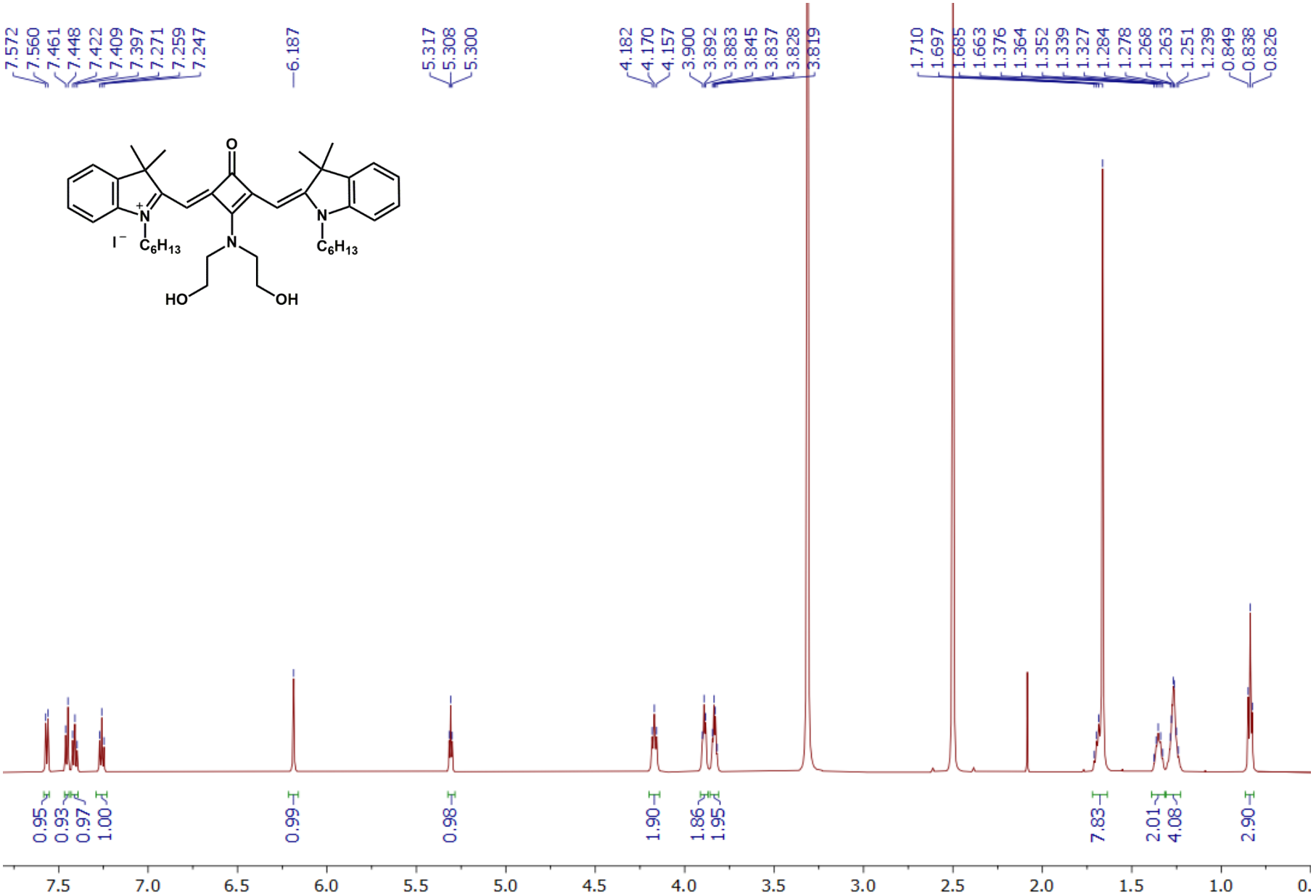

Figure S1. ^{1}H NMR spectrum of squaraine dye **11a** (600 MHz, DMSO-d_6, ppm).

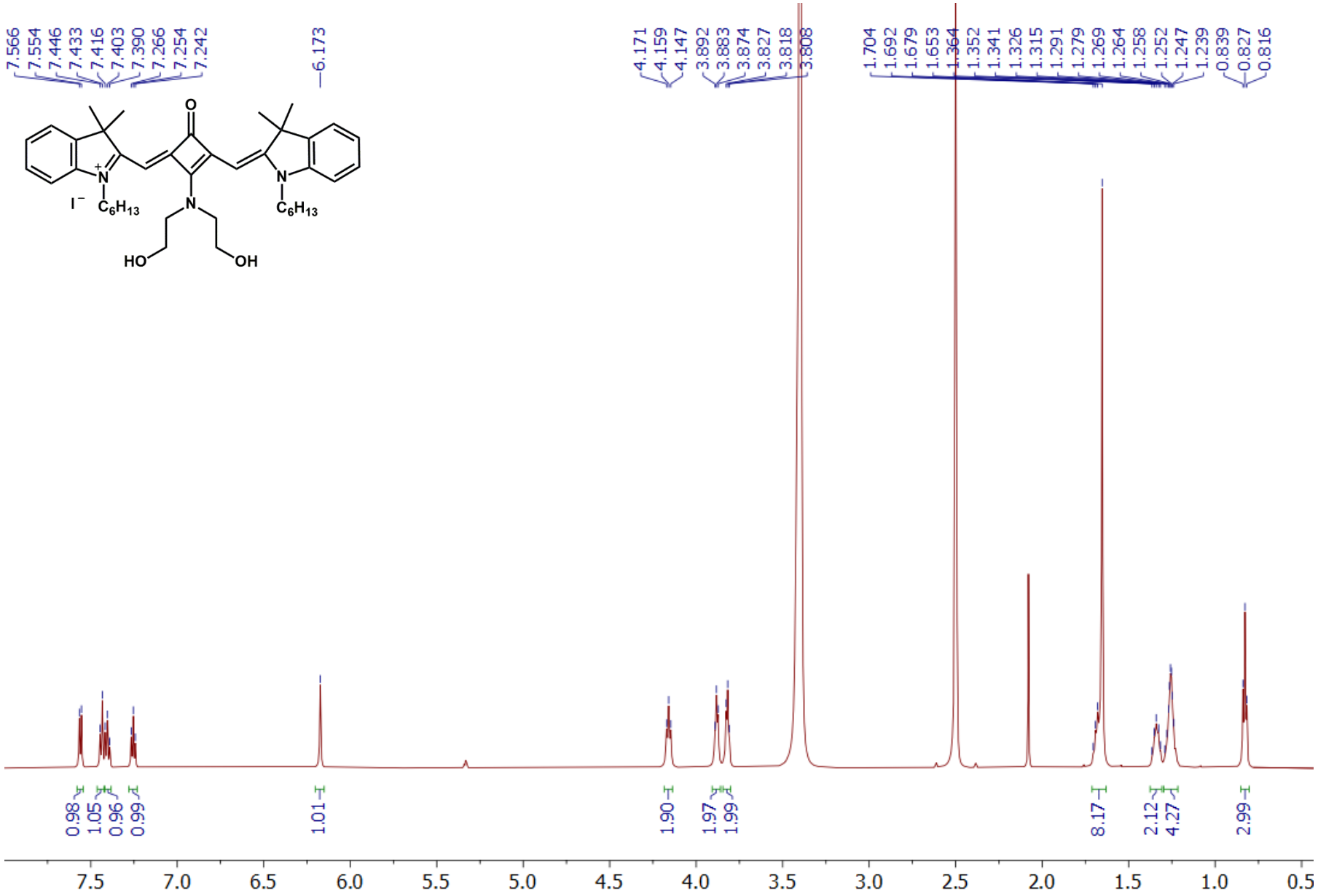

Figure S2. ^{1}H NMR spectrum of squaraine dye **11a** (600 MHz, DMSO-d_6+D_2O ppm).

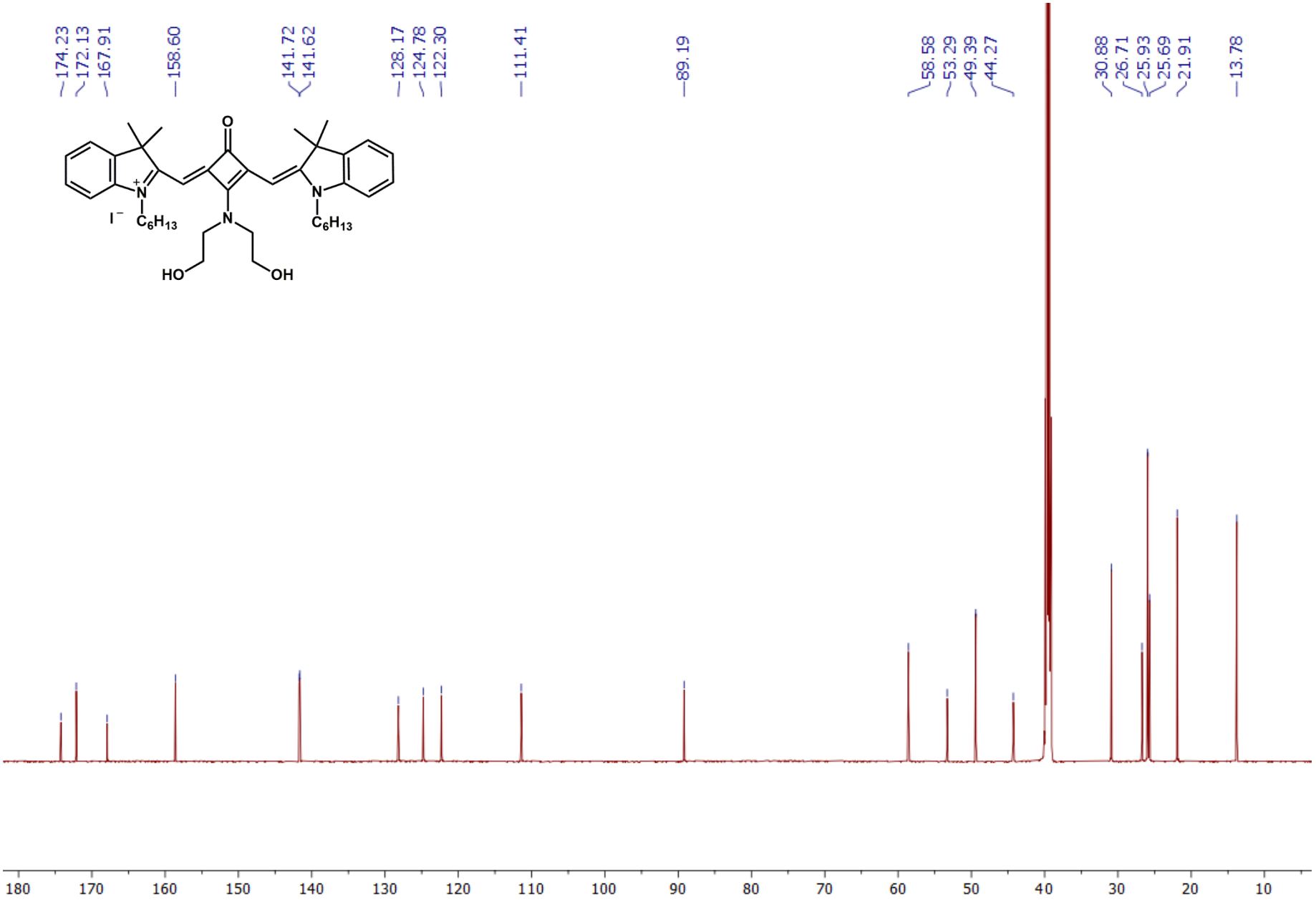

Figure S3. ^{13}C NMR spectrum of squaraine dye **11a** (150.90 MHz, DMSO-d_6, ppm).

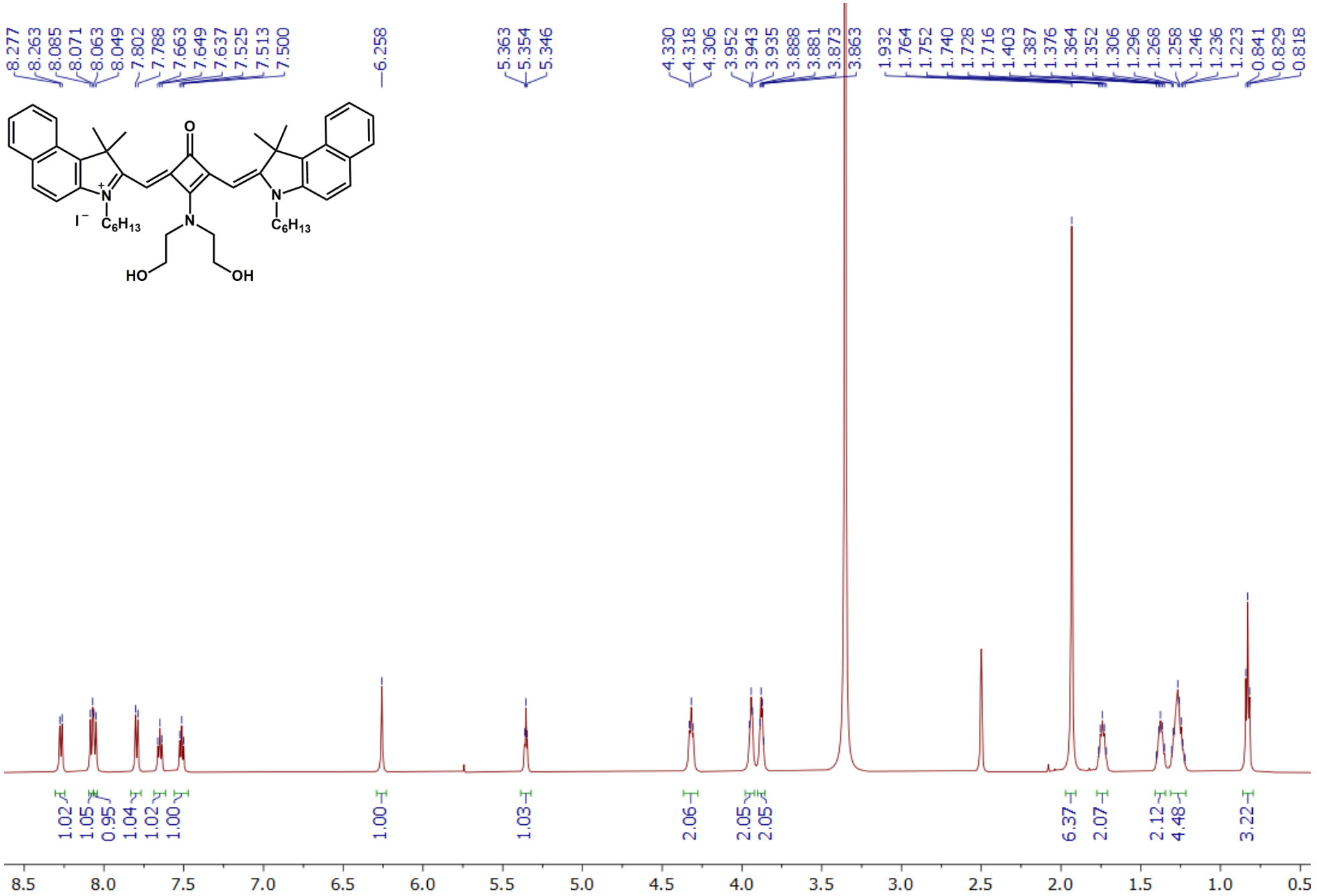

Figure S4. ^{1}H NMR spectrum of squaraine dye **11b** (600 MHz, DMSO-d_6, ppm).

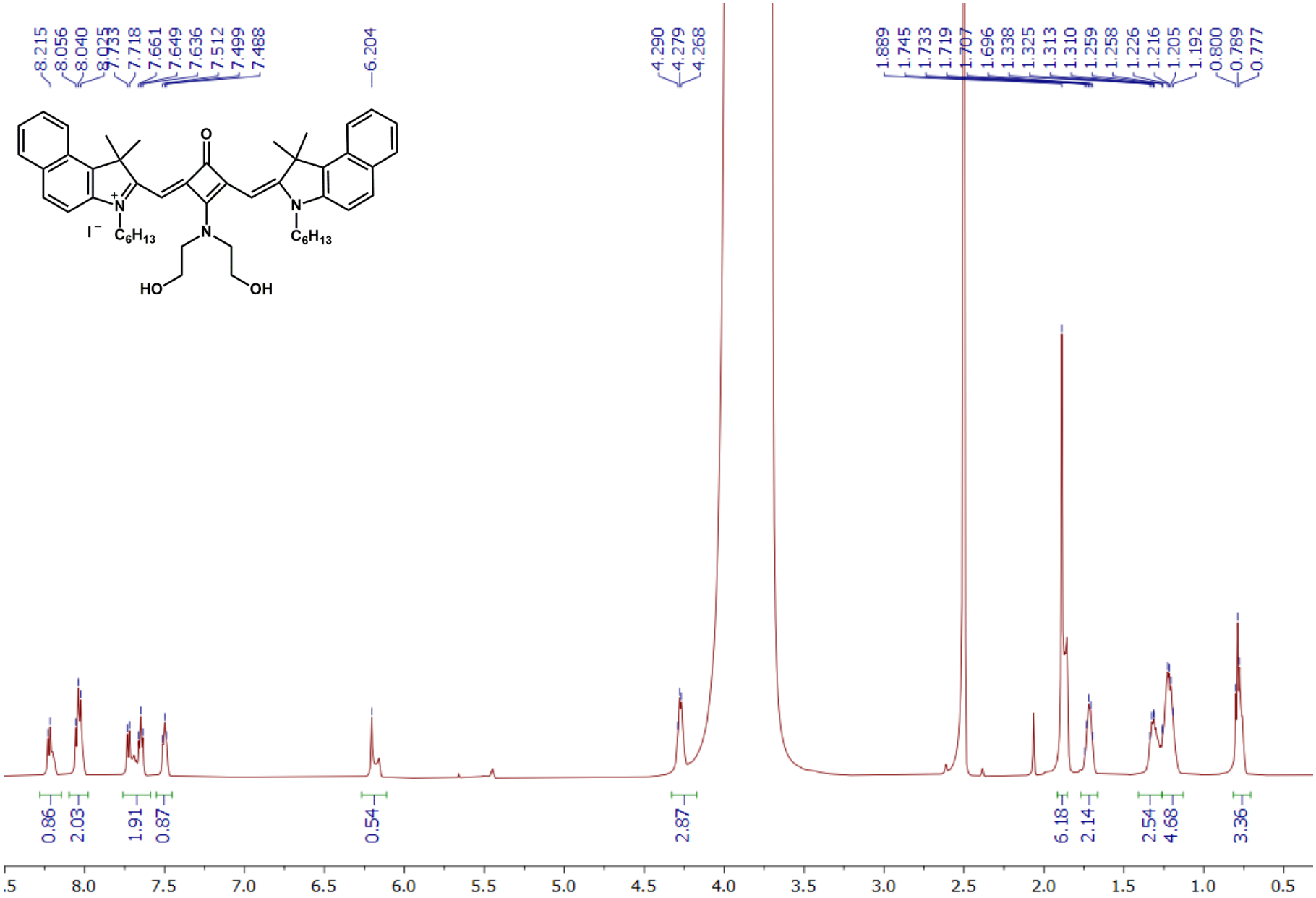

Figure S5. ^{1}H NMR spectrum of squaraine dye **11b** (600 MHz, DMSO-d_6 + D_2O, ppm).

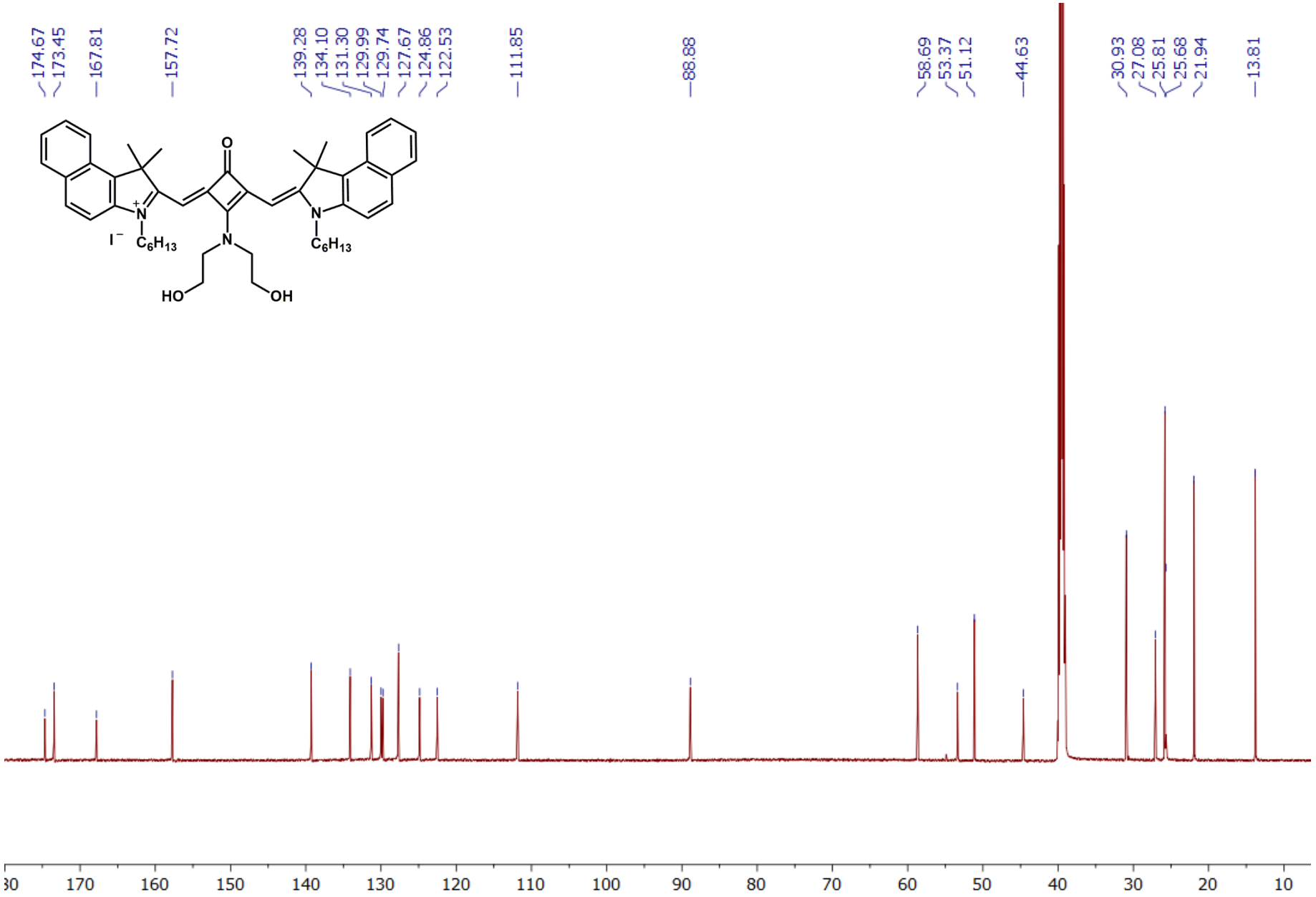

Figure S6. ^{13}C NMR spectrum of squaraine dye **11b** (150.0 MHz, DMSO-d_6, ppm).

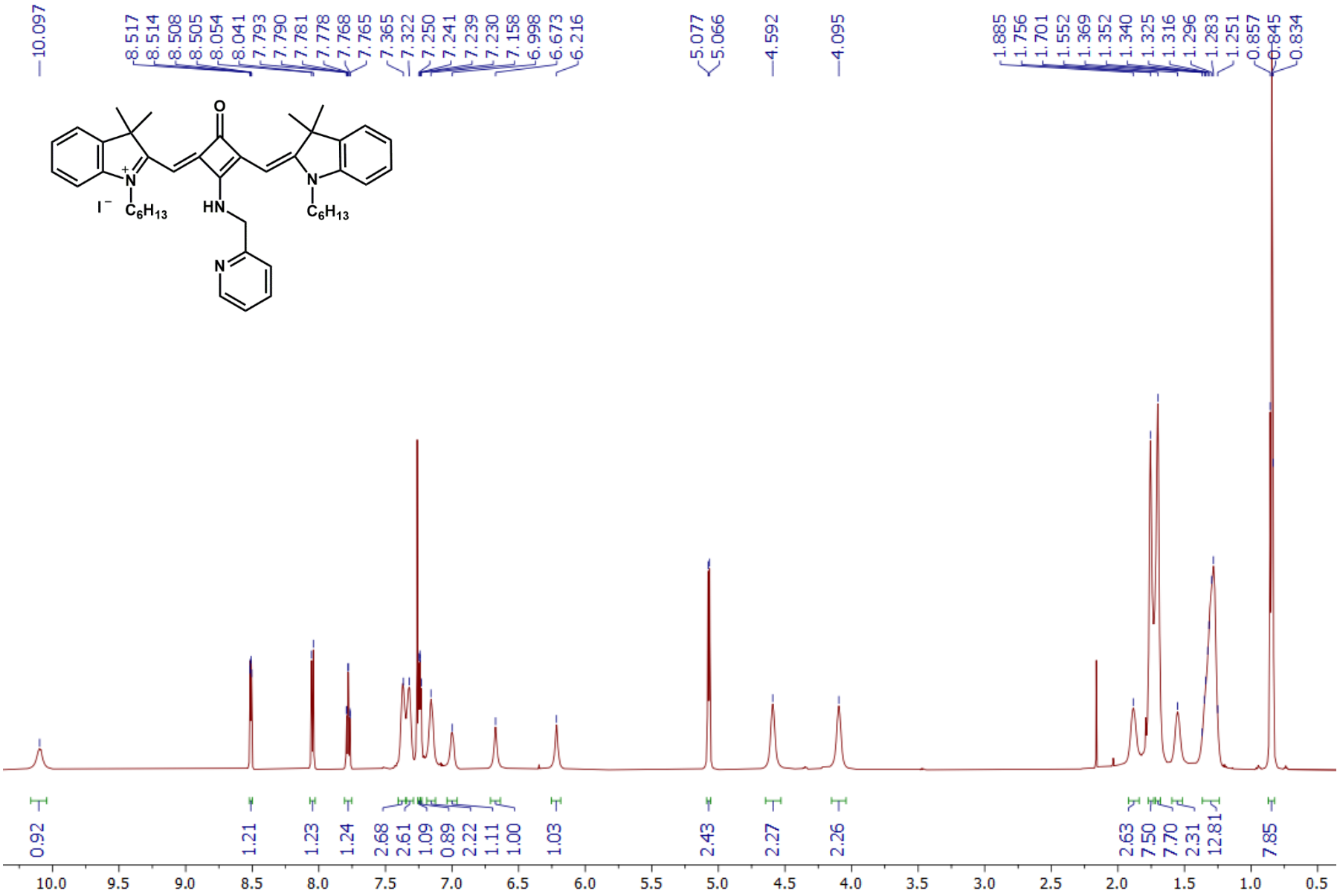

Figure S7. ^{1}H NMR spectrum of squaraine dye **12a** (600 MHz, $CDCl_3$, ppm).

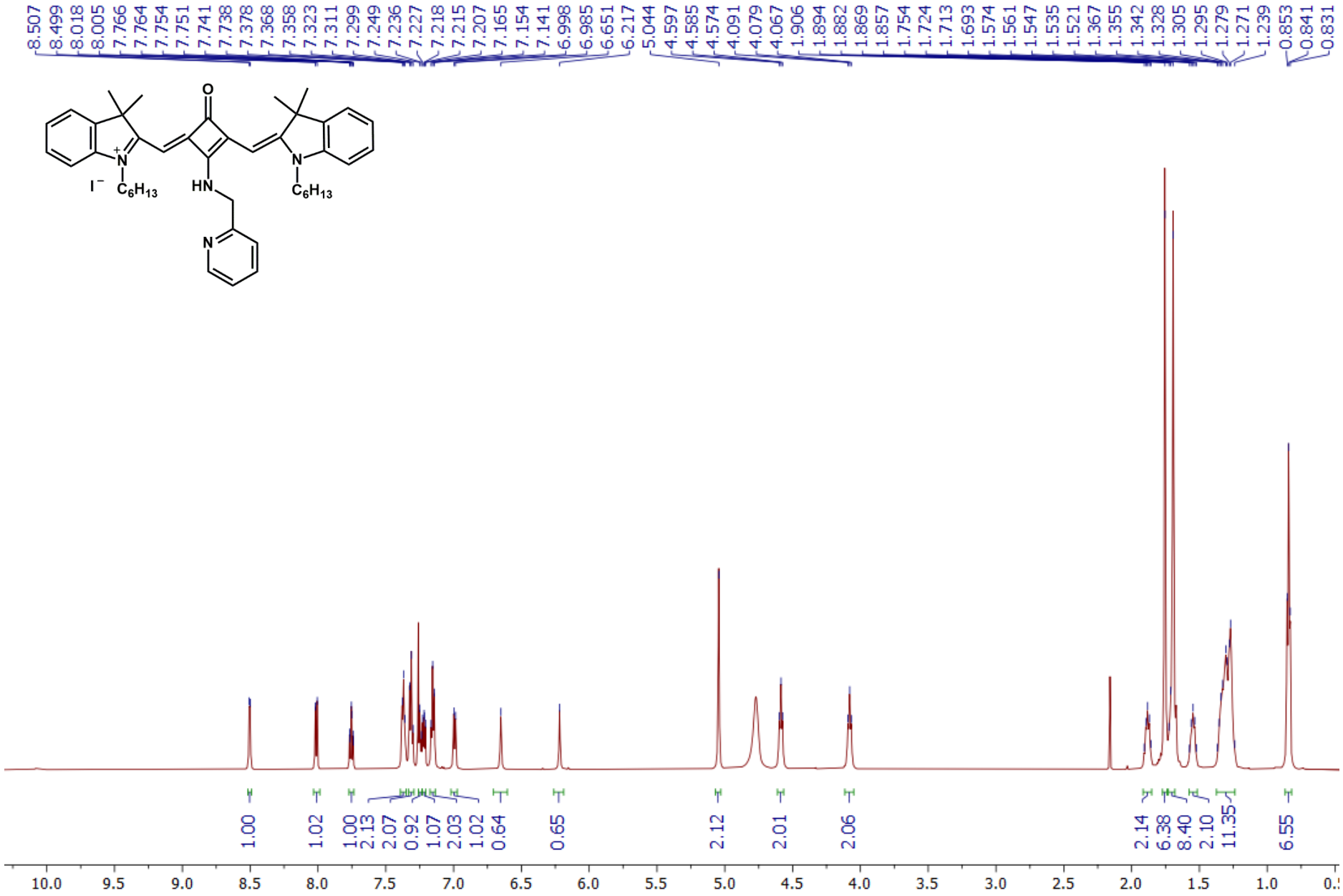

Figure S8. ^{1}H NMR spectrum of squaraine dye **12a** (600 MHz, $CDCl_3$+D_2O, ppm).

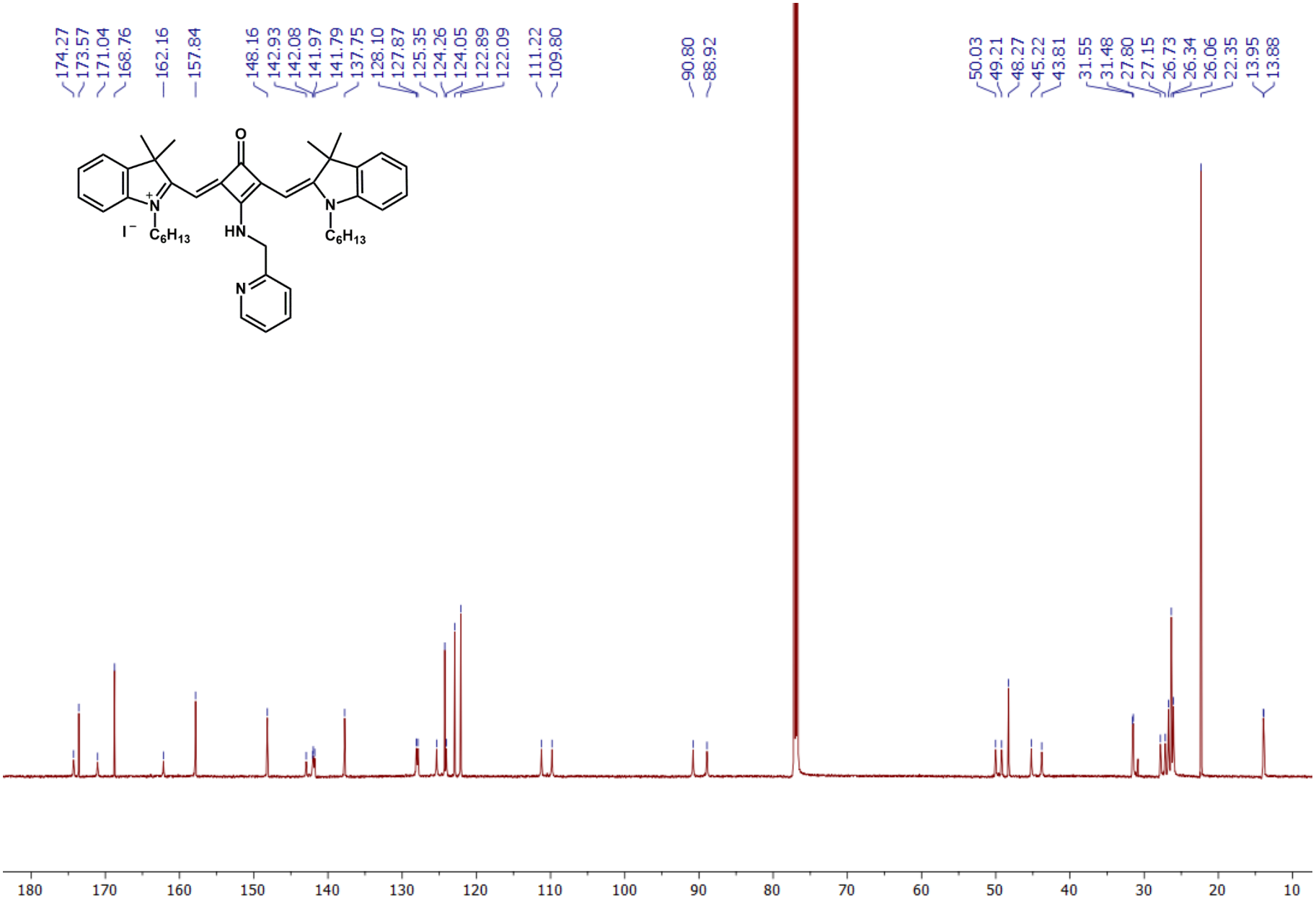

Figure S9. ^{13}C NMR spectrum of squaraine dye **12a** (150.0 MHz, $CDCl_3$, ppm).

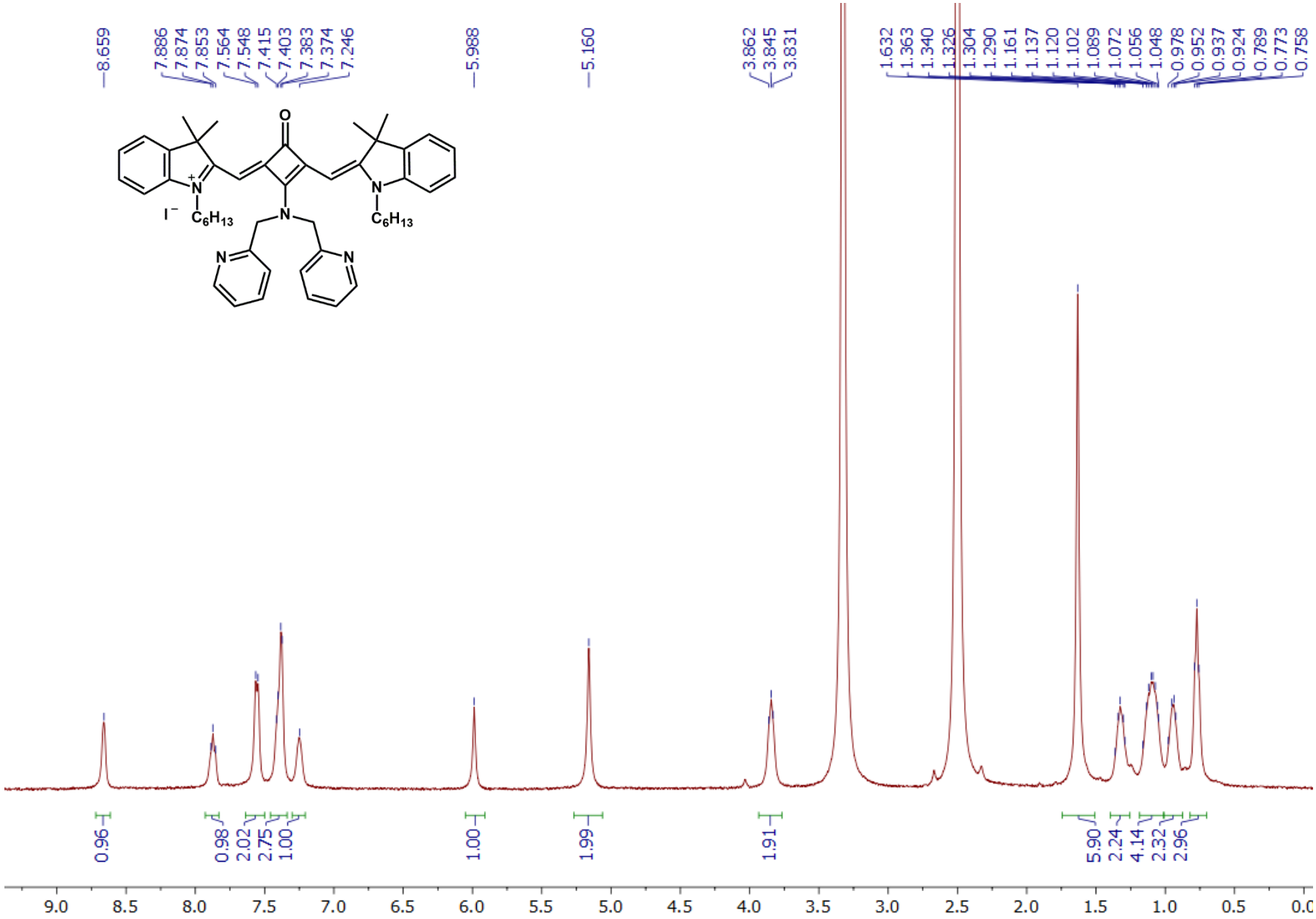

Figure S10. ^{1}H NMR spectrum of squaraine dye **13a** (400 MHz, DMSO-d_6, ppm).

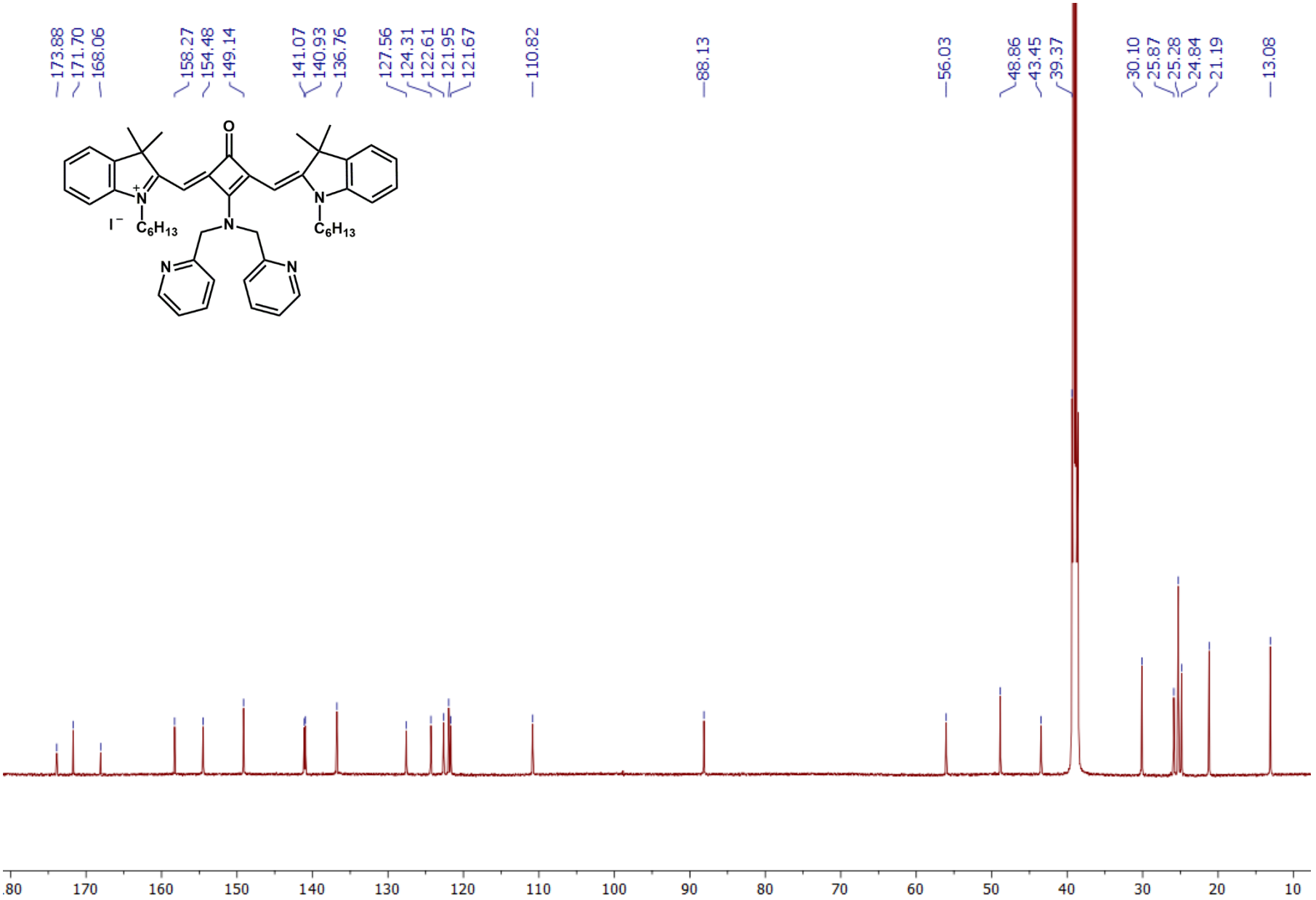

Figure S11. ^{13}C NMR spectrum of squaraine dye **13a** (150.0 MHz, DMSO-d_6, ppm).

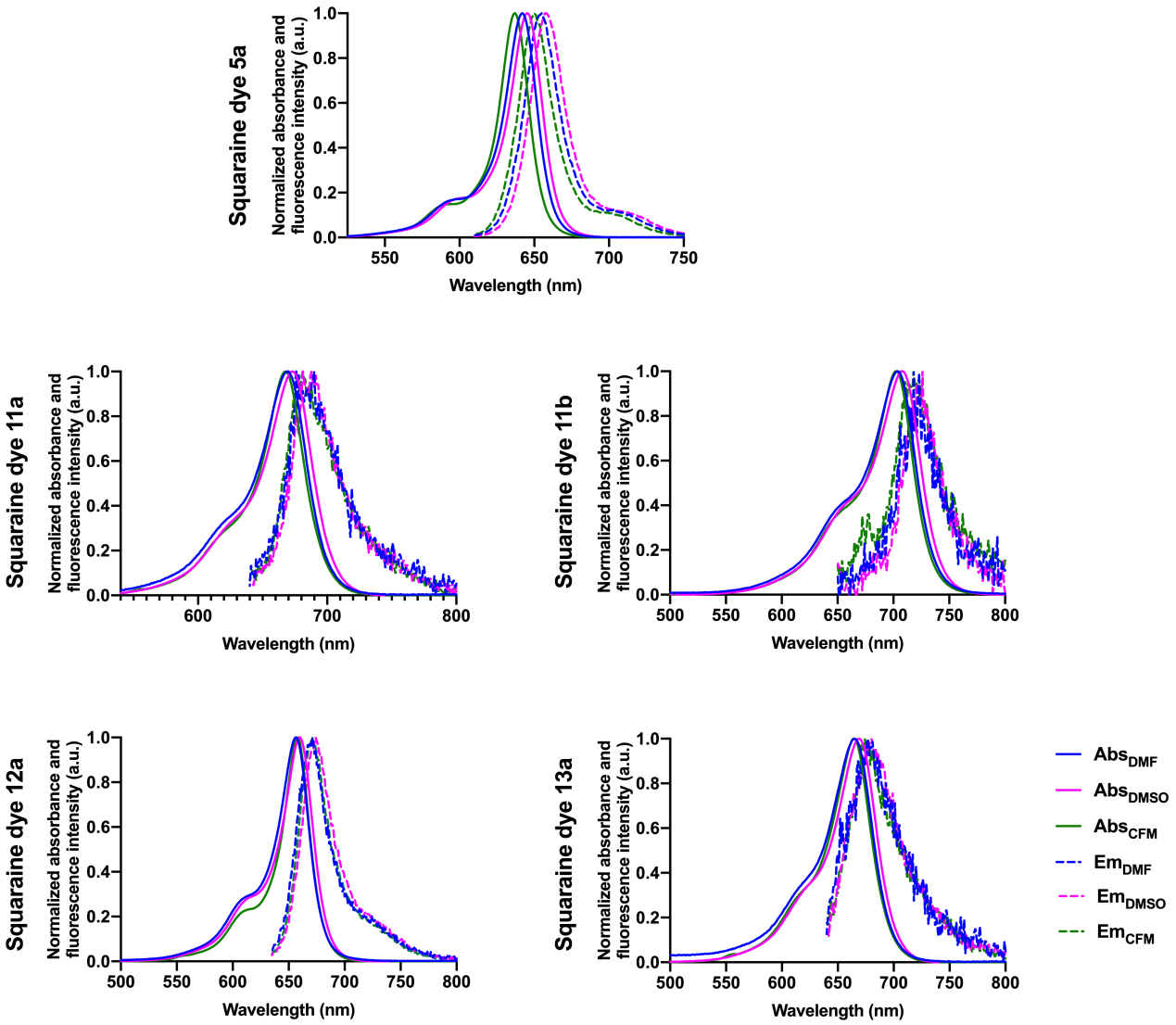

Figure S12. Visible absorption (Abs) and emission (Em) spectra of squaraine dyes **5a**, **11a**,**b**, **12a**, and **13a** obtained in dimethylformamide (DMF), dimethyl sulfoxide (DMSO) and chloroform (CFM). Absorbance and fluorescence intensity were normalized to 1.0 for more straightforward analysis and are presented as arbitrary units (a.u.).

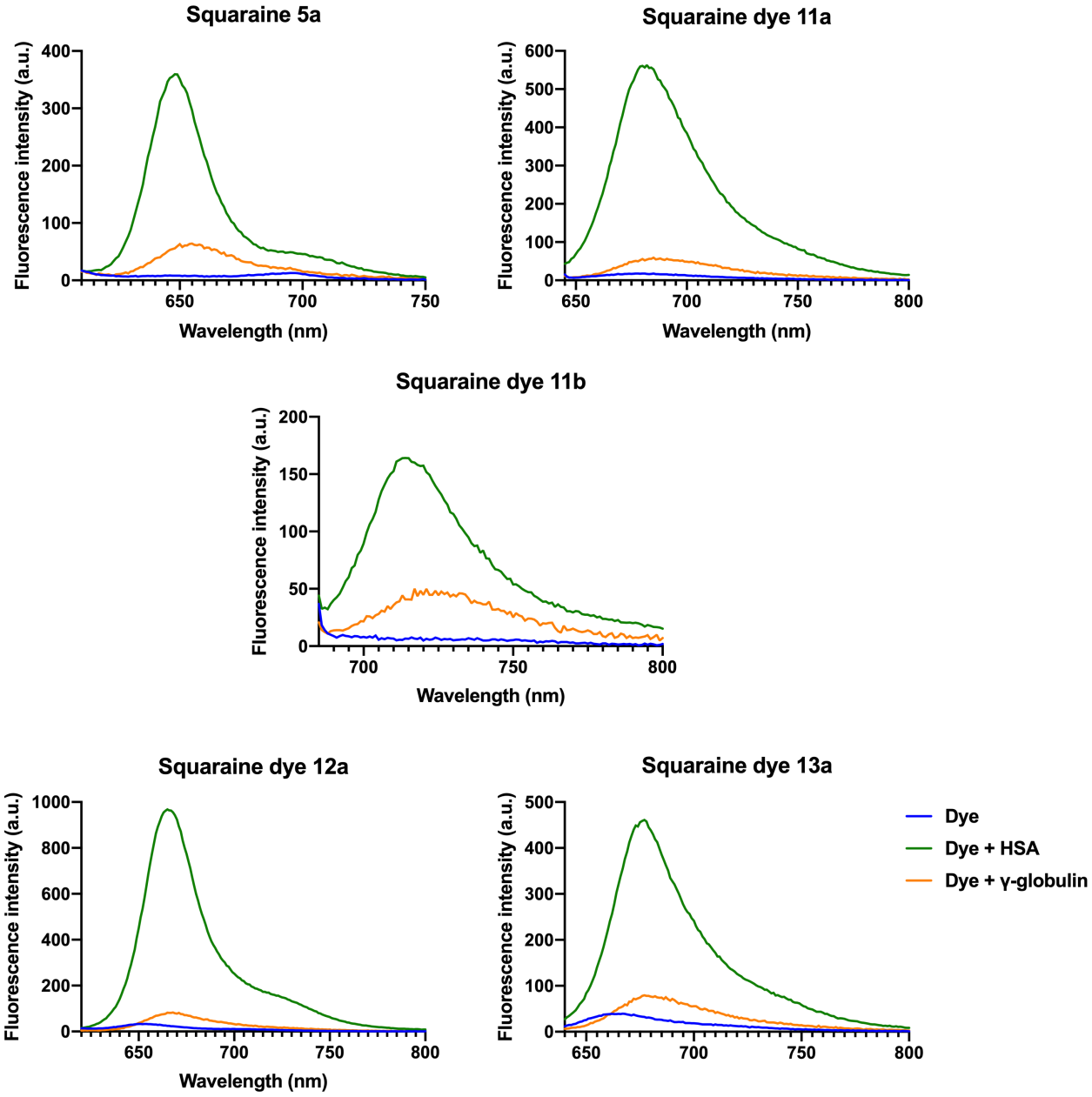

Figure S13. Fluorescence spectra of squaraine dyes **5a**, **11a**,**b**, **12a**, and **13a** in phosphate buffer pH 7.4 at a concentration of 2.0 μM in the presence and absence of human γ-globulin and serum albumin proteins and at a concentration of 3.0 μM. Spectra were obtained at the incubation time with the highest albumin-dye interaction and fluorescence intensity is presented as arbitrary units (a.u.).

Table S1. Estimated free binding energy and interactions list of warfarin and squaraine dyes **5a**, **11a**,**b**, **12a**, and **13a** in Sudlow site I of human serum albumin.

Protein: 2BXD (Sudlow's Site I)		Ligand					
		Warfarin	**5a**	**11a**	**11b**	**12a**	**13a**
Estimated Free Binding Energy (Kcal/mol)		-8.80	-12.08	-11.07	-12.15	-13.12	-12.34
Interactions	**Classic H-Bonds**	TYR150 HIS242 ARG222 ARG257	---	LYS195 LYS199 ARG218 ARG222	LYS195 ARG222 ASP451	ARG218 ARG222	ARG222
	Non-classic H-Bonds[a]	---	ARG218 PRO447 ASP451	ARG218	ARG218	ARG218	ARG218
	Van der Waals	---	---	---	---	---	---
	Electrostatics[b]	LYS199	LYS195 ARG218 ARG222 ASP451	LYS195 LYS199 ARG222	LYS195 LYS199 ARG218	LYS195 LYS199	LYS195 ARG218 ARG222 HIS242 GLU292 ASP451
	Miscellaneous	---	---	---	CYS448[d]		---
	Hydrophobic	LYS195 TRP214 ALA215 ARG218 LEU219 LEU238	LYS195 TRP214 ALA215 ARG218 LEU219 LEU238 ALA291 PRO447 CYS448	LYS195 LYS199 PHE211 TRP214 LEU238 HIS242 ALA291 PRO447 CYS448	LYS195 LYS199 PHE211 LEU238 HIS242 ALA291 LYS436 PRO447 CYS448	ALA194 LYS195 LEU198 PHE211 TRP214 ALA215 LEU238 ALA291 PRO447 CYS448 TYR452 VAL455	TYR150 LYS195 LEU198 LYS199 TRP214 ARG218 LEU219 HIS242 ALA291 VAL343 PRO447 CYS448 VAL455
	Unfavorable[c]	---	ARG218	---	LYS195 ARG218	---	LYS199 ARG222

Kcal/mol = units of Estimated Free Binding Energy, Kilocalorie per mole; [a] Non-classical H-bonds: carbon-hydrogen; π-donor hydrogen bond; [b] Electrostatic interactions: π-cation; π-anion; attractive charge; salt bridge; [c] Unfavorable interactions: charge repulsion; [d] π-Sulfur interactions.

Table S2. Estimated free binding energy and interactions list of ibuprofen and squaraine dyes **5a**, **11a**,**b**, **12a**, and **13a** in Sudlow site II of human serum albumin.

Protein: 2BXG (Sudlow's Site II)		Ligand					
		Ibuprofen	**5a**	**11a**	**11b**	**12a**	**13a**
Estimated free binding energy (Kcal/mol)		-7.42	-8.36	-8.83	-10.21	-8.87	-9.41
Interactions	**Classical H-Bonds**	ARG410 TYR411	---	LYS351 ASN483	ARG349	ASN483	---
	Non-Classical H-Bonds[a]	---	ARG348	ASN483	LYS351 ASN483	---	SER480
	Van der Waals	---	---	---	---	---	---
	Electrostatics[b]	---	---	---	GLU479	---	---
	Miscellaneous	---	THR352[e]	---	CYS487[d]	---	---
	Hydrophobic	ILE388 CYS392 LEU407 LEU430 VAL433 CYS437 CYS438 ALA449 LEU453	ARG348 LYS351 PRO379 LEU380 PRO486 CYS487 ALA490	PRO379 LEU380 PRO486 CYS487 ALA490	THR352 GLU376 LEU380 PRO486 CYS487 ALA490	ARG348 LYS351 PRO379 LEU380 CYS476 PRO486 CYS487 ALA490	ARG348 LYS351 THR352 LEU380 ARG484 PRO486 CYS487 ALA490
	Unfavorable[c]	---	---	---	---	---	---

Kcal/mol = units of Estimated Free Binding Energy, Kilocalorie per mole; [a] Non-classical H-bonds: carbon-hydrogen; π-donor hydrogen bond; [b] Electrostatic interactions: π-cation; π-anion; attractive charge; salt bridge; [c] Unfavorable interactions: charge repulsion; [d] π-Sulfur interactions; [e] π-Lone-pair interactions.

Table S3: Estimated free binding energy and interactions of squaraine dyes **5a**, **11a**,**b**, **12a**, and **13a** in human serum albumin.

Protein: 2BXG (All Protein)		Ligand				
		5a	**11a**	**11b**	**12a**	**13a**
Estimated free binding energy (Kcal/mol)		-9.09	-6.84	-9.67	-8.66	-9.25
Interactions	**Classical H-Bonds**	---	ASN109 GLU425	LEU115	LYS106	---
	Non-Classical H-Bonds[a]	LEU115 TYR138 GLU141	---	ARG145	HYS105 ASP107	---
	Van der Waals	---	---	---	---	---
	Electrostatics[b]	ARG117	GLU425	ARG186 GLU425	ASP107	GLU141 ARG144
	Miscellaneous	---	---	---	---	MET123[d]
	Hydrophobic	LEU115 PRO118 MET123 PHE134 LYS137 ILE142 TYR161 LEU182 ARG186	PRO110 PRO421 VAL424 LEU463 ILE563	PRO110 ILE142 ARG145 TYR161 LEU182 ARG186 LYS190	MET87 HYS105 LYS106 PRO110 LEU112 LYS466	PHE36 PRO118 VAL122 ALA126 PHE134 LYS137 TYR140
	Unfavorable[c]	ARG117	---	---	ASP108	---

Kcal/mol = units of Estimated Free Binding Energy, Kilocalorie per mole; [a] Non-classical H-bonds: carbon-hydrogen; π-donor hydrogen bond; [b] Electrostatic interactions: π-cation; π-anion; attractive charge; salt bridge; [c] Unfavorable interactions: charge repulsion; [d] π-Sulfur interactions.

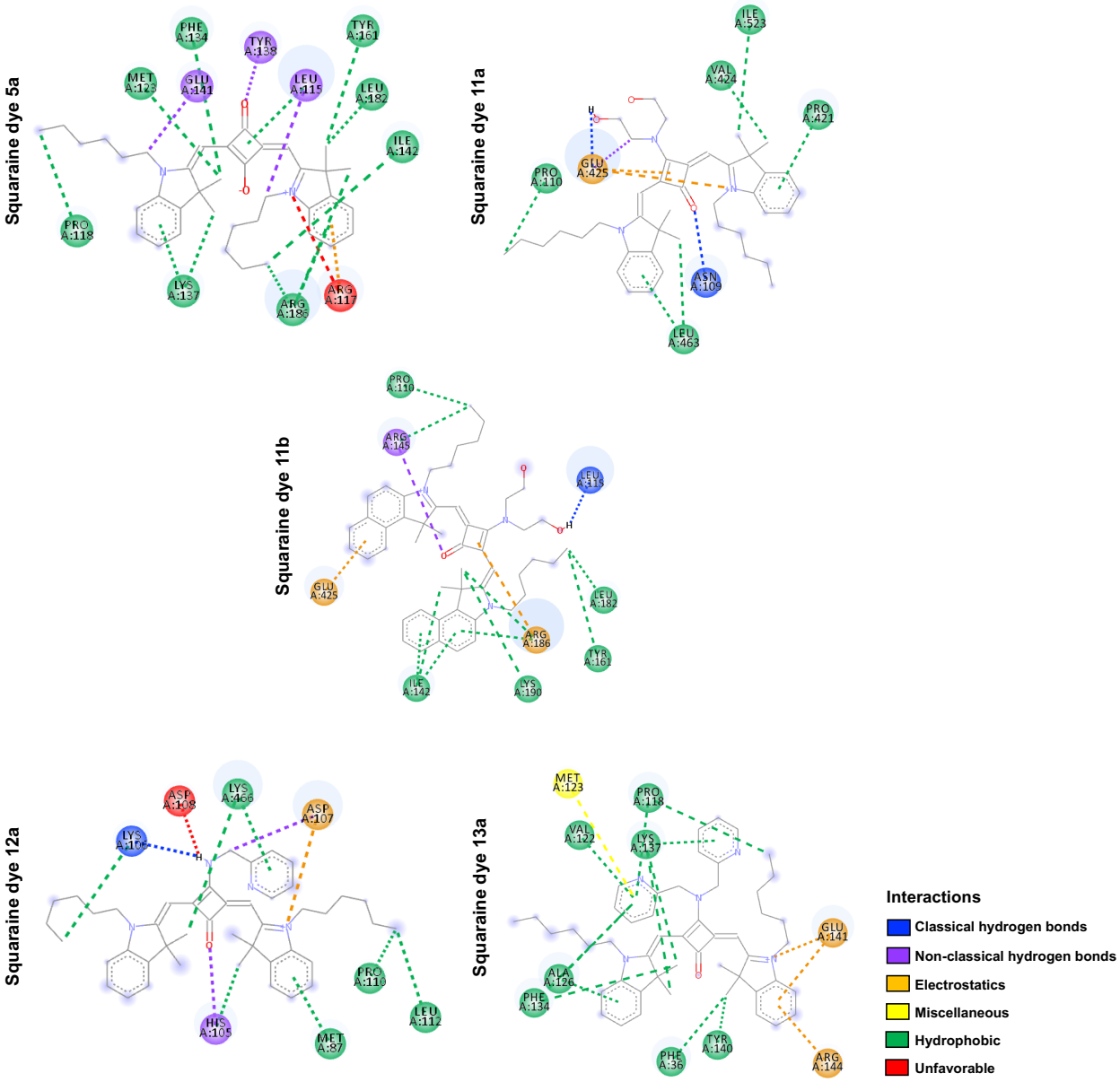

Figure S14. Binding modes and interactions of squaraine dyes **5a**, **11a**,**b**, **12a**, and **13a** with amino acid residues of human serum albumin protein.