Aggregate Formation and Photoreactivity in Phospholipid Vesicles and Langmuir–Blodgett Multilayers: Topologically Controlled Photodimerization of Amphiphilic Styrenes

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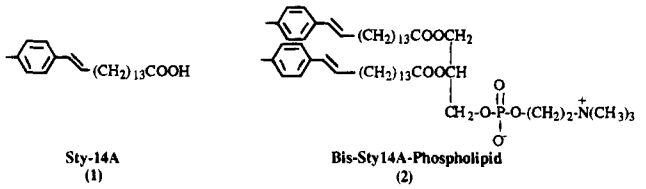
Abstract: The amphiphilic styrene fatty acid **1** and its corresponding phosphatidylcholine derivative **2** have been found to exhibit aggregate formation and topologically controlled photodimerization in Langmuir–Blodgett (LB) assemblies and phospholipid vesicles, respectively. For both compounds, formation of the β or syn, head-to-head photodimer is the chief photoreaction observed upon irradiation in the assemblies; a trace of the cis styrene is observed on irradiation in the phospholipid vesicles. Changes in the absorption spectrum and a lack of fluorescence in the assemblies, compared to dilute organic solutions, suggest that **1** and **2** exist as "H" aggregates in both the LB films and vesicles. Monte Carlo simulations suggest that the most stable structure in a monolayer is a simple translation aggregate. Energy minimization gives a cross sectional area in good agreement with that measured for films at the air–water interface. The calculated structure has nearest neighbor separation within the "magic distance" for solid state photodimerization of 4.10 Å. The relatively small calculated tilt angle suggests that dimers can be formed without substantial reorganization. The λ_{max} for the aggregate estimated by an extended dipole calculation shows good agreement with the measured absorption maximum. Vesicles of **2**, either pure or with excess saturated phospholipid, give topologically controlled formation of the β dimer via photolysis of an aggregated form.

Introduction

Topologically controlled photodimerization and photoaddition reactions have been well studied for crystalline solids of a variety of substances;[1–3] related examples have been reported for Langmuir–Blodgett (LB) multilayers, reversed micelles, and other types of organized media.[4–8] In the latter, high effective local concentrations of reactive chromophores, often in fixed or controlled relationship to one another, can lead to detectable aggregates which are characterized by altered spectra and photophysics compared to the solution monomer.[9–14] Some of the major questions concerning aggregation of organic chromophores, especially aromatic and unsaturated hydrocarbons, include the extent of delocalization or π-interaction in ground and excited states and the factors which control aggregate size, structure, and reactivity.[12,14–17] As part of a study of the range of aggregates formed between diverse and multifunctional organic chromophores in microheterogeneous media, we have recently studied a series of functionalized fatty acids which should presumably incorporate into a variety of assemblies in a predictable manner.[14,15] Herein we report an investigation of an amphiphilic styrene fatty acid (**1**) and its corresponding phosphatidylcholine derivative (**2**) in LB assemblies and in aqueous solution, respectively. We find that both **1** in LB assemblies and **2** in aqueous vesicles give topologically controlled formation of a single dimer via photolysis of an aggregated form.



Sty-14A (1) Bis-Sty14A-Phospholipid (2)

Experimental Section

Materials. Sodium bicarbonate (Baker Analyzed Reagent) and cadmium chloride $2^1/_2$ hydrate (Baker Analyzed Reagent) were used as received. Chloroform (Baker, HPLC grade) for monolayer work was used as received. All other solvents were used as received except where otherwise specified. Langmuir–Blodgett films were formed using water deionized and polished with a Millipore purification system.

Synthesis of Styrene 1 (Sty-14A). Unlabeled **1** was prepared as reported previously:[18] 1,16-Hexadecanedioic acid (Lancaster) was

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converted to the dimethyl ester; the diester was hydrolyzed to the monoester monoacid by barium hydroxide and isolated as its barium salt. The monoacid was converted to its acid chloride by treatment with oxalyl chloride; a Friedel–Crafts coupling with toluene/$AlCl_3$ led to a keto ester, which was reduced by $NaBH_4$ to the corresponding alcohol. The alcohol was converted to the corresponding tosyslate, which afforded the styrene ester via base-catalyzed elimination. Hydrolysis afforded **1**: mp 83.7–84.5 °C; λ_{max} 256 nm (in methanol, acetonitrile, or chloroform); ^{1}H-NMR δ 1.29 (m), 1.47 (m), 1.66 (m), 2.21 (m), 2.35 (m), 2.35 (t), 6.19 (m), 6.37 (d), 7.12 (d), 7.26 (d).

^{13}C-labeled **1** was prepared via the dinitrile.[19] 1,14-Tetradecanediol (Aldrich, 1 g, 4.35 mmol, 1 equiv) and *p*-toluenesulfonyl chloride (Aldrich, 1.83 g, 9.57 mmol, 2.2 equiv) were mixed and partially dissolved in 2 mL of dry methylene chloride. Anhydrous pyridine (Aldrich, 35 mmol, 8 equiv) was injected dropwise to the solution under nitrogen at 0 °C. The solution was kept at temperatures below 20 °C by immersion in a water bath with stirring for 3 h. Cold, aqueous hydrochloric acid (10%) was added to the solution until it was acid to pH paper. The mixture was then extracted three times with methylene chloride, and the organic layers were combined, washed with water and saturated sodium chloride, and dried over anhydrous sodium sulfate. Removal of the solvent afforded a light yellow solid. Recrystallization from ethanol yielded white crystals of the 1,14-tetradecanediol ditosylate in 92% yield. R_f = 0.28 (20/80 ethyl acetate/hexane). A mixture of the 1,14-tetradecanediol ditosylate (1 g, 1.86 mmol, 1 equiv) and dry ^{13}C-labeled sodium cyanide (Aldrich, dried at 90 °C under vacuum overnight prior to use, 0.23 g, 4.46 mmol, 2.45 equiv) was treated with 10 mL of anhydrous dimethyl sulfoxide (Aldrich) and heated gently (below boiling) for 0.5–1 h. Water was added, and the mixture was extracted with methylene chloride four times. The organic extracts were combined, washed twice with saturated sodium chloride, and dried over anhydrous magnesium sulfate. Removal of the solvent afforded a yellow solid, which was purified by being passed through a silica column using 20/80 ethyl acetate/hexane. The dinitrile was obtained as a white solid. R_f = 0.37 (20/80 ethyl acetate/hexane); yield = 95%; ^{13}C-NMR ($CDCl_3$): δ = 120.6 (C*N).

The labeled dinitrile (0.55 g, 2.2 mmol, 1 equiv) in 2.2 mL of dry benzene was reacted with a solution of *p*-tolylmagnesium bromide in ether (Aldrich, 1 M, 2.2 mL, 1 equiv) by dropwise addition of the latter solution under nitrogen at 0 °C.[20] The resultant yellow slurry was allowed to warm to room temperature and stirred for an additional 2 h. The red slurry which was left was cooled in an ice bath and treated with 2.7 mL of water and 0.54 mL of 6 M aqueous sulfuric acid. The organic solvent was removed by rotary evaporation, and the remaining mixture was extracted with four portions of methylene chloride. The combined methylene chloride extracts were washed with saturated potassium carbonate and water and then dried over magnesium sulfate. The crude product was dissolved in 5/95 ethyl acetate/hexane and passed twice through a silica column. The *p*-tolyl-14-cyano tetradecyl ketone was obtained as a white solid in 37% yield. R_f = 0.51 (20/80 ethyl acetate/hexane); ^{13}C-NMR ($CDCl_3$): δ 200.9 (PhC*=O), 120.6 (C*N).

The keto nitrile was converted to the styrene nitrile by the following procedure. To a solution of *p*-tolyl-14-cyano tetradecyl ketone (0.26 g, 0.758 mmol, 1 equiv) in methanol (19.5 mL) was added sodium borohydride (Aldrich, 0.06 g, 1.52 mmol, 2 equiv). The resulting clear solution was stirred at room temperature overnight. After acidification with aqueous hydrochloric acid (10%) the mixture was extracted four times with methylene chloride. The organic extracts were combined and dried over anhydrous magnesium sulfate. The solvent was removed, and the residue was used (after drying under vacuum) directly in the next step without further purification. The hydroxy nitrile (0.26 g, 0.75 mmol, 1 equiv) and *p*-toluenesulfonic acid monohydrate (Aldrich, 0.03 g, 0.15 mmol, 0.2 equiv) were mixed and dissolved in 22 mL of benzene. The flask was connected to a Dean–Stark trap and the reaction mixture allowed to reflux (3 h) until no additional water was collected. The crude product was passed through a silica column using ethyl acetate/hexane (5/95). The labeled styrene nitrile was obtained in 78% yield. R_f = 0.36 (10/90 ethyl acetate/hexane). ^{13}C-NMR ($CDCl_3$): δ 130.3 (PhC*H=CH), 120.6 (C*N).

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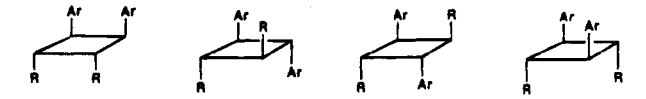
Scheme 1. Possible Isomeric Photodimer Products[a]



trans-syn-trans dimer (3,7) | trans-anti-trans (4) | trans-cis-trans (5) | trans-trans-trans (6)

[a] **3a–6a**: Ar = phenyl, R = $(CH_2)_4CH_3$. **3b–6b**: Ar = phenyl, R = COOH. **7**: Ar = *p*-tolyl, R = $(CH_2)_{13}$COOH.

The styrene nitrile (0.19 g, 0.58 mmol, 1 equiv) was dissolved in diethylene glycol (Aldrich, 19.5 mL) with heating.[21] A 3 M potassium hydroxide solution (1.95) was added dropwise at room temperature. The mixture was refluxed for 24 h; the resulting red solution was acidified with 10% aqueous hydrochloric acid and extracted with four portions of methylene chloride. Purification by passing an ethyl acetate solution over silica afforded the crude product; recrystallization from methanol gave white crystals of **1** in 75% yield. R_f = 0.18 (20/80 ethyl acetate/hexane); mp 81–82 °C; IR (KBr) 1660, 2929 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ 1.29 (m), 1.47 (m), 1.66 (m), 2.21 (m), 2.35 (s), 2.35 (t), 6.19 (m), 6.05–6.62 (dd), 7.12 (d), 7.26 (d); ^{13}C-NMR ($CDCl_3$) δ 179.4 (HOC*=O), 130 (PhC*H=CH). Anal. Calcd for $^{12}C_{21}{}^{13}C_2H_{36}O_2$: C, 79.71; H 10.47. Found: C, 78.92; H, 10.61.

Bis(styrene) Phospholipid 2. The conversion of **1** to **2** was accomplished by a literature preparation coupling the mixed anhydride of **1** to *sn*-glycero-3–phosphocholine (Sigma).[22,23] All glassware was flame-dried. Methylene chloride was distilled over calcium hydride. Triethylamine was dried over Linde type 4-Å molecular sieves for 30 min and distilled from barium oxide. *sn*-Glycero-3-phosphocholine (cadmium chloride complex, Sigma) was dried under vacuum before use. 4-(*N*,*N*-Dimethylamino)pyridine (DMAP) was recrystallized from chloroform/ether (1/1), and trimethylacetyl chloride was obtained from Aldrich. Rexyn I-300, mixed resin, was obtained from Fisher.

Sty-14A (0.5 g, 1.45 mmol, 1 equiv) was mixed with 30 mL of dry methylene chloride. Triethylamine (250 μL, 1.74 mmol, 1.2 equiv) was injected into the reaction mixture under nitrogen, followed by 720 μL (5.8 mmol, 4 equiv) of trimethylacetyl chloride. The colorless solution was stirred at room temperature for 6 h. The solution turned orange. The methylene chloride was removed under vacuum, and the crude mixed anhydride was dried in a desiccator under vacuum for 1 h.

The crude mixed anhydride (0.5 g, 1.167 mmol, 4 equiv) was mixed with *sn*-glycero-3-phosphocholine as a cadmium chloride complex (0.128 g, 0.29 mmol, 1 equiv) and DMAP (0.071 g, 0.58 mmol, 2 equiv). The mixture was dissolved in 15 mL of dry methylene chloride, and the solution was stirred at room temperature for 40 h. After the solvent was removed, the residue was passed through a Rexyn I-300 column using methanol/chloroform/water, 5/4/1, v/v/v, as eluent. Benzene/ethanol, 3/2, v/v, was used to remove water as an azeotrope. The crude yellow product was recrystallized from chloroform/ether to yield white crystals. The isolated yield of the product was 30%: R_f = 0.23 (methanol/chloroform/water, 25/6.5/4, v/v/v); ^{1}H-NMR ($CDCl_3$) δ 1.25 (m), 1.45 (m), 1.58 (m), 2.18 (m), 2.28 (t), 2.32 (s), 3.35 (s), 3.79 (m), 3.97 (m), 4.13 (m), 4.38 (m), 5.22 (m), 6.17 (m), 6.33 (d), 7.08 (d), 7.23 (d); λ_{max} 356 nm (methanol or acetonitrile); FAB MS calcd for $C_{54}H_{88}O_8NP$ MW 910.2792, found 910.6283.

^{13}C-Labeled 2. Procedures similar to those described above were used. The isolated yield of product was 53%: R_f = 0.22 in methanol/chloroform/water, 25/6.5/4, v/v/v; ^{1}H-NMR ($CDCl_3$) δ 6.04–6.60 (dd) (all other peaks same as for **2**); ^{13}C-NMR ($CDCl_3$) δ 130 (PhC*H=CH), 179–179.3 (C*OO); FAB MS calcd for $^{12}C_{50}{}^{13}C_4H_{88}O_8NP$ MW 914.2346, found 913.6414.

Model Compounds 3a–6a. The model cyclobutane dimers **3a–6a** (Scheme 1) were prepared by similar methods as outlined in Scheme 2 and reported in detail for **3a** as follows. The precursor dimers of

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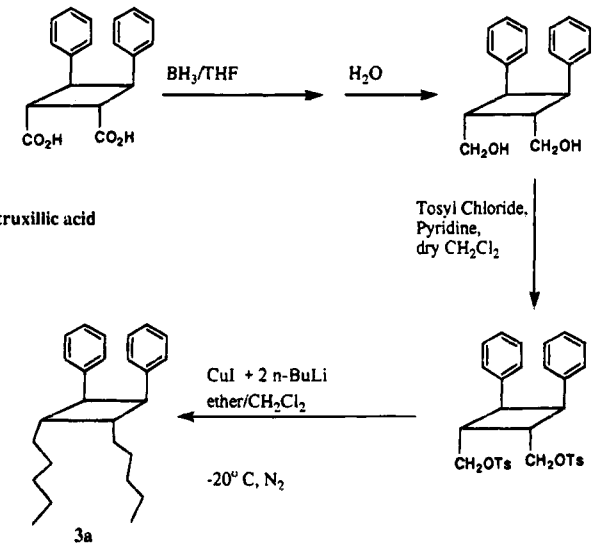
Scheme 2. Synthesis of Compound **3a**



requisite stereochemistry for **3a**–**6a**, β-truxillic acid[24] (**3b**, R = COOH), δ-truxillic acid[25] (**4b**, R = COOH), α-truxinic acid[26] (**5b**, R = COOH) and ϵ-truxinic acid[27] (**6b**, R = COOH), respectively, were synthesized by procedures available in the literature. β-Truxillic acid (0.8 g, 2.8 mmol, 1 equiv) was dissolved in 30 mL of dry tetrahydrofuran under nitrogen. The solution was treated by dropwise addition of the borane–tetrahydrofuran complex (Aldrich, 1 M, 7.5 mL, 8/3 equiv) while cooling in an ice bath. The colorless mixture was refluxed under nitrogen for 2 h. Water was added to quench excess borane. After the THF was removed by rotary evaporation, the remaining mixture was extracted with four 20 mL portions of ether. The ether layers were combined and dried over anhydrous sodium sulfate. The crude product (a colorless oil) was recovered by rotary evaporation and recrystallized to give the diol as a white solid in 93% yield. The β-diol (0.6 g, 2.2 mmol, 1 equiv) and *p*-toluenesulfonyl chloride (Aldrich, 0.94 g, 4.9 mmol, 2.2 equiv) were mixed and partially dissolved in 3 mL of dry methylene chloride. Dry pyridine (Aldrich, 1.45 mL,18 mmol, 8 equiv) was injected dropwise under nitrogen at 0 °C. The resulting light yellow solution was stirred over a water bath below 20 °C for 2 h and then acidified by addition of 10% hydrochloric acid. The mixture was extracted three times with methylene chloride. The combined methylene chloride solutions were washed with water and saturated sodium chloride and dried over anhydrous sodium sulfate. The crude product, obtained by rotary evaporation, was reduced to the hydrocarbon as follows.[28] A suspension of copper(I) iodide (Aldrich, 99.999%, dried with phosphorus pentoxide at 90 °C under vacuum overnight, 0.58 g, 3 mmol, 4 equiv) in 4 mL of freshly distilled ether at −30 °C was treated by dropwise addition of an *n*-butyllithium solution in hexane (Aldrich, 2.5 M, 2.4 mL, 8 equiv). A yellow slurry formed immediately upon addition of the *n*-butyllithium; as the remainder was added, a dark red-brown solution was obtained. The solution was stirred for 10 min at −30 °C. The β-ditosylate (0.44 g, 0.75 mmol, 1 equiv) was dissolved in 3 mL of freshly distilled ether and then added dropwise to the lithium di-*n*-butylcuprate solution at −30 °C. The reaction mixture was stirred at −20 °C for 1.5 h. A saturated solution of ammonium chloride was added to the reaction mixture at −20 °C, and the resulting mixture was stirred for 10 min. This mixture was extracted with three portions of ether. The ether layers were combined, washed twice with saturated sodium carbonate and once with water, and dried over sodium sulfate. Removal of the solvent afforded a yellow liquid, which was purified by being passed through a silica column using hexane. **3a** was obtained as a very pale yellow liquid: R_f (hexane) = 0.29; ^{1}H-NMR ($CDCl_3$) δ 0.87 (t), 1.24 (m), 1.63 (m), 2.76 (m), 3.56 (m), 6.90–7.05 (m).

4a, 5a, and **6a** were obtained by similar procedures. **4a**: ^{1}H-NMR ($CDCl_3$) δ 0.80 (t), 1.17 (m), 1.56 (m), 2.02 (m), 2.90 (d), 7.12–729 (m). **5a**: R_f = 0.39 (hexane); ^{1}H-NMR ($CDCl_3$) δ 0.77 (t), 1.0–1.2 (m), 2.94 (m), 3.40 (d), 7.20–7.32 (m). **6a**: R_f = 0.35 (hexane); ^{1}H-NMR ($CDCl_3$) δ 0.74 (t), 1.08 (m), 1.55 (m), 2.33 (m), 2.55 (d), 7.18–7.30 (m).

Monolayer Film and Multilayer Deposition Studies. The general methods for preparing Langmuir–Blodgett films and assemblies and the cleaning of the substrates have been described elsewhere.[11,29] Styrene **1** was found to form stable films at pressures of 20 dyn/cm^2 which could be transferred to quartz supports as Y-type multilayers. Up to 45 layers could be coated on each side of a slide with maintenance of a good transfer ratio. For preparative isolation of Langmuir–Blodgett film photolysis products, the coated slides were irradiated at 300 nm in a Rayonet photochemical reactor for 15 min. The photolysis products were washed from the slides by Soxhlet extraction with HPLC grade chloroform, concentrated, and examined by 300 MHz ^{1}H-NMR and ^{13}C-NMR.

The styrene phospholipid **2** forms a fairly stable monolayer film at the air–water interface with a mean molecular area of 63 Å^2. A single layer of the film could be transferred to a quartz support at a surface pressure of 18 dyn/cm^2; however, good multilayer assemblies could not be obtained.

Vesicle Preparation. Solutions of the bis(styrene) phosphatidylcholine **2** in chloroform were transferred to a scintillation vial; the solvent was evaporated by flushing with nitrogen, and the residue was dispersed in deionized water with sonication to give a solution formally 6.24×10^{-4} M in **2.** The sonication with an Ultrasonic, Inc., Model W220f probe sonicator (setting 6.5 (35 W)) was carried out during four 15 min periods with an intervening 5 min delay for cooling. The stock vesicle solution was centrifuged for 30 min at 3500 rpm using a Fisher Scientific centrifuge; the slightly translucent supernatant fraction was carefully removed by a pipet.

Spectra. Absorption spectra were recorded on an IBM 9430 UV–visible spectrophotometer. Fluorescence spectra were recorded on a SPEX 111 CM spectrofluorimeter containing two single beam monochromators and a 150 W Xe light source and a thermoelectrically cooled photodetector. NMR spectra were recorded on a GE 300 MHz spectrometer.

Results and Discussion

Styrene **1** was prepared as reported previously.[18] A doubly ^{13}C labeled styrene, containing ^{13}C at the α-olefinic and carboxylate carbons, was also prepared by a different route involving condensation of $^{13}CN^-$ with 1,14-tetradecanediol ditosylate and subsequent Grignard reaction of *p*-tolylmagnesium bromide with the resulting dinitrile. The conversion of the keto nitrile to doubly labeled **1** was accomplished by reduction, tosylation, and elimination to yield the styrene, followed by hydrolysis of the nitrile to the acid. The conversion of **1** to **2** (for both labeled and unlabeled compounds) was accomplished by procedures developed for other modified phosphatidylcholine derivatives.[22,23] **1** forms stable monolayer films when spread from chloroform solution at the air–water interface showing isotherms very similar to that of arachidic acid with a limiting molecular area of 21 Å^2; the films are readily transferred to quartz supports at a pressure of 20 mN/cm^2. The absorption spectra of **1** in LB films and organic solutions are compared in Figure 1. Phospholipid **2**, soluble in organic solvents, forms clear solutions when dispersed in water alone or together with the saturated phospholipid, dipalmitoylphosphatidylcholine (DPPC), by probe sonication, followed by centrifugation under conditions generally leading to small unilamellar vesicles. The absorption spectra of **2** in water and

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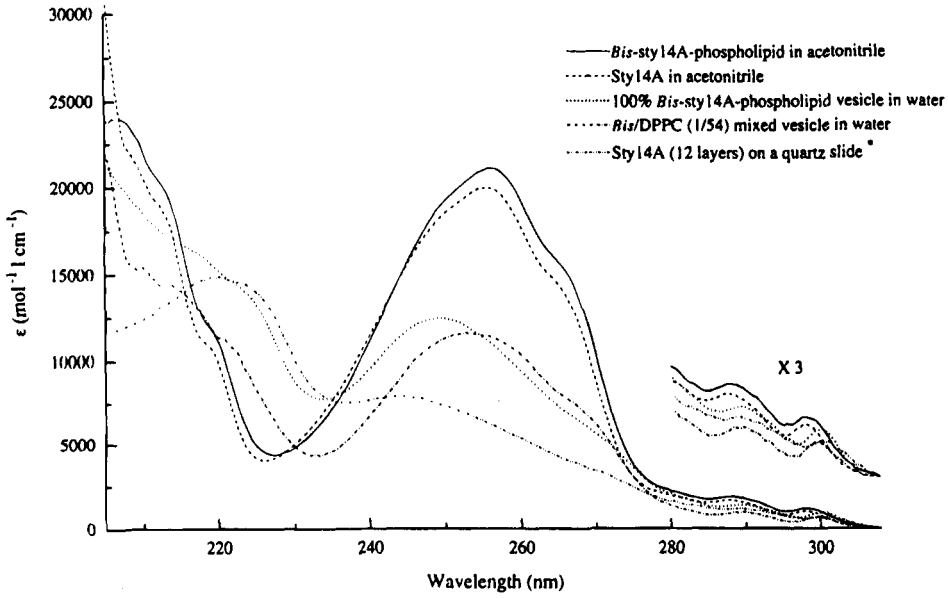

Figure 1.

water containing **2** and DPPC in a ratio of 1/54 are also shown in Figure 1. Although **1** and **2** exhibit strong fluorescence when dissolved in dilute organic solvents, no fluorescence is observed from **1** in the LB films or from **2** in water or water with DPPC. Irradiation of **1** in LB films at $\lambda = 300$ nm (on the edge of the UV absorption) gives rise primarily to a single product; a fast atom bombardment mass spectrum of the photoproduct mixture from unlabeled **1** gives a molecular weight of 688.6, indicating that the product is a dimer. A similar reaction is observed when aqueous vesicles of **2** or **2**/DPPC are irradiated under the same conditions. The photoproduct from **1** irradiated in the supported assemblies was recovered by Soxhlet extraction with chloroform. The photoproduct from irradiation of **2** was recovered after hydrolysis of the phospholipid by reflux with KOH in water.

^{1}H- and ^{13}C-NMR spectra of the photoproducts from **1** and **2** in LB films and vesicles, respectively, together with the mass spectral data, indicate that the predominant product in both cases is a cyclobutane dimer formed by 2 + 2 cycloaddition across the ethylenic bond similar to those formed in photolysis of crystals of cinnamic acid and related compounds.[1,2,26] The isosbestic points observed during the irradiation together with the isolation and detection of one major product[30] (**7**) suggest that the photoreaction occurs with a topological control enforced by the ordered arrangement of the monomer (or dimer in the case of **2**). As shown in Scheme 1, there are four possible dimers arising from addition of two trans units of **1**. In order to determine which dimer is in fact formed in these irradiations, the similarly functionalized cyclobutane dimers **3a**−**6a** were synthesized as shown in Scheme 2 from the corresponding cinnamate photodimers (**3b**−**6b**, R = COOH).[24−27] As shown in Table 1, the ^{1}H-NMR spectrum of **7** in the aromatic and cyclobutane proton regions is very similar to that of the β-dimer **3a** and distinctly different from those of the other three possible photodimers. It is therefore reasonable to conclude that the primary photoproduct in both the LB assemblies and phospholipid vesicles is the β-dimer which arises from a parallel head-to-head alignment of the styrene chromophores in both organized media.

The ^{13}C- and ^{1}H-NMR spectra of photoproduct **7** recovered from photolysis of the doubly ^{13}C labeled **1** and **2** in LB films and vesicles, respectively, also are consistent with formation

(30) The only other product detectable from irradiation of the aqueous phospholipid solutions is a trace of the *cis*-styrene.

Table 1. ^{1}H-NMR Chemical Shifts for Photodimer **7** and Model Compounds **3a**−**6a**[a]

	δ_A (ppm)	δ_B (ppm)	aromatic region
7	3.47 (d)	2.69 (m)	6.85 (m)
3a	3.56 (d)	2.76 (m)	6.98 (m)
4a	2.90 (m)	2.02 (m)	7.21 (m)
5a	3.40 (dd)	2.94 (m)	7.29 (m)
6a	2.55 (t)	2.33 (m)	7.22 (m)

[a] ^{1}H-NMR data from $CDCl_3$: proton A is on the cyclobutane ring, adjacent to a phenyl; proton B is on the cyclobutane ring adjacent to the fatty acid chain.

of a single cyclobutane dimer. In the ^{1}H spectrum of labeled **1** the peak assigned to the α-vinyl proton is strongly split (doublet of doublets, $\delta = 6.09-6.60$); this peak is replaced upon photolysis by a split peak ($\delta = 3.3-3.72$) for **7** in the region assigned to the cyclobutane protons. The ^{13}C spectra are even simpler; for **1** the two singlets at $\delta = 178$ and 130 are replaced in the photoproduct (**7**) from LB films and vesicles by two singlets at $\delta = 180$ and 49.1. The simplicity of the ^{13}C-NMR spectra makes it especially easy to follow the reaction in different media. When **1** or **2** is dissolved in an organic solvent such as dilute ($10^{-4}-10^{-5}$ M) acetonitrile and irradiated under the same conditions used for the LB films or vesicles, it is found that a new peak grows in at $\delta = 129$ concurrent with a bleaching of the long-wavelength transitions in the UV spectrum. This peak can be reasonably assigned to *cis*-**1**, which is anticipated to be the major photoproduct under conditions where the dimerization cannot occur. Careful analysis of the proton-decoupled ^{13}C-NMR spectra from irradiated samples of **1** and **2** in pure LB films and vesicles indicates that there are traces of the 129 ppm peak observable in both cases for samples subjected to prolonged irradiation. In the vesicles there appear also to be traces of other products giving ^{13}C signals near $\delta =$ 47.4 and 47.2 which could be due to traces of other photodimers.

The fact that both pure vesicles of **2** and mixed vesicles, where **2** is diluted with the saturated phospholipid DPPC in 20−54-fold excess, give the same photoproduct in comparable purity (compared to cis or other photodimers), as indicated by ^{13}C-NMR spectra, suggests that both intermolecular and intramolecular photodimerization processes may occur in the vesicles. This is somewhat surprising since the dilute vesicles show absorption spectra very similar to those of monomer in dilute solution, and it would be reasonable to suspect that the styrene

groups at the ends of two chains of the same overall length might be sufficiently offset in the phospholipid bilayer to result in a mismatch inhibiting intramolecular dimerization.

The shifts in absorption spectra for both **1** and **2** in the organized assemblies resemble those previously observed with *trans*-stilbene fatty acid derivatives[10,11,15] for which an "H" type of aggregation has been suggested. However, the spectral shifts observed with the styrenes are much smaller in magnitude, which might be taken as evidence that the aggregate size for the styrene is smaller.[31] Monte Carlo simulations[32] on assemblies of **1** suggest that the most stable structure in the monolayer may be a simple translation aggregate. Energy minimization on a single layer consisting of 23 molecules of **1** gives a cross sectional area per molecule in the layer of 20.72 Å^2, which is within experimental error of the measured value (21 Å^2). In the lowest energy structure each styrene has nearest neighbors in the translation layer with a separation between adjacent and nearly parallel double bonds of 4.10 Å, within the "magic distance" of 3.5−4.2 Å,[2] while the next nearest neighbor is separated by a considerably larger distance (5.05 Å). The relatively small calculated "tilt angle" of 37.2° with respect to the normal allows the two double bonds in a nearest neighbor pair to react without substantial reorganization. It is also possible to calculate the predicted aggregate absorption spectral shifts for this structure using the extended dipole approximation developed by Czekklely, Forsterling, and Kuhn.[33] For this computation a transition dipole moment of 4.66 D was estimated from the oscillator strength of the monomer at 256 nm in cyclohexane solution. The dipole length was estimated as 4.44 Å, and a dielectric constant of 2.5 was assumed. The predicted λ_{max} for the aggregate in the global minimum structure is 241 nm, in fairly good agreement with the observed value of 244 nm.

The aggregates characterized in this study and their photophysical/photochemical behavior offer an interesting contrast among the intermediate size aggregates recently observed with stilbene amphiphiles[15] and the much larger aggregates occurring with similarly functionalized squaraines.[14] The quite different aggregate sizes and properties from different monomeric structures indicate that the individual chromophore molecular properties exert a much greater control than might have been previously expected. Thus, while hydrophobic and/or packing interactions may be crucial in controlling the macrostructure formed by association of functionalized amphiphiles, the specific π-interactions leading to the "supramolecular" assembly and its reactivity appear determined largely by the specific properties of the molecular unit.

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(31) That the aggregate size is greater than 2 is suggested by the observation of a more pronounced shift for **2** in the "pure" vesicle than for what should be an isolated dimer in the 1/54 DPPC-diluted vesicle; the observation of dimer **7** as the predominant product in each case indicates that both intra- and intermolecular dimerization can occur for the bis(styrene) phospholipid.

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