

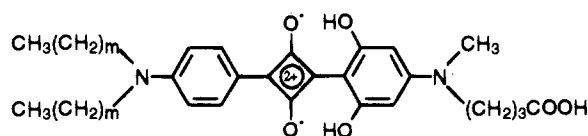
Amphiphilic Squaraine Dye Aggregates: Evidence for a Cyclic Chiral Structure as a General Supramolecular Structure for Aggregates of Dyes and Aromatic Molecules

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The formation of aggregates exhibiting blue shifts of the major long wavelength transitions in the absorption spectrum, often referred to as "H" aggregates, has been observed for a wide variety of aromatic molecules and dyes, especially for compounds in which the chromophores involved may be anticipated to be arranged in parallel stacks or "card packs".^{1–3} Such aggregates are frequently encountered in crystals⁴ and in organized assemblies such as Langmuir–Blodgett (LB) films and multilayers,^{1–3} where a combination of high effective concentrations and enforced organization should favor such packing. In very recent work, we have carried out a systematic study of the aggregates formed from *trans*-stilbene fatty acids and phospholipids.^{5,6} These investigations have led to evidence that the unit aggregate structure formed from the stilbenes is a chiral cyclic tetramer which may be envisioned as a fragment of an extended glide or herringbone lattice.⁶ Our results suggest that the "unit aggregate" may have considerable stabilization and may be reasonably considered a true "supramolecular" entity; the extended aggregate may be most correctly described as a mosaic of these unit structures. Investigations with structurally similar molecules such as related 1,4-diphenyl-1,3-butadienes, 1,6-diphenyl-1,3,5-hexatrienes, and *trans*-azobenzenes suggest that these chromophores may form small cyclic chiral aggregates of very similar structure and stability.⁷ Squaraine dyes such as **1** and **2**, which have strong absorption in the visible and structures quite different from the aforementioned compounds, also exhibit a strong tendency to form "H" aggregates in crystals, films, and arrested crystallites in solution.^{8–10} In the present paper, we present results obtained in a study of the aggregation of these molecules in solution and microheterogeneous media which lead us to propose a remarkably similar unit aggregate for the squaraines and suggest that a cyclic tetramer may be a very stable and general supramolecular structure.



Squaraine **1**: $m = 7$; **2**: $m = 3$

Squaraines **1** and **2**¹¹ form stable LB films at the air–water interface which can be readily transferred to optically transparent rigid supports; in both cases, these squaraines, similar to several others examined in different studies, exhibit strong blue shifts

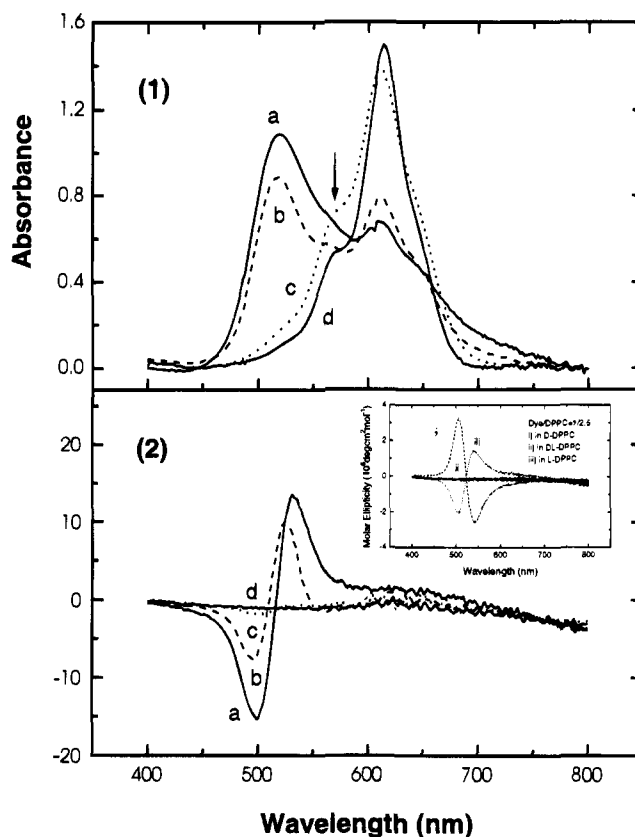


Figure 1. Squaraine **1** (1×10^{-5} M) dispersed in L-DMPC vesicles: (1) absorption (the arrow shows shoulder attributable to the dimer) and (2) CD spectra. Molar ratio of squaraine **1** to DMPC: (a) 1:2.5; (b) 1:5; (c) 1:10; (d) 1:50. Inset: CD spectra of squaraine **1** (1×10^{-6} M) dispersed in D-, L-, and DL-DPPC.

in their long-wavelength transitions (520 nm) compared to the maxima (650 nm) in dilute organic solutions.^{8–10} Unlike some of the other squaraines previously examined, these dyes are stable in the presence of water and can be prepared as aggregate (same λ_{\max} as for LB film) or monomer or a mixture of the two in dimethyl sulfoxide (DMSO)–water mixed solvent solutions. The dimer previously observed with other structurally similar squaraines,¹⁰ is not directly observable in these solutions (there is an isosbestic point between monomer and aggregate).¹² It is possible to examine the equilibration between aggregate and monomer over a moderate temperature range. The aggregate/monomer ratio decreases sharply as the temperature is raised from 5 to 55 °C. A Benesi–Hildebrand¹³ analysis of the equilibrium between monomer (M) and aggregate (Agg), where n is the aggregation number, according to eqs 1 and 2 for **2** in 50% (v/v) DMSO–water (A is the absorbance of aggregate at any concentration and A_0 is the absorbance of pure aggregate (no monomer present)), leads to an aggregation number of 4.1 ± 0.6 , $\Delta H_0 = -46$ kcal/mol, and $\Delta S_0 = -40$ cal/mol deg.

$$nM = \text{Agg} \quad (1)$$

$$\ln A = n \ln(A_0 - A) + \text{constant} \quad (2)$$

A similar analysis for **1** gives $\Delta H_0 = -40.7$ kcal/mol and $\Delta S_0 = -37.4$ cal/mol deg with $n = 5.2 \pm 0.5$.

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(12) Dimer formation ($\lambda_{\max} = 585$ nm for **1**) may be forced by adding γ -cyclodextrin to the solutions.

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Table 1. Predicted Possible Structures and Properties of Squaraine **2** Monolayers

structure	layer type	unit cell dimensions ^a			surface area ^b	tilt angle ^c	λ_1^d	λ_2^d	ratio ^e	energy ^f
		<i>a</i>	<i>b</i>	γ						
1	translation	7.98	4.23	91.33	33.71	42.25	513			
2	glide	17.91	4.66	90.00	41.75	55.51	565	596	0.69	1.09
3	translation	8.69	4.56	90.46	39.66	51.92	550			2.18
4	glide	14.97	5.59	90.00	41.83	32.80	518	632	0.19	4.14
5	translation	8.22	5.01	86.88	41.10	49.02	560			5.57
6	glide	8.28	8.84	90.00	36.60	41.30	527	659	0.01	5.62
7	glide	8.70	8.59	90.00	37.36	40.80	528	659	0.00	6.53
exptl					38.0	51	520	655		

^a Unit cell dimensions *a* and *b* in angstroms; angle γ in degrees.

^b Surface area/molecules in Å². ^c Tilt of transition moment with respect to surface normal in degrees. ^d Exciton spectra peaks in nanometers. λ_1 and λ_2 for the glide layer as a result of the Davydov splitting. ^e Computed ratio of the oscillator strengths $f(\lambda_2)/f(\lambda_1)$ for the Davydov splitting. ^f Energy above the apparent global minimum (structure 1) in kilocalories.

1 can be incorporated as a "guest" into phospholipid vesicles in water. As shown in Figure 1, the absorption spectrum for relatively high ratios of squaraine to phospholipid (dimyristoylphosphatidylcholine (DMPC) or dipalmitoylphosphatidylcholine (DPPC)) shows a predominance of the blue-shifted (520 nm) aggregate, similar to the spectra obtained in LB films or in DMSO–water mixtures. At lower dye/DMPC ratios (<1:10), the spectrum of the monomer is dominant, and a small trace of dimer can also be detected. The value for *n* for **1** in the DMPC–water solutions was estimated to be 3.5 ± 1 . The vesicles obtained for DMPC–**1** mixtures were analyzed by light scattering;¹⁴ interestingly, it was found that structures considerably larger than simple DMPC vesicles (diameter ≈ 12 nm)¹⁵ were obtained for both concentrated (dye/DMPC = 1:2.5) and dilute (1:10) mixtures, with measured values of 175 and 292 nm (diameters), respectively.¹⁶ Additional evidence concerning the aggregate structure and aggregate incorporation into the mixed vesicles is provided by examining the circular dichroism spectra of the **1**–DMPC mixtures in water. When **1** is dispersed in L-DMPC (R isomer), the blue-shifted aggregate shows a strong biphasic induced circular dichroism (ICD) spectrum in the range 450–550 nm whose crossing point coincides with the λ_{max} of the major exciton band (Figure 1). As shown in Figure 1, when the ratio of DMPC to dye is increased so that appreciable amounts of dimer and monomer are present, the ICD signal still corresponds to the aggregate exciton, with little or no signal corresponding to the former two species. This is reasonable since the squaraine chromophore is achiral, and in dilute vesicles, the monomer and dimer are likely too far removed from the chiral center in the phospholipid host for there to be a strong chiral perturbation of the chromophore. The observation of a strong ICD from the aggregate suggests that the aggregate is chiral, as has been suggested recently for other systems.^{6,17–19} The signal obtained when **1** is dispersed in water with D-DPPC (Figure 1) is the inverse of that obtained when the dye is dispersed with L-DPPC under the same conditions, while no ICD is observed when the dye is dispersed in DL-DPPC. Neither the absorption nor the ICD spectra for **1** show changes as the solutions are heated through the phase transition temperature for DPPC (43 °C).

(14) We thank Dr. Thomas Whitesides for providing the light scattering measurements.

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(16) The polydispersities of the vesicles are 0.19 and 0.18, respectively. Evidence for large vesicles is also shown by membrane filtration experiment, in which the mixed vesicles cannot be extruded through 100 nm filters, through which pure DMPC and DPPC can be easily extruded.

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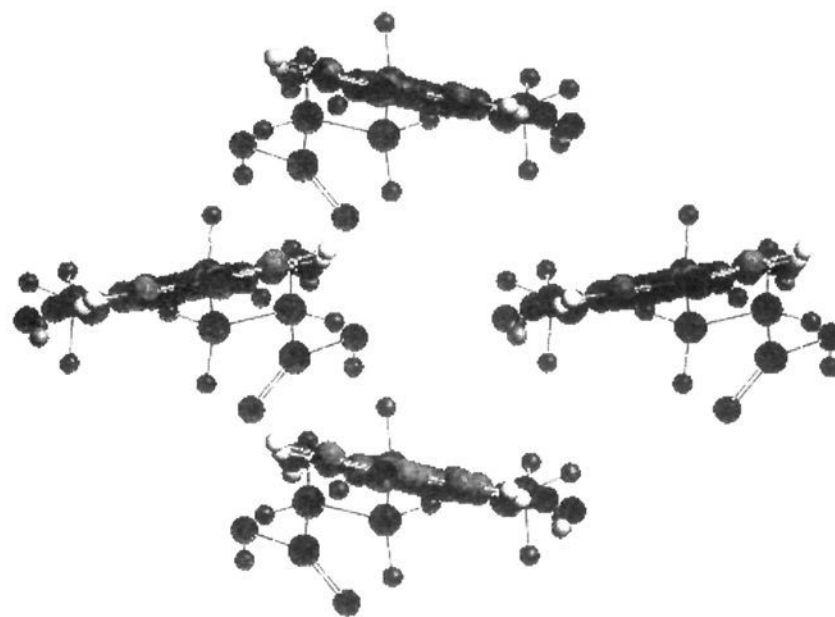


Figure 2. "Overhead" view of a tetramer unit within the simulated monolayer assembly of squaraine **2** (23 molecules) in the glide layer arrangement, which has reasonable agreement with experimental data (structure 6 in Table 1).

Monte Carlo simulations^{10,20,21} for a monolayer of **2** indicate that a glide layer or herringbone arrangement should be the lowest energy arrangement that shows reasonable agreement between measured and calculated values for molecular area, exciton shifts, and tilt angle of **2** in the monolayer (Table 1).²² From the measured aggregation numbers, the strong indications of a chiral structure for the unit aggregate, and the molecular simulations, we propose the pinwheel structure shown in Figure 2 for the unit aggregate. This structure is essentially the same as that proposed earlier for the aggregates of trans-stilbene and it seems especially reasonable for aggregates of the squaraines. As pointed out for the stilbenes, the "pinwheel" structure permits "T" interactions between the component molecules and can be related to the most stable configuration for the dimer of benzene and other aromatics.^{23–27} To gain some idea of the strength of the various interactions that may occur for the squaraines, it is useful to compare the stabilization of the dimer of a compound structurally similar to **2** with the aggregates of **1**. For the dimer, values of $\Delta H_0 = -6.8$ kcal/mol and $\Delta S_0 = -1.83$ cal/mol deg were obtained;¹⁰ presumably, the dimer has a face-to-face or near-parallel arrangement of the squaraines. In contrast, the proposed tetramers have stabilizations of ~ 40 – 46 kcal/mol where there are four "T" interactions and perhaps a very weak face-to-face interaction.²⁸ This leads to a minimum estimate that the "T" interactions must be on the order of 10 kcal/mol each, which seems quite reasonable for the squaraines.

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