Electronic Supplementary Material (ESI) for Polymer Chemistry

Supplementary information for:

A one component methodology for the fabrication of honeycomb films from biocompatible amphiphilic block copolymer hybrids: A linear-dendritic-linear twist

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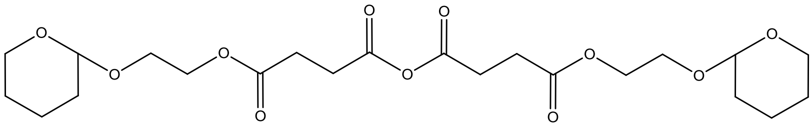
Chemicals:

N,N'-dicyclohexylcarbodiimide (DCC, 99%) and magnesium sulfate (99%) were purchased from Acros. Benzyl alcohol (anhydrous, 99.8%), tin (II)-2-ethylhexanoate ($Sn(Oct)_2$), dimethylaminopyridine (DMAP, 99%), N,N,N',N",N"-pentamethyldiethylenetriamine (PMDETA, 99%), CuBr (99%), CaH_2,tetraethylene glycol and sodium bisulfate were obtained from Sigma-Aldrich. Succinic anhydride, dichloromethane (analysis), methanol (analysis), toluene (Seccosolv) and dimethylformamide (Seccosolv) were purchased from Merck. Pyridine (AnalaR Normapur), p-toluenesulfonic acid (pTSA) and THF (unstabilized, HPLC) were obtained from VWR. 2,2-Dimethoxy-2-phenylacetopheneone (Irgacure 651) was purchased from Ciba. Ɛ-caprolactone (99%) was distilled over CaH_2 and stored over 4 Å molecular sieves under argon (g). Lactide (Sigma-aldrich) was recrystallized from toluene and stored under argon (g).

Monoprotected TEG-THP was synthesized as reported elsewhere (Angew. Chem. Int. Ed. 2010, 46, 6881-6884). PEG2k-N3 was synthesized as reported elsewhere (Langmuir 2008, 24, 2732-2739). PEG2k-SH and allyl-G3-OH were synthesized as reported elsewhere (Polymer chemistry 2011, 2, 394-402).

Synthesis of THP protected TEG anhydride



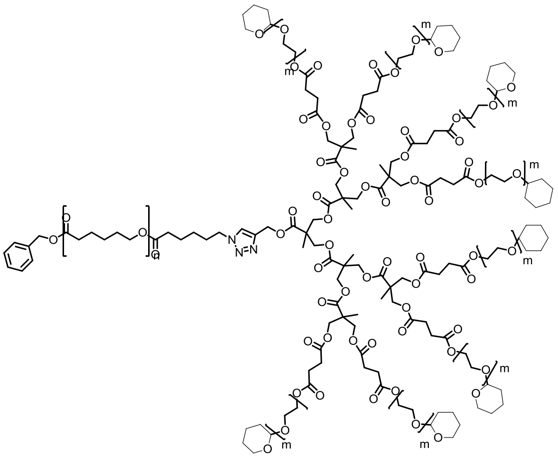
Synthesis of THP-protected TEG- succinic acid.

In a round bottom flask were added TEG (4 g, 14 mmol), DMAP (0,34 g, 2.8 mmol), pyridine (3.38 ml, 42 mmol) and dichloromethane (5 ml). Succinic anhydride (1.72 g, 17 mmol) was dissolved in dichloromethane (5 ml) and the solution was slowly added to the round bottom flask. The reaction was left to react over night. The excess anhydride was quenched with water. The solution was extracted 3 times with $NaHSO_4$, dried on $MgSO_4$ and concentrated. Yield: 3g (56 %).^{1}H-NMR ($CDCl_3$) δ(ppm):1.47-1.81 (6H,m, **-CH$_2$-CH$_2$-CH$_2$**-CH- THP), 2.63 (4H,s, **-CH$_2$**-C(=O)), 3.46-3.66 (14H,m, **-CH$_2$**-O- TEG), 3.83 (2H,m, **-CH$_2$**-O- THP), 4.23 (2H,m, **-CH$_2$**-O-C(=O)), 4.62 (1H,m, **-CH-**). ^{13}C-NMR ($CDCl_3$) δ(ppm):19.52, 25.52, 29.09, 29.30, 30.63, 62.30, 64.00, 66.73, 69.11, 70.60, 70.62, 70.68, 70.70, 70.78, 90.03, 172.25, 176.15.

Synthesis of THP protected TEG anhydride

THP-protected TEG- succinic acid (3 g, 7.92 mmol) was dissolved in DCM (5 ml). The solution was placed on an ice bath and a solution of DCC (817 mg, 3.96 mmol) in DCM (1 ml) was slowly added to the system. The reaction was left to proceed over night. The product was filtered and washed with ether. Yield: 2,657 g (91 %). ^{1}H-NMR ($CDCl_3$) δ(ppm):1.47-1.80 (6H,m, **-CH$_2$-CH$_2$-CH$_2$**-CH- THP), 2.58-2.63 (2H,m, **-CH$_2$**-C(=O)), 2.65-2.77 (2H,m, -C(=O)**-CH$_2$-**), 3.42-3.64 (14H,m, **-CH$_2$**-O- TEG), 3.82 (2H,m, **-CH$_2$**-O- THP), 4.23 (2H,m, **-CH$_2$**-O-C(=O)), 4.61 (1H,m, **-CH-**). ^{13}C-NMR ($CDCl_3$) δ(ppm):19.53, 25.57, 28.56, 30.32, 30.71, 62.37, 64.24, 66.78, 69.13, 70.61, 70.68, 70.74, 70.79, 70.88, 99.07, 167.99, 171.79.

Synthesis of PCL240-G3-TEG-THP



Polymerization of Ɛ-caprolactone (Bz-PCL$_{240}$)

A flame dried 50 mL round bottom flask equipped with a stir bar was charged with 28 µl (0,27 mmol) of benzyl alcohol. The flask was sealed with a septum and 1 ml of dry toluene was added. After heating at 110 °C, toluene was removed under vacuum for a period of 10 min and the flask was refilled with argon. 15 ml of dry toluene and 9.7 ml (87 mmol) of Ɛ-caprolactone were added to the flask. Finally, 1.7 ml of a 0.1 mmol/ml Sn(Oct)$_2$ stock solution in dry toluene (0,17 mmol) was added. The reaction was allowed to proceed at 110 °C until a conversion of 75 % had been reached, as observed by ^{1}H-NMR. The reaction vessel was removed from the oil bath, diluted with 30 ml of dichloromethane and precipitated in 1l of methanol. The white precipitate was filtered off and dried under vacuum. Yield: 6.69 g (95 %). ^{1}H-NMR (CDCl$_3$) δ(ppm): 1.34-1.42 (m, PCL backbone, -CH$_2$-**CH$_2$**-CH$_2$-), 1.56-1.66 (m, PCL backbone, - **CH$_2$**-CH$_2$-**CH$_2$-**), 2.29-2.33 (t, PCL backbone, J = 8.0 Hz, -**CH$_2$**-C(=O)-), 3.65 (2H, m, -**CH$_2$**-OH), 4.06 (t, backbone, J = 6.7 Hz, -**CH$_2$**-O-), 5.11 (2H,s, Bz-**CH$_2$**-O-), 7.35 (5H,m, Bz).

Synthesis of Bz-PCL$_{240}$-N$_3$

In a round bottom flask were added Bz-PCL$_{240}$ (1 g, 0.039 mmol), DMAP (1 mg, 0.008 mmol), pyridine (9 µl, 0,12 mmol) and 1 ml dichloromethane. 6-azidohexanoic anhydride (52 mg, 0,19 mmol) was dissolved in 1 ml dichloromethane and the solution was slowly added to the round bottom flask. The reaction was left to proceed over night. After precipitation on methanol, the product was collected as a white powder. Yield: 972 mg (96%). %). ^{1}H-NMR (CDCl$_3$) δ(ppm): 1.36-1.38 (m, PCL backbone and azide, -CH$_2$-**CH$_2$**-CH$_2$-), 1.59-1.65 (m, PCL backbone and azide, - **CH$_2$**-CH$_2$-**CH$_2$-**), 2.28-2.36 (t,PCL backbone, J = 8.0 Hz, -**CH$_2$**-C(=O)-), 2.37 (2H, m, -**CH$_2$**-N$_3$), 3.27 (2H,t, J = 6.7 Hz, -C(=O)-O-**CH$_2$**-CH$_2$- azide), 4.06 (t, backbone, J = 6.7 Hz, -**CH$_2$**-O-), 5.11 (2H,s, Bz-**CH$_2$**-O-), 7.35 (5H,m, Bz).

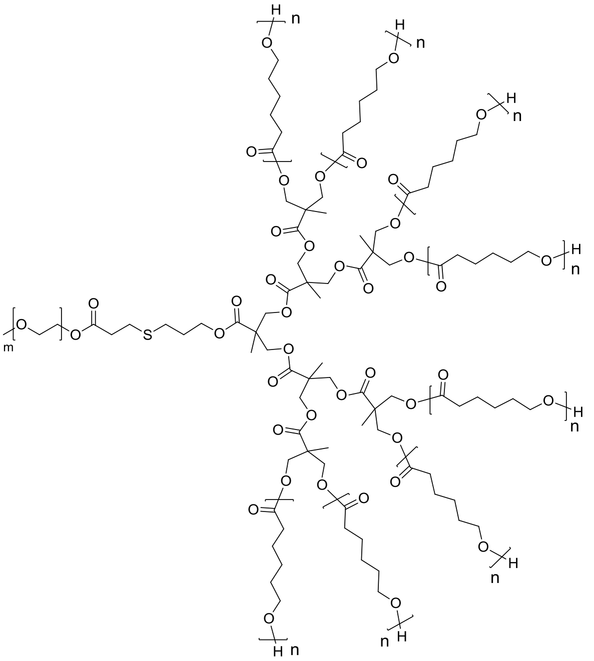
Synthesis of Bz-PCL$_{240}$-G3-OH

In a round bottom flask were added Bz-PCL$_{240}$-N$_3$ (500 mg, 0,019 mmol) and alk-G3-OH (20 mg, 0,023 mmol). The system was degassed by three vacuum/argon cycles (2min/2min). 1 ml of DMF and CuBr (2.8 mg, 0,019 mmol) were added to the system. The system was degassed again with 3 vacuum/argon cycles. PMDETA (4 µl, 0.019 mmol) was added to the system. The reaction was left to react over night at 30 °C. The product was precipitated in cold methanol and collected as a white powder. Yield: 360 mg (70 %). ^{1}H-NMR ($CDCl_3$) δ(ppm):1.07 (12H, s, -CH_3, third generation),1.24-1.27 (9H,m, - CH_3), 1.33-1.41 (m, PCL backbone and azide, -CH_2-**CH_2**-CH_2-), 1.60-1.68 (m,PCL backbone and azide, **- CH_2**-CH_2-**CH_2-**), 2.28-2.32 (t, PCL backbone, J = 8.0 Hz, **-CH_2**-C(=O)-), 3.40 (8H,s, -CH_2-O**H**), 3.710-3.79 (16H,m, **-CH_2**-OH), 4.05 (t, PCL backbone, J = 6.7 Hz, **-CH_2**-O-),4.21-4.30 (12H,m, **-CH_2**-O- dendron), 5.11 (2H,s, Bz-**CH_2**-O-), 5.27 (2H,s, triazole-**CH_2**-O-), 7.35 (5H, m, Bz), 7.76 (1H,s, triazole).

Synthesis of Bz-PCL$_{240}$-G3-TEG-THP

To a round bottom flask were added Bz-PCL$_{240}$-G3-OH (150 mg, 0.0056 mmol), DMAP (1 mg, 0.0089 mmol), pyridine (10 µl, 0.013 mmol) and dichloromethane (0.5 ml). THP protected TEG anhydride (50 mg, 0.067 mmol) was dissolved in dichloromethane (0.5 ml) and the solution was slowly added to the round bottom flask. The reaction was left to proceed over night. After precipitation in cold methanol, the product was obtained as a white powder (65 mg, 38 %). ^{1}H-NMR ($CDCl_3$) δ(ppm): 1.20-1.25 (21H,m, - CH_3), 1.34-1.38 (m, PCL backbone and azide, -CH_2-**CH_2**-CH_2-), 1.60-1.70 (m,PCL backbone, azide and THP **- CH_2**-CH_2-**CH_2-**), 2.28-2.32 (t, PCL backbone, J = 8.0 Hz, **-CH_2**-C(=O)-), 2.63 (32H,s, -C(=O)**-CH_2-CH_2**-C(=O)-), 3.58-3.70 (128H,m, **-CH_2-CH_2**-O-TEG), 3.82 (16H,m, **-CH_2**-O- THP), 4.05 (t, PCL backbone, J = 6.7 Hz, **-CH_2**-O-), 4.21-4.26 (46H,m, **-CH_2**-O- dendron and **-CH_2**-O-C(=O) THP), 4.62 (8H,t, J = 3.6 Hz, **-CH**-), 5.11 (2H,s, Bz-**CH_2**-O-), 5.24 (2H,s, triazole-**CH_2**-O-), 7.35 (5H,m, Bz), 7.73 (1H, s, triazole).

Synthesis of PEG2k-S-G3-PCL30



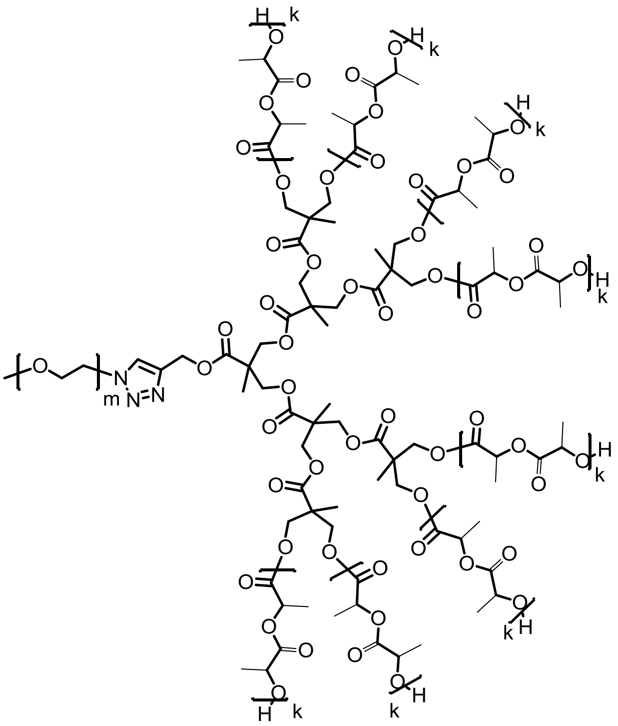
Synthesis of allyl-G3-PCL30

A flame dried round bottom flask equipped with a stir bar was charged with 238 mg (0.3 mmol) of allyl-G3-OH. The flask was sealed with a septum and 1 mL of dry toluene was added. After heating at 110 °C, toluene was removed under vacuum for a period of 10 min and the flask was refilled with argon. 2 ml of dry toluene and 10 g (87.6 mmol) of Ɛ-caprolactone were added to the flask. Finally, 440 µl of a 1 mmol/ml Sn(Oct)$_2$ stock solution in dry toluene (0,2 mmol) was added. The reaction was allowed to proceed at 110 °C until a conversion of 75 % had been reached, as observed by ^{1}H-NMR. The reaction vessel was removed from the oil bath, diluted with dichloromethane and precipitated in cold methanol. The white precipitate was filtered off and dried under vacuum. Yield: 8.08 g. 1H-NMR(CDCl$_3$) δ(ppm) = 1.22 (21H,s, **H$_3$C**-C), 1.28-1.38 (m, backbone, -CH$_2$-**CH$_2$**-CH$_2$-), 1.59-1.65 (m, backbone, **-CH$_2$**-CH$_2$-**CH$_2$-**), 2.29 (t, backbone, J = 7.6 Hz, **-CH$_2$**-C(=O)-), 3.63 (16H,t, J = 6.5 Hz, **-CH$_2$**-OH), 4.05 (t, backbone, J = 6.6 Hz, **-CH$_2$**-O-), 4.16 (28H,m, **-CH$_2$**-O- dendron), 4.61 (2H,d, J = 5.8 Hz,
H$_2$C=CH-**CH$_2$**-O-), 5.23-5.34 (1H, m, H$_2$C=**CH**-CH$_2$-O-), 5.89 (1H, m, **H$_2$C**=CH-CH$_2$-O-).

Synthesis of PEG2k-S-G3-PCL30

A flame dried round bottom flask equipped with a stir bar was charged with 500 mg, (0.018 mmol) of allyl-G3-PCL30 and 354 g (0.18 mmol) of PEG2k-SH. After complete dissolution of the materials in unstabilized THF, DMPA was added in catalytic amount and the solution was purged with argon for 2 min. The solution was then exposed to UV for 60 min using a high pressure mercury lamp (Oriel lamp). The product was purified by precipitation in cold methanol and collected as a white powder. Yield: 445 mg (83 %). ^{1}H-NMR (CDCl$_3$) δ(ppm) =1.20 (21H, s, dendron **-CH$_3$**), 1.32-1.40 (m, PCL backbone –CH$_2$-**CH$_2$**-CH$_2$-), 1.59-1.67 (m, PCL backbone –**CH$_2$**-CH$_2$-**CH$_2$**-), 2.29 (t, PCL backbone , J = 7.4 Hz, –**CH$_2$**-C(=O)-), 2.67 (2H, m, -C(=O)-**CH$_2$**-CH$_2$-S-CH$_2$), 2.75 (2H, m, -C(=O)-CH$_2$-**CH$_2$**-S-CH$_2$), 2.90 (2H, m, -C(=O)-CH$_2$-CH$_2$-S-**CH$_2$**), 3.36 (3H, s, -O**CH$_3$**), 3.63 (m, PEG backbone –**CH$_2$-CH$_2$**-O-), 4.05 (t, J = 6.6 Hz, PCL backbone –**CH$_2$**-O-), 4.17-4.25 (6H,m, -O-CH$_2$ **-CH$_2$**-O-C(=O), S-CH$_2$-CH$_2$-**CH$_2$**-O-C(=O)-, dendron –**CH$_2$**-O-).

Synthesis of PEG2k-G3-PLA 30



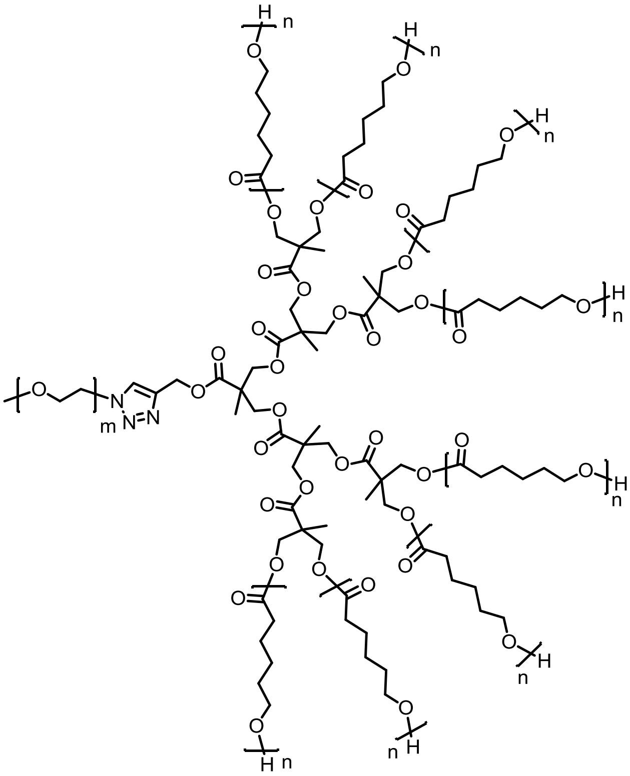
Synthesis of acetylene-G3-PLA30

A flame dried 5 mL round bottom flask equipped with a stir bar was charged with 19 mg (0,022 mmol) of acetylene-G3-OH. The flask was sealed with a septum and 1 ml of dry toluene was added. After heating at 110 °C, toluene was removed under vacuum for a period of 10 min and the flask was refilled with argon. 2 ml of dry toluene and 1 g (2,94 mmol) of lactide were added to the flask. Finally, 34 µl of a 1 mmol/ml $Sn(Oct)_2$ stock solution in dry toluene (0,035 mmol) was added. The reaction was allowed to proceed at 110 °C until a conversion of 75 % had been reached, as observed by ^{1}H-NMR. The reaction vessel was removed from the oil bath, diluted with dichloromethane and precipitated in cold methanol. The white precipitate was filtered off and dried under vacuum. Yield: 398 mg (52 %). ^{1}H-NMR ($CDCl_3$) δ(ppm): 1.20-1.25 (21H,m, -CH_3), 1.47-1.56 (m, PLA backbone, -CH_3), 2.72 (8H, s, -O**H**), 4.24-4.35 (28H, m, -**CH_2**-O- dendron), 4.71 (2H,s, Ac-**CH_2**- O-), 5.12-5.26 (m, PLA backbone, -**CH**(CH_3)-O).

Synthesis of PEG2k-G3-PLA30

In a round bottom flask were added PEG2k-N_3 (6.5 mg, 0,0032 mmol) and Ac-G3-PLA30 (100 mg, 0,0026 mmol). The system was degassed by three vacuum/argon cycles (2min/2min). 1 ml of DMF and CuBr (40 µl of a 10mg/ml solution in DMF, 0.0026 mmol) were added to the system. The system was degassed again with 3 vacuum/argon cycles. PMDETA (0.5 µl, 0.0026 mmol) was added to the system. The reaction was left to react over night at 30 °C. The product was precipitated in cold methanol and collected as a white powder. Yield: 54 mg (51 %). ^{1}H-NMR ($CDCl_3$) δ(ppm): 1.21 (21H, m, -CH_3), 1.35-1.43 (m, PCL backbone, -CH_2-**CH_2**-CH_2-), 1.60-1.66 (m, PCL backbone, **CH_2**-CH_2-**CH_2-**), 2.28-2.32 (t, PCL backbone, J = 8.0 Hz, -**CH_2**-C(=O)-), 3.62-3.66 (m, PEG backbone, -O-**CH_2**-**CH_2**-O-), 4.24-4.35 (28H, m, -**CH_2**-O- dendron), 5.12-5.28 (m, PLA backbone, -**CH**(CH_3)-O), 7.79 (1H, s, triazole).

Synthesis of PEG1k-G3-PCL30



In a round bottom flask were added PEG1k-N_3 (15 mg, 0,0072 mmol) and Ac-G3-PCL30 (400 mg, 0,0060 mmol). The system was degassed by three vacuum/argon cycles (2min/2min). 1 ml of DMF and CuBr (0.86 mg, 0.0060 mmol) were added to the system. The system was degassed again with 3 vacuum/argon cycles. PMDETA (1.2 µl, 0.0060 mmol) was added to the system. The reaction was left to react over night at 30 °C. The product was precipitated in cold methanol and collected as a white powder. Yield: 338 mg (83 %). ^{1}H-NMR ($CDCl_3$) δ(ppm): 1.16-1.25 (21H, m, -CH_3), 1.43-1.56 (m, PLA backbone, -CH_3), 2.72 (8H, s, -O**H**), 3.60-3.64 (m, PEG backbone, -O-**CH_2**-**CH_2**-O-),4.06 (t, PCL backbone, J = 6.7 Hz, -**CH_2**-O-), 4.14-4.25 (28H, m, -**CH_2**-O- dendron), 4.54 (8H,t, J = 3.6 Hz, -**CH**-),5.24 (2H, s, triazole-**CH_2**-O-), 7.81 (1H, s, triazole).

Radius of gyration

The radius of gyration was determined by THF SEC using the Flory-Fox equation.

Sample	Radius of gyration (nm)
PEG2k-G0-PCL60	4.0
PEG2k-G1-PCL60	5.4
PEG2k-G2-PCL60	6.7
PEG2k-G3-PCL60	8.8
PEG2k-G1-PCL30	4.0
PEG2k-G2-PCL30	5.3
PEG2k-G3-PCL30	7.0
PEG2k-G4-PCL30	8.3
PEG2k-G0-PCL240	6.0
PEG2k-G1-PCL120	6.8
PEG2k-G4-PCL15	6.3

Thermal properties

The crystallization temperature and enthalpy of crystallization were determined using DSC

	T_c (°C)	ΔH_c (J/g)
PEG2k-G0-PCL240	32.0	62.1
PEG2k-G1-PCL120	29.8	58.1
PEG2k-G2-PCL60	27.8	60.1
PEG2k-G3-PCL30	31.7	57.7
PEG2k-G4-PCL15	23.0	48.8
PEG2k-G0-PCL60	28.5	89.0
PEG2k-G1-PCL60	28.6	60.8
PEG2k-G2-PCL60	27.8	60.1
PEG2k-G3-PCL60	24.6	62.5
PEG2k-G1-PCL30	27.0	51.3
PEG2k-G2-PCL30	26.7	60.4
PEG2k-G3-PCL30	31.7	57.7
PEG2k-G4-PCL30	24.9	65.0
PEG1k-G3-PCL30	27.2	63.0
PEG5k-G3-PCL60	27.1	63.2
PEG2k-S-G3-PCL3	28.4	56.9
PEG2k-G3-PLA30	/	/
PCL240-G3-TEG-T	30.1	54.7
PCL240-G3-TEG-O	37.1	46.0

Contact angle

Sample	Spin coated film (°)	Isoporous film (°)
PEG2k-G0-PCL60	41 ± 1	51 ± 2
PEG2k-G1-PCL60	72 ± 3	81 ± 3
PEG2k-G2-PCL60	77 ± 1	121 ± 5
PEG2k-G3-PCL60	74 ± 4	123 ± 3
PEG2k-G1-PCL30	41 ± 2	/
PEG2k-G2-PCL30	67 ± 3	75 ± 1
PEG2k-G3-PCL30	73 ± 1	119 ± 3
PEG2k-G4-PCL30	74 ± 4	118 ± 3
PEG2k-G0-PCL240	75 ± 3	83 ± 11
PEG2k-G1-PCL120	70 ± 1	86 ± 10
PEG2k-G4-PCL15	73 ± 2	86 ± 4
PEG2k-S-G3-PCL30	71 ± 6	110 ± 6
PEG1k-G3-PCL30	69 ± 1	115 ± 7
PEG5k-G3-PCL60	77 ± 2	76 ± 17
PEG2k-G3-PLA30	79 ± 3	113 ± 6
PCL240-G3-TEG-THP	80 ± 2	95 ± 7
PCL240-G3-TEG-OH	57 ± 3	74 ± 3

Stability of the films.

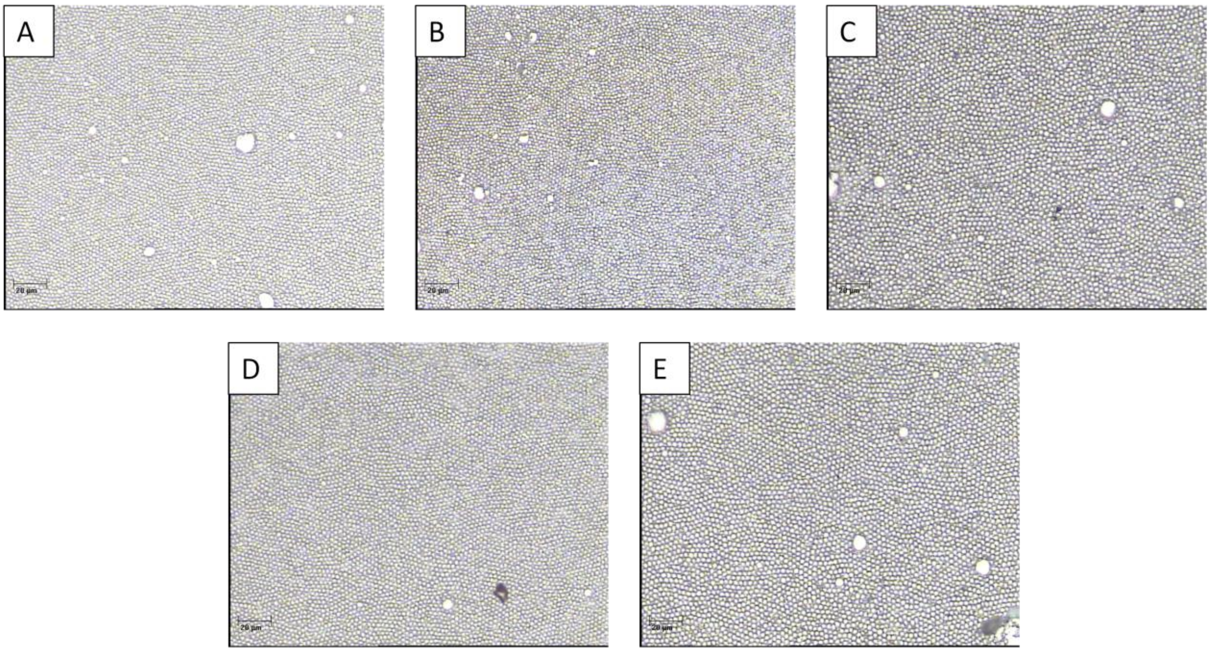


Figure S1: Optical images of honeycomb film cast from PEG2k-G3-PCL30 before immersion in solution (A), after immersion for 3h in PBS at 25 °C (B), in PBS at 37 °C (C), in water at 25 °C (D) and in methanol at 25 °C.

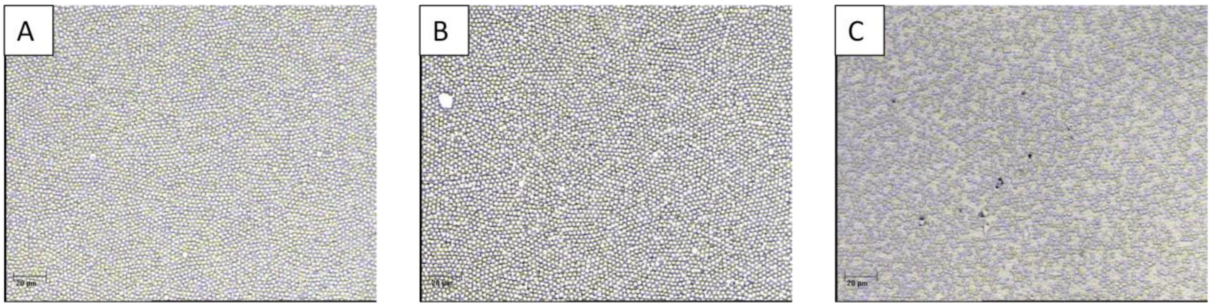


Figure S2: Optical images of honeycomb film cast from PEG2k-G3-PCL30 before heating (A), after heating for 5 min at 48 °C (B) and 50 °C (C).