

Supporting Information for

Isoselective Ring-Opening Polymerization and Asymmetric Kinetic Resolution Polymerization of *rac*-Lactide Catalyzed by Bifunctional Iminophosphorane-Thiourea/Urea Catalysts

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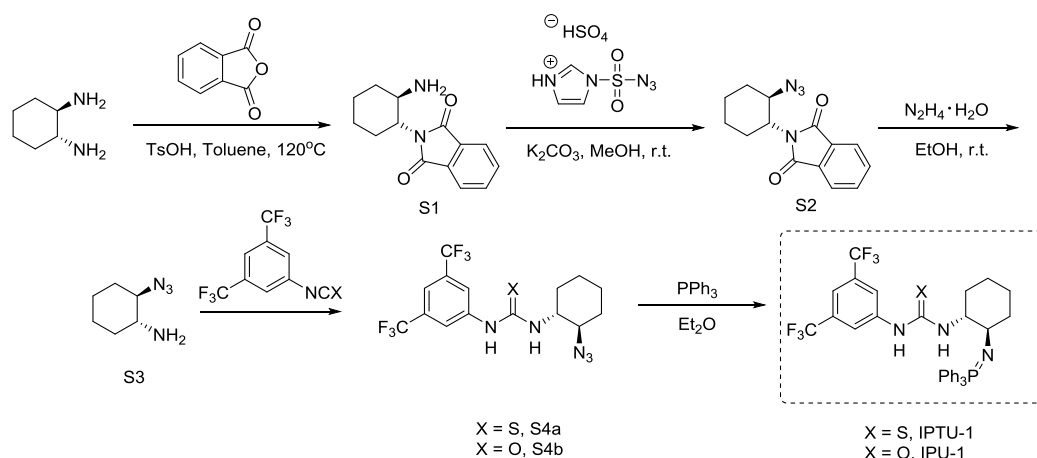
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1. Preparation of the iminophosphorane-thiourea/urea-1/2 catalysts

1.1 Preparation of *rac*/(*R*, *R*) iminophosphorane-thiourea/urea bifunctional catalysts IPTU/IPU-1



Scheme S1. Synthesis of iminophosphorane-thiourea/urea bifunctional catalyst IPTU/IPU-1

The *rac*-IPTU/IPU-1 were synthesized from (+/-)-*trans*-1,2-diaminocyclohexane and the (*R*, *R*)-IPTU/IPU-1 were synthesized from (1*R*, 2*R*)-(-)-1,2-diaminocyclohexane.

The preparation process of these iminophosphorane-thiourea/urea catalysts is based on the relevant literature.¹⁻⁴ *p*-TsOH·H₂O (1.1 equiv.) in toluene was heated to reflux for removing water, followed by the addition of diaminocyclohexane (1.0 equiv.) and phthalic anhydride (1.0 equiv.) at room temperature. The mixture was again heated to remove water overnight and allowed to cool to room temperature. The obtained white solid was filtered and stirred in DCM with saturated sodium bicarbonate solution at room temperature overnight. The organic layer was dried and condensed under vacuo to afford **S1** without further purification (82%).

S1 (1.0 equiv.) and imidazol-azido sulfate (1.2 equiv.) was stirred in MeOH by the addition of K₂CO₃ (1.7 equiv.) and CuSO₄·5H₂O (0.01 equiv.) at room temperature for 12 h. After quenched with water and extracted by ether, the combined organic phase was dried and concentrated, the compound **S2** was obtained (75%) by flash column chromatography (PE: EA = 10:1). Residue obtained from the mixture **S2** and hydrazine (N₂H₄·H₂O) in ethanol, was dissolved in ester, then the mixture was washed by hydrochloric acid solution and saturated sodium bicarbonate solution, the organic layer was dried and condensed under vacuo to afford **S3** (64%)

The crude **S3** was dissolved in THF, then 3, 5-bis (trifluoromethyl) phenyl isothiocyanate/isocyanate (1 equiv.) was added dropwise and the solution was stirred at room temperature for 12 h. Solvent were removed the crude product **S4** was purified by flash column chromatography (PE/EA = 9:1, 88%).

Under an argon atmosphere, PPh₃ (1.1 equiv.) was added to the solution of **S4** (1.0 equiv.) in Et₂O at room temperature for 24 h, and the reaction solvent was concentrated under a stream of N₂. Then pentane was added and the resultant precipitate was filtered to obtain catalyst **IPTU/IPU-1** as a white solid (80%).

S4a: ^1H NMR (400 MHz, Chloroform-*d*, 298 K) δ 8.44 (s, 1H), 7.88 (s, 2H), 7.69 (s, 1H), 6.24 (s, 1H), 3.90 (s, 1H), 3.29 (s, 1H), 2.38 – 2.11 (m, 2H), 1.92 – 1.72 (m, 2H), 1.54 (m, 1H), 1.41 – 1.16 (m, 3H).

S4b: ^1H NMR (400 MHz, Chloroform-*d*, 298 K) δ 7.87 (s, 2H), 7.51 (s, 1H), 7.00 (s, 1H), 4.71 (s, 1H), 3.51 (s, 1H), 3.20 (m, 1H), 2.16 (m, 1H), 1.81 (m, 1H), 1.64 – 1.21 (m, 6H).

IPTU-1: ^1H NMR (400 MHz, Chloroform-*d*, 298 K) δ 7.64 – 7.52 (m, 9H), 7.50 – 7.45 (m, 8H), 7.27 (s, 1H), 3.79 – 3.68 (m, 1H), 2.89 – 2.76 (m, 1H), 2.03 (s, 1H), 1.69 (m, 1H), 1.53 – 1.41 (m, 2H), 1.35 – 1.18 (m, 5H), 0.98 (m, 1H). LRMS (ESI) calcd for $[\text{C}_{33}\text{H}_{30}\text{F}_6\text{N}_3\text{PS} + \text{H}]^+$: 646.1880. Found: 646.1771. ^{19}F NMR (376 MHz, Chloroform-*d*, 298 K) δ -62.78. ^{31}P NMR (162 MHz, Chloroform-*d*, 298 K) δ 18.11.

IPU-1: ^1H NMR (400 MHz, Chloroform-*d*, 298 K) δ 7.71 – 7.35 (m, 17H), 7.20 (s, 1H), 3.54 – 3.25 (m, 1H), 3.05 – 2.66 (m, 1H), 1.96 (m, 1H), 1.68 (m, 1H), 1.52 (m, 2H), 1.26 (m, 5H), 1.02 (m, 1H). LRMS (ESI) calcd for $[\text{C}_{33}\text{H}_{30}\text{F}_6\text{N}_3\text{OP} + \text{H}]^+$: 630.2109, Found: 630.2021. ^{19}F NMR (376 MHz, Chloroform-*d*, 298 K) δ -62.87. ^{31}P NMR (162 MHz, Chloroform-*d*, 298 K) δ 13.89.

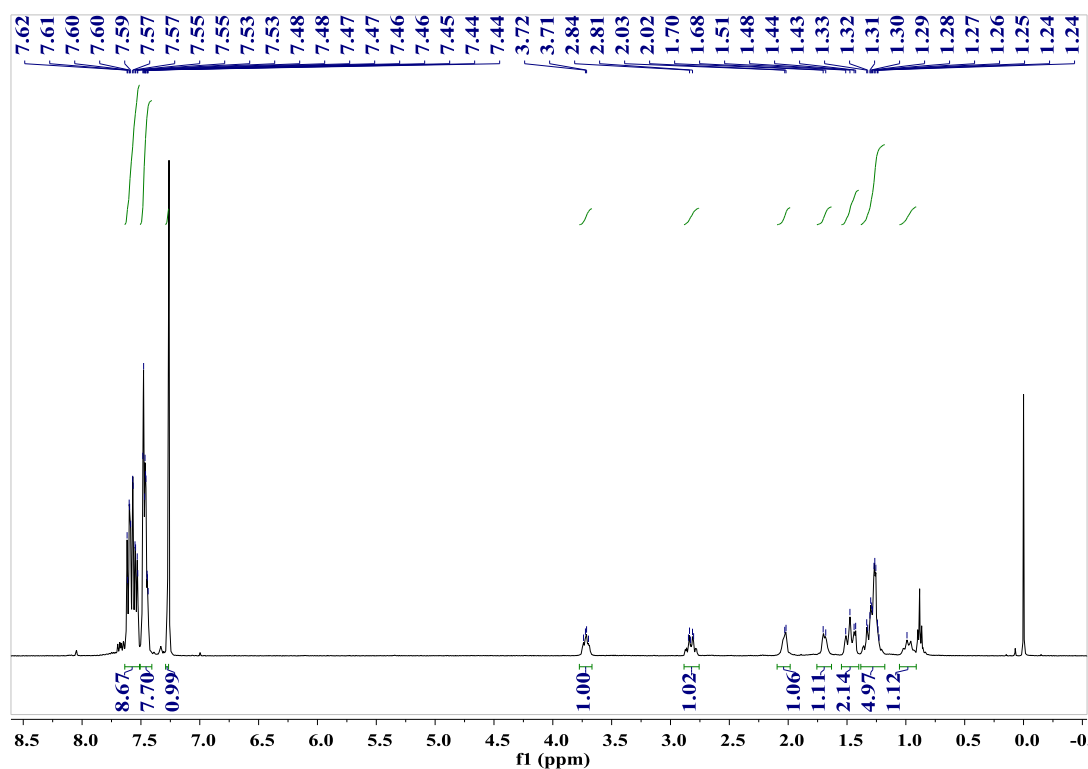


Figure S1a. ^1H NMR spectrum of catalyst IPTU-1 (400 MHz, Chloroform-*d*, 298 K).

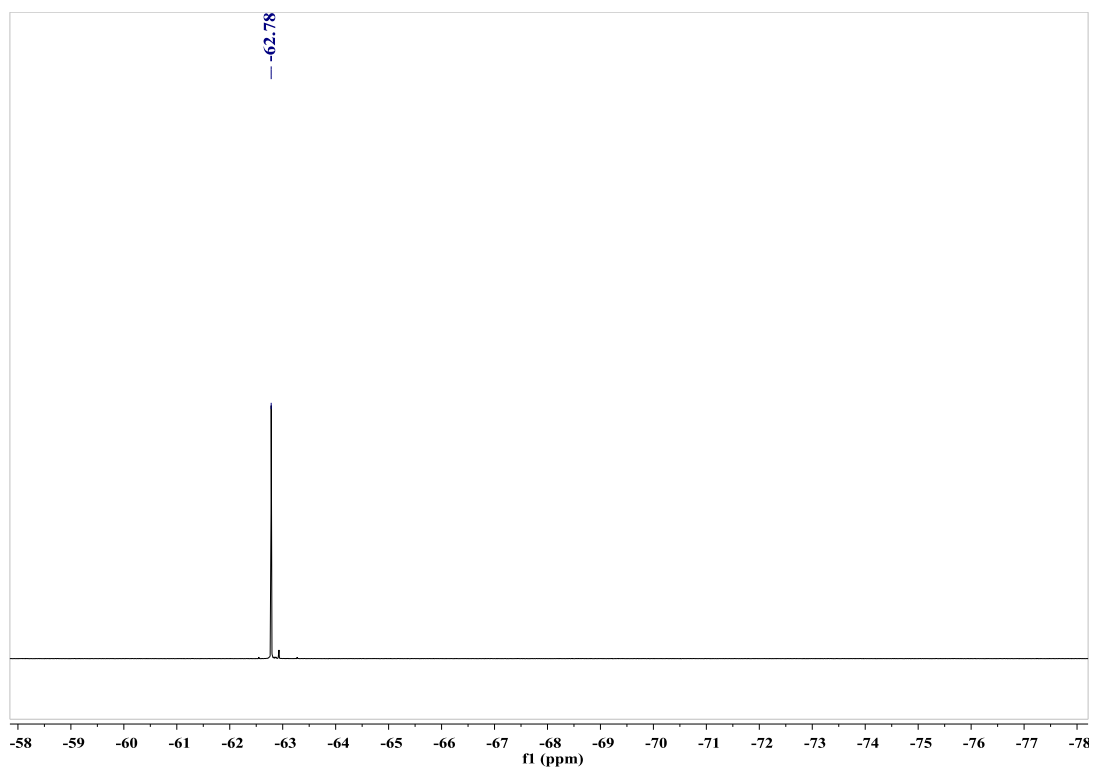


Figure S1b. ^{19}F NMR spectrum of catalyst IPTU-1 (376 MHz, Chloroform-*d*, 298 K).

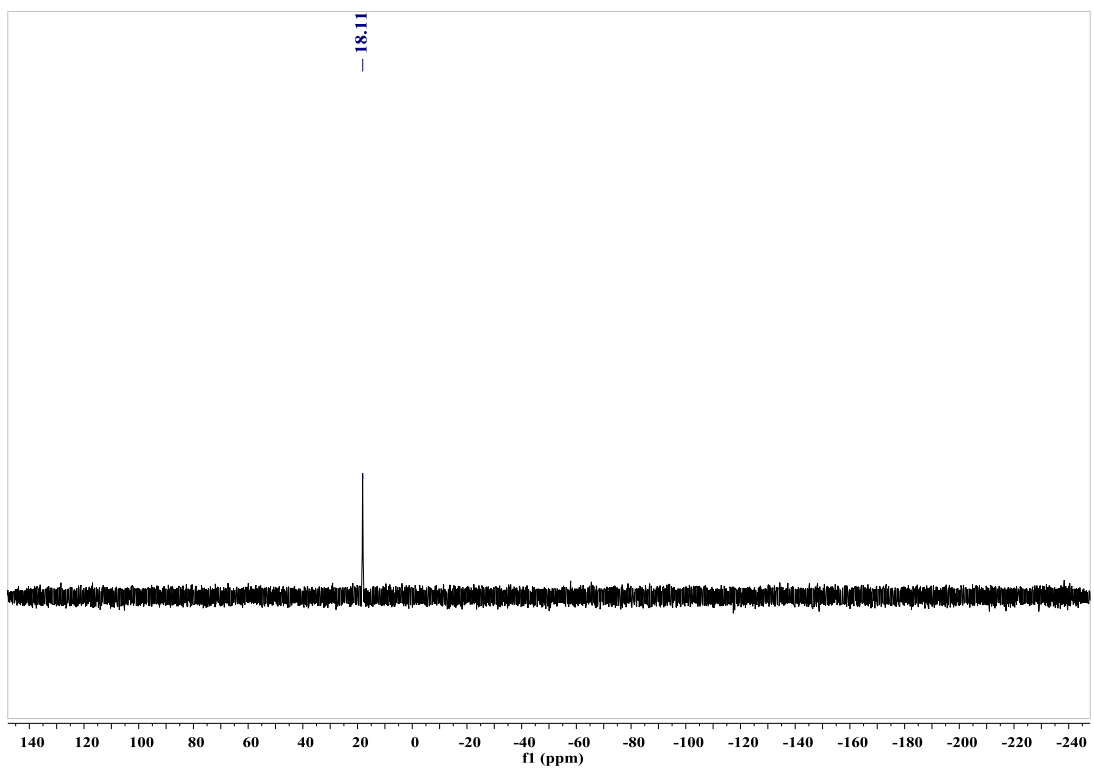


Figure S1c. ^{31}P NMR spectrum of catalyst IPTU-1 (162 MHz, Chloroform-*d*, 298 K).

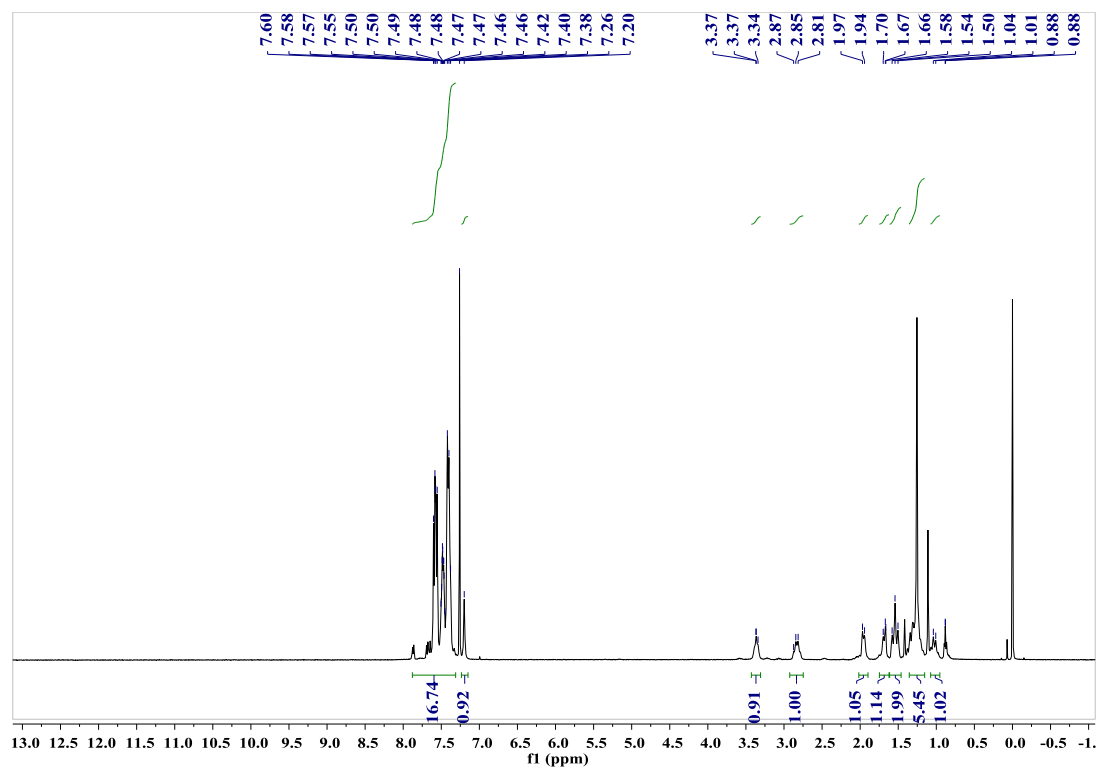


Figure S2a. ^1H NMR spectrum of catalyst IPU-1 (400 MHz, Chloroform- d , 298 K).

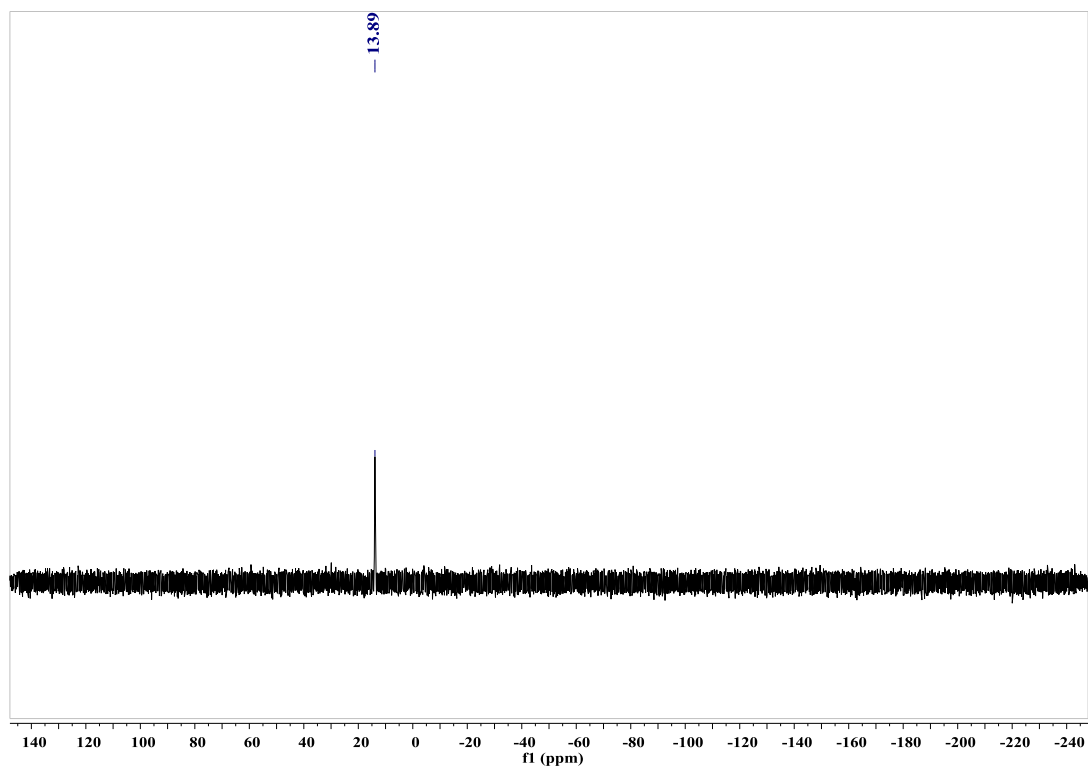


Figure S2b. ^{19}F NMR spectrum of catalyst IPU-1 (376 MHz, Chloroform- d , 298 K).

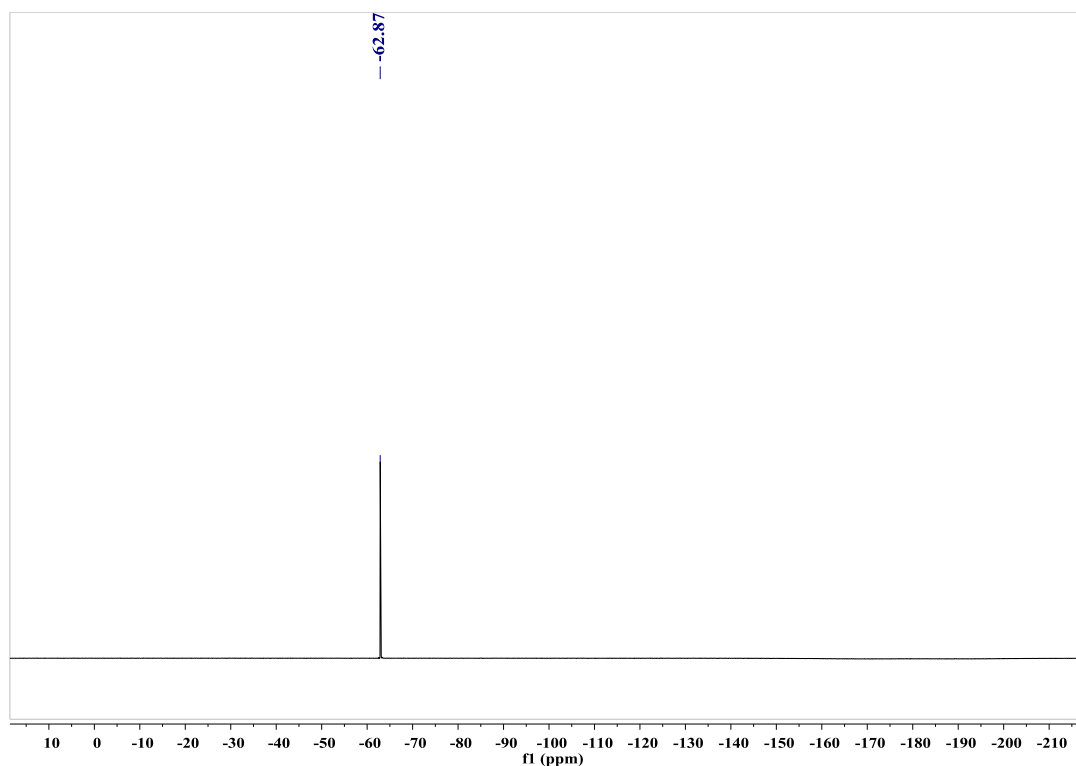
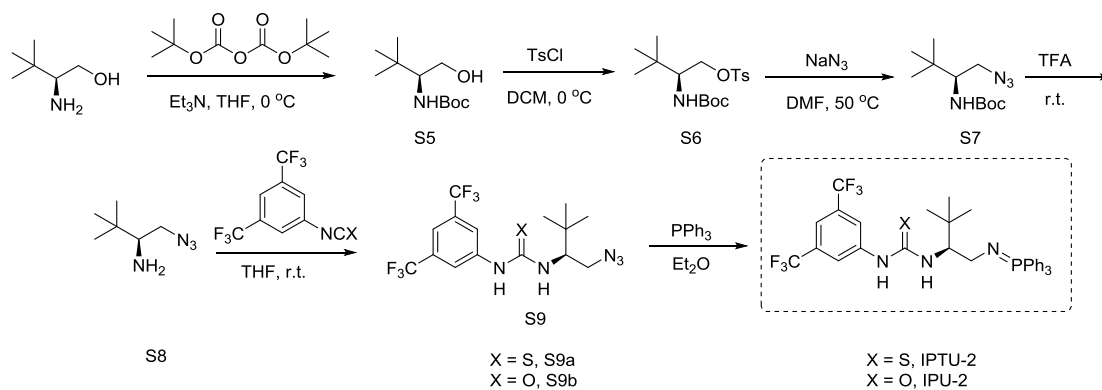


Figure S2c. ^{31}P NMR spectrum of catalyst IPU-1 (162 MHz, Chloroform-*d*, 298 K).

1.2 Preparation of chiral-iminophosphorane-thiourea/urea bifunctional catalyst IPTU/IPU-2



Scheme S2. Synthesis of iminophosphorane-thiourea/urea bifunctional catalyst IPTU/IPU-2

The preparation process of these iminophosphorane-thiourea/urea catalysts is based on the relevant literature.¹⁻⁴

(*S*)-*tert*-Leuciol (1.0 equiv.) was stirred with di-*tert*-butyl dicarbonate (1.0 equiv.) and Et_3N (1.0 equiv.) in THF at 0 °C for 12 h, after quenched with saturated ammonium chloride solution, the organic phase was combined and washed by saturated sodium chloride solution, the rude **S5** was obtained (95%) by removing the solvent.

To the solvent of **S5** (1.0 equiv.), TsCl (1.0 equiv.) and Et_3N (1.0 equiv.) were added in DCM. The mixture was washed by saturated sodium bicarbonate solution and saturated sodium chloride

solution, then organic phase is concentrated and **S6** was obtained by flash column chromatography (PE/EA = 20:1, 89%).

NaN₃ (1.1 equiv.) was added into **S6** (1.0 equiv.) in the DMF at 50 °C for 12 h, after quenched with water and extracted by ether, the organic phase was removing by rotary evaporation to obtain the rude **S7** (43%).

S7 (1.0 equiv.) was added into the trifluoroacetate (TFA, 10.0 equiv.) at room temperature for 4 h. TFA was evaporated under a stream of N₂, the residue dissolved in Et₂O and sodium hydroxide solution was added until PH = 14, the combined organics were dried over Na₂SO₄ and concentrated to obtain **S8** (64%).

S8 (1.0 equiv.) and 3, 5-bis (trifluoromethyl) phenyl isothiocyanate/isocyanate (1.0 equiv.) were dissolved in THF, and the solution was stirred at room temperature for 16 h. After evaporation of the solvents, the crude product was purified by flash column chromatography (PE/EA = 4:1) to yield **S9** as a white solid (86%).

To **S9** (1.0 equiv.) in Et₂O (3.0 mL) under an argon atmosphere, PPh₃ was added into Et₂O at room temperature for 48 h, and the reaction solvent was concentrated under a stream of N₂. Then pentane was added and the resultant thick precipitate was filtered to obtain catalyst **IPTU/IPU-2** as a white solid (75%).

S9a: ¹H NMR (400 MHz, Chloroform-*d*, 298 K) δ 8.17 (s, 1H), 7.83 (s, 2H), 7.74 (s, 1H), 6.20 (d, *J* = 8.4 Hz, 1H), 4.62 (s, 1H), 3.81 (dd, *J* = 12.8, 4.1 Hz, 1H), 3.48 (dd, *J* = 12.7, 6.2 Hz, 1H), 1.01 (s, 9H).

S9b: ¹H NMR (400 MHz, Chloroform-*d*, 298 K) δ 7.94 – 7.78 (m, 2H), 7.57 – 7.44 (m, 1H), 7.13 (s, 1H), 5.00 (d, *J* = 9.8 Hz, 1H), 3.84 (s, 1H), 3.63 (dd, *J* = 12.6, 3.8 Hz, 1H), 3.34 (dd, *J* = 12.6, 7.8 Hz, 1H), 0.98 (s, 9H).

IPTU-2: ¹H NMR (400 MHz, Chloroform-*d*, 298 K) δ 7.78 – 7.34 (m, 18H), 3.76 (br, 1H), 3.49 – 3.33 (t, *J* = 10.4 Hz, 1H), 3.03 (q, *J* = 10.4 Hz, 1H), 0.96 (s, 9H). LRMS (ESI) calcd for [C₃₃H₃₂F₆N₃OP + H]⁺: 648.2037, Found: 648.1759. HRMS (ESI) calcd for [C₃₃H₃₂F₆N₃PS + H]⁺: 648.2037, Found: 648.2035. ³¹P NMR (162 MHz, Chloroform-*d*, 298 K) δ 20.37. ¹⁹F NMR (376 MHz, Chloroform-*d*, 298 K) δ -62.77.

IPU-2: ¹H NMR (400 MHz, Chloroform-*d*, 298 K) δ 7.81 – 7.34 (m, 18H), 3.54 (br, 1H), 3.03 (d, *J* = 12.8 Hz, 1H), 2.39 (br, 1H), 0.90 (s, 9H). LRMS (ESI) calcd for [C₃₃H₃₂F₆N₃OP + H]⁺: 632.2265, Found: 632.2125. ¹⁹F NMR (376 MHz, Chloroform-*d*, 298 K) δ -62.98. ³¹P NMR (162 MHz, Chloroform-*d*, 298 K) δ 30.81.

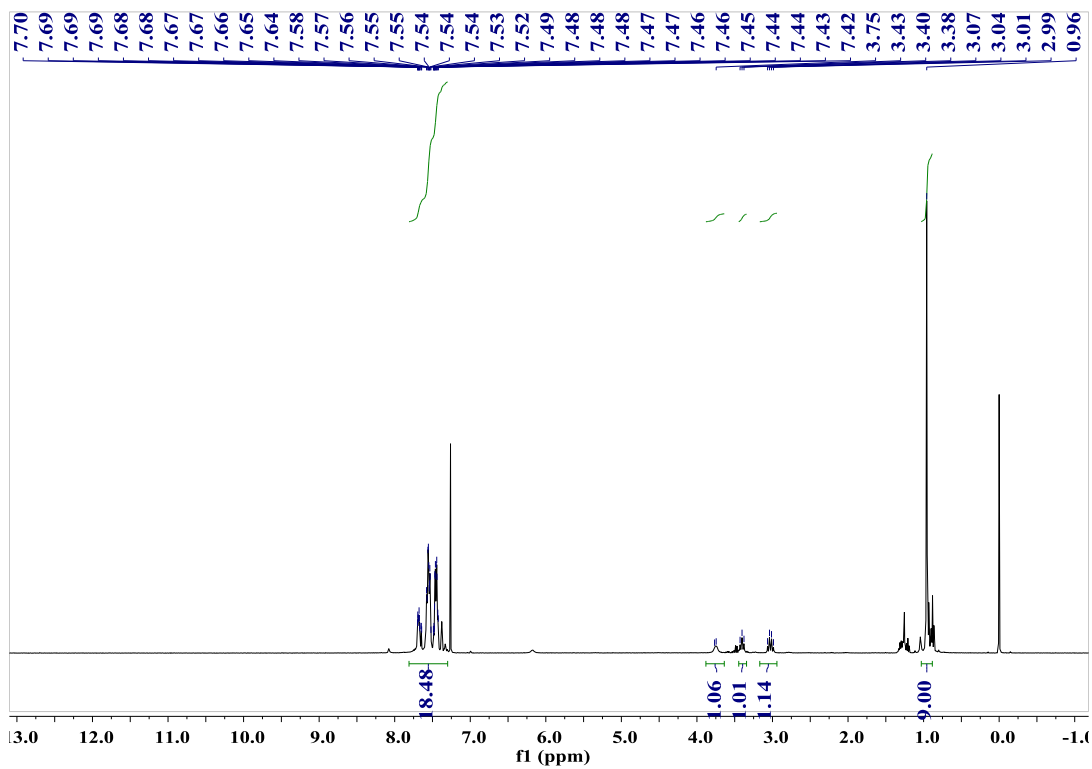


Figure S3a. ^1H NMR spectrum of catalyst IPTU-1 (400 MHz, Chloroform-*d*, 298 K).

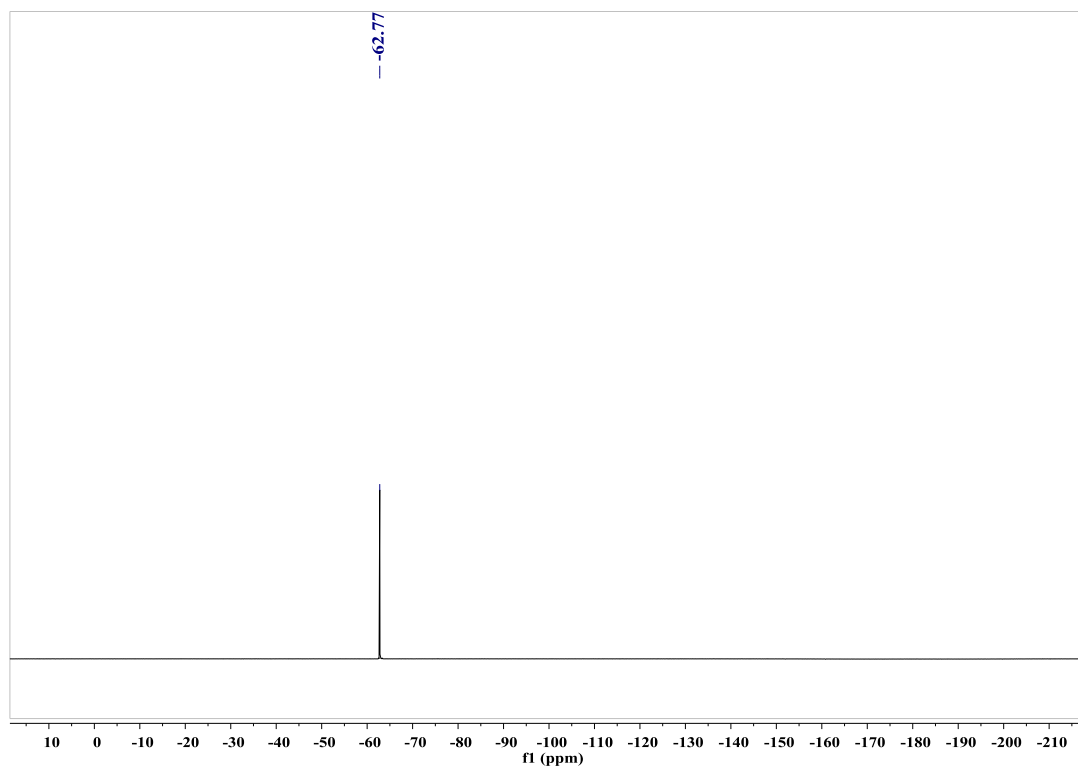


Figure S3b. ^{19}F NMR spectrum of catalyst IPTU-2 (376 MHz, Chloroform-*d*, 298 K).

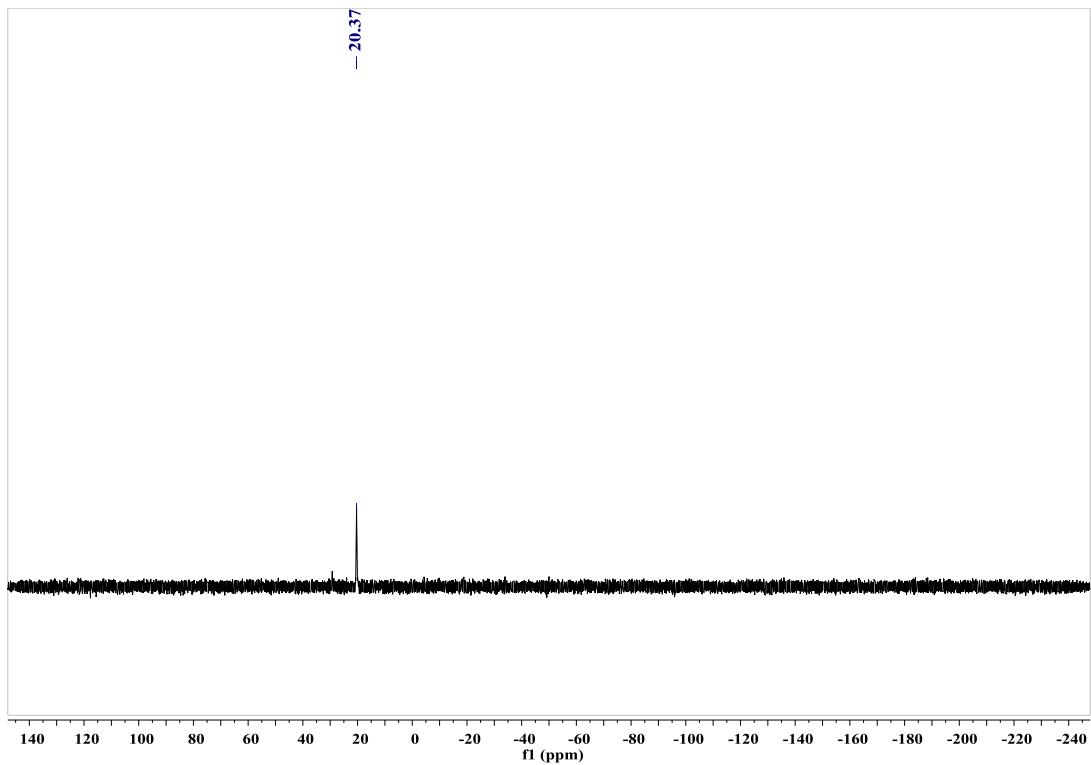


Figure S3c. ³¹P NMR spectrum of catalyst IPTU-2 (162 MHz, Chloroform-*d*, 298 K).

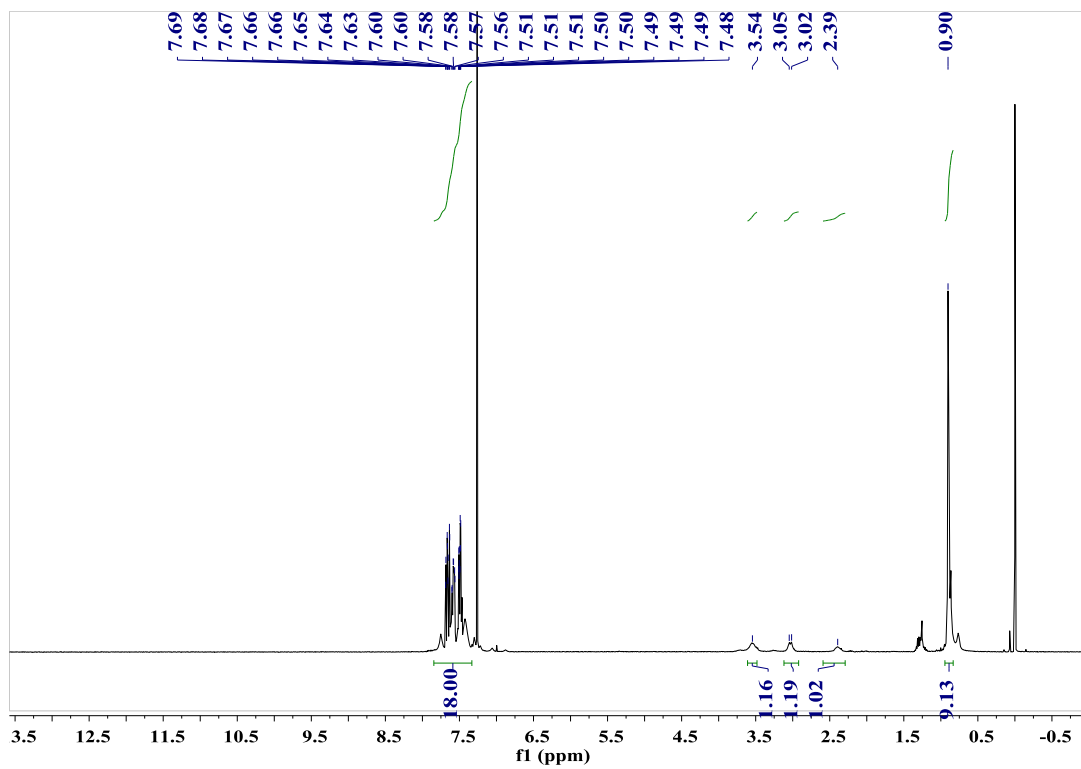


Figure S4a. ¹H NMR spectrum of catalyst IPU-2 (400 MHz, Chloroform-*d*, 298 K).

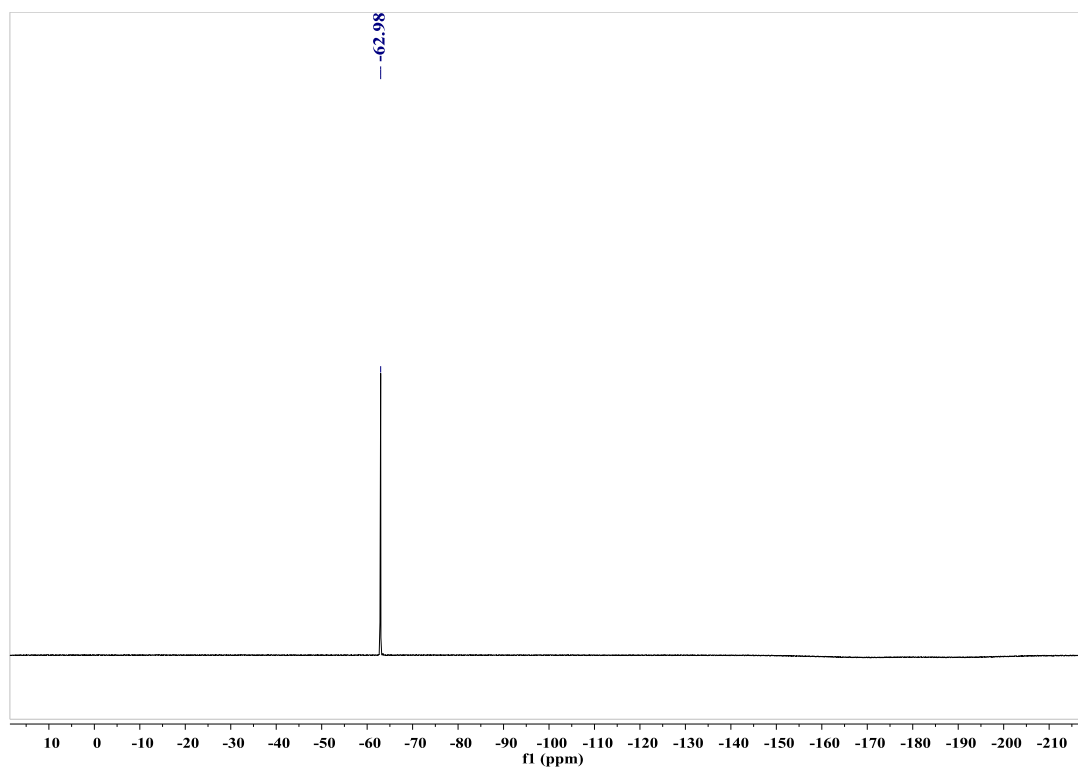


Figure S4b. ^{19}F NMR spectrum of catalyst IPTU-2 (376 MHz, Chloroform-*d*, 298 K).

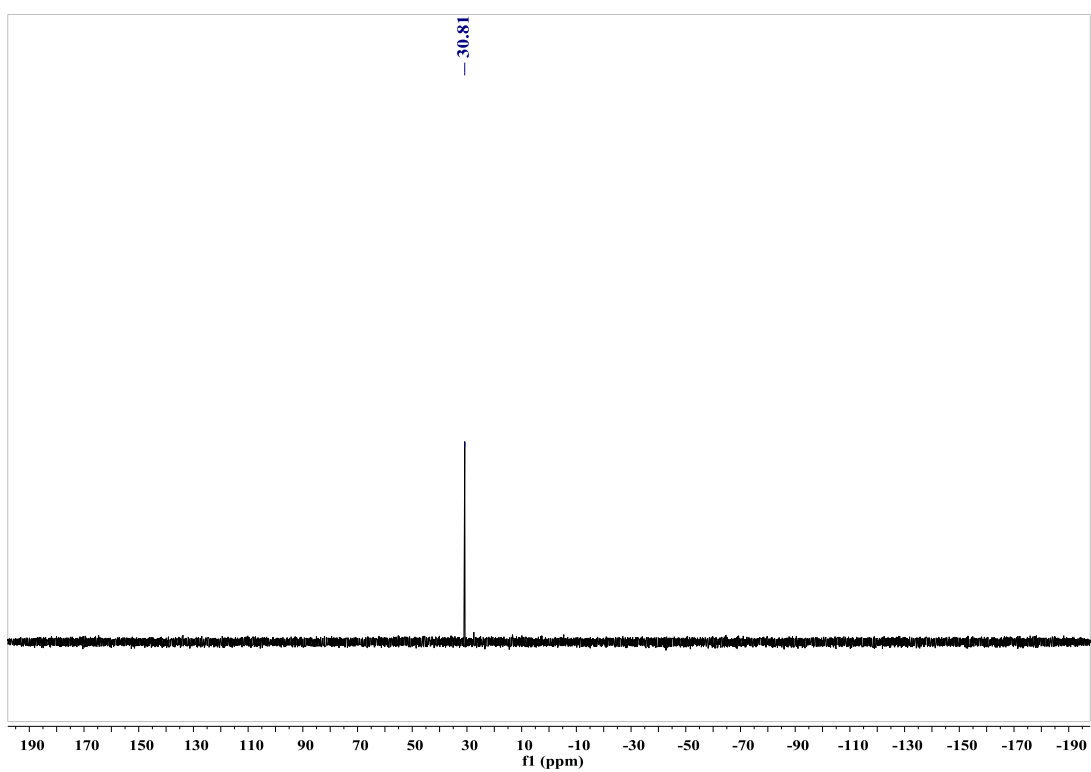


Figure S4c. ^{31}P NMR spectrum of catalyst IPU-2 (162 MHz, Chloroform-*d*, 298 K).

2. Isoselective ring-opening polymerization of *rac*-lactide catalyzed by bifunctional iminophosphorane-thiourea/urea catalysts

Table S1. Polymerization of *rac*-lactide using *rac*-IPTU-1

Entry ^a	Catalyst	[M]/[Cat.]/[I]	T (°C)	Time (h)	Conv. ^b (%)	M_n^c (g/mol)	\bar{D}^c	$P_m(\text{CEC})^d$	$P_m(\text{ESC})^d$
1	IPTU-1	100:5:0.33	25	19	94	26700	1.15	0.66	0.77
2		100:5:0.67	25	15	90	1610	1.13	0.70	0.78
3 ^e		100:5:1	0	71	90	15400	1.17	0.99	0.99
4	IPTU-1	100:5:1	25	1	13	200	1.37	--	--
5				2	23	1600	1.08	--	--
6				3	37	3200	1.12	--	--
7				4	43	4000	1.11	--	--
8				5	61	5500	1.12	0.68	0.77
9				5.5	66	6100	1.11	0.67	0.76
10				6	71	6600	1.12	0.67	0.76
11				6.5	74	6700	1.13	0.69	0.78
12				7	80	7300	1.12	0.64	0.73
13				7.5	85	7700	1.12	0.66	0.75
14				8	88	7800	1.14	0.68	0.79
15				9	90	8400	1.10	0.70	0.78
16				9.5	93	8600	1.11	0.68	0.77
17				10	94	8700	1.11	0.70	0.81

^a Polymerizations were conducted in CH_2Cl_2 (1 M) at 25 °C unless otherwise stated. ^b Monomer conversion was determined and calculated by ^1H NMR spectrum in CDCl_3 . ^c Apparent number-average molar mass (M_n) and dispersity (\bar{D}) value were determined by GPC in THF using polystyrene standards for calibration, and corrected using the Mark–Houwink factor 0.58 for polylactide. ^d Probability of finding *meso* dyads calculated from homonuclear decoupled ^1H NMR spectrum after deconvolution; calculations are based on CEC/ESC mechanism. ^e $[\textit{rac}\text{-LA}]_0 = 0.5 \text{ mol/L}$.

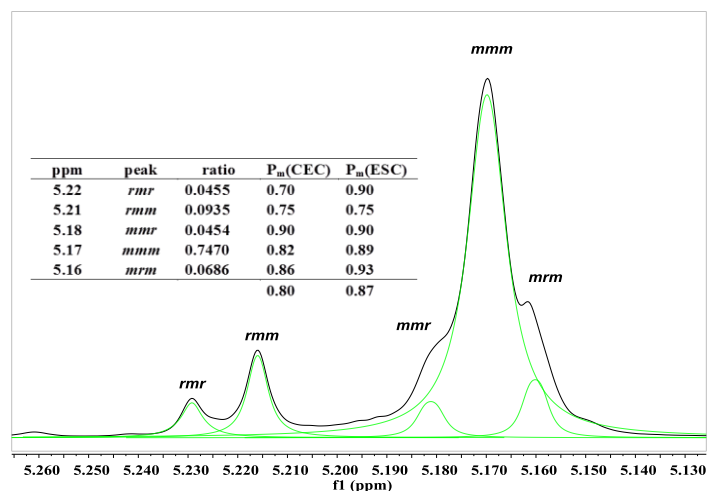


Figure S5. The homodecoupled ^1H NMR spectrum after deconvolution of the sample (Table 1, entry 14).

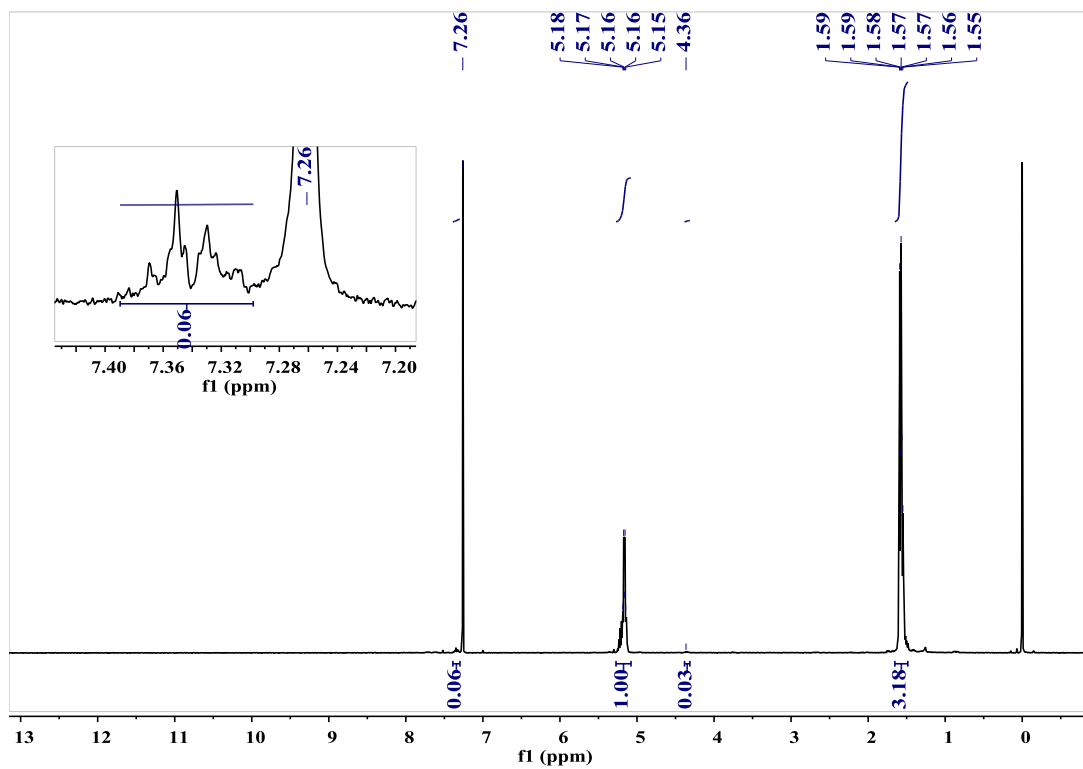


Figure S6. ^1H NMR spectrum of polylactide (400 MHz, Chloroform-*d*, 298 K) (Table 1, entry 5).

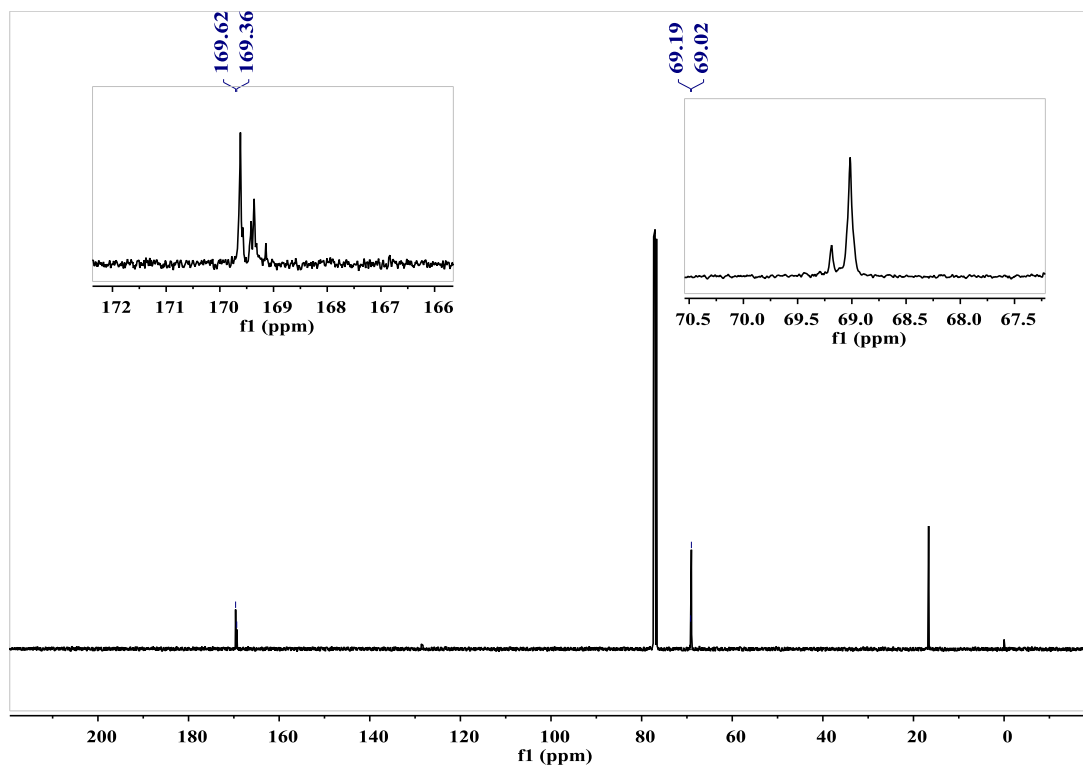
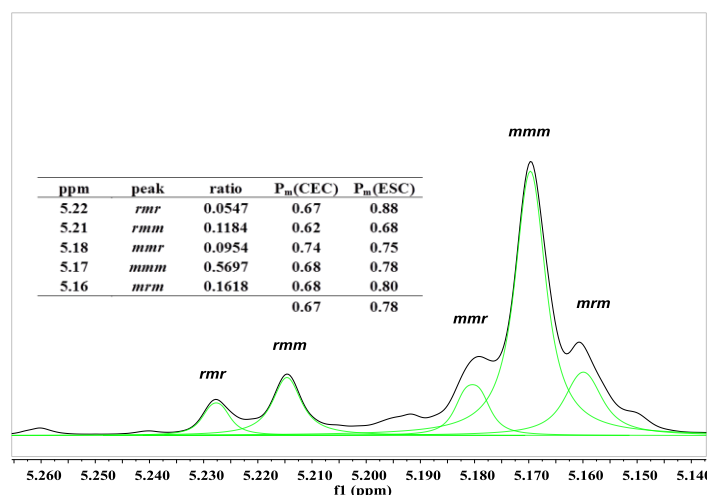


Figure S7. ^{13}C NMR spectrum of polylactide (100 MHz, Chloroform-*d*, 298 K) (Table 1, entry 5).

Table S2. Polymerization of *rac*-lactide using (*R,R*)-IPTU /IPU-1 and (*S*)-IPTU/IPU-2

Entry ^a	Catalyst	[M]/[Cat.]/[I]	T (°C)	Time (h)	Conv. ^b (%)	M_n^c (g mol ⁻¹)	\bar{D}^c	$P_m(\text{CEC})^d$	$P_m(\text{ESC})^d$
1	IPTU-1	100:5:2	-40	60	79	2400	1.13	0.65	0.75
2	IPU-1	100:5:2	-40	2	96	2900	1.14	0.75	0.83
3 ^e	IPTU-2	100:5:2	25	0.5	97	4900	1.16	0.68	0.76
4 ^f			0	6	87	3300	1.13	0.59	0.67
5			-40	20	83	2600	1.12	0.69	0.79
6 ^e	IPU-2	100:5:2	25	0.5	97	4300	1.15	0.66	0.74
7 ^f			0	4	86	4400	1.18	0.64	0.72
8			-40	20	66	1600	1.15	0.65	0.75

^a Polymerizations were conducted in CH₂Cl₂, $[rac\text{-LA}]_0/[Cat.]_0/[BnOH]_0 = 100/5/2$, $[rac\text{-LA}]_0 = 0.25$ mol/L. ^b Monomer conversion were determined and calculated by ¹H NMR spectrum in CDCl₃. ^c Apparent number-average molar mass (M_n) and dispersity (\bar{D}) value were determined by GPC in THF using polystyrene standards for calibration, and corrected using the Mark–Houwink factor 0.58 for polylactide. ^d Probability of finding *meso* dyads calculated from homonuclear decoupled ¹H NMR spectrum after deconvolution; calculations were based on CEC/ESC mechanism. ^e $[rac\text{-LA}]_0 = 1$ mol/L. ^f $[rac\text{-LA}]_0 = 0.5$ mol/L.

Figure S8. Homodecoupled ¹H NMR spectrum after deconvolution of polylactide (Table 2, entry 1).

3. Asymmetric kinetic resolution polymerization of *rac*-lactide catalyzed by chiral bifunctional iminophosphorane-thiourea/urea- catalysts

Table S3. Kinetic studies of Polymerization using *rac*/D/L-LA initiated by *rac*/(*R,R*)-IPTU-1

Entry ^a	<i>rac</i> -IPTU-1				(R,R)-IPTU-1			
	Time (h)	Conv. ^b for <i>rac</i> -LA	Conv. ^b for D-LA	Conv. ^b for L-LA	Time (h)	Conv. ^b for <i>rac</i> -LA	Conv. ^b for D-LA	Conv. ^b for L-LA
1	0.5	0.07	0.09	0.10	0.5	0.24	0.31	0.31
2	1	0.11	0.17	0.15	1	0.32	0.41	0.38
3	1.5	0.21	0.30	0.28	2	0.39	0.47	0.45
4	2	0.22	0.31	0.30	2.5	0.46	0.50	0.48

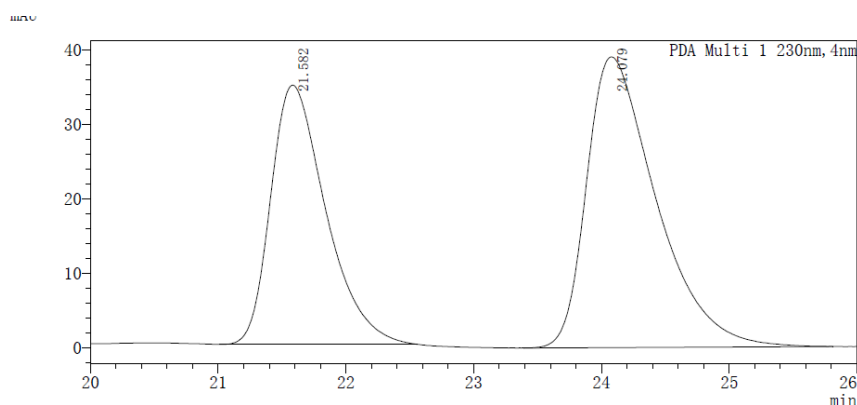
5	3	0.40	0.50	0.50	3.5	0.48	0.61	0.59
6	4	0.48	0.57	0.59	4	0.59	0.66	0.64
7	5	0.61	0.70	0.71	4.5	0.66	0.66	0.70
8	5.5	0.64	0.73	0.74	5	0.68	0.73	0.73
9	6	0.67	0.76	0.78	6	0.75	0.80	0.76
10	7	0.75	0.84	--	7	0.78	--	0.81
11	8	0.81	0.87	0.86	8	0.83	0.81	
12	9	0.85	0.88	0.89	9	0.84	0.87	0.89
13	10	0.88	0.91	0.91	10	0.88	--	--

^a Polymerizations were conducted in CH₂Cl₂ (1 M) at 25 °C, and [LA]₀/[IPTU-1]₀/[BnOH]₀ = 100:5:1. ^b Monomer conversion was determined and calculated by ¹H NMR spectrum in CDCl₃.

Table S4. Kinetic studies of Polymerization using D/L-LA initiated by (R, R)-IPTU-1

Entry ^a	Time (h)	Conv. ^b for D-LA	Conv. ^b for L-LA
1	3.5	0.20	0.25
2	7	0.24	0.31
3	16	0.32	0.40
4	22	0.36	0.44
5	40	0.45	0.54
6	52	0.55	0.64
7	64	0.62	0.72
8	74	0.66	0.76
9	86	0.69	0.80

^a Polymerizations were conducted in CH₂Cl₂ (0.25 M) at -40 °C, and [LA]₀/[(R, R)-IPTU-1]₀/[BnOH]₀ = 100:5:1. ^b Monomer conversion was determined and calculated by ¹H NMR spectrum in CDCl₃.



<峰表>

PDA Ch1 230nm

峰号	保留时间	面积	高度	面积%
1	21.582	1044752	34811	41.437
2	24.079	1476532	39021	58.563
总计		2521284	73832	100.000

Figure S9. HPLC chromatograms of the unreacted monomer determined using a UV (230 nm) detector (Table 3, entry 6).

4. References

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2. M. Formica, G. Sorin, A. J. M. Farley, J. D'iaz, R. S. Paton and Darren J. Dixon, *Chem. Sci.*, 2018, **34**, 6969-6974.
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