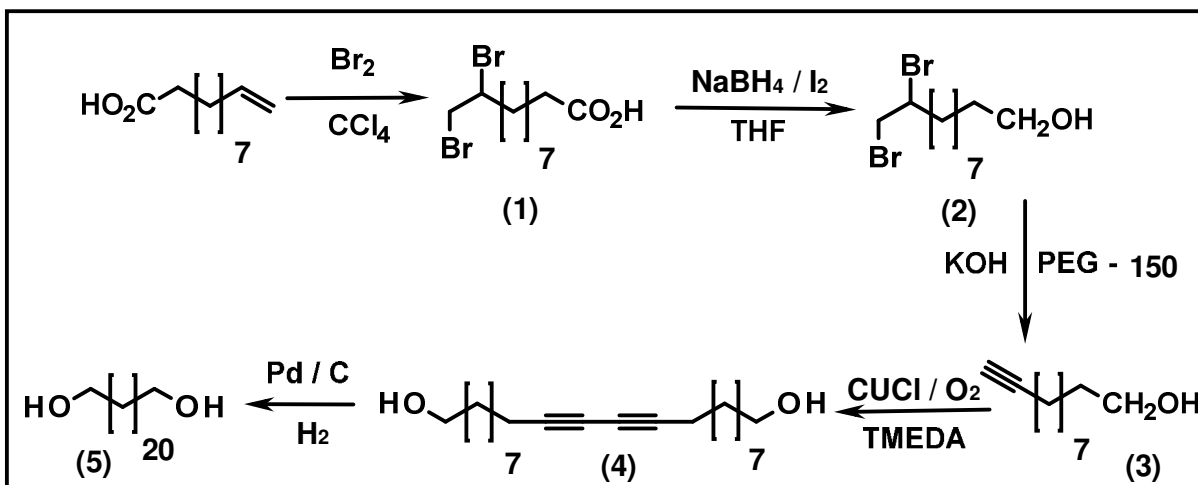


SUPPLEMENTARY INFORMATION

Periodically Grafted Amphiphilic Copolymers: Nonionic Analogues of Ionenes

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Synthesis of diol monomers:



Scheme: 1

10,11-Dibromoundecanoic acid (1)¹

5.0 gm (27.17 mmol, 1 eq.) of undecylenic acid was dissolved in 20 ml of dry CCl₄ and the mixture was cooled to 0 °C. To the reaction vessel, 4.5 gm (27.17 mmol, 1 eq.) bromine was added in dropwise. The reaction mixture was allowed to stir at room temperature for two hours. After which the CCl₄ was removed under reduced pressure and the contents were poured into a petri dish. Upon standing for 1-2 days, the dibromo acid crystallizes completely and the yield was nearly quantitative.

¹H NMR (δ, ppm, CDCl₃): 1.25 (m, 10H, -(CH₂)₅CH₂CH₂CO₂H); 1.55 (m, 2H, -(CH₂)₅CH₂CH₂CO₂H); 1.70 (m, 1H, -(CH₂)₅CH_bH_aCHBrCH₂Br); 2.00 (m, 1H, -(CH₂)₅CH_bH_aCHBrCH₂Br); 2.28 (t, 2H, -(CH₂)₅CH₂CH₂CO₂H); 3.55 (m, 1H, CH₂CHBrCH₂Br); 3.78 (m, 1H, CH₂CHBrCH_bH_aBr); 4.10 (m, 1H, CH₂CHBrCH_bH_aBr).

10,11-Dibromoundecan-1-ol (2)²

1.6 gm of NaBH₄ (45.86 mmol, 1.2 eq.) was taken in 60 ml of dry THF. To the slurry I₂ (4.9gm, 19.1 mmol, 0.5 eq.) in THF (30 ml) was added slowly during 2.5 hours at 0 °C

followed by the THF solution of 10,11-Dibromoundecanoic acid (9 gm, 38.2 mmol, 1 eq.). The reaction mixture was allowed to stir for additional two hours at room temperature. After completion of the reaction, dilute HCl (16 ml, 3 N) was added carefully. The reaction mixture was washed with 3 N NaOH and then with brine solution. The separated organic layer was collected and passed through anhydrous Na₂SO₄. The product was used as such for the next step without further purification. Crude yield was 75%.

¹H NMR (δ, ppm, CDCl₃): 1.25 (m, 12H, -(CH₂)₆CH₂CH₂OH); 1.52 (m, 2H, -(CH₂)₆CH₂CH₂OH); 1.70 (m, 1H, -(CH₂)₅CH_bH_aCHBrCH₂Br); 2.06 (m, 1H, -(CH₂)₅CH_bH_aCHBrCH₂Br); 3.55 (m, 1H, -CH₂CHBrCH₂Br); 3.60 (t, 2H, -(CH₂)₆CH₂CH₂OH); 3.78 (m, 1H, -CH₂CHBrCH_bH_aBr); 4.10 (m, 1H, CH₂CHBrCH_bH_aBr).

Undec-10-yn-1-ol (3)³

A mixture of PEG-150 (15 ml) and KOH pellets (2.7gm, 48.4 mmol, 4 eq.) were stirred and heated in an oil bath at 80 °C for about 0.5 hour during which time when all the KOH dissolved forming a homogeneous solution. The reaction mixture was cooled and compound **2** (4 gm, 12.1 mmol, 1 eq.) was added dropwise over a period of 20 minutes. The mixture was heated in an oil bath at 80 °C for 2 hours. After completion, water (50ml) was added and the mixture was extracted with 9:1 hexane/chloroform (5x100 ml). The combined organic layers were washed with water followed by brine and finally passed through anhydrous Na₂SO₄. The crude product was distilled in Kugelröhr apparatus under reduced pressure (125 °C and 2 torr) to yield a colorless oil in 70% yield.

¹H NMR (δ, ppm, CDCl₃): 1.30 (m, 12H, -(CH₂)₆CH₂CH₂OH); 1.55 (m, 2H, -(CH₂)₆CH₂CH₂OH); 1.94 (t, 1H, -CH₂CCH); 2.18 (m, 2H, -CH₂CCH); 3.64 (t, 2H, -(CH₂)₆CH₂CH₂OH).

Docosa-10,12-diyne-1,22-diol (4)⁴

4.0 gm (23.8 mmol, 1 eq.) of **3** in 50 ml of methanol, 0.414 g (3.57 mmol, 0.15 eq.) of tetramethylethylenediamine and 0.12 gm (1.19 mmol, 0.05 eq.) of Cu(I)chloride was taken in the reaction vessel. The reaction mixture was stirred with continuous purging of oxygen for one hour. After completion of the reaction, 2 ml of 1 N HCl was added to the reaction mixture in ice cold condition. After further addition of 10 ml of brine solution, cooled and filtered, the precipitated product was isolated by filtration and washed with cold dilute HCl solution and finally with cold water to obtained a white crystalline product. The crude product was recrystallized from dry toluene to give a final yield of 60%.

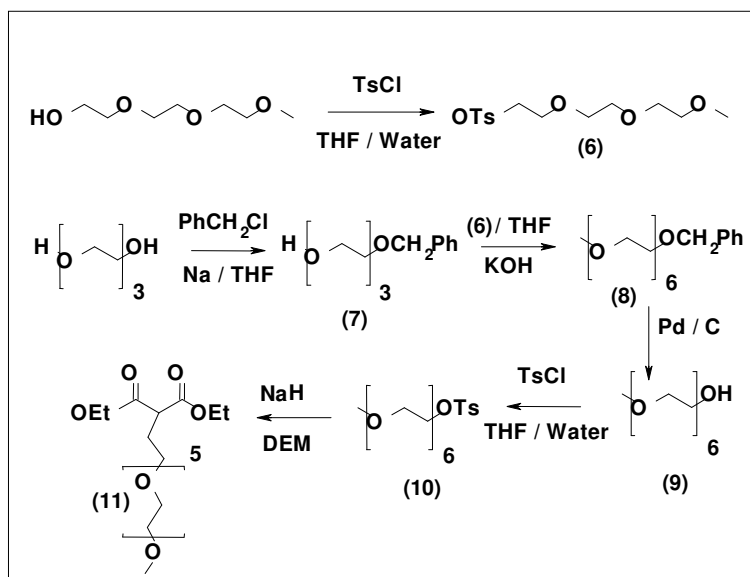
¹H NMR (δ, ppm, CDCl₃): 1.23 (m, 24H, -CCCH₂(CH₂)₆CH₂CH₂OH); 1.40 (m, 4H, -CCCH₂(CH₂)₆CH₂CH₂OH); 2.18 (t, 4H, -CCCH₂CH₂-); 3.64 (t, 4H, -(CH₂)₆CH₂CH₂OH).

Docosane-1,22-diol (5)

1.0 gm (2.99 mmol) of **4** in 20 ml of toluene was taken in high pressure hydrogenation apparatus along with 0.2 g Pd/C (10% by weight) and one drop of conc. HCl as an activator. The contents were maintained at 55 psi (H₂) under mechanical agitation for 3 hours. After completion, the reaction mixture was filtered and the toluene was removed under reduced pressure. The crude product was purified by distillation in Kugelröhr apparatus under reduced pressure (220 °C and 2 torr), while a small amount of lower boiling fraction was discarded. The liquid distillate solidified to a white highly crystalline material in room temperature. The yield was 80% after distillation.

¹H NMR (δ, ppm, CDCl₃): 1.30 (m, 36H, -(CH₂)₁₈CH₂CH₂OH); 1.56 (m, 4H, -(CH₂)₁₈CH₂CH₂OH); 3.64 (t, 4H, -(CH₂)₅CH₂CH₂OH).

Synthesis of the diester monomer



Scheme: 2

Triethyleneglycol monomethyl ether tosylate (6)⁵

20 gm (121.9 mmol 1 eq.) of triethyleneglycol monomethyl ether was taken in 70 ml THF and the contents were cooled in an water-ice bath. To the cooled solution, sodium hydroxide (14.6 gm, 365.8 mmol, 3 eq.) in 70 ml water was added. Tosylchloride (30 gm, 158.5 mmol, 1.3 eq.) in 50 ml THF was then added slowly using a dropping funnel over 30 min. After the addition, the contents were allowed to warm up to ambient temperature and stirred overnight. After completion of reaction, the separated organic

layer was collected and the aqueous layer was extracted twice with diethyl ether (2 x 50 ml). The combined organic layer was washed with 10 % sodium hydroxide solution, followed by saturated brine and water. It was dried over anhydrous sodium sulphate, filtered and concentrated to obtain the pure product as viscous liquid in nearly quantitative yield.

^1H NMR (δ , ppm, CDCl_3): 2.45 (s, 3H, $-\text{OSO}_2\text{ArCH}_3$); 3.37 (s, 3H, $-\text{OCH}_3$); 3.7-3.5 (m, 10H, $-\text{OCH}_2\text{CH}_2\text{O}-$); 4.16 (t, 2H, $-\text{CH}_2\text{OSO}_2\text{ArCH}_3$); 7.45 (d, 2H, $-\text{OSO}_2\text{ArHCH}_3$); 7.8 (d, 2H, $-\text{OSO}_2\text{ArHCH}_3$).

Triethyleneglycol monobenzylate (7)

Triethylene glycol (45 gm, 300 mmol, 2 eq.) was taken in 30 ml dry methanol and small pieces of metallic sodium (3.45 gm, 150 mmol, 1 eq.) were slowly added to it. After complete dissolution of sodium, methanol was removed completely under reduced pressure. The resulting monosodium salt was dissolved in dry THF and benzyl chloride (17.5 gm, 138 mmol, 0.91 eq.) was added to it. The contents were refluxed under nitrogen atmosphere for 24 h. After cooling the reaction mixture, the THF was removed under reduced pressure, water was added and the contents were extracted with diethyl ether (3 x 50 ml). The combined organic layer was dried over anhydrous sodium sulphate, filtered and concentrated to yield the crude product. Pure compound **7** was obtained by vacuum distillation at 180 °C and 2 torr as a colorless liquid in 72 % yield.

^1H NMR (δ , ppm, CDCl_3): 2.56 (t, 1 H, OH); 3.72-3.60 (m, 12 H, $-\text{OCH}_2\text{CH}_2\text{O}-$); 4.57 (s, 2 H, $\text{ArCH}_2\text{O}-$); 7.35-7.26 (m, 5 H, **ArH**).

Hexaethylene glycol monomethyl ether benzylate (8)

Compound **6** (35.7 gm, 112.5 mmol, 1.2 eq.) and compound **7** (22.5 gm, 93.75 mmol, 1 eq.) were taken along with potassium hydroxide (15.75 gm, 281.25 mmol, 3 eq.) in dry THF. The contents were refluxed for 2 days in the presence of a catalytic amount of potassium iodide. After completion, the reaction mixture was cool down to room temperature and THF was removed under reduced pressure, water was added and the contents were extracted with diethyl ether (3 x 50 ml). The combined organic layer was dried over anhydrous sodium sulphate, filtered and concentrated to obtain the liquid crude product. The compound was taken to the next step without further purification. Crude yield = 75 %.

^1H NMR (δ , ppm, CDCl_3): 3.382 (s, 3H, OCH_3); 3.69-3.53 (m, 24 H, $-\text{OCH}_2\text{CH}_2\text{O}-$); 4.57 (s, 2 H, $\text{ArCH}_2\text{O}-$); 7.35-7.26 (m, 5 H, **ArH**).

Hexaethylene glycol monomethyl ether (9)

Crude compound **8** (14 gm, 30 mmol) obtained from previous step was taken in a Parr hydrogenation apparatus along with (500 mg) of 10 wt-% palladium in charcoal. 30 ml methanol was used as solvent along with one drop of conc. HCl as an activator. The

contents were maintained at 55 psi (H_2) under mechanical agitation for 5 h. After completion, the reaction mixture was neutralized with solid $NaHCO_3$, filtered and passed over silica-gel column to obtain crude colourless oil. Distillation at $220\text{ }^\circ\text{C}$ under reduced pressure (2 torr) in Kugelröhr apparatus gave the pure product as a colourless liquid in 85 % yield.

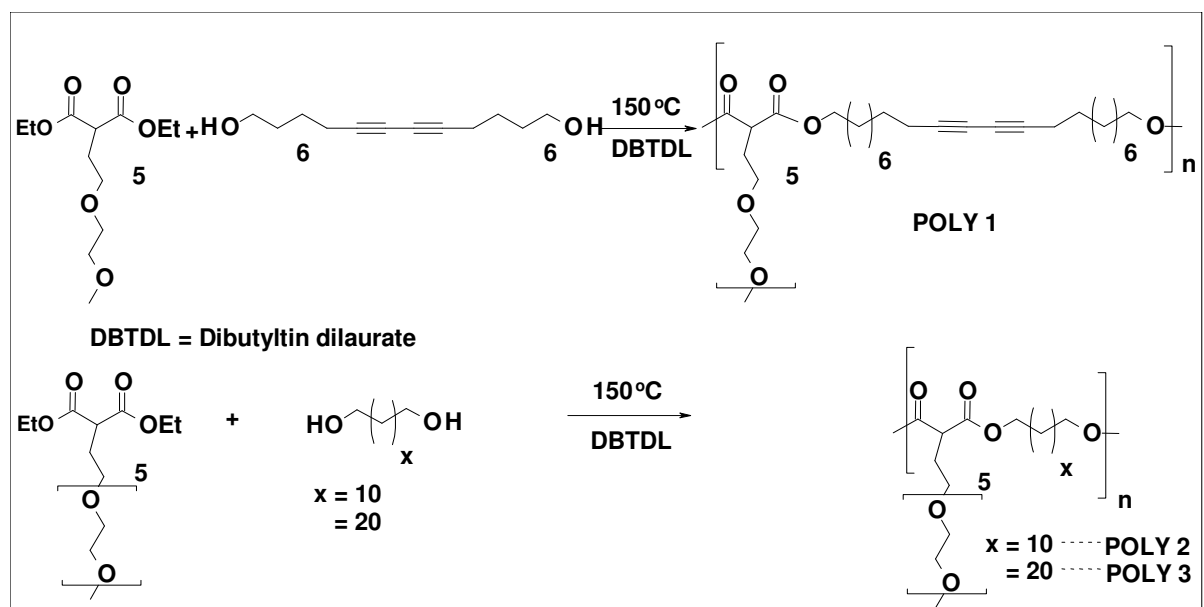
1H NMR (δ , ppm, $CDCl_3$): 3.38 (s, 3H, OCH_3); 3.72-3.55 (m, 24 H, $-OCH_2CH_2O-$).

Hexaethylene glycol monomethyl ether tosylate (10)

Compound **9** (6 gm, 20.3 mmol, 1 eq.) was taken in 20 ml THF and the contents were cooled in ice bath. Sodium hydroxide (2.43 gm, 60.9 mmol, 3 eq. as 50 % aq. solution) was added to it. Tosylchloride (5.02 gm, 26.4 mmol, 1.3 eq.) in 25 ml THF was added slowly using a dropping funnel over 30 min. After the addition, the contents were allowed to warm up to ambient temperature and stirred overnight. The separated organic layer was collected and the aqueous layer was extracted with diethyl ether (2 x 30 ml). The combined organic layer was washed with 10 % sodium hydroxide solution, followed by saturated brine and water. It was dried over anhydrous sodium sulphate, filtered and concentrated to obtain the pure product as viscous liquid in nearly quantitative yield.

1H NMR (δ , ppm, $CDCl_3$): 2.45 (s, 3H, $-OSO_2ArCH_3$); 3.37 (s, 3H, $-OCH_3$); 3.7-3.5 (m, 22H, $-OCH_2CH_2O-$); 4.16 (t, 2H, $-CH_2OSO_2ArCH_3$); 7.45 (d, 2H, $-OSO_2ArHCH_3$); 7.8 (d, 2H, $-OSO_2ArHCH_3$).

Synthesis of (11): We have discussed it in the main text.



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heme 3: Synthesis of Polymers

Polymer 1 (PGAC-C22-DA):

1.0 gm (2.28 mmol, 1 eq.) of **11** (diester) along with 0.76 gm (2.28 mmol, 1 eq.) **4** (diol) and 2 mol% catalyst (Dibutyltin dilaurate) was taken in a polymerization vessel. Initially dry N₂ was purged through the reaction mixture for 15 minutes and purging was continued for additional 15 minutes under melt condition to ensure homogeneous mixing between all components. The reaction mixture was heated to 150 °C for two hours under N₂ purging. At the next stage, polymerization vessel was connected with Kugelrohr apparatus and the polymerization was continued for another 1 hour under reduced pressure and 150 °C. The resulting polymer was dissolved in THF and filtered, the filtrate was concentrated under reduced pressure to a viscous solution and precipitated in methanol. The polymers were further purified by dissolution in THF and precipitated into methanol. Finally **Polymer 1** obtained with 73% yield after two reprecipitations.

¹H NMR (δ, ppm, CDCl₃): 1.25 (m, 20H, -CCCH₂CH₂(CH₂)₅CH₂CH₂OCO-); 1.51 (q, 4H, -CCCH₂CH₂(CH₂)₅CH₂CH₂OCO-); 1.61 (q, 4H, -CCCH₂CH₂(CH₂)₅CH₂CH₂OCO-); 2.1 (q, 2H, -OCOCHCH₂CH₂O-); 2.2 (t, 4H, -CCCH₂CH₂(CH₂)₅CH₂CH₂OCO-); 3.39 (s, 3H, -OCH₃); 3.70-3.50 (m, 22H, -OCH₂CH₂O-); 3.53 (t, 1H, -OCCHCOO); 4.12 (m, 4H, -OCOCH₂-).

Found C, 65.97%; H, 9.37% (C_{3.8}H_{6.4}O requires: C, 66.93%; H, 9.61%).

Polymer 2 (PGAC-C12):

1.0 gm (2.28 mmol, 1 eq.) of **11** (diester) along with 0.46 gm (2.28 mmol, 1 eq.) dodecane diol and 2 mol% catalyst (Dibutyltin dilaurate) was taken in a polymerization vessel. Initially dry N₂ was purged through the reaction mixture for 15 minutes and purging was continued for additional 15 minutes under melt condition to ensure homogeneous mixing between all components. The reaction mixture was heated to 150 °C for two hours under N₂ purging. At the next stage, polymerization vessel was connected with Kugelrohr apparatus and the polymerization was continued for another 1 hour under reduced pressure and 150 °C. The resulting polymer was dissolved in THF and filtered, the filtrate was concentrated under reduced pressure to a viscous solution and precipitated in methanol. The polymers were further purified by dissolution in THF and precipitated into methanol. Finally **Polymer 2** obtained with 75% yield after two reprecipitations.

¹H NMR (δ, ppm, CDCl₃): 1.25 (m, 16H, -OCOCH₂CH₂(CH₂)₈CH₂CH₂OCO-); 1.62 (m, 4H, -OCOCH₂CH₂(CH₂)₈CH₂CH₂OCO-) 2.17 (q, 2H, -OCH₂CH₂CHCOO-); 3.38 (s, 3H, -OCH₃); 3.70-3.50 (m, 22H, -OCH₂CH₂O-); 3.53 (t, 1H, -OCOCHCH₂CH₃); 4.12 (m, 4H, -OCOCH₂CH₂(CH₂)₁₈CH₂CH₂OCO-).

Found C, 61.01%; H, 9.60% (C_{2.8}H_{5.2}O requires: C, 61.30%; H, 9.49%).

Polymer 3 (PGAC-C22): We have discussed it discussed in the main text.

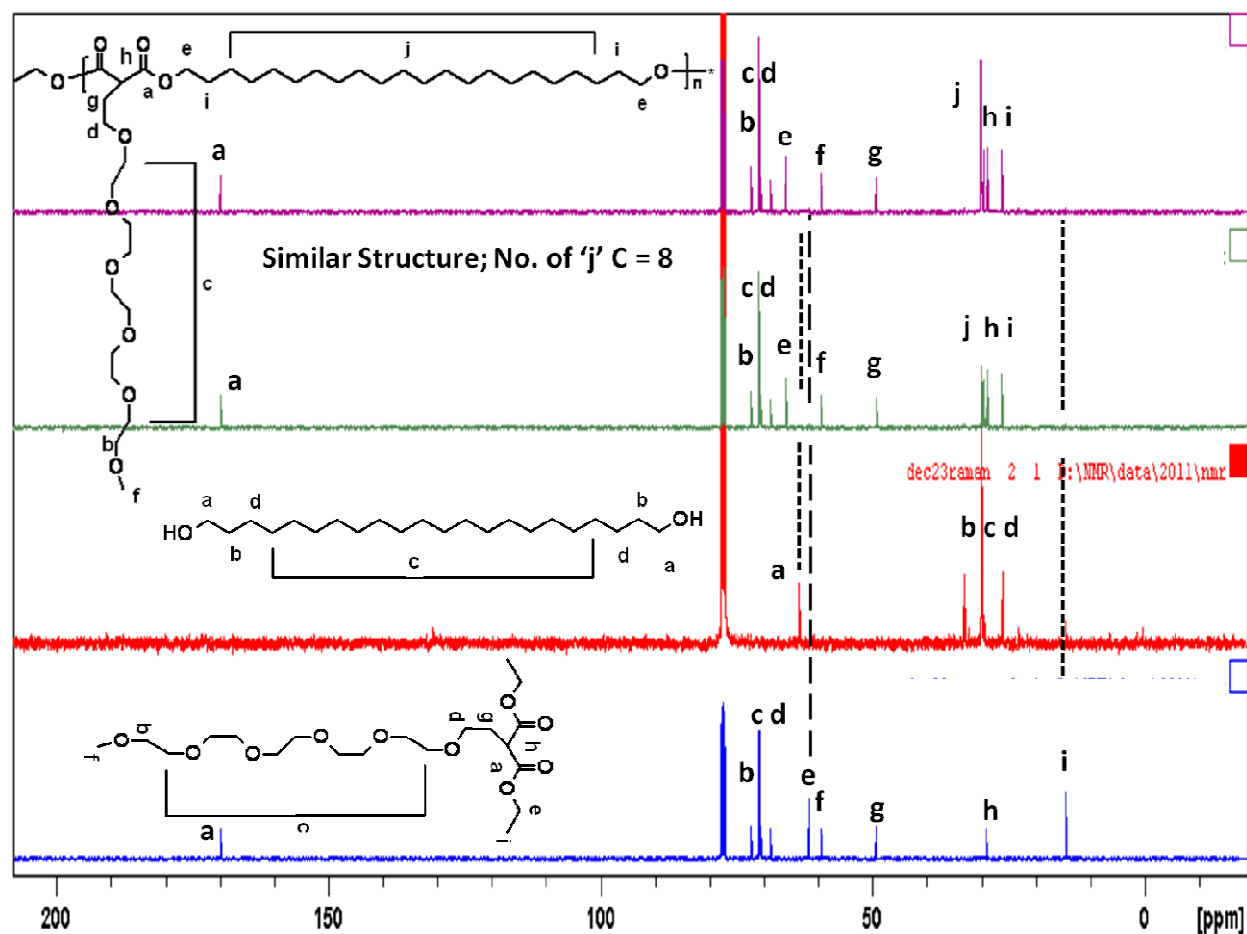


Figure S1: ^{13}C NMR spectra of the two monomers, namely the PEGylated malonate ester A and the C-22 diol, along with those of the two polymers PGAC-C12 and PGAC-C22. The peaks due to the ethyl ester groups (e and f) in the monomer are clearly shifted in the polymers; the end-group signals are not visible suggesting that the polymerization has occurred to fairly high levels of conversion implying the formation of reasonably high molecular weights.

AFM images with height profile

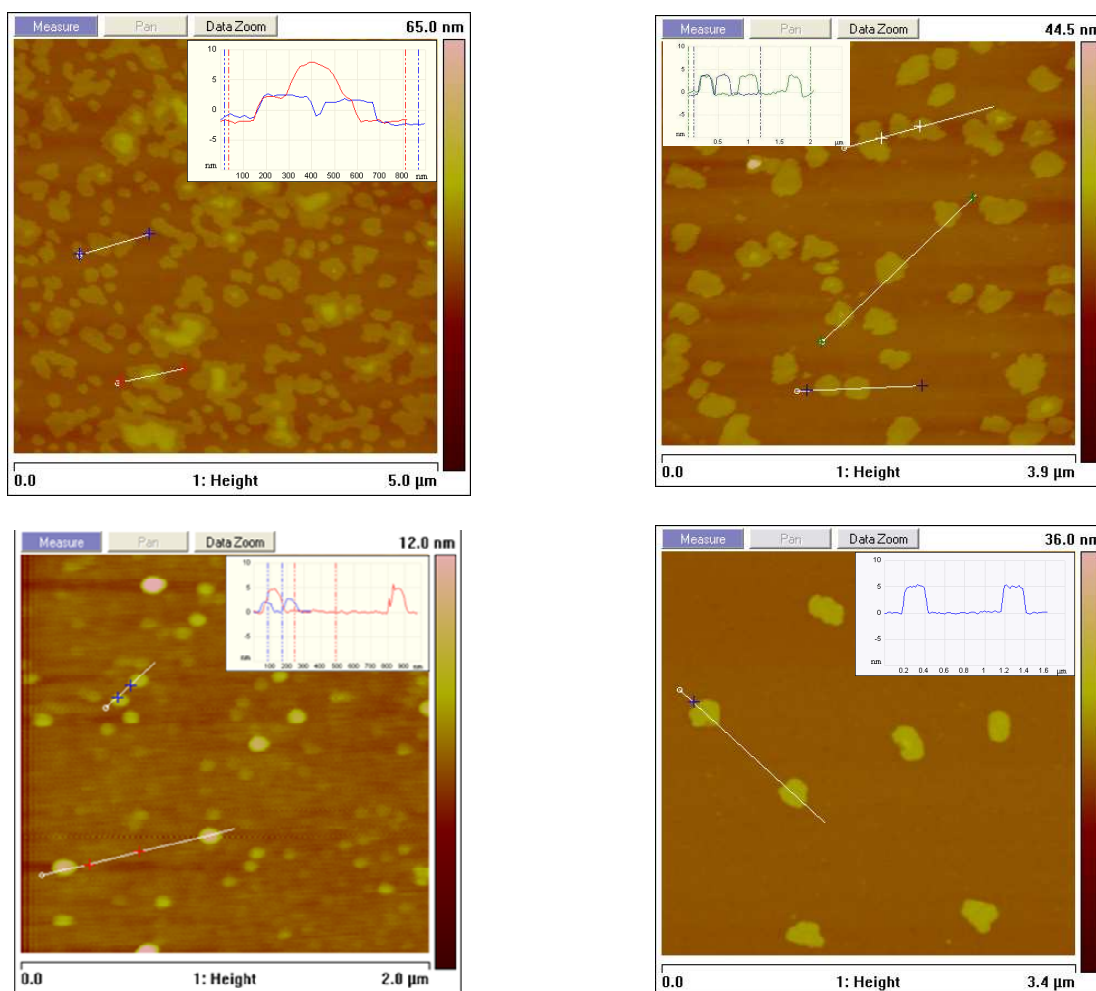
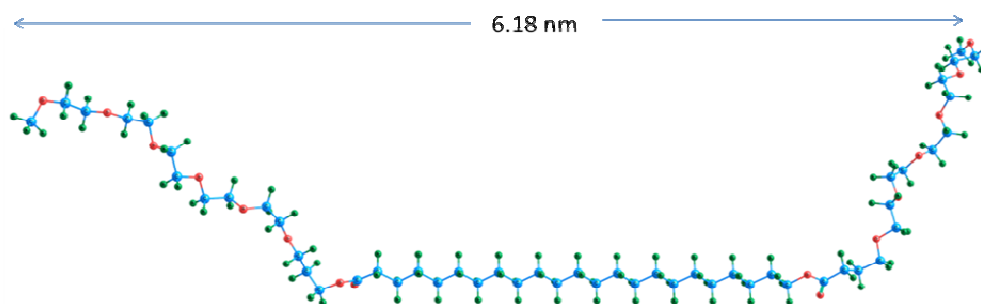


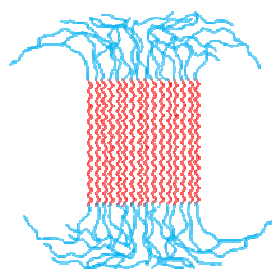
Figure S2: Top (left) is the AFM image of PGAC-C22 on piranha treated silicon wafer prior to annealing and top (right) is the image after thermal annealing; in the former there is clear evidence for the presence of one layer on top of the other, but the flatness of the structure is still retained. Additionally, the height on silicon wafer is slightly lower (~4.5 nm) than on mica suggesting that the PEG chains may be flattened on the hydrophilic surface because of stronger interactions. Bottom (left) AFM image of PGAC-C12 showing poorly formed structures that reveal the importance of the crystallization of the alkylene segment in stabilizing the folded zigzag structure. **Bottom (right) is the AFM image of PGAC-C22 (THF solution of PGAC-C22 was slowly added into water, resulting solution was used for AFM imaging) casted on mica surface.**

Estimated end-to-end distance of model system



To gain an idea of the thickness of the folded structure, we carried out an energy minimization calculation of a model system containing a central C-22 alkylene segment flanked by two hexaethylene glycol monomethyl ether units. As seen above the PEG units contain a significant number of gauche conformations that leads to a significantly smaller end-to-end distance than will be expected for an *all-trans* conformation. This value is still higher than the value seen from the AFM images and the SAXS studies. In the former case, a further flattening of the PEG chains may occur upon deposition on a hard mica or silicon surface, while in the latter a certain extent of inter-digitation of the segments could also occur.

A schematic depiction of the nature of the aggregate formed is given below.



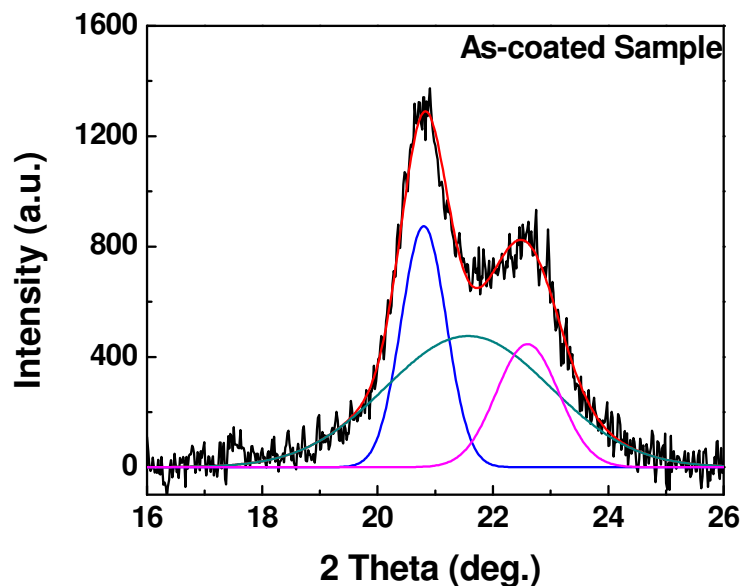


Figure S3: WAXS pattern of as-coated PGAC-C22 sample, along with the de-convolution showing two crystalline peaks and an amorphous halo.

SAXS Experiment: Bulk morphology of PGACs

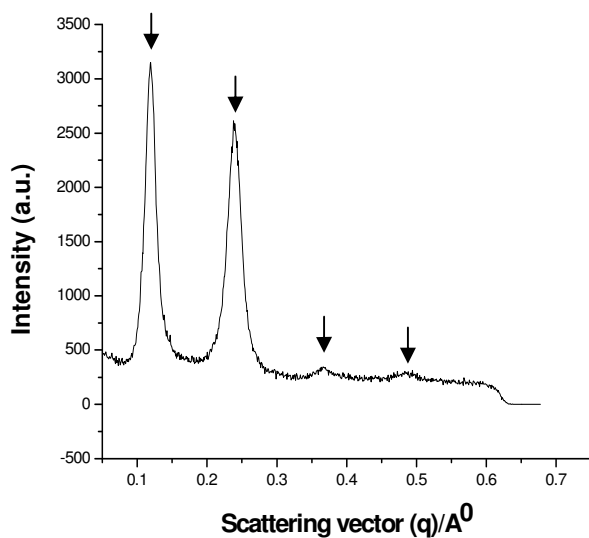


Figure S4: SAXS diagram of PGAC-C22 using a SAXS machine with an extended q -range.

Small angle X-ray scattering studies were performed using a Hecus S3-Micro System equipped with a one-dimensional position sensitive detector. Data was recorded at a

sample-to-detector distance 25.75 cm, using a wavelength, λ of 1.542 Å ($\text{CuK}\alpha$). Samples were taken in sealed glass capillaries and the diffraction patterns were collected at 30 °C. The exposure time was set to 2000 s and the diffraction patterns were calibrated using silver behenate.

The diffraction patterns of PGAC-C22 sample shows peaks up to fourth order and the ratio of peak positions relate as 1:2:3:4 confirming their layered kind of structure (lamella). From the scattering vector of the primary reflection, d -spacing was calculated to be 5.2 nm, which is consistent with the AFM results.

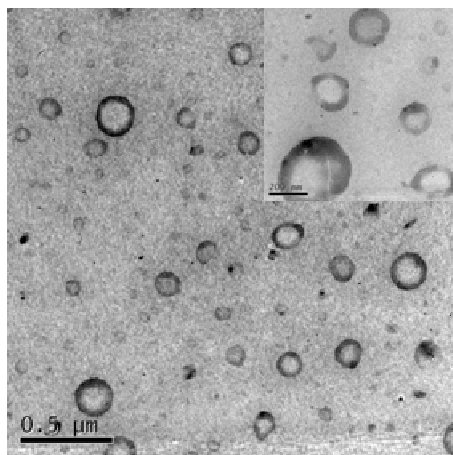


Figure S5. TEM image of vesicles formed by nonionene-C22; inset shows a higher magnification picture.

Molecular weight of PGACs

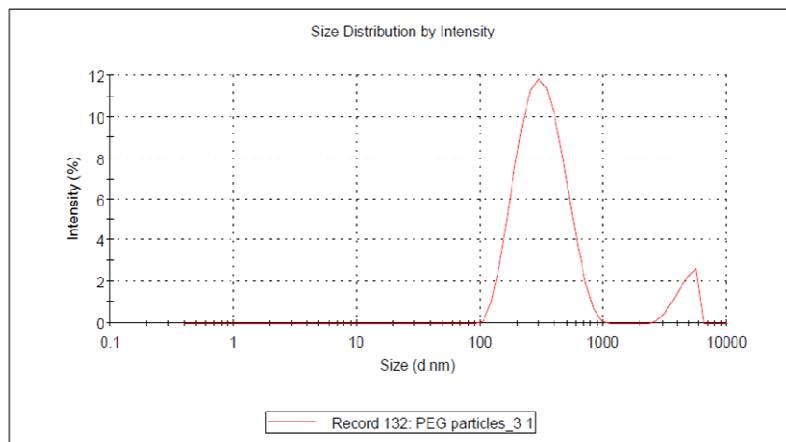
Polymer	M_n	M_w	PDI
PGAC-C22-DA	10800	24700	2.3
PGAC-C12	9800	26000	2.65
PGAC-C22	18700	432000	23*

* Possibly a reflection of aggregate formation

Particle size measurement by Dynamic Light Scattering (Figure S6)

PGAC-C22 was dispersed in water from THF solution and the organic solvent was removed latter, which appeared as a light blue color solution. The final concentration of polymers in water was 0.025mg/mL

	Diam. (nm)	% Intensity	Width (nm)
Z-Average (d.nm): 306.5	Peak 1: 333.2	91.6	142.6
PdI: 0.319	Peak 2: 4611	8.4	825.2
Intercept: 0.696	Peak 3: 0.000	0.0	0.000
Result quality : Refer to quality report			



DSC Thermogram of an aqueous dispersion

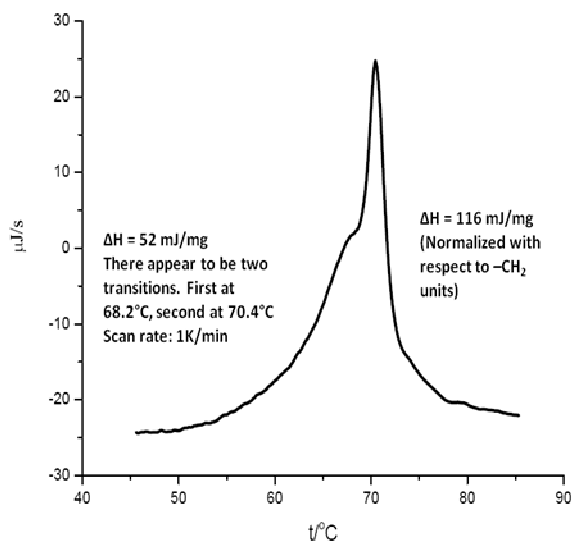


Figure S7. DSC thermogram of an aqueous dispersion of PGAC-C22 (1 mg/mL). The enthalpy of melting has been normalized with respect to the wt-fraction of alkylene segment in the polymer. The solution was prepared by adding a fixed volume of a THF solution (of known concentration) into a fixed amount of water; after removal of THF in ultrasonic bath, the final concentration was adjusted to 1 mg/mL.

References

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