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*Supporting informations for*

# ADMET polymerization of α,ω-unsaturated glycolipids: synthesis and physico-chemical properties of the resulting polymers

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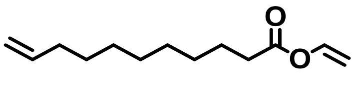
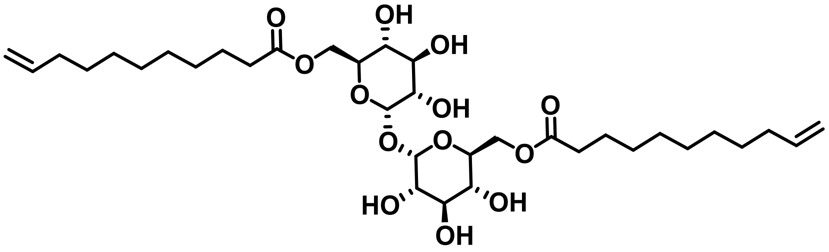
## Experimental and Supporting Information

## Experimental Methods

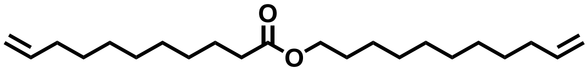
## Synthesis



***Vinyl undecenoate (1) (transvinylation of undecenoic acid):*** Undecenoic acid (1 eq) and a 15 eq. excess of vinyl acetate (VAc) was poured in a vial for the microwave reactor. Then, the palladium acetate (0.05 eq.), and the potassium hydroxide (0.10 eq.) were added and the resulting reaction mixture was stirred under microwave at 60 °C for 2 h. The reaction mixture was diluted in DCM and then filtrated over celite to remove the palladium acetate, before removing the solvent with a rotary evaporator. The resulting residue was purified by silica gel flash chromatography using an elution gradient of 2-5% MeOH in DCM to give the vinyl undecenoate. Yield: 95 %. $^1$H NMR (DMSO-$d_6$, 400MHz, δ (ppm)): 7.29 (m, 1H, =C<u>H</u>-OCO-), 5.81 (m, 1H, -C<u>H</u>=CH$_2$), 4.97 (m, 2H, C<u>H</u>$_2$=CH-), 4.88 (d, 1H, CH$_2$=C<u>H</u>-OCO-), 4.56 (d, 1H, CH$_2$=C<u>H</u>-OCO-), 2.37 (t, 4H, -C<u>H</u>$_2$-COO-), 2.04 (m, 4H, -C<u>H</u>$_2$-CH=CH-), 1.67 (m, 4H, -C<u>H</u>$_2$-CH$_2$-COO-), 1.30 (m, 20H, aliphatic -C<u>H</u>$_2$-).



***Trehalose diundecenoate (2) (enzymatic esterification of trehalose):*** The lipase (2.8 g) was added to a mixture of trehalose (3 g, 9 mmol), vinyl ester (6.8 g, 22 mmol, 2.5 eq) in dry acetone (40 mL). The reaction mixture was stirred at 45 °C for 72 hr. After the reaction time, THF was added to well dissolve the diesters of trehalose, then the reaction mixture was filtered and solvent was removed in rotary evaporator. The obtained crude product was purified by silica gel flash chromatography using an elution gradient of 5-25% methanol in EtOAc-DCM (1:1) to give pure trehalose diesters as white solids. Yield: 50 %. $^1$H NMR (DMSO-$d_6$, 400MHz, δ (ppm)): 5.78 (m, 2H, -C<u>H</u>=CH2), 5.04 (d, 2H, -O<u>H</u>, H4), 4.94 (m, 4H, C<u>H</u>2=CH-), 4.89 (d, 2H, -O<u>H</u>, H3), 4.82 (d, 2H, -C<u>H</u>-, H1), 4.76 (d, 2H, -O<u>H</u>, H2), 4.21 (d, 2H, -C<u>H</u>-, H6), 4.04 (m, 2H, -C<u>H</u>-, H6), 3.89 (m, 2H, -C<u>H</u>-, H5), 3.55 (m, 2H, -C<u>H</u>-, H3), 3.26 (m, 2H, -C<u>H</u>-, H2), 3.13 (m, 2H, -C<u>H</u>-, H4), 2.27 (t, 4H, -C<u>H</u>2-COO-), 2.01 (m, 4H, -C<u>H</u>2-CH=CH-), 1.51 (m, 4H, -C<u>H</u>2-CH2-COO-), 1.33-1.25 (m, 20H, aliphatic -C<u>H</u>2-) ).



***Undecenyl undecenoate (3) (transesterification):*** Undecenol (12.8 g, 0.08 mol.) was blended with 10-methylundecenoate (15 g, 0.08 mol.). TBD (5% mol.) was added as a catalyst. The reaction was performed under a nitrogen flow at 120°C for 2h, then the temperature was increased to 160 °C for 2h more under dynamic vacuum. Purification over silica gel flash chromatography was performed using cyclohexane/ethyl acetate 94/6 eluent. Yield: 76%. $^1$H NMR (400MHz, CDCl$_3$, δ (ppm)): 5.8 (m, 1H, -CH=CH$_2$), 4.9 (m, 2H, CH$_2$=CH-), 4.0 (t, 2H, -CH$_2$COO-), 2.2 (t, 2H, -COOCH$_2$-), 2.0 (m, 4H, -CH$_2$-CH=CH-), 1.5-1.2 (m, 26H, aliphatic -CH$_2$-).

## Synthesis of polymers

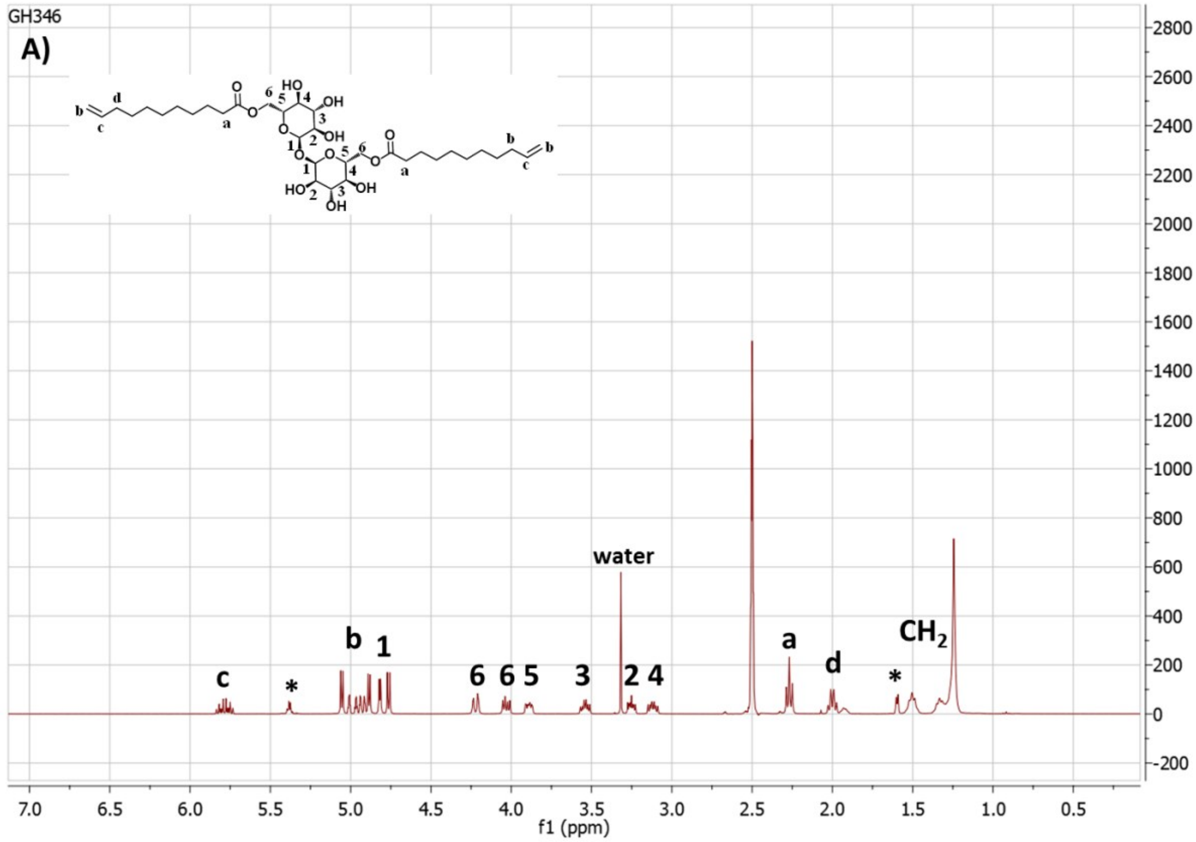
### *ADMET polymerization*

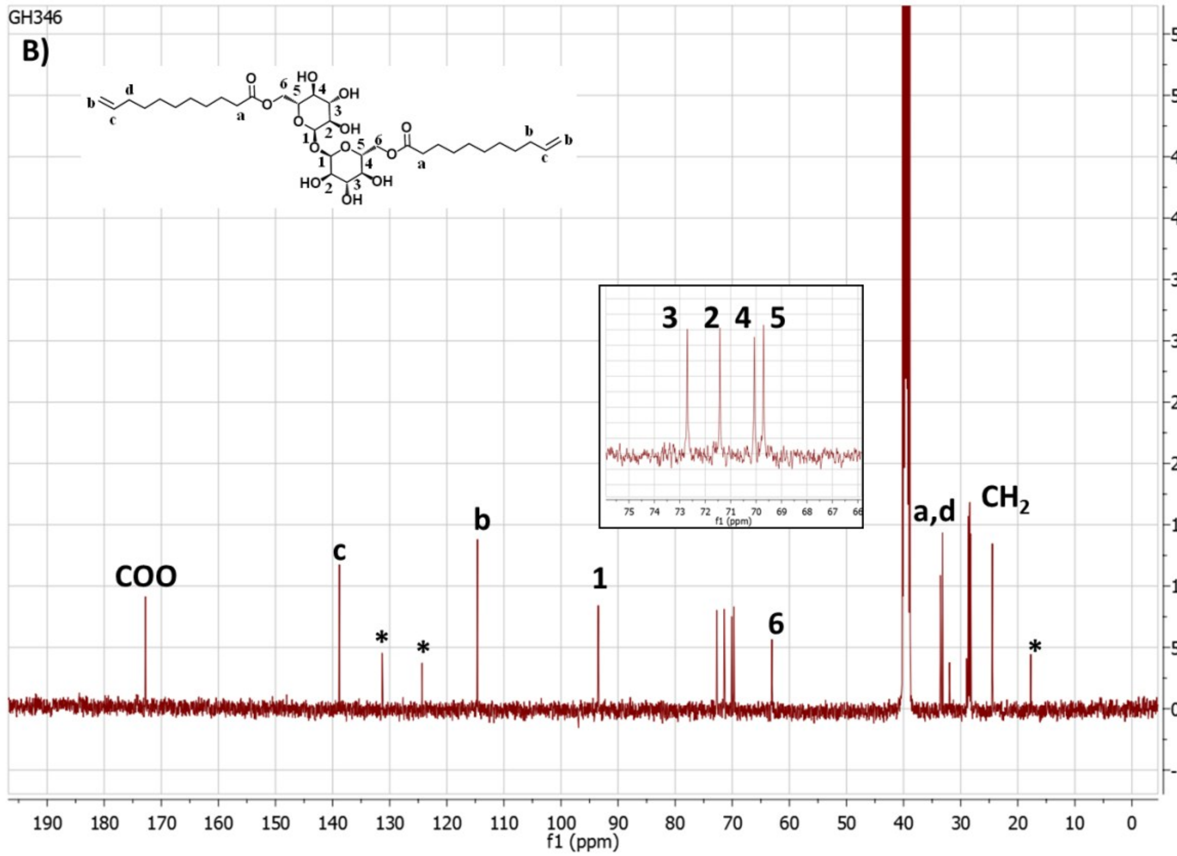
***Homopolymers (P0 and P100):*** Into a flame-dried Schlenk flask equipped with bubbler, undecenyl undecenoate (P0) (0.1 g, 0.3 mmol.) or trehalose diundecenoate (P100) (0.2 g, 0.3 mmol.) dried over-night under vacuum was dissolved in 2 mL of dry THF. Hoveyda-Grubbs 2nd generation metathesis catalyst (4 mol.%) was added and the reaction mixture was stirred under nitrogen atmosphere for 24 h at 45 °C. Then, 3 ml of ethyl vinyl ether were introduced into the flask to quench the reaction. The final glyco-polyester was purified by precipitation in cold methanol.

***Copolymers (P33, P50 and P67):*** Into a flame-dried round Schlenk flask, trehalose diundecenoate (0.2 g, 0.3 mmol.) and the corresponding amount of undecenyl undecenoate (see **Erreur ! Source du renvoi introuvable.**) were mixed and dried over-night under vacuum. Then, the diene monomers were dissolved in 2 mL of dry THF and Hoveyda-Grubbs 2nd generation (4 mol.%) was added. The reaction mixture was stirred at 45 °C under nitrogen atmosphere for 24 h. Then, 3 mL of ethyl vinyl ether and 4 mL of THF were introduced to the flask. The final copolymers were purified by precipitation in cold methanol.

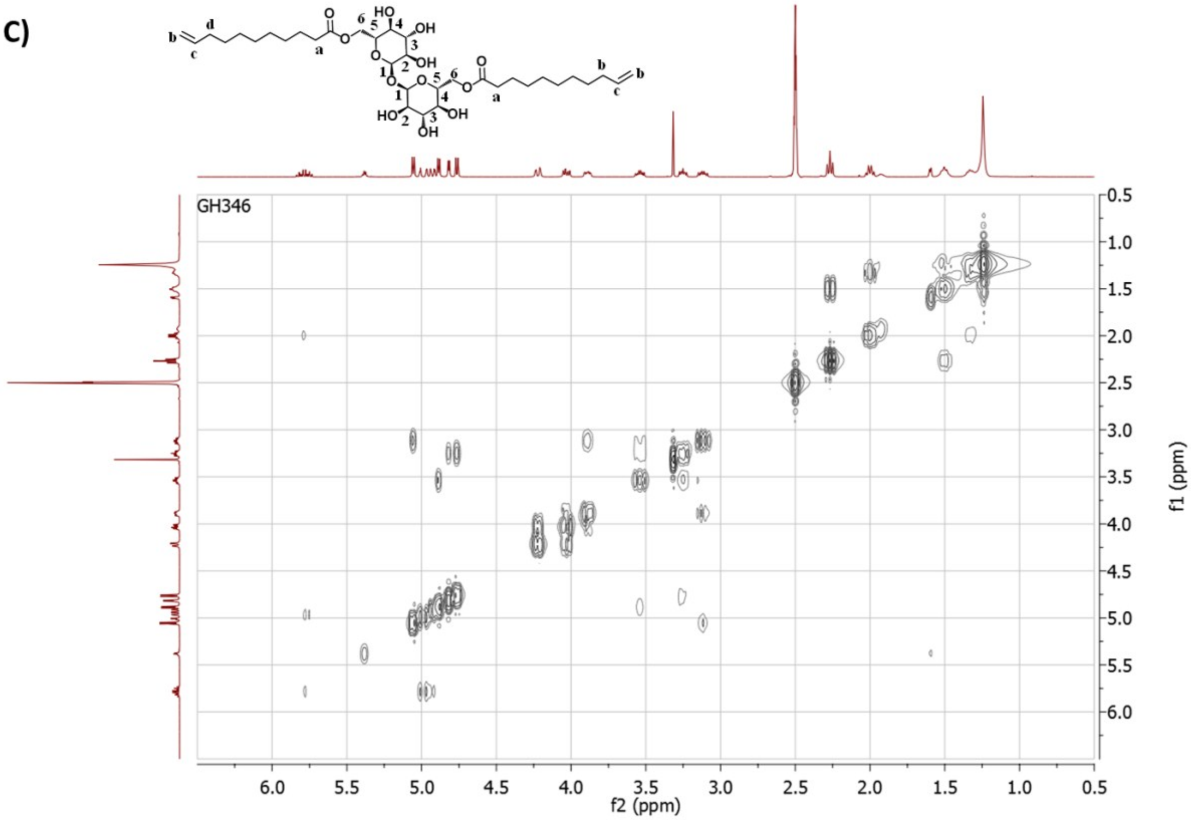
**Preparation of polymer self-assemblies in water**

The nano-particles were prepared using solvent displacement method by dialysis. (Co)polymers were solubilized in DMF and polymer solutions were then poured into dialysis membranes with molecular weight cutoff of 1kD. The membranes were beforehand soaked for 15 min and rinsed with deionized water. The membranes were then submerged in 2 L of deionized water and dialyzed under gentle magnetic stirring for 12 h. After 2 h and 4 h, the dialysis solution was replaced by fresh deionized water. At the end of the dialysis, milky solutions present inside the dialysis membranes were recover.


GH346
A)
c
*
b
1
6
6
5
3
2
4
water
a
d
*
CH₂
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)
2800
2600
2400
2200
2000
1800
1600
1400
1200
1000
800
600
400
200
0
-200


GH346
B)
COO
c
*
*
b
1
6
a,d
CH₂
*
3
2
4
5
75
74
73
72
71
70
69
68
67
66
f1 (ppm)
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)
550
500
450
400
350
300
250
200
150
100
50
0
-50

**C)**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f2 (ppm)
f1 (ppm)
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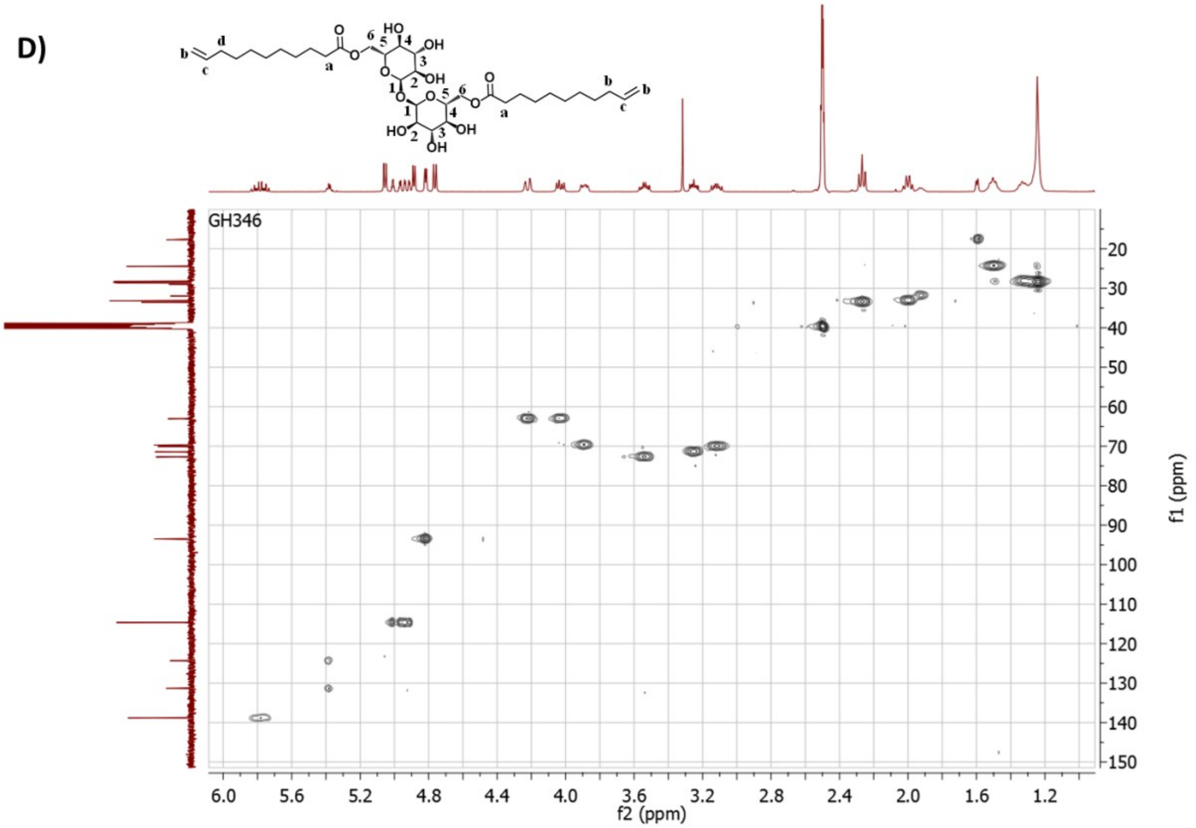
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
HO
OH
a
b
c
d
1
2
3
4
5
6

**D)**


GH346
f2 (ppm)
f1 (ppm)
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5.6
5.2
4.8
4.4
4.0
3.6
3.2
2.8
2.4
2.0
1.6
1.2
20
30
40
50
60
70
80
90
100
110
120
130
140
150
HO
OH
a
b
c
d
1
2
3
4
5
6

**E)**

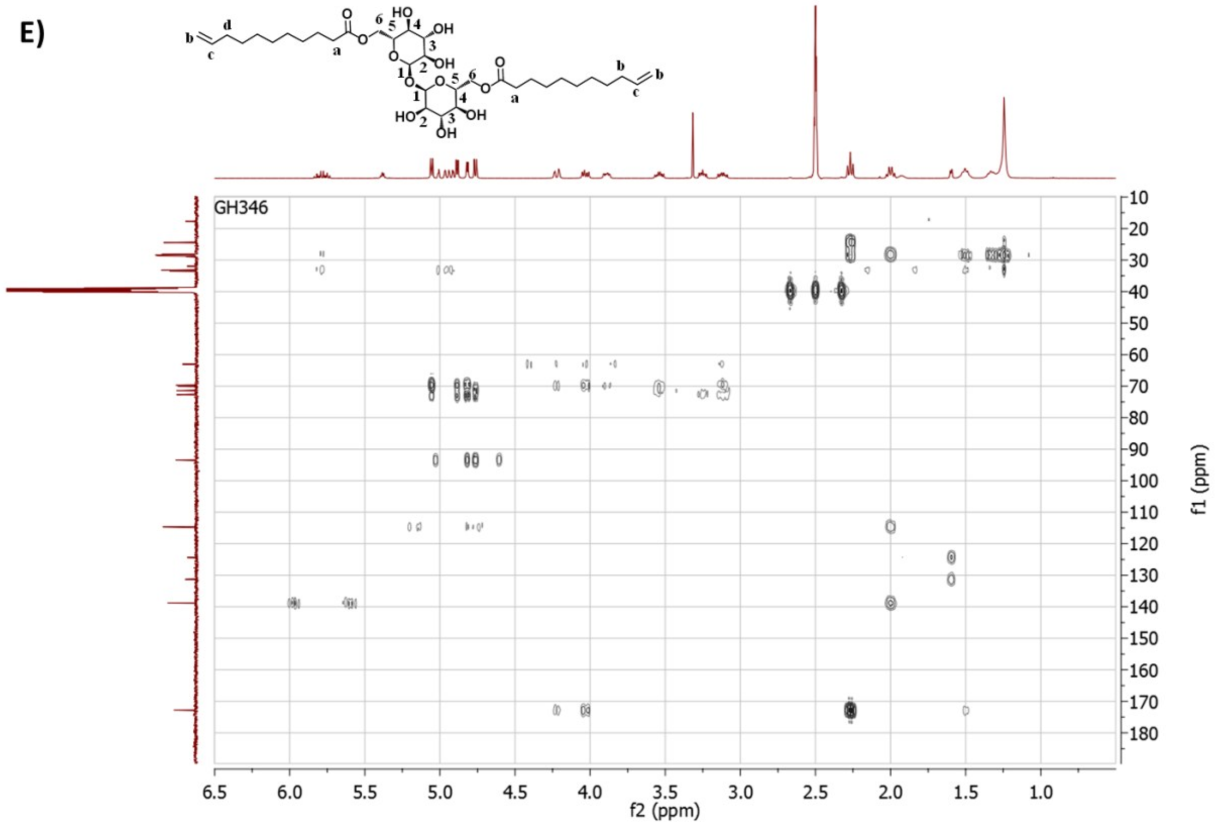
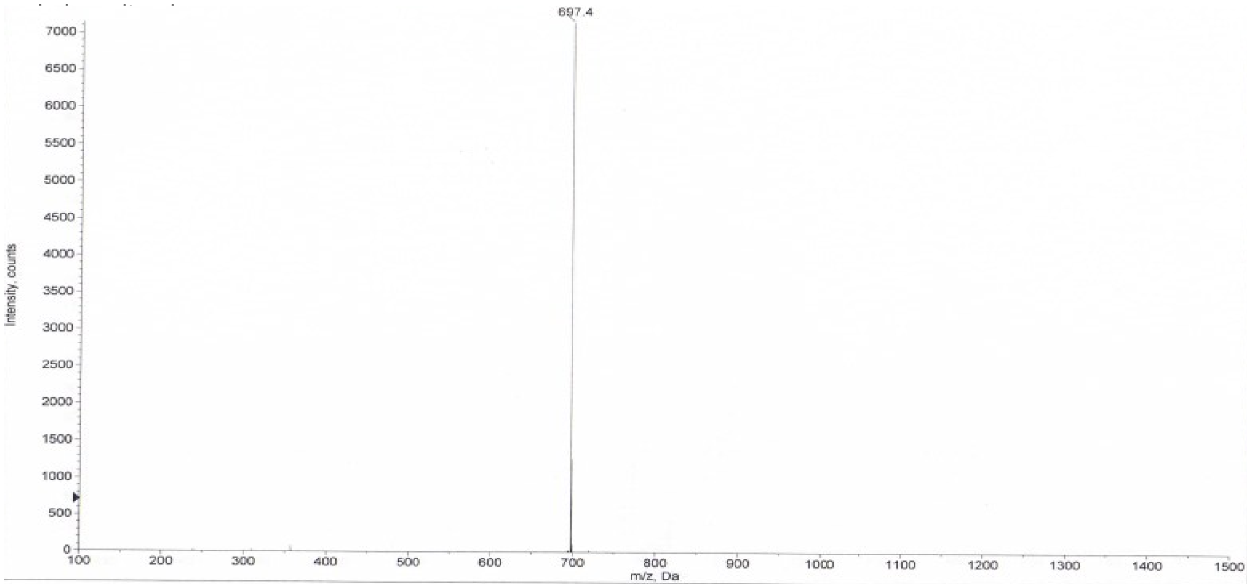


**Fig. S1** NMR spectra of trehalose diundecenoate performed in DMSO-d$_6$. A) $^1$H NMR, B) $^{13}$C NMR, C) $^1$H COSY NMR, D) $^1$H-$^{13}$C HSQC NMR, E) $^1$H-$^{13}$C HMBC NMR. *correspond to isomerized double bonds of



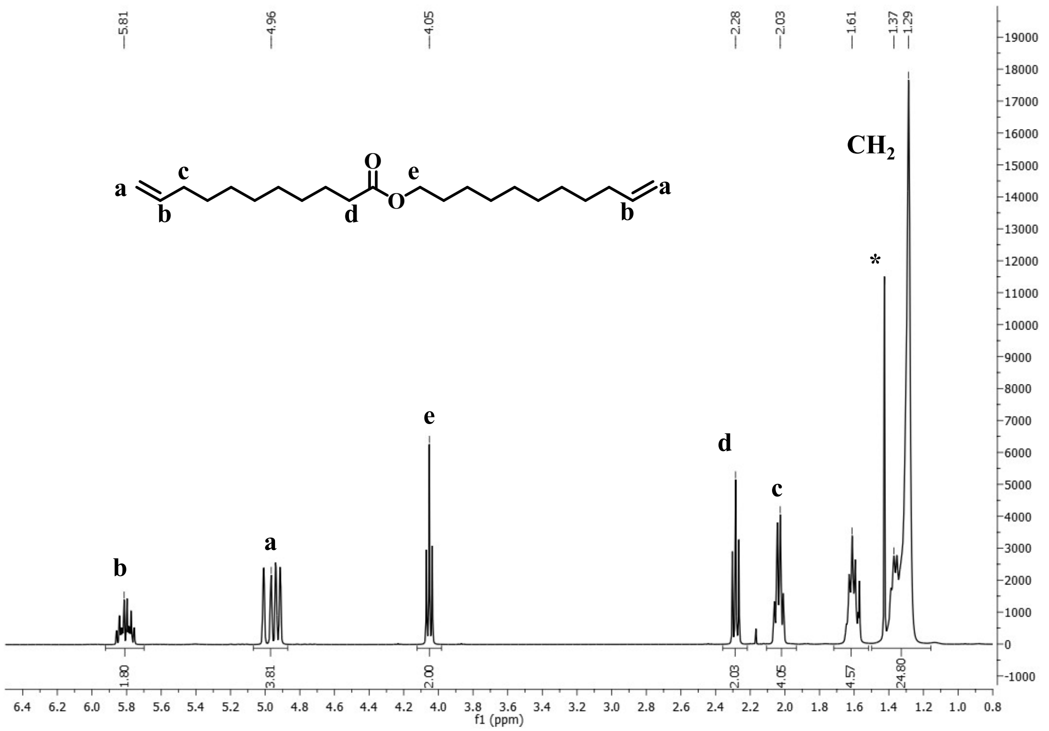
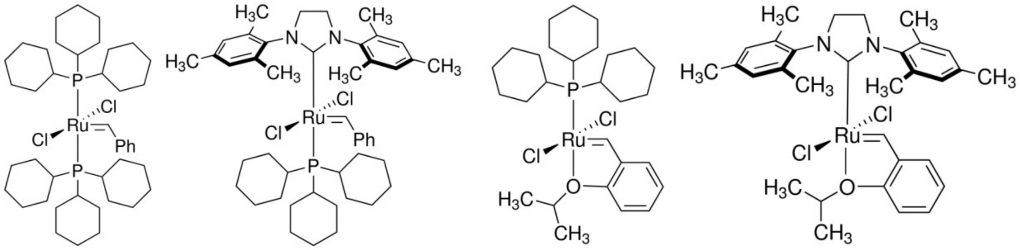


**Fig. S3** $^{1}$H NMR spectrum of undecenyl undecenoate performed in $CDCl_3$.



(G1)
Grubbs 1st generation catalyst

(G2)
Grubbs 2nd generation catalyst

(HG1)
Hoveyda-Grubbs 1st generation catalyst

(HG2)
Hoveyda-Grubbs 2nd generation catalyst

**Fig. S4** Chemical structures of the ruthenium-based metathesis catalysts tested

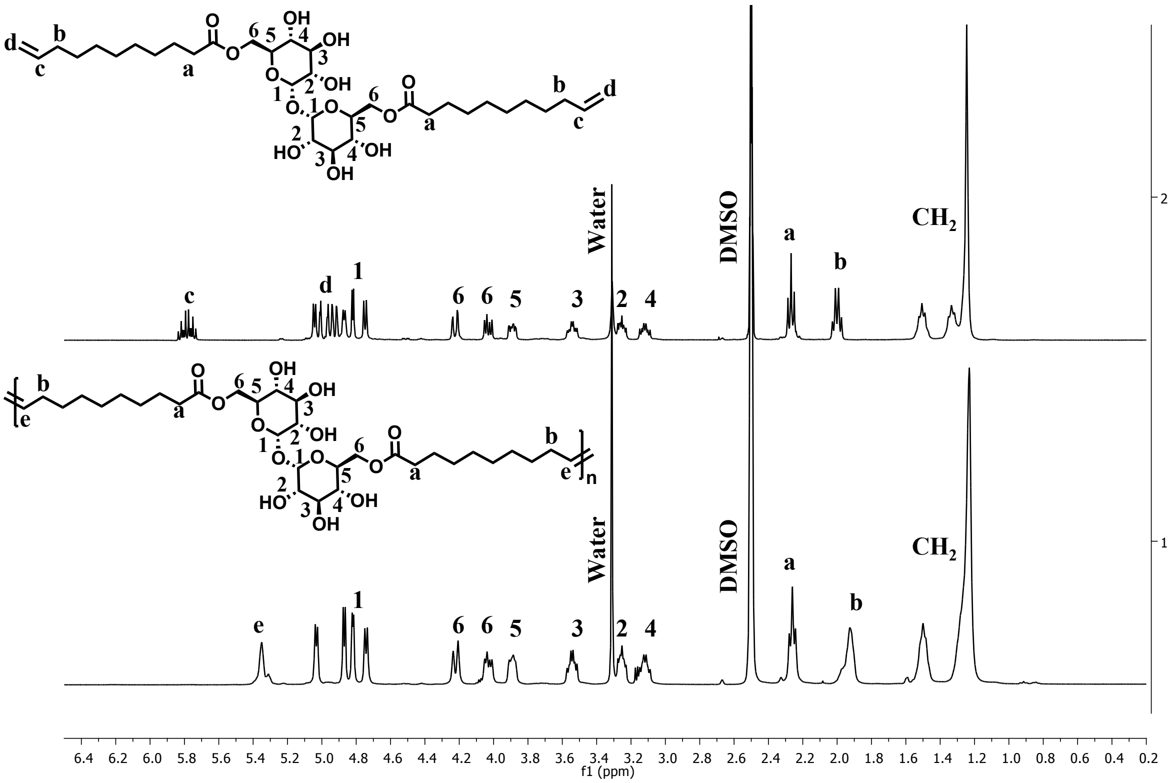


**Fig. S5** Stacked $^1$H NMR spectra of trehalose diundecenoate (top) and the homopolymer P100 synthesized by ADMET from trehalose diundecenoate (bottom) performed in DMSO-d$_6$.

| Entry | Catalyst | $\bar{M}_n$$^a$ (g.mol$^{-1}$) | Đ$^a$ |
|---|---|---|---|
| **1** | G1 | 10000 | 1.9 |
| **2** | G2 | 17000 | 3.1 |
| **3** | HG1 | 4700 | 1.3 |
| **4** | HG2 | 13200 | 2.1 |

**Table S1**: SEC data of poly(trehalose undecenoate) synthesized by ADMET with respect to various ruthenium-based catalysts $^a$Determined by SEC in DMF, PS calibration

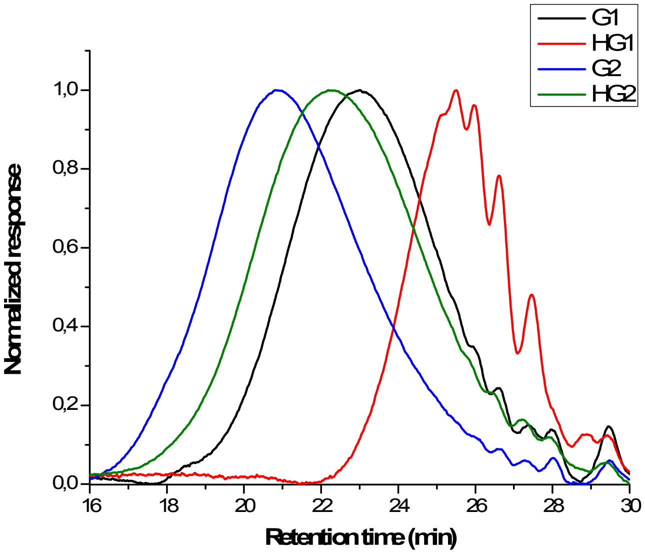


**Figure S6**: SEC traces of poly(trehalose undecenoate) synthesized by ADMET polymerization with different metathesis catalysts performed in DMF (LiBr, PS standards)

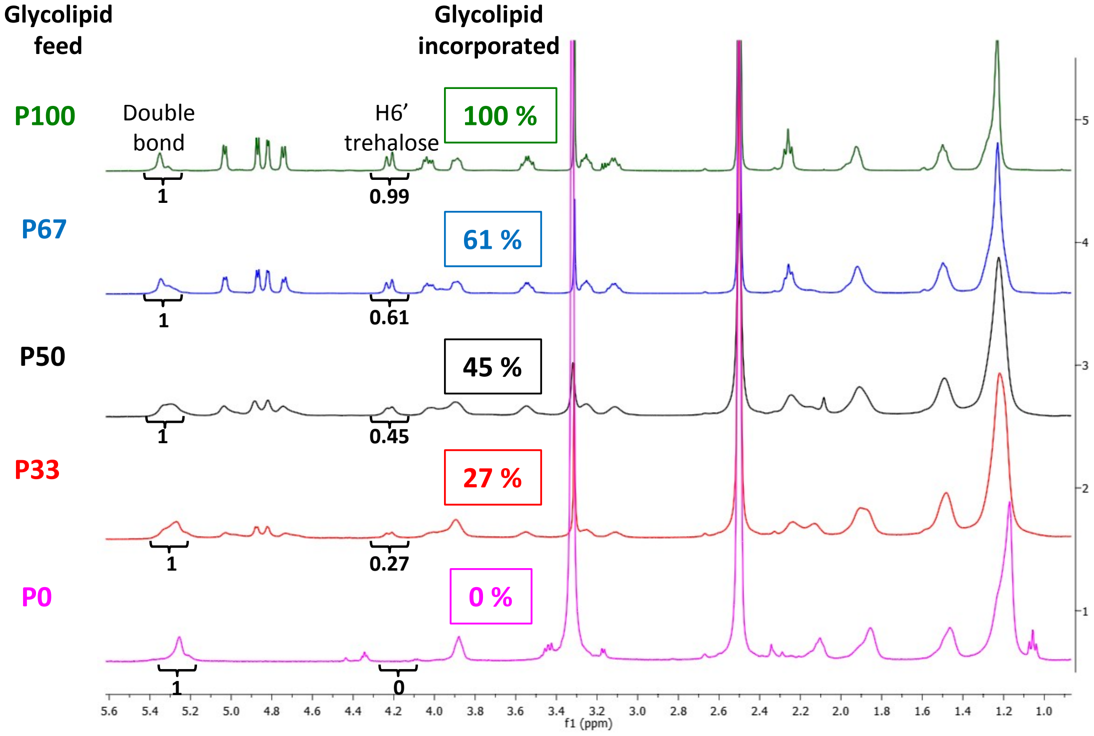


**Fig. S7** $^{1}H$ NMR spectra in DMSO of the copolymers obtained by ADMET, with ratio of trehalose undecenoate incorporated (100 % = 100 % trehalose diundecenoate).

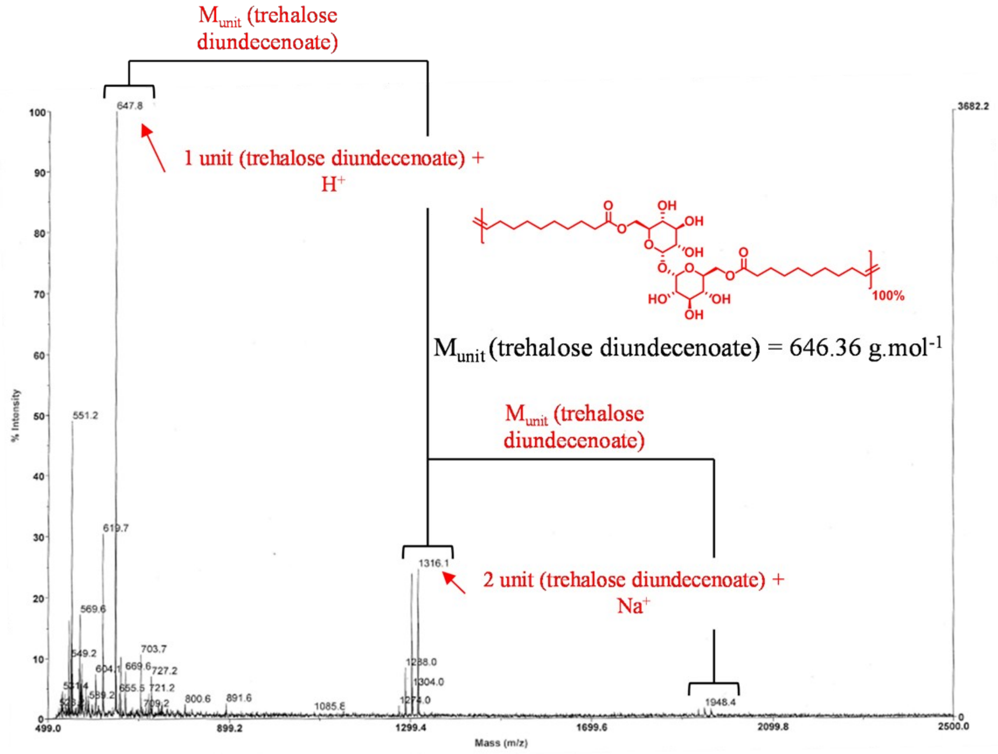


**Fig. S8** MALDI-TOF analysis of P100 (Matrix 2,5-dihydroxybenzoic acid (DHB))

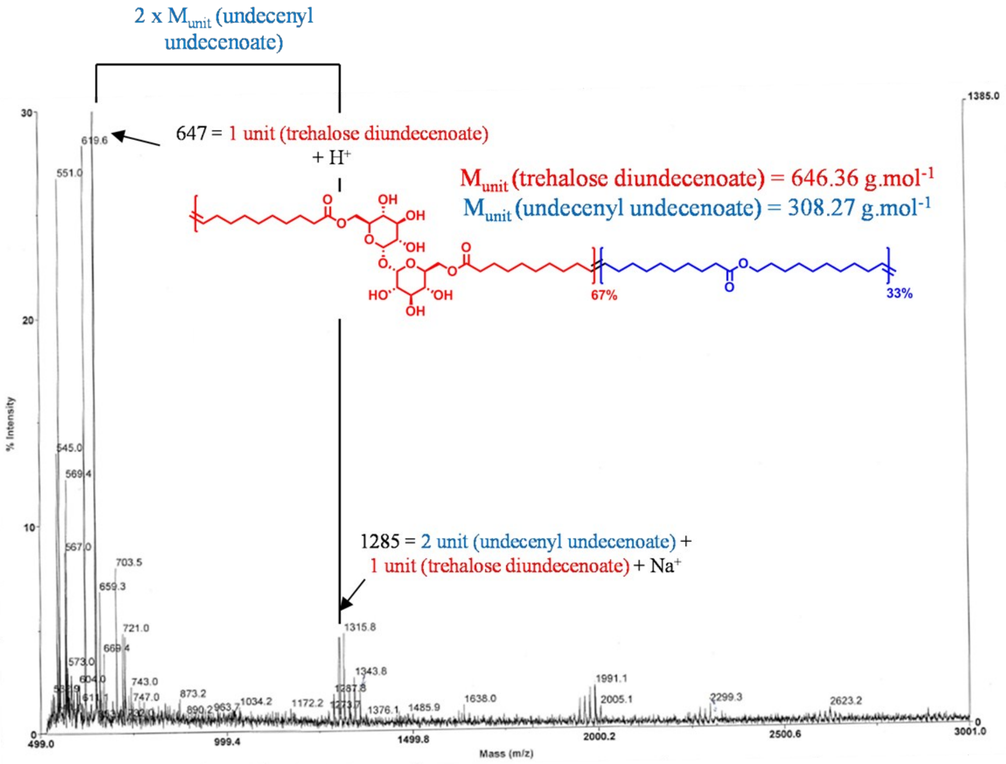


**Fig. S9** MALDI-TOF analysis of P67 (Matrix 2,5-dihydroxybenzoic acid (DHB))

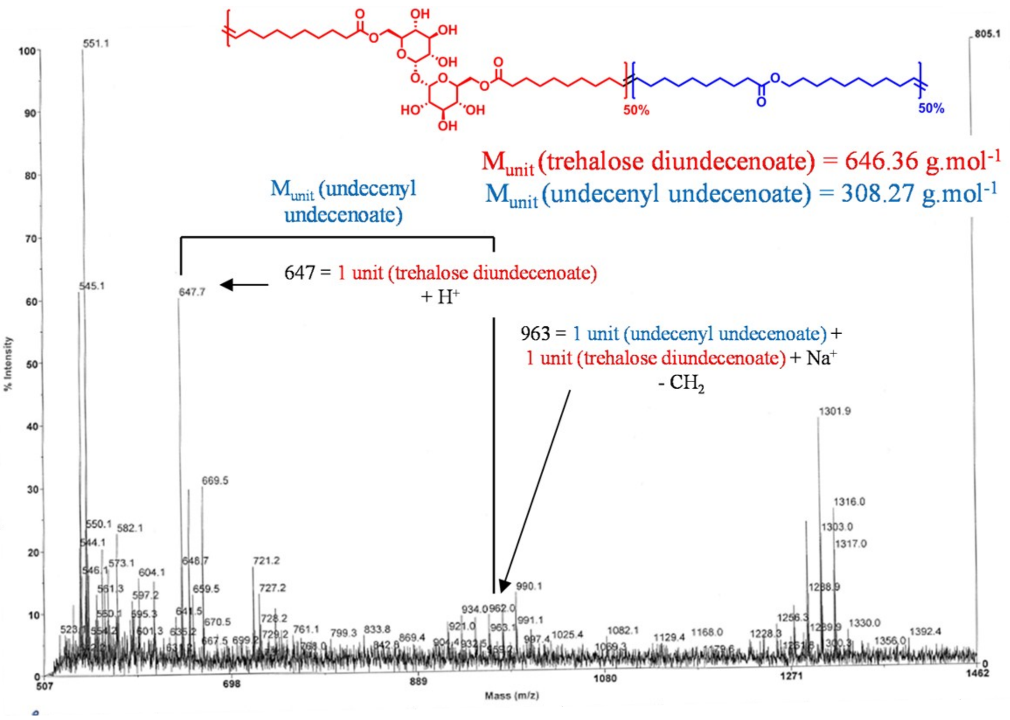


**Fig. S10** MALDI-TOF analysis of P50 (Matrix 2,5-dihydroxybenzoic acid (DHB))

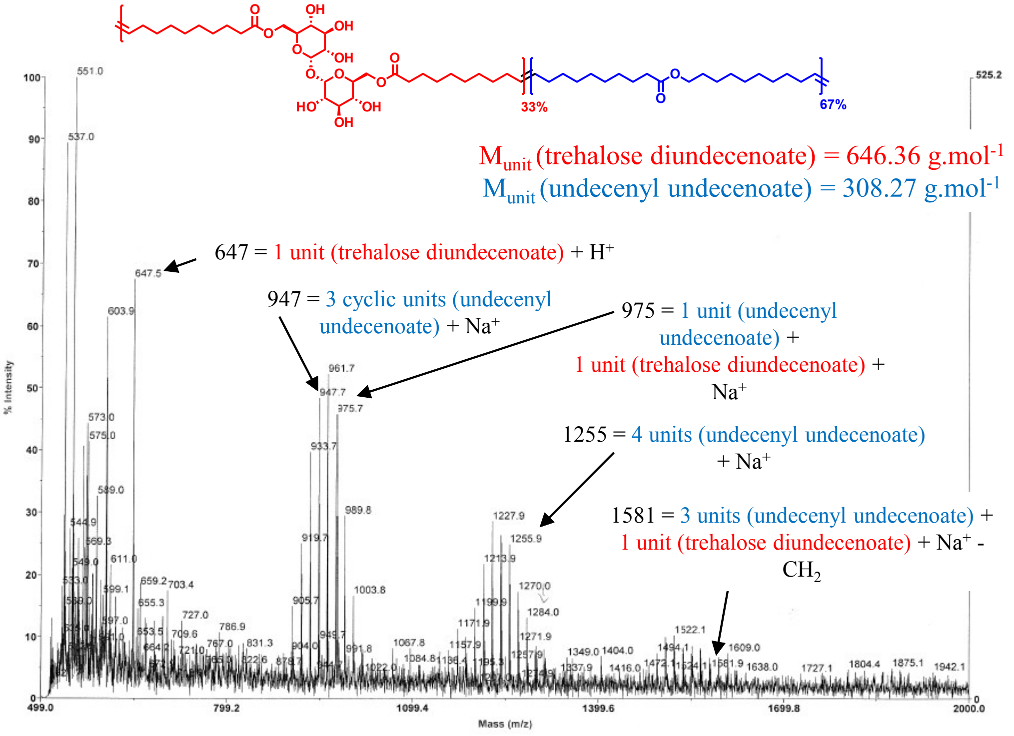


**Fig. S11** MALDI-TOF analysis of P33 (Matrix 2,5-dihydroxybenzoic acid (DHB))

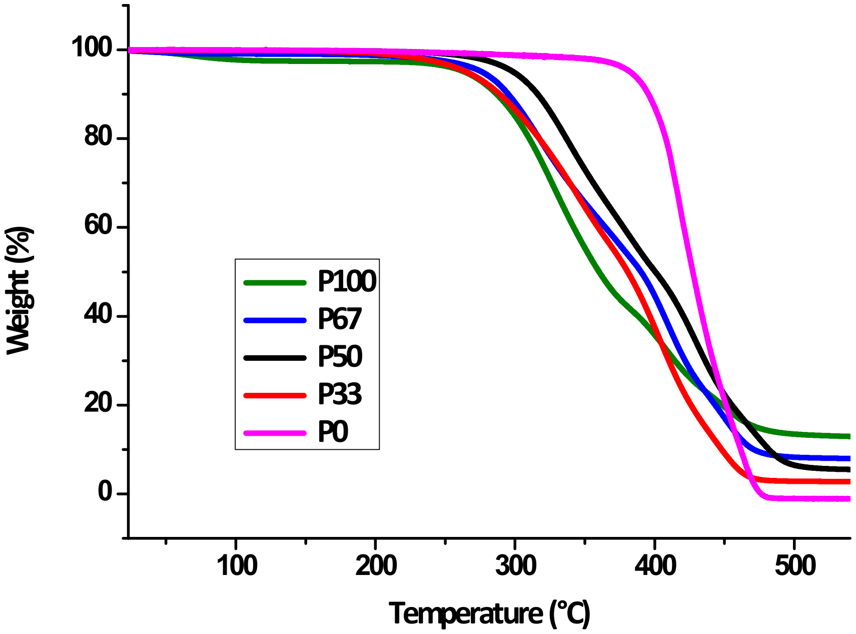


**Fig. S12** TGA curves of (co)polymers obtained by ADMET polymerization.

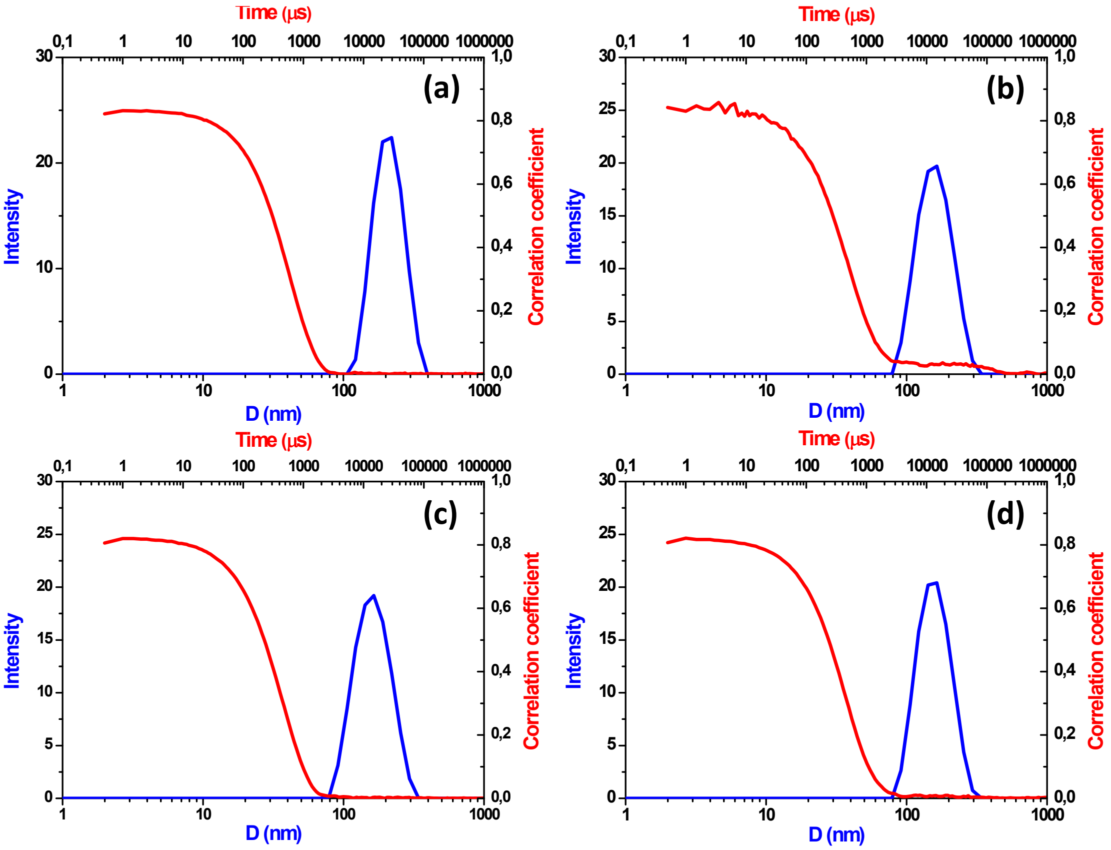


**Fig. S13** Auto-correlation functions (red) and relaxation time and size distributions (blue) (determined at 90°) obtained from Dynamic Light Scattering (DLS) from self-assemblies in water: (a) P100, (b) P67, (c) P50, (d) P33