Electronic Supplementary Material (ESI) for Green Chemistry.

Tandem thionation of biomass derived levulinic acid with Lawesson Reagent

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Supporting information

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1. Experimental section

1.1 Materials:

Levulinic acid (98%), Lawesson Reagent (LR, 95%), angelica lactone (AL, 98%) and 2-methylthiophene (98%) were purchased from TCI Shanghai, China.

Standard sample of 5-methylthiophene-2-thiol (compound **5**) with a 95% purity was kindly provided by Enamine Ltd..

All the other chemicals were analytical reagents and purchased from Sinopharm Chemical Reagent Co., Ltd., China.

All the chemicals are used without any pre-treatments except toluene applied in Table S1.

1.2 Reaction:

1.2.1 Thionation of LA

In a typical experiment, 15 mL toluene, 4 mmol LA and 1-5 mmol LR were added to a dried flask and heated to target temperature within 25 min in an oil bath under magnetic stirring. The reaction time was started to record as soon as the system reached working temperature. After reaction, the liquid was cooled down to temperature quickly, filtrated and stored for later analysis.

1.2.2 Integrated synthesis of thionation products from cellulose

For the production of cellulose derived crude LA, 15 g microcrystalline cellulose (90 μm) was added to 100 mL 0.5 mol/L H_2SO_4 solution. The reaction was then conducted in a 400 mL Hastelloy-C high pressure reactor (Dalian-controlled Plant, Dalian, China). The reactor was heated to 180 ^oC quickly and under vigorous stirring for 1 h. After reaction, the reactor was cooled down to room temperature and the liquid product was separated with coke by vacuum filtration. The product was then analyzed by a Waters e2695 HPLC equipped with a Bio-Rad Aminex HPX-87H column and a Waters 2414 refractive index detector, providing an LA yield of 44%. The pH of product was then adjusted to 2 to neutralize H_2SO_4 by the addition of CaO. After filtration, 25 mL crude LA solution was distilled and a viscous dark liquid was obtained, which was subsequently extracted by 15 mL toluene twice. The extracts were mixed and analyzed by an Agilent 7890A GC. About 85% LA was transferred into toluene phase and a LA concentration of 2.4 wt% (about 2.5 mmol in 15 mL toluene) was obtained. Then 1.25 equiv. LR was added to the solution and the reaction was conducted in a flask at 110 ^oC for 40 min.

1.2.3 Purification of compound 5

After reaction, 4 mmol water was added to the flask and the system was kept at 90 ^oC for another 10 min to convert LR residues to water soluble MPPA. The liquid product was then cooled down and washed by 30 mL 10 wt% $NaHCO_3$ aqueous solution, during which MPPA was neutralized and extracted into water phase while compound **5** still remained in toluene phase because of its weaker acidity than carbonic acid. Na_2CO_3 with a little stronger alkalinity was also appropriate for the washing process. However, **5** was converted to its sodium salt and transferred to aqueous phase if the product was washed by NaOH solution. After bubbling CO_2 into the aqueous phase, **5** could be regenerated and extracted into organic phase (e.g. ethyl acetate, diethyl ether) with a recovery up to 95%, which also proved the weaker acidity of **5** than carbonic acid.

After washing, the liquid product was diluted to remove toluene. A yellow, transparent oil was obtained and further purified by column chromatography using silica gel (spherical, 100-200 mesh) with a petroleum ether/ethyl acetate (3/1) as the eluting solvent.

MPPA partially precipitated after cooling down was separated by filtration and a white crystal was obtained. The solid was then stored in N_2 for further characterization.

1.3 Characterization:

The composition of liquid product was diluted by toluene and then analyzed by GC and GC-MS.

For the quantitative analysis of LA, an Agilent 7890A GC-FID instrument equipped by an Agilent DB-WAXETR column (15.0 m × 250 μm × 0.25 μm) was applied because the response of LA was poor on GC-MS. The following programmed temperature was used in the analysis: 313 K (2 min) – 10 K/min – 553 K (2 min).The carrier gas was N_2 with a flow rate of 1.2 mL min^{-1} and the split ratio was 1:20. External standard method was applied to measure the mass of unreacted LA in the product. C_{LA} was calculated as the following equations.

$$C_{LA}(\%) = \left(1 - \frac{m_{LA}}{m_{LA\_initial}}\right) \times 100\%$$

The *semi*-quantitative analysis of **1** was measured using the external standard curve of LA on GC considering that their structures are quite similar.

For the quantitative analysis of AL and compound **5** and **6**, a Thermofisher Trace 1300 & ISQ LT GC-MS instrument with a TR-5MS column (15.0 m × 250 μm × 0.25 μm) was applied. The following programmed temperature was used in the analysis: 313 K (2 min) – 10 K/min – 553 K (2 min). The carrier gas was He with a flow rate of 1.2 mL min^{-1} and the split ratio was 1:50. The mass spectra were obtained by electron impact ionization (EI), at an electron energy of 70 eV and with a 25 μA emission current. External standard method was applied to measure the mass of AL, 5 and 6 in the product as the following equations.

$$Yield\ of\ AL\ (\%) = \left(\frac{m_{AL}/98}{m_{LA\_initial}/116}\right) \times 100\%$$

$$Yield\ of\ 5\ (\%) = \left(\frac{m_5/130}{m_{LA\_initial}/116}\right) \times 100\%$$

$$Yield\ of\ 6\ (\%) = \left(\frac{m_6/98}{m_{LA\_initial}/116}\right) \times 100\%$$

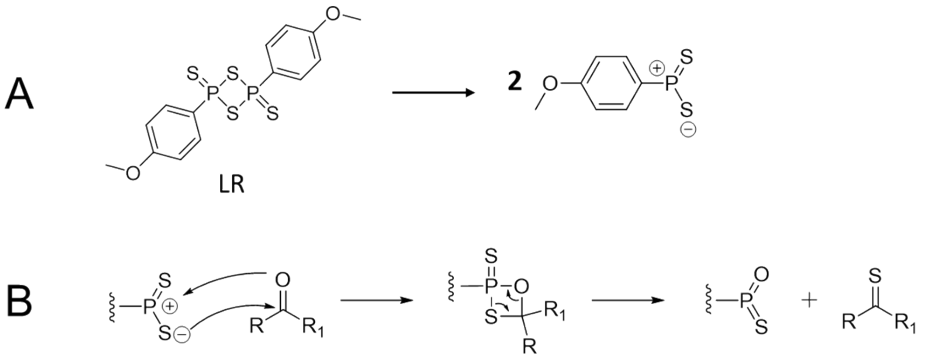
The *semi*-quantitative analysis of **2, 3** and **4b** was measured using the external standard curve of AL on GC considering their highly similarity structure.

^{1}H and ^{13}C NMR spectra were collected on a Bruker AVANCE III 600 MHz instrument.

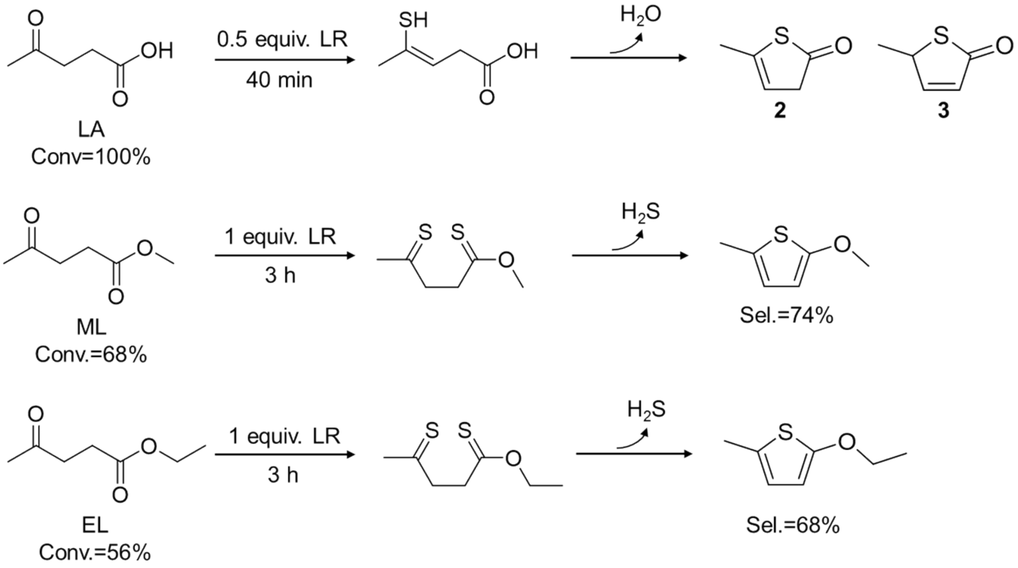
SEM analysis of solid MPPA was carried out by a Zeiss Sigma OXFORD X-Max scanning electron microscope with an accelerating voltage of 15 kV.

2. Supplementary materials

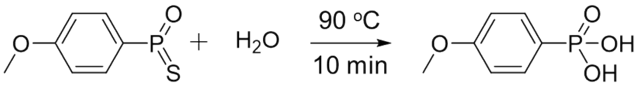
2.1 Supplementary schemes



Scheme S1 Mechanism of: A) decomposition of LR to two thionated phosphorus ylides and B) thionated phosphorus ylide promoted thionation of carbonyl group.



Scheme S2 Different thionation-cyclization mechanisms between LA and other 1,4-dicarbonyl molecules such as ML and EL. Reaction conditions: 15 mL toluene, 4 mmol substrate, 110 ^{o}C.



Scheme S3 Hydrolysis of LR residue to P-(4-methoxyphenyl)-phosphonic acid (MPPA).

2.2 Supplementary figures

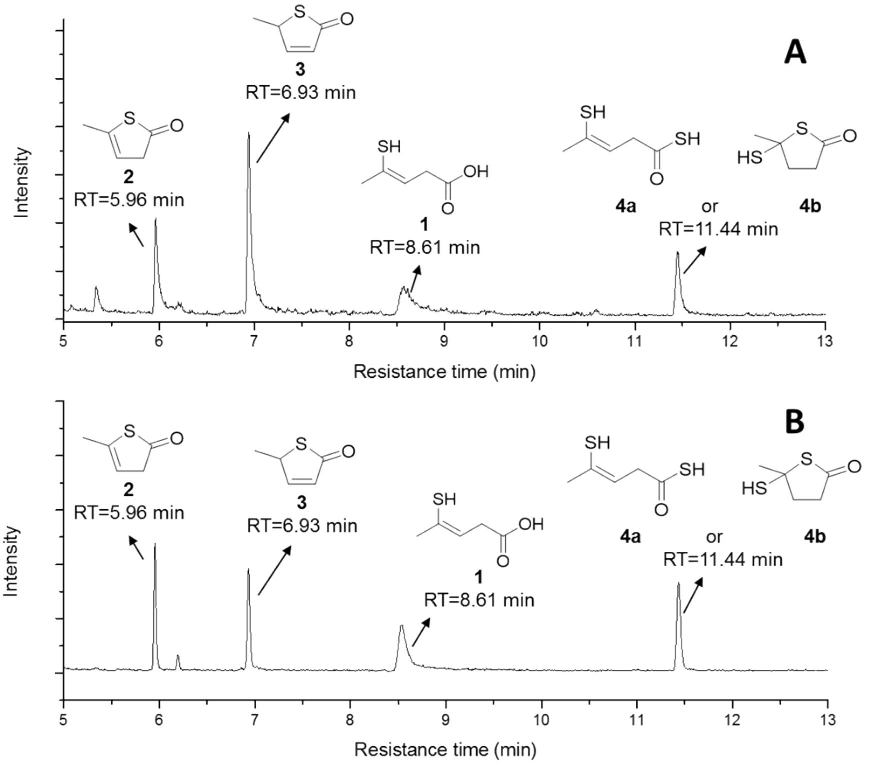


Figure S1 GC-MS spectra of the product. Reaction conditions of: A) 15 mL toluene, 4 mmol LA, 2 mmol LR, 90 °C, 40 min; B) 15 mL toluene, 4 mmol LA, 4mmol LR, 70 °C, 40 min.

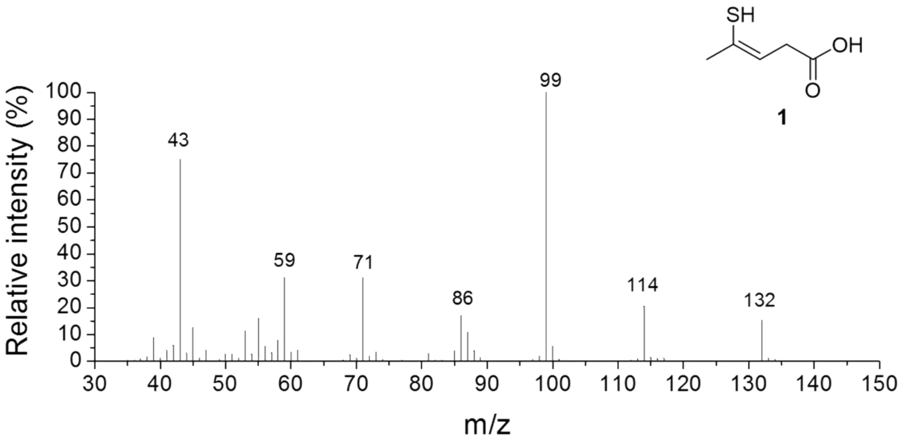


Figure S2 Mass spectrum of intermediate **1**.

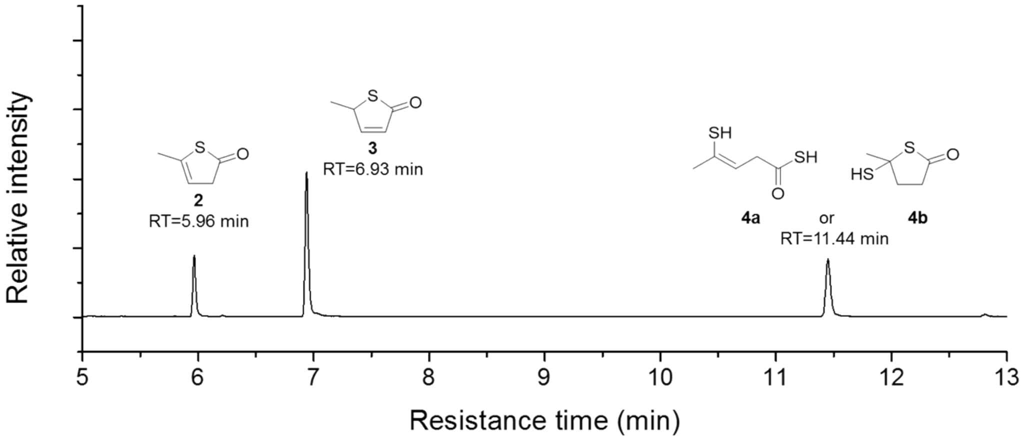


Figure S3 GC-MS TIC spectrum of the completely mono-thionated product. Reaction conditions: 15 mL Toluene, 4 mmol LA, 2 mmol LR, 90 °C, 40 min

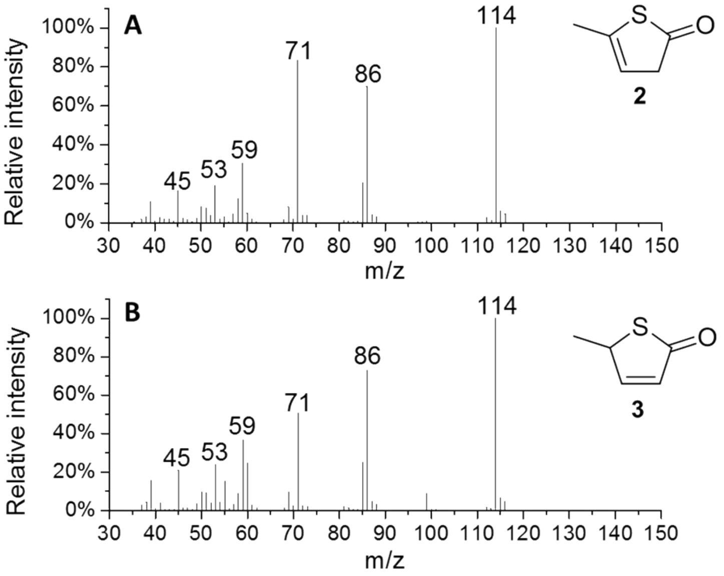


Figure S4 Mass spectra of compound **2** and **3**.

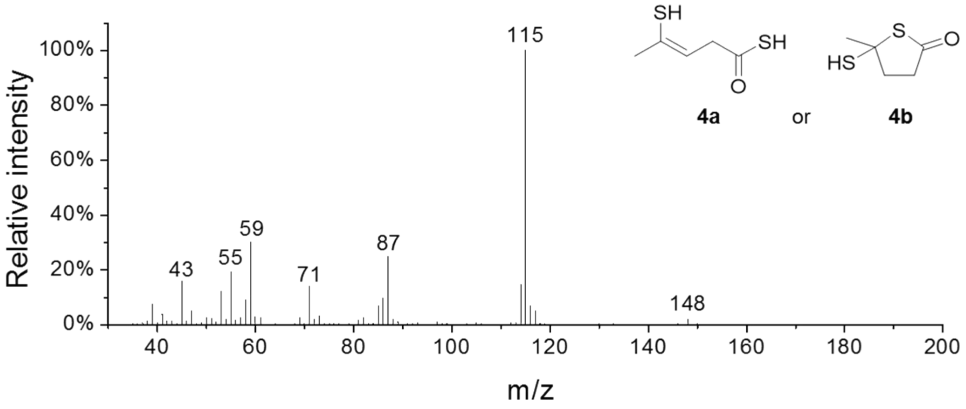


Figure S5 Mass spectrum of compound **4**.

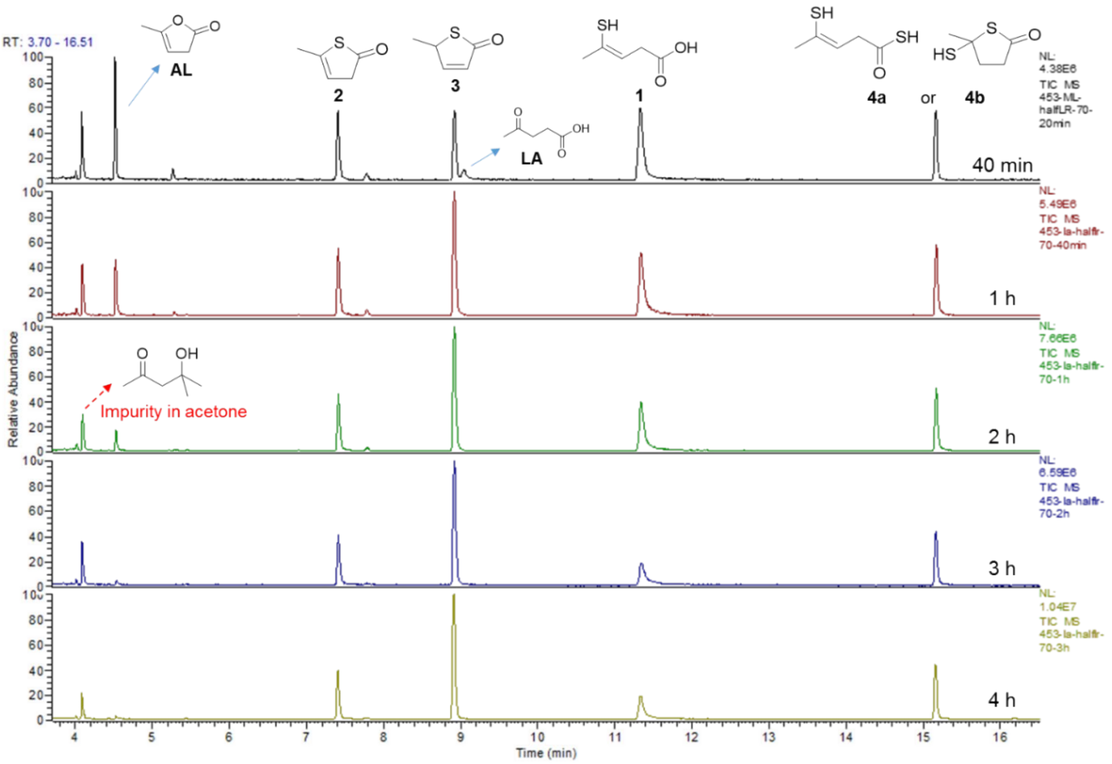


Figure S6 Reaction time affected product distribution at 70 ^{o}C monitored by GC-MS.

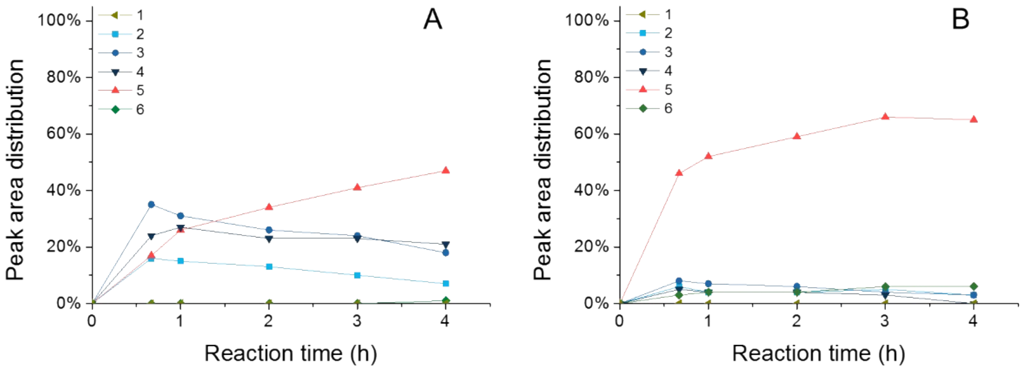


Figure S7 Product distribution under reaction temperature of: A) 90 °C; B) 110 °C. Reaction conditions: 15 mL toluene, 4 mmol LA, 4 mmol LR.

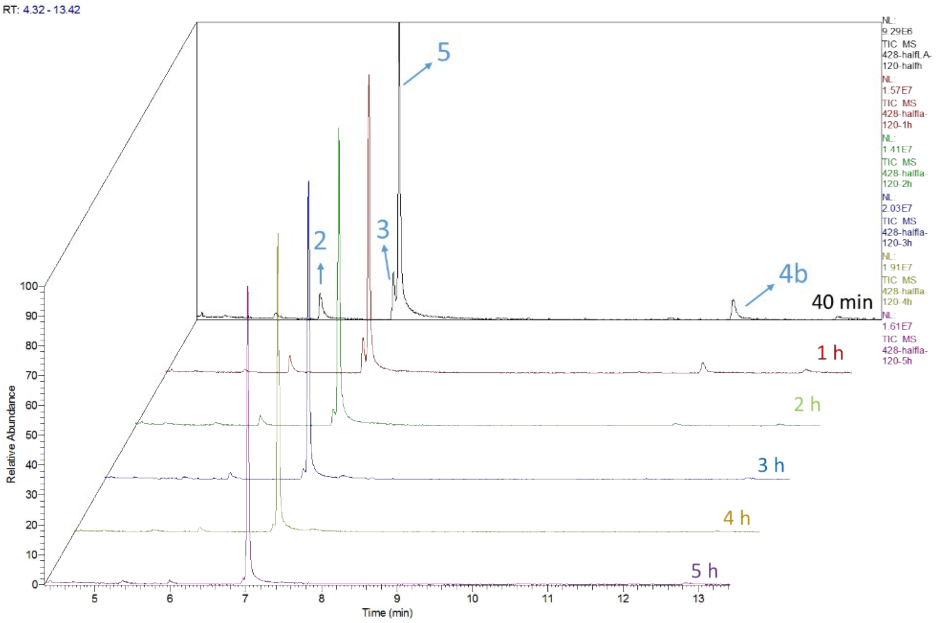


Figure S8 GC-MS monitored thionation of LA. Reaction conditions: 15 mL toluene, 4 mmol LA, 4 mmol LR, 110 °C.

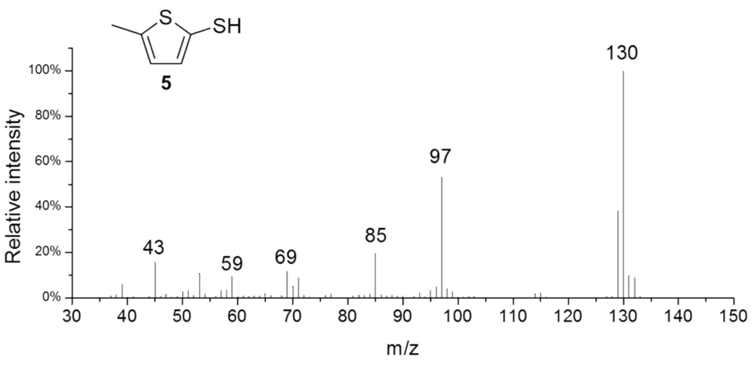


Figure S9 Mass spectrum of compound **5**.

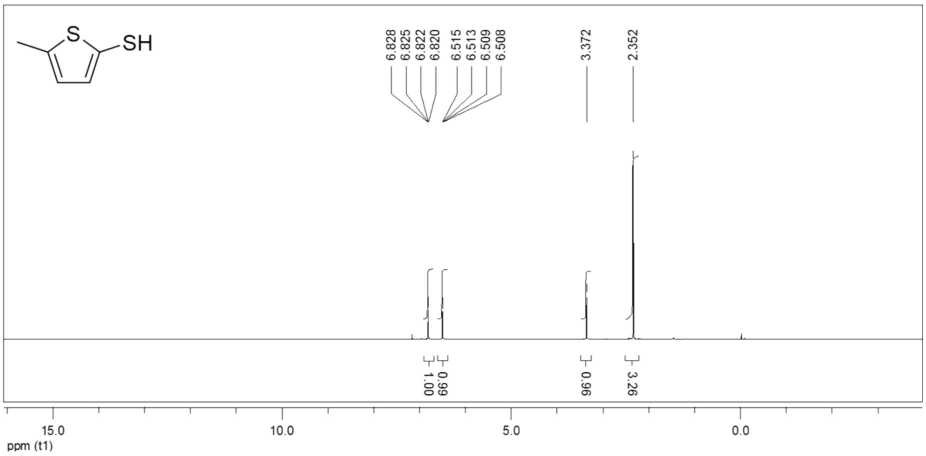


Figure S10 ^{1}H NMR spectrum of compound **5** in $CDCl_3$. δ=6.83-6.82 (dd, J=1.5, 3.3 Hz, 1 H), 6.52-6.51 (dd, J=0.9, 2.7 Hz, 1 H), 3.37 ppm (s, 1 H), 2.35 ppm (s, 3 H).

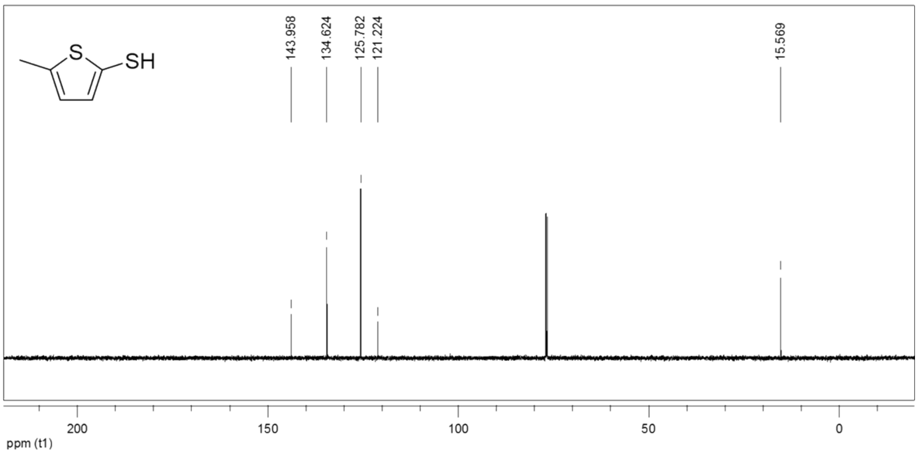


Figure S11 ^{13}C NMR spectrum of compound **5** in $CDCl_3$. δ=144.0, 134.6, 125.8, 121.2, 15.6 ppm.

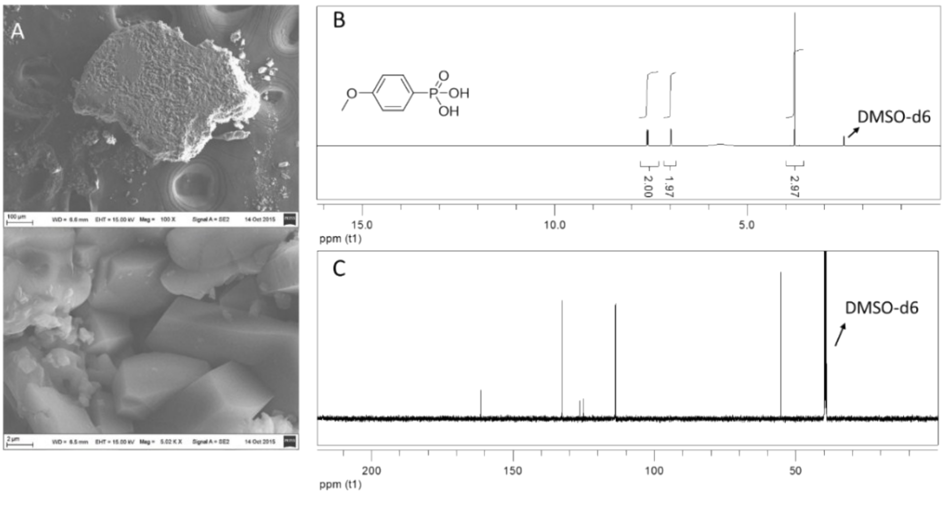


Figure S12 (A) SEM images of crystalline MPPA; (B) ^{1}H NMR spectrum and (C) ^{13}C NMR spectrum of MPPA in DMSO-d6.

2.3 Supplementary table

Table S1 Water affected thionation of AL.

Solvent	Reaction time	C_{AL}[a] (%)	$Y_{\mathbf{2}}$[b] (%)	$Y_{\mathbf{3}}$[b] (%)	$Y_{\mathbf{4b}}$[b] (%)	$Y_{\mathbf{5}}$[c] (%)
Dried toluene [d]	40 min	17	7	3	1	4
	3 h	46	13	8	3	10
Untreated toluene	40 min	58	11	19	3	17
	3 h	74	34	21	5	24
Toluene+0.02 g H_2O	40 min	83	18	41	15	14
	1 h	87	18	44	11	20

[a]: percentage conversion of AL, measured by external standard method; [b]: yield of **2**, **3** and **4b**, *semi*-quantified using the standard curve of AL; [c]:yield of 5, measured by external standard method; [d]: dried by 4 Å zeolite (10 wt% of toluene) for 24 h.