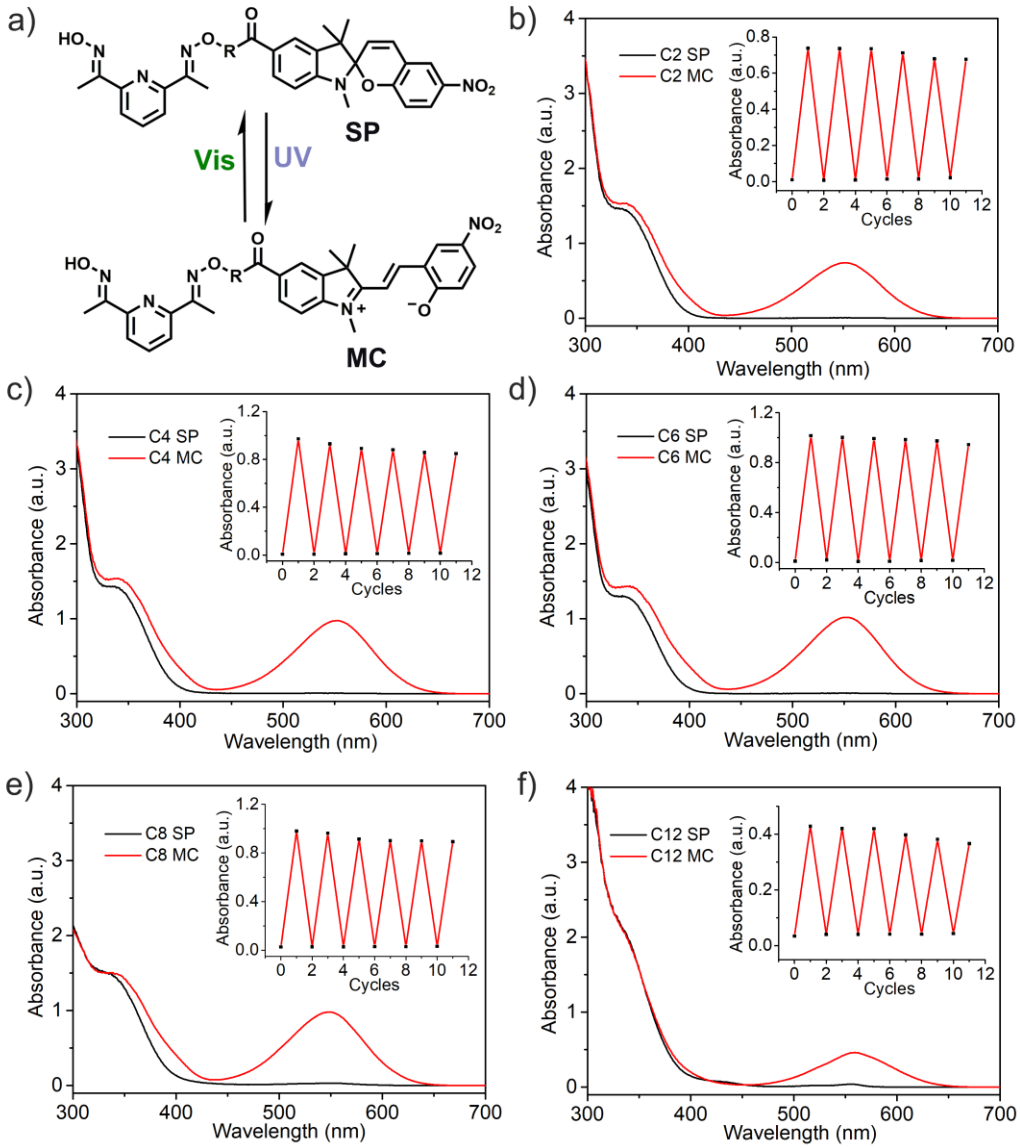


Figure S2. The photoisomerization of transducer in solutions (0.17 mM in CH_3CN/H_2O = 9/1 at 298 K). a) Schematic representation of the photoisomerization of transducers under UV and Vis irradiation. b-f) The absorption evolution of b) **C2**, c) **C4**, d) **C6**, e) **C8**, and f) **C12** before and after 365 nm UV light irradiation (2 mW cm^{-2}). The inset was the switching cycles followed by UV-Vis spectroscopy under alternating irradiation with 365 nm UV light (2 mW cm^{-2}, 10 s) and 530 nm visible light (2 mW cm^{-2}, 2 min). The detection wavelength is at 550 nm.

5. Molecular dynamics simulation of C8 isomers in the lipid bilayers

Two systems were constructed including the **C8** isomers (before and after photo

irradiation) were performed as described in Experimental section in the main text. For the snapshots of **C8** isomers in lipid bilayers (Figure 1a), water and the lipid bilayer are shown in the line model, the precatalyst and photoresponsive groups are shown in the VDW model, and the linker is shown in the CPK model. The white, red, cyan, blue and gray balls represent hydrogen, oxygen, carbon, nitrogen and Zn^{2+}, respectively.

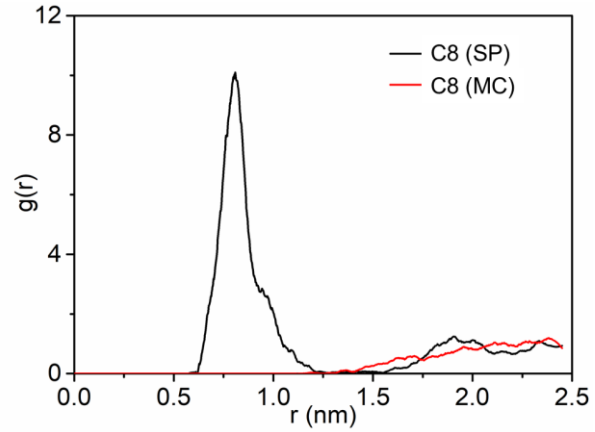


Figure S3. The radial distribution function between N atom of precatalyst group and Zn^{2+} for **C8** isomers.

6. Zn^{2+} binding of C8 determined by UV-Vis absorption

Based on the reported reference, the binding stoichiometry between pyridine-oxime and Zn^{2+} is 1:1.[1] UV-vis absorption titration was used to determine the binding constant.[2]

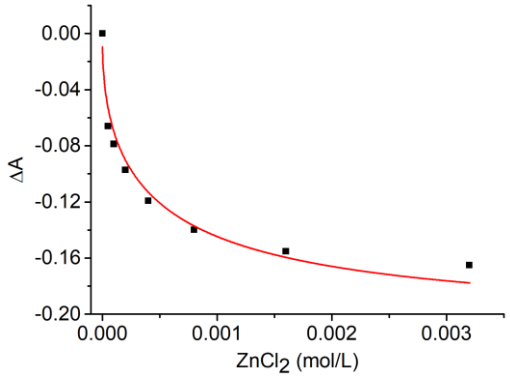


Figure S4. Binding constant determination of 50 μM **C8** in EtOH/HEPES buffer (V/V = 9/1) at 298 K with $ZnCl_2$ by tracking the absorption variation at 290 nm. For 1:1 binding: K = 1562 M^{-1}, ΔG = -18.2 KJ mol^{-1}.

7. Membrane stability analysis

DLS analysis:

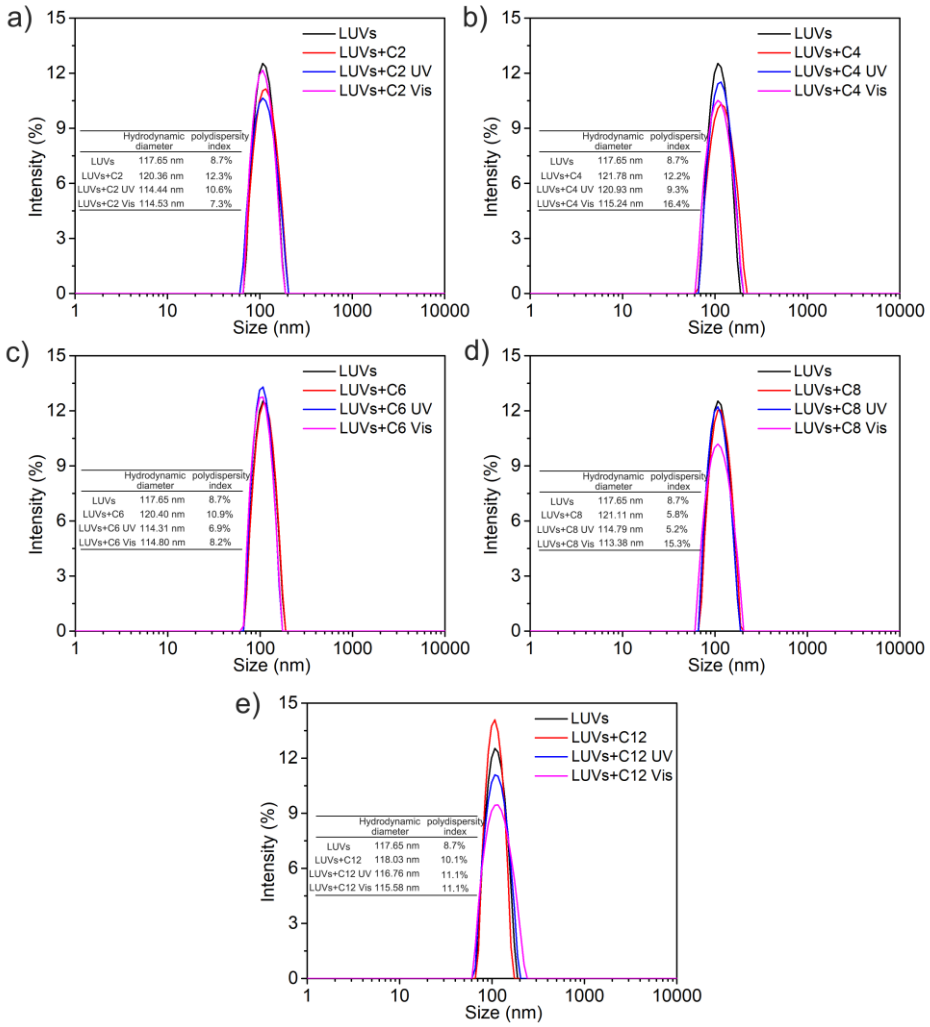


Figure S5. The hydrodynamic radius distribution and the corresponding polydispersity index of LUVs determined by DLS assay.

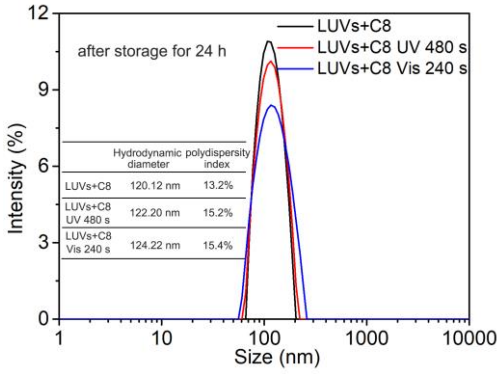


Figure S6. The DLS data of **C8**-loaded LUV samples without and with UV/Vis

irradiation after 24 h storage at room temperature. The irradiation time was determined according to the cumulative alternating irradiation time experienced in the following 10 h process of light signal transduction.

Calcein leakage experiments:

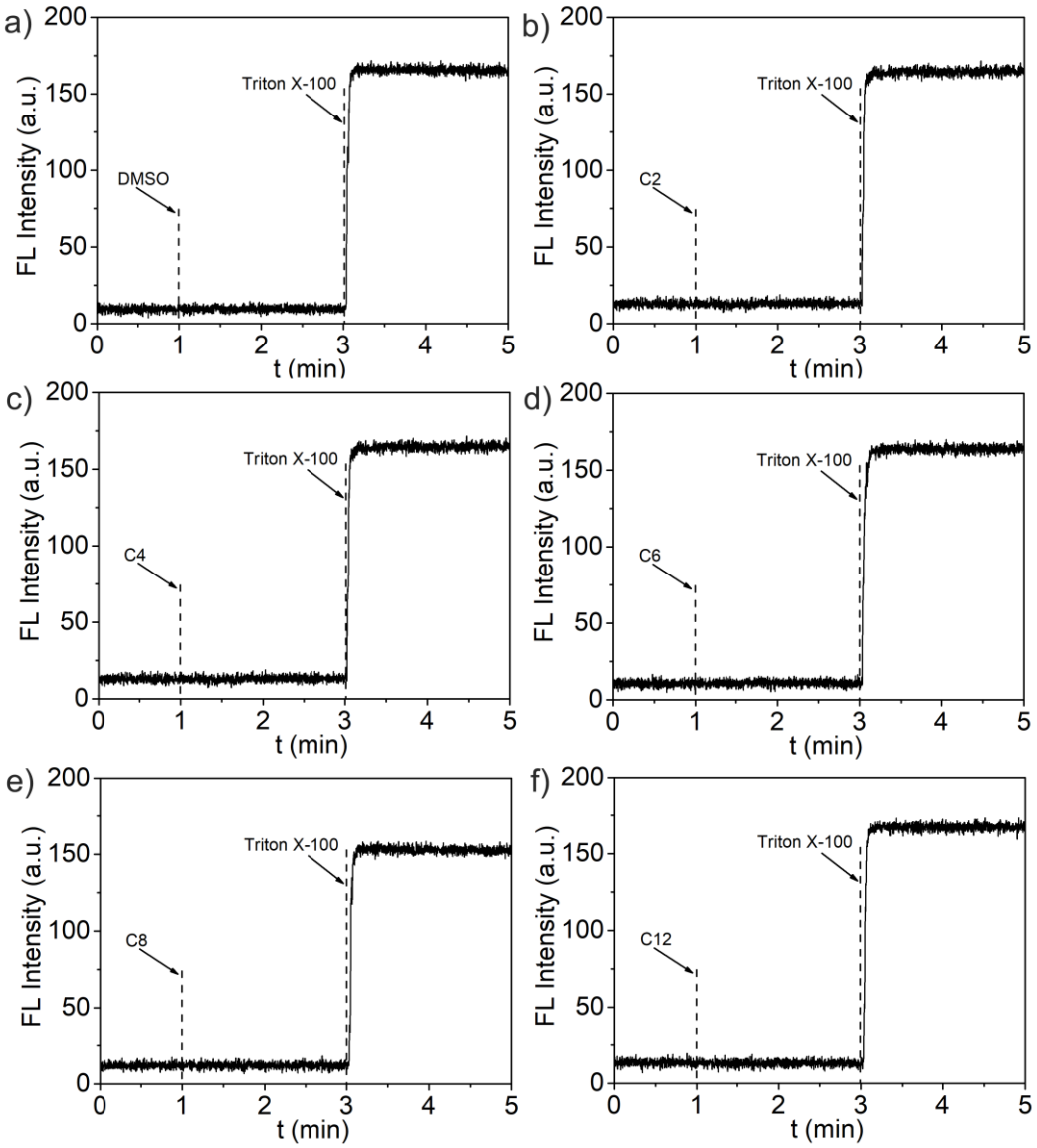


Figure S7. Calcein leakage assay. The addition of 10 μL DMSO (a), and transducers **C2** b), **C4** c), **C6** d), **C8** e) and **C12** f) at 10.0 μM in DMSO.

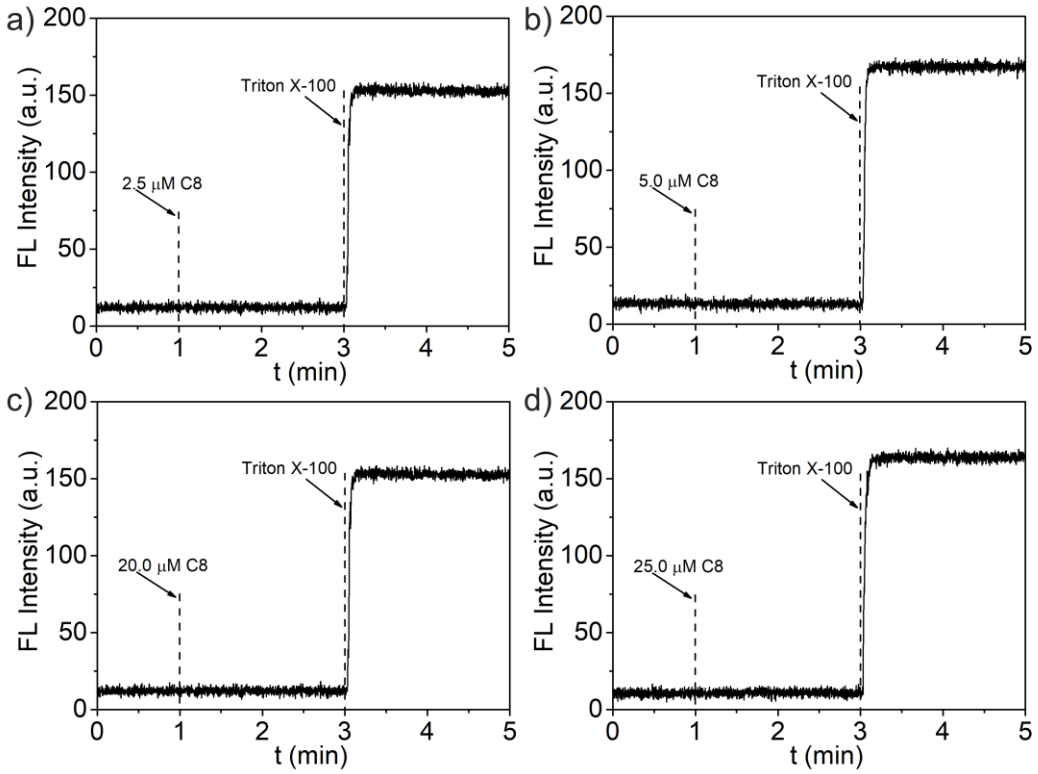


Figure S8. Calcein leakage assay. The addition of transducer **C8** at different concentrations of 2.5 μM a), 5.0 μM b), 20.0 μM c) and 25.0 μM d), respectively.

8. Membrane loading analysis

Taking **C8** as the example, 250 μL of above-prepared LUVs was transferred to a quartz cuvette followed by addition of 1.0 μL **C8** contained solution (10 mM in DMSO) under a slow stirring condition. The molar ratio of added **C8** was 2.0 mol% to lipids. After 10 min, the vesicles were purified to remove the unloaded **C8** by three mini-column centrifugation with SephadexG-50 (1000 r/min, 1 min). Finally, the purified vesicles (**LUVs-C8**) were diluted by HEPES buffer to reach a total volume of 1.0 mL, which was analyzed by HPLC analysis. The detection wavelength was at 254 nm. The solution before the column purification (**LUVs+C8**) was also diluted to 1.0 mL and analyzed as control. The membrane loading was calculated by comparing the integral area at 6.2 minutes of retention time of **C8**.

Membrane loading mol% (relative to lipids) = $(A_{LUVs\text{-}C8}/A_{LUVs+C8} \times C_{C8})/C_{LUVs} \times 100\%$

$A_{LUVs\text{-}C8}$ means the integral area of **LUVs-C8** at 6.2 minutes, $A_{LUVs+C8}$ means the integral area of **LUVs+C8** at 6.2 minutes, C_{C8} means the added concentration of **C8**

(10 μM), C_{LUVs} means the concentration of lipid (0.5 mM), respectively.

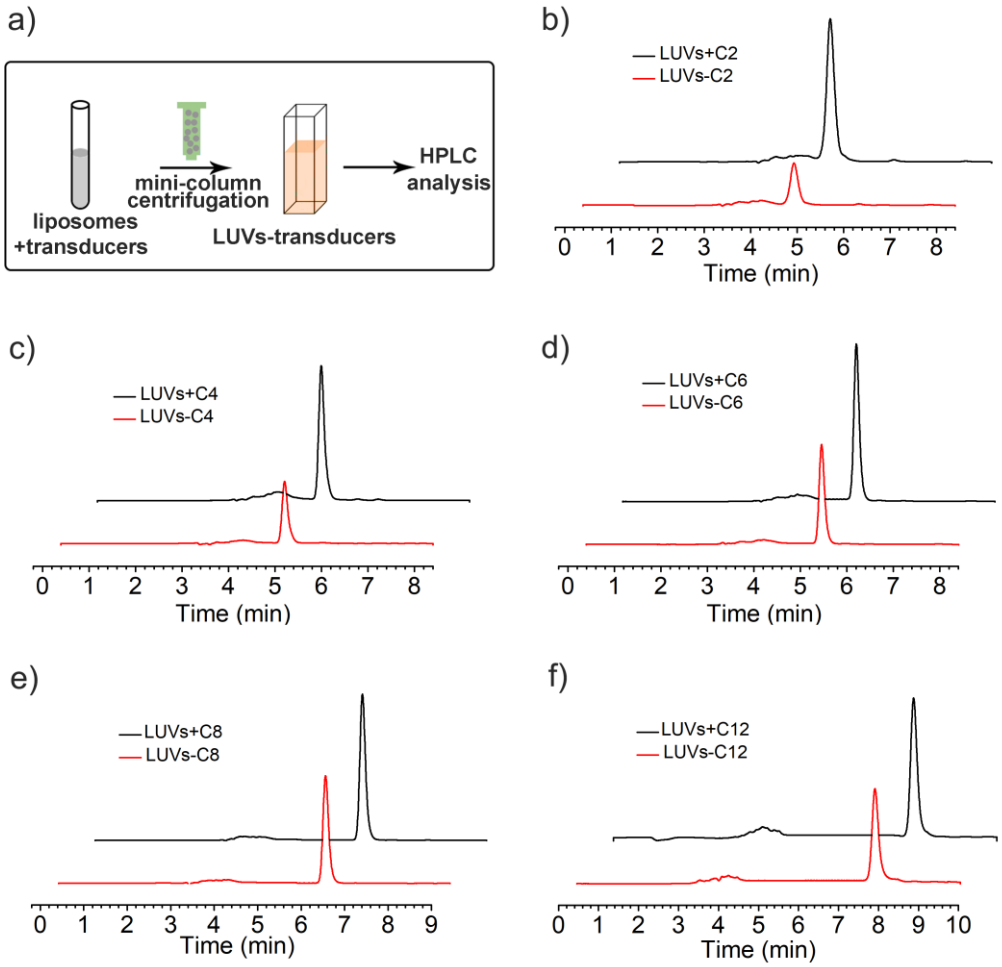


Figure S9. HPLC analysis for membrane loading. a) Schematic representation of the experiment of membrane loading analysis. b-f) The corresponding HPLC spectra for the membrane loading calculation of **C2** b), **C4** c), **C6** d), **C8** e), and **C12** f), respectively.

9. Photoisomerization effect on C8 loading in lipid bilayers

To observe if the photoisomerization affects the membrane loading, the sample of **LUVs-C8** liposomes as prepared above was further irradiated with a LED 365 nm light (2 mW cm^{-2}, 10 s), and another mini-column centrifugation was performed to remove the molecules that may escape from the membrane and obtain vesicles **LUVs-C8 UV**. All vesicle samples were diluted to 1.0 mL with HEPES solution, and UV-Vis absorption spectra was recorded and the absorbance at 365 nm was compared. To decrease the comparison error, the UV-Vis absorption spectra of **LUVs-C8 UV** was recorded after recovering **C8** into SP structure by 530 nm irradiation.

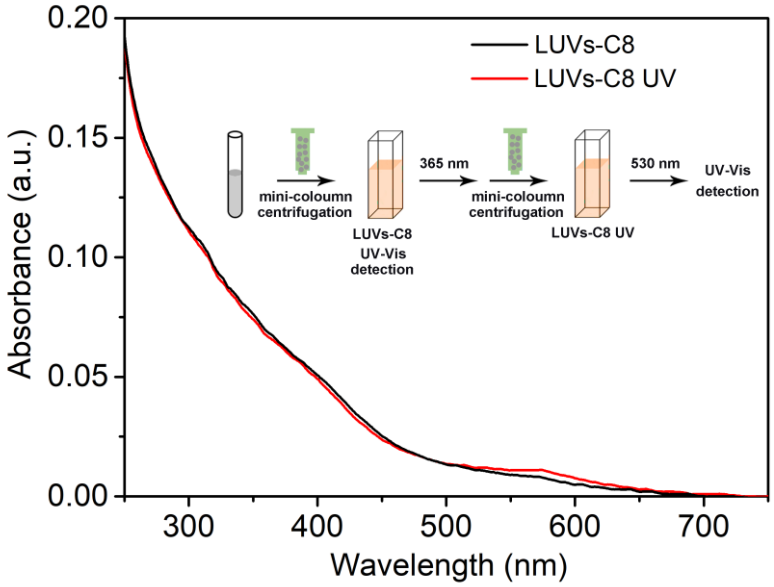


Figure S10. The UV-Vis absorption spectra of membrane-loading **C8** before and after UV irradiation. After comparing the absorption value at 365 nm, more than 90% **C8** was remained in the lipid membrane, indicating that the photoisomerization would not cause transducer **C8** to escape from the lipid membrane.

10. Photostability of MC isomer of C8 in lipid bilayers

The photostability of UV irradiated **C8** (MC state) in the lipid bilayers was measured by tracking the evolution of UV-Vis absorption spectra of **LUVs-C8 UV** in dark.

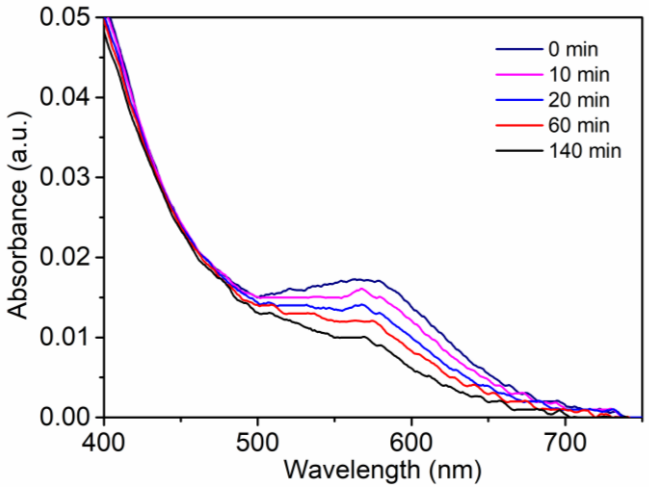


Figure S11. The UV-Vis absorption evolution for dark recovery of **LUVs-C8 UV**.

11. Catalytic hydrolysis of transducers in aqueous

The structure-activity relationship and the effect of photoisomerization were

investigated in aqueous. Compound **15** (10.0 μM) and zinc chloride (10.0 μM) were dissolved in 10 mM HEPES buffer, then, the stock solution containing transducers in DMSO (final concentration 10.0 μM) was added and the time dependent change in fluorescence intensity (λ_{em} = 510 nm) was monitored under excitation wavelength λ_{ex} = 405 nm. After 2h, the solution was irradiated with a LED 365 light (2 mW cm^{-2}). To keep transducers in MC state, the illumination was performed for ten seconds every five minutes. After another 2h, the solution was irradiated with a LED 530 nm light (2 mW cm^{-2}), and the illumination was also performed for 2 minutes to make transducers in SP state. The data under alternative UV and visible light irradiation was tracked and collected every 0.5 h, and the temperature was kept at 25 °C by a temperature controller.

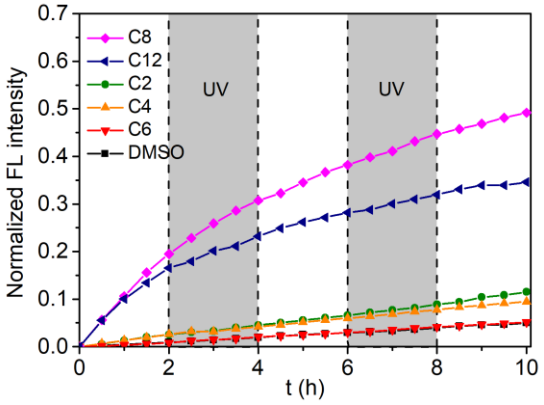
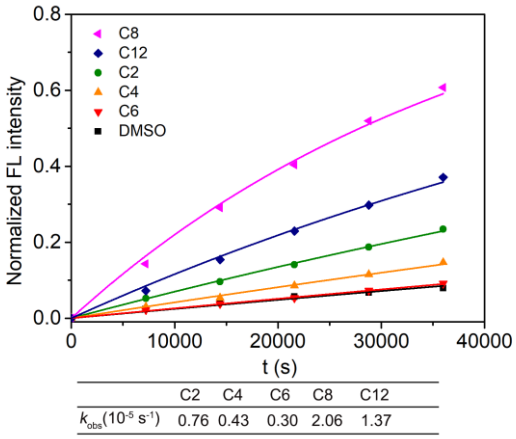


Figure S12. Time-dependence of the normalized fluorescence emission intensity at 510 nm (λ_{ex} = 405 nm) of 10 mM HEPES buffer containing compound **15** (10.0 μM) and zinc chloride (10.0 μM) after the addition of transducers (10.0 μM) by alternative irradiation with 365-nm UV and 530-nm visible light.

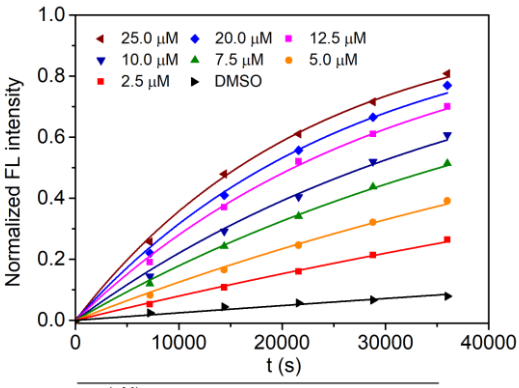
12. Signal transduction assay

First-order rate curve fitting for signal transduction: After observing the data, we found that the data error increased after 10 h, and the fitted curves show poor correlation index. It is reasonable since the long-time reaction will lead to the error caused by concentration change and possible vesicle leakage, which will affect the data fitting. Therefore, for better fitting, the data of the first 10 hours were used for the first-order rate curve fitting (see the equation in the main text).



	C2	C4	C6	C8	C12
k_{obs}(10^{-5} s^{-1})	0.76	0.43	0.30	2.06	1.37

Figure S13. K_{obs} fitting for time-dependence of normalized fluorescence intensity at 510 nm (λ_{ex} = 405 nm) of vesicles after the addition of transducers **C2**, **C4**, **C6**, **C8** and **C12** (10.0 μM).



c (μM)	2.5	5.0	7.5	10.0	12.5	20.0	25.0
k_{obs}(10^{-5} s^{-1})	0.68	1.10	1.59	2.06	2.60	2.90	3.27

Figure S14. K_{obs} fitting for time-dependence of normalized fluorescence intensity at 510 nm (λ_{ex} = 405 nm) of vesicles after the addition of transducers **C8** at different concentrations.

Additional control experiments: 1) The absence of Zn^{2+} in the vesicles. The vesicles were prepared as for LUVs⊃**15**, except a 10 mM HEPES buffer (100 mM KCl, pH = 7.0) containing 0.5 mM compound **15** was used for hydration process. The final liposomes were diluted to reach a total lipid concentration of 1 mM, assuming 100% retention of lipid during the gel filtration process. The experiment process for the exploration of signal transduction of **C8** at 10.0 μM was similar to the transduction activity test.

2) The absence of precatalyst head. Compound **12** (without the precatalyst head) was used as the transducer at the concentration of 10.0 μM. The vesicles were prepared as described in the main text. The final liposomes were diluted reach a total lipid

concentration of 1 mM, assuming 100% retention of lipid during the gel filtration process. The experiment process for the exploration of signal transduction was similar to the transduction activity test.

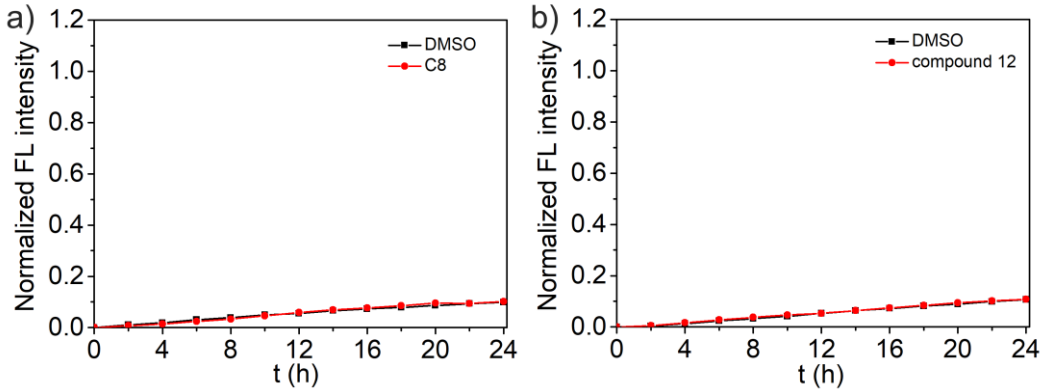


Figure S15. Time-dependence of normalized fluorescence intensity at 510 nm (λ_{ex} = 405 nm) after the addition of a) transducers **C8** to LUVs⊃**15** without Zn^{2+} in the vesicles and b) compound **12** to LUVs⊃**15**. The black line shows the normalized fluorescence intensity for a DMSO control.

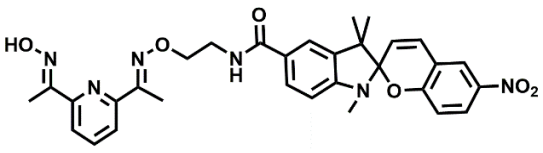
13. References

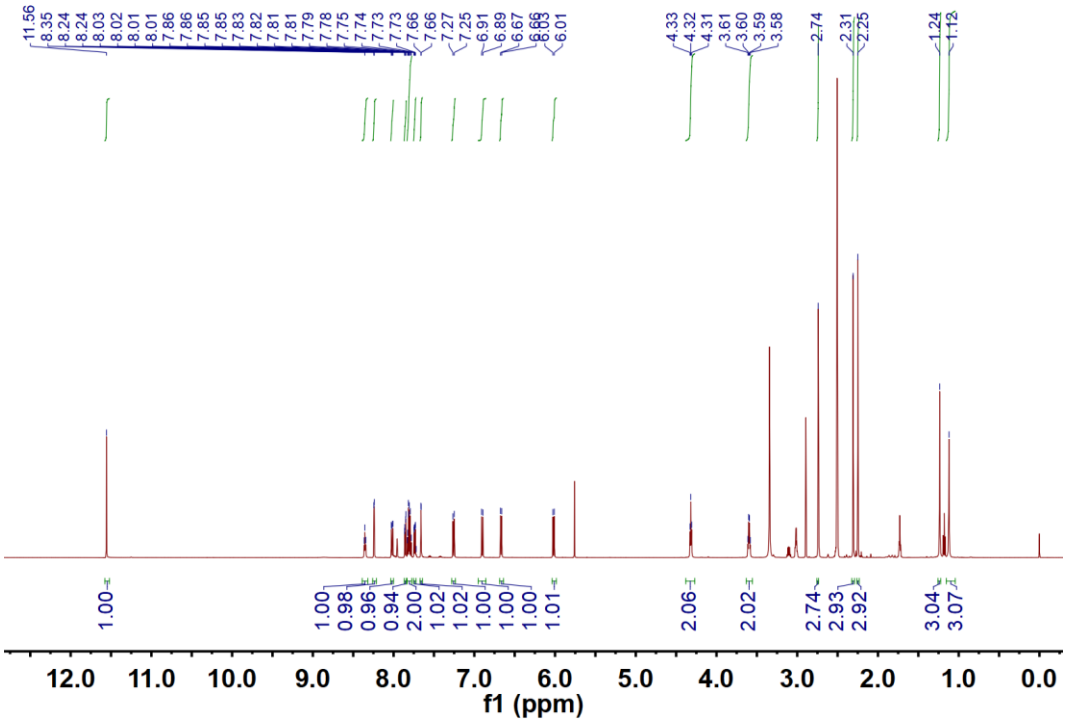
1. A. K. Yatsimirsky, P. Gómez-Tagle, S. Escalante-Tovar, L. Ruiz-Ramírez, *Inorg. Chim. Acta*, 1998, **273**, 167-174.

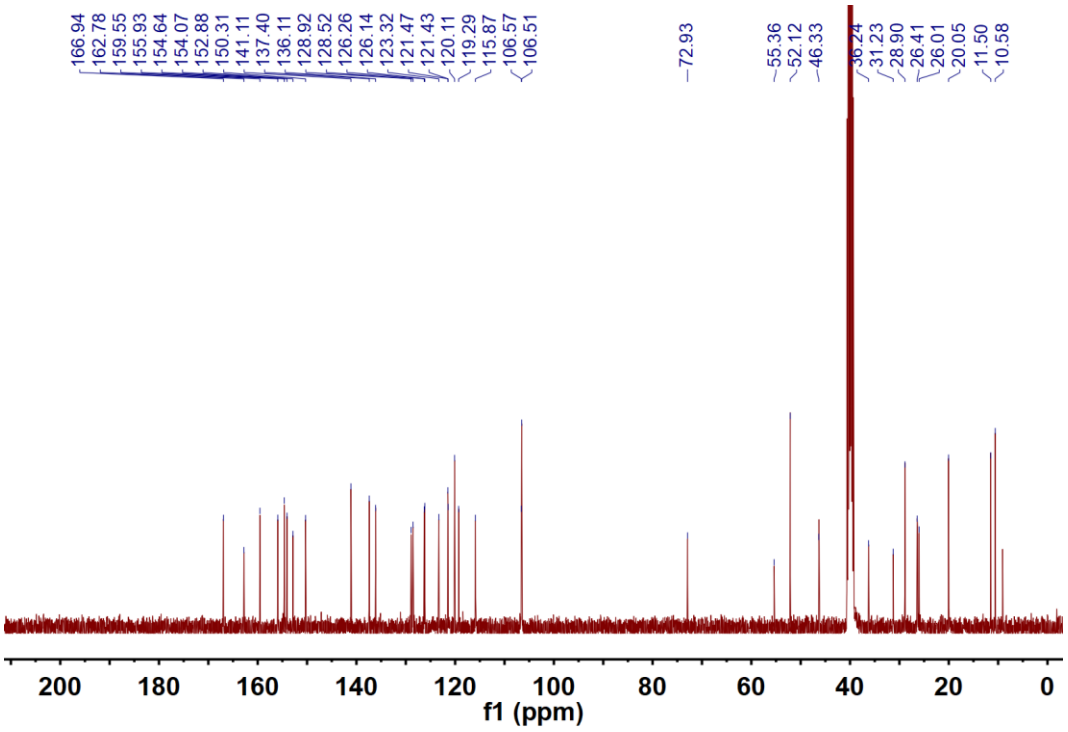
2. P. Thordarson, *Chem. Soc. Rev.* 2011, **40**, 1305-1323.

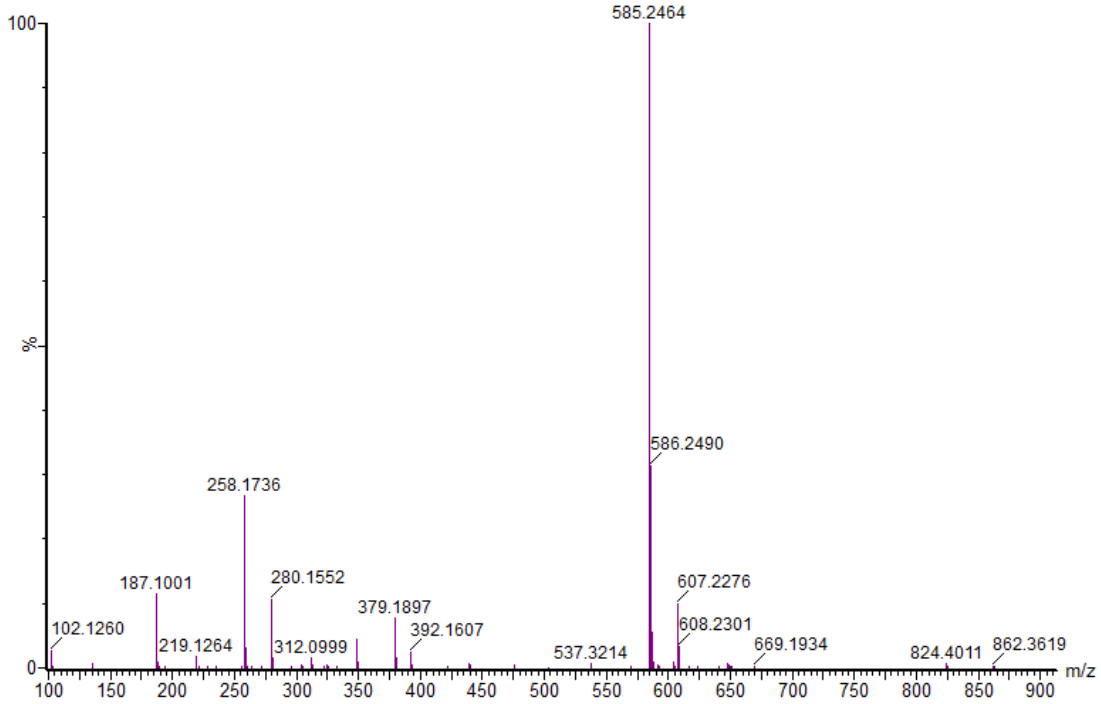
14. Appendix: ^{1}H NMR, ^{13}C NMR and Mass spectra for New Compounds:

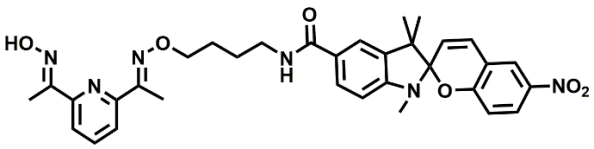
Compound **C2**



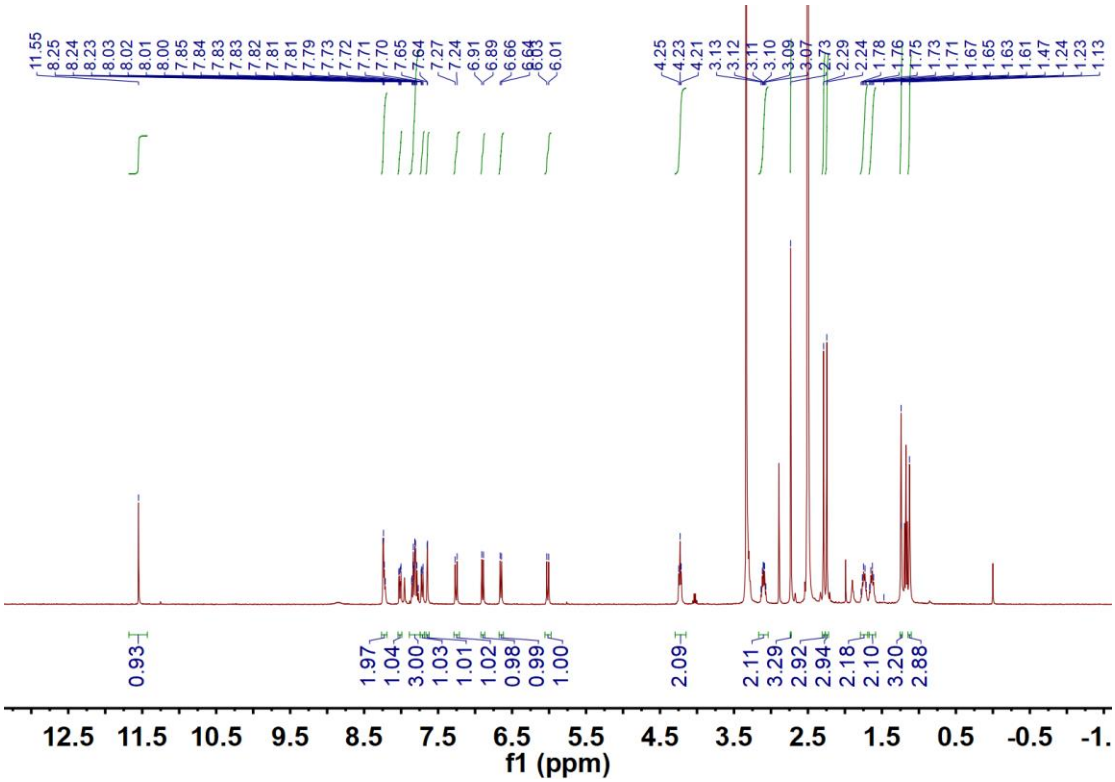

11.56
8.35
8.24
8.24
8.03
8.02
8.01
8.01
7.86
7.86
7.85
7.85
7.83
7.82
7.81
7.81
7.79
7.78
7.75
7.74
7.73
7.73
7.66
7.66
7.27
7.25
6.91
6.89
6.67
6.66
6.01
4.33
4.32
4.31
3.61
3.60
3.59
3.58
2.74
2.31
2.25
1.24
1.12
1.00
1.00
0.98
0.96
0.94
2.00
1.02
1.02
1.00
1.00
1.00
1.01
2.06
2.02
2.74
2.93
2.92
3.04
3.07
12.0
11.0
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
f1 (ppm)

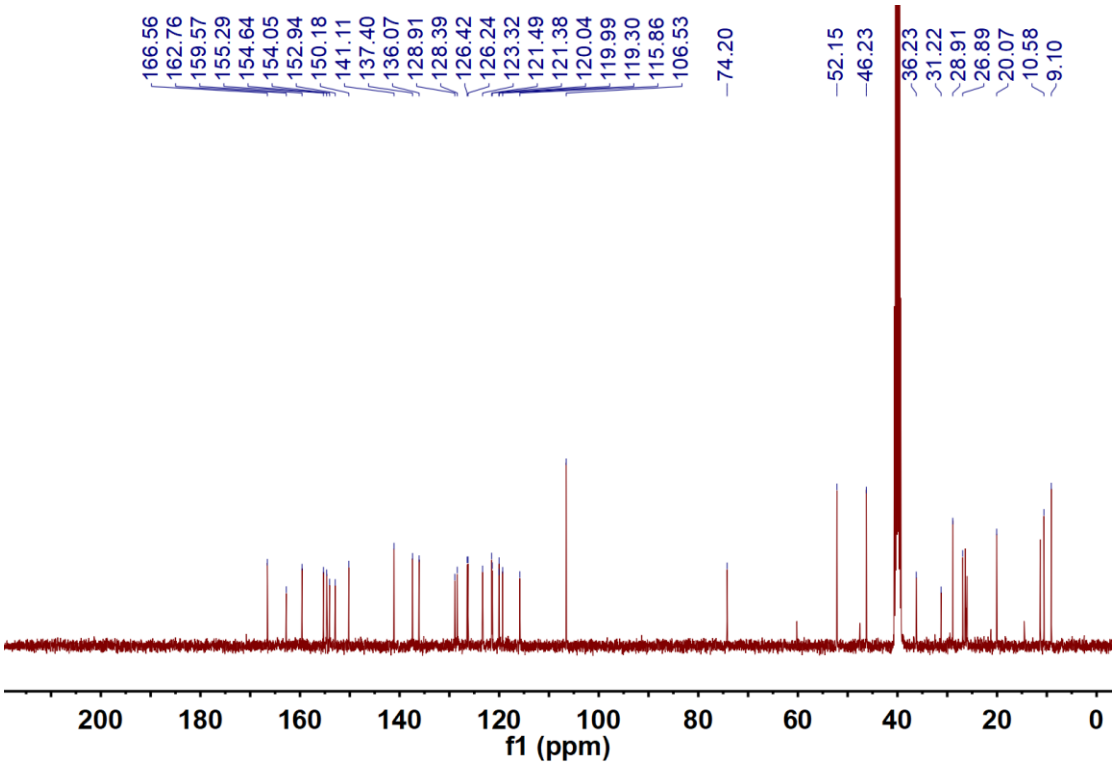

166.94
162.78
159.55
155.93
154.64
154.07
152.88
150.31
141.11
137.40
136.11
128.92
128.52
126.26
126.14
123.32
121.47
121.43
120.11
119.29
115.87
106.57
106.51
72.93
55.36
52.12
46.33
36.24
31.23
28.90
26.41
26.01
20.05
11.50
10.58
200
180
160
140
120
100
80
60
40
20
0
f1 (ppm)

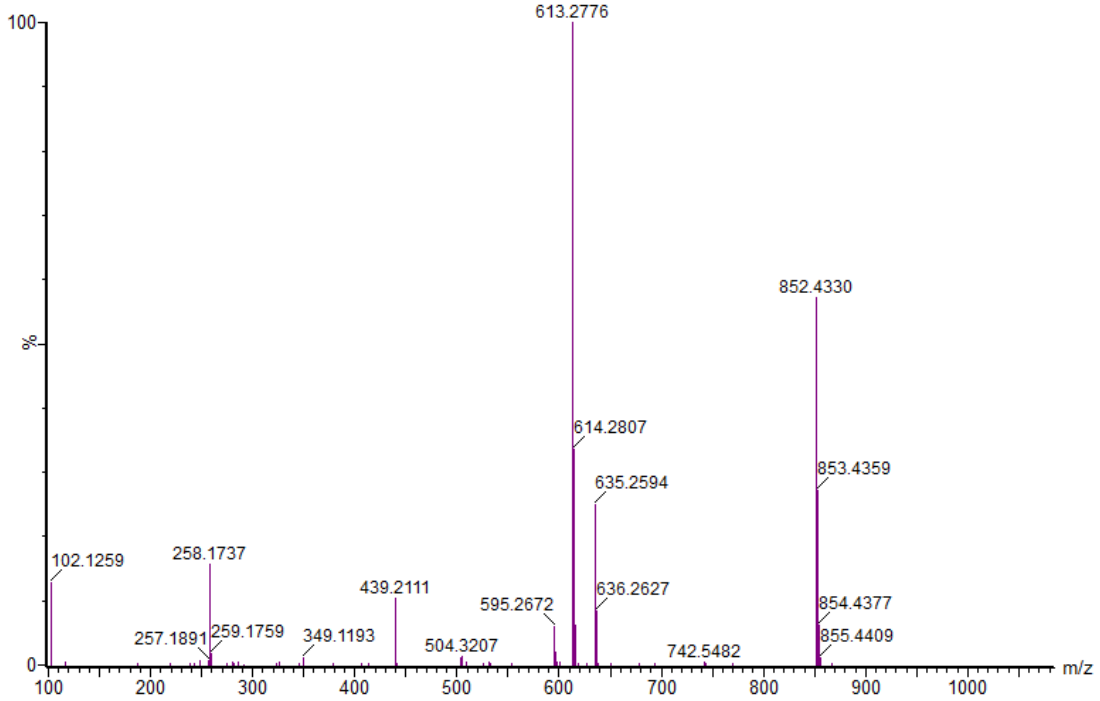

585.2464
586.2490
258.1736
187.1001
280.1552
607.2276
379.1897
608.2301
102.1260
219.1264
312.0999
392.1607
537.3214
669.1934
824.4011
862.3619
m/z

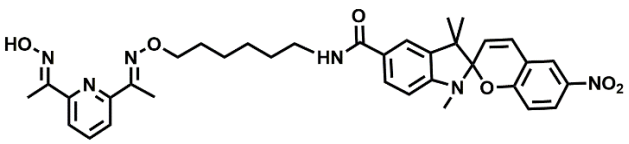

HO
N
N
O
N
H
O
N
O
NO2

Compound **C4**

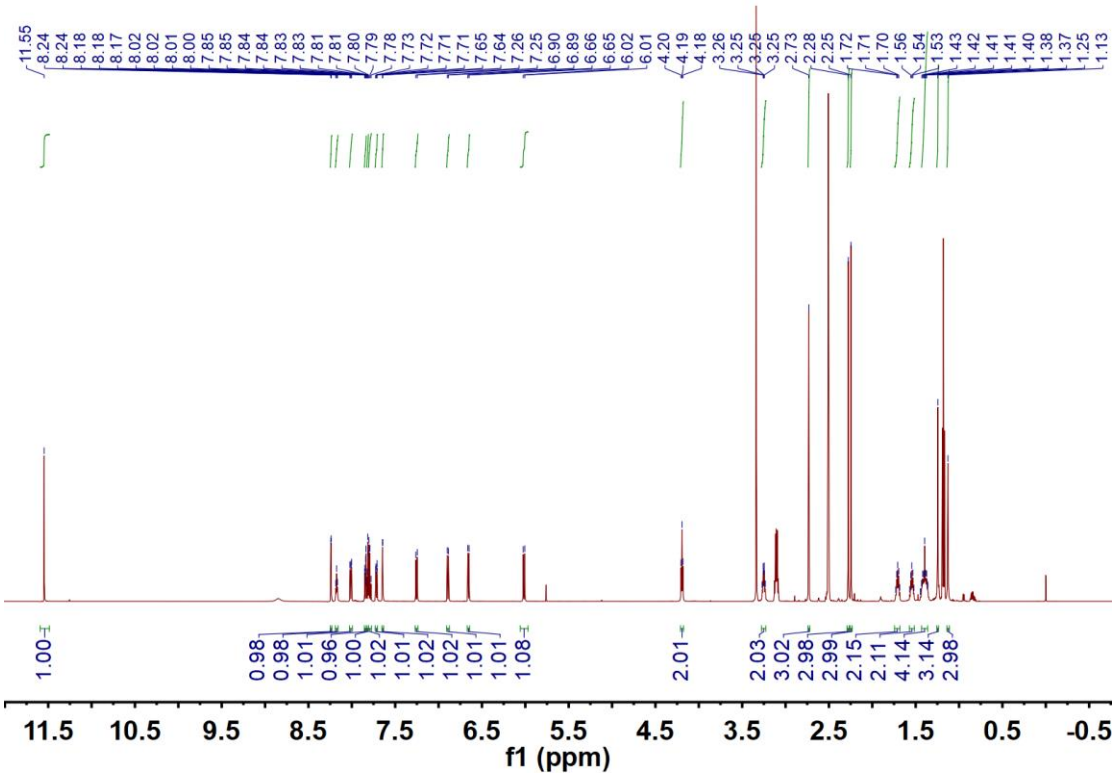

f1 (ppm)

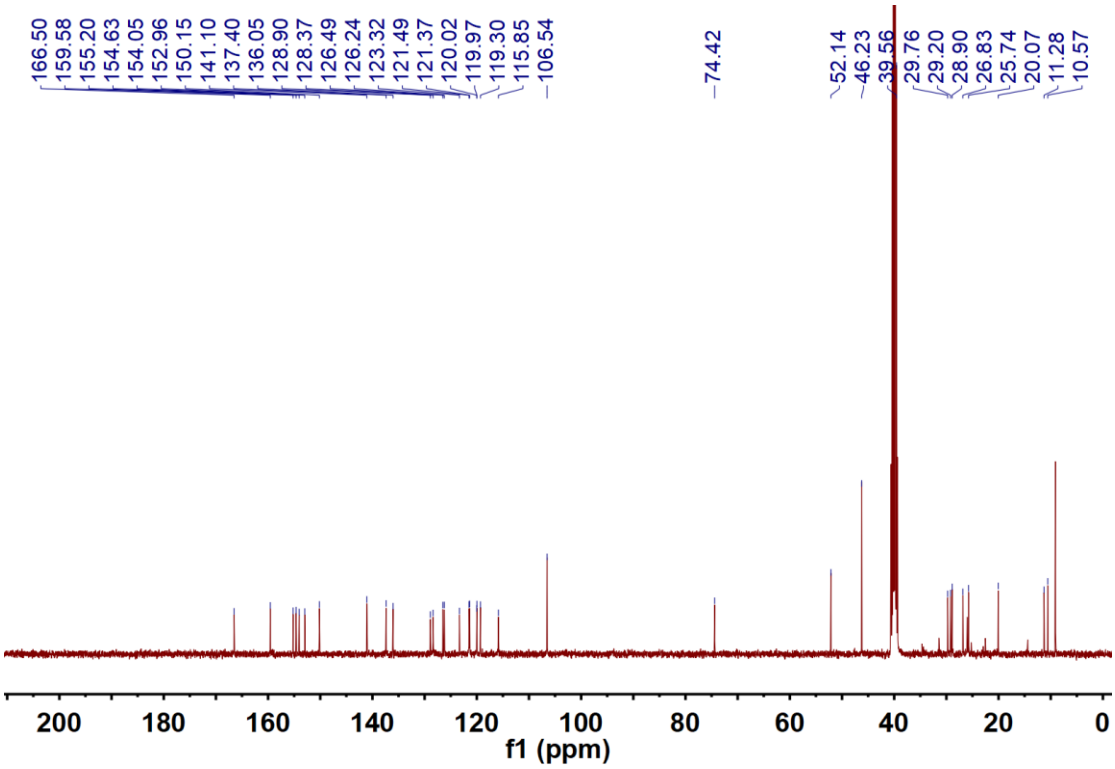

166.56
162.76
159.57
155.29
154.64
154.05
152.94
150.18
141.11
137.40
136.07
128.91
128.39
126.42
126.24
123.32
121.49
121.38
120.04
119.99
119.30
115.86
106.53
74.20
52.15
46.23
36.23
31.22
28.91
26.89
20.07
10.58
9.10
200
180
160
140
120
100
80
60
40
20
0
f1 (ppm)

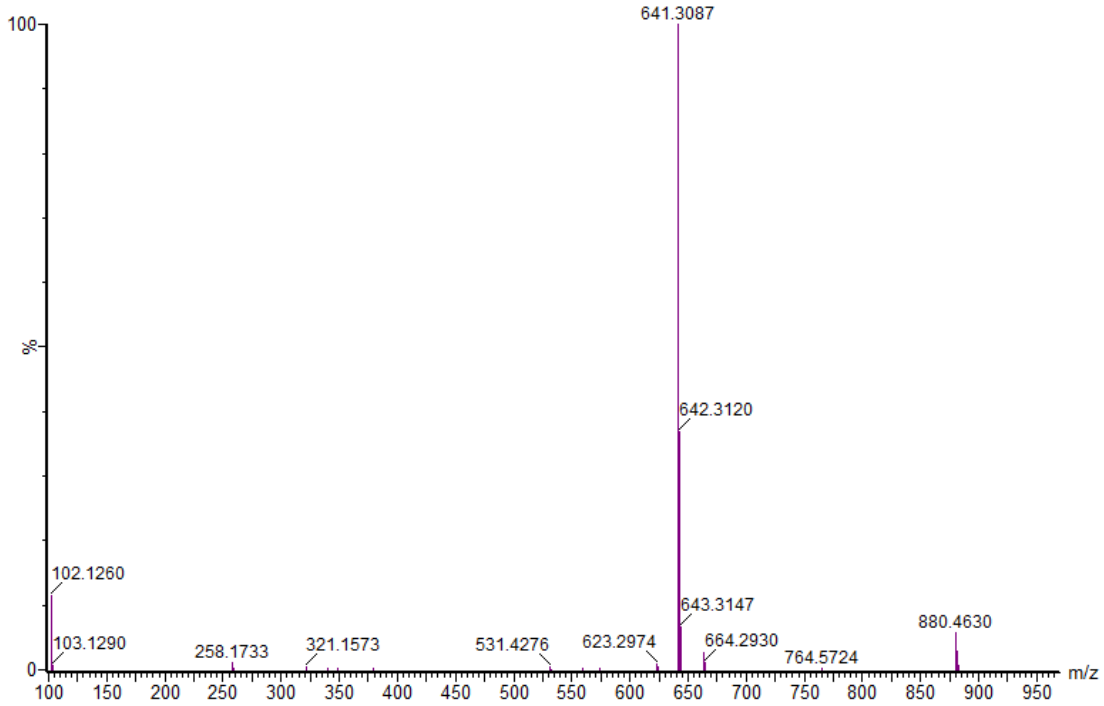

100
%
0
613.2776
852.4330
614.2807
853.4359
635.2594
102.1259
258.1737
439.2111
595.2672
636.2627
854.4377
257.1891
259.1759
349.1193
504.3207
742.5482
855.4409
100
200
300
400
500
600
700
800
900
1000
m/z

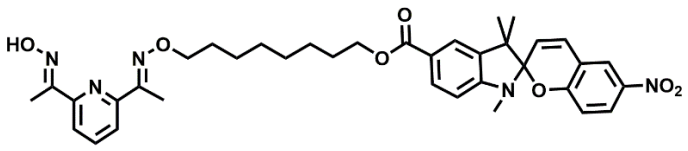

HO
N
N
O
N
HN
O
N
O
NO2

Compound **C6**

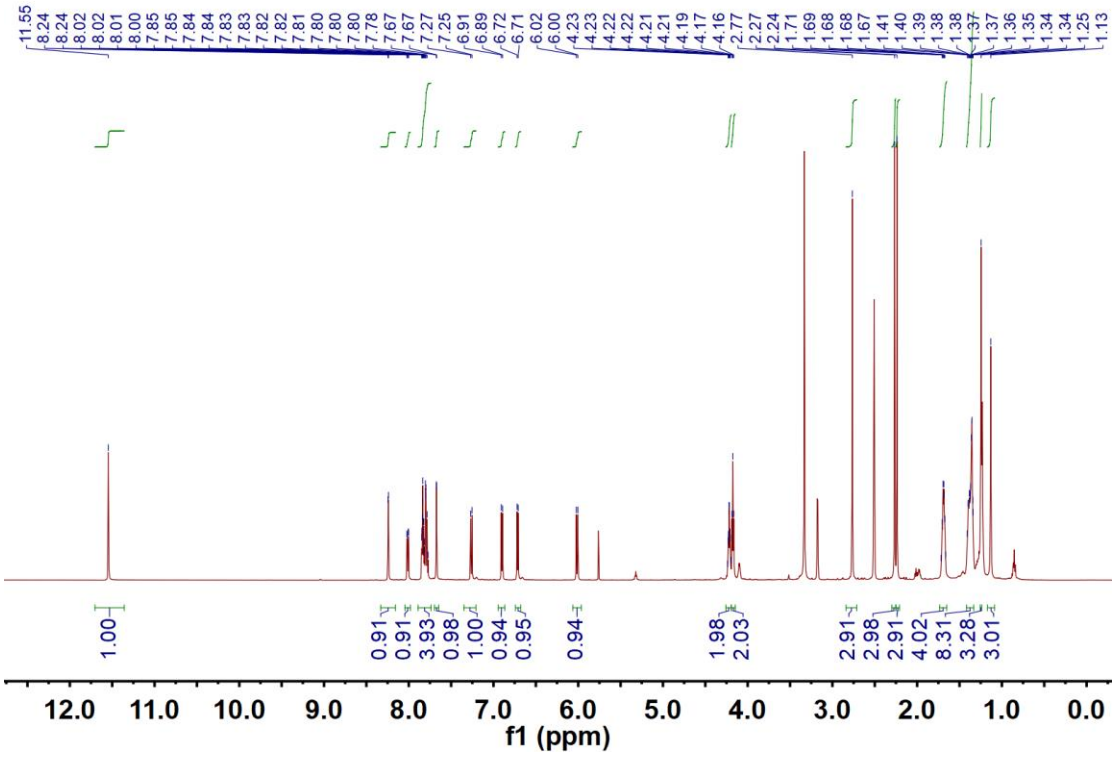

11.55
8.24
8.24
8.18
8.18
8.17
8.02
8.02
8.01
8.00
7.85
7.85
7.84
7.84
7.83
7.83
7.81
7.81
7.80
7.79
7.78
7.73
7.72
7.71
7.71
7.65
7.64
7.26
7.25
6.90
6.89
6.66
6.65
6.02
6.01
4.20
4.19
4.18
3.26
3.25
3.25
3.25
2.73
2.28
2.25
1.72
1.71
1.70
1.56
1.54
1.53
1.43
1.42
1.41
1.41
1.40
1.38
1.37
1.25
1.13
1.00
0.98
0.98
1.01
0.96
1.00
1.02
1.01
1.02
1.02
1.01
1.01
1.08
2.01
2.03
3.02
2.98
2.99
2.15
2.11
4.14
3.14
2.98
11.5
10.5
9.5
8.5
7.5
6.5
5.5
4.5
3.5
2.5
1.5
0.5
-0.5
f1 (ppm)

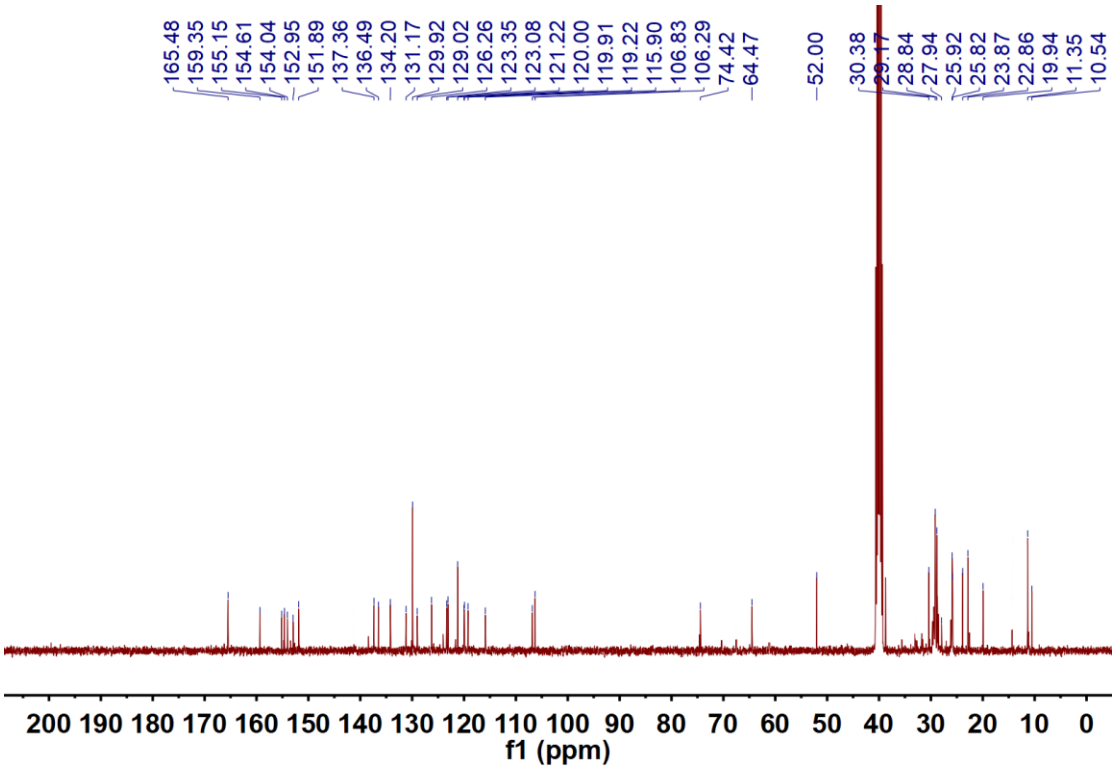

166.50
159.58
155.20
154.63
154.05
152.96
150.15
141.10
137.40
136.05
128.90
128.37
126.49
126.24
123.32
121.49
121.37
120.02
119.97
119.30
115.85
106.54
74.42
52.14
46.23
39.56
29.76
29.20
28.90
26.83
25.74
20.07
11.28
10.57
200
180
160
140
120
100
80
60
40
20
0
f1 (ppm)

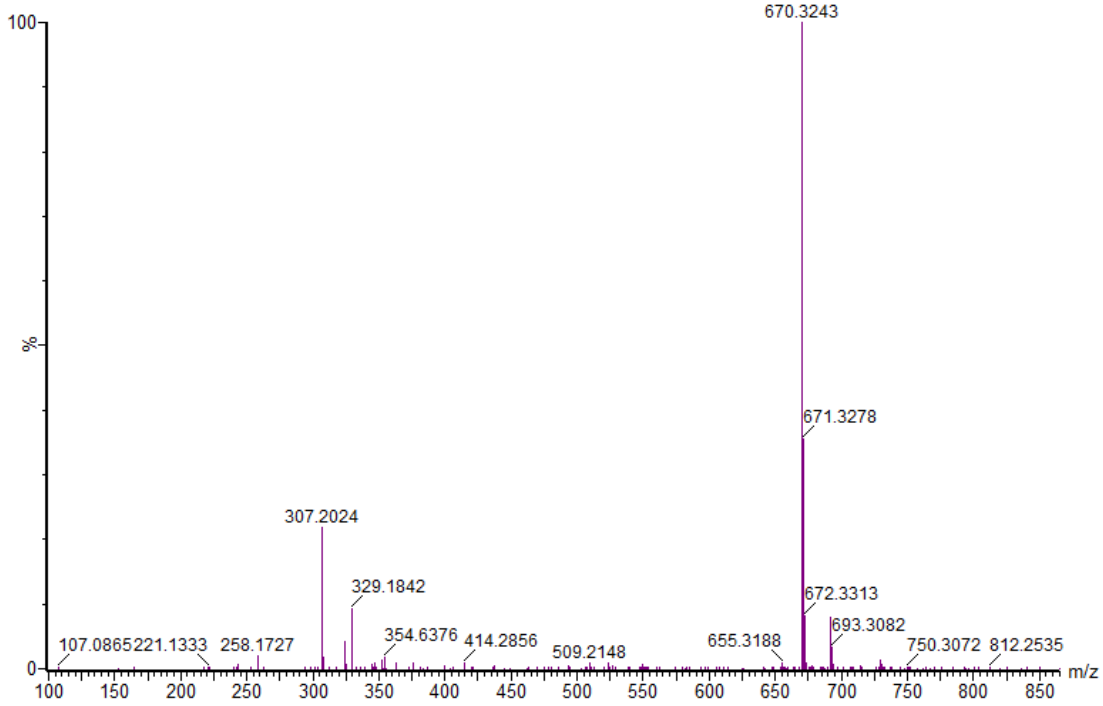

641.3087
642.3120
643.3147
102.1260
103.1290
258.1733
321.1573
531.4276
623.2974
664.2930
764.5724
880.4630
100
%
0
m/z
100 150 200 250 300 350 400 450 500 550 600 650 700 750 800 850 900 950

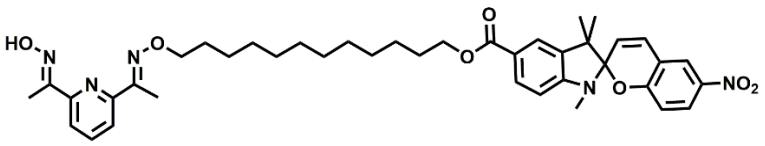

HO
N
N
O
N
O
O
N
O
NO2

Compound **C8**

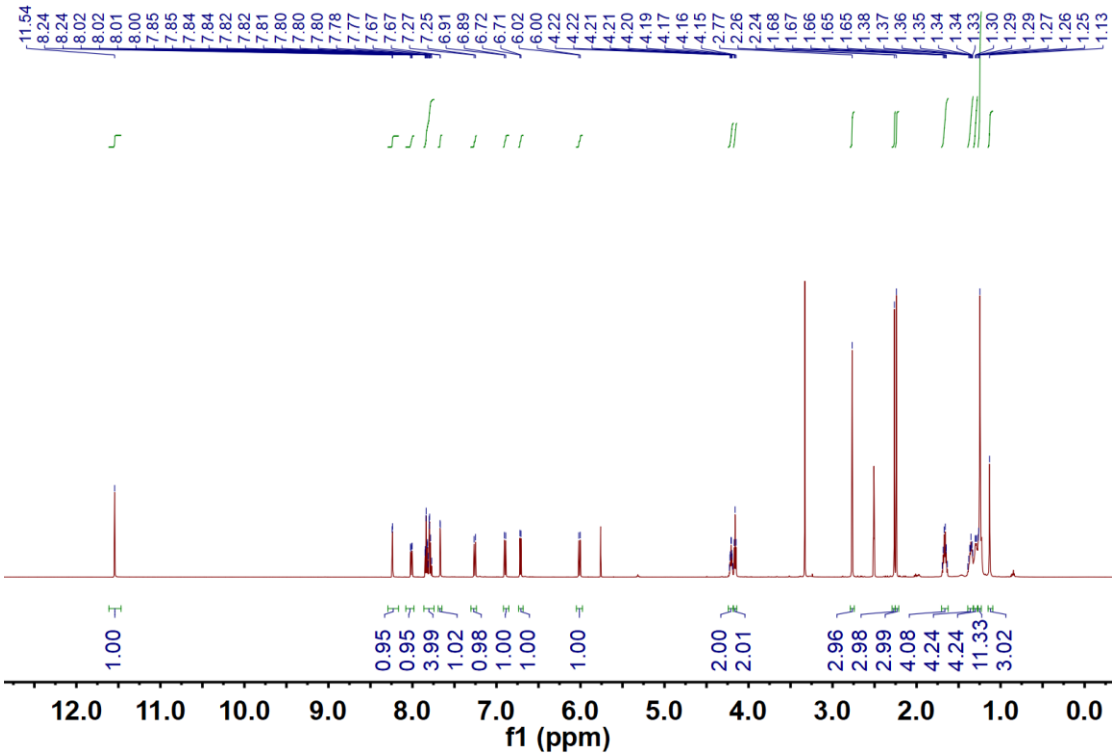

11.55
8.24
8.24
8.02
8.02
8.01
8.00
7.85
7.85
7.84
7.84
7.83
7.83
7.82
7.82
7.81
7.80
7.80
7.80
7.78
7.67
7.67
7.27
7.25
6.91
6.89
6.72
6.71
6.02
6.00
4.23
4.23
4.22
4.22
4.21
4.21
4.19
4.17
4.16
2.77
2.27
2.24
1.71
1.69
1.68
1.68
1.67
1.41
1.40
1.39
1.38
1.38
1.37
1.37
1.36
1.35
1.34
1.34
1.25
1.13
1.00
0.91
0.91
3.93
0.98
1.00
0.94
0.95
0.94
1.98
2.03
2.91
2.98
2.91
4.02
8.31
3.28
3.01
12.0 11.0 10.0 9.0 8.0 7.0 6.0 5.0 4.0 3.0 2.0 1.0 0.0
f1 (ppm)

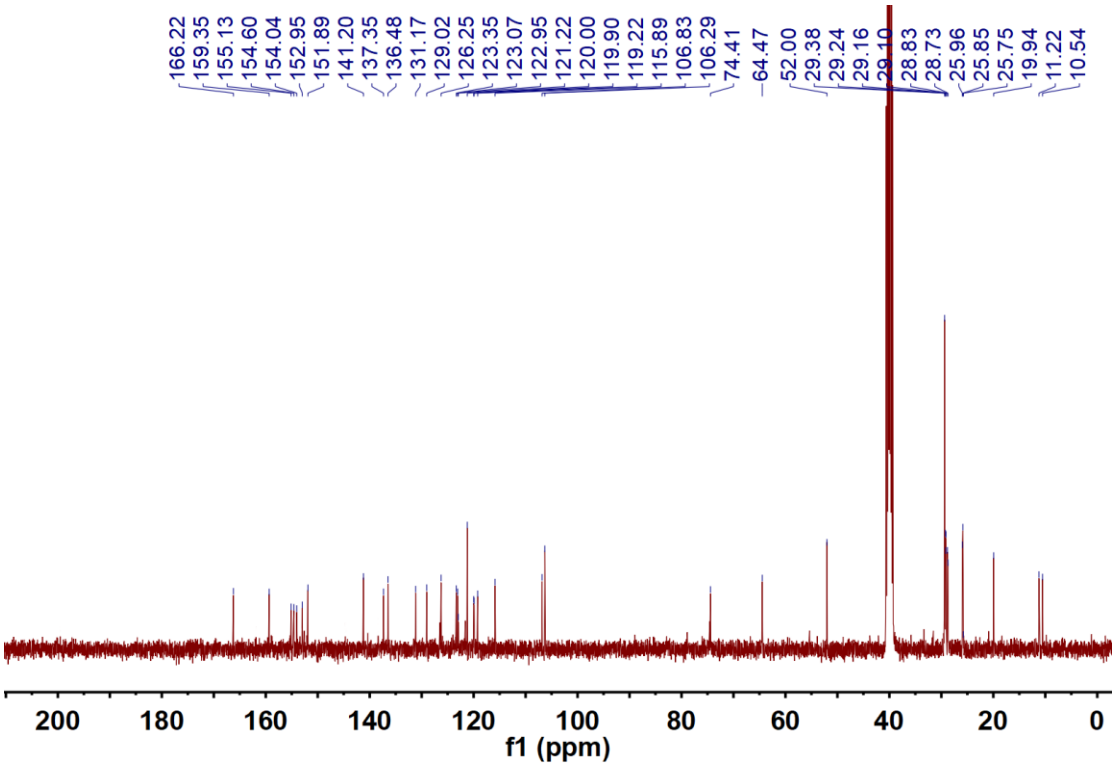


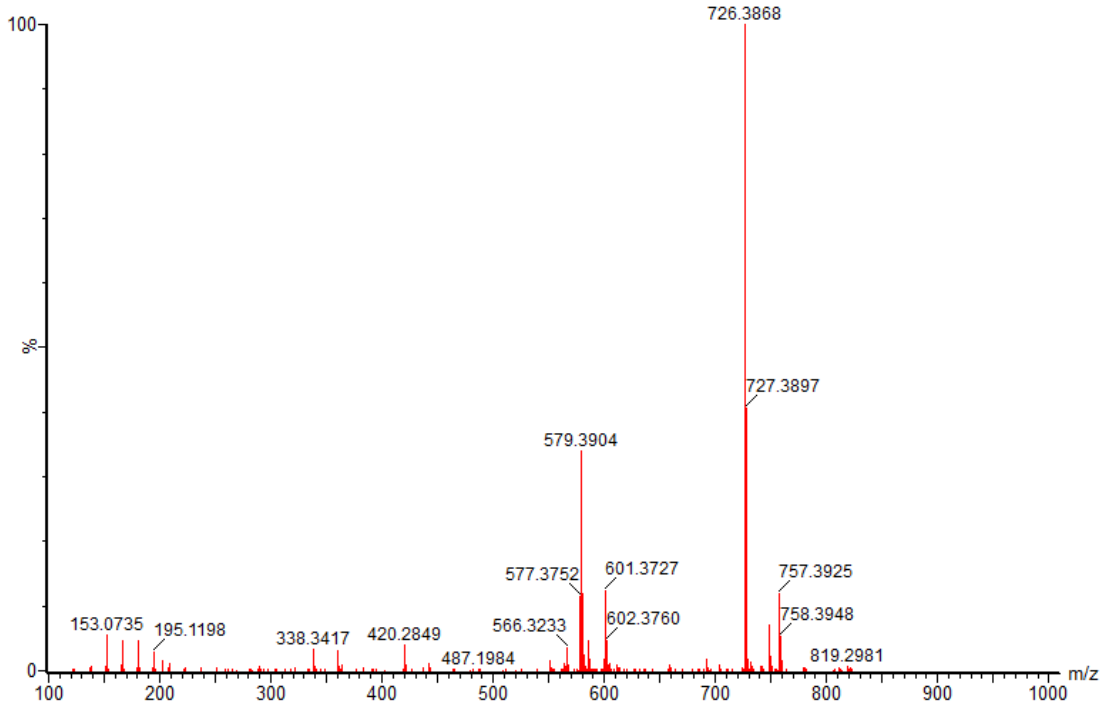




Compound **C12**


11.54
8.24
8.24
8.02
8.02
8.01
8.00
7.85
7.85
7.84
7.84
7.82
7.82
7.81
7.80
7.80
7.80
7.78
7.77
7.67
7.67
7.27
7.25
6.91
6.89
6.72
6.71
6.02
6.00
4.22
4.22
4.21
4.21
4.20
4.19
4.17
4.16
4.15
2.77
2.26
2.24
1.68
1.67
1.66
1.65
1.65
1.38
1.37
1.36
1.35
1.34
1.34
1.33
1.30
1.29
1.29
1.27
1.26
1.25
1.13
1.00
0.95
0.95
3.99
1.02
0.98
1.00
1.00
1.00
2.00
2.01
2.96
2.98
2.99
4.08
4.24
4.24
11.33
3.02
12.0
11.0
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
f1 (ppm)


166.22
159.35
155.13
154.60
154.04
152.95
151.89
141.20
137.35
136.48
131.17
129.02
126.25
123.35
123.07
122.95
121.22
120.00
119.90
119.22
115.89
106.83
106.29
74.41
64.47
52.00
29.38
29.24
29.16
29.10
28.83
28.73
25.96
25.85
25.75
19.94
11.22
10.54
200
180
160
140
120
100
80
60
40
20
0
f1 (ppm)


726.3868
100
%
727.3897
579.3904
577.3752
601.3727
757.3925
758.3948
153.0735
195.1198
338.3417
420.2849
566.3233
602.3760
487.1984
819.2981
0
m/z
100
200
300
400
500
600
700
800
900
1000