

Anionic synthesis and end-functionalization of polymyrcene in a flow microreactor system

Katia Pérez,^{a,b} Sébastien Leveneur,^c Fabrice Burel,^a Julien Legros,^b and Daniela Vuluga^{*,a}

a INSA Rouen, Normandie Univ, UNIROUEN, CNRS, PBS, 76000 Rouen, France

b CNRS, INSA Rouen, Normandie Univ, UNIROUEN, COBRA, 76000 Rouen, France

c Normandie Univ, INSA Rouen, UNIROUEN, LSPC, EA4704, 76000 Rouen, France

Table of Contents

Materials and Methods	3
Typical experimental procedures	4
<i>Synthesis of poly(myrcene) under batch conditions</i>	<i>4</i>
<i>Synthesis of poly(myrcene) under flow conditions</i>	<i>7</i>
<i>Synthesis of poly(myrcene) quenched with TMSCl under flow conditions</i>	<i>9</i>
<i>Synthesis of poly(myrcene) functionalized quenched CO₂ under batch conditions</i>	<i>11</i>
<i>Synthesis of poly(myrcene) quenched with CO₂ under flow conditions</i>	<i>13</i>

Materials and Methods

Reagents and materials: Myrcene was purchased from Sigma-Aldrich or Acros (distilled from CaH_2) and dissolved in anhydrous THF (distilled from benzophenone/sodium) for the reaction. Organolithiums compounds were purchased from Sigma-Aldrich or Acros as a 2.5 M solution in hexanes and diluted to the wanted title with *n*-hexane (distilled from CaH_2) and titrated by menthol/bipyridine method before usage. Methanol was purchased from Sigma-Aldrich or Acros and was used as received. TMSCl was freshly distilled. Adapters, ferrules and connexions were purchased from CIL. Microflow reactors were cut from stainless steel tubing also purchased from CIL. Micromixers were custom manufactured by MG-63 (vide infra for schematics). Reagents were fed in the reactors by mean of Harvard Apparatus PHD Ultra syringe pumps, and SGE gas-tight glass syringes.

Reaction conditions: All experiments were run under oxygen and moisture-free environment. Glassware was dried under vacuum using a Schlenk line by heating the flask with a heat-gun before cycling dry argon and vacuum. Stainless steel reactors were dried overnight in a 120 °C oven, before cooling in a desiccator over silica gel under vacuum. Flow experiments were run in a tap water bath cooled at 10 °C. Flow experiments: three dead volumes of reagents were run through the system before collection to ensure reactor equilibrium, then approximately between 2-5 mL were collected for analysis.

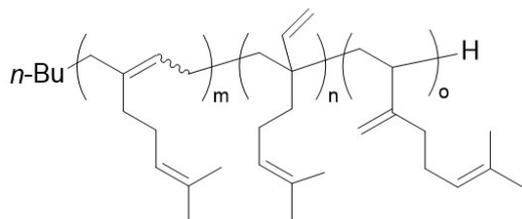
NMR Analysis: ^1H and ^{13}C NMR Spectra were recorded on a Bruker 300 MHz spectrometer and worked with MestReNova software, chemical shifts are given in part per millions (ppm) relative to the residual solvent (7.26 and 77.16 respectively for CDCl_3). Spectra were calibrated on residual non-deuterated solvent peaks.

Gel Permeation Chromatography (GPC): GPC chromatograms were recorded on a PL-GPC 50 Plus, treated with GPC offline software. GPC was calibrated with polymethyl methacrylate (PMMA) a pre-weighed polymer standard from Agilent. Samples were diluted in dichloromethane and injected into the GPC (30°C, 1mL/min, 2 mixed-C column).

Infrared analysis: Infrared spectra were recorded on a Perkin Elmer ATR universal sampler 100 spectrum.

Typical experimental procedures

Synthesis of poly(myrcene) under batch conditions



2.6 mL of anhydrous THF is introduced in a reactor under inert atmosphere (Ar) and then cooled with a 10° C water bath. Then, 1.4 mL of hexane is introduced and 0.19 mL of *n*-BuLi (2.5 M in hexanes) is injected. After 5 minutes, 1.4 mL of myrcene (8 mmol) is introduced in one portion. After the time selected (1, 2, 8 min, etc.), the reaction is quenched with methanol: water (2/2 mL). The quenched mixture is extracted with dichloromethane (3 x 10 mL), washed with water (20 mL), dried over magnesium sulfate, and concentrated under vacuum to afford a crude mixture, analyzed by mean of NMR (data in accordance with the literature.¹).

¹H NMR (300 MHz, CDCl₃) δ (ppm)= 5.67, 5.13, 4.75, 1.69, 1.62 and 0.87 (3 H).

¹³C NMR (75 MHz, CDCl₃) δ (major isomer) (ppm) = 139.04, 131.21, 124.51, 36.96, 30.67, 27.01, 26.83, 25.71, and 17.73.

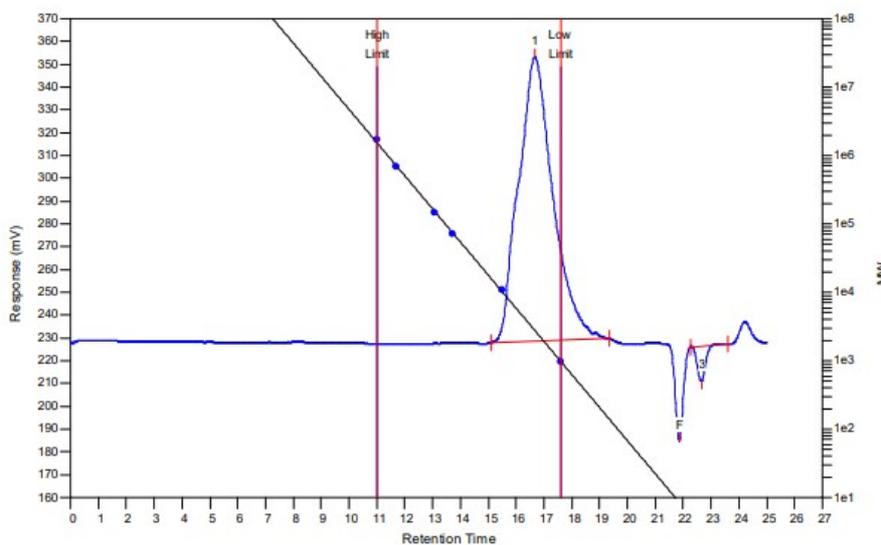


Fig. 1. GPC of poly(myrcene) in batch

¹ (a) J.M. Bolton, M.A. Hillmyer, T.R. Hoye, Sustainable Thermoplastic Elastomers from Terpene-Derived Monomers, ACS Macro Lett. 3 (2014) 717–720. <https://doi.org/10.1021/mz500339h>. (b) S. Loughmari, A. Hafid, A. Bouazza, A. El Bouadili, P. Zinck, M. Visseaux, Highly stereoselective coordination polymerization of β-myrcene from a lanthanide-based catalyst: Access to bio-sourced elastomers, Journal of Polymer Science Part A: Polymer Chemistry. 50 (2012) 2898–2905. <https://doi.org/10.1002/pola.26069>.

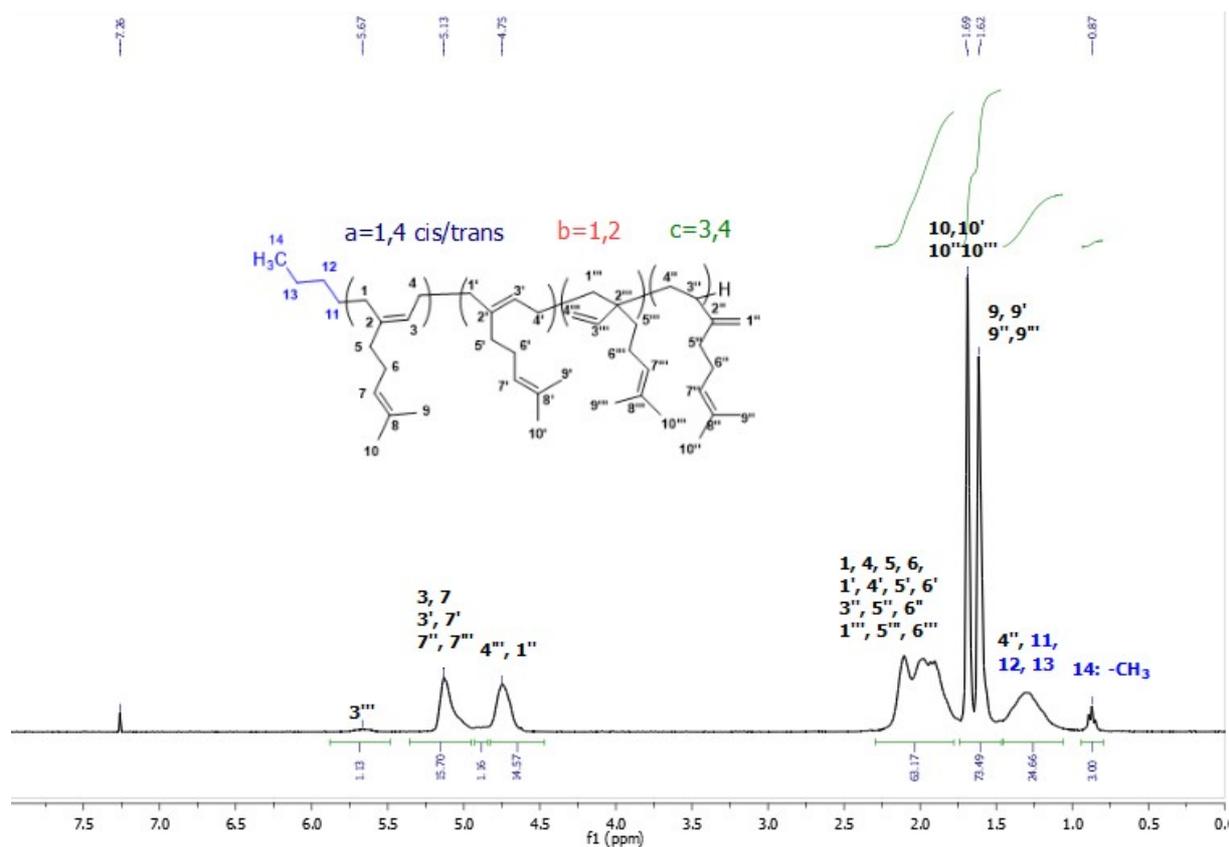


Fig 2. ^1H NMR (300 MHz, CDCl_3) spectrum of polymyrcene in batch at 10°C . Microstructure calculations: $b=1.13(1\text{H})$; $c=(14.57-1.13)/2=6.72(1\text{H})$; $a=(15.70-6.72-1.13)/2=3.92(1\text{H})$; $a=3.92/11.77=33\%$, $b=1.13/11.77=10\%$, $c=6.72/11.77=57\%$

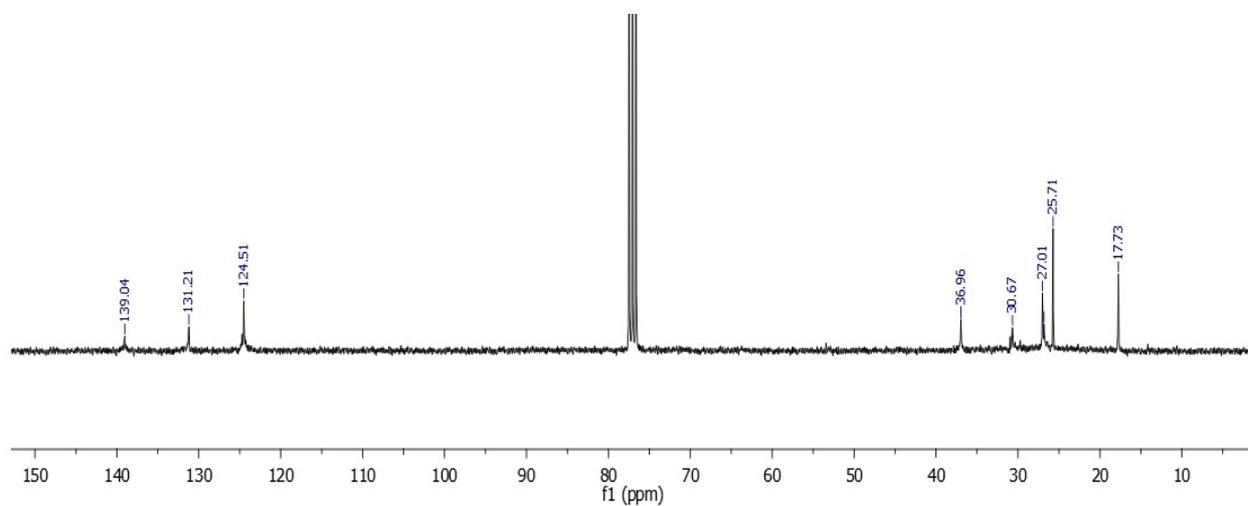


Fig 3. ^{13}C NMR (75 MHz, CDCl_3) spectrum of polymyrcene in batch at 10°C .

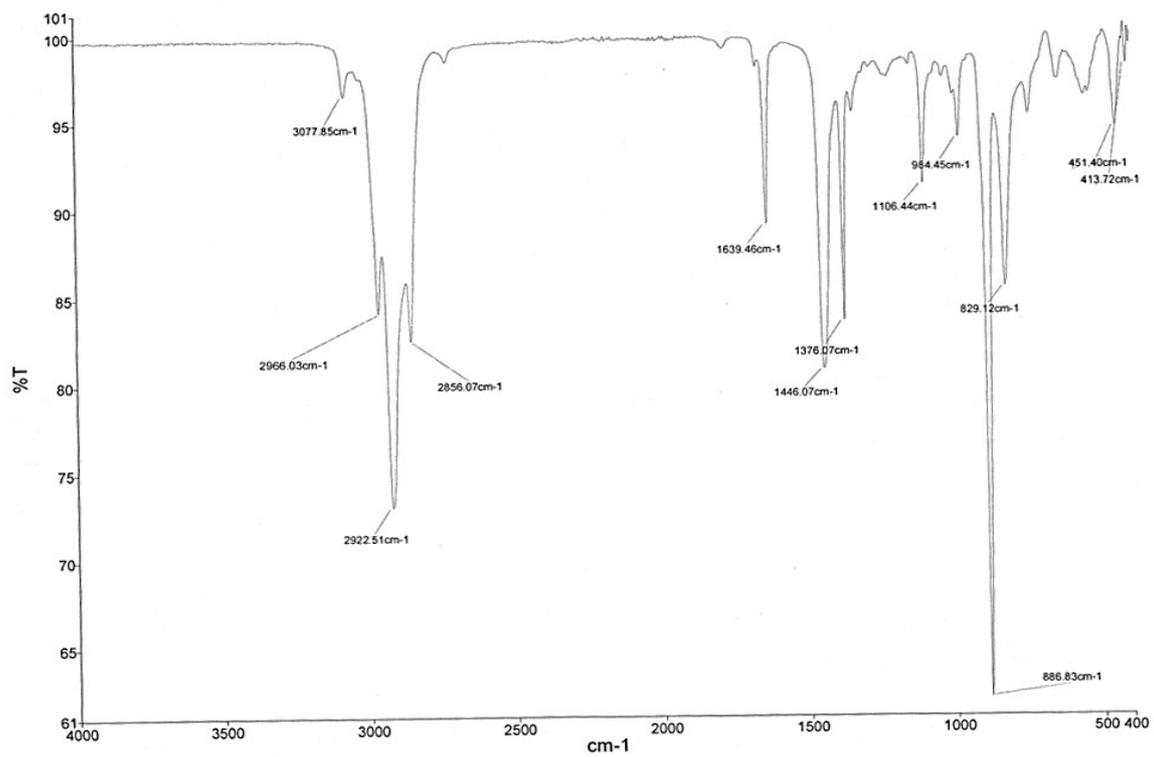
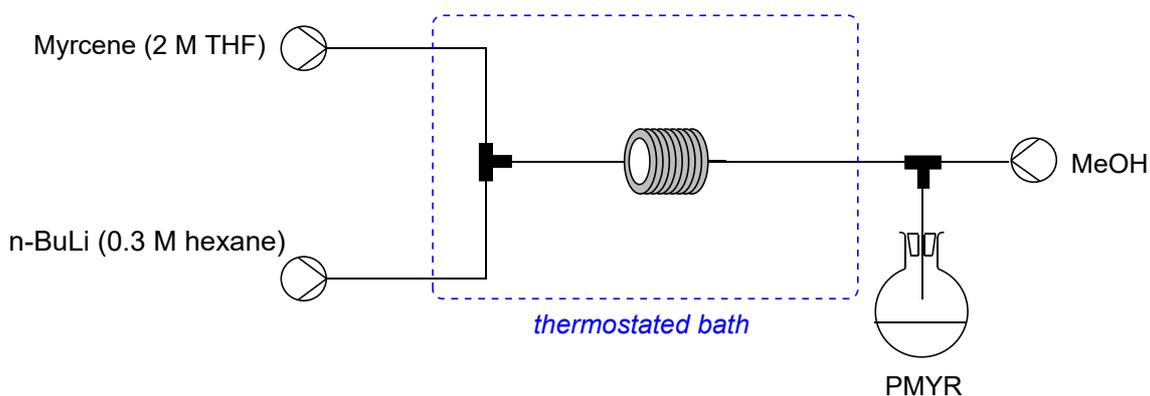


Fig 4. Infrared spectrum of polymyrcene in batch at 10°C.

Synthesis of poly(myrcene) under flow conditions



The system is composed of a first inlet containing a solution of Myrcene in THF (2 M) and a second inlet with *n*-BuLi solution (0.3 M in hexanes). The solutions are passed through a T-Shape micromixer (stainless steel, 500 μm of internal diameter (ID)). The resulting mixture is passed through a microreactor (stainless steel, 750 μm ID, 1 m length). This microreactor is submerged in a 10° C water bath. The resulting solution is introduced in a second T-shape micromixer (500 μm ID) to be quenched with methanol, flow rate 0.1 mL/min. The quenched mixture is passed through a second tube of 300 mm length and 750 μm ID before collection in a vial containing 2 mL water. The quenched mixture is extracted with dichloromethane (3 x 10 mL), washed with water (20 mL), dried over magnesium sulfate, and concentrated under vacuum to afford a crude mixture, analyzed by mean of NMR (confirming previous literature report)

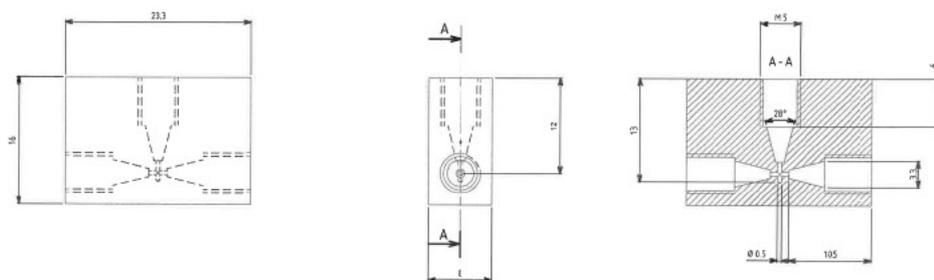


Fig 5. 0.5 mm, Θ 90° Micromixers design.

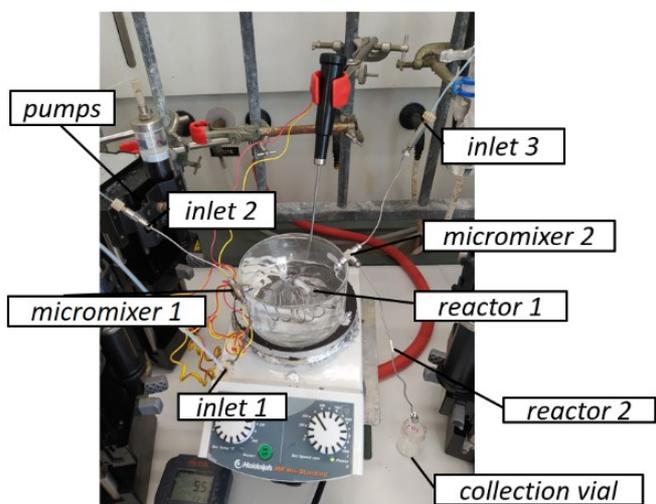


Fig 6. Experimental setup in microflow conditions

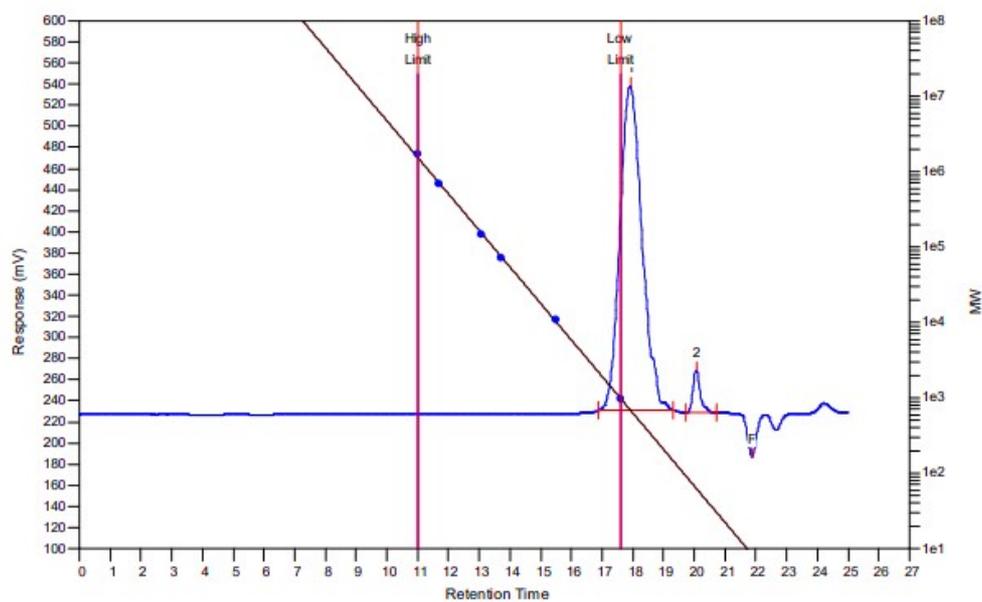
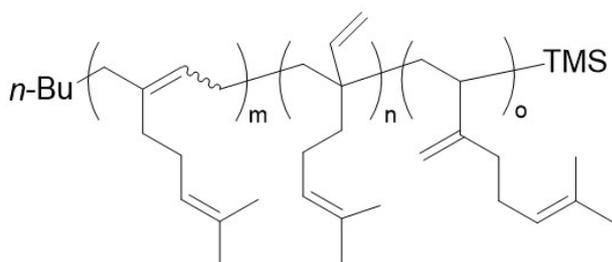
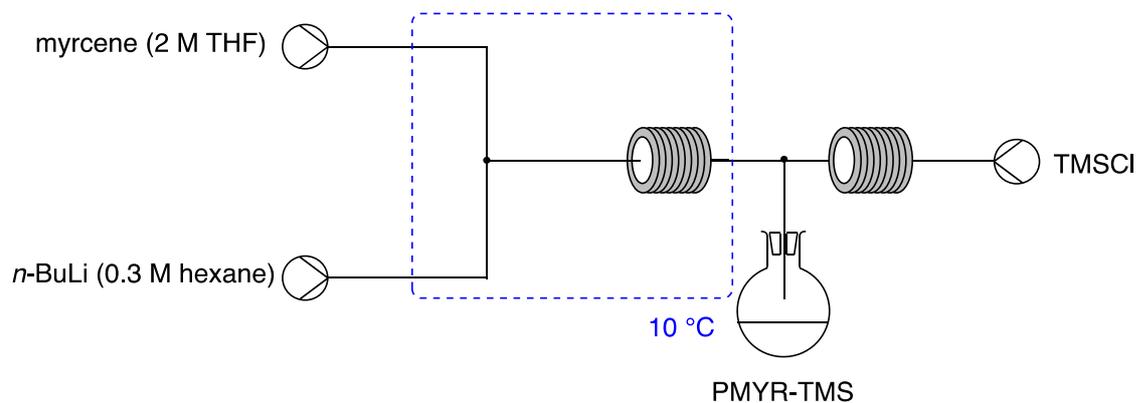


Fig 7. GPC of polycyclohexene in microflow conditions, flow rate polycyclohexene/*n*-BuLi/Methanol: 0.25/0.1/0.1 mL/min respectively at 10°C.

Synthesis of poly(myrcene) quenched with TMSCl under flow conditions



The system is composed of a first inlet containing a solution of Myrcene in THF (2 M) and a second inlet with *n*-BuLi solution (0.3 M in hexanes). The solutions are passed through a T-Shape micromixer (stainless steel, 500 μm of internal diameter (ID)). The resulting mixture is

passed through a microreactor (stainless steel, 750 μm ID, 3 m length). This microreactor is submerged in a 10° C water bath. The resulting solution is introduced in a second T-shape micromixer (500 μm ID) to be quenched with TMSCl, flow rate 0.1 mL/min. The quenched mixture is passed through a second tube of 300 mm length and 750 μm ID before collection in a vial containing 2 mL of HCl (2 N). The quenched mixture is extracted with dichloromethane (3 x 10 mL), washed with water (20 mL), dried over magnesium sulfate, and concentrated under vacuum to afford a crude mixture, analyzed by mean of NMR (confirming previous literature report).

^1H NMR (300 MHz, CDCl_3) δ (ppm)= 5.68, 5.14, 4.76, 1.70, 1.63, 0.88 (3 H), 0.04 and 0.03. (TMS).

^{13}C NMR (75 MHz, CDCl_3) δ (ppm) = 146.31, 139.14, 131.46, 124.72, 115.83, 113.21, 109.24, 35.03, 33.20, 32.23, 31.55, 29.86, 27.18, 26.87, 26.54, 25.85, 22.82, 22.54, 17.84, 14.27 and -0.37.

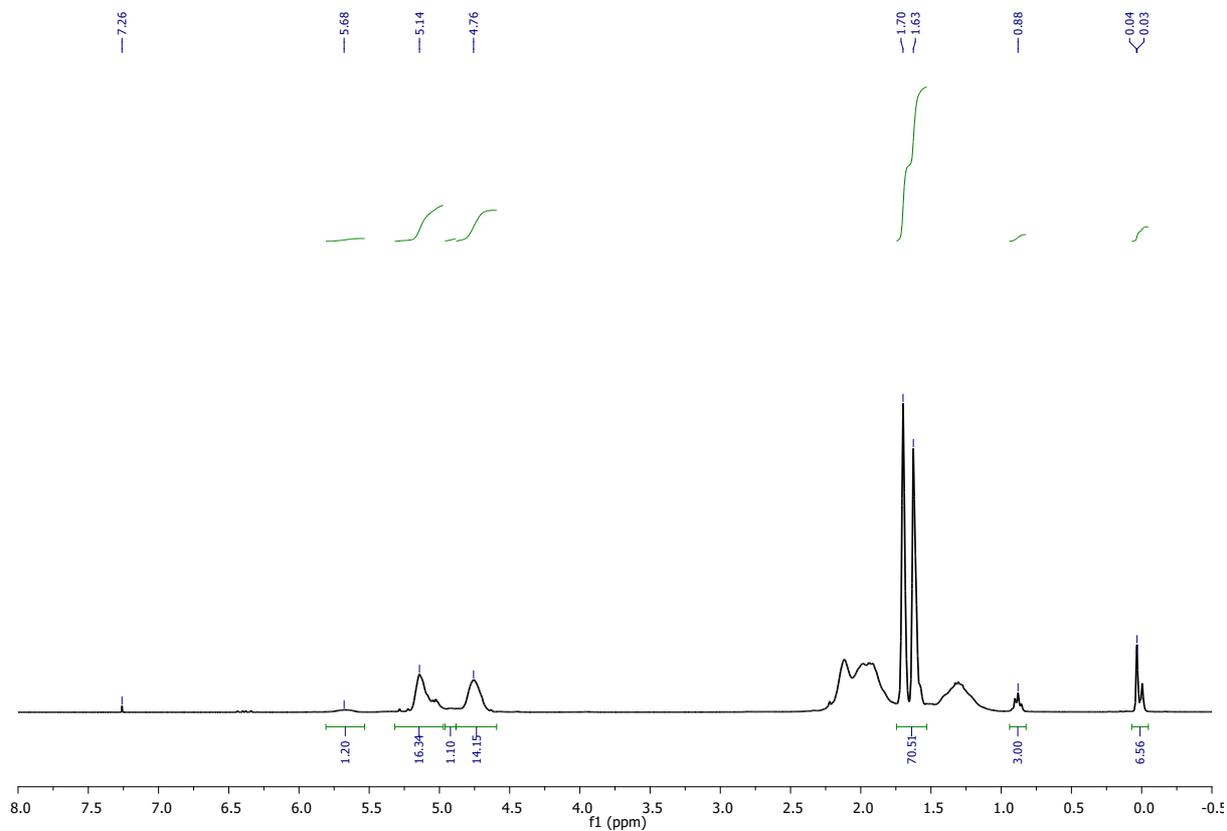


Fig 8. ^1H NMR (300 MHz, CDCl_3) of polymyrcene with TMS end-group, MF: flow rate myrcene/n-BuLi/TMSCl: 0.25:0.1:0.1 mL/min respectively at 10°C . Functionalization degree: $6,56/9 \times 100 = 73\%$.

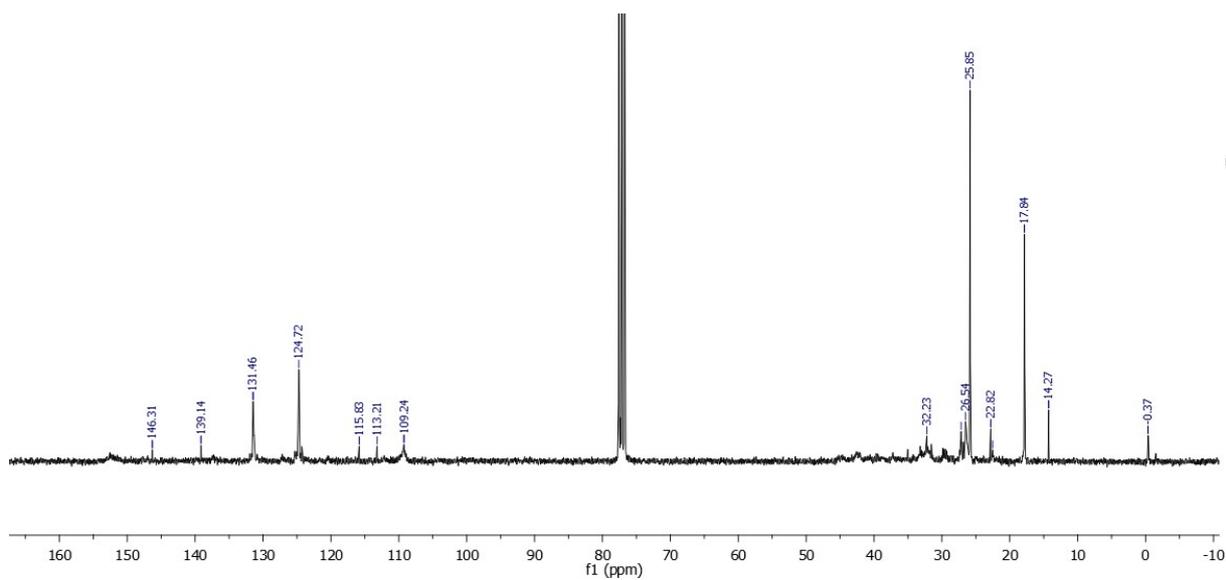
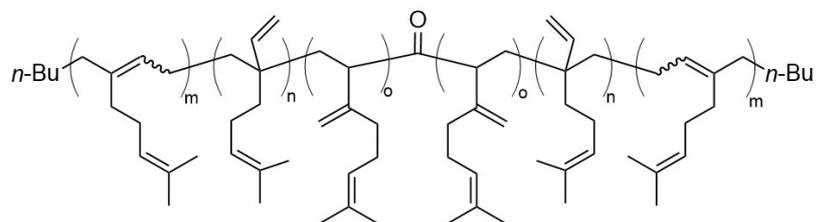


Fig 9: ^{13}C NMR (75 MHz, CDCl_3) of polymyrcene with TMS end-group, MF: flow rate myrcene/n-BuLi/TMSCl 0.25:0.1:0.1 mL/min respectively at 10°C .

Synthesis of poly(myrcene) functionalized quenched CO₂ under batch conditions



2.6 mL of anhydrous THF is introduced in a reactor under inert atmosphere (Ar) and then cooled with a 10° C water bath. Then, 1.4 mL of hexane is introduced and 0.19 mL of *n*-BuLi (2.5 M in hexanes) is injected. After 10 minutes, 1.4 mL of myrcene (8 mmol) is introduced in one portion. Directly from the gas bottle CO₂ is introduced with a needle. Then, the reaction was left under 1 bar at least 1 min. The reaction is quenched with of HCl (2 N).

The quenched mixture is extracted with dichloromethane (3 x 10 mL), washed with water (20 mL), dried over magnesium sulfate, and concentrated under vacuum to afford a crude mixture, analyzed by mean of NMR.

¹H NMR (300 MHz, CDCl₃) δ (ppm)= 5.15, 4.77, 3.10, 2.14, 1.71, 1.64, and 0.89 (3 H).

¹³C NMR (75 MHz, CDCl₃) δ (ppm) = 207.19, 152.30, 131.43, 124.69, 109.27, 32.19, 31.02, 29.82, 26.52, 25.80, 17.80, 14.23.

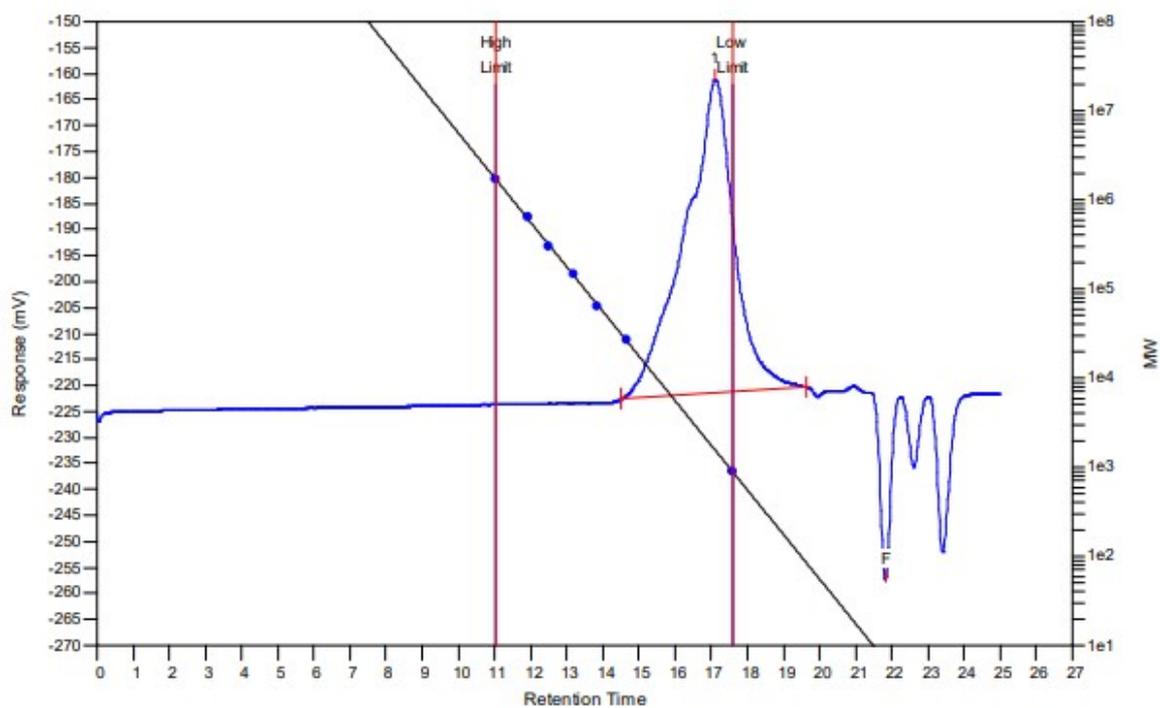


Fig 10. GPC of polymyrcene ketone in batch at 10°C.

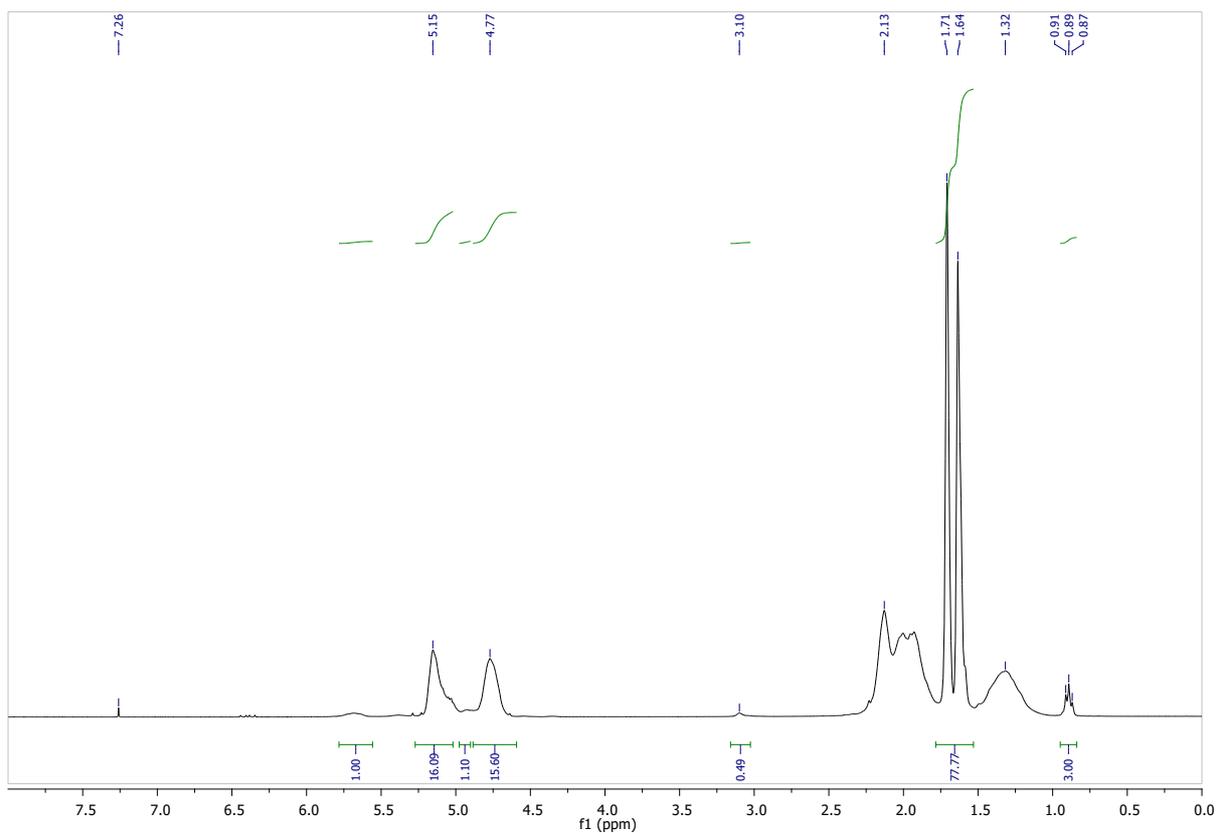


Fig 11. ¹H NMR (300 MHz, CDCl₃) of polymyrcene ketone in batch at 10°C.

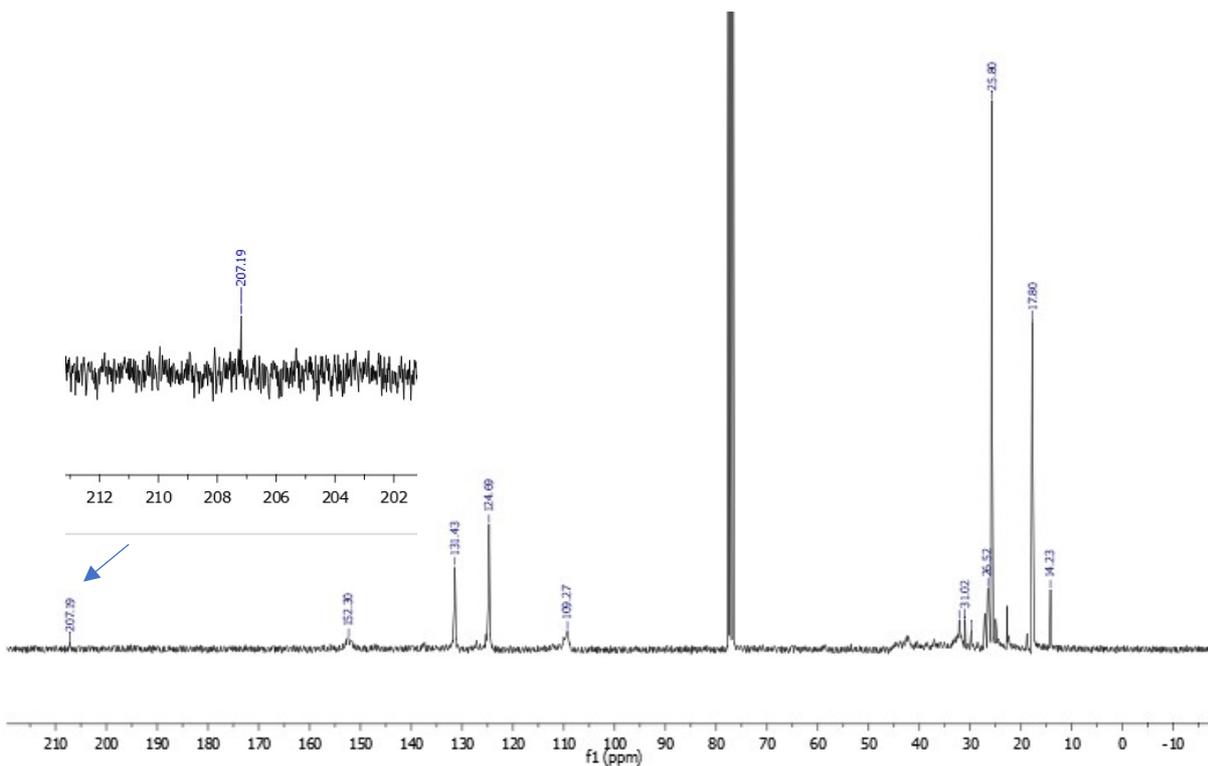


Fig 12. ^{13}C NMR (300 MHz, CDCl_3) of polymyrcene ketone in batch at 10°C .

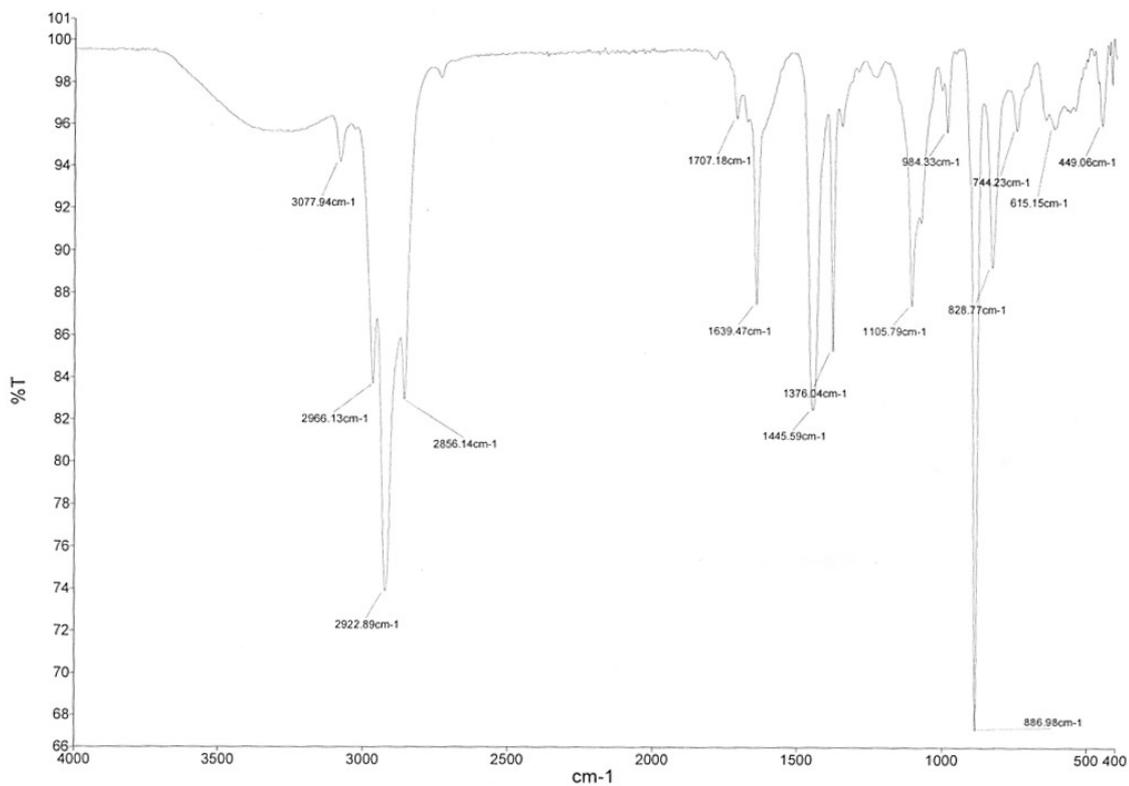
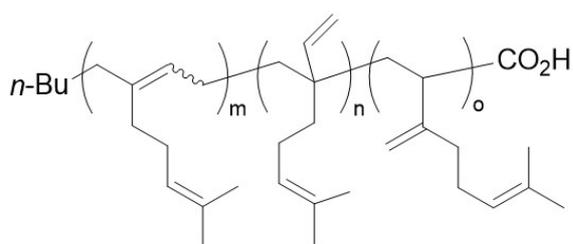
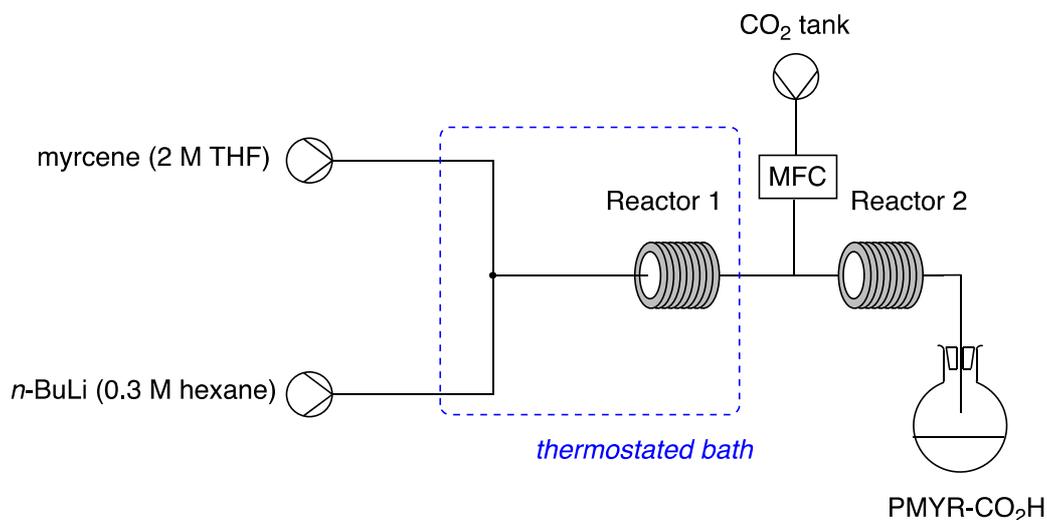


Fig 13. FTIR of polymyrcene ketone in batch (carbonyl group signal 1707.18 cm^{-1}) at 10°C .

Synthesis of poly(myrcene) quenched with CO₂ under flow conditions



For the functionalization of poly(myrcene) with CO₂ a similar system in continuous flow was used as previously mentioned. However, in the second micromixer, instead of methanol, CO₂ gas is introduced by connecting a gas tank to a mass flow controller (Bronkhorst High-Tech BV). This inlet is connected to a second reactor (Reactor 2: ID = 0.75 mm, L = 30 cm) to generate the PMYR functionalized with a carboxyl group, before collection in a vial containing 2 mL of HCl 2 N. The procedure for collection, extraction and analysis of the sample was performed as above.

¹H NMR (300 MHz, CDCl₃) δ (ppm) = 5.61, 5.12, 4.74, 3.06, 1.68, 1.60 and 0.86 (3 H).

¹³C NMR (75 MHz, CDCl₃) δ (ppm) = 178.48, 177.89, 152.44, 150.01, 149.19, 146.86, 146.20, 139.10, 131.34, 124.68, 115.76, 113.08, 109.29, 108.67, 36.16, 34.99, 32.19, 31.53, 27.22, 27.11, 26.84, 26.50, 26.43, 25.78, 22.78 and 17.77.

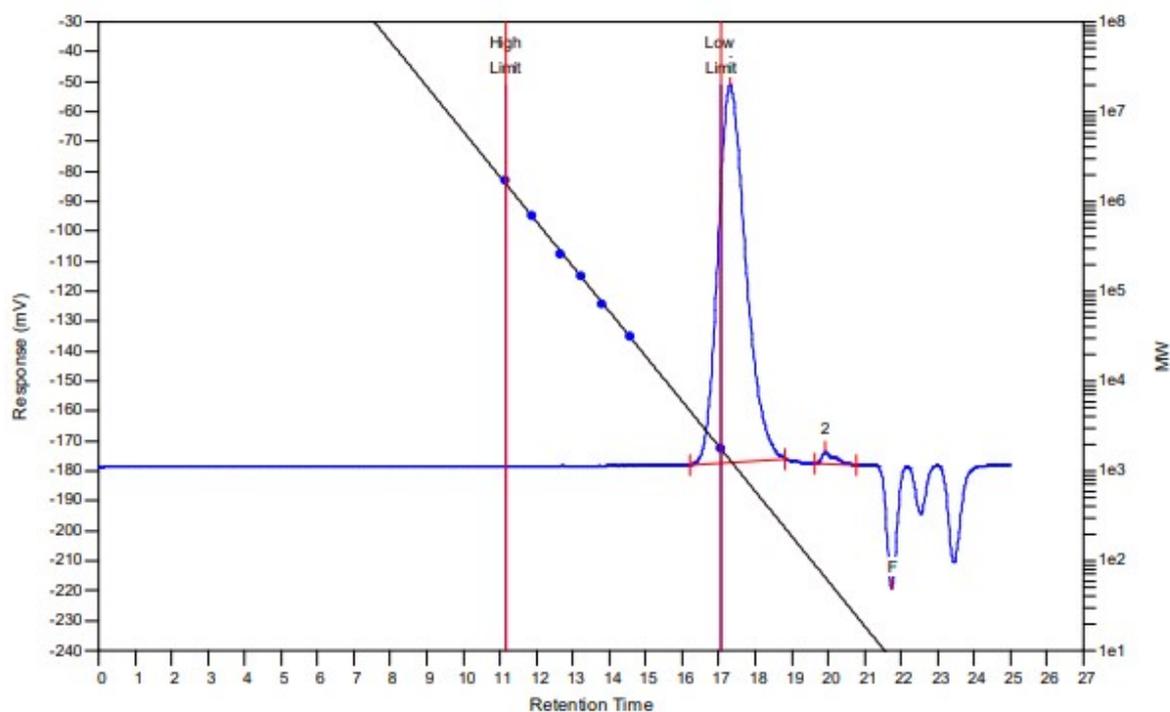


Fig 14. GPC of polymyrcene end-group acid, MF conditions: flow rate myrcene/n-BuLi/CO₂ 0.25:0.1:1.36 mL/min respectively at 10°C.

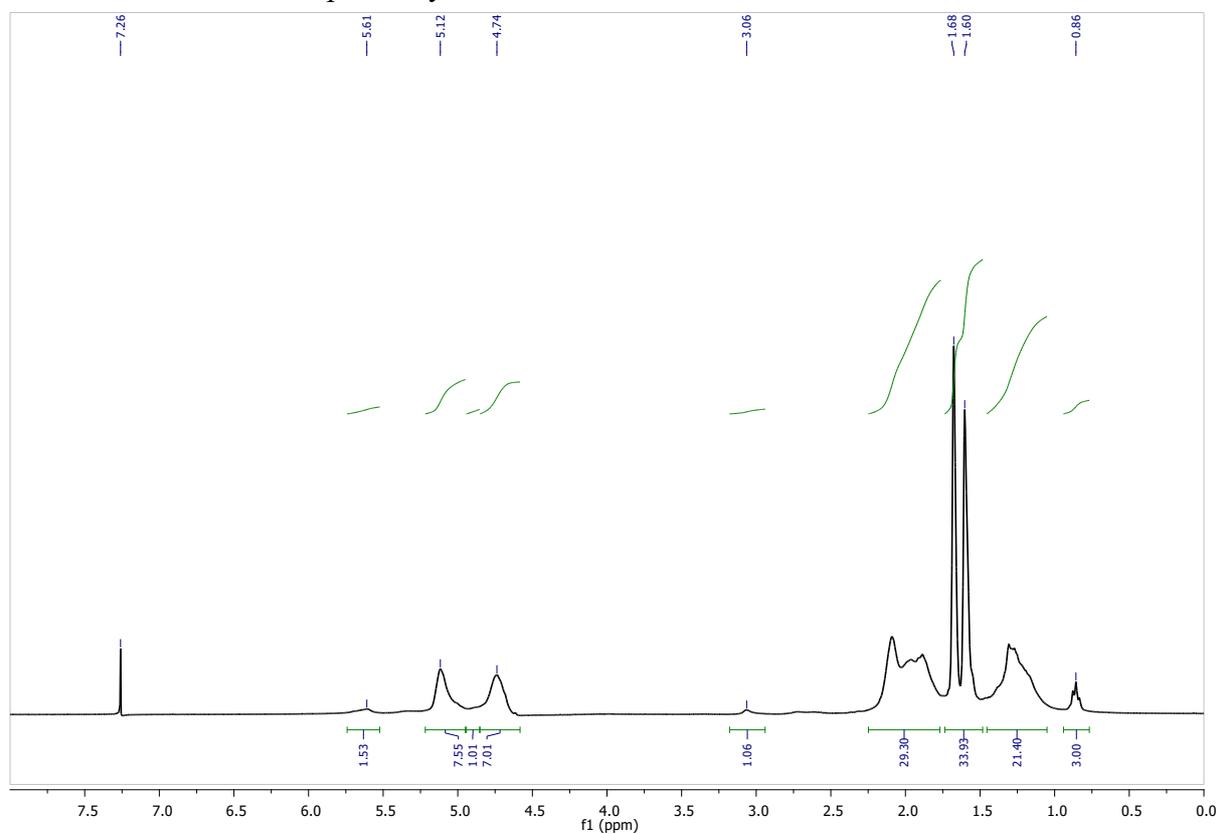


Fig 15. ¹H NMR of polymyrcene end-group acid, MF conditions: flow rate myrcene/n-BuLi/CO₂ 0.25:0.1:1.36 mL/min respectively, at 10°C. Functionalization degree: 95%.

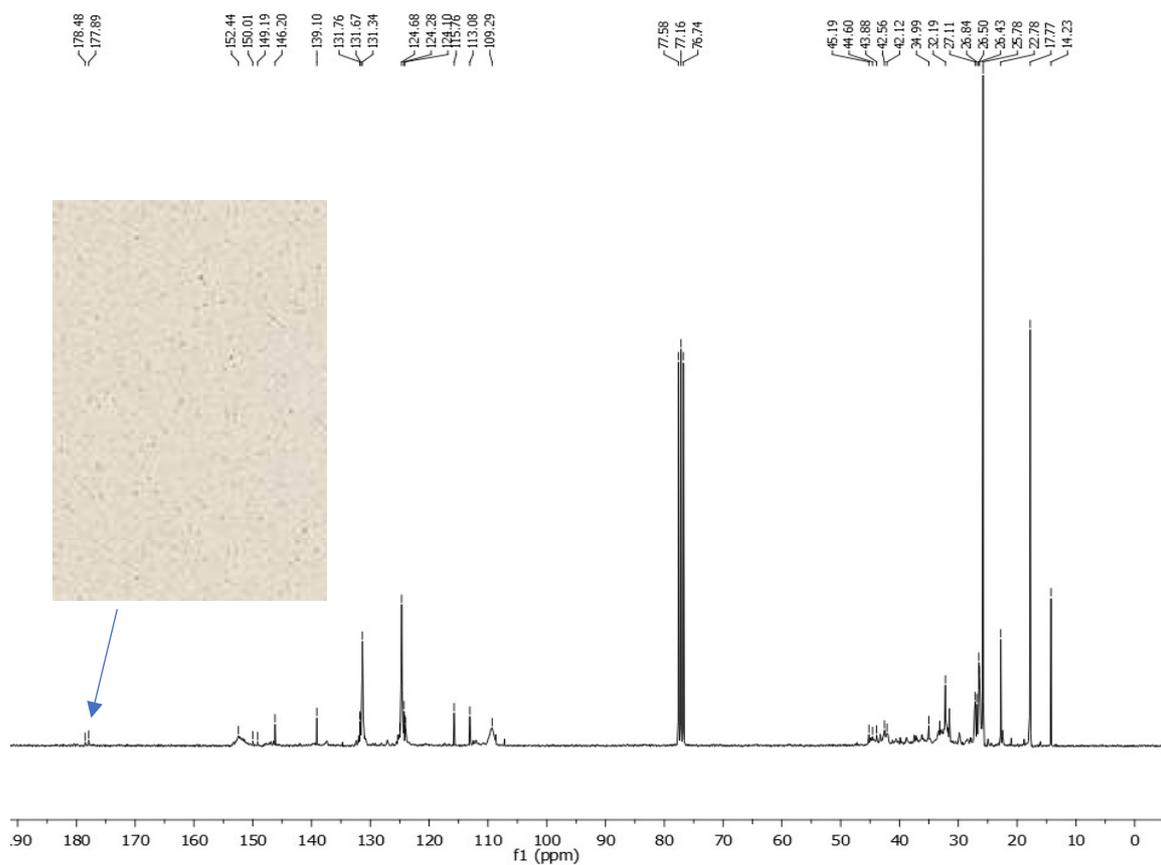


Fig 16. ^{13}C NMR of polymycene end-group acid, MF conditions: flow rate myrcene/n-BuLi/ CO_2 0.25:0.1:1.36 mL/min respectively at 10°C

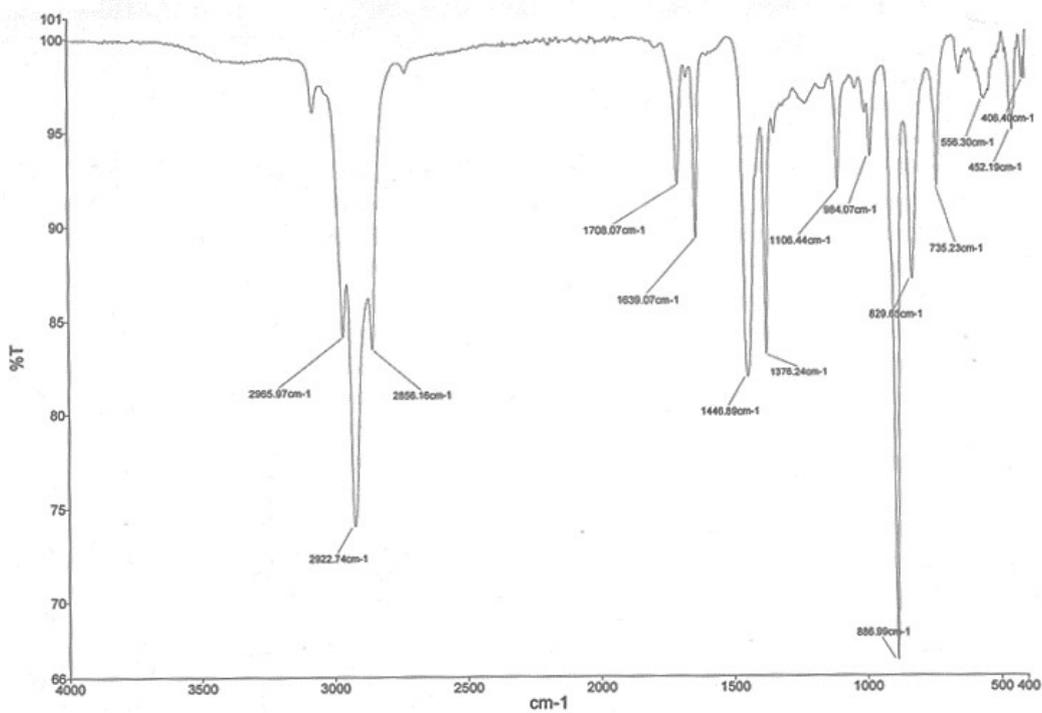


Fig 17. FTIR of polymycene end-group acid (carbonyl group signal 1708.07 cm^{-1}). MF conditions: flow rate myrcene/n-BuLi/ CO_2 0.25:0.1:1.36 mL/min respectively at 10°C .