Electronic Supplementary Material (ESI) for Polymer Chemistry.

Organocatalyzed ring-opening polymerization (ROP) of functional β-lactones: New insights into the ROP mechanism and poly(hydroxyalkanoate)s (PHAs) macromolecular structure

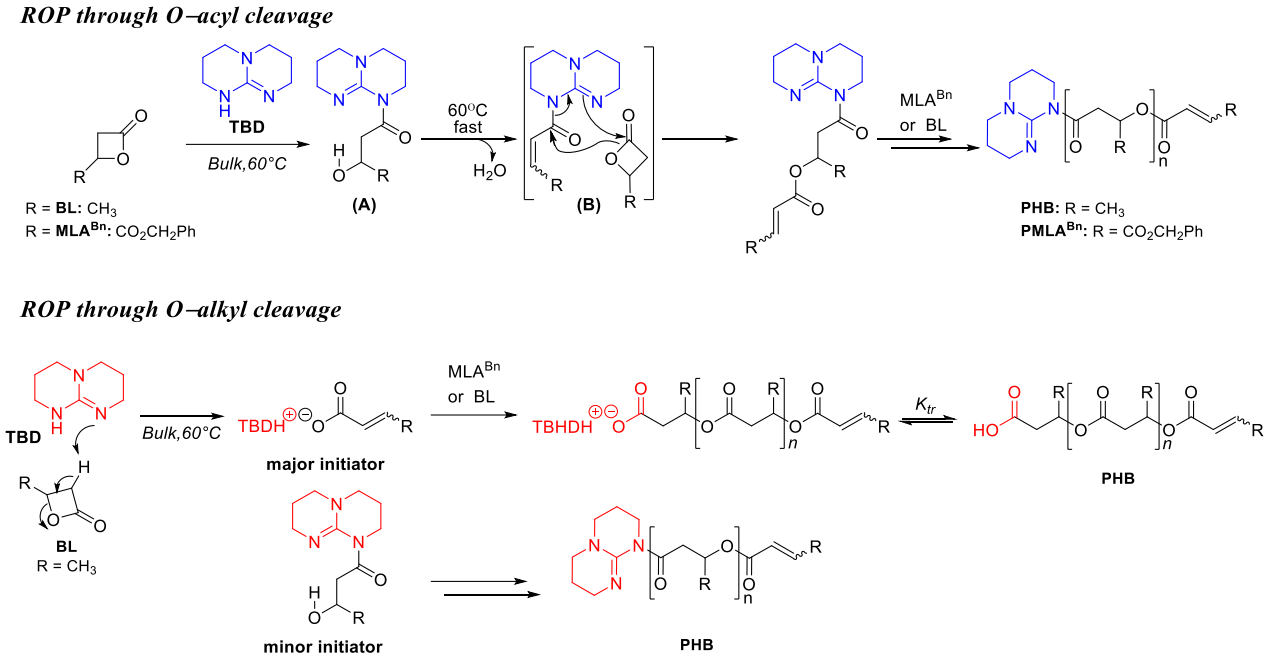
Rama M. Shakaroun,[a,b] Philippe Jéhan,[c] Ali Alaaeddine,*[b] Jean-François Carpentier,*[a] and Sophie M. Guillaume*[a]

[a.] *Univ. Rennes, CNRS, Institut des Sciences Chimiques de Rennes, UMR 6226, F-35042 Rennes, France. E-mail: sophie.guillaume@univ-rennes1.fr, jean-francois.carpentier@univ-rennes1.fr*

[b.] *Univ. Libanaise, Campus Universitaire Rafic Hariri Hadath, Faculté des Sciences, Laboratoire de Chimie Médicinale et des Produits Naturels, Beirut, Lebanon. E-mail: Alikassem.alaaeddine@ul.edu.lb*

[c.] *Centre Régional de Mesures Physiques de l'Ouest-CRMPO, ScanMAT UMS 2001, Université de Rennes 1*

Table of content



Scheme S1. Previously proposed mechanisms for the TBD-organocatalyzed ROP of BL and MLA^{Bn} showing *O*-acyl cleavage (top), and of BL showing *O*-alkyl cleavage (bottom).[1,2]

[1] C. G. Jaffredo, J.-F. Carpentier and S. M. Guillaume, *Polym. Chem.*, 2013, **4**, 3837-3850.

[2] S. Moins, C. Henoumont, J. De Winter, A. Khalil, S. Laurent, S. Cammas-Marion and O. Coulembier, *Polym. Chem.*, 2018, **9**, 1840-1847

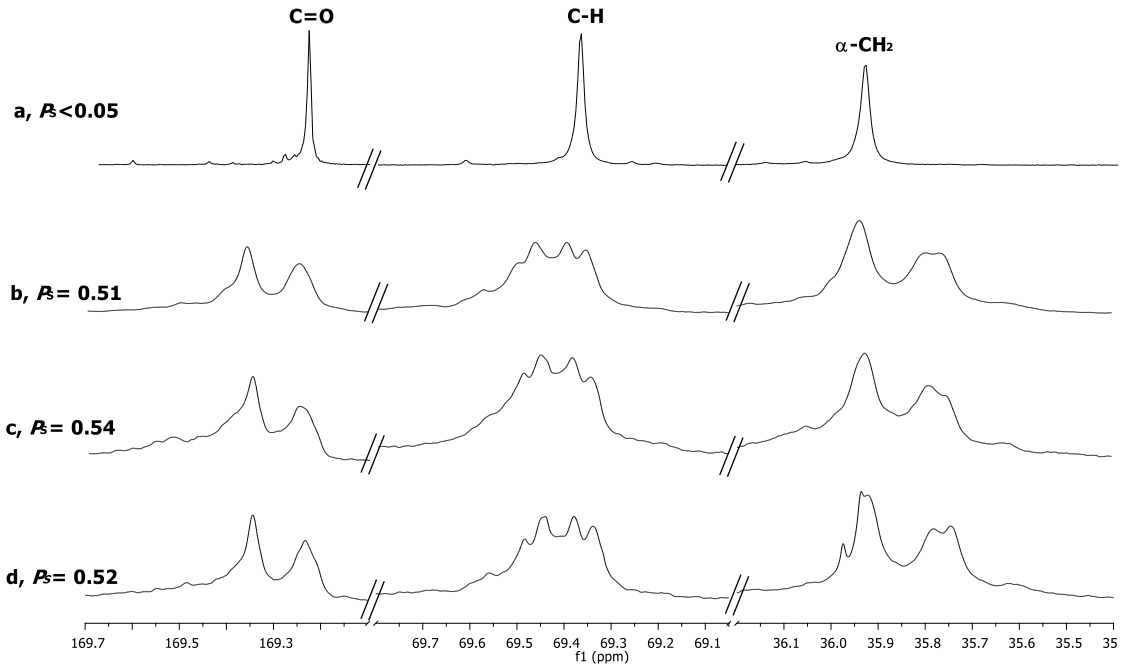


Figure S1. Regions of the $^{13}C\{^{1}H\}$ NMR spectra (125 MHz, $CDCl_3$, 23 ˚C) of $PBPL^{OBn}$ prepared by the ROP of *rac*-BPL^{OBn} (except for the top spectrum **a**: by the ROP of enantiopure (*S*)-BPL^{OBn}) in the presence of DBU-spectrum **b** (Figure 7; Table 3, entry 3), TBD-spectrum **c** (Figure 5; Table 2, entry 7), or BEMP-spectrum **d** (Figure 3; Table 1, entry 9), revealing atactic $PBPL^{OBn}$.

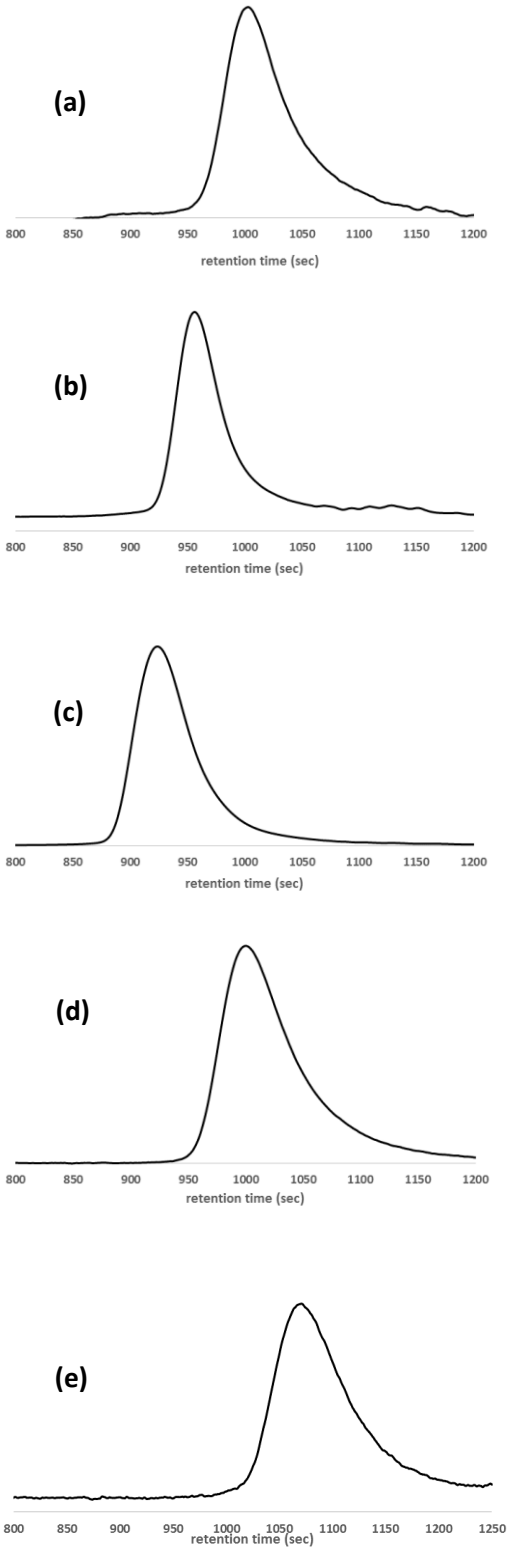


Figure S2. SEC t*rac*es of PBPL^{OR}s prepared from the ROP of *rac*-BPL^{OR}s mediated by the organocatalyst BEMP (a) and (b) (Table 1, entries 3,4, respectively); TBD (c) & (d) (Table 2, entries 5,7, respectively); DBU (e) (Table 3, entry 3).

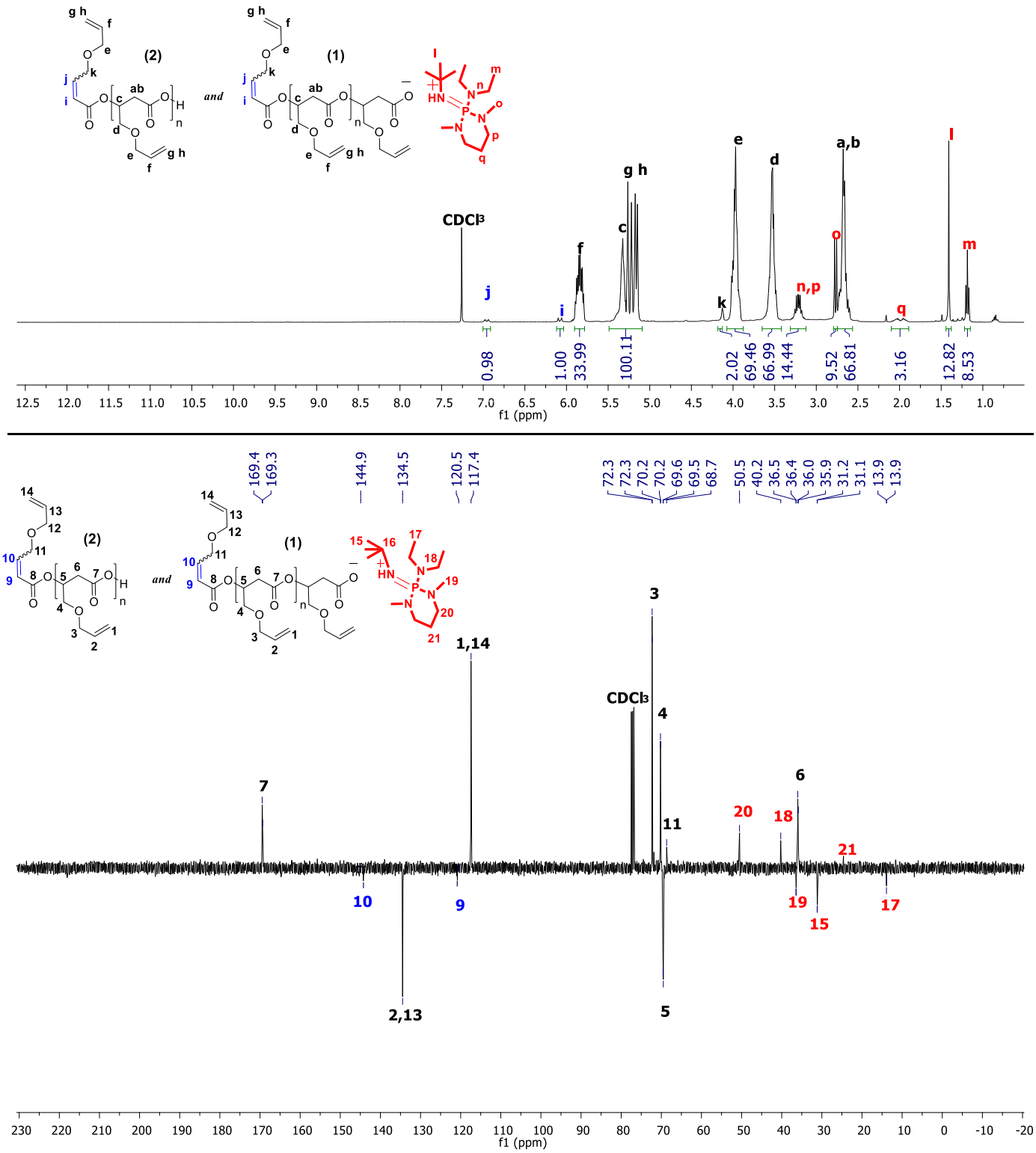


Figure S3. ^{1}H (500 MHz, $CDCl_3$, 25 °C) (top) and J-MOD (125 MHz, $CDCl_3$, 25 °C) (bottom) NMR spectra of PBPL^{OAll} recovered from the ROP of *rac*-BPL^{OAll} mediated by BEMP (Table 1, entry 3).

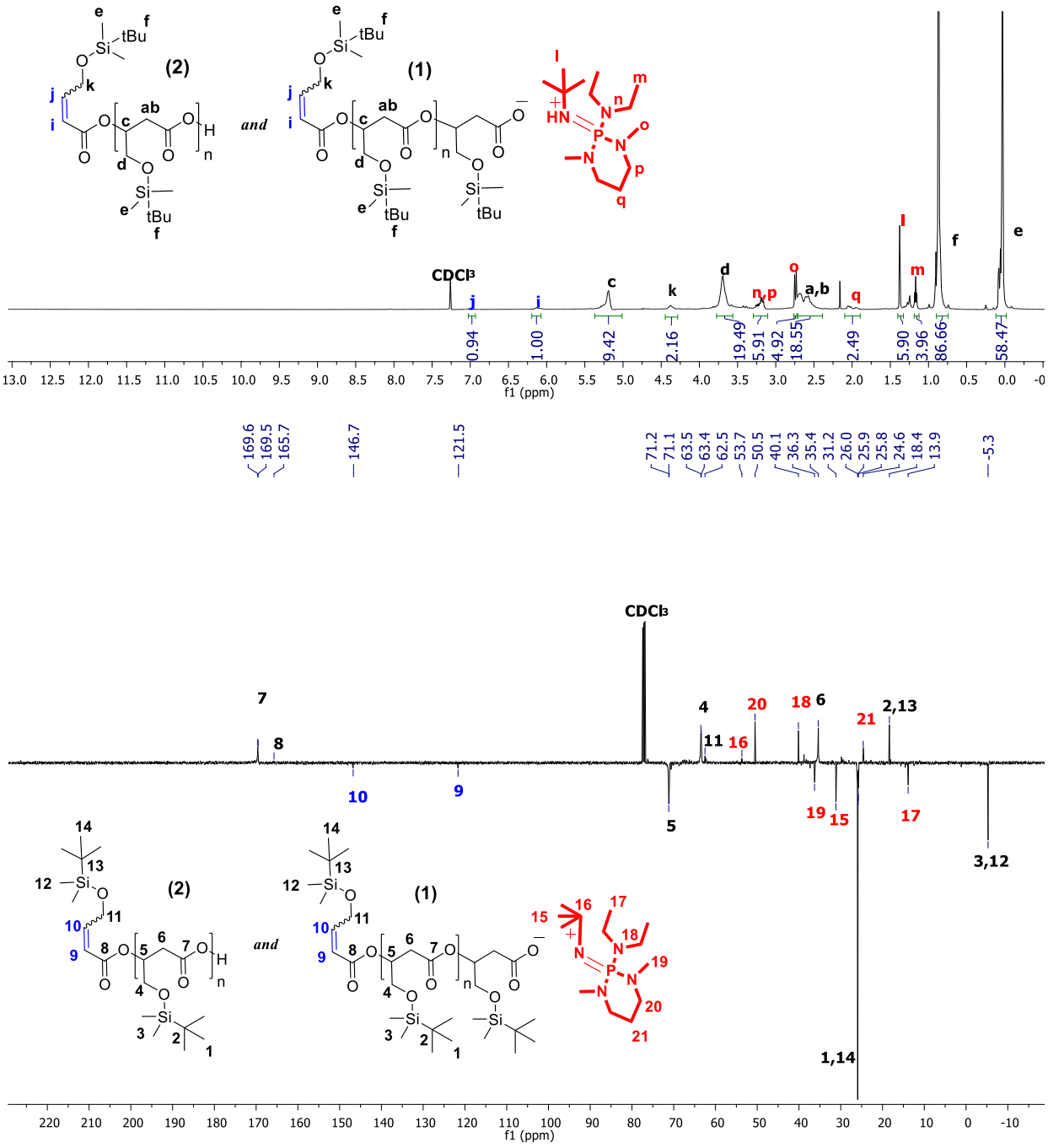


Figure S4. ^{1}H (500 MHz, $CDCl_3$, 25 °C) (top) and J-MOD (125 MHz, $CDCl_3$, 25 °C) (bottom) NMR spectra of $PBPL^{OTBDMS}$ recovered from the ROP of *rac*-BPL^{OTBDMS} mediated by BEMP (Table 1, entry 14).

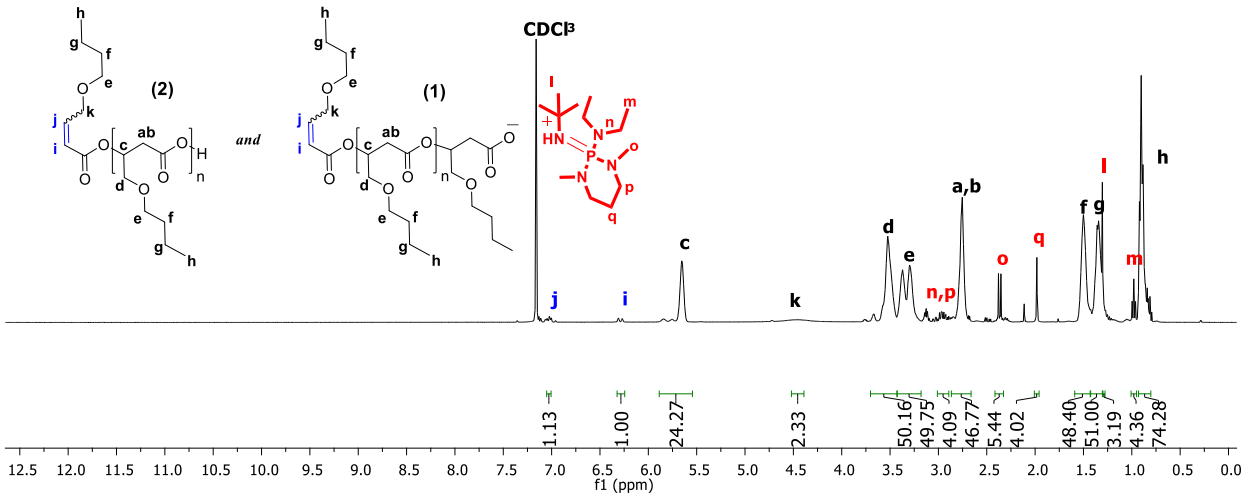


Figure S5. ^{1}H (500 MHz, $CDCl_3$, 25 °C) NMR spectrum of PBPL^{OnBu} recovered from the ROP of *rac*-BPL^{OnBu} mediated by BEMP (Table 1, entry 6).

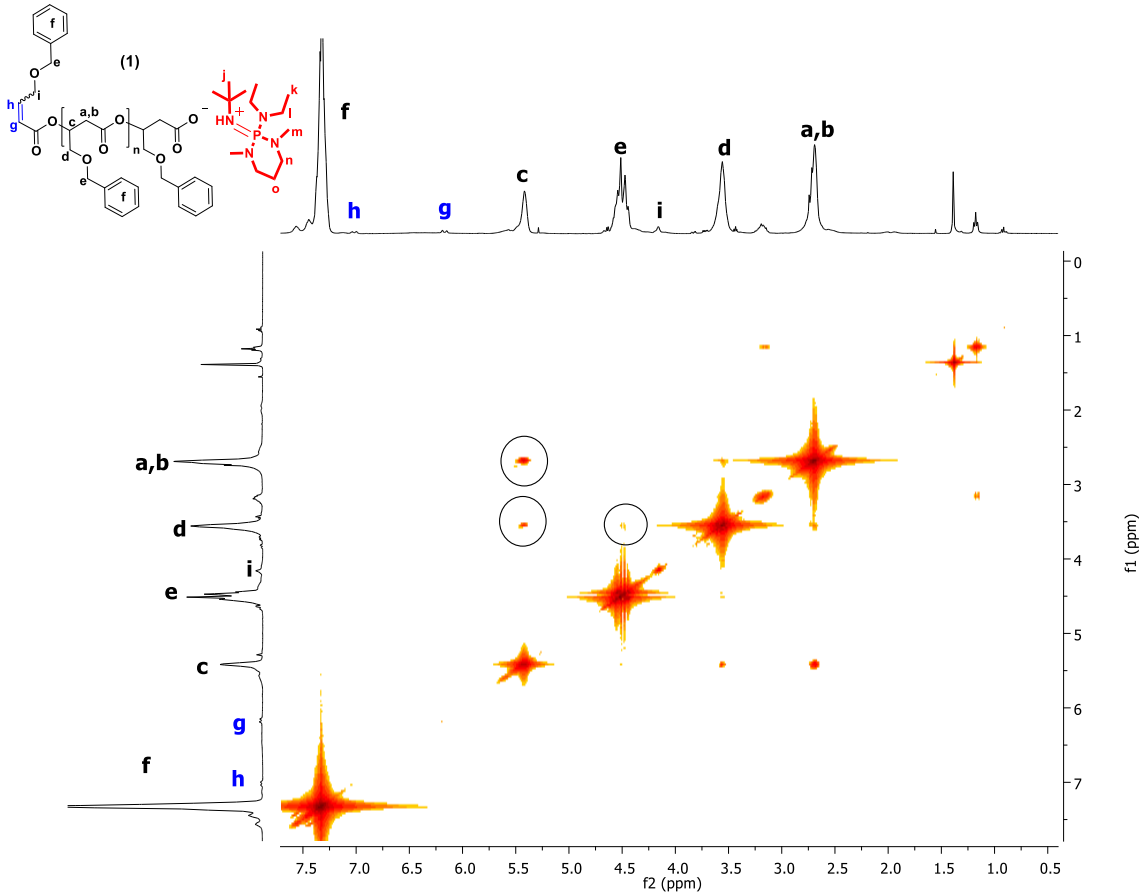


Figure S6. ^{1}H-^{1}H COSY (500 MHz, $CDCl_3$, 25 °C) NMR spectrum of PBPL^{OBn} recovered from the ROP of *rac*-BPL^{OBn} mediated by BEMP (Table 1, entry 12), supporting the signals' assignments of the ^{1}H NMR spectrum.

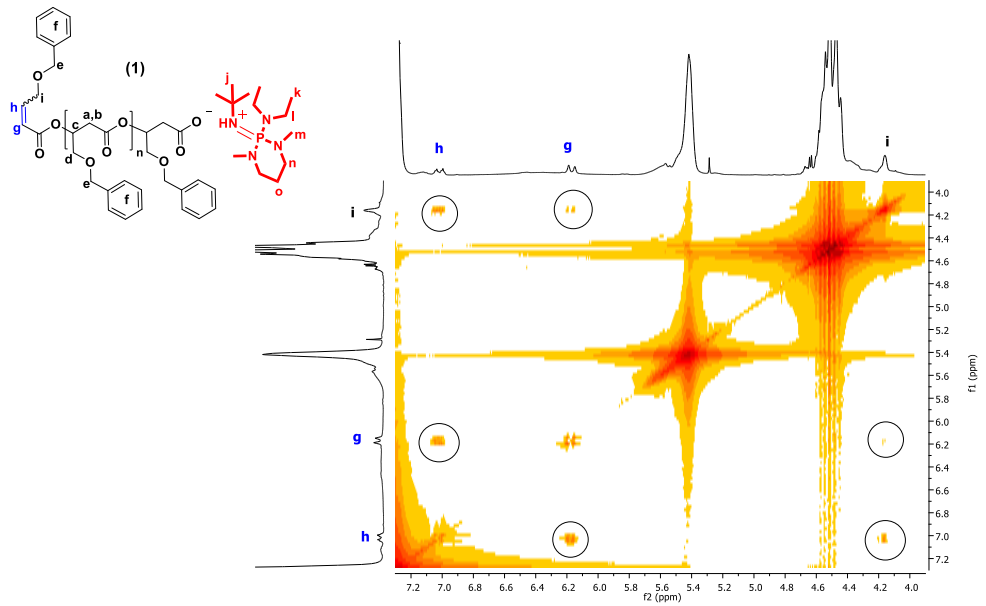


Figure S7. ^{1}H-^{1}H COSY (500 MHz, $CDCl_3$, 25 ˚C) NMR zoomed spectra of PBPL^{OBn} recovered from the ROP of *rac*-BPL^{OBn} mediated by BEMP supporting the α-crotonate end-capping group (Table 1, entry 12).

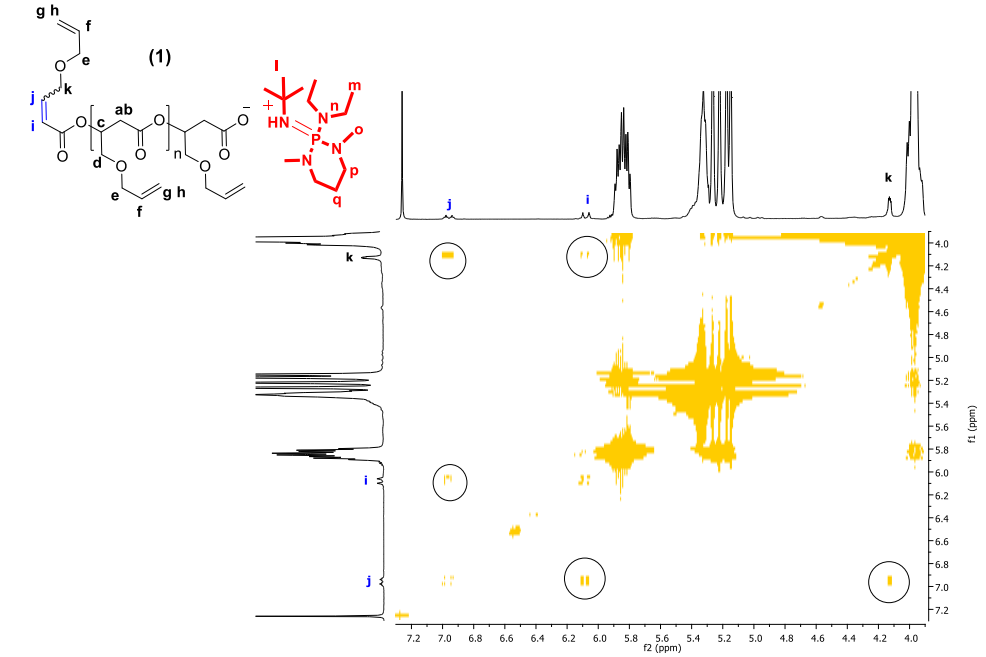


Figure S8. ^{1}H-^{1}H COSY (500 MHz, $CDCl_3$, 25 ˚C) NMR zoomed spectra of PBPL^{OAll} recovered from the ROP of *rac*-BPL^{OAll} mediated by BEMP supporting the α-crotonate end-capping group (Table 1, entry 3).

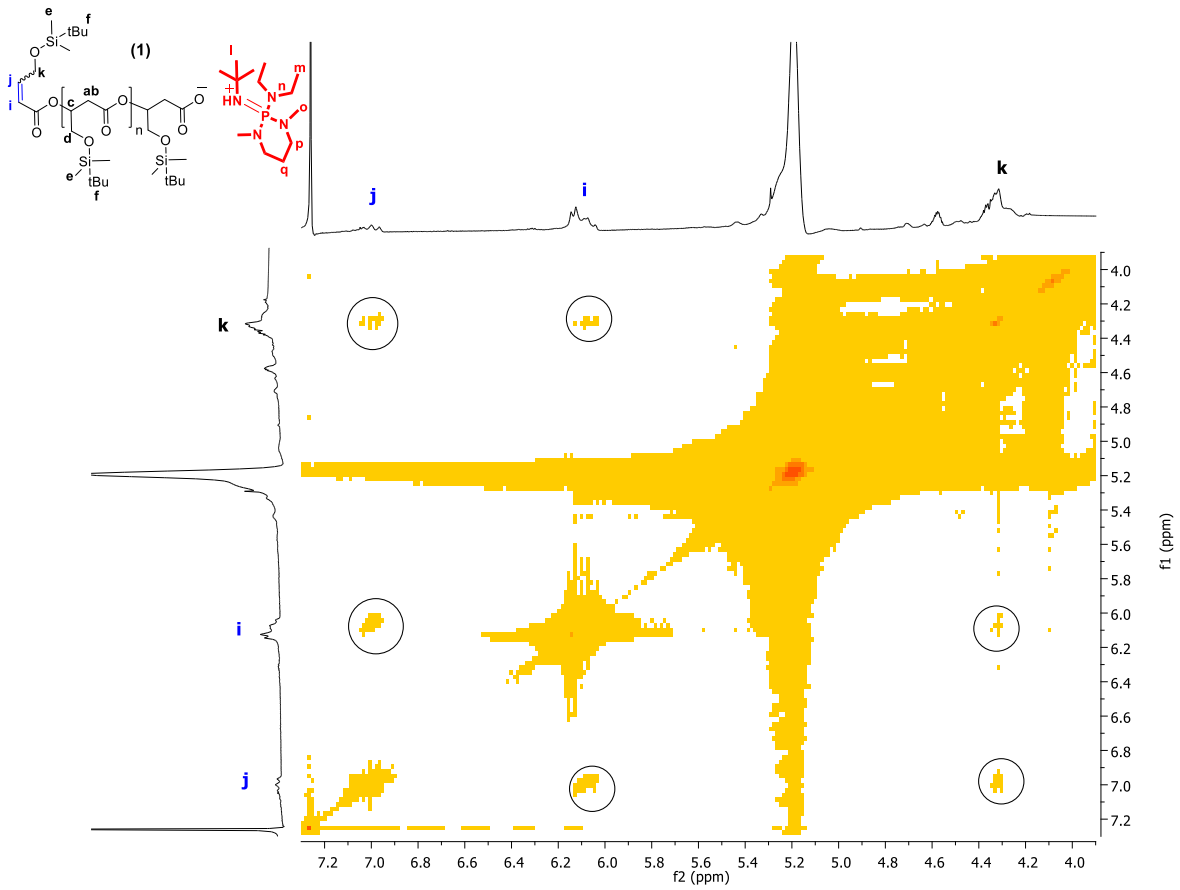


Figure S9 ^{1}H-^{1}H COSY (500 MHz, $CDCl_3$, 25 ˚C) NMR zoomed spectrum of PBPL^{OTBDMS} recovered from the ROP of *rac*-BPL^{OTBDMS} mediated by BEMP supporting the α-crotonate end-capping group (Table 1, entry 15).

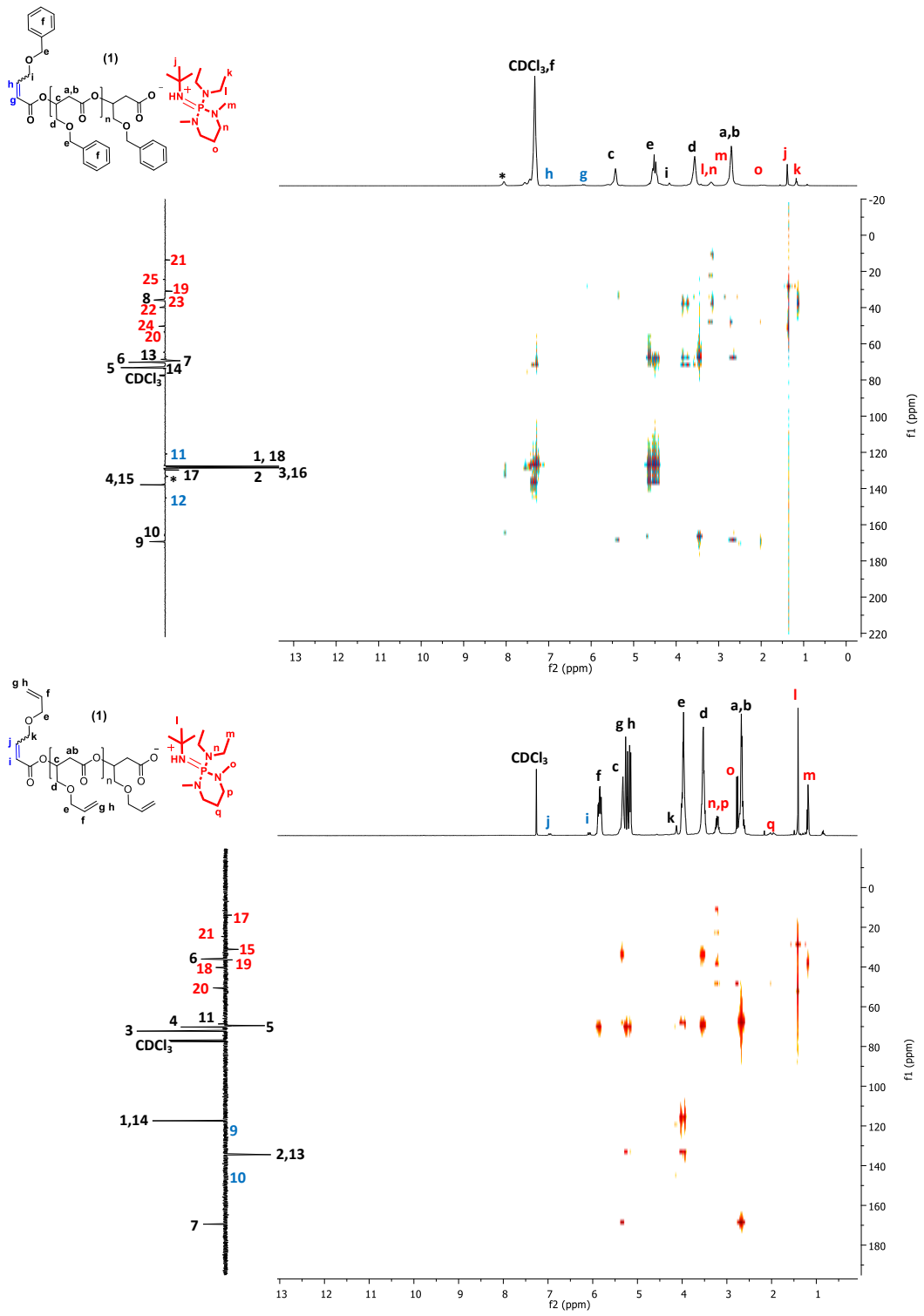


Figure S10. ^{1}H-^{13}C HMBC (500 MHz, $CDCl_3$, 25 ˚C) NMR spectra of $PBPL^{OBn}$ (top) and $PBPL^{OAll}$ (bottom) recovered from the ROP of *rac*-BPL^{OBn} and *rac*-BPL^{OAll} mediated by BEMP, respectively (Table 1, entries 12,3).

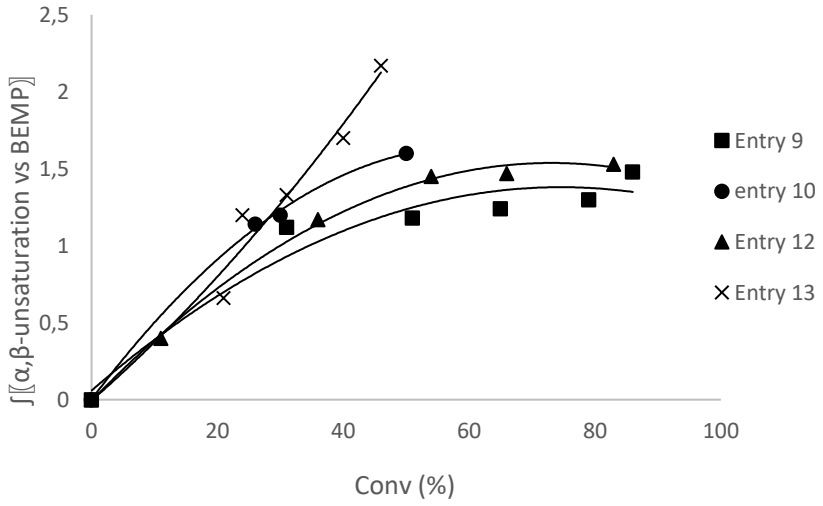


Figure S11. ^{1}H NMR monitoring of the molar content of the crotonate with respect to BEMP as a function of *rac*-BPL^{OBn} consumption for the ROP of *rac*-BPL^{OBn} mediated by BEMP, using the methine ($\delta_{CHC(O)O}$ 6.17 ppm) and methyl ($\delta_{NC(CH3)3}$ 1.39 ppm) resonances, respectively (Table 1, entries 9,10,12,13).

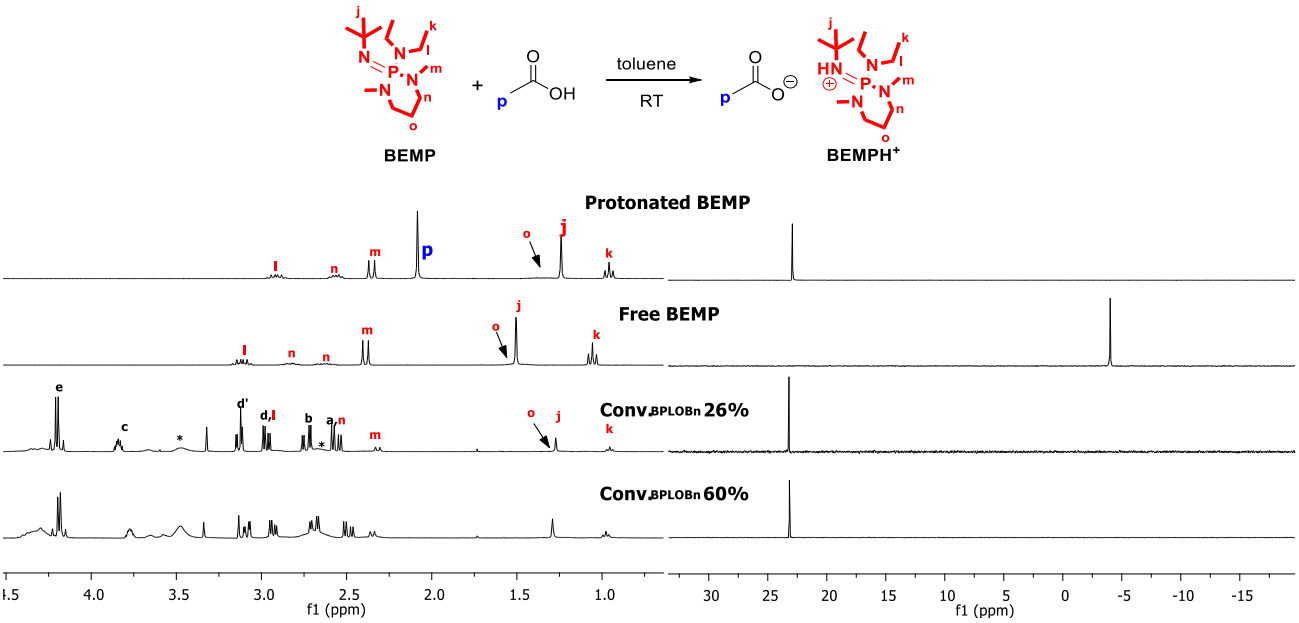


Figure S12. ^{1}H (left, 400 MHz, C_6D_6, 25 °C) and ^{31}P (right) (121 MHz, C_6D_6, 25 °C) NMR monitoring of the ROP of *rac*-BPL^{OBn} mediated by BEMP in dry C_6D_6 (to avoid adventitious protonation by H_2O) (Table 1, entry 12) as compared to free and protonated BEMP ($[BEMPH]^+[CH_3COO]^-$; prepared from the equimolar reaction of BEMP with acetic acid in dry toluene under inert conditions).

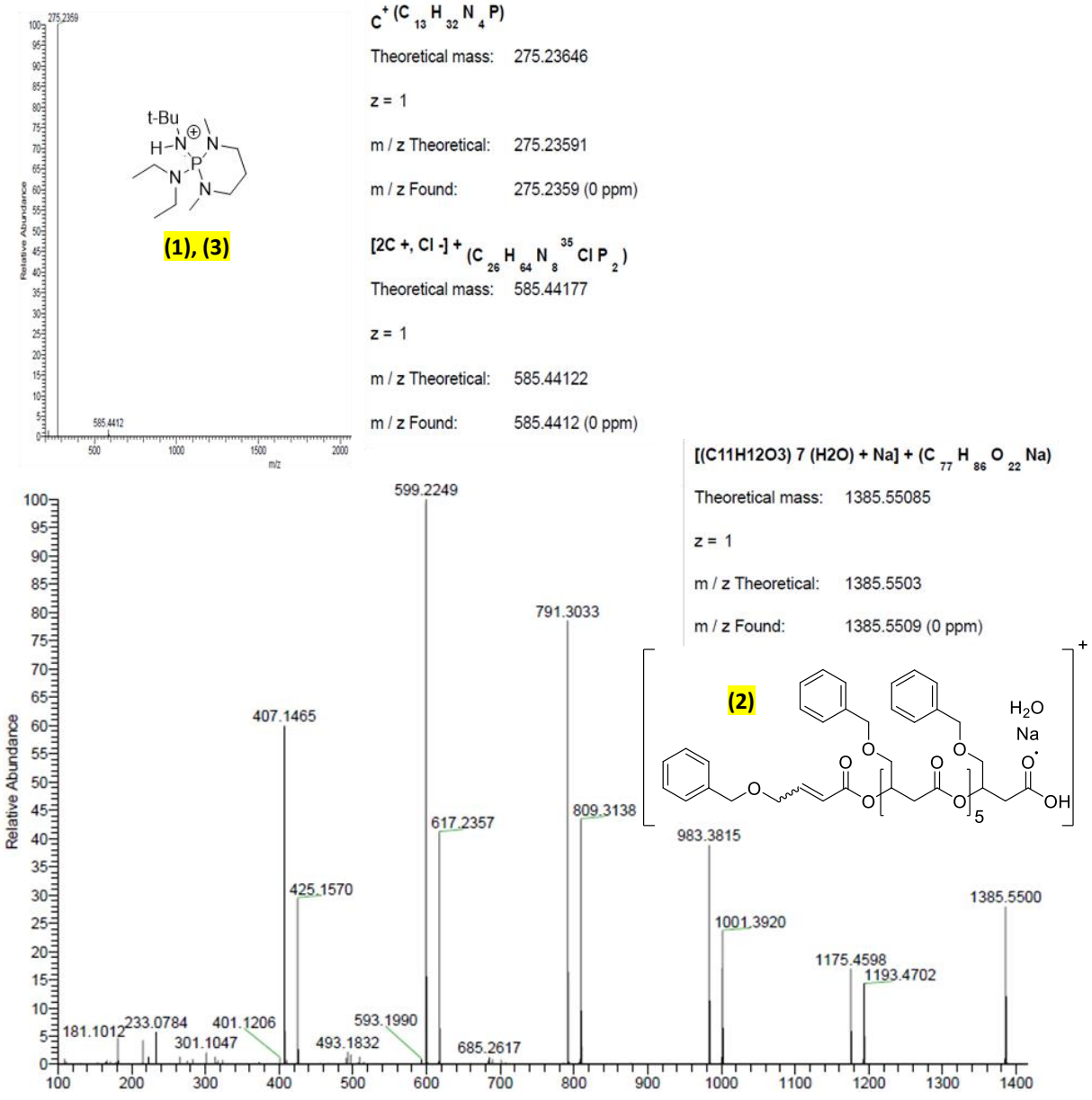


Figure S13. ESI mass spectrum of PBPL^{OBn} (CH_2Cl_2, NaCl) sample freshly synthesized from the ROP of *rac*-BPL^{OBn} mediated by BEMP (Table 1, entry 7); showing BEMPH$^+$ (Scheme 2, **1** & **3**) and PBPL^{OBn} macromolecules end-capped with both an α-crotonate and an ω-carboxylic acid end-groups (Scheme 2, **2**); ionized by Na^+ in presence of adventitious H_2O.

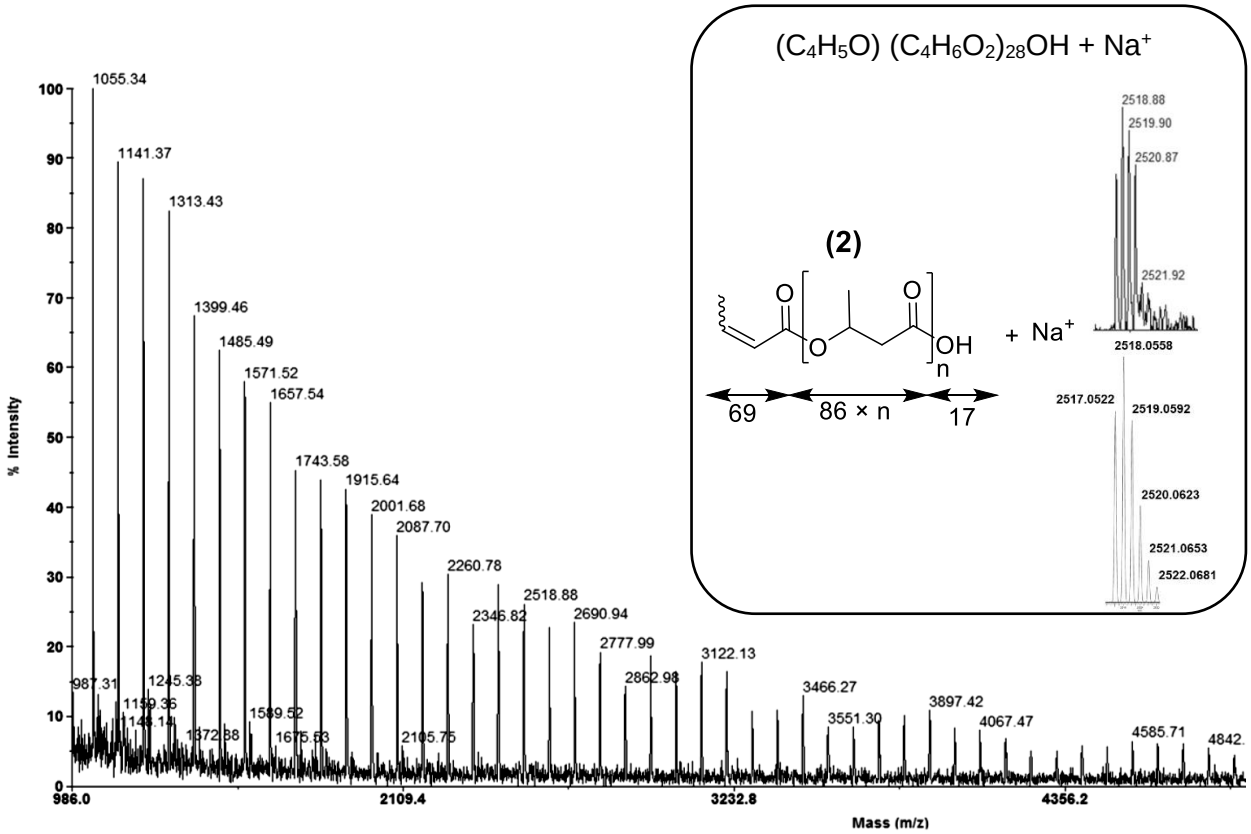


Figure S14. MALDI-ToF mass spectrum (positive mode, DCTB matrix, Na^+ cationizing salt) of a PHB sample prepared from the ROP of *rac*-BL mediated by BEMP (ESI, Figure S10 in reference 3).[3] Reinterpretation shows that the zoomed region corresponds to the simulated (bottom) and experimental (top) spectra of PHB macromolecules end-capped with both an α-crotonate and an ω-carboxylic acid end-groups (alike species Scheme 2-**2**).

[3] C. G. Jaffredo, J.-F. Carpentier and S. M. Guillaume, *Macromol. Rapid Commun.* **2012**, *33*, 1938−1944.

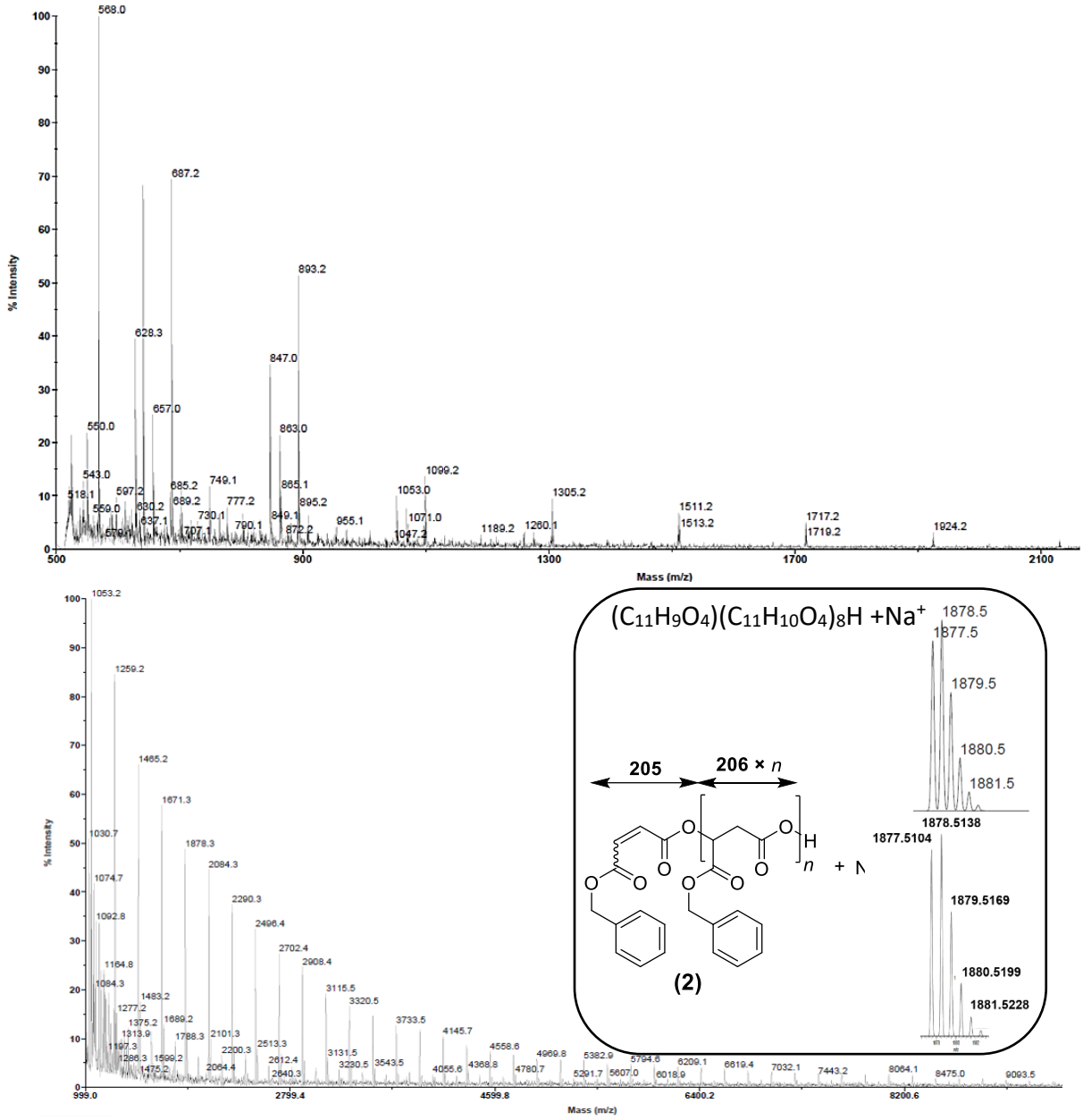


Figure S15. MALDI-ToF mass spectra of a PMLA^{Bn} sample freshly synthesized from the ROP of *rac*-MLA^{Bn} mediated by BEMP, using α-cyano-4-hydroxycinnamic acid (CHCA) as matrix (no cationizing salt) (top) (Figure S11 of reference 1), and of the same sample but not freshly synthesized using trans-3-indoleacrylic acid (IAA) matrix in the presence of Na^+ cationizing salt (bottom) (Figure S13 of reference 1).[1] Reinterpretation of the top spectrum shows that in the absence of a cationizing agent, a non-conclusive spectrum is obtained. Also, the bottom spectrum shows a population corresponding to PMLA^{Bn} which can only be observed in the presence of cationizing agent, with the zoomed region corresponding to the simulated (bottom) and experimental (top) spectra of PMLA^{Bn} macromolecules end-capped with both an α-crotonate and an ω-carboxylic acid end-groups, alike species Scheme 2-**2**.[1]

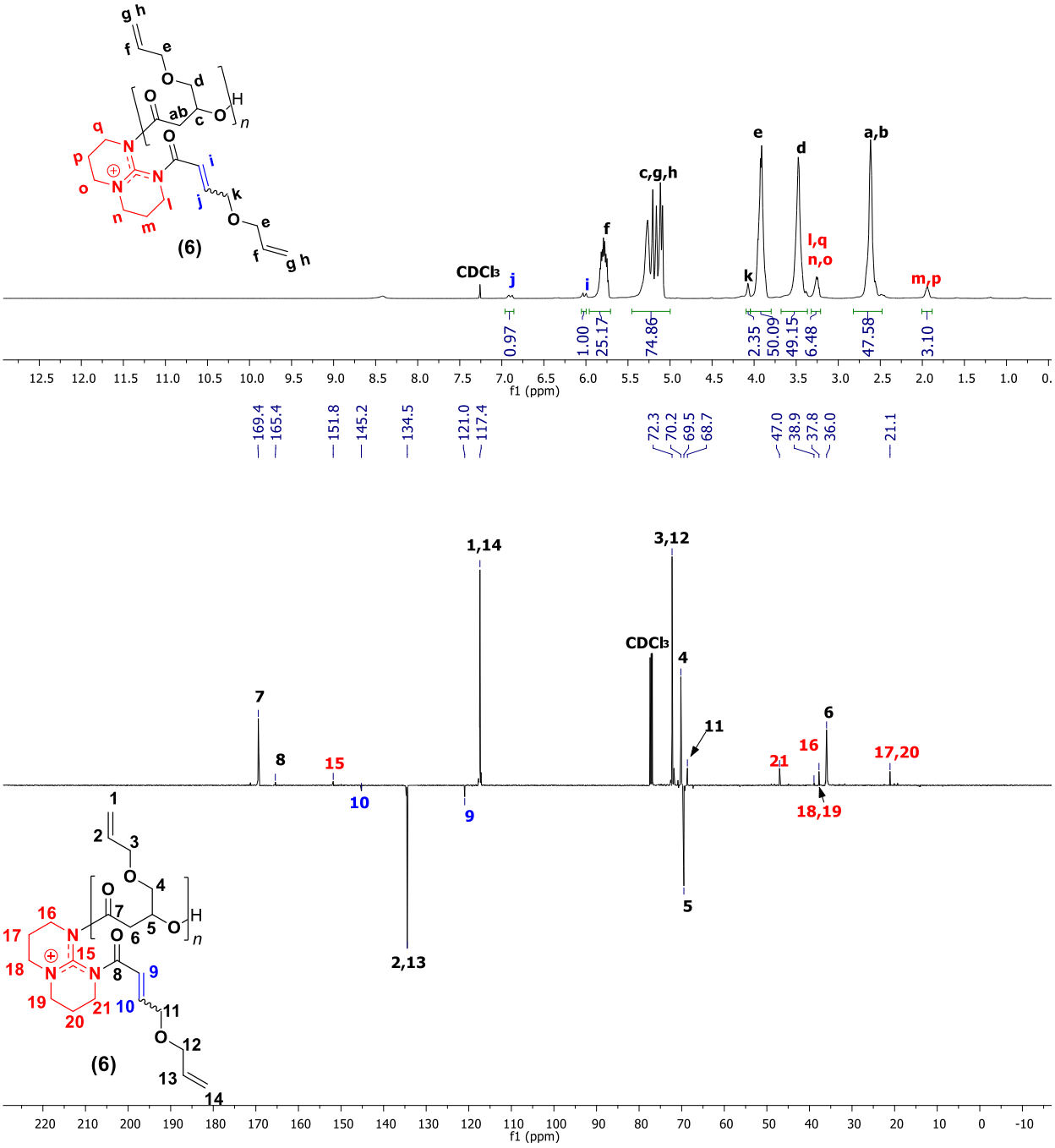


Figure S16. ^{1}H (500 MHz, $CDCl_3$, 25 °C) (top) and J-MOD (125 MHz, $CDCl_3$, 25 °C) (bottom) NMR spectra of $PBPL^{OAll}$ recovered from the ROP of *rac*-BPL^{OAll} mediated by TBD (Table 2, entry 1).

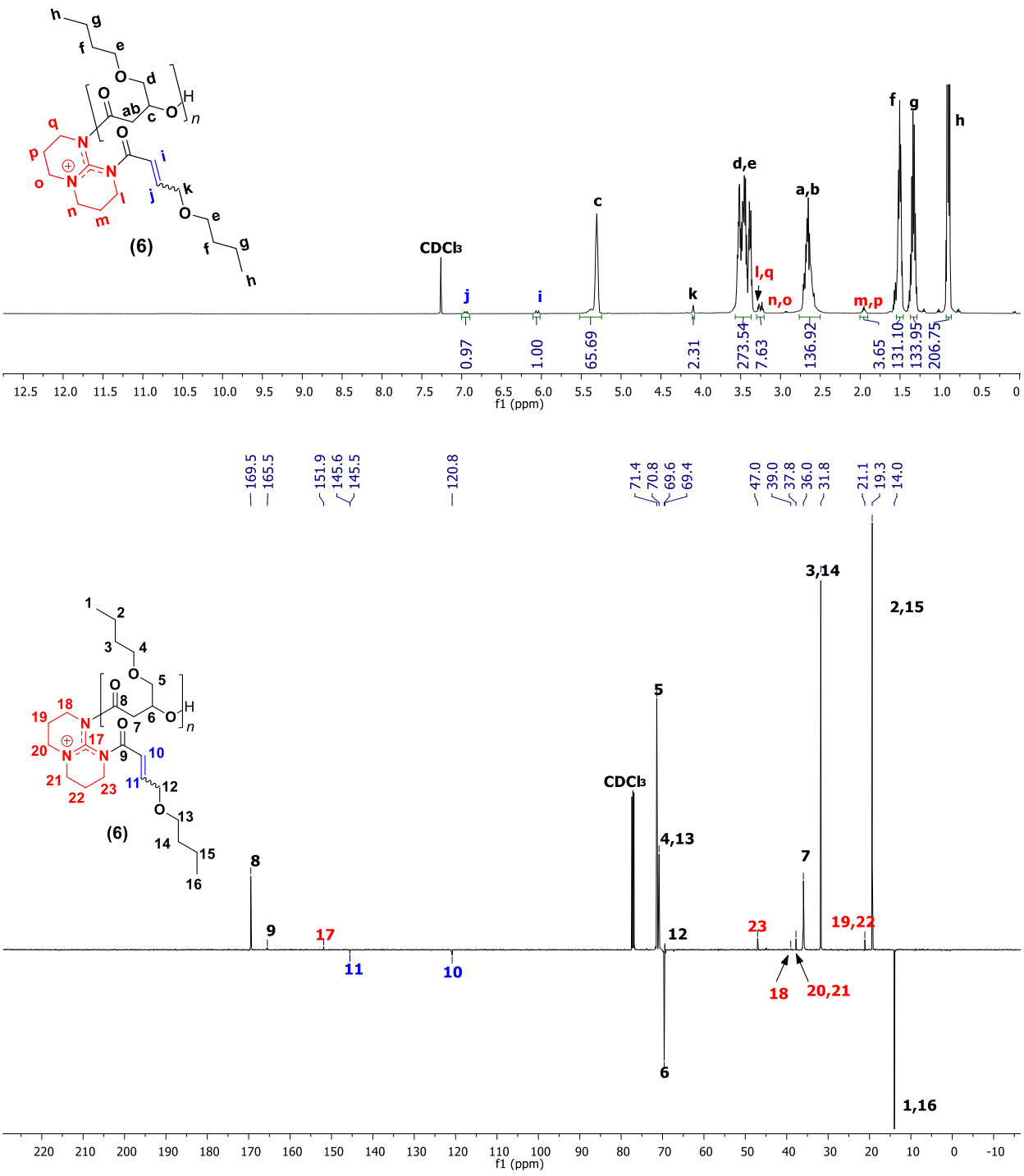


Figure S17. ^{1}H (500 MHz, $CDCl_3$, 25 °C) (top) and J-MOD (125 MHz, $CDCl_3$, 25 °C) (bottom) NMR spectra of PBPL^{OnBu} recovered from the ROP of *rac*-BPL^{OnBu} mediated by TBD (Table 2, entry 5).

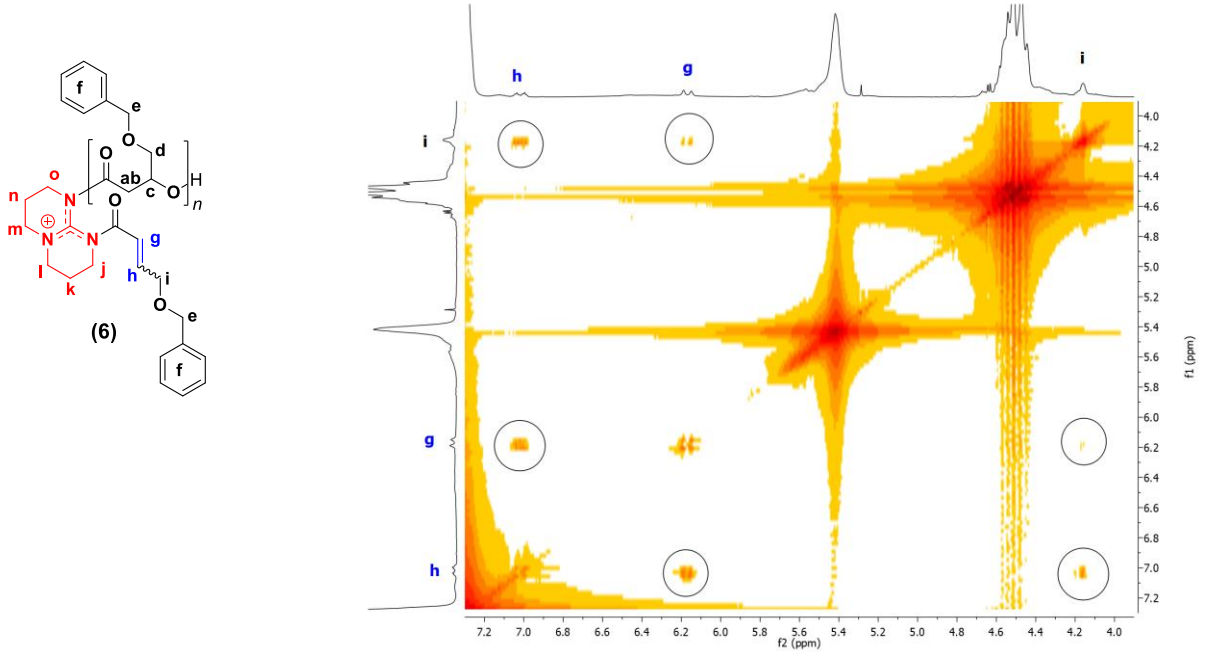


Figure S18. ^{1}H-^{1}H COSY (500 MHz, $CDCl_3$, 25 ˚C) NMR zoomed spectrum of PBPL^{OBn} recovered from the ROP of *rac*-BPL^{OBn} mediated by TBD supporting the α-crotonate end-capping group (Table 2, entry 7).

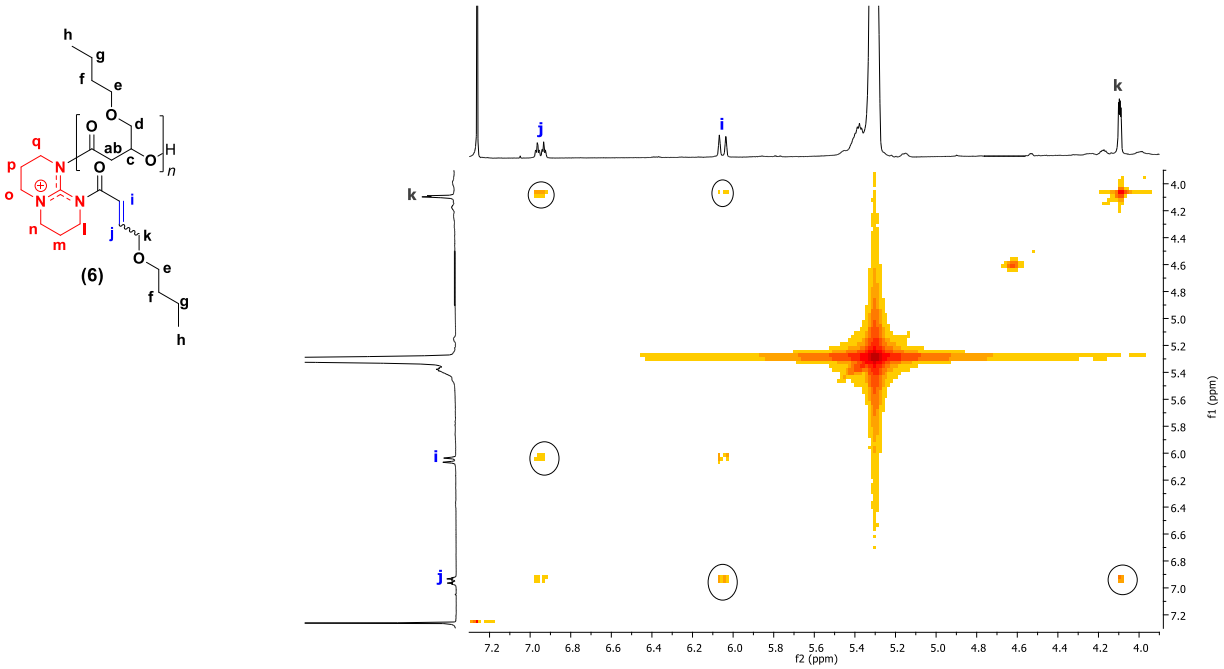


Figure S19. ^{1}H-^{1}H COSY (500 MHz, $CDCl_3$, 25 ˚C) NMR zoomed spectrum of PBPL^{OnBu} recovered from the ROP of *rac*-BPL^{OnBu} mediated by TBD supporting the α-crotonate end-capping group (Table 2, entry 5).

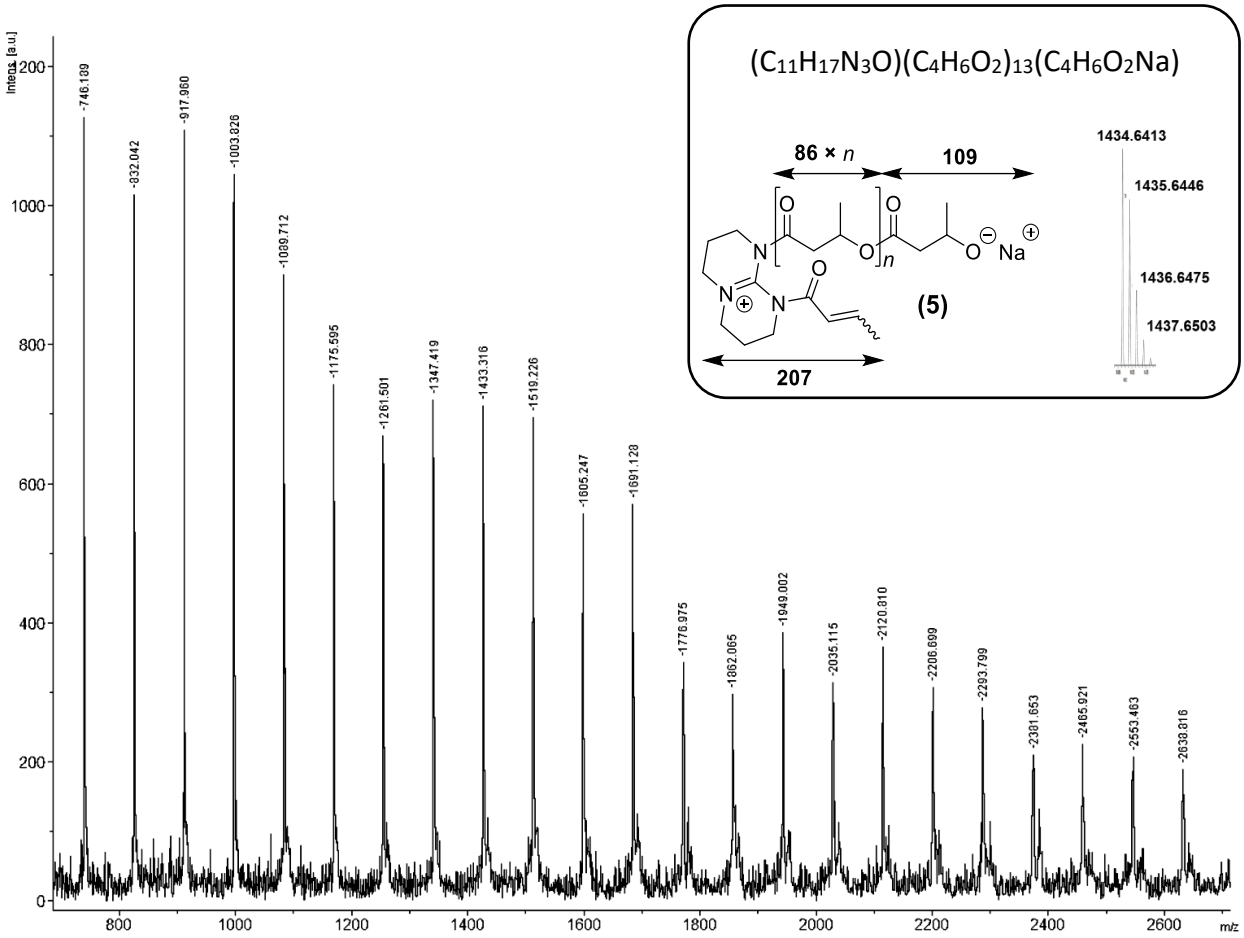
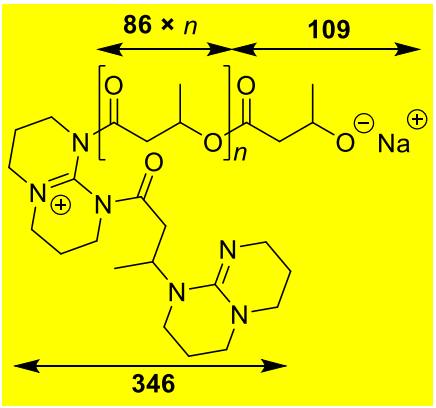


Figure S20. MALDI–ToF mass spectrum (positive mode, DCTB matrix, Na^+ cationizing salt) of a PHB sample synthesized from the ROP of *rac*-BL mediated by TBD (as reproduced from Figure 4 in reference 3).[3] Reinterpretation shows that the zoomed regions correspond to the simulated (bottom) and experimental (top) spectra of a zwitterionic species alike species Scheme 3-**5**.

Note that a putative TBD Michael-addition product onto the crotonate moiety was not observed (absence of the following calculated *m/z* signals):



n= 4. *m/z*: 799.4218 (100.0%)
n= 5. *m/z*: 863.4761 (100.0%)
n= 6. *m/z*: 971.4948 (100.0%)
n= 7. *m/z*: 1057.5316 (100.0%)
n= 8. *m/z*: 1143.5683 (100.0%)
n= 9. *m/z*: 1229.6051 (100.0%)
n= 10. *m/z*: 1315.6419 (100.0%)

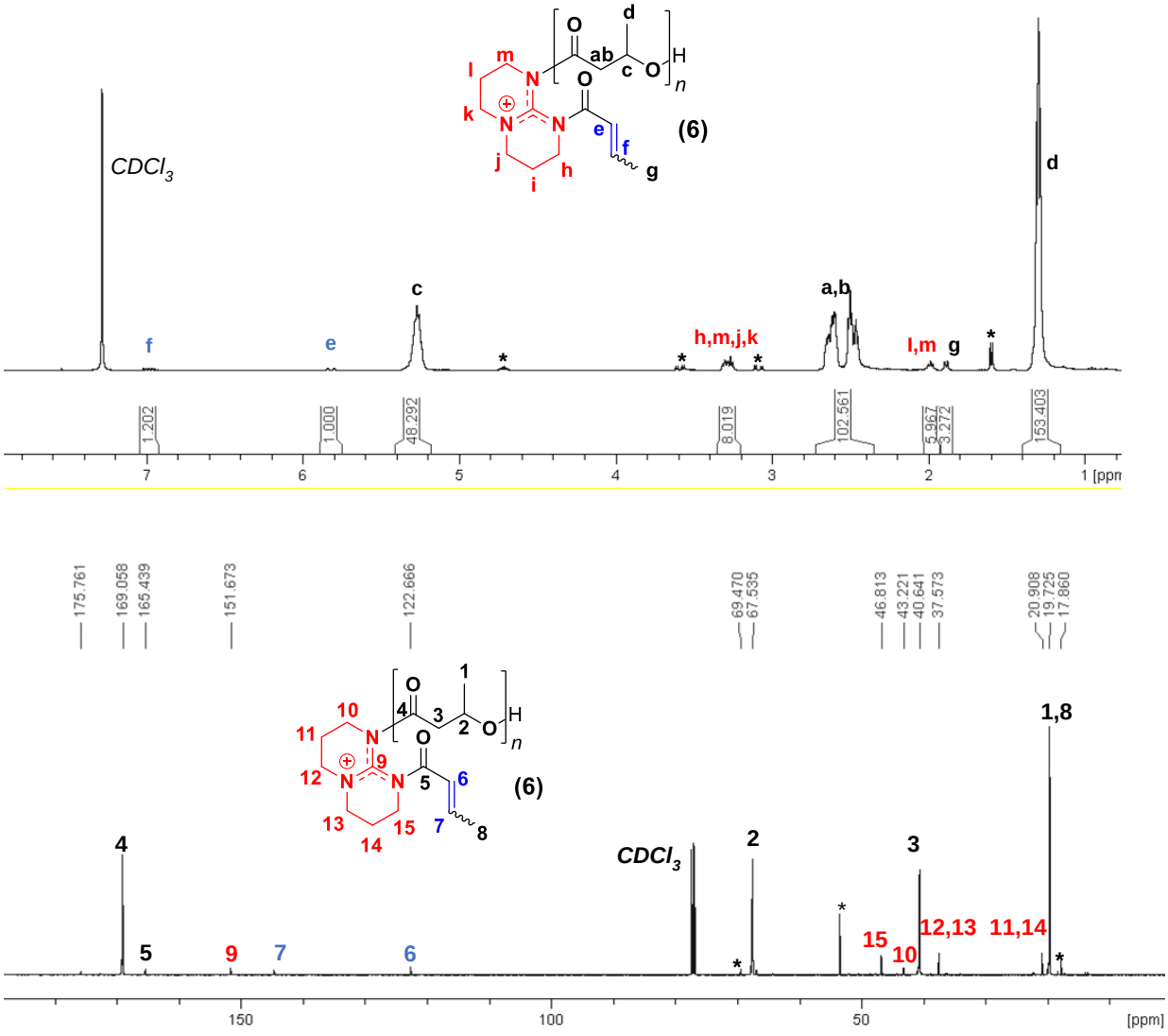


Figure S21. ^{1}H and $^{13}C\{^{1}H\}$ NMR (500 and 125 MHz, $CDCl_3$, 25 °C) spectra of a precipitated PHB sample prepared by ROP of BL mediated by TBD in bulk monomer (no solvent) at 60 °C (* marker stands for residual BL monomer) as reproduced from reference 3).[3]

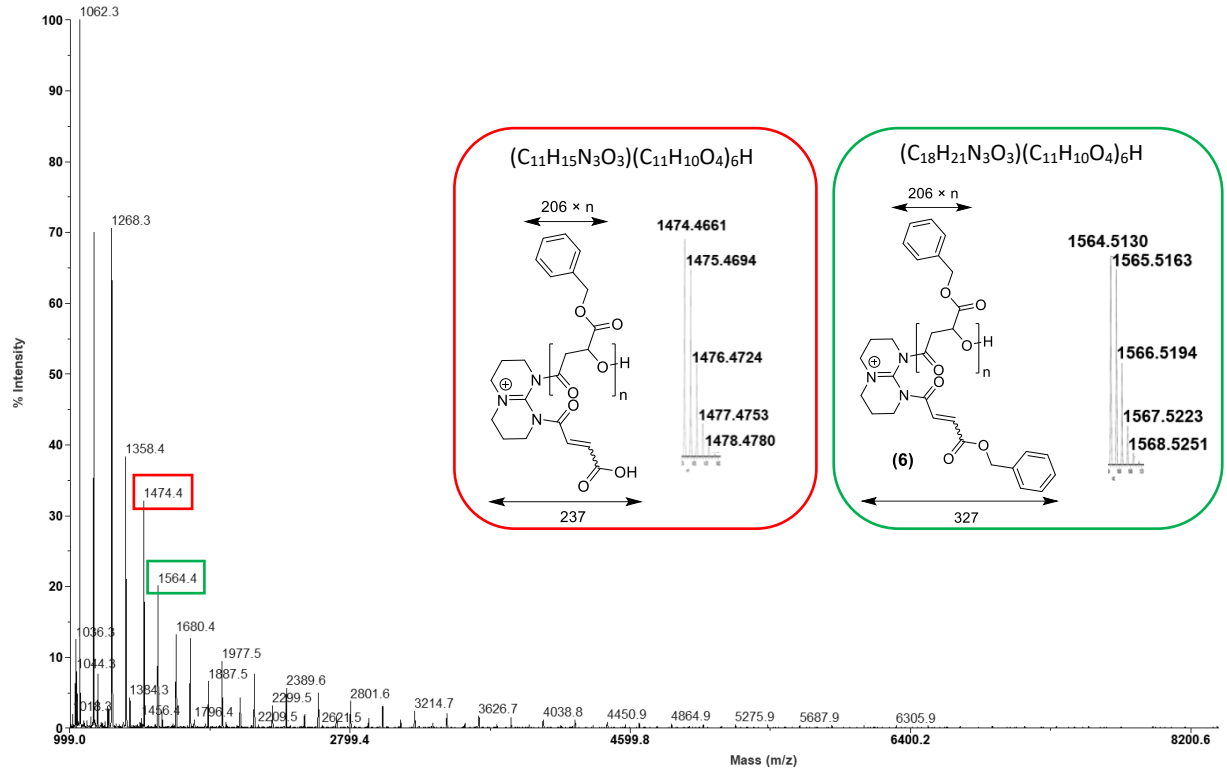


Figure S22. MALDI-ToF mass spectrum (trans-3-indoleacrylic acid (IAA) matrix, no ionization agent) of a PMLA^{Bn} sample freshly synthesized from the ROP of *rac*-MLA^{Bn} mediated by TBD (as reproduced from Figure 7 from reference 3).[3] Reinterpretation shows that the zoomed regions correspond to the simulated (bottom) and experimental (top) spectra of PMLA^{Bn} macromolecules end-capped with an α-TBD-benzyloxycrotonate-TBD and ω-hydroxy end-groups (population **II**; Scheme 3-**6**), and of the same macromolecular species depleted of the benzylium ion $[C_6H_5CH_2]^+$ depicted in red).

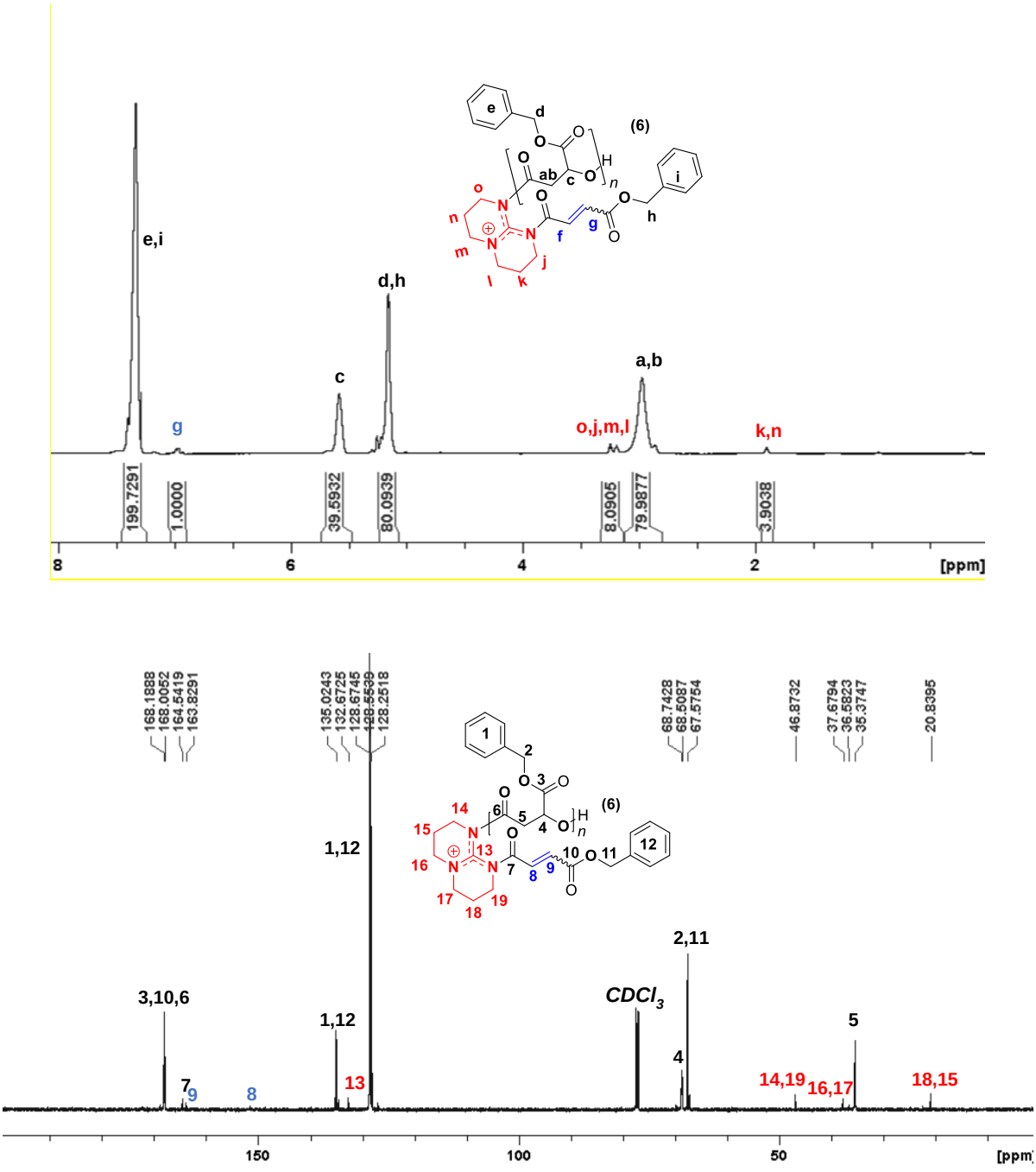


Figure S23. ^{1}H and $^{13}C\{^{1}H\}$ NMR (500 and 125 MHz, $CDCl_3$, 25 °C) spectra of a twice-precipitated $PMLA^{Bn}$ sample prepared by ROP of MLA^{Bn} mediated by TBD in bulk monomer (no solvent) at 60 °C (* label stands for residual CH_2Cl_2) as reproduced from reference 1.

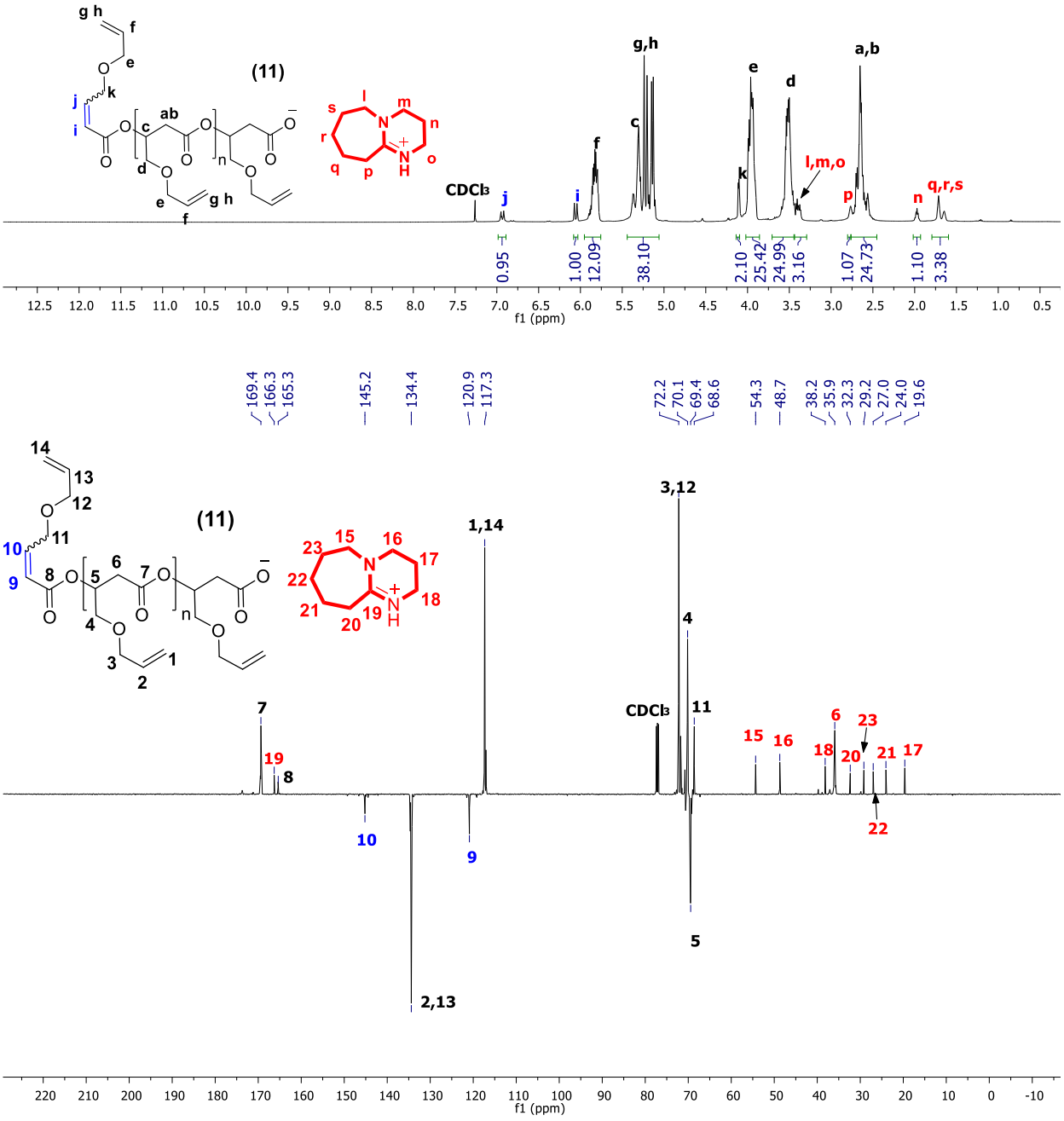


Figure S24. ^{1}H (500 MHz, $CDCl_3$, 25 °C) (top) and J-MOD (125 MHz, $CDCl_3$, 25 °C) (bottom) NMR spectra of $PBPL^{OAll}$ recovered from the ROP of *rac*-BPL^{OAll} mediated by DBU (Table 3, entry 1).

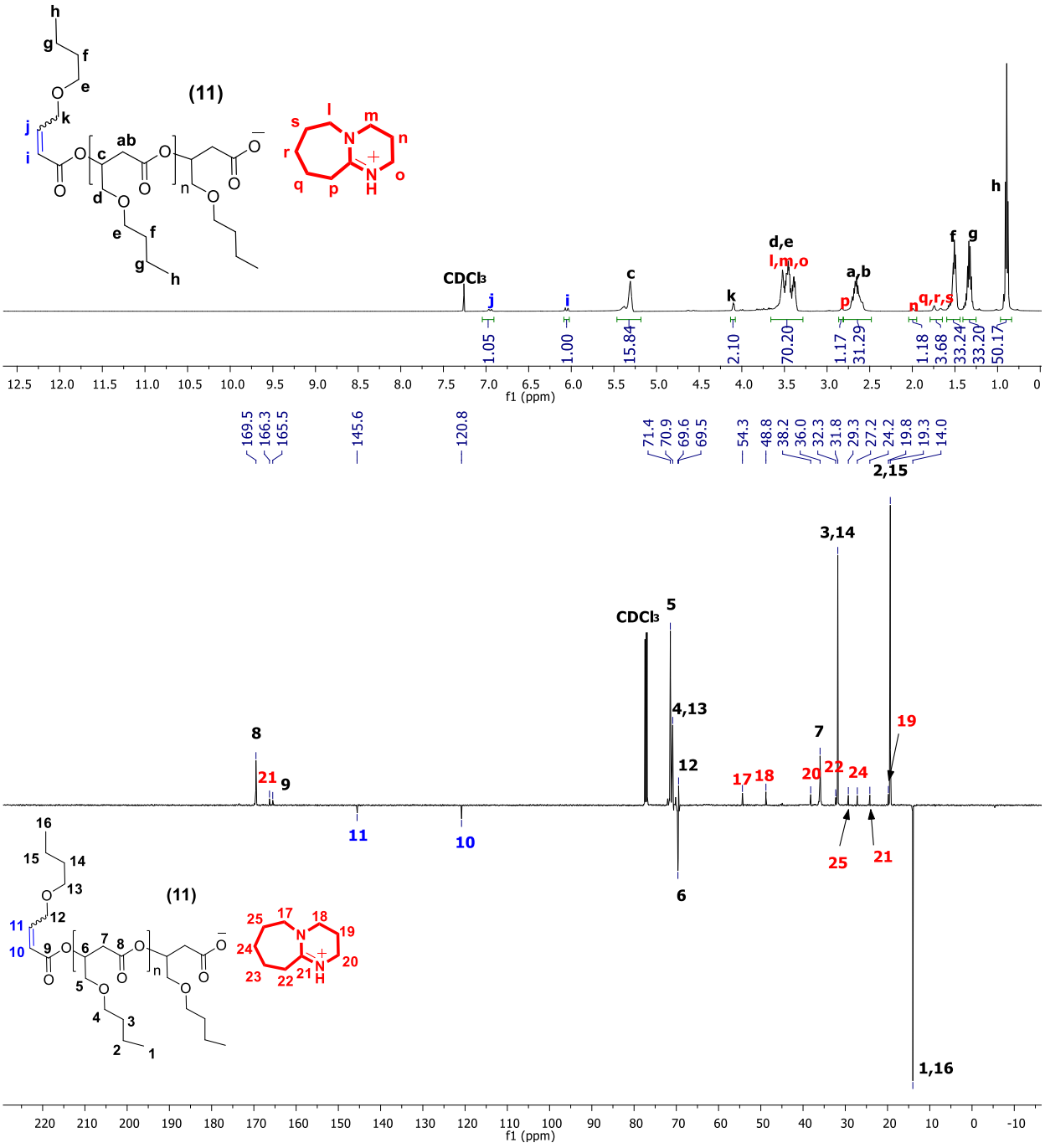


Figure S25. ^{1}H (500 MHz, $CDCl_3$, 25 °C) (top) and J-MOD (125 MHz, $CDCl_3$, 25 °C) (bottom) NMR spectra of $PBPL^{OBu}$ recovered from the ROP of *rac*-BPL^{OBu} mediated by DBU (Table 3, entry 3).

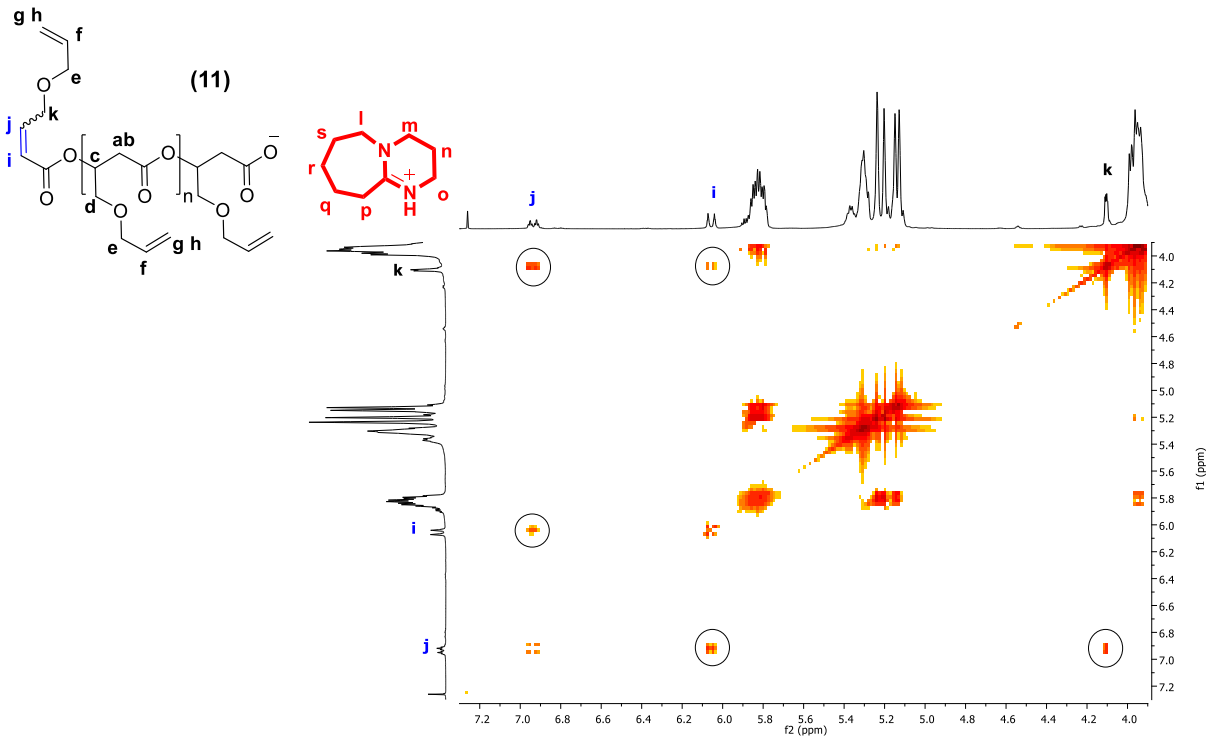


Figure S26. ^{1}H-^{1}H COSY (500 MHz, $CDCl_3$, 25 ˚C) NMR zoomed spectrum of $PBPL^{OAll}$ recovered from the ROP of *rac*-BPL^{OAll} mediated by DBU supporting the α-crotonate end-capping group (Table 3, entry 1).

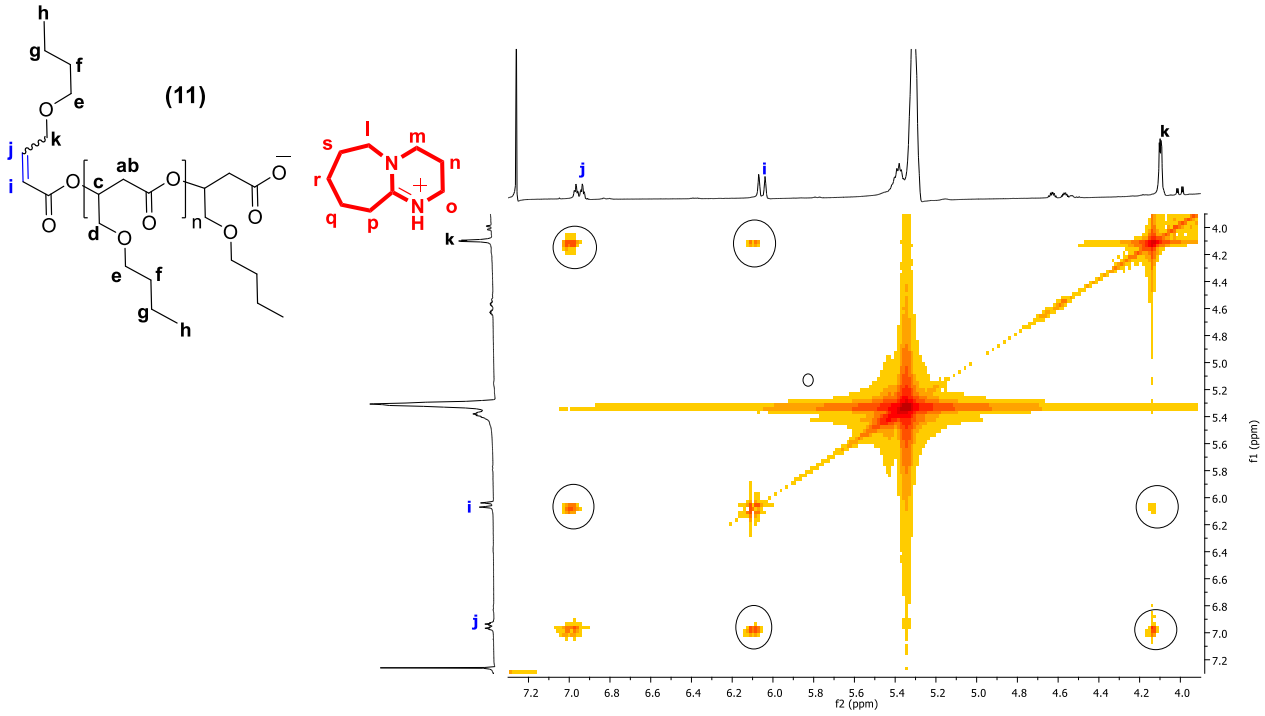


Figure S27. ^{1}H-^{1}H COSY (500 MHz, $CDCl_3$, 25˚C) NMR zoomed spectra of $PBPL^{OnBu}$ recovered from the ROP of *rac*-BPL^{OnBu} mediated by DBU supporting the α-crotonate end-capping group (Table 3, entry 2).

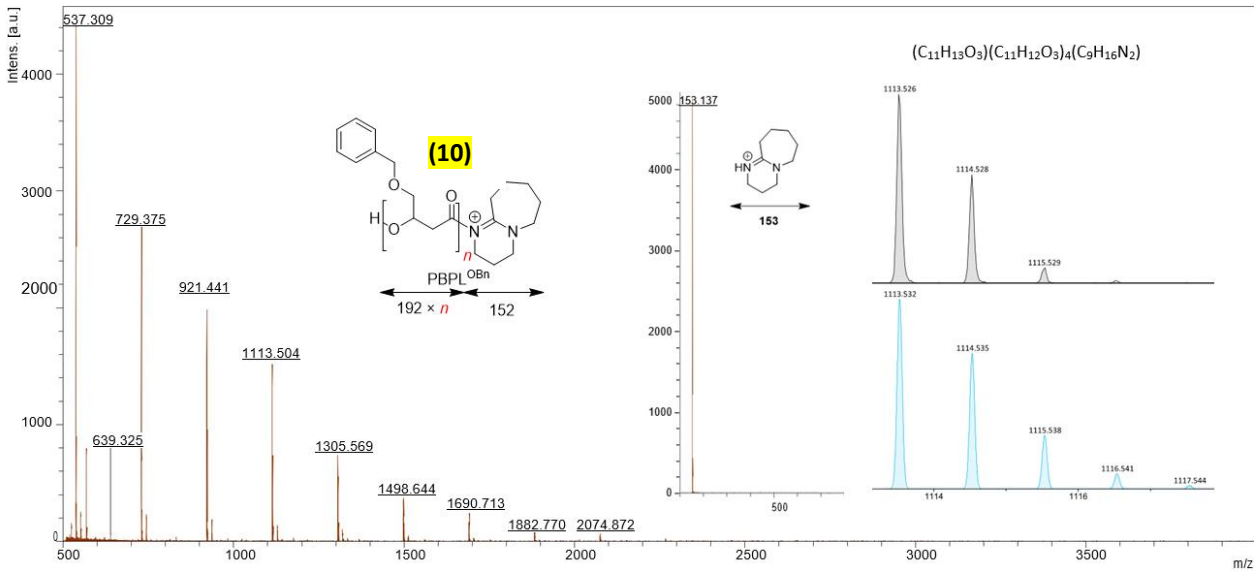


Figure S28. MALDI-ToF mass spectrum (DCTB matrix, no Na^+ cationizing salt) of a sample freshly synthesized from the ROP of *rac*-BPL^{OBn} mediated by DBU (Table 3, entry 3); see the zoomed regions corresponding to the simulated (blue, bottom) and experimental (black, top) spectra of PBPL^{OBn} macromolecules end-capped with both an α–hydroxyester and ω-DBU-groups (Figure 8, population **I,** Scheme 4-**10**).

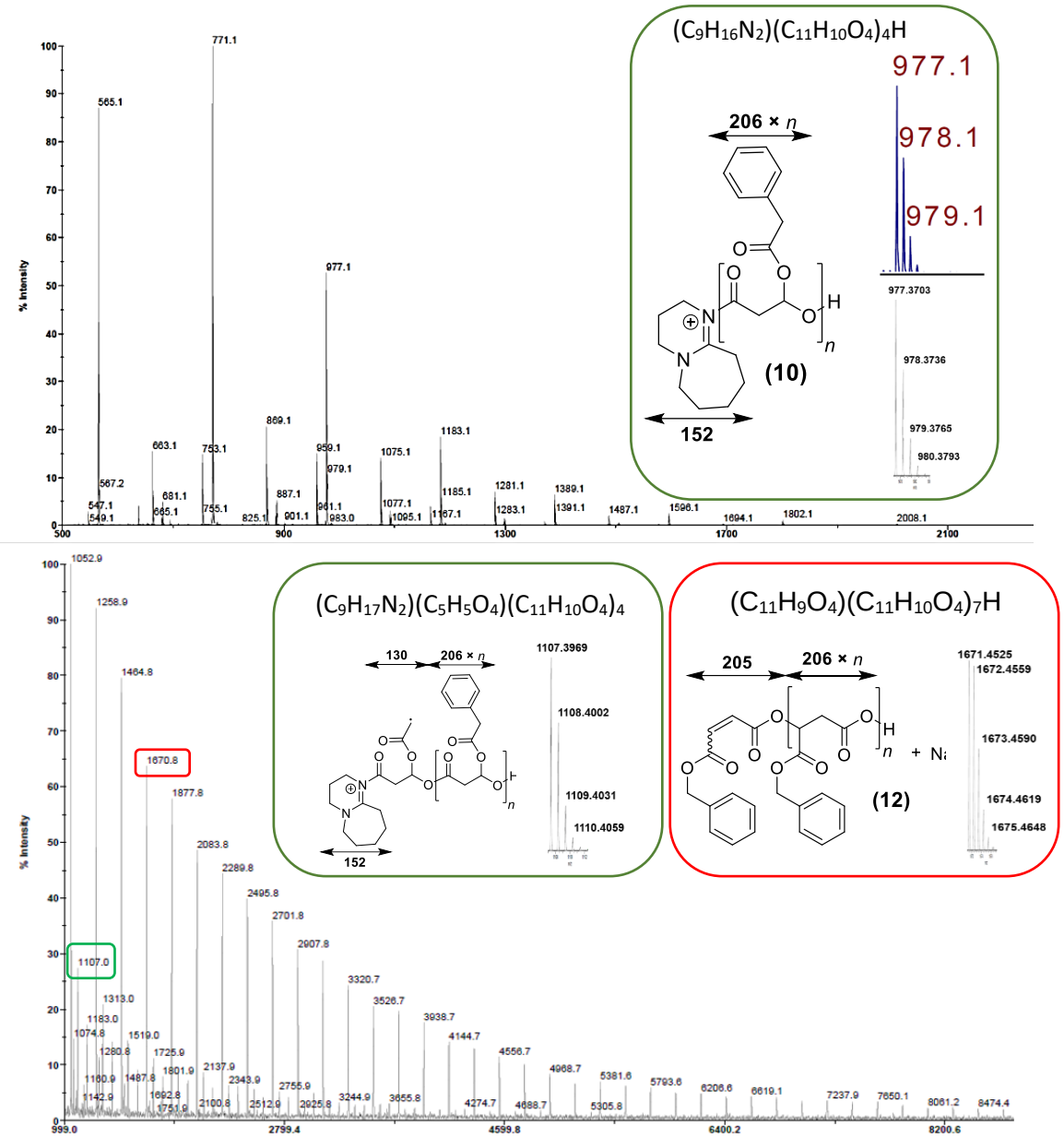


Figure S29. MALDI-ToF mass spectra of a PMLA^{Bn} sample freshly synthesized from the ROP of *rac*-MLA^{Bn} mediated by DBU, using α-cyano-4-hydroxycinnamic acid (CHCA) as matrix (no cationizing salt) (Top) (ESI, Figure S10 of reference 1), and of the same sample not freshly synthesized using trans-3-indoleacrylic acid (IAA) matrix in the presence of Na^+ cationizing salt (bottom) (ESI, Figure S12 of reference 1).[1] Reinterpretation of the top spectrum shows the zoomed regions corresponding to the simulated (bottom) and experimental (top) spectra of PMLA^{Bn} macromolecules end-capped with both an α-hydroxy and ω-DBU$^+$ groups (population **I**, Scheme 4-**10**). Also, the bottom spectrum shows a population corresponding to PMLA^{Bn} which can only be observed in the presence of cationizing agent, with the zoomed region corresponding to the simulated (bottom) and experimental (top) spectra of PMLA^{Bn} macromolecules end-capped with both an α-crotonate and an ω-carboxylic acid end-groups, alike species Scheme 4-**12**.

Comments on the TBD-catalyzed ROP of β-lactones as previously reported in the literature.[1,2]

In the first work reported in 2013 on the ROP of MLA^{Bn} promoted by TBD, we suggested that TBD initiates polymerization via a nucleophilic pathway as depicted in Scheme S1 with BL.[1] A subsequent study reported by Coulembier and co-workers in 2018 disclaimed that TBD could ring-open MLA^{Bn} upon acting as a nucleophile.[2] However, according to our considerations, several spectroscopic and spectrometric characterizations as well as features implemented in the polymerization procedure as developed in Coulembier's work,[2] are not in full support of this latter statement of a weak nucleophilic behavior of TBD.

First, Coulembier's study involved a bulkier monomer than MLA^{Bn}, namely *rac*-benzylcarbonyl-3,3-dimethyl-2-oxetanone (dMMLA^{Bn}), which brings into consideration some steric effects that may impede the 1,2 attack of TBD on the C=O of dMMLA^{Bn} (Figure S30-B), unlike the attack on the less hindered MLA^{Bn} (Figure S30-A) or BL.

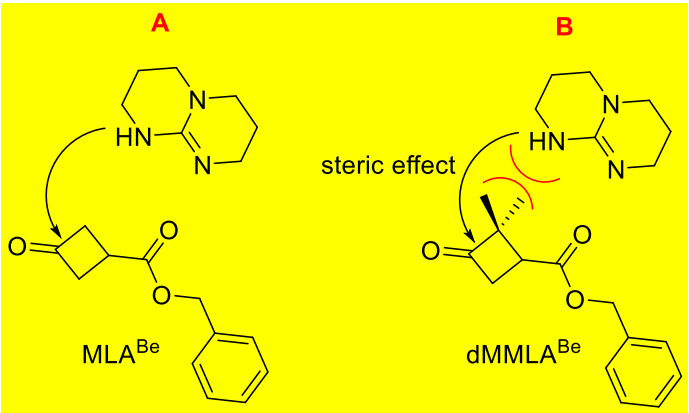


Figure S30: TBD's approach of MLA^{Bn} (A)[1] and dMMLA^{Bn} (B),[2] In bulk (no solvent).

Furthermore, the oligomer resulting from the ROP of dMMLA^{Bn} mediated by TB, features, as based on ESI MS claims, a water end-capping molecule. Coulembier *et al.* rationalized the formation of such a macromolecule, by the anionic ROP mediated by residual water (refer to Scheme 2 in their publication).[2] Consequently, this statement confirms the presence of significant amounts of water in their polymerization medium.[2] This residual water can indeed lead to the formation, upon reaction with TBD, of TBDH$^+$, thereby depleting TBD from its nucleophilic feature.[4] Note that in our work, efforts were made to avoid any water traces. [1] The two experiments are thus not comparable.

Moreover, the ^{1}H-NMR spectrum reported by Coulembier *et al.* of their "as-used TBD" (i.e. as received TDB) in $CDCl_3$ is peculiar, in that is exhibits two sets of alike signals (refer to Figure 1a in their paper; Figure S31-top).[2] ^{1}H NMR analyses of our TBD (98%, Aldrich; used as received) does not show this same latter pattern, regardless of the deuterated solvent used for the NMR analysis. The ^{1}H NMR spectrum of our TBD is exactly matching the literature data (Figure S31-middle and -

[4] A. Dzienia, P. Maksym, B. Hachuła, M. Tarnacka, T. Biela, S. Golba, A. Zięba, M. Chorążewski, K. Kaminski and M. Paluch, *Polym. Chem.*, 2019, **10**, 6047-6061.

bottom, respectively). The comparison of the experimental results of the ROP mediated by two such distinct batches of TBD is thus questionable.

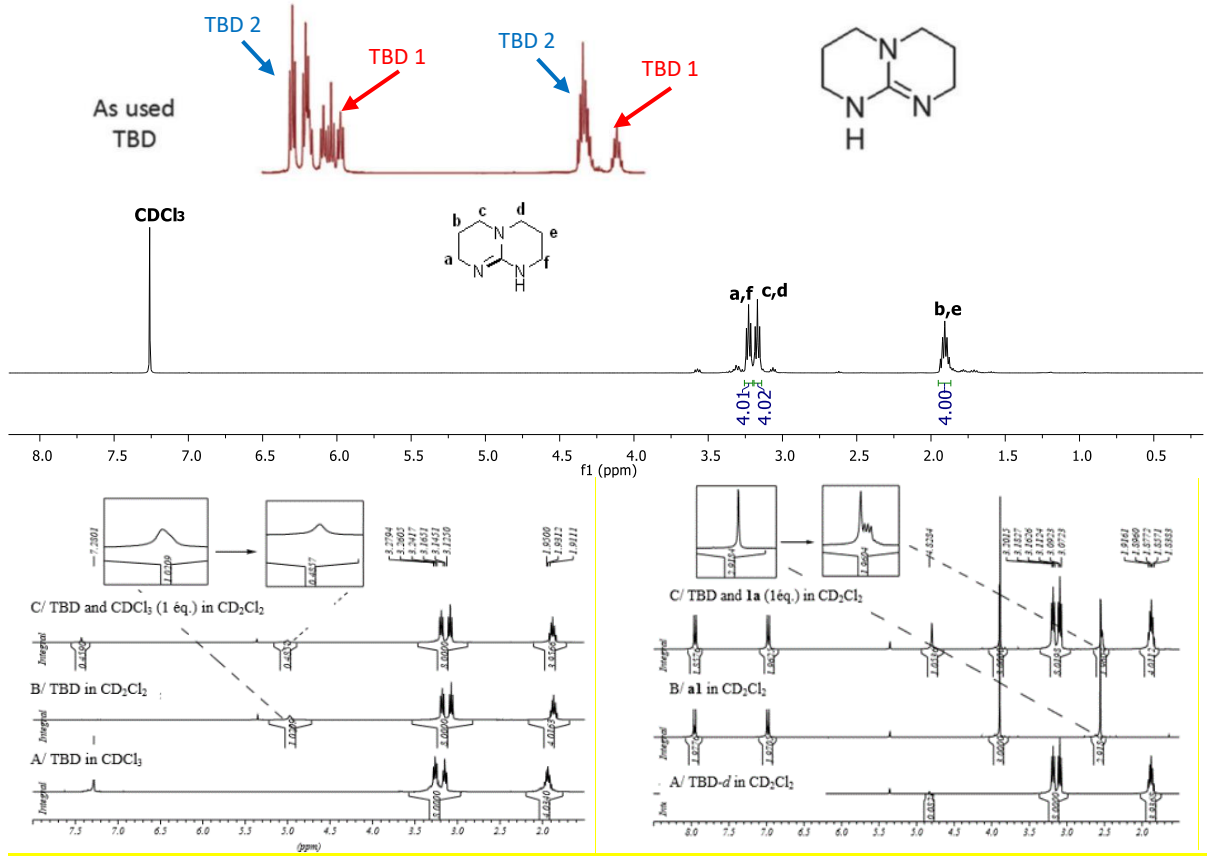


Figure S31: ^{1}H NMR spectra of "as-used" TBD reported by Coulembier *et al.* in 2018 in $CDCl_3$ (top),[2] the TBD used in our present and prior studies[1,3] (middle), and of TBD as reported in the literature (bottom).[5]

Finally, Coulembier and co-workers reproduced[2] the ROP of BL using TBD in bulk, under the same experimental conditions than those we reported previously.[1,3] MALDI-ToF MS analysis of the PHB sample that we isolated only exhibits a single population assigned to a zwitterionic species alike species Scheme 3-**5** (Figure S20). On the contrary, the MALDI-ToF MS analysis of the PHB sample analyzed using the same conditions (same DCTB matrix and Na^+ cationizing salt) and reported by Coulembier *et al.* clearly exhibits four distinct populations (Figure 6 in their publication).[2] Population (b) reported therein is the same as the sole population previously reported by us (Figure S20).[3] On the other hand, population (d) observed in Coulembier's work is therein claimed to originate from H_2O initiation, that is from residual water (refer to our above-mentioned comment) in the reaction medium, which then acts as the initiating species. Again, our observation do not evidence the presence of water as initiator under our reaction conditions, thereby precluding any direct comparison.

[5] C. Sabot, K. A. Kumar, C. Antheaume and C. Mioskowski, *J. Org. Chem.*, 2007, **72**, 5001-5004.