

Supporting Information

One-step Construction of Aminosquaraine Backbone

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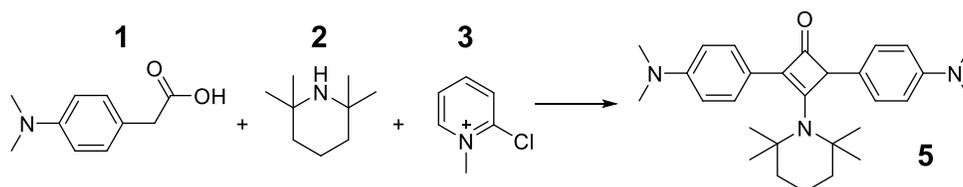
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General

Materials. Anhydrous dichloromethane (DCM) was dried by a column packed with alumina. All deuterated solvents were purchased from Cambridge Isotope Laboratories, Inc. and used as received. All other chemicals were purchased from Sigma-Aldrich (St. Louis, MO, USA) and used as received unless otherwise specified.

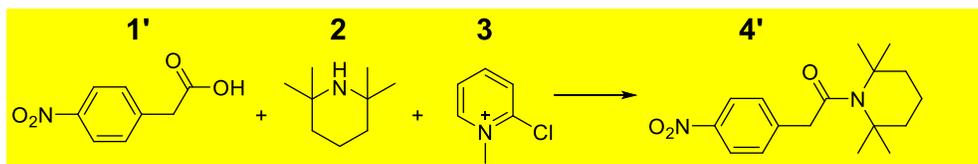
Instrumentation. NMR spectra were recorded on Varian U500 (500 MHz) spectrometer. Mass spectra were recorded on Waters Q-TOF Ultima ESI. UV-Vis spectra were recorded on Perkin Elmer lambda 25.

Scheme S1. Synthesis of aminosquaraine dye **5**



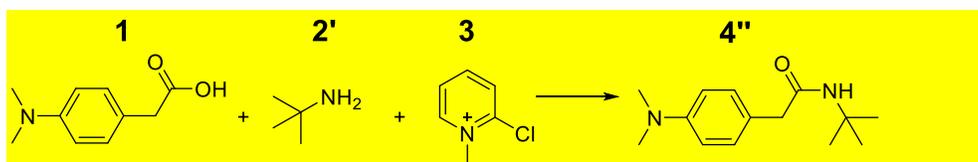
Synthesis of aminosquaraine dye **5.** 4-(Dimethylamino)phenylacetic acid (**1**, 1.00 g, 5.59 mmol) was dissolved in 100 mL anhydrous DCM, followed by the addition of 2-chloro-1-methylpyridinium iodide (**3**, 2.14 g, 8.38 mmol). After 15 min, 2,2,6,6-tetramethylpiperidine (**2**, 2.36 g, 16.7 mmol) was added dropwise. Then the mixture was allowed to react at room temperature for 24 h. After that, the mixture was diluted with DCM (100 mL), and washed with saturated NaHCO₃ solution (3 × 50 mL) and brine (3 × 50 mL). The organic phase was dried by anhydrous Na₂SO₄. After the solvent was removed by vacuum, the residue was purified by column chromatography (hexane/EtOAc = 5:1 to 2:1, v/v) to give brown solid as the final product (160 mg, yield 12%). ¹H NMR (500 MHz, CDCl₃): δ 7.45 (d, *J* = 8.5 Hz, 2H, Ph-H), 7.17 (d, *J* = 8.5 Hz, 2H, Ph-H), 6.71 (m, 4H, Ph-H), 4.70 (s, 1H, -CH), 2.96 (s, 6H, -CH₃), 2.92 (s, 6H, -CH₃), 1.80 (m, 2H, -CH₂), 1.68 (m, 2H, -CH₂), 1.51 (m, 2H, -CH₂), 1.32 (s, 6H, -CH₃), 1.16 (s, 6H, -CH₃), ¹³C NMR (125 MHz, CDCl₃), δ 189.9, 169.4, 150.2, 150.0, 132.8, 130.9, 129.3, 125.5, 121.0, 113.1, 112.4, 70.7, 58.2, 41.0, 40.7, 38.3, 32.5, 27.4, 15.7 (Figure S1). ESI-MS (low resolution, positive mode): calculated for C₂₉H₄₀N₃O, *m/z*, 446.3 [M + H]⁺; found 446.2 [M + H]⁺.

Scheme S2. Synthesis of amide 4'



Synthesis of 4'. 4-Nitrophenylacetic acid (**1'**, 0.200 g, 1.10 mmol) was dissolved in 20 mL anhydrous DCM, followed by the addition of 2-chloro-1-methylpyridinium iodide (**3**, 0.423 g, 1.66 mmol). After 15 min, 2,2,6,6-tetramethylpiperidine (**2**, 0.467 g, 3.31 mmol) was added dropwise. Then the mixture was allowed to react at room temperature for 24 h. After that, the mixture was diluted with DCM (100 mL), and washed with saturated NaHCO₃ solution (3 × 50 mL) and brine (3 × 50 mL). The organic phase was dried by anhydrous Na₂SO₄. After the solvent was removed by vacuum, the residue was purified by column chromatography (hexane/EtOAc = 2:1 v/v) to give grey solid as the final product (120 mg, yield 36%). ¹H NMR (500 MHz, CDCl₃): δ 8.16 (d, *J* = 8.5 Hz, 2H, Ph-H), 7.47 (d, *J* = 8.5 Hz, 2H, Ph-H), 3.81 (s, 2H, -CH₂), 2.92 (s, 6H, -CH₃), 1.79 (m, 6H, -CH₂), 1.47 (s, 12H, -CH₃), ¹³C NMR (125 MHz, CDCl₃), δ 173.8, 146.9, 145.0, 130.4, 123.7, 56.5, 46.4, 36.7, 30.5, 14.6 (Figure S3). ESI-MS (low resolution, positive mode): calculated for C₁₇H₂₅N₂O₃, *m/z*, 305.2 [M + H]⁺; found 305.2 [M + H]⁺.

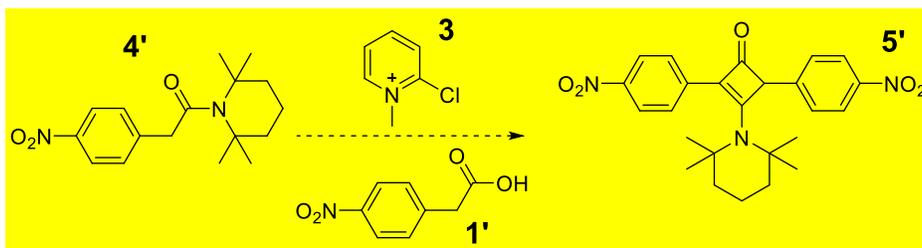
Scheme S3. Synthesis of amide 4''



Synthesis of 4''. 4-(Dimethylamino)phenylacetic acid (**1**, 0.200 g, 1.12 mmol) was dissolved in 20 mL anhydrous DCM, followed by the addition of 2-chloro-1-methylpyridinium iodide (**3**, 0.428 g, 1.68 mmol). After 15 min, *t*-butylamine (**2'**, 0.241 g, 3.30 mmol) was added dropwise. Then the mixture was allowed to react at room temperature for 24 h. After that, the mixture was diluted with DCM (100 mL), and washed with saturated NaHCO₃ solution (3 × 50 mL) and brine (3 × 50 mL). The organic phase was dried by anhydrous Na₂SO₄. After the solvent was removed by vacuum, the residue was purified by column chromatography (hexane/EtOAc = 2:1 v/v) to give grey solid as the final product (126 mg, yield 47%). ¹H NMR (500 MHz, CDCl₃), δ 7.08 (d, *J* = 8.5 Hz, 2H, Ph-H), 6.71 (d, *J* = 8.5 Hz, 2H, Ph-H), 5.23 (br, 1H, N-H), 3.38 (s, 2H, -CH₂),

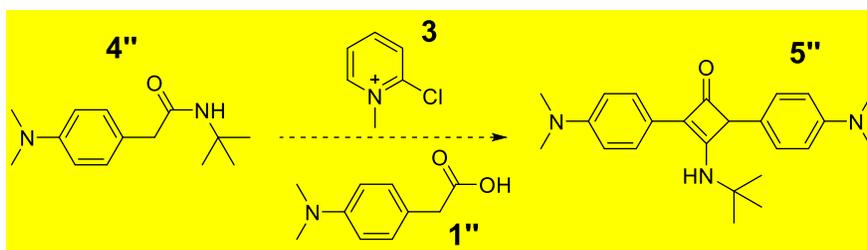
2.94 (s, 6H, -CH₃), 1.26 (s, 12H, -CH₃), ¹³C NMR (125 MHz, CDCl₃), δ 171.6, 149.9, 130.3, 123.3, 113.3, 51.3, 44.2, 40.9, 29.0 (Figure S4). ESI-MS (low resolution, positive mode): calculated for C₁₄H₂₃N₂O, m/z, 235.2 [M + H]⁺; found 235.2 [M + H]⁺.

Scheme S4. Attempt to synthesize squaraine dye starting from 4'



Attempt to synthesize squaraine dye 5' starting from 4': Compound 4' (50 mg, 0.164 mmol), 4-nitrophenylacetic acid (1', 30 mg, 0.164 mmol), 2-chloro-1-methylpyridinium iodide (3, 42 mg, 0.164 mmol), and triethylamine (17 mg, 0.164 mmol) were dissolved in DCM (20 mL) and allowed to react at room temperature for 24 h. After that, the solution was characterized by ESI to detect the existence of aminosquaraine dye 5'. No peak for 5' was detected (Figure S5). Finally, the mixture was dried by vacuum and ran through column chromatography. No 5' was identified. Part of the starting compound 4' was recovered (17 mg, recovery ratio = 34%).

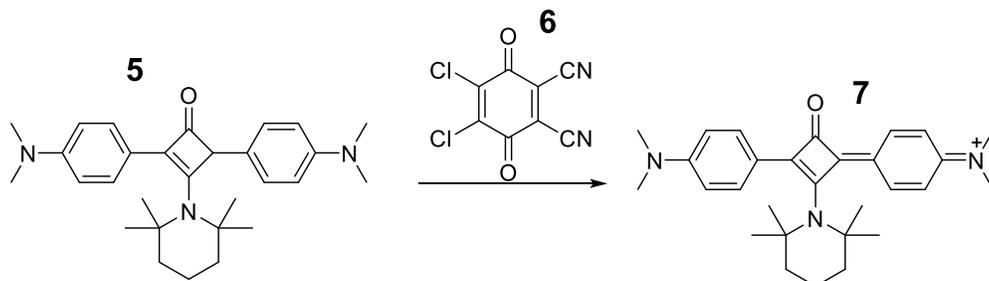
Scheme S5. Attempt to synthesize squaraine dye starting from 4''



Attempt to synthesize squaraine dye 4'' starting from 4'': Compound 4'' (50 mg, 0.214 mmol), 4-(dimethylamino)phenylacetic acid (1'', 38 mg, 0.214 mmol), 2-chloro-1-methylpyridinium iodide (3, 55 mg, 0.214 mmol), and triethylamine (21 mg, 0.214 mmol) were dissolved in DCM (20 mL) and allowed to react at room temperature for 24 h. After that, the solution was characterized by ESI to detect the existence of aminosquaraine dye 5''. No peak for 5'' was detected (Figure S6). The solution was diluted to 0.1 mM (calculated based on the original concentration of starting amide 4'') and added DDQ (0.2 mM). No long wavelength

absorption was detected for the mixture (Figure S7). Finally, the mixture was dried by vacuum and ran through column chromatography. No **5''** was identified. Part of the starting compound **4''** was recovered (40 mg, recovery ratio = 80%).

Scheme S6. Oxidation of reduced aminosquaraine dye **5** by DDQ



Oxidation of reduced aminosquaraine dye 5 by DDQ: Reduced aminosquaraine dye **5** (6.0 mg, 0.013 mmol) was dissolved in deuterated chloroform (550 μL). Later, DDQ (**6**, 3.0 mg, 0.013 mmol) was added. Instant color change from light yellow to deep green was observed. The mixture was directly characterized by ^1H NMR and ESI to confirm the structure of oxidized species **7**. ^1H NMR (500 MHz, CDCl_3), δ 8.41 (br, 4H, Ph-H), 6.93 (br, 4H, Ph-H), 3.67 (br, 12H, CH_3), 2.05 (br, 2H, $-\text{CH}_2$), 1.82 (br, 4H, $-\text{CH}_2$), 1.46 (br, 12H, $-\text{CH}_3$) (Figure S8), ESI-MS (low resolution, positive mode): calculated for $\text{C}_{29}\text{H}_{38}\text{N}_3\text{O}$, m/z , 444.3 $[\text{M}]^+$; found 444.3 $[\text{M}]^+$. The UV-Vis absorption characterization was also performed and compared with the solution of reactants **5** and **6**, respectively.

Titration of 5 by DDQ to determine the reaction equivalents: Deuterated chloroform solution of **5** and **6** were prepared both in concentration of 0.024 mM. Four portions of **6** solution (volume of each portion was 125 μL) was added to 500 μL solution of **5**. The ^1H NMR spectra was taken after each addition. The quantity ratios of **5** and **7** in the mixtures were recorded based on the NMR peaks integral and used for the plotting of titration curve (Figure S9).

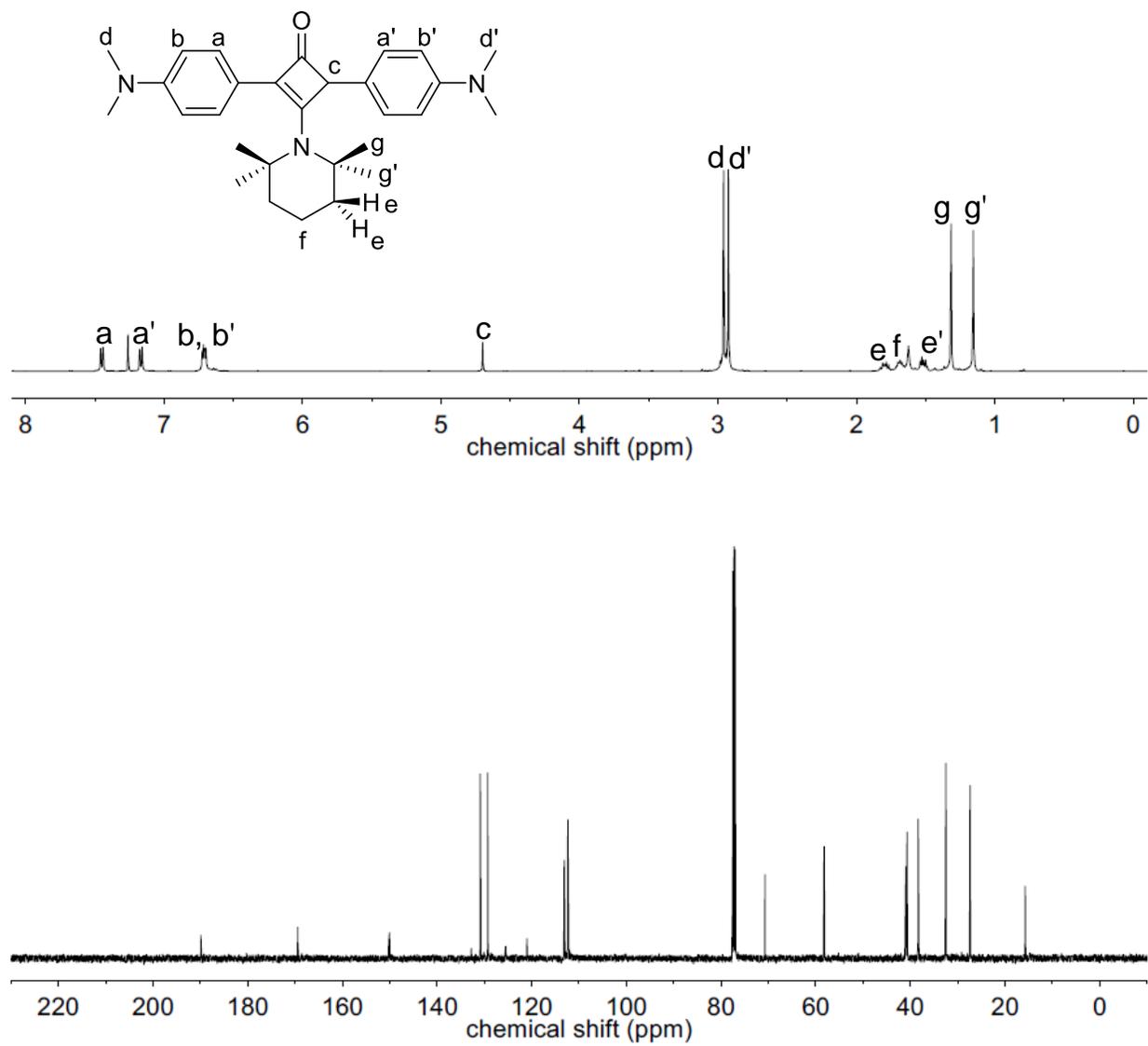


Figure S1. ^1H NMR and ^{13}C NMR spectra of compound 5.

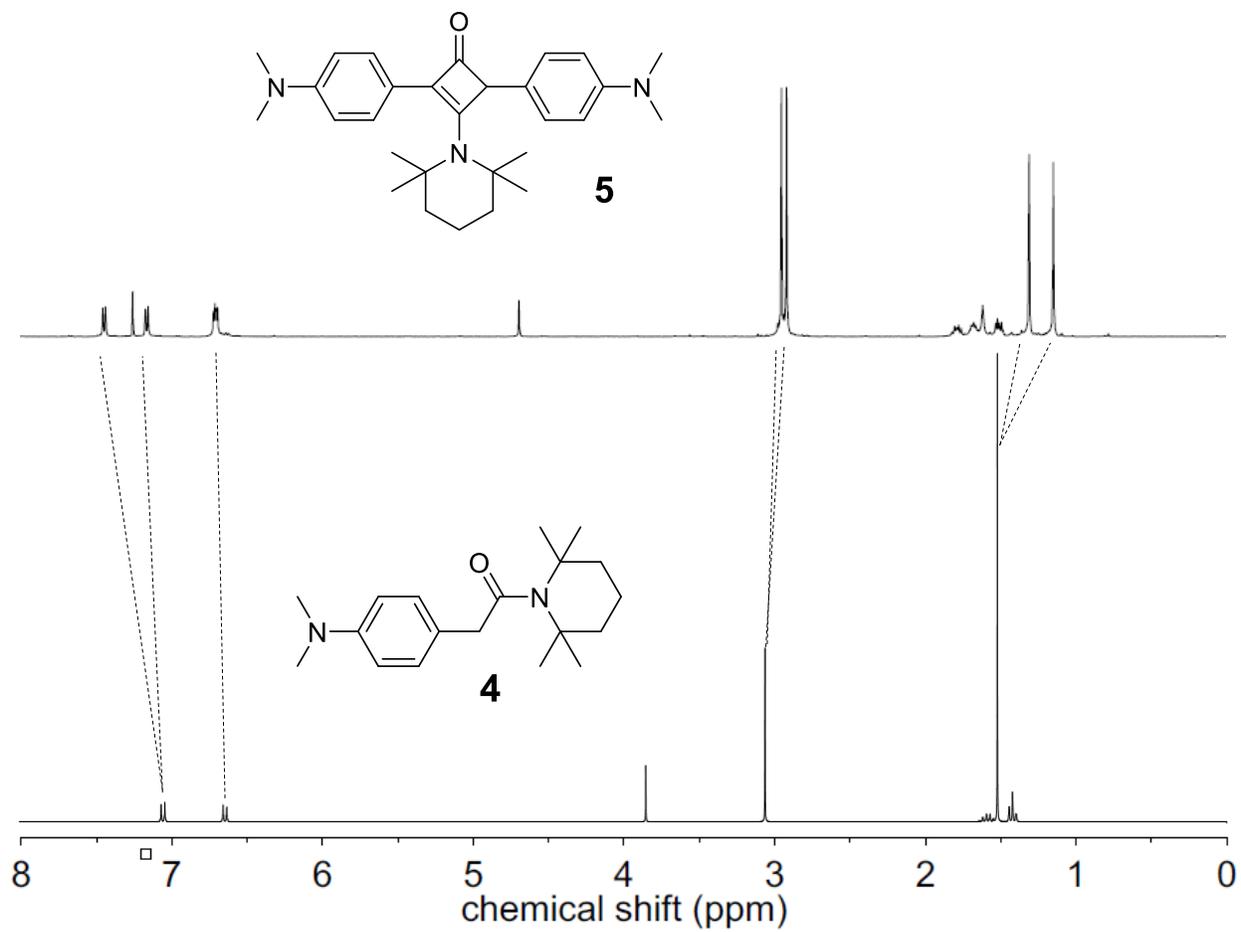


Figure S2. Comparison of ¹H NMR spectra of reduced aminosquaraine **5** and expected amide compound **4** (spectrum of **4** was simulated by chemdraw).

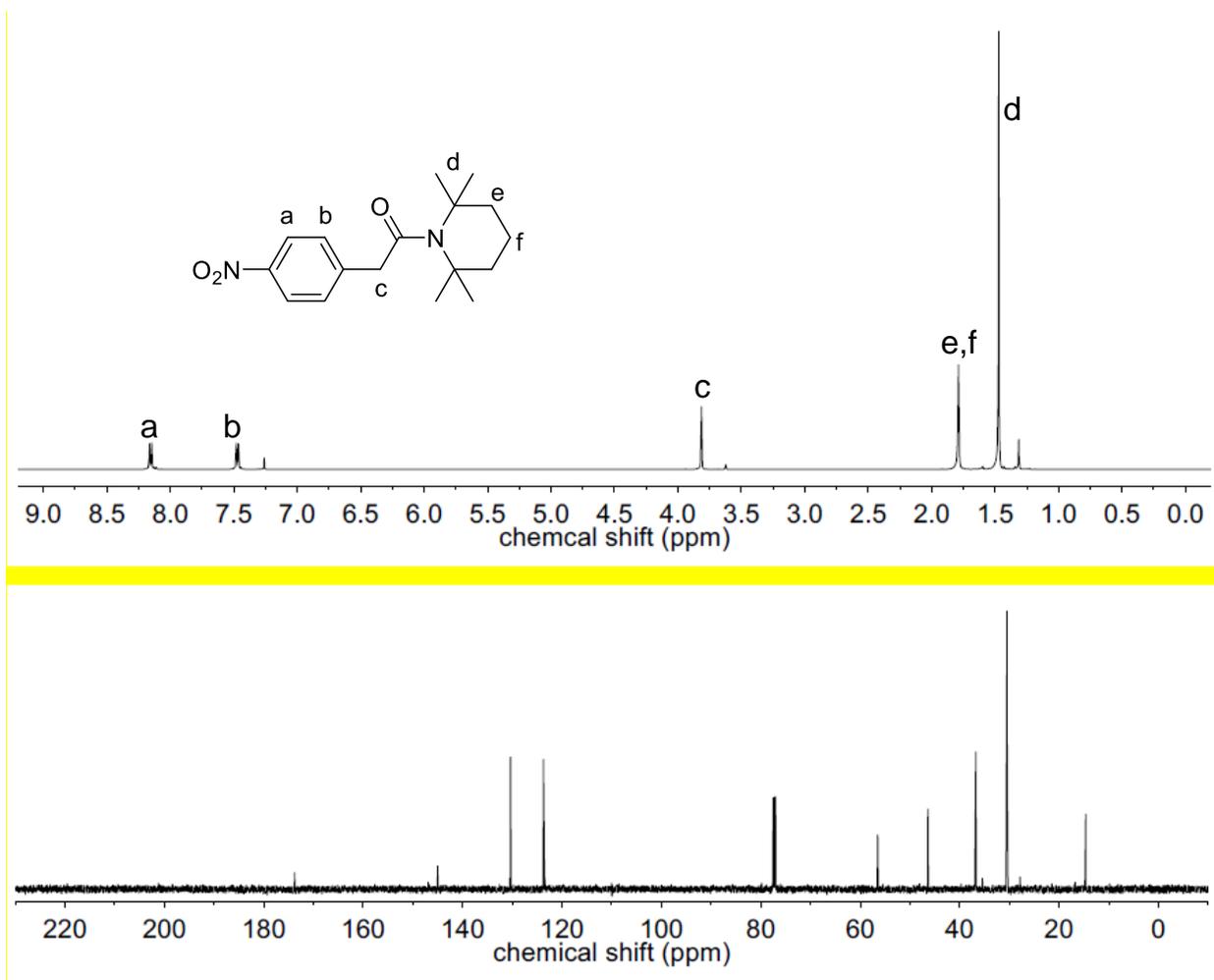


Figure S3. ^1H NMR and ^{13}C NMR spectra of compound 4'.

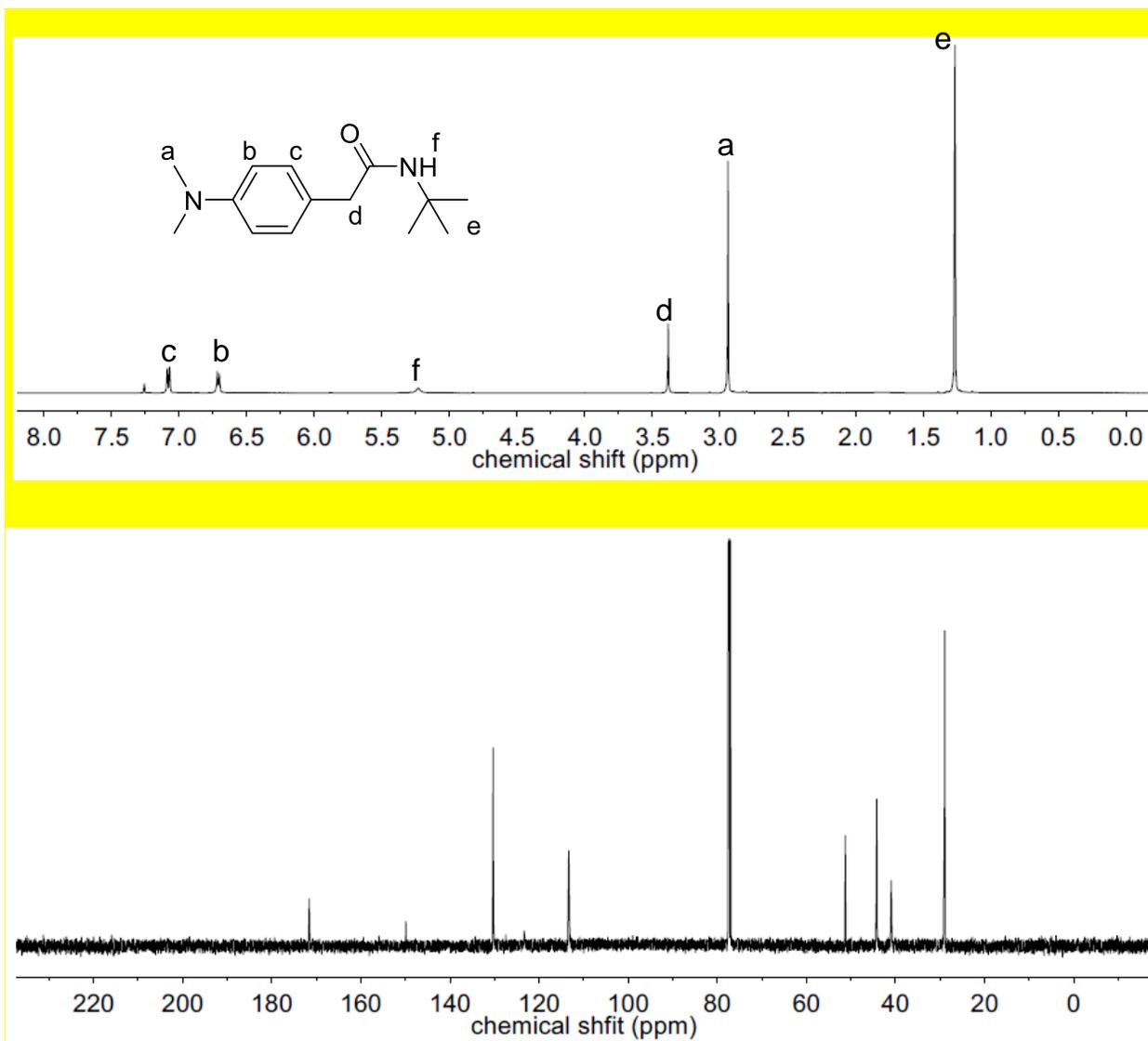


Figure S4. ^1H NMR and ^{13}C NMR spectra of compound 4''.

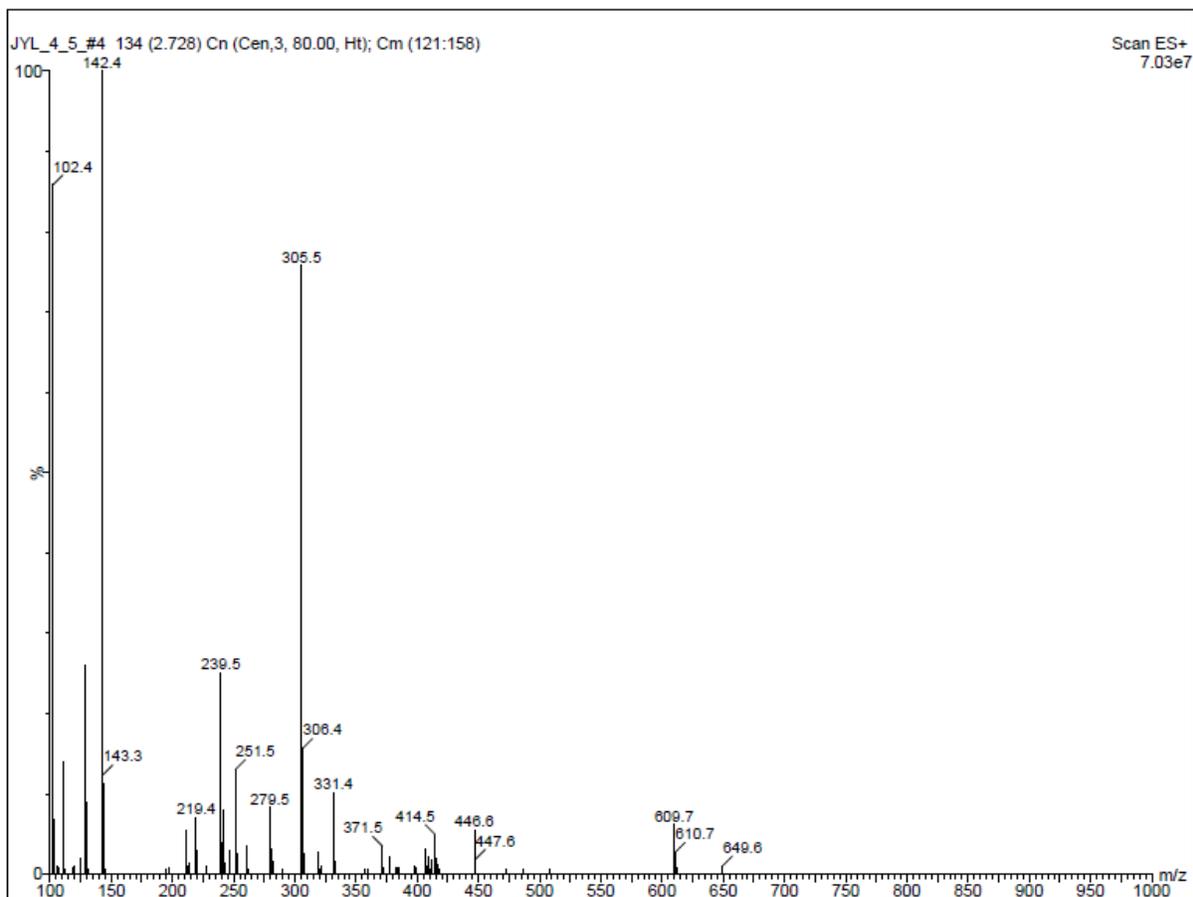


Figure S5. ESI spectrum taken after mixing **4'**, **1'**, **3** for 24 h at room temperature. Peak for starting compound **4'** was detected (calculated for $C_{17}H_{25}N_2O_3$, m/z, 305.2 $[M + H]^+$). No peak for targeted compound **5'** (calculated for $C_{25}H_{27}N_3O_5$, m/z, 450.2 $[M + H]^+$) was detected.

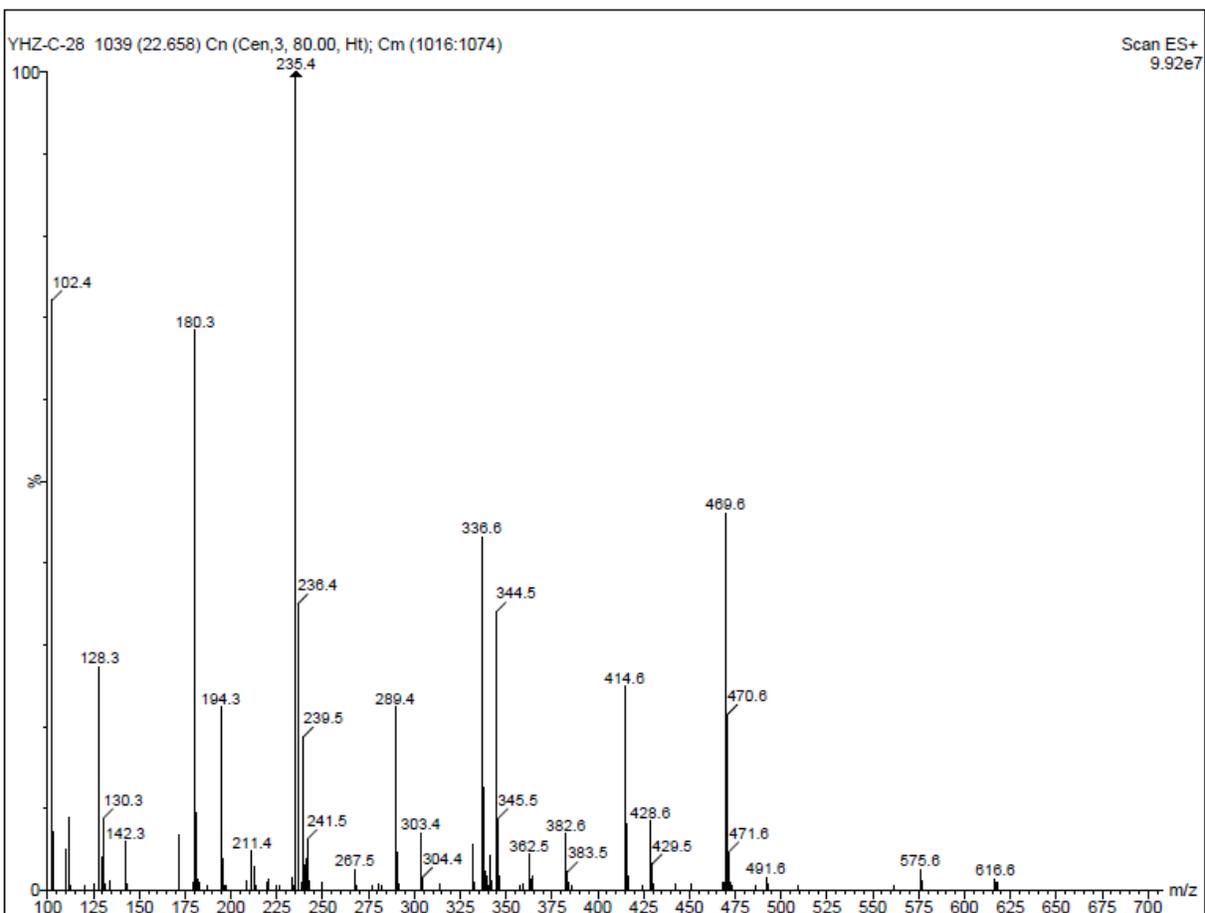


Figure S6. ESI spectrum taken after mixing **4''**, **1''**, **3** for 24 h at room temperature. Peak for starting compound **4''** was detected (calculated for $C_{14}H_{23}N_2O$, m/z , 235.2 $[M + H]^+$). No peak for targeted compound **5''** (calculated for $C_{24}H_{31}N_3O$, m/z , 377.2 $[M + H]^+$) was detected.

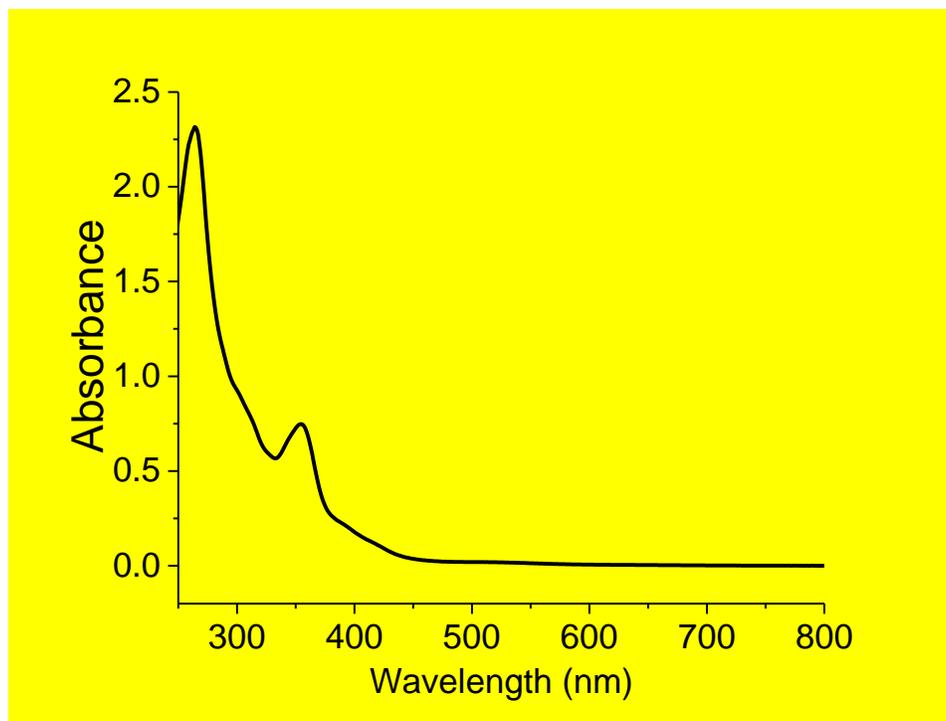


Figure S7. UV-Vis spectrum of 4'', 1'', 3 mixture ($[4'']_0 = 0.05\text{mM}$, after 24 h reaction at room temperature) with the addition of DDQ (0.1 mM). No detectable peak was observed in long wavelength range ($>500\text{ nm}$), demonstrating no squaraine structure was formed.

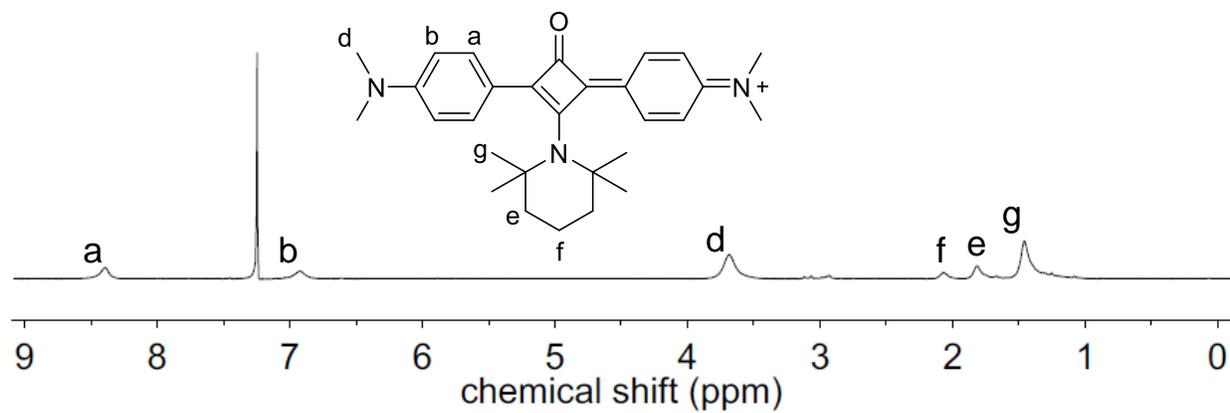


Figure S8. ^1H NMR spectrum of compound 7.

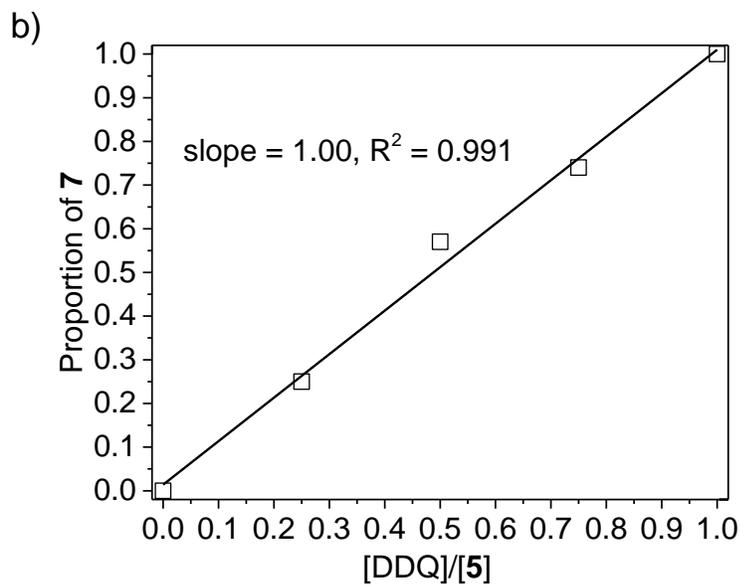
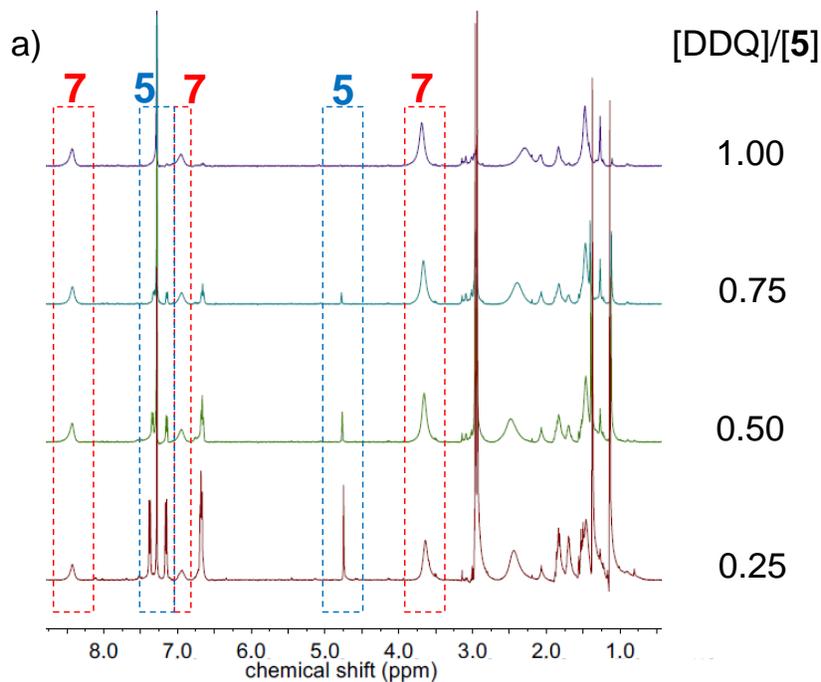


Figure S9. Titration of **5** by DDQ to determine the reaction stoichiometry. a) ^1H NMR spectra taken after mixing DDQ and **5** with variant ratios; b) Relation between proportion of **7** and ratio of $[\text{DDQ}]/[\mathbf{5}]$. The slope shows the 1:1 stoichiometry.