

# Iron acetate plus small amides: a cheap and simple catalyst system for the synthesis of PLLA and PLLA-PCL blockcopolymers

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## Introduction

### Poly-L-lactic acid (PLLA)

Poly(lactic acid) is the most well-known and used bio-derived polymer at present. As a hydrolytically degradable and biocompatible polyester it is also of huge interest for the biomedical field. It is mostly synthesised via ring-opening polymerisation (ROP) of a dimeric lactone (lactide) consisting of two lactic acid units, which in turn is produced by fermentation of sugars. In this work L-lactide is used as monomer.

### Ring opening polymerisation (ROP)

The most commonly and industrially used catalyst for ROP is  $\text{Sn}(\text{Oct})_2$ . Despite strict regulations, there are concerns about residual toxic tin ions in materials designed for resorption in the body. In addition, tin mining has a large impact on the environment and is at high risk from the effects of global warming. For these reasons, research has been conducted on metals to substitute tin in catalysts for ROP. One metal that is of low toxicity and large abundance is iron.

### Previous Work: ROP of morpholine-2,5-diones

Different metals were tested as catalysts for the ROP of morpholinediones.

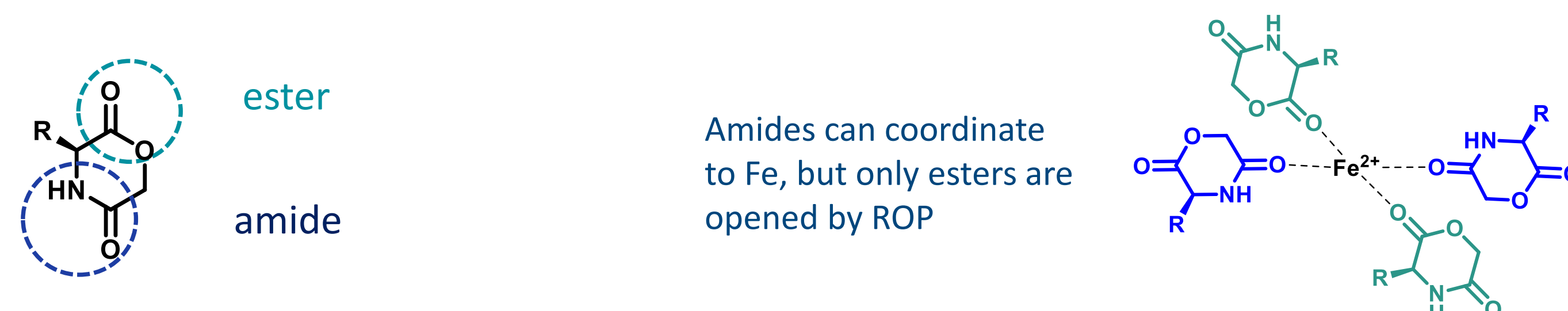
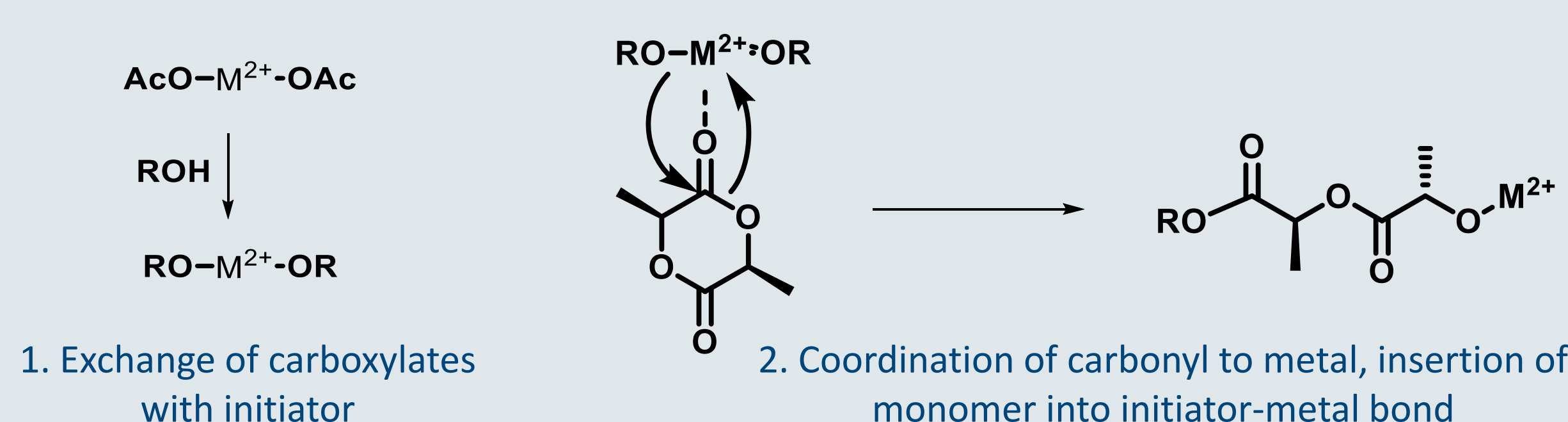
$\text{Fe}(\text{OAc})_2$  gave better results than  $\text{Sn}(\text{Oct})_2$  [1].

Initial experiments showed that  $\text{Fe}(\text{OAc})_2$  could polymerise L-lactide when combined with secondary amides as non-polymerisable catalytic adjuncts [2].

### Polycaprolactone (PCL)

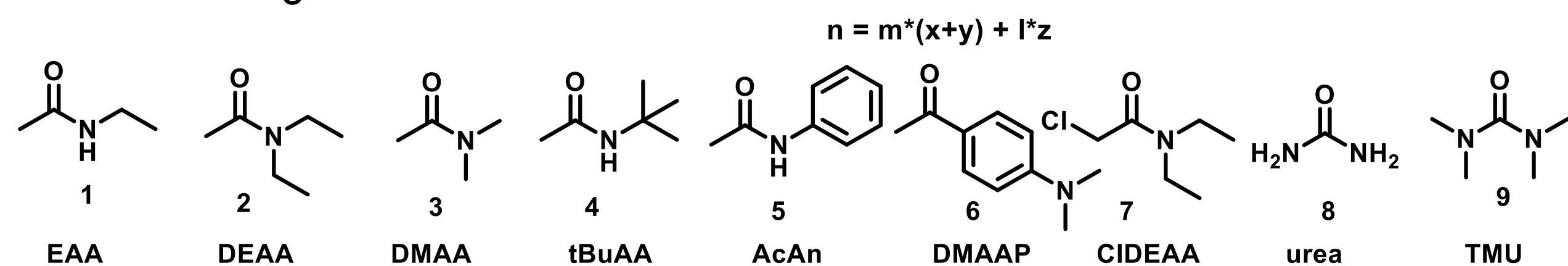
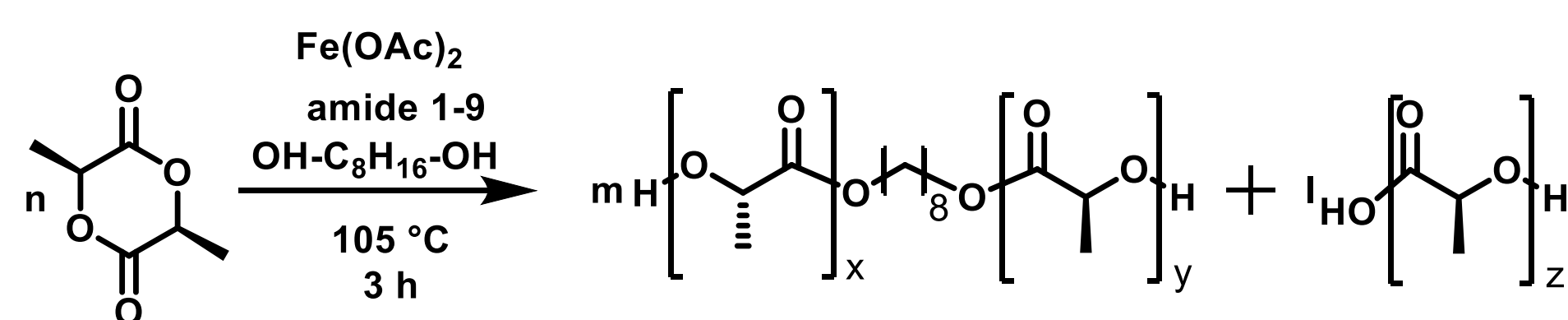
PCL is another biodegradable and biocompatible polyester, which is produced via ROP of  $\epsilon$ -caprolactone (CL). PLLA and PCL have complimentary material properties in terms of elasticity/hardness, degradation rate inside the body, etc so that by copolymerisation materials can be designed for many different specific applications.

#### Coordination-insertion mechanism for metal-catalysed ROP



## Catalyst optimisation

### Screening of amides

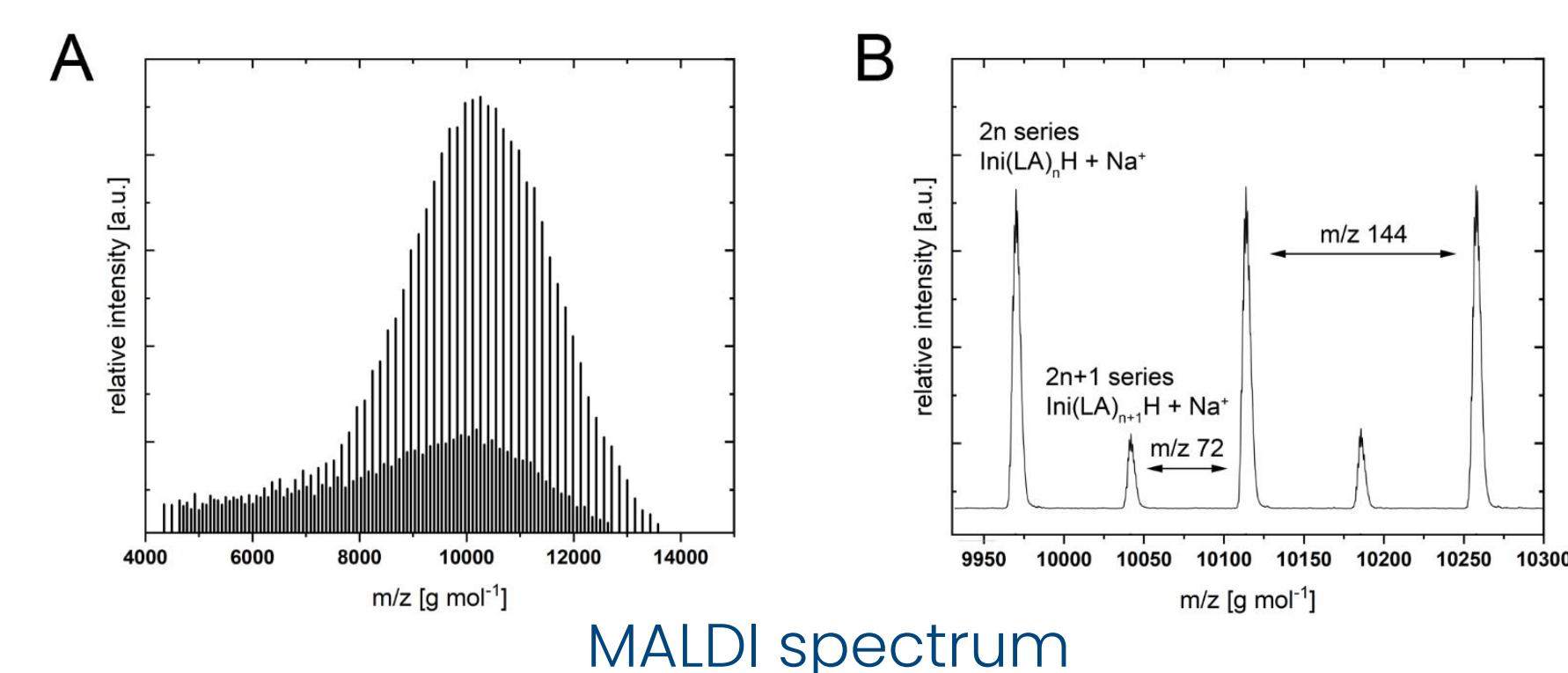


Amide	1 EAA	2 DEAA	3 DMAA	4 tBuAA	5 AcAn	6 DMAAP	7 CIDEAA	8 urea	9 TMU
Conv [%]	77	93	93	44	29	15	39	88*	87
Initiator [%]	74	94	99	75	83	79	89	45	91
$M_n$ (NMR)	8790	11280	9424	4040	4160	2440	4980	5490 1572	9885

- best conversions and initiator incorporation was achieved with small tertiary amides (electron density donation via alkyl substituents)
- Bulkier groups on the amide N or electron withdrawing substituents next to the carbonyl reduced the yield

Polymer	$M_n$ MALDI [g mol <sup>-1</sup> ]	$M_w$ MALDI [g mol <sup>-1</sup> ]	$\bar{D}$ MALDI	2n:2n+1 [%]	$M_n$ GPC [g mol <sup>-1</sup> ]	$M_w$ GPC [g mol <sup>-1</sup> ]	$\bar{D}$ GPC	$[\alpha]_D^{22}$ [°]
PLLA-EAA	8655	9000	1.04	66	14100	14700	1.04	-153
PLLA-DEAA	9780	10120	1.03	79	14500	15000	1.04	-154
PLLA-DMAA	7745	7989	1.03	68	12200	13000	1.06	-150
PLLA-urea	6120 2503	6255 2652	1.02 1.06	78	3240 (bimodal)	5600	1.72	-147
PLLA-TMU	9470	9820	1.04	68	12500	14400	1.16	-151

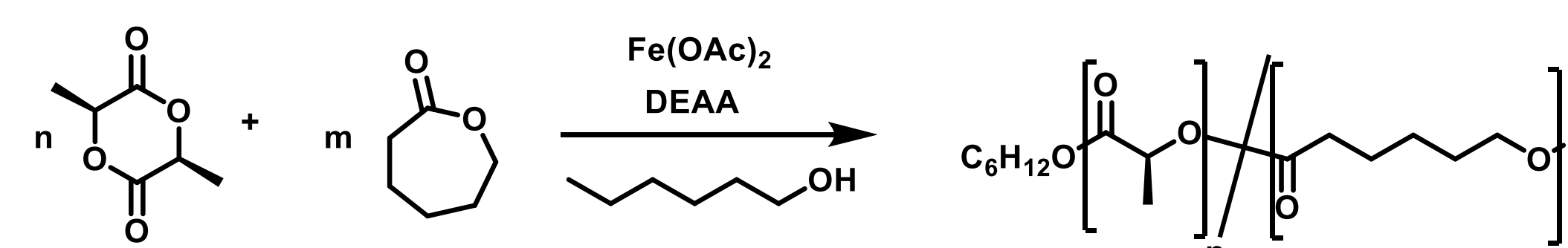
Target mass: 15 kg mol<sup>-1</sup>



- optical rotation  $[\alpha]_D$  is a measure of lactide racemisation during reaction
- No racemisation took place except for PLLA-urea

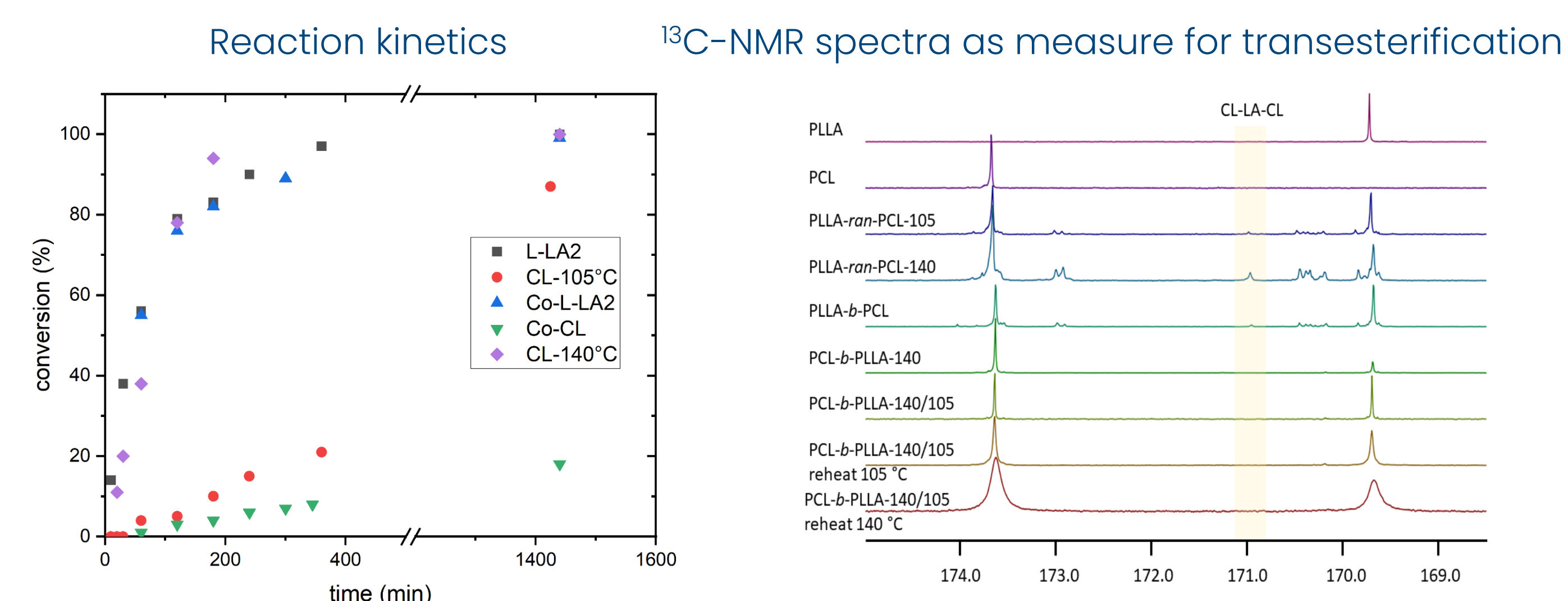
- Ratio of 2n:2n+1 from MALDI spectrum is a measure of transesterification
- Transesterification is fairly low here, but increases with prolonged reaction times

## Copolymers



The ability of the catalyst to achieve different microstructures of PLLA-PCL copolymers was investigated with 1:1 mixtures of monomers. Randomness R can be calculated from the NMR spectra (value between 0 and 1)

Polymer	Reaction time	Temp [°C]	Conv LA [%]	Conv CL [%]	Molar ratio LA:CL	R	$M_n$ (GPC) [g mol <sup>-1</sup> ]	$M_w$ (GPC) [g mol <sup>-1</sup> ]	$\bar{D}$ (GPC)
PLLA- <i>ran</i> -PCL-105	7 d	105	>99	97	45:55	0.20	3300	6400	1.94
PLLA- <i>ran</i> -PCL-140	48 h	140	92	91	42:58	0.30	4000	12900	3.22
PLLA- <i>b</i> -PCL-105	7 d	105	>99	91 <sup>a</sup>	50:50	0.19	2500	7300	2.92
PCL- <i>b</i> -PLLA-140	48 h	140	86 <sup>b</sup>	>99	27:73	0.07	5000	9100	1.82
PCL- <i>b</i> -PLLA-140-105	30 h	140/ 105	80 <sup>c</sup>	97	47:53	0.04	7100	10400	1.47



- Due to the difference in reactivity, the randomness R of the copolymers is low
- Highly blocky copolymers can be achieved
- Transesterification happens only when CL monomer is present during chain growth

## Conclusions

- $\text{Fe}(\text{OAc})_2$  with small, cheap tertiary amides is a good catalyst for the synthesis of PLLA of low dispersity up to 25 kg mol<sup>-1</sup> in the melt
- Racemisation of lactide is avoided
- PCL-PLLA blockcopolymers of very low randomness can be produced