Supporting Information for publication

Polyhydroxyalkanoate-based amphiphilic diblock copolymers as original biocompatible nanovectors

Ghislaine Barouti,[a] Kathleen Jarnouen,[b] Sandrine Cammas-Marion,[c,*] Pascal Loyer,[b,*] and Sophie M. Guillaume[a,*]

[a] Institut des Sciences Chimiques de Rennes, UMR 6226 CNRS - Université de Rennes 1, Campus de Beaulieu, 263 Avenue du Général Leclerc, F-35042 Rennes Cedex, France
[b] INSERM, UMR991, Liver, Metabolisms and Cancer, CHU Pontchaillou, F-35033 Rennes Cedex - Université de Rennes 1, F-35043 Rennes Cedex, France
[c] Ecole Nationale Supérieure de Chimie de Rennes - Institut des Sciences Chimiques de Rennes, UMR 6226 CNRS - Université de Rennes 1, 11 Allée de Beaulieu CS 50837, F-35708 Rennes Cedex, France

[*] Corresponding authors: sophie.guillaume@univ-rennes1.fr; pascal.loyer@univ-rennes1.fr; sandrine.marion.1@ensc-rennes.fr

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Figure S8. ^{1}H NMR (400 MHz, $CDCl_3$, 23 °C) spectrum of TBD–PMLABe$_{17100}$-*b*-PHB$_{1700}$–crotonate synthesized from the sequential ROP of BL (in bulk) and MLABe (in toluene) using TBD (Table 1, entry 5).

Figure S9. ^{1}H NMR (400 MHz, $CDCl_3$, 23 °C) spectrum of PMLABe$_{8600}$-*b*-PHB$_{2300}$ synthesized from the sequential ROP of BL (in bulk) and MLABe (in toluene) using TBD (Table 1, entry 6) (* marker stands for residual water in $CDCl_3$ and unidentified impurities).

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Figure S12. DOSY NMR (400 MHz, acetone-d_6, 23 °C) spectrum of HO–PMLA$_{800}$-*b*-PHB$_{7300}$–C(O)^{n}Pr obtained upon hydrogenolysis of TBD–PMLABe$_{1700}$-*b*-PHB$_{7300}$–crotonate (Table 2, entry 1; Table 1, entry 2, respectively).

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Figure S14. DOSY NMR (400 MHz, acetone-d_6, 23 °C) spectrum of HO–PMLA$_{8500}$-*b*-PHB$_{1900}$–C(O)^{n}Pr obtained upon hydrogenolysis of TBD–PMLABe$_{17100}$-*b*-PHB$_{1700}$–crotonate (Table 2, entry 6; Table 1, entry 5, respectively).

Figure S15. DSC trace (second heating cycle) of PMLA$_{3300}$-*b*-PHB$_{3100}$ synthesized from the hydrogenolysis of PMLABe$_{6500}$-*b*-PHB$_{3100}$ (Table 2, entry 3 *vs.* Table 1, entry 3, respectively).

Figure S16. DSC trace (second heating cycle) of a PMLA sample ($M_{n,theo}$ = 30 000 g.mol^{-1}) synthesized from the hydrogenolysis of a PMLABe ($M_{n,theo}$ = 60 000 g.mol^{-1}) prepared by anionic ROP of MLABe in bulk initiated by benzoate tetraethylammonium.[11] The thermogram was recorded according to the following cycles: –50 to +70 °C at 10 °C·min^{-1}; +70 to –50 °C at 10 °C·min^{-1}; –50 °C for 5 min; –50 to +150 °C at 10 °C·min^{-1}; +150 to –100 °C at 10 °C·min^{-1}.

Figure S17. DLS analysis of nanoparticles derived from $PMLA_{3300}$-*b*-PHB_{3100} (Table 2, entry 3) using various NaCl concentrations *in PBS*. Self-assembly of the copolymer was performed from the nanoprecipitation method in three solutions of water with salt concentrations ranging from 0.05 M to 0.15 M. As monitored by DLS, analysis of the nanoparticles revealed that 0.15 M was the optimized value.

Figure S18. Determination of the CMC of the $PMLA_{3300}$-*b*-PHB_{3100}-based nanoparticles (Table 2, entry 3) in PBS ($[NaCl]_0$ = 0.15 mol.L^{-1}, pH 7.4) by surface tension measurements.

Figure S19. MTT assays in progenitor and hepatocyte HepaRG and SK-MEL-28 cells incubated with $PMLA_{800}$-*b*-PHB_{7300} based nanoparticles (circles: 24 h; triangles: 48 h; squares: 2 weeks). Statistical analyses: *, $p < 0.05$; **, $p < 0.01$; ***, $p < 0.001$.

Figure S20. Flow cytometry analysis of fluorescence (FL4H channel) in progenitor HepaRG cells incubated for 24 h with $PMLA_{800}$-*b*-PHB_{7300} and $PMLA_{3300}$-*b*-PHB_{3100} nanoparticles loaded DiD Oil. The M1 gate represents the autofluorescence of control HepaRG cells (dotted line histogram), and M2 gate records the fluorescence of cells incubated with nanoparticles (plain line histogram).

Grams scale **sequential ring-opening copolymerization of BL and MLABe promoted by TBD at 60 °C *in bulk*.**

While the *bulk* ROP of BL promoted by TBD proceeded as expected.[1,2] the 1–3 g of PHB were recovered as a highly viscous oil. The subsequent addition of MLABe, even though a less viscous material than the PHB macroinitiator, did not allow to generate a homogeneous reaction medium. As a result, the control of the copolymerization remained very sluggish whichever the various $[BL]_0$:$[MLABe]_0$ ratios (Table S1). Although the NMR spectra of the samples obtained agreed with literature data,[1] the molar mass of the PHB and PMLABe blocks in the copolymers, as determined by NMR (PMLABe-PHB $M_{n,NMR}$; note that to obtain the exact molar mass of the TBD–PMLABe-*b*-PHB–crotonate, this value should be incremented by the molecular weight of the two chain ends, namely M_{TBD} = 139 g.mol^{-1} and $M_{C(O)CHCHCH3}$ = 69 g.mol^{-1}, *i.e.* TBD–PMLABe-*b*-PHB–crotonate $M_{n,NMR}$ = PMLABe-PHB $M_{n,NMR}$ + 208 g.mol^{-1}), did not match well the calculated theoretical molar mass values (PMLABe-PHB $M_{n,theo}$; based on the conversion of both monomers). Moreover, the SEC chromatograms of the thus formed copolymer samples showed bimodal traces suggesting (given the heterogeneity of the reaction medium), the presence of both PHB homopolymer along with PMLABe-*b*-PHB copolymers (Figure S1). Correspondingly, a DOSY NMR spectrum of the same copolymer sample clearly showed that the ^{1}H NMR signals observed (since the PHB homopolymer and the targeted PMLABe-*b*-PHB copolymers feature the same TBD and crotonate chain end-groups,[1,2] they cannot be differentiated from ^{1}H NMR analysis) belonged to two distinct macromolecular species (Figure S2). The thus implemented sequential *bulk* copolymerization of BL and then MLABe at a larger scale, hence revealed unsuccessful for the controlled synthesis of large amounts of well-defined PMLABe-*b*-PHB copolymers.

Copolymerization of MLABe from the TBD–PHB–crotonate macroinitiator in *solution* at 60 °C using a *PHB initial concentration of 0.5 mol.L^{-1}*.

In comparison to the bulk procedure (Table S1), the copolymerization of MLABe from the TBD–PHB–crotonate macroinitiator in *toluene* at $[PHB]_0$ = 0.5 mol.L^{-1}, within 2–6 h, was slightly more controlled in terms of $M_{n,theo}/M_{n,NMR}$ agreement (*i.e.* PMLABe-PHB $M_{n,theo}$ [theoretical molar mass of each block of the TBD–PMLABe-*b*-PHB–crotonate copolymers *not including* either the TBD or the –C(O)CHCHCH$_3$ chain-end groups] / PMLABe-PHB $M_{n,NMR}$ [note that to obtain the exact molar mass of the TBD–PMLABe-*b*-PHB–crotonate, this latter value should be incremented by the molecular weight of the two chain ends, namely M_{TBD} = 139 g.mol^{-1} and $M_{C(O)CHCHCH3}$ = 69 g.mol^{-1}, *i.e.* TBD–PMLABe-*b*-PHB–crotonate $M_{n,NMR}$ = PMLABe-PHB $M_{n,NMR}$ + 208 g.mol^{-1}]) (Table S2). More particularly, the SEC chromatograms were all monomodal; however, the dispersity values ranged from $Đ_M$ = 1.4–1.7, a data still a little high in light of the ones previously obtained from the bulk route with lower loadings of comonomers ($Đ_M$ = 1.13–1.40),[1] and most likely suggesting a faster rate of propagation *vs.* the rate of initiation, and/or the occurrence of some side reactions (transesterification reactions typically encountered in the ROP of cyclic esters and involving intermolecular (reshuffling) and intramolecular (backbiting) reactions).[3]

^{1}H and DOSY NMR characterization of the PHB macroinitiator and the PMLABe-*b*-PHB copolymers.

^{1}H NMR characterization of the PHB macroinitiator[2] and the PMLABe-*b*-PHB isolated copolymers (Figures S5, S7, respectively) confirmed the formation of TBD/crotonate end-capped PMLABe-*b*-PHB copolymers, in agreement with previously reported data.[1] The guanidine methylene and vinylene methine chain-ends signals were clearly identified in the ^{1}H NMR spectra and well-resolved from the signals of the repeating units, thereby allowing the molar mass to be measured by NMR analysis with a good reliability (Table 1). Taking into account these chain-end signals and the intensity ratio between the methine signals of PMLABe (–OC*H*(CO_2CH_2Ph)CH_2 at δ 5.50 ppm) and PHB (–OC*H*(CH_3)CH_2 at δ 5.23 ppm), each block length could thus be estimated (Table 1; refer to Experimental Section). The copolymers with different sizes of PMLABe/PHB segments displayed the corresponding signals of the PHA repeating units in correspondingly varying relative intensities (Figures S6–S9). The values thus determined (PMLABe-PHB $M_{n,NMR}$) matched fairly well the calculated values (PMLABe-PHB $M_{n,theo}$; Table 1). DOSY NMR experiments[4,5,6] on diluted acetone-d_6 solutions of TBD–PMLABe-*b*-PHB–crotonate revealed that, as shown on the DOSY map, ^{1}H NMR signals of PMLABe and PHB present a unique diffusion coefficient (110.10^{-11} $m^2.s^{-1}$), thereby supporting an efficient polymerization of MLABe from the PHB macroinitiator (Figure S11). This diffusion coefficient is lower than that of TBD–PHB–crotonate ($120.10^{-11}m^2.s^{-1}$, Figure S10), in agreement with the higher molar mass of the block copolymer. DOSY analysis thus supported the absence of any residual PHB prepolymer or PMLABe homopolymer, and the presence of a unique macromolecular species in the sample, namely TBD–PMLABe-*b*-PHB–crotonate, in agreement with the above SEC (Figures S3,S5) and ^{1}H NMR analyses.

Nanoprecipitation of the PMLA-*b*-PHB copolymers using *distilled water*.

The nanoprecipitation method carried out using *distilled water*, resulted in ill-defined nano-objects displaying several populations, as evidenced by the very large polydispersity index values measured by DLS (PDI = 0.65–1.21; Table S3). This behavior most likely resulted from the unbalanced forces between the hydrophobic interactions within the PHB inner core and the electrostatic repulsions of the outer hydrophilic corona resulting from the lateral carboxylate groups of the PMLA block (*i.e.* carboxylic acid functions in distilled water at pH = *ca.* 5.5), as previously observed on related PMLA copolymers.[7,8] To solve this issue, the subsequent preparations of PMLA/PHB objects were performed by nanoprecipitation of the PMLA-*b*-PHB copolymers into a *Phosphate Buffer Saline (PBS) aqueous solution* containing NaCl ($[NaCl]_0$ = 0.15 $mol.L^{-1}$, a concentration which also favorably corresponds to the NaCl molarity in physiological conditions; Figure S17) used to neutralize the $–COO^-$ outer shell charges, at pH 7.4, according to the previously established procedure.[8,9,10]

Table S1. Sequential ring-opening copolymerization of BL and MLABe initiated by TBD at 60 °C *in bulk*. [1]

Entry	$[BL]_0$: $[MLABe]_0$: $[TBD]_0$	BL, MLABe Reaction Time [a]	BL, MLABe, conv. [b] (%)	PMLABe-PHB $M_{n,theo}$ [c]	PMLABe-PHB $M_{n,RMN}$ [d]	PMLABe-*b*-PHB $M_{n,SEC}$ [e]	$Đ_M$ [f]
1	17:34:1	1h40, 2h	84, 90	6300-1250	4000-1500	2700	1.42
2	28:24:1	1h50, 2h30	99, 100	4900-2400	4100-1600	1300	2.09
3	30: 25:1	1h30, 1h20	65, 100	5200-1700	6800-5100	3900	1.47
4	30: 25:1	2h30, 1h20	98, 86	4400-2500	5100-3300	5000	1.29
5	39: 14:1	3h, 1h	100, 91	2600-3400	5200-4200	3400	2.12
6	58: 48:1	5h, 6h	94, 100	9900-4700	10300-5300	5700	1.65
7	58: 24:1	5h, 1h30	94, 100	4900-4700	2700-6800	3400	3.08

[a] The reaction time was not necessarily optimized. [b] Monomer conversion determined by ^{1}H NMR analysis of the crude reaction mixture (refer to the Experimental Section). [c] Theoretical molar mass of each block of the TBD–PMLABe-*b*-PHB–crotonate copolymers (*not including* either the TBD or the –C(O)CHCHCH$_3$ chain-end groups) calculated from the relations: $\{[BL]_0/[TBD]_0 \times Conv_{BL} \times M_{BL}\}$ and $\{[MLABe]_0/[TBD]_0 \times Conv._{MLABe} \times M_{MLABe}\}$, respectively, with M_{BL} = 86 g.mol^{-1} and M_{MLABe} = 206 g.mol^{-1}. [d] Experimental molar mass values determined by ^{1}H NMR analysis of the isolated polymer, from ^{1}H resonances of both terminal groups (*i.e.*, base and –C(O)CHCHCH$_3$, refer to the Experimental Section). [e] Experimental molar mass values determined by SEC in THF at 30 °C *vs.* polystyrene standards (uncorrected values; refer to the Experimental Section). [f] Dispersity values determined by SEC analysis in THF at 30 °C.

Table S2. Sequential ring-opening copolymerization of BL (in bulk) and MLABe (in toluene) initiated by TBD at 60 °C,[a] with $[PHB]_0$ = 0.5 mol.L^{-1}.[b]

Entry	$[BL]_0$:$[MLABe]_0$:$[TBD]_0$ [a]	BL, MLABe Reaction Time [c] (h)	BL,MLABe Conv. [d] (%)	PMLABe-PHB $M_{n,theo}$ [e] (g.mol^{-1})	PMLABe-PHB $M_{n,NMR}$ [f] (g.mol^{-1})	PMLABe-*b*-PHB $M_{n,theo}$ [g] (g.mol^{-1})	PMLABe-*b*-PHB $M_{n,sec}$ [h] (g.mol^{-1})	$Đ_M$ [i]
1	29:05:1	2.5, 2	100, 100	1000-2500	1900-3200	3750	3200	1.63
2	29:10:1	2.5, 6.5	100, 100	2100-2500	2500-4000	4750	2500	1.50
3	29:20:1	2.5, 6	100, 100	4100-2500	6400-4600	6800	5700	1.52
4	29:30:1	2.5, 7	100, 94	5800-2500	7000-3000	8500	6400	1.47
5	58:05:1	4, 2	100, 84	900-5000	2200-4200	6050	7200	1.44
6	58:10:1	4, 3	100, 81	1700-5000	3500-6000	6900	5500	1.62
7	58:20:1	4, 6	100, 86	3500-5000	5300-2200	8750	3700	1.71
8	58:30:1	4, 48	100, 100	6200-5000	4700-3800	11 400	3200	1.72

[a] General conditions used: ROP of BL performed in *bulk* and of MLABe performed in *toluene*, both at 60 °C (refer to the Experimental Section). [b] Initial concentration of PHB in toluene prior to the addition of MLABe. [c] The reaction time was not necessarily optimized. [d] Monomers' conversion determined by ^{1}H NMR of the crude reaction mixture (refer to the Experimental Section). [e] Theoretical molar mass of each block of the TBD–PMLABe-*b*-PHB–crotonate copolymers (*not including* either the TBD or the –C(O)CHCHCH$_3$ chain-end groups) calculated from the relations: $\{[BL]_0/[TBD]_0 \times Conv_{BL} \times M_{BL}\}$ and $\{[MLABe]_0/[TBD]_0 \times Conv._{MLABe} \times M_{MLABe}\}$, respectively, with M_{BL} = 86 g.mol^{-1} and M_{MLABe} = 206 g.mol^{-1}. [f] Experimental molar mass values determined by ^{1}H NMR analysis of the isolated block copolymer (*not including* either the TBD or the –C(O)CHCHCH$_3$ chain-end groups) from the resonances of both terminal groups (*i.e.*, base *and* –C(O)CHCH$_2$H$_3$; refer to the Experimental Section). [g] Theoretical molar mass of the TBD–PMLABe-*b*-PHB–crotonate *including* the chain end-groups calculated from the relation PHB-PMLABe $M_{n,theo}$ + M_{TBD} + $M_{C(O)CHCHCH3}$, with M_{TBD} = 139 g.mol^{-1}, $M_{C(O)CHCHCH3}$ = 69 g.mol^{-1}. [h] Experimental molar mass values determined by SEC analysis in THF at 30 °C *vs.* polystyrene standards (uncorrected value; refer to the Experimental Section). [i] Dispersity determined by SEC analysis in THF at 30 °C.

Table S3. Characteristics of the PMLA-*b*-PHB copolymers based nano-objects obtained by nanoprecipitation of $PMLA_{3300}$-*b*-PHB_{3100} (Table 2, entry 3) *in distilled water*.

Entry	$[PMLA\text{-}PHB]_0$ [a] in distilled H_2O ($mg.L^{-1}$)	D_h [b] (nm)	PDI[c]
1	0.5	43,323,1944,98263	1.21
2	2.5	26,82,1262,11826	0.65
3	5	30,160,2520,30220	0.82
4	7.5	32,149,3504,44802	0.91
5	10	23,108,2682,35190	0.70

[a] Concentration of the PMLA-*b*-PHB copolymer in PBS. [b] Diameter given as the average number distribution. [c] Polydispersity index of the nanoparticle size measured from DLS.

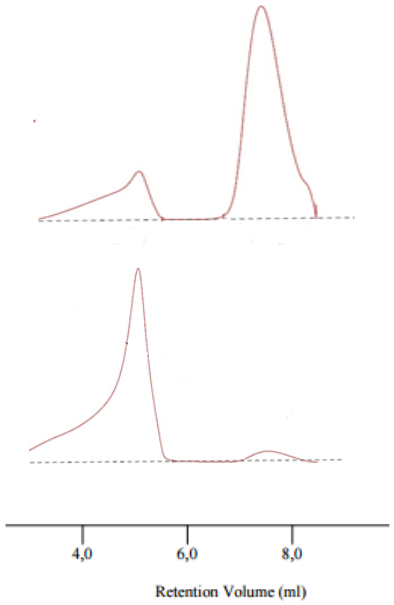


Figure S1. SEC chromatograms of the sample recovered from the sequential *bulk* copolymerization of BL and then MLABe mediated by TBD (top trace), and of a mixture of this same sample along with the corresponding PHB macroinitiator (bottom trace; $M_{n,SEC}$ = 5700 $g.mol^{-1}$, $Đ_M$ = 1.65; Table S1, entry 6).

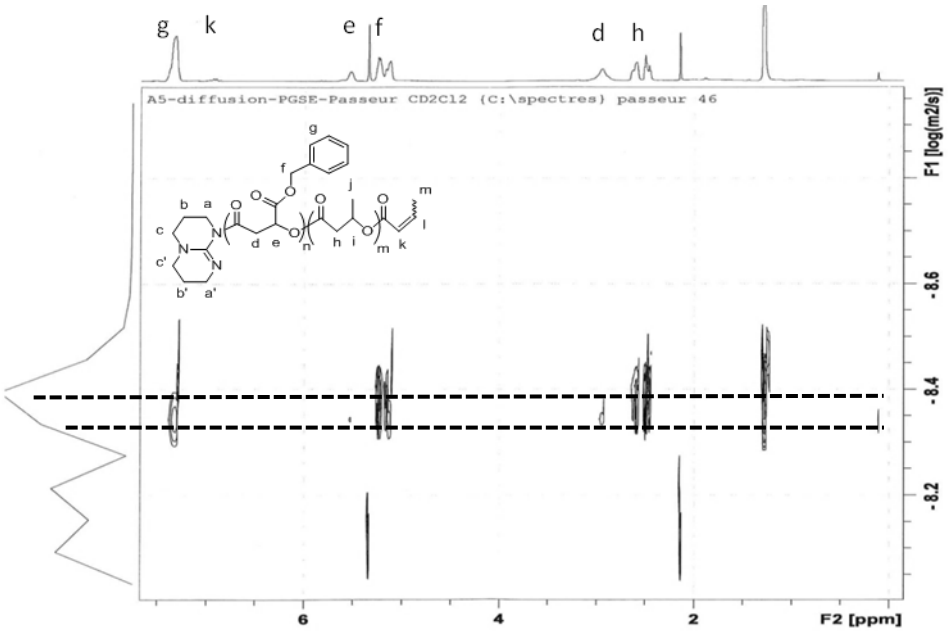


Figure S2. DOSY NMR (400 MHz, CD_2Cl_2, 23 °C) spectrum of PMLABe$_{5200}$-*b*-PHB$_{4200}$ recovered from the sequential *bulk* copolymerization of BL and then MLABe mediated by TBD (Table S1, entry 5).

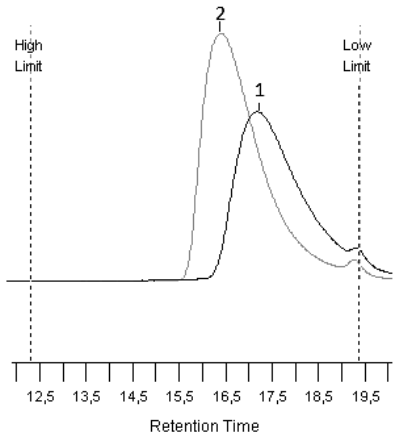


Figure S3. SEC chromatograms of the PHB macroinitiator ($M_{n,SEC}$ = 4500 g.mol^{-1}, $Đ_M$ = 1.26) and the corresponding TBD–PMLABe$_{6500}$-*b*-PHB$_{3100}$–crotonate block copolymer ($M_{n,SEC}$ = 6000 g.mol^{-1}, $Đ_M$ = 1.25) obtained by the sequential copolymerization of BL ($M_{n,NMR}$ = 3400 g.mol^{-1}, Figure S5) and then MLABe mediated by TBD in toluene (Table 1, entry 3). Note that the small peak appearing at the low limit (high retention time) is inherent to the SEC apparatus and appears in all chromatograms (Figure S4). Following the evolution of the molar mass by SEC from the PHB precursor to the ensuing PMLABe-*b*-PHB copolymer showed the shift of the trace to lower elution times, *i.e.* an increase of the molar mass, thereby highlighting the efficiency of the solution ROP of MLABe from the TBD–PHB–crotonate macroinitiator. Also, the absence of the PHB macroinitiator trace in the SEC chromatogram of the copolymer, revealed the complete consumption of PHB during the polymerization of MLABe.

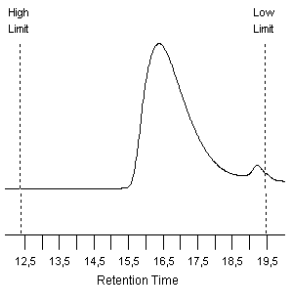
			
PMLABe$_{1700}$-*b*-PHB$_{7300}$ $M_{n,SEC}$ = 5400 g.mol^{-1} $Đ_M$ =1.26	PMLABe$_{6500}$-*b*-PHB$_{3100}$ $M_{n,SEC}$ = 6000 g.mol^{-1} $Đ_M$ = 1.25	PMLABe$_{8600}$-*b*-PHB$_{2300}$ $M_{n,SEC}$ = 4600 g.mol^{-1} $Đ_M$ = 1.23	PMLABe$_{15000}$-*b*-PHB$_{1600}$ $M_{n,SEC}$ = 2700 g.mol^{-1} $Đ_M$ = 1.26

Figure S4. SEC chromatograms of PMLABe-*b*-PHB copolymers recovered from the sequential copolymerization of BL (in bulk) and then MLABe (in toluene), mediated by TBD (Table 1, entries 2, 3, 6, 7).

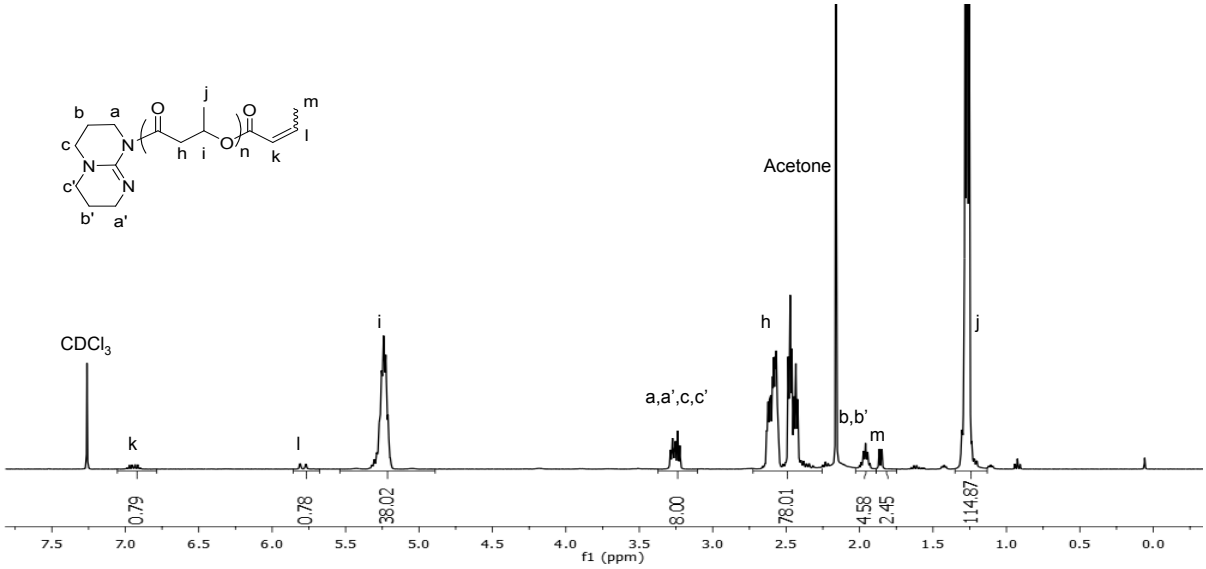


Figure S5. ^{1}H NMR (400 MHz, $CDCl_3$, 23 °C) spectrum of TBD–PHB$_{3400}$–crotonate synthesized from the bulk ROP of BL using TBD ($M_{n,SEC}$ = 4500 g.mol^{-1}, $Đ_M$ = 1.26; Table 1, entry 3).

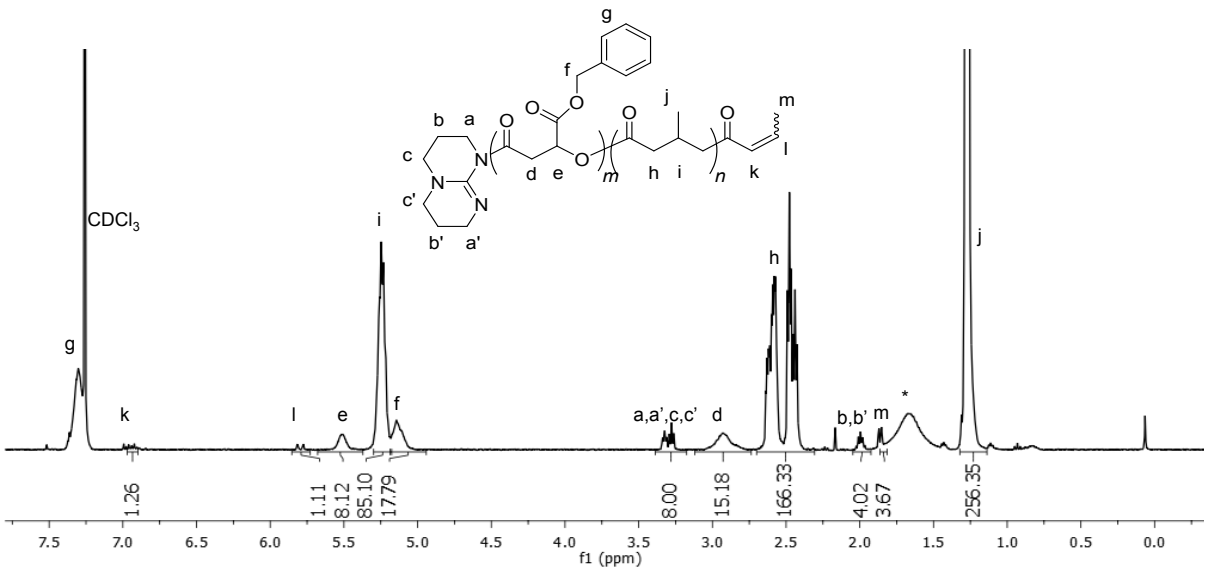


Figure S6. ^{1}H NMR (400 MHz, $CDCl_3$, 23 °C) spectrum of TBD–PMLABe$_{1700}$-*b*-PHB$_{7300}$–crotonate synthesized from the sequential ROP of BL (in bulk) and MLABe (in toluene) using TBD (Table 1, entry 2) (* marker stands for residual water in $CDCl_3$).

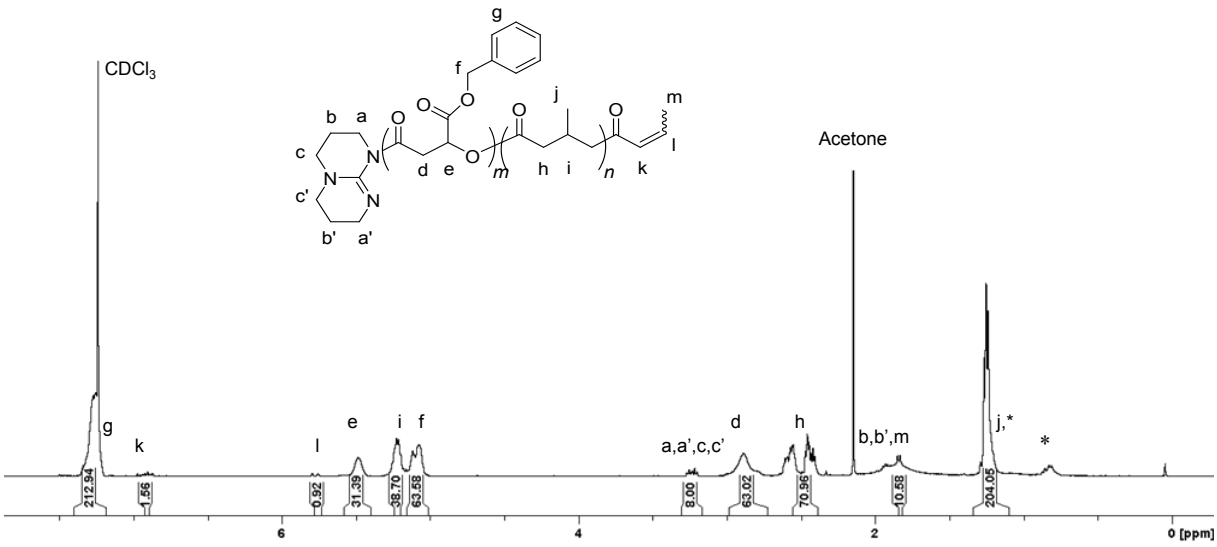


Figure S7. ^{1}H NMR (400 MHz, $CDCl_3$, 23 °C) spectrum of TBD–PMLABe$_{6500}$-*b*-PHB$_{3100}$–crotonate synthesized from the sequential ROP of BL (in bulk) and MLABe (in toluene) using TBD (Table 1, entry 3) (* marker stands for a residual unidentified impurity).

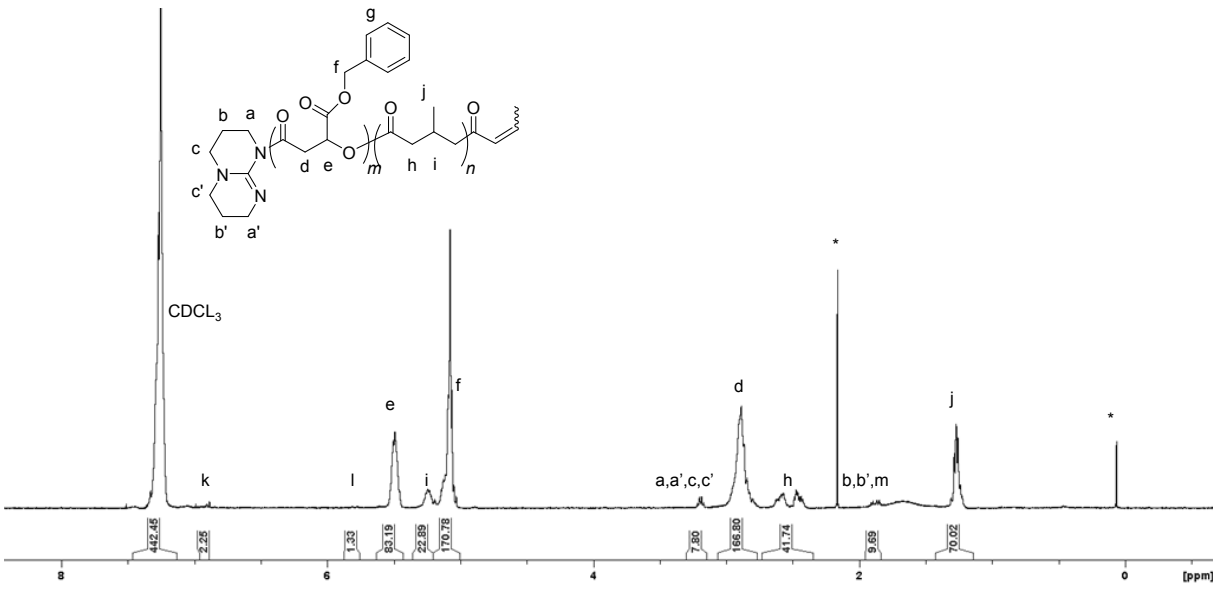


Figure S8. ^{1}H NMR (400 MHz, $CDCl_3$, 23 °C) spectrum of TBD–PMLABe$_{17100}$-*b*-PHB$_{1700}$–crotonate synthesized from the sequential ROP of BL (in bulk) and MLABe (in toluene) using TBD (Table 1, entry 5). Note that the repeating unit signals of both blocks (d,e,h,i,j) in the present spectrum of PMLABe$_{17100}$-*b*-PHB$_{1700}$ display the same integration values as in the spectrum of the deprotected sample of PMLA$_{8500}$-*b*-PHB$_{1900}$ reported Figure 1 (Table 2, entry 6), respectively.

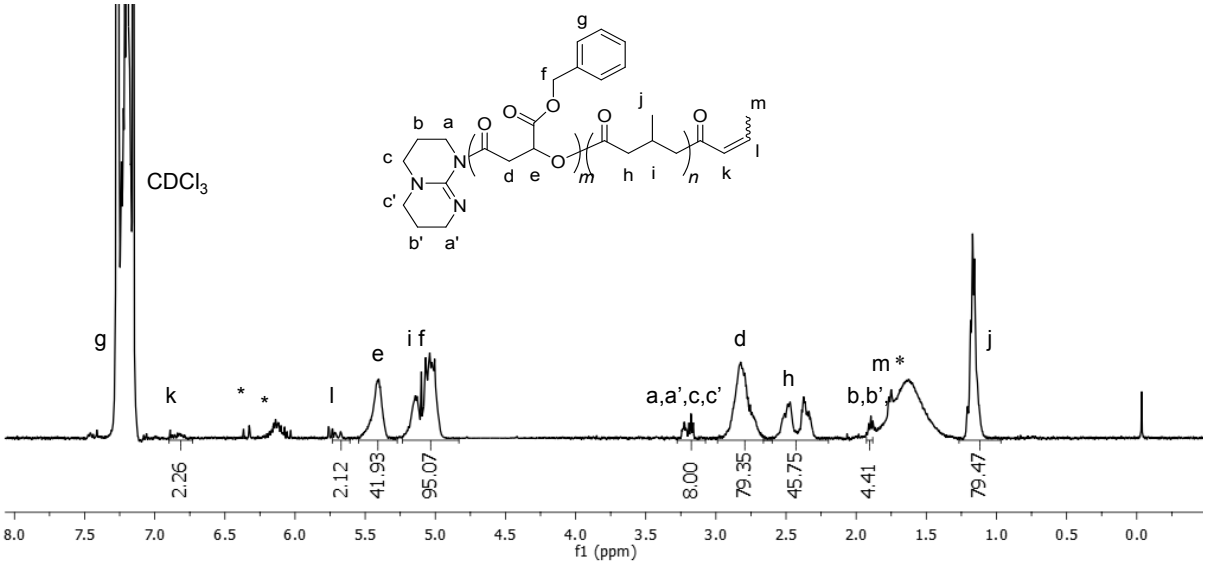


Figure S9. ^{1}H NMR (400 MHz, $CDCl_3$, 23 °C) spectrum of PMLABe$_{8600}$-*b*-PHB$_{2300}$ synthesized from the sequential ROP of BL (in bulk) and MLABe (in toluene) using TBD (Table 1, entry 6) (* marker stands for residual water in $CDCl_3$ and unidentified impurities).

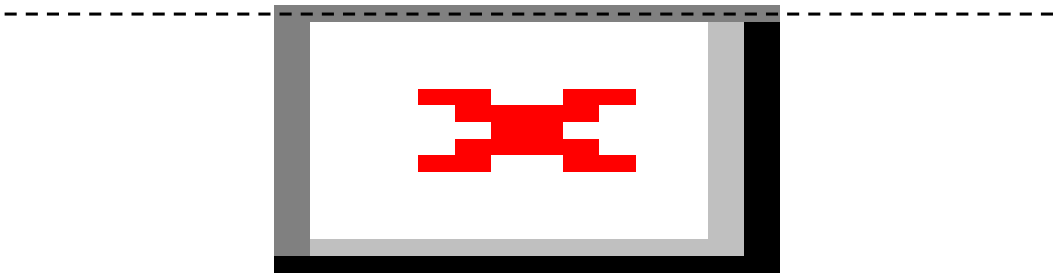


Figure S10. DOSY NMR (400 MHz, acetone-d_6, 23 °C) spectrum of TBD–PHB_{3400}–crotonate synthesized from the ROP of BL (in bulk; Table 1, entry 3).

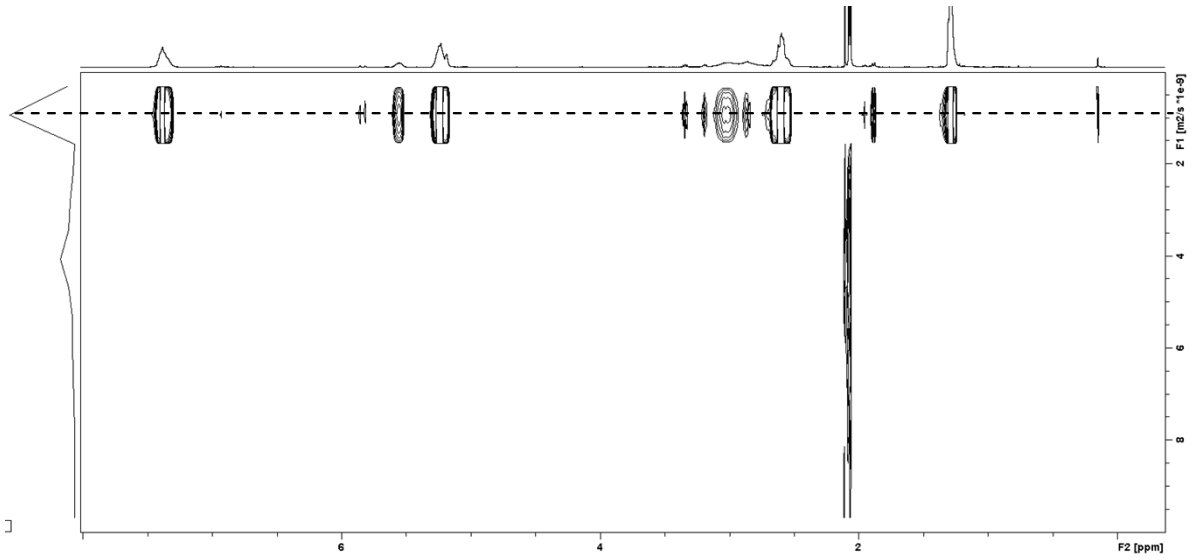


Figure S11. DOSY NMR (400 MHz, acetone-d_6, 23 °C) spectrum of TBD–$PMLABe_{6500}$-*b*-PHB_{3100}–crotonate synthesized from the sequential ROP of BL (in bulk) and MLABe (in toluene) using TBD (Table 1, entry 3).

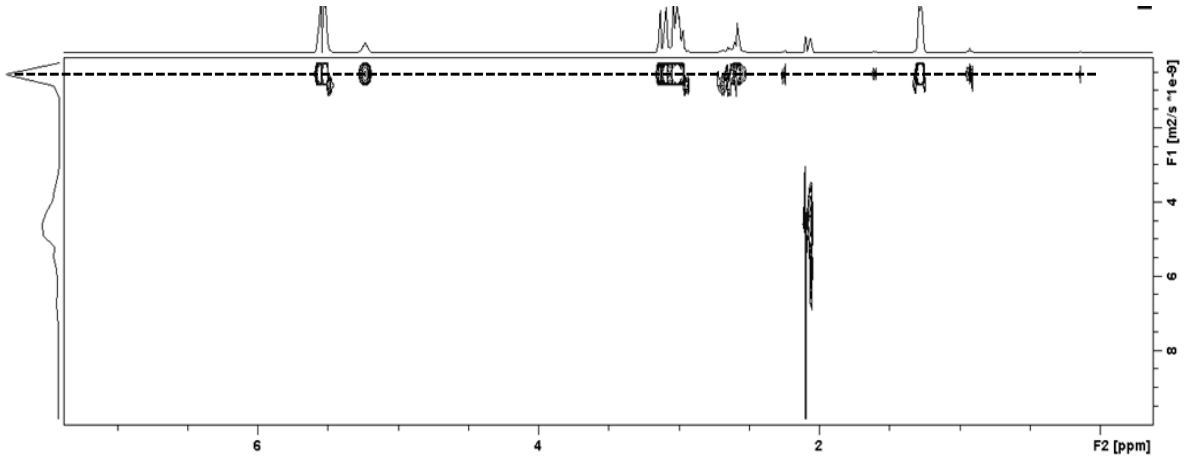


Figure S12. DOSY NMR (400 MHz, acetone-d_6, 23 °C) spectrum of HO–PMLA$_{800}$-*b*-PHB$_{7300}$–C(O)^{n}Pr obtained upon hydrogenolysis of TBD–PMLABe$_{1700}$-*b*-PHB$_{7300}$–crotonate (Table 2, entry 1; Table 1, entry 2, respectively).

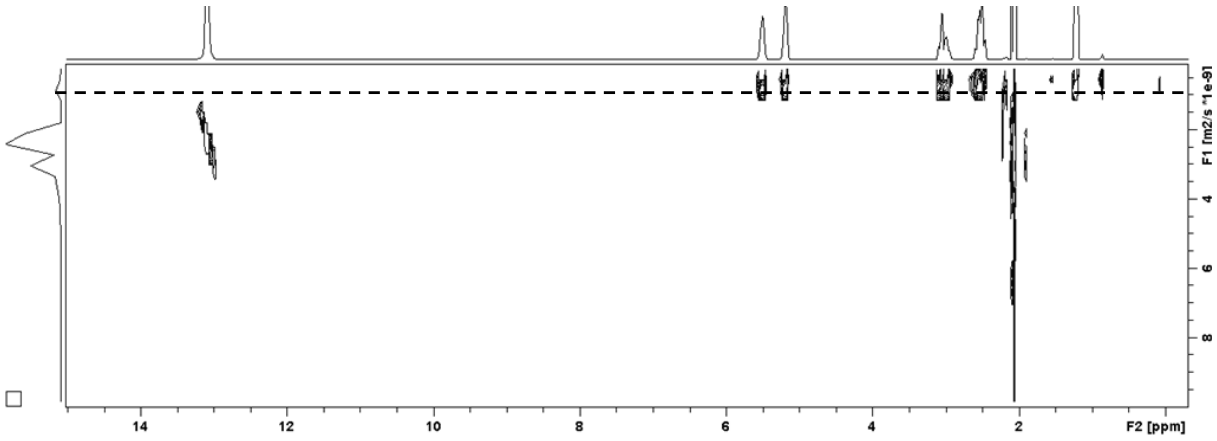


Figure S13. DOSY NMR (400 MHz, acetone-d_6/TFA (80/20, *v*/*v*), 23 °C) spectrum of HO–PMLA$_{3300}$-*b*-PHB$_{3100}$–C(O)^{n}Pr (Table 2, entry 3) obtained upon hydrogenolysis of TBD–PMLABe$_{6500}$-*b*-PHB$_{3100}$–crotonate synthesized from the sequential ROP of BL (in bulk) and MLABe (in toluene) using TBD (Table 1, entry 3).

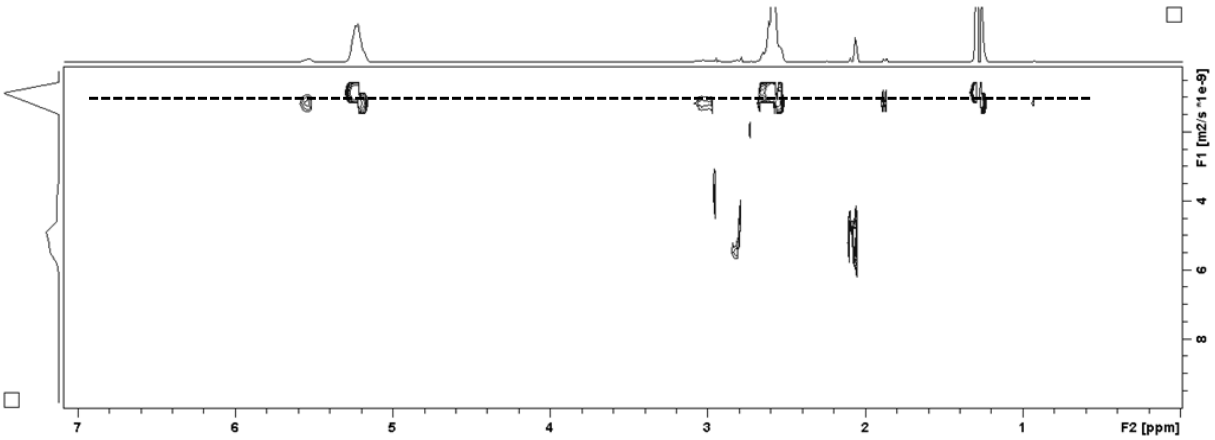


Figure S14. DOSY NMR (400 MHz, acetone-d_6, 23 °C) spectrum of HO–PMLA$_{8500}$-*b*-PHB$_{1900}$–C(O)^{n}Pr obtained upon hydrogenolysis of TBD–PMLABe$_{17100}$-*b*-PHB$_{1700}$–crotonate (Table 2, entry 6; Table 1, entry 5, respectively).

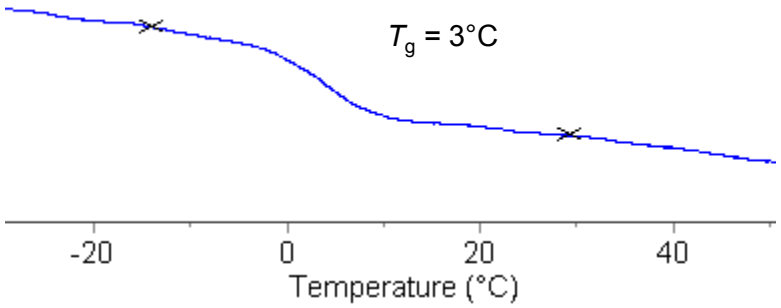


Figure S15. DSC trace (second heating cycle) of PMLA$_{3300}$-*b*-PHB$_{3100}$ synthesized from the hydrogenolysis of PMLABe$_{6500}$-*b*-PHB$_{3100}$ (Table 2, entry 3 *vs.* Table 1, entry 3, respectively).

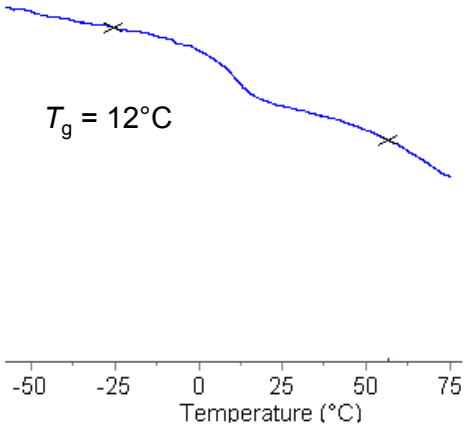
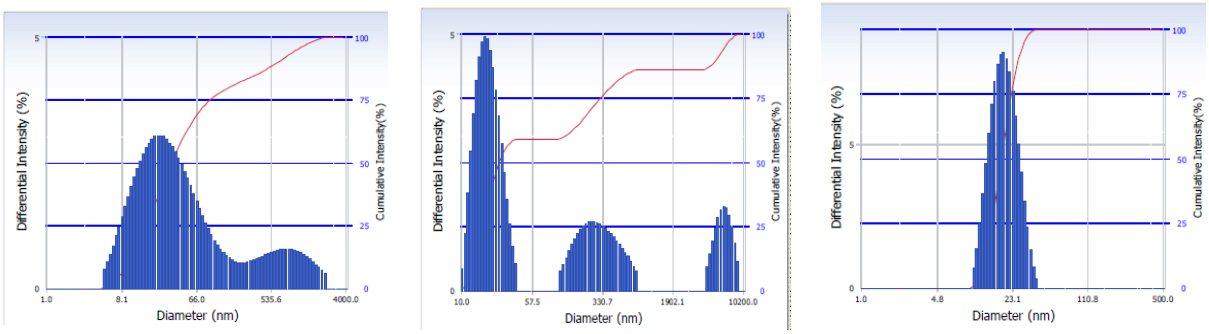


Figure S16. DSC trace (second heating cycle) of a PMLA sample ($M_{n,theo}$ = 30 000 g.mol^{-1}) synthesized from the hydrogenolysis of a PMLABe ($M_{n,theo}$ = 60 000 g.mol^{-1}) prepared by anionic ROP of MLABe in bulk initiated by benzoate tetraethylammonium.[11] The thermogram was recorded according to the following cycles: –50 to +70 °C at 10 °C·min^{-1}; +70 to –50 °C at 10 °C·min^{-1}; –50 °C for 5 min; –50 to +150 °C at 10 °C·min^{-1}; +150 to –100 °C at 10 °C·min^{-1}.



PI= 0.29, [NaCl] = 0.05 M PI= 0.25, [NaCl] = 0.1 M PI= 0.19, [NaCl] = 0.15 M

Figure S17. DLS analysis of nanoparticles derived from PMLA$_{3300}$-*b*-PHB$_{3100}$ (Table 2, entry 3) using various NaCl concentrations *in PBS*. Self-assembly of the copolymer was performed from the nanoprecipitation method in three solutions of water with salt concentrations ranging from 0.05 M to 0.15 M. As monitored by DLS, analysis of the nanoparticles revealed that 0.15 M was the optimized value.

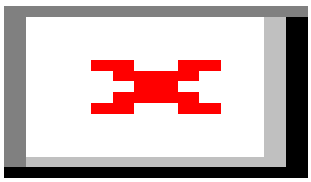


Figure S18. Determination of the CMC of the PMLA$_{3300}$-*b*-PHB$_{3100}$-based nanoparticles (Table 2, entry 3) in PBS ([NaCl]$_0$ = 0.15 mol.L^{-1}, pH 7.4) by surface tension measurements.

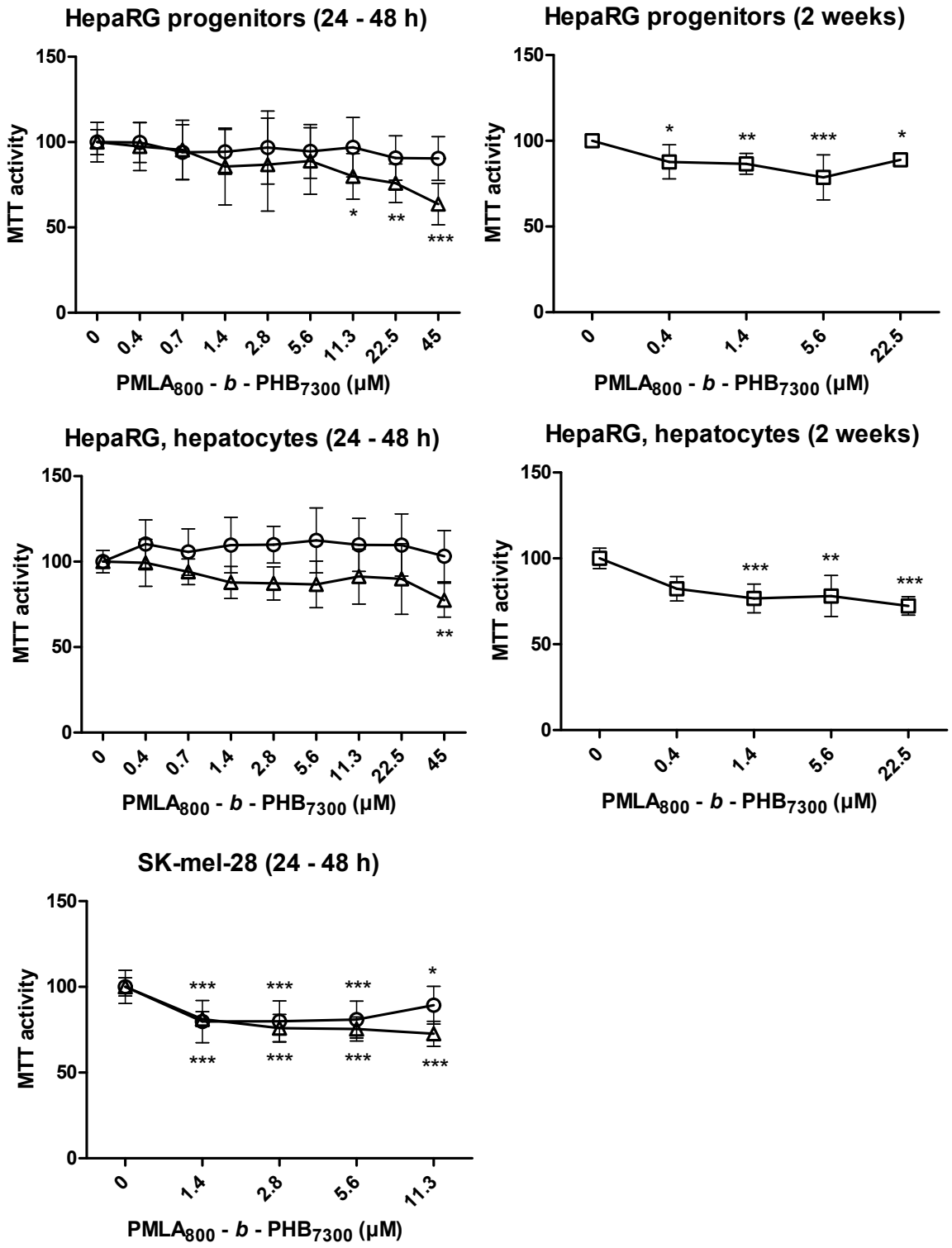


Figure S19. MTT assays in progenitor and hepatocyte HepaRG and SK-MEL-28 cells incubated with $PMLA_{800}$-*b*-PHB_{7300} based nanoparticles (circles: 24 h; triangles: 48 h; squares: 2 weeks). Statistical analyses: *, $p < 0.05$; **, $p < 0.01$; ***, $p < 0.001$.

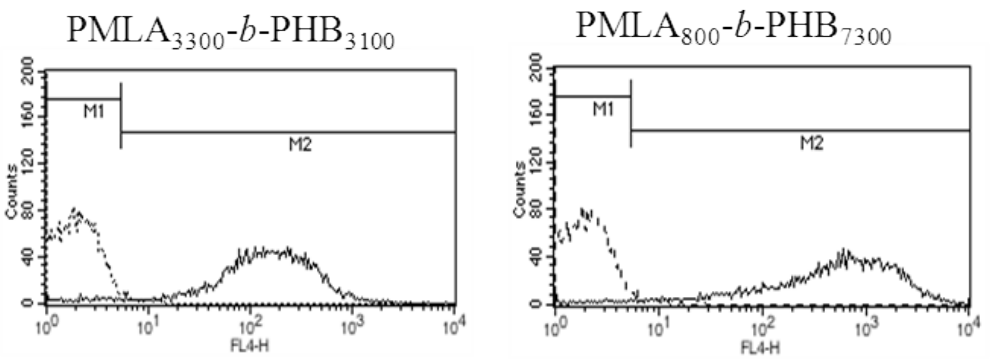


Figure S20. Flow cytometry analysis of fluorescence (FL4H channel) in progenitor HepaRG cells incubated for 24 h with $PMLA_{800}$-*b*-PHB_{7300} and $PMLA_{3300}$-*b*-PHB_{3100} nanoparticles loaded DiD Oil. The M1 gate represents the autofluorescence of control HepaRG cells (dotted line histogram), and M2 gate records the fluorescence of cells incubated with nanoparticles (plain line histogram).

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