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COMMUNICATION

Sterol-containing tetraphenylethenes: synthesis, aggregation-induced emission, and organogel formation

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Cholesterol- and stigmasterol-containing tetraphenylethenes (TPEs) (TPE-Chol and TPE-Stig) are facilely synthesized in satisfactory yields by Cu (I)-catalyzed click reaction of 1,2-bis(4-azidomethylphenyl)-1,2-diphenylethene and cholesteryl-4-ethylbenoate and sigmasteryl 11-(4-ethynylphenoxy)undecanoate, respectively. Whereas they are nonluminescent in solution, they become highly emissive when aggregated in the condensed phase. The molecules of TPE-Stig can self-assemble in methanol solution, generating organogels with gelation-induced emission characteristics.

Keywords sterols, tetraphenylethenes, aggregation-induced emission, gel

1 Introduction

Sterols are an important class of naturally occurring organic substances and their derivatives are of great importance in biology, medicine, and chemistry [1,2]. Sterols include all the sex hormones, adrenal cortical hormones, bile acids, the molting hormones of insects, and many other physiologically active substances of animals. Examples are represented by cholesterol and stigmasterol, which are, respectively, essential components of mammalian cell membranes and used as a precursor for the manufacture of synthetic progesterone, a valuable human hormone. Incorporation of such naturally occurring species into optical materials is of interest because the resultant luminogens may exhibit intriguing light-emitting and biologic properties. They may be liquid crystalline and optically active because most of the steroids are mesogens and chiral [3,4].

Besides these attractive attributes, they may be capable of self-assembling into efficient low-molecular-weight organic gelators driven by noncovalent interactions such as van der Waals forces under appropriate conditions [5–10]. In the gel state, the luminophores may assemble and align in a one-dimensional fashion, which may result in interesting fluorescence phenomena [11–15]. Thus, these fluorescent organogels may find high-technological applications such as in optical devices and sensors. Attracted by such a prospect, in this paper we attached cholesterol and stigmasterol into tetraphenylethene (TPE), an archetypal luminogen with an aggregation-induced emission (AIE) feature by click chemistry [16]. Whereas the hybrid molecules are nonluminescent in the solution state, they become highly emissive in the aggregate state as nanoparticle suspensions in poor solvents or as thin films and gels in the condensed phase [17–19].

2 Results and discussions

The synthetic routes to the sterol-containing TPEs (TPE-Chol and TPE-Stig) are depicted in Scheme 1. A methylated TPE (2MeTPE) was first prepared by McMurry cross coupling reaction of 4-methylbenzophenone catalyzed by $Zn/TiCl_4$ [20–22]. The methyl groups of 2MeTPE were then brominated by NBS and converted into azido functionalities by substitution reaction with sodium azide. "Click reactions" of diazide-containing 2N3TPE with sterol-containing phenylacetylenes (EBA-Chol and EBA-Stig) were catalyzed by $CuSO_4$/sodium ascorbate in EtOH/THF/H_2O, which furnished the desirable products, TPE-Chol and TPE-Stig, in satisfactory yields after simple filtration and solvent washing [23–28]. All the molecules were characterized spectroscopically and gave satisfactory analysis data corresponding to their structures (See Experimental Section for details). An example of the ^{1}H NMR spectrum of TPE-Stig is shown in Figure 1. For comparison, the spectra of its monomers 2N3TPE and EBA-Stig are also given in the same figure. The spectrum of TPE-Stig is somehow an adduct of its two monomers, with some notable discriminations. The spectrum shows no resonances of the ethynyl proton of EBA-Stig at δ of 2.99. The resonance peaks of the phenyl protons of EBA-Stig and methylene protons of 2N3TPE at δ of 7.42, 6.82, and 4.25 are down-field shielded to 7.51, 6.97, and 5.45, respectively, after the click reaction due to the formation of triazole rings in TPE-Stig. It is well-known that the Cu(I)-catalyzed azide-alkyne click reactions yield 1,4-disubstitued 1,2,3-triazoles. As expected, TPE-Stig obtained from the click reaction of

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EBA-Stig and 2N3TPE initiated by $CuSO_4$/sodium ascorbate exhibits a diagnostic peak for the 1,4-isomeric unit at δ of 7.69. No other unexpected signals are found and all the peaks can be readily assigned, suggesting that the structure of the product is indeed TPE-Stig, as shown in Scheme 1. The solubility in common organic solvents is low for TPE-Chol due to its rigid structure and strong intermolecular interactions. On the contrary, it is pretty high for TPE-Stig, thanks to its long aliphatic alkyl chains.

Both TPE-Chol and TPE-Stig are almost nonluminescent when molecularly dissolved in solvents, but become highly emissive in the condensed phase. Figure 2 shows the photoluminescence (PL) spectra of TPE-Stig in THF and THF/water mixtures as an example. The PL spectrum in THF is basically a flat line parallel to the abscissa. When a large amount of water is added into the THF solution, intense emission at ~457 nm is recorded under identical measurement conditions. The higher the water content, the stronger the light emission. At a water fraction of 95%, the PL intensity is more than 100-fold higher than that in pure THF. Since water is a non-solvent for TPE-Stig, its molecules must be aggregated in the solvent mixtures with high water fractions. The mixtures are, however, macroscopically homogenous with no precipitates, suggesting that the aggregates are of nanodimension. Apparently, the emissions of TPE-Stig are induced by aggregate formation; in other words, it is AIE-active. In the solution state, the active intramolecular rotation (IMR) of its phenyl blades has consumed the energy of excitons via rotational relaxation channels, hence rendering it nonemissive in THF. In the aggregate state, the IMR process is restricted, which blocks the nonradiative decay pathways and thus makes it highly luminescent. The spectrum shifts slightly to

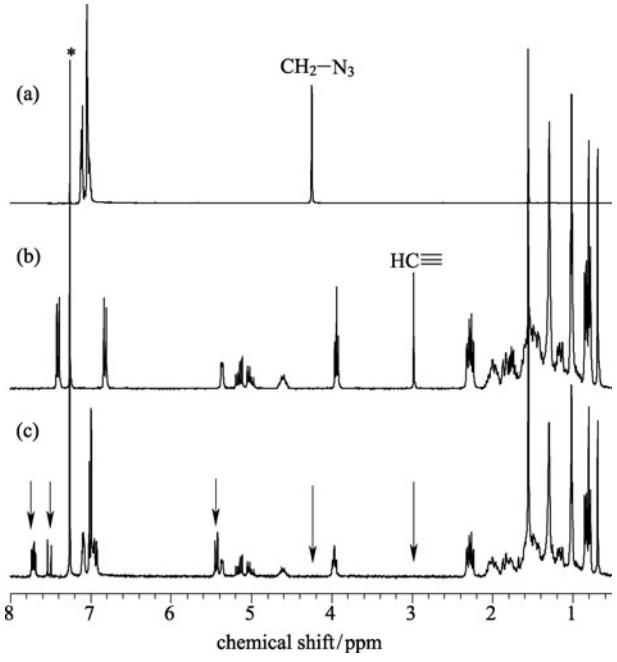
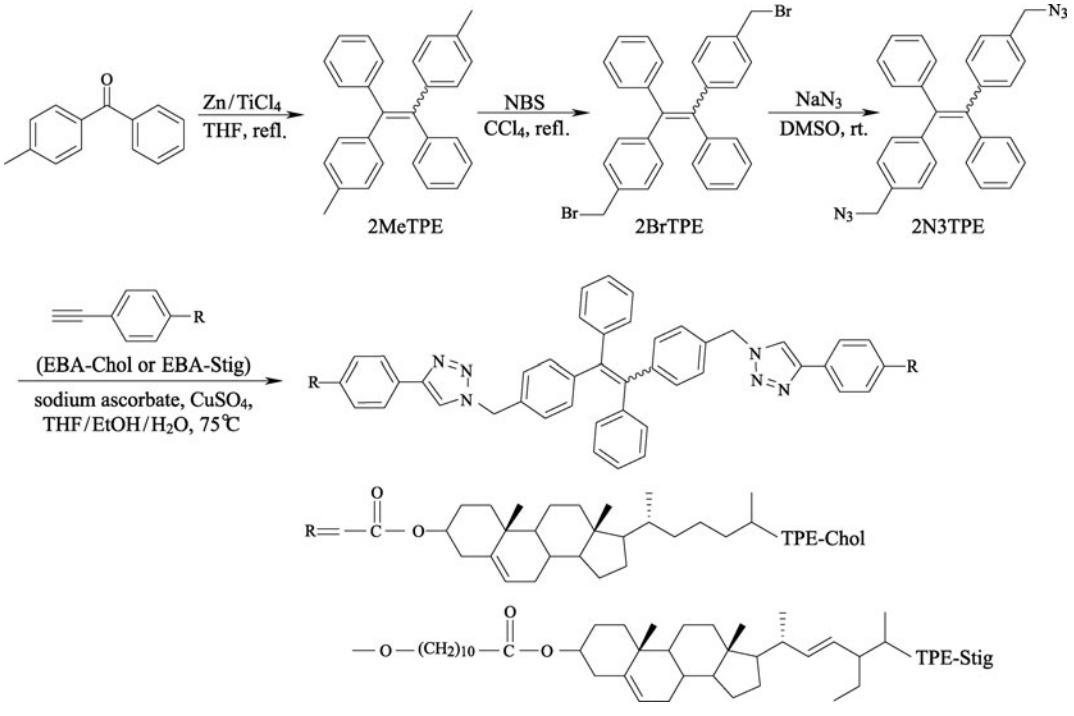


Figure 1 ^{1}H NMR spectra of (a) 2N3TPE, (b) EBA-Stig, and (c) TPE-Stig in chloroform-*d*. The solvent peaks are marked with asterisks.



Scheme 1 Synthetic routes for the sterol-containing tetraphenylethenes.

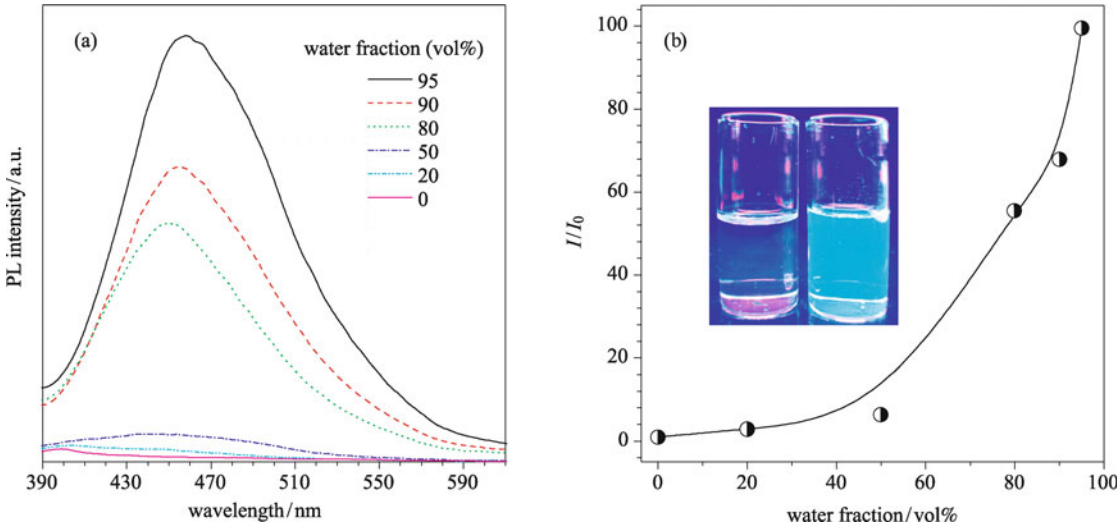


Figure 2 (a) Photoluminescence spectra of TPE-Stig in THF and THF/water mixtures with different water fractions. Concentration: 10 μM; excitation: 355 nm. (b) Plot of PL intensity versus composition of the THF/water mixture. Inset: fluorescent images of TPE-Stig in THF solution and THF/water mixture with 95% water fraction.

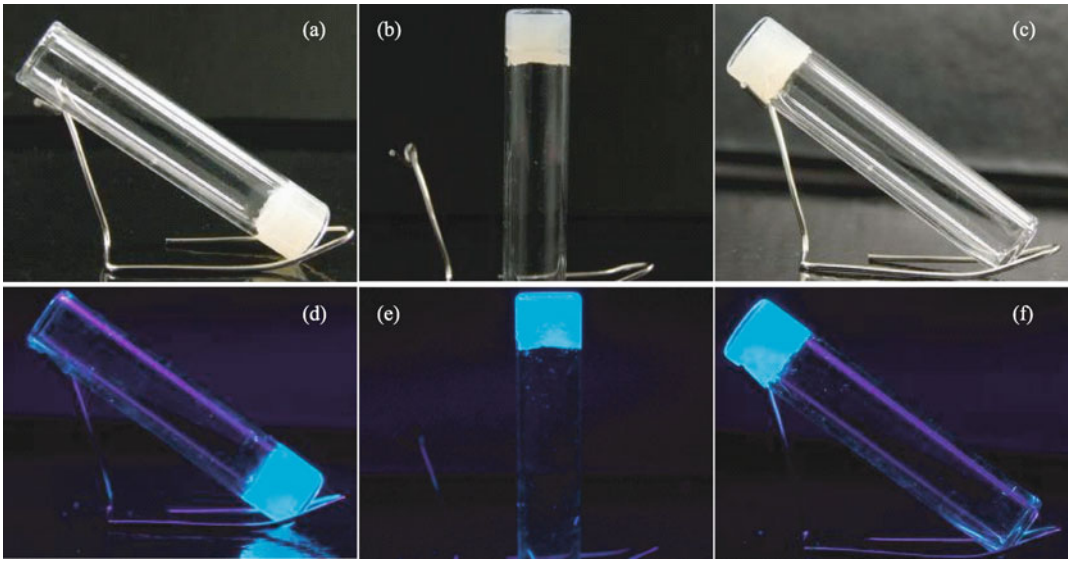


Figure 3 Fluorescent images of organogels of TPE-Stig formed in methanol (~0.5 wt%) taken under ((a) – (c)) normal room lightning and ((d) – (f)) UV irradiation.

the longer wavelengths in mixtures with high water content, probably due to the change in the packing mode of the dye molecules from crystalline to amorphous in the aggregates [29]. The photograph shown in the inset of Figure 2 clearly manifests the nonluminescent and emissive natures of the molecular isolated species and aggregate particles. The fluorescence quantum yields of the thin films of TPE-Chol and TPE-Stig measured by the integrating sphere are 29.3% and 31.4%, respectively.

TPE-Stig is an efficient gelator. Although it is not soluble in methanol, it dissolves readily with the aid of a few drops of THF and gentle heating. When the solution is cooled to room temperature, organogels of TPE-Stig is, interestingly, formed. The viscosity of the solution is so high that it exhibits no gravitational flow and the tube can be turned upside down without any solvent leakage (Figure 3). Under normal room light illumination, the organogels appear white but emit an intense blue light upon UV irradiation. The morphology of the organogel was investigated by scanning electron (SEM) and transmission electron (TEM) microscopes. The SEM images reveal entangled three-dimensional networks constructed from bundles of fibrous aggregates (Figs. 4(a) and 4(b)). This should be responsible for the observed gelation. A clear network structure is observed in the TEM pictures

(Figs. 4(c) and 4(d)). The width of the fibers is around 50 nm and their length can be extended to tens of micrometers.

The self-assembly of TPE-Stig molecules into three-dimensional organogels should strongly rigidify their molecular conformations and constrain the IMR process. Thus, the organogels are expected to show intense light upon photoexcitation. This is indeed the case. As depicted in Figure 5, before gel formation, the methanol solution of TPE-Stig is

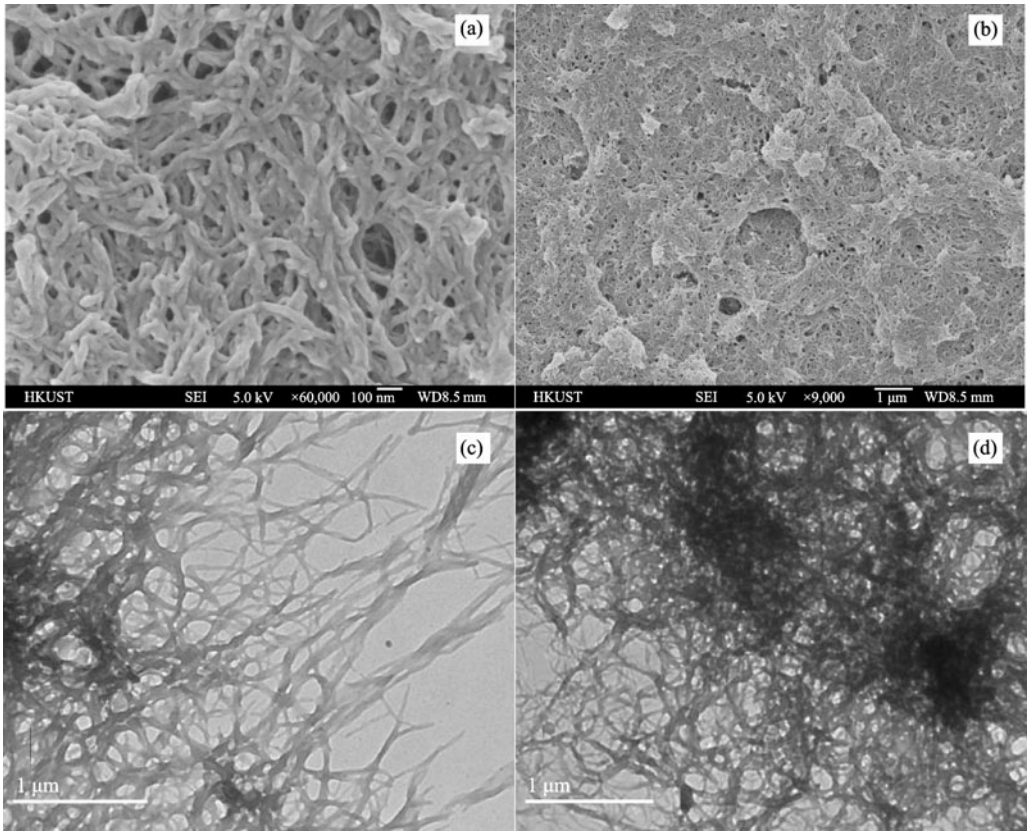


Figure 4 (a), (b) SEM and (c), (d) TEM images of organogels of TPE-Stig.

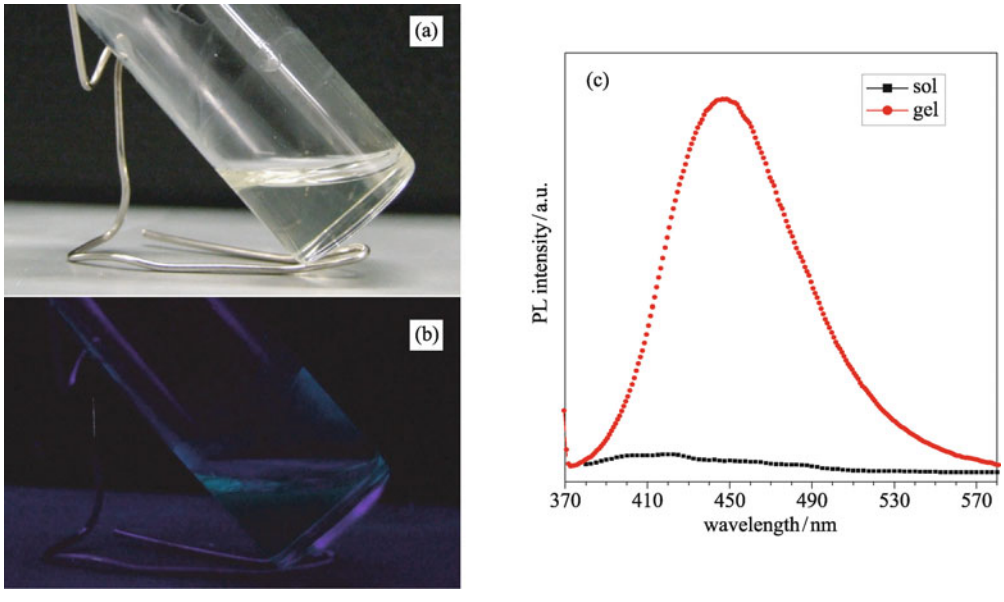


Figure 5 Fluorescent images of hot methanol (~0.5 wt%) of TPE-Stig taken under (a) normal room lightning and (b) UV irradiation. (c) Photoluminescence spectra of hot methanol solution and gel of TPE-Stig.

weakly emissive. When the solution solidifies, a strong PL signal is recorded, whose intensity is more than 18 times higher than that of the solution, demonstrating an interesting phenomenon of gelation-induced emission.

3 Conclusion

In this paper, sterol-containing TPEs are synthesized in high yields by Cu(I) catalyzed azide-alkyne click reaction of 2N3TPE and EBA-Chol and EBA-Stig, respectively. All the dye molecules are AIE-active. Self-assembly of TPE-Stig molecules generates organogels, which exhibit a novel phenomenon of gelation-induced emission.

4 Experimental section

4.1 Materials and instrumentations

THF was distilled from sodium benzophenone ketyl under nitrogen immediately prior to use. All the chemicals and other regents were purchased from Aldrich and used as received without further purification. Compounds, namely cholesteryl-4-ethylbenoate (EBA-Chol) and sigmasteryl 11-(4-ethynylphenoxy)undecanoate (EBA-Stig) were synthesized according to previous papers [30,31]. ^{1}H and ^{13}C NMR spectra were measured on a Bruker AV 400 spectrometer in $CDCl_3$ using tetramethylsilane (TMS; δ = 0) as internal reference. Photoluminescence spectra of the dye molecules were recorded on a Perkin-Elmer LS 55 spectrofluorometer. High resolution mass spectra (HRMS) were recorded on a GCT premier CAB048 mass spectrometer operating in MALDI-TOF mode. Morphologies of the organogels were imaged on JEOL-6300 scanning electron and JEOL 2010F transmission electron microscopes.

4.2 Synthesis

1,2-Bis(4-methylphenyl)-1,2-diphenylethene (**2MeTPE**): In a three-necked flask equipped with a magnetic stirrer, were added zinc powder (7.7 g, 120 mmol), 4-methylbenzophenone (6 g, 30.6 mmol), and 60 mL of THF. The mixture was cooled to −5°C and $TiCl_4$ (6.6 mL, 60 mmol) was slowly added by a syringe. The mixture was warmed to room temperature, stirred for 0.5 h, and then heated to reflux for 12 h. After being cooled to room temperature, the reaction was quenched with 10% K_2CO_3 aqueous solution and extracted with CH_2Cl_2. The organic layer was collected and concentrated. The crude product was purified by silica-gel chromatography to give a white solid in 92% yield (5.07 g). ^{1}H NMR ($CDCl_3$, 300 MHz), δ (TMS, ppm): 7.01–7.11 (m, 10H), 6.90 (d, 8H), 2.24 and 2.26 (two singlets, 6H). HRMS (MALDI-TOF): *m*/*z* 360.3255 [M^+, calcd 360.1878].

1,2-Bis(4-bromomethylphenyl)-1,2-diphenylethene (**2BrTPE**): In a flask equipped with a magnetic stirrer were added 2MeTPE (1.5 g, 4.1 mmol), *n*-bromosuccinimide (1.5 g, 8.5 mmol), benzoyl peroxide (50 mg) and 50 mL of CCl_4. The mixtures were refluxed for 8 h. After being cooled to room temperature, the solution was filtrated and the filtrate was condensed. The crude product was purified by silica-gel chromatography to give a white solid of **2BrTPE** in 61% yield (1.31 g). ^{1}H NMR ($CDCl_3$, 300 MHz), δ (TMS, ppm): 7.09–7.15 (m, 10H), 6.96–7.03 (m, 8H), 4.41 and 4.43 (two singlets, 4H). ^{13}C NMR ($CDCl_3$, 75 MHz), δ (TMS, ppm): 144.46, 144.40, 143.93, 143.87, 141.49, 136.61, 136.51, 132.31, 131.98, 129.20, 129.10, 128.51, 128.42, 127.42, 127.33, 34.24.

1,2-Bis(4-azidomethylphenyl)-1,2-diphenylethene (**2N3TPE**): In a flask equipped with a magnetic stirrer were added 2BrTPE (0.3 g, 0.58 mmol), sodium azide (0.083 g, 1.28 mmol), and 15 mL of DMSO. After stirring at room temperature for 24 h, the solution was poured into 100 mL of water and extracted with CH_2Cl_2. The crude product was purified by silica-gel chromatography to give a light yellow solid in 95% yield (0.24 g). ^{1}HNMR ($CDCl_3$, 300 MHz), δ (TMS, ppm): 7.09–7.14 (m, 6H), 6.99–7.06 (m, 12H), 4.25 (s, 4H). ^{13}C NMR ($CDCl_3$, 75 MHz), δ (TMS, ppm): 143.79, 143.33, 140.90, 140.87, 133.50, 131.82, 131.37, 127.85, 127.73, 126.76, 54.63, 54.61.

TPE-Chol: Into a 20 mL Schlenk tube were suspended 0.076 g (0.17 mmol) of 2N3TPE and 0.194 g (0.38 mmol) of EBA-Chol in 15 mL of water/THF/ethanol mixture (1/1/1, *v*/*v*/*v*). 0.3 mmol of freshly prepared 1 mol·L^{-1} aqueous solution of sodium ascorbate was added followed by 7.5 mg (0.03 mmol) of copper(II) sulfate in 100 μL of water. The solution was stirred vigorously at 75°C overnight. The reaction mixture was diluted with water (50 mL), and the white precipitate was collected by filtration. After washing with water and ethanol, the precipitate was dried under vacuum to afford 0.188 g (76%) of pure product as a white powder. ^{1}HNMR ($CDCl_3$, 300 MHz), δ (TMS, ppm): 8.07 (d, 4H), 7.87 (t, 2H), 7.70 (d, 4H), 7.12 – 6.96 (m, 18H), 5.46 (d, 4H), 5.42 (s, 2H), 4.88 (m, 2H), 2.47 (d, 4H), 2.05 – 0.8 (m, 82H). ^{13}C NMR ($CDCl_3$, 75 MHz), δ (TMS, ppm): 166.38, 147.92, 144.86, 143.61, 141.51, 140.26, 135.38, 133.52, 133.23, 132.65, 131.87, 130.91, 130.86, 128.58, 128.18, 128.09, 127.60, 126.04, 123.54, 121.02, 75.49, 57.40, 56.84, 50.75, 43.02, 40.44, 40.21, 38.92, 37.74, 37.35, 36.88, 46.49, 32.64, 32.59, 28.93, 28.71, 28.59, 24.99, 24.52, 23.51, 23.25, 21.75, 20.08, 19.42, 12.56.

TPE-Stig: It was synthesized according to the same procedure mentioned above using 0.076 g (0.17 mmol) of 2N3TPE and 0.254 g (0.38 mmol) of EBA-Stig. White powder; yield 78%

(0.24 g). ^{1}HNMR ($CDCl_3$, 300 MHz), δ (TMS, ppm): 7.69 (t, 2H), 7.51 (d, 4H), 7.10 (m, 6H), 6.97 – 6.93 (m, 16H), 5.45 (d, 4H), 5.37 (d, 2H), 5.19 – 4.97 (m, 4H), 4.60 (m, 2H, OCH), 3.97 (m, 4H), 2.34 – 0.68 (m, 122H). ^{13}C NMR ($CDCl_3$, 75 MHz), δ (TMS, ppm): 174.02, 159.94, 144.69, 143.66, 143.62, 141.47, 140.41, 139.01, 133.79, 133.54, 132.58, 132.47, 131.86, 129.95, 128.56, 128.48, 128.09, 128.0, 127.62, 127.54, 127.46, 123.70, 123.27, 123.18, 119.42, 119.37, 119.31, 119.25, 119.21, 115.53, 115.48, 115.40, 74.37, 68.78, 57.47, 56.61, 51.92, 50.73, 42.90, 41.20, 40.31, 38.85, 37.69, 37.30, 35.41, 32.58, 30.19, 30.07, 29.95, 29.80, 29.61, 28.51, 26.72, 26.11, 25.74, 25.05, 21.91, 21.79, 21.71, 20.02, 19.68, 12.95, 12.74.

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