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# **Multi- and Heterometallic ProPhenol Catalysts for Cyclic Ester Ring-Opening Polymerisation**

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Doctor of Philosophy  
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*For my dearest little one, Yuuki-chan.*

(although I wouldn't expect you to read this thesis the first thing when you come out)

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*Alhamdulillahilladhi bi ni'matihi tatimmussolihat.*

## Lay Summary

Increasing societal reliance on plastic has led to the continuous growth of petroleum-based plastic production, which raises significant environmental and economic concerns. To address the detrimental issues stemming from plastic overconsumption, extensive research efforts have focused on the development and circular use of renewable and biodegradable alternatives to conventional fossil-based plastics. Biodegradable polyesters, such as poly(lactic acid) and poly( $\epsilon$ -caprolactone), are of high value and importance in many commodity applications. These polymers can be produced by the polymerisation of compounds called cyclic esters. These reactions are performed with the aid of catalysts that allow reactions to be efficiently carried out at a faster rate and under milder reaction conditions. Some of the best-performing catalysts are metal-based, with examples spanning across almost the entire periodic table. More recent catalyst development has focused on systems where two or more metals work cooperatively, showcasing better catalytic performance than the single metal analogues. The work in this thesis therefore aims to understand and explore the origin of enhanced catalyst performance stemming from the interaction(s) of multiple different metal centres within a catalyst.

## Abstract

Plastic is an integral part of daily life, utilised in many sectors spanning from domestic to industrial purposes. However, high societal reliance on plastic products as well as the durability of plastic have led to rising environmental concerns. This has prompted urgent research into sustainable and biodegradable alternatives. Polymers such as aliphatic polyesters (*i.e.* poly(lactic acid) (PLA), poly( $\epsilon$ -caprolactone) (PCL) and poly( $\delta$ -valerolactone) (PVL)) are attractive candidates owing to their desirable properties, biodegradability and biocompatibility. The ring-opening polymerisation (ROP) of cyclic esters is an efficient route for producing well-controlled biodegradable polyesters, typically performed using organometallic catalysts. Heterometallic cooperativity is of key interest in polymerisation catalysis, with many heterometallic complexes outperforming the homometallic counterparts in terms of activity and control. In heterometallic systems, synergistic interactions between different metals depend on the position of proximate metals within a ligand scaffold; this plays a significant role in monomer coordination and the subsequent ring-opening process. The work in this thesis aims to exploit and understand the synergistic effects stemming from heterometal interactions in the ring-opening (co)polymerisation of cyclic esters, for multimetallic complexes based on the ProPhenol ligand scaffold.

While heterometallic cooperativity has delivered enhanced catalyst performance in the ROP of cyclic esters, so far this has been almost exclusively limited to their homopolymerisation. The work in Chapter 2 outlines heterobimetallic cooperativity and trade-offs in the synthesis of PCL-PLA block copolymers, comparing the catalyst performance and control to the homobimetallic analogue. Specifically, this study shows that heterometallic Mg/Zn and Ca/Zn catalysts, based on the ProPhenol ligand, show significant activity enhancements in the synthesis of PCL-*b*-PLA diblock copolymers, outperforming the Zn/Zn analogue with the activity order Ca/Zn > Mg/Zn > Zn/Zn. The excellent activity accompanies good (co)polymerisation control, generating well-defined PCL-*b*-PLA block copolymer structures. Interestingly, the catalyst activity order is completely reversed upon the sequential addition of  $\epsilon$ -caprolactone as the third monomer in an attempt to generate PCL-PLA-PCL triblock copolymers. This demonstrates that the features of heterometallic “ate” catalysts that boost polymerisation activity can also enhance competitive undesired transesterification processes. Overall, this chapter highlights the importance of the choice of the metal combination to generate well-defined block copolymer microstructures, especially when targeting multi-block copolymer structures.

Heterometallic complexes can be accessed through several different synthetic pathways, including transmetallation and sequential deprotonation routes. Many s-block metals exhibit high catalyst activities in polymerisation owing to the Lewis acidity of the metal (facilitating monomer coordination), yet often give poor control. In contrast, catalysts based on earth-abundant aluminium often show good polymerisation control yet lower activities. Heterometallic catalysts have the potential to combine these features to deliver improved performance. Chapter 3 describes synthetic approaches to prepare novel heterotrimetallic ProPhenol complexes based on inexpensive and low-toxicity metals, by combining an alkali metal (Na or K) with two aluminium centres ( $\text{AlMe}_3$ ,  $\text{AlEt}_3$  or  $\text{Al}^i\text{Bu}_3$ ). These complexes were characterised in the solution-state by NMR spectroscopy, and in the solid-state *via* single crystal X-ray diffraction. The molecular structures provide insight into the metal coordination geometry and different bonding modes for the two Al centres; where one Al centre sits in a 'pocket' within the ligand scaffold, while the other is coordinated through a dative bond to  $\text{AlR}_3$  from a benzylic oxygen of the ProPhenol ligand.

Chapter 4 builds upon the work in Chapter 3, and probes the reactivity of these  $\text{Na/Al}_2$  complexes through NMR studies. The abstraction of the datively bound  $\text{AlR}_3$  unit was investigated as a route to form bimetallic mono/trivalent Na/Al analogues of the di/divalent Mg/Zn and Ca/Zn complexes reported in Chapter 2. However, the  $\text{AlR}_3$  group persisted in the presence of a range of Lewis donors. Therefore, heterotrimetallic  $\text{Na/Al}_2$  complexes were directly tested for the ROP of cyclic esters using benzyl alcohol as an initiator, as aluminium analogues of a previously reported  $\text{Na/Zn}_2$  ProPhenol complex. PCL, PLA and PVL were successfully generated with good control, albeit at relatively low activity rates ( $0.068\text{ h}^{-1}$ ,  $0.053\text{ h}^{-1}$  and  $0.195\text{ h}^{-1}$ ). Notably, reactivity studies of the heterotrimetallic  $\text{Na/Al}_2$  complex with Lewis base additives provided insight into the different roles of sodium and aluminium metals in cyclic ester polymerisation.

## Publications

### Publications in Peer Reviewed Journals

- [1] M. Abdul Rahman, T. J. Neal and J. A. Garden, *Chem. Commun.*, 2024, **60**, 5530–5533.
- [2] P. A. Lowy, M. Abdul Rahman, G. S. Nichol, C. A. Morrison and J. A. Garden, *ChemCatChem*, 2024, **16**, e202301338.
- [3] E. Fazekas, P. A. Lowy, M. Abdul Rahman, A. Lykkeberg, Y. Zhou, R. Chambenahalli and J. A. Garden, *Chem. Soc. Rev.*, 2022, **51**, 8793–8814.
- [4] E. Fazekas, P. A. Lowy, M. Abdul Rahman and J. A. Garden, in *Comprehensive Organometallic Chemistry IV*, Elsevier, 2022, pp. 193–304.

### Conference Presentations (Oral)

- [1] M. Abdul Rahman, T. J. Neal, J. A. Garden, A Game of Tug-of-War: Balancing Enhanced Activity and Control in Multimetallic Complexes for Block Copolymer Synthesis, *IUPAC Macro 2024 50<sup>th</sup> World Conference*, University of Warwick, Warwick, UK, **2024**.
- [2] M. Abdul Rahman, J. A. Garden, Heterometallic Alkali Metal/Al ProPhenol Catalysts for the Ring-Opening Polymerisation of Cyclic Esters, *Universities of Scotland Inorganic Chemistry (USIC) Conference*, University of Edinburgh, Edinburgh, UK, **2024**.
- [3] M. Abdul Rahman, J. A. Garden, Heterometallic Alkali Metal/Al ProPhenol Catalysts for the Ring-Opening Polymerisation of Cyclic Esters, *Joseph Black Conference*, University of Edinburgh, Edinburgh, UK, **2024**. Runner-up Oral Presentation Prize.

## Conference Presentations (Poster)

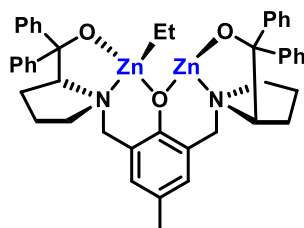
- [1] M. Abdul Rahman, T. J. Neal, J. A. Garden, A Game of Tug-of-War: Balancing Enhanced Activity and Control in Multimetallic Complexes for Block Copolymer Synthesis, *Chemical Science Symposium 2023: Chemistry of Polymers*, The Royal Society of Chemistry, Burlington House, London, UK, **2023**.
- [2] M. Abdul Rahman, T. J. Neal, J. A. Garden, A Game of Tug-of-War: Balancing Enhanced Activity and Control in Multimetallic Complexes for Block Copolymer Synthesis, *Joseph Black Conference*, University of Edinburgh, Edinburgh, UK, **2023**.
- [3] M. Abdul Rahman, T. J. Neal, J. A. Garden, A Game of Tug-of-War: Balancing Enhanced Activity and Control in Multimetallic Complexes for Block Copolymer Synthesis, *EaStCHEM Conference for Early Career Researchers*, Edinburgh, UK, **2023**.
- [4] M. Abdul Rahman, T. J. Neal, J. A. Garden, A Game of Tug-of-War: Balancing Enhanced Activity and Control in Multimetallic Complexes for Block Copolymer Synthesis, *ScotCHEM: Polymer & Soft Materials Conference II*, Edinburgh, UK, **2023**.

## Abbreviations

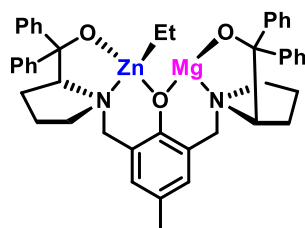
|                         |                                                            |
|-------------------------|------------------------------------------------------------|
| <b>CDCl<sub>3</sub></b> | Deuterated chloroform                                      |
| <b>conc.</b>            | Concentrated                                               |
| <b>conv.</b>            | Conversion                                                 |
| <b>COSY</b>             | Correlation spectroscopy                                   |
| <b>d</b>                | Doublet                                                    |
| <b>Đ</b>                | Dispersity                                                 |
| <b>DOSY</b>             | Diffusion-ordered spectroscopy                             |
| <b>DSC</b>              | Differential scanning calorimetry                          |
| <b>EA</b>               | Elemental analysis                                         |
| <b>equiv.</b>           | Equivalent                                                 |
| <b>Et</b>               | Ethyl                                                      |
| <b>EtOH</b>             | Ethanol                                                    |
| <b>h</b>                | Hour                                                       |
| <b>HMDS</b>             | 1,1,1,3,3,3-hexamethyldisilazide                           |
| <b>HMDS(H)</b>          | 1,1,1,3,3,3-hexamethyldisilazane                           |
| <b>HSQC</b>             | Heteronuclear Single Quantum Correlation                   |
| <b>LA</b>               | Lactide                                                    |
| <b>M</b>                | Molar                                                      |
| <b>m.p.</b>             | Melting point                                              |
| <b>MALDI-ToF</b>        | Matrix assisted laser desorption ionisation-time of flight |
| <b>Me</b>               | Methyl                                                     |
| <b>MeOH</b>             | Methanol                                                   |
| <b>M<sub>n</sub></b>    | Number average molecular weight (molar mass)               |
| <b>M<sub>w</sub></b>    | Weight average molecular weight (molar mass)               |
| <b>Mt</b>               | Million metric ton                                         |
| <b>MW</b>               | Molecular weight                                           |
| <b>NMR</b>              | Nuclear magnetic resonance                                 |
| <b>PCL</b>              | Poly(ε-caprolactone)                                       |
| <b>P<sub>i</sub></b>    | Probability of isotactic enchainment                       |
| <b>P<sub>s</sub></b>    | Probability of syndiotactic enchainment                    |
| <b>PLA</b>              | Poly(lactic acid)                                          |
| <b>ppm</b>              | Parts per million                                          |

|                         |                               |
|-------------------------|-------------------------------|
| <b>q</b>                | Quintet                       |
| <b><i>rac</i></b>       | Racemic                       |
| <b>ROP</b>              | Ring-opening polymerisation   |
| <b>r. t.</b>            | Room temperature              |
| <b>s</b>                | Singlet                       |
| <b>SEC</b>              | Size-exclusion chromatography |
| <b>t</b>                | Triplet                       |
| <b><i>tert</i></b>      | Tertiary                      |
| <b><math>T_g</math></b> | Glass transition temperature  |
| <b>THF</b>              | Tetrahydrofuran               |
| <b><math>T_m</math></b> | Melting temperature           |
| <b>XRD</b>              | X-ray diffraction             |

## Compounds Prepared and/or Investigated within this Thesis

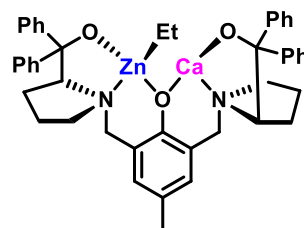


[LZn<sub>2</sub>Et<sub>2</sub>]



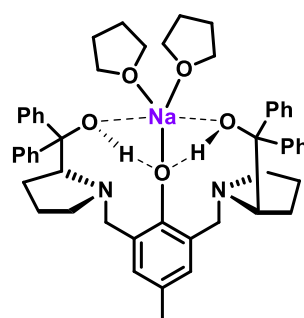
+ 1 HMDSH + 1 THF

[LMgZnEt]

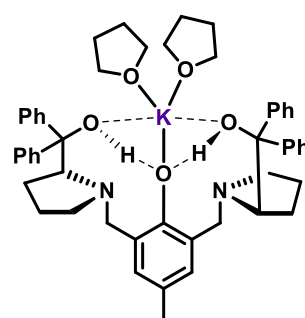


+ 1 HMDSH + 1 THF

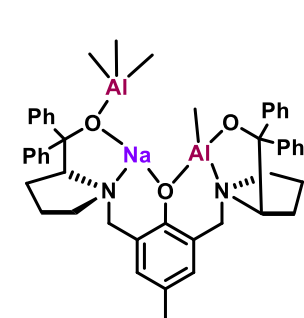
[LCaZnEt]



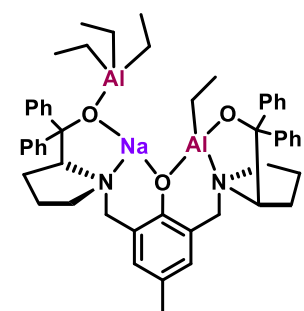
[LH<sub>2</sub>Na(THF)<sub>2</sub>]



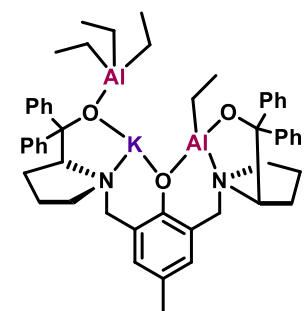
[LH<sub>2</sub>K(THF)<sub>2</sub>]



[LNaAlMe·AlMe<sub>3</sub>]



[LNaAlEt·AlEt<sub>3</sub>]



[LKAIEt·AlEt<sub>3</sub>]

## Table of Contents

|                                                                                                                                                                            |      |
|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------|
| Declaration .....                                                                                                                                                          | ii   |
| Acknowledgements.....                                                                                                                                                      | iv   |
| Lay Summary .....                                                                                                                                                          | vi   |
| Abstract .....                                                                                                                                                             | vii  |
| Publications .....                                                                                                                                                         | ix   |
| Publications in Peer Reviewed Journals .....                                                                                                                               | ix   |
| Conference Presentations (Oral) .....                                                                                                                                      | ix   |
| Conference Presentations (Poster) .....                                                                                                                                    | x    |
| Abbreviations .....                                                                                                                                                        | xi   |
| Compounds Prepared and/or Investigated within this Thesis .....                                                                                                            | xiii |
| <b>Chapter 1</b> General Introduction to Organometallic Catalyst Development for Cyclic Ester Ring-Opening Polymerisation.....                                             | 1    |
| 1.1 Plastic: A Balance of Potential and Problem.....                                                                                                                       | 2    |
| 1.2 Biodegradable Polymers: A Promising Alternative to Conventional Plastics.....                                                                                          | 3    |
| 1.2.1 Poly(lactic acid).....                                                                                                                                               | 3    |
| 1.2.2 Poly( $\epsilon$ -caprolactone).....                                                                                                                                 | 5    |
| 1.3 Ring-Opening Polymerisation: An Efficient Route to Prepare Aliphatic Polyesters.....                                                                                   | 6    |
| 1.3.1 The Mechanisms of Ring-Opening Polymerisation using Organometallic Catalysts .....                                                                                   | 6    |
| 1.3.2 Polymer Microstructures and Common Side Reactions in the ROP of Cyclic Esters .....                                                                                  | 8    |
| 1.4 Development of Organometallic Catalysts for Cyclic Ester ROP .....                                                                                                     | 11   |
| 1.4.1 Highly Efficient Monometallic Catalysts in the ROP of Cyclic Esters .....                                                                                            | 12   |
| 1.4.2 Multi- and Heterometallic Catalysts in the ROP of Cyclic Esters .....                                                                                                | 17   |
| 1.4.3 Organometallic ProPhenol Complexes in Cyclic Ester Polymerisation .....                                                                                              | 26   |
| 1.5 Aims of the PhD Research.....                                                                                                                                          | 29   |
| <b>Chapter 2</b> Heterometallic Cooperativity in Block Copolymer Synthesis: Balancing Activity and Control to Deliver Well-Defined PCL- <i>block</i> -PLA Copolymers ..... | 31   |
| 2.1 Overview.....                                                                                                                                                          | 32   |
| 2.2 Introduction .....                                                                                                                                                     | 33   |
| 2.3 Results and discussion .....                                                                                                                                           | 36   |
| 2.3.1 Synthesis and Characterisation of PCL- <i>block</i> -PLA Copolymer.....                                                                                              | 36   |
| 2.3.2 Accessing Higher Order PCL-PLA Block Copolymers with Multimetallic ProPhenol Complexes .....                                                                         | 44   |
| 2.3.3 Cooperativity vs Competition in Heterometallic Systems.....                                                                                                          | 48   |
| 2.4 Conclusions .....                                                                                                                                                      | 51   |

|                  |                                                                                                                                                                                                                                  |           |
|------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------|
| 2.5              | Future Work .....                                                                                                                                                                                                                | 52        |
| 2.6              | Experimental .....                                                                                                                                                                                                               | 53        |
| 2.6.1            | Synthesis of Complexes <b>[LZn<sub>2</sub>Et]</b> , <b>[LMgZnEt]</b> and <b>[LCaZnEt]</b> .....                                                                                                                                  | 53        |
| 2.6.1.1          | Complex <b>[LZn<sub>2</sub>Et]</b> .....                                                                                                                                                                                         | 53        |
| 2.6.1.2          | Complex <b>[LMgZnEt]</b> .....                                                                                                                                                                                                   | 53        |
| 2.6.1.3          | Complex <b>[LCaZnEt]</b> .....                                                                                                                                                                                                   | 54        |
| 2.6.2            | General experimental procedure for the synthesis of PCL .....                                                                                                                                                                    | 55        |
| 2.6.3            | General experimental procedure for the synthesis of PCL- <i>b</i> -PL(L)A .....                                                                                                                                                  | 55        |
| 2.6.4            | General experimental procedure for the synthesis of PCL-PLA-PCL copolymer .....                                                                                                                                                  | 55        |
| <b>Chapter 3</b> | <b>The Synthesis and Characterisation of Structurally Well-Defined Alkali Metal/Aluminium Heterotrimetallic ProPhenol Complexes .....</b>                                                                                        | <b>57</b> |
| 3.1              | Overview .....                                                                                                                                                                                                                   | 58        |
| 3.2              | Introduction .....                                                                                                                                                                                                               | 59        |
| 3.3              | Results and Discussion.....                                                                                                                                                                                                      | 62        |
| 3.3.1            | Synthesis of Novel Heterotrimetallic Alkali Metal (AM)/Aluminium ProPhenol Complexes .....                                                                                                                                       | 62        |
| 3.3.2            | Structural Analysis of Heterotrimetallic Alkali Metal/Aluminium Complexes .....                                                                                                                                                  | 66        |
| 3.3.3            | Solution-State Analysis of Heterotrimetallic Alkali Metal/Aluminium Complexes.....                                                                                                                                               | 74        |
| 3.3.3.1          | Comparison between AM/Zn <sub>2</sub> ProPhenol Complex with AM/Al <sub>2</sub> ProPhenol Complex ..                                                                                                                             | 79        |
| 3.4              | Conclusions .....                                                                                                                                                                                                                | 82        |
| 3.5              | Future Work .....                                                                                                                                                                                                                | 83        |
| 3.6              | Experimental .....                                                                                                                                                                                                               | 85        |
| 3.6.1            | Synthesis of Complexes <b>[LH<sub>2</sub>Na(THF)<sub>2</sub>]</b> , <b>[LH<sub>2</sub>K(THF)<sub>2</sub>]</b> , <b>[LNaAlMe·AlMe<sub>3</sub>]</b> , <b>[LNaAlEt·AlEt<sub>3</sub>]</b> and <b>[LKAIEt·AlEt<sub>3</sub>]</b> ..... | 85        |
| 3.6.1.1          | Complex <b>[LH<sub>2</sub>Na(THF)<sub>2</sub>]</b> .....                                                                                                                                                                         | 85        |
| 3.6.1.2          | Complex <b>[LH<sub>2</sub>K(THF)<sub>2</sub>]</b> .....                                                                                                                                                                          | 85        |
| 3.6.1.3          | Complex <b>[LNaAlMe·AlMe<sub>3</sub>]</b> .....                                                                                                                                                                                  | 86        |
| 3.6.1.4          | Complex <b>[LNaAlEt·AlEt<sub>3</sub>]</b> .....                                                                                                                                                                                  | 87        |
| 3.6.1.5          | Complex <b>[LKAIEt·AlEt<sub>3</sub>]</b> .....                                                                                                                                                                                   | 88        |
| 3.6.2            | X-ray Crystallographic Data and Refinement Details.....                                                                                                                                                                          | 89        |
| <b>Chapter 4</b> | <b>Reactivity Studies of Heterotrimetallic Na/Al ProPhenol Complexes .....</b>                                                                                                                                                   | <b>90</b> |
| 4.1              | Overview .....                                                                                                                                                                                                                   | 91        |
| 4.2              | Introduction .....                                                                                                                                                                                                               | 92        |
| 4.3              | Results and Discussion.....                                                                                                                                                                                                      | 94        |
| 4.3.1            | Reactivity Studies of <b>[LNaAlEt·AlEt<sub>3</sub>]</b> with Different Lewis Bases .....                                                                                                                                         | 94        |
| 4.3.1.1          | Reaction of <b>[LNaAlEt·AlEt<sub>3</sub>]</b> with TEPO .....                                                                                                                                                                    | 94        |

|                  |                                                                                                                                                                                 |     |
|------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----|
| 4.3.1.2          | Reaction of [LNaAlEt·AlEt <sub>3</sub> ] with DMAP.....                                                                                                                         | 97  |
| 4.3.1.3          | Reaction of [LNaAlEt·AlEt <sub>3</sub> ] with PMDETA.....                                                                                                                       | 100 |
| 4.3.2            | Reactivity Insights: <i>In Situ</i> Alcoholysis of [LNaAlEt·AlEt <sub>3</sub> ] Complex .....                                                                                   | 102 |
| 4.3.3            | Reactivity of [LNaAlEt·AlEt <sub>3</sub> ] in the Polymerisation of CL, LA and VL.....                                                                                          | 108 |
| 4.3.3.1          | Synthesis of PCL- <i>block</i> -PLA Copolymer with [LNaAlEt·AlEt <sub>3</sub> ].....                                                                                            | 115 |
| 4.4              | Conclusion.....                                                                                                                                                                 | 119 |
| 4.5              | Future Work.....                                                                                                                                                                | 120 |
| 4.6              | Experimental .....                                                                                                                                                              | 121 |
| 4.6.1            | NMR-scale reaction of [LNaAlEt·AlEt <sub>3</sub> ] complex with triethylphosphine oxide (TEPO), 4-dimethylamido pyridine (DMAP) or pentamethyldiethylenetriamine (PMDETA) ..... | 121 |
| 4.6.1.1          | Large-scale reaction of [LNaAlEt·AlEt <sub>3</sub> ] complex with triethylphosphine oxide (TEPO).....                                                                           | 121 |
| 4.6.2            | General experimental procedure for the synthesis of PCL, PLA and PVL .....                                                                                                      | 121 |
| 4.6.3            | Experimental procedure for the synthesis of PCL- <i>b</i> -PLA .....                                                                                                            | 122 |
| 4.6.4            | Experimental procedure for the synthesis of PCL-PLA-PCL copolymer .....                                                                                                         | 122 |
| <b>Chapter 5</b> | An Outlook n Multi- and Heterometallic ProPhenol Catalysts for Polymer Synthesis .                                                                                              | 123 |
| <b>Chapter 6</b> | General Experimental Techniques.....                                                                                                                                            | 127 |
| 6.1              | Materials.....                                                                                                                                                                  | 128 |
| 6.2              | Manipulation of Air- and Moisture-sensitive Compounds .....                                                                                                                     | 128 |
| 6.2.1            | Schlenk Techniques.....                                                                                                                                                         | 128 |
| 6.2.2            | Glove Box .....                                                                                                                                                                 | 129 |
| 6.3              | Instrumentation for Characterisation .....                                                                                                                                      | 129 |
| 6.3.1            | Nuclear Magnetic Resonance (NMR) Spectroscopy .....                                                                                                                             | 129 |
| 6.3.1.1          | Preparation of Diffusion Order Spectroscopy (DOSY) External Calibration Plots.....                                                                                              | 130 |
| 6.3.2            | Mass Spectrometry.....                                                                                                                                                          | 136 |
| 6.3.3            | Elemental Analysis.....                                                                                                                                                         | 136 |
| 6.3.4            | X-Ray Diffraction.....                                                                                                                                                          | 136 |
| 6.3.5            | Size-Exclusion Chromatography .....                                                                                                                                             | 136 |
| 6.3.6            | Differential Scanning Calorimetry.....                                                                                                                                          | 137 |
| 6.4              | Determination of Percentage Monomer Conversions .....                                                                                                                           | 138 |
| 6.5              | Determination of Polymer Tacticity .....                                                                                                                                        | 138 |
| 6.6              | Calculations for Randomness Factor, <i>R</i> , and Number-Average Sequence Length, <i>I</i> , in PCL- <i>b</i> -PLA Copolymer Structure .....                                   | 140 |
| <b>Chapter 7</b> | Bibliography.....                                                                                                                                                               | 142 |

# **Chapter 1**

## **General Introduction to Organometallic Catalyst Development for Cyclic Ester Ring-Opening Polymerisation**

## 1.1 Plastic: A Balance of Potential and Problem

Plastic is an integral part of daily life, with utilisation in many sectors spanning from domestic to industrial purposes. The demand for virgin plastic products has skyrocketed over the past half century. Population growth and the rise in per capita incomes have contributed to a steep increase in plastic consumption, with global cumulative manufacture of primary plastic being forecast to reach 34 billion tonnes by 2050.<sup>1,2</sup> Material versatility, high durability and substantial economic benefits from its production are key influences for high dependency on plastics, more than other commodities, including steel and aluminium.<sup>3-5</sup> Plastic resins are utilised widely for multiple purposes such as in packaging, transportation, building and construction as well as medical equipment and supplies. For instance, the on-set of the Coronavirus 2019 (COVID-19) global pandemic led to a significant decrease of global economic activity in 2020, accompanied by a high demand for certain plastics in the healthcare sector due to the soaring need for personal protective equipment (PPE) including surgical face masks and single-use medical tools.<sup>6,7</sup> Additionally, the growth of e-commerce (online retail) in recent years and a shift from restaurant dine-ins to food take-away and deliveries have raised the demand for single-use plastic packaging.<sup>8</sup> Despite the extensive range of functional properties delivered by plastics, which leads to their significant role in general life, the vast majority of plastics are made of monomers derived from non-renewable petrochemical feedstocks such as ethylene and propylene.<sup>1</sup>

The increasing reliance on plastics is detrimental in many ways, and has come with a significant environmental price. Therefore, efficient recycling management post-consumption is a pressing necessity to treat these polymeric materials. A study revealed that in the span of 55 years (1950 – 2005), 8 300 million metric tons (Mt) of virgin plastics were manufactured, from which approximately 6 300 Mt of plastic waste was produced.<sup>1</sup> Worryingly, a 2018 statistic showed that less than 10% of plastics produced are being recycled.<sup>2</sup> On top of this, although there has been a significant global increase of secondary plastic production (*i.e.* recycled products), from 6.8 Mt in 2000 to 29.1 Mt in 2019, this quantity only really constitutes 6% of the entire plastic production.<sup>3,5</sup> In addition, rising concerns over the depletion of fossil-based feedstocks in recent decades have prompted urgent research into the developments of sustainable and biodegradable polymers as potential plastic alternatives to address problems arising from overflowing post-consumer plastic waste.<sup>9,10</sup>

## 1.2 Biodegradable Polymers: A Promising Alternative to Conventional Plastics

Polymers such as aliphatic polyesters (*e.g.* poly(lactic acid) (PLA) and poly( $\epsilon$ -caprolactone) (PCL)) and polycarbonates (*e.g.* poly(trimethylene carbonate)) are attractive candidates owing to their desirable properties, biodegradability and biocompatibility.<sup>11,12</sup> However, despite gaining considerable interest, the commercialisation of biodegradable polymers is challenged by the relatively high production cost and inferior properties compared to conventional plastics. Therefore, advances on the design of biodegradable materials with improved and/or tailored properties is necessary to produce comparable materials of high performance as promising candidates to replace conventional plastics. This development should come hand in hand with increasing the efficiency of biodegradable polymer production to ensure that these polymers are able to economically compete with the current industrial plastic manufacture.

### 1.2.1 Poly(lactic acid)

PLA is a versatile fully bio-derived and biodegradable aliphatic polyester, generally synthesised *via* the ring-opening polymerisation (ROP) of the cyclic dimer of lactic acid, lactide (LA). Currently, the industrial production of LA is mainly achieved *via* the microbial fermentation of carbohydrates.<sup>13</sup> Lactic acid (2-hydroxypropanoic acid), exists in two enantiomeric configurations, L(+)- and D(-)-lactic acid. Due to the chirality of lactic acid, lactide is present in three different forms: the optically active stereoisomers (L,L-LA (*S,S*) and D,D-LA (*R,R*)), as well as the optically inactive L,D-lactide isomer (known as *meso*-lactide) (Figure 1.1, left). *Rac*-LA (also known as D,L-LA) is a racemic (50:50) mixture of the enantiopure isomers. The mechanical and physical properties of polymers, such as melting point, tensile strength, and stiffness, are highly controlled by polymer crystallinity, which in turn depends on the stereochemistry of the polymer backbone, known as the tacticity (Figure 1.1; refer to [Section 1.3.2](#) for further details). For instance, enriched isotacticity or syndiotacticity increases the crystallinity of PLA owing to a more efficient chain packing.<sup>14</sup> Poly-L-lactic acid (PLLA) and poly-D-lactic acid (PDLA) are semi-crystalline, while poly-D,L-lactic acid (PDLLA) and poly(*meso*-lactic acid) are amorphous when there is no control over the order of insertion of the monomers into the polymer chain.<sup>15–17</sup> The bulk properties of PLA vary depending on the different microstructures of PLA, affecting the polymer thermal and mechanical properties (see [Section 1.3.2](#)). Therefore, controlling the L/D-LA ratio is key to tuning the material properties of PLA for specific applications.

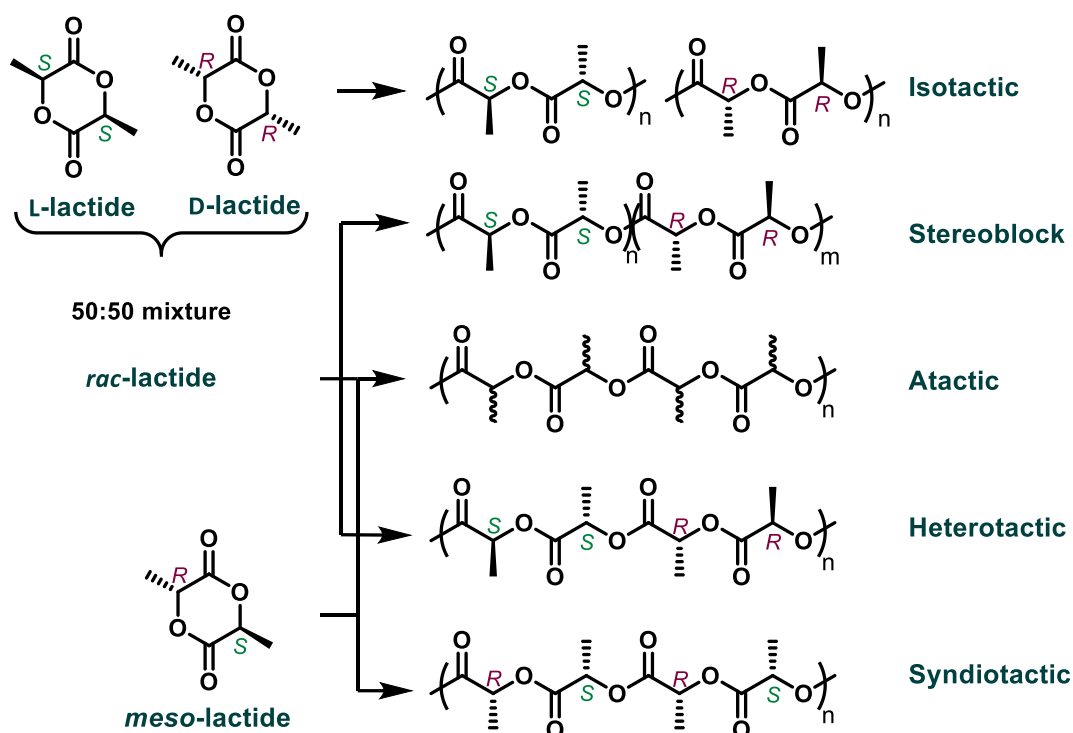


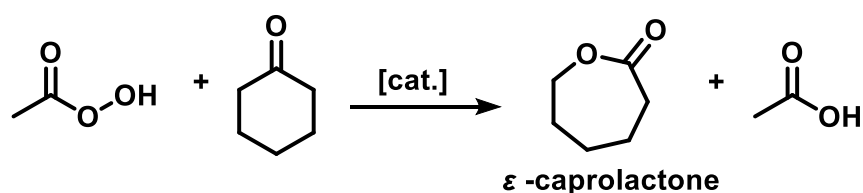
**Figure 1.1** Some possible microstructures in PLA chain derived from ROP of different LA isomers.<sup>18,19</sup>

Although PLA homopolymer exhibits relatively good mechanical and thermal properties, its commercial use is limited due to its hydrophobicity, brittleness, high crystallinity and thermal instability.<sup>15,20</sup> These drawbacks have prompted extensive research into various PLA modifications to enhance the material properties, thus expanding its potential applications. Among the common modification techniques include copolymerisation with other monomer units, the preparation of PLA composites (for instance through the addition of natural fibres) or the addition of suitable plasticisers to enhance PLA flexibility and processability.<sup>15,21</sup>

PLA degradation can occur through the simple hydrolysis of ester bonds in the polymer backbone. It is worth noting that the degree and rate of PLA degradation are dependent on several variables, such as the polymer structure and size, the ratio of stereoisomers as well as the temperature of hydrolysis. At temperatures beyond 200 °C, PLA undergoes thermal degradation as well as hydrolysis, lactide reformation, oxidative chain scission and transesterification reactions.<sup>20</sup> Interestingly, the decomposition of PLA into carbon dioxide and water in an industrial composting environment (*i.e.* temperature above 50 °C) takes approximately between six months and two years, in comparison to 500 to 1 000 years for conventional plastics.<sup>22,23</sup> The 'closed-loop' lifecycle and impressive biodegradability render PLA as part of the potential economic and environmental solutions for the current issues revolving conventional plastic.

### 1.2.2 Poly( $\epsilon$ -caprolactone)

Poly( $\epsilon$ -caprolactone) (PCL) is one of the earliest synthetic polyesters, first discovered by van Natta and co-workers in the early 1930s through the ROP of  $\epsilon$ -caprolactone (CL). Industrially, the CL monomer unit is derived from cyclohexanone oxidation using peracetic acid in the presence of catalyst or initiator (Scheme 1.1).



**Scheme 1.1** Industrial production of  $\epsilon$ -caprolactone at Solvay.

PCL is widely recognised for its biodegradability, impressive mechanical properties and miscibility with a wide range of other polymers (such as poly(vinyl chloride) and poly(bisphenol-A)).<sup>24–26</sup> The molecular weight and crystallinity of PCL influence the mechanical, physical and thermal properties. PCL is a semi-crystalline biocompatible polymer with an exceptional blend-compatibility, which has further attracted research interest in biomedical fields, with applications in tissue engineering and drug delivery systems.<sup>27–29</sup>

The biodegradation of PCL takes several months to several years (typically 2 – 4 years).<sup>9,24</sup> The relatively slow degradation rate of PCL, compared to other polyesters such as PLA and poly(glycolide) (PGA), is attributed to the hydrophobic nature coupled with high crystallinity and olefinic character of PCL.<sup>30</sup> PCL can undergo complete biodegradation in the presence of a wide range of microbes.<sup>9</sup> The biodegradability depends on the polymer structure as well as local environmental conditions and driving forces such as enzymes and hydrolysis of the aliphatic ester linkages. It is noteworthy that enzymatic PCL degradation increases the rate of decomposition; however some studies suggest that this can only occur in the environment but not *in vivo*.<sup>31,32</sup> Generally, the amorphous phase in the PCL structure would undergo initial degradation, consequently extending the degree of polymer crystallinity while keeping the molecular weight constant. Subsequently, ester bonds are cleaved, leading to the loss of polymer mass.<sup>24</sup> As with PLA, the applications of PCL homopolymers are limited, in this case due to the hydrophobicity and poorly controlled biological interactions.<sup>33</sup> The material properties and biodegradability, as well as the rate of *in vivo* PCL hydrolysis can, however, be improved and modified by introducing functionality to CL to produce functionalised PCL or through PCL copolymerisation with other monomers, such as LA.<sup>27,29,34</sup>

## 1.3 Ring-Opening Polymerisation: An Efficient Route to Prepare Aliphatic Polyesters

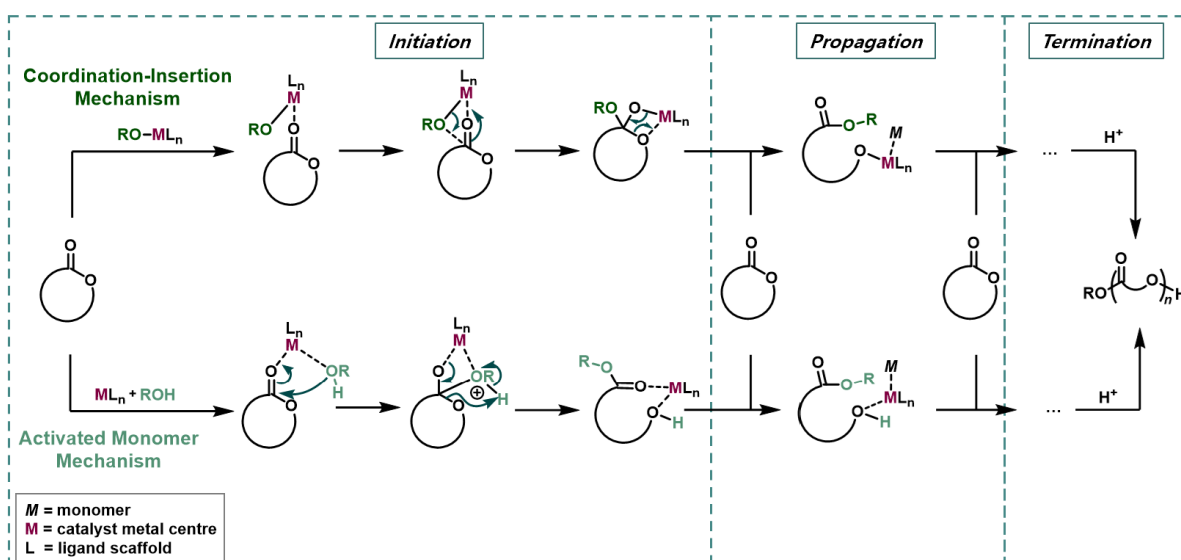
The synthesis of aliphatic polyesters can be efficiently achieved through the ring-opening polymerisation (ROP) of cyclic ester (lactone) monomers, a reaction driven by the relief of ring strain.<sup>35</sup> ROP is a chain-growth polymerisation where one end of the growing polymer chain is active for the insertion of new monomer units. ROP is an attractive and efficient synthetic route for producing polyesters with narrow dispersities, high molecular weight and polymer end-group fidelity through improved control over the resultant polymer molecular structure.<sup>36</sup> Unlike the alternative traditional diol/diacid polycondensation reaction, which generates by-products (*e.g.* water and alcohols) and often requires extreme reaction conditions (*i.e.*  $T \geq 150\text{ }^{\circ}\text{C}$ , prolonged reaction time), ROP generally operates under milder reaction conditions and avoids the formation of low molecular weight by-products.<sup>37</sup> Furthermore, and especially relevant for LA, ROP allows control over the order of monomer insertion into polymer chain, enabling the alteration of PLA backbone stereochemistry and subsequently the polymer material properties (refer to [Section 1.2.1](#)).<sup>36</sup> Owing to the high polymerisation selectivity and impressive control, ROP has been widely employed in industrial-scale production of various aliphatic polyesters, and continues to garner interest in the area of polymerisation catalysis.<sup>38,39</sup>

Most industrial chemical processes proceed with the aid of catalytic systems which provide an alternative lower activation energy pathway for chemical reactions. This enables reactions to be performed efficiently under milder practical conditions at a faster rate. Catalyst development for ROP has been expanding over many decades, ranging from enzymatic<sup>40</sup> and organic<sup>41–43</sup> to organometallic<sup>44</sup> catalysts. Organometallic catalysis for ROP is of particular interest due to their relatively high efficiency (*i.e.* low catalyst loading with excellent turnover frequencies (TOF)), generating polymers with high molecular weights and monomer conversions. However, most organometallic catalysts that exhibit impressive performance are also air- and moisture-sensitive, consequently hampering the application for large-scale industrial syntheses. There has been a rapid evolution in the research area of organometallic catalysts supported by various ligand designs and synthesis, incorporating earth-abundant metals with low-toxicity and improved air and moisture tolerance.

### 1.3.1 The Mechanisms of Ring-Opening Polymerisation using Organometallic Catalysts

Organometallic catalysts are usually composed of a Lewis acidic metal (electron pair acceptor) with a nucleophilic moiety acting as an initiating group (*i.e.* alkyl, alkoxide or halide), embedded within a

ligand scaffold. The ROP of cyclic esters using organometallic catalysts commonly proceeds *via* a coordination-insertion mechanism (Scheme 1.2, top). Through the coordination-insertion route, the polymerisation is initiated by a Lewis basic monomer (electron pair donor) coordinating to the Lewis acidic metal centre through a dative interaction. This leads to subsequent activation of the carbonyl group for nucleophilic attack, prompting the ring-opening of the cyclic ester unit through an acyl-oxygen cleavage. In the coordination-insertion pathway, the nucleophile is typically a metal-alkoxide group, either isolated or formed *in situ* through alcoholysis of a metal-alkyl precursor. The propagation step involves coordination and insertion of subsequent monomers into the polymer chain, generating new metal-alkoxide units for further monomer insertion.



**Scheme 1.2** The ROP of cyclic esters through a proposed coordination-insertion (top) or activated monomer (bottom) mechanism, using a monometallic catalyst.<sup>44</sup> L refers to ligand, M refers to metal centre and OR refers to either the initiating group or the growing polymer chain.

ROP may also operate through an alternative route, the activated monomer mechanism (Scheme 1.2, bottom). Identical to the coordination-insertion mechanism, the monomer is activated through metal coordination, yet in this case, nucleophilic attack occurs from an exogenous protic nucleophile (typically an alcohol or an amine). In both pathways, monomer coordination and nucleophilic attack are key mechanistic steps. Finally, the termination of the polymerisation cycle is triggered through hydrolysis and/or alcoholysis (typically with a protic source, *e.g.* water or acidified methanol).

The mechanism which a catalyst system follows is dependent on the catalyst structure and reactivity.<sup>45</sup> In general, catalysts featuring reactive metal-alkoxide units or functional groups that are susceptible to *in situ* alcoholysis typically follows a coordination-insertion mechanism.<sup>46</sup> On the other hand, catalysts that do not comprise of any co-ligand unit, or bear metal-R bonds that are less or

unreactive towards alcohol would often observe the activated monomer mechanism upon the addition of exogeneous alcohol.

Where the polymer features a stereocentre in the backbone, such as PLA, the stereocontrol of the polymer produced can be generated *via* an enantiomorphic site-controlled or a chain-end-controlled mechanism.<sup>36</sup> Through the enantiomorphic site-controlled pathway, the chirality of the inserted monomer is dictated by the chirality of the metal catalyst, typically influenced by the configuration of the surrounding ligand. On the contrary, in a chain-end-control mechanism, the chirality of a growing polymer chain is determined by the chirality of a propagating chain end connected to the catalyst. This mechanism usually features achiral metal complexes that are more sterically hindered.<sup>14</sup> Therefore, careful choice of the metal and ligand design can tune the metal Lewis acidity and provide accessible sites for efficient monomer coordination and subsequent nucleophilic attack in the ring-opening of monomer units.

### 1.3.2 Polymer Microstructures and Common Side Reactions in the ROP of Cyclic Esters

Since the first use of ROP techniques for the synthesis of aliphatic polyesters, specifically PLA, the quest for well-controlled polymerisation methods has continued to grow.<sup>47</sup> Different approaches have been adopted towards achieving highly controlled polymer structures including the design and alteration of catalyst structures, optimisation of polymerisation conditions and the utilisation of functionalised monomers to control polymerisation activity. Efficient control over properties, including polymer chain length (number average molecular weight,  $M_n$ ) and molecular weight distribution (dispersity,  $\mathcal{D}$ ), is critical to produce polymers with tailored properties for specific applications. These values can be determined through size-exclusion chromatography (SEC) analysis, a technique which allows polymer chains to be separated by the differences of polymer hydrodynamic volume (size).

The manipulation of polymer tacticity is key for altering polymer microstructure, and thus the thermal and mechanical properties (*i.e.* crystallinity, melting point, melting temperature ( $T_m$ ) and glass transition temperature ( $T_g$ )), which in turn dictate polymer performance.<sup>36</sup> Polymer tacticity is determined using NMR spectroscopy and can be quantified through the relative intensity of deconvoluted  $^1\text{H}\{\text{H}\}$  NMR or  $^{13}\text{C}\{\text{H}\}$  NMR signals that are characteristics for diads, triads or tetrads.<sup>18,19</sup> In the case of PLA generated through LA polymerisation, the homonuclear decoupled  $^1\text{H}$  NMR spectrum gives rise to singlet resonances for the methine protons ( $\delta = 5.15 - 5.25$  ppm) (refer to Chapter 6, [Section 6.5](#) for the determination of PLA tacticity). Polymer tacticity can be described as

the probability of isotactic and syndiotactic linkages, expressed as  $P_i$  and  $P_s$ , respectively (where  $0 < P < 1$ ;  $P_i + P_s = 1.00$ ). PLA generated with  $P_i = 1.00$  (and thus  $P_s = 0.00$ ) describes perfectly isotactic PLA,  $P_s = 1.00$  (and  $P_i = 0.00$ ) represents perfectly heterotactic PLA, whereas  $P_i = P_s = 0.50$  describes a perfectly atactic PLA (refer to Figure 1.1, [Section 1.2.1](#)).

Catalyst efficiency in generating well-controlled polyesters also depends on the susceptibility towards undesired side reactions, such as transesterification and chain transfer reactions (Figure 1.2, *vide infra*).<sup>48</sup> Transesterification generally proceeds at a slower rate than the rate of monomer propagation (*i.e.*  $k_{tr} < k_{pr}$ ), yet can outcompete the propagation rate at lower monomer concentration as polymerisation progresses. Intramolecular transesterification can lead to cyclisation and/or the backbiting of M-OR polymer chain end onto an internal carbonyl group, consequently generating cyclic oligomers (Figure 1.2, top). Intermolecular transesterification involves carbonyl attack of a polymer chain from an external M-OR of a growing polymer, resulting in polymer chain redistributions (Figure 1.2, middle).<sup>49</sup> It is important to note that due to chain sequence rearrangements, transesterification can lead to a loss of stereoselectivity (such as with *rac*-LA or *meso*-LA, refer to Figure 1.1 for monomer structure). Overall, transesterification leads to broadening of the molecular weight distribution (broad  $\mathcal{D}$ ). Chain transfer reactions commonly occur in the presence of exogeneous alcohol, involving the transfer of the active part of a propagating polymer chain to another molecule. Consequently, shorter polymer chains are formed, generally resulting in a narrow molecular weight distribution (narrow  $\mathcal{D}$ ).

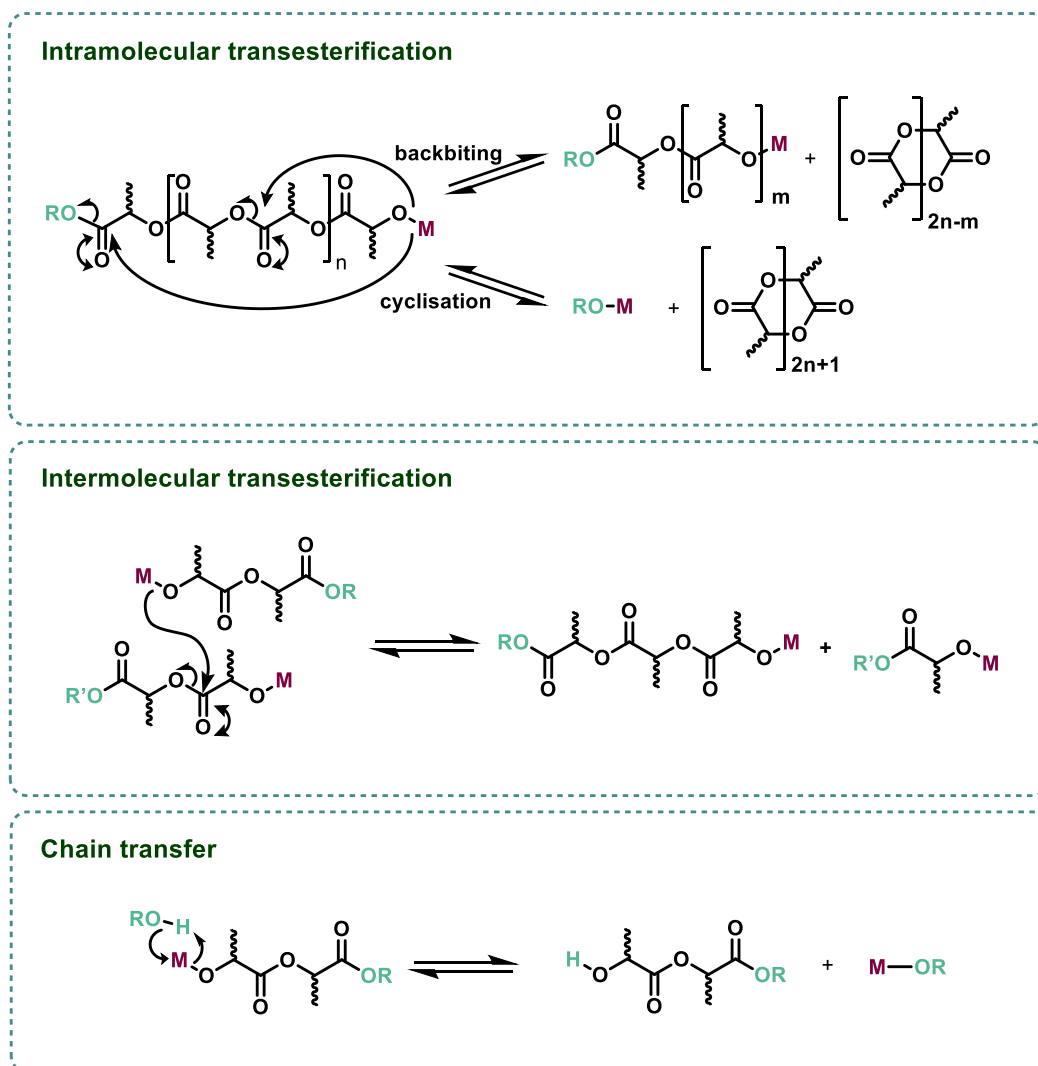


**Figure 1.2** Typical side reactions during the ROP of cyclic esters (shown here is LA). **M** refers to metal centre and OR refers to either the initiating group or the growing polymer chain.

Other than that, a loss of stereocontrol can occur as a result of epimerisation, also known as racemisation (Figure 1.3). Epimerisation can take place in the presence of an electropositive and Brønsted basic metal catalyst, resulting in the change of stereochemistry of a chiral monomer (*i.e.* L-LA) *in situ*.<sup>48,50</sup> Metal compounds with high Brønsted basicity can result in monomer deprotonation. Instead of altering the stereochemistry of a polymer chain, monomers are more susceptible to epimerisation due to the relatively entropically favourable delocalisation of the negative charge in a cyclic molecule.<sup>50,51</sup> Epimerisation results in the change of polymer tacticity (*e.g.* isotactic to atactic, determined by deconvoluted  $^1\text{H}\{\text{H}\}$  NMR analysis), thus altering the mechanical and thermal properties of polymer (determined by thermal analysis techniques, *e.g.* differential scanning calorimetry (DSC)).

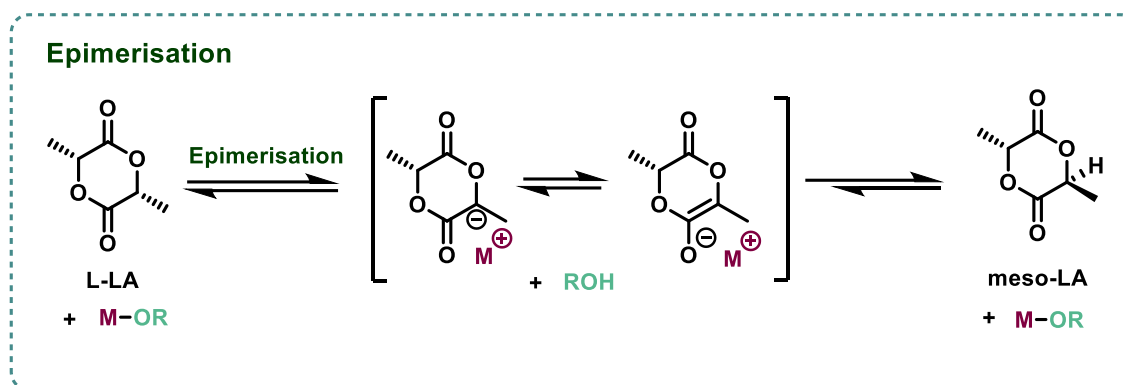


**Figure 1.3** Epimerisation of L-LA resulting in the change of configuration around the stereocentre.

## 1.4 Development of Organometallic Catalysts for Cyclic Ester ROP

Among the earliest metal-based catalysts in cyclic ester ROP is tin(II) bis(2-ethylhexanoate),  $\text{Sn}(\text{Oct})_2$  (**1**, Figure 1.4).<sup>52</sup> To date, **1** is still the standard catalyst used industrially owing to its solubility in many cyclic esters, good stability and catalytic performance.<sup>53</sup> **1** can be used to produce high molecular weight PLA ( $M_n > 100 - 1\,000 \text{ kg mol}^{-1}$ ) *via* the bulk polymerisation of LA, in the presence of an alcohol co-initiator (*e.g.* butanol) to produce PLA with high activity. Cyclic ester polymerisation with **1** is generally proposed to proceed *via* the coordination-insertion mechanism, where the Sn-alkoxide bond generated upon the addition of alcohol co-initiator can undergo monomer coordination and ring-opening (refer to Scheme 1.2).<sup>54,55</sup> However, **1** does not display stereocontrol over the propagating polymer chain, therefore, is not viable for use in the synthesis of some polymers (such as PLA from *rac*-LA) with specifically targeted microstructures. In addition, toxicity issues with **1** have also sparked a drive to explore alternative initiators based on less toxic metals while still maintaining good activity and control over the polymer properties.

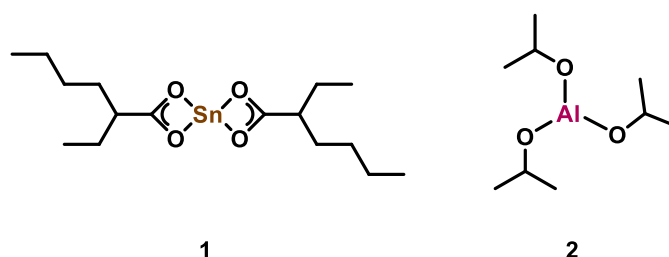


**Figure 1.4** Early examples of cyclic ester ROP catalysts.

Simple Al alkoxides (*i.e.*  $\text{Al}(\text{iOPr})_3$ , **2**, Figure 1.4) have also been reported for the bulk polymerisation of LA.<sup>56,57</sup> However, **2** was found to be inferior to **1** in terms of polymerisation activity, displaying an induction period of several minutes and a remarkably slow propagation rate in LA ROP. This occurrence was suggested to stem from an equilibrium observed between a tetramer and trimer

state of the Al salt, where the trimeric form of **2** is more active than the tetramer.<sup>58</sup> Although a range of Al alkoxides have been developed, as with **1**, no stereocontrol was observed, which limits the synthesis of PLA with good thermal and mechanical properties.

The development of organometallic catalysts exerting a higher degree of stereocontrol has since been realised through the incorporation of ancillary ligands. Efficient catalyst systems that exhibit good activity as well as good selectivity and control are governed by ligand architecture, choice of metal and polymerisation conditions (*e.g.* temperature, solvent, reaction time). Over a period of decades, metals ranging from all across the periodic table have been incorporated in homo- and heterometallic (mixed-metal) catalysts for cyclic ester polymerisation.<sup>48</sup> The review of organometallic catalyst development for the ROP of cyclic esters presented within this thesis is by no means comprehensive as this field is vast and has been extensively reviewed elsewhere.<sup>44,46,59,60</sup> Instead, this introduction focuses mainly on selected examples based on Earth-abundant metals, and also includes several catalysts systems that incorporate more scarce metals but have displayed outstanding catalytic performance.

#### 1.4.1 Highly Efficient Monometallic Catalysts in the ROP of Cyclic Esters

Catalysts based on s-block metals (*i.e.* alkali metals: Li, Na, K; alkaline-earth metals: Mg, Ca, Sr) are desirable due to the high abundance, lack of colour and innocuous nature of the metals.<sup>61,62</sup> In the generation of aliphatic polyesters applied in the biomedical field, these features are especially valuable as traces of metal catalyst in the polymers formed could give detrimental effects to human physiology. Alkali metal complexes often display high polymerisation activity due to the relatively large metal size, which aids monomer coordination, yet they often exhibit poor control.<sup>63</sup> The design of alkali metal complexes featuring an active metal centre sandwiched between bulky electron-rich ligands and crown ethers or cryptand-222 have been adopted to overcome the poor polymerisation control.<sup>63,64</sup> Among alkali metal-based catalysts with a sandwich-type conformation displaying high activity and selectivity is the system introduced by Zhang *et. al.* (Figure 1.5, **3a** and **3b**).<sup>65</sup> Notably, 400 equiv. LA were converted within just 5 min (with 10 equiv. BnOH, -60 °C, THF). The high polymerisation activity was attributed to the use of an electron-rich ligand. The exceptional isoselectivity and polymerisation control ( $P_i \leq 0.86$ ,  $\bar{D} = 1.0 - 1.1$ ) were attributed to steric congestion around the metal centre which prevents undesirable coordination of ester group of the growing polymer chain, consequently minimising transesterification reaction.

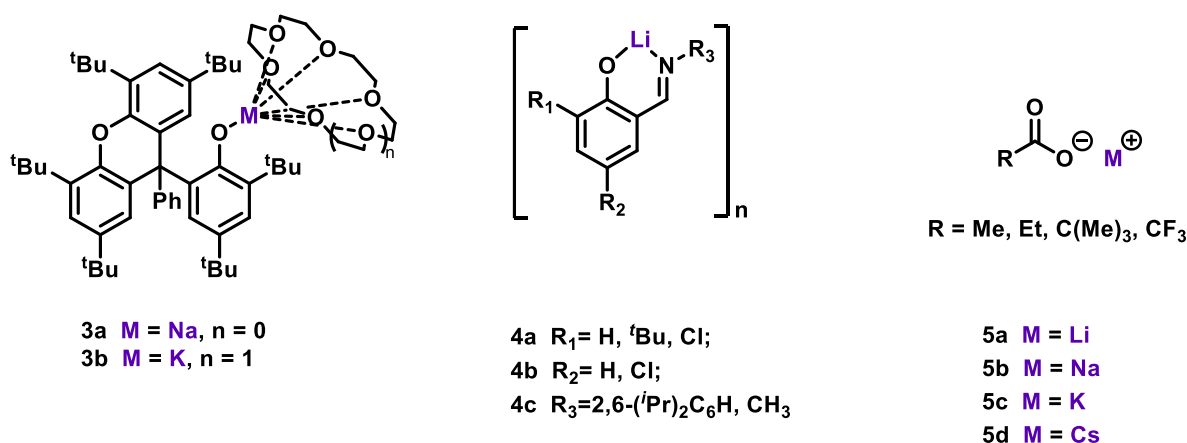


**Figure 1.5** Examples of homometallic alkali metal complexes for the ROP of cyclic esters.<sup>65–67</sup>

Garden and co-workers reported a range of half-salen Li complexes with diverse electronic and steric effects exhibited by the ligands (**4**, Figure 1.5).<sup>66</sup> These lithium complexes could initiate the ROP of LA even in the absence of any external initiator (such as BnOH), however the activity was significantly enhanced in the presence of BnOH ( $k_{\text{obs}} \leq 7.43 \times 10^{-2} \text{ s}^{-1}$ ). Interestingly, it was observed that in the latter case, the ROP mechanism switches from coordination-insertion to an activated monomer route, consequently altering the resultant PLA structure from cyclic to linear. As part of the rigorous effort to shift the current conventional plastic manufacture to greener polymer alternatives, it is essential for the catalysts used in large-scale polymer production to be practical, environmentally benign and straightforward to synthesise. Moving towards this goal, a series of simple and efficient alkali metal carboxylates were reported for the ROP of a range of cyclic esters, including LA, CL, and VL (**5**, Figure 1.5).<sup>67</sup> Complexes **5b** – **5c** were used in combination with 3-phenyl-1-propanol (PPA) as an initiator in cyclic ester polymerisations under bulk conditions ( $[\text{cat.}]:[\text{PPA}]:[\text{monomer}] = 1:2:100$ , 80 – 100 °C), producing polymer with targeted molecular weight and narrow dispersities ( $\mathcal{D} = 1.07 - 1.13$ ). Although the polymerisation is well-controlled, the polymerisation activity reflects a trend following the alkali metal size. The polymerisation rate increased with the increasing cation size of the catalyst and in the presence of more electron-donating groups on the alkyl moiety. Mechanistic insight through NMR, MALDI-ToF and Fourier transform infrared (FTIR) analyses revealed a dual activation mechanism, by which the metal centre activates both the monomer and propagating chain end, through the coordination of propagating chain end/initiator hydroxyl group. The size of the metal (which acts a counteranion) and the choice of the carboxylate substituent R is therefore key to tune the polymerisation activity and control.

Mg complexes supported by a chiral oxazolinyl aminophenolate ligand delivering rapid and highly isoselective LA ROP have been reported (**6**, Figure 1.6).<sup>68</sup> The mixture of racemic complex **6a** and **6b**

produced high molecular weight PLA ( $M_n = 461 \text{ kg mol}^{-1}$ ), integrating extremely high polymerisation activity and isoselectivity ( $\text{TOF} \leq 54\,000 \text{ h}^{-1}$ ,  $P_i = 0.80$ ). Detailed NMR studies suggested that the high isoselectivity is influenced by both the ligand chirality and the dimeric structure of the active species. Kol and co-workers reported a series of magnesium complexes bearing a tetradentate monoanionic {ONNN}-type ligand (**7**, Figure 1.6). These complexes displayed an exceptional combination of extremely high activity and living character of isoselective LA ROP, generating PLA with targeted molecular weights and narrow dispersities ( $\mathcal{D} = 1.04 - 1.14$ ). Complex **7a** displayed the highest activity, impressively converting 5 000 equiv. LA within 5 min (with 1 equiv. BnOH, RT, DCM) to produce highly isotactic PLA ( $P_i = 0.91$ ). In another study, **7a** was employed in the synthesis of block-stereoblock copolymers of PLA and PCL through a one-pot sequential monomer polymerisation.<sup>69</sup> Long chain copolymers with 100 – 800 repeat units were generated with the targeted molecular weights and narrow dispersities ( $\mathcal{D} = 1.07 - 1.18$ ) within 10 min. Furthermore, by replacing BnOH initiator with 1,4-benzenediol, BAB-type triblock copolymer of PLA/PCL was achieved while retaining the high block integrity of the polymer chain, reflecting minimal transesterification during the copolymer synthesis. High monomer loadings were tolerated with this system, indicating the truly living nature of these catalysts.

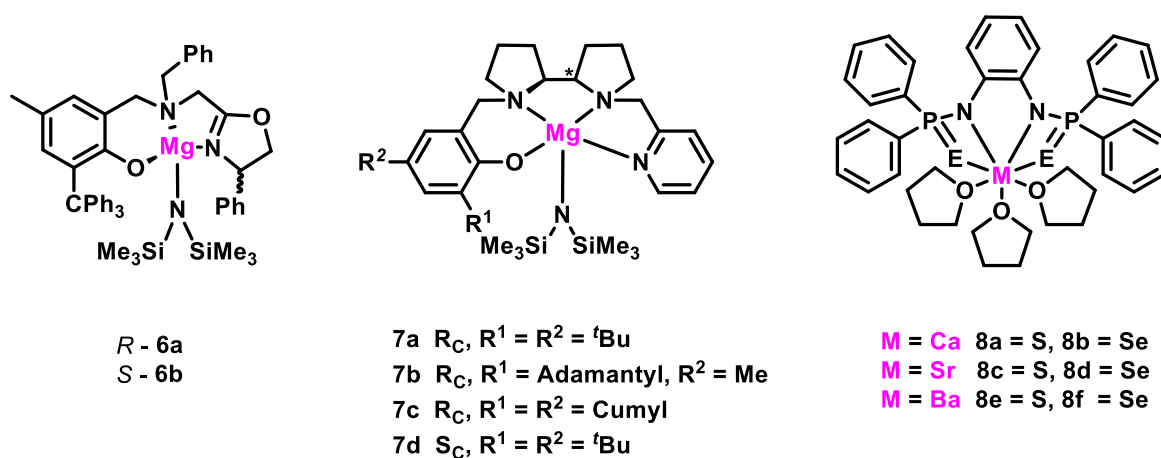


**Figure 1.6** Examples of monometallic complexes based on alkaline earth metals for cyclic ester ROP.<sup>68,70,71</sup>

Extremely active achiral alkaline-earth metals catalysts bearing 1,2-phenylene(bis-diphenylphosphino-chalcogen amine) ligands were reported by Panda and co-workers in the living ROP of LA (**8**, Figure 1.6).<sup>71</sup> **8f** exhibited the highest polymerisation activity, converting 1 000 equiv. LA within 10 min under mild conditions (25 °C, toluene). The study revealed that the polymerisation rate and stereoselectivity are influenced by the size of the alkaline earth metal ions; larger metals displayed higher catalytic activities ( $\text{Ba} > \text{Sr} > \text{Ca}$ ) but with inverse isoselectivity control ( $\text{Ca} > \text{Sr} > \text{Ba}$ ).

All complexes displayed extremely high activity in the ROP of CL, consuming 1 000 equiv. CL in less than 0.5 min.

Catalysts based on the most abundant metal in the Earth's crust, Al, have long gained special attention in cyclic ester ROP due to the low toxicity and impressive polymerisation control of several Al catalysts, albeit with many exhibiting somewhat low polymerisation activity.<sup>14,72–74</sup> The first highly stereoselective catalyst reported for the ROP of LA was an enantiomerically pure aluminium complex **9** supported by chiral binaphthyl Schiff base (also known as salen) ligand, developed by Spassky *et al.* (Figure 1.7).<sup>75</sup> Optically active isotactic PLA ( $P_i \leq 0.88$ ) was produced with a narrow dispersity ( $\mathcal{D} = 1.05$ ) at 19% conversion. Good polymerisation control was retained ( $\mathcal{D} = 1.05 - 1.27$ ) even at prolonged reaction time ( $> 48$  h, 70 °C, toluene), suggesting a well-controlled polymerisation with minimal transesterification reaction. Following this successful catalysis, a wide range of metal complexes supported by functionalised salen backbones were studied for providing good polymerisation activity and control in LA ROP, with most being Al-based complexes.<sup>18,76,77</sup> In general, polymerisation rate is enhanced for Al-salen complexes containing electron-withdrawing substituents on the phenoxy donors resulting from enhanced electrophilicity of the Al metal centre.

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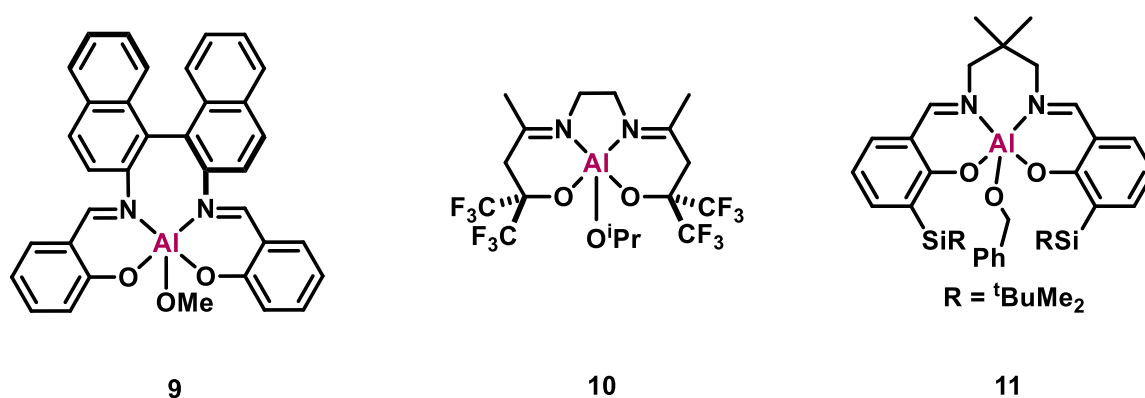


**Figure 1.7** Examples of Al-based monometallic complexes displaying high polymerisation control.<sup>75,76,78</sup>

Aluminium alkoxide complexes featuring trimethylfluoryl substituents have also been reported for LA and CL ROP (**10**, Figure 1.7).<sup>78</sup> High activities were observed in CL polymerisation with TOF up to 180 – 200 h<sup>-1</sup> (100 equiv. CL, RT, THF or bulk). The experimental molecular weights matched the expected values even at a high monomer loading ( $\leq 600$  equiv. CL). While low activity was observed for LA polymerisation in THF at RT (TOF  $\approx 6$  h<sup>-1</sup>), high activities were obtained under melt conditions (TOF  $\leq 1\,260$  h<sup>-1</sup>), yielding isotactic-enriched stereoblock PLA ( $P_i \leq 0.87$ ). In 2007, Nomura *et al.* reported the synthesis of PLA exhibiting the highest stereocontrol up to that point ( $P_i \leq 0.98$ ), which was achieved using an Al-salen complex incorporating bulky but flexible Si<sup>t</sup>BuMe<sub>2</sub> *ortho*-phenoxy

substituents (**11**, Figure 1.7).<sup>76</sup> Highly stereoblock PLA was successfully generated in solution (1.0 mol% catalyst loading, 70 °C, toluene) and high isoselectivity was retained under bulk polymerisation condition at 210 °C, producing PLA of  $P_i = 0.81$ , making this system potentially relevant for industrial applications.

Developing catalysts that can deliver high activity while retaining good stereoselectivity under elevated conditions (*i.e.* solvent-free, high temperature) is essential to ensure catalysts adaptability for industrial use. Amine tris(phenolate) ligand-supported complexes based on Group 4 metals, **12b** and **12c**, were reported to successfully achieve this demand (Figure 1.8).<sup>79</sup> Both Zr and Hf complexes displayed high activity, achieving quantitative LA conversion within 30 min under melt conditions (300 equiv. LA, 130 °C). Gratifyingly, the rapid conversion was accompanied by a high degree of stereoselectivity and good control ( $P_s > 0.90$ ,  $\bar{D} = 1.19 - 1.22$ ), with potential for large-scale PLA production. The inferior activity and control observed for Ti complex **12a** could be due to the difference in the coordination mode of the growing PLA chain on the metal centre (*vs* Zr and Hf), reflecting the importance of metal size and coordination environment in dictating catalyst overall behaviour.<sup>79–81</sup>

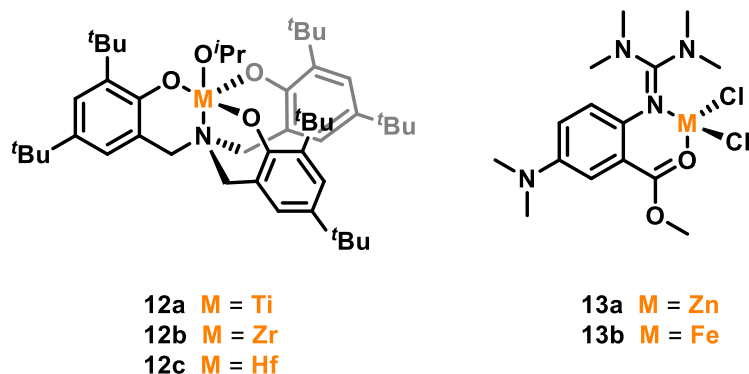


**Figure 1.8** Efficient cyclic ester ROP catalysts based on d-block metals.<sup>79,82</sup>

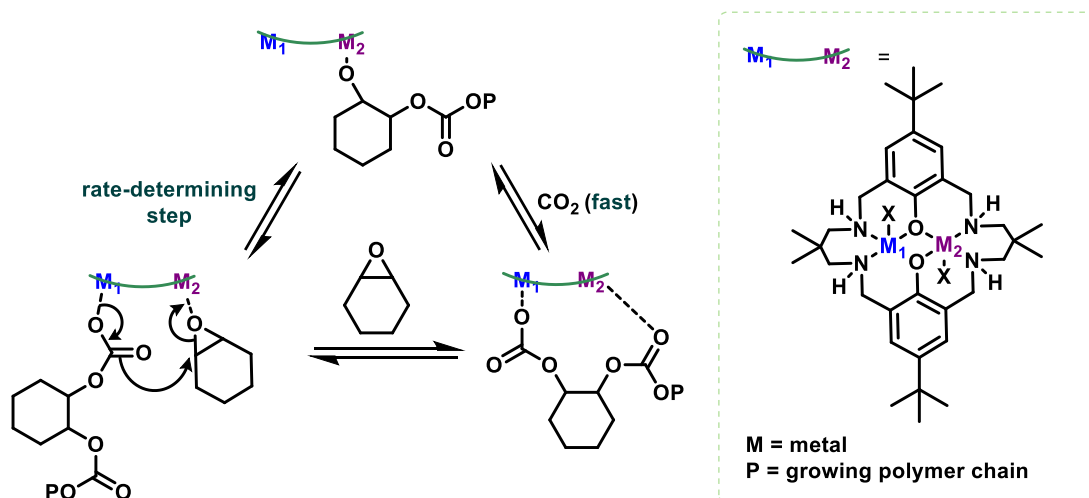
Far surpassing the performance and versatility of the current industrially employed catalyst,  $\text{Sn}(\text{Oct})_2$  (**1**, Figure 1.4), Herres-Pawlis and co-workers established a series of robust guanidine complexes, including the most recent catalysts Zn and Fe guanidine catalysts (**13a** and **13b**, Figure 1.8).<sup>82,83</sup> Both catalysts are active for the polymerisation of unpurified technical grade LA as well as recrystallised LA in bulk polymerisation with high monomer loading (5 000 equiv. LA, 150 °C), showcasing the robustness of the system for industrial LA production. Impressively, the polymerisation activity of **13b** outperformed that of **1**, where the propagation rate of the Fe complex was over 6.5 times higher ( $k_{pr} = 55.4 \times 10^{-2} \text{ L mol}^{-1} \text{ s}^{-1}$  *vs*  $8.4 \times 10^{-2} \text{ L mol}^{-1} \text{ s}^{-1}$ ).<sup>82</sup> **13b** is the first biocompatible metal catalyst reported that surpassed the polymerisation activity of toxic **1** under industrially relevant condition.

Notably, in a more recent investigation, the Herres-Pawlis group also employed **13b** in the copolymerisation of CL, LA and glycolide, accessing two opposite polymer microstructures through the manipulation of polymerisation conditions.<sup>84</sup> Highly ordered PLA-*b*-PGA-*b*-PCL-*b*-PGA-*b*-PLA pentablock copolymers were successfully generated *via* a sequential addition of monomers under melt condition at 150 °C. Conversely, performing the polymerisation by mixing the monomers at 180 °C led to high transesterification, resulting in the formation of copolymers with high degree of randomness (refer Figure 1.2 and see Chapter 2, [Section 2.3.1](#) and Chapter 6, [Section 6.6](#) for more details).

### 1.4.2 Multi- and Heterometallic Catalysts in the ROP of Cyclic Esters

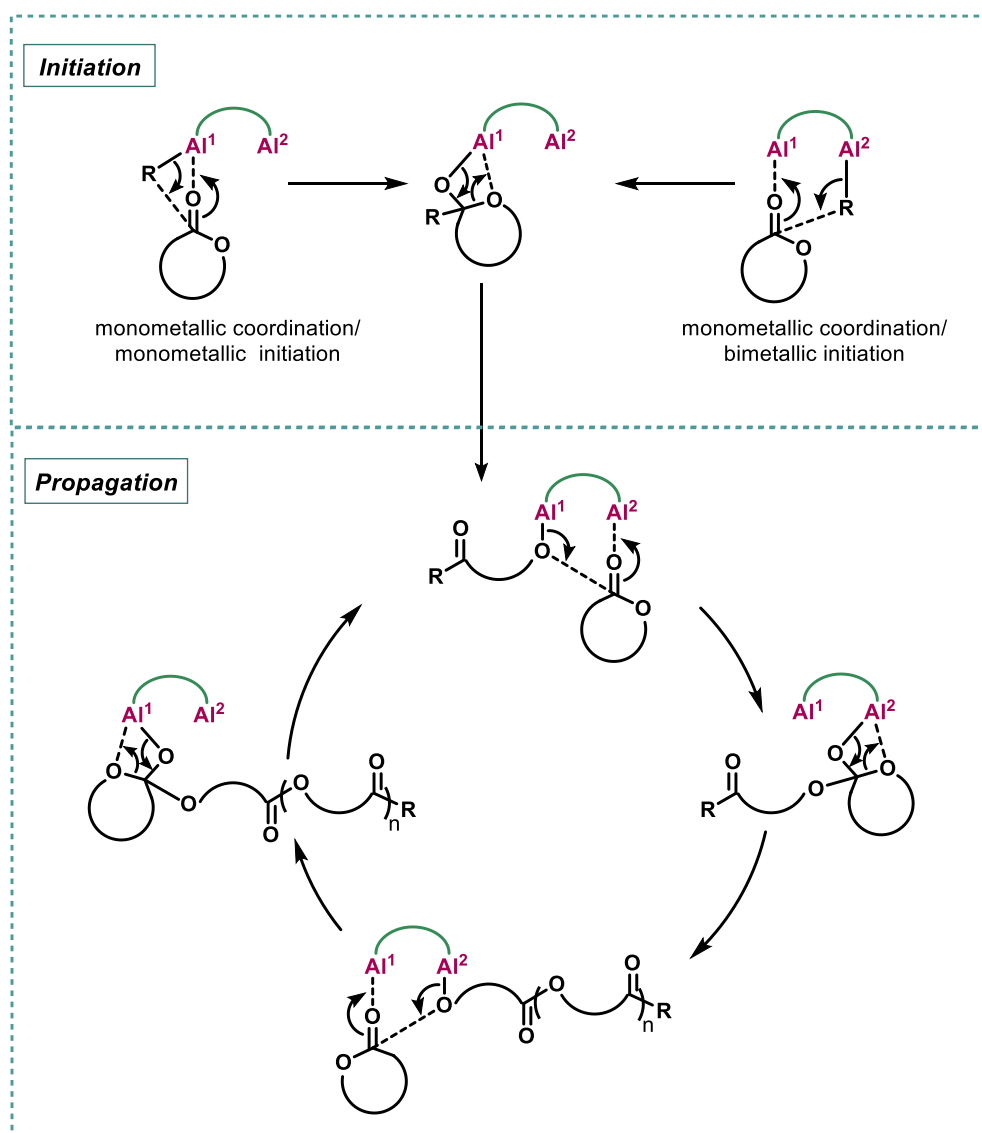
The concept of multi- and heterometallic cooperativity has seen a surge in attention and application in recent years for enhancing ROP catalysis.<sup>46,59,85</sup> The cooperativity between metals in multi- and heterometallic systems depends on the metal-metal distance, complex geometry and, in the case of heterometallic catalysts, the choice of metal combinations.

This concept has been particularly well-explored in the ring-opening copolymerisation (ROCOP) of carbon dioxide and epoxides (as well as some other monomer combinations), where bimetallic catalysts are proposed to enable improved monomer coordination, hence facilitating metal carbonate attack on epoxide.<sup>86,87</sup> Through kinetic and computational studies, it was revealed that ROCOP in the presence of bimetallic catalysts based on a macrocyclic ligand scaffold proceed *via* a “chain-shuttling” mechanism whereby both metals aid in catalysis by playing distinct roles in the cycle (Scheme 1.3). The rate determining step was found to correlate to epoxide coordination on one metal centre and the nucleophilic attack of a carbonate group bonded to the other metal.<sup>86,87</sup>



**Scheme 1.3** “Chain-shuttling” mechanism proposed for a bimetallic catalyst system based on a macrocyclic ligand scaffold.<sup>86</sup>

While this concept is understood in ROCOP, the mechanism by which metal cooperativity enhances the activity in some multi- and heterometallic catalysis is still not fully understood in the ROP of cyclic esters. In ROP catalysts featuring multiple metal centres, most of the hypothesised mechanisms have been based on the coordination-insertion pathway (refer Scheme 1.2).<sup>46,88–90</sup> Several investigations on cyclic ester ROP using bimetallic catalyst systems are proposed to follow a “chain shuttling” mechanism.<sup>88,89</sup> Through the chain-shuttling pathway, the Lewis basic monomer can coordinate to the metal bearing an initiating group, from which the nucleophilic attack also takes place (Scheme 1.4, top left).



**Scheme 1.4** Proposed initiation and chain-shuttling (in the propagation step) mechanism for cyclic ester homopolymerisation using several bimetallic Al catalyst systems.<sup>88,89</sup>

Alternatively, in another study the cyclic ester monomer was also proposed to coordinate to one of the metals ( $Al^1$ ) with the initiating group provided by a proximal Al centre ( $Al^2$ ) (Scheme 1.4, top

right).<sup>89</sup> The initiation step (*i.e.* whether the initiating group comes from either the coordinating, or a vacant neighbouring metal) is influenced by the ligand framework as well as the sterics around the metal centres. The propagation step proceeds with the coordination of a subsequent monomer to the neighbouring Al, which triggers the cyclic ester ring-opening by the propagating chain end. The polymerisation continues through the coordination of monomer on the vacant Al site by the “shuttling” of propagating chain between the metal centres following ring-opening.<sup>46</sup> Other mechanisms are also available, for example where the polymer chain does not shuttle between the two metals during propagation, but one metal always provides the monomer coordination site whereas the other always provides the nucleophilic source.

From the work by Yuan, Yao and co-workers, bimetallic complexes **15a** – **15f** were proposed to follow the “chain shuttling” mechanism, and displayed activities between two and eight times higher than their respective monometallic counterparts **14a** – **14f** in the polymerisation of CL (Figure 1.9).<sup>89</sup> For instance, bimetallic catalyst **15e** displayed a greater activity than the monometallic analogue **14e** by almost four-fold (*i.e.*  $k_{\text{obs}} = 1.28 \times 10^{-4} \text{ s}^{-1}$  vs  $3.38 \times 10^{-5} \text{ s}^{-1}$ ) under the same reaction conditions (70 °C, toluene, 400 equiv. and 200 equiv. CL for polymerisation with **15e** and **14e**, respectively). Moving down Group 13, a series of Schiff base-supported Ga initiators were developed for LA and  $\epsilon$ -CL ROP (**16**; in toluene, 100 °C, with 4 equiv. BnOH).<sup>91</sup> These initiators generated polymers with narrow dispersities ( $\mathcal{D}_{\text{PLA}} = 1.10 - 1.21$ ,  $\mathcal{D}_{\text{PCL}} = 1.06 - 1.12$ ) and PLA with enriched isotacticity ( $P_i \leq 0.78$ ). Impressively, a sequential addition of monomers through both orders of addition (*i.e.* ‘PCL first’ and ‘PLA first’ routes) produced well-defined PCL-PLLA and PLLA-PCL block copolymers. The ability of **16** to produce PLLA-*b*-PCL copolymer with good control ( $\mathcal{D}_{\text{PCL-PLLA}} = 1.17 - 1.25$ ;  $\mathcal{D}_{\text{PLLA-PCL}} = 1.24 - 1.32$ ) coupled with the retainment of ‘blocky’ microstructure is particularly notable as accessing PLA-PCL block copolymers *via* the ‘PLA first’ route is typically challenging and often results in polymer microstructure scrambling, thus leading to the formation of random copolymers instead (refer to Chapter 2, [Section 2.2](#) for more details).<sup>92</sup> Mehrkhodavandi and co-workers introduced a series of enantiopure and racemic dinuclear In complexes (**17**, Figure 1.9) that were active for LA ROP with good control ( $\mathcal{D} = 1.04 - 1.26$ ). In particular, complex **17a** afforded high molecular weight PLA from a high LA loading of over 2 100 equiv. ( $M_n < 350 \text{ kg mol}^{-1}$ ,  $\mathcal{D} = 1.04$ ).<sup>93</sup>

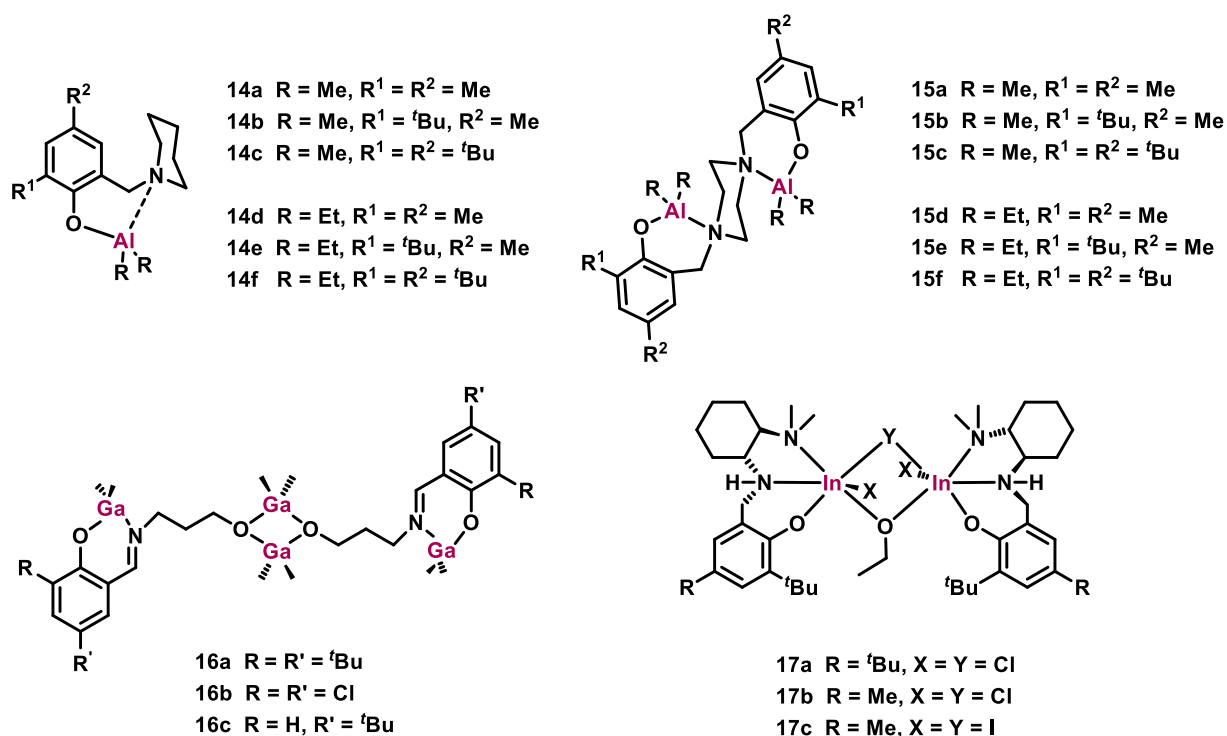


**Figure 1.9** Examples of homobimetallic complexes based on Group 13 metals.<sup>89,91,93</sup>

Tolman, Hillmyer and co-workers reported mono- and dinuclear zinc alkoxide complexes supported by a diiminophenolate ligand (**19** and **20**, Figure 1.10).<sup>94</sup> Notably, dimeric alkoxide complex **20** displayed high activity (96% conversion in 5 min), whereas the monomeric analogue **19**, without an alkoxide initiating/propagating group, was inactive towards LA ROP. Complex **20** exhibited good control, producing high molecular weight PLA with narrow dispersities ( $M_n < 130 \text{ kg mol}^{-1}$ ,  $\bar{D} \geq 1.40$ ) at low catalyst loadings ( $< 0.1 \text{ mol\%}$  catalyst loading). Since these pioneering studies, a range of highly active bimetallic zinc catalysts have been reported for cyclic ester ROP. Of particular note are the dinuclear zinc complexes reported by Williams and co-workers (**22a** – **22d**, Figure 1.10). Supported by diphenylamine-based macrocycle ligands, these complexes show exceptional activity in *rac*-LA ROP ( $\text{TOF} \leq 60\,000 \text{ h}^{-1}$ ,  $0.1 \text{ mol\%}$  catalyst loading,  $25^\circ\text{C}$ ), with bimetallic complex **22b** exhibiting enhanced activity compared to the monometallic counterpart **21** (*i.e.*  $45\,000 \text{ h}^{-1}$  vs  $14\,300 \text{ h}^{-1}$ ), under the same conditions.<sup>95</sup> Interestingly, the conformation of the ancillary macrocyclic ligand was shown to control both the Zn-Zn distance and the ROP activity. Di-zinc catalysts adopting a “folded” ligand conformation (**22a**) ( $\text{TOF} = 20\,300 \text{ h}^{-1}$ ) outperformed those with a “planar” conformation (**22c**) ( $\text{TOF} = 30 \text{ h}^{-1}$ ) under identical conditions ( $0.1 \text{ mol\%}$  catalyst loading,  $25^\circ\text{C}$ , THF). The striking activity difference between these two conformations was attributed to enhanced accessibility of zinc active sites in the “folded” **22a** complex, facilitating both monomer coordination and insertion simultaneously. Both Zn-alkoxide (Zn-O<sup>*i*</sup>Pr) and Zn-bis(trimethylsilyl)amide (Zn-HMDS) initiators were

investigated; higher polymerisation rates were observed using HMDS complexes **22a** – **22b** while the alkoxide analogues **22c** – **22d** displayed better control. Varying the Zn-Zn proximity by increasing the diamine chain length altered the activity; complex **22a** was found to be 1.5 times faster than **22b**, reflecting the higher efficiency of intermetallic cooperation stemming from the closer proximity of the metal centres.

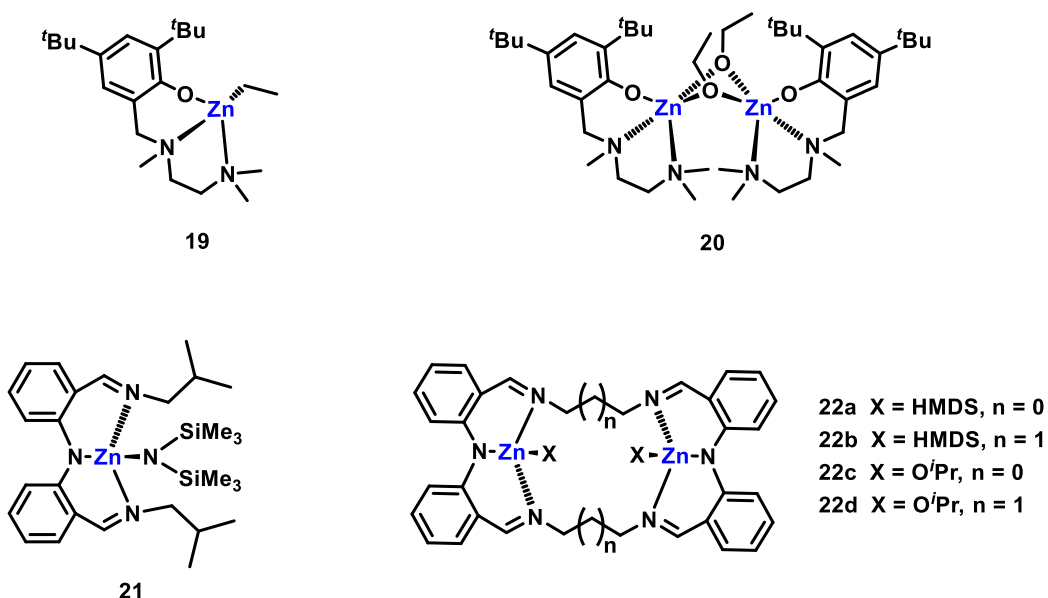


**Figure 1.10** Examples of homobimetallic complexes based on Zn.<sup>94,95</sup>

The design, synthesis and application of heterometallic (mixed-metal) complexes have garnered attention across various fields of research due to the potential for heterometallic cooperativity stemming from the unique electronic structures and the properties of the different metals.<sup>46,85,96</sup> Importantly, synergistic interaction between metals generally requires metals to be in close proximity, which is often dictated by the ligand structure. In ligand systems containing M-O-M' framework (such as ProPhenol complexes, refer to [Section 1.4.3](#)), the incorporation of metals with different electronegativity values allows the formation of “ate”-type complexes which alters the electronic properties of each metal centre.<sup>97</sup> “Ate” activation can be accessed by pairing a hard metal (*e.g.* Group 1 and 2) with a softer, more carbophilic metal (*e.g.* Zn), resulting in the transfer of the anionic ligands to the more carbophilic metal.<sup>61,97</sup> This feature can lead to the enhancement of polymerisation activity by facilitating the two key steps in ROP: the monomer coordination (onto the more Lewis acidic metal) and nucleophilic attack (through increased nucleophilicity of the M-R bond) (Figure 1.11).

"Ate" activation:

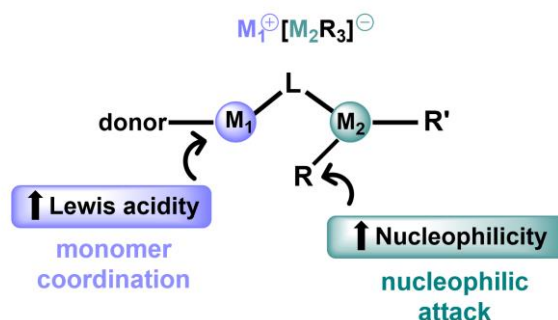


**Figure 1.11** The concept of "ate" activation arising from heterometallic cooperativity, resulting in polymerisation activity enhancement.

Dinuclear Li/Mg and Li/Zn catalysts based on bisphenol ligands (Figure 1.12, **23**) were reported to produce highly heterotactic PLA from LA ROP (in THF/toluene, RT, with 1 equiv. neopentyl alcohol).<sup>98</sup> The high stereoselectivity observed when these polymerisations were conducted in THF/toluene ( $P_s = 0.84$ ; cf.  $P_s = 0.54$  in THF alone and  $P_s = 0.64$  in toluene alone) was attributed to steric hindrance around the metal centre, leading to better stereocontrol following a chain-end control mechanism. In contrast, reduced stereocontrol in coordinating solvents such as THF was attributed to metal dissociation, consequently decreasing the steric hindrance and therefore polymerisation selectivity. Williams and co-workers investigated the performance of a series of heterometallic complexes **24a** – **24e** featuring Co(III) combination with s-block metals, Co(III)M(I/II) (where M = Na(I), K(I), Ca(II), Sr(II), Ba(II)), for three polymerisation reactions: propylene oxide (PO)/CO<sub>2</sub> ROCOP, PO/phthalic anhydride ROCOP, and LA ROP.<sup>62</sup> The study revealed a correlation between polymerisation rates and selectivity with the Lewis acidity of s-block metals, in which Co(III)M(I/II) catalysts bearing weakly Lewis acidic M (*i.e.* higher  $pK_a$ ;  $pK_a$  of  $[M(OH_2)_m]^{n+} = K > Na > Ba > Sr > Ca$ ) displayed greater polymerisation rates. In the ROP of LA ([cat.]:[PO]:[LA] = 1:1000:100, 50 °C; PO was used as solvent and initiator), this system was hypothesised to follow the coordination-insertion mechanism. M(I/II)-OR intermediate nucleophilic attack at the LA coordinated to Co(III) was proposed as the rate-limiting step. It was tentatively hypothesised that reducing the s-block metal Lewis acidity resulted in the destabilisation of M(I/II)-OR intermediate, hence causing higher LA insertion lability (and faster rates). **24b** was the most active catalyst and the only complex displaying PLA isoselectivity (TOF = 912 h<sup>-1</sup>,  $P_i = 0.71$ ).

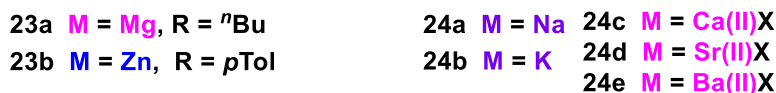


**Figure 1.12** Examples of heterometallic catalysts incorporating alkali and alkali-earth metal.<sup>62,98</sup>

A series of heterometallic complexes of the form Al(III)M(I/II) (where M = Li(I), Mg(II), Ca(II), Zn(II)), was investigated by the Garden group (Figure 1.13, **25b** – **25e**) for LA ROP.<sup>99</sup> Complex **25c** and **25e** displayed enhanced activity ( $k_{\text{obs}} = 1.8 \times 10^{-3} \text{ s}^{-1}$  and  $k_{\text{obs}} = 8.8 \times 10^{-3} \text{ s}^{-1}$ , respectively) outperforming the mono-Al analogue **25a** ( $k_{\text{obs}} = 0.8 \times 10^{-3} \text{ s}^{-1}$ ) by 2- and 11- fold, respectively ([cat.]:[PO]:[LA] = 1:50:100, 120 °C, toluene). On the other hand, both **25b** and **25d** displayed inferior activities compared to **25a**. DFT studies revealed that the Cl initiating group bridged between the two heterometals through a dative bond, which elongates and weakens the Al—Cl bond thus increasing the polymerisation rate. This study highlights the influence of heterometallic interaction on the complex co-ligand, affecting the polymerisation initiation and propagation steps. The enhanced activity of **25c** and **25e** was attributed to an increased rigidity of the catalysts framework which leads to close intermetallic proximity, whereas the rigid square pyramidal geometry around the Al centre results in improved monomer coordination.



**Figure 1.13** Examples of heterometallic catalysts combining Al with mono- and di-valent metals.<sup>99,100</sup>

More recently, highly active heterometallic Al/Mg catalysts **26a** and **26b** were reported for LA and L-LA ROP under very mild polymerisation conditions ([cat.]:[LA] = 1:400, 0 – 23 °C, THF).<sup>100</sup> **26a** displayed an outstanding activity ( $\text{TOF} \leq 24\,770\text{ h}^{-1}$ ), affording quantitative conversion of LA and L-LA in 1.0 and 1.6 min, respectively, with great polymerisation control ( $M_n = 54.5 - 58.1\text{ kg mol}^{-1}$ ,  $\bar{D} = 1.10 - 1.12$ ). The PLA produced displayed a significant level of heterotacticity ( $P_s = 0.80$ ), while PLLA was generated without epimerisation. A slightly reduced activity observed for **26b** was attributed to the bulky *t*Bu group hampering the propagation step. Importantly, the heterometallic catalyst displayed first-order kinetics with respect to the catalyst and LA, indicating a synergic intermolecular interaction between Al and Mg. Notably, these complexes also show enhanced activity compared to their previously reported Al- and Mg-monometallic counterparts.<sup>101</sup> This Al/Mg system is the most active heterometallic system incorporating Al metal reported for LA ROP thus far.

In the development of heterometallic catalysts featuring low-toxicity main group metals paired with transition metals, Ti is interesting owing to its biocompatibility. A Ti(IV) complex supported by a tetradentate ligand and incorporating sodium, **27**, was shown to be active for the ROP of CL, yielding up to 97% conversion to PCL (100 – 200 equiv. CL, toluene, 60 °C, 2 h), albeit with broad dispersities ( $\bar{D} = 1.60 - 2.50$ ).<sup>102</sup> The incorporation of Na into the Ti-ligand scaffold resulted in a Lewis acidity increase of Ti and the weakening of Ti-O*i*Pr bond, thus potentially assisting nucleophilic attack.

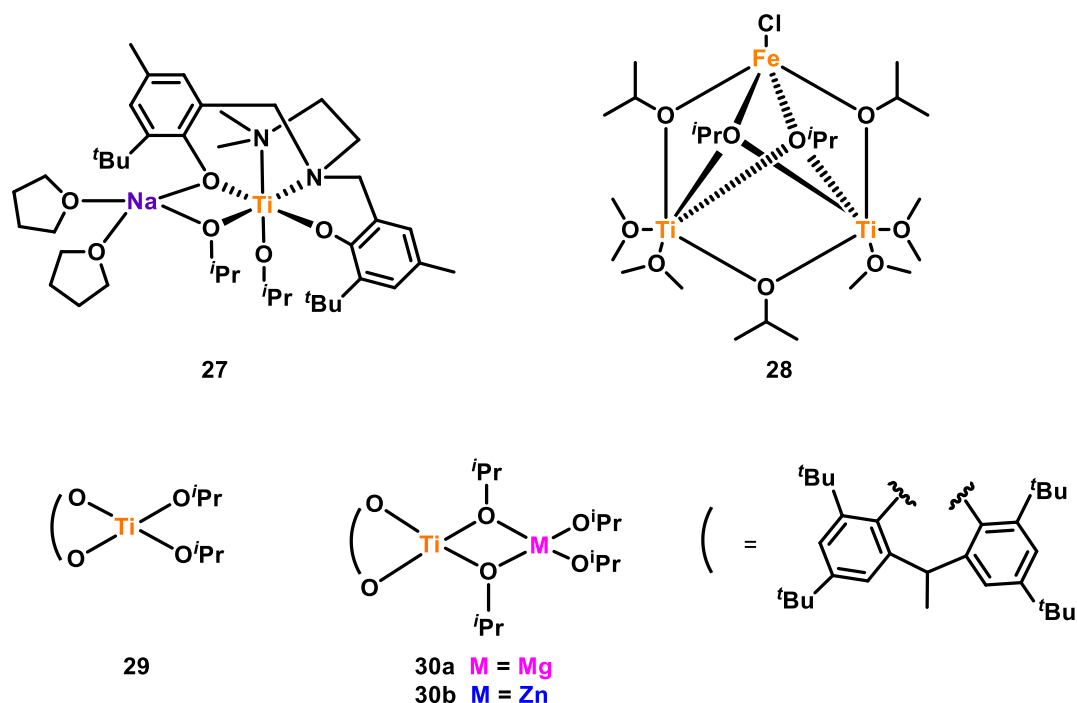


Figure 1.14 Ti-based heterometallic complexes for the ROP of LA and CL.<sup>102–104</sup>

The heterotrimetallic Fe(II)/Ti(IV) complex **28** is active for the bulk polymerisation of CL and LA, and was also successfully applied to the solution polymerisation of CL.<sup>103</sup> This complex is one of the few heterometallic complexes reported bearing two biocompatible metals within the same molecular framework, and is thus particularly interesting. For the bulk polymerisation of CL, quantitative conversions were achieved in a relatively short time (0.08 – 0.5 h, 250 – 3 000 equiv. CL, 90 – 120 °C), with relatively broad dispersities ( $\bar{D}$  = 1.51 – 2.46), without the presence of any co-initiators. In an activity comparison study for the ROP of L-LA, heterobimetallic Ti(I)/M complexes (where M = Mg(II), Zn(II); **30a** – **30b**) showed activity enhancement relative to the monometallic complex **29**.<sup>104</sup> **30b** displayed the fastest polymerisation rate, delivering 91% L-LA conversion within 0.5 h (*cf.* 89% L-LA conversion by **30a** in 3.5 h) with good control ( $\bar{D}$  = 1.27). The enhanced activity of **30b** was attributed to differences in the electronic configurations as well as charge densities of M; a smaller charge density was proposed to result in a more labile M-OR bond, thus increasing the polymerisation rate.

Heterometallic cooperativity has exhibited promise as a foundation for ROP catalyst design, giving superior catalyst performance which stems from improved monomer activation and nucleophilic attack. Among the catalysts reported to show synergistic interactions, heterometallic systems featuring combinations of a Lewis acidic metal (*i.e.* larger metals from Group 1 or lanthanides) with electronegative metals (*i.e.* Al, Co, Zn) often display enhanced polymerisation activities. The former (large Lewis acidic metal) component allows the coordination of more monomer units, consequently enhancing catalyst activities while the latter component (the more electronegative metal) aids in efficient nucleophilic attack on the carbonyl unit (refer to Scheme 1.2). However, it is also important to note that not all heterometallic complexes outperform their homometallic counterparts.<sup>99,105</sup> While the factors that influence heterometallic cooperativity are still emerging, computational studies have been used to provide helpful insights and better understanding of heterometal synergy, which will aid the choice of metal combinations in future catalyst design.

Additionally, to harness the full potential from intermetallic communication in both homo- and heterometallic complexes, understanding of the chemical/electronic environments around the metal active sites must be elucidated. Three important aspects generally considered in the design of catalysts are: i) catalytic activity, ii) reaction scope and iii) reaction selectivity. Yet, in the effort to move towards greener chemistry, incorporating metals that are abundant and sustainable, non-toxic and easy to handle are also crucial for practical application in the synthesis of biodegradable polymers.

### 1.4.3 Organometallic ProPhenol Complexes in Cyclic Ester Polymerisation

Several organometallic complexes supported by the commercially available ProPhenol ligand ((*S,S*)-(+)-2,6-bis[2-(hydroxydiphenylmethyl)-1-pyrrolidinyl-methyl]-4-methylphenol) (Figure 1.15)<sup>106</sup> have displayed impressive activity and/or control in cyclic ester ROP. The experimental work described within this thesis therefore focuses on the further development and performance of organometallic complexes based on the ProPhenol ligand. First developed by Trost and Ito in 2000, catalysts based on this chiral aza-crown ligand have since been widely utilised in numerous asymmetric transformation reactions, including Aldol,<sup>106</sup> alkynylations and conjugation reactions,<sup>107</sup> as well as Mannich reactions.<sup>108,109</sup>

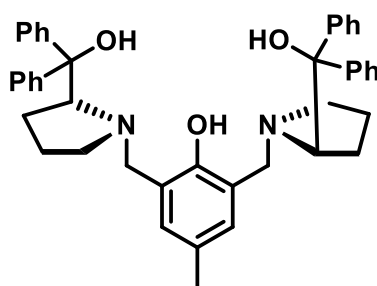


**Figure 1.15** Structure of a ProPhenol ligand, a proline-derived ligand with a phenolic backbone, featuring multiple coordination sites for metal occupancy.<sup>106</sup>

Upon treatment with two equivalents of a metal-alkyl reagent, such as  $\text{Et}_2\text{Zn}$  or  $\text{Bu}_2\text{Mg}$ , the ProPhenol ligand readily forms a chemically inequivalent bimetallic complex. The complex consists of a Lewis acidic site for activation of electrophiles and a Brønsted basic site for a pronucleophile activation through simple deprotonation, a feature which may present an advantage for the ROP of cyclic esters (Figure 1.16).<sup>110</sup>

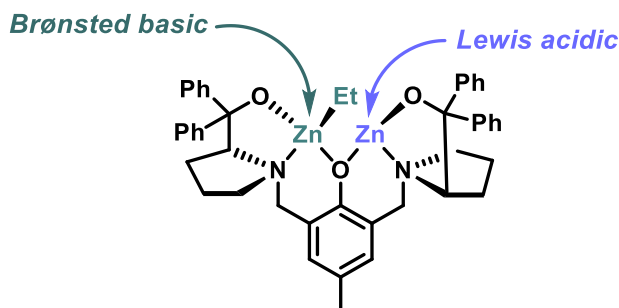


**Figure 1.16** Bimetallic Zn-ProPhenol complex featuring two chemically inequivalent Zn centres.<sup>110,111</sup> In cyclic ester ROP, the Lewis acidic metal could provide an efficient site for Lewis basic monomer coordination, whereas a nucleophilic alkyl/alkoxide group on the Brønsted basic metal may facilitate carbonyl attack.

In 2015, Rajashekhar *et al.* reported the first series of ProPhenol complexes for the ROP of LA and CL, incorporating Group 4 (*i.e.* Ti(IV), Hf(IV) and Zr(IV)) transition metals (**31a** – **31c**, Figure 1.17).<sup>81</sup>

The polymerisation of both cyclic esters was performed under solvent free conditions and converted up to 98% of 200 equiv. LA or CL (at 140 °C and 80 °C, respectively) within 2 – 9 min, while exhibiting impressive polymerisation control ( $M_n = 24.0 - 33.0 \text{ kg mol}^{-1}$ ,  $\bar{D} = 1.05 - 1.12$ ). The narrow polymer dispersities are reflective of well-controlled polymer propagation with this system. Gratifyingly, in the ROP of LA, both **31b** and **31c** also displayed high stereocontrol, generating PLA with isotactic-enriched stereoblock microstructures ( $P_i = 0.78$  and  $0.71$ , respectively) whereas **31a** produced atactic PLA. The stereocontrol observed with **31b** and **31c** was attributed to the higher coordination numbers of these complexes compared to **31a** which enable polymer chains to coordinate to the metal centre through the carbonyl group, thus facilitating LA monomer to approach the metal centre for further coordination.<sup>80</sup>

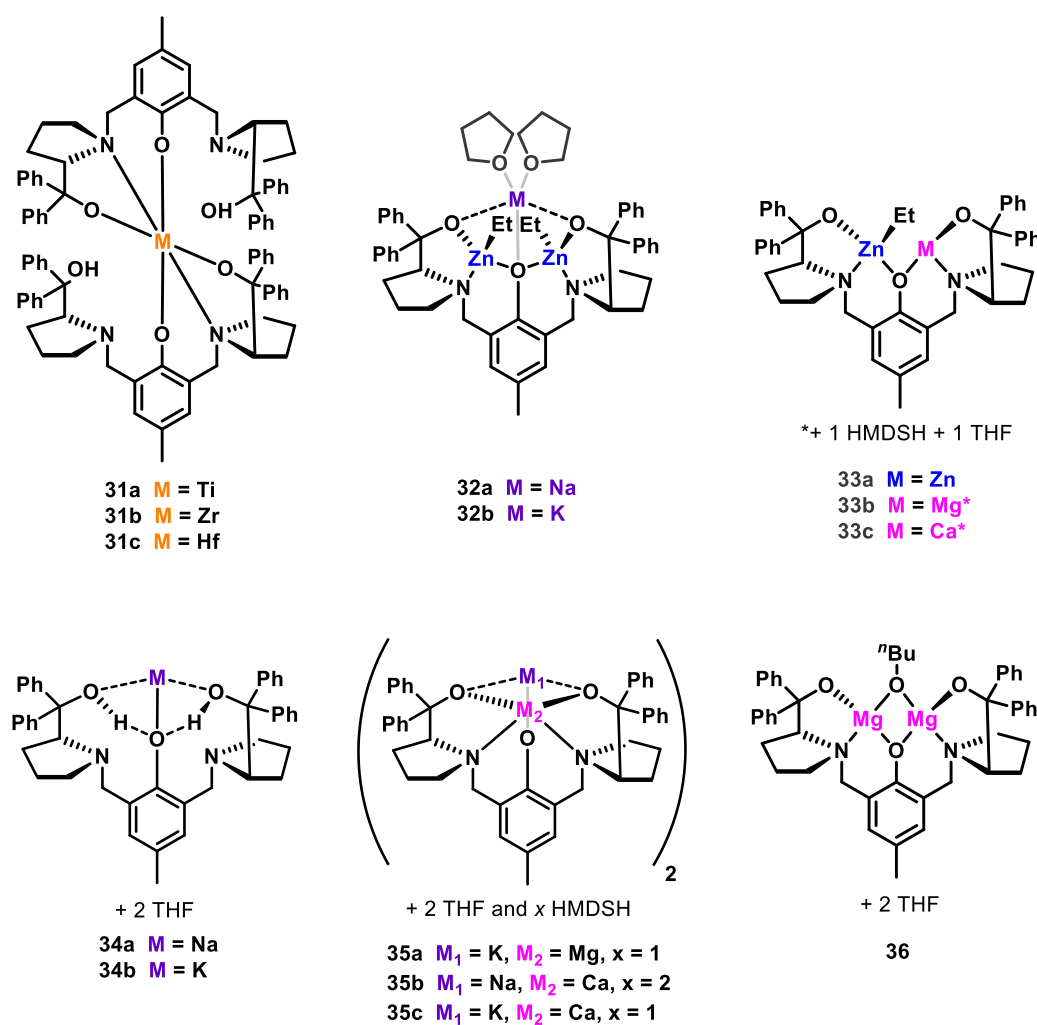


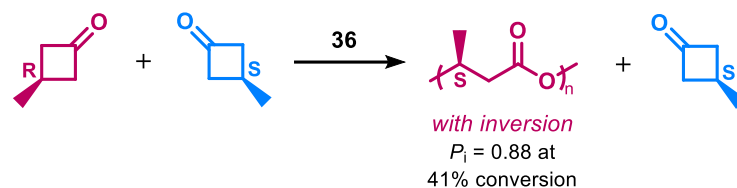
**Figure 1.17** Organometallic ProPhenol complexes reported for cyclic ester ROP.<sup>81,112–116</sup>

Remarkably active trimetallic catalysts in the ROP of LA featuring a Na/Zn<sub>2</sub> ProPhenol heterocombination were reported by Garden and co-workers, **32a**, where the high activity was attributed to “ate” activation observed in the catalyst structure by solution-state NMR analysis.<sup>112</sup>

**32a** displayed excellent activities ( $k_{\text{obs}} = 3.2 \times 10^{-3} \text{ s}^{-1}$ ) with moderate control ( $\bar{D} = 1.40$ ) in the ROP of 100 equiv. LA (with 2 equiv. BnOH,  $[M] = 1.0 \text{ M}$  in THF, RT). Changing Na to K (*i.e.* from **32a** to **32b**) enhanced the activity by five-fold ( $k_{\text{obs}} = 1.7 \times 10^{-2} \text{ s}^{-1}$ ), reflecting the important role of the alkali metal in monomer coordination and activation, with larger K proposed to give better site availability for monomer coordination. The incorporation of the alkali metal was also discovered to labilise the Zn-Et bond, consequently facilitating nucleophilic attack and the ring opening of LA. However, neither of the catalysts exhibited isoselectivity in the LA polymerisation.

In another study, highly active di/divalent heterometallic catalysts (**33b** and **33c**) were investigated and compared against their di/divalent homometallic *bis*-Zn analogue, **33a**.<sup>113,114</sup> **33c** displayed the highest activity, with 82% conversion in 1.25 min (100 equiv. LA,  $[M] = 1.0 \text{ M}$  in toluene, 60 °C), outperforming **33b** which gave similar activities to **33a** (87% conversion in 10 min). Both **33b** and **33c** were also compared against the respective *bis*-Mg and *bis*-Ca analogues, and showed enhanced activities compared to their homometallic counterparts. DFT studies revealed the presence of THF and HMDSH coordinated to the Group 2 metals (*i.e.* Mg and Ca) in heterometallic **33b** and **33c**, with the larger Ca(II) providing additional coordination sites. Subsequently, the monomers were proposed to coordinate to either Mg or Ca, while Zn served as the source of nucleophile.<sup>114</sup> A simple yet elegant method of harnessing heterometallic cooperativity was showcased in an investigation combining homometallic alkali metal ProPhenol complexes (**34a** – **34b**) with simple salt additives ( $\text{Zn}(\text{OBn})_2$ ,  $\text{Mg}(\text{OBn})_2$  or  $\text{Ca}(\text{OBn})_2$ ) *in situ*.<sup>115</sup> This method circumvents challenging heterometallic synthesis, yet proved to deliver excellent polymerisation activities as isolated heterometallic complexes **35**. The activity enhancements were ascribed to Lewis acidic metal-based activation of the carbonyl group towards nucleophilic attack.

Most recently, Coates and co-workers developed **36** for the ROP of *rac*- $\beta$ -butyrolactone (*r*- $\beta$ -BL), through an enantioselective, kinetic resolution approach, generating highly isotactic poly(3-hydroxybutyrate) (PHB).<sup>116</sup> **36** polymerised *r*- $\beta$ -BL with a stereochemical inversion to produce (*S*)-PHB with  $P_i = 0.98$  at 41% monomer conversion, the highest degree of isotacticity for *r*- $\beta$ -BL ROP reported to date, under various conditions (Scheme 1.5). Further investigation revealed that neither pure (*R*)- $\beta$ -BL nor (*S*)- $\beta$ -BL polymerisation was favoured, as only minimal monomer conversion was observed in both cases, suggesting that the presence of the opposite enantiomer is key for activating the catalyst to perform kinetic resolutions.



**Scheme 1.5** Enantioselective polymerisation of *r*-β-BL with **36**, yielding highly isotactic (*S*)-PHB through a stereochemical inversion.<sup>116</sup>

Despite the outstanding performance and potential, these are the only catalysts based on ProPhenol reported for cyclic ester ROP thus far. The ProPhenol ligand motif features multiple coordination sites for metal occupancy, thus enabling various different metal combinations for accessing hetero- or multimetallic complexes to gain catalytic activity enhancement. Depending on the catalyst structure (*i.e.* complex rigidity, ligand fluxionality and accessibility of metal centre(s)), the polymerisation (stereo)control can be anticipated, as demonstrated by several studies in literature.<sup>81,116</sup>

## 1.5 Aims of the PhD Research

The overall aim of this PhD research project was to explore the synergistic heterometallic interaction of mixed-metal ProPhenol complexes in the ring-opening polymerisation of cyclic esters. In previous heterometallic complexes, the enhanced polymerisation rate was attributed to “ate” activation arising from the intermetallic interaction of different metal combinations. Here, this concept was explored further to understand the pros and cons of assimilating “ate” character in the design of heterometallic catalysts for cyclic ester ROP. Given the impressive activity and/or stereocontrol observed with ProPhenol complexes reported in literature, new heterometallic ProPhenol complexes which incorporate structural features expected to deliver enhanced polymerisation performance (*e.g.* proximal mixed metals with different electronegativities, accessible metal centres for monomer coordination) were also targeted. Structural insights into the new catalysts were determined through X-ray crystallographic analysis, and compared against the structure of related ProPhenol complexes to identify key similarities and differences that give rise to the polymerisation activity and control. A further aim was to develop an understanding on how the different metals, and metal valencies (*e.g.* di/divalent vs mono/trivalent) influenced the catalyst structure and performance in cyclic ester homo- and copolymerisations. The catalyst behaviour was elucidated through multinuclear NMR spectroscopic experiments including <sup>1</sup>H, <sup>13</sup>C, COSY, HSQC, NOESY and DOSY while the catalytic activity was investigated through kinetic studies. The resultant polymers generated were analysed by NMR spectroscopy, SEC and MALDI-ToF mass spectrometry analyses to gain insights of the polymer microstructures and polymerisation control.

The work in Chapter 2 focused on probing a series of previously reported heterometallic divalent/divalent ProPhenol complexes (**33b** – **33c**, Figure 1.17) in the synthesis of PCL-*block*-PLA copolymers, by comparing the catalyst performance against the homobimetallic *bis*-Zn counterpart, **33a**. Specifically, this chapter investigated the balance of enhanced activity and control delivered by “ate” complexes in the copolymerisation of LA and CL. The catalyst activities were compared by performing kinetic studies, while the control towards block copolymer synthesis was investigated by analysing the copolymer microstructure and molecular weight distribution by NMR spectroscopy and SEC, respectively. The potential of the ProPhenol catalysts was tested further in the formation of higher-order block PCL-PLA copolymer, by targeting PCL-PLA-PCL triblock copolymer.

With the aim to develop cooperative heterometallic catalysts incorporating innocuous, Earth-abundant metals, a series of heterometallic ProPhenol complexes combining Group 1 metals (Na or K) with Al was targeted. The pairing of s-block metals that typically exhibit high activity but poor control, with Al, which often displays the slow polymerisation but high levels of control was envisioned to deliver improved performance in ROP. The novel complexes prepared were analysed in the solution-state by NMR spectroscopy, and in the solid-state by single crystal X-ray diffraction studies.

Chapter 4 aimed to investigate the reactivity of the newly synthesised Na/Al<sub>2</sub> heterometallic ProPhenol complexes presented in Chapter 3. One of the (datively bound) Al centres was envisaged to undergo chemical abstraction through the reaction with a range of Lewis donors. While the abstraction was proven futile, some understanding on the behaviour of Lewis basic monomer coordination to the Na/Al<sub>2</sub> complex was achieved through NMR studies. Subsequently, the work in this chapter aimed to study the complex activity and control in the ROP of *rac*-lactide,  $\epsilon$ -caprolactone and  $\delta$ -valerolactone. Overall, Chapter 3 and 4 aimed to investigate the different roles of Na and Al in the ROP of cyclic esters.

## Chapter 2

Heterometallic Cooperativity in  
Block Copolymer Synthesis:  
Balancing Activity and Control to Deliver  
Well-Defined PCL-*block*-PLA Copolymers

## 2.1 Overview

While heterometallic cooperativity has delivered enhanced catalyst performance in the ring-opening polymerisation (ROP) of cyclic esters, so far this has primarily been limited to their homopolymerisation. In “ate” complexes, the metals are electronically connected through a bridging M-O-M' unit, and this is a common structural feature in heterometallic catalysts for cyclic ester homopolymerisation. However, to date, none have been reported for the block copolymerisation of cyclic esters, in spite of the potential activity enhancements.

In this chapter, we show that heterometallic Mg/Zn and Ca/Zn catalysts, based on a ProPhenol ligand, show significant activity enhancements in the synthesis of PCL-*b*-PLA diblock copolymers, outperforming the Zn/Zn analogue with the activity order Ca/Zn > Mg/Zn > Zn/Zn. The excellent activity accompanies good polymerisation control, generating well-defined PCL-*b*-PLA copolymer structures. Intriguingly, this catalyst activity order is reversed upon the sequential addition of  $\epsilon$ -caprolactone as the third monomer. Instead of forming PCL-PLA-PCL triblock copolymers, analysis of the copolymer microstructures shows that transesterification occurs to generate random copolymers. The degree of transesterification is higher with Ca/Zn and Mg/Zn. The features of heterometallic “ate” catalysts that boost polymerisation activity can thus also enhance competitive transesterification processes, governed by the choice of the heterometal and the monomer.

## 2.2 Introduction

The ROP of cyclic esters produces aliphatic polyesters that are promising alternatives to conventional hydrocarbon-based polymers, yet their applications remain limited by their material properties. For example, PLA is bioderived and biodegradable but is also brittle.<sup>117</sup> This can be overcome by copolymerising the parent monomer, LA, with other cyclic esters such as CL, to harness the complementary thermal, physical and mechanical properties of both polymers.<sup>56</sup> The material properties can be further tuned by altering the copolymer composition, chain lengths and architecture (*e.g.* block, gradient or random, see Figure 2.1). For example, diblock and triblock copolymers of PCL-PLA and PCL-PLA-PCL can give higher elongation-at-break values than PLA.<sup>118</sup> Katiyar *et. al.* investigated the effects of different block lengths and stereocomplexation of PLA/PCL copolymer on the resultant polymer mechanical and thermal properties.<sup>119</sup> The study reported an increase of elongation-at-break from just a factor of nine for diblock PLA-PCL copolymer to several hundred-fold in triblock PLA-PCL-PLA copolymer, in comparison to pure PLA. Accordingly, PCL-PLA copolymers have diverse applications in biomedicine,<sup>120</sup> compatibilisation<sup>121</sup> and packaging production.<sup>122</sup>

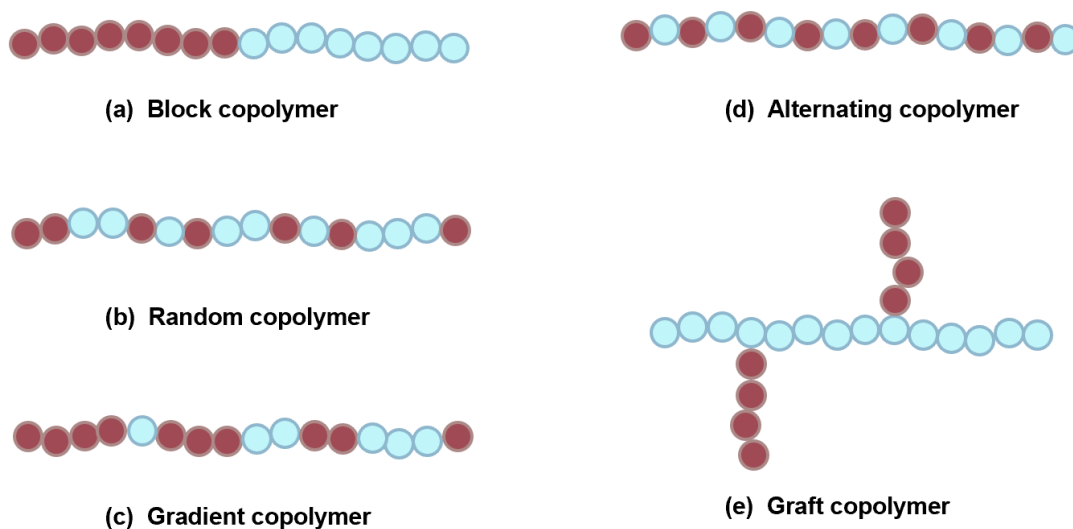


**Figure 2.1** Examples of different copolymer structures.

The sequential addition of two (or more) cyclic ester monomers to a metal-based catalyst is a particularly attractive method of producing block copolymers, as this is a simple, one-pot, living polymerisation method where some catalysts have delivered high activities and exquisite polymerisation control.<sup>123</sup> However, transesterification can disrupt the block structure to give random copolymers, and thus the relative rates of propagation and transesterification are key to controlling the copolymer structures.<sup>113</sup> To achieve the targeted block copolymers, it is essential to

avoid transesterification as this can rearrange the block structure to give random copolymers. The polymer structure is therefore influenced by the relative rates of propagation and transesterification, and faster propagation of the second monomer added facilitates the synthesis of well-controlled diblock copolymers.<sup>84</sup>

The work in this chapter investigated the synthesis of PCL-*block*-PLA copolymers through the sequential addition of LA monomer to a living PCL\* chain. This route to PCL-PLA block copolymers is more commonly reported in literature than the reverse monomer addition sequence, known as the 'PLA first' route. The addition of CL into a PLA\* chain often leads to scrambling of the copolymer structure to cause randomisation, or the inactivity of PLA\* chain to polymerise CL monomers resulting in low conversion.<sup>56,69</sup> While the exact reason for the occurrence remains unclear, some studies have suggested that the randomisation originates from the rate of CL transesterification into the PLA\* chain being higher than the rate of CL propagation ( $k_{tr} > k_p$ ).<sup>92,124</sup>

Previously, our group reported a *bis*-Zn catalyst for cyclic ester ROP (**[LZn<sub>2</sub>Et]**, Figure 2.2), which successfully generated PCL-PLA block copolymers *via* sequential monomer addition of CL then LA, without transesterification disrupting the block structure.<sup>113</sup> The analogous heterometallic Mg/Zn (**[LMgZnEt]**) and Ca/Zn (**[LCaZnEt]**) catalysts successfully homopolymerised LA and CL, which outperformed homometallic **[LZn<sub>2</sub>Et]** with an overall activity trend of Ca/Zn > Mg/Zn > *bis*-Zn (Figure 2.2).<sup>114</sup> These performance enhancements were attributed to the "ate" structure of the heterometallic complexes. Pairing a hard metal (*e.g.* Group 1 and 2) with a softer, more carbophilic metal (*e.g.* Zn) can result in anionic "ate" activation.<sup>61,85</sup> This can simultaneously enhance the Lewis acidity of the Group 2 metal (*i.e.* facilitating monomer coordination), and the nucleophilicity of the Zn-Et/OR unit (enhancing ring-opening and enchainment).<sup>44</sup> Despite the advantages of heterometallic complexes, their use in the preparation of block copolymers from cyclic esters is surprisingly limited.<sup>125</sup>

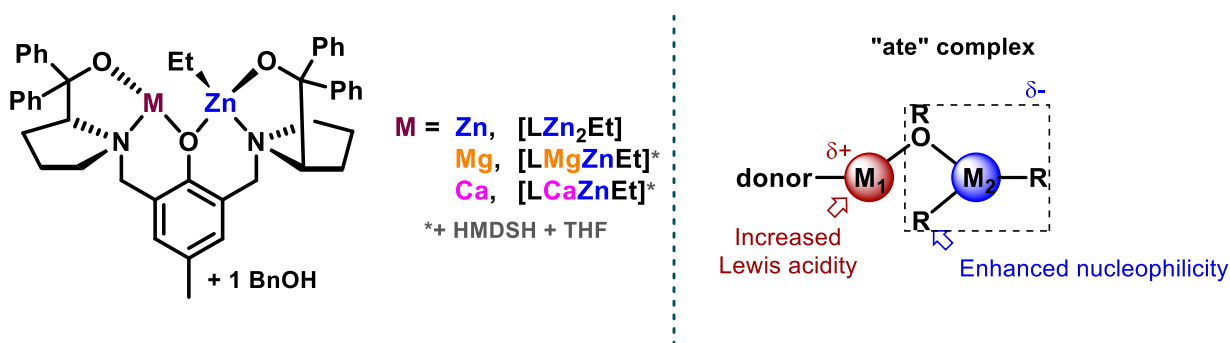


**Figure 2.2** General structural motifs of "ate" complexes and heterometallic ProPhenol structures tested for cyclic ester block copolymers in this chapter.

To the best of our knowledge, the only homogeneous heterometallic catalysts reported for the preparation of block copolymers from the living polymerisation of cyclic ester monomers have been switchable catalyst systems. Several heterometallic catalysts can switch between cyclic ester ROP and the ring-opening copolymerisation (ROCOP) of epoxides/anhydrides or epoxides/CO<sub>2</sub>, including electrochemically switchable systems.<sup>126–129</sup> Chemical or mechanistic “switches” can also be employed. For example, in 2020, Williams *et. al.* utilised Zn(II)/Mg(II) catalyst in the presence of 1,4-benzenedimethanol (BDM) (Figure 2.3, left) for the preparation of ABA-triblock polyester featuring poly(cyclohexene carbonate) (PCHC) as the hard A block, and poly( $\epsilon$ -decalactone) (PDL) as the soft B block.<sup>127</sup> Upon DL consumption through ROP to generate PDL, the addition of phthalic anhydride/cyclohexane oxide mixture triggered a mechanistic ‘switch’ from ROP to ROCOP, enabling the formation of PCHC blocks extending from the PDL chain.

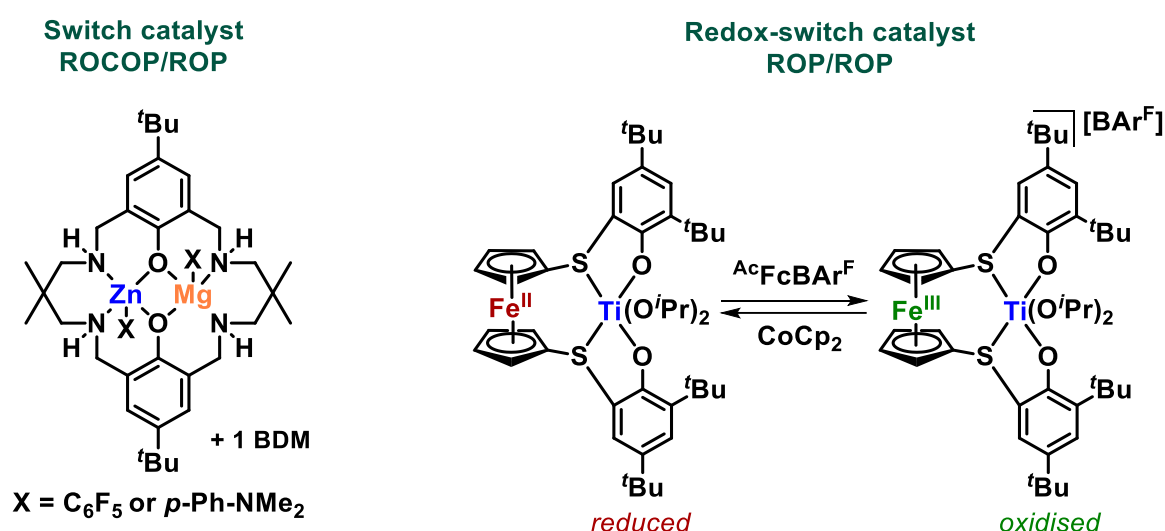


**Figure 2.3** Examples of literature reported heterometallic switch catalysts.<sup>126,130</sup>

Most of the switchable catalyst systems reported to date are ROP/ROCOP switches, where only one of the monomers is a cyclic ester. In a rather unusual example, Diaconescu and co-workers reported a redox-switchable Fe/Ti catalyst, where changing the oxidation state of the ferrocene unit switched between LA and CL ROP (Figure 2.3, right).<sup>130</sup> In a one-pot mixture of LA and CL monomer and the initiator, switching (thiolfan\*)Ti(O<sup>i</sup>Pr)<sub>2</sub> (thiolfan\* = 1,1'-bis(2,4-di-<sup>t</sup>Bu-6-thiophenoxy)ferrocene)) complex from the reduced ferrocenyl unit to its oxidised form (*i.e.* Fe(II) to Fe(III)) upon the addition of AcFcBAR<sup>F</sup> triggered the ROP of CL, while LA remained unreacted. Conversely, the reduction of [(thiolfan\*)Ti(O<sup>i</sup>Pr)<sub>2</sub>][BAR<sup>F</sup>] *via* the addition of CoCp<sub>2</sub> halted LA polymerisation but activated CL ROP.

*In situ* switching of the initiator redox state allowed the copolymerisation of LA and CL to produce multiblock PLA-PCL copolymers in one-pot.

The relative lack of heterometallic catalysts for cyclic ester block copolymerisations is surprising, as several heterometallic catalysts have been reported to efficiently homopolymerise several different cyclic esters, such as LA, CL,  $\delta$ -valerolactone and  $\beta$ -butyrolactone.<sup>112,113,131</sup> In this chapter, we unlock the potential of heterometallic catalysts featuring a M-O-M' electronic bridge within a ProPhenol scaffold, to prepare block copolymers from cyclic esters (M and M' refer to two different metals). This work also provides some insight into how the choice of the heterometal influences the copolymer structure. Overall, we reveal which heterometallic catalyst features lead to trade-offs between activity and control over the polymer structure.

## 2.3 Results and discussion

### 2.3.1 Synthesis and Characterisation of PCL-*block*-PLA Copolymer

Complexes [LZn<sub>2</sub>Et], [LMgZnEt] and [LCaZnEt] are efficient catalysts for the homopolymerisation of LA and CL,<sup>113,114</sup> and were selected for this study as the divalent nature of all three metals enables direct comparisons to be drawn between the three catalysts. Differences in the catalyst activity and resultant polymer structures therefore can be attributed to the nature of the metal instead of differences in the number of co-ligands or initiating units. In this work, the polymerisation conditions were modified slightly compared to those reported previously; the reaction temperature was increased from 60 °C to 70 °C to improve LA solubility in the copolymerisations and to elevate the catalyst activities.<sup>113</sup> The synthesis of PCL<sub>100</sub>-PLA<sub>100</sub> diblock copolymers was targeted, with CL added as the first monomer because the addition of LA to a living PCL\* chain is generally more straightforward than the addition of CL to a PLA\* chain (\*denotes the active chain end).<sup>132,133</sup>

**Table 2.1** Catalyst activity of **[LZn<sub>2</sub>Et]**, **[LMgZnEt]** and **[LCaZnEt]** for CL homopolymerisation in toluene at 70 °C at different time points.

| <b>[LZn<sub>2</sub>Et]</b> |                     | <b>[LMgZnEt]</b> |                     | <b>[LCaZnEt]</b> |                     |
|----------------------------|---------------------|------------------|---------------------|------------------|---------------------|
| <b>Time (s)</b>            | <b>CL conv. (%)</b> | <b>Time (s)</b>  | <b>CL conv. (%)</b> | <b>Time (s)</b>  | <b>CL conv. (%)</b> |
| 30                         | 30                  | 30               | 87                  | 30               | 91                  |
| 60                         | 54                  | 60               | 94                  | 60               | 95                  |
| 90                         | 72                  | 90               | 97                  | 120              | 98                  |
| 120                        | 82                  | 100              | 97                  | 180              | 98                  |
| 150                        | 89                  | 120              | 98                  |                  |                     |
| 180                        | 93                  | 130              | 98                  |                  |                     |
| 240                        | 96                  |                  |                     |                  |                     |
| 300                        | 98                  |                  |                     |                  |                     |

CL conversion to PCL was determined from PCL signal integrals with respect to CL monomer signals *via* <sup>1</sup>H NMR spectroscopy (refer to Chapter 6, [Section 6.4](#) for details).

All three catalysts exhibited excellent activity in the homopolymerisation of CL ([CL] = 1 M in toluene, 1 equiv. of BnOH), achieving essentially complete conversion of 100 equiv. CL to PCL within 5 minutes (**[LZn<sub>2</sub>Et]**: 5 min; **[LMgZnEt]**: 2.5 min, **[LCaZnEt]**: 2 min, as determined by <sup>1</sup>H NMR spectroscopy, Table 2.1). Due to the rapid conversion of CL, especially with **[LMgZnEt]** and **[LCaZnEt]**, the polymerisation rates of CL were not determined. Notably, lower *M<sub>n</sub>* values of PCL (at 98% CL conv.) were obtained when using heterometallic **[LCaZnEt]** (*M<sub>n</sub>* = 22.9 kg mol<sup>-1</sup>) and **[LMgZnEt]** (*M<sub>n</sub>* = 27.7 kg mol<sup>-1</sup>) compared to **[LZn<sub>2</sub>Et]** (*M<sub>n</sub>* = 32.5 kg mol<sup>-1</sup>), indicating a greater degree of transesterification of the polymers generated using the heterometallic complexes (Figure 2.6, *vide infra*).

Upon almost complete CL conversion (>98%), 100 equiv. of LA was added to the living PCL\* chain. Heterometallic **[LCaZnEt]** was significantly more active than **[LMgZnEt]** or **[LZn<sub>2</sub>Et]**, consuming over 95% of *rac*-LA in only 20 mins, whereas **[LMgZnEt]** and **[LZn<sub>2</sub>Et]** required 1 hr and 2.5 hr, respectively (Table 2.2 and Figure 2.3).

**Table 2.2** Catalyst activity of **[LZn<sub>2</sub>Et]**, **[LMgZnEt]** and **[LCaZnEt]** for LA co-polymerisation from a living PCL\* chain, in toluene at 70 °C, at different time points.

| <b>[LZn<sub>2</sub>Et]</b> |              | <b>[LMgZnEt]</b> |              | <b>[LCaZnEt]</b> |              |
|----------------------------|--------------|------------------|--------------|------------------|--------------|
| Time (min)                 | LA conv. (%) | Time (min)       | LA conv. (%) | Time (min)       | LA conv. (%) |
| 2                          | 15           | 1                | 35           | 1                | 58           |
| 4                          | 21           | 3                | 65           | 3                | 80           |
| 8                          | 37           | 5                | 71           | 5                | 87           |
| 15                         | 56           | 10               | 79           | 7                | 90           |
| 30                         | 72           | 20               | 87           | 10               | 92           |
| 60                         | 89           | 30               | 91           | 15               | 93           |
| 96                         | 94           | 40               | 93           | 20               | 96           |
| 150                        | 95           | 50               | 94           | 25               | 98           |
|                            |              | 60               | 95           | 30               | 98           |
|                            |              | 90               | 96           |                  |              |
|                            |              | 120              | 97           |                  |              |

LA conversion to PLA was determined from PLA signal integrals with respect to LA monomer signals *via* <sup>1</sup>H NMR spectroscopy (refer to Chapter 6, [Section 6.4](#) for details).

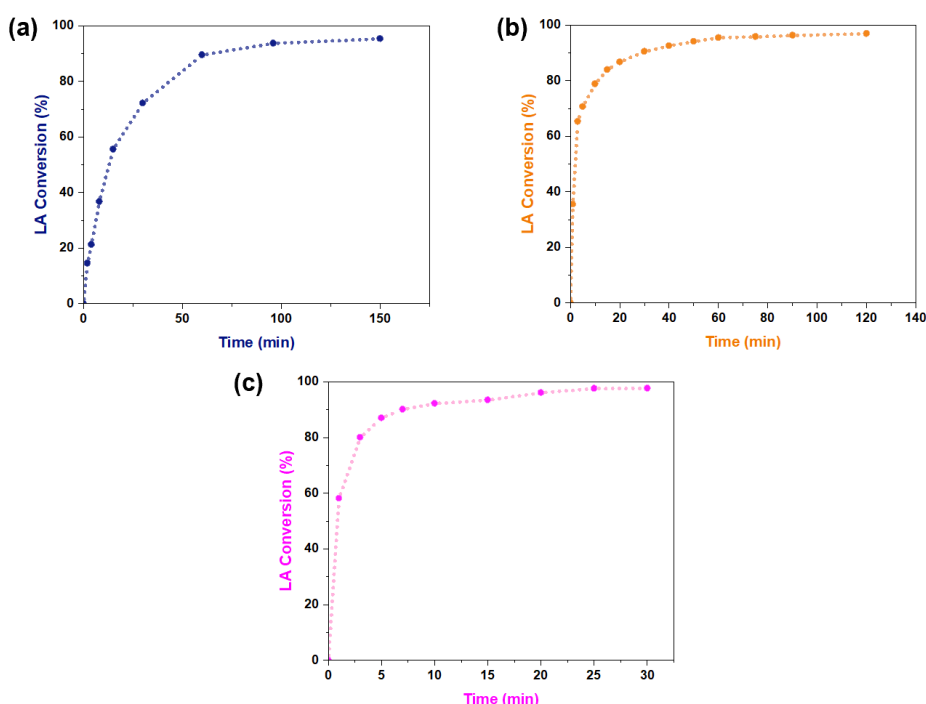


**Figure 2.3** Conversion plots of *rac*-LA co-polymerisation from a living PCL\* chain generated by catalysts (a) **[LZn<sub>2</sub>Et]**, (b) **[LMgZnEt]** and (c) **[LCaZnEt]**. Polymerisation conditions: [cat.]:[BnOH]:[CL]:[LA] = 1:1:100:100, [CL] = 1.0 M, [LA] = 0.5 M in toluene at 70 °C.

Strikingly, from the kinetic studies on the *rac*-LA ROP (*i.e.* second block), **[LZn<sub>2</sub>Et]** displayed a first-order rate constant for the *rac*-LA ROP ( $k_{\text{obs}} = 0.052 \text{ min}^{-1}$ ), whereas **[LMgZnEt]** and **[LCaZnEt]** were second-order in monomer ( $k_{\text{obs}} = 0.295 \text{ min}^{-1}$  and  $1.17 \text{ min}^{-1}$ , respectively) under identical

reaction conditions (Figure 2.4). This differs from the homopolymerisation of *rac*-LA with **[LMgZnEt]** and **[LCaZnEt]**, which displayed a first-order kinetics when the ROP of LA is initiated by the active catalyst rather than a PCL\* chain.<sup>114</sup>

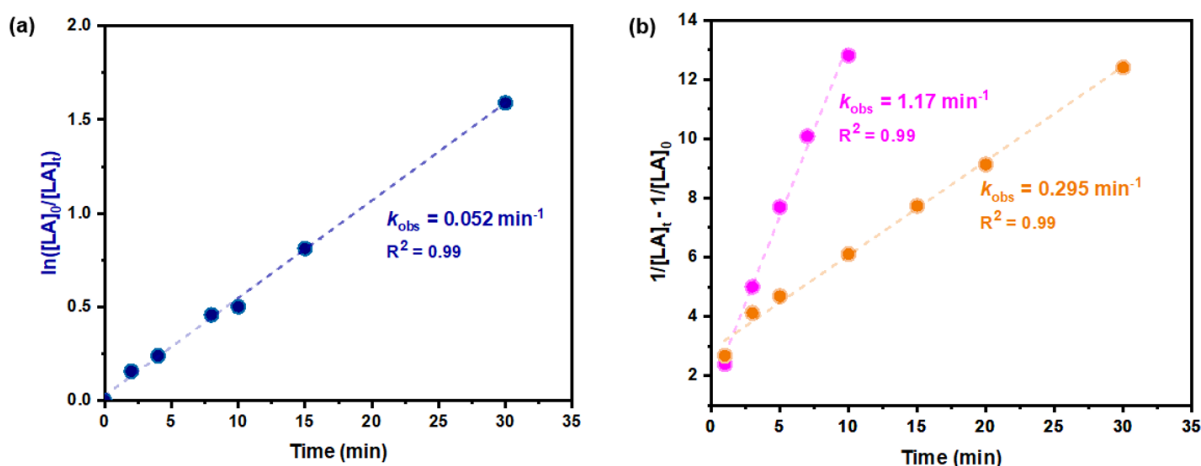


**Figure 2.4** Kinetic plots of *rac*-LA co-polymerisation from a living PCL\* chain generated by catalysts (a) **[LZn<sub>2</sub>Et]** (first-order) and (b) **[LMgZnEt]** and **[LCaZnEt]** (second-order). Polymerisation conditions: [cat.]:[BnOH]:[CL]:[LA] = 1:1:100:100, [CL] = 1.0 M, [LA] = 0.5 M in toluene at 70 °C.

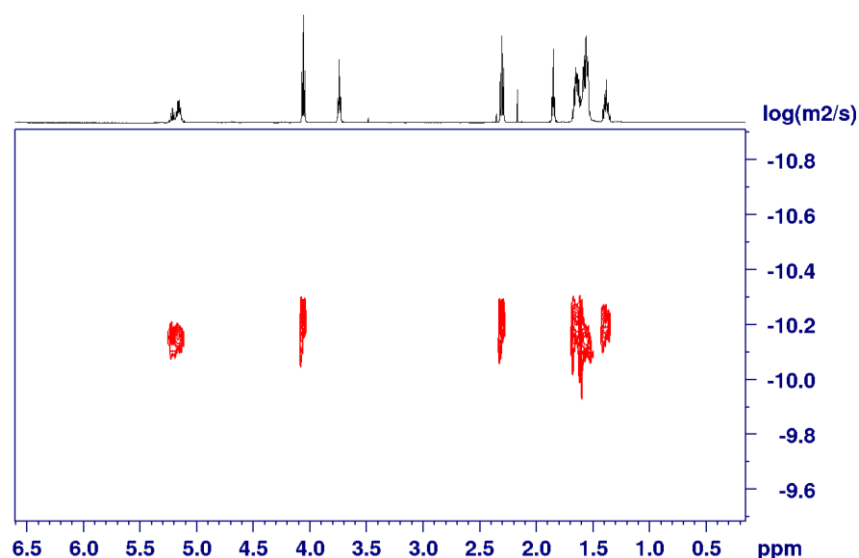


**Figure 2.5** Example DOSY NMR spectrum of PCL-*b*-PLA with a 1:100:100 **[LMgZnEt]**:CL:LA ratio.

The formation of a copolymer was supported by diffusion order NMR spectroscopy (DOSY NMR, Figure 2.5), as a single diffusion coefficient was observed for both PCL and PLA resonances. Providing further evidence for the synthesis of block copolymers, monomodal SEC traces were obtained that showed a significant increase in the  $M_n$  values upon incorporation of *rac*-LA as the second block (Figure 2.6 (a – c)). The dispersities were relatively low for all three catalysts (Table 2.3, entries 1 – 3,

*vide infra*), and were generally narrower for the copolymers than the PCL precursors (Figure 2.6). This indicates that the second step of the copolymerisation (LA ROP) was living in nature.<sup>69</sup>

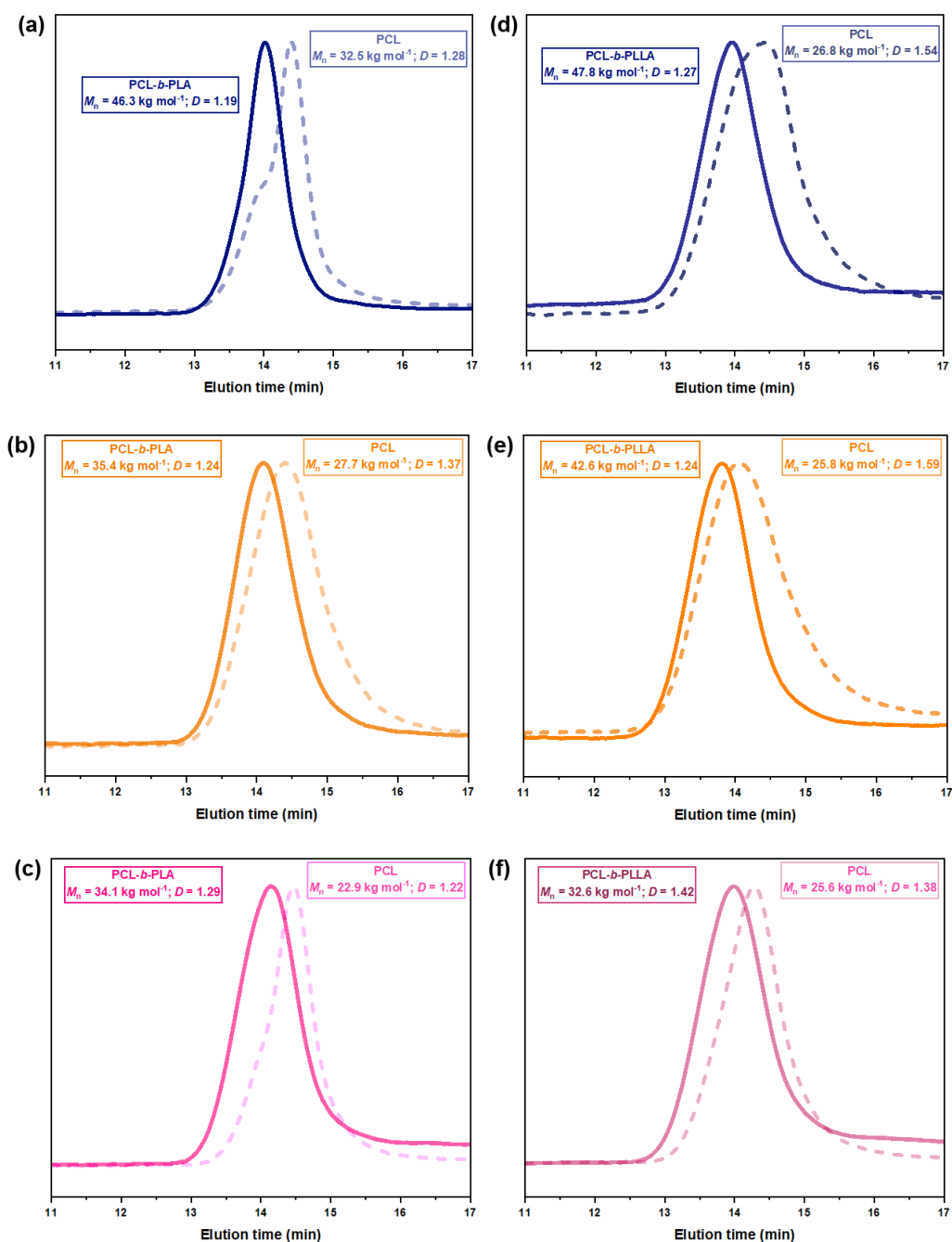
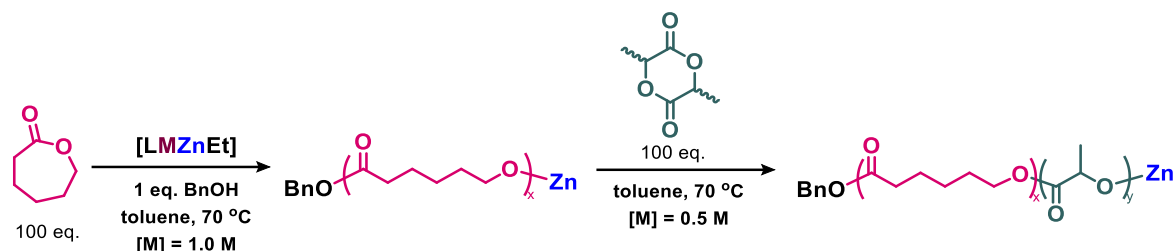


**Figure 2.6** Overlay of SEC traces of PCL and PCL-*b*-PLA catalysed by (a) [LZn<sub>2</sub>Et], (b) [LMgZnEt] and (c) [LCaZnEt] in toluene at 70 °C (Table 2.2).

**Table 2.3** PCL-PLA and PCL-PLLA diblock copolymers prepared using catalysts **[LZn<sub>2</sub>Et]**, **[LMgZnEt]** and **[LCaZnEt]**, with a 100:100:1:1 ratio of [CL]:[LA]:[cat.]:[BnOH] in toluene solvent.



|   | Cat.                       | Polymer <sup>a</sup> | $M_{n,obs}^b$<br>(kg mol <sup>-1</sup> ) | $M_{n,calc}^c$<br>(kg mol <sup>-1</sup> ) | $\bar{D}^b$ | $P_i^d$ | Comp.<br>(PCL:PLA) <sup>e</sup> | $I_{CL}, I_{LA}^{e,f}$ | $R^{e,g}$ |
|---|----------------------------|----------------------|------------------------------------------|-------------------------------------------|-------------|---------|---------------------------------|------------------------|-----------|
| 1 | <b>[LZn<sub>2</sub>Et]</b> | PCL-PLA              | 46.3                                     | 24.9                                      | 1.19        | 0.51    | 54:46                           | 119, 100               | 0.02      |
| 2 | <b>[LMgZnEt]</b>           |                      | 35.4                                     | 25.2                                      | 1.24        | 0.48    | 50:50                           | 100, 99                | 0.02      |
| 3 | <b>[LCaZnEt]</b>           |                      | 34.1                                     | 25.3                                      | 1.29        | 0.49*   | 57:43                           | 68, 50                 | 0.04      |
| 4 | <b>[LZn<sub>2</sub>Et]</b> | PCL-PLLA             | 47.8                                     | 25.3                                      | 1.27        | 1.00    | 57:43                           | 62, 50                 | 0.04      |
| 5 | <b>[LMgZnEt]</b>           |                      | 42.6                                     | 24.8                                      | 1.34        | 1.00    | 57:43                           | 68, 50                 | 0.04      |
| 6 | <b>[LCaZnEt]</b>           |                      | 32.6                                     | 25.0                                      | 1.42        | 0.62*   | 58:42                           | 70, 50                 | 0.03      |

[a] [CL] = 1 M, [LA] = 0.5 M in toluene, 70 °C (refer to [Section 2.6](#) for details). [b] Determined by SEC analysis using polystyrene standards in THF, values uncorrected to enable comparisons between crude homopolymers and copolymers. [c] Calculated from monomer conversions,  $M_{n,calc} = ((M_{CL} \times ([M]/[I]) \times CL \text{ conv.}) + (M_{LA} \times ([M]/[I]) \times LA \text{ conv.}))$ , assuming 1 chain per catalyst. [d] Determined by deconvoluted <sup>1</sup>H{H} NMR spectroscopy.<sup>18</sup> \*Values subject to error due to LA epimerisation with **[LCaZnEt]** (*vide infra*).<sup>36</sup> [e] Composition determined from PCL/PLA <sup>1</sup>H NMR integrals for purified copolymer samples (refer to Chapter 6 for further details). [f]  $I$ : number sequence length [g] Randomness factor,  $R$ :  $R = 0$  (blocky structure),  $R = 1$  (fully random).

The block structure was further investigated by <sup>1</sup>H NMR spectroscopy to obtain key information on the composition, structure and average sequence length of the PCL-PLA copolymers. The polymer composition was calculated by comparing the relative integrals of the PCL and PLA <sup>1</sup>H NMR resonances. In all cases, the composition of the copolymers was concordant with the targeted 50:50 PCL:PLA composition. The randomness factor,  $R$ , gives insight into whether the copolymer has a well-defined block structure ( $R = 0$ ), a purely random structure ( $R = 1$ ), or somewhere in-between (refer to randomness calculation, [Section 6.6](#) for details).<sup>134</sup> Gratifyingly, all complexes generated highly defined ‘blocky’ PCL-*b*-PLA structures, with  $R$  factors ranging from 0.02 to 0.04. Furthermore, the average monomer sequence lengths in PCL-*b*-PLA,  $I_{CL}$  and  $I_{LA}$ , were also relatively close to the target values ( $(I_{CL}, I_{LA}) = (119, 100)$  and  $(100, 99)$  for **[LZn<sub>2</sub>Et]** and **[LMgZnEt]**, respectively), albeit with **[LCaZnEt]** delivering somewhat shorter  $I_{CL}$  and  $I_{LA}$  values ( $(I_{CL}, I_{LA}) = (68, 50)$ ). Overall, these results show that all three complexes are all highly efficient catalysts for the production of well-defined PCL-*b*-PCL diblock copolymers.

None of the catalysts displayed any stereocontrol for *rac*-LA ROP, and all generated atactic PLA blocks in the diblock copolymers as determined by deconvoluted <sup>1</sup>H{H} NMR analysis. This corresponds with

previous observations when using these catalyst systems for the homopolymerisation of *rac*-LA.<sup>113,114</sup> Interestingly, upon substituting *rac*-LA for L-LA, **[LZn<sub>2</sub>Et]** and **[LMgZnEt]** generated isotactic PLLA blocks (Table 2.3, entries 4 – 5), whereas **[LCaZnEt]** gave an atactic PLA block (entry 6). This was attributed to epimerisation, an issue that has been encountered with some other alkaline earth metal-based catalysts (refer to Chapter 1, [Section 1.3.2](#)).<sup>135</sup> Kricheldorf and co-workers investigated the extent of L-LA racemisation with different metal salt initiators (*i.e.* metal oxide, carbonate, carboxylate), and observed that catalysts with higher Brønsted basicity (*i.e.* Ca vs Mg) generally gave a greater degree of racemisation due to deprotonation of the methine C-H of L-LA.<sup>50</sup> The L-LA monomer is more prone to suffer from racemisation than the PLLA polymer chain, as negative charge delocalisation in a cyclic molecule is more entropically favoured, which may explain the epimerisation observed even at low L-LA conversions.

The PCL-*b*-PLA diblock copolymers synthesised by all three catalysts displayed similar thermal behaviour, with a single melting temperature ( $T_m$  ~56 °C) corresponding to the  $T_m$  of PCL homopolymer, but no PLA  $T_m$ , reflecting the amorphous state of the atactic PLA block (Tables 2.3 and 2.4, entries 1 – 3; Figure 2.7). Additionally, the formation of diblock microstructures was further supported through the observation of glass transition temperature ( $T_g$ ) by DSC analysis. Where ‘blocky’ character in a copolymer is retained, two distinct  $T_g$  values, of each polymer component, are expected. In contrast, a random copolymer generally exhibits one  $T_g$  value, resulting from short sequences of randomly distributed monomers along the copolymer chain.<sup>136</sup> In all cases, two  $T_g$  values were observed for PCL (-62.6 – -60.4 °C) and PLA (25.1 – 30.4 °C), indicating that insignificant randomisation occurs in the block copolymer chain.<sup>137</sup>

When L-LA was used instead of *rac*-LA, catalysts **[LZn<sub>2</sub>Et]** and **[LMgZnEt]** gave polymers with a  $T_m$  value of 156 – 158 °C, due to the crystalline phase of the isotactic PLLA block (Table 2.4, entries 4 and 5; Figure 2.8 (a – b)), whereas no  $T_m$  was observed in the copolymers produced using **[LCaZnEt]**. This was attributed to the amorphous nature of the PLA block resulting from L-LA epimerisation (Table 2.4, entry 6; Figure 2.8 (c)). As all catalysts displayed high activities and delivered well controlled diblock copolymer structures, we further attempted to access higher-order triblock PCL-PLA-PCL copolymers and study the activity and control of all three catalysts.

**Table 2.4** Thermal properties of PCL-*b*-PLA and PCL-*b*-PLLA copolymers analysed by DSC.

|   | Cat.                  | Polymer  | PCL        |            | Degree of crystallinity, $\chi_{\text{PCL}}$ (%) <sup>138</sup> | P(L)LA     |            | Degree of crystallinity, $\chi_{\text{PLA}}$ (%) <sup>138</sup> |
|---|-----------------------|----------|------------|------------|-----------------------------------------------------------------|------------|------------|-----------------------------------------------------------------|
|   |                       |          | $T_g$ (°C) | $T_m$ (°C) |                                                                 | $T_g$ (°C) | $T_m$ (°C) |                                                                 |
| 1 | [LZn <sub>2</sub> Et] | PCL-PLA  | -62.6      | 56.3       | 20                                                              | 25.1       | -          | -                                                               |
| 2 | [LMgZnEt]             |          | -62.2      | 55.8       | 16                                                              | 30.4       | -          | -                                                               |
| 3 | [LCaZnEt]             |          | -60.4      | 55.7       | 23                                                              | 29.9       | -          | -                                                               |
| 4 | [LZn <sub>2</sub> Et] | PCL-PLLA | -62.8      | 55.3       | 18                                                              | 26.0       | 156.5      | 23                                                              |
| 5 | [LMgZnEt]             |          | -62.2      | 54.7       | 15                                                              | -          | 163.2      | 28                                                              |
| 6 | [LCaZnEt]             |          | -59.8      | 55.8       | 24                                                              | -          | -          | -                                                               |

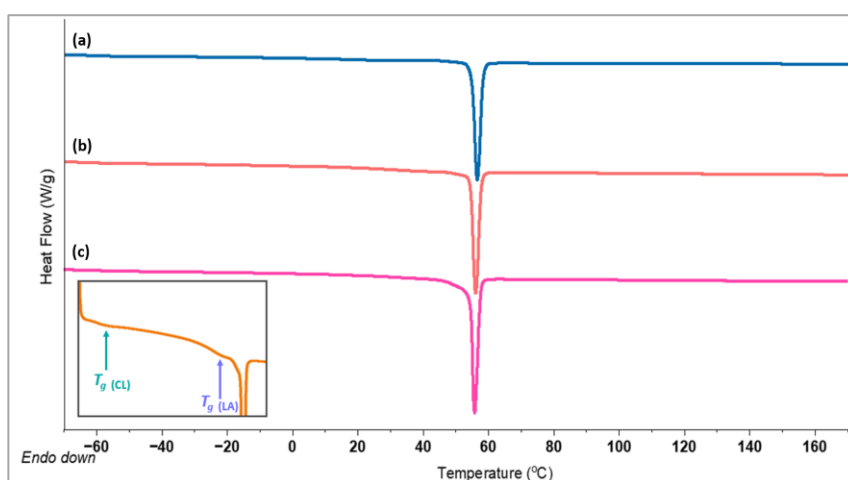


**Figure 2.7** DSC thermograms for PCL-*b*-PLA copolymers catalysed by (a) [LZn<sub>2</sub>Et], (b) [LMgZnEt] and (c) [LCaZnEt].

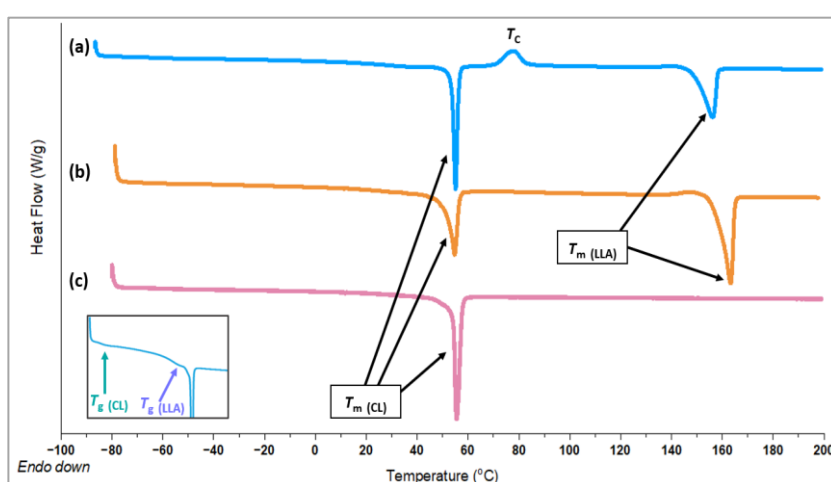


**Figure 2.8** DSC thermograms for PCL-*b*-PLLA copolymers catalysed by (a) [LZn<sub>2</sub>Et], (b) [LMgZnEt] and (c) [LCaZnEt].

### 2.3.2 Accessing Higher Order PCL-PLA Block Copolymers with Multimetallic ProPhenol Complexes

The synthesis of triblock PCL-PLA-PCL copolymers were attempted through the addition of CL as the third monomer onto the growing PCL-PLA\* block copolymer chain. The PCL-*b*-PLA precursor was synthesised using higher monomer concentrations ( $[CL_1] = 1.76$  M,  $[LA] = 0.88$  M in toluene) with a subsequent batch of neat CL ( $CL_2$ ) added *in situ*, as increased concentration improved  $CL_2$  conversion in the 'third block'.<sup>139–142</sup>

Intriguingly, homometallic  $[LZn_2Et]$  outperformed heterometallic complexes  $[LMgZnEt]$  and  $[LCaZnEt]$  in the conversion of  $CL_2$  as the third block after 24 h, reaching 73% conversion vs 42% for  $[LMgZnEt]$  and 16% for  $[LCaZnEt]$  (Table 2.5, entries 1 – 3). This is a striking difference from the CL and LA homopolymerisations and the synthesis of PCL-*b*-PLA diblock copolymers, where the activity trend was  $[LCaZnEt] > [LMgZnEt] > [LZn_2Et]$ . Moreover, only  $[LZn_2Et]$  produced a copolymer with a significantly increased  $M_n$  value compared to the PCL-*b*-PLA (and the PCL) precursor (Table 2.5, Figures 2.9 – 2.10).

**Table 2.5** Investigations into the extension of PCL-PLA diblock copolymers into PCL-PLA-PCL copolymers using catalysts  $[LZn_2Et]$ ,  $[LMgZnEt]$  and  $[LCaZnEt]$  in toluene solvent at 70 – 100 °C.

|                | Cat.        | Polymer     | $CL_2$<br>conv.<br>(%) <sup>a</sup> | $M_{n,obs}$<br>(kg mol <sup>-1</sup> ) <sup>b</sup> | $M_{n,calc}$<br>(kg mol <sup>-1</sup> ) <sup>c</sup> | $\bar{D}^b$ | Comp.<br>(PCL:PLA) <sup>d</sup> | $I_{CL}, I_{LA}^{d,e}$ | $R^{d,f}$ |
|----------------|-------------|-------------|-------------------------------------|-----------------------------------------------------|------------------------------------------------------|-------------|---------------------------------|------------------------|-----------|
| 1 <sup>g</sup> | $[LZn_2Et]$ | PCL-PLA     | -                                   | 49.7                                                | 25.4                                                 | 1.23        | 53:47                           | 100, 112               | 0.02      |
|                |             | PCL-PLA-PCL | 73                                  | 56.3                                                | 33.8                                                 | 1.48        | 64:36                           | 9, 5                   | 0.31      |
| 2 <sup>g</sup> | $[LMgZnEt]$ | PCL-PLA     | -                                   | 32.6                                                | 25.4                                                 | 1.37        | 50:50                           | 96, 95                 | 0.02      |
|                |             | PCL-PLA-PCL | 42                                  | 31.3                                                | 30.1                                                 | 1.56        | 53:47                           | 9, 8                   | 0.23      |
| 3 <sup>g</sup> | $[LCaZnEt]$ | PCL-PLA     | -                                   | 28.9                                                | 25.4                                                 | 1.43        | 50:50                           | 51, 50                 | 0.04      |
|                |             | PCL-PLA-PCL | 16                                  | 28.9                                                | 27.3                                                 | 1.44        | 63:37                           | 21, 13                 | 0.13      |
| 4 <sup>h</sup> | $[LMgZnEt]$ | PCL-PLA     | -                                   | 31.0                                                | 25.3                                                 | 1.43        | 49:51                           | 96, 100                | 0.02      |
|                |             | PCL-PLA-PCL | 90                                  | 31.5                                                | 35.6                                                 | 1.55        | 67:33                           | 4, 2                   | 0.76      |
| 5 <sup>h</sup> | $[LCaZnEt]$ | PCL-PLA     | -                                   | 26.4                                                | 25.1                                                 | 1.60        | 45:55                           | 83, 100                | 0.02      |
|                |             | PCL-PLA-PCL | 48                                  | 22.8                                                | 30.6                                                 | 1.62        | 63:37                           | 7, 4                   | 0.38      |

[a] Determined from PCL/PLA signal integrals with respect to CL/LA monomer signals *via* <sup>1</sup>H NMR spectroscopy (refer to Section 6.4 for details); [b] Determined by SEC analysis using polystyrene standards in THF, values uncorrected to enable comparisons between crude homopolymers and copolymers; [c] Calculated from monomer conversions,  $M_{n,calc} = ((M_{CL} \times ([M]/[I]) \times CL \text{ conv.}) + (M_{LA} \times ([M]/[I]) \times LA \text{ conv.}) + (M_{CL} \times ([M]/[I]) \times CL_2 \text{ conv.}))$ , assuming 1 chain per catalyst. [d] Determined from PCL/PLA signal integrals by <sup>1</sup>H NMR spectroscopy of copolymer samples, using crude aliquots for PCL-PLA precursors and purified samples for the final PCL-PLA-PCL copolymers; [e] *I*: number average sequence length; [f] Randomness factor,  $R$ :  $R = 0$  (blocky structure),  $R = 1$  (fully random); [g] 100:100:100:1:1  $[CL_1]:[LA]:[CL_2]:[cat.][BnOH]$  where  $[CL_1] = 1.76$  M,  $[LA] = 0.88$  M solution in toluene and  $CL_2$  was added neat, at 70 °C; [h] 100:100:100:1:1  $[CL_1]:[LA]:[CL_2]:[cat.][BnOH]$  where  $[CL_1] = 2$  M,  $[LA] = 1$  M solution in toluene and  $CL_2$  was added neat, at 100 °C.

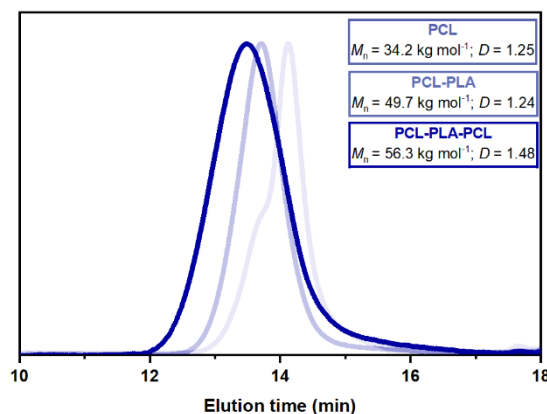


**Figure 2.9** SEC traces of PCL homopolymer, PCL-*b*-PLA and PCL-PLA-PCL copolymers catalysed by **[LZn<sub>2</sub>Et]** (Table 2.4, entry 1).

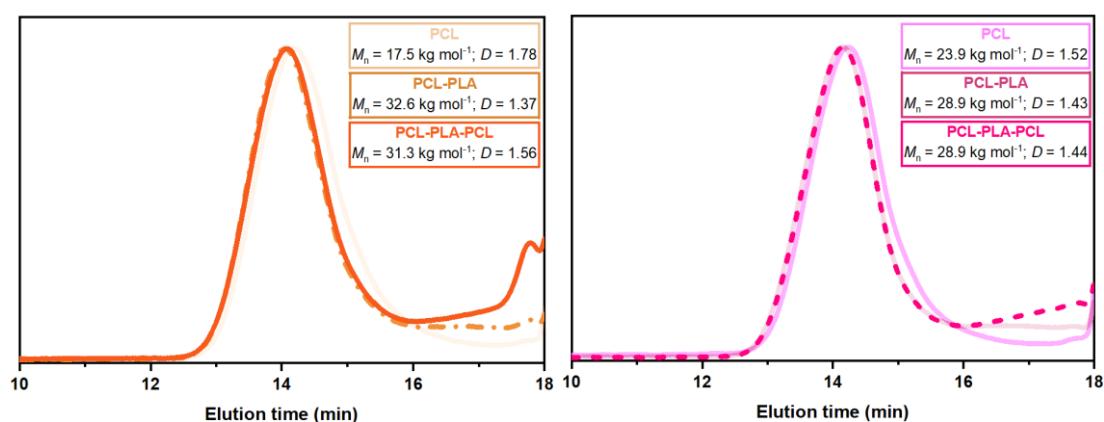


**Figure 2.10** SEC traces of PCL homopolymer, PCL-*b*-PLA and PCL-PLA-PCL copolymers catalysed by **[LMgZnEt]** (left) and **[LCaZnEt]** (right) (Table 2.4, entries 2 – 3).

To increase the conversion of CL<sub>2</sub> using **[LMgZnEt]** and **[LCaZnEt]**, both the temperature and the monomer concentrations were increased (100 °C, [CL<sub>1</sub>] = 2 M, [LA] = 1 M, [CL<sub>2</sub>] = neat, in toluene). This gave higher CL<sub>2</sub> conversions, achieving 90% and 48% conversion with **[LMgZnEt]** and **[LCaZnEt]**, respectively (Table 2.5, entries 3 and 5). However, this increased conversion came at the expense of increased transesterification and randomisation of the polymer microstructure, as confirmed by the increased *R* factors and shorter average sequence lengths (*e.g.* Table 2.4, entry 4; *R* increases from 0.02 for PCL-*b*-PLA to 0.76 for PCL-PLA-PCL). Additionally, despite 90% conversion of the third monomer, the  $M_n$  value increased only slightly (from 31.0 kg mol<sup>-1</sup> for PCL-*b*-PLA to 31.5 kg mol<sup>-1</sup> for PCL-PLA-PCL, Figure 2.11). This indicates that intramolecular transesterification occurs forming lower molar mass species, concomitantly preventing an increase of the copolymer molecular weight. This undesired side reaction was evidenced by the observation of pronounced low molecular weight tailing in the SEC chromatograms (Figure 2.9 vs Figures 2.10 and 2.11).<sup>143</sup>

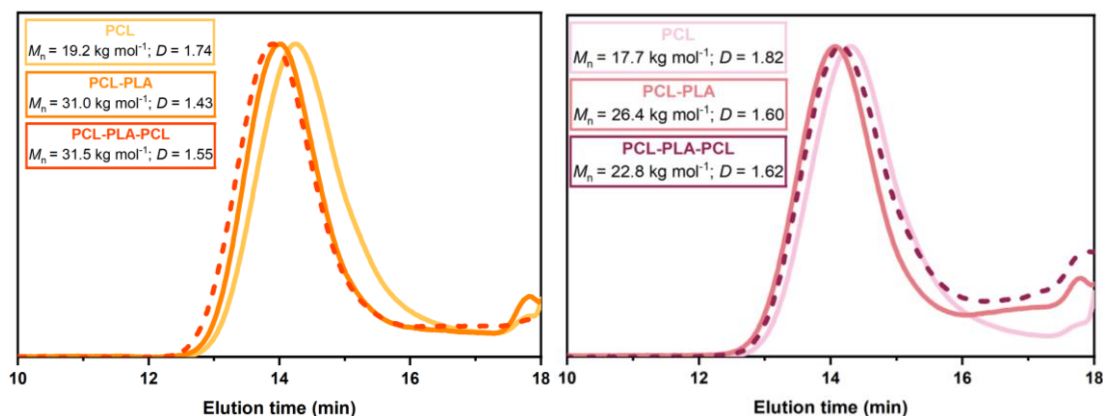


**Figure 2.11** SEC traces of PCL homopolymer, PCL-*b*-PLA and PCL-PLA-PCL copolymers catalysed by [LMgZnEt] (left) and [LCaZnEt] (right) at elevated temperature (100 °C) and increased monomer concentration (Table 2.4, entries 4 – 5).

The experimental data suggests that with [LMgZnEt] and [LCaZnEt], higher CL<sub>2</sub> conversion is generally linked to increased transesterification (Table 2.5, entries 2 vs 3; 4 vs 5), which makes it challenging to draw direct comparisons between the different catalysts. Yet [LCaZnEt] gives very short average sequence lengths even at just 48% conversion, which are lower than the average sequence lengths observed with catalyst [LMgZnEt] at a similar, albeit slightly lower conversion (entries 2 and 5), indicating that a greater extent of transesterification occurs with [LCaZnEt] than [LMgZnEt]. This is corroborated by the shorter  $M_n$  values observed for resultant copolymers generated by the heterometallic catalysts. For example, with [LCaZnEt], the  $M_n$  value decreased from 26.4 kg mol<sup>-1</sup> to 22.8 kg mol<sup>-1</sup> upon addition of CL<sub>2</sub>, which correlated with a visual decrease in the polymerisation viscosity upon addition of CL<sub>2</sub>.

Transesterification appears to outcompete the propagation of CL<sub>2</sub> when using heterometallic [LMgZnEt] and [LCaZnEt], with [LCaZnEt] giving the poorest control on the basis of the  $R$  and  $I$  values as well as DOSY analysis. Specifically, the DOSY spectra gave a single diffusion coefficient for the PCL-PLA-PCL copolymers synthesised using [LZn<sub>2</sub>Et] and [LMgZnEt] (Figure 2.12 (a and b)), yet multiple diffusion coefficients were observed for the copolymers prepared using [LCaZnEt] (Figure 2.12 (c)). The latter indicates the presence of multiple polymer species in solution due to transesterification, which may be catalysed by the large and Lewis acidic calcium coordinating and activating carbonyl units from the polymer chain towards transesterification.

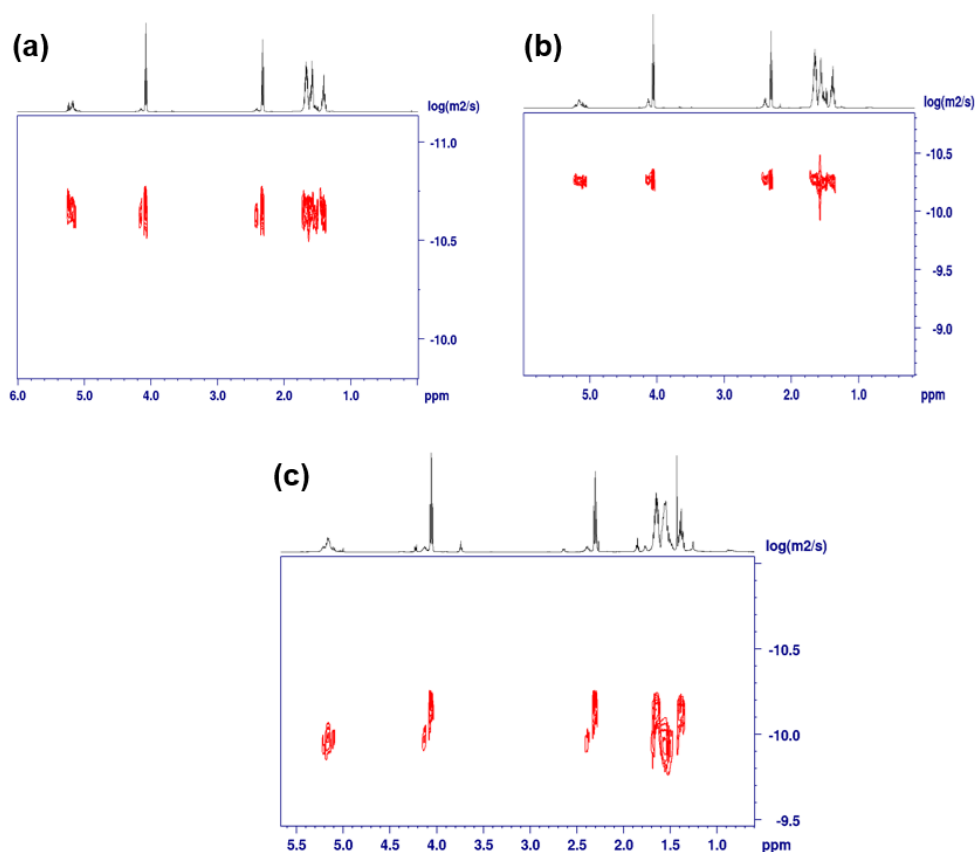
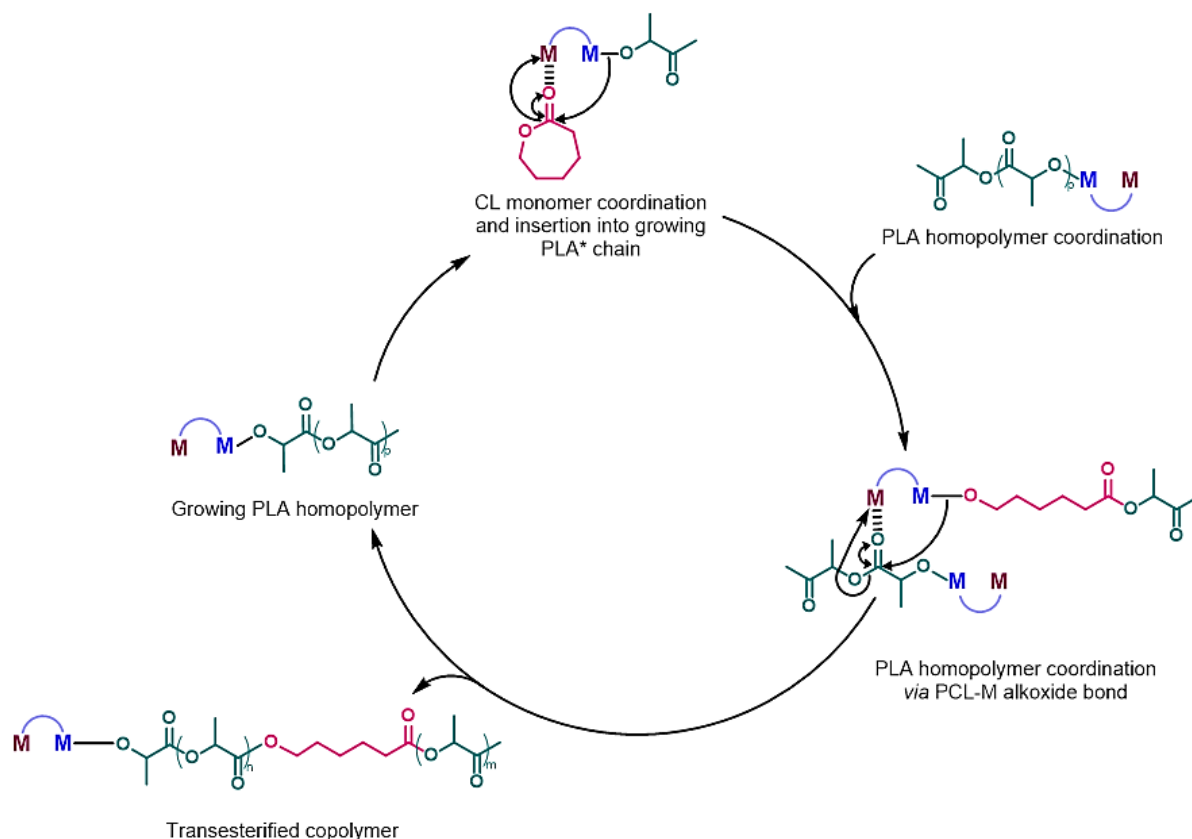


**Figure 2.12** DOSY NMR spectra of the purified PCL-PLA-PCL copolymer catalysed by (a) **[LZn<sub>2</sub>Et]**, (b) **[LMgZnEt]** and (c) **[LCaZnEt]**. Polymerisation conditions: 100:100:100:1:1 [CL<sub>1</sub>]:[LA]:[CL<sub>2</sub>]:[cat.]:[BnOH] where [CL<sub>1</sub>] = 1.76 M, [LA] = 0.88 M solution and CL<sub>2</sub> was added neat, in toluene solvent at 70 °C (using **[LZn<sub>2</sub>Et]**) or 100 °C (using **[LMgZnEt]** and **[LCaZnEt]**).

While the direct comparison of the triblock and diblock structures was somewhat limited by the different copolymer compositions, the triblock copolymers clearly have a less well-defined “blocky” structure than the diblock copolymers. This was evidenced by the lower average sequence lengths (*l*) and higher randomness factors (*R*), which increased from *R* = 0.02 – 0.04 for the diblock copolymers to *R* = 0.13 – 0.76 for the triblock copolymers (refer Table 2.5).<sup>144</sup> The loss of the block structure was attributed to transesterification, as evidenced by notable CL-LA linkage resonances at 4.11 ppm in the <sup>1</sup>H NMR spectra (refer to [Section 6.6](#) for further details).

### 2.3.3 Cooperativity vs Competition in Heterometallic Systems

Taken together, these observations indicate that transesterification is initiated by the incorporation of CL into the propagating PCL-PLA\* chain. This phenomenon has been observed previously in the synthesis of PLA-PCL copolymer *via* the 'PLA first' route.<sup>141</sup> The randomisation of the copolymer microstructure is proposed to occur *via* propagation of CL monomer followed by intermolecular transesterification of PLA\* homopolymer *via* the reactive PCL-[M] alkoxide bond (Scheme 2.1).



**Scheme 2.1** Proposed mechanism for CL-initiated transesterification of PLA\* polymer chain.<sup>141</sup>

In the 'PLA first' route, the randomisation observed upon CL incorporation into growing PLA\* has been attributed to the higher rate of CL transesterification relative to the rate of CL propagation ( $k_{tr} > k_p$ ).<sup>92,124</sup> Conversely, the addition of LA to growing PCL\* in the 'PCL first' route generally does not lead to transesterification ( $k_{tr} < k_p$ ),<sup>69</sup> thus producing well-defined PCL-*b*-PLA block copolymer, as observed in this work (Section 2.3.1). A key difference observed between these two routes is the presence of a pendant substituent (*i.e.* Me group) neighbouring the alkoxide bond of PLA chain, which is absent on the PCL chain. In the attempted synthesis of PCL-PLA-PCL copolymer (Section 2.3.2), the lack of a sterically demanding substituent on the PCL-[M] alkoxide bond may enable the coordination of PLA homopolymer, thus initiating intermolecular transesterification.

Overall, this work revealed that different catalysts can result in different degrees of transesterification upon addition of CL to the PCL-PLA\* chain, highlighting the influence the (hetero)metal exerts over the copolymer structure for PCL-PLA-PCL copolymers (Figure 2.13). The features of heterometallic “ate” catalysts that enhance propagation also enhance transesterification. An increased metal Lewis acidity ( $\text{Ca} > \text{Mg} > \text{Zn}$ ) can facilitate monomer coordination (propagation) or polymer coordination (transesterification), and can simultaneously enhance the nucleophilicity of the M-OR unit towards both reactions (Scheme 2.2, *vide infra*).

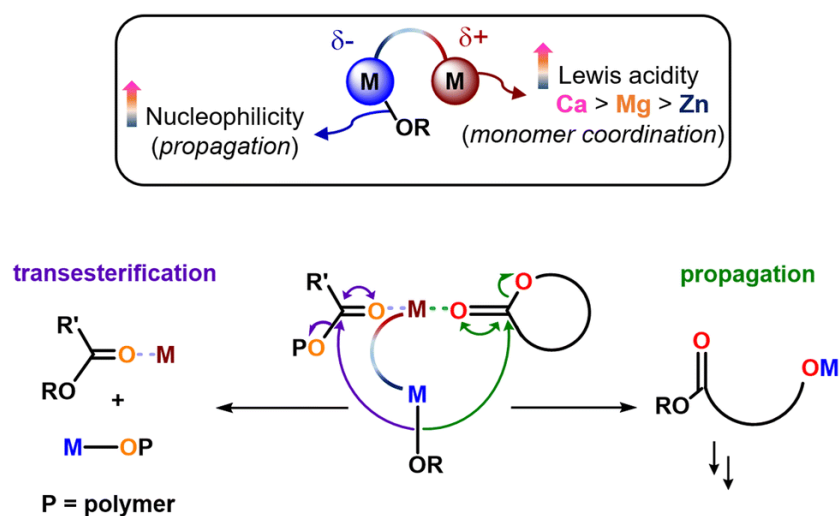
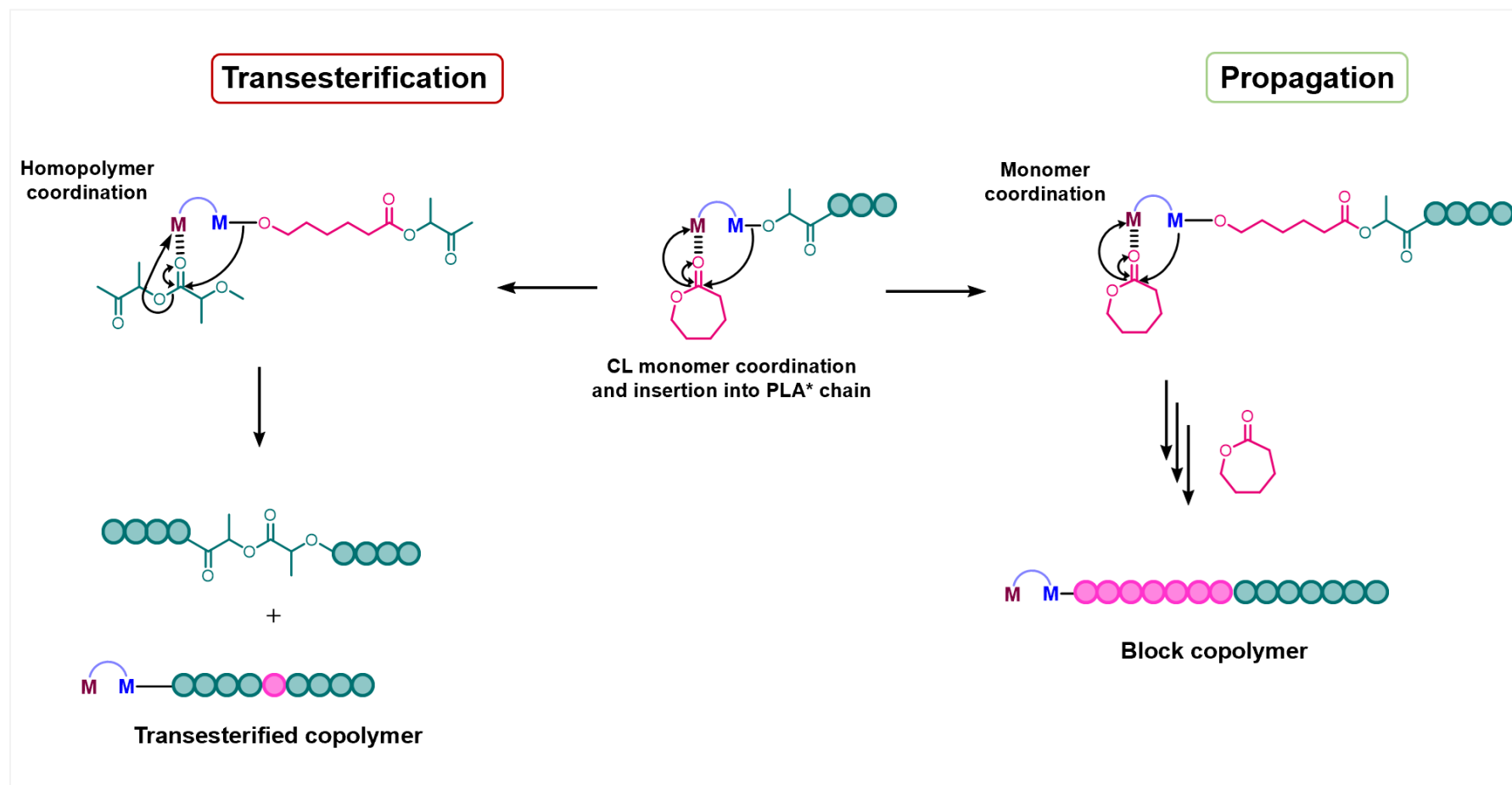


**Figure 2.13** The competition between propagation and transesterification is controlled by the nature of the (hetero)metal (top figure).



**Scheme 2.2** Summary of reaction pathways available following  $\epsilon$ -caprolactone (CL) insertion, either 1) propagation to produce block copolymers (right) or 2) transesterification to give random copolymers (left).<sup>141</sup>

## 2.4 Conclusions

In this chapter, we showcase the first report of a homogeneous, heterometallic “ate” catalyst for the synthesis of well-controlled PCL-*b*-PLA diblock copolymers. The heterometallic Ca/Zn and Mg/Zn complexes outperform the homometallic *bis*-Zn analogue in terms of activity, showcasing that heterometallic cooperativity enhancements can be translated from PLA and PCL homopolymers to diblock copolymers. In contrast, investigations into PCL-PLA-PCL triblock copolymers revealed that addition of CL<sub>2</sub> as the third monomer triggered transesterification, with heterometallic [LMgZnEt] and [LCaZnEt] giving more random polymer structures than homometallic [LZn<sub>2</sub>Et].

The transesterification trend of [LCaZnEt] > [LMgZnEt] > [LZn<sub>2</sub>Et] upon addition of CL<sub>2</sub> matches the catalyst propagation rate in the homopolymerisation of CL or LA and the synthesis of PCL-PLA diblock copolymers. Addition of CL<sub>2</sub> converts the metal-PLA\* alkoxide bond into a metal-PCL\* alkoxide bond, whereupon transesterification significantly outcompetes propagation for both [LMgZnEt] and [LCaZnEt] resulting in low conversions of CL<sub>2</sub> as the third monomer. This shows that heterometallic catalysts can deliver activity enhancements in ROP but this needs to be carefully balanced, as the catalyst features that lead to enhanced activities can also enhance transesterification side-reactions. Specifically, both Lewis acid coordination of a Lewis donor monomer and nucleophilic attack/ring-opening are key steps in cyclic ester ROP.<sup>44</sup> Notably, Lewis acid catalysed transesterification also involves the Lewis activation of a carbonyl unit and nucleophilic attack. The nature of the (hetero)metals is thus key in controlling the competition between propagation and transesterification.

The enhanced activity of heterometallic complexes in cyclic ester ROP has previously been ascribed to the formation of “ate” structures, which simultaneously enhances the Lewis acidity of one metal (*e.g.* Mg or Ca) to aid monomer coordination, and the nucleophilicity of another (*e.g.* Zn-OR bond) to enhance nucleophilic attack and ring-opening.<sup>114</sup> While these two catalyst features facilitate ROP, they can also facilitate transesterification through a Lewis acid activation mechanism. Therefore, a careful choice of metal combinations in heterometallic complexes is imperative to harness both high activity and good control in the synthesis of well-defined PCL-P(L)LA block copolymers.

## 2.5 Future Work

Synergistic effect in heterometallic complexes stemming from “ate” character translates into significant activity enhancement in PCL-*b*-PLA synthesis, accompanied by good polymerisation control of the diblock copolymer. Given the striking loss of control observed in higher order block copolymer generated by the heterometallic catalysts compared to the *bis*-Zn counterpart, it would be interesting to further investigate if this concept generally applies to other heterometallic complexes. Three key questions include: are the trade-offs between polymerisation activity and control generally more prominent in higher degree block copolymers, are these trade-offs specific to certain catalytic systems with specific ligand scaffolds or features, or is the trade-off exclusively influenced by the choice of (hetero)metal combination? Extending this study to other catalytic systems will allow better understanding of different roles of the metals, and may provide clearer insight into the origins of cooperativity (or inferiority) performance in multi- or heterometallic complexes.

Randomisation of copolymer microstructure was observed in this study, particularly in the formation of PCL-PLA-PCL copolymer, where CL monomer was added sequentially to the growing PCL-PLA\* chain. In general, the synthesis of well-defined block copolymers requires the rate of propagation to be greater than the rate of monomer transesterification (*i.e.*  $k_p > k_{tr}$ ), where both rates are influenced by multiple factors. For example, the rate of propagation is enhanced from an increased ring strain of lactones, whereas the greater steric bulk of a growing polymer lowers the rate of transesterification. Therefore, to better understand the origin of transesterification in block copolymers synthesis, specifically through the ‘PLA first’ route, a more comprehensive study of heterometallic cooperativity in block copolymer formation is accessible by testing different combination of lactones. Sterically more hindered monomers, such as 7-methyl-2-oxepanone or 2-methyl- $\epsilon$ -caprolactone, can be tested in place of CL to investigate if bulkier substituents of lactones lower the rate of monomer transesterification into PLA\* chain. Consequently, linear chain propagation would outcompete transesterification ( $k_p > k_{tr}$ ), and the formation of well-defined block copolymer structure can thus be realised. It would be valuable to discover if enhanced activity and control could be achieved with heterometallic catalysts in higher order block copolymers if transesterification could be controlled or minimised with more sterically hindered monomers.

Investigation into the activity and resultant copolymer structures generated by the homometallic complexes and the heterometallic counterparts, and comparing the common features of monomer combinations could pave way to better understand the balance between activity and control seen in these catalytic systems.

## 2.6 Experimental

### 2.6.1 Synthesis of Complexes [LZn<sub>2</sub>Et], [LMgZnEt] and [LCaZnEt]

All three complexes were prepared according to literature procedure. <sup>1</sup>H NMR and <sup>13</sup>C NMR spectra of the products were consistent with reported literature values.

#### 2.6.1.1 Complex [LZn<sub>2</sub>Et]

In a glovebox, (*S,S*)-(+)-2,6-bis[2-(hydroxydiphenylmethyl)-1-pyrrolidinyl-methyl]-4-methylphenol (500 mg, 0.79 mmol) was weighed into a Schlenk flask and dissolved in dry THF (15 mL). ZnEt<sub>2</sub> (193.3 mg, 1.57 mmol) was added into a separated Schlenk flask and dissolved in dry THF (5 mL). The metal solution was added dropwise into the ligand solution. The resulting mixture was stirred for 18 h at ambient temperature under an argon atmosphere. THF was subsequently removed *in vacuo*, yielding a pale-orange powder (495 mg, 79%). <sup>1</sup>H and <sup>13</sup>C NMR spectra of the products were consistent with reported literature values.<sup>113</sup>

**<sup>1</sup>H NMR** (500 MHz, CDCl<sub>3</sub>) δ 7.98 (d, 2 H), 7.72 (d, 2 H), 7.35 – 7.23 (m, 4 H), 7.22 – 7.13 (m, 6 H), 7.10 – 7.01 (m, 4 H), 6.66 (d, 2 H), 4.40 (d, 1 H), 3.70 (s, 1 H), 3.62 (d, 1 H), 3.28 (d, 1 H), 2.65 – 2.58 (m, 1 H), 2.54 (d, 1 H), 2.50 – 2.42 (m, 1 H), 2.31 – 2.17 (m, 2 H), 2.16 (s, 3 H), 2.13 – 2.03 (m, 2 H), 1.68 – 1.59 (m, 1 H), 1.52 (t, 3 H), 1.40 – 1.30 (m, 1 H), 1.26 (m, 2 H), 1.14 – 1.02 (m, 1 H), 0.96 – 0.83 (m, 1 H), 0.69 (q, 2 H), 0.02 – -0.11 (m, 1 H).

**<sup>13</sup>C NMR** (126 MHz, CDCl<sub>3</sub>) δ 157.05, 151.92, 151.83, 151.41, 146.40, 131.77, 131.71, 128.64, 128.00, 127.67, 127.59, 127.50, 127.42, 127.07, 126.73, 126.42, 126.28, 126.20, 125.36, 125.05, 122.09, 81.56, 77.93, 77.36, 75.01, 70.84, 68.13, 61.48, 59.82, 57.51, 55.15, 28.83, 25.77, 25.11, 21.71, 21.20, 20.42, 13.44, 1.17, -2.97.

#### 2.6.1.2 Complex [LMgZnEt]

In a glovebox, (*S,S*)-(+)-2,6-bis[2-(hydroxydiphenylmethyl)-1-pyrrolidinyl-methyl]-4-methylphenol (500 mg, 0.78 mmol) was weighed into a Schlenk flask and dissolved in dry THF (10 mL). Mg(HMDS)<sub>2</sub> (270.3 mg, 0.78 mmol) was slowly added to the ligand solution, and the resulting mixture was stirred for 15 min at room temperature. ZnEt<sub>2</sub> (97.0 mg, 0.78 mmol) dissolved in THF (3 mL) was slowly added and left to stir for 16 h in the glove box. THF was subsequently removed *in vacuo*, yielding a pale orange powder (698 mg, 91%). <sup>1</sup>H and <sup>13</sup>C NMR spectra of the products were consistent with reported literature values.<sup>114</sup>

**<sup>1</sup>H NMR** (500 MHz, THF-*d*<sub>8</sub>) δ 8.09 – 8.00 (m, 2 H), 7.88 (dd, 2 H), 7.80 (d, 2 H), 7.64 (d, 4 H), 7.23 – 7.13 (m, 4 H), 7.09 (t, 2 H), 6.97 (ddd, 2 H), 6.95 – 6.89 (m, 1 H), 6.69 – 6.63 (m, 1 H), 6.60 (d, 1 H), 4.12 (d, 1 H), 3.88 – 3.80 (m, 2 H), 3.71 (s, 1 H), 3.67 – 3.61 (m, 4 H), 2.68 (ddd, 1 H), 2.56 (dd, 1 H), 2.47 – 2.40 (m, 4 H), 2.40 – 2.34 (m, 2 H), 2.29 – 2.13 (m, 4 H), 2.06 (s, 3 H), 1.83 – 1.75 (m, 4 H), 1.58 – 1.49 (m, 6 H), 0.92 (t, 3 H), 0.07 (s, 21 H), 0.02 – -0.10 (m, 2 H).

**<sup>13</sup>C NMR** (126 MHz, THF-*d*<sub>8</sub>) δ 158.98, 156.45, 156.12, 156.09, 156.06, 132.20, 132.13, 128.08, 127.84, 127.68, 127.58, 127.54, 127.08, 126.97, 126.92, 126.87, 125.58, 125.37, 125.08, 125.05, 124.43, 79.52, 77.05, 75.30, 71.31, 60.36, 58.86, 55.34, 30.02, 29.79, 20.37, 20.27, 13.89, 2.95, - 0.20.

### 2.6.1.3 Complex [LCaZnEt]

In a glovebox, (*S,S*)-(+)-2,6-bis[2-(hydroxydiphenylmethyl)-1-pyrrolidinyl-methyl]-4-methylphenol (500 mg, 0.79 mmol) was weighed into a Schlenk flask and dissolved in dry THF (10 mL) in the glove box. Ca(HMDS)<sub>2</sub>(THF)<sub>2</sub> (395.9 mg, 0.79 mmol) was added to the ligand solution. The resulting mixture was stirred for 15 min at ambient temperature under an argon atmosphere in the glove box. ZnEt<sub>2</sub> (97.0 mg, 0.79 mmol) dissolved in dry THF (2 mL) was subsequently added and the reaction mixture was stirred for 16 h at ambient temperature under an argon atmosphere in the glove box. THF was subsequently removed *in vacuo*, resulting in a pale-yellow powder (479 mg, 61%). <sup>1</sup>H and <sup>13</sup>C NMR spectra of the products were consistent with reported literature values.<sup>114</sup>

**<sup>1</sup>H NMR** (500 MHz, THF-*d*<sub>8</sub>) δ 8.06 (d, 2 H), 7.75 – 7.78 (dd, 4 H), 7.56 (d, 2 H), 7.05 – 7.11 (m, 8 H), 6.87 – 6.94 (m, 4 H), 6.64 (dd, 2 H), 4.12 (d, 1 H), 4.01 (d, 1 H), 3.78 (m, 2 H), 3.63 – 3.60 (m, 4 H), 2.70 (d, 2 H), 2.65 – 2.53 (m, 1 H), 2.40 – 2.24 (m, 1 H), 2.24 – 2.15 (m, 2 H), 2.04 (s, 3 H), 1.57 (m, 1 H), 1.79 – 1.76 (m, 4 H), 1.51 – 1.38 (m, 2 H), 1.23 – 1.14 (m, 2 H), 1.01 (t, 3 H), 0.04 (s, 19 H), 0.07 – - 0.18 (m, 2 H).

**<sup>13</sup>C NMR** (126 MHz, THF-*d*<sub>8</sub>) δ 161.42, 158.08, 157.43, 156.69, 156.60, 133.52, 131.88, 127.77, 127.56, 127.43, 127.37, 127.22, 126.99, 125.53, 125.12, 122.72, 80.19, 79.87, 77.60, 70.74, 59.73, 59.27, 55.36, 30.29, 29.15, 26.55, 20.60, 20.53, 14.34, 2.85, -0.06.

### 2.6.2 General experimental procedure for the synthesis of PCL

In a glovebox, CL (100 equiv., 2.5 mmol, 277.0  $\mu$ L) was dissolved in dry toluene (1.5 mL) in an air-tight vial equipped with a magnetic stirrer bar. In a separate vial, catalyst **[LZn<sub>2</sub>Et]**, **[LMgZnEt]** and **[LCaZnEt]** (1 equiv., 25  $\mu$ mol) was dissolved in toluene solvent, and BnOH was added (1 equiv., 25  $\mu$ mol, total volume = 1.0 mL). Both solutions were stirred at 70 °C for 1 h using DrySyn heating blocks. The polymerisation of CL was initiated by the addition of the catalyst/BnOH solution to the CL solution ([CL] = 1.0 M; combined volume = 2.5 mL). Aliquots of propagating PCL chains were taken periodically over the reaction time to monitor monomer conversion and polymer growth. Upon completion, PCL was quenched by the addition of chloroform and purified by precipitation from cold acidified methanol to remove any residual unconverted monomer and traces of metal catalyst.

### 2.6.3 General experimental procedure for the synthesis of PCL-*b*-PL(L)A

The copolymerisation to prepare PCL-*b*-PL(L)A diblock copolymers was carried out *via* a sequential addition of L- or *rac*-LA after the full conversion of CL to PCL (using the homopolymerisation procedure presented above). In a separate air-tight vial equipped with a magnetic stirrer bar, LA (100 equiv., 2.5 mmol, 360.3 mg) was dissolved in toluene (2.5 mL) and stirred at 70 °C for 1 h. Subsequently, the LA solution was added to the propagating PCL\* chain in toluene (total volume = 5.0 mL, [LA] = 0.5 M). Please note that the CL polymerisation was allowed to proceed for one minute beyond the time determined for high conversion by <sup>1</sup>H NMR analysis (**[LZn<sub>2</sub>Et]**: 5 min, **[LMgZnEt]**: 2.5 min, **[LCaZnEt]**: 2 min), prior to the addition of the LA solution, to help ensure that only traces of unreacted CL were present from the homopolymerisation step. Aliquots of the PCL-P(L)A copolymerisation were taken periodically to monitor monomer conversion and polymer growth (refer to [Section 6.4](#)). Upon completion (**[LZn<sub>2</sub>Et]**: 2.5 h, **[LMgZnEt]**: 2 h, **[LCaZnEt]**: 20 mins), the PCL-PL(L)A copolymerisation was quenched by the addition of chloroform and purified by precipitation from cold acidified methanol to remove any residual unconverted monomer and traces of metal catalyst.

### 2.6.4 General experimental procedure for the synthesis of PCL-PLA-PCL copolymer

In a glovebox, in an air-tight vial equipped with a magnetic stirrer bar, catalyst **[LZn<sub>2</sub>Et]**, **[LMgZnEt]** and **[LCaZnEt]** (1 equiv., 25  $\mu$ mol) was dissolved in toluene solvent, and BnOH was added (1 equiv., 25  $\mu$ mol, total volume = 1.0 mL). In a separate air-tight vial with a magnetic stirrer bar, CL (100

equiv., 2.5 mmol, 277.0  $\mu\text{L}$ ) was dissolved in toluene (total volume = 1.42 mL or 1.25 mL, for respective  $[\text{CL}] = 1.76 \text{ M}$  or  $2.0 \text{ M}$  in the first step *i.e.* CL homopolymerisation). The polymerisation of CL was initiated by the addition of catalyst/BnOH solution, and was allowed to proceed for one minute beyond the time determined for high conversion by  $^1\text{H}$  NMR analysis (**[LZn<sub>2</sub>Et]**: 5 min, **[LMgZnEt]**: 2.5 min, **[LCaZnEt]**: 2 min) prior to LA addition. Subsequently, the LA solution (100 equiv., 2.5 mmol, 360.3 mg in 1.42 mL or 1.25 mL of toluene) was added to the propagating PCL\* chain in toluene to give a respective total volume = 2.84 mL or 2.50 mL ( $[\text{LA}] = 0.88 \text{ M}$  or  $1.0 \text{ M}$ ) in the second step of PCL-PLA copolymerisation). The reaction mixture was stirred for a set period of time (see above protocol for the synthesis of PCL-*b*-PLA for details), prior to the addition of neat  $\text{CL}_2$  (100 equiv., 2.5 mmol, 277.0  $\mu\text{L}$ ) as the third “block”. Note that the LA polymerisation was also allowed to react for 1 minute beyond the time point in which each catalyst achieved  $\geq 95\%$  LA conversion (**[LZn<sub>2</sub>Et]**: 2.5 h, **[LMgZnEt]**: 2 h, **[LCaZnEt]**: 20 mins), prior to the addition of  $\text{CL}_2$  for the third “block”, to help ensure complete conversion of the LA monomer. In all cases, the polymerisation of  $\text{CL}_2$  was allowed to proceed for 24 h. Upon completion of each polymerisation step, aliquots of PCL, PCL-PLA diblock and PCL-PLA-PCL (co)polymers were taken and quenched by the addition of excess chloroform. The final resultant copolymers were purified by precipitation from cold acidified methanol to remove any residual unconverted monomer and traces of metal catalyst.

## **Chapter 3**

# **The Synthesis and Characterisation of Structurally Well-Defined Alkali Metal/Aluminium Heterotrimetallic ProPhenol Complexes**

### 3.1 Overview

The past decade has seen a surge of interest in the exploitation of heterometallic cooperativity for the ROP of cyclic esters.<sup>46,96</sup> Among the best performing catalysts reported to date are catalysts featuring metal combinations with zinc (Zn) as one of the components. Coupled with impressive reactivity, the low toxicity of Zn is an additional attraction in the field of ROP, as poly(lactone)s have found application in the biomedical field. However, Zn has been identified as an element under serious threat in the next century;<sup>145</sup> therefore, sourcing polymerisation catalysts based on cheap, earth-abundant metal such as aluminium (Al) would be fitting to realise the effort towards more sustainable chemistry.

Introducing a trivalent Al centre into a ProPhenol ligand scaffold, in place of divalent Zn, could be coupled with incorporation of an alkali metal, to generate mono/trivalent metal analogues of the di/divalent metal complexes as described in Chapter 2. However, the switch to a trivalent Al opens up the potential for significant changes in the structure and bonding. In this chapter, four novel heterotrimetallic ProPhenol complexes were synthesised and fully characterised, including by single-crystal X-ray diffraction studies. The combination of AM with Al yielded a heterotrimetallic complex with an asymmetric structure, differing from the previously reported symmetrical AM/Zn<sub>2</sub> ProPhenol complex.

## 3.2 Introduction

Environmental and sustainability concerns have led to rising efforts in the development of aliphatic polyesters to address the urgent need for greener alternatives for petrochemical polymers. Specifically, the past decade has witnessed a surge of advancement in the design and synthesis of highly active, selective and well-controlled catalysts for cyclic ester polymerisation. Within organometallic catalysis, different approaches have been taken to access high performance catalysts, including through the alteration of ligand scaffolds and/or by exploiting harmonic cooperation of different metals within a catalyst system.

Although the vast majority of heterometallic complexes have demonstrated enhanced performances in cyclic ester ROP,<sup>46,85,96</sup> there have also been reports of some catalysts displaying inferior performance compared to their homometallic counterparts. Despite some trends for cooperativity emerging within multi- and/or heterometallic complexes, there is still a myriad of overarching design principles that are still not fully understood.<sup>46</sup> The origin of cooperativity (or lack thereof) in heterometallic complexes could stem from several factors such as metal-metal proximity, the flexibility and conformation of ligand framework as well as the balance of electronics between different metal combinations. It is important to note that while some experimental observations hint towards the different roles of different metals, there has not yet been any detailed mechanistic studies for cyclic ester ROP with heterometallic systems that fits for all cases.<sup>62</sup>

Understanding of discrete metal complexes, typically through X-ray crystallography, may allow correlation between the heterometal interactions or the overall complex structure with polymerisation activity and/or selectivity. Among different metal combinations, pairing alkali metal (AM) with aluminium (Al) is particularly interesting for cyclic ester polymerisation. Owing to their biocompatibility, a range of polyesters including PLA, PCL, PGA and poly( $\delta$ -valerolactone) (PVL) have seen rapid growth in biological and pharmaceutical sectors, for various uses spanning from tissue engineering to surgical implant applications.<sup>146</sup> Cheap, earth-abundant, weakly pigmented and low toxicity AM/Al catalysts are therefore desirable for generating polyesters. Catalysts based on AM have demonstrated high activity for lactone polymerisation, yet often generate moderate or poorly controlled polymers at ambient to high temperature.<sup>63,147</sup> On the other hand, aluminium-based complexes typically produce controlled polymers and have been widely reported for cyclic ester ROP.<sup>72,73</sup> However, aluminium catalysts often require demanding conditions (*i.e.* high temperature, high catalyst loading and/or long reaction times) to be effective.

Taking the different performance enhancements and drawbacks that either the monometallic AM or Al catalysts display, we aimed to design a discrete heterometallic complex that could harness

cooperativity between the two metals for the synthesis of polyesters with high catalytic activity and selectivity. This work was inspired by polymerisation enhancement observed in the previous heterometallic ProPhenol complexes attributed to “ate” activation;<sup>114</sup> therefore, AM aluminate ProPhenol complexes were targeted. Within the heterometallic AM/Al ProPhenol complex, the combination of organoalkali metal with organoaluminium was proposed to generate alkali metal aluminates,  $AM^+[AlR_4]^-$ , through electronic modulation occurring *via* the M-O-M' framework.<sup>148</sup>

Over recent years, AM aluminate compounds have been utilised in many organic transformations<sup>149,150</sup> including in hydroboration processes,<sup>151</sup> C-X bond formation<sup>152</sup> and C-H activation catalysis<sup>153</sup> (Figure 3.1). Cooperative AM/Al complexes has also been explored for use as (co)catalysts in polymer chemistry, and much focus has been on vinyl polymerisation.<sup>150,154</sup> Yet, the examples of such complexes in cyclic ester polymerisation remain scarce.<sup>155</sup>

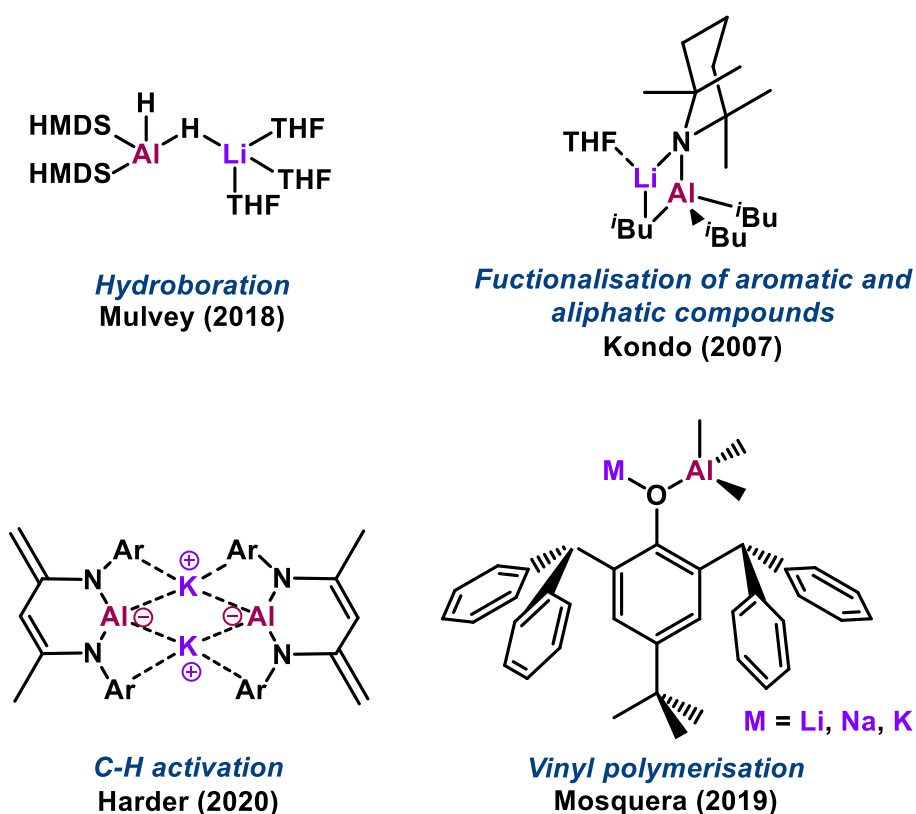
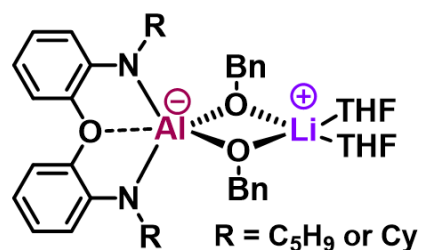


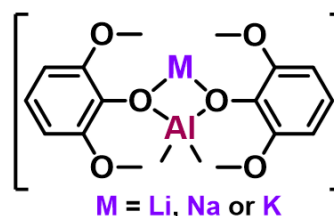
**Figure 3.1** Examples of alkali metal aluminates utilised in different areas of catalysis.<sup>150–153</sup>

Among the earliest work on Al/AM complexes designed for LA polymerisation is a study by Dagorne and co-workers in 2010, which reported Li/Al anionic bis-alkoxide complexes supported by NON-type tridentate ligands (Figure 3.2).<sup>156</sup> The heterometallic complexes readily undergo LA polymerisation under mild conditions (82 – 85% conv., 230 equiv. LA, RT, in  $CH_2Cl_2$ ), whereas the monometallic Li and Al analogues were completely inactive for LA ROP under similar conditions

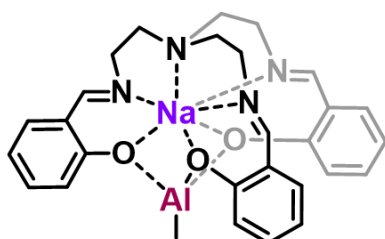
tested. The authors hypothesised that cooperativity observed from the Li/Al complexes originated from the (partial) dissociation of the complex under catalytic condition to form neutral Al alkoxide complex  $\{(RN-o-C_6H_4)_2O\}Al(OCH_2Ph)$  which activates and coordinates the monomer, whereas the  $LiOCH_2Ph$  species initiates LA ROP.



Dagorne (2010)



Mosquera (2014)



Garden (2022)

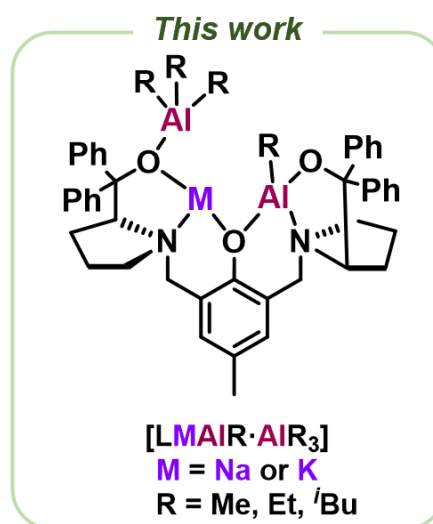


**Figure 3.2** Literature examples of AM/Al heterobimetallic complexes investigated for LA polymerisation and the heterotrimetallic ProPhenol complexes presented in this chapter.<sup>155–157</sup>

In 2014, Mosquera and co-workers investigated a series of heterobimetallic AM/Al “ate” species (AM = Li, Na, K), where the  $AM^+$  in each complex is ‘encapsulated’ by the  $\{AlMe_2(2,6-(MeO)_2C_6H_3O)_2\}^-$  structural motif.<sup>155</sup> These complexes are active in the ROP of L-LA (with 1 equiv. BnOH, Li/Al: 75%, Na/Al: 48%, K/Al: 20% conv., 100 equiv. L-LA, 125 °C, in toluene). Recent studies from the Garden group reported a Na/Al “ate” complex based on the TrenSal ligand, which showcased an interesting structural transformation compared to the homometallic complex. The incorporation of Na resulted in a geometry change of Al from octahedral in the monometallic Al complex, to tetrahedral in the heterobimetallic complex.<sup>157</sup> The insertion of Na also switched the inactive mono-Al complex for LA ROP to an active heterometallic catalyst (with 1 equiv. BnOH, 77% conv., 100 equiv. LA, RT, toluene), due to the presence of accessible monomer coordination sites at Al in the latter.

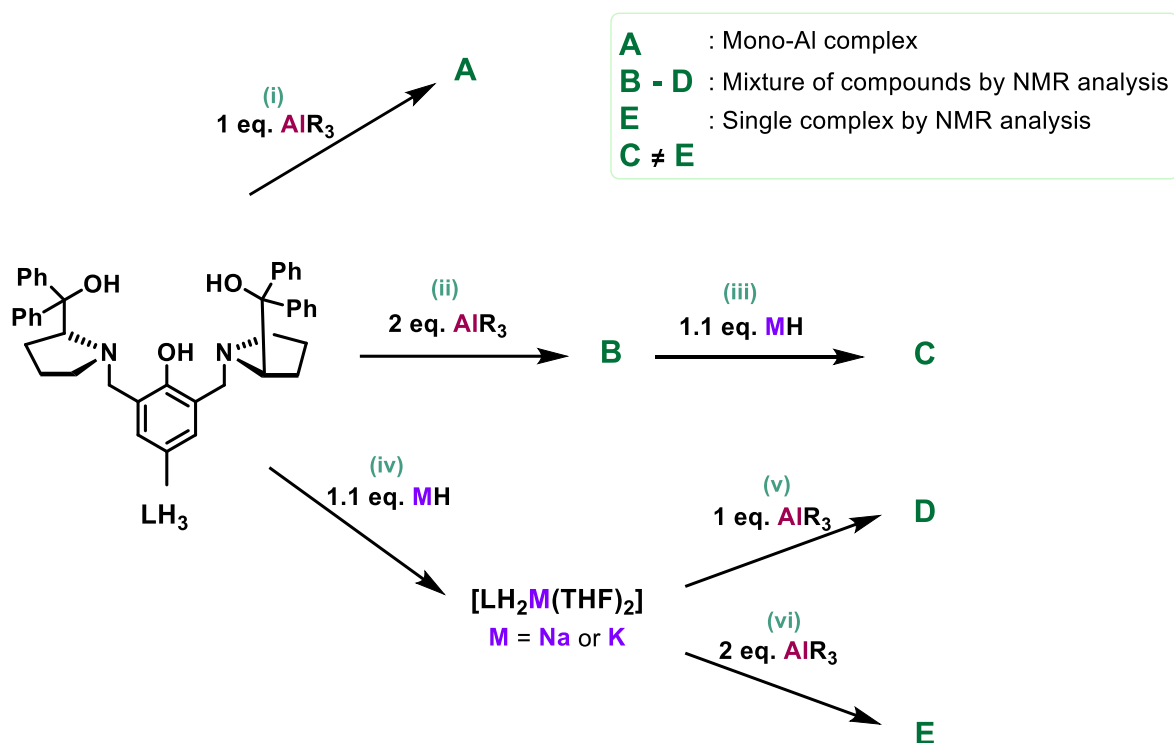
These catalysts showcased the significance of mixed-metal systems, which have the potential to change the metal geometry to activate the catalyst, or can further boost the catalyst activity and/or control. These complexes all share a common structural feature, where the heterometals are connected by oxygen atom(s) within the ligand to generate an M-O-M' motif, which allows for electronic modulation to take place.

In this work, a series of trimetallic AM/Al<sub>2</sub> complexes based on a ProPhenol Trost ligand were synthesised *via* a sequential deprotonation method (Scheme 3.1, *vide infra*). Structural characterisation, through X-ray crystallography and NMR spectroscopy, reveals two different bonding modes for the two Al centres. To the best of our knowledge, this work reports the first structurally well-defined AM/Al heterotrimetallic complexes bearing the ProPhenol ligand.

### 3.3 Results and Discussion

#### 3.3.1 Synthesis of Novel Heterotrimetallic Alkali Metal (AM)/Aluminium ProPhenol Complexes

Heterometallic complexes can be accessed through different methodologies, such as *via* sequential deprotonation, coordination, salt metathesis and/or transmetalation routes. Insights from previous computational and experimental studies on ProPhenol metal complexes show that multiple metals (up to three metals, thus far) can be held within this ligand scaffold.<sup>81,111,112,114,116</sup> The binding of metals in the ProPhenol ligand framework and the resultant structures are influenced by several factors, such as the different acidity of the ligand OH (phenol and benzoxy), metal ionic radii, oxophilicity and valency. To develop heterometallic AM/Al ProPhenol complexes, several synthetic pathways towards bi- and trimetallic complexes were explored, based on sequential deprotonation methods (Scheme 3.1).



**Scheme 3.1** Possible synthetic pathways attempted to access heterometallic AM/Al ProPhenol complexes. Reaction conditions: (i) 1 equiv.  $\text{AlEt}_3$  in THF, 16 h, RT; (ii) 2 equiv.  $\text{AlEt}_3$  in THF, 16 h, RT; (iii) 1.1 equiv. NaH in THF, 4 – 24 h, added *in situ* to **B**; (iv) 1.1 equiv. NaH or KH in THF, 4 h, RT;<sup>112</sup> (v) 1 equiv.  $\text{AlEt}_3$  in THF or toluene, 16 h, RT; (vi) 2 equiv.  $\text{AlEt}_3$  in THF or toluene, 16 h, RT.

Initially, we investigated whether the complexation of Al into the ProPhenol scaffold could be achieved by either di- or trideprotonation of three of the hydroxyl groups. Some previous studies on ProPhenol complexes have shown that the ligand geometry can lead towards an inclination for dideprotonation to occur.<sup>81</sup> Here, a ProPhenol ligand was firstly deprotonated with triethyl aluminium,  $\text{AlEt}_3$  (1-2 equivalents) (Scheme 3.1, (i)). One equivalent of the aluminium reagent generates a mono-Al ProPhenol complex **A**.  $^1\text{H}$  NMR spectroscopy shows a significant shift of the  $^1\text{H}$  NMR resonances compared to the ProPhenol ligand, indicating successful trideprotonation and Al complexation into the ligand framework (Figure 3.3). This was evidenced by the absence of both phenol and benzoxyl *OH* resonances, as well as the absence of Al-Et signals in the resultant complex. Contrary to previously reported monometallic AM ProPhenol complexes,  $[\text{LH}_2\text{Na}(\text{THF})_2]$  and  $[\text{LH}_2\text{K}(\text{THF})_2]$ , **A** appears asymmetric in solution (benzene- $d_6$ ) which is likely to arise from Al...N coordination in one of the ligand pockets to generate a tetrahedral coordination geometry around the Al centre.<sup>158,159</sup> The asymmetric nature was reflected from different chemical environments of the meta-phenolic proton of the complex, where coupling was observed between these two proton resonances through COSY NMR. Additionally, there are additional signals around the aromatic region (7.0 ppm – 8.5 ppm) compared to the free symmetric ligand, suggesting that the peripheral phenolic rings on each side of the ligand framework are in different chemical environments.

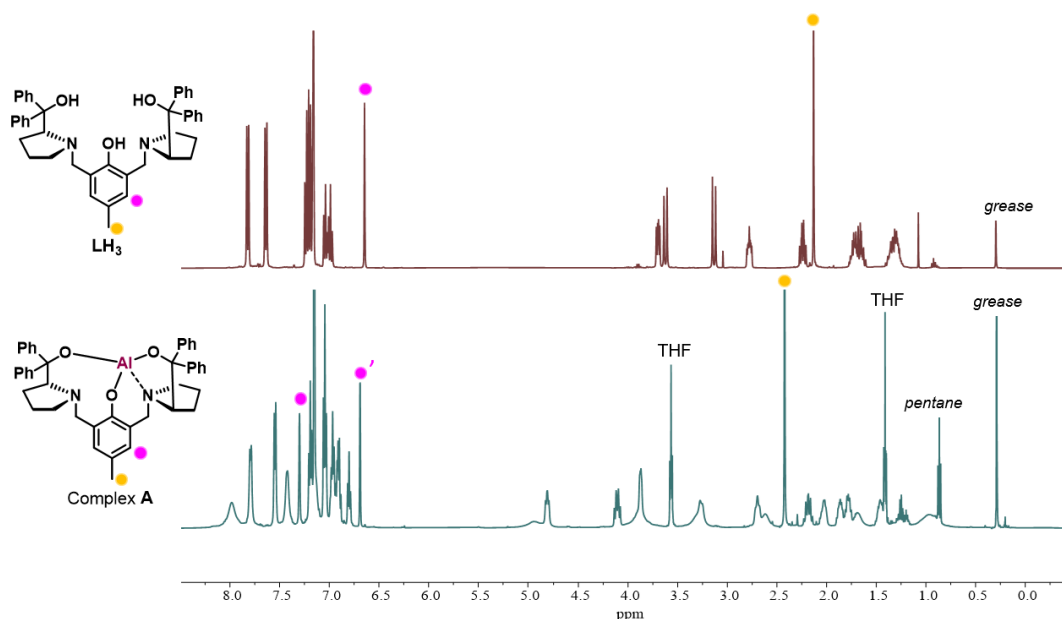


**Figure 3.3** Overlay of  $^1\text{H}$  NMR spectra (benzene- $d_6$ ) of ProPhenol ligand (top) and complex **A** (bottom) at 298 K, showing signals shift and the loss of symmetry of ProPhenol ligand scaffold. The Al-Et resonances (0.35 and 1.16 ppm)<sup>160</sup> are absent in complex **A**, indicating trideprotonation of the ligand by  $\text{AlEt}_3$  and successful Al complexation.

Additionally, complex **A** exists as a dimeric species in solution (benzene- $d_6$ ), as determined by DOSY (diffusion-ordered spectroscopy) analysis (Figure 3.4). DOSY NMR is a useful spectroscopic technique for the identification of solution-state structures and the separation of compounds present in a solution based on their different diffusion coefficients.<sup>161,162</sup> Using DOSY, the approximate molecular weights of complexes in solutions are calculated by interpolating the logarithmic diffusion coefficient (logD) values of the compounds on a calibration plot of reference standards, with known molar masses in a specific solvent (refer to Chapter 6, [Section 6.3.1.1](#)).

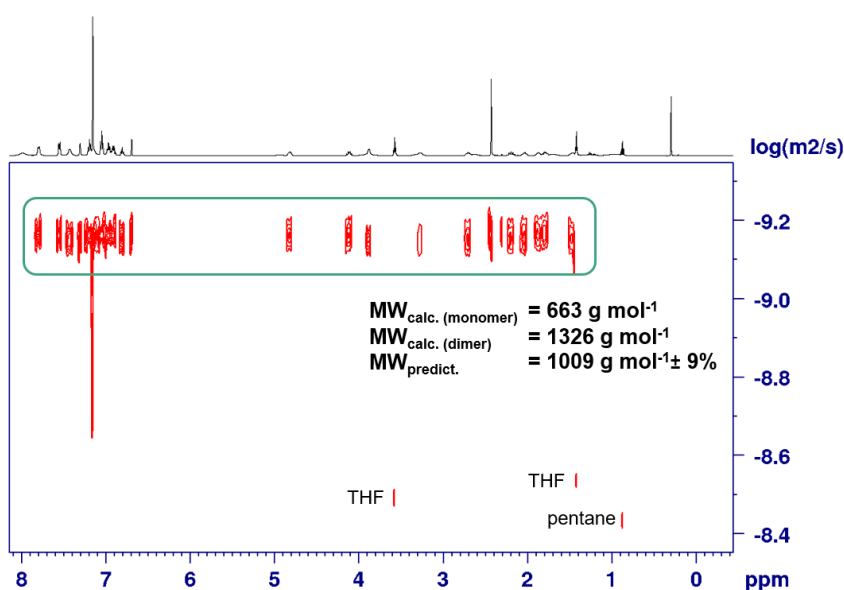


**Figure 3.4** DOSY NMR spectrum (benzene- $d_6$ ) of complex **A** at 298 K.

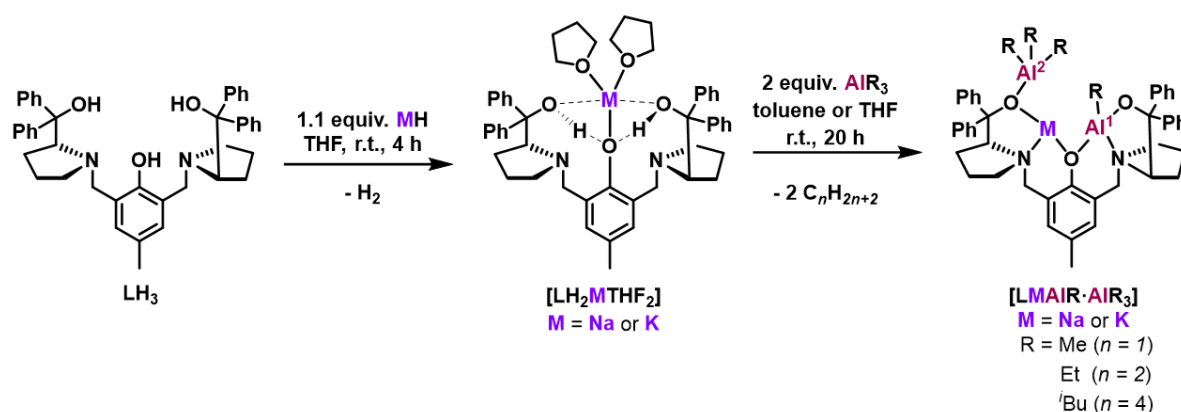
Complex **A** was successfully isolated and purified by recrystallisation from pentane/THF mixture, however, the crystals were unsuitable for X-ray diffraction studies. However, this synthesis route was not explored further for sequential deprotonation with AM base due to the absence of alkyl (initiating) group in the complex, which is key for nucleophilic attack to occur following the coordination-insertion mechanistic pathway in cyclic ester ROP.

Next, to generate Al complexes bearing Al-alkyl (initiating) groups, we looked into the synthetic pathway of accessing a bimetallic Al complex. Earlier investigations reported the spontaneous formation of dinuclear metal complexes when treated with two equivalents of alkyl metal reagent (*i.e.* ZnEt<sub>2</sub> or MgBu<sub>2</sub>).<sup>110,163</sup> However, treatment of the ligand with two equivalents of AlEt<sub>3</sub> to access a dinuclear Al complex **B** generated a mixture of undefined compounds as well as some unreacted AlEt<sub>3</sub>, as identified by <sup>1</sup>H and DOSY NMR (Scheme 3.1, (ii)). The inaccessibility of a stable dialuminium complex (*cf.* ProPhenol-Zn<sub>2</sub> or Mg<sub>2</sub>) could be attributed to the difference in metal valency. While the complexation of one Al metal may be possible (*i.e.* complex **A** formation), having two equivalents of Al, coupled with the presence of trialkyl substituents, may sterically hinder Al occupancy into the ligand framework, as hinted by the unreacted AlEt<sub>3</sub> resonances. Although “complex **B**” was not isolated as a pure compound, the formation of heterometallic Al/AM complex **C** was also attempted through *in situ* reaction of **B** with one equivalent of AM hydride (Scheme 3.1 (iii)). However, this method also led to the formation of a mixture of products. Therefore, a different strategy was investigated, where deprotonation with an AM reagent was performed prior to deprotonation with a trialkyl aluminium species.

Monometallic alkali metal complexes [LH<sub>2</sub>Na(THF)<sub>2</sub>] and [LH<sub>2</sub>K(THF)<sub>2</sub>] were prepared according to literature procedures, through the mono-deprotonation of the phenolic-OH of ProPhenol ligand, LH<sub>3</sub>, with NaH or KH, respectively (Scheme 3.1, (iv)).<sup>112</sup> An attempt to access a bimetallic AM/Al ProPhenol complex **D**, [LMAIR<sub>n</sub>] (where M = Na or K; R = alkyl group), was carried out *via* the addition of one equivalent of trialkyl aluminium reagent to the isolated [LH<sub>2</sub>M(THF)<sub>2</sub>] (M = Na or K). Unfortunately, instead of achieving the target heterobimetallic complex, undefined mixtures of species were present in the resultant product solution, as indicated by multiple product signals in the <sup>1</sup>H NMR spectra and several diffusion coefficients observed in the DOSY NMR spectra. Therefore, metalation of the isolated [LH<sub>2</sub>M(THF)<sub>2</sub>] precursor was investigated, using two equivalents of the respective trialkyl aluminium, AlR<sub>3</sub>, (where R = Me, Et, *i*Bu) (Scheme 3.2).

Four different metal reagent pairings were investigated (*i.e.* [LH<sub>2</sub>Na(THF)<sub>2</sub>]/AlMe<sub>3</sub>, [LH<sub>2</sub>Na(THF)<sub>2</sub>]/AlEt<sub>3</sub>, [LH<sub>2</sub>Na(THF)<sub>2</sub>]/Al(*i*Bu)<sub>3</sub> and [LH<sub>2</sub>K(THF)<sub>2</sub>]/AlEt<sub>3</sub>). In all cases, the reaction was accompanied by a discolouration from a dark yellow to a pale yellow solution coupled with

effervescence, indicating alkane gas elimination due to deprotonative metalation. This gave the formation of a single reaction product in each case assigned as heterotrimetallic complex **E**, as identified by X-ray crystallography and NMR spectroscopy analysis. Complexes **[LNaAlMe·AlMe<sub>3</sub>]**, **[LNaAlEt·AlEt<sub>3</sub>]** and **[LKAIEt·AlEt<sub>3</sub>]** were successfully isolated in low to moderate yields (32 – 63%). The synthesis of **[LNaAl<sup>i</sup>Bu·Al(<sup>i</sup>Bu)<sub>3</sub>]** was also investigated and the complex was successfully crystallised. However, isolation of the pure compound was surprisingly challenging due to enhanced solubility of the Al(<sup>i</sup>Bu)<sub>3</sub> unit, resulting in a mixture of **[LNaAl<sup>i</sup>Bu·Al(<sup>i</sup>Bu)<sub>3</sub>]** and traces of excess Al(<sup>i</sup>Bu)<sub>3</sub> reagent observed in solution-state NMR analysis.



**Scheme 3.2** Synthesis of heterometallic **[LNaAlMe·AlMe<sub>3</sub>]**, **[LNaAlEt·AlEt<sub>3</sub>]**, **[LNaAl<sup>i</sup>Bu·Al(<sup>i</sup>Bu)<sub>3</sub>]** and **[LKAIEt·AlEt<sub>3</sub>]** complexes.

### 3.3.2 Structural Analysis of Heterotrimetallic Alkali Metal/Aluminium Complexes

Complexes **[LNaAlMe·AlMe<sub>3</sub>]**, **[LNaAlEt·AlEt<sub>3</sub>]**, **[LNaAl<sup>i</sup>Bu·Al(<sup>i</sup>Bu)<sub>3</sub>]** and **[LKAIEt·AlEt<sub>3</sub>]** were recrystallised from concentrated benzene solvent and pentane antisolvent by either vapour diffusion or solvent layering at room temperature, yielding colourless crystals suitable for XRD analysis in all cases. Structural characterisation through X-ray crystallography confirmed successful deprotonation and subsequent binding of two Al metals to the AM precursor complexes, in all cases. Within each compound, the two Al metals are in different chemical environments, where one Al centre is situated “inside” a cavity of the ProPhenol ligand framework (denoted as Al<sup>1</sup> hereon), while another Al is datively bonded and located peripherally on the “outside” sphere of the ligand scaffold (denoted as Al<sup>2</sup>) (see AM/Al<sub>2</sub> complex in Scheme 3.2, *vide supra*).

The spatial arrangement of atoms within the unit cell are influenced by the alkyl groups attached to the Al metal centre (*i.e.* AlMe<sub>3</sub>, AlEt<sub>3</sub> or Al(<sup>i</sup>Bu)<sub>3</sub>). Complex **[LNaAlMe·AlMe<sub>3</sub>]** crystallised as a tetragonal crystal lattice in the *P*4<sub>1</sub> space group, whereas complex **[LNaAl<sup>i</sup>Bu·Al(<sup>i</sup>Bu)<sub>3</sub>]** crystallised in the triclinic *P*1 space group. Both **[LNaAlEt·AlEt<sub>3</sub>]** and **[LKAIEt·AlEt<sub>3</sub>]** complexes crystallised in a

monoclinic crystal system with  $P2_1$  space group. Additionally, the central alkali metal (Na and K) in the precursor complexes rearranged to fill one of the inner ‘pockets’ of the ProPhenol ligand framework (refer Figures 3.5 – 3.9) in the heterotrimetallic complexes.

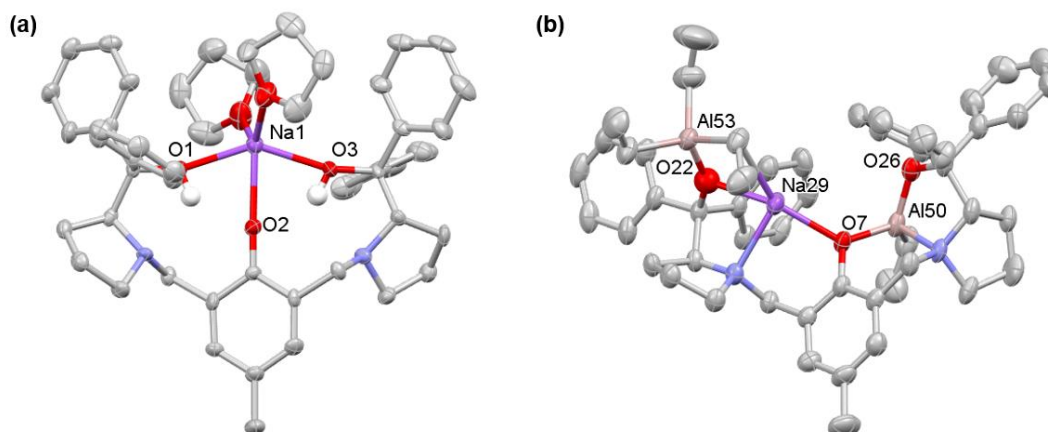


**Figure 3.5** Molecular structures of (a)  $[\text{LH}_2\text{NaTHF}_2]$  precursor complex showing Na occupying a central position within the ProPhenol ligand,<sup>112</sup> and (b)  $[\text{LNaAlEt}\cdot\text{AlEt}_3]$  where Na rearranges to fill in one side of the inner ‘pockets’ of ProPhenol ligand framework. Molecular structures are displayed with displacement ellipsoids at the 50% and 30% probability level, respectively. Colour scheme: grey = C, light purple = N, red = O, purple = Na, pink = Al, white = H.

In the case of heterometallic complexes based on Na analogues, it is interesting to note that the deprotonation of benzylic  $\text{OH}$ 's with two equivalents of aluminium alkyl results in a decreased coordination number at Na from pentacoordinate to tetracoordinate. In the  $[\text{LH}_2\text{NaTHF}_2]$  precursor complex, the Na centre is supported by the coordination of two THF molecules resulting in a coordination number of five.<sup>112</sup> However, the THF molecules are absent upon Al metalation in the resultant Na/Al<sub>2</sub> complexes, presumably due to the increased steric bulk resulting from two Al moieties with alkyl groups occupying the ligand cavity. This hinders the coordination of THF molecules to Na. The geometry and  $\tau_4$  character (where  $\tau_4 = 0.00$  is for a perfect square planar and  $\tau_4 = 1.00$  reflects a perfect tetrahedral geometry) around the four-coordinate Na and Al metal centres were investigated according to the calculation method established by Houser and co-workers, and are discussed below.<sup>164</sup> A structural comparison of these complexes is shown (Figures 3.6 – 3.8) and summarised in Tables 3.2 and 3.3 (*vide infra*).

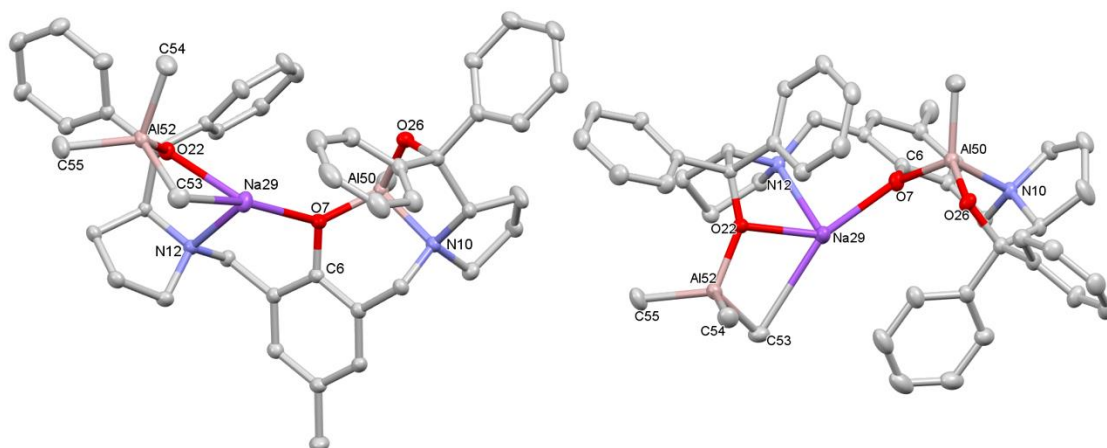


**Figure 3.6** Front (left) and top (right) views of molecular structure of **[LNaAlMe·AlMe<sub>3</sub>]** with displacement ellipsoids at the 50% probability level. Hydrogen atoms, and co-crystallised benzene-*d*<sub>6</sub> solvent molecules were omitted for clarity. Colour scheme: grey = C, light purple = N, red = O, purple = Na, pink = Al.

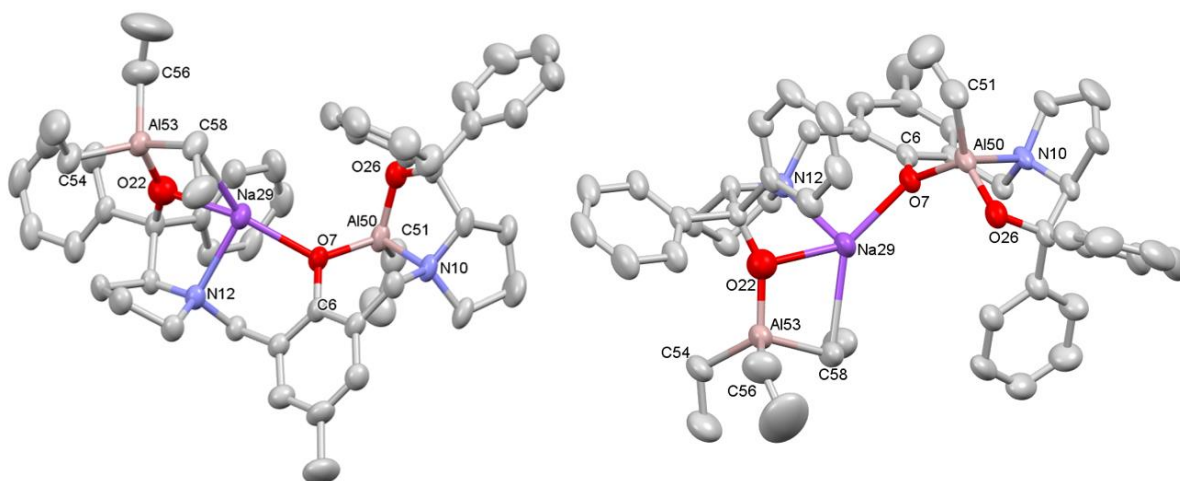


**Figure 3.7** Front (left) and top (right) views of molecular structure of **[LNaAlEt·AlEt<sub>3</sub>]** with displacement ellipsoids at the 30% probability level, with hydrogen atoms removed for clarity. Colour scheme: grey = C, light purple = N, red = O, purple = Na, pink = Al.

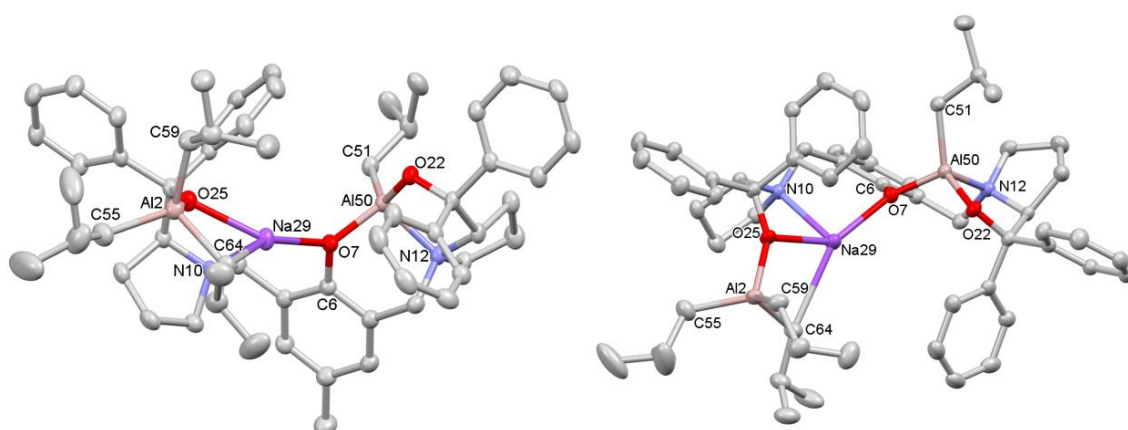


**Figure 3.8** Front (left) and top (right) views of molecular structure of **[LNaAl<sup>*i*</sup>Bu·Al(<sup>*i*</sup>Bu)<sub>3</sub>]** with displacement ellipsoids at the 50% probability level. Hydrogen atoms were omitted for clarity. Colour scheme: grey = C, light purple = N, red = O, purple = Na, pink = Al.

In the Na/Al<sub>2</sub> complexes, the geometry of Na centre of all three species lies in between distorted tetrahedral and square planar complex ( $\tau_4$  values: **[LNaAlMe·AlMe<sub>3</sub>]** = 0.48; **[LNaAlEt·AlEt<sub>3</sub>]** = 0.52; **[LNaAl(<sup>i</sup>Bu)·Al(<sup>i</sup>Bu)<sub>3</sub>]** = 0.49). This tetracoordinate geometry is achieved through the presence of an agostic interaction of Na with the C—H bond from Al<sup>2</sup>; this Na···Me-Al interaction (as is the case for K, see below) can help to stabilise the Na centre.<sup>165,166</sup> The agostic interaction is weak, as reflected by the elongated Na···C bond lengths (**[LNaAlMe·AlMe<sub>3</sub>]**, Na29-C53; 2.970(2) Å, **[LNaAlEt·AlEt<sub>3</sub>]**, Na29-C58; 2.718(8) Å, **[LNaAl(<sup>i</sup>Bu)·Al(<sup>i</sup>Bu)<sub>3</sub>]**, Na29-C63;a 2.798(2) Å) compared to the calculated Na—C bond distance of 2.50 Å (quantified by the sum of the Na and C atomic radii, Table 3.2, *vide infra*).<sup>167</sup> Interestingly, between the Na/Al<sub>2</sub> complexes, comparable angles and bond lengths are also observed around all three metal centres, suggesting that the steric from different substituents play a very small role in changing the structure of the overall complex. Generally, the rearrangement of Na in the heterometallic complexes creates more space around the alkali metal centre compared to the **[LH<sub>2</sub>Na(THF)<sub>2</sub>]** precursor complex; visually, almost half of the coordination sphere of Na appears to be accessible for Lewis base coordination.

When moving from Na to K, the metal coordination sphere increases from tetracoordinate for Na to heptacoordinate for K, which can be attributed to the larger ionic radius of K. A similar agostic interaction of K with the C—H bond from Al<sup>2</sup>-Et is present in the **[LKAIEt·AlEt<sub>3</sub>]** complex, albeit with longer K···C bond distance (K29-C56; 3.033(2) Å). Furthermore, there are three additional agostic interactions around the K metal centre with proximal aromatic rings to complete the coordination number of seven (see Figure 3.9). These interactions are much weaker, reflected by the more elongated K···C bonds distances. The closest interaction is the bond that exists between K and the central phenolic ring (K29-C6; 3.291(2) Å) resulting from K occupancy inside the ligand pocket. The remaining two bonding interactions are the coordination of K to two opposite benzyl rings with comparable bond distances between the two (*i.e.* K29-C39; 3.364(2) Å and K29-C45; 3.366(2) Å, Table 3.2).

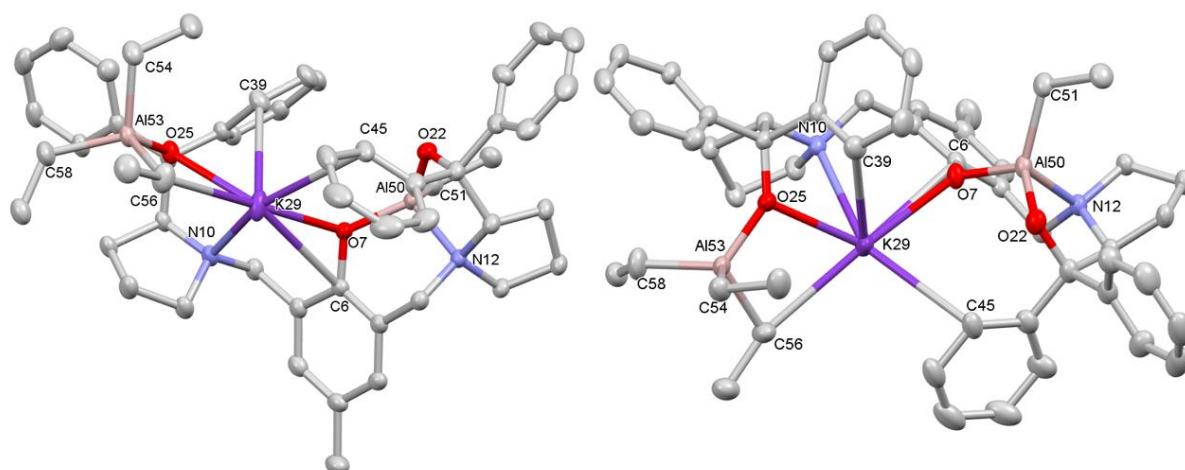
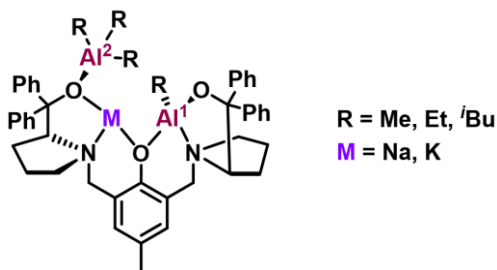


**Figure 3.9** Front (left) and top (right) views of molecular structure of **[LKAlEt.AIEt<sub>3</sub>]** with displacement ellipsoids at the 50% probability level, with hydrogen atoms and a benzene co-crystal removed for clarity. Colour scheme: grey = C, light purple = N, red = O, dark purple = K, pink = Al.

Different alkyl substituents in the Na/Al<sub>2</sub> analogues, as well as the different AM (*i.e.* Na vs K) within the heterometallic complexes have insignificant impact on the overall geometry around the Al centres. This is reflected from similar  $\tau_4$  character around the Al metal centres in all four complexes, which all occupy a slightly distorted tetrahedral geometry (Table 3.1).<sup>164</sup> When comparing between the two Al centres in different environments (*i.e.* Al<sup>1</sup> vs Al<sup>2</sup>, Table 3.1), Al<sup>1</sup> which is accommodated in the inside pocket of the ProPhenol ligand is observed to be more distorted from a perfect tetrahedral geometry in all cases. On the other hand, Al<sup>2</sup> which is loosely bonded to the oxygen of the benzylic moiety on the outer sphere experiences less distortion, resulting in an almost-perfect tetrahedral geometry, as the environment around Al<sup>2</sup> centre is not affected by the constraints of the ligand scaffold.

**Table 3.1** Comparison of  $\tau_4$  character around aluminium centres for [LNaAlMe<sub>2</sub>·AlMe<sub>3</sub>], [LNaAlEt<sub>2</sub>·AlEt<sub>3</sub>], [LNaAl<sup>*i*</sup>Bu·Al(<sup>*i*</sup>Bu)<sub>3</sub>] and [LKAIEt<sub>2</sub>·AlEt<sub>3</sub>] complexes.



|                                                                            | $\tau_4$ (Al <sup>1</sup> ) | $\tau_4$ (Al <sup>2</sup> ) |
|----------------------------------------------------------------------------|-----------------------------|-----------------------------|
| [LNaAlMe·AlMe <sub>3</sub> ]                                               | 0.89                        | 0.96                        |
| [LNaAlEt·AlEt <sub>3</sub> ]                                               | 0.89                        | 0.95                        |
| [LNaAl( <sup><i>i</i></sup> Bu)·Al( <sup><i>i</i></sup> Bu) <sub>3</sub> ] | 0.88                        | 0.95                        |
| [LKAIEt·AlEt <sub>3</sub> ]                                                | 0.89                        | 0.92                        |

$\tau_4$  character is determined using a calculation method established by Houser and co-workers.<sup>164</sup> Al<sup>1</sup> refers to Al centre inside a pocket of the ProPhenol ligand. Al<sup>2</sup> refers to datively bonded Al located outside the ProPhenol ligand pocket.

However, taking a closer look at the difference between the Al<sup>2</sup> geometries, the larger K atom leads to greater distortion of the tetrahedral Al<sup>2</sup> coordination environment. This could stem from the longer bond distance of the agostic AM...HC-Al bond for the K/Al<sub>2</sub> analogue (*i.e.* **[LKAIEt·AlEt<sub>3</sub>]**, K1-C56; 3.033(2) Å *vs* **[LNaAlEt·AlEt<sub>3</sub>]**, Na29-C58; 2.718(8) Å). On top of that, the greater ionic radius of K occupying the flexible ligand backbone could also result in a more “open” ligand framework in the **[LKAIEt·AlEt<sub>3</sub>]** complex (**[LKAIEt·AlEt<sub>3</sub>]**’s Al<sup>1</sup>...Al<sup>2</sup>; 7.244(9) Å *vs* **[LNaAlEt·AlEt<sub>3</sub>]**’s Al<sup>1</sup>...Al<sup>2</sup>; 6.674(2) Å), hence bending or opening up the ligand scaffold to a greater extent.

**Table 3.2** Selected bond lengths for complexes [LNaAlMe·AlMe<sub>3</sub>], [LNaAlEt·AlEt<sub>3</sub>], [LNaAl<sup>i</sup>Bu·Al(<sup>i</sup>Bu)<sub>3</sub>] and [LKAIEt·AlEt<sub>3</sub>], as determined by XRD.

| [LNaAlMe·AlMe <sub>3</sub> ] |              | [LNaAlEt·AlEt <sub>3</sub> ] |              | [LNaAl <sup>i</sup> Bu·Al( <sup>i</sup> Bu) <sub>3</sub> ] |              | [LKAIEt·AlEt <sub>3</sub> ] |              |
|------------------------------|--------------|------------------------------|--------------|------------------------------------------------------------|--------------|-----------------------------|--------------|
| Bond                         | Distance (Å) | Bond                         | Distance (Å) | Bond                                                       | Distance (Å) | Bond                        | Distance (Å) |
| Na29-O7                      | 2.306(1)     | Na29-O7                      | 2.273(4)     | Na29-O7                                                    | 2.304(2)     | K29-O7                      | 2.620(1)     |
| Na29-O22                     | 2.282(1)     | Na29-O22                     | 2.284(4)     | Na29-O25                                                   | 2.299(2)     | K29-O25                     | 2.655(1)     |
| Na29-N12                     | 2.462(1)     | Na29-N12                     | 2.420(5)     | Na29-N10                                                   | 2.427(3)     | K29-N10                     | 2.783(1)     |
| Na29-C53                     | 2.970(2)     | Na29-C58                     | 2.718(8)     | Na29-C63                                                   | 2.798(2)     | K29-C6                      | 3.291(2)     |
| Al50-O7                      | 1.788(2)     | Al50-O7                      | 1.773(4)     | Al50-O7                                                    | 1.786(2)     | K29-C39                     | 3.364(2)     |
| Al50-O26                     | 1.739(1)     | Al50-O26                     | 1.724(4)     | Al50-O22                                                   | 1.737(2)     | K29-C56                     | 3.033(2)     |
| Al50-N10                     | 2.001(1)     | Al50-N10                     | 1.988(5)     | Al50-N12                                                   | 1.997(2)     | K29-O7                      | 2.620(1)     |
| Al50-C51                     | 1.942(2)     | Al50-C51                     | 1.944(9)     | Al50-C51                                                   | 1.950(2)     | K29-O25                     | 2.655(1)     |
| Al52-O22                     | 1.791(1)     | Al53-O22                     | 1.780(4)     | Al2-O25                                                    | 1.805(1)     | K29-N10                     | 2.783(1)     |
| Al52-C53                     | 2.016(2)     | Al53-C58                     | 2.005(7)     | Al2-C55                                                    | 2.005(4)     | K29-C6                      | 3.291(2)     |
| Al52-C54                     | 2.006(2)     | Al53-C54                     | 1.994(7)     | Al2-C59                                                    | 2.037(3)     | K29-C45                     | 3.366(2)     |
| Al52-C55                     | 1.988(2)     | Al53-C56                     | 1.985(1)     | Al2-C63                                                    | 2.036(4)     | K29-C56                     | 3.033(2)     |
|                              |              |                              |              |                                                            |              | Al50-O7                     | 1.768(1)     |
|                              |              |                              |              |                                                            |              | Al50-O22                    | 1.735(1)     |
|                              |              |                              |              |                                                            |              | Al50-N12                    | 1.994(1)     |
|                              |              |                              |              |                                                            |              | Al50-C51                    | 1.953(2)     |
|                              |              |                              |              |                                                            |              | Al53-O25                    | 1.798(1)     |
|                              |              |                              |              |                                                            |              | Al53-C54                    | 2.013(2)     |
|                              |              |                              |              |                                                            |              | Al53-C56                    | 2.028(2)     |
|                              |              |                              |              |                                                            |              | Al53-C58                    | 1.992(2)     |

**Table 3.3** Selected bond angles for complexes [LNaAlMe·AlMe<sub>3</sub>], [LNaAlEt·AlEt<sub>3</sub>], [LNaAl<sup>i</sup>Bu·Al(<sup>i</sup>Bu)<sub>3</sub>] and [LKAIEt·AlEt<sub>3</sub>], as determined by XRD.

| [LNaAlMe·AlMe <sub>3</sub> ] |            | [LNaAlEt·AlEt <sub>3</sub> ] |            | [LNaAl <sup>i</sup> Bu·Al( <sup>i</sup> Bu) <sub>3</sub> ] |            | [LKAIEt·AlEt <sub>3</sub> ] |            |
|------------------------------|------------|------------------------------|------------|------------------------------------------------------------|------------|-----------------------------|------------|
| Bond                         | Angles (°) | Bond                         | Angles (°) | Bond                                                       | Angles (°) | Bond                        | Angles (°) |
| O7-Na29-N12                  | 84.85(4)   | O7-Na29-N12                  | 88.5(2)    | O7-Na29-N10                                                | 85.69(7)   | O7-K29-N10                  | 75.64(4)   |
| O7-Na29-O22                  | 135.03(5)  | O7-Na29-O22                  | 145.5(2)   | O7-Na29-O25                                                | 140.91(8)  | O7-K29-O25                  | 119.68(4)  |
| O7-Na29-C53                  | 157.10(5)  | O7-Na29-C58                  | 141.1(2)   | O7-Na29-C63                                                | 150.53(9)  | O7-K29-C56                  | 176.21(5)  |
| C53-Na29-O22                 | 67.56(5)   | O22-Na29-C58                 | 72.2(2)    | O25-Na29-C63                                               | 68.53(8)   | O25-K29-C56                 | 64.04(4)   |
| N12-Na29-O22                 | 74.11(4)   | O22-Na29-N12                 | 74.5(1)    | O25-Na29-N10                                               | 74.22(7)   | O25-K29-N10                 | 64.29(3)   |
| N12-Na29-C53                 | 109.19(5)  | N12-Na29-C58                 | 120.1(2)   | N10-Na29-C63                                               | 110.06(9)  | N10-K29-C56                 | 107.37(5)  |
| C53-Al52-O22                 | 102.65(6)  | C58-Al53-O22                 | 103.1(3)   | C63-Al2-O25                                                | 97.8(1)    | C56-Al53-O25                | 104.72(7)  |
| C53-Al52-C54                 | 108.93(7)  | C58-Al53-C54                 | 110.0(3)   | C63-Al2-C55                                                | 110.9(1)   | C56-Al53-C54                | 106.59(8)  |
| C53-Al52-C55                 | 109.09(8)  | C58-Al53-C56                 | 107.8(4)   | C63-Al2-C59                                                | 115.3(1)   | C56-Al53-C58                | 108.96(8)  |
| O22-Al52-C55                 | 114.73(7)  | C54-Al53-O22                 | 116.2(2)   | O25-Al2-C59                                                | 105.2(1)   | C58-Al53-O25                | 118.28(7)  |
| O22-Al52-C54                 | 109.40(7)  | O22-Al53-C56                 | 108.9(3)   | O25-Al2-C55                                                | 110.9(1)   | O25-Al53-C54                | 111.36(6)  |
| O7-Al50-C51                  | 114.29(7)  | O7-Al50-51                   | 115.0(3)   | O7-Al50-C51                                                | 110.53(9)  | O7-Al50-C51                 | 115.41(6)  |
| O7-Al50-N10                  | 98.71(6)   | O7-Al50-N10                  | 100.6(2)   | O7-Al50-N12                                                | 99.75(9)   | O7-Al50-N12                 | 99.83(5)   |
| O7-Al50-O26                  | 114.12(6)  | O7-Al50-O26                  | 112.5(2)   | O7-Al50-O22                                                | 113.20(9)  | O7-Al50-O22                 | 112.17(6)  |
| O26-Al50-N10                 | 90.51(6)   | O26-Al50-N10                 | 90.2(2)    | O22-Al50-N12                                               | 90.54(9)   | O22-Al50-N12                | 91.29(6)   |
| O26-Al50-C51                 | 119.90(7)  | O26-Al50-C51                 | 118.1(3)   | O22-Al50-C51                                               | 123.3(1)   | O22-Al50-C51                | 119.08(6)  |
|                              |            |                              |            |                                                            |            | C6-K29-O7                   | 23.50(3)   |
|                              |            |                              |            |                                                            |            | O7-K29-C45                  | 79.24(4)   |
|                              |            |                              |            |                                                            |            | C45-K29-C39                 | 94.21(4)   |
|                              |            |                              |            |                                                            |            | C39-K29-O25                 | 52.44(4)   |
|                              |            |                              |            |                                                            |            | C39-K29-N10                 | 76.93(4)   |

### 3.3.3 Solution-State Analysis of Heterotrimetallic Alkali Metal/Aluminium Complexes

The heterotrimetallic complexes,  $[\text{L}(\text{AM})\text{AlR}\cdot\text{AlR}_3]$  (where AM = Na or K; R = Me, Et), were also characterised in the solution-state by multinuclear NMR spectroscopic methods ( $^1\text{H}$ ,  $^{13}\text{C}$ , 2D COSY, HSQC and DOSY) and elemental analyses. NMR spectroscopy analysis of the resultant heterotrimetallic complexes is in alignment with the molecular structure obtained by XRD analysis, implying that the solid-state structures are maintained in solution. The  $^1\text{H}$  NMR spectra revealed shifts of the product proton resonances compared to those of the precursor (*e.g.*  $[\text{LNaAlEt}\cdot\text{AlEt}_3]$  vs  $[\text{LH}_2\text{Na}(\text{THF})_2]$ ), indicating the successful metalation and incorporation of aluminium alkyl units (Figure 3.10).

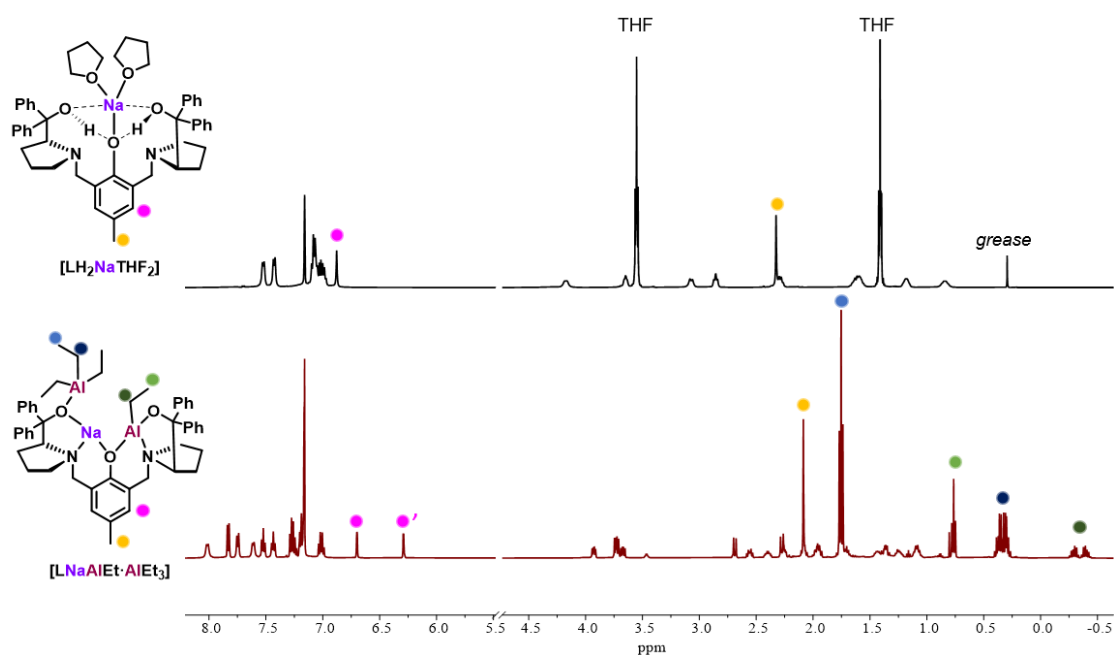


**Figure 3.10** Overlay of  $^1\text{H}$  NMR spectra (benzene- $d_6$ ) of  $[\text{LH}_2\text{Na}(\text{THF})_2]$  precursor (top) and  $[\text{LNaAlEt}\cdot\text{AlEt}_3]$  (bottom) complexes at 298 K, highlighting the incorporation of two Al moieties from two sets of ethyl groups, as well as the loss of complex symmetry upon reaction with  $\text{AlEt}_3$ .

Interestingly, unlike the symmetrical heterotrimetallic ProPhenol complexes based on AM/ $\text{Zn}_2$  previously synthesised by the Garden group (refer to Chapter 1, Figure 1.17),<sup>112</sup> metalation of  $[\text{LH}_2\text{Na}(\text{THF})_2]$  with two equivalents of aluminium alkyl gave an asymmetric heterometallic complex. The presence of a doublet of doublets at 6.29 and 6.70 ppm in the  $^1\text{H}$  NMR spectrum of  $[\text{LNaAlEt}\cdot\text{AlEt}_3]$  indicates the loss of symmetry from the precursor  $[\text{LH}_2\text{Na}(\text{THF})_2]$ , suggesting that the two protons on the *meta*-positions of the resultant complex are inequivalent. Furthermore, the coupling of these *meta*-phenolic protons in the COSY NMR spectrum confirms that the two heterometals are part of the same complex.<sup>114</sup> In addition, the complexation of Al in two different environments was corroborated by the appearance of two sets of distinctive Al-ethyl signals in the

high-field region (-1.10 - -0.26 ppm and -0.36 - 1.75 ppm, respectively, see Figure 3.10); one resonance representing one alkyl group coordinated to one Al centre ( $\text{Al}^1$ ), and another set of resonances representing three alkyl groups coordinated to a different Al centre ( $\text{Al}^2$ ). The datively bound triethyl- $\text{Al}^2$  moiety observed in the solid-state remains part of the complex in solution, as seen from the shifted triethyl- $\text{Al}^2$  signals (vs uncoordinated  $\text{AlEt}_3$  at 0.35 and 1.16 ppm)<sup>160</sup> in benzene- $d_6$ ). In addition, DOSY NMR showed that both sets of ethyl groups have the same diffusion coefficient as the ligand resonances (Figure 3.11).

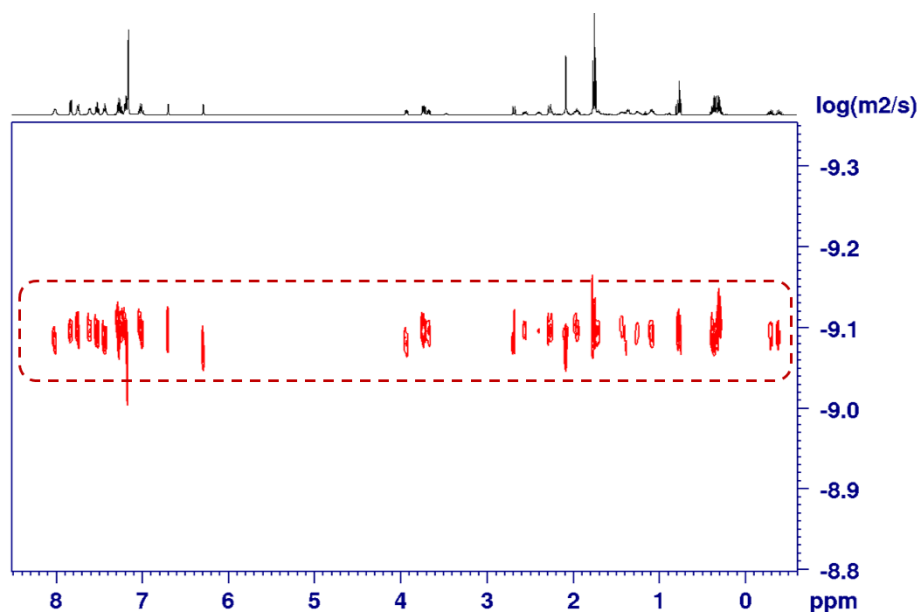


**Figure 3.11** Example DOSY NMR of  $[\text{LNaAlEt} \cdot \text{AET}_3]$  in benzene- $d_6$  at 298 K; where  $\text{MW}_{\text{predicted}}$  of complex is obtained through comparison to calibration plot.

(refer to Table 3.4 (*vide infra*), and Chapter 6, [Section 6.3.1.1](#) for more details)

The Na which initially occupied the central cavity of  $[\text{LH}_2\text{Na}(\text{THF})_2]$  shifts to the adjacent ‘pocket’ to accommodate the occupancy of  $\text{Al}^1$ , resulting in the deprotonation of the adjacent benzylic OH accompanied by the loss of the complex symmetry. This is interesting, as previous investigations revealed a selective deprotonation of phenolic-OH ProPhenol with 1.1 equiv. NaH, and further equivalents of NaH (with a total of  $\leq 3$  equiv.) did not deprotonate either of the benzylic OH groups. This suggests that metal rearrangements within the ProPhenol scaffold to occupy the most stable conformation may drive further deprotonation of the benzylic OH’s, which otherwise was not achieved even with a strong metal hydride Brønsted base such as NaH or KH. Other than that, further deprotonation of the benzylic OH’s might also be attributed to the smaller size of Al (vs Na and K), enabling the complexation of two Al’s into the  $[\text{LH}_2\text{M}(\text{THF})_2]$  framework.

The influence of different alkali metals and alkyl substituents upon the resultant heterometallic AM/Al complex was also investigated. In solution, both  $[\text{LNaAlMe} \cdot \text{AlMe}_3]$  and  $[\text{LKAIEt} \cdot \text{AlEt}_3]$  complexes display a similar trend; both are asymmetric and show the same 1:3 ratio of alkyl groups

coordinated to Al, with DOSY NMR confirming that the complex is monomeric in benzene- $d_6$  and that the  $\text{AlR}_3$  unit remains coordinated in solutions (refer to Figure 3.12 and Table 3.4).

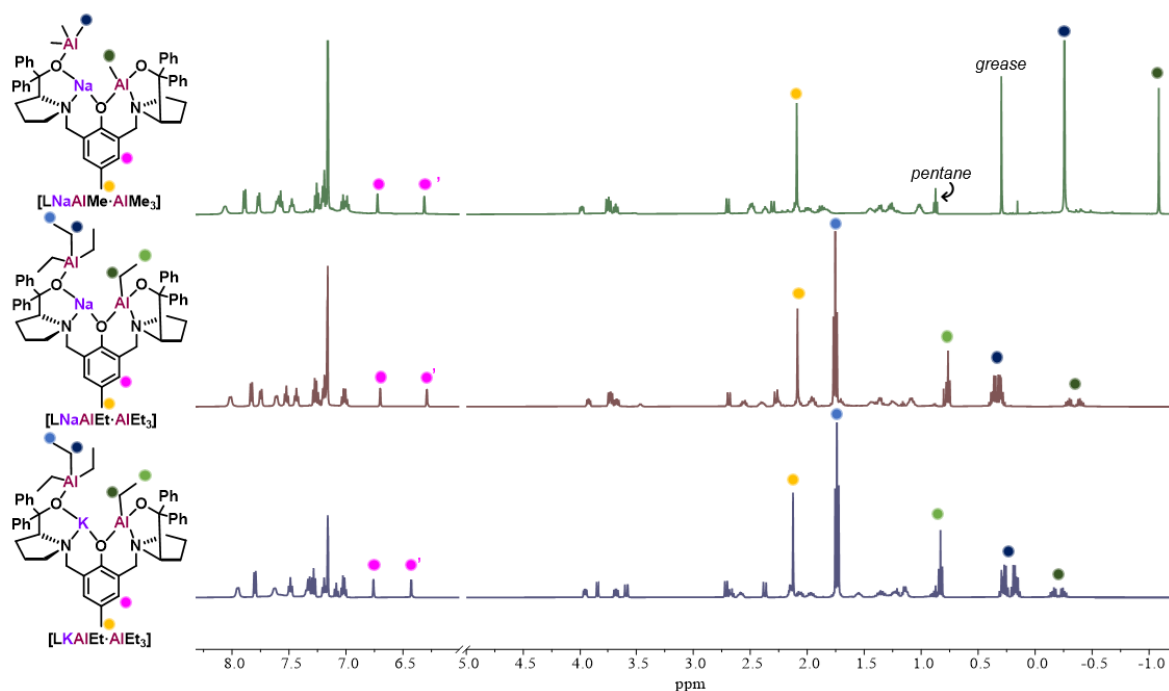


**Figure 3.12** Overlay of  $^1\text{H}$  NMR spectra (benzene- $d_6$ ) of  $[\text{LNaAlMe}\cdot\text{AlMe}_3]$  (top),  $[\text{LNaAlEt}\cdot\text{AlEt}_3]$  (middle) and  $[\text{LKAIEt}\cdot\text{AlEt}_3]$  (bottom) complexes at 298 K.

**Table 3.4** Predicted molecular weights by DOSY NMR for heterotrimetallic AM/ $\text{Al}_2$  complexes in benzene- $d_6$  at 298 K.

|   | Complex                              | MW <sub>calc.</sub><br>(g mol <sup>-1</sup> ) | Diffusion<br>coefficient, D<br>(m <sup>2</sup> s <sup>-1</sup> ) | MW <sub>predict</sub><br>(g mol <sup>-1</sup> ) |
|---|--------------------------------------|-----------------------------------------------|------------------------------------------------------------------|-------------------------------------------------|
| 1 | $[\text{LNaAlMe}\cdot\text{AlMe}_3]$ | 772.92                                        | -9.057                                                           | 700                                             |
| 2 | $[\text{LNaAlEt}\cdot\text{AlEt}_3]$ | 829.03                                        | -9.089                                                           | 790                                             |
| 3 | $[\text{LKAIEt}\cdot\text{AlEt}_3]$  | 845.14                                        | -9.095                                                           | 800                                             |

It is noteworthy that the methyl resonances bound to the Al of  $[\text{LNaAlMe}\cdot\text{AlMe}_3]$  are significantly shifted upfield ( $\text{Al}^1\text{Me}$ , -1.08 ppm;  $\text{Al}^2\text{Me}_3$ , -0.28 ppm) compared to the methylene ( $-\text{CH}_2\text{CH}_3$ ) resonances of both the  $[\text{LNaAlEt}\cdot\text{AlEt}_3]$  ( $\text{Al}^1\text{Et}$ , -0.24 – -0.45 ppm;  $\text{Al}^2\text{Et}_3$ , 0.43 – 0.26 ppm) and  $[\text{LKAIEt}\cdot\text{AlEt}_3]$  ( $\text{Al}^1\text{Et}$ , -0.11 – -0.30 ppm;  $\text{Al}^2\text{Et}_3$ , 0.32 – 0.14 ppm) complexes (refer to Figure 3.12, *vide supra*). This reflects the greater  $\sigma$ -electron donating nature/effect of ethyl group (*cf.* methyl) towards the Al metal centre, resulting in lesser shielding effect by electron density on the ethyl substituent. Additionally, the greater shielding effect in  $[\text{LNaAlMe}\cdot\text{AlMe}_3]$  is in line with “ate” character observed in mixed-metal complexes bearing AM/Al with methyl substituents.<sup>168</sup> The

formation of “ate” structures may occur with the close proximity of AM and the datively bonded  $\text{Al}^2$  via a AM-O-Al bridge to generate  $\text{AM}^+[\text{AlR}_4]^-$ -type complexes. When methyl substituents are present in aluminate compounds, a short methyl...alkali metal contact (*i.e.* an agostic interaction), is driven by the  $\sigma$ -electron density in the C—H bond. However, recent reports supported by computational studies have demonstrated that the  $\text{sp}^3$  C atom forming the carbon...alkali metal is highly electron-dense.<sup>169</sup> Consistent with literature precedent, the  $^{13}\text{C}\{^1\text{H}\}$  NMR of  $\text{Al}^2(\text{CH}_3)_3$  resonance has a greater upfield shift at -4.20 ppm in the  $^{13}\text{C}\{^1\text{H}\}$  NMR spectrum, relative to  $[\text{LNaAlEt}\cdot\text{AlEt}_3]$  and  $[\text{LKAIEt}\cdot\text{AlEt}_3]$  complexes (4.70 and 5.21 ppm, respectively), confirmed by HSQC NMR analysis.<sup>168,170</sup>

The effect of different alkali metals (*i.e.*  $[\text{LNaAlEt}\cdot\text{AlEt}_3]$  vs  $[\text{LKAIEt}\cdot\text{AlEt}_3]$ ) upon the extent of “ate” character can be seen through the different chemical shifts of the  $\text{Al}^2\text{-(CH}_2\text{CH}_3)_3$  resonances by  $^1\text{H}$  NMR analysis (yellow box, Figure 3.13). Electronic modulation within a heterometallic complex results in unequal electron distribution between the two metals, with partial negative charge ( $\delta^-$ ) being transferred to the more electronegative metal.<sup>97,171</sup> Within these AM/ $\text{Al}_2$  complexes, the lower electronegativity of K ( $\chi_{\text{K}} = 0.82$  vs Na,  $\chi_{\text{Na}} = 0.93$ )<sup>172</sup> results in greater  $\delta^-$  transfer to Al, thus increasing the polarity of Al—Et bond which is reflected by an upfield shift of the  $\text{Al}^2\text{-(CH}_2\text{CH}_3)_3$  resonance in  $[\text{LKAIEt}\cdot\text{AlEt}_3]$  vs  $[\text{LNaAlEt}\cdot\text{AlEt}_3]$  (0.22 ppm vs 0.34 ppm, see Figure 3.13). On the other hand, the opposite is observed for  $\text{Al}^1\text{-(CH}_2\text{CH}_3)_3$ . In the complexes,  $\text{Al}^1$  is bonded to two oxo- groups and one ethyl, and thus the  $\text{Al}^1$  centre is neutrally charged. However, the less shielded Et group in  $[\text{LKAIEt}\cdot\text{AlEt}_3]$  could still be influenced by the electronic communication between the three metals through the bridging phenoxy oxygens within the  $\text{Al}^1\text{-O-AM-O-Al}^2$  framework. The greater  $\delta^-$  on  $\text{Al}^2$  of  $[\text{LKAIEt}\cdot\text{AlEt}_3]$ , due to greater “ate” character arising from K/ $\text{Al}^2$  interactions, may be balanced by a smaller  $\delta^-$  charge on the  $\text{Al}^1$  fragment, which in turn decreases the  $\text{Al}^1\text{—Et}$  bond polarity. This is evidenced by the more downfield signal of  $[\text{LKAIEt}\cdot\text{AlEt}_3]$  (-0.21 ppm) compared to the  $[\text{LNaAlEt}\cdot\text{AlEt}_3]$  resonance (-0.35 ppm).

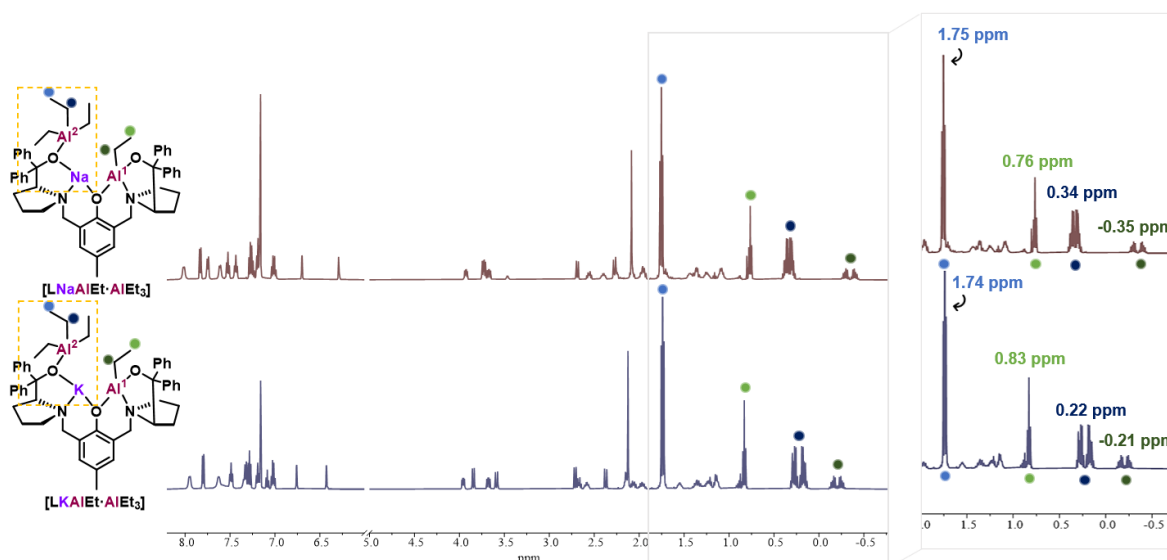


**Figure 3.13** Overlay of  $^1\text{H}$  NMR spectra (benzene- $d_6$ ) of  $[\text{LNaAlEt}\cdot\text{AlEt}_3]$  (top) and  $[\text{LKAlEt}\cdot\text{AlEt}_3]$  (bottom) complexes at 298 K. The greater  $\text{Al}^2\text{—Et}$  bond polarity of  $[\text{LKAlEt}\cdot\text{AlEt}_3]$  is reflected through the more upfield Et resonance, attributed to greater partial negative charge around the  $\text{Al}^2$  metal (highlighted in yellow box, left).

These trimetallic complexes have multiple metal centres available for the coordination of Lewis basic monomers, and initiation/propagation could take place from the  $\text{Al}^1\text{R}$  and/or  $\text{Al}^2\text{R}_3$  nucleophiles. To allow for comparison between different catalysts, we sought to investigate the abstraction of datively bonded  $\text{Al}^2\text{R}_3$  to form bimetallic mono/trivalent AM/Al analogues of the di/divalent M/Zn (where M = Zn, Mg or Ca) complexes investigated in Chapter 2. The abstraction of the  $\cdot\text{AlEt}_3$  moiety from the complex was hypothesised to occur at high temperatures, due to the weak nature of the dative  $\text{O—Al}^2$  bond, which could form heterobimetallic AM/Na complex. Intriguingly, the  $\cdot\text{AlEt}_3$  moiety retained the bonding at high temperature (100 °C, in toluene- $d_8$ ), as observed from the persistent  $\text{Al}^2\text{—}(\text{CH}_2\text{CH}_3)_3$  resonances between 0.0 and 0.5 ppm (Figure 3.14). Moreover, there were insignificant changes to the signal splitting in the  $^1\text{H}$  NMR spectra obtained under a range of temperature (–30 °C to 100 °C, see Figure 3.14). However, an upfield shift of the  $\text{Al}^2\text{—Et}_3$  signals were observed transitioning from lower to higher temperature, with the most significant resonance shift occurring for  $\text{Al}^2\text{—}(\text{CH}_2\text{CH}_3)_3$  (1.79 ppm at –30 °C to 1.48 ppm at 100 °C). Relating the bonding modes of  $\cdot\text{AlEt}_3$  to this observation, X-ray diffraction studies revealed an agostic interaction between the AM (Na or K) and one of the C—H bond from  $\text{Al}^2$  (refer Section 3.3.2, *vide supra*). In the solution-state, all three ethyl groups are in identical chemical environment, as evidenced by a single resonance observed in the  $^1\text{H}$  (and  $^{13}\text{C}\{^1\text{H}\}$ ) NMR spectra, at 0.26 – 0.40 (0.33) ppm and 1.74 – 1.77 (1.80) ppm, for the methylene and methyl group, respectively. At higher temperature, faster rotation of the ethyl groups may decrease the effect of  $\text{HC}\cdots\text{AM}$  agostic

interaction, and this consequently results in greater electron density on the ethyl groups, hence causing the protons to be more shielded.

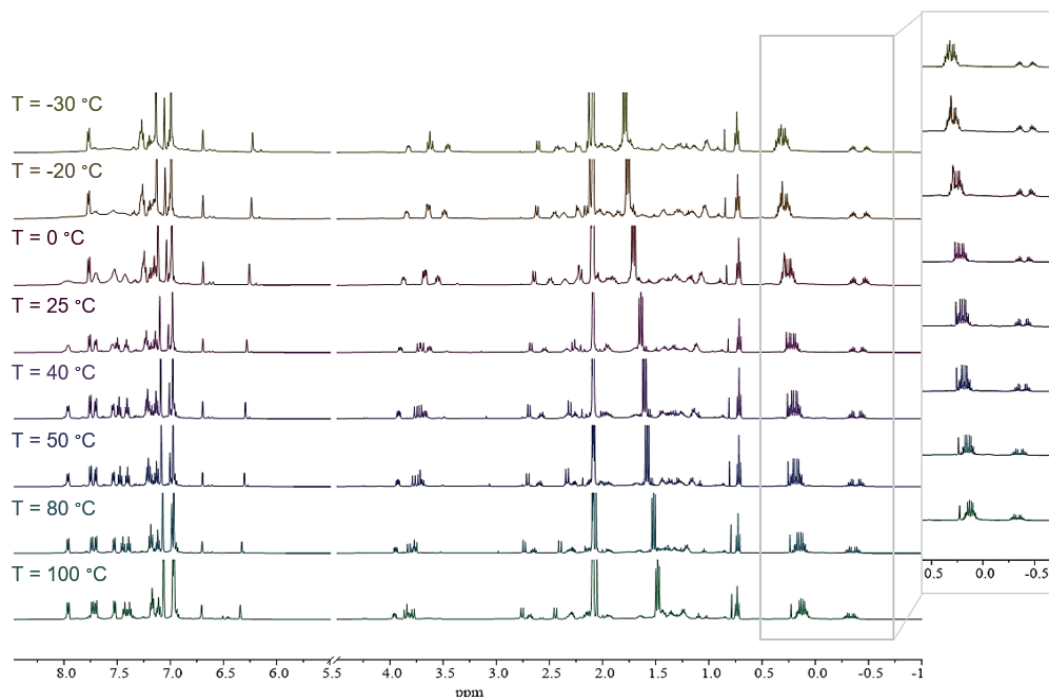
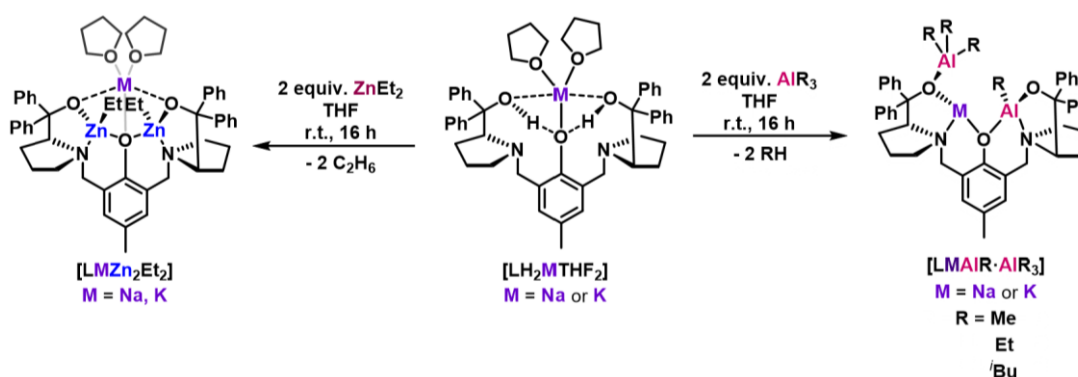


**Figure 3.14** Overlay of  $^1\text{H}$  NMR spectra of  $[\text{LNaAlEt}\cdot\text{AlEt}_3]$  at various temperature in toluene- $d_8$ .

### 3.3.3.1 Comparison between AM/ $\text{Zn}_2$ ProPhenol Complex with AM/ $\text{Al}_2$ ProPhenol Complex

The heterotrimetallic ProPhenol complexes based on AM/ $\text{Zn}_2$  reported previously by the Garden group,  $[\text{LNaZn}_2\text{Et}_2]$  and  $[\text{LKZn}_2\text{Et}_2]$ , have demonstrated heterometal cooperativity in the ROP of LA (refer to [Section 1.4.3](#), Chapter 1).<sup>112</sup> Although structural information of the AM/ $\text{Zn}_2$  complexes was only available through computational studies, it is interesting to observe the significant structural differences in the analogous heterotrimetallic complexes generated through sequential deprotonation of the AM precursor complexes with two equivalents of alkyl Zn and Al (Scheme 3.3).



**Scheme 3.3** Similar synthetic route *via* sequential deprotonation of AM precursor complexes generating different structures of AM/ $\text{Zn}_2$  (left) and AM/ $\text{Al}_2$  (right) complexes.

Unlike the **[LMAIR·AIR<sub>3</sub>]** complex(es), there was no rearrangement of the central AM of the precursor complex(es) in the AM/Zn<sub>2</sub> analogues (Figure 3.15). Both Zn share the same chemical environment, as evidenced from two resonances (*i.e.* Zn-CH<sub>2</sub>-CH<sub>3</sub>) from the two ethyl units of **[LMZn<sub>2</sub>Et<sub>2</sub>]** in <sup>1</sup>H NMR spectrum. On the other hand, rearrangement of AM in the heterometallic AM/Al<sub>2</sub> complexes resulted in two different Al environments (*i.e.* Al<sup>1</sup> is situated inside the ProPhenol pocket whilst Al<sup>2</sup> is datively bound outside the ProPhenol pocket). The different Al environments, and increased valency of Al compared to Zn, gives rise to four ethyl units that could act as initiating groups in cyclic ester ROP.

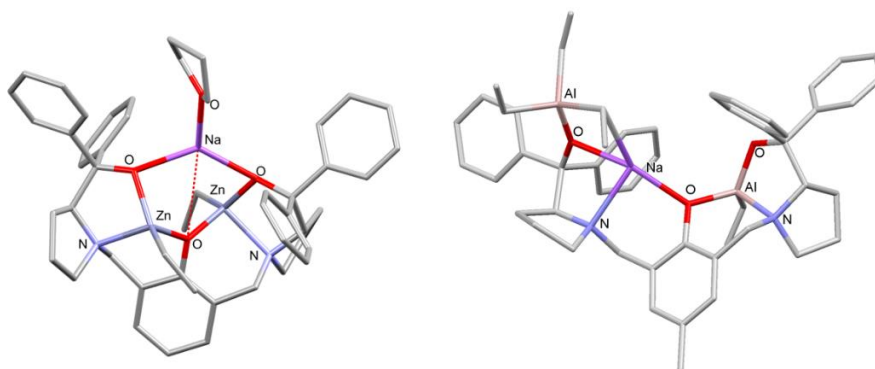


**Figure 3.15** Structural difference between **[LNaZn<sub>2</sub>Et<sub>2</sub>]** (left) and **[LNaAlEt·AlEt<sub>3</sub>]** (right). The reported structure for **[LNaZn<sub>2</sub>Et<sub>2</sub>]** was computed at  $\omega$ B97XD/6-311++g(d,p)/6-31g(d)/cpcm=tetrahydrofuran/298K level of theory.<sup>112</sup> The molecular structure for **[LNaAlEt·AlEt<sub>3</sub>]** was obtained from a single crystal with displacement ellipsoids at the 30% probability level.

Other than that, Na is more exposed and located slightly “above” the inner cavity of the ligand scaffold of **[LNaZn<sub>2</sub>Et<sub>2</sub>]**, potentially making the AM more accessible for monomer coordination. In contrast, the Na centre of **[LNaAlEt·AlEt<sub>3</sub>]** is positioned more deeply inside the ligand pocket. However, it is also worth noting that the AM of the AM/Al<sub>2</sub> is tetracoordinate without additional THF molecules coordinated around the metal centre, which could also be advantageous for monomers to coordinate readily. Unlike the AM/Al<sub>2</sub> heterotrimetallic complexes investigated within this chapter, the AM/Zn<sub>2</sub> complexes are symmetrical in solution-state as evidenced from NMR spectroscopic analysis. These complexes displayed “ate” (*i.e.* zincate) character in solution, where the Zn—Et groups of both complexes were observed shifted upfield compared to that of homobimetallic complex **[LZn<sub>2</sub>Et]**. Similar to this work where **[LKAIEt·AlEt<sub>3</sub>]** displays greater “ate” character (see previous section) in solution, as the increased polarity of the Zn—Et bond was also reflected through a higher upfield shift of the Zn—Et resonance in the K/Zn<sub>2</sub> vs the Na/Zn<sub>2</sub> analogue. All heterotrimetallic ProPhenol complexes based on AM/Zn<sub>2</sub> and AM/Al<sub>2</sub> were monomeric in solution, in THF-*d*<sub>8</sub> and benzene-*d*<sub>8</sub>, respectively.

Overall, the heterotrimetallic AM/Al<sub>2</sub> are interesting catalyst candidates for cyclic ester polymerisation. As the AM/Zn<sub>2</sub> ProPhenol analogues have shown impressive performance for LA polymerisation arising from heterometallic synergy and “ate” activation within the complex, the AM/Al<sub>2</sub> analogues that have demonstrated similar character were anticipated to deliver good polymerisation performance. Of course, the differences observed between the AM/Zn<sub>2</sub> and AM/Al<sub>2</sub> complexes, such as the AM coordination modes and number of alkyl (initiating) groups, may influence the catalyst behaviour. Nevertheless, the well-defined molecular structures obtained from this work were envisaged to provide valuable information on the catalyst activity and performance, which is further described in Chapter 4.

### 3.4 Conclusions

Harnessing the reactivity enhancements available with multimetallic complexes has gained momentum in many areas of catalysis. Although comprehensive and precise mechanistic studies for multimetallic ROP have yet to be established, both computational and experimental studies are starting to provide invaluable insights into the beneficial features of synergic heterometallic catalysts, including the formation of “ate” complexes.

In this chapter, the formation of heterometallic ProPhenol complexes based on AM (Na and K) and Al was investigated through sequential metallation of a ProPhenol ligand. Upon optimising the order of addition and the reaction stoichiometry, four novel heterotrimetallic complexes ( $[\text{LNaAlMe}\cdot\text{AlMe}_3]$ ,  $[\text{LNaAlEt}\cdot\text{AlEt}_3]$ ,  $[\text{LNaAl}^i\text{Bu}\cdot\text{Al}(^i\text{Bu})_3]$  and  $[\text{LKAIEt}\cdot\text{AlEt}_3]$ ) were gratifyingly synthesised. This was achieved *via* reaction with an AM hydride, followed by further deprotonation of the isolated AM precursor complex with two equivalents of a trialkyl aluminium reagent. To the best of our knowledge, these are the first examples of well-defined heterotrimetallic complexes based on the ProPhenol ligand successfully isolated and characterised by X-ray crystallography.

The molecular structure provides interesting insight into the metal coordination geometry. Differing from previously reported AM/ $\text{Zn}_2$  ProPhenol complexes, the reaction of the monometallic AM precursor with two equivalents of  $\text{AlR}_3$  generated asymmetric heterotrimetallic species upon the rearrangement of AM within the ProPhenol ligand. The coordination number around Na decreased from five in the  $[\text{LH}_2\text{NaTHF}_2]$  precursor complex to four in all of the Na/ $\text{Al}_2$  complexes, whereas the K of the K/ $\text{Al}_2$  analogue is heptacoordinate to satisfy the larger coordination sphere.

The heterometallic complexes bear “ate” character as observed by NMR spectroscopy. Analysis of the XRD and NMR data indicates that an alkali metal aluminate,  $\text{AM}^+[\text{AlR}_4]^-$  is formed around the datively bound  $\text{Al}^2$  moiety. The difference in “ate” character between the Na/ $\text{Al}_2$  and K/ $\text{Al}_2$  complexes was observed by  $^1\text{H}$  NMR spectroscopy. In solution, K/ $\text{Al}_2$  analogue displays a greater “ate” character, attributed to the lower electronegativity of K. This consequently increased the partial negative charge around the Al metal centre of the  $[\text{L}(\text{AM})\text{AlR}\cdot\text{AlR}_3]$  moiety, reflected through a greater upfield shift of the  $\text{Al}-\text{Et}$  unit.

The different alkyl substituents attached to the Al centre (Me, Et or  $^i\text{Bu}$ ) have an insignificant impact on the overall molecular structure of the complexes, as seen from the comparable bond angles and geometry around the metal centres. Interestingly, the two Al centres coordinated to the complex are in completely different chemical environments with distinct bonding modes. One Al centre occupies the inner cavity of the ProPhenol ligand scaffold, whereas the other Al centre is datively

bound to a benzylic oxygen on the 'outer' part of the ligand framework. This molecular structure is also retained in solution-state, as evidenced by NMR spectroscopy analysis. Further investigation to access a bimetallic mono/trivalent AM/Al complex by removing the datively bound  $\text{AlR}_3$  moiety was attempted through subjecting the trimetallic complex under elevated temperature in solution. Intriguingly, the  $\text{AlR}_3$  remained persistent on the complex under the range of temperature tested (-30 to 100 °C). The heterotrimetallic complexes studied within this chapter have potential to act as efficient cyclic ester ROP catalysts, and may be more sustainable alternatives for the high-performing heterometallic ProPhenol catalysts based on Zn. Furthermore, access into the molecular structures of these complexes could provide valuable insight of the roles of different metals within the heterometallic ProPhenol system in cyclic ester polymerisation, which is explored in detail in Chapter 4.

### 3.5 Future Work

Reported herein are structurally well-defined novel heterometallic ProPhenol complexes based on AM and Al, designed for the ROP of cyclic ester. Structural insights gained from this study such as the ProPhenol ligand flexibility, metal bonding and connectivity, as well as the overall complex geometry are among determining factors for cooperativity observed in multimetallic systems for cyclic ester polymerisation.

As with previously reported heterometallic ProPhenol analogues, solution-state studies hint towards "ate" character being present within these AM/ $\text{Al}_2$  complexes too. DFT calculations would be a powerful method of providing more in-depth insight into the electronic properties of these complexes, especially those arising from intermetallic communication. For instance, natural bond orbital analysis can provide information on electron density distribution within a molecule whereas natural population analysis delivers quantitative information of atomic charges based on their electronic structure and bonding manners.<sup>173,174</sup> These theoretical insights would be useful to compliment and rationalise the hypothesis on heterometallic catalysts activity enhancement that stems from "ate"-type activation.

The work presented in this chapter showcased great structural similarity between Na and K analogues of the AM/ $\text{Al}_2$  complexes. More significant differences are seen with relation to the bonding around the AM centre (*i.e.* higher coordination number around K vs Na) and the overall ligand flexibility/geometry. Extending this study to heavier alkali metals would be a valuable complement to the structural studies of AM/ $\text{Al}_2$  ProPhenol complexes. So far, the largest metallic

ProPhenol complexes reported are based on transition metal of Group 4 (*i.e.* Ti, Zr, Hf), comprising of two ProPhenol ligands per metal centre.<sup>81</sup> Hence, extending the library of AM/Al<sub>2</sub> complexes with larger Group 1 elements Rb and Cs (ionic radii of Rb<sup>+</sup> = 152 pm; Cs<sup>+</sup> = 181 pm)<sup>175</sup> may provide understanding on the fluxionality of ProPhenol ligand scaffold. This information is valuable not only in the context of cyclic ester ROP but is equally beneficial for other stereo- and/or regioselective catalytic reactions. It would be worth studying the effect of heavier AM on the “ate” character of the resultant trimetallic complexes resulting from different Lewis acidity, and how this would in turn alter the polarity of Al—alkyl bond.

In a similar vein, replacing Al with low-toxicity, earth abundant Fe to access a series of mono/trivalent ProPhenol complexes is also worth investigating. Numerous high-performing Fe complexes for cyclic ester polymerisation have been reported.<sup>176</sup> Therefore, combining the strong track record of Fe catalysts with active AM can be anticipated to further enhance the polymerisation activity and selectivity. Furthermore, Fe can bear a variety of oxidation states (most commonly +2 and +3), which would vary the coordination geometries; this provides another opportunity to vary the electronics as well as the steric availability at the metal centres.

In this work, AM/Al<sub>2</sub> complexes were accessed through a sequential deprotonation route, initially yielding a monometallic AM precursor before finally generating a trimetallic AM/Al<sub>2</sub> complex. An initial attempt to access bimetallic complex *via* the removal of datively bound AlR<sub>3</sub> at an elevated temperature was unsuccessful, and so this was further probed using chemical means in Chapter 4. Alternatively, a bimetallic AM/Al ProPhenol complex could potentially be accessed through other synthetic pathways (*i.e.* salt metathesis, transmetalation), and/or by using a broader range of aluminium reagents beyond aluminium alkyls (*i.e.* aluminium hydrides, aluminium alkoxides or mixed aluminium alkyl and halide species, *e.g.* AlEt<sub>2</sub>Cl). Perhaps the difference in electronic properties of different metal reagents could stabilise AM/Al ProPhenol complexes with a single Al centre, giving a straightforward access to heterobimetallic species.

## 3.6 Experimental

### 3.6.1 Synthesis of Complexes $[\text{LH}_2\text{Na}(\text{THF})_2]$ , $[\text{LH}_2\text{K}(\text{THF})_2]$ , $[\text{LNaAlMe}\cdot\text{AlMe}_3]$ , $[\text{LNaAlEt}\cdot\text{AlEt}_3]$ and $[\text{LKAIEt}\cdot\text{AlEt}_3]$

#### 3.6.1.1 Complex $[\text{LH}_2\text{Na}(\text{THF})_2]$

In a glovebox, (*S,S*)-(+)-2,6-bis[2-(hydroxydiphenylmethyl)-1-pyrrolidinyl-methyl]-4-methylphenol (1.0 g, 1.56 mmol) was dissolved in dry THF (20 mL). NaH (41.2 mg, 1.716 mmol) was slowly added into the solution to yield  $[\text{LH}_2\text{Na}(\text{THF})_2]$ . The mixtures were stirred for 2 h at room temperature in the glovebox. Solvent was removed *in vacuo* to yield products as a pale yellow powder (676.4 mg, 54%).  $^1\text{H}$  and  $^{13}\text{C}$  NMR spectra of the products were consistent with reported literature values.<sup>112</sup>

$^1\text{H}$  NMR (500 MHz,  $\text{THF}-d_8$ )  $\delta$ : 9.97 (s, 2 H), 7.60 – 7.54 (m, 4 H), 7.38 – 7.33 (m, 4 H), 7.29 (dd, 4 H), 7.23 – 7.16 (m, 2 H), 7.09 – 6.99 (m, 6 H), 6.58 (s, 2 H), 4.49 (d, 2 H), 3.81 (dd, 2 H), 3.64 – 3.60 (m, 6 H), 3.08 (d, 2 H), 2.69 (ddd, 2 H), 2.33 (ddd, 2 H), 2.10 (s, 3 H), 2.01 – 1.89 (m, 2 H), 1.81 – 1.75 (m, 6 H), 1.60 (ddt, 2 H), 1.30 – 1.23 (m, 2 H), 0.42 – 0.28 (m, 2 H).

$^{13}\text{C}$  NMR (126 MHz,  $\text{THF}-d_8$ )  $\delta$ : 166.39, 149.14, 148.30, 129.36, 128.56, 128.41, 127.32, 81.04, 71.08, 68.27, 67.27, 67.10, 61.91, 55.42, 30.76, 26.43, 25.21, 25.05, 20.86.

#### 3.6.1.2 Complex $[\text{LH}_2\text{K}(\text{THF})_2]$

In a glovebox, (*S,S*)-(+)-2,6-bis[2-(hydroxydiphenylmethyl)-1-pyrrolidinyl-methyl]-4-methylphenol (1.0 g, 1.56 mmol) was dissolved in dry THF (20 mL). KH (68.8 mg, 1.716 mmol) was slowly added into the solution to yield  $[\text{LH}_2\text{K}(\text{THF})_2]$ . The mixtures were stirred for 2 h at room temperature in the glovebox. Solvent was removed *in vacuo* to yield products as dark brown/orange powder (1033.0 mg, 88%).  $^1\text{H}$  and  $^{13}\text{C}$  NMR spectra of the products were consistent with reported literature values.<sup>112</sup>

$^1\text{H}$  NMR (500 MHz,  $\text{THF}-d_8$ )  $\delta$ : 10.28 (s, 2 H), 7.71 (dd, 2 H), 7.44 (dd, 2 H), 7.26 (t, 4 H), 7.16 (t, 2 H), 7.10 – 6.97 (m, 6 H), 6.52 (s, 2 H), 3.74 (dd, 2 H), 2.88 (d, 2 H), 2.75 (dt, 2 H), 2.30 – 2.21 (m, 2 H), 2.06 (s, 3 H), 1.54 (ddt, 2 H), 1.30 – 1.22 (m, 2 H), 0.59 – 0.46 (m, 2 H).

$^{13}\text{C}$  NMR (126 MHz,  $\text{THF}-d_8$ )  $\delta$ : 166.56, 150.34, 148.92, 130.28, 128.94, 128.43 (d), 127.93, 127.38, 126.77, 126.09, 116.25, 80.62, 70.23, 68.27, 60.66, 55.21, 30.91, 26.43, 23.55, 20.83.

### 3.6.1.3 Complex [LNaAlMe·AlMe<sub>3</sub>]

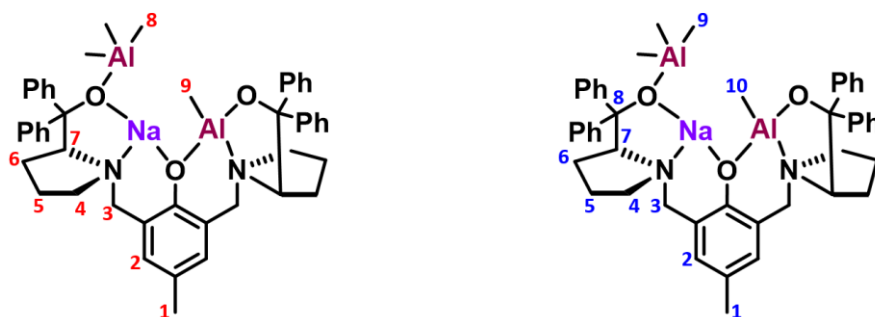


**Figure 3.16** Labelled structures for [LNaAlMe·AlMe<sub>3</sub>] for <sup>1</sup>H (left) and <sup>13</sup>C (right) NMR assignments.

In a glovebox, complex [LH<sub>2</sub>Na(THF)<sub>2</sub>] (402.5 mg, 0.5 mmol) was dissolved in dry THF or toluene (10 mL). AlMe<sub>3</sub> (2.0 M in toluene, 0.5 mL, 1.0 mmol) was added slowly. The reaction mixture was stirred for 16 h at room temperature in the glovebox. THF solvent was removed *in vacuo*. The resulting off-white compound was washed with pentane (3 × 5 mL) and dried *in vacuo* to yield [LNaAlMe·AlMe<sub>3</sub>] as an off-white powder (165.1 mg, 42.7%).

**<sup>1</sup>H NMR** (500 MHz, C<sub>6</sub>D<sub>6</sub>) δ: 8.06 (d, 2 H, Ar-H), 7.89 (dd, 2 H, Ar-H), 7.77 (dd, 2 H, Ar-H), 7.59 (dddd, 4 H, Ar-H), 7.48 (t, 2 H, Ar-H), 7.26 (t, 2 H, Ar-H), 7.18 (t, 2 H, Ar-H), 7.03 (t, 2 H, Ar-H), 6.99 (t, 2 H, Ar-H), 6.72 (d, 1 H, H<sub>2</sub>), 6.31 (d, 1 H, H<sub>2</sub>'), 3.99 (dd, 1 H, H<sub>7</sub>), 3.74 (dd, 2 H, H<sub>3</sub>/H<sub>3</sub>'), 3.68 (dd, 1 H, H<sub>7</sub>'), 2.70 (d, 1 H, H<sub>3</sub>), 2.53 – 2.44 (m, 2 H, H<sub>6</sub>), 2.37 (ddd, 1H, H<sub>4</sub>), 2.30 (d, 1 H, H<sub>3</sub>'), 2.09 (s, 3 H, H<sub>1</sub>), 1.99 (m, 1 H, H<sub>4</sub>), 1.93 – 1.79 (m, 2 H, H<sub>4</sub>), 1.48 – 1.40 (m, 2 H, H<sub>5</sub>), 1.40 – 1.31 (m, 2 H, H<sub>5</sub>), 1.08 – 0.95 (m, 2 H, H<sub>6</sub>), -0.26 (s, 9 H, H<sub>8</sub>), -1.08 (s, 3 H, H<sub>9</sub>) ppm.

**<sup>13</sup>C NMR** (126 MHz, C<sub>6</sub>D<sub>6</sub>) δ: 152.91 (C-Ar), 152.10 (C-Ar), 151.19 (C-Ar), 149.39 (C-Ar), 148.78 (C-Ar), 133.95 (C-Ar), 130.87 (C-Ar), 129.35 (C-Ar), 129.27 (C-Ar), 127.26 (C-Ar), 127.16 (C-Ar), 126.67 (C-Ar), 126.00 (C-Ar), 125.90 (C-Ar), 125.43 (C-Ar), 125.38 (C-Ar), 82.63 (C<sub>8</sub>), 79.73 (C<sub>8</sub>'), 73.84 (C<sub>7</sub>'), 72.68 (C<sub>7</sub>), 59.14 (C<sub>8</sub>), 58.65 (C<sub>8</sub>'), 56.62 (C<sub>4</sub>), 56.14 (C<sub>4</sub>'), 30.56 (C<sub>6</sub>), 29.60 (C<sub>6</sub>'), 24.25 (C<sub>5</sub>), 21.41 (C<sub>5</sub>'), 20.54 (C<sub>1</sub>), -4.15 (C<sub>9</sub>) ppm.

N.B. C<sub>10</sub> not located in <sup>13</sup>C NMR, similar precedent observed in literature.<sup>177,178</sup>

**Elemental analysis:** Calculated: C, 73.04; H, 7.17; N, 3.62%. Found: C, 70.85; H, 6.49; N, 3.24%

### 3.6.1.4 Complex [LNaAlEt·AlEt<sub>3</sub>]

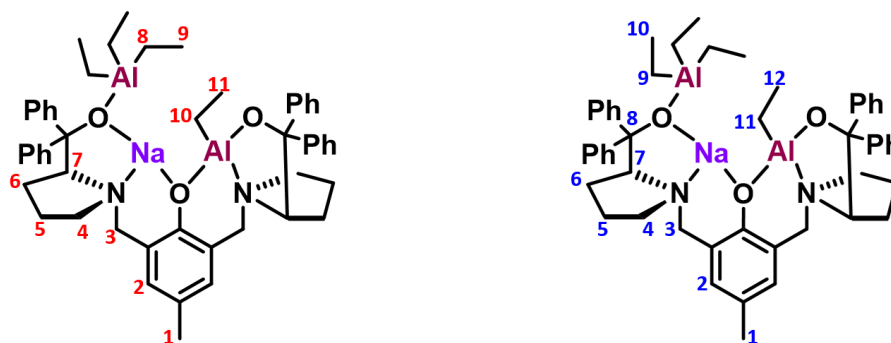


**Figure 3.17** Labelled structures for [LNaAlEt·AlEt<sub>3</sub>] for <sup>1</sup>H (left) and <sup>13</sup>C (right) NMR assignments.

In a glovebox, complex [LH<sub>2</sub>Na(THF)<sub>2</sub>] (644.0 mg, 0.8 mmol) was dissolved in dry THF (10 mL). AlEt<sub>3</sub> (182.7 mg, 1.6 mmol) was dissolved in THF (2 mL) and added dropwise to the solution of complex [LH<sub>2</sub>Na(THF)<sub>2</sub>], with effervescence being observed upon the addition. The reaction mixture was stirred for 16 h at room temperature in the glovebox. The solvent was removed *in vacuo*, resulting in the formation of an off-white powder. Recrystallisation of the product at room temperature from benzene with *n*-pentane layering afforded colourless crystals of complex [LNaAlEt·AlEt<sub>3</sub>] (416.5 mg, 62.8%).

**<sup>1</sup>H NMR** (500 MHz, C<sub>6</sub>D<sub>6</sub>) δ: 8.01 (d, 2 H, Ar-H), 7.86 – 7.80 (m, 2 H, Ar-H), 7.75 (d, 2 H, Ar-H), 7.61 (d, 2 H, Ar-H), 7.52 (t, 2 H, Ar-H), 7.44 (t, 2 H, Ar-H), 7.34 – 7.26 (ddd, 3 H, Ar-H), 7.21 – 7.18 (dt, 3 H, Ar-H), 7.06 – 6.97 (m, 2 H, Ar-H), 6.70 (d, 1 H, H<sub>2</sub>), 6.29 (d, 1 H, H<sub>2</sub>'), 3.93 (dd, 1 H, H<sub>7</sub>), 3.73 (dd, 2 H, H<sub>3</sub>/H<sub>3</sub>'), 3.67 (dd, 1 H, H<sub>7</sub>'), 2.69 (d, 1 H, H<sub>3</sub>), 2.56 (ddd, 1 H, H<sub>6</sub>), 2.40 (ddt, 1 H, H<sub>6</sub>'), 2.27 (d, 1 H, H<sub>3</sub>'), 2.26 – 2.23 (m, 2 H, H<sub>5</sub>'), 2.09 (s, 3 H, H<sub>1</sub>), 2.08 – 2.04 (m, 2 H, H<sub>4</sub>), 2.02 – 1.91 (m, 2 H, H<sub>6</sub>), 1.75 (t, 9 H, H<sub>9</sub>), 1.40 – 1.34 (m, 2 H, H<sub>5</sub>), 1.28 – 1.20 (m, 2 H, H<sub>5</sub>), 1.13 – 1.05 (m, 2 H, H<sub>4</sub>), 0.76 (t, 3 H, H<sub>11</sub>), 0.41 – 0.25 (m, 6 H, H<sub>8</sub>), -0.24 – -0.46 (m, 2 H, H<sub>10</sub>) ppm.

**<sup>13</sup>C NMR** (126 MHz, C<sub>6</sub>D<sub>6</sub>) δ: 152.63 (C-Ar), 152.42 (C-Ar), 149.31 (C-Ar), 148.68 (C-Ar), 134.16 (C-Ar), 130.45 (C-Ar), 129.47 – 129.23 (C-Ar), 129.10 (C-Ar), 126.81 (C-Ar), 126.13 (C-Ar), 125.51 (C-Ar), 125.38 (C-Ar), 82.11 (C<sub>8</sub>), 79.18 (C<sub>8</sub>'), 74.04 (C<sub>7</sub>), 73.11 (C<sub>7</sub>'), 58.97 (C<sub>3</sub>), 58.52 (C<sub>3</sub>'), 56.09 (C<sub>4</sub>), 55.55 (C<sub>4</sub>'), 30.26 (C<sub>6</sub>), 29.74 (C<sub>6</sub>'), 24.01 (C<sub>5</sub>), 21.21 (C<sub>5</sub>'), 20.49 (C<sub>1</sub>), 11.91 (C<sub>10</sub>), 8.41 (C<sub>12</sub>), 4.67 (C<sub>9</sub>), -3.17 (C<sub>11</sub>) ppm.

**Elemental analysis:** Calculated: C, 73.89; H, 7.66; N, 3.38%. Found: C, 73.95; H, 7.33; N, 3.14%

### 3.6.1.5 Complex [LKAIEt·AlEt<sub>3</sub>]

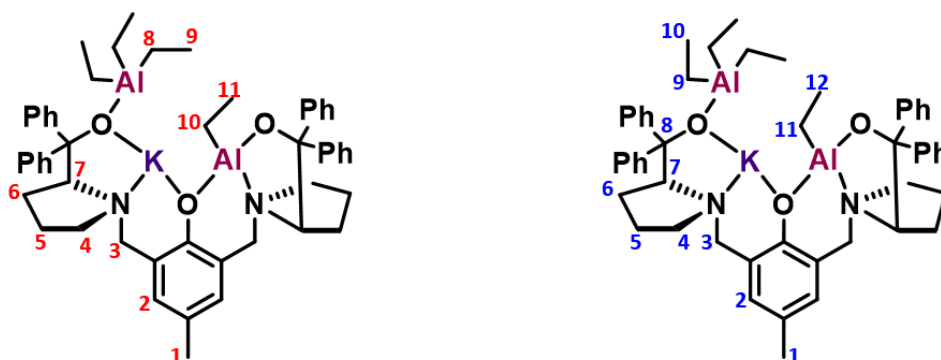


**Figure 3.18** Labelled structures for [LKAIEt·AlEt<sub>3</sub>] for <sup>1</sup>H (left) and <sup>13</sup>C (right) NMR assignments.

In a glovebox, complex [LH<sub>2</sub>K(THF)<sub>2</sub>] (656.9 mg, 0.8 mmol) was dissolved in dry THF (10 mL). AlEt<sub>3</sub> (114.2 mg, 1.6 mmol) was dissolved in THF (2 mL) and added dropwise to the orange solution of complex [LH<sub>2</sub>K(THF)<sub>2</sub>], with effervescence being observed upon the addition with a colour change from orange to pale yellow. The reaction mixture was stirred for 16 h at room temperature in the glovebox. The solvent was removed *in vacuo*, resulting in off-white powder. Recrystallisation of the product at room temperature from benzene with *n*-pentane layering afforded colourless single crystals of complex [LKAIEt·AlEt<sub>3</sub>] (217.6 mg, 32.2%).

**<sup>1</sup>H NMR** (500 MHz, C<sub>6</sub>D<sub>6</sub>) δ: 7.95 (d, 2 H, Ar-H), 7.83 – 7.77 (dd, 2 H, Ar-H), 7.63 (d, 3 H, Ar-H), 7.49 (t, 2 H, Ar-H), 7.38 – 7.32 (m, 3 H, Ar-H), 7.31 – 7.26 (t, 3 H, Ar-H), 7.23 – 7.16 (m, 2 H, Ar-H), 7.09 (tt, 1 H, Ar-H), 7.02 (m, 2 H, Ar-H), 6.76 (d, 1 H, H<sub>2</sub>), 6.43 (d, 1 H, H<sub>2</sub>'), 3.96 (dd, 1 H, H<sub>7</sub>), 3.85 (d, 1 H, H<sub>3</sub>), 3.68 (dd, 1 H, H<sub>7</sub>'), 3.59 (d, 1 H, H<sub>3</sub>'), 2.71 (d, 1 H, H<sub>3</sub>), 2.69 – 2.63 (m, 1 H, H<sub>4</sub>), 2.58 (ddt, 1 H, H<sub>6</sub>), 2.37 (d, 1 H, H<sub>3</sub>'), 2.18 – 2.13 (m, 2 H, H<sub>4</sub>'), 2.12 (s, 3 H, H<sub>1</sub>), 2.06 (m, 1 H, H<sub>4</sub>), 2.01 – 1.93 (m, 1 H, H<sub>6</sub>), 1.77 (d, 1 H, H<sub>5</sub>), 1.74 (t, 9 H, H<sub>9</sub>), 1.55 (m, 1 H, H<sub>5</sub>), 1.41 – 1.31 (m, 1 H, H<sub>6</sub>'), 1.28 – 1.20 (m, 1 H, H<sub>6</sub>'), 1.17 – 1.10 (m, 2 H, H<sub>5</sub>'), 0.83 (t, 3 H, H<sub>11</sub>), 0.33 – 0.11 (m, 6 H, H<sub>8</sub>), -0.10 – -0.31 (m, 2 H, H<sub>10</sub>).

**<sup>13</sup>C NMR** (126 MHz, C<sub>6</sub>D<sub>6</sub>) δ: 153.04 (d) (C-Ar), 151.54 (C-Ar), 150.07 (C-Ar), 148.67 (C-Ar), 134.81 (C-Ar), 130.70 (C-Ar), 128.99 (C-Ar), 127.44 (C-Ar), 126.75 (C-Ar), 126.50 (C-Ar), 126.17 (C-Ar), 125.86 (C-Ar), 125.30 (C-Ar), 125.21 (C-Ar), 83.30 (C<sub>8</sub>), 79.22 (C<sub>8</sub>'), 74.12 (C<sub>7</sub>), 72.54 (C<sub>7</sub>'), 59.54 (C<sub>3</sub>), 57.48 (C<sub>3</sub>'), 56.30 (C<sub>4</sub>), 54.80 (C<sub>4</sub>'), 30.22 (C<sub>6</sub>), 30.12 (C<sub>6</sub>'), 24.45 (C<sub>5</sub>), 21.82 (C<sub>5</sub>'), 20.56 (C<sub>1</sub>), 12.24 (C<sub>10</sub>), 8.36 (C<sub>12</sub>), 5.42 (C<sub>9</sub>), -2.68 (C<sub>11</sub>).

**Elemental analysis:** Calculated: C, 72.48; H, 7.51; N, 3.31%. Found: C, 70.99; H, 7.55; N, 3.19%

### 3.6.2 X-ray Crystallographic Data and Refinement Details

**Table 3.5** Crystallographic data and collection and refinement details for complexes [LNaAlMe·AlMe<sub>3</sub>], [LNaAl<sup>i</sup>Bu·Al(<sup>i</sup>Bu)<sub>3</sub>], [LNaAlEt·AlEt<sub>3</sub>] and [LKAIEt·AlEt<sub>3</sub>].

|                                                    | [LNaAlMe·AlMe <sub>3</sub> ]                                                    | LNaAl <sup>i</sup> Bu·Al( <sup>i</sup> Bu) <sub>3</sub>                         | [LNaAlEt·AlEt <sub>3</sub> ]                                                    | [LKAIEt·AlEt <sub>3</sub> ]                                                    |
|----------------------------------------------------|---------------------------------------------------------------------------------|---------------------------------------------------------------------------------|---------------------------------------------------------------------------------|--------------------------------------------------------------------------------|
| <b>Formula</b>                                     | C <sub>65</sub> H <sub>73</sub> Al <sub>2</sub> N <sub>2</sub> NaO <sub>3</sub> | C <sub>59</sub> H <sub>79</sub> Al <sub>2</sub> N <sub>2</sub> NaO <sub>3</sub> | C <sub>51</sub> H <sub>63</sub> Al <sub>2</sub> N <sub>2</sub> NaO <sub>3</sub> | C <sub>51</sub> H <sub>61</sub> Al <sub>2</sub> KN <sub>2</sub> O <sub>3</sub> |
| <b><i>D</i><sub>calc.</sub>/ g cm<sup>-3</sup></b> | 1.22                                                                            | 1.125                                                                           | 1.165                                                                           | 1.216                                                                          |
| <b><i>μ</i>/mm<sup>-1</sup></b>                    | 0.108                                                                           | 0.877                                                                           | 0.113                                                                           | 0.197                                                                          |
| <b>Formula Weight</b>                              | 1025.31                                                                         | 941.19                                                                          | 828.98                                                                          | 843.126                                                                        |
| <b>Colour</b>                                      | colourless                                                                      | clear colourless                                                                | colourless                                                                      | colourless                                                                     |
| <b>Shape</b>                                       | block-shaped                                                                    | block-shaped                                                                    | block-shaped                                                                    | plate-shaped                                                                   |
| <b>Size/mm<sup>3</sup></b>                         | 0.74×0.52×0.26                                                                  | 0.22×0.15×0.07                                                                  | 0.26×0.15×0.13                                                                  | 0.26×0.15×0.13                                                                 |
| <b><i>T</i>/K</b>                                  | 100                                                                             | 120.00(10)                                                                      | 249.7                                                                           | 100                                                                            |
| <b>Crystal System</b>                              | tetragonal                                                                      | triclinic                                                                       | monoclinic                                                                      | monoclinic                                                                     |
| <b>Flack Parameter</b>                             | 0.01(2)                                                                         | -0.030(13)                                                                      | 0.00(6)                                                                         | 0.006(7)                                                                       |
| <b>Space Group</b>                                 | <i>P</i> 4 <sub>3</sub>                                                         | <i>P</i> 1                                                                      | <i>P</i> 2 <sub>1</sub>                                                         | <i>P</i> 2 <sub>1</sub>                                                        |
| <b><i>a</i>/Å</b>                                  | 10.1065(3)                                                                      | 10.7389(3)                                                                      | 11.0792(6)                                                                      | 11.0534(13)                                                                    |
| <b><i>b</i>/Å</b>                                  | 10.1065(3)                                                                      | 11.4495(4)                                                                      | 19.3556(11)                                                                     | 18.555(2)                                                                      |
| <b><i>c</i>/Å</b>                                  | 54.653(2)                                                                       | 13.5631(4)                                                                      | 11.1649(6)                                                                      | 11.3129(13)                                                                    |
| <b><i>α</i>/°</b>                                  | 90                                                                              | 67.955(3)                                                                       | 90                                                                              | 90                                                                             |
| <b><i>β</i>/°</b>                                  | 90                                                                              | 89.898(2)                                                                       | 99.090(3)                                                                       | 97.053(5)                                                                      |
| <b><i>γ</i>/°</b>                                  | 90                                                                              | 66.019(3)                                                                       | 90                                                                              | 90                                                                             |
| <b><i>V</i>/Å<sup>3</sup></b>                      | 5582.3(4)                                                                       | 1389.74(8)                                                                      | 2364.2(2)                                                                       | 2302.6(5)                                                                      |
| <b><i>Z</i></b>                                    | 4                                                                               | 1                                                                               | 2                                                                               | 2                                                                              |
| <b><i>Z</i>'</b>                                   | 1                                                                               | 1                                                                               | 1                                                                               | 1                                                                              |
| <b>Wavelength/Å</b>                                | 0.71073                                                                         | 1.54184                                                                         | 0.71073                                                                         | 0.71073                                                                        |
| <b>Radiation type</b>                              | Mo K <sub>α</sub>                                                               | Cu K <sub>α</sub>                                                               | Mo K <sub>α</sub>                                                               | Mo K <sub>α</sub>                                                              |
| <b><i>θ</i><sub>min</sub>/°</b>                    | 2.149                                                                           | 3.573                                                                           | 2.138                                                                           | 2.12                                                                           |
| <b><i>θ</i><sub>max</sub>/°</b>                    | 30.517                                                                          | 75.722                                                                          | 21.112                                                                          | 30.56                                                                          |
| <b>Measured Refl's.</b>                            | 203719                                                                          | 23144                                                                           | 68307                                                                           | 157332                                                                         |
| <b>Indep't Refl's</b>                              | 17073                                                                           | 9661                                                                            | 5100                                                                            | 14059                                                                          |
| <b>Refl's I≥2 <i>σ</i>(I)</b>                      | 16461                                                                           | 9399                                                                            | 4700                                                                            | 13036                                                                          |
| <b><i>R</i><sub>int</sub></b>                      | 0.0354                                                                          | 0.0249                                                                          | 0.0534                                                                          | 0.0472                                                                         |
| <b>Parameters</b>                                  | 728                                                                             | 621                                                                             | 537                                                                             | 592                                                                            |
| <b>Restraints</b>                                  | 86                                                                              | 3                                                                               | 2                                                                               | 163                                                                            |
| <b>Largest Peak</b>                                | 0.258                                                                           | 0.305                                                                           | 0.362                                                                           | 0.4807                                                                         |
| <b>Deepest Hole</b>                                | -0.151                                                                          | -0.166                                                                          | -0.142                                                                          | -0.1881                                                                        |
| <b>Goodness-of-fit on F<sup>2</sup></b>            | 1.048                                                                           | 1.036                                                                           | 1.055                                                                           | 1.0408                                                                         |
| <b><i>R</i>1, <i>wR</i><sub>2</sub> (all data)</b> | 0.0304, 0.079                                                                   | 0.0355, 0.0930                                                                  | 0.0462, 0.1128                                                                  | 0.0438, 0.1084                                                                 |
| <b><i>R</i>1, <i>wR</i><sub>2</sub></b>            | 0.0287, 0.0772                                                                  | 0.0344, 0.0918                                                                  | 0.0415, 0.1093                                                                  | 0.0392, 0.1049                                                                 |
| <b><i>R</i><sub>1</sub> (all data)</b>             | 0.0304                                                                          | 0.0355                                                                          | 0.0462                                                                          | 0.0438                                                                         |
| <b><i>R</i><sub>1</sub></b>                        | 0.0287                                                                          | 0.0344                                                                          | 0.0415                                                                          | 0.0392                                                                         |

## Chapter 4

### Reactivity Studies of Heterotrimetallic Na/Al ProPhenol Complexes

## 4.1 Overview

The formation of heterobimetallic mono/trivalent **[LNaAlEt]** ProPhenol complexes was targeted, to provide a comparison with the bimetallic di/divalent ProPhenol complexes, **[LZn<sub>2</sub>Et]**, **[LMgZnEt]** and **[LCaZnEt]**, which were the focus of Chapter 2. Routes to convert trimetallic **[LNaAlEt·AlEt<sub>3</sub>]** into bimetallic **[LNaAlEt]** through the removal of the datively coordinated AlEt<sub>3</sub> unit by the addition of Lewis bases, including TEPO, DMAP and PMDETA, was investigated. While none of these Lewis bases abstracted the ·AlEt<sub>3</sub> moiety, NMR spectroscopic studies provided some insight into the potential interactions of Lewis donors with heterotrimetallic **[LNaAlEt·AlEt<sub>3</sub>]**. These observations provide some insight into the potential roles of the different metals in cyclic ester polymerisation. To enable catalytic comparison with the previously reported heterotrimetallic Na/Zn<sub>2</sub> ProPhenol complex **[LNaZn<sub>2</sub>Et<sub>2</sub>]**, **[LNaAlEt·AlEt<sub>3</sub>]** was tested for the ROP of CL, LA and VL in the presence of 2 equiv. BnOH as a co-initiator. PCL, PLA and PVL were successfully generated with good control, albeit with relatively low activity rates ( $k_{\text{obs}}$  values of 0.068 h<sup>-1</sup>, 0.053 h<sup>-1</sup> and 0.195 h<sup>-1</sup>, respectively).

## 4.2 Introduction

It has been established in several fields that heterometallic cooperativity can deliver superior performance compared to the homometallic counterparts.<sup>179</sup> Understanding and fine-tuning heterometallic cooperativity therefore offers an additional mode of enhancing catalyst activity, beyond the typical variables in a monometallic system where the catalyst performance is generally influenced by the ligand motif, choice of metal ( $M_1$ ), and the nature of co-ligands. In the ROP of cyclic esters, catalyst features such as the metal-metal distance, ligand flexibility and metal electronic properties, can all influence the catalyst performance.<sup>46</sup> Yet not all heterometallic complexes display cooperativity, and some perform less well than their homometallic analogues. Therefore, in order to design catalysts that harness heterometallic cooperativity to enhance catalyst performance, it is important to understand the factors that enable heterometallic cooperativity. This generally involves understanding the role of the different metals in the reaction mechanisms. This can be challenging to determine, as introducing heterometals can vary other factors, such as the number of co-ligands or initiating units.<sup>46</sup> Therefore, deeper investigations into catalyst behaviour under polymerisation conditions, such as through NMR spectroscopic and/or XRD analysis, is crucial to provide enhanced understanding of structure-activity relationships.

This chapter aimed to prepare a bimetallic mono/trivalent alkali metal (AM)/Al complex from the heterotrimetallic  $[LNaAlEt \cdot AlEt_3]$  complex reported in Chapter 3, and to compare its performance against the bimetallic di/divalent ProPhenol complexes investigated in Chapter 2. The targeted mono/trivalent AM/Al  $[LNaAlEt]$  was envisioned to form *via* the abstraction of the  $\cdot AlEt_3$  unit by a range of Lewis bases, yet the datively bound  $AlEt_3$  was surprisingly persistent. Therefore, heterometallic  $[LNaAlEt \cdot AlEt_3]$  was tested in cyclic ester (co)polymerisations, to provide a comparison to  $[LNaZn_2Et_2]$ , with a specific focus on CL, LA and VL monomers.

As discussed in the previous chapter ([Section 3.3.3.1](#)),  $[LNaAlEt \cdot AlEt_3]$  presents different position and connectivity of the alkali metal, as well as different number of alkyl (potential initiating) groups than the Na/Zn<sub>2</sub> analogue,  $[LNaZn_2Et_2]$ . More importantly, the combination of alkali metal (*i.e.* Na or K) with Earth-abundant Al, in place of Zn, is anticipated to result in different catalytic behaviour between  $[LNaAlEt \cdot AlEt_3]$  and  $[LNaZn_2Et_2]$ . Zn-based organometallic catalysts have been extensively utilised in the ROP of cyclic esters, typically exhibiting high activity coupled with good polymerisation control.<sup>44,94</sup> On the other hand, although Al-based catalysts are generally known to deliver polymers with good selectivity and stereocontrol, most reported Al catalysts display relatively poor catalytic activity, often requiring high catalyst loadings and/or long reaction times.<sup>44,72</sup> The different valencies of Zn(II) and Al(III) makes direct comparisons challenging due to

the different number of initiating groups, co-ligands and/or catalyst structures. Nonetheless, Mu and co-workers presented bimetallic Zn and Al catalysts supported by anilido-aldimine ligands for the ROP of CL (Figure 4.1, left).<sup>180</sup> The polymerisation by both bimetallic catalysts were determined to follow the coordination-insertion mechanism, where the active catalyst species were formed through alcoholysis of the M—alkyl complexes with BnOH. The stoichiometry of BnOH was reported to influence the catalyst activity. The *bis*-Zn complex outperformed the activity of *bis*-Al (98% CL conv. in 1 min by *bis*-Zn vs 92% in 20 min by *bis*-Al) under the same conditions ([cat.]:[BnOH]:[M] = 1:2:100, 70 °C, toluene). The higher activity of *bis*-Zn was attributed to the lower bond dissociation energy of Zn—O (284 kJ mol<sup>-1</sup>) than that of Al—O (512 kJ mol<sup>-1</sup>), as well as the sterically more accessible Zn metal centres for monomer coordination. In another study of Zn and Al complexes based on an *N,N,O*-chelate ligand (Figure 4.1, right), both Zn and Al catalysts were found active for CL polymerisation in the presence of BnOH.<sup>181</sup> However, while the *bis*-Zn complex was active for LA polymerisation under mild condition (with 2 equiv. BnOH, [LA] = 0.5 M in toluene, 50 °C), the mono-Al analogue was completely inactive, with or without BnOH as a co-initiator. Interestingly, the Zn analogue also displayed high stereoselectivity in the ROP of LA ( $P_s \leq 0.73$ , in THF at 0 °C).

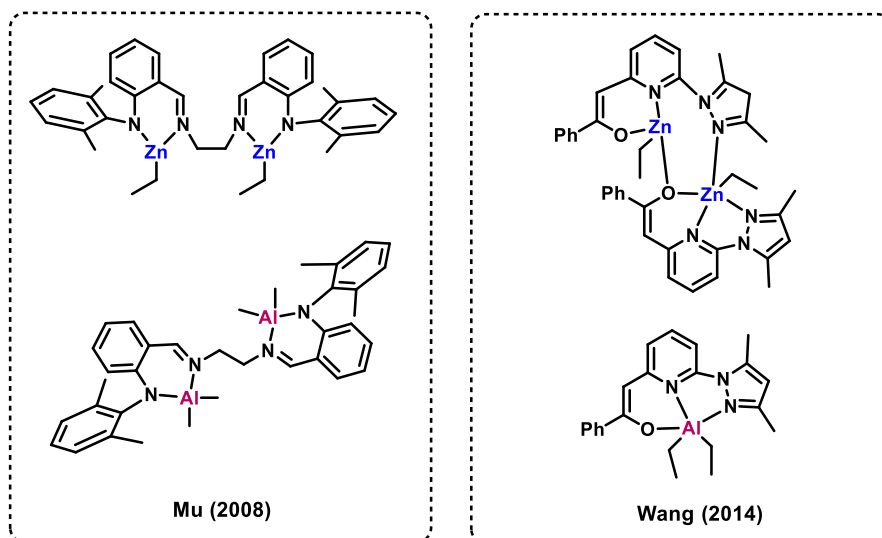


**Figure 4.1** Examples of Zn- and Al catalysts, each pair supported by the same ligand system, reported for the ROP of cyclic esters.<sup>180,181</sup>

Overall, this chapter provides insight into the addition of Lewis donors to [LNaAlEt·AlEt<sub>3</sub>], which offers an understanding of how [LNaAlEt·AlEt<sub>3</sub>] could operate as a catalyst in the ROP of cyclic esters. In general, Lewis bases are not only capable of abstracting a metal from a heterometallic structure, but can also act as a probe to understand the Lewis basicity of different metals, which is a key feature within cyclic ester ROP.<sup>182</sup>

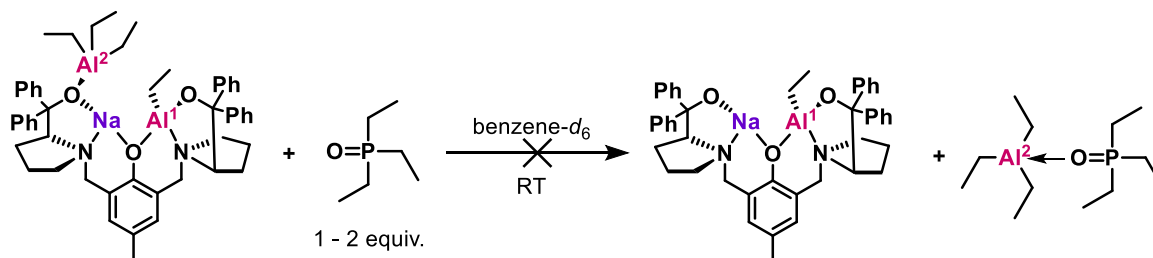
## 4.3 Results and Discussion

### 4.3.1 Reactivity Studies of [LNaAlEt·AlEt<sub>3</sub>] with Different Lewis Bases

The conversion of heterotrimetallic [LNaAlEt·AlEt<sub>3</sub>] into a heterobimetallic [LNaAlEt] analogue by chemical abstraction of the datively bound ·AlEt<sub>3</sub> unit was attempted through the use of Lewis donors. Specifically, [LNaAlEt·AlEt<sub>3</sub>] was reacted with triethylphosphine oxide (TEPO), 4-dimethylamido pyridine (DMAP) or pentamethyldiethylenetriamine (PMDETA), which could mimic the coordination of Lewis basic cyclic ester monomer and allow monitoring of complex changes by NMR analysis. The resultant products analysed by NMR spectroscopy in benzene-*d*<sub>6</sub> revealed that none of the Lewis bases investigated successfully removed the ·AlEt<sub>3</sub> unit, thus reflecting the stability of [LNaAlEt·AlEt<sub>3</sub>] (*vide infra*).

#### 4.3.1.1 Reaction of [LNaAlEt·AlEt<sub>3</sub>] with TEPO

Complex [LNaAlEt·AlEt<sub>3</sub>] was first reacted with triethylphosphine oxide (TEPO) to access [LNaAlEt] (Scheme 4.1). The strongly polarised O—P bond of Lewis basic TEPO was anticipated to interact with the Al centre of AlEt<sub>3</sub>, while also serving as a probe molecule in <sup>31</sup>P NMR analysis.<sup>183,184</sup>



**Scheme 4.1** Predicted AlEt<sub>3</sub> abstraction by TEPO from complex [LNaAlEt·AlEt<sub>3</sub>] to yield the targeted heterobimetallic complex [LNaAlEt].

The reaction of [LNaAlEt·AlEt<sub>3</sub>] with TEPO (1 – 2 equiv.) in benzene-*d*<sub>6</sub> altered the complex structure, as seen from a shift of the <sup>1</sup>H NMR resonances (Figure 4.2 (b, c), *cf.* unreacted [LNaAlEt·AlEt<sub>3</sub>], (Figure 4.2 (a)). The most prominent changes were observed around the aromatic region (6.95 – 8.04 ppm). The addition of 1 equivalent TEPO to [LNaAlEt·AlEt<sub>3</sub>] also resulted in signals broadening around the upfield region (0.61 – 1.26 ppm). The addition of 2 equivalents TEPO also gave rise to two broad resonances at the same chemical shift as unreacted TEPO, indicating that not all of the TEPO added is coordinated to a metal centre. Overall, both spectra indicate that at least one equivalent of TEPO is coordinated to the complex.

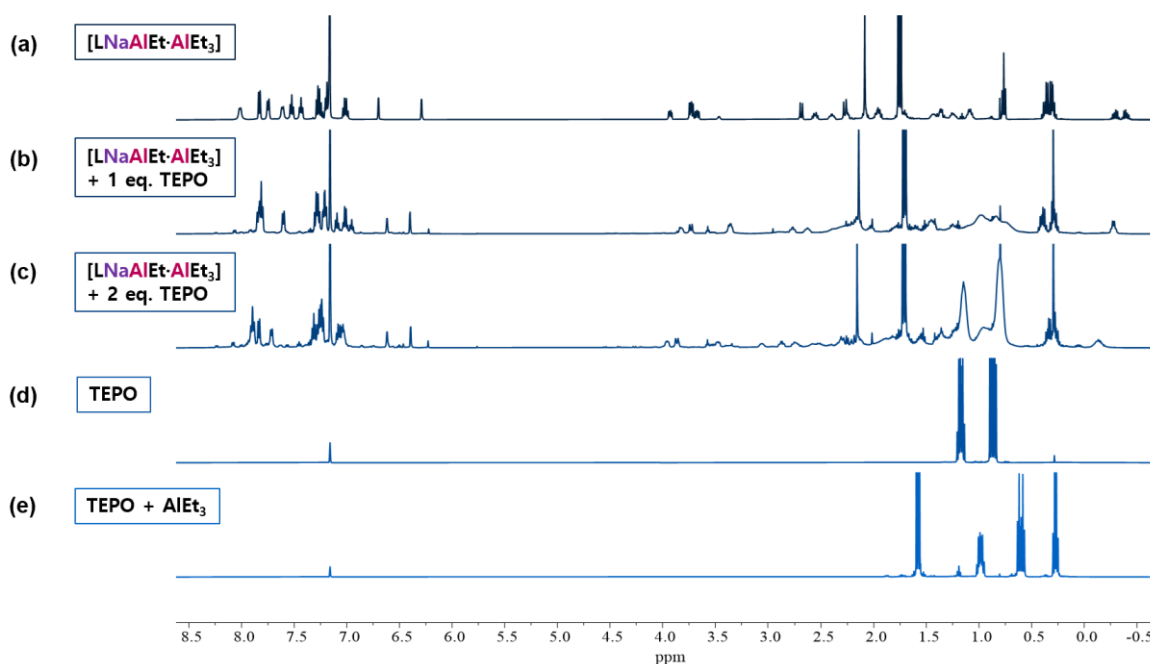


**Figure 4.2** Overlay of  $^1\text{H}$  NMR spectra (from top to bottom) of  $[\text{LNaAlEt}\cdot\text{AlEt}_3]$ , the reaction of  $[\text{LNaAlEt}\cdot\text{AlEt}_3]$  with TEPO (1 – 2 equiv.), unreacted TEPO and the reaction of  $\text{AlEt}_3$  with TEPO (1 equiv.), in benzene- $d_6$  at 298 K.

The presence of TEPO resonances closer to that of ‘free’ TEPO (Figure 4.2 (d)) and the absence of signals coinciding with the 1:1 reaction of  $\text{AlEt}_3$  with TEPO (Figure 4.2 (e)) indicate that TEPO does not abstract the  $\cdot\text{AlEt}_3$  unit from the ProPhenol complex. Instead, at least one TEPO molecule is proposed to coordinate to the ProPhenol complex, causing a rearrangement of the structure. Suggesting that the asymmetric nature of the trimetallic ProPhenol complex was retained in both cases, two doublets were observed at 6.39 and 6.62 ppm, which correspond to the inequivalent *meta*-phenolic protons of the ProPhenol backbone. These are notably shifted from the *meta*-phenolic protons of  $[\text{LNaAlEt}\cdot\text{AlEt}_3]$ , which are present at 6.28 and 6.69 ppm. The reaction of 1 equiv. TEPO with  $[\text{LNaAlEt}\cdot\text{AlEt}_3]$  was repeated in a larger scale (0.2 mmol) and the reaction product isolated as off-white powder. DOSY NMR analysis of the product revealed a single diffusion coefficient for the ProPhenol complex, where the ethyl resonances of the  $\cdot\text{AlEt}_3$  unit have the same diffusion coefficient as the rest of the ProPhenol complex (Figure 4.3).

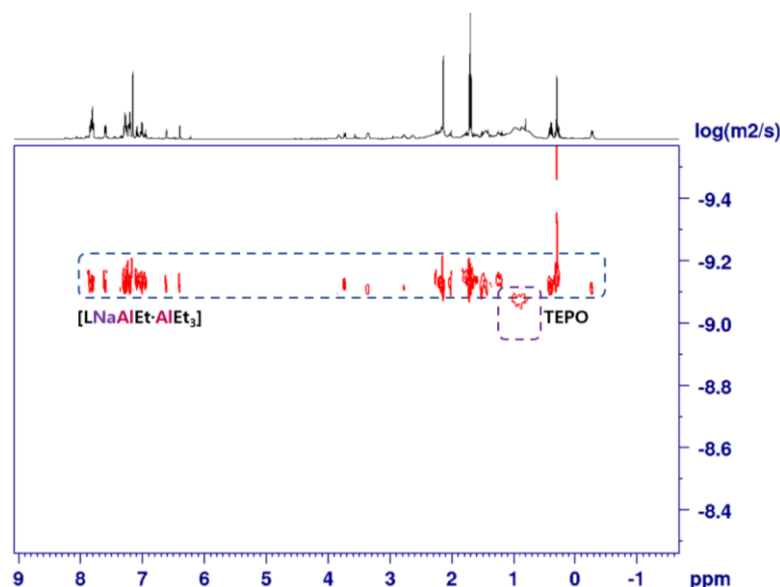


**Figure 4.3** DOSY NMR spectrum of isolated product of **[LNaAlEt·AlEt<sub>3</sub>]** reaction with TEPO (1 equiv.) showing the ethyl resonance of  $\cdot\text{AlEt}_3$  appearing in the same diffusion coefficient as the rest of ProPhenol complex as the major product, in benzene-*d*<sub>6</sub> at 298 K.

The resonance of TEPO appeared at a slightly lower diffusion coefficient than the rest of ProPhenol complex. However, the change in the chemical shifts of **[LNaAlEt·AlEt<sub>3</sub>]** indicate that TEPO is interacting with the complex. It is therefore plausible that TEPO coordinates to **[LNaAlEt·AlEt<sub>3</sub>]** through an equilibrium process, and the lower diffusion coefficient observed in the DOSY analysis is due to the averaging of these signals. To provide further insight into the coordination, future investigations could compare the diffusion coefficient of ‘free’ TEPO with the diffusion coefficient of the **[LNaAlEt·AlEt<sub>3</sub>]/TEPO** mixture. Overall, <sup>1</sup>H and DOSY NMR confirmed the stability of **[LNaAlEt·AlEt<sub>3</sub>]** even in the presence of TEPO as a hard Lewis base.

<sup>31</sup>P NMR spectroscopy revealed a single phosphorus signal at 73.18 ppm from the reaction of **[LNaAlEt·AlEt<sub>3</sub>]** with 1 equiv. TEPO (Figure 4.4 (a)), a significant shift from 45.91 ppm for ‘free’ TEPO (Figure 4.4 (e)). As the tetracoordinated Al<sup>1</sup> unit of **[LNaAlEt·AlEt<sub>3</sub>]** is sterically more hindered around the metal centre, it is likely that the signal at 73.18 ppm reflected TEPO coordination to the Al<sup>2</sup> metal centre of the  $\cdot\text{AlEt}_3$  moiety. Providing further support for this coordination mode, the signal at 73.18 ppm lies relatively close to the phosphorus signal observed from the combination of TEPO with neat AlEt<sub>3</sub> (65.80 ppm, Figure 4.4 (f)). This may suggest the preference for Lewis basic monomer to coordinate to the AlEt<sub>3</sub> centre of the **[LNaAlEt·AlEt<sub>3</sub>]** complex in the polymerisation. Intriguingly, the addition of 2 equiv. TEPO to **[LNaAlEt·AlEt<sub>3</sub>]** resulted in a significant upfield shift of the phosphorus signal from 73.18 ppm to a sharp resonance at 49.04 ppm accompanied by a discreet broad signal around 62.40 – 68.75 ppm. Notably, the resonance at 49.04 ppm lies close to

that of TEPO when it is combined with the mono-sodium ProPhenol precursor,  $[\text{LH}_2\text{Na}(\text{THF})_2]$ , which gave rise to a single resonance at 49.37 ppm. This suggests that subsequent monomers (coordination of  $\geq 2$  monomer units) coordinate to the Na metal centre. The shift of the other  $^{31}\text{P}$  resonance, from 73.18 ppm to 62.40 – 68.75 ppm, may arise from an increased lability of the first unit of monomer coordinating to the  $\text{AlEt}_3$  metal centre due to increased steric bulk and the introduction of another Lewis donor.

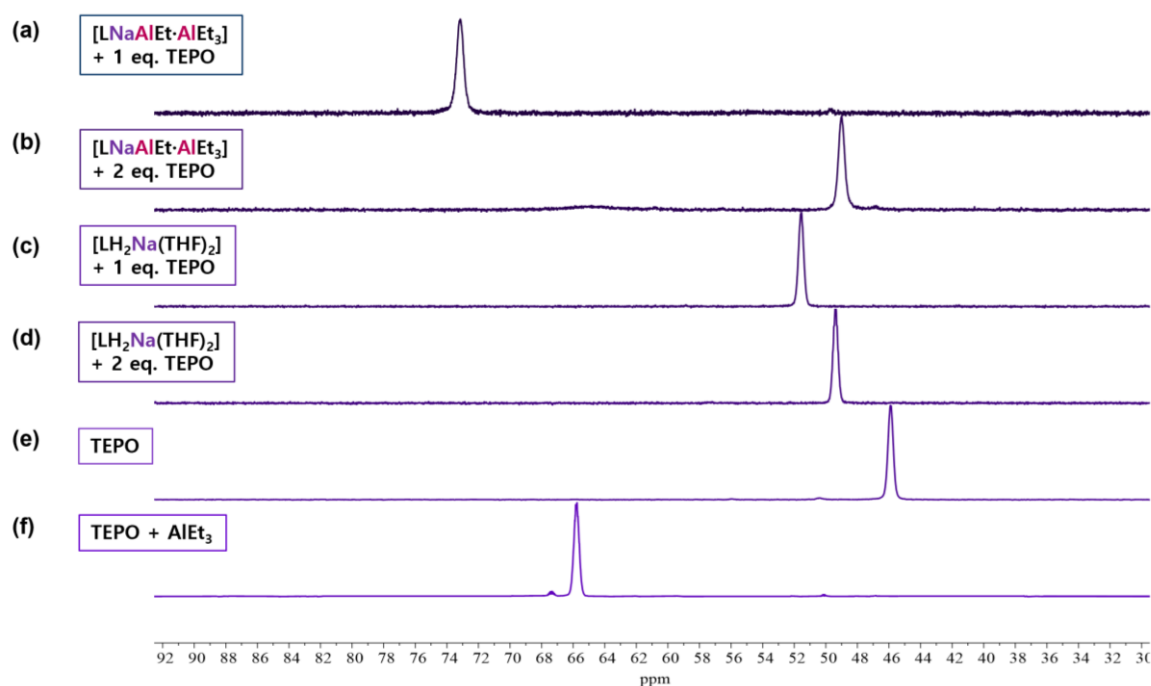


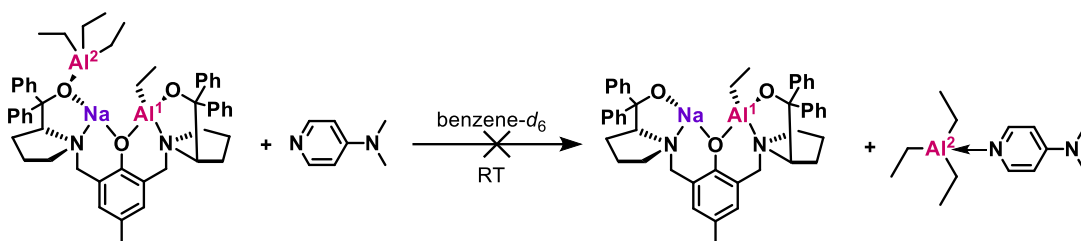
**Figure 4.4** Overlay of  $^{31}\text{P}$  NMR spectra (top to bottom) of  $[\text{LNaAlEt}\cdot\text{AlEt}_3]$ , reaction of  $[\text{LNaAlEt}\cdot\text{AlEt}_3]$  with TEPO (1 – 2 equiv.), reaction of  $[\text{LH}_2\text{Na}(\text{THF})_2]$  with TEPO (1 – 2 equiv.), unreacted TEPO and reaction of  $\text{AlEt}_3$  with TEPO (1 equiv.), in benzene- $d_6$  at 298 K.

Although the highly polarised P—O bond of TEPO was unable to abstract the datively bound  $\cdot\text{AlEt}_3$  of  $[\text{LNaAlEt}\cdot\text{AlEt}_3]$  to form a heterobimetallic  $[\text{LNaAlEt}]$  complex, TEPO coordination to the ProPhenol complex was observed by NMR spectroscopy analysis. The reactivity studies of  $[\text{LNaAlEt}\cdot\text{AlEt}_3]$  with TEPO provides an insight of possible monomer coordination on the complex.

#### 4.3.1.2 Reaction of $[\text{LNaAlEt}\cdot\text{AlEt}_3]$ with DMAP

Next,  $[\text{LNaAlEt}\cdot\text{AlEt}_3]$  was reacted with 4-dimethylamido pyridine (DMAP), to investigate the potential for DMAP to abstract the  $\cdot\text{AlEt}_3$  moiety (Scheme 4.2), as observed in other systems.<sup>185,186</sup> Similar to the reactivity with TEPO, the addition of DMAP (1 – 2 equiv.) to  $[\text{LNaAlEt}\cdot\text{AlEt}_3]$  in benzene- $d_6$  caused a change in the  $[\text{LNaAlEt}\cdot\text{AlEt}_3]$   $^1\text{H}$  NMR resonances, indicating an interaction between DMAP and the complex (Figures 4.5 (a-c)). Suggesting that the  $\text{AlEt}_3$  unit was not

abstracted from the ProPhenol scaffold, the  $^1\text{H}$  NMR spectra of  $[\text{LNaAlEt}\cdot\text{AlEt}_3]$  and DMAP (1 or 2 equiv.) did not include the expected signals expected from  $\text{DMAP}\cdot\text{AlEt}_3$ , as determined through comparison to this species (Figure 4.5 (e)).



**Scheme 4.2** Targeted formation of heterobimetallic  $[\text{LNaAlEt}]$  complex through  $\cdot\text{AlEt}_3$  abstraction with DMAP.

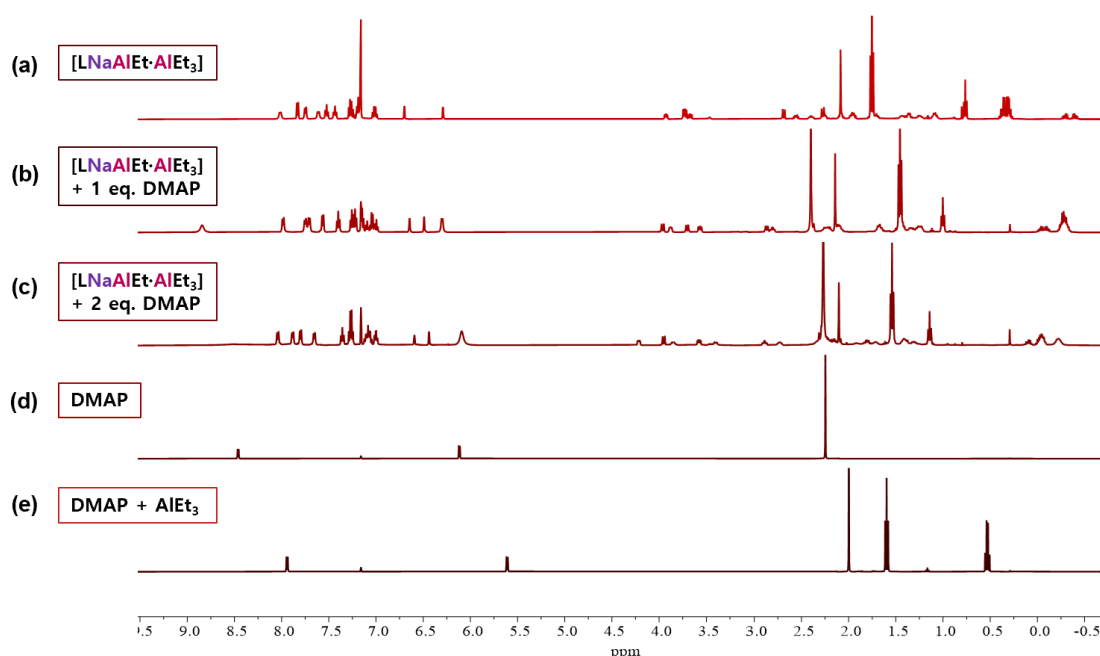


**Figure 4.5** Overlay of  $^1\text{H}$  NMR spectra (from top to bottom) of  $[\text{LNaAlEt}\cdot\text{AlEt}_3]$ , the reaction of  $[\text{LNaAlEt}\cdot\text{AlEt}_3]$  with DMAP (1 – 2 equiv.), unreacted DMAP and the reaction of  $\text{AlEt}_3$  with DMAP (1 equiv.), in benzene- $d_6$  at 298 K.

Notably, upon DMAP (1 equiv.) addition, the chemical shifts of the two types of ethyl group,  $\text{AlEt}$  and  $\text{AlEt}_3$ , appeared in inversed order relative to that of unreacted  $[\text{LNaAlEt}\cdot\text{AlEt}_3]$  (Figures 4.5 (a – b)). The signals of  $\text{Al}^1\text{Et}$  are shifted downfield ( $[\text{LNaAlEt}\cdot\text{AlEt}_3]$ : -0.24 – -0.45 and 0.78 – 0.75 ppm;  $[\text{LNaAlEt}\cdot\text{AlEt}_3]/\text{DMAP}$ : 0.01 – -0.14 ppm and 1.49 – 1.43 ppm), whereas the signals of  $\cdot\text{Al}^2\text{Et}_3$  are shifted upfield ( $[\text{LNaAlEt}\cdot\text{AlEt}_3]$ : 0.43 – 0.26 ppm and 1.78 – 1.73 ppm;  $[\text{LNaAlEt}\cdot\text{AlEt}_3]/\text{DMAP}$ : -0.21 – -0.35 ppm and 1.03 – 0.97 ppm). Additionally, the inversed shifts of the ethyl groups were

also observed from the methylene carbon atoms ( $\text{CH}_2\text{CH}_3$  and  $(\text{CH}_2\text{CH}_3)_3$ ) via  $^{13}\text{C}$  NMR spectroscopy, which was further confirmed by HSQC NMR analysis (Figure 4.7).

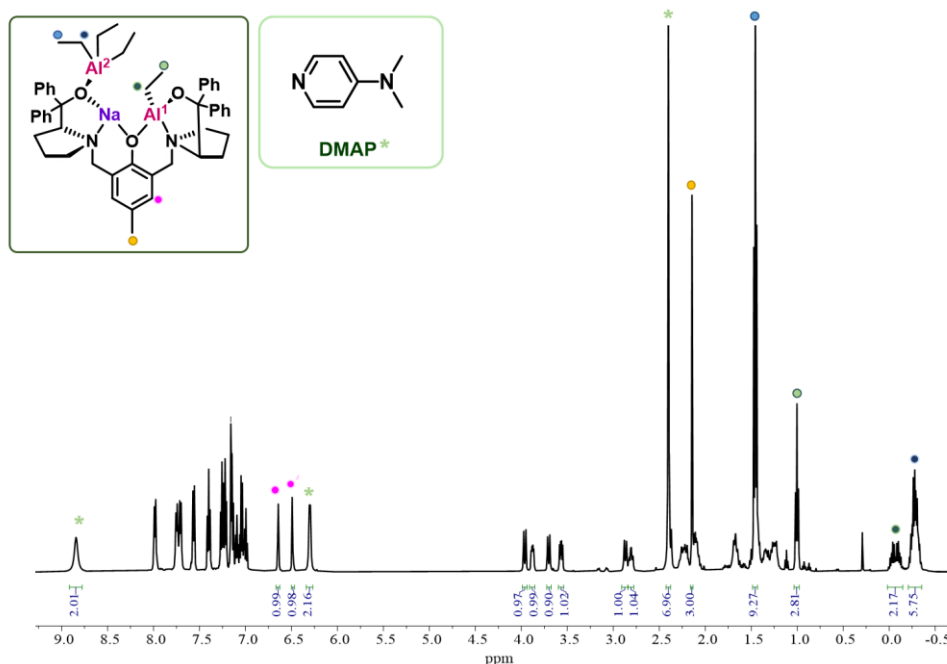


**Figure 4.6**  $^1\text{H}$  NMR spectrum of  $[\text{LNaAlEt}\cdot\text{AlEt}_3]$  reaction with DMAP (1 equiv.), in benzene- $d_6$  at 298 K. The  $\cdot\text{Al}^2-(\text{CH}_2\text{CH}_3)_3$  resonance of  $[\text{LNaAlEt}\cdot\text{AlEt}_3]$  is shifted upfield in the presence of DMAP, whereas the ethyl resonance of  $\text{Al}^1-\text{CH}_2\text{CH}_3$  is shifted downfield.

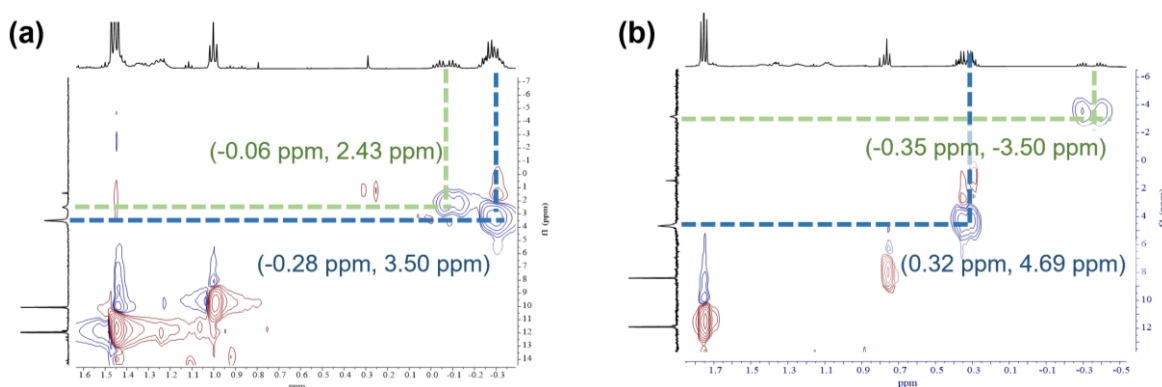


**Figure 4.7** HSQC NMR zoomed-in spectra of (a)  $[\text{LNaAlEt}\cdot\text{AlEt}_3]$  and (b)  $[\text{LNaAlEt}\cdot\text{AlEt}_3]$  combined with DMAP (1 equiv.), in benzene- $d_6$  at 298 K, showing an inversed shifts of the methylene carbon resonances of  $[\text{LNaAlEt}\cdot\text{AlEt}_3]$ .

The upfield shift of the  $\cdot\text{Al}^2\text{Et}_3$  resonances indicates that Lewis basic DMAP is coordinated to the  $\text{Al}^2$  metal centre, resulting in shielding of the ethyl groups. Other than that, DOSY NMR analysis of  $[\text{LNaAlEt}\cdot\text{AlEt}_3]$  combined with 1 equiv. of DMAP revealed that the ethyl signals of both  $\text{AlEt}$  and  $\cdot\text{AlEt}_3$  moieties have the same diffusion coefficient as each other, and as the DMAP resonances (Figure 4.8). Similar to TEPO, the reaction of  $[\text{LNaAlEt}\cdot\text{AlEt}_3]$  with DMAP resulted in the Lewis base coordination to  $\cdot\text{AlEt}_3$ , yet did not successfully abstract the  $\cdot\text{AlEt}_3$  unit from  $[\text{LNaAlEt}\cdot\text{AlEt}_3]$  complex,

under the reaction conditions tested (room temperature, in toluene or benzene solvent). Nonetheless, NMR spectroscopy analysis hints towards DMAP molecule (1 equiv.) coordination to  $\text{Al}^2$  metal centre, which is parallel to the observation of  $[\text{LNaAlEt}\cdot\text{AlEt}_3]$  reaction with TEPO (1 equiv.), despite the structural difference of the Lewis bases.<sup>187,188</sup> The reactivity studies of  $[\text{LNaAlEt}\cdot\text{AlEt}_3]$  with DMAP correlates with the reactivity studies with TEPO – both indicate that 1 equivalent of Lewis donor coordinates to the  $\cdot\text{AlEt}_3$  unit, which still remains as part of the heterotrimetallic complex.

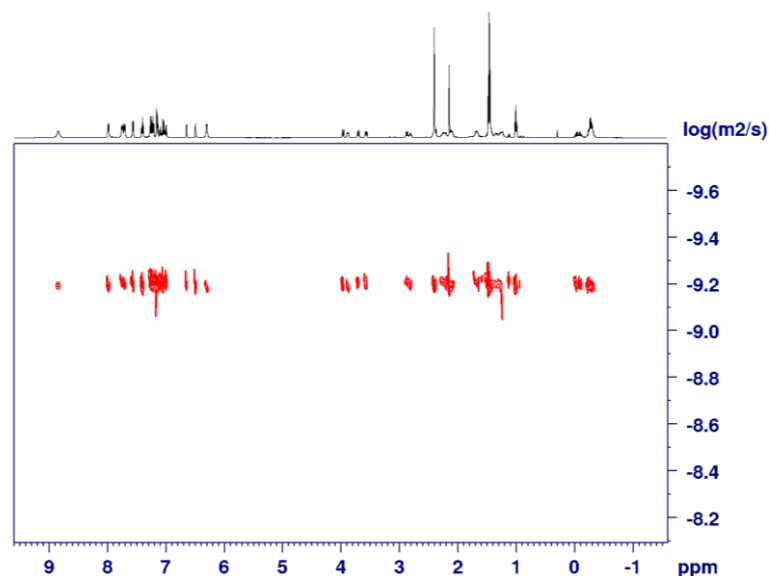


**Figure 4.8** DOSY NMR spectrum of isolated product of  $[\text{LNaAlEt}\cdot\text{AlEt}_3]$  reaction with DMAP (1 equiv.) showing the DMAP resonances appearing at the same diffusion coefficient as the rest of the ProPhenol complex, in benzene- $d_6$  at 298 K.

#### 4.3.1.3 Reaction of $[\text{LNaAlEt}\cdot\text{AlEt}_3]$ with PMDETA

Finally,  $[\text{LNaAlEt}\cdot\text{AlEt}_3]$  was reacted with the tridentate ligand,  $N,N',N'',N'''$ -penta-methyldiethylenetriamine (PMDETA). In a study of aluminium dialkyl halide complex,  $\text{AlR}_2\text{X}$  (where  $\text{R} = \text{Me}, ^i\text{Bu}, ^t\text{Bu}$ ;  $\text{X} = \text{Cl}, \text{Br}, \text{I}$ ) PMDETA chelation of Al occurred, which even enabled the formation of a cationic Al complex through the displacement of a halide.<sup>189</sup> Due to the tridentate nature of PMDETA, it was anticipated to chelate the  $\text{Al}^2$  metal centre, either abstracting  $\text{Al}^2\text{Et}_3$  or blocking monomer coordination to the  $\text{Al}^2$  centre. However, no coordination between PMDETA and  $[\text{LNaAlEt}\cdot\text{AlEt}_3]$  was observed in the solution state (benzene- $d_6$ ), as evidenced by the unchanged resonances of  $[\text{LNaAlEt}\cdot\text{AlEt}_3]$  in the  $^1\text{H}$  NMR spectrum (Figure 4.9).

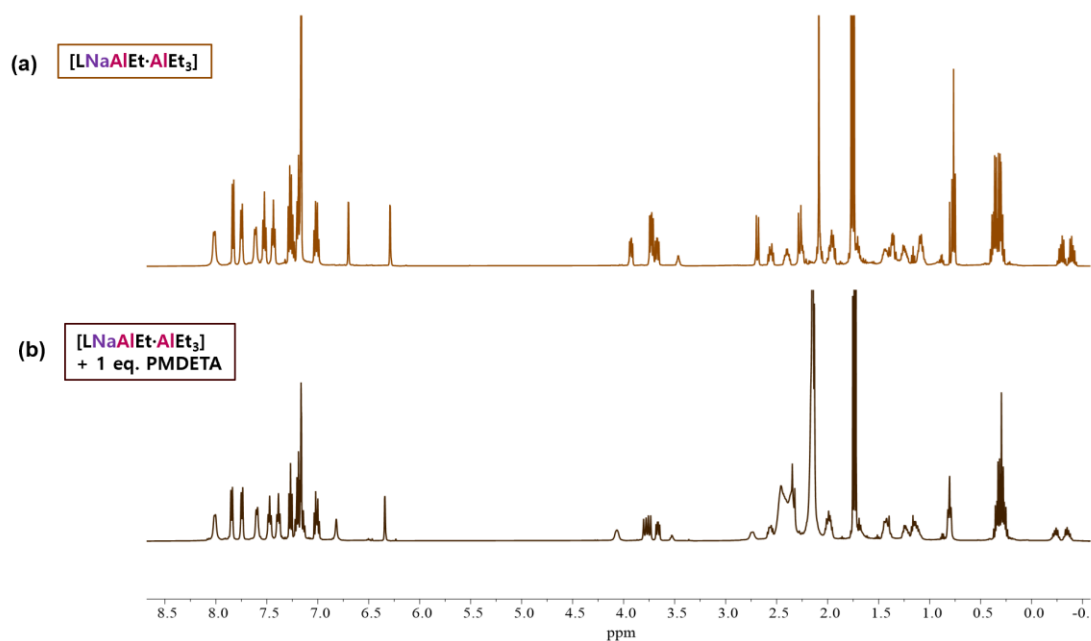


**Figure 4.9**  $^1\text{H}$  NMR spectra of (a)  $[\text{LNaAlEt}\cdot\text{AlEt}_3]$  and (b)  $[\text{LNaAlEt}\cdot\text{AlEt}_3]$  reaction with PMDETA (1 equiv.), in benzene- $d_6$  at 298 K.

In addition, DOSY NMR also confirmed that PMDETA did not coordinate to the  $[\text{LNaAlEt}\cdot\text{AlEt}_3]$  complex (Figure 4.10). This was evidenced by two distinguished diffusion coefficients with the PMDETA resonances appearing with a significantly lower molecular weight diffusion coefficient than that of  $[\text{LNaAlEt}\cdot\text{AlEt}_3]$ .

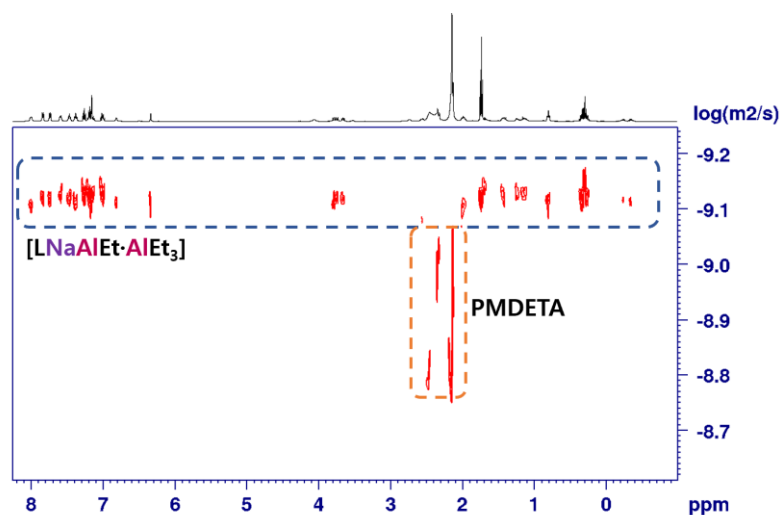


**Figure 4.10** DOSY NMR spectrum of  $[\text{LNaAlEt}\cdot\text{AlEt}_3]$  reaction with PMDETA (1 equiv.), in benzene- $d_6$  at 298 K, showing PMDETA resonances at a lower molecular weight diffusion coefficient than the  $[\text{LNaAlEt}\cdot\text{AlEt}_3]$  resonances.

Overall, these reactivity studies revealed the stability of **[LNaAlEt·AlEt<sub>3</sub>]** in the presence of several Lewis bases, under the reaction conditions tested. Despite the unsuccessful attempts to abstract the datively bound  $\cdot\text{AlEt}_3$  unit of the **[LNaAlEt·AlEt<sub>3</sub>]** complex with TEPO, DMAP and PMDETA, these reactivity studies provided some insights into the preferred and/or available coordination site(s) on the complex. These observations can be translated to the preferred site for Lewis basic monomer coordination in the polymerisation of cyclic esters, which may help to build a better understanding of the roles played by the different metals in the heterotrimetallic ProPhenol complex.

#### 4.3.2 Reactivity Insights: *In Situ* Alcoholysis of **[LNaAlEt·AlEt<sub>3</sub>]** Complex

As the targeted mono/trivalent **[LNaAlEt]** complex was not successfully generated through the abstraction of the  $\cdot\text{AlEt}_3$  unit, the heterotrimetallic **[LNaAlEt·AlEt<sub>3</sub>]** complex was investigated for the ROP of CL. Different from the previously reported AM/Zn<sub>2</sub> analogue, **[LNaZn<sub>2</sub>Et<sub>2</sub>]** which features two ethyl groups (refer to Chapter 3, [Section 3.3.3.1](#)), **[LNaAlEt·AlEt<sub>3</sub>]** bears four potential initiating units (*i.e.* four Al-ethyl groups). In cyclic ester ROP, Al-alkyl units are generally inefficient at initiating the ring-opening of monomers, and therefore require conversion into more reactive Al alkoxide initiating species through alcoholysis.<sup>44,73,190</sup> The *in situ* alcoholysis of complex **[LNaAlEt·AlEt<sub>3</sub>]** with 1, 2 and 4 equivalents of BnOH was therefore investigated by NMR analysis in toluene-*d*<sub>8</sub> at 70° C to mimic typical polymerisation conditions. In all cases, NMR spectroscopy revealed that traces of some of the Al-Et groups of **[LNaAlEt·AlEt<sub>3</sub>]** remained on the complex. This was indicated by distinctive Al-Et resonances in the 1.2 – 0.7 ppm and -0.3 – -0.5 ppm region of the <sup>1</sup>H NMR spectra, reflecting incomplete alcoholysis of the ethyl groups, even in the presence of excess BnOH (*i.e.* 4 equiv.) (refer to Figures 4.11 and 4.12 (b)).

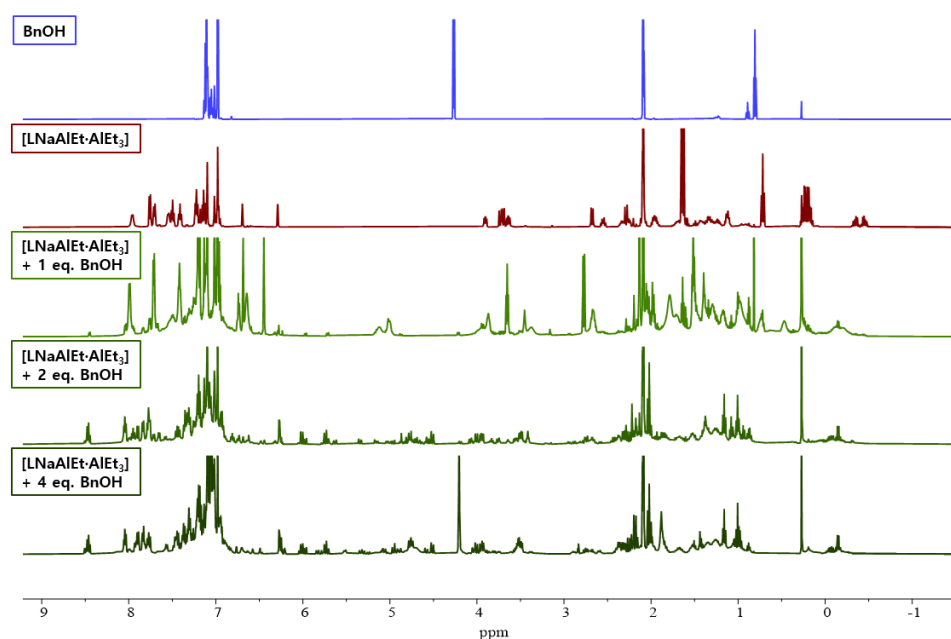


**Figure 4.11**  $^1\text{H}$  NMR spectra of BnOH,  $[\text{LNaAlEt}\cdot\text{AlEt}_3]$ , and reaction of  $[\text{LNaAlEt}\cdot\text{AlEt}_3]$  with different equivalents of BnOH in toluene- $d_8$  at 343 K.

While Lewis bases did not abstract the  $\cdot\text{AlEt}_3$ , the alcoholysis product (*i.e.*  $\text{Al}(\text{OBn})_3$ ) may be easier to abstract. However, DOSY NMR revealed the presence of the Al-Et signals in a very similar diffusion coefficient to the major complex (Figure 4.12), further confirming the incomplete alcoholysis of the ethyl groups to form the targeted benzoxide species,  $[\text{LNaAlOBn}\cdot\text{Al}(\text{OBn})_3]$ . Notably, in the reaction of  $[\text{LNaAlEt}\cdot\text{AlEt}_3]$  with 2 equiv. BnOH, the benzoxy resonances also appear in a similar diffusion coefficient as the major species (Figure 4.12(a)), indicating that the Al-OBn unit(s) are likely to still be part of the complex.

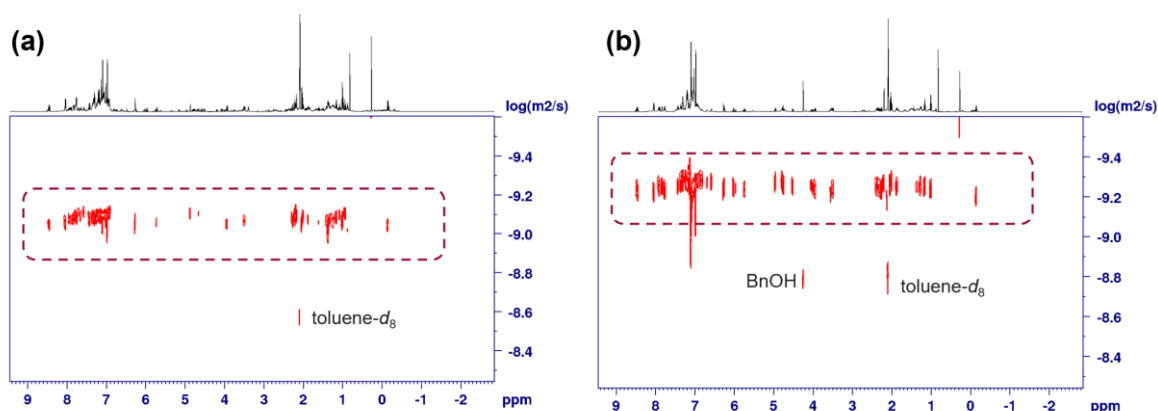


**Figure 4.12** DOSY NMR spectra of  $[\text{LNaAlEt}\cdot\text{AlEt}_3]$  complex reaction with a) 2 equiv. and b) 4 equiv. of BnOH in toluene- $d_8$  at 70 °C, showing multiple components with a similar diffusion coefficient and Al-Et signals present with a very similar diffusion coefficient to the major complex resonances.

Other than that, the shifts and change of splitting of the Al-Et signals in the  $[\text{LNaAlEt}\cdot\text{AlEt}_3]/\text{BnOH}$  reactions compared to the unreacted  $[\text{LNaAlEt}\cdot\text{AlEt}_3]$  complex, together with the appearance of new signals, may suggest complex rearrangement and/or scrambling of the  $[\text{LNaAlEt}\cdot\text{AlEt}_3]$  structure as well as the formation of new compounds. However, due to chemical shifts overlap and poor DOSY resolution to extract compounds with diffusion parameters where there are small molecular weight differences, it was not possible to identify the different components present from the reactions.

The alcoholysis of  $[\text{LNaAlEt}\cdot\text{AlEt}_3]$  with BnOH was also attempted in  $\text{THF-}d_8$  at room temperature. Similar to the previous observation in  $\text{toluene-}d_8$ , ethyl signals persisted around the upfield regions (1.1 – 0.7 ppm and -0.1 – -0.6 ppm) suggesting the presence of some Al-Et bonds, even in the presence of 4 equivalents of BnOH. However, differently from the reaction in  $\text{toluene-}d_8$ , the reaction of  $[\text{LNaAlEt}\cdot\text{AlEt}_3]$  with BnOH (1, 2 and 4 equiv.) resulted in more defined resonances of product mixtures (Figure 4.13). In  $\text{THF-}d_8$ , unreacted BnOH signals appear when 2 equiv. of BnOH were added, as evidenced by a doublet observed at 4.55 ppm.<sup>66</sup>

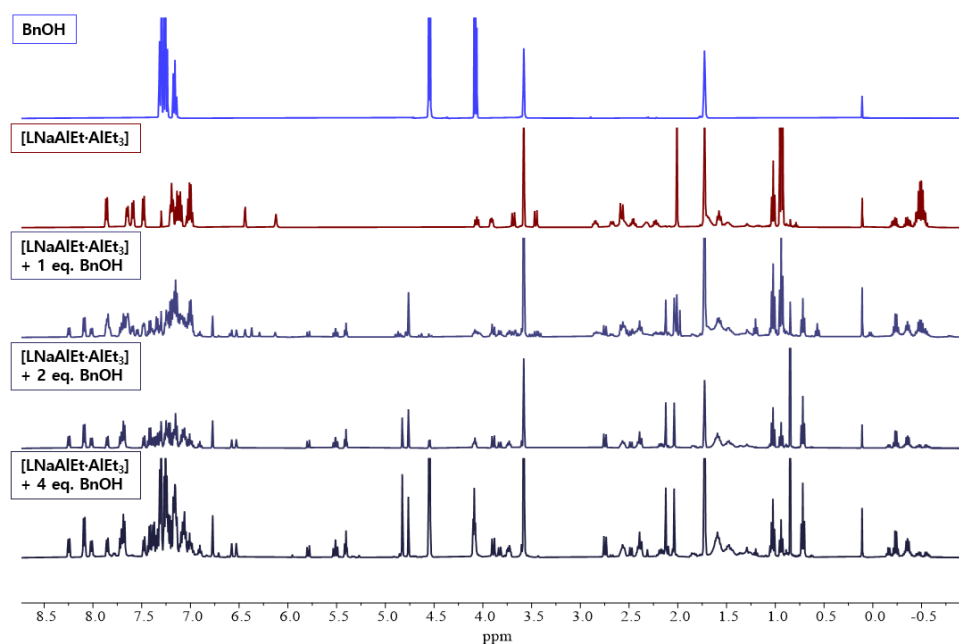


**Figure 4.13**  $^1\text{H}$  NMR spectra of BnOH,  $[\text{LNaAlEt}\cdot\text{AlEt}_3]$  and reaction of  $[\text{LNaAlEt}\cdot\text{AlEt}_3]$  with different equivalents of BnOH in  $\text{THF-}d_8$  at 300 K.

Interestingly, the addition of 2 and 4 equiv. of BnOH to  $[\text{LNaAlEt}\cdot\text{AlEt}_3]$  yielded similar product resonances in the  $^1\text{H}$  NMR spectra.  $^1\text{H}$  and DOSY NMR analyses indicated the complete loss of  $[\text{LNaAlEt}\cdot\text{AlEt}_3]$  following the formation of a multi-component mixture with at least three major species present (refer to Figures 4.13 and 4.14), as well as some unreacted BnOH.

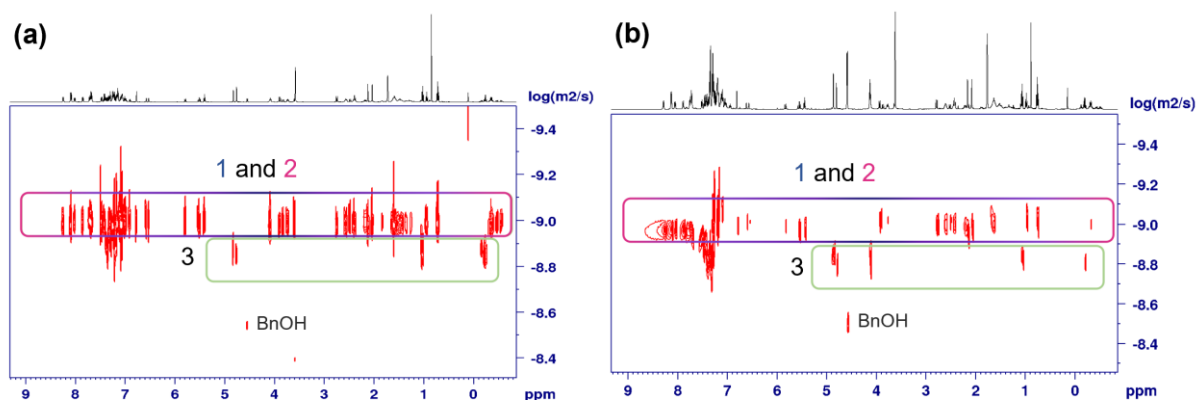


**Figure 4.14** DOSY NMR spectra of  $[\text{LNaAlEt}\cdot\text{AlEt}_3]$  complex reaction with a) 2 equiv. and b) 4 equiv. of BnOH in  $\text{THF-}d_8$  at room temperature, showing a mixture of at least three components.

NMR spectroscopy ( $^1\text{H}$ , COSY, HSQC and DOSY NMR) analysis suggested that compounds **1** and **2** are ProPhenol complexes, which are present in a 1:1 ratio. This is evidenced by two resonances at 2.13 and 2.03 ppm, which correlate to the distinctive methyl group on the phenolic ring of the ProPhenol ligand backbone (Figure 4.15). ProPhenol compound **1** is a symmetric compound, evidenced by a singlet *meta*-phenolic resonance observed at 6.77 ppm which corresponds to two H atoms, and couples to the methyl resonance at 2.13 ppm in the 2D COSY NMR. On the other hand, asymmetric ProPhenol compound **2** is postulated to be a bimetallic Na/Al ProPhenol complex. The coupling of two doublets in the *meta*-phenolic region, at 6.58 and 5.53 ppm, as seen by COSY NMR, suggests the presence of two inequivalent *meta*-phenolic protons, arising from the asymmetry of the complex. Further coupling of these resonances to the methyl phenolic signal at 2.03 ppm was observed in the COSY spectrum. Two proton resonances with a 2:3 ratio at -0.51 and 0.94 ppm, which may correspond to an Al-ethyl group in **2**, was observed by  $^1\text{H}$  NMR, and the coupling between these protons was confirmed by COSY NMR. Finally, the Al-ethyl resonances corresponding in integrations to OBn is in a 1:2 ratio. Compound **3** is thus tentatively hypothesised to be a dimeric mono-ethyl, *bis*-benzoxy aluminium species (Figure 4.15).

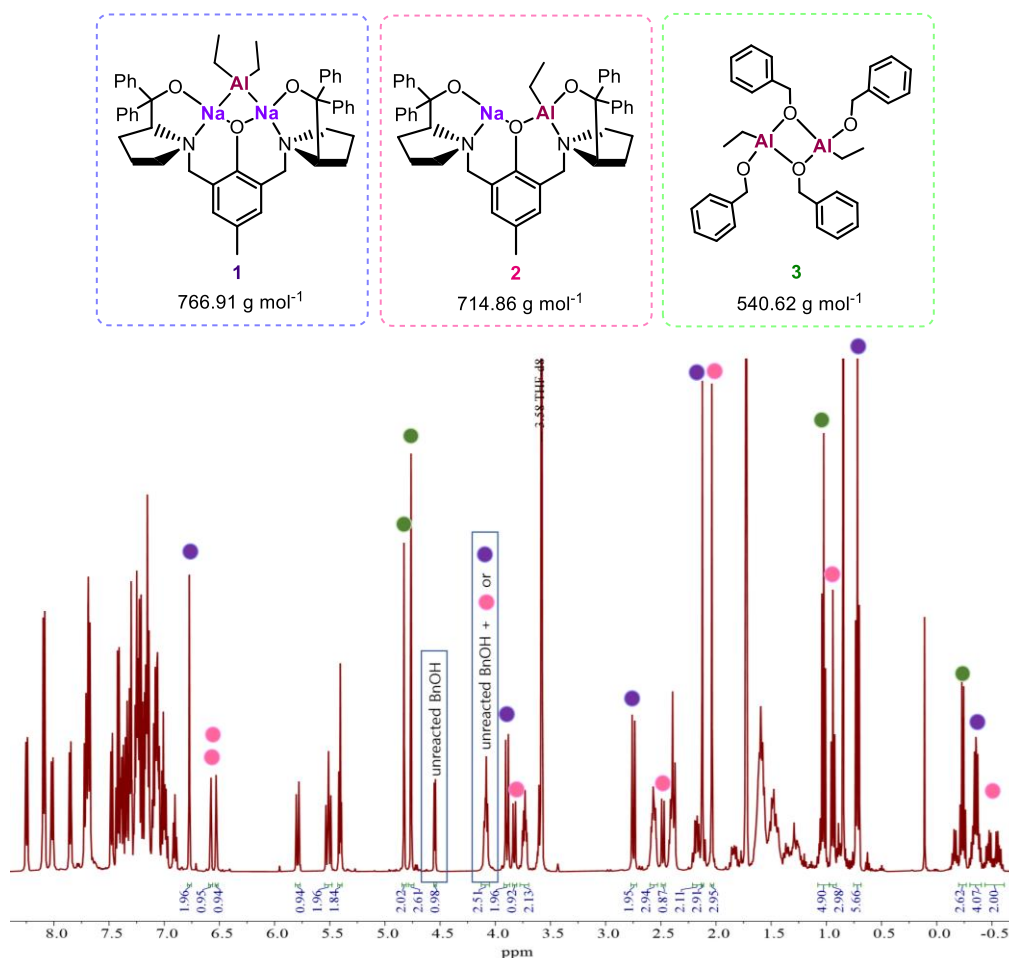


**Figure 4.15**  $^1\text{H}$  NMR spectrum of  $[\text{LNaAlEt}\cdot\text{AlEt}_3]$  with 2 equiv.  $\text{BnOH}$ , yielding at least three different compounds, in  $\text{THF-}d_8$  at 298 K. The hypothesised compounds are distinguished by different coloured labels (symmetric ProPhenol compound **1** – purple; asymmetric ProPhenol compound **2** – pink; *bis*-Al benzoxy compound **3** – green).

The diffusion coefficients obtained from DOSY NMR were compared against a calibration plot to obtain predicted molecular weights for each component (refer to Chapter 6, [Section 6.3.1.1](#), for additional details). The reaction of complex  $[\text{LNaAlEt}\cdot\text{AlEt}_3]$  with  $\text{BnOH}$  (2 equiv.) yielded multiple compounds, which all had lower molecular weights than the  $[\text{LNaAlEt}\cdot\text{AlEt}_3]$  precursor (Figure 4.16). ProPhenol compounds **1** and **2** have identical predicted molecular weights ( $690\text{ g mol}^{-1}$ ) whereas compound **3** had a lower diffusion coefficient, corresponding to a lower molecular weight species ( $480\text{ g mol}^{-1}$ ) with no ProPhenol signals present in the DOSY NMR spectrum. The predicted molecular weights of the postulated compounds were within the expected error for DOSY, which was determined to be  $\pm 8\%$  in the calibration plot. The predicted and calculated molecular weights were within  $\pm 8\%$  difference for complex  $[\text{LNaAlEt}\cdot\text{AlEt}_3]$  and compound **2** in  $\text{toluene-}d_8$ , with slightly higher differences for compounds **1** and **3**, where the calculated molecular weights were 10% and 11% lower than those of the predicted values, respectively.

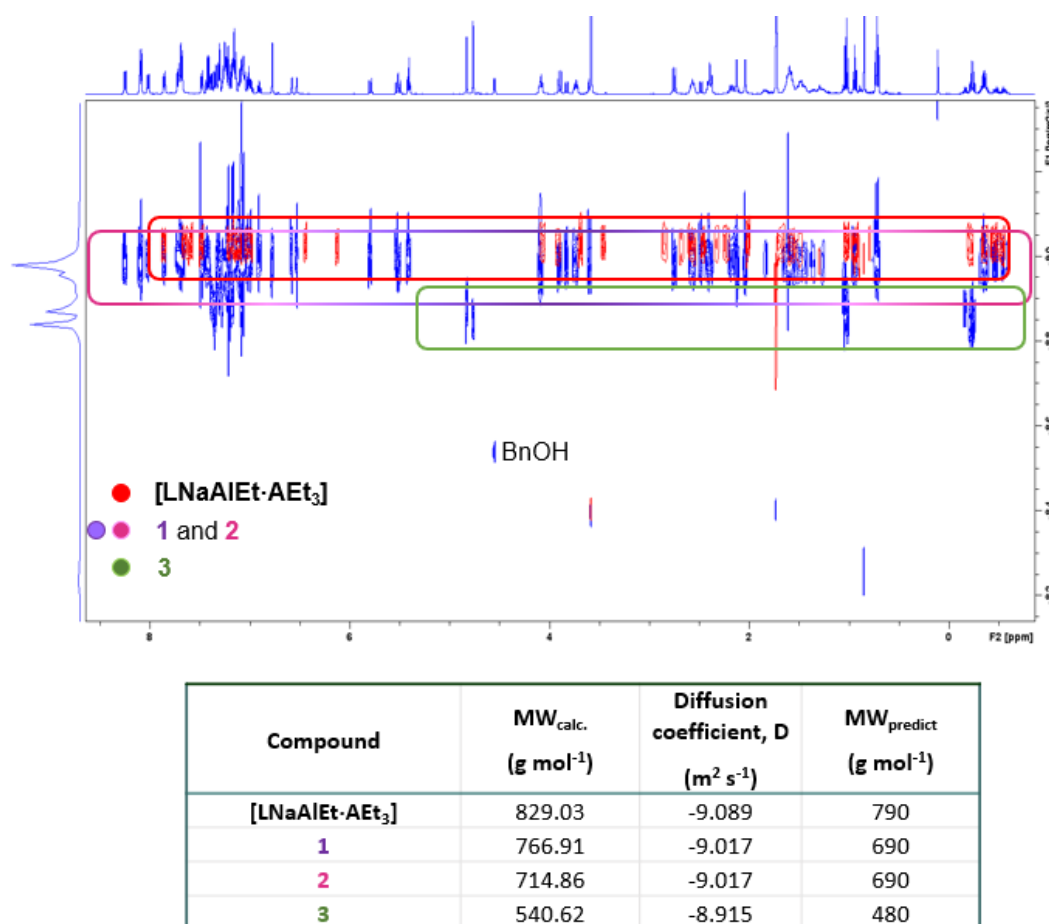


**Figure 4.16** Overlay of DOSY NMR spectra of [LNaAlEt·AET<sub>3</sub>] (red diffusion coefficient) with the product mixture from the reaction of [LNaAlEt·AET<sub>3</sub>] with 2 equiv. BnOH (blue diffusion coefficient), with predicted molecular weights of the three components obtained from DOSY NMR calibration plot of standards in THF-*d*<sub>8</sub> at 298 K (refer to [Section 6.3.1.1](#) for details).

Overall, the NMR-scale addition of BnOH (1, 2 ad 4 equiv.) to [LNaAlEt·AET<sub>3</sub>] under the reaction conditions tested did not yield the targeted benzoxide species, [LNaAlOBn·Al(OBn)<sub>3</sub>], in either toluene-*d*<sub>8</sub> or THF-*d*<sub>8</sub> solvents. Partial alcoholysis or complex rearrangements were evidenced by the Al-Et signals observed in the upfield region of the <sup>1</sup>H NMR spectra (refer to Figures 4.15 and 4.16), and multi-components product mixtures were observed in both cases. Nevertheless, at least three metallic complexes were tentatively assigned from the reaction in THF-*d*<sub>8</sub>. The presence of multiple species could make it challenging to identify the active species involved in the cyclic ester ROP mechanism, as monomer activation could occur at multiple metal centres. However, the ring-opening of monomer could preferentially occur from the postulated compound **3** due to the presence of labile O—Bn bonds, which can facilitate nucleophilic attack on the monomer compared to Al-alkyl units.<sup>190</sup> Importantly, other catalysts have previously been reported where a mixture of species in solution deliver exceptionally high activity in ROP, including those based on the Trost ligand, and thus these catalyst systems were tested in the ROP of various cyclic esters.<sup>115</sup>

### 4.3.3 Reactivity of [LNaAlEt·AlEt<sub>3</sub>] in the Polymerisation of CL, LA and VL

THF is a Lewis donor and thus has the potential to abstract metals from the [LNaAlEt·AlEt<sub>3</sub>] complex, especially when used in excess as a solvent compared to the 1 or 2 equivalents of TEPO, DMAP or PMDETA added in [Section 4.3.1](#). While a mixture of products was observed in both the NMR spectra of [LNaAlEt·AlEt<sub>3</sub>] combined with BnOH in toluene-*d*<sub>8</sub> and THF-*d*<sub>8</sub>, the reaction in toluene-*d*<sub>8</sub> did not appear to have a bimetallic Al (*i.e.* (EtAlOBn<sub>2</sub>)<sub>2</sub> dimer, compound **3**) species. Therefore, toluene was chosen as the polymerisation solvent. Two equivalents of BnOH were added as a co-initiator to allow a more straightforward comparison with the reported [LNaZn<sub>2</sub>Et<sub>2</sub>] catalyst.<sup>112</sup> Initial studies revealed that [LNaAlEt·AlEt<sub>3</sub>] is active in the ROP of CL (2 equiv. BnOH, 70 °C, 1.0 M in toluene), yielding almost quantitative PCL with moderate dispersity (98% conversion in 24 h, *Đ* = 1.46), albeit with relatively low activity. Although the CL polymerisation with [LNaAlEt·AlEt<sub>3</sub>] was carried out in different solvents (*i.e.* toluene vs THF), it was apparent that the activity of [LNaAlEt·AlEt<sub>3</sub>] is significantly inferior compared to the Na/Zn<sub>2</sub> analogue [LNaZn<sub>2</sub>Et<sub>2</sub>] even when performed at an elevated temperature and prolonged reaction time (see Table 4.1).

**Table 4.1** ROP of CL using complexes [LNaAlEt·AlEt<sub>3</sub>] and [LNaZn<sub>2</sub>Et<sub>2</sub>] with 2 equiv. BnOH.

|                  | Cat.                                  | Time, <i>t</i> | Conv. (%) <sup>a</sup> | <i>M</i> <sub>n</sub> (obs, corr)<br>(kDa) <sup>b</sup> | <i>M</i> <sub>n</sub> (calc)<br>(kDa) <sup>c</sup> | <i>Đ</i> <sup>b</sup> |
|------------------|---------------------------------------|----------------|------------------------|---------------------------------------------------------|----------------------------------------------------|-----------------------|
| 1                | [LNaAlEt·AlEt <sub>3</sub> ]          | 4 min          | 0                      | n/a                                                     | n/a                                                | n/a                   |
| 2                | [LNaAlEt·AlEt <sub>3</sub> ]          | 24 h           | 98                     | 6.6                                                     | 5.6                                                | 1.46                  |
| 3 <sup>112</sup> | [LNaZn <sub>2</sub> Et <sub>2</sub> ] | 5 s            | 53                     | 5.2                                                     | 3.0                                                | 1.52                  |
| 4 <sup>112</sup> | [LNaZn <sub>2</sub> Et <sub>2</sub> ] | 20 s           | 83                     | 4.6                                                     | 4.7                                                | 1.62                  |

100:1:2 monomer:catalyst:BnOH, [LNaAlEt·AlEt<sub>3</sub>]: 1 M in toluene, 70 °C; [LNaZn<sub>2</sub>Et<sub>2</sub>]: 1 M in THF, RT. <sup>a</sup>Conversion calculated using <sup>1</sup>H NMR spectroscopy. <sup>b</sup>*M*<sub>n</sub> (obs) and *Đ* determined by SEC using polystyrene standards in THF, values corrected by correction factor for PCL (0.56).<sup>191</sup> <sup>c</sup>*M*<sub>n</sub> (calc) = *M*<sub>CL</sub> × ([M]/[I]) × CL conversion assuming 2 chains per catalyst.

The poor activity of [LNaAlEt·AlEt<sub>3</sub>] raised a few questions: ‘What is the role of each metal in the complex? Does the lack of anticipated multimetallic cooperativity come from just the ‘uncooperative’ metal combinations, or does the structural motif play a part? Does [LNaAlEt·AlEt<sub>3</sub>] follow a different polymerisation mechanism than the [LNaZn<sub>2</sub>Et<sub>2</sub>] catalyst?’ Further investigation of the activity and control of [LNaAlEt·AlEt<sub>3</sub>] for the ROP of cyclic ester (CL, LA and VL) was carried out.

As heterotrimetallic [LNaAlEt·AlEt<sub>3</sub>] showed activity for CL polymerisation in the preliminary polymerisation studies, more detailed studies were performed for the ROP of CL, LA and VL (Table 4.2). The polymerisation was run using BnOH (2 equiv.) as a co-initiator, at 70 °C with 1.0 M monomer concentration in toluene and a loading ratio of [cat.]:[BnOH]:[M] = 1:2:100.

**Table 4.2** Kinetic studies of CL, LA and VL ROP of with complex **[LNaAlEt·AlEt<sub>3</sub>]**.

|    | <b>M<sup>a</sup></b> | <b>Time<br/>(h)</b> | <b>Conv.<br/>(%)<sup>b</sup></b> | <b>M<sub>n(calc)</sub><br/>(1 initiator)<sup>c</sup></b> | <b>M<sub>n(calc)</sub><br/>(2 initiators)<sup>c</sup></b> | <b>M<sub>n(obs, corr)</sub><sup>d</sup></b> | <b>Đ<sup>d</sup></b> |
|----|----------------------|---------------------|----------------------------------|----------------------------------------------------------|-----------------------------------------------------------|---------------------------------------------|----------------------|
| 1  | CL                   | 1                   | 16                               | 1.8                                                      | 0.9                                                       | 1.5                                         | 1.43                 |
| 2  |                      | 2                   | 20                               | 2.2                                                      | 1.1                                                       | 1.9                                         | 2.12                 |
| 3  |                      | 3                   | 24                               | 2.8                                                      | 1.4                                                       | 2.1                                         | 1.45                 |
| 4  |                      | 4                   | 29                               | 3.3                                                      | 1.7                                                       | 2.2                                         | 1.68                 |
| 5  |                      | 5                   | 33                               | 3.8                                                      | 1.9                                                       | 2.6                                         | 1.48                 |
| 6  |                      | 6                   | 37                               | 4.2                                                      | 2.1                                                       | 2.8                                         | 1.40                 |
| 7  |                      | 7                   | 41                               | 4.7                                                      | 2.3                                                       | 3.2                                         | 1.39                 |
| 8  |                      | 8                   | 45                               | 5.1                                                      | 2.6                                                       | 3.4                                         | 1.46                 |
| 9  | LA                   | 1                   | 8                                | 1.1                                                      | 0.6                                                       | 0.8                                         | 1.12                 |
| 10 |                      | 2                   | 13                               | 1.8                                                      | 0.9                                                       | 1.1                                         | 1.16                 |
| 11 |                      | 3                   | 16                               | 2.3                                                      | 1.1                                                       | 1.2                                         | 1.19                 |
| 12 |                      | 4                   | 20                               | 2.9                                                      | 1.4                                                       | 1.5                                         | 1.22                 |
| 13 |                      | 5                   | 27                               | 3.9                                                      | 1.9                                                       | 1.8                                         | 1.22                 |
| 14 |                      | 6                   | 29                               | 4.2                                                      | 2.1                                                       | 1.8                                         | 1.21                 |
| 15 |                      | 7                   | 30                               | 4.4                                                      | 2.2                                                       | 2.4                                         | 1.17                 |
| 16 | VL                   | 1                   | 14                               | 1.4                                                      | 0.7                                                       | 1.0                                         | 1.20                 |
| 17 |                      | 2                   | 24                               | 2.4                                                      | 1.2                                                       | 1.5                                         | 1.39                 |
| 18 |                      | 3                   | 38                               | 3.8                                                      | 1.9                                                       | 2.5                                         | 1.21                 |
| 19 |                      | 4                   | 51                               | 5.1                                                      | 2.5                                                       | 3.0                                         | 1.27                 |
| 20 |                      | 5                   | 61                               | 6.1                                                      | 3.0                                                       | 3.6                                         | 1.34                 |
| 21 |                      | 6                   | 68                               | 6.8                                                      | 3.4                                                       | 5.0                                         | 1.32                 |
| 22 |                      | 7                   | 74                               | 7.4                                                      | 3.7                                                       | 5.5                                         | 1.29                 |
| 23 |                      | 8                   | 78                               | 7.8                                                      | 3.9                                                       | 5.8                                         | 1.27                 |

Polymerisation conditions: [cat.]:[BnOH]:[M] = 1:2:100, [M] = 1.0 M, in toluene at 70 °C. [a] M = monomer; [b] Determined from polymer (PCL, PLA or PVL) signal integrals with respect to monomer (CL, LA or VL) signal integrals *via* <sup>1</sup>H NMR spectroscopy (refer to [Section 6.4](#) for details); [c] Calculated from monomer conversions,  $M_{n,calc} = M_M \times ([M]/[I]) \times M_{conv.}$ , where I = number of initiator; [d]  $M_{n,obs}$  and  $\bar{D}$  values determined by SEC analysis using polystyrene standards in THF.  $M_{n,obs}$  values corrected by correction factor (0.56 for PCL, 0.58 for PLA and 0.57 for PVL).<sup>191</sup>

In the presence of BnOH (2 equiv.), **[LNaAlEt·AlEt<sub>3</sub>]** is active for CL, LA and VL polymerisation, generating PCL, PLA and PVL with generally good control, with monomodal SEC traces observed in all cases. The lowest polymer dispersity was observed for PLA ( $\bar{D}$  = 1.12 – 1.22), followed by PVL ( $\bar{D}$  = 1.20 – 1.39) and PCL ( $\bar{D}$  was generally in the range of 1.39 – 1.68 apart from Entry 2,  $\bar{D}$  = 2.12; this higher value may arise from poorer initiation efficiency thus lower control in the early stages of the polymerisation). In the polymerisation of CL, the experimental molecular weight ( $M_{n,obs(corr)}$ ) values of the polymer lie in between the theoretical molecular weights ( $M_{n,calc}$ ) values for one and two

chains initiated per catalyst. However, as the polymerisations evolved to higher monomer conversion, the  $M_{n,obs}$  values are in better agreement with the  $M_{n,calc}$  values for two chains per catalyst until the late stage of polymerisation (see Figure 4.17). Furthermore, while the  $M_{n,obs}$  of PLA is in a good agreement with two chains per catalyst throughout (Figure 4.18), the  $M_{n,obs}$  of PVL fits better with the  $M_{n,calc}$  for two chains per catalyst until the middle stage of polymerisation before deviating towards one chain at the late stage of polymerisation (Figure 4.19).

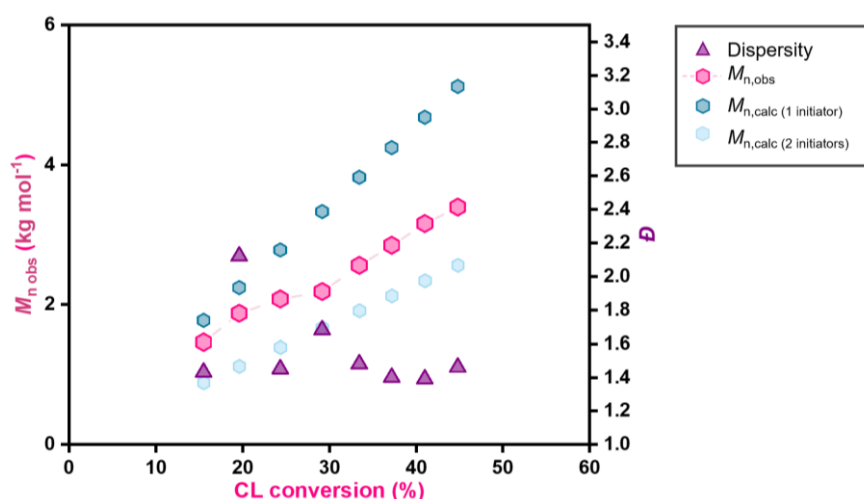


**Figure 4.17** Comparison between  $M_{n(obs)}$  and  $M_{n(calc)}$  for one and two initiators and the dispersity values at increasing conversions of CL with  $[LNaAlEt \cdot AlEt_3]/2$  equiv. BnOH.

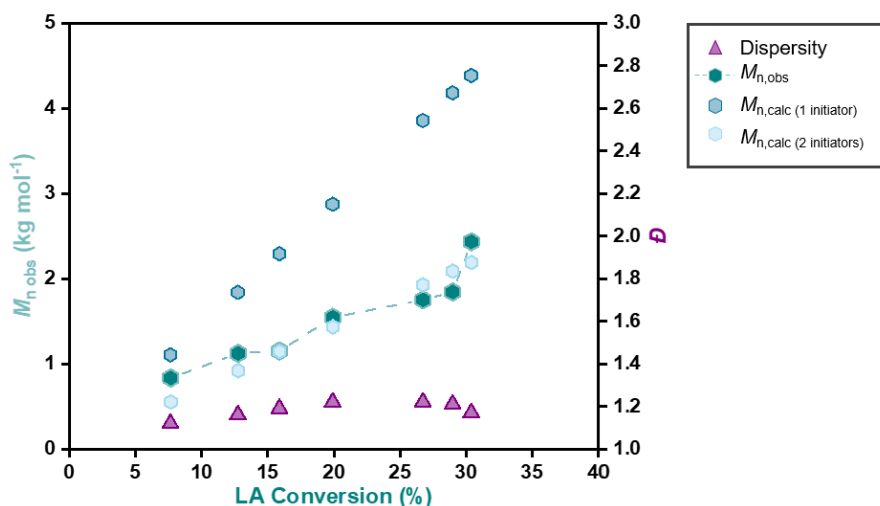


**Figure 4.18** Comparison between  $M_{n(obs)}$  and  $M_{n(calc)}$  for one and two initiators and the dispersity values at increasing conversions of LA with  $[LNaAlEt \cdot AlEt_3]/2$  equiv. BnOH.

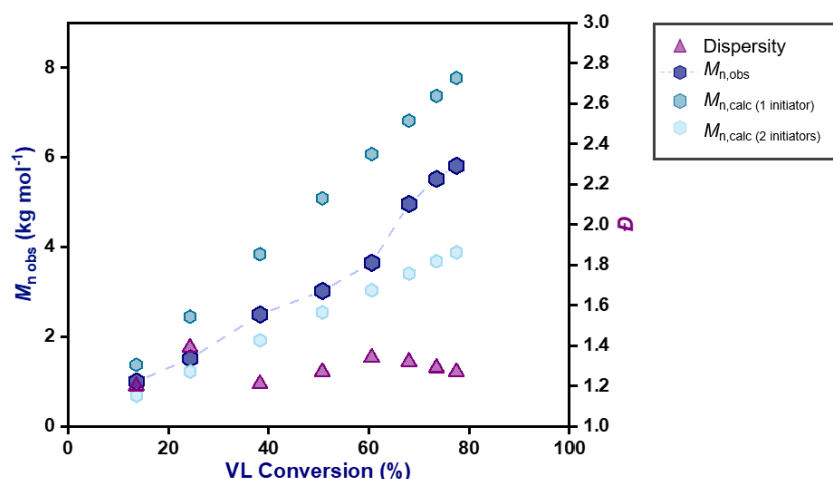


**Figure 4.19** Comparison between  $M_{n(obs)}$  and  $M_{n(calc)}$  for one and two initiators and the dispersity values at increasing conversions of VL with  $[LiNaAlEt_2 \cdot AlEt_3]/2$  equiv. BnOH.

Analysis of PCL and PVL by Matrix-Assisted Laser Desorption Ionization-Time of Flight (MALDI-ToF) analysis showed the presence of benzoxide (BnO) end-capped polymers (Figures 4.20 – 4.21). It should be mentioned that, although  $Li^+$  was used as the cationising agent, possible traces of  $Na^+$  in the mass spectroscopy instrument was also accounted for in the MALDI-ToF analysis (*e.g.* PVL and PLA analyses). The  $\alpha$ -OBn/ $\omega$ -H end groups observed in the PCL and PVL polymer structures suggest the formation of an active benzoxide species, perhaps partially, from the reaction of BnOH and  $[LiNaAlEt_2 \cdot AlEt_3]$  which could initiate the polymerisation of CL and VL. Nonetheless, based on the MALDI-ToF spectrum analysis, the formation of cyclic polymer in CL ROP is also probable (Figure 4.20). The possible overlap of  $\alpha$ -OBn/ $\omega$ -OH capped PCL and cyclic PCL peaks may explain the discrepancies seen between the theoretical and observed polymer molecular weight values and broad polymer dispersities. However, it is important to note that MALDI-ToF is not quantitative and the analysis must be coupled with other analytical method(s).  $^1H$  NMR spectroscopic studies of PCL, PVL as well PLA purified by acidified MeOH confirmed the presence of OBn-capped polymer, evidenced by a singlet resonance observed at 5.21 ppm which corresponds to the  $-CH_2-$  methylene protons of the benzoxy group. It is worth mentioning that in the cyclic ester ROP set-up, the monomers were combined with  $[LiNaAlEt_2 \cdot AlEt_3]$  and stirred for 1 h prior to the addition of BnOH (2 equiv.) as a co-initiator (refer to [Section 4.6.2](#) for details). This order of addition could drive polymerisation through both the coordination-insertion and activated monomer mechanism pathways, yielding OBn-capped polymers either way (refer to Scheme 1.2, Chapter 1). The ROP may proceed *via* coordination-insertion mechanism in the case where  $[LiNaAlEt_2 \cdot AlEt_3]$  undergoes alcoholysis at the first instance upon BnOH addition, to generate a reactive metal-alkoxide bond prior to monomer ring-opening. Conversely, if rapid initiation occurs from the exogeneous BnOH to ring-open catalyst-coordinated monomer(s), the activated monomer mechanism could occur instead. Additionally,  $[LiNaAlEt_2 \cdot AlEt_3]$  alcoholysis and nucleophilic attack of the carbonyl unit (*i.e.*

initiation of ROP) may both take place upon BnOH addition to the catalyst/monomer mixture, thus leading to simultaneous occurrence of both mechanisms.

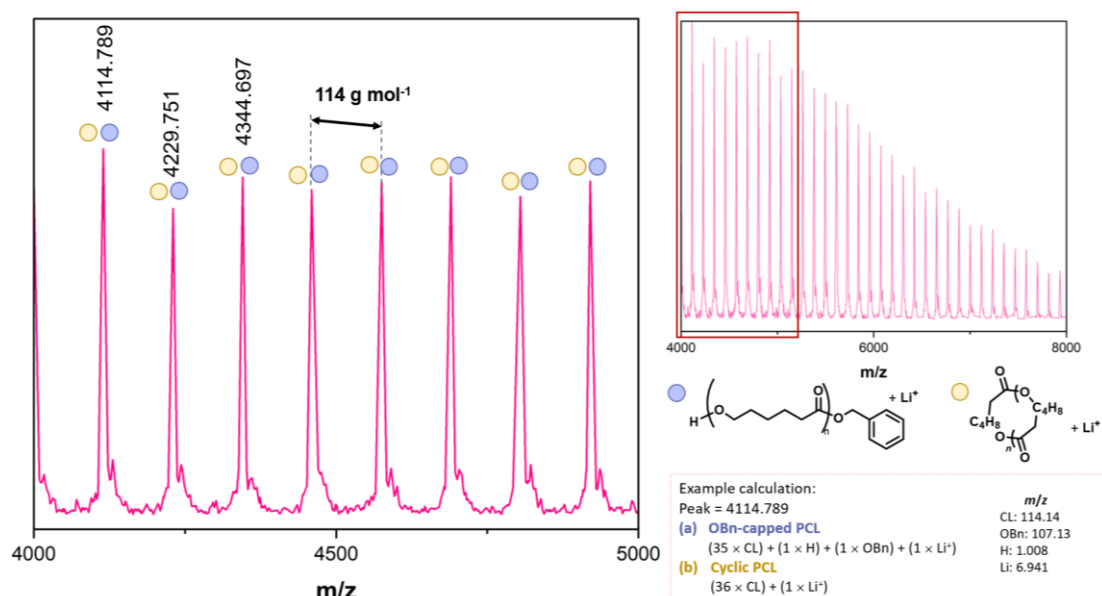


**Figure 4.20** MALDI-ToF spectrum of PCL prepared with  $[\text{LNaAlEt} \cdot \text{AlEt}_3]/2$  BnOH in toluene at 70 °C at 45% conversion, showing the peaks corresponding to a series of (i) benzoxo-end capped PCL ( $[\text{M} + \text{Li}^+]$ ; purple) and (ii) cyclic PCL ( $[\text{M} + \text{Li}^+]$ ; yellow).

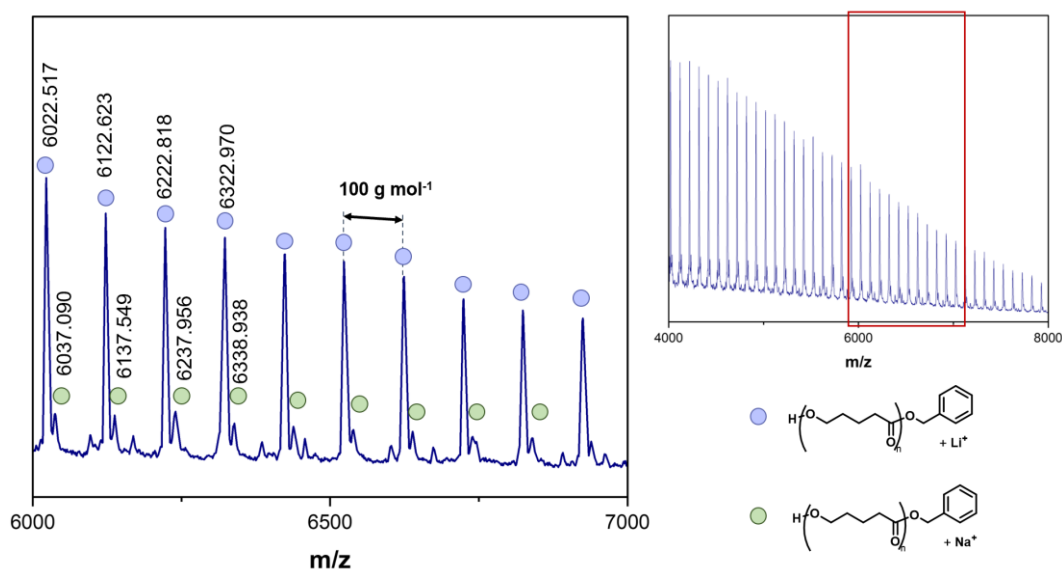


**Figure 4.21** MALDI-ToF spectrum of PVL prepared with  $[\text{LNaAlEt} \cdot \text{AlEt}_3]/2$  BnOH in toluene at 70 °C at 78% conversion, showing the peaks corresponding to a series of (i) benzoxo-end capped PVL ( $[\text{M} + \text{Li}^+]$ ; purple, and  $[\text{M} + \text{Na}^+]$ ; yellow).

End group analysis of PLA by MALDI-ToF also confirmed the presence of the expected  $\alpha$ -OBn/ $\omega$ -OH as well as  $\alpha$ -OH/ $\omega$ -OH end capped polymers (major series),  $\alpha$ -OMe/ $\omega$ -OH capped polymers possibly generated during the purification of crude PLA with acidified MeOH (minor series),<sup>192–194</sup> and cyclic PLA (minor series) (Figure 4.22). Although MALDI-ToF and SEC analyses showed a controlled LA ROP (*i.e.*  $\Delta(m/z) = 144 \text{ g mol}^{-1}$  and narrow  $\mathcal{D}$ ) indicating minimal transesterification,  $[\text{LNaAlEt} \cdot \text{AlEt}_3]/2$

equiv. BnOH produced atactic PLA, as determined by  $^1\text{H}\{\text{H}\}$  NMR analysis ( $P_i = 0.49$ ), reflecting the lack of stereocontrol of the catalyst system.

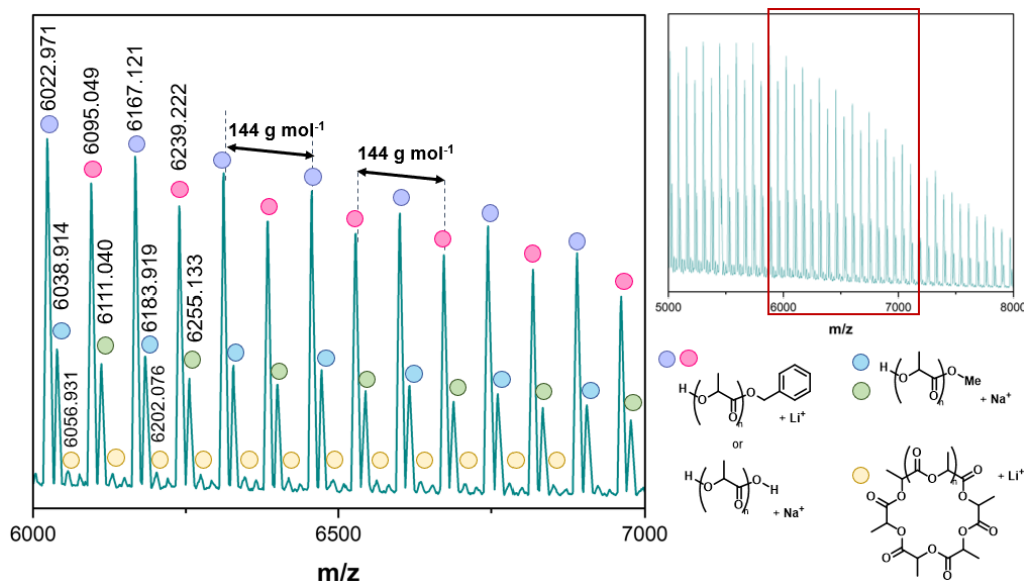


**Figure 4.22** MALDI-ToF spectrum of PLA prepared with  $[\text{LNaAlEt}\cdot\text{AlEt}_3]/2$  BnOH in toluene at  $70^\circ\text{C}$  at 30% conversion, showing the peaks corresponding to a series of (i) benzoxy-end capped PLA ( $[\text{M} + \text{Li}^+]$ , purple) (ii) methoxy-end capped PLA ( $[\text{M} + \text{Na}^+]$ , green and blue), (iii) hydroxy-end capped PLA ( $[\text{M} + \text{Na}^+]$ , pink) and (iv) cyclic PLA ( $[\text{M} + \text{Li}^+]$ , yellow).

Each of the polymerisations displayed first-order kinetics in monomer, following an activity order of  $\text{VL} \gg \text{CL} > \text{LA}$ . The rates of polymerisation are in the order of decreasing free enthalpy of the cyclic esters polymerisation at 298 K ( $k_{\text{obs,VL}} = 0.195 \text{ h}^{-1} \gg k_{\text{obs,CL}} = 0.068 \text{ h}^{-1} > k_{\text{obs,LA}} = 0.053 \text{ h}^{-1}$ ) (refer to Figures 4.23 – 4.26), opposite to the expected order of polymerisation activity based on the ring strain ( $\text{LA} > \text{CL} > \text{VL}$ , Figure 4.23).<sup>195</sup> The ring-opening of cyclic esters is driven by release of monomer ring strain,<sup>196</sup> yet here the trends of ring-strain and the  $k_{\text{obs}}$  values are inverted. This difference could be explained by the accessibility of monomer to the metal active site.<sup>197</sup> For example, LA with the lowest Gibbs energy bears bulky methyl substituents adjacent to the carbonyl bond, which may decrease the accessibility of the catalyst metal centre therefore decreasing the rate of polymerisation.

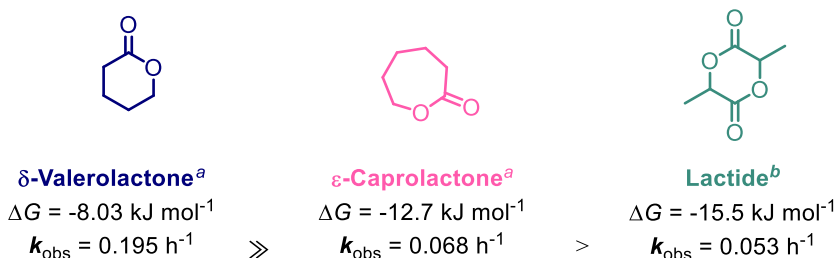


**Figure 4.23** Polymerisation of different cyclic esters catalysed by  $[\text{LNaAlEt}\cdot\text{AlEt}_3]$ , displaying an increased polymerisation rate with decreasing Gibbs free energy for ROP at 298 K.

[a] [monomer] = 10 M, conducted neat; [b] [monomer] = 1 M, conducted in solvent.<sup>195</sup>

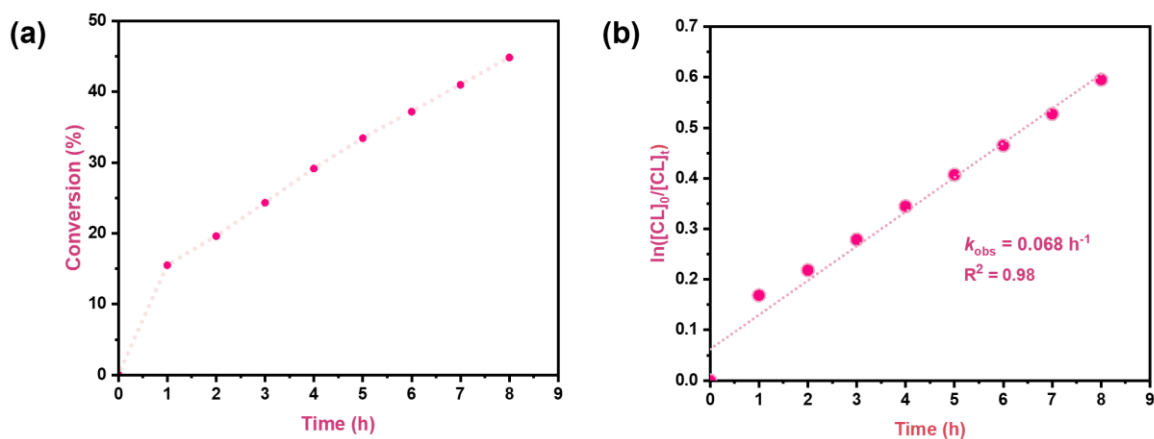


**Figure 4.24** CL polymerisation (a) conversion and (b) kinetic plots generated by complex  $[LNaAlEt \cdot AlEt_3]$ . Polymerisation conditions: [cat.]:[BnOH]:[CL] = 1:2:100, [CL] = 1.0 M, in toluene at 70 °C.

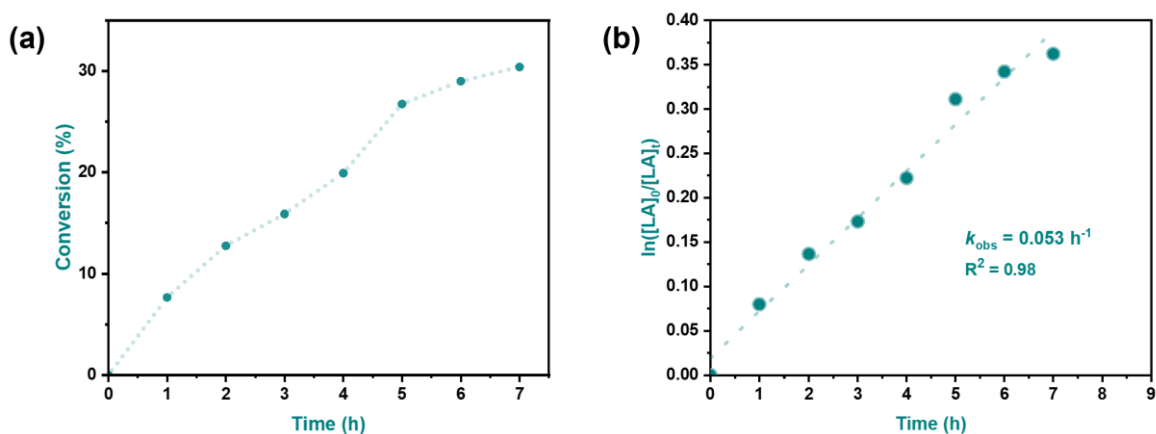


**Figure 4.25** LA polymerisation (a) conversion and (b) kinetic plots generated by complex  $[LNaAlEt \cdot AlEt_3]$ . Polymerisation conditions: [cat.]:[BnOH]:[LA] = 1:2:100, [LA] = 1.0 M, in toluene at 70 °C.

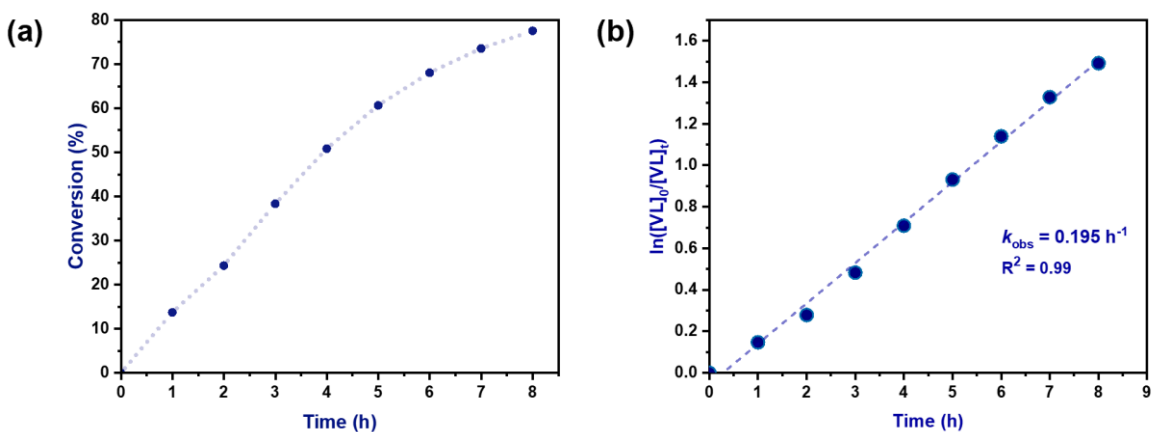


**Figure 4.26** VL polymerisation (a) conversion and (b) kinetic plots generated by complex  $[LNaAlEt \cdot AlEt_3]$ . Polymerisation conditions: [cat.]:[BnOH]:[VL] = 1:2:100, [VL] = 1.0 M, in toluene at 70 °C.

Although a direct comparison is not possible due to different polymerisation conditions (*i.e.* monomer loading, reaction temperature, solvent and different number of initiators), **[LNaAlEt·AlEt<sub>3</sub>]** shows relatively low activity for cyclic ester polymerisation compared to the heterotrimetallic Zn analogue, **[LNaZn<sub>2</sub>Et<sub>2</sub>]** and other ProPhenol complexes reported for cyclic ester ROP. Based on literature trends for Na/Al complexes, available monomer coordination sites at Al may be key for efficient polymerisation to take place.<sup>156,157,198</sup> The inferiority of **[LNaAlEt·AlEt<sub>3</sub>]** could be due to the unavailability of Al<sup>2</sup> metal centre to accommodate more than one monomer, as seen from the reactivity studies with TEPO (refer to [Section 4.3.1.1](#)), and where the sterically congested Al<sup>1</sup> metal centre likely has no available monomer coordination site. This may result in preferential coordination of monomer units on the Na centre. The preference for TEPO ( $\geq 2$  molecules), reflective of monomer units, to coordinate to Na metal centre may be linked to the relatively low polymerisation activity, as some previous literature has shown that alkali metal/Al complexes typically operate *via* monomer coordination to Al and an alkali metal-alkoxide unit providing the source of a nucleophile.<sup>156,157</sup> Looking into the structure of **[LNaAlEt·AlEt<sub>3</sub>]**, the rearrangement of Na in the ligand scaffold creates more space around the alkali metal centre in comparison to the **[LNaZn<sub>2</sub>Et<sub>2</sub>]** analogue (refer to structure comparisons, [Section 3.3.3.1](#)). While the available coordination site around Na may facilitate monomer coordination and improve catalyst activity, Lewis basic monomer units could also coordinate simultaneously, or even interchangeably, onto the highly Lewis acidic Al<sup>2</sup> metal centre.<sup>198,199</sup> This could have hampered the polymerisation efficiency, consequently lowering the overall catalyst activity.

#### 4.3.3.1 Synthesis of PCL-*block*-PLA Copolymer with **[LNaAlEt·AlEt<sub>3</sub>]**

To further explore the catalyst potential, **[LNaAlEt·AlEt<sub>3</sub>]** (with 2 equiv. BnOH) was tested for the synthesis of PCL<sub>100</sub>-PLA<sub>100</sub> block copolymer (at 70 °C, [CL] = 1.0 M, [LA] = 0.5 M, in toluene). PCL-*b*-PLA was successfully formed *via* sequential addition of LA onto the growing PCL\* chain as evidenced by a single diffusion coefficient for PCL and PLA resonances in DOSY NMR, coupled with an increased polymer MW observed by SEC analysis (Figure 4.27, *vide infra*). The monomodal SEC traces for PCL-*b*-PLA copolymer showed a significant increase of  $M_n$  upon the incorporation of LA into the PCL\* chain, increasing from 9.6 kg mol<sup>-1</sup> (PCL) to 21.7 kg mol<sup>-1</sup> (PCL-*b*-PLA). The copolymer synthesis is well-controlled with narrow dispersity value observed for PCL-*b*-PLA ( $\mathcal{D}$  = 1.23). The lower dispersity for the copolymer, compared to the PCL homopolymer ( $\mathcal{D}$  = 1.59), reflects the living nature of the LA ROP step in the second block.<sup>69</sup>

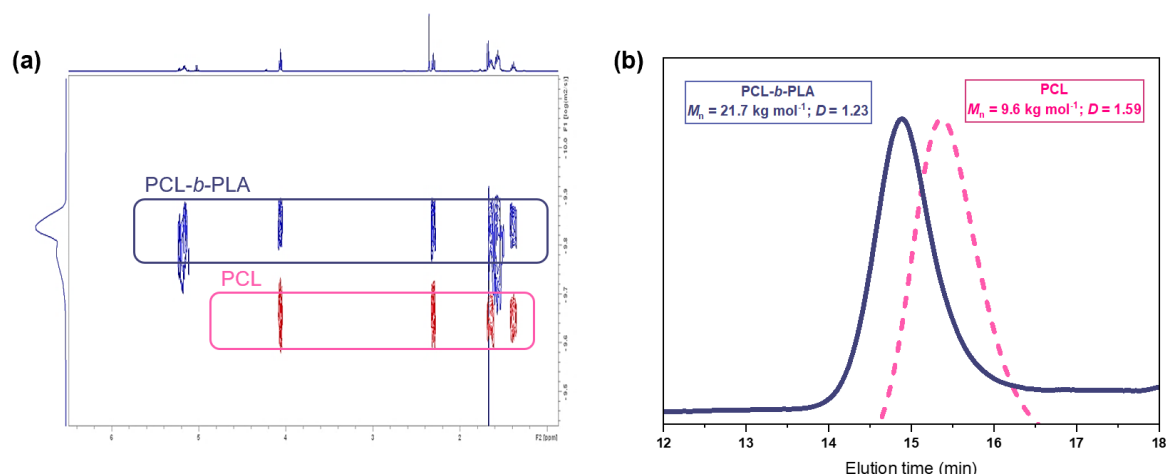


**Figure 4.27** DOSY NMR and SEC analysis confirming the formation of PCL-*b*-PLA copolymer generated by **[LNaAlEt·AlEt<sub>3</sub>]**, at 70 °C in toluene. (a) Overlay of DOSY NMR spectra of PCL precursor (red traces) with PCL-*b*-PLA copolymer (blue traces) showing a single diffusion coefficient product with increased molecular weight. (b) Overlay of monomodal SEC traces of PCL (pink traces) and PCL-*b*-PLA (purple traces) displaying an increased molecular weight of the PCL-*b*-PLA copolymer from PCL homopolymer.

Unlike the highly active divalent ProPhenol complexes (**[LZn<sub>2</sub>Et]**, **[LMgZnEt]** and **[LCaZnEt]**) that generated PCL-*b*-PLA copolymer rapidly with an average total polymerisation time of 2 h (refer to Chapter 2, [Section 2.3.1](#)), **[LNaAlEt·AlEt<sub>3</sub>]** displays much poorer activity. The synthesis of PCL-*b*-PLA copolymer with **[LNaAlEt·AlEt<sub>3</sub>]** required a total of 107 hours, converting only 90 equiv. CL and 84 equiv. LA units, in the PCL and PLA block, respectively (Figure 4.28). Notably, the CL conversion to PCL was impeded at 90%, and did not proceed further upon the addition of LA, even though **[LNaAlEt·AlEt<sub>3</sub>]** displays a higher polymerisation rate for CL compared to LA in the homopolymerisation studies (refer to [Section 4.3.3](#)).

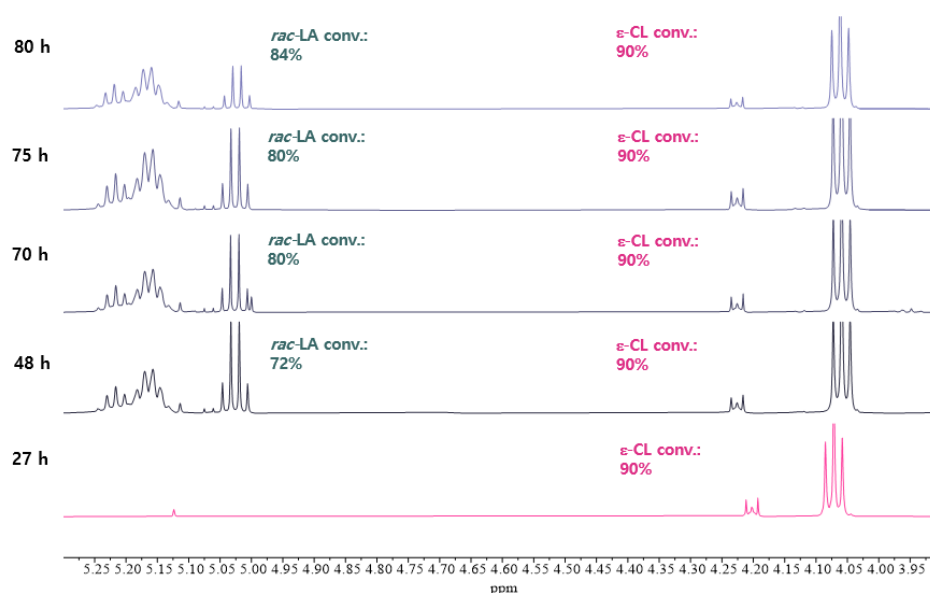


**Figure 4.28** Overlay of <sup>1</sup>H NMR spectra of CL and LA conversions progress by time for the synthesis of PCL (bottom spectrum) and PCL-*b*-PLA copolymer.

Furthermore, the PLA growth from PCL\* chain as a second block does not appear to be disrupted by the remaining 10 equiv. of CL monomer in the polymerisation. Impressively, despite the prolonged polymerisation time, the presence of unreacted CL and the use of a relatively high temperature (80 h after LA addition, at 70 °C in toluene), the PCL-*b*-PLA copolymer formed retained a 'blocky' structure (Figure 4.29), as evidenced by the randomness factor being close to 0.00 ( $R = 0.08$ ; number average sequence lengths,  $l_{\text{CL}}$  and  $l_{\text{LA}} = 26$  and 25, respectively).<sup>134</sup>

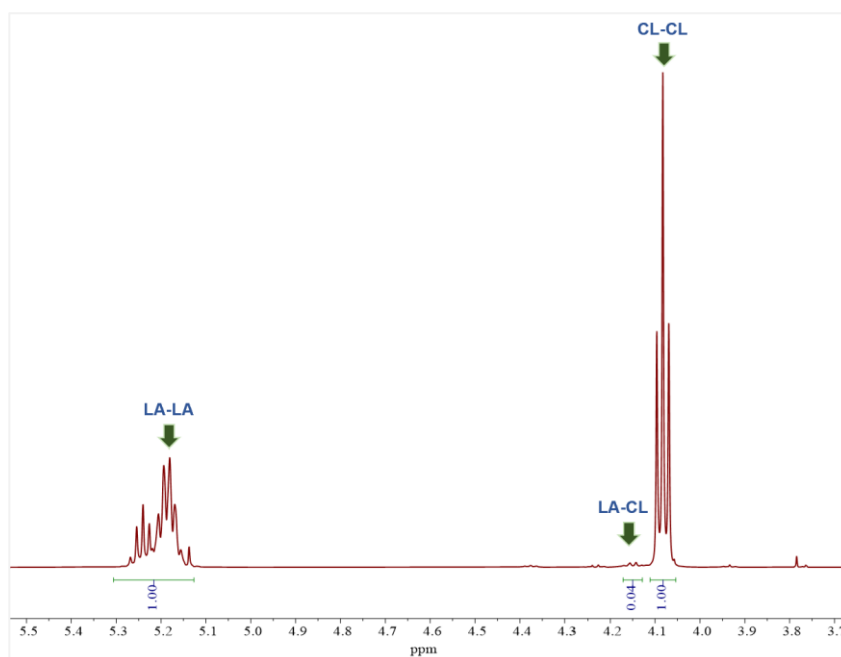


**Figure 4.29** <sup>1</sup>H NMR spectrum of purified PCL-*b*-PLA showing retained 'block' structure of the copolymer, reflected by minor LA-CL diad integral arising from a relatively small degree of randomisation (refer to Chapter 6, [Section 6.6](#), for randomness factor,  $R$ , calculation).

Subsequently, [**LNAlEt·AlEt<sub>3</sub>**] (with 2 equiv. BnOH) was tested for the synthesis of PCL-PLA-PCL triblock copolymers by the sequential addition of neat CL to the PCL-PLA\* diblock propagating chain. For these reactions, the PCL-PLA diblock copolymer precursor was prepared by adding LA after the quantitative conversion of the first CL block (CL<sub>1</sub>). This was to ensure that all of the CL in the third block was from the conversion of the newly added, second batch of CL (CL<sub>2</sub>). However, the conversion of LA to PLA appears to reach a maximum value of 81% after 72 hours reaction time (Figure 4.30, bottom). Unfortunately, upon the addition of neat CL<sub>2</sub> to the PCL-PLA polymer medium, no conversion was observed even after 96 hours of reaction time (Figure 4.30, top). The prolonged polymerisation period was accompanied by a visual decrease of the polymerisation viscosity, potentially indicating that transesterification to lower molecular weight species has occurred. In addition, a colour change from the initial light yellow to a darker yellow solution occurred, which may indicate the decomposition of the active catalyst.

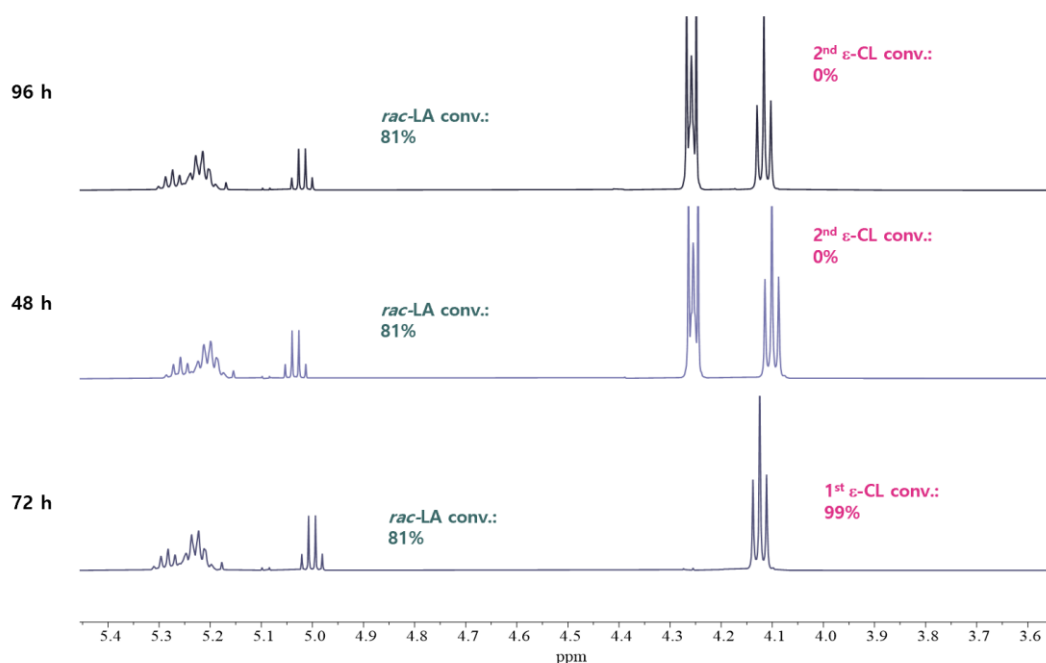


**Figure 4.30** Overlay of  $^1\text{H}$  NMR spectra of CL conversions after 48 h and 96 h in the attempted synthesis of PCL-PLA-PCL triblock copolymer, starting from PCL-PLA\* diblock copolymer (bottom).

Previous studies have shown that the addition of CL to a propagating PLA\* chain can instigate randomisation of (block) copolymer structure resulting from transesterification, including the work described here in Chapter 2.<sup>200</sup> Apart from that, the complete inactivity of some catalysts towards CL polymerisation in the presence of LA monomer units or a PLA\* chain, as observed with  $[\text{LNaAlEt}\cdot\text{AlEt}_3]$  in this case, has also been reported.<sup>132,201,202</sup> For most of the reported catalysts, inclusive of  $[\text{LNaAlEt}\cdot\text{AlEt}_3]$  and divalent ProPhenol complexes (Chapter 2), the homopolymerisation rate of CL is much higher than that of LA.<sup>203</sup> However, in the copolymerisation of CL/LA, the net reactivities of CL and LA are reversed relative to their reactivities in homopolymerisation. Consequently, LA is typically preferentially polymerised. It is worth mentioning that, although this phenomenon has been observed for over three decades since the first report,<sup>204</sup> there has not yet been any solid explanation of this occurrence on a molecular level.<sup>205</sup> In the attempt to generate PCL-PLA-PCL triblock copolymers with  $[\text{LNaAlEt}\cdot\text{AlEt}_3]$ , the presence of LA monomer units is therefore hypothesised to have completely hampered the polymerisation of  $\text{CL}_2$ , resulting in zero conversion even after a prolonged reaction time.

## 4.4 Conclusion

In order to harness the full potential of synergic heterometallic complexes for polymer catalysis, it is essential to understand the roles of different metals, as well as the influence of the overall complex structure on the polymerisation activity and/or control. The work in this chapter investigated the role of three different metal centres (*i.e.* Na, covalently bonded Al<sup>1</sup> and datively bound Al<sup>2</sup>) of a heterotrimetallic ProPhenol complex, **[LNaAlEt·AlEt<sub>3</sub>]**, the structure of which was presented in Chapter 3.

In Chapter 3, the presence of “ate” character observed by NMR spectroscopy around the datively bound Al<sup>2</sup> moiety was envisaged to promote high activity of the catalyst in the ROP of cyclic esters. The formation of an alkali metal aluminate, AM<sup>+</sup>[AlR<sub>4</sub>]<sup>-</sup>, unit around the Na/Al<sup>2</sup> moiety was hypothesised to promote better monomer coordination onto the Lewis acidic Na, and simultaneously allow enhanced propagation rate from the more nucleophilic Al<sup>2</sup>—Et unit. In this chapter, the role of the different metals was proven to be more intricate. The reactivity studies of **[LNaAlEt·AlEt<sub>3</sub>]** with different Lewis bases indicate the preferential coordination of a single Lewis base (or a monomer) unit onto the datively bound Al centre, Al<sup>2</sup>. However, the addition of more Lewis base (*i.e.* ≥ 2 units) may shift the coordination to the more spatially accessible Na centre. This observation suggests the possibility of monomer coordination on multiple sites, which could be influenced by the size of the monomer units. The potential for multiple monomer coordination sites may consequently stunt the overall polymerisation performance, as observed from the poor performance of **[LNaAlEt·AlEt<sub>3</sub>]** in the cyclic ester polymerisation. Nonetheless, it is important to emphasise the stability of **[LNaAlEt·AlEt<sub>3</sub>]** towards several Lewis bases tested. The predicted loosely bound dative ·AlEt<sub>3</sub> unit was not abstracted by any of the Lewis bases, and rather, this was retained as part of the heterotrimetallic complex under the conditions investigated.

Furthermore, it is also worth highlighting the formation of multiple compounds observed from the reaction of **[LNaAlEt·AlEt<sub>3</sub>]** with BnOH as a co-initiator (in toluene and THF solvents). Although the structural insights into **[LNaAlEt·AlEt<sub>3</sub>]** gained in Chapter 3 are valuable, the complex does not necessarily retain its structure under polymerisation conditions (70 °C, 2 equiv. BnOH, in toluene). Therefore, due to the formation of multiple species in the polymerisation medium, it is rather challenging to determine the active species involved in the cyclic ester polymerisation, as well as the mechanism(s) by which polymerisation proceeds. As BnOH was added to the mixture of monomer and **[LNaAlEt·AlEt<sub>3</sub>]**, the polymerisation could proceed *via* either, or simultaneously through both, the coordination-insertion and activated monomer mechanisms.

## 4.5 Future Work

The reactivity studies of  $[\text{LNaAlEt}\cdot\text{AlEt}_3]$  with different Lewis bases conducted in the first part of this chapter provided an insight into the possible role of different metals in this system. Nevertheless, more in-depth investigations would deliver enhanced understanding of the active catalyst form during the polymerisation reaction, including the potential coordination and/or interaction of monomer units with the complex. Analysis of crude polymer samples by atmospheric pressure photoionisation (APPI) or electrospray ionisation (ESI)-mass spectrometry may be carried out to characterise the catalysts that may take part in the propagation step. As observed from the reaction of  $[\text{LNaAlEt}\cdot\text{AlEt}_3]$  with BnOH (1, 2 and 4 equiv.), generating an active benzoxide species was synthetically challenging and resulted in the formation of multiple species. Mass spectroscopy may also therefore be used to identify the major species formed from this reaction, when coupled with other analytical method such as DOSY NMR. Importantly, DFT studies could be utilised to determine the preferential monomer coordination site(s) onto  $[\text{LNaAlEt}\cdot\text{AlEt}_3]$  and predict the most stable form of catalyst/monomer interaction. A combination of these analyses may provide a more solid understanding of this heterometallic system and further provide better rationale of the origin of any cooperativity (or lack thereof) in the ROP of cyclic esters.

In several heterometallic ProPhenol complexes previously studied for LA ROP, the greater “ate” character present within a catalyst system was inferred to result in much enhanced catalytic activity (*e.g.*  $[\text{LKZn}_2\text{Et}] \gg [\text{LNaZn}_2\text{Et}]; [\text{LCaZnEt}] \gg [\text{LMgZnEt}] \sim [\text{LZn}_2\text{Et}]$ ).<sup>112,114</sup> In spite of the presence of multiple unidentified species from the reaction of  $[\text{LNaAlEt}\cdot\text{AlEt}_3]$  with BnOH, it would be interesting to investigate the impact of more electropositive K of  $[\text{LKAIEt}\cdot\text{AlEt}_3]$  on the overall polymerisation activity. Comparing the catalysts performance may also indicate if the “ate” character observed in the heterometallic complexes still retains influence over the catalyst performance under the polymerisation (solution-state) conditions.

Heterotrimetallic  $[\text{LNaAlEt}\cdot\text{AlEt}_3]$  (with 2 equiv. BnOH as a co-initiator) is active for CL, LA and VL ROP and generated polymers with good control, albeit with a relatively low activity (in toluene). Contrary to the reaction in toluene- $d_8$ , NMR spectroscopic studies of  $[\text{LNaAlEt}\cdot\text{AlEt}_3]$  alcoholysis with different equivalents of BnOH (in THF- $d_8$ ) revealed the formation of more defined compounds. Therefore, it would be interesting to test and compare the activity of this system in THF as the active catalyst form will presumably differ than that present in toluene. Perhaps, the formation of several compounds in THF could act synergistically and result in better polymerisation activity and/or control. Of course, to confirm this postulation, further analyses mentioned earlier will be necessary to confirm the catalyst behaviour in the polymerisation process.

## 4.6 Experimental

### 4.6.1 NMR-scale reaction of [LNaAlEt·AlEt<sub>3</sub>] complex with triethylphosphine oxide (TEPO), 4-dimethylamido pyridine (DMAP) or pentamethyldiethylenetriamine (PMDETA)

In a glovebox, [LNaAlEt·AlEt<sub>3</sub>] (0.02 – 0.05 mmol) was weighed in a vial equipped with a magnetic stirrer bar. The Lewis bases (TEPO, DMAP or PMDETA) were weighed separately in another vial with different equivalents (1 – 2 equiv., 0.02 – 0.10 mmol) and were dissolved in benzene-*d*<sub>6</sub>. Complex [LNaAlEt·AlEt<sub>3</sub>] was subsequently added to the Lewis base solution, stirred for 15 minutes at room temperature, and then transferred to a J. Youngs tap NMR tube for NMR spectroscopic analysis.

#### 4.6.1.1 Large-scale reaction of [LNaAlEt·AlEt<sub>3</sub>] complex with triethylphosphine oxide (TEPO)

In a glovebox, [LNaAlEt·AlEt<sub>3</sub>] (0.2 mmol, 165.8 mg) was weighed into a Schlenk flask and dissolved in dry benzene (5 mL). TEPO (0.2 mmol, 26.8 mg) was added, and the reaction mixture was stirred for 2 h at room temperature. The solvent was subsequently removed *in vacuo*, yielding an off-white powder. The resultant solid product was further analysed by NMR spectroscopy.

### 4.6.2 General experimental procedure for the synthesis of PCL, PLA and PVL

In a glovebox, CL, LA or VL (100 equiv., 2.5 mmol) was dissolved in dry toluene (1.5 mL) in an air-tight vial equipped with a magnetic stirrer bar. In a separate vial, catalyst [LNaAlEt·AlEt<sub>3</sub>] (1 equiv., 25 μmol, 20.7 mg) was dissolved in toluene solvent. Both solutions were heated and stirred separately at 70 °C for 1 h using DrySyn heating blocks, and the two solutions were combined and mixed by stirring after 1 h. The polymerisation was initiated by the addition of a BnOH stock solution to the CL, LA or VL/catalyst solution ([M] = 1.0 M; combined volume = 2.5 mL). Aliquots of the propagating PCL, PLA or PVL chains were taken every hour over an 8 hour period, and were quenched with wet CDCl<sub>3</sub> outside the glovebox. These quenched aliquots were subsequently analysed by <sup>1</sup>H NMR spectroscopy and SEC to monitor monomer conversion and polymer growth. Upon completion, the polymer was quenched by the addition of wet chloroform and purified by precipitation from cold acidified methanol, to remove any residual unconverted monomer and traces of metal catalyst for SEC analysis.

#### 4.6.3 Experimental procedure for the synthesis of PCL-*b*-PLA

The copolymerisation to prepare PCL-*b*-PLA diblock copolymers was carried out *via* the sequential addition of *rac*-LA after the full conversion of CL to PCL (using the homopolymerisation procedure presented above). In a separate air-tight vial equipped with a magnetic stirrer bar, LA (100 equiv., 2.5 mmol, 360.3 mg) was dissolved in toluene (2.5 mL) and stirred at 70 °C for 1 h. Subsequently, the LA solution was added to the propagating PCL\* chain in toluene (total volume = 5.0 mL, [LA] = 0.5 M). Aliquots of the PCL-PLA copolymerisation were taken periodically to monitor monomer conversion and polymer growth by <sup>1</sup>H NMR spectroscopy and SEC analyses. Upon completion, the PCL-PLA copolymerisation was quenched by the addition of chloroform and purified by precipitation from cold acidified methanol to remove any residual unconverted monomer and traces of metal catalyst.

#### 4.6.4 Experimental procedure for the synthesis of PCL-PLA-PCL copolymer

In a glovebox, in an air-tight vial equipped with a magnetic stirrer bar, catalyst [LN<sub>2</sub>AlEt·AlEt<sub>3</sub>] (1 equiv., 25 µmol, 20.7 mg) and CL (100 equiv., 2.5 mmol, 277.0 µL) were dissolved in toluene (total volume = 1.42 mL, [CL] = 1.76 M in the first step *i.e.* CL homopolymerisation). The polymerisation of CL was initiated by the addition of BnOH (1 equiv., 25 µmol), and was allowed to proceed for 24 h to reach quantitative (99%) CL conversion. Subsequently, LA solution (100 equiv., 2.5 mmol, 360.3 mg in 1.42 mL of toluene) was added to the propagating PCL\* chain in toluene to give a total volume = 2.84 mL ([LA] = 0.88 M) in the second step of PCL-PLA copolymerisation). Aliquots of the PCL-PLA copolymerisation were taken periodically to monitor monomer conversion and polymer growth by <sup>1</sup>H NMR spectroscopy and SEC analyses. The reaction mixture was stirred for up to 72 h, observing LA conversion capped at 81%. Finally neat CL<sub>2</sub> (100 equiv., 2.5 mmol, 277.0 µL) was added as the third “block”. Aliquots of the polymerisation medium were taken periodically and analysed by <sup>1</sup>H NMR spectroscopy for up to 96 h.

## **Chapter 5**

### **An Outlook on Multi- and Heterometallic ProPhenol Catalysts for Polymer Synthesis**

Once championed as one of the most versatile materials with applications across many sectors, plastic is now often demonised for the resultant and escalating plastic pollution, placing plastic under environmental scrutiny for over a decade. Since its commercialisation in the 1950s, plastic production has undergone an exceptionally rapid growth, exceeding the manufacture of other materials such as wood and glass.<sup>5,206,207</sup> Plastic has also played a pivotal role in global economical and societal development over the years. In Western Europe, the average plastic consumption per person is estimated to be around 150 kg per annum, reflecting our high reliance on plastic in the modern age.<sup>208,209</sup>

Nevertheless, despite the adaptability and increasing utilisation of plastic materials, there is no doubt that plastic plays a rather complex role in terms of sustainability. On one hand, plastic has made positive contributions towards a more sustainable future across diverse industries, by improving the functionality and durability of materials at a relatively low cost.<sup>210</sup> On the other hand, plastic is frequently seen as a major threat towards sustainability, partially because the vast majority of plastic monomers (*i.e.* ethylene, propylene) are derived from fossil hydrocarbons.<sup>211</sup> According to a 2016 report from the Ellen MacArthur Foundation, 90% of plastics are derived from fossil fuel, which currently constitutes about 6% of global oil consumption.<sup>212</sup> Alarmingly, with the current surge in plastic demand and production, the use of plastic is forecast to double in the next 20 years, and is projected to account for 20% of the total oil consumption by 2050.<sup>212</sup>

Aside from concerns over depleting finite raw materials, the durability of plastic, which is a desirable feature for many applications, poses significant challenges for plastic disposal and post-consumer management. Plastic degradation rates vary depending on the plastic type, sizes and the degradation environments. For example, the degradation of common plastic items such as high-density polyethylene (HDPE) milk bottles and laundry detergent pods are estimated to take around half a millennium to degrade on average, while industrial HDPE pipes may take thousands of years to fully degrade.<sup>213</sup> As of 2015, it was reported that from around 6 300 Mt of plastic waste generated, only 9% had been recycled, 12% had been incinerated while the rest ended up in landfills or natural environments.<sup>206</sup> The consequential plastic waste has resulted in leaks into oceans. This is not only detrimental to the oceanic ecosystems but is also damaging the quality of planetary lives on the whole. Cumulative efforts from government and policy makers, industry and manufacturers, as well as improved general public awareness is crucial to combat the detrimental effects of plastic pollution. On top of that, chemistry plays a key role in designing effective strategies to understand and mitigate plastic impacts, and to offer more sustainable alternatives to the current plastic production, utilisation and end-of-life management.

The shift from conventional plastic production to sustainable polymers based on renewable resources (*i.e.* PLA and PGA) has steadily advanced and has even gained momentum over the past few years.<sup>214,215</sup> Although renewable-based aliphatic polyesters are a promising contribution towards realising a more sustainable future, the large-scale transition to polyesters is currently limited by their high production cost as well as inferior mechanical properties and reduced overall performances.<sup>216</sup> In order to generate greener alternative polymers that are on par with conventional plastics, the understanding of polymer designs and synthesis, and the resultant properties of the polymeric materials is crucial. Copolymerisation of two or more different homopolymers with different compositions and polymer chain microstructure can provide access to different properties for specific applications. Furthermore, insights into the distinct roles, potentials and drawbacks of different metal centres in a multimetallic system are important to access tuneable polymer chains with precise architectures. The work presented in Chapter 2 demonstrates the balance between catalytic activity and control achieved using different ProPhenol heterometallic catalysts (Zn/Zn, Mg/Zn, Ca/Zn), specifically for the synthesis of PCL-*block*-PLA copolymers. Exploring and exploiting this investigation further for the synthesis of other target copolymers (*e.g.* gradient and statistical copolymers) of various monomer combinations can pave a way towards understanding heterometallic synergy in other catalytic systems. Identifying common features in multimetallic complexes that contribute towards the precision of different (co)polymer structures would help chemists to design well-defined catalysts that are not only efficient and cost-effective, but more importantly are adaptable for industrial-scale polymer production. The informed synthesis of biobased (co)polymers with tuneable material properties would help to provide cheaper and more accessible alternatives to conventional plastics, to meet the increased demand for bio-based polymers.

Despite the synthetic challenges to access multi- and heterometallic complexes, there is an extensive interest in these complexes owing to the cooperativity and activity enhancements demonstrated across different fields of catalysis, including polymer chemistry.<sup>85,217</sup> However, the understanding of the key multimetallic catalyst design features for the ROP of cyclic ester is still in its somewhat nascent stage. Structural insights of metal complexes through crystallographic analysis can be valuable for understanding catalyst features that influence cooperativity, hence enabling prediction of catalyst performances. Although some trends of cooperative catalyst structures are emerging, clear mechanistic understanding of the polymerisation cycle and individual heterometal roles are essential to bring this field to its full potential and to reap the full benefits of intermetallic communication.<sup>46</sup> DFT calculations can provide useful insights into the interaction between monomers and the active catalyst site(s). For example, polymer tacticity can

be influenced by the monomer orientation and coordination mode as well as the catalyst framework structure, electronics and chirality. DFT modelling and visualisation of ROP allows the prediction of the most feasible polymerisation route, bringing us a step closer to comprehending the ROP mechanisms for multi- and heterometallic catalysts.

The ProPhenol ligand scaffold is chiral, and has been used extensively for accessing bimetallic complexes that have exhibited impressive performance and enantioselectivity for many organic transformations.<sup>111</sup> Thus far, a total of 13 ProPhenol complexes have been reported for the ROP of different lactones (*i.e.* LA, CL and *rac*- $\beta$ -BL; refer to Chapter 1, [Section 1.4.3](#)),<sup>81,112–116</sup> with 4 additional new ProPhenol complexes presented in this thesis. The complexes reported in literature have shown excellent activity, coupled with impressive stereocontrol in some cases. Collating these literature findings with additional computational studies would provide an interesting and critical insight for the design and synthesis of future ProPhenol metal complexes for cyclic ester ROP. In addition, designing robust catalysts that are tolerant to industrial conditions is critical for pragmatic and commercially viable polymer production. Therefore, future synthetic refinement and/or modification may focus on combining different Earth-abundant and low-toxicity metals, and modifying the ProPhenol ligand backbone to develop air-stable heterometallic catalysts which deliver heterometallic synergy. Ligand modification could focus on altering the ligand substituents and incorporating different functional groups to tailor the steric environment around the metal active site (for improved selectivity) and tune the electronics of the metal centres (for enhanced activity).

Several high-performance ROP catalysts have also been utilised for ring-opening co-polymerisation (ROCOP) reactions.<sup>218,219</sup> Owing to similarities between the ROP and ROCOP mechanisms and some shared catalyst features,<sup>85</sup> the scope of polymer catalysis using ProPhenol complexes could potentially be extended to the ROCOP of epoxides with anhydrides or carbon dioxide to generate sustainable polyesters and polycarbonates. The electronic modulation that gives rise to “ate” character, as seen in several ProPhenol complexes, could also be exploited to deliver enhanced activity in ROCOP. Additionally, from the structural studies of heterotrimetallic AM/Al<sub>2</sub> ProPhenol complexes in this study, the intermetallic proximities of the AM and both Al metal centres (*i.e.* Al<sup>1</sup> and Al<sup>2</sup>) were determined within the range of intermetallic distance (3 — 5 Å) required for optimum cooperativity.<sup>220</sup> Therefore, these complexes are anticipated to display activity for ROCOP, which can be further extended with other ProPhenol complexes. It would be interesting to investigate the activity and selectivity of all the ProPhenol complexes for both ROP and ROCOP through systematic comparison studies, to draw key similarities and differences between the catalysts and consequently extract information on critical factors for future catalysts development.

## **Chapter 6**

### **General Experimental Techniques**

## 6.1 Materials

All manipulations involving air- or moisture-sensitive compounds were performed either in a glove box or using standard Schlenk techniques under argon atmosphere. All reagents and solvents were purchased from Sigma-Aldrich, Fisher Scientific, Fluorochem, Acros Organics, and used without further purification unless stated otherwise. Dry solvents (THF, toluene, and pentane) were collected from a solvent purification system (Innovative Technologies), dried over activated 4 Å molecular sieves and stored under argon. Benzene was dried overnight over CaH<sub>2</sub>, degassed three times by freeze-pump-thaw and vacuum transferred under reduced pressure, then stored over activated 4 Å molecular sieves under argon.

Anhydrous NMR solvents (benzene-*d*<sub>6</sub>, CDCl<sub>3</sub>, THF-*d*<sub>8</sub>, and toluene-*d*<sub>8</sub>) for air- and moisture-sensitive compounds used for NMR spectroscopy analysis were dried overnight over CaH<sub>2</sub>, degassed three times by freeze-pump-thaw and vacuum transferred under reduced pressure, then stored over activated 4 Å molecular sieves under argon.

*Rac*-lactide (99%, Sigma-Aldrich) and L-lactide were purified by double recrystallization from toluene followed by sublimation, and stored at -18 °C in a glove box freezer. Benzyl alcohol (BnOH), ε-caprolactone (99%, Alfa Aesar) and δ-valerolactone (99%, Thermo Scientific Chemicals) were dried over CaH<sub>2</sub>, distilled under reduced pressure and stored over activated 4 Å molecular sieves prior to use.

## 6.2 Manipulation of Air- and Moisture-sensitive Compounds

This project entailed the use of air- and moisture-sensitive organometallic reagents, complexes and monomers. All manipulations involving such compounds were performed either in a glove box or using standard Schlenk techniques under a dry and inert argon atmosphere.

### 6.2.1 Schlenk Techniques

The Schlenk line used in this project comprised two independent components, with one connected to a high vacuum pump and the second connected to an inlet of dry, oxygen-free argon gas. The Schlenk line featured five two-way taps, coated with high vacuum grease to ensure an efficient seal, which were used to connect the reaction apparatus to the Schlenk line *via* tubing. The Schlenk taps enabled the introduction of vacuum or argon into the connected apparatus, most commonly a Schlenk flask. The Schlenk set-up also included a solvent trap, where volatiles (*e.g.* solvent) were condensed when the trap was placed in a Dewar flask with liquid nitrogen, thus preventing the

volatiles from reaching and potentially damaging the vacuum pump. Prior to each Schlenk-based procedure, the reaction apparatus was connected to the Schlenk line and was evacuated and refilled with argon gas three times (one 10 min. evacuation, followed by two 5 min. evacuations) to remove any oxygen/moisture from the reaction vessel.

### 6.2.2 Glove Box

The air- and moisture-sensitive reagents, complexes and monomers were manipulated and stored in an argon-filled MBraun glove box to prevent decomposition. This included analytical preparation (for NMR spectroscopy and elemental analysis), reactions (metalation and polymerisation), purification (crystallisation set-up and filtration) and the determination of the mass of solid reactants, catalysts and products. In general, when introducing chemicals or equipment into the glove box, the item was placed in the small glove box antechamber *via* the outer port door, with the inner port door remaining closed. Once the outer port door was sealed, the antechamber was evacuated for 10 min., refilled with argon, then evacuated for 5 min. (and refilled with argon) twice more. Certain equipment (*e.g.* sublimation kit) required the use of the larger glove box antechamber, which was evacuated for 20 min. and refilled with argon gas three times. After performing the three vacuum/argon cycles, the chemicals and/or equipment were safely introduced into the main body of the glove box through the inner port door without introducing significant quantities of oxygen and water. The oxygen and water levels were continuously monitored *via* built-in sensors, with the values displayed on the LCD control panel. To ensure these levels remained low, the glove box was regenerated regularly by passing H<sub>2</sub>/argon gas through the catalyst and removing water from the molecular sieves by heating under vacuum.

## 6.3 Instrumentation for Characterisation

### 6.3.1 Nuclear Magnetic Resonance (NMR) Spectroscopy

1D NMR (<sup>1</sup>H, 1H{<sup>1</sup>H}, <sup>13</sup>C) and 2D NMR (COSY, HSQC, DOSY, HMBC) spectra were recorded on Bruker AVA500 or PRO500 spectrometer at 300 K operating at 500 MHz. Chemical shifts ( $\delta$ ) are given in ppm, and coupling constants (*J*) are reported in Hertz (Hz). Integration is provided and assignments are indicated. <sup>1</sup>H and <sup>13</sup>C NMR spectra were referenced with respect to the residual peaks of deuterated solvents (benzene-*d*<sub>6</sub>: 7.26 ppm, 128.1 ppm; CDCl<sub>3</sub>: 7.27 ppm, 77.0 ppm; THF-*d*<sub>8</sub>: 3.58 ppm, 25.3 ppm; toluene-*d*<sub>8</sub>: 2.08 ppm, 20.4 ppm). Multiplicities are indicated by s (singlet), d (doublet), dd (doublet of doublet), m (multiplet), t (triplet) and q (quartet).

The Diffusion-Ordered Spectroscopy (DOSY) NMR experiments were performed at 298 K on a Bruker Ascend 2 channel instrument operating at a frequency of 500 MHz for proton resonance under TopSpin (version 4.3, Bruker Biospin, Karlsruhe) and equipped with a z-gradient DCH/5mm tuneable “CryoProbe”™ probe and a GRASP II gradient spectroscopy accessory providing a maximum gradient output of 53.5 G/cm (5.35G/cmA). Diffusion ordered NMR data was acquired using the Bruker pulse program dstebpgp3s with a spectral width of 10330 Hz (centred on 6.175 ppm) and 32768 data points. A relaxation delay of 2 s was employed along with a diffusion time ( $\Delta$ ) of 100 ms and a longitudinal eddy current delay (LED) of 5 ms. Bipolar gradients pulses ( $\delta/2$ ) of 1.5 ms and homospoil gradient pulses of 0.6 ms were used. The gradient strengths of the 3 homospoil pulses were -13.17%, -17.13%, -15.37%. 16 experiments were collected with the bipolar gradient strength, initially at 5% (1<sup>st</sup> experiment), linearly increased to 95% (16<sup>th</sup> experiment). All gradient pulses were smooth-square shaped (SMSQ10.100) and after each application a recovery delay of 200  $\mu$ s used. The experiment was run with 16 scans per increment, employing one stimulated echo with two spoiling gradients.

DOSY plots were generated and the NMR spectra formatted by using the DOSY processing module of TopSpin. Parameters were optimised empirically to find the best quality of data for presentation purposes. Diffusion coefficients were calculated by fitting intensity data to the Stejskal-Tanner expression

#### 6.3.1.1 Preparation of Diffusion Order Spectroscopy (DOSY) External Calibration Plots

Calibration plots in benzene-*d*<sub>6</sub>, THF-*d*<sub>8</sub> and toluene-*d*<sub>8</sub> were formed through DOSY analysis of a range of standards spanning the molecular weight range of 136.24 to 622.67 g mol<sup>-1</sup> [adamantane, 136.25; 2-phenylpyridine, 155.20; pyrene, 202.26; tri(*o*-tolyl)-phosphine, 304.37; tetraphenylphthaline, 432.50 and 2,2'-bis(diphenylphosphino)-1,1'-binaphthyl (BINAP), 622.67, Tables 6.1, 6.2 and 6.3].<sup>221</sup> Adamantane was run a total of four times and the average observed Log D was used. Furthermore, adamantane was used as an internal standard for all other standards used. From the diffusion coefficients of the external standards, linear calibration graphs were obtained by plotting logD vs logMW (Figures 6.1 – 6.3). Following DOSY analysis of the product, the diffusion coefficient obtained for the signals corresponding to the product allowed an estimate of the MW of the species present in solution through use of the equation  $y = mx + c$ .

**Table 6.1** Diffusion coefficients of standards in benzene- $d_6$  solution compared to their molecular weight.

| Calibration factors<br>(from the plot equation $y = mx + c$ ): |                            |                           | Gradient,<br>m:   |                     | Intercept,<br>c:           |                           |              |                      |            |
|----------------------------------------------------------------|----------------------------|---------------------------|-------------------|---------------------|----------------------------|---------------------------|--------------|----------------------|------------|
|                                                                |                            |                           | -0.6515           |                     | -7.2021                    | Uncorrected<br>adamantane |              |                      |            |
| Calibrant                                                      | MW <sub>real</sub><br>(Da) | log<br>MW <sub>real</sub> | Observed<br>Log D | Normalised<br>Log D | MW <sub>calc</sub><br>(Da) | Difference                | Error<br>(%) | Log D <sub>obs</sub> | Difference |
| Adamantane                                                     | 136.24                     | 2.13                      | -8.6160           | -8.6160             | 147.99                     | 11.75                     | 8.63         | -                    | -          |
| 2-Phenylpyridine                                               | 155.20                     | 2.19                      | -8.6244           | -8.6212             | 152.45                     | -2.75                     | 1.77         | -8.6192              | 0.0031875  |
| Pyrene                                                         | 202.26                     | 2.31                      | -8.6726           | -8.6694             | 180.76                     | -21.50                    | 10.63        | -8.6192              | 0.0031875  |
| Tri(o-tolyl)-phosphine                                         | 304.37                     | 2.48                      | -8.8322           | -8.8241             | 317.74                     | 13.37                     | 4.39         | -8.6241              | 0.0080875  |
| Tetraphenyl-naphthalene                                        | 432.55                     | 2.64                      | -8.9570           | -8.9547             | 493.89                     | 61.34                     | 14.18        | -8.6183              | 0.0022875  |
| BINAP                                                          | 622.67                     | 2.79                      | -9.0090           | -9.0037             | 593.53                     | -29.14                    | 4.68         | -8.6213              | 0.0052875  |
|                                                                |                            |                           |                   |                     |                            | Avg. error<br>(%)         | 8.47         |                      |            |

**Table 6.2** Diffusion coefficients of standards in THF-*d*<sub>8</sub> solution compared to their molecular weight.

| Calibration factors<br>(from the plot equation $y = mx + c$ ): |                            |                           | Gradient,<br>m:   |                     | Intercept,<br>c:           |                           |              |                      |            |
|----------------------------------------------------------------|----------------------------|---------------------------|-------------------|---------------------|----------------------------|---------------------------|--------------|----------------------|------------|
|                                                                |                            |                           | -0.6061           |                     | -7.2251                    | Uncorrected<br>adamantane |              |                      |            |
| Calibrant                                                      | MW <sub>real</sub><br>(Da) | log<br>MW <sub>real</sub> | Observed<br>Log D | Normalised<br>Log D | MW <sub>calc</sub><br>(Da) | Difference                | Error<br>(%) | Log D <sub>obs</sub> | Difference |
| Adamantane                                                     | 136.24                     | 2.13                      | -8.5512           | -8.5512             | 154.14                     | 17.90                     | 13.14        | -                    | -          |
| 2-Phenylpyridine                                               | 155.20                     | 2.19                      | -8.5405           | -8.5385             | 148.00                     | -7.20                     | 4.64         | -8.5532              | 0.002      |
| Pyrene                                                         | 202.26                     | 2.31                      | -8.5823           | -8.5843             | 173.47                     | -28.79                    | 14.23        | -8.5492              | -0.002     |
| Tri(o-tolyl)-phosphine                                         | 304.37                     | 2.48                      | -8.7359           | -8.7363             | 310.93                     | 6.56                      | 2.15         | -8.5508              | -0.0004    |
| Tetraphenyl-naphthalene                                        | 432.55                     | 2.64                      | -8.8482           | -8.8484             | 476.37                     | 43.82                     | 10.13        | -8.5510              | -0.0002    |
| BINAP                                                          | 622.67                     | 2.79                      | -8.9056           | -8.9071             | 592.44                     | -30.23                    | 4.85         | -8.5497              | -0.0015    |
|                                                                |                            |                           |                   |                     |                            | Avg. error<br>(%)         | 8.19         |                      |            |

**Table 6.3** Diffusion coefficients of standards in toluene-*d*<sub>8</sub> solution compared to their molecular weight.

| Calibration factors<br>(from the plot equation $y = mx + c$ ): |                            |                           | Gradient,<br>m:   |                     | Intercept,<br>c:           |                           |              |                      |            |
|----------------------------------------------------------------|----------------------------|---------------------------|-------------------|---------------------|----------------------------|---------------------------|--------------|----------------------|------------|
|                                                                |                            |                           | -0.6466           |                     | -7.1808                    | Uncorrected<br>adamantane |              |                      |            |
| Calibrant                                                      | MW <sub>real</sub><br>(Da) | log<br>MW <sub>real</sub> | Observed<br>Log D | Normalised<br>Log D | MW <sub>calc</sub><br>(Da) | Difference                | Error<br>(%) | Log D <sub>obs</sub> | Difference |
| Adamantane                                                     | 136.24                     | 2.13                      | -8.57928          | -8.57928            | 145.49                     | 9.25                      | 6.79         | -                    | -          |
| 2-Phenylpyridine                                               | 155.20                     | 2.19                      | -8.5933           | -8.58978            | 152.93                     | -2.27                     | 1.46         | -8.5828              | 0.00352    |
| Pyrene                                                         | 202.26                     | 2.31                      | -8.64542          | -8.6407             | 184.12                     | -18.14                    | 8.97         | -8.584               | 0.00472    |
| Tri(o-tolyl)-phosphine                                         | 304.37                     | 2.48                      | -8.8015           | -8.80178            | 320.99                     | 16.62                     | 5.46         | -8.579               | -0.00028   |
| Tetraphenyl-naphthalene                                        | 432.50                     | 2.64                      | -8.914            | -8.90488            | 479.16                     | 46.66                     | 10.79        | -8.5884              | 0.00912    |
| BINAP                                                          | 622.67                     | 2.79                      | -8.9713           | -8.9736             | 587.62                     | -35.05                    | 5.63         | -8.5814              | -0.0023    |
|                                                                |                            |                           |                   |                     |                            | Avg. error<br>(%)         | 6.52         |                      |            |

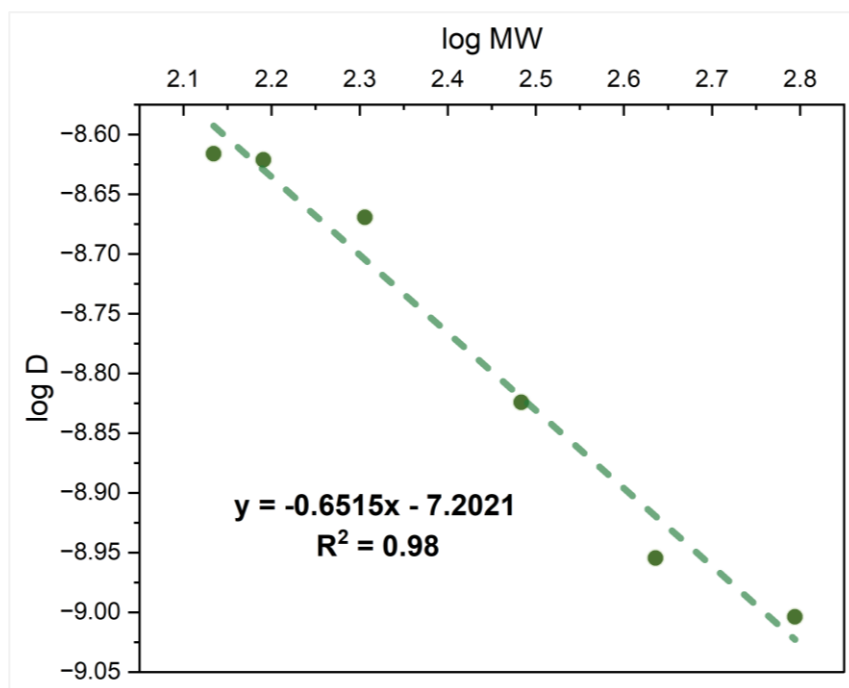


**Figure 6.1** Plot of logD vs logMW constructed from the <sup>1</sup>H DOSY NMR data of adamantane, 2-phenylpyridine, pyrene, tri(*o*-tolyl)-phosphine, tetraphenylphthaline and 2,2'-bis(diphenylphosphino)-1,1'-binaphthyl (BINAP) standards in benzene-*d*<sub>6</sub>.

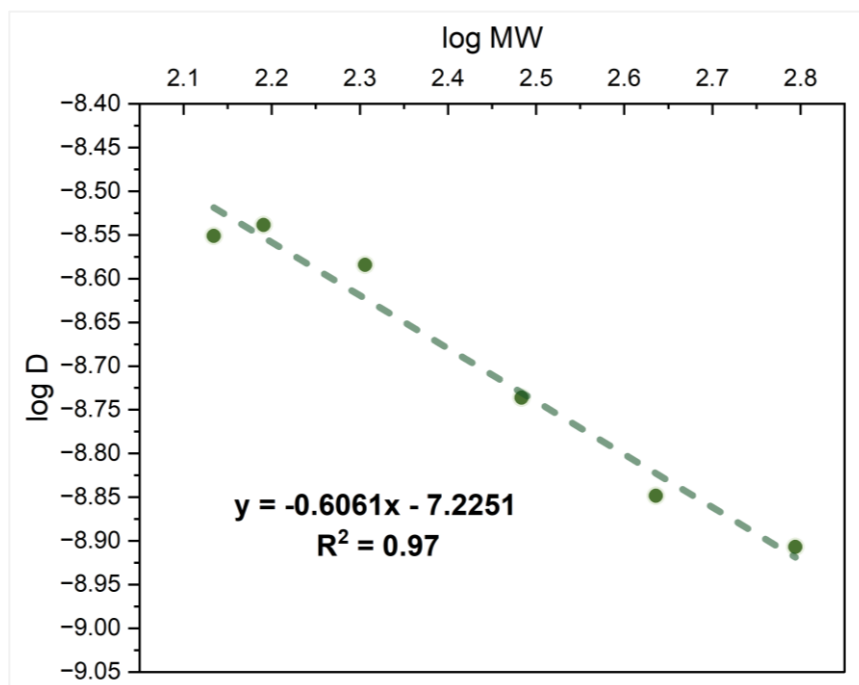


**Figure 6.2** Plot of logD vs logMW constructed from the <sup>1</sup>H DOSY NMR data of adamantane, 2-phenylpyridine, pyrene, tri(*o*-tolyl)-phosphine, tetraphenylphthaline and 2,2'-bis(diphenylphosphino)-1,1'-binaphthyl (BINAP) standards in THF-*d*<sub>8</sub>.

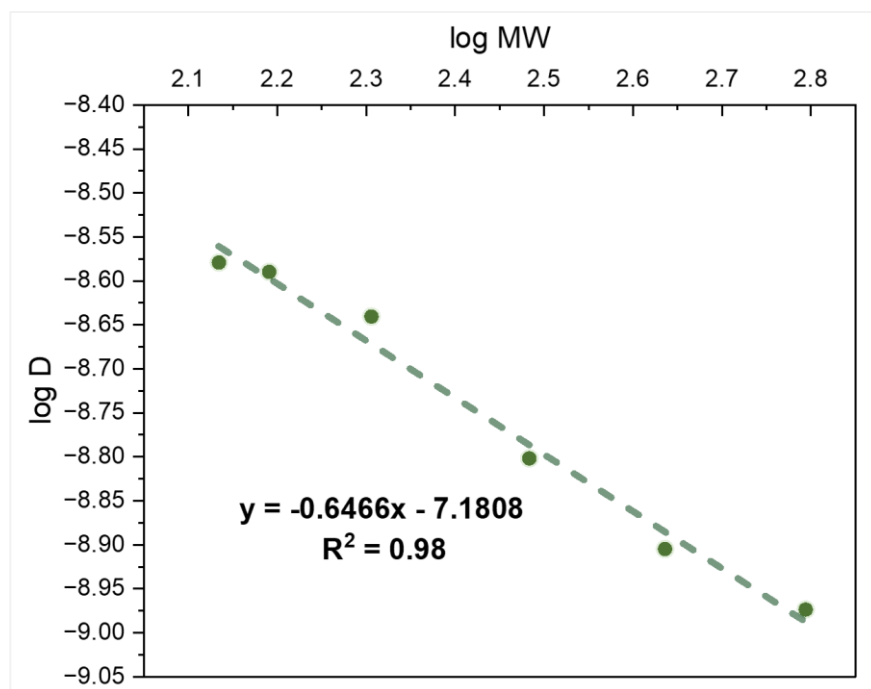


**Figure 6.3** Plot of logD vs logMW constructed from the  $^1\text{H}$  DOSY NMR data of adamantane, 2-phenylpyridine, pyrene, tri(o-tolyl)-phosphine, tetraphenylphthaline and 2,2'-bis(diphenylphosphino)-1,1'-binaphthyl (BINAP) standards in toluene- $d_8$ .

### 6.3.2 Mass Spectrometry

Mass spectrometry (MS) was performed by the University of Edinburgh, School of Chemistry, Mass Spectrometry Laboratory.

#### MALDI-ToF

MALDI-ToF MS analyses were performed using a Bruker Daltonics UltrafleXtreme™ instrument with a double time-of-flight (ToF) mass analyser (MALDI-ToF/ToF MS) in either reflectron positive (RP) or linear positive (LP) mode. Calibration was performed in either RP or LP mode against a 10 mg mL<sup>-1</sup> solution of red phosphorus in THF. Data are reported in the form of *m/z*. The sample to be analysed, dithranol matrix and LiI cationising agent were dissolved in THF at 10 mg mL<sup>-1</sup> and the solutions were mixed in a 2:2:1 volume ratio. A droplet (2 µL) of the resultant mixture was spotted on to the sample plate and submitted for MALDI-ToF MS analysis.

### 6.3.3 Elemental Analysis

The percentage C, H, N values of the elemental composition of the complexes synthesised in this project were assessed by elemental microanalysis, which was performed by Ms. Orfhlaith McCullough at London Metropolitan University.

### 6.3.4 X-Ray Diffraction

Single crystal X-ray diffraction work was performed by Dr Gary Nichol. In each case, the crystals were first coated in paratone or perfluoroether oil, then suitable single crystal was selected on a Mitegen tip and mounted on the diffractometer. Structural analyses of complexes **[LNaAlMe·AlMe<sub>3</sub>]** and **[LNaAl(*i*Bu)·Al(*i*Bu)<sub>3</sub>]** were performed with a Rigaku Oxford Diffraction SuperNova diffractometer with Mo K<sub>α</sub> radiation at a temperature of 120 K. Analyses of complexes **[LNaAlEt·AlEt<sub>3</sub>]** and **[LKAIEt·AlEt<sub>3</sub>]** were performed with a Bruker D8 VENTURE diffractometer with Cu K<sub>α</sub> radiation. The data of complex **[LNaAlEt·AlEt<sub>3</sub>]** were measured at 270 K, and the temperature lowered to 250 K at a rate of 60 K/hour, while the crystal of **[LKAIEt·AlEt<sub>3</sub>]** was kept at a temperature of 100 K during data collection.

### 6.3.5 Size-Exclusion Chromatography

Polymer samples (2 – 10 mg) were dissolved in GPC grade THF (1 mL) and filtered using a 0.2 µm PTFE syringe filter. SEC analyses of the filtered polymer samples were carried out in GPC grade THF at a flow rate of 1 mL min<sup>-1</sup> at 35 °C on an Agilent 1260 Infinity II GPC/SEC single detector system

with mixed bed C PLgel columns (300 x 7.5 mm). The RI detector was calibrated using a narrow molecular weight polystyrene standards.

### 6.3.6 Differential Scanning Calorimetry

DSC experiments were performed using a DSC (DSC 2500, TA Instruments) with a refrigerated cooling accessory (RCS90). In all experiments, the DSC cell was purged with nitrogen at 50 mL min<sup>-1</sup>. Indium was used to calibrate the cell constant. Materials were sealed in Tzero aluminium pans with a pierced hole on the lid. Runs were performed at a ramp rate of 5°C/min from -80 °C to 200 °C.

The relative degree of crystallisation ( $x_c$ ) can be measured by the following equation:<sup>138</sup>

$$x_c = \frac{\Delta H_m}{\Delta H_f} \times 100$$

where  $\Delta H_m$  is the enthalpy change associated with melting the sample and  $\Delta H_f$  the is the theoretical enthalpy of melting for a 100% crystalline sample.

## 6.4 Determination of Percentage Monomer Conversions

The monomer conversion in each ROP reaction was quantified by  $^1\text{H}$  NMR spectroscopy through the relative integration of the  $\epsilon$ -CL, *rac*-LA or  $\delta$ -VL signals at 4.22, 5.01 or 4.35 ppm, respectively, and the corresponding PCL, PLA or PVL signals at 4.06, 5.15-5.25 or 4.08 ppm, respectively (Figure 6.4), and by inputting the integrals into the following equation:

$$\text{Percentage polymer conversion} = \left( \frac{\text{polymer integration}}{\text{polymer integration} + \text{monomer integration}} \right) \times 100$$

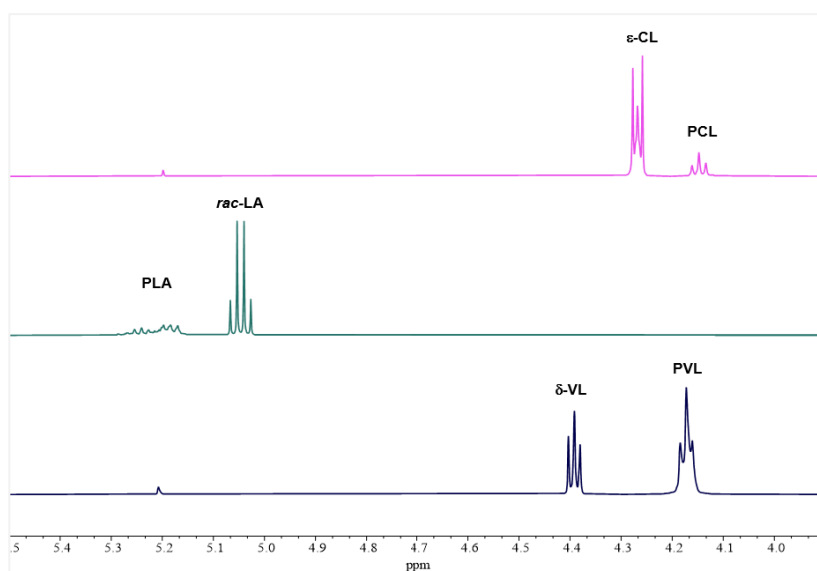


**Figure 6.4** Example  $^1\text{H}$  NMR spectra in  $\text{CDCl}_3$  used to determine conversions of  $\epsilon$ -CL to PCL (top), *rac*-LA to PLA (middle) and  $\delta$ -VL to PVL (bottom).

## 6.5 Determination of Polymer Tacticity

The tacticity of PLA was determined by the analysis of deconvoluted  $^1\text{H}\{^1\text{H}\}$  NMR spectrum of the polymer (Figure 6.5), which decouples the splitting effect of the methyl and methine protons of PLA ( $\delta = 5.15\text{--}5.25$  ppm).<sup>19,36</sup> The probability of syndiotactic ( $P_s$ ) or isotactic ( $P_i$ ) enchainment in the polymer chain can then be determined quantitatively from the equations in Figure 6.6. This is calculated by the integration of the five possible tetrads of PLA generated from *rac*-LA by  $^1\text{H}\{^1\text{H}\}$  NMR spectroscopy, each with a distinct chemical shift (Figure 6.5, *vide infra*).

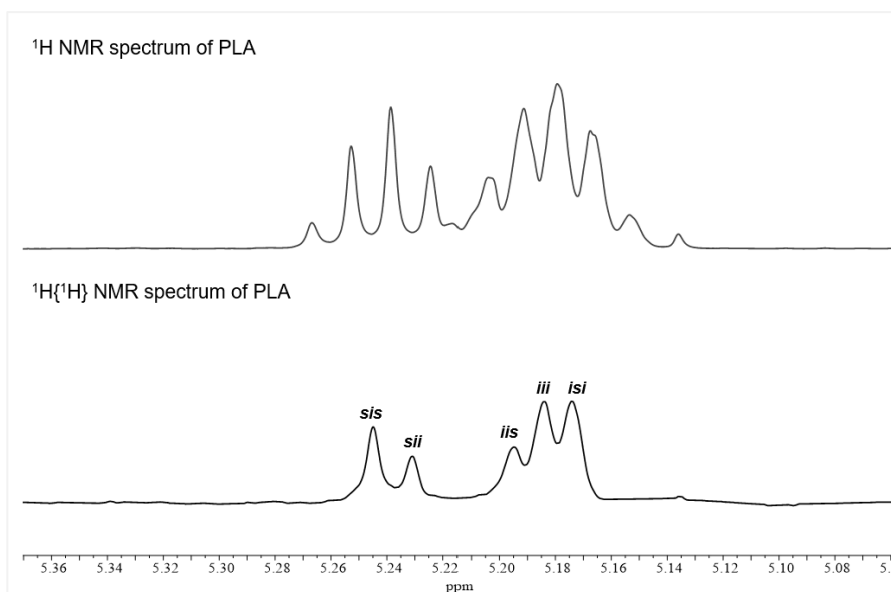


**Figure 6.5** Example  $^1\text{H}$  (top) and deconvoluted  $^1\text{H}\{^1\text{H}\}$  (bottom) NMR spectra used to determine PLA tacticity, in  $\text{CDCl}_3$  (500 MHz, 298 K).

| Tetrad          | Probability                 |
|-----------------|-----------------------------|
| $sis$           | $\frac{P_s^2}{2}$           |
| $sii$           | $\frac{P_s P_i}{2}$         |
| $iis$           | $\frac{P_s P_i}{2}$         |
| $iii$           | $P_i^2 + \frac{P_s P_i}{2}$ |
| $isi$           | $\frac{P_s^2 + P_s P_i}{2}$ |
| $P_s + P_i = 1$ |                             |

**Figure 6.6** The five possible tetrads for PLA generated from *rac*-LA and the equations used to determine the probability of isotactic or syndiotactic enchainment in the polymer chain.<sup>18,19</sup>

## 6.6 Calculations for Randomness Factor, $R$ , and Number-Average Sequence Length, $I$ , in PCL-*b*-PLA Copolymer Structure

The relative integrals ( $i$ ) of CL-CL, LA-LA, CL-LA and LA-CL  $^1\text{H}$  NMR diad resonances of the copolymer structure were used to quantify the degree of randomisation resulting from transesterification.

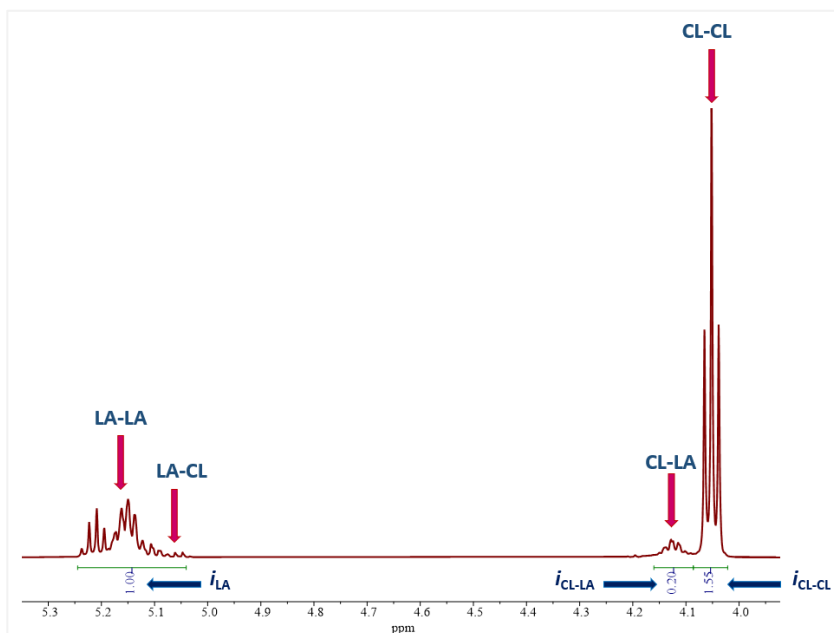


**Figure 6.7** Example  $^1\text{H}$  NMR spectrum of PCL-PLA-PCL copolymer generated with  $[\text{LZn}_2\text{Et}]$  (Chapter 2, Table 2.4, entry 1); where the relative integrals of diad resonances at 5.0 – 5.3 and 4.0 – 4.2 ppm were used for quantifying the randomness factor,  $R$ , and number-average sequence lengths,  $I$ . Note that another set of CL-LA linkage resonance resulting from transesterification appears at 2.37 ppm, which further confirmed these  $R$  and  $I$  values.<sup>134</sup>

The randomness factor,  $R$ , and number-average sequence lengths ( $I$ ) for CL and LA chain were calculated using the following equations:<sup>134</sup>

$$i_{\text{CL}} = i_{\text{CL-CL}} + i_{\text{CL-LA}} \quad \text{and} \quad i_{\text{LA}} = i_{\text{LA-LA}} + i_{\text{LA-CL}}$$

Where  $f_{\text{CL}}$  and  $f_{\text{LA}}$  are relative mole fractions of PCL and PLA in the copolymer, respectively.

$$f_{\text{CL}} = \frac{i_{\text{CL}}}{i_{\text{LA}} + i_{\text{CL}}} \quad \text{and} \quad f_{\text{LA}} = \frac{i_{\text{LA}}}{i_{\text{LA}} + i_{\text{CL}}}$$

Following this, the average diad relative molar fractions  $f_{\text{C-C}}$ ,  $f_{\text{C-L}}$ , and  $f_{\text{L-L}}$ , were calculated:

$$f_{\text{C-C}} = f_{\text{CL}} \times f_{\text{C-C/CL}}$$

$$f_{\text{C-L}} = f_{\text{CL}} \times f_{\text{C-L/CL}}$$

$$f_{L-L} = 1 - (f_{C-C} + f_{C-L})$$

Where,

$$f_{C-C/CL} = \frac{i_{CL-CL}}{i_{CL}} \quad \text{and} \quad f_{C-L/CL} = \frac{i_{CL-LA}}{i_{CL}}$$

Randomness factor,  $R$  and the number-average sequence length for CL and LA chain ( $l_{CL}$  and  $l_{LA}$ ) are calculated using the following equations:<sup>134</sup>

$$R = \frac{f_{C-L}}{2 \times f_{LA} \times f_{CL}}$$

$$l_{CL} = \frac{2f_{CL}}{f_{CL-LA}} \quad l_{LA} = \frac{2f_{LA}}{f_{CL-LA}}$$

## Chapter 7

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