***Electronic supplementary information** for:*

Rare Earth Metal-Mediated Ring-opening Polymerisation of Cyclic Phosphoesters

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Experimental section

Materials and methods

All chemicals were purchased from Merkel or Aladdin and used without further purification unless otherwise noted. Toluene, diethyl ether and THF were dried by a MBraun SPS-800 and used as received. Cp_2YbMe was prepared according to a literature[1] Triethylamine and ethylene glycol was purified by refluxing over CaH_2 and subsequently distilled under vacuum before use. All monomers were dry, and stored over molecular sieve (3Å) before use. All syntheses and manipulations of air- and moisture-sensitive materials were carried out in flamed Schlenk-type glassware on a dual-manifold Schlenk line, or in an inert gas-filled glovebox.

Characterization

^{1}H NMR spectra were obtained using a Bruker NMR spectrophotometer (300 MHz). Gel permeation chromatography (GPC) measurements were conducted with a PL-GPC120 equipped with a Waters Styragel column (HT3) using DMF as the eluent, and the molecular weights were calibrated with polystyrene standards.

Synthesis

Methylphosphonic dichloride (MePCl).

A mixture of dimethyl methylphosphonate (50 g, 0.40 mol) and DMF (0.30 g, 4.10 mmol) was added to $SOCl_2$ (119.86 g, 1.01 mol) at room temperature. After completion of the addition, the solution was refluxed overnight. During the reaction, a lot of HCl gas was generated. MePCl was collected by fractional distillation as colorless oil (45 g, yield 90%). ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.52 (d, J = 16.4 Hz, 3H). ^{31}P NMR (161 MHz, $CDCl_3$): δ 31.75**.**

2-Methyl-2-oxo-1,3,2-dioxaphospholane (MePPn).

MePCl (38.10 g, 0.29 mol) and ethylene glycol (17.79 g, 0.29 mol) were dissolved in 250 mL of dry DCM and cooled to 0 °C. At this temperature Et_3N (60.91 g, 0.60 mol) in 100mL of dry DCM was added within 1h. The solution was allowed to warm to room temperature and was stirred overnight. The solvent was removed under vacuum and the residue was purified by flash chromatography. MePPn was collected by fractional distillation as colorless oil

(19.97 g, 57%). ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.69 (d, J = 17.5 Hz, 3H), 4.25-4.37 (m, 2H), 4.42-4.56 (m, 2H). ^{31}P NMR (161 MHz, $CDCl_3$): δ 48.57**.**

2-methoxy-2-oxo-1,3,2-dioxaphospholane (MePP).

2-Chloro-2-oxo-1,3,2-dioxaphospholane (COP) was prepared according to a previously published procedure.[2] The THF (50 mL) solution of COP (15 g, 0.12 mol) were added to a solution of methanol (3.89 g, 0.12 mol) and Et_3N (13.52 g, 0.13 mol) in anhydrous THF (100 mL) under N_2 atmosphere,. The temperature was maintained at 0 °C until complete addition, after which it was allowed to warm to room temperature for 2h. The formed salt was removed by filtration and the filtrate was concentrated under vacuum to yield a crude product. MePP was purified by fractional distillation as a colorless oil (14.93 g, 89%). ^{1}H NMR (300 MHz, $CDCl_3$): δ 3.86 (d, J = 11.8 Hz, 3H), 4.35-4.49 (m, 4H). ^{31}P NMR (161 MHz, $CDCl_3$): δ 18.06**.**

2-*iso*-Propoxy-2-oxo-1,3,2-dioxaphospholane (iPrPP).

To a solution of isopropanol (7.30 g, 0.12 mol) and Et_3N (13.52 g, 0.13 mol) in anhydrous THF (100 mL) at 0 °C under N_2, was added COP (15 g, 0.12 mol) in THF (50 mL). The temperature was maintained at 0 °C until complete addition, after which the reaction was performed for another 2h at room temperature. The formed salt was removed by filtration and the filtrate was concentrated under vacuum to yield a crude product. iPrPP was collected by fractional distillation as colorless oil (17.34 g, 87%). ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.37 (d, J = 6.2 Hz, 2H), 4.30-4.48 (m, 4H), 4.71-4.82 (hept, J = 6.3 Hz, 1H). ^{31}P NMR (161 MHz, $CDCl_3$): δ 16.87**.**

Dibutyl butylphosphonate (DBP).

To a 250 mL round-bottom flask equipped with a reflux condenser, was charged with tributyl phosphite (50 g, 0.20 mol) and 1,3-diiodopropane (18.38 g, 0.10 mol). The mixture was heated at 160 °C for 2h. DBP was collected by fractional distillation as a colorless oil (49 g, 98%). ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.91 (t, 9H), 1.30−1.46 (m, 6H), 1.65−1.66 (m, 6H), 1.69−1.77 (m, 2H), 3.91−4.07 (m, 4H).

***n*-Butyl-Phosphonic acid dichloride (^{n}BuPCl).**

To a 100 mL three-necked round-bottom flask equipped with a reflux condenser, was charged with DBP (30 g, 0.12 mol). The mixture was heated at 150 °C for 3h. After phosphorus pentachloride (49.91 g, 0.24 mol) was added in small portions, the reaction was at maintained 150 °C for another 1h. ^{n}BuPCl

was collected by fractional distillation as a colorless oil (17.82 g, 85%). ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.97 (t, 3H), 1.43-1.57 (m, 2H), 1.74-1.90 (m, 2H), 2.53-2.63 (m, 2H).

2-*n*-Butyl-2-oxo-1,3,2-dioxaphospholane (^{n}BuPPn).

^{n}BuPCl (15 g, 0.09 mol) and ethylene glycol (5.32 g, 0.09 mol) were dissolved in 250 mL dry ether and cooled to 0 °C. Afterthat, Et_3N (19.08 g, 0.19 mol) in 100 mL dry ether was added within 1h. Then, the solution was warmed to room temperature and was stirred overnight. The salt was removed by filtration and the filtrate was concentrated under vacuum to yield a crude product. ^{n}BuPPn was collected by fractional distillation as a colorless oil (7.46 g, 53%). ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.94 (t, J = 6.3 Hz, 3H), 1.45 (h, J = 7.2 Hz, 1H), 1.56-1.71 (m, 2H), 1.92-2.03 (m, 2H), 4.23-4.35 (m, 2H), 4.43-4.56 (m, 2H). ^{31}P NMR (161 MHz, $CDCl_3$): δ 51.42**.**

Polymerisation

Representative procedure: The monomer was placed in a flame-dried ampoule with dry toluene. The rare-earth complex was dissolved in dry toluene and placed in another flame-dried ampoule. The polymerization was conducted by the addition of the monomer solution to the rare-earth complex solution at -40 °C. Polymerization was terminated by the addition of methanol after indicated time. The polymer was purified by pouring the reaction mixture into 100 mL of diethyl ether and the subsequent freeze-drying.

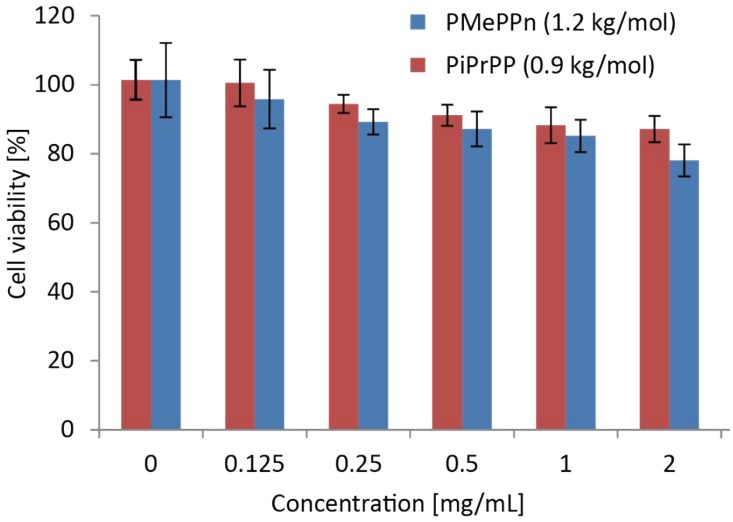
Block copolymerisation

Block copolymerisation of ^{n}BuPPn and MePPn was conducted at -40 °C. In view of the poor solubility of PMePPn in toluene, we use ^{n}BuPPn (80 eq.) as the first feed monomer, the completely conversion was monitored by ^{1}H NMR, after that it was divided into two parts and one was terminated by methanol. MePPn was added into another parts as the second monomer to get P(BuPPn-*b*-PMePPn).

***In vitro* toxicity assay**

1×10^4 NIH 3T3 and Raw 264.7 cells in 100 μL DMEM were seeded in each well of 96-well plate for overnight growth. Then, the cells were treated with different concentrations (0, 0.125, 0.25, 0.5, 1, and 2 mg/mL) of PMePPn and PiPrPP for 24 h. For MTT assay, each well was added 20 μL of 5 mg mL^{-1} MTT solution. After incubated for 3.5 h, 150 μL of DMSO was added into each well after the cell culture medium was removed. Then the absorbance was recorded at 490 nm using a microplate reader after the plate was shaken for 10 min.

(A)



(B)

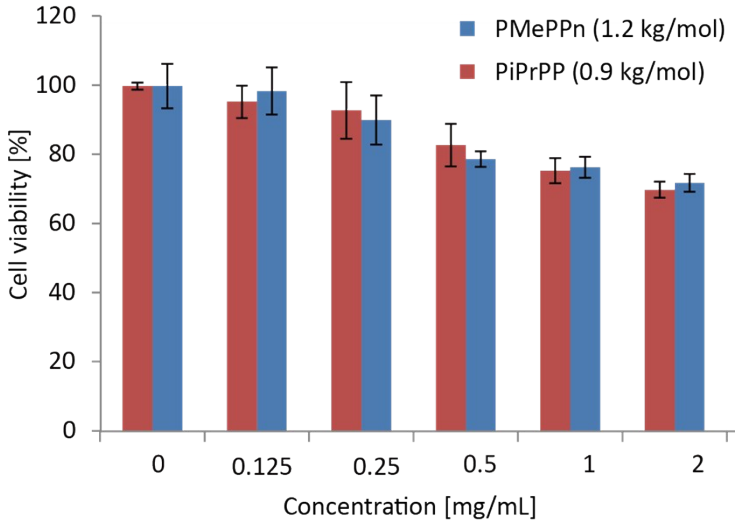


Figure S1. Cell viability of (A) NIH-3T3 cells after 24 h and (B) Raw 267.4 cells after 24 h of incubation with polymer samples

Characterization

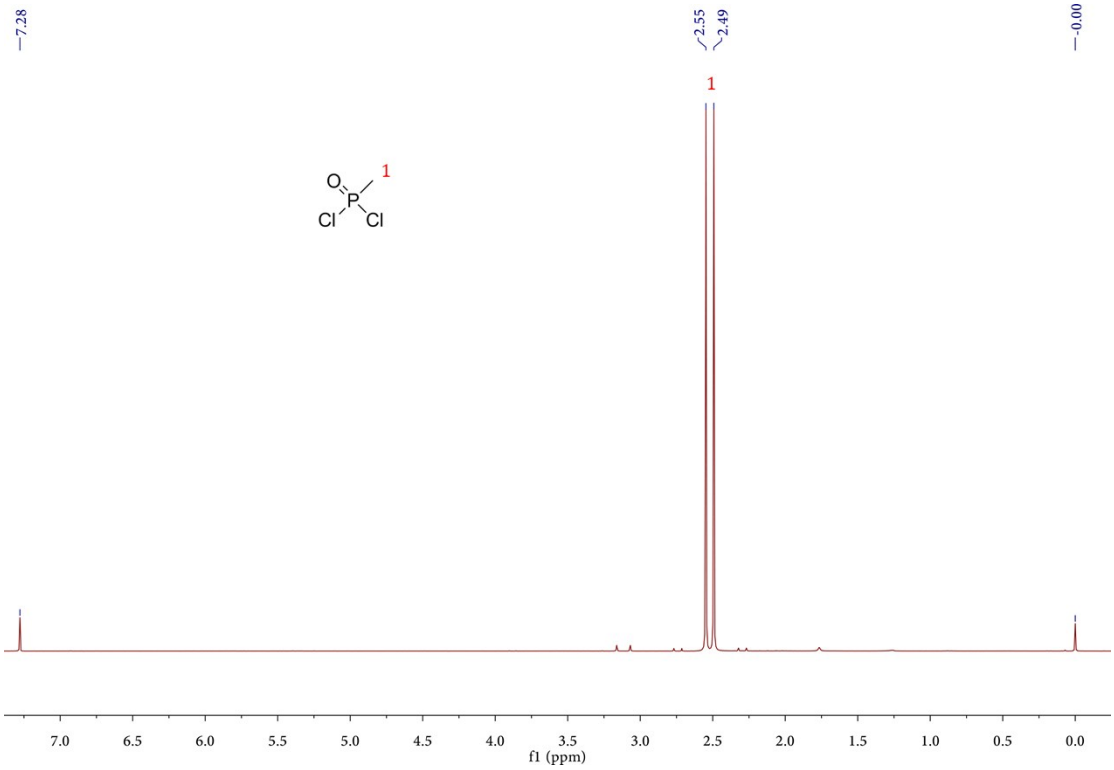


Figure S2. ^{1}H (300 MHz) NMR spectra of MePCl in $CDCl_3$.

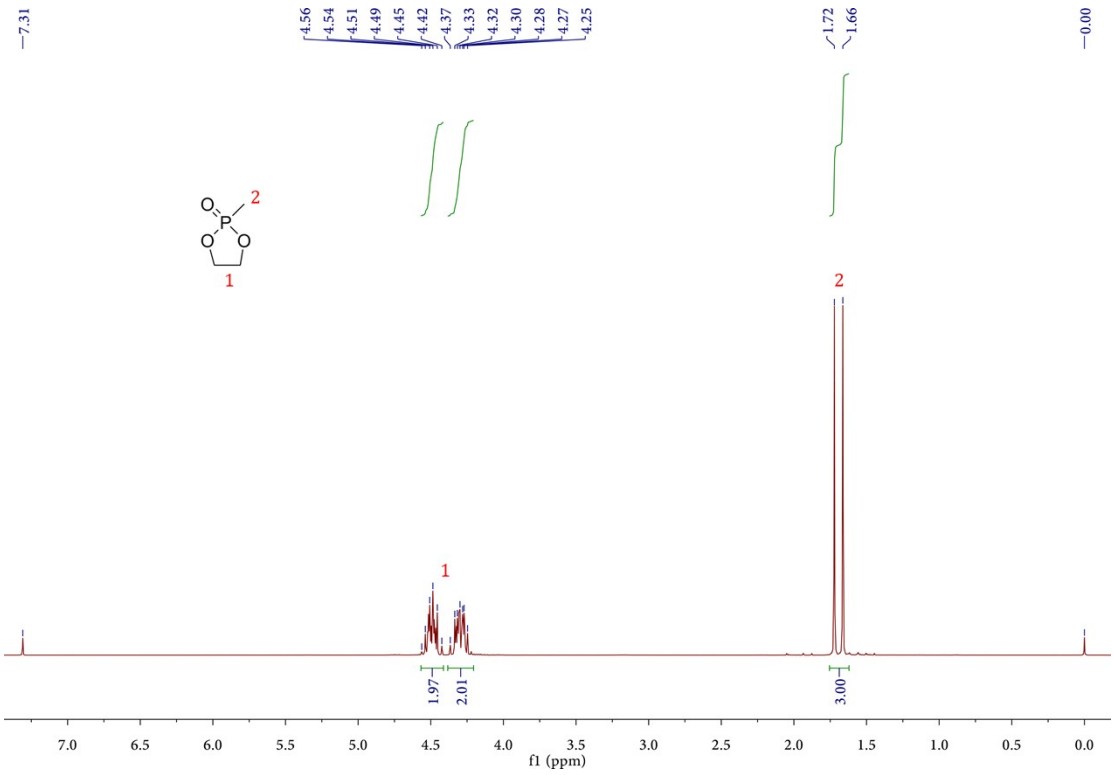


Figure S3. ^{1}H (300 MHz) NMR spectra of MePPn in $CDCl_3$.

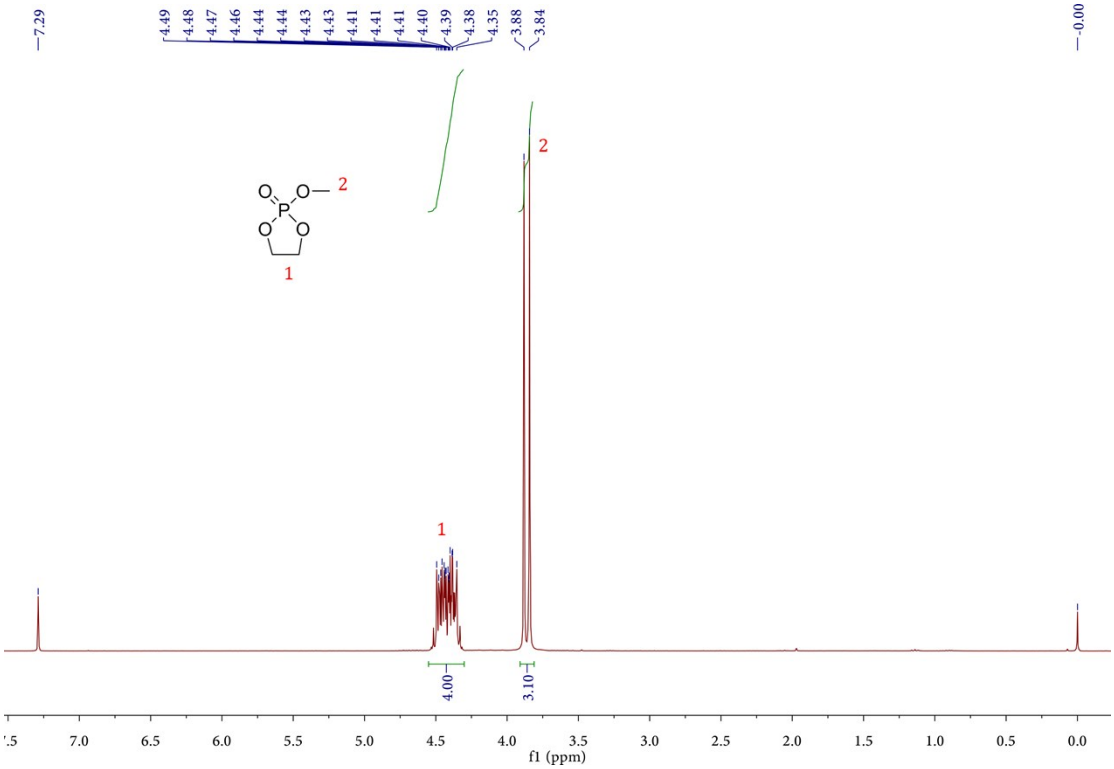


Figure S4. ^{1}H (300 MHz) NMR spectra of MePP in $CDCl_3$.

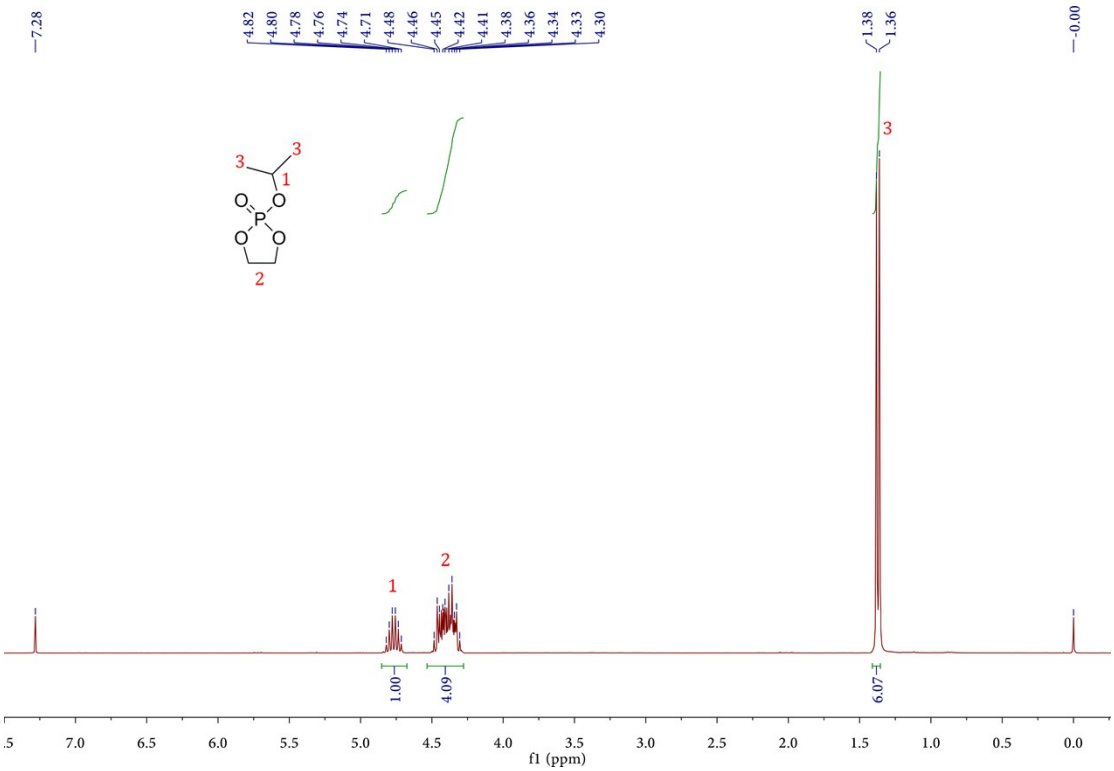


Figure S5. ^{1}H (300 MHz) NMR spectra of iPrPP in $CDCl_3$.

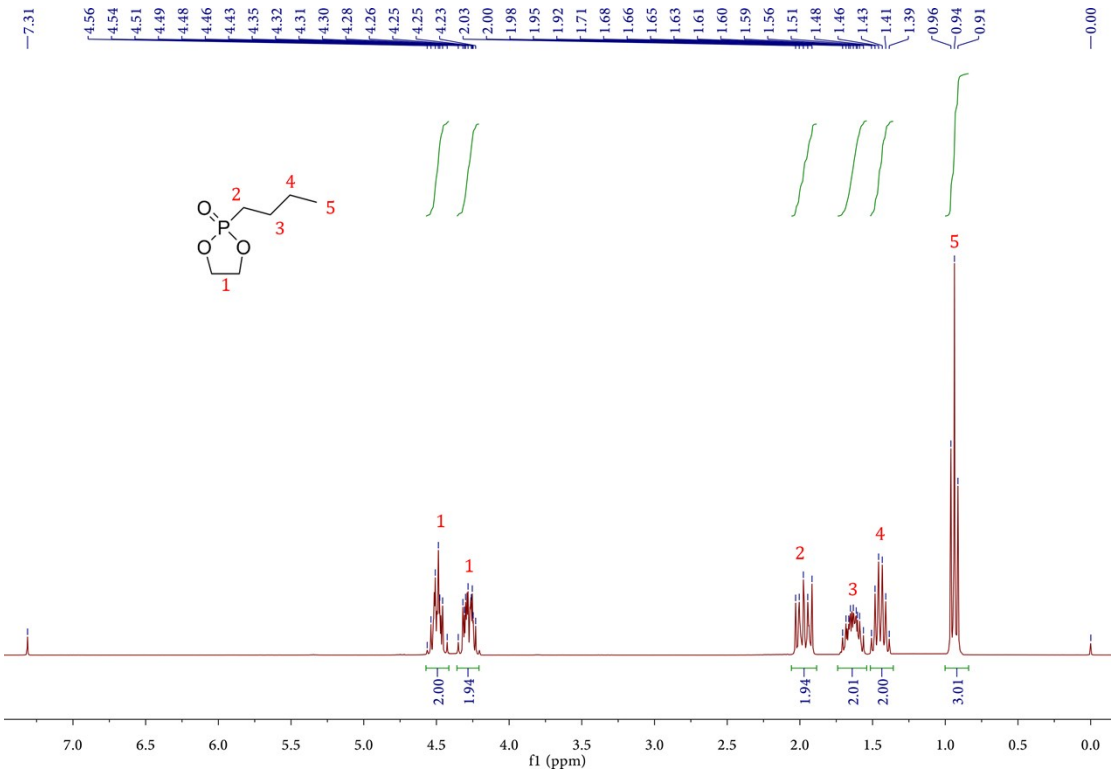


Figure S6. ^{1}H (300 MHz) NMR spectra of ^{n}BuPPn in $CDCl_3$.

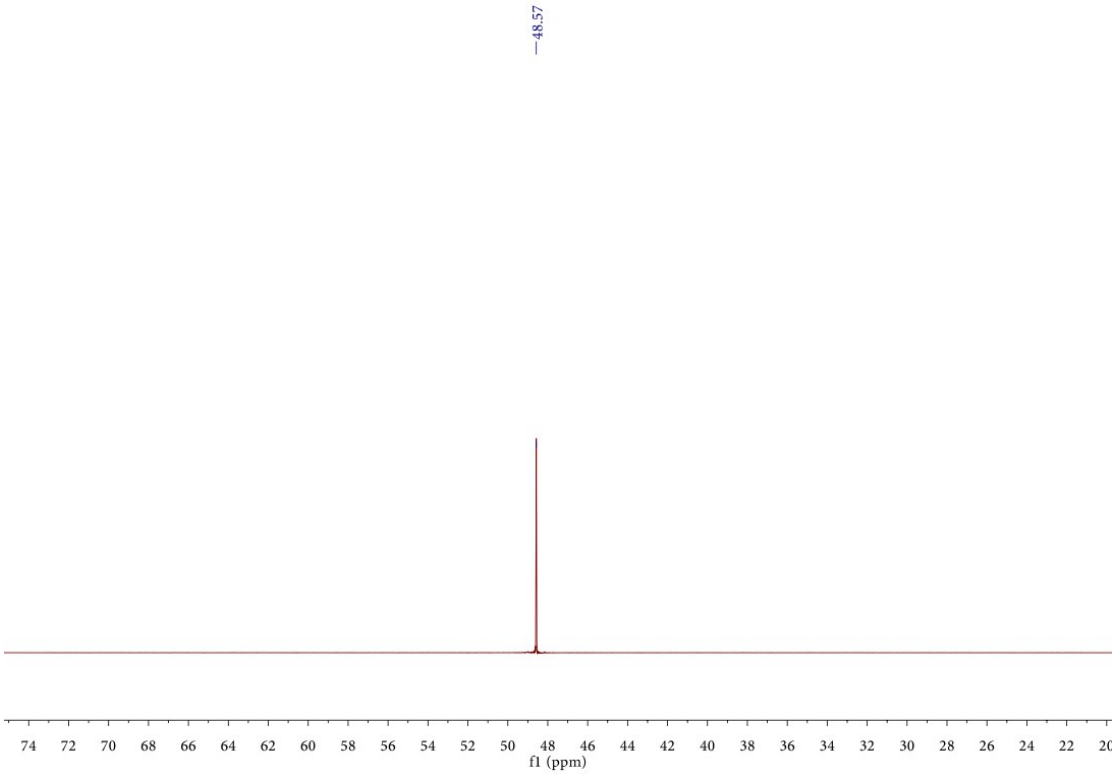


Figure S7. ^{31}P (161 MHz) NMR spectra of MePPn in $CDCl_3$.

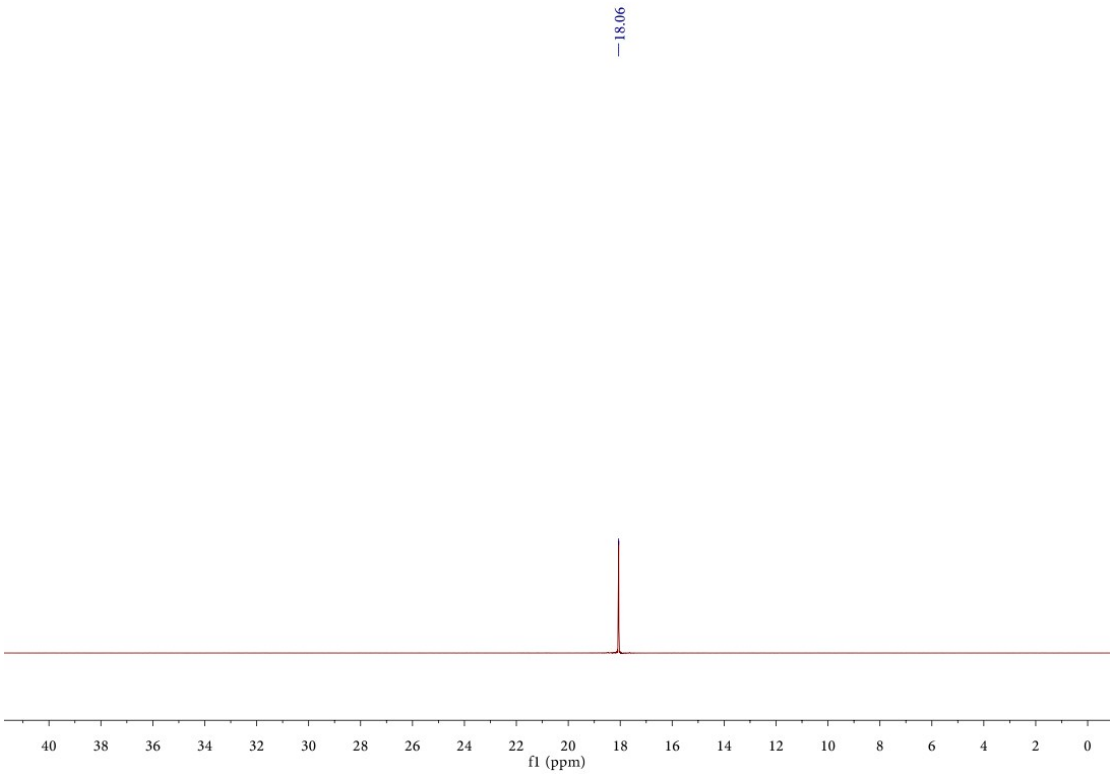


Figure S8. ^{31}P (161 MHz) NMR spectra of MePP in $CDCl_3$.

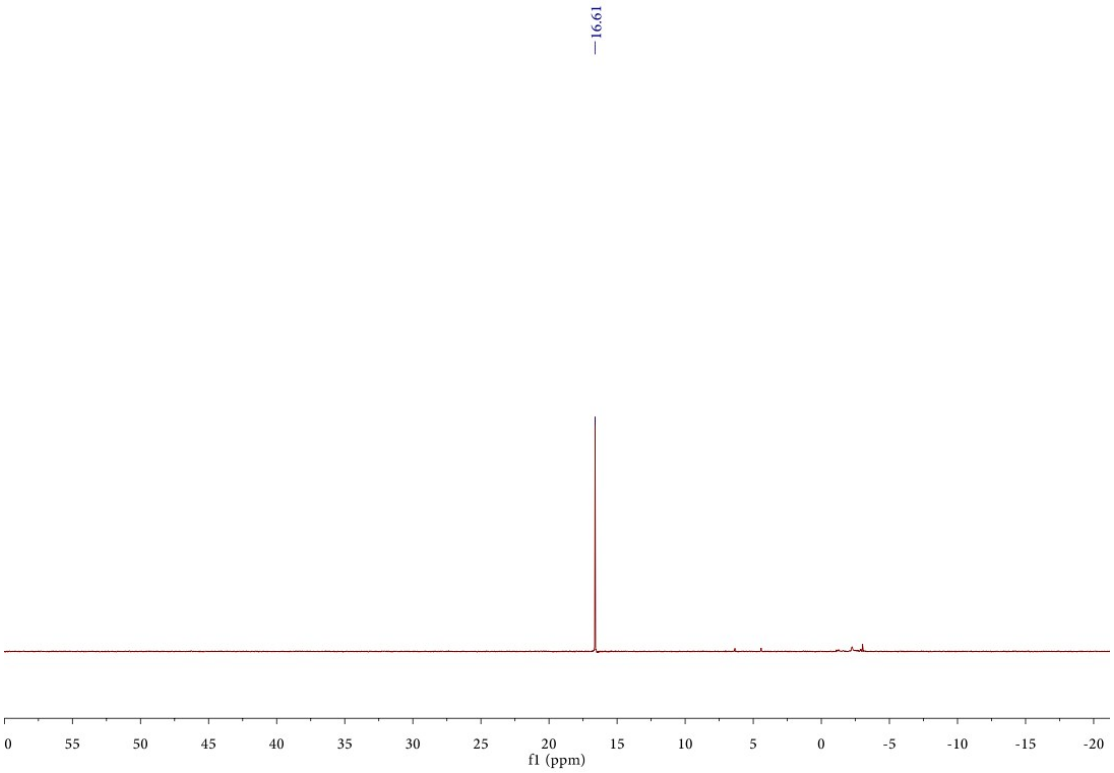


Figure S9. ^{31}P (161 MHz) NMR spectra of iPrPP in $CDCl_3$.

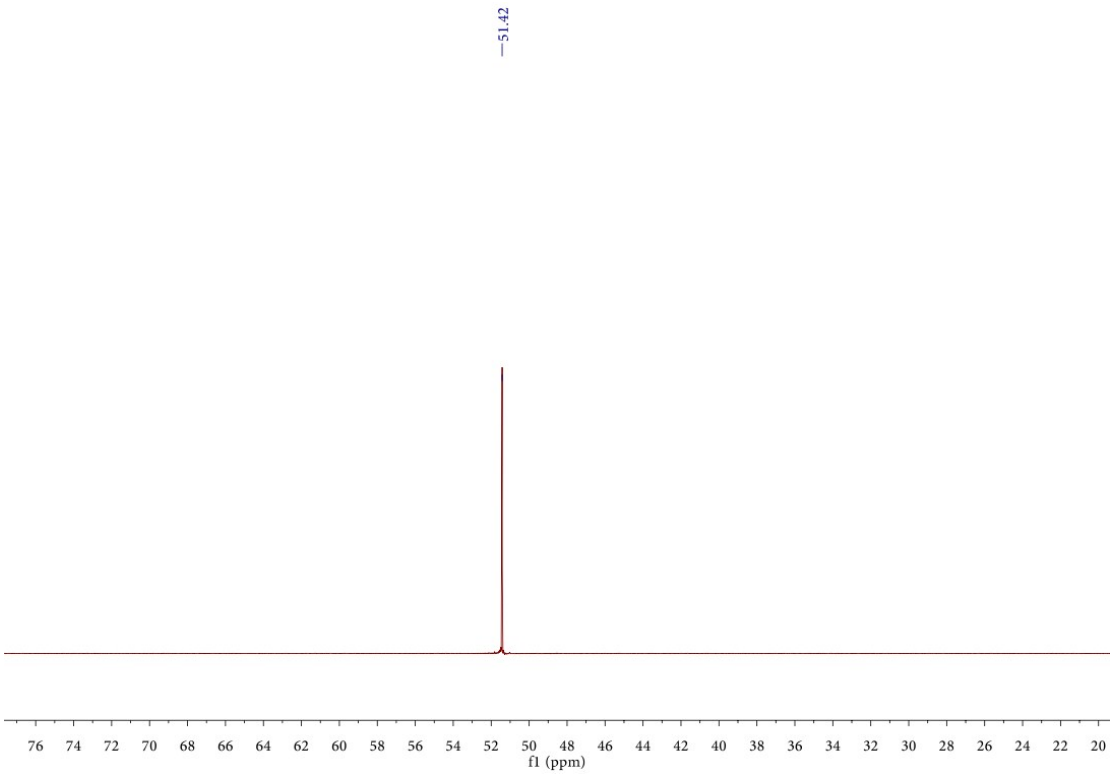


Figure S10. ^{31}P (161 MHz) NMR spectra of ^{n}BuPPn in $CDCl_3$.

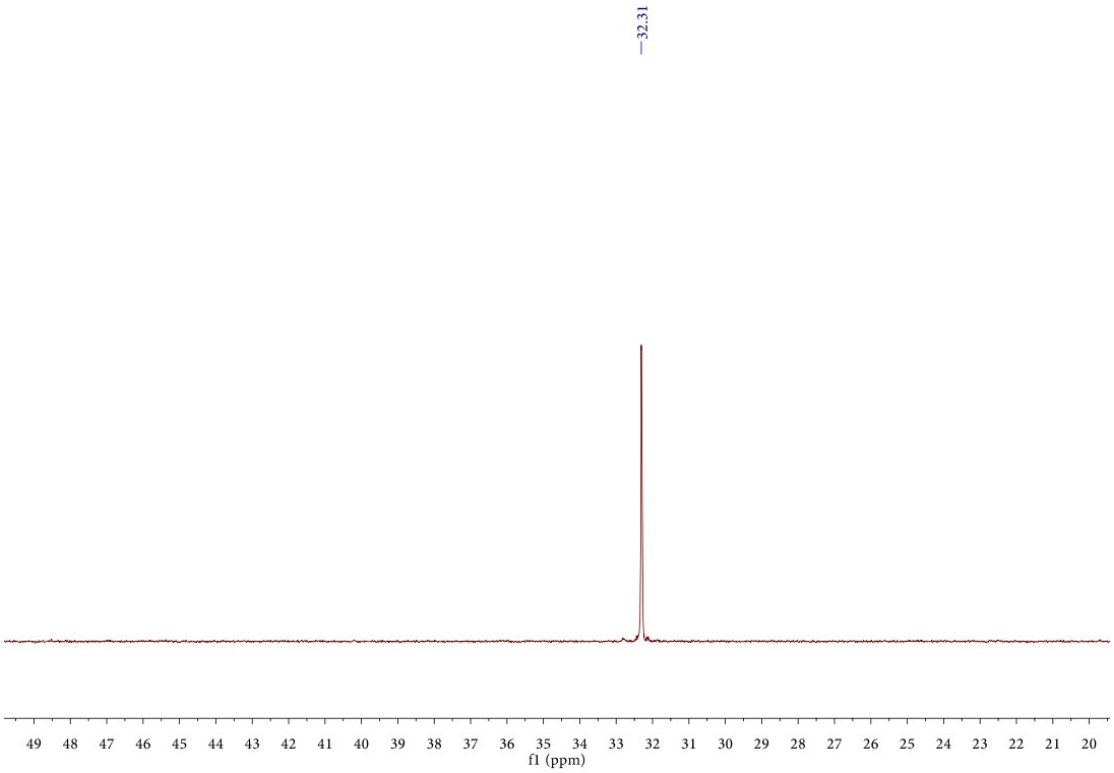


Figure S11. ^{31}P (161 MHz) NMR spectra of PMePPn in $CDCl_3$.

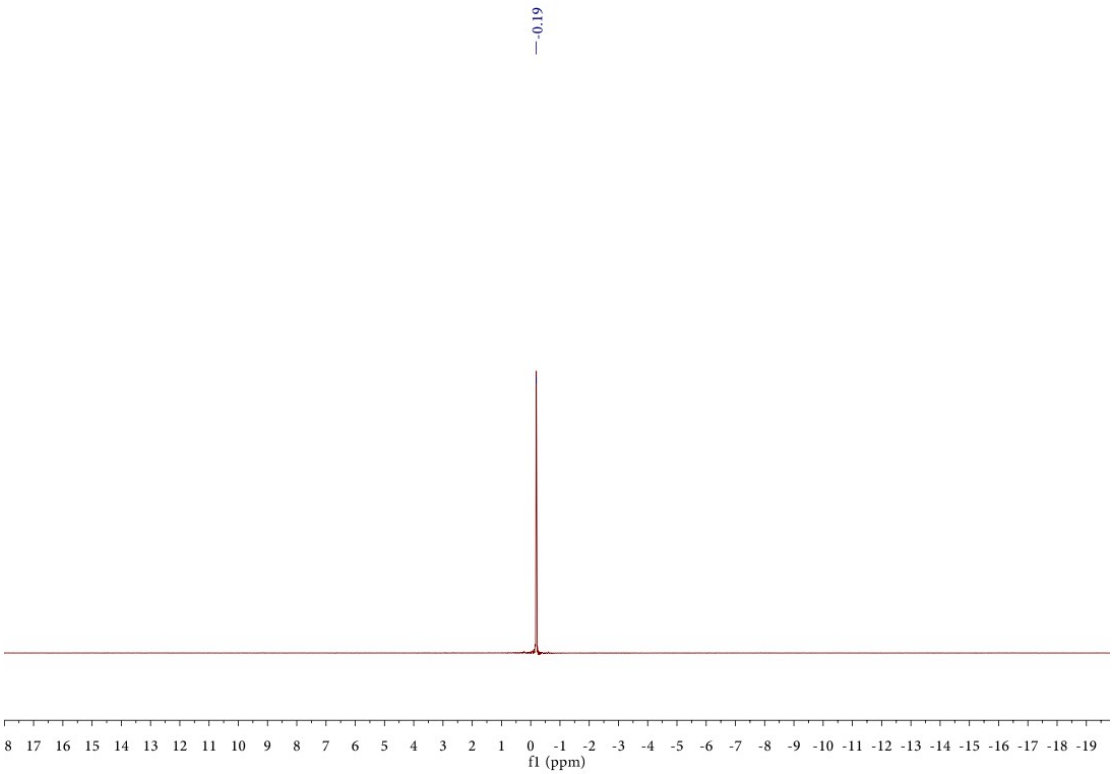


Figure S12. ^{31}H (161 MHz) NMR spectra of PMePP in $CDCl_3$.

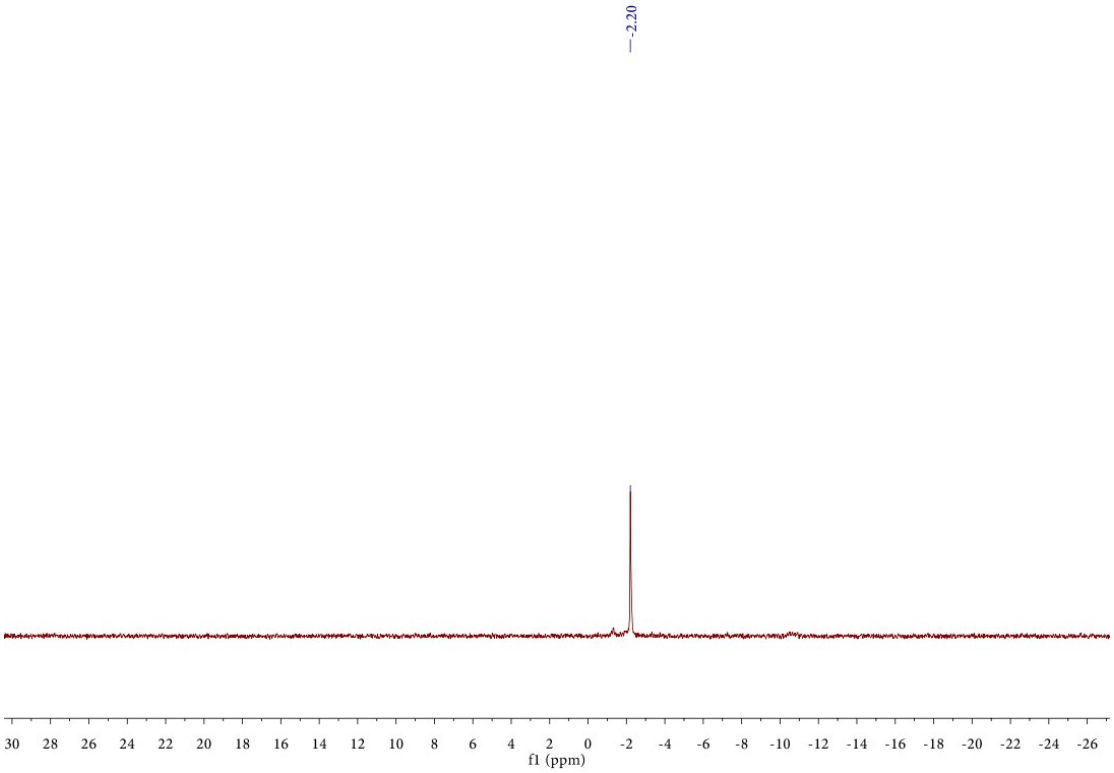


Figure S13. ^{31}P (161 MHz) NMR spectra of PiPrPP in $CDCl_3$.

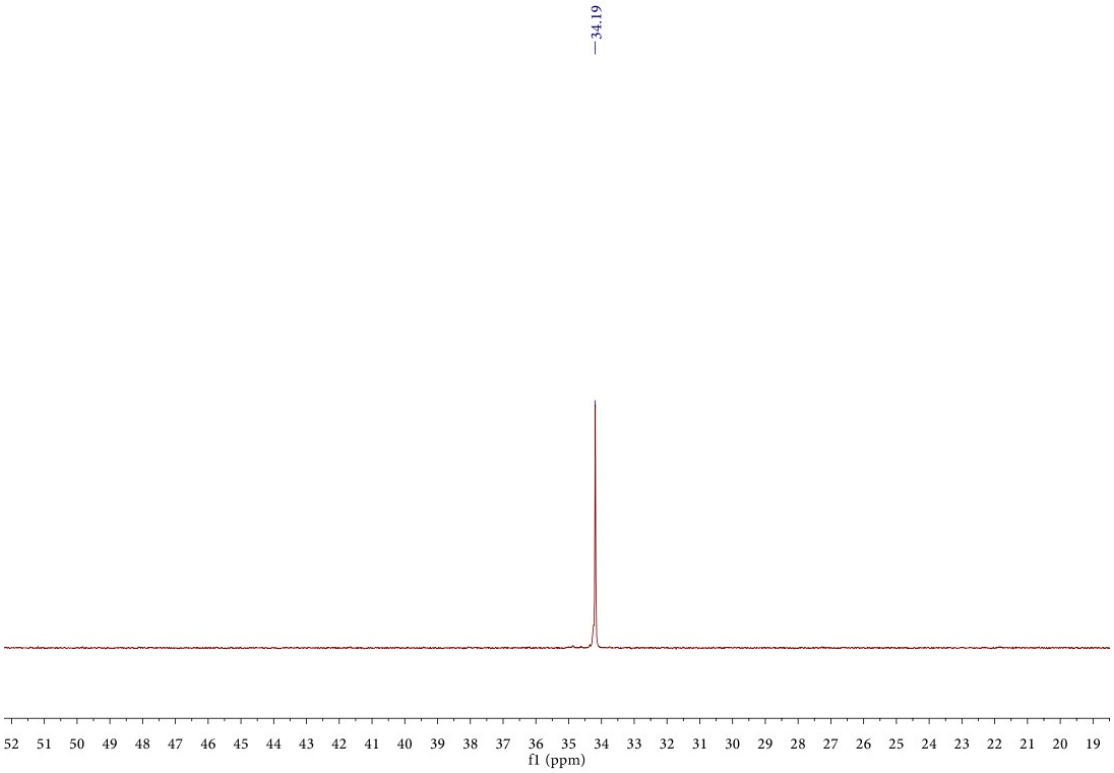


Figure S14. ^{31}H (161 MHz) NMR spectra of PBuPPn in $CDCl_3$.

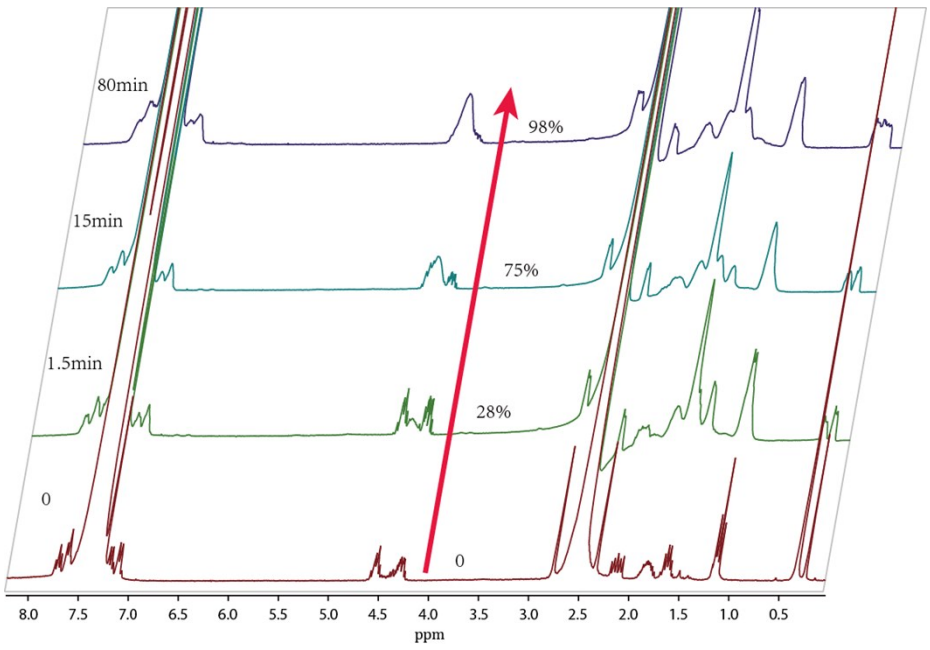


Figure S15. In-situ ^{1}H NMR investigation of the polymerisation of ^{n}BuPPn.

GPC traces for copolymerisation investigation

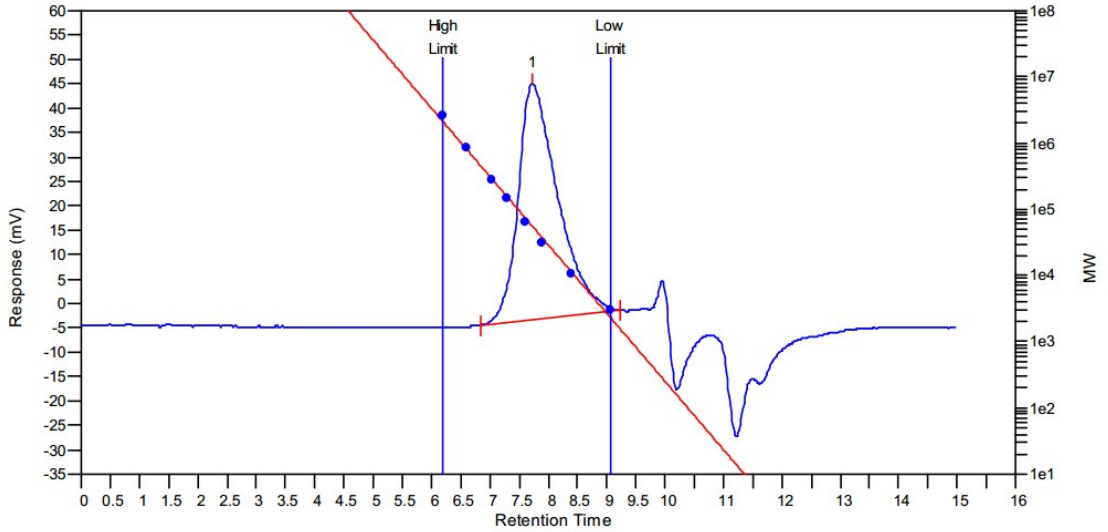


Figure S16. GPC trace for PBuPPn, $M_n = 2.5\times10^4$ g/mol.

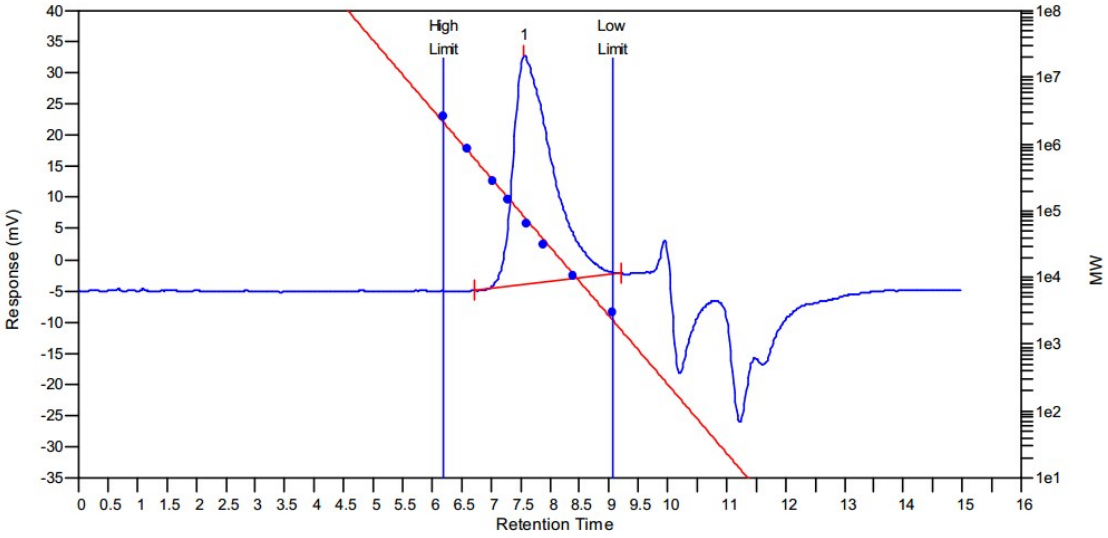


Figure S17. GPC trace for diblock copolymer P(BuPPn-*b*-MePPn), $M_n = 3.1\times10^4$g/mol.

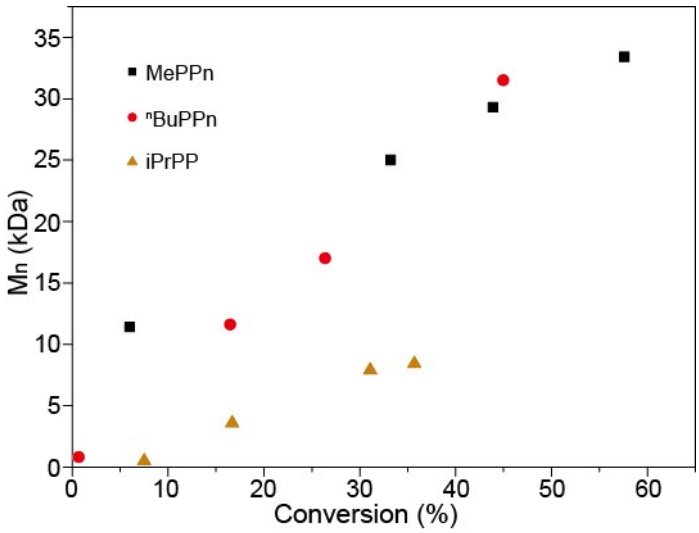


Figure S 18. Development of molar mass of PMePPn, PbuPPn and PiPrPP as a function of the monomer conversion.

References

(1) U. B. Seemann, J. E. Dengler and B. Rieger, Angew. Chem. Int. Ed., 2010, 49, 3489.

(2) G. Becker and F. R. Wurm, Tetrahedron, 2017, 73, 3536.