Supplementary Information

Generalizing Metallocene Mechanochemistry to Ruthenocene Mechanophores

Ye Sha,[1] Yudi Zhang,[2] Enhua Xu,[3] C. Wayne McAlister,[1] Tianyu Zhu,[1] Stephen L. Craig[2]* and Chuanbing Tang[1]*

[1]Department of Chemistry and Biochemistry, University of South Carolina, Columbia, South Carolina 29208, United States
[2]Department of Chemistry, Duke University, Durham, North Carolina 27708, United States
[3]Graduate School of System Informatics, Kobe University, Kobe 657-8501, Japan

1. General experimental details

1.1 Materials

Ruthenocene (98%), n-butyllithium (2.5 M in hexane, 98%), *N,N,N′,N′*-tetramethylethylenediamine (TMEDA, 98%), 2-hydroxyethyl 2-bromoisobutyrate (98%), dicyclohexylcarbodiimide (DCC, 99%), *N,N,N′,N″,N″*-pentamethyldiethylenetriamine (PMDETA, 99%), dimethylaminopyridine (DMAP, 98%), tetrabutylammonium bromide (TBAB, 99%), allyl alcohol (97%), ethyl vinyl ether (EVE, 99%), Grubbs II and III catalysts (98%) were purchased from Sigma-Aldrich and used as received. Cyclooctene-*g*DCC monomer was synthesized and freshly distilled before use according to literature.[1] Methoxy-cyclooctene was synthesized and freshly distilled before use according to our previous work.[2] Ruthenocenedicarboxylic acid was prepared according to our previous work.[3] Methyl acrylate (99%) was passed through a basic alumina column to remove inhibitors. All solvents were thoroughly dried and freshly distilled before use unless otherwise stated. All synthetic procedures were conducted under N_2 protection unless otherwise stated.

1.2 Characterization methods

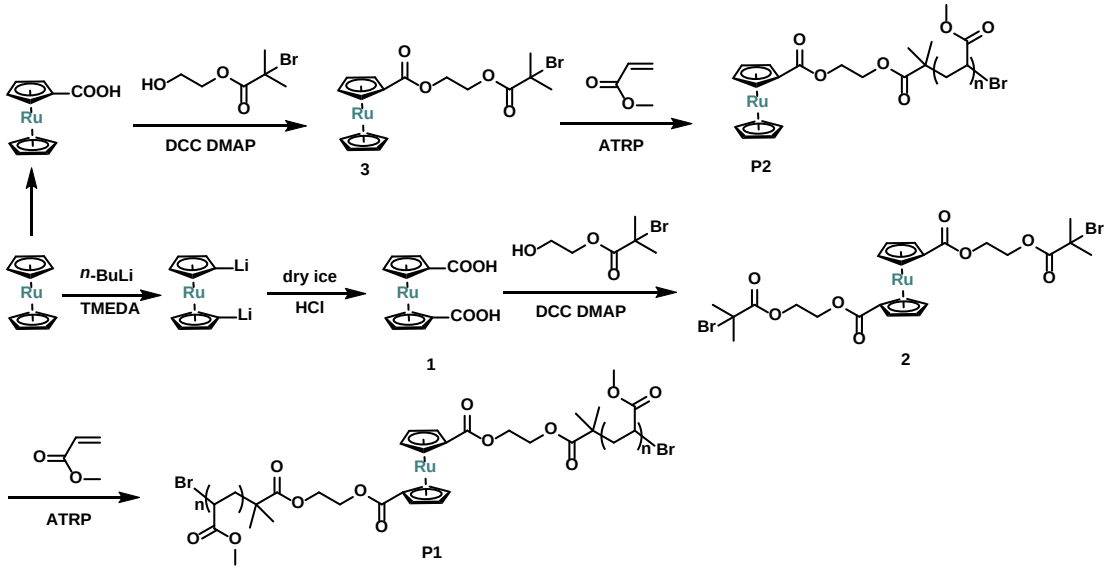
^{1}H NMR and ^{13}C NMR spectra were recorded on a Bruker Avance III HD 300 spectrometer or a 400 MHz Varian NMR or spectrometer sing $CDCl_3$ or CD_3CN as solvents. The chemical shifts are reported with respect to $CHCl_3/CDCl_3$($\delta(^1H)$ =7.26 ppm, $\delta(^{13}C)$ =77.0 ppm) or CH_3CN/CD_3CN($\delta(^1H)$ =1.94 ppm). EI mass spectra were collected on a Waters Micromass Q-Tof mass spectrometer, and the ionization source was positive ion electrospray. Gel permeation chromatography (GPC) was performed with THF as eluent at a flow rate of 1 mL/min at 35 °C on a Waters-GPC system equipped with a refractive index (RI) detector by using narrow dispersed polystyrene as the molecular weight standard. Or GPC was performed with a series of double columns (Agilent Technology PL gel, 179911GP-503 (103Å) and 179911GP-504 (104 Å)) in THF with an elution rate of 4 mL/min at room temperature, molecular weight was calibrated using an inline Wyatt Optilab DSP Interferometric Refractometer (RI) and Wyatt Dawn EOS multi-angle light scattering (MALS) detector.

1.3 Sonication test

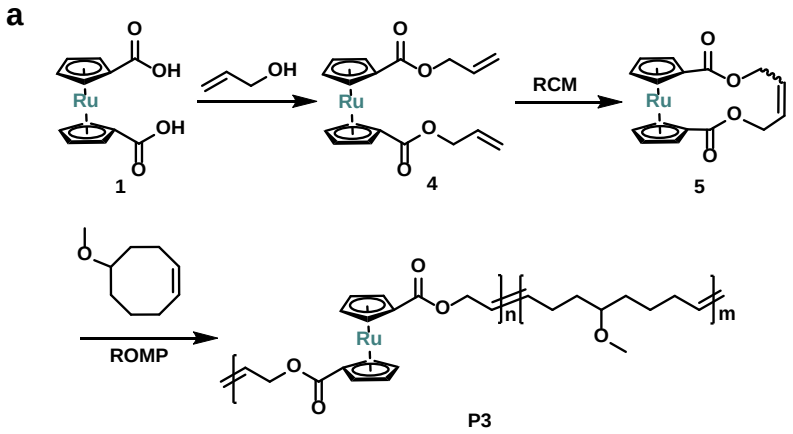
Sonication experiments were conducted on a Vibra cell Model VCX500 sonicator at 20 kHz with a 13 mm replaceable tip titanium probe purchased from *Sonics & Materials*. Sonication was carried out on 2 mg/mL polymer solutions in selective solvents in a 20 mL suslick vessel immersed in an ice-water bath. The solutions were thoroughly degassed with N_2 for 20 min before sonication and exposed in N_2 stream during the entire sonication process. Pulsed ultrasound was performed at a power of 8.7 W/cm^2 and the sonication sequence was set as 1s on 1s off. Alternatively, the sonication was performed under equally vigorous N_2 protection on a Vibra cell Model VC600 sonicator at 20 kHz with a 13 mm replaceable tip titanium probe from Sonics and Materials. The sonication parameters were set with 50% duty cycle (1s on 1s off) and output control at 6. The samples can be taken out at specific time intervals using a degassed syringe for further analysis. It should be noted that the sonication times are reported as the cumulative “on” time of the sonication experiment rather than elapsed

clock time.

2. Synthetic procedures



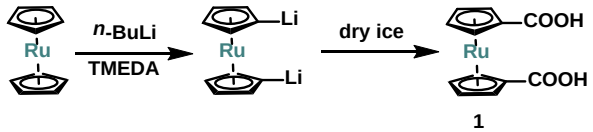
Scheme S1. Synthesis of single site-labeled main-chain ruthenocene-containing polymers by ATRP.



Scheme S2. (a) Synthesis of main-chain ruthenocene-containing polymer **P3**.

2.1 Synthesis of small molecules

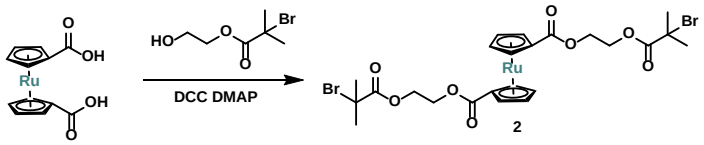
2.1.1 Synthesis of 1,1'-ruthenocenedicarboxylic acid (1)



Ruthenocene (4.62 g, 20 mmol) was dissolved in 150 mL dry hexane. Another flask was filled with n-butyl lithium (32 mL, 80 mmol, 2.5 M), TMEDA (8.3 mL, 52 mmol) and 100 mL hexane. The diluted n-butyl lithium solution was transferred into the ruthenocene solution at -78 ^{o}C via a degassed syringe and the resulting solution was stirred at room temperature for another 19 h. The mixture solution was cooled to -78 ^{o}C and small piece of dry ice was added every 15 min during 3 h. The reaction mixture

was quenched by adding water and acidified by adding concentrated HCl until pH reaches 1. The off-white precipitated product was filtered and washed using water and dried without further purification (5.1 g, 80% yield). ^{1}H NMR (300 MHz, DMSO) δ = 12.20 (s, 2H), 5.04 (t, 4H), 4.79 (t, 4H).

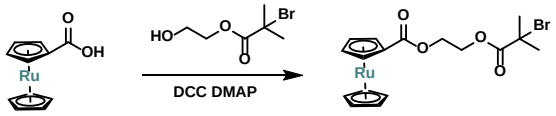
2.1.2 Synthesis of difunctional ruthenocene-based ATRP initiator (2)



2

1,1'-Ruthenocenedicarboxylic acid (0.9396 mmol, 300 mg), 2-hydroxyethyl 2-bromoisobutyrate (2.255 mmol, 327 µL, 476 mg), DMAP (0.1879 mmol, 23 mg) and DCC (1.879 mmol, 387.7 mg) were dissolved in 10 mL dry DCM. The reaction was stirred at room temperature overnight. The resultant mixture was filtered and the filtrate was purified by silica flash chromatography (hexane:ethyl acetate=3.2:1 as eluent). The product was obtained as off-white powder (470 mg, 71% yield). ^{1}H NMR (300 MHz, $CDCl_3$) δ = 5.18 (m, 4H), 4.75 (m, 4H), 4.41 (m, 8H), 1.96 (s, 12H). ^{13}C NMR (75 MHz, $CDCl_3$) δ = 171.34, 168.59, 74.52, 73.27, 63.61, 61.64, 55.41, 30.63. HRMS-EI (70 eV) m/z: calcd for $C_{24}H_{28}Br_2O_8Ru$ 705.9184, found 705.9198.

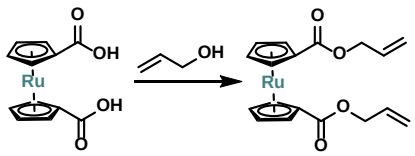
2.1.3 Synthesis of monofunctional ruthenocene-based ATRP initiator (3)



3

Ruthenocene dicarboxylic acid (1.090 mmol, 300 mg), 2-hydroxyethyl 2-bromoisobutyrate (1.199 mmol, 174 µL) and DMAP (0.1090 mmol, 13.31 mg) and DCC (1.090 mmol, 224.9 mg) were dissolved in 7 mL dry DCM. The reaction was stirred at room temperature overnight. The resultant mixture was filtered and the filtrate was purified by silica flash chromatography (hexane:ethyl acetate=5:1 as eluent). The product was obtained as an off-white grey powder (230 mg, 45% yield). ^{1}H NMR (300 MHz, $CDCl_3$) δ = 5.11 (m, 2H), 4.66 (m, 2H), 4.55 (s, 5H), 4.36 (m, 4H), 1.91 (s, 6H). ^{13}C NMR (75 MHz, $CDCl_3$) δ = 171.30, 169.96, 74.80, 72.85, 71.74, 71.54, 63.63, 61.41, 55.31, 30.61. HRMS-EI (70 eV) m/z: calcd for $C_{17}H_{19}BrO_4Ru$ 469.9505, found 469.9507.

2.1.4 Synthesis of diallyl 1,1'-ruthenocenedicarboxylate (4)

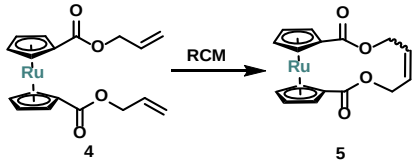


1 4

1,1'-Ruthenocenedicarboxylic acid (1.566 mmol, 500 mg), allyl alcohol (3.758 mmol, 255.6 uL, 218.3 mg) and DMAP (0.3132 mmol, 38.26 mg) were dissolved in 20 mL dry DCM. Then DCC (3.132 mmol, 646.2 mg) dissolved in 10 mL DCM was added

into the system dropwise at an ice-water bath. The reaction was stirred at room temperature overnight. The resultant mixture was filtered and the filtrate was washed with saturated $NaHCO_3$ solution, deionized water, saturated brine and dried over $MgSO_4$. The crude product was purified by silica flash chromatography (hexane:ethyl acetate=5:1 as eluent). The product was obtained as a light grey oil (450 mg, 72% yield). ^{1}H NMR (300 MHz, $CDCl_3$) δ = 5.94 (ddd, 2H), 5.27 (m, 4H), 5.16 (m, 4H), 4.72 (m, 4H), 4.63 (d, 4H). ^{13}C NMR (75 MHz, $CDCl_3$) δ = 168.71, 132.44, 117.78, 74.37, 73.23, 71.74, 64.83. EI-MS: (m/z): 400 (M^+, 100%)

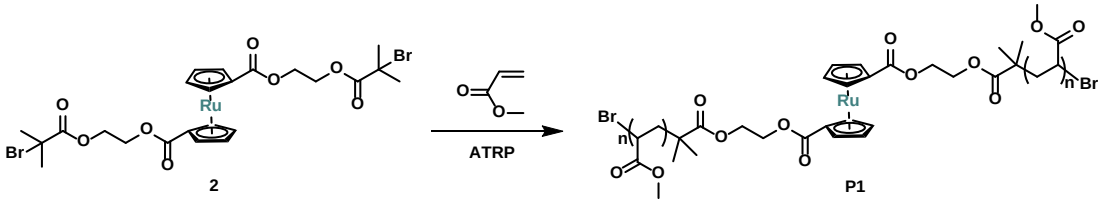
2.1.5 Synthesis of 1,1'-(2-butenyl)ruthenocenedicarboxylate (5)



Diallyl 1,1'-Ruthenocenedicarboxylate (**4**, 112.6 mg, 0.2819 mmol) was dissolved in 200 mL anhydrous degassed DCM, Grubbs II catalyst (11.97 mg, 0.01410 mmol) was added and the resulting solution was heated to reflux for 55 min. Several drops of EVE were added to quench the reaction. The solvent was removed and product was purified by flash silica column chromatography three times (hexane: ethyl acetate=3:1 as the eluent). The product was obtained as an off-white solid (70 mg, 67% yield), which can be further purified by recrystallization from methanol. ^{1}H NMR (300 MHz, $CDCl_3$) δ = 6.5-6.1 (m, 2H), 5.3-4.5 (m, 12H). ^{13}C NMR (75 MHz, $CDCl_3$) δ = 168.76, 135.01 (trans), 131.45 (cis), 74.18, 73.66, 61.59, 58.96. HRMS-EI (70 eV) m/z: calcd for $C_{16}H_{14}BrO_4Ru$ 371.9936, found 371.9943.

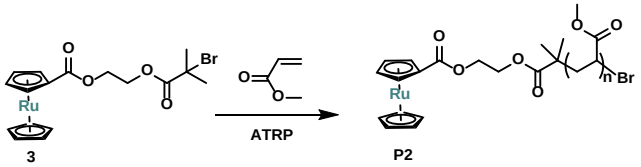
2.2 Synthesis of polymer

2.2.1 Synthesis of P1



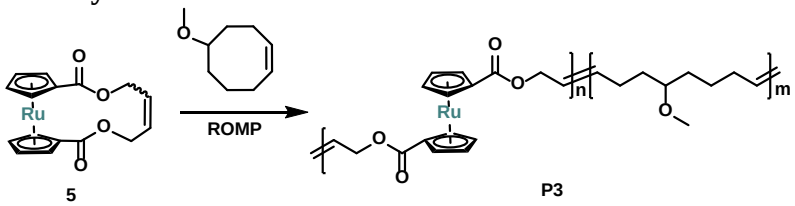
PMDETA (0.2 mmol, 0.0347 g, 41.8 μL), methyl acrylate (100 mmol, 10 g) and difunctional ruthenocene-containing ATRP initiator **2** (0.1 mmol, 0.0706 g) were placed in a 50 mL Schlenk flask and thoroughly degassed. Then CuBr (0.2 mmol, 28.7 mg) was quickly added to the reaction system and purged nitrogen. Then reaction flask was then immersed in a preheated 70 ^{o}C oil bath and reacted for totally solidification within 8 h. The crude product was opened to air and diluted with dichloromethane (20 mL) and precipitated into cold methanol five times to remove impurities. The product was obtained after evaporation under reduced pressure as a colorless oil (8 g, 80% yield).

2.2.2 Synthesis of P2



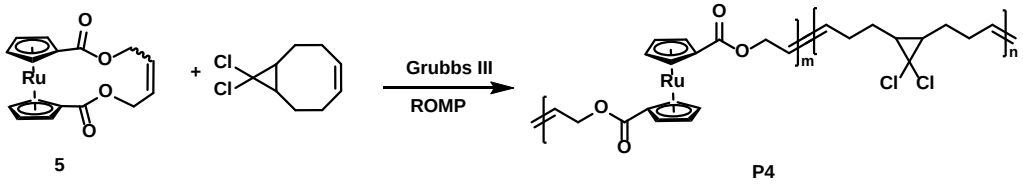
PMDETA (0.2 mmol, 0.0347 g, 41.8 μL), methyl acrylate (200 mmol, 20 g) and monofunctional ruthenocene-containing ATRP initiator **3** (0.2 mmol, 0.0938 g) were placed in a 50 mL Schlenk flask and thoroughly degassed. Then CuBr (0.2 mmol, 28.7 mg) was quickly added to the reaction system and purged nitrogen. Then reaction flask was then immersed in a preheated 70 ^{o}C oil bath and reacted for 20 h with a conversion of 60% determined from ^{1}H NMR. The crude product was opened to air and diluted with dichloromethane and precipitated into cold methanol five times to remove impurities. The product was obtained after evaporation under reduced pressure as a colorless oil (17 g, 85% yield).

2.2.3 Synthesis of P3



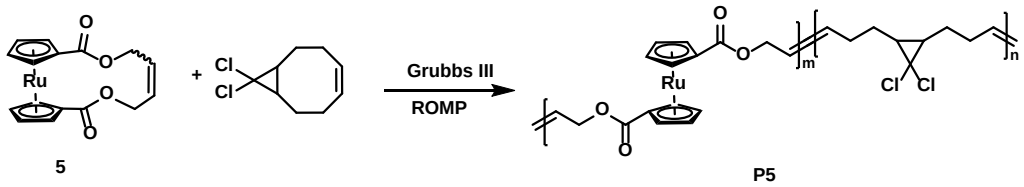
1,1'-(2-Butenyl)ruthenocenedicarboxylate (**5**, 13.94 mg, 0.038 mmol) and 5-methoxy-1-cyclooctene (100 mg, 0.71 mmol) were dissolved in 0.9 mL anhydrous chloroform. The solution was fully degassed. A solution of Grubbs II catalyst (0.637 mg, 0.75 μmol) in 0.15 mL chloroform was added to initiate the polymerization at 25 ^{o}C. After the reaction was conducted for 4 h, several drops of EVE were added to quench the catalyst. The polymer was precipitated into cold methanol three times and subsequently dried under vacuum. An off-white color solid was obtained (100 mg, 88% yield).

2.2.4 Synthesis of P4



1,1'-(2-Butenyl)ruthenocenedicarboxylate (**5**, 25.1 mg, 0.068 mmol) and *g*DCC-cyclooctene (56 mg, 0.29 mmol) were dissolved in 0.35 mL anhydrous DCM. The solution was fully degassed by purging N_2. A solution of Grubbs III catalyst (0.32 mg, 0.38 μmol) in 0.01 mL DCM was added to initiate the polymerization at room temperature and reacted for 3 h, several drops of EVE were added to quench the catalyst. The polymer was precipitated into methanol three times and subsequently dried to constant weight. An off-white color solid was obtained (48 mg, yield 60%).

2.2.5 Synthesis of P5



1,1'-(2-Butenyl)ruthenocenedicarboxylate (**5**, 8 mg, 0.022 mmol) and *g*DCC-cyclooctene (78.3 mg, 0.41 mmol) were dissolved in 0.2 mL anhydrous DCM. The solution was fully degassed by purging N_2. A solution of Grubbs III catalyst (0.38 mg, 0.45 μmol) in 0.01 mL DCM was added to initiate the polymerization at room temperature and reacted for 3 h, several drops of EVE were added to quench the catalyst. The polymer was precipitated into methanol three times and subsequently dried to constant weight. An off-white color solid was obtained (60 mg, yield 70%).

3. Sonication of P1 and P2

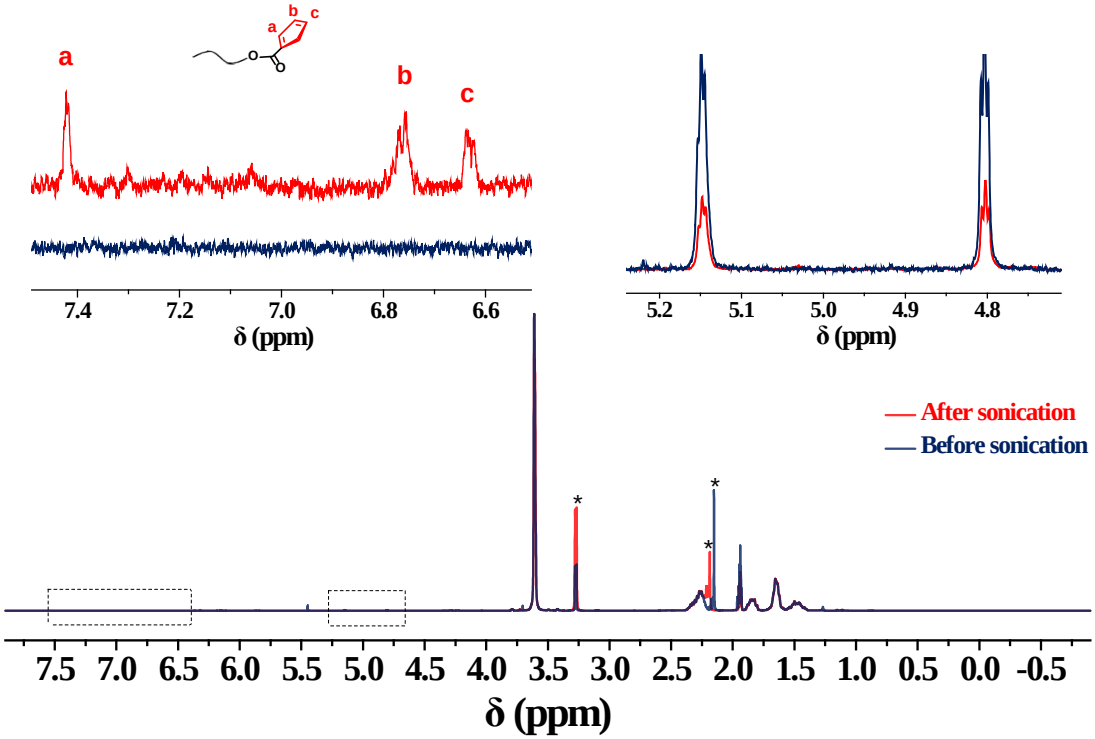


Figure S1. Normalized ^{1}H NMR spectra of **P1** before sonication and after sonication for 1 h (CD_3CN).

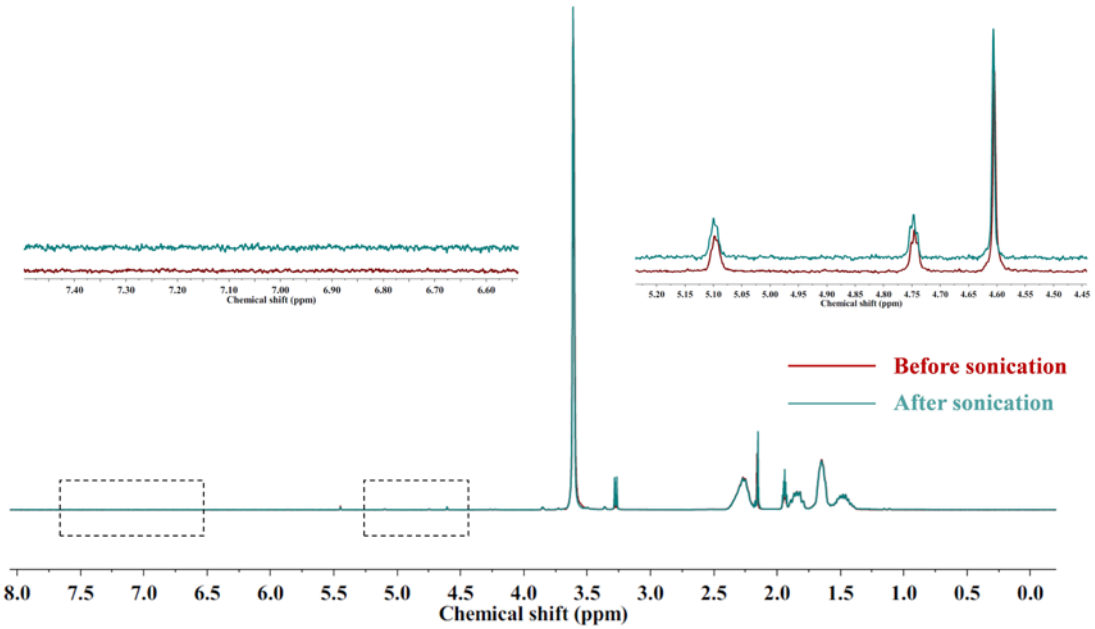


Figure S2. ^{1}H NMR (CD_3CN) spectra of **P2** before and after sonication in acetonitrile for 1 h.

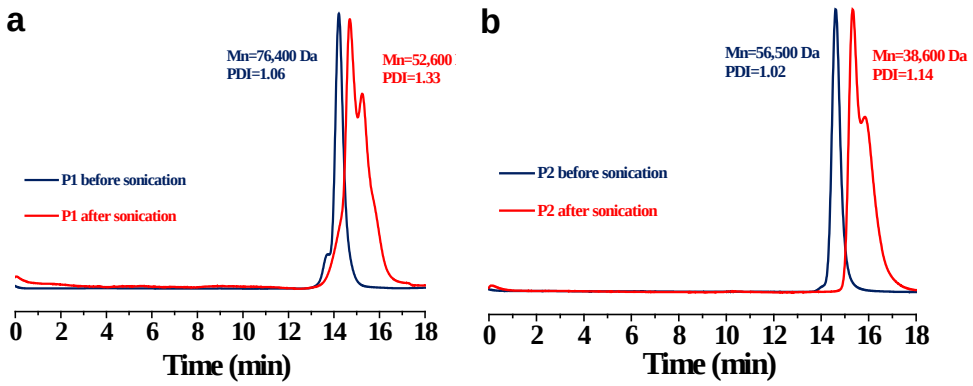


Figure S3. GPC elution traces (RI detector) of (a) **P1**, (b) **P2** before and after sonication in acetonitrile for 1 h.

4. Sonication of P3 in THF

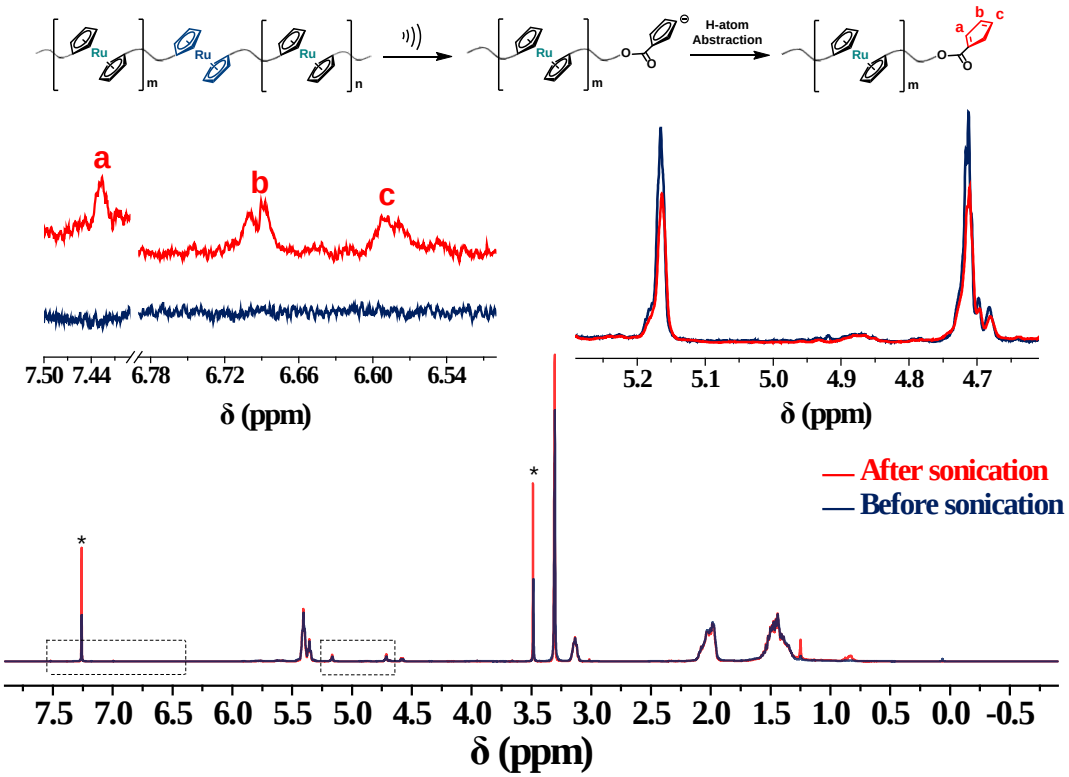
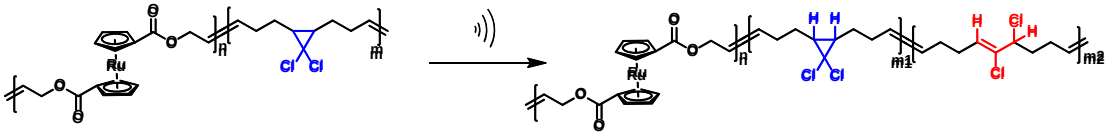


Figure S4. ^{1}H NMR ($CDCl_3$) spectra of **P3** before and after sonication for 1 h.

5. Relative mechanical strength analysis of ruthenocene

During ultrasonication, two competitive mechanochemical processes between ruthenocene scission and ring opening of *g*DCC and were combined in the same polymer chain as shown in Scheme S1.



Scheme S3. Ultrasonication-induced ring-opening of *g*DCC.

Ring-opening ratio (Φ_i) was determined from ^{1}H NMR spectra after sonication at elapsed time by integrating new generated characteristic proton peaks to see how many cyclopropane units were opened. Chain scission cycles were determined based on the following equation:

$$\text{Scission Cycle} = \frac{\ln(M_{n,0}) - \ln(M_{n,t})}{\ln 2}$$

where $M_{n,t}$ represents the molecular weight of **P4** sonicated for t min, $M_{n,0}$ represents the initial molecular weight of **P4** before sonication.

6. TBAB facilitated chain scission

40 mg **P5** and 3.37 mg TBAB (same equivalent weight of ruthenocene that **P5** has) were dissolved and sonicated in 20 mL THF. Aliquot was taken out at different time intervals. Then solvent was evaporated and the resulting polymer was washed to

remove TBAB and dried under vacuum for further ^{1}H NMR and GPC measurement to determine the ring-opening ratio (Φ_i).

7. Computational details

7.1 Computational methods

The stretched structure evolution of ruthenocene was explored with Q-chem 4.3 package. 1,1'-Ruthenocenedicarboxylic allyl diester was selected as the model structure as shown in Figure S5 to describe the stretching of the polymer chain. Previous work demonstrated that PBE function can well describe the structure of ruthenocene,[4-6] herein, unrestricted PBE function was employed to describe the system. An effective core potential was used to describe the scalar relativistic effects of Ru atom with 28 core electrons. We use def2-tzvp Stuttgart ECP for Ru atoms in all ruthenocene derivatives, along with the def2-tzvp basis set for Ru and def2-svp basis set for C, O and H atoms. In a typical COGEF calculation, the end-to-end distance of the model compound was fixed to mimic the external force, meanwhile all other fully relaxed geometry optimization was carried out. Varying the end-to-end distance of the model compound simulates an isometric stretching scenario and generates the COGEF potential. The relationship of force and stretching distance can be obtained from the first derivate of potential to distance.

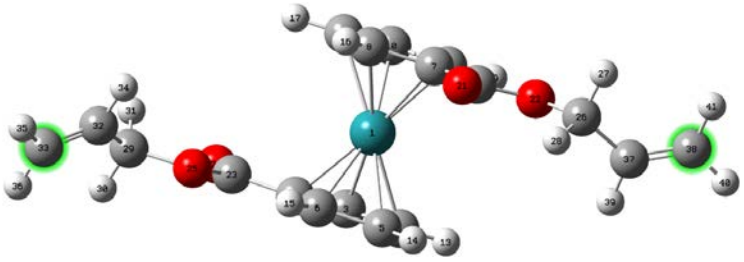


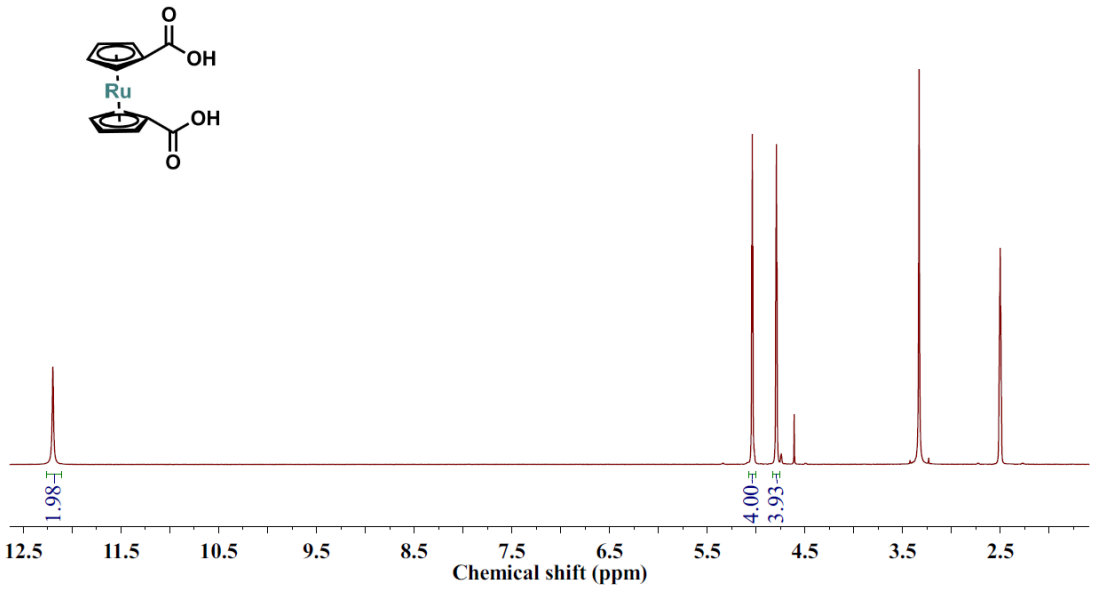
Figure S5. Model ruthenocene-based compound for stretching simulation. The distance between highlighted C33 and C38 was fixed to a constant value during optimization to mimic the specific force.

7.2 Electrostatic potential mapping

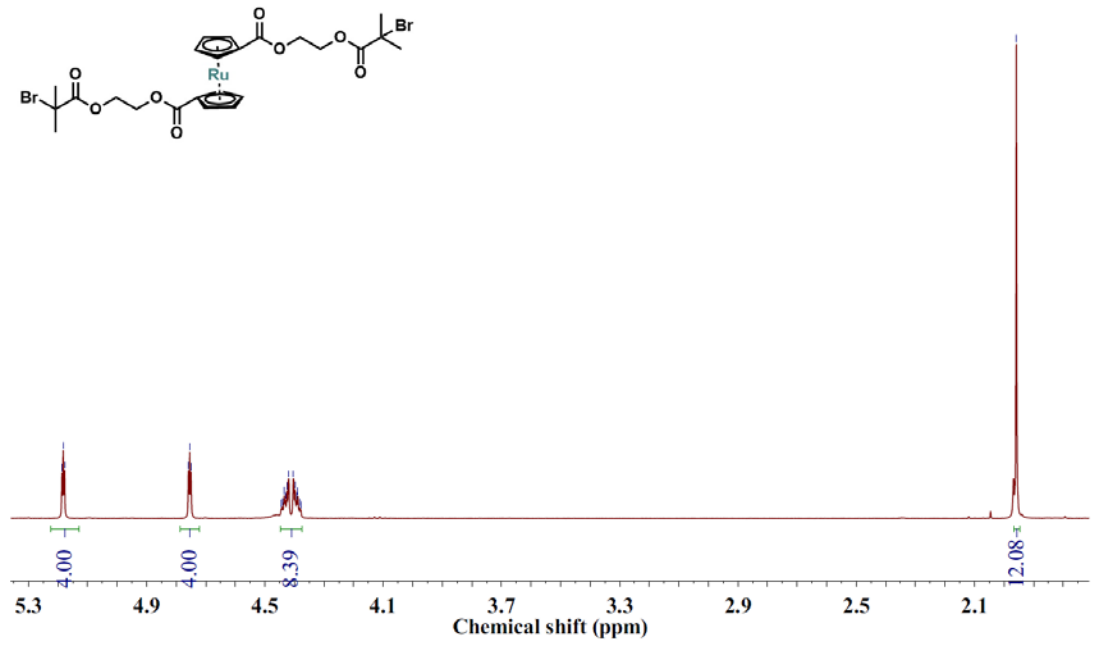
The electrostatic potential of each structure is plotted using GaussView. The exported wave function files of optimized structures were used as input to map the electrostatic potential plot. The contour surface is defined based on the Van der Waals surface proposed by Bader with electron density of 0.001.[7]

8. Spectra

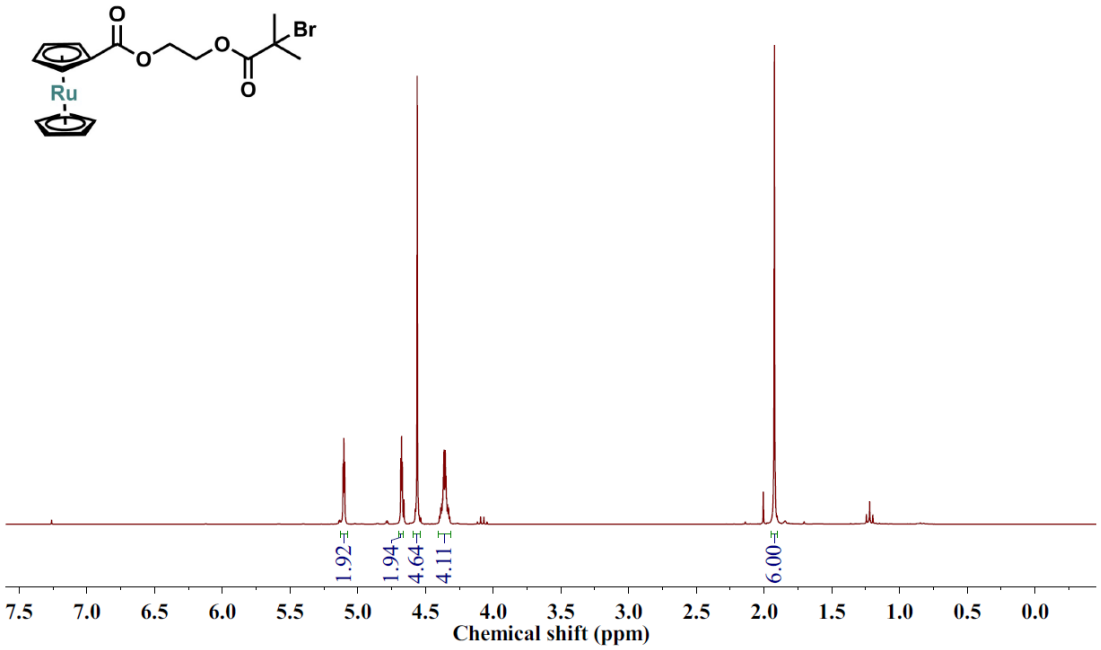
8.1 ^{1}H NMR Spectra



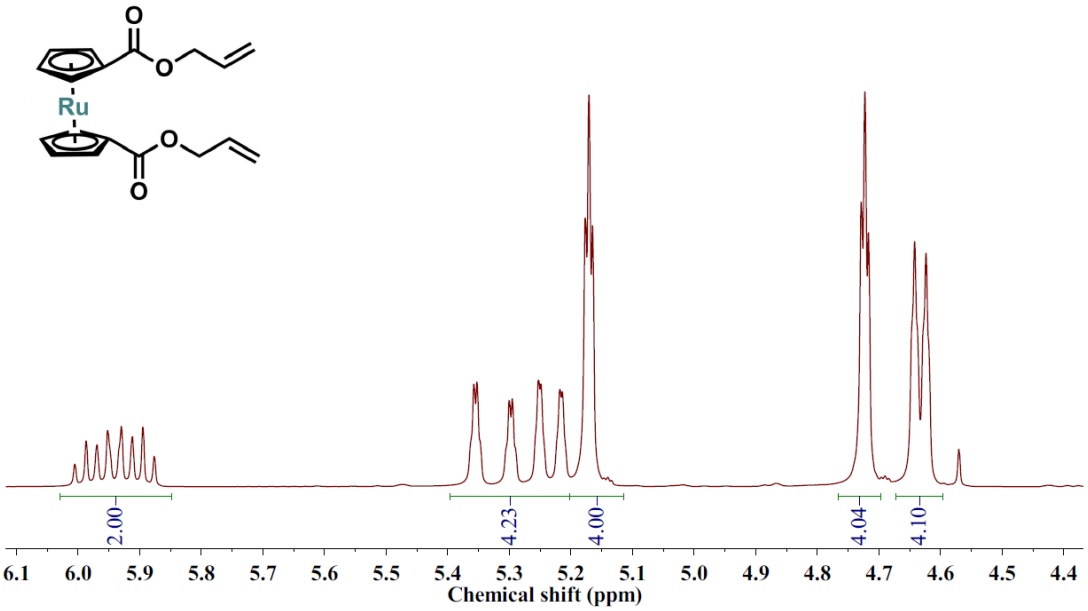
DMSO-d_6 as solvent



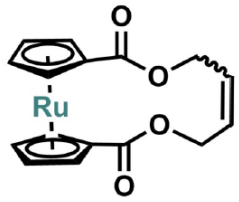
$CDCl_3$ as solvent

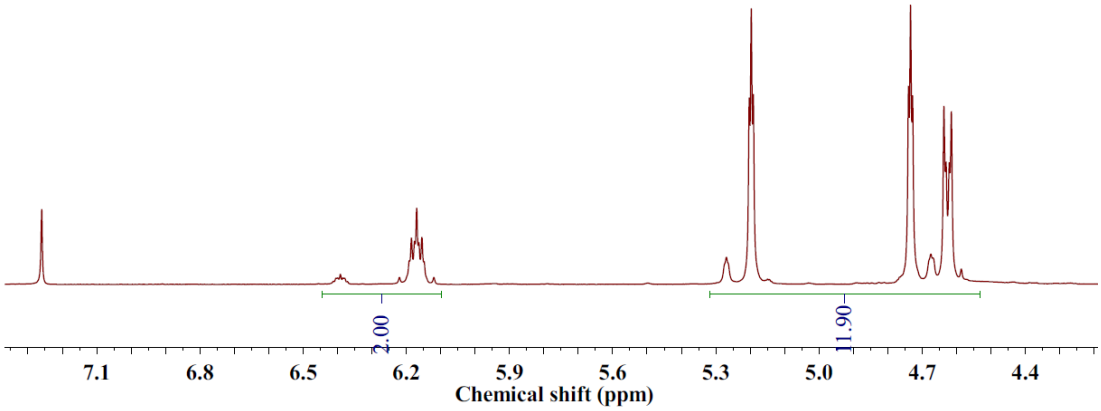


$CDCl_3$ as solvent



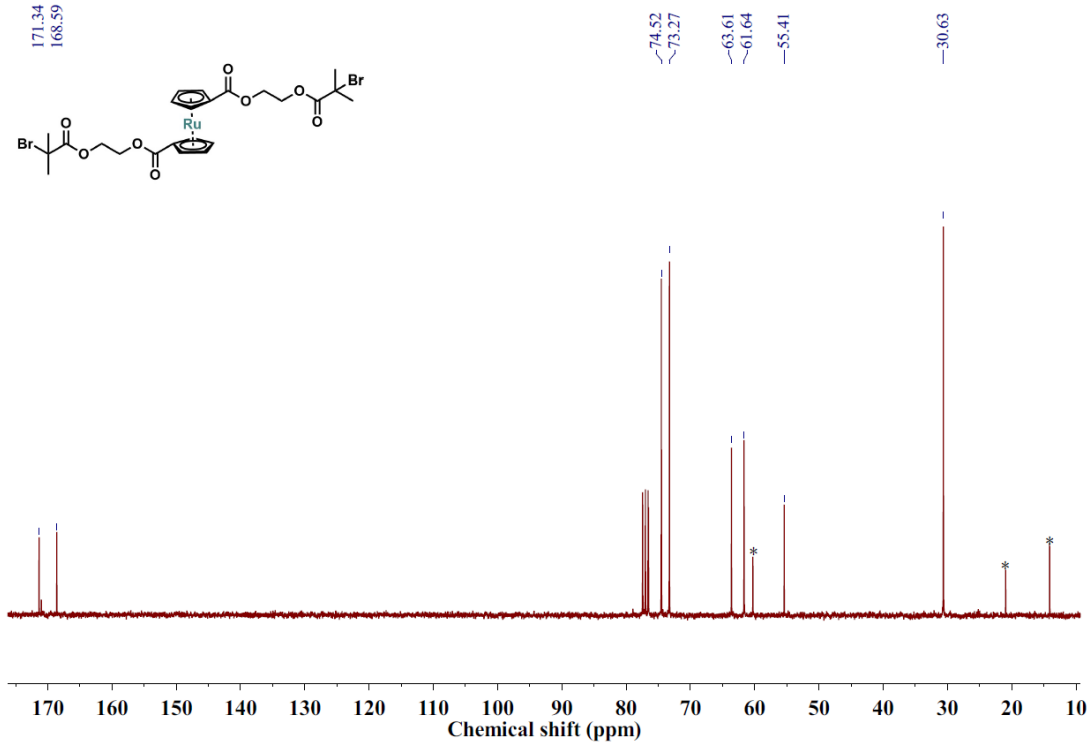
$CDCl_3$ as solvent



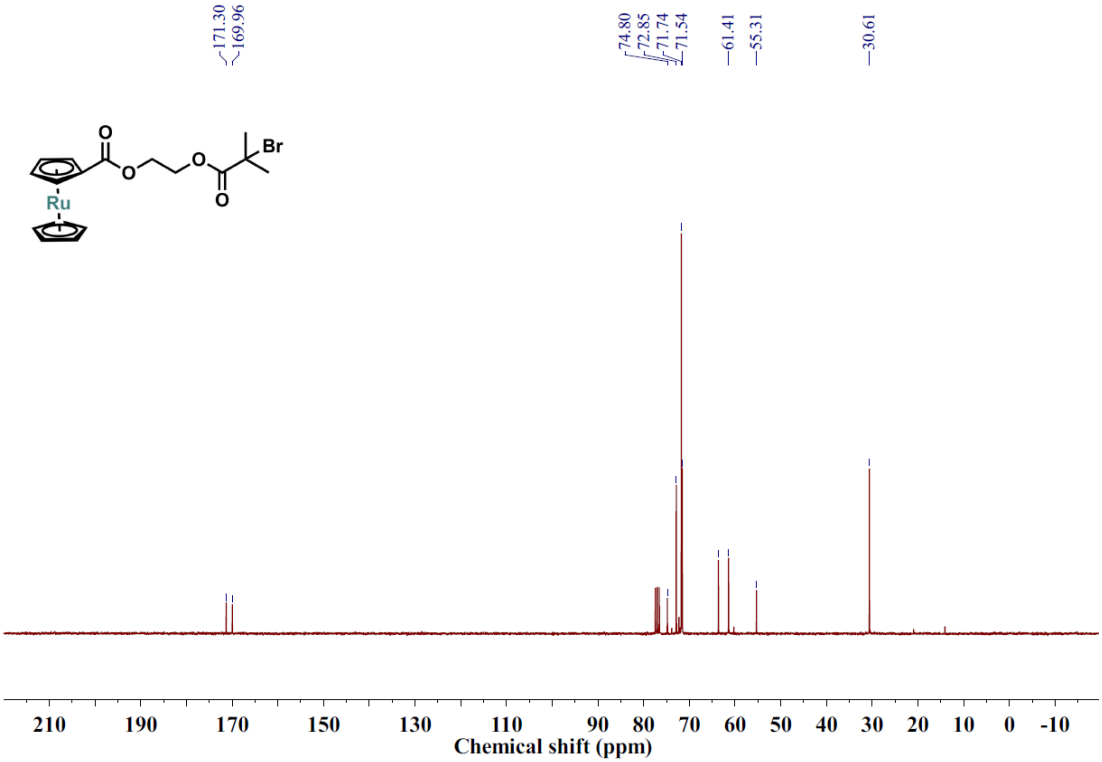


$CDCl_3$ as solvent

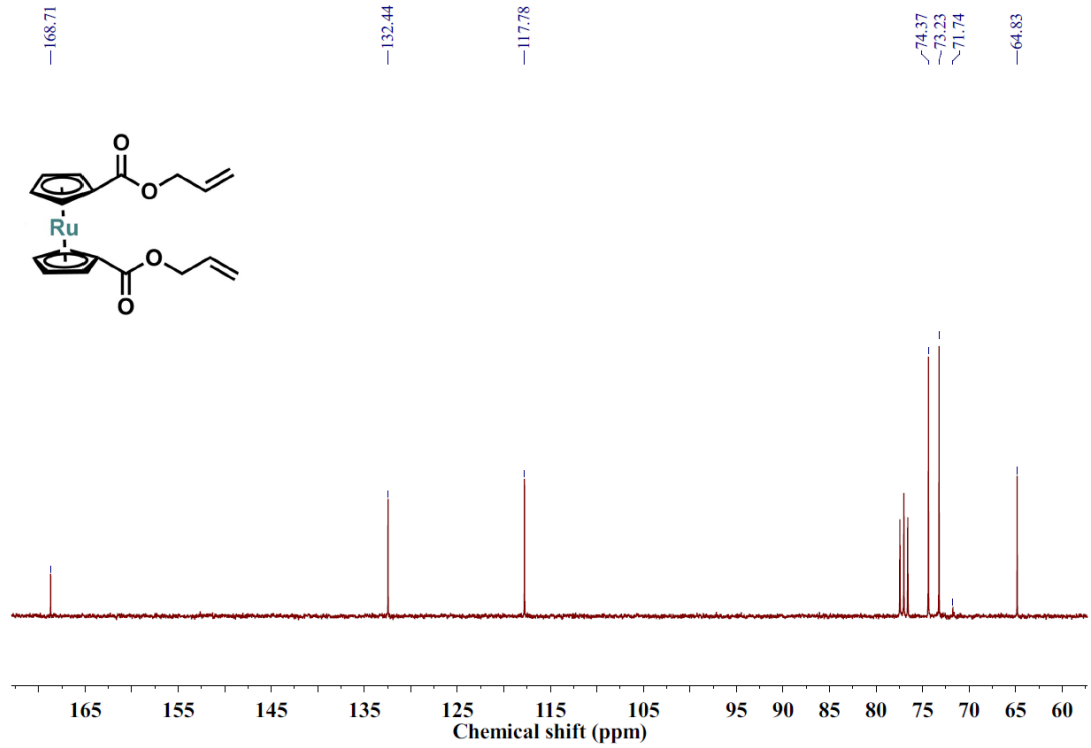
8.2 ^{13}C NMR Spectra



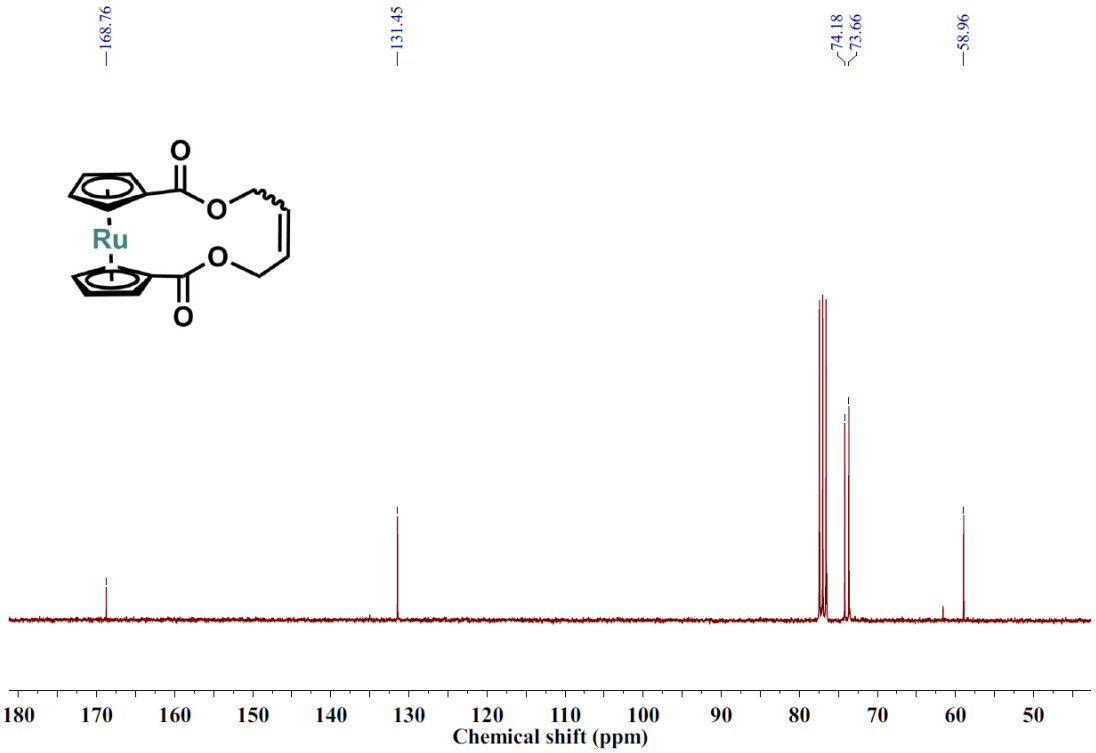
$CDCl_3$ as solvent



$CDCl_3$ as solvent

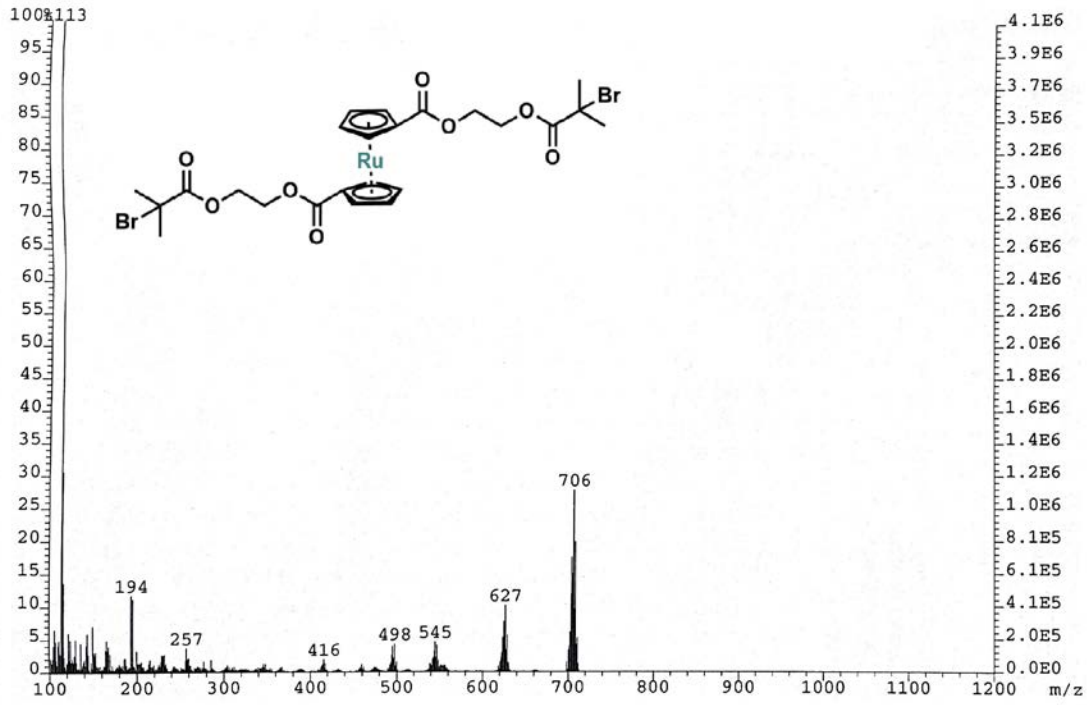


$CDCl_3$ as solvent

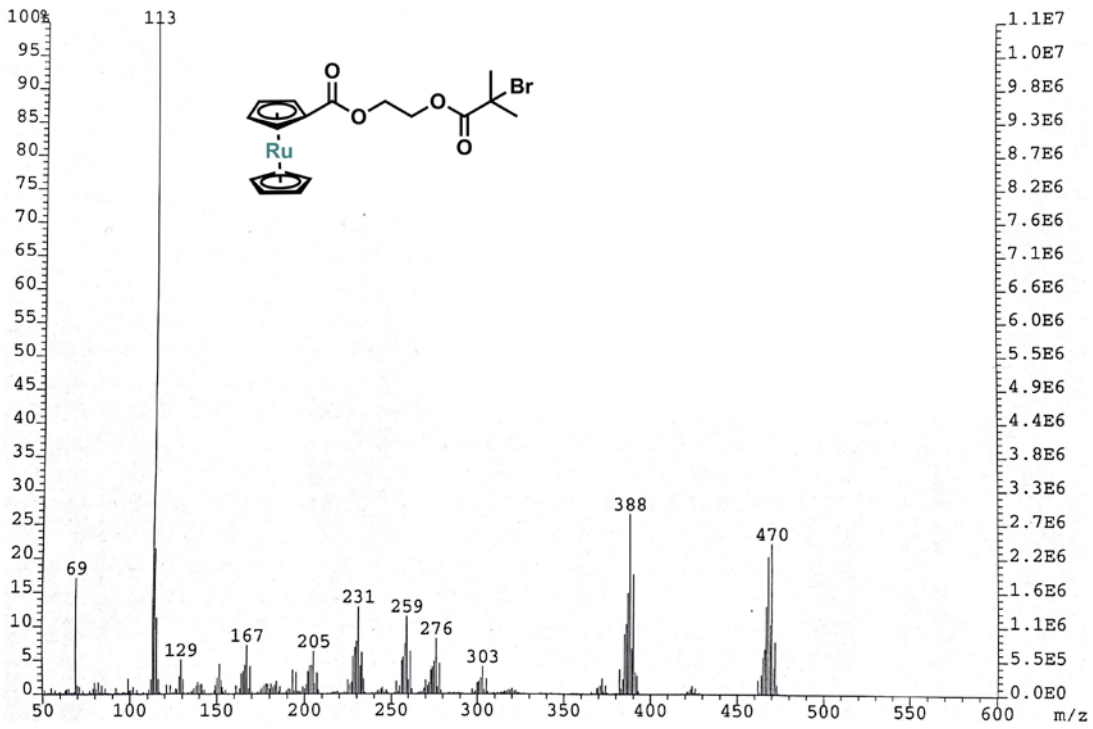


$CDCl_3$ as solvent

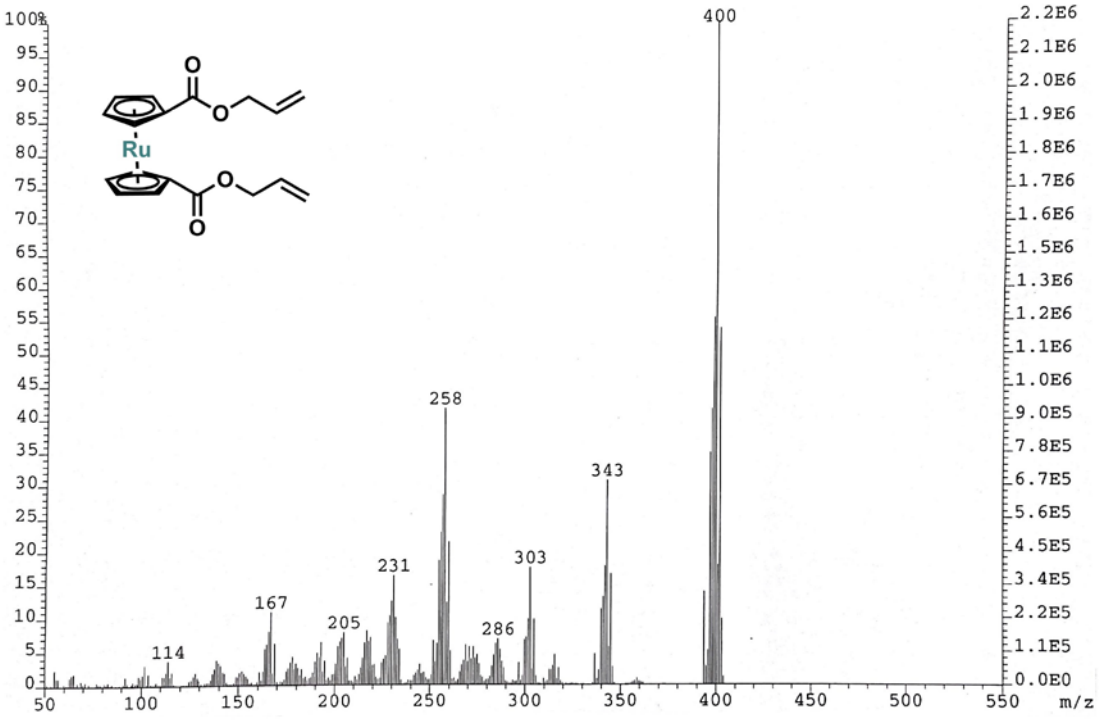
8.3 Mass spectra



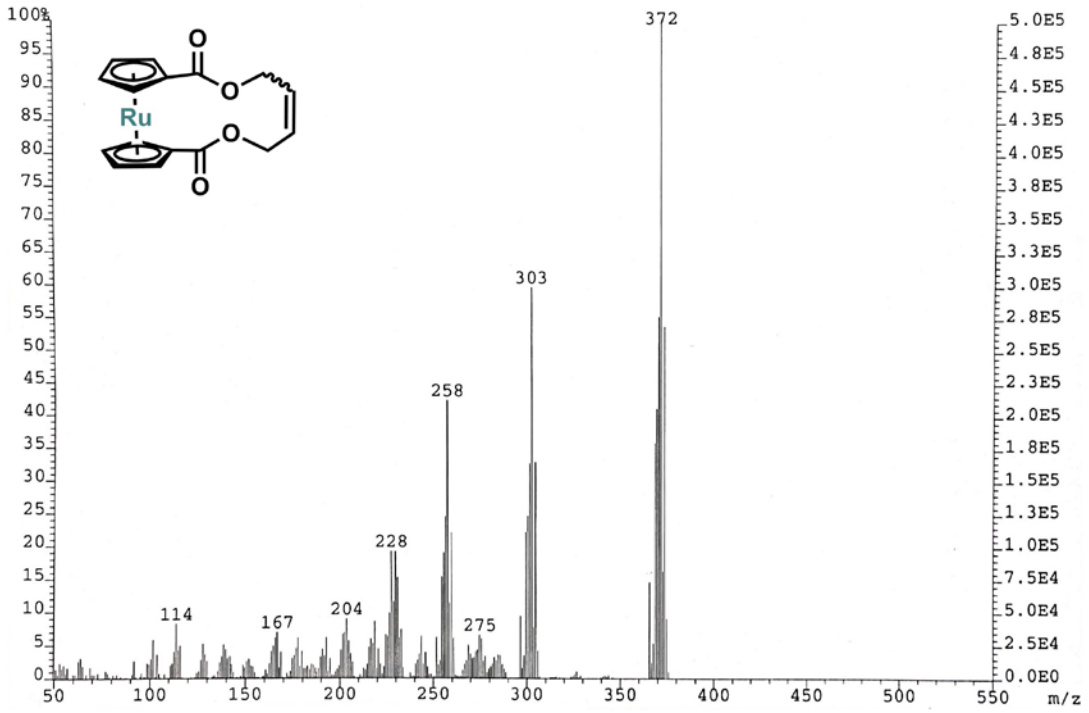
Compound **2**



Compound **3**



Compound **4**



Compound **5**

9. References

(1) Chien, C. T.; Tsai, C. C.; Tsai, C. H.; Chang, T. Y.; Tsai, P. K.; Wang, Y. C.; Yan, T. H. Novel ambiphilic dichlorocarbenoid equivalent in alkene cyclopropanation and carbonyl olefination. *J. Org. Chem.* **2006,** *71*, 4324-4327.

(2) Sha, Y.; Zhang, Y. D.; Xu, E. H.; Wang, Z.; Zhu, T. Y.; Craig, S. L.; Tang, C. B. Quantitative and Mechanistic Mechanochemistry in Ferrocene Dissociation. *ACS Macro Lett.* **2018,** *7*, 1174-1179.

(3) Yan, Y.; Zhang, J. Y.; Qiao, Y. L.; Ganewatta, M.; Tang, C. B. Ruthenocene-Containing Homopolymers and Block Copolymers via ATRP and RAFT Polymerization. *Macromolecules* **2013,** *46*, 8816-8823.

(4) Vargas-Caamal, A.; Pan, S.; Ortiz-Chi, F.; Cabellos, J. L.; Boto, R. A.; Contreras-Garcia, J.; Restrepo, A.; Chattaraj, P. K.; Merino, G. How strong are the metallocene-metallocene interactions? Cases of ferrocene, ruthenocene, and osmocene. *Phys. Chem. Chem. Phys.* **2016,** *18*, 550-556.

(5) Takayanagi, T.; Takahashi, K.; Fujihara, T.; Sato, M. On the accuracy of density-functional methods for determining structures of dicationic binuclear ruthenocene derivatives bridged by an unsaturated molecule. *J. Mol. Struct.* **2007,** *806*, 85-92.

(6) Borissova, A. O.; Antipin, M. Y.; Perekalin, D. S.; Lyssenko, K. A. Crucial role of Ru center dot center dot center dot H interactions in the crystal packing of ruthenocene and its derivatives. *Crystengcomm* **2008,** *10*, 827-832.

(7) Bader, R. F. W. A quantum theory of molecular structure and its applications. *Chem. Rev.* **1991,** *91*, 893-928.