Electronic Supplementary Information

Supramolecular capture of highly polar amidosquaraine dye in water with nanomolar affinity and large turn-on fluorescence

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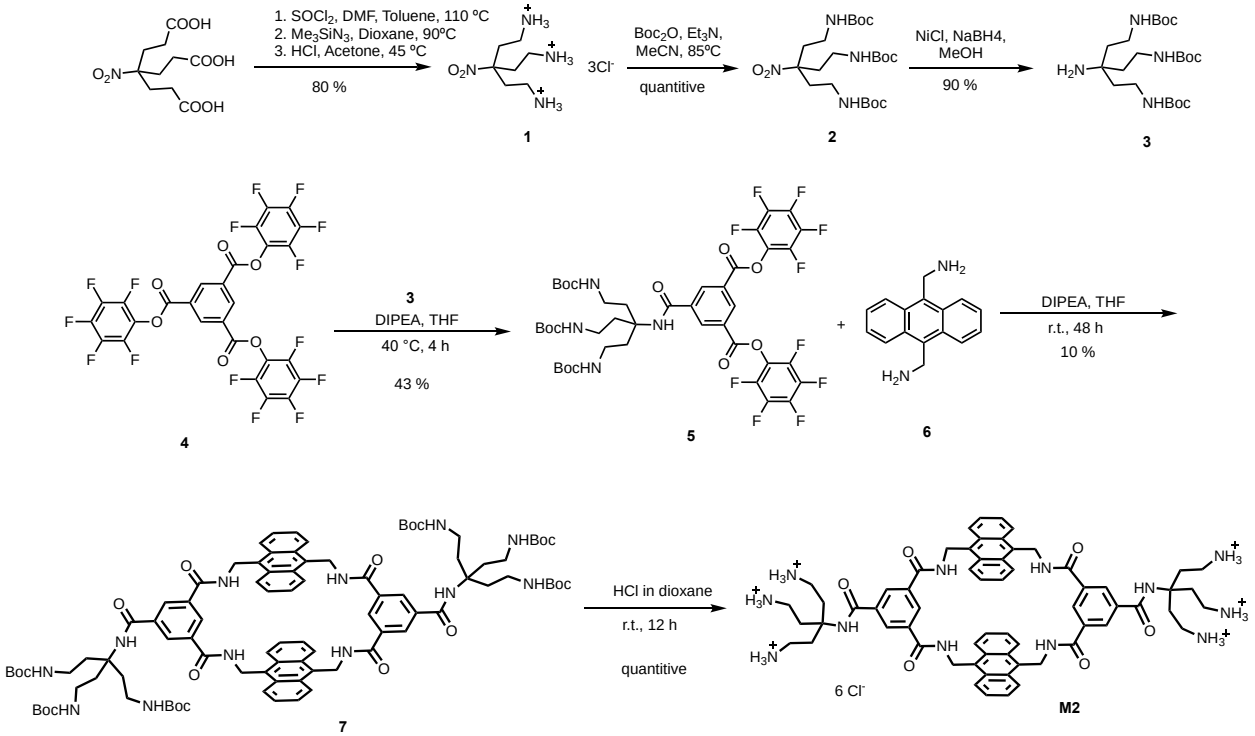
Content

1. Materials and Instrumentation

All chemicals and solvents were purchased as reagent grade and used without further purification unless otherwise noted. Reactions were monitored by TLC plate (precoated with 60 Å silica gel, F254) purchased from SILICYCLE and visualized by UV light (254, 365 nm) or $KMnO_4$ stain. Flash column chromatography was performed using silica gel (silicaFlash P60 from SILICYCLE) as the stationary phase. ^{1}H and ^{13}C NMR spectra were recorded on Bruker AVANCE III HD 400 and 500 MHz spectrometers at 25 °C. Chemical shift is presented in ppm and referenced by residual solvent peak. Mass spectrometry (MS) was performed using a Bruker microTOF II spectrometer. Absorption spectra were collected using an Evolution 201 UV-Vis Spectrometer with ThermoInsight software. Fluorescence spectra were collected using a Horiba Fluoromax-4 fluorometer with FluorEssence software.

2. Synthesis and Compound Characterization

Compounds **M1**,[1] **1**,[2] **2**,[2] **3**,[2] **4**,[1] **6**,[3] **8**,[4] and **9**,[5] were synthesized according to previously reported procedures.



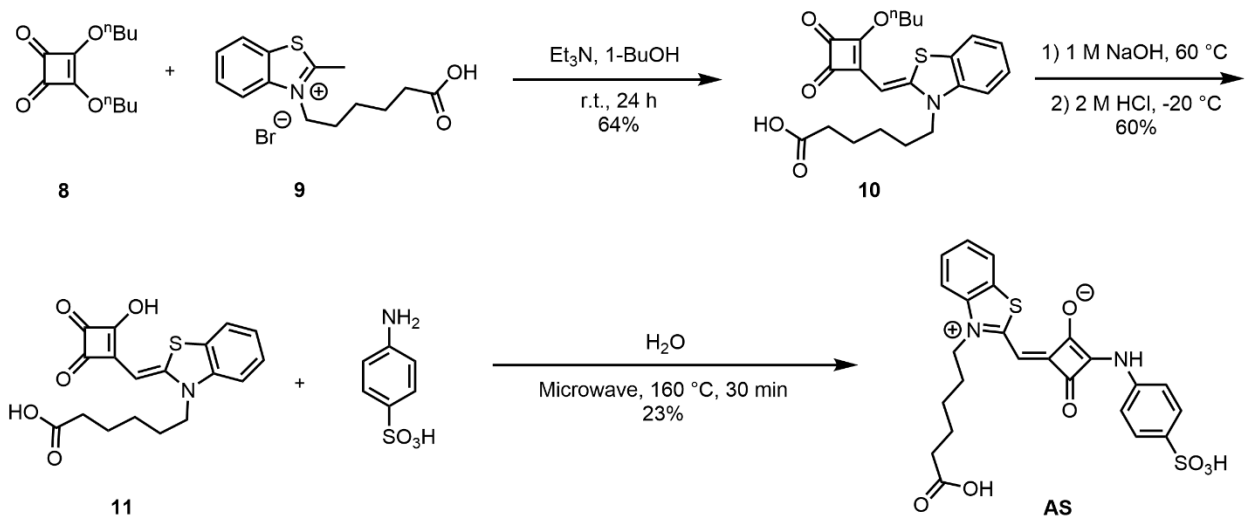
Scheme S1: Synthesis of **M2**.

*Synthesis of **5***

To a stirred suspension of tris-pentafluorophenyl ester **4** (1.00 g, 1.42 mmol) and amino-hexa-ester **3** (0.60 g, 0.65 mmol) in 5 mL dry THF was added DIPEA (1 mL). The reaction mixture was heated at 40 °C for 4 hours, after which the clear solution was concentrated to dryness with a rotary evaporator. The resulting oil was purified via column chromatography (hexane:EtOAc, 6:4 to 4:6) to yield bis-pentafluorophenyl ester **5** as a white solid (0.94 g, 43%). ^{1}H NMR (500 MHz, $CDCl_3$, 25 °C): δ 9.04 (t, *J* = 1.4 Hz, 1H), 9.00 (d, *J* = 1.6 Hz, 2H), 8.23 (bs, 1H), 4.91 (bs, 3H), 3.19 (m, 6H), 2.10 (m, 6H), 1.34 (s, 27H). HRMS (ESI-TOF) m/z: $[M+H]^+$ calcd for $C_{43}H_{47}F_{10}N_4O_{11}^+$ 985.3076; found 985.3099.

*Synthesis of **M2***

5 (0.5135 g, 0.52 mmol) was dissolved in 70 mL dry THF in a plastic syringe. Compound **6** (0.118 g, 0.52 mmol) and DIPEA (5.0 mL) were dissolved in 70 mL dry THF in a separate plastic syringe. Another 500 mL of dry THF were added to a dry roundbottom flask, and the above two solutions were added by syringe pump to the flask over a period of 24 hours under an argon atmosphere. The mixture was then stirred for a further 24 hours. The solvent was removed under reduced pressure and the crude product was dissolved in a 50 mL dichloromethane and filtered. The solvent was removed from the filtrate under reduced pressure and the residue was purified by column chromatography using 0-10% MeOH in chloroform to obtain the crude product, which was further purified by reverse-phase C18 column chromatography using 70-80% acetone in H_2O to obtain **7** as a yellow solid (10%) whose structure was confirmed by mass spectrometry. HRMS (ESI-TOF) m/z: $[M+K]^+$ calcd for $C_{94}H_{120}KN_{12}O_{18}^+$ 1743.8475; found 1743.8538. Protected macrocycle **7** **(**10 mg) was then stirred overnight in a mixture of 200 µL concentrated HCl and 200 µL dioxane. The solvent was then removed under reduced pressure to obtain **M2** as a pale yellow solid (15 mg, quant.). ^{1}H NMR (500 MHz, CD_3OD, 25 °C): δ 8.58 (d, *J* = 1.4 Hz, 4H), 8.27 (dd, *J* = 7.5, 1.6 Hz, 8H), 7.90 (t, *J* = 1.4 Hz, 2H), 7.45 (dd, *J* = 7.5, 1.6 Hz, 8H), 5.50 (s, 8H), 3.10-3.15 (m, 12H), 2.33-2.37 (m, 12H). HRMS (ESI-TOF) m/z: $[M+2H]^+$ calcd for $C_{64}H_{73}N_{12}O_6^+$ 1105.5771; found 1105.5784.



Scheme S2: Synthesis of **AS**.

*Synthesis of **10***

Compounds **8** (1.35 g, 6 mmol) and **9** (2.06 g, 6 mmol) were suspended in 15 mL of 1-butanol, then 1.0 mL of triethylamine were added to the suspension. The mixture was protected from light and stirred overnight, then the solvent was removed *in vacuo*. The dark orange precipitate was purified with column chromatography (0-8% methanol in dichloromethane) to yield semisquaraine **10** as yellow powder (1.60 g, 64%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.48 (d, *J* = 7.5 Hz,1H), 7.35 (t, *J* = 7.5 Hz,1H), 7.17 (t, *J* = 7.5 Hz, 1H), 7.07 (d, *J* = 7.5 Hz, 1H), 5.49 (s, 2H), 4.82 (t, *J* = 7.0 Hz, 2H), 4.00 (t, *J* = 7.5 Hz, 2H), 2.41 (t, *J* = 7.0 Hz, 2H), 1.84 (m, *J* = 2.0 Hz, 4H), 1.75 (m, *J* = 2.0 Hz, 2H), 1.52 (m, *J* = 1.5 Hz, 4H), 1.00 (t, *J* = 1.5 Hz, 3H). ^{13}C NMR (126 MHz, DMSO-d_6) δ 192.41, 185.02, 184.50, 174.37, 171.94, 159.19, 140.93, 127.23, 125.80, 123.57, 122.39, 112.14, 78.91, 72.89, 44.95, 33.54, 31.58, 26.19, 25.62, 24.21, 18.22, 13.58. HRMS (LC-MS/MS) m/z: $[M+H]^+$ calcd for $C_{22}H_{26}NO_5S^+$ 416.1526; found 416.1542.

*Synthesis of **11***

To compound **10** (415 mg, 1 mmol), 30 mL of 100 mM aquous NaOH solution was added. The suspension was stirred and heated at 70 °C for 10 hours, and formed a clear orange solution. The mixture was then cooled to -10 °C in a brine ice bath, then 2 M HCl was added to the mixture dropwise to adjust the pH to 5~6, and orange precipitate crashed out. The precipitate was filtered out, rinsed with cold acetone, dried under high vacuum, and yielded **11** as dark-orange solid (215 mg, 60%). ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.64 (d, *J* = 8.0 Hz, 1H), 7.29 (m, *J* = 8.5 Hz, 2H), 7.08 (t, *J* = 8.0 Hz, 1H), 5.58 (s, 1H), 3.99 (t, *J* = 7.0 Hz, 2H), 2.21 (t, *J* = 7.0 Hz, 2H), 1.65 (m, *J* = 1.5 Hz, 2H), 1.56 (m, *J* = 1.5 Hz, 1H), 1.39 (m, *J* = 1.5 Hz, 2H). ^{13}C NMR (126 MHz, DMSO-d_6) δ 191.97, 175.48, 174.41, 141.47, 126.70, 125.97, 122.31, 121.91, 110.80, 80.21, 44.53, 33.60, 25.87, 25.77, 24.24. HRMS (LC-MS/MS) m/z: $[M+H]^+$ calcd for $C_{18}H_{18}NO_5S^+$ 360.0900; found 360.0925.

*Synthesis of **AS***

Compound **11** (54 mg, 0.15 mmol) and 4-aminobenzenesulfonic acid (130 mg, 0.75 mmol) were suspended in water. The reaction was heated to 160 °C in a microwave reactor for 30 minutes. The reaction mixture was cooled to room temperature and the solvent was removed under reduced pressure. The residue was purified by reverse-phase column chromatography (0-50% MeOH in 0.5% $NH_3 \cdot H_2O$) and yielded **AS** as a dark-pink solid (15 mg, 23%). ^{1}H NMR (400 MHz, D_2O) δ7.52 (d, *J* = 7.5 Hz, 2H), 7.40 (d, *J* = 7.0 Hz, 1H), 7.08 (m, *J* = 7.0 Hz, 3H), 6.99 (d, *J* = 7.0 Hz,1H), 6.92 (d, *J* = 7.0 Hz,1H), 5.44 (s, 2H), 3.85 (t, *J* = 5.5 Hz, 2H), 2.14 (t, *J* = 2.0 Hz, 2H), 1.64 (m, *J* = 1.5 Hz, 2H), 1.55 (m, *J* = 1.5 Hz, 2H), 1.34 (m, *J* = 1.5 Hz, 2H). ^{13}C NMR (126 MHz, D_2O) δ 183.90, 181.71, 140.92, 136.77, 127.40, 126.86, 126.46, 123.93, 122.00, 120.71, 111.95, 46.02, 37.72, 26.39, 26.27, 25.89, 23.46. HRMS (ESI) m/z: $[M-H]^-$ calcd for $C_{24}H_{21}N_2O_7S_2^-$ 513.0796; found 513.0781.

^{1}H and ^{13}C NMR and Mass Spectra

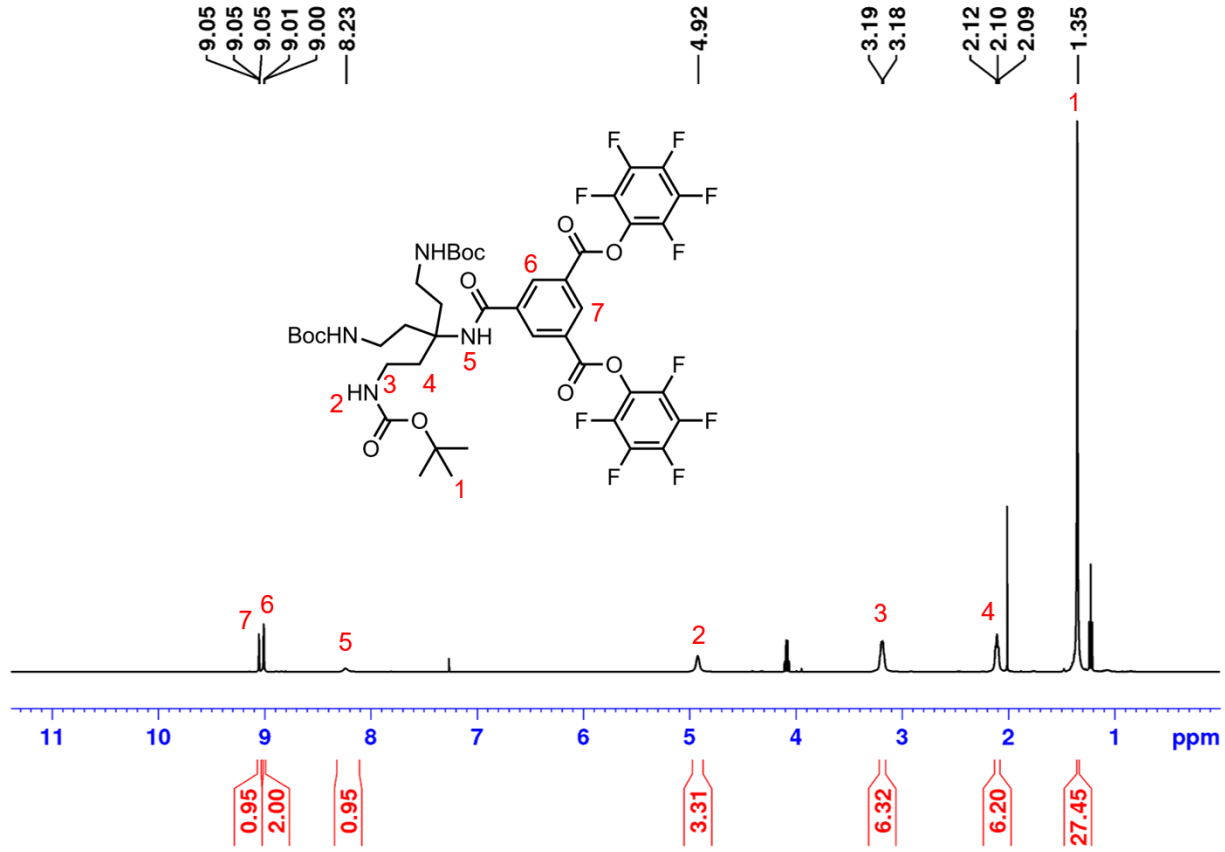


Figure S1: ^{1}H NMR (500 MHz, $CDCl_3$, 25 °C) of **5**.

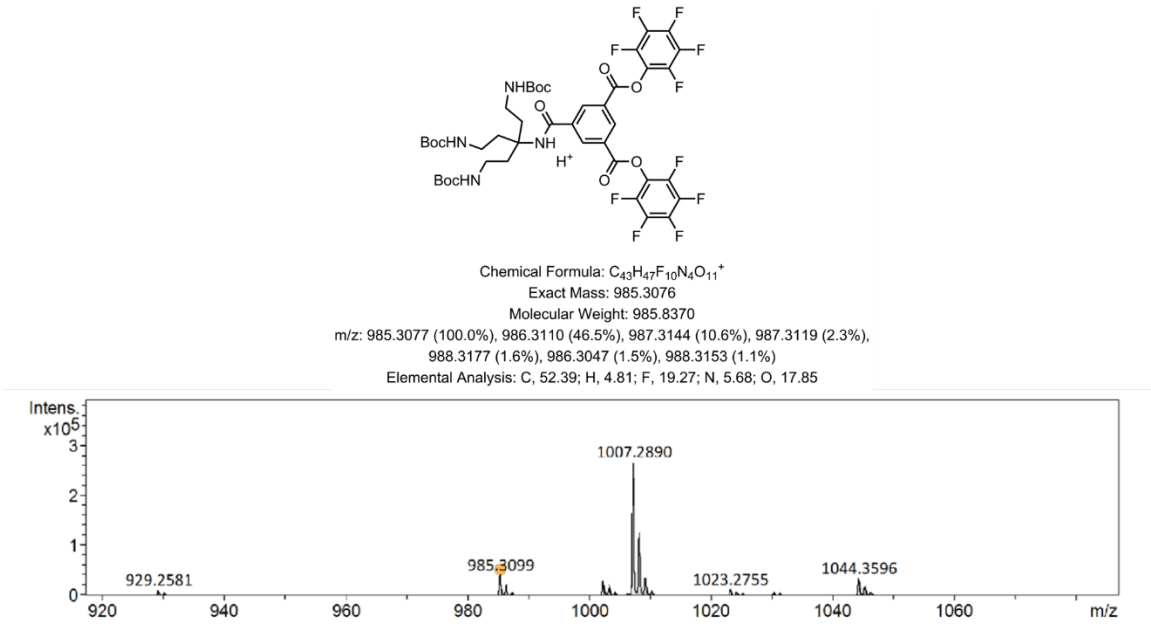


Figure S2: HRMS (ESI-TOF) of **5**.

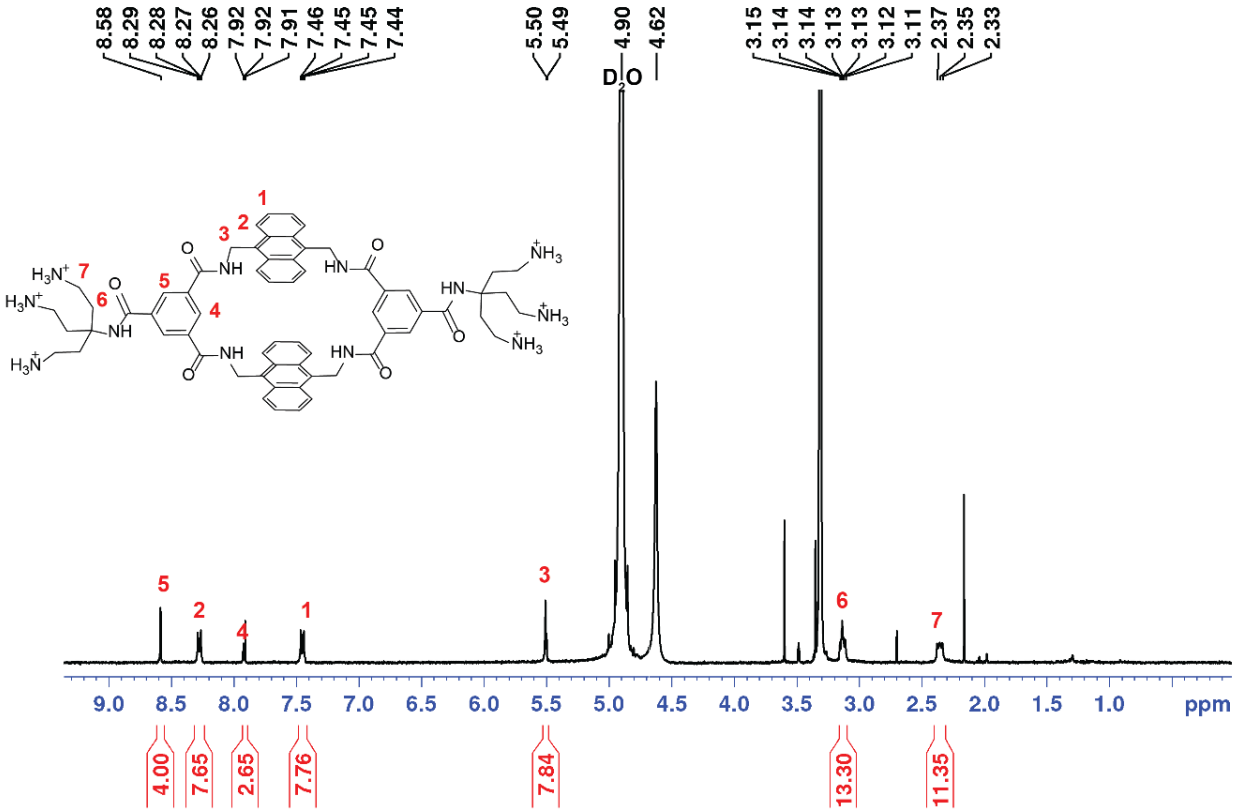
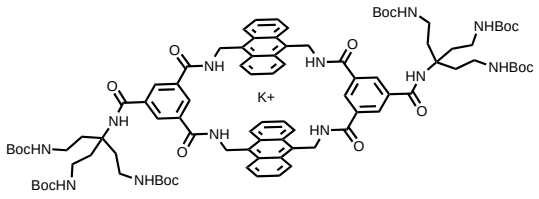
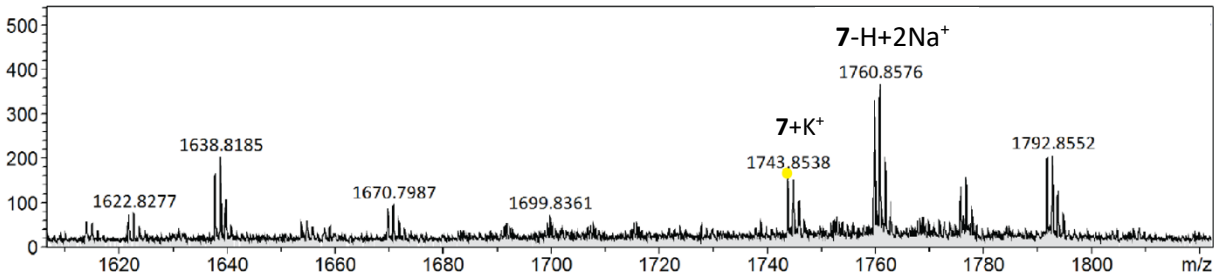
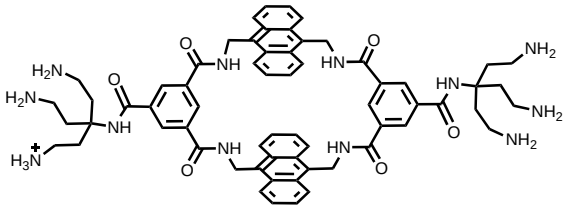


Figure S3: ^{1}H NMR (500 MHz, CD_3OD/D_2O, 25 °C) of **M2**.



Chemical Formula: $C_{94}H_{120}KN_{12}O_{18}^{+}$
Exact Mass: 1743.8475





Chemical Formula: $C_{64}H_{73}N_{12}O_{6}^{+}$
Exact Mass: 1105.5771

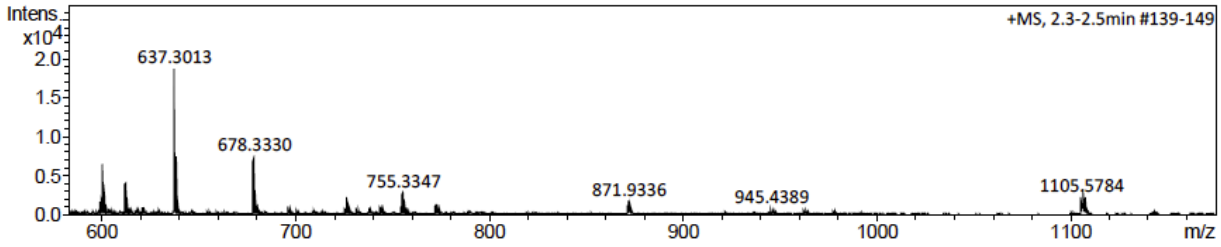


Figure S4: (*top*) HRMS (ESI-TOF) of precursor **7.** (*bottom*) HRMS (ESI-TOF) of **M2**.

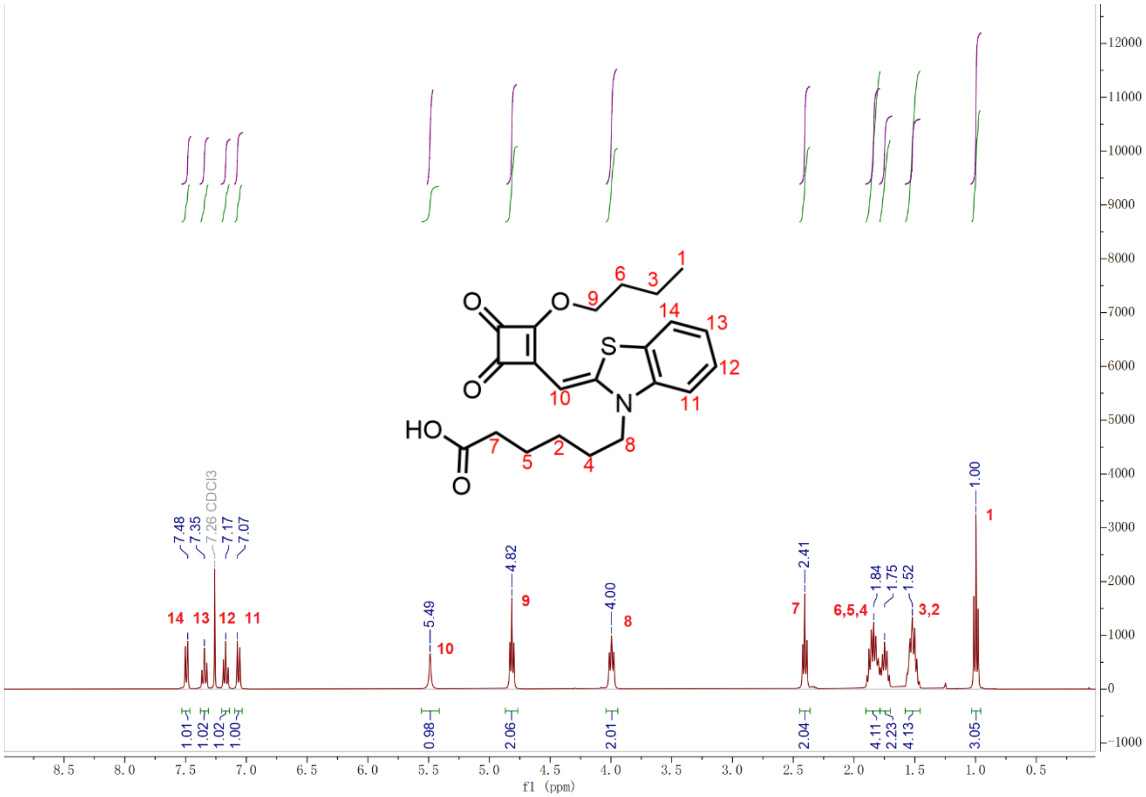


Figure S5: ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C) of **10**.

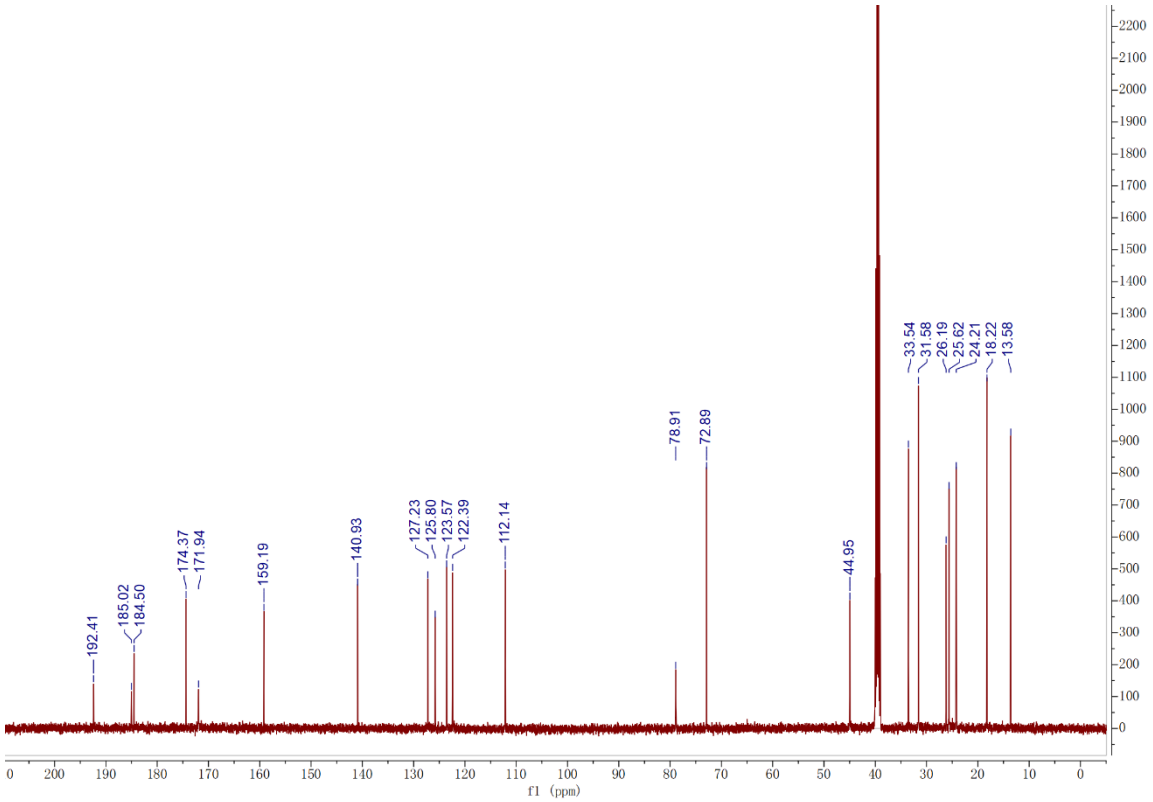
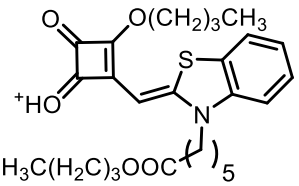


Figure S6: ^{13}C NMR (126 MHz, DMSO-d_6, 25 °C) of **10**



Chemical Formula: $C_{22}H_{26}NO_5S^+$

Exact Mass: 416.1526

Molecular Weight: 416.5115

m/z: 416.1526 (100.0%), 417.1560 (23.8%), 418.1484 (4.5%), 418.1593 (2.7%), 419.1518 (1.1%), 418.1569 (1.0%)

Elemental Analysis: C, 63.44; H, 6.29; N, 3.36; O, 19.21; S, 7.70

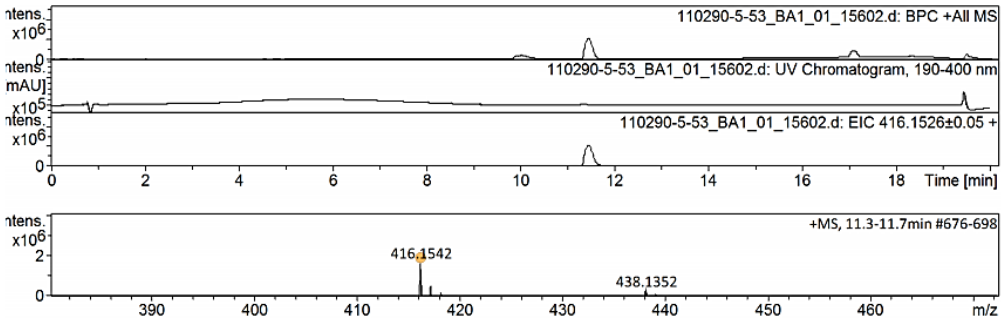


Figure S7: HRMS (LC-MS/MS) of **10**.

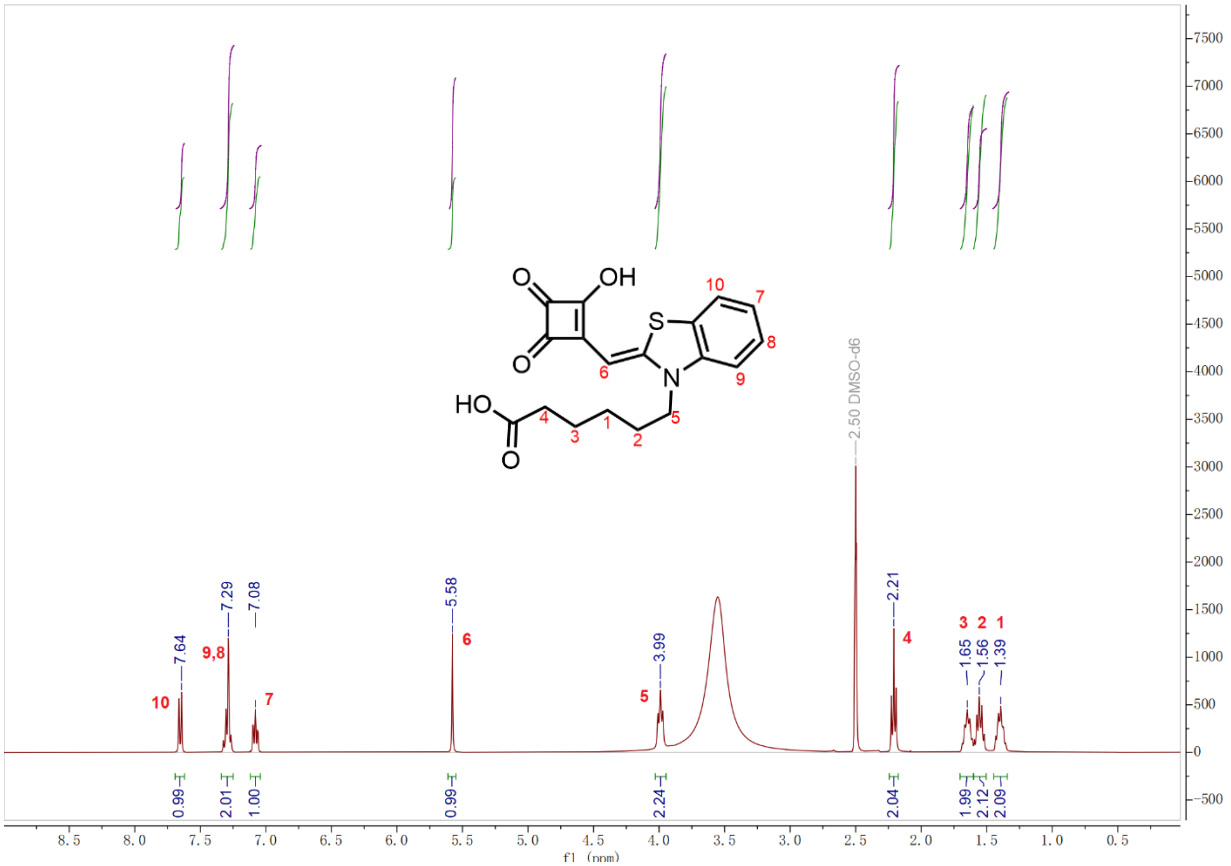


Figure S8: ^{1}H NMR (400 MHz, DMSO-d_6, 25 °C) of **11**.

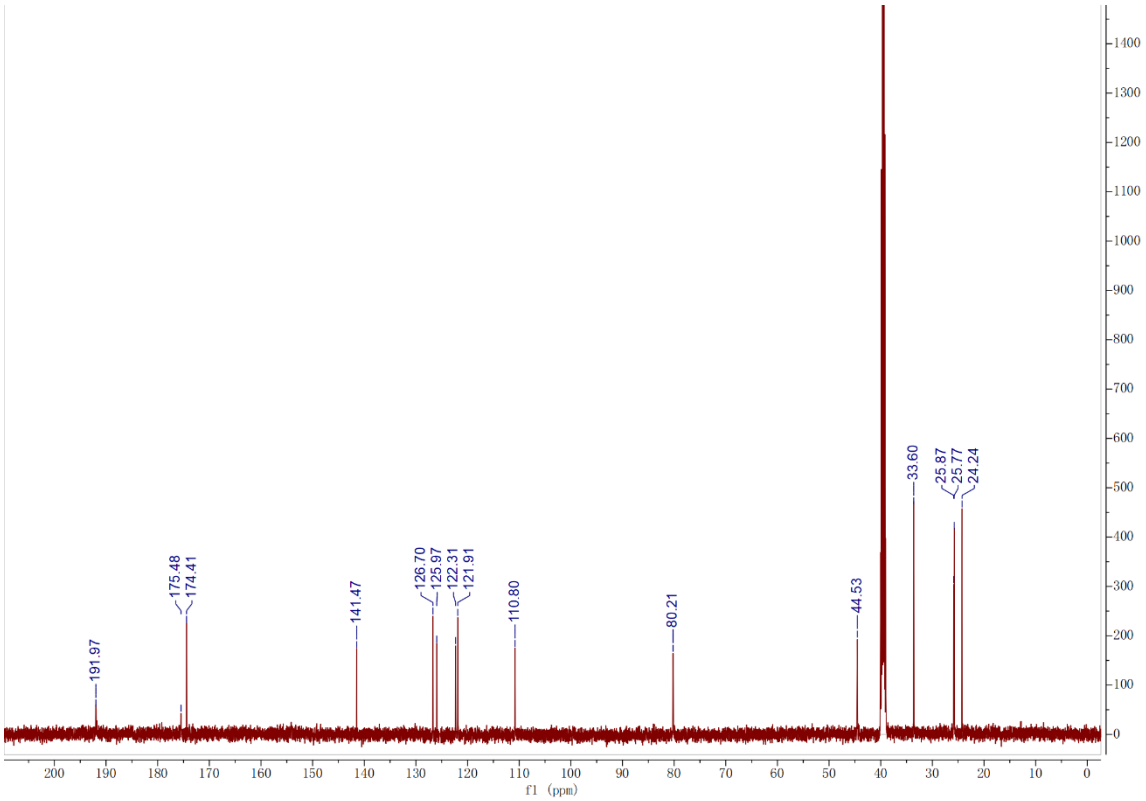
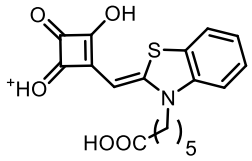


Figure S9: ^{13}C NMR (126 MHz, DMSO-d_6, 25 °C) of **11**



Chemical Formula: $C_{18}H_{18}NO_5S^+$
Exact Mass: 360.0900
Molecular Weight: 360.4035
m/z: 360.0900 (100.0%), 361.0934 (19.5%), 362.0858 (4.5%), 362.0967 (1.8%), 362.0943 (1.0%)
Elemental Analysis: C, 59.99; H, 5.03; N, 3.89; O, 22.20; S, 8.90

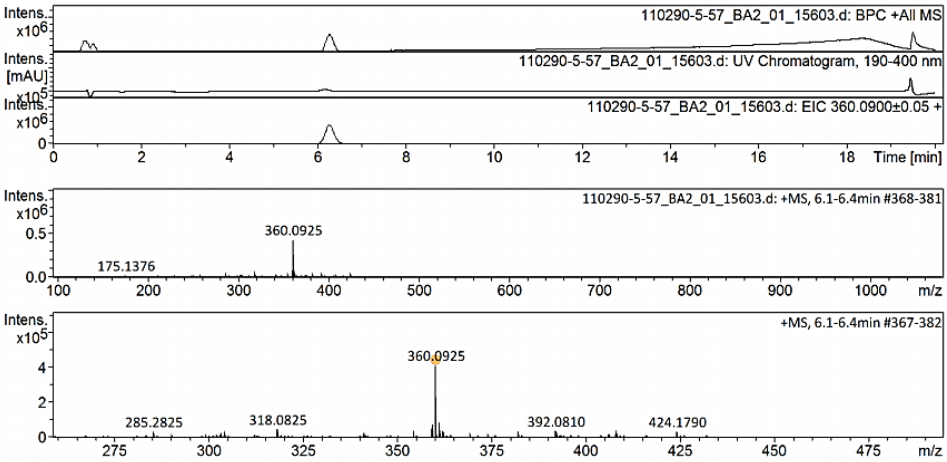


Figure S10: HRMS (LC-MS/MS) of **11**.

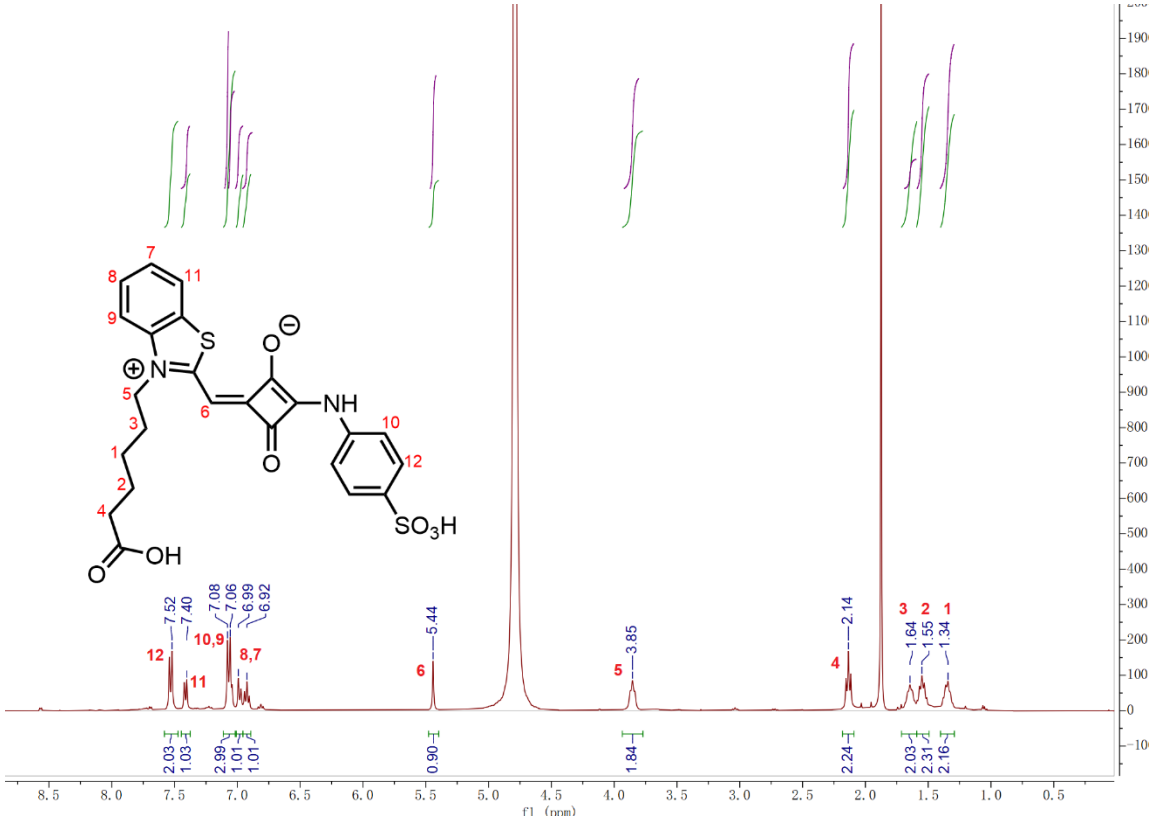


Figure S11: ^{1}H NMR (400 MHz, D_2O, 25 °C) of **AS** (potassium salt).

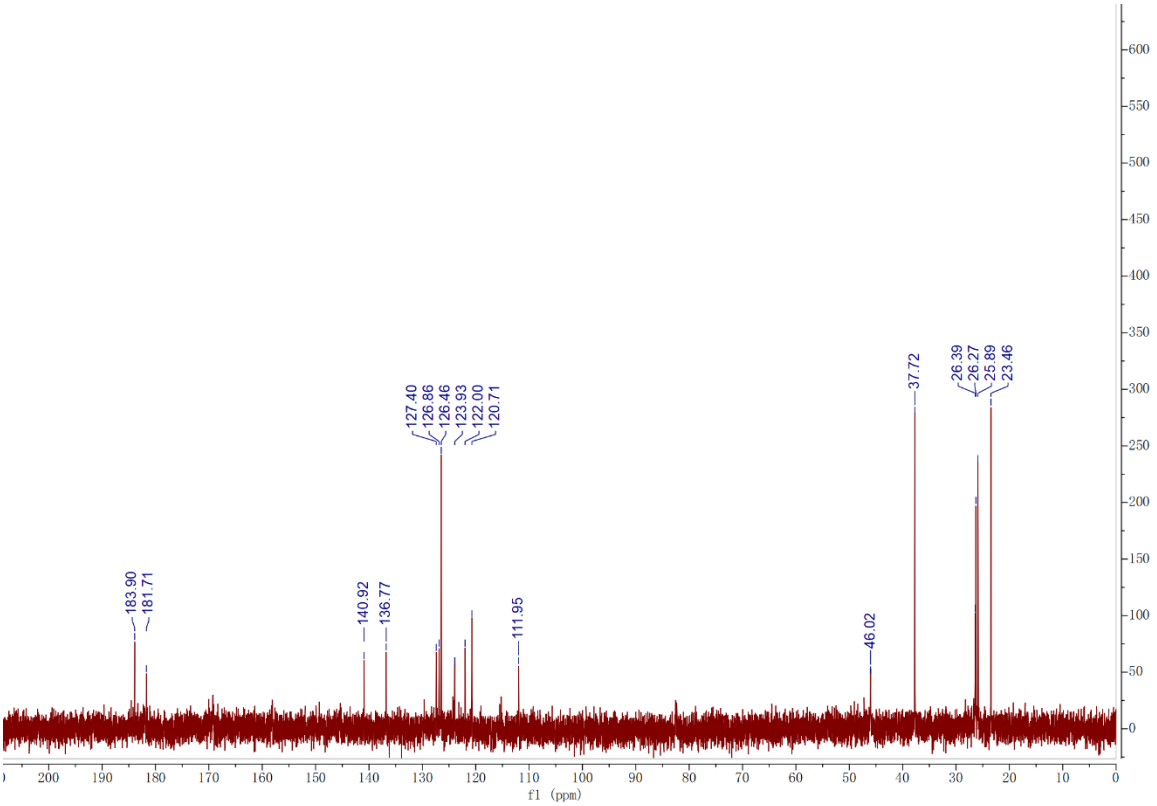
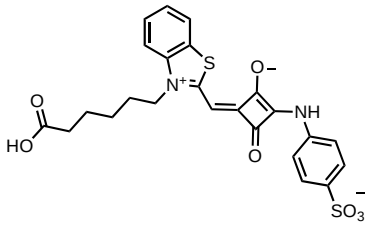
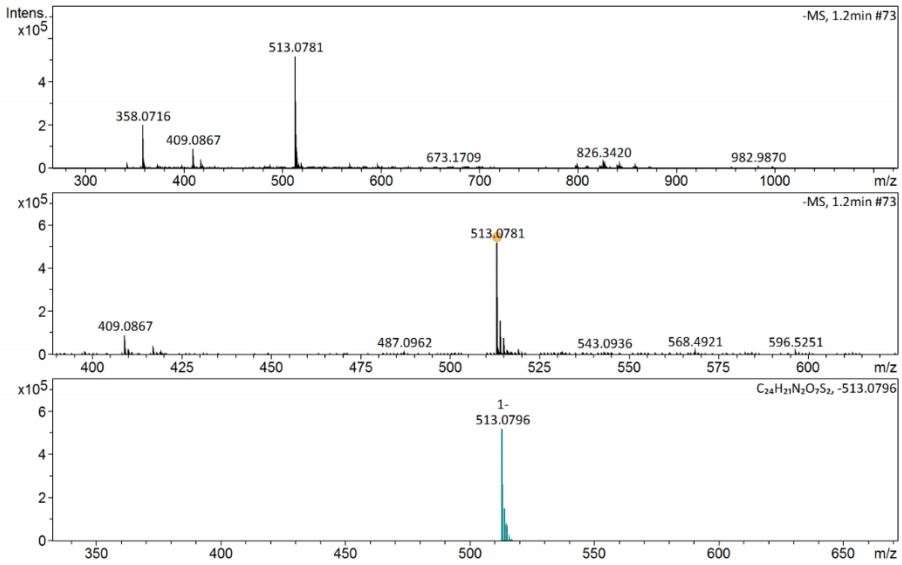
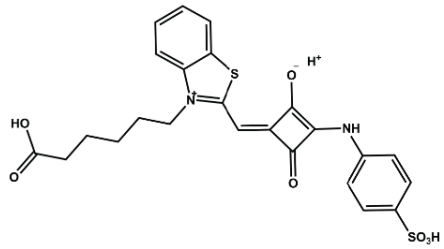


Figure S12: ^{13}C NMR (126 MHz, D_2O, 25 °C) of **AS** (potassium salt.



Chemical Formula: $C_{24}H_{21}N_2O_7S_2^-$
Exact Mass: 513.0796
m/z: 513.0796 (100.0%), 514.0829 (26.0%), 515.0754 (4.5%), 515.0754 (4.5%), 515.0863 (3.2%), 515.0838 (1.4%), 516.0787 (1.2%), 516.0787 (1.2%)





Chemical Formula: $C_{24}H_{23}N_2O_7S_2^+$
Exact Mass: 515.0941
Molecular Weight: 515.5781
m/z: 515.0942 (100.0%), 516.0975 (26.0%), 517.0900 (9.0%), 517.1009 (3.2%), 518.0933 (2.3%), 516.0936 (1.6%), 517.0984 (1.4%)
Elemental Analysis: C, 55.91; H, 4.50; N, 5.43; O, 21.72; S, 12.44

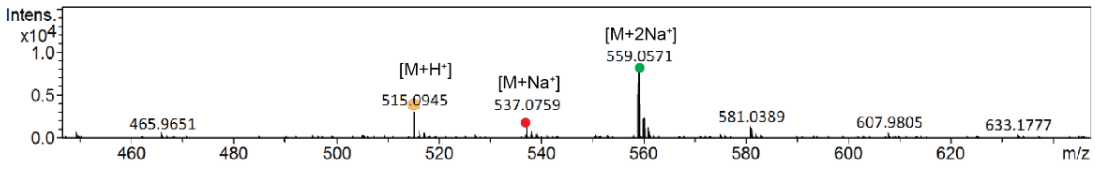


Figure S13: HRMS (ESI) of **AS**. (*top*) negative ion, (*bottom*) postive ion.

3. Photophysical Data and Titration Studies

Fluorescence titration method

All fluorescence measurements were made in triplicate on a Horiba Fluoromax 4 spectrometer with a slit width of 2 nm. Stock solutions of **AS**, generally 0.03-3 μM, were prepared, and stock solutions of tetralactam host (0.6-60 μM) were made by using guest solution as solvent (to keep the concentration of guest constant during the titration). A solution of guest (1 mL) was placed in the cuvette and host solution was titrated into guest solution. Spectral changes were recorded after each aliquot addition. The association constants were calculated using the titration data with specifically written non-linear least squares fitting equations for 1:1 binding within Origin Lab™ 8.6 software.[6] Note that the titration curves presented in Figures 1, S14, and S16, are representative uncorrected data, and that the curve fitting equation includes a small [H]/[G] correction factor (accounts for weighing errors) to match 1:1 binding. The values of K_a are reported as the mean of three measurements with the error equal to the standard deviation.

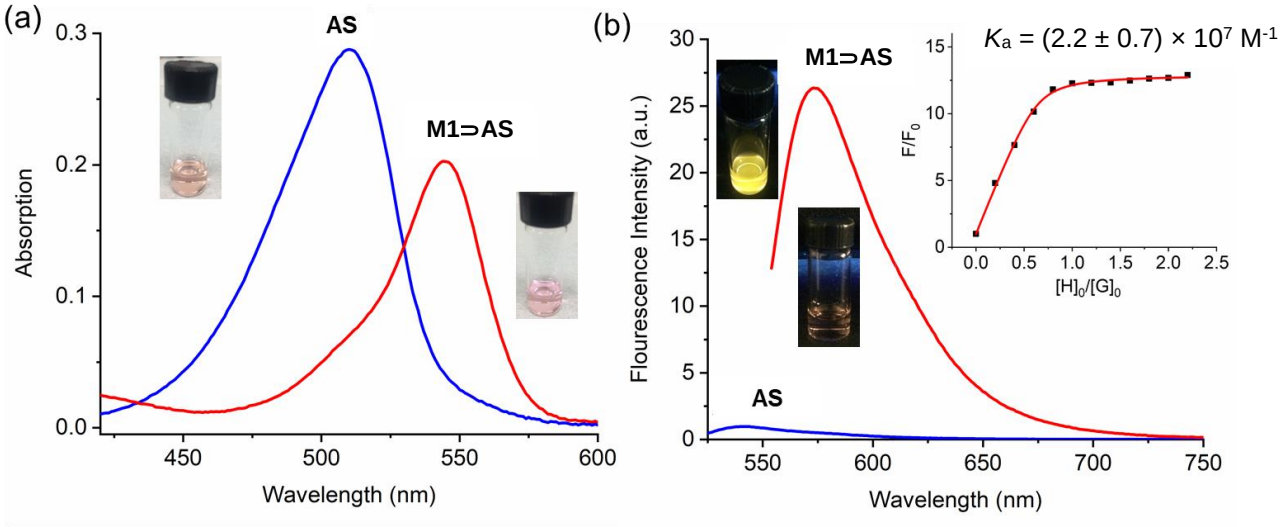


Figure S14: (a) Absorption spectra for 10 μM **AS** (blue) and **M1⊃AS** (red) in water at 25 °C ($\lambda_{\mathbf{AS}}$ = 510 nm; $\lambda_{\mathbf{AM1\supset AS}}$ = 545 nm). (b) Emission spectra for 10 μM **AS** (blue) and **M1⊃AS** (red) in PBS at 25 °C ($\lambda_{ex\ \mathbf{AS}}$ = 510 nm, $\lambda_{em\ \mathbf{AS}}$ = 541 nm; $\lambda_{ex\ \mathbf{AM1\supset AS}}$ = 545 nm, $\lambda_{em\ \mathbf{AM1\supset AS}}$ = 575 nm). Insert: Representative fluorescence titration isotherm with fitting to 1:1 association model.

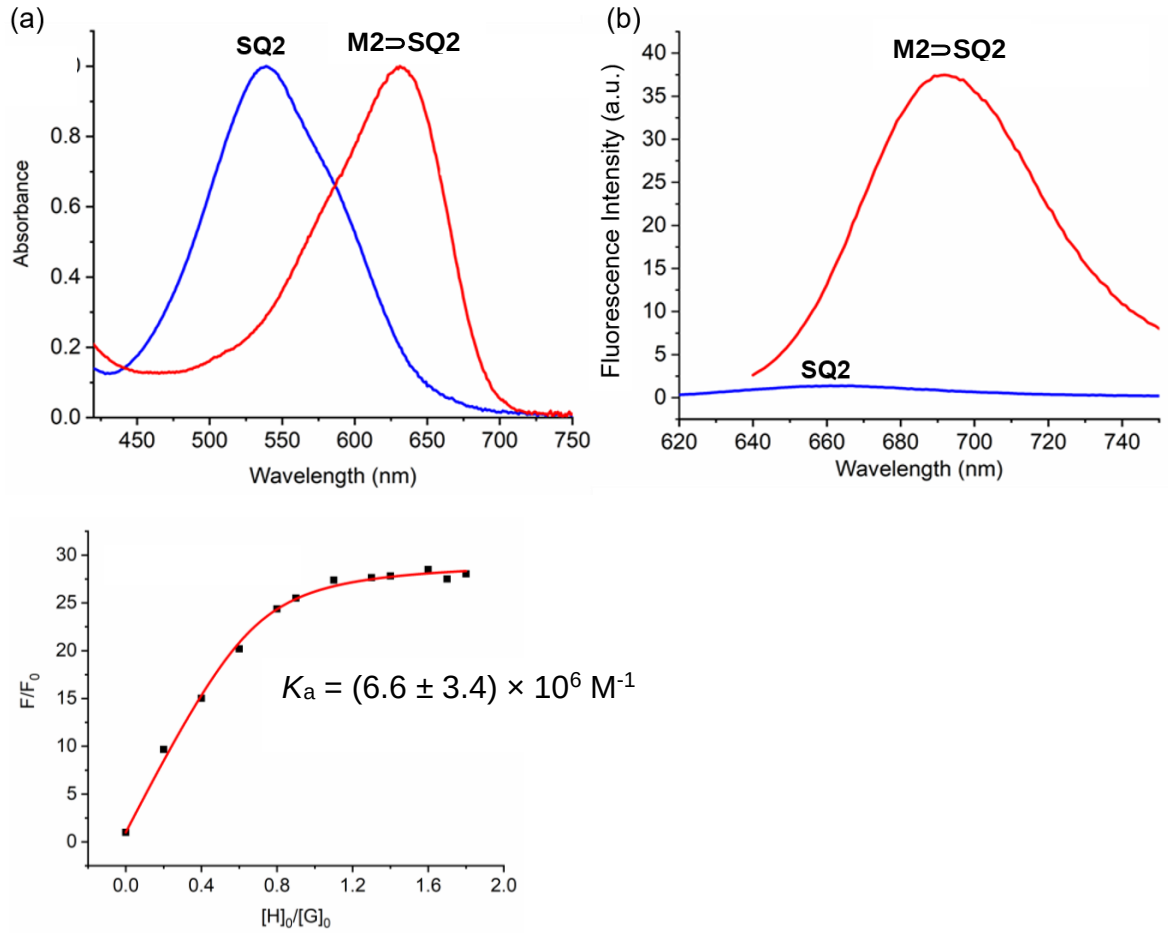


Figure S15: (a) Absorption spectra for 10 μM **SQ2** (blue) and **M2⊃SQ2** (red) in PBS at 25 °C. (b) Emission spectra for 10 μM **SQ2** (blue) and **M2⊃SQ2** (red) in PBS, pH 7.4, at 25 °C. ($\lambda_{ex\ \mathbf{SQ2}}$ = 610 nm, $\lambda_{ex\ \mathbf{AM2\supset SQ2}}$ = 640 nm. (c) Representative fluorescence titration experiment that added increasing equivalents of **M2** to a solution of **SQ2 (**10 μM) in PBS, pH 7.4, at 25 °C; isotherm fitted to a 1:1 binding model.

4. NMR Studies of M1⊃AS Complex

The **M2⊃AS** complex is soluble in water at the low micromolar levels employed for absorption and fluorescence studies, but it is aggregated and not fully soluble at the high micromolar/millimolar levels needed for NMR studies. In contrast, the polyanionic complex **M1⊃AS** is soluble at millimolar concentration in water and NMR spectra exhibit sharp lines that enable structure elucidation. Atom assignments were based on comparisons with spectra of the free components and confirmed with COSY (Figure S16b). Shown in Figure S16a is a comparison of ^{1}H NMR spectra for free **M1**, free **AS**, and the **M1⊃AS** complex. Threading of **M1** produced the following diagnostic complexation-induced changes in NMR chemical shifts:

(a) Downfield migration of **M1** isophthalamide protons A and B which each appear as two equal-intensity singlets, consistent with **M1** encapsulation of unsymmetric **AS** in either a cis or trans conformation as described below in section *6. Molecular Modeling*.
(b) Upfield migration of **M1** anthracene protons D and E and separation into four peaks each; this is due to the anisotropic shielding by the encapsulated unsymmetric **AS**.
(c) Separation of **M1** benzylic protons into four peaks; this is due to the anisotropic shielding by the encapsulated unsymmetric **AS**.
(d) Upfield migration of encapsulated **AS** proton 5 reflecting shielding by the anthracene sidewalls
(e) Downfield migration of **AS** anilide protons 6 and 7 reflecting locations outside the cavity of **M1** and deshielding by the peripheries of the anthracene sidewalls and isophthalamide bridging units of **M1**. This is strong evidence that the **AS** anilide ring is proximal to the isophthalamide bridging units of **M1** (see Figure S20 for homologous molecular model) and supports the guest back-folding concept in article Figure 2c.

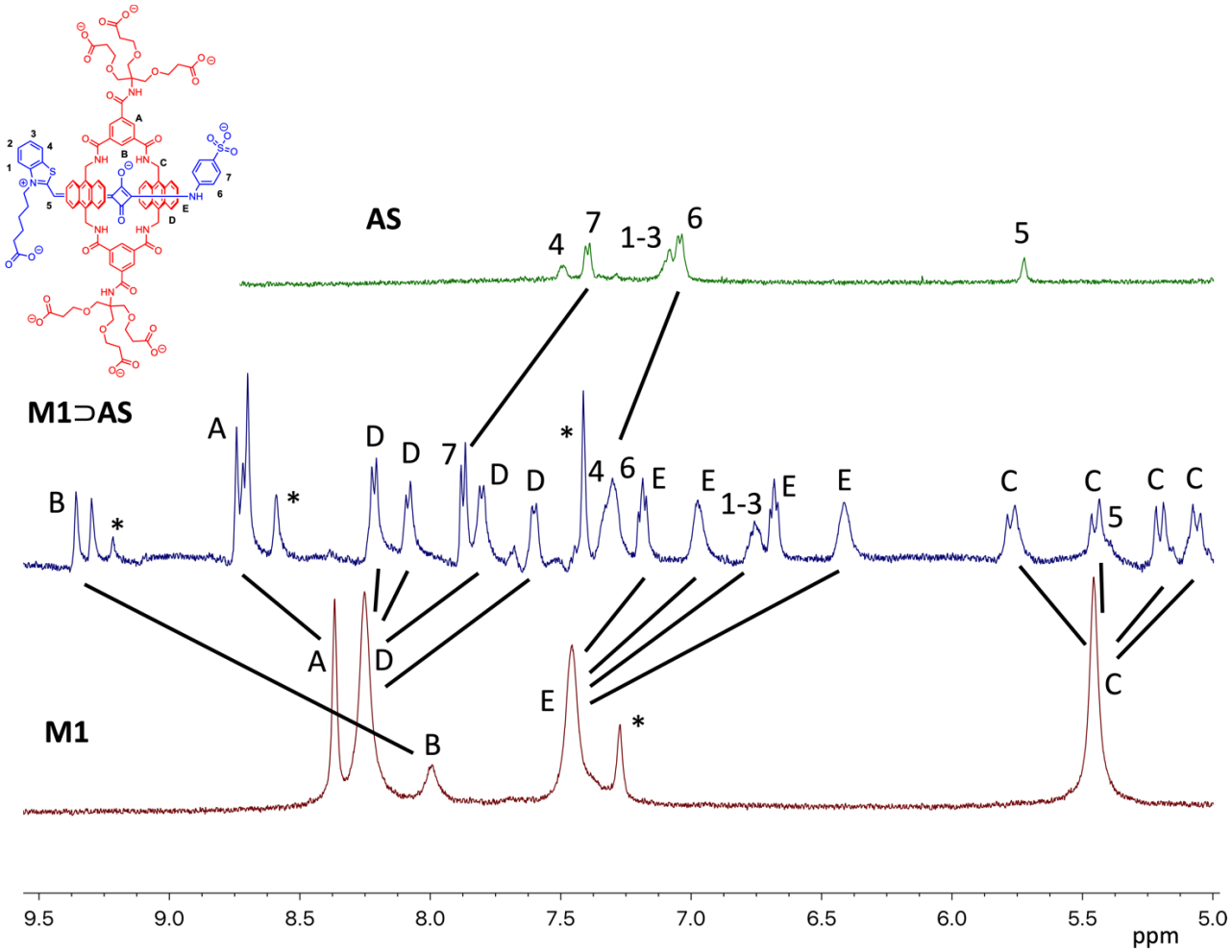


Figure S16a: Partial ^{1}H NMR spectrum (500 MHz, D_2O, 25 °C) of **AS** (2 mM, ammonium salt), **M1⊃AS** (2 mM), and **M1** (2 mM). The singlets labeled with * are unassigned but tentatively attributed to NH residues on **M1**, **AS**, or ammonium counter cation that have not fully exchanged with the solvent.

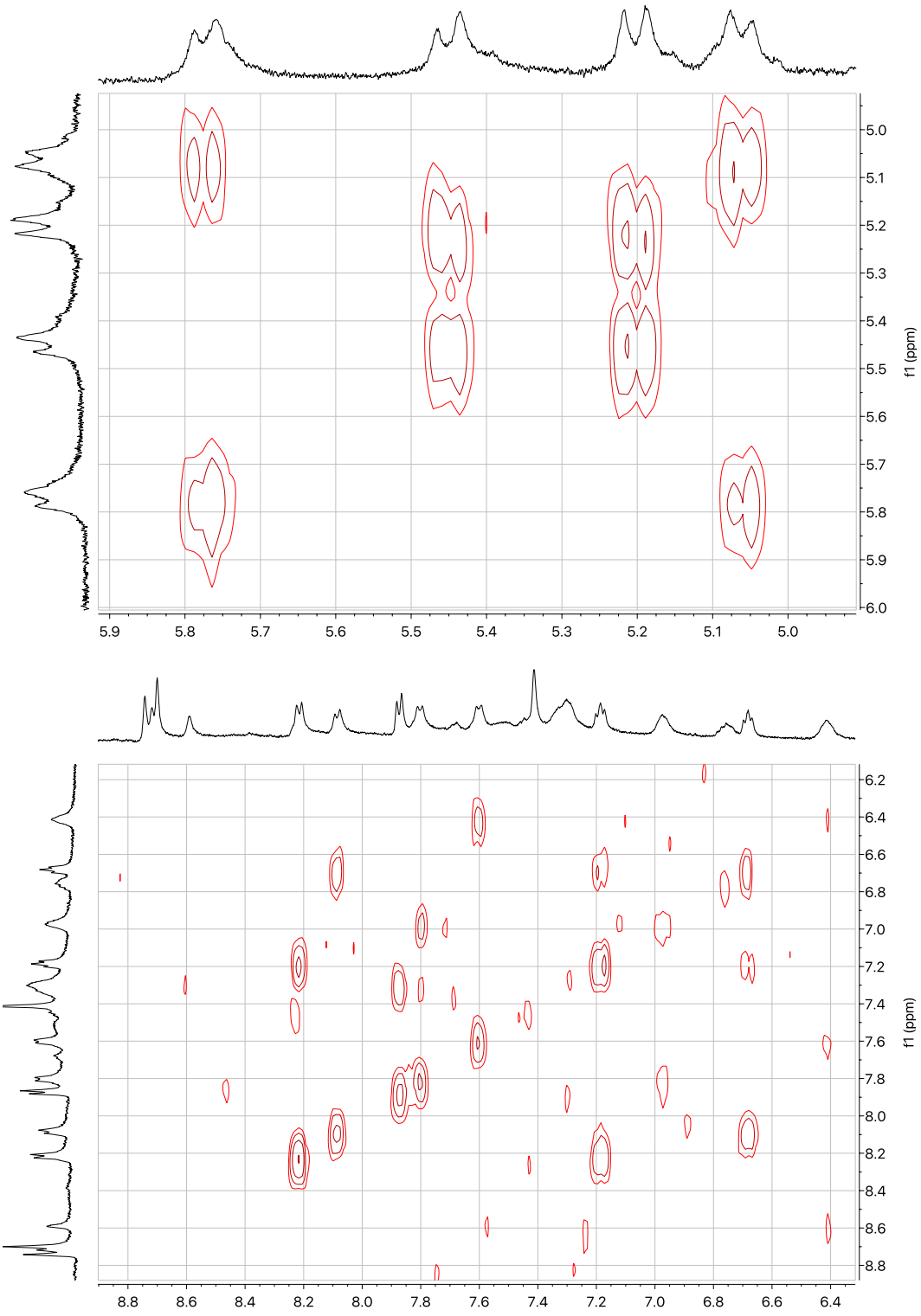


Figure S16b: Partial views of a ^{1}H COSY spectrum (500 MHz) of **M**1⊃**AS** in D_2O showing key cross peaks that support the atom assignments in Figure S16a.

5. Liposome Leakage Studies

Liposome Preparation

A lipid film of 1-palmitoyl-2-oleoyl-*sn*-glycero-3-phosphocholine (POPC) was formed from a chloroform solution under reduced pressure and dried under high vacuum overnight. Standard thin film hydration methods were conducted using HEPES buffer (10 mM HEPES, 3 mM $CaCl_2$, pH 7.4) containing **AS** (500 µM), followed by a brief vortex dispersion and five freeze/thaw cycles. Lipid suspensions were extruded 21 times through a 0.2 µm poly-carbonate filter (Whatman) to produce a suspension of large unilamellar vesicles. Unencapsulated dye was removed by use of a single-use PD-10 desalting column (GE Healthcare) using cold buffer as an eluent. For studies using carboxyfluorescein (**CF**), the same lipid film hydration method was used with a loading concentration of 50 mM **CF** followed by removal of unencapsulated dye. The POPC liposomes containing encapsulated dye (**AS** or **CF**) are stable for several days at 25 °C.

Dye Leakage Experiments

Liposome leakage at 25 °C was induced by mixing phospholipase A_2 (5 U/mL, PLA_2 from honey bee venom) with a dispersion of 500 µM POPC@**AS** liposomes in 10 µM **M2**, 10 mM HEPES buffer, 3 mM $CaCl_2$ (pH 7.4), or 500 µM POPC@**CF** liposomes in 10 mM HEPES buffer, 3 mM CaCl2 (pH 7.4). A final addition of Triton X-100 detergent achieved 100 % dye release. The percentage of dye released *F* (%) was calculated using the following equation:

$$F\ (\%) = 100\ (F_t - F_0)/(F_{total} - F_0)$$

where F_t is the intensity at the measured time point, F_0 is the intensity at t = 0, and F_{total} is the intensity after treatment with Triton X-100.

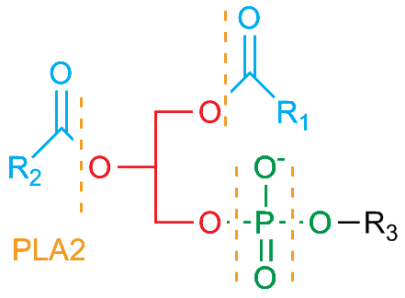


Figure S17: Phospholipase A2 (PLA_2) hydrolyzes the fatty ester group at the *sn*-2 position of glycerophospholipids.

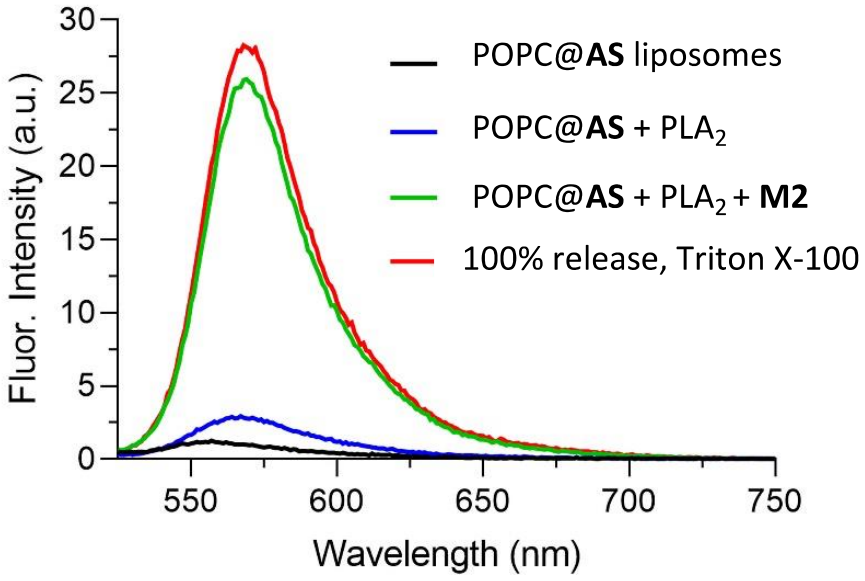


Figure S18: Fluorescence spectra (ex: 510 nm) of POPC liposomes containing 500 µM of **AS** (POPC@**AS** liposomes) before (black) and 30 minutes after addition of PLA_2 (5 U/mL) in the absence (blue) or presence (green) of **M2** (10 µM). Addition of Triton X-100 detergent produced 100% dye release (red).

Due to an assay artifact, the maximum percentage of **AS** release in Figures 3 and S18 only reaches 90%. The **M2⊃AS** complex is weakly solvatochromic[7] and the Triton X-100 detergent added at the end of the assay slightly increases its fluorescence intensity. Thus, the fluorescence intensity for 100% release of **AS** (red line in Figure S18) is artificially high which means that the calculated percentage of dye released *F* (%) is about 10% lower than its actual value. This artifact does not change the kinetic profile for the PLA_2-induced leakage which is the key assay output value. If desired, this artifact can be removed from the graphs by simply including a correction factor in the equation to calculate released dye, or by using a different method to lyse the liposomes at the end of the assay (e.g., instead of detergent, add a lytic peptide such as melittin).

An analogous PLA_2-induced liposome leakage experiment was conducted using POPC liposomes containing 50 mM carboxyfluorescein (POPC@**CF** liposomes) and a very similar leakage rate was observed (Figure S19), strongly suggesting that PLA_2-mediated hydrolysis of POPC and concomitant destruction of the membrane is the slow and rate determining step in each case. The subsequent steps are rapid; that is, rapid escape of the entrapped dye (**AS** or **CF**) and rapid capture of released **AS** by **M2**.

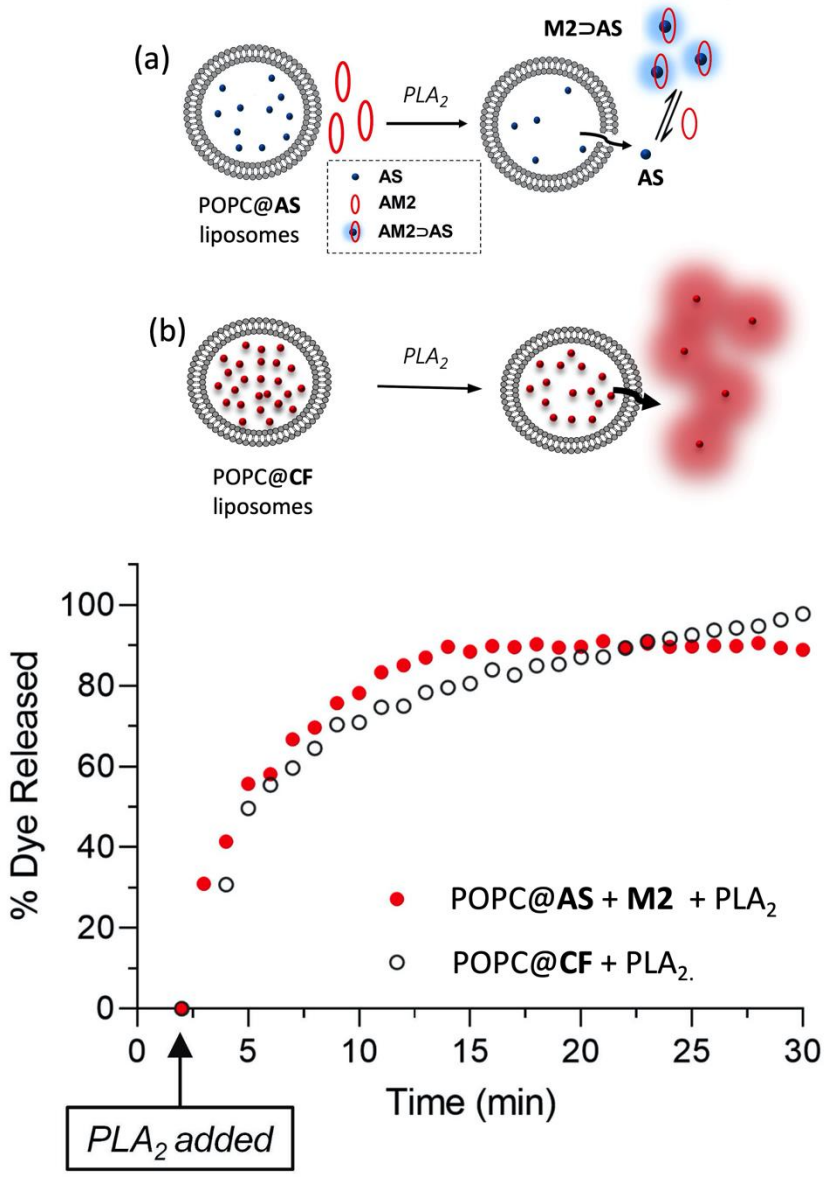


Figure S19: Comparison of dye leakage assays: (a) POPC@**AS** liposomes containing 500 µM **AS** and the external solution containing 10 µM **M2**, or (b) POPC@**CF** liposomes containing 50 mM of carboxyfluorescein (**CF**). In each case, leakage was triggered by addition of PLA_2 (5 U/mL), and the external solution contained 10 mM HEPES buffer and 3 mM $CaCl_2$ (pH 7.4) at 25 °C; a final addition of Triton X-100 detergent achieved 100 % dye release. The leakage profiles are very similar.

6. Molecular Modeling

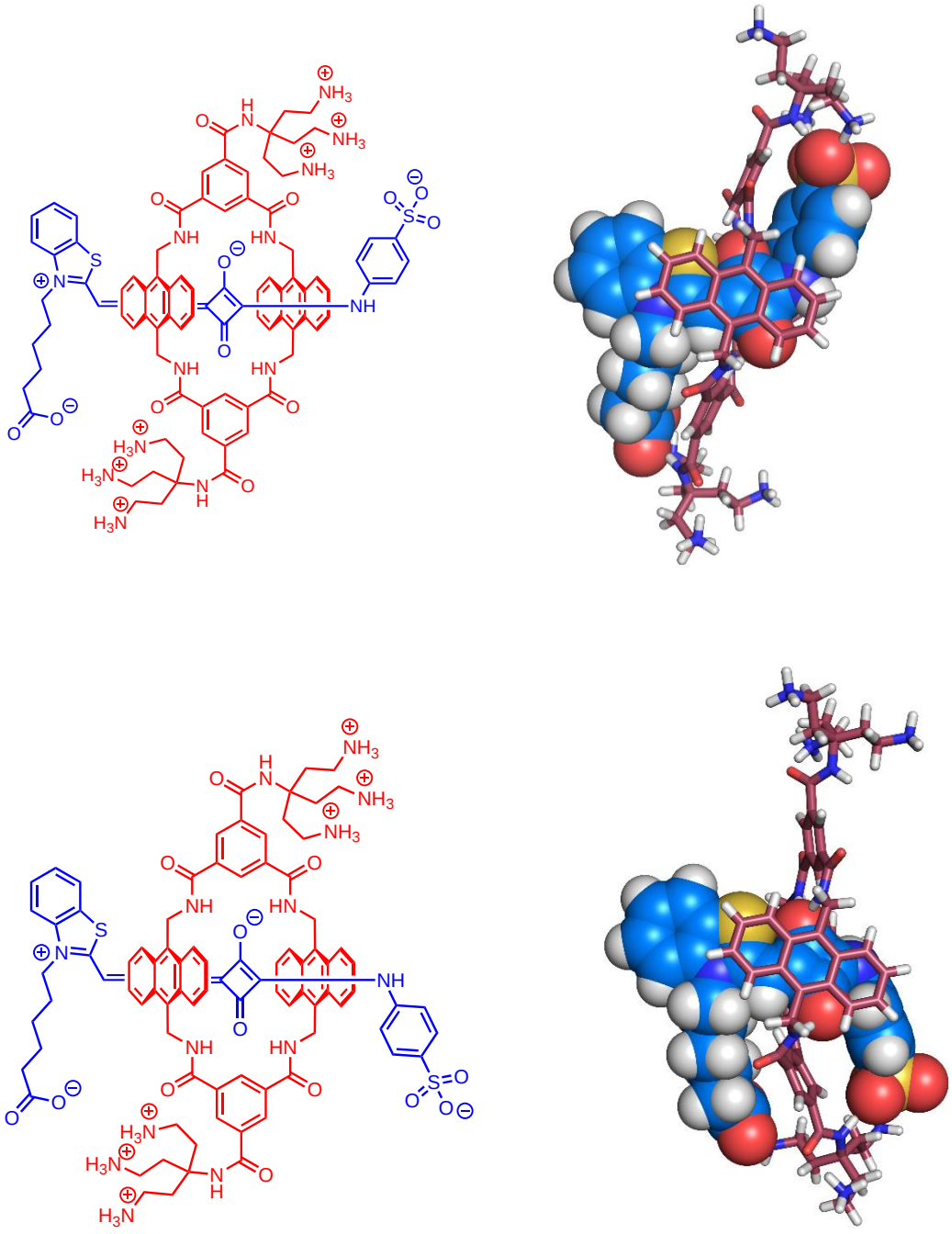


Figure S20: Molecular models of two energy-minimized states for **M2⊃AS**; (top) encapsulated **AS** in *trans*-conformation, (bottom) encapsulated **AS** in *cis*-conformation. Modeling used the semiempirical method within the MOPAC program and was generated at the PM7 level. The dielectric constant of the solvent was set at 78.5 for water at 25 °C.

Cartesian Coordinates of **M2⊃AS,** *trans-c*onformation, at the PM7 Level

Final Energy = -18918.72585 eV

EPS=78.5 PM7 CHARGE=4 EF xyz GNORM=0.100 SHIFT=80

C	-0.791	0.13794	0.25031
C	-2.0188	-0.2879	0.74343
C	-2.1667	-1.5987	1.1976
C	-1.04	-2.4339	1.23113
C	0.16924	-2.0446	0.64585
C	0.28945	-0.7367	0.16907
C	-3.559	-2.0075	1.55287
C	1.37249	-2.9164	0.49276
C	-0.6578	1.53517	-0.1798
O	-4.3671	-1.1327	1.86085
O	2.46044	-2.3623	0.32114
O	-1.2475	2.43323	0.4122
N	-3.9182	-3.3242	1.40263
N	1.23217	-4.2909	0.47445
C	-5.3116	-3.7153	1.46705
C	2.39255	-5.1074	0.14334
C	2.26117	-6.6083	0.41296
C	-5.5338	-5.2182	1.3357
C	2.31919	-7.0733	1.76415
C	2.23898	-8.4659	2.04586
C	2.08802	-9.3976	0.96735
C	2.1785	-7.5456	-0.6695
C	2.09685	-8.9401	-0.3905
C	2.48676	-6.182	2.85635
C	2.60515	-6.6122	4.17538
C	2.53489	-7.9603	4.4526
C	2.34005	-8.8652	3.40825
C	2.18002	-7.1545	-2.0373
C	2.12604	-8.0629	-3.0946
C	2.05328	-9.41	-2.8219
C	2.03081	-9.8345	-1.4952
C	1.90332	-10.888	1.26278
C	-5.8074	-5.7973	0.05286
C	-5.9995	-7.1988	-0.0562
C	-5.9684	-8.0022	1.12645
C	-5.7264	-7.4192	2.41347
C	-5.4741	-6.0301	2.51075
C	-5.9044	-5.0283	-1.1394

C	-0.4155	-4.5576	-3.4122
C	-0.4051	-3.1903	-3.7442
C	-1.3477	-2.3172	-3.1868
C	-2.3152	-2.8161	-2.3228
C	-2.3067	-4.1866	-1.9978
S	-1.2034	-0.5589	-3.53
O	0.17415	-0.2261	-3.1302
O	-2.1757	0.16312	-2.705
O	-1.3856	-0.4079	-4.9613
H	-5.1304	-12.722	7.35908
H	-4.0087	-13.624	6.32912
H	-2.6973	-11.249	6.7428
H	-2.4066	-12.128	5.23326
H	-4.7623	-11.693	4.53674
H	-5.0745	-10.82	6.02646
H	-0.82	-9.7705	5.92771
H	-0.7195	-10.052	4.22135
H	-3.1125	-10.072	3.93727
H	-3.3818	-9.2597	5.46384
H	-5.8597	-3.1524	0.7055
H	-5.7475	-3.3294	2.39522
H	3.26814	-4.7259	0.68619
H	2.64236	-4.8775	-0.8941
H	2.39342	-11.189	2.19074
H	2.4159	-11.508	0.52029
H	-6.6666	-9.8316	0.11004
H	-6.8751	-9.8413	1.80726
H	2.44547	2.96704	-0.7731
H	1.14199	3.34892	0.30489
H	0.35004	2.786	-3.9322
H	1.51642	3.99799	-3.4607
H	-0.3882	4.99361	-2.3515
H	-1.042	4.39312	-0.861
H	1.08117	5.71743	-0.5374
H	2.52245	5.34029	-1.5354
H	2.56637	1.45582	-2.5023
H	3.17427	2.51393	-3.7986
H	-1.7729	3.24036	-3.6377

C	-6.1755	-5.5867	-2.3884
C	-6.3316	-6.9502	-2.4976
C	-6.2317	-7.7385	-1.3533
C	-5.1883	-5.496	3.79624
C	-5.2101	-6.2616	4.95937
C	-5.5092	-7.6031	4.87292
C	-5.7407	-8.1729	3.62102
C	-6.1799	-9.5018	1.02943
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N	-4.9336	-10.23	1.18208
C	0.0176	-12.215	2.18519
C	-4.9264	-11.595	1.09835
O	0.68793	-12.638	3.12216
O	-5.872	-12.272	0.6937
C	-1.4006	-12.688	2.08739
C	-2.4183	-11.874	1.55921
C	-3.7418	-12.31	1.63652
C	-1.7187	-13.969	2.62492
C	-3.0467	-14.402	2.69189
C	-4.04	-13.538	2.23654
C	-3.4705	-15.822	2.95262
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C	2.29039	2.0009	-3.4082
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N	2.80658	5.28036	0.53525
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C	-7.1655	-16.755	3.41782
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C	-4.8829	-19.571	2.69996
C	-6.7184	-17.415	0.39693
C	-7.8087	-15.393	3.10136
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N	-6.6305	-16.675	-0.9016
N	-8.3016	-14.763	4.3277
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H	-8.0744	-13.732	4.36104
H	-7.6713	-15.016	5.12158
H	-3.0829	-18.551	2.21836
H	-5.6895	-16.69	-1.3247
H	-9.2705	-14.883	4.6273
H	-3.7776	2.59218	-2.1862
H	2.6966	0.35432	-4.6684
H	3.66901	4.71674	0.53055
H	-5.0949	-15.391	4.19261
H	-5.084	-13.826	2.29396
H	-0.9172	-14.617	2.97962
H	-2.1911	-10.923	1.09277
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H	2.01736	-10.135	-3.6309
H	2.1458	-7.7116	-4.1229
H	2.21875	-6.1094	-2.3266
H	2.31985	-9.9131	3.69477
H	2.66829	-8.3155	5.47099

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C	-1.2529	-8.2728	-0.2725
C	-1.3759	-6.901	-0.8478
O	-1.1403	-9.4239	-0.6701
O	-1.9431	-5.2813	0.88182
C	-1.2229	-8.1626	2.30645
C	-1.3181	-7.4994	3.5748
N	-1.3214	-8.0896	4.77277
S	-1.4174	-5.8026	3.80568
C	-1.4562	-7.2354	5.86626
C	-1.44	-5.9021	5.49903
C	-1.6083	-7.5691	7.22936
C	-1.6866	-6.5415	8.17563
C	-1.5773	-5.2108	7.78726
C	-1.4593	-4.8658	6.44063
C	-1.317	-9.5383	4.97902
C	-2.7602	-10.015	4.97304
C	-2.9986	-11.329	5.69179
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C	-4.8536	-12.926	6.31912
C	-6.0065	-13.571	5.61071
O	-6.9196	-12.876	5.0845
O	-5.9679	-14.833	5.47335
N	-1.2345	-6.4349	-2.0798
C	-1.3563	-5.0828	-2.5157

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H	-1.8288	-6.7835	9.22835
H	-1.6012	-4.424	8.5403
H	-1.3975	-3.8254	6.13154
H	-5.5722	-8.209	5.77248
H	-5.015	-5.7933	5.92028
H	-4.9423	-4.4435	3.92045
H	-5.9674	-9.2364	3.61799
H	-6.346	-8.8046	-1.5183
H	-6.5279	-7.4051	-3.4645
H	-6.2476	-4.9524	-3.2676
H	-5.757	-3.9523	-1.1292
H	-4.123	-9.6934	1.45801
H	-3.2231	-4.0412	1.13463
H	0.29932	-4.7197	0.49247
H	-0.0617	-10.982	0.47758
H	-0.8815	-7.0462	-2.8098
H	0.35004	-5.2041	-3.8305
H	0.35102	-2.8117	-4.425
H	-3.06	-2.1666	-1.8726
H	-3.0579	-4.5576	-1.3053
H	-0.9415	-9.205	2.32738

Cartesian Coordinates of **M2⊃AS,** *cis*-conformation, at the PM7 Level

Final Energy = -18918.06159 eV

EPS=78.5 PM7 CHARGE=4 EF xyz GNORM=0.100 SHIFT=80

C	-0.5774	0.21216	0.09323
C	-1.8763	-0.2781	0.1507
C	-2.1291	-1.6456	-0.0526
C	-1.059	-2.5111	-0.3146
C	0.25422	-2.0377	-0.2707
C	0.48799	-0.6664	-0.0754
C	-3.5602	-2.0569	0.0055
C	1.46475	-2.8816	-0.4505
C	-0.3573	1.67396	0.15562
O	-4.4082	-1.1747	-0.1302
O	2.48705	-2.3094	-0.8349
O	-1.0056	2.3901	0.90946

C	-1.508	-9.7867	-2.9338
C	-1.8481	-11.039	-3.4588
C	-3.1698	-11.305	-3.8253
C	-4.1328	-10.305	-3.7303
C	-3.7693	-9.0525	-3.213
S	-3.6221	-12.992	-4.2477
O	-2.7912	-13.805	-3.3554
O	-5.055	-13.137	-3.9456
O	-3.3169	-13.129	-5.66
H	-3.0204	-14.315	5.38394
H	-1.981	-14.004	3.99545
H	-1.9687	-11.817	6.06177

N	-3.8674	-3.3656	0.27245
N	1.42297	-4.2156	-0.1095
C	-5.2364	-3.7506	0.5498
C	2.6649	-4.9667	-0.1168
C	2.57176	-6.4084	0.36462
C	-5.4356	-5.2572	0.58624
C	2.64108	-6.6953	1.76497
C	2.69381	-8.0443	2.21119
C	2.65195	-9.1006	1.24642
C	2.53138	-7.464	-0.5956
C	2.63493	-8.8084	-0.159
C	2.66079	-5.6697	2.74716
C	2.76055	-5.9297	4.11338
C	2.83236	-7.2359	4.54808
C	2.79327	-8.2702	3.61306
C	2.38348	-7.2293	-1.9895
C	2.4155	-8.2507	-2.9369
C	2.59282	-9.552	-2.5197
C	2.69237	-9.8216	-1.1562
C	2.49521	-10.557	1.69072
C	-5.8928	-5.9327	-0.5881
C	-6.1178	-7.3302	-0.5426
C	-5.7507	-8.0607	0.63412
C	-5.3555	-7.379	1.82643
C	-5.2	-5.9724	1.80483
C	-6.1585	-5.2563	-1.8117
C	-6.7304	-5.882	-2.9172
C	-7.0468	-7.2195	-2.8398
C	-6.7287	-7.9291	-1.6808
C	-4.8279	-5.3335	3.01908
C	-4.6851	-6.0191	4.22461
C	-4.8492	-7.3869	4.24639
C	-5.1496	-8.0548	3.06088
C	-5.75	-9.5811	0.62155
N	1.16498	-11.05	1.36957
N	-4.4092	-10.15	0.60893
C	0.51054	-12.038	2.05477
C	-4.2728	-11.502	0.39699
O	0.87857	-12.511	3.11854
O	-5.2405	-12.227	0.15638
C	-0.7119	-12.532	1.37111
C	-1.846	-11.701	1.23318
C	-2.9236	-12.135	0.46979
C	-0.6886	-13.832	0.84673
C	-1.7564	-14.249	0.06278

H	-1.2283	-11.896	4.47148
H	-3.6159	-12.003	3.48653
H	-4.1938	-12.227	5.12737
H	-0.6491	-9.4981	6.10286
H	-0.1787	-9.7592	4.4622
H	-2.6588	-9.8486	3.81691
H	-3.0696	-9.7045	5.52019
H	-5.9039	-3.2591	-0.1643
H	-5.5338	-3.2849	1.49545
H	3.39887	-4.4222	0.49185
H	3.10072	-4.8946	-1.1188
H	2.68024	-10.728	2.75022
H	3.22847	-11.192	1.18138
H	-6.2883	-10.005	-0.2256
H	-6.2902	-9.9761	1.49006
H	2.9203	3.06472	0.08155
H	1.64404	3.37297	1.2266
H	0.77443	3.71222	-3.0161
H	1.8852	4.90657	-2.3638
H	0.174	5.61134	-0.9218
H	-0.3381	4.729	0.48598
H	1.84248	5.8643	0.80851
H	3.22599	5.5226	-0.2712
H	2.57209	1.91586	-2.6473
H	3.68409	3.23033	-2.175
H	-1.4882	3.49847	-1.9785
H	-1.8584	5.23488	-1.8508
H	3.05055	4.82071	2.61643
H	3.91212	6.05628	1.96579
H	3.35327	4.19572	-4.3972
H	2.32345	2.96268	-4.8093
H	-2.2689	3.34391	0.38052
H	-3.4471	3.70163	-0.7269
H	-3.8987	-17.53	0.28917
H	-5.3364	-17.888	-0.6427
H	-4.0694	-15.821	-3.6577
H	-4.8457	-14.969	-2.3109
H	-2.7254	-17.768	-3.3384
H	-4.1841	-18.594	-2.8275
H	-2.3767	-19.986	-2.2378
H	-2.9595	-19.341	-0.6955
H	-6.8244	-16.345	-2.521
H	-6.061	-17.294	-3.8389
H	-6.3447	-15.789	-0.1786
H	-4.8052	-15.01	0.20608

C	-2.8202	-13.367	-0.169
C	-1.9092	-15.658	-0.4043
O	-1.4139	-16.622	0.16551
N	0.52005	2.18486	-0.7889
C	0.99991	3.58878	-0.8477
C	2.08255	3.74362	0.28879
C	1.58553	3.85301	-2.2886
C	-0.174	4.62205	-0.5945
C	2.63216	5.14884	0.56726
C	2.77778	2.98498	-2.7353
C	-1.5224	4.35274	-1.2977
N	3.53262	5.11808	1.75248
N	3.09116	3.22446	-4.1703
N	-2.5842	4.06986	-0.299
N	-2.7046	-15.809	-1.5114
C	-3.8299	-16.76	-1.7484
C	-4.6046	-17.097	-0.43
C	-4.697	-15.957	-2.766
C	-3.3071	-18.051	-2.45
C	-2.4923	-19.072	-1.6461
C	-6.059	-16.344	-3.3004
C	-5.3519	-15.941	0.25308
N	-1.1275	-18.613	-1.3588
N	-6.4367	-15.278	-4.2806
N	-5.5358	-16.212	1.6761
C	-1.4821	-6.7328	0.27602
C	-0.9497	-7.752	1.12774
C	-0.841	-8.5832	-0.056
C	-1.6473	-7.5852	-0.7791
O	-0.4206	-9.7127	-0.25
O	-1.8472	-5.4983	0.52827
C	-0.6859	-8.0572	2.40185
C	-0.9141	-7.3376	3.60152
N	-1.0791	-7.885	4.80931
S	-0.9431	-5.6265	3.722
C	-1.3421	-6.9806	5.83211
C	-1.2917	-5.6607	5.39844
C	-1.6357	-7.2479	7.18631
C	-1.8624	-6.1779	8.06106
C	-1.7988	-4.8648	7.60819
C	-1.512	-4.5828	6.27093
C	-0.9834	-9.3345	5.07214
C	-2.3031	-10.07	4.82825
C	-2.1308	-11.582	5.00294
C	-3.3272	-12.38	4.47281

H	-0.6521	-18.182	-2.1601
H	-0.5234	-19.352	-0.9822
H	-6.1055	-14.317	-3.9771
H	-7.4377	-15.187	-4.4775
H	-5.7601	-15.319	2.19736
H	-4.6052	-16.36	2.15524
H	-1.1426	-17.877	-0.6179
H	-5.9386	-15.361	-5.1791
H	-6.1818	-16.924	2.00931
H	-2.8618	4.8863	0.26173
H	3.89346	2.64535	-4.4752
H	4.35322	4.50242	1.64808
H	-2.6402	-15.01	-2.1782
H	-3.6473	-13.654	-0.8085
H	0.15044	-14.493	1.04648
H	-1.8846	-10.745	1.7341
H	0.91976	1.47905	-1.4038
H	-2.7106	0.39683	0.33136
H	1.51306	-0.3051	-0.0447
H	-1.2455	-3.5417	-0.5852
H	2.80831	-10.869	-0.8884
H	2.62862	-10.362	-3.2435
H	2.29784	-8.0243	-3.9933
H	2.21112	-6.2288	-2.3779
H	2.88639	-9.2725	4.02166
H	2.94349	-7.4586	5.60644
H	2.79376	-5.1096	4.82551
H	2.59044	-4.6231	2.46086
H	-1.706	-8.2573	7.58197
H	-2.0942	-6.3747	9.1081
H	-1.9813	-4.0466	8.30465
H	-1.4738	-3.5562	5.91681
H	-4.7751	-7.9369	5.17914
H	-4.4624	-5.4726	5.13601
H	-4.658	-4.2614	3.0558
H	-5.2783	-9.1325	3.13531
H	-6.9901	-8.9827	-1.6992
H	-7.5152	-7.725	-3.6801
H	-6.9404	-5.3172	-3.8212
H	-5.9333	-4.2003	-1.9321
H	-3.6144	-9.5254	0.61644
H	-3.146	-4.0955	0.38856
H	0.55421	-4.6869	0.16341
H	0.73968	-10.714	0.50049
H	-2.8574	-6.8575	-2.1952

C	-2.9992	-13.871	4.3818
C	-3.9175	-14.672	3.49016
O	-5.0854	-14.256	3.24208
O	-3.4694	-15.747	2.98178
N	-2.247	-7.6356	-1.9542
C	-2.4718	-8.7905	-2.748

H	-0.4771	-9.6101	-2.6427
H	-1.0904	-11.814	-3.5428
H	-5.1624	-10.501	-4.0151
H	-4.5278	-8.2868	-3.1127
H	-0.2667	-9.0487	2.51342

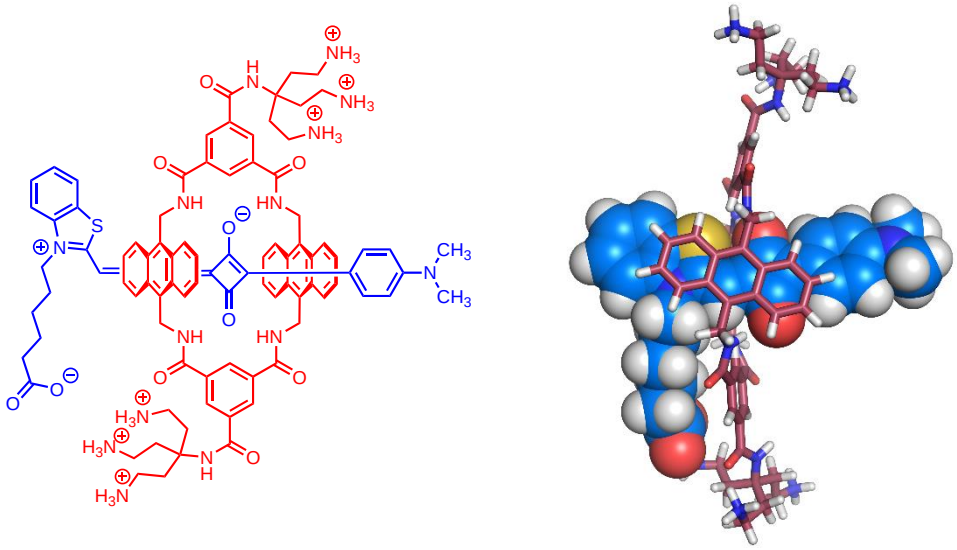

Figure S21: Molecular model of energy-minimized **M2⊃SQ2.** The model was generated by semiempirical method within the MOPAC program at the PM7 level. The dielectric constant of the solvent was set at 78.5 for water at 25 °C.

Cartesian Coordinates of **M2⊃SQ2** at the PM7 Level

Final Energy = - 18185.01645 eV

EPS=78.5 PM7 CHARGE=4 EF xyz GNORM=0.100 SHIFT=80

C	-0.7863	0.8656	0.4506
C	-2.0387	0.3380	0.7350
C	-2.1815	-1.0447	0.9075
C	-1.0472	-1.8651	0.8524
C	0.2016	-1.3499	0.5152
C	0.3269	0.0313	0.3468
C	-3.5655	-1.5599	1.1066
C	1.4384	-2.1539	0.3036
C	-0.6240	2.3163	0.2377
O	-4.4235	-0.7672	1.4922

H	-1.0662	-11.6904	3.0082
H	-3.5225	-11.9822	2.4348
H	-3.8883	-12.0267	4.1523
H	-0.2625	-9.3174	4.3934
H	-0.2331	-9.4183	2.6638
H	-2.7016	-9.7255	2.5942
H	-2.8024	-9.5627	4.3417
H	-5.7632	-2.8842	0.0256
H	-5.6778	-3.0270	1.7235
H	3.3697	-3.8792	0.5422

O	2.5017	-1.5321	0.2152
O	-1.2481	3.1477	0.8854
N	-3.8319	-2.8609	0.7641
N	1.3535	-3.5171	0.1487
C	-5.1821	-3.3780	0.8122
C	2.5648	-4.2764	-0.0912
C	2.4642	-5.7772	0.1386
C	-5.2437	-4.8913	0.6836
C	2.4589	-6.2696	1.4823
C	2.4886	-7.6675	1.7239
C	2.4938	-8.5659	0.6093
C	2.4996	-6.6779	-0.9723
C	2.5629	-8.0721	-0.7324
C	2.4269	-5.3995	2.6052
C	2.4453	-5.8557	3.9205
C	2.5031	-7.2107	4.1594
C	2.5230	-8.0957	3.0809
C	2.4715	-6.2499	-2.3277
C	2.5820	-7.1283	-3.4059
C	2.7092	-8.4789	-3.1677
C	2.6887	-8.9378	-1.8542
C	2.3472	-10.0681	0.8168
C	-5.3254	-5.4861	-0.6157
C	-5.4235	-6.8921	-0.7301
C	-5.4394	-7.6927	0.4541
C	-5.2954	-7.1061	1.7501
C	-5.1997	-5.6979	1.8640
C	-5.3043	-4.7286	-1.8187
C	-5.3986	-5.3075	-3.0839
C	-5.4960	-6.6774	-3.1935
C	-5.4973	-7.4520	-2.0361
C	-5.0557	-5.1469	3.1663
C	-5.0185	-5.9267	4.3204
C	-5.1075	-7.2970	4.2101
C	-5.2378	-7.8725	2.9471
C	-5.5944	-9.1932	0.3121
N	1.0643	-10.5510	0.3217
N	-4.3190	-9.8496	0.1053
C	0.6698	-11.8460	0.5471
C	-4.2443	-11.0234	-0.5956
O	1.3675	-12.6687	1.1304
O	-5.1877	-11.4936	-1.2326
C	-0.6669	-12.2614	0.0349
C	-1.7335	-11.3550	-0.1258
C	-2.9917	-11.8262	-0.5025
C	-0.8610	-13.6357	-0.1987

H	2.9052	-4.0197	-1.0972
H	2.4274	-10.3843	1.8570
H	3.1534	-10.6088	0.3070
H	-6.3024	-9.4462	-0.4845
H	-6.0565	-9.6491	1.1927
H	2.6833	3.3252	0.1482
H	1.4071	3.8726	1.1959
H	0.7827	3.9320	-3.1014
H	1.9889	5.0565	-2.4944
H	0.2806	6.0700	-1.2305
H	-0.3453	5.4018	0.2492
H	1.9254	6.2794	0.6125
H	3.3104	5.6920	-0.3543
H	2.3584	1.9960	-2.4020
H	3.5831	3.2458	-2.0569
H	-1.5607	4.0693	-2.1458
H	-1.8016	5.8320	-2.1109
H	2.8923	5.2218	2.5563
H	3.9401	6.2956	1.8886
H	3.4209	3.9296	-4.3985
H	2.2852	2.7531	-4.6878
H	-2.3671	4.1118	0.2217
H	-3.5059	4.4702	-0.9224
H	-4.0011	-17.5720	0.3225
H	-5.4313	-18.2714	-0.4081
H	-4.8922	-16.4415	-3.7760
H	-5.7976	-15.6822	-2.4925
H	-2.7602	-17.9003	-3.1610
H	-4.1360	-18.9266	-2.8414
H	-2.4246	-20.1407	-1.9533
H	-3.1303	-19.4331	-0.4989
H	-7.0964	-17.8133	-2.1305
H	-6.2139	-18.5503	-3.5007
H	-6.7020	-16.2378	-0.1304
H	-5.2437	-15.2519	0.0774
H	-0.6786	-18.4590	-1.8796
H	-0.7479	-19.3299	-0.4720
H	-7.8927	-16.0981	-3.6608
H	-8.3033	-17.6057	-4.1833
H	-5.9021	-15.4361	2.1374
H	-4.7950	-16.5183	2.1095
H	-1.3451	-17.8051	-0.5256
H	-7.0778	-16.7921	-4.9222
H	-6.3981	-17.0430	2.1636
H	-2.8514	5.6758	-0.0031
H	3.8035	2.3372	-4.2423

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C	-3.1572	-13.1911	-0.7508
C	-2.3650	-15.5438	-0.8388
O	-1.7182	-16.4220	-0.2874
N	0.2448	2.6701	-0.7812
C	0.8837	3.9957	-0.9219
C	1.9266	4.1136	0.2574
C	1.5660	4.0553	-2.3412
C	-0.1754	5.1639	-0.8093
C	2.6307	5.4575	0.4692
C	2.6739	3.0185	-2.6204
C	-1.5365	4.9576	-1.5095
N	3.4554	5.4006	1.7084
N	3.0551	3.0284	-4.0576
N	-2.6250	4.8105	-0.5102
N	-3.3918	-15.8259	-1.7169
C	-4.2361	-17.0466	-1.7768
C	-4.8290	-17.3555	-0.3626
C	-5.3711	-16.6467	-2.8068
C	-3.4141	-18.2595	-2.3547
C	-2.6079	-19.1967	-1.4285
C	-6.5341	-17.6112	-3.0450
C	-5.6795	-16.2351	0.2569
N	-1.2772	-18.6896	-1.0787
N	-7.4959	-16.9886	-3.9997
N	-5.7633	-16.3920	1.7048
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C	-1.1786	-6.8535	-0.3207
C	-1.0108	-7.5073	-1.6261
C	-1.2295	-6.2150	-2.2450
O	-0.8055	-8.6661	-1.9738
O	-1.6750	-4.3889	-0.6913
C	-1.0866	-7.3887	0.9072
C	-1.2175	-6.8713	2.2509
N	-1.1294	-7.6618	3.4198
S	-1.4113	-5.1496	2.5828
C	-1.2635	-6.8363	4.5429
C	-1.4090	-5.5214	4.2686
C	-1.2578	-7.2427	5.9390
C	-1.3762	-6.2667	7.0181
C	-1.5188	-4.9599	6.7236
C	-1.5495	-4.5490	5.3274
C	-0.8577	-9.0912	3.5002
C	-2.1543	-9.9008	3.5248
C	-1.8695	-11.3953	3.6915
C	-3.1091	-12.2494	3.4130

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H	-3.6219	-15.0571	-2.3450
H	-4.1589	-13.5401	-0.9811
H	-0.0437	-14.3346	-0.0274
H	-1.5931	-10.3024	0.0760
H	0.5540	1.8822	-1.3471
H	-2.9134	0.9801	0.8067
H	1.3130	0.4424	0.1534
H	-1.1442	-2.9173	1.0673
H	2.7792	-10.0138	-1.7262
H	2.8029	-9.1805	-3.9911
H	2.5542	-6.7494	-4.4234
H	2.3246	-5.2050	-2.5844
H	2.5729	-9.1461	3.3481
H	2.5163	-7.5868	5.1786
H	2.4002	-5.1521	4.7462
H	2.3606	-4.3228	2.4752
H	-1.2329	-8.2912	6.2031
H	-1.3563	-6.6209	8.0429
H	-1.6197	-4.2055	7.4953
H	-1.7301	-3.5108	5.0804
H	-5.0549	-7.9220	5.0967
H	-4.8894	-5.4591	5.2921
H	-4.9300	-4.0773	3.3119
H	-5.2746	-8.9575	2.9280
H	-5.5378	-8.5276	-2.1853
H	-5.5464	-7.1494	-4.1696
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H	-5.1729	-3.6511	-1.7953
H	-3.5270	-9.4551	0.5925
H	-3.1124	-3.4712	0.3417
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H	0.5454	-9.9481	-0.3102
H	-0.8364	-8.4372	0.8952
C	-1.2512	-5.8157	-3.6705
C	-1.6624	-4.5260	-4.0020
C	-1.6602	-4.0886	-5.3323
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C	-1.2222	-4.9064	-6.3833
H	-2.0014	-3.0756	-5.5140
C	-0.8186	-6.2066	-6.0201
C	-0.8481	-6.6686	-4.6884
H	-0.4747	-6.9072	-6.7754
H	-0.5184	-7.6806	-4.4712
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O	-3.4884	-15.8187	2.5133
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H	-1.8331	-13.9205	2.9149
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H	-1.1783	-6.1172	-8.9814
H	0.4426	-5.5508	-8.4781
H	-0.4684	-4.6569	-9.6796

7. References

1 C. Ke, H. Destecroix, M. P. Crump and A. P. Davis, *Nat. Chem.*, 2012, **4**, 718–23.

2 X. Zhao and K. S. Schanze, *Chem. Commun.*, 2010, **46**, 6075–6077.

3 J. J. Gassensmith, E. Arunkumar, L. Barr, J. M. Baumes, K. M. DiVittorio, J. R. Johnson, B. C. Noll and B. D. Smith, *J. Am. Chem. Soc.*, 2007, **129**, 15054–15059.

4 S. Friães, A. M. Silva, R. E. Boto, D. Ferreira, J. R. Fernandes, E. B. Souto, P. Almeida, L. F. Vieira and L. V Reis, *Bioorg. Med. Chem.*, 2017, **25**, 3803–3814.

5 T. S. Jarvis and B. D. Smith, *Supramol. Chem.*, 2019, **31**, 140–149.

6 E. M. Peck, W. Liu, G. T. Spence, S. K. Shaw, A. P. Davis, H. Destecroix and B. D. Smith, *J. Am. Chem. Soc.*, 2015, **137**, 8668–8671.

7 T. S. Jarvis, F. M. Roland, K. M. Dubiak, P. W. Huber and B. D. Smith, *J. Mater. Chem. B*, 2018, **6**, 4963–4971.