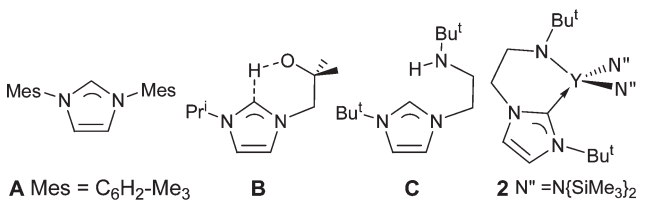
Bifunctional yttrium(III) and titanium(IV) NHC catalysts for lactide polymerisation†

Dipti Patel, Stephen T. Liddle, Shaheed A. Mungur, Mark Rodden, Alexander J. Blake and Polly L. Arnold*

Received (in Cambridge, UK) 10th October 2005, Accepted 13th January 2006
First published as an Advance Article on the web 25th January 2006
DOI: 10.1039/b514406j

Lewis acidic yttrium(III) and titanium(IV) derivatives of anionic, metal-tethered carbenes apparently act as bifunctional catalysts for the polymerisation of D,L-lactide, using a combination of Lewis acid and base functionalities to initiate ring opening of the cyclic monomer; the alcohol- and amino-functionalised carbenes from which they derive provide models for the first insertion step, and also display metal-free polymerisation catalysis to generate polylactic acid.

In addition to their traditional role in late metal chemistry, N-heterocyclic carbenes (NHCs) of the form **A** are increasingly being used as additives to enhance the reactivity of Lewis acidic homogeneous catalysts.[1–3] NHCs with simple hydrocarbyl N-substituents are also effective nucleophilic catalysts in their own right, for example catalysing the polymerisation of lactide to polylactic acid, PLA.[4,5] Polylactide polymers are biodegradable, bioresorbable and available from renewable feedstocks, and thus useful as future alternatives to polyethylene, and in medical materials applications.[6,7] Therefore, the control of their physical properties by using cheap, non-toxic polymerisation catalysts to tune the polymer molecular weights and stereochemistry is a desirable goal. Metal alkoxides are the most common catalysts currently used,[8–10] while metal-free catalysts offer the potential for cheap and particularly environmentally friendly catalysis.[11,12] The mechanism of catalysis by NHCs is presumed to involve NHC activation of the monomer, followed by addition of an equivalent of benzyl alcohol initiator to form the ring-opened adduct from which polymerisation continues, releasing the NHC.[13] Whilst anionic or strongly nucleophilic promoters (such as NHCs) give high activities, they have been less investigated than the metal alkoxides, due to concerns that they will also catalyse damaging transesterification,[14] and racemisation side-reactions when the initiator is re-released in solution.



University of Nottingham, University Park, Nottingham, UK NG7 2RD. E-mail: polly.arnold@nottingham.ac.uk; Fax: +44 115 9513563
† Electronic supplementary information (ESI) available: Characterising data and polymerisation data for complexes and polymers. See DOI: 10.1039/b514406j

Recently, two metal NHC complexes have been reported as D,L-lactide polymerisation catalysts. One, (1-ethyl-3-methylimidazol-2-ylidene)silver(I) chloride, is thermally decomposed to liberate the NHC as the active catalyst,[15] while the other, $[Zn(C\{NMesCH\}_2)(OBz)(\mu_2\text{-}OBz)]_2$ uses a bound NHC to control the reactivity, although the results do not rule out a catalytic contribution from a small amount of free NHC present.[16] To date there have been no reports of the use of asymmetric NHC-based ligands in metal-based initiators for the polymerisation of lactide, or the incorporation of NHCs into bifunctional catalysts—single-component catalysts that activate both substrates in a reaction.

We have been studying the use of anionic functional groups pendant to the NHC to provide a 'tether' by which an electropositive metal may be bound more strongly to the soft carbene centre, *e.g.* **2**.[17–19]

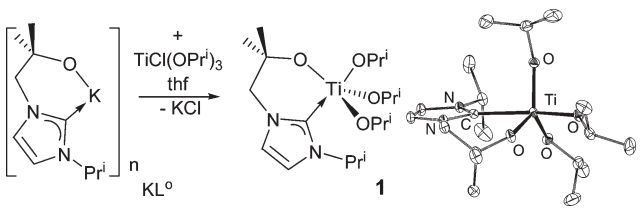
Herein, we report the synthesis of the first tethered titanium alkoxy-NHC complex, and show how this and the related yttrium complex **2** can act as bifunctional catalysts[20–22] for lactide polymerisation, using both Lewis acid and base functionalities to initiate ring opening. The free ligands **B** and **C** provide models for the first insertion step, and also display metal-free catalysis.

Treatment of $[TiCl(OPr^i)_3]$ with an equivalent of KL^O affords the colourless titanium alkoxide $[Ti(L^O)(OPr^i)_3]$ **1**, in moderate yield, Scheme 1, confirmed by NMR spectroscopy, elemental analysis and a single crystal X-ray diffraction study, see ESI.‡ The complex is remarkably air stable, and may be sublimed in good yield (10^{-3} mbar, 80 °C).

The chemical shift of the carbenic carbon in **1** is 189.5 ppm. This compares with a shift of 198.7 for HL^O (**B**) and 185.8 ppm for **2**.[19] The titanium–carbon distance of 2.293(2) Å lies at the long end of the range of reported titanium(IV) alkyl distances but is similar to the values of the four previously reported Ti–C_{NHC} complexes.[23]

The activities of **1**, **2**, the zwitterionic proligand **B**, and aminocarbene ligand **C**, as catalysts for the polymerisation of D,L-lactide are collated in Table 1.

If the carbenic carbon is available to react as a nucleophilic initiator, both **B** and **C** could catalyse the polymerisation



Scheme 1 Synthesis, and displacement ellipsoid drawing of **1** (50% probability).

Table 1 Activity of complexes for D,L-lactide polymerisation

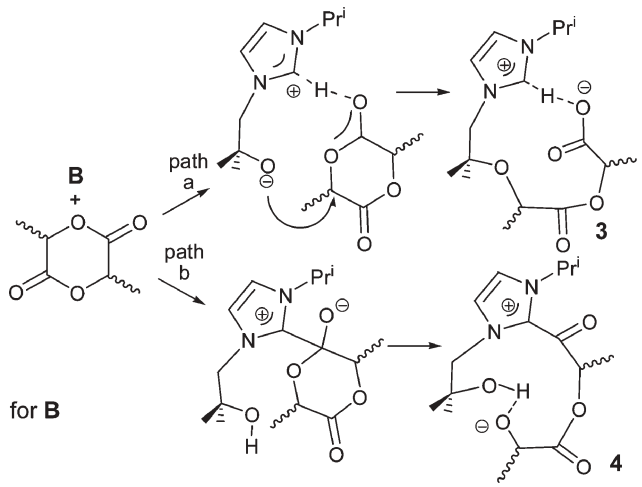
Run	Complex (+initiator = I)	Catalyst : I : monomer	Time/min	Yield (%)	MW	PDI
1	HL^O (**B**)	5 : 0 : 100	5	100	27 100	1.46
2	HL^N (**C**)	1 : 0 : 100	15	100	45 000	1.29
3	**1**	1 : 0 : 100	1	60	1800	1.19
4	**1**	1 : 0 : 100	2	85	2300	1.17
5	**1**	5 : 0 : 100	24 h	65	3600	1.05
6	**1a**	5 : 0 : 100	24 h	72	3500	1.05
7	**2**	1 : 0 : 10 000	15	85	66 000	1.47
8	**2**	1 : 0 : 100	0.18	60	65 000	1.19
9	**2**	1 : 0 : 100	2	75	77 000	1.19
10	**2**	4 : 0 : 100	60	100	28 000	1.53
11	**A** + I	1 : 1.5 : 200	0.25	85	>25 000	1.18
12	**C** + I[a]	1 : 0.5 : 100	15	100	8900	1.25
13	**2** + I	1 : 0.5 : 100	2	75	7400	1.20[b]

[a] I = $PhCH_2OH$; data for **A** from ref. 13. [b] Determined for the polymer sample corresponding to the higher molecular weight portion of the bimodal GPC trace.

reaction.[24] Additionally, **B** could also behave as an alkoxide initiator for polymerisation.[17] Interestingly, the reaction of **B** with one equivalent of D,L-lactide in thf, pyridine or toluene affords two compounds, Scheme 2.

These are identified as the coordination insertion product **3** (HL^O behaving as an alkoxide initiator, path a), and the carbene attack product **4** (HL^O behaving as a carbene nucleophile initiator, path b). Due to the greater disparity in the acidity of the amine and NHC functional groups compared with **B**, **C** behaves chemically more like a carbene, and forms only the analogous 'path b' product, *i.e.* the amine carbene analogue of **4**.

Despite the lower activity of **B** as a catalyst, sequential additions of up to five monomer equivalents clearly show the beginning of chain growth from **4**, forming polymers with an imidazolium end group, as determined by MALDI mass spectrometry. Further, **B** exhibits moderate activity as a catalyst at loadings of 5 mol%.[25] The amine **C** also generates polylactide with high molecular weights after one hour at room temperature. The relative rates are in accord with our previous observations that **B** exists as a hydrogen-bonded structure, a more inert resting state than exists for **C**. At low catalyst loading (1 mol%) both the molecular weight and the distribution are comparable to that of a sample of **A** with added benzyl alcohol initiator, but neither **B** nor **C** requires an additional equivalent of alcohol promoter to form the ring-opened adduct. Catalyst **C** retains its activity with the inclusion of 0.5 mol% of benzyl alcohol but the polymer molecular weights are significantly lower, and the GPC trace shows a bimodal distribution of polymer, so the polymer is poorly defined.

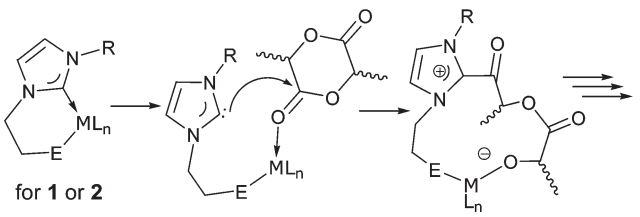


Scheme 2

The titanium complex **1** initially displays fast polymerisation catalysis at room temperature, which is more controlled than that of the ligand **B** for the first minute, after which the molecular weight distribution becomes bimodal, so resultant polymers are poorly defined (see ESI†). Complex **1** is more active than its precursor $[TiCl(OPr^i)_3]$, which requires higher temperatures.[26]

The distribution of polymer weights (PDI) for PLA made by **1** becomes broader with increased reaction time; this is not due to a mixture of alkoxide and labilised NHC initiation sites. MALDI mass spectrometric analysis of the polymer shows clearly that all chains are terminated by an imidazolium group (from the NHC). Thus the ring-opening initiation is exclusively by nucleophilic attack by the NHC group, and **1** must also be catalysing deleterious transesterification processes throughout the chain growth reaction. A further 100 equivalents of monomer are polymerised by a sample of **1**·polymer when added 48 h later. Catalyst **1** functions as a masked, and thus highly water and air-stable, source of an NHC. This is supported by another comparison with a titanium complex of L^N isolated in our laboratory, **1a** (see ESI†) $[Ti(L^N)(OPr^i)_2Br]$, which even at 5% loading, shows extremely good control over the polydispersity during monomer polymerisation up to about 75% conversion, but is very slow, and only generates polymers with molecular weights of 3500 after 24 h, Table 1 entry 6.[27]

The more Lewis acidic yttrium complex **2** exhibits faster catalysis than **1**, to make higher molecular weight polymers compared with **C**, with much greater conversions achieved than with **1** before the onset of deleterious side-reactions. Complex **2** is extremely active even at very low—0.01%—concentrations. The polydispersity is very narrow for the polymer made by **2**, even after the majority of the monomer feedstock has been exhausted. ^1H and ^{13}C HETCOR NMR analysis shows the polymer to be highly regular heterotactic poly(*rac*-lactide). The addition of benzyl alcohol as a protic initiator drastically reduces the activity and polydispersity control of **2**, consistent with a change in the mechanism which is normally observed in Lewis acid-catalysed ring opening polymerisations.[28]



Scheme 3

The activity difference between **1** and **2** cannot be explained by differences in the ability to eliminate a carbene ligand, but we know from competition experiments with a range of substrates that the NHC is more labile at Y(III) than Ti(IV) (see ESI and ref. 19). Most simply, as described in Scheme 3, **2** is the most capable of functioning as a combined Lewis acid and Lewis base, or bifunctional catalyst, in order to hold the monomer and initiate chain growth. It is germane to compare this behaviour with that of a bifunctional organocatalyst originally designed for Michael additions,[29] which was very recently shown also to act as a bifunctional catalyst for lactide polymerisation.[11] The compound, $ArNHCSNH(C_6H_4\text{-}2\text{-}NMe_2)$ combines a hydrogen bonding thiourea group which activates the lactide monomer, and a Brønsted basic tertiary amino group which activates the initiating benzyl alcohol and gives excellent selectivity for polymerisation over transesterification. In our yttrium system **2**, (without alcohol initiator) the Lewis acidic metal coordinates the lactide, and the labilised NHC functions as the ring-opening nucleophile.

In summary, the data for the metal complexes suggest a bifunctional catalyst system, Scheme 3. This combines an initiating nucleophilic attack on the metal-coordinated monomer by the labilised carbene, followed by coordination insertion polymerisation of the rest of the lactide monomer. The most effective combination of 'protected' hemilabile NHC and Lewis acidic metal is provided by the Y(III) complex **2**, suggesting that further chain growth occurs *via* monomer insertion at the metal.

Comparison of the functionalised organic NHC compounds **B** and **C** demonstrate that the more accessible carbene centre affords a more active nucleophilic catalyst. This provides a new opportunity to control the activation and polymerisation of a polar monomer. Work is now in progress to measure the catalytic activities of complexes of chiral variants of **B** and **C**.[3]

We thank Dr M. F. Wyatt from the EPSRC National Mass Spectrometry service for the MALDI data, the EPSRC (PLA, STL, SAM, MR, and funding for a diffractometer), the Nuffield Foundation, and the Royal Society.

Notes and references

‡ Analytically pure $Ti(OPr^i)_3L^O$ is a waxy colourless solid which can be sublimed (80 °C, 10^{-3} mbar), and manipulated briefly in air as a solid. Anal. calcd. for $C_{19}H_{38}N_2O_4Ti$: C, 56.15; H, 9.42; N, 6.89. Found: 56.25; H, 9.39; N, 6.96. Monoclinic, $P2_1/n$ a = 9.389(2), b = 14.878(3), c = 17.833(4) Å, β = 104.608(3)°, V = 2410.6(15) Å^3, μ = 0.377 mm^{-1}, Z = 4 D_x = 1.120 Mg m^{-3} 5486 independent reflections. Final R_1 [3875 $F > 4\sigma(F)$] = 0.0479 and wR(all F^2) was 0.137. CCDC 279173. For crystallographic data in CIF or other electronic format see DOI: 10.1039/b514406j

1 W. A. Herrmann, *Angew. Chem., Int. Ed.*, 2002, **41**, 1290.
2 R. W. Alder, M. E. Blake, L. Chaker, J. N. Harvey, F. Paolini and J. Schutz, *Angew. Chem., Int. Ed.*, 2004, **43**, 5896.
3 P. L. Arnold, M. Rodden, K. M. Davis, A. C. Scarisbrick, A. J. Blake and C. Wilson, *Chem. Commun.*, 2004, 1612.
4 S. Csihony, D. A. Culkin, A. C. Sentman, A. P. Dove, R. M. Waymouth and J. L. Hedrick, *J. Am. Chem. Soc.*, 2005, **127**, 9079.
5 E. F. Connor, G. W. Nyce, M. Myers, A. Mock and J. L. Hedrick, *J. Am. Chem. Soc.*, 2002, **124**, 914.
6 M. H. Chisholm and Z. P. Zhou, *J. Mater. Chem.*, 2004, **14**, 3081.
7 O. Dechy-Cabaret, B. Martin-Vaca and D. Bourissou, *Chem. Rev.*, 2004, **104**, 6147.
8 E. L. Marshall, V. C. Gibson and H. S. Rzepa, *J. Am. Chem. Soc.*, 2005, **127**, 6048.
9 L. F. Zhang, Z. Q. Shen, C. P. Yu and L. Fan, *J. Mol. Catal. A: Chem.*, 2004, **214**, 199.
10 R. D. Kohn, Z. D. Pan, J. Q. Sun and C. F. Liang, *Catal. Commun.*, 2003, **4**, 33.
11 A. P. Dove, R. C. Pratt, B. G. G. Lohmeijer, R. M. Waymouth and J. L. Hedrick, *J. Am. Chem. Soc.*, 2005, **127**, 13798.
12 M. Myers, E. F. Connor, T. Glauser, A. Mock, G. Nyce and J. L. Hedrick, *J. Polym. Sci., Part A: Polym. Chem.*, 2002, **40**, 844.
13 G. W. Nyce, T. Glauser, E. F. Connor, A. Mock, R. M. Waymouth and J. L. Hedrick, *J. Am. Chem. Soc.*, 2003, **125**, 3046.
14 G. W. Nyce, J. A. Lamboy, E. F. Connor, R. M. Waymouth and J. L. Hedrick, *Org. Lett.*, 2002, **4**, 3587.
15 A. C. Sentman, S. Csihony, R. M. Waymouth and J. L. Hedrick, *J. Org. Chem.*, 2005, **70**, 2391.
16 T. Jensen, L. Breyfogle, M. Hillmyer and W. Tolman, *Chem. Commun.*, 2004, 2504.
17 P. L. Arnold, M. Rodden and C. Wilson, *Chem. Commun.*, 2005, 1743.
18 S. T. Liddle and P. L. Arnold, *Organometallics*, 2005, **24**, 2597.
19 P. L. Arnold, S. A. Mungur, A. J. Blake and C. Wilson, *Angew. Chem., Int. Ed.*, 2003, **42**, 5981.
20 M. Shibasaki, M. Kanai and K. Funabashi, *Chem. Commun.*, 2002, 1989.
21 H. Groger, *Chem.–Eur. J.*, 2001, **7**, 5246.
22 M. S. Shibasaki and H. T. Arai, *Angew. Chem., Int. Ed. Engl.*, 1997, **36**, 1236.
23 P. Shukla, J. A. Johnson, D. Vidovic, A. H. Cowley and C. D. Abernethy, *Chem. Commun.*, 2004, 360.
24 S. Csihony, T. T. Beaudette, A. C. Sentman, G. W. Nyce, R. M. Waymouth and J. L. Hedrick, *Adv. Synth. Catal.*, 2004, **346**, 1081.
25 *N.B.*, after consumption of the monomer and standing for 5 h, the analysed polymer has a poorly defined molecular weight distribution due to subsequent transesterification reactions.
26 J. G. Verkade and J. Kindel, *US Pat.*, 2005/0009687 A1, 2005.
27 S. A. Mungur, A. J. Blake, C. Wilson, J. McMaster and P. L. Arnold, *Organometallics,* 2006, in press.
28 H. Y. Ma and J. Okuda, *Macromolecules*, 2005, **38**, 2665.
29 T. Okino, Y. Hoashi and Y. Takemoto, *J. Am. Chem. Soc.*, 2003, **125**, 12672.

