Dalton Transactions

PAPER

View Article Online
View Journal | View Issue

Cite this: *Dalton Trans.*, 2014, **43**, 12095

Synthesis and characterisation of unsymmetrical Zr(IV) amine tris(phenolate) complexes and their application in ROP of *rac*-LA†

Thomas R. Forder,[a,b] Mary F. Mahon,[a] Matthew G. Davidson,[a] Timothy Woodman[c] and Matthew D. Jones*[a]

Received 29th April 2014,
Accepted 24th June 2014

DOI: 10.1039/c4dt01260g

www.rsc.org/dalton

Unsymmetrical amine tris(phenolate) ligands have been prepared and complexed to Zr(IV). In the solid-state dimeric species are observed, which persist in solution. The complexes show interesting coordination chemistry and the nature of which is discussed. These complexes are analogues of a highly stereoselective C_3-symmetric Zr(IV) amine tris(phenolate) alkoxide and have been prepared, characterised and trialled for the ring-opening of *rac*-lactide providing insight into the effect of symmetry and ligand steric bulk on selectivity. The polymerisations have been investigated in solution and under the industrially preferred melt conditions (130 °C). The rate law for the ROP has been determined – with $Zr_2(\mathbf{1})_2(O^iPr)_2$, a pseudo first order dependency was seen, however for $Zr_2(\mathbf{2})_2(O^iPr)_2$ this changed to a half order dependency in initiator.

Introduction

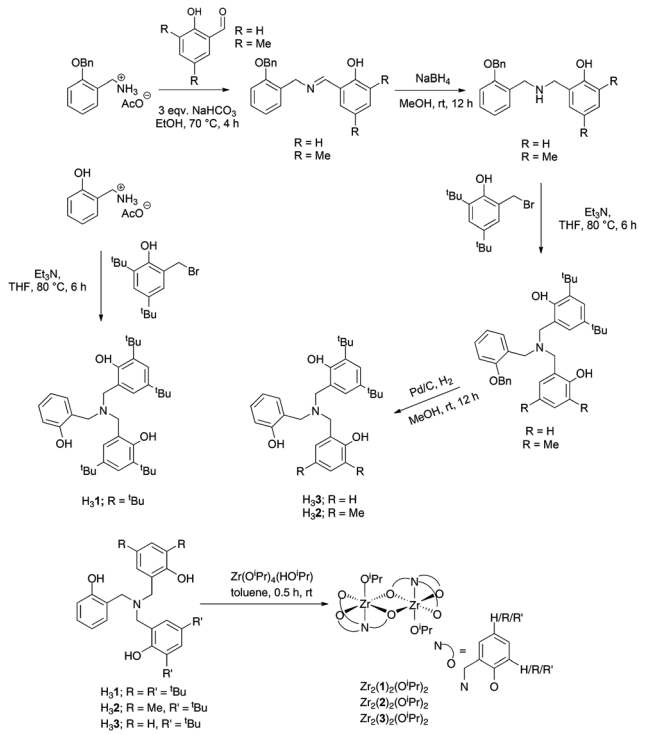
The controlled ring-opening polymerisation (ROP) of *rac*-lactide (*rac*-LA) through the use of stereo-selective metal alkoxides has received continued interest due to the ability to produce polymeric material with well-defined thermal and mechanical properties.[1] Such control provides one route to widening the potential applications of this environmentally favourable renewable plastic.[2–6] The polymer itself (PLA) has found many uses from packing material to high value biomedical applications.[7] There are numerous examples in the literature of discrete metal complexes that are efficient (in terms of molecular weight control and tacticity). Examples of stereo-selective initiators vary significantly in both metal centre and ligand architecture.[8–15] Whilst recent publications have shown that for some metal–ligand systems it is possible to switch from isotactically- to heterotactically-enriched polylactide by altering ligand structure,[16,17] it is on the whole difficult to predict selectivity without potentially arduous and time consuming synthesis and polymerisation trials. Group 4 metals initiators are an important class of complexes for the controlled ROP of cyclic esters.[18] For example, Group 4 amine tris(phenolate) complexes have received considerable interest for their structure and reactivity for ROP of *rac*-LA.[19–22] A C_3-symmetric Zr(IV) amine tris(phenolate) alkoxide has previously been shown to be extremely active for the controlled ROP of *rac*-LA, yielding highly heterotactic polylactide.[19] This metal complex has been shown to have a C_3-symmetric propeller-like arrangement similar to that for other amine tris(phenolate) complexes and can undergo axial flipping between the *P* and *M* enantiomers.[21,23] Complexes with such ligands are prevalent in the literature;[24–26] however there are no examples of unsymmetrical variants.

Results and discussion

Metal complex synthesis

To further understand the influence of initiator symmetry and steric bulk of the ligand, a systematic alteration of ligand architecture was carried out to remove symmetry and provide stepwise removal of the sterically-bulky substituents about the metal centre. Unlike the one-pot synthesis of the aforementioned amine tris(phenolate) *via* a modified Mannich reaction,[21] one unsymmetrical analogue ($H_3\mathbf{1}$) had to be accessed through the utilisation of a salicylammonium salt and a 3,5-disubstituted salicylbromide. Synthesis of amine tris(phenolate) ligands with further removal of steric bulk or a fully unsymmetrical structure ($H_3\mathbf{2}$–$\mathbf{3}$) required utilising a benzyl-protected imine bis(phenolate) intermediate.† $Zr(O^iPr)_4$-

[a]*Department of Chemistry, University of Bath, Claverton Down, Bath BA2 7AY, UK. E-mail: mj205@bath.ac.uk; Fax: +44 (0)1225 386231; Tel: +44 (0)1225 384908*
[b]*Doctoral Training Centre in Sustainable Chemical Technologies, University of Bath, Bath BA2 7AY, UK*
[c]*Department of Pharmacy and Pharmacology, University of Bath, Bath BA2 7AY, UK*
† Electronic supplementary information (ESI) available: Full characterisation and experimental procedures. CCDC 959185 and 959186. For ESI and crystallographic data in CIF or other electronic format see DOI: 10.1039/c4dt01260g



Scheme 1 Synthesis of unsymmetrical Zr(IV) amine tris(phenolate) complexes and ligands.

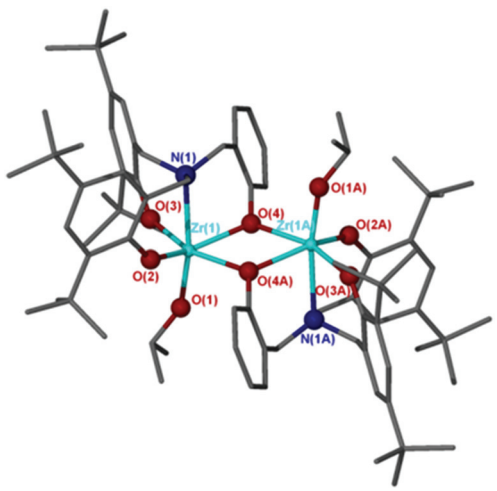


Fig. 1 Molecular structure for $Zr_2(\mathbf{1})_2(O^iPr)_2$: hydrogen atoms, lattice solvent and ligand disorder have been removed for clarity.

(HO^iPr) was coordinated with 1 eq. of $H_3\mathbf{1}$–$\mathbf{3}$ to yield dimeric complexes $Zr_2(\mathbf{1})_2(O^iPr)_2$, $Zr_2(\mathbf{2})_2(O^iPr)_2$ and $Zr_2(\mathbf{3})_2(O^iPr)_2$ respectively (Scheme 1).

The dimer motif was observed in the solid-state with the less-sterically demanding phenolate acting as a bridge between two metal centres (Fig. 1), the NMR spectra (in non-coordinating solvents) indicates that this structure is retained in solution.† Both Zr(IV) centres are six-coordinate and adopt a pseudo-octahedral geometry. As with the C_3-symmetric monomeric complex, the nitrogen donor and alkoxide remain in an axial orientation.[19] Contrary to the monomeric species, the dimer motif is not fluxional and the rigid structure results in the six protons of the methylene bridges of each ligand appearing as discrete diastereotopic doublets in the ^{1}H NMR spectrum.† When the ^{1}H NMR spectrum for $Zr_2(\mathbf{1})(O^iPr)_2$ was run in d_8-THF, at an elevated temperature (333 K), two doublets and a singlet were observed for the methylene bridges, indicating that the complex can be broken down in a coordinating solvent to form a monomeric species.† Interestingly, from solution-state DOSY NMR spectroscopic analysis the hydrodynamic volume of $Zr_2(\mathbf{1})_2(O^iPr)_2$ was 635 Å^3 (*cf.* 505 Å^3 for the C_3 symmetric monomer complex[19] and 606 Å^3 for $Zr_2(\mathbf{3})_2(O^iPr)_2$ – in d^8-Tol). When the DOSY was recoded in d^8-THF, which is believed to break the dimer into a monomer, for $Zr_2(\mathbf{1})_2(O^iPr)_2$ the hydrodynamic volume is 493 Å^3, analogous to the known monomeric species.

Discerning dimer motifs

For $Zr_2(\mathbf{2})_2(O^iPr)_2$ and $Zr_2(\mathbf{3})_2(O^iPr)_2$ analysis of the ^{1}H NMR spectra indicated the presence of multiple sets of diastereotopic doublets, which presumably are due to three possible isomers for this motif (Fig. 2). With a restriction that an unsubstituted phenolate would adopt the bridging role, the dimer can consist of an enantiomeric pair (Λ,Δ) that requires the ^{t}Bu-substituted phenolate arms to adopt a transoid arrangement across the dimer (Fig. 2a and b). For the ^{t}Bu-substituted arms to be arranged cisoid the dimer must consist of a Λ,Λ or Δ,Δ pairing (Fig. 2c).

Geometry can be further distinguished by the arrangement of the ^{t}Bu-substituted phenolate arm with respect to the bridging phenolate arm of the same ligand. This leads to the resolution of two forms of the transoid dimer (Fig. 2a and b) whereas the cisoid dimer arrangement requires there to always be a *trans*/*cis* pairing. Through variable temperature (208 K–358 K) ^{1}H NMR spectroscopy it was determined that these isomers are not exchanging, providing further evidence of the non-fluxional nature of the dimer motif.† We have further prepared $H_3\mathbf{2}$ and subsequent $Zr_2(\mathbf{2})_2(O^iPr)_2$ (Fig. 3) in which each arm of the tris(phenolate) is differently substituted.

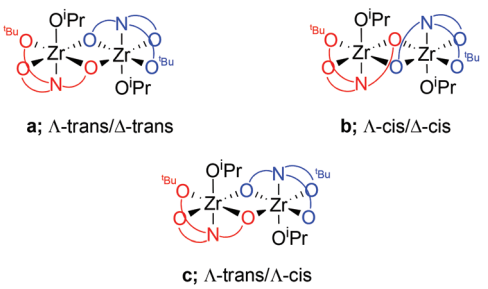


Fig. 2 Possible isomers for the dimer $Zr_2(\mathbf{3})_2(O^iPr)_2$. Methylene bridges, phenolates and substituents have been pictorially represented for clarity. ^{t}Bu annotation indication which phenolate arm is di-^{t}Bu-substituted. Only one enantiomer for each isomer is shown for clarity.

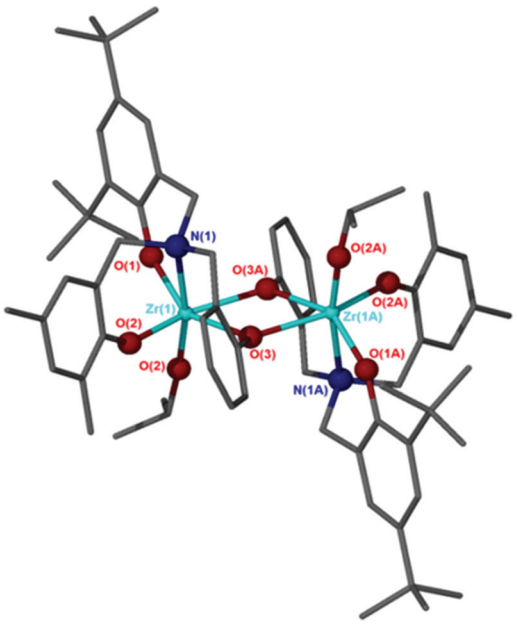


Fig. 3 Molecular structure for $Zr_2(\mathbf{2})_2(O^iPr)_2$: hydrogen atoms, lattice solvent and ligand disorder have been removed for clarity.

Polymerisation of *rac*-lactide

Complexes $Zr_2(\mathbf{1–3})_2(O^iPr)_2$ were tested for the ROP of *rac*-LA under solvent free conditions and compared with that previously reported for the C_3-symmetric analogue (Table 1).[18] All initiators showed high activity with comparable conversion to the C_3-symmetric analogue being achieved in under 30 minutes under industrially-relevant melt conditions.

Analysis of the polymer microstructure by homonuclear decoupled ^{1}H NMR spectroscopy revealed that heterotactic-enriched PLA was obtained for $Zr_2(\mathbf{1–3})_2(O^iPr)_2$ with no significant difference in selectivity between each initiator ($P_r \approx 0.7$, Table 1). Polymeric material produced in solution (toluene, 0.5 M) at a lower reaction temperature was found to have similar or lower heterotactic enrichment. Analysis of polymeric material using size-exclusion chromatography (SEC) found that polymer weight distribution ($Đ$) increased with further removal of sterically-bulky ligand substituents and that, compared to the C_3-symmetric analogue, molecular weight control was lost. MALDI-ToF MS of the polymer from $Zr_2(\mathbf{3})_2(O^iPr)_2$ indicated the presence of the H- and O^iPr end groups, as expected from the coordination insertion mechanism.†

Table 1 Polymerisation data for *rac*-LA with initiators $Zr_2(\mathbf{1–3})_2(O^iPr)_2$

Initiator	Time (h)	Conv.[c] (%)	M_n [d]	$Đ$[d]	P_r [e]
C_3-symm. Zr[18]	0.1	78	32 300	1.22	0.96
$Zr_2(\mathbf{1})_2(O^iPr)_2$ [a]	0.5	76	66 900	1.40	0.72
$Zr_2(\mathbf{2})_2(O^iPr)_2$ [a]	0.5	80	19 100	1.54	0.71
$Zr_2(\mathbf{3})_2(O^iPr)_2$ [a]	0.5	87	41 900	1.76	0.70
$Zr_2(\mathbf{1})_2(O^iPr)_2$ [b]	1	94	22 500	1.54	0.64
$Zr_2(\mathbf{2})_2(O^iPr)_2$ [b]	3	65	20 300	1.08	0.65
$Zr_2(\mathbf{3})_2(O^iPr)_2$ [b]	3	50	9750	1.08	0.69

Conditions: [a] [M]/[I] = 300, 130 °C, solvent free. [b] Solution (toluene) [M]/[I] = 100, 80 °C ($[M]_0$ = 0.5 mol dm^{-3}). [c] As determined *via* ^{1}H NMR spectroscopy. [d] Determined from GPC (in THF) referenced to polystyrene. [e] P_r is the probability of racemic enchainment, calculated from the ^{1}H homonuclear decoupled NMR spectra.

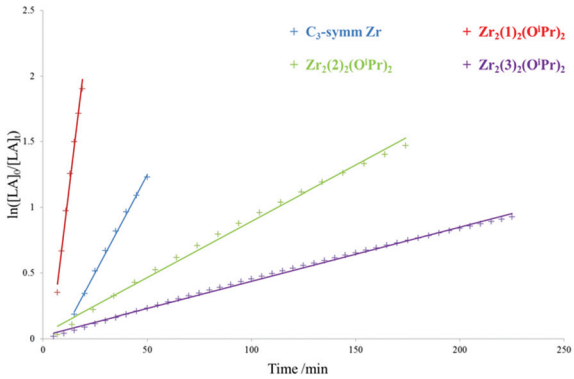


Fig. 4 First order plots for $\ln([LA]_o/[LA]_t)$ *versus* time using $Zr_2(\mathbf{1–3})_2(O^iPr)_2$ and the C_3-symmetric analogue (toluene-d_8, 353 K, $[LA]_0$ = 0.50 M, [M]/[I] = 100).

Solvent-based kinetic studies for the ROP of *rac*-LA were carried out in toluene-d_8 at 253 K for complexes $Zr_2(\mathbf{1–3})_2(O^iPr)_2$ and compared with the C_3-symmetric analogue. All polymerisations were found to be first order with respect to monomer (Fig. 4). Under the conditions used a first order rate constant (k_{app}) of 3.0×10^{-2} min^{-1} was found for the C_3-symmetric Zr(IV) amine tris(phenolate) complex (*cf.* 1.4×10^{-2} min^{-1} for L-LA). A larger rate constant of 13.0×10^{-2} min^{-1} was observed for $Zr_2(\mathbf{1})_2(O^iPr)_2$ whilst pseudo first-order plots for the polymerisation of *rac*-LA initiated by $Zr_2(\mathbf{2})_2(O^iPr)_2$ and $Zr_2(\mathbf{3})_2(O^iPr)_2$ identified relatively lower rate constants of 0.86×10^{-2} and 0.41×10^{-2} min^{-1} respectively. Compared to the C_3-symmetric complex, removal of the ^{t}Bu substituents from one arm of the amine tris(phenolate) ligand to yield $Zr_2(\mathbf{1})_2(O^iPr)_2$ increases the relative rate of polymerisation of *rac*-LA. Further removal of steric bulk to $Zr_2(\mathbf{2})_2(O^iPr)_2$ and subsequently $Zr_2(\mathbf{3})_2(O^iPr)_2$ leads to a lowering in rate below that observed for the C_3-symmetric analogue (Fig. 4).

It was deemed reasonable to assume that the ROP-active species of $Zr_2(\mathbf{1–3})_2(O^iPr)_2$ would not be dimeric; due to the lactide coordination step required in both initiation and propagation.[27] To further investigate the polymerisation kinetics and mechanism k_{app} was determined for a variety of initiator concentrations and a plot of $\ln k_{app}$ *vs.* $\ln[I]_0$ was used to determine the order of the process with respect to the initiator, and hence the rate law $-d[LA]/dt = k[LA]^1[I]^x$ (Fig. 5). Gradients of each linear plot indicated that, as expected, order with respect to the monomeric C_3-symmetric zirconium initiator to be pseudo first-order (x = 1.05). The order with respect to initiator for $Zr_2(\mathbf{1})_2(O^iPr)_2$ was also essentially first order (x = 1.22), whilst for $Zr_2(\mathbf{3})_2(O^iPr)_2$ it was found to be of half order dependency (x = 0.43).

^{1}H NMR spectroscopic studies of $Zr_2(\mathbf{1})_2(O^iPr)_2$ in a coordinative solvent (THF-d_8) at an elevated temperature of 333 K, found that the AX spin system for the diastereotopic protons

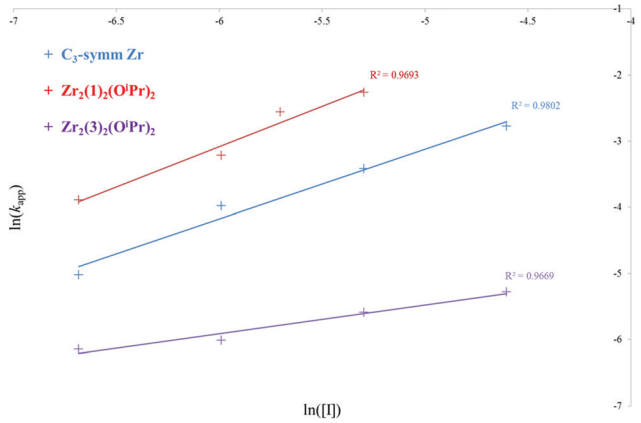


Fig. 5 ln–ln plots for determining reaction order with respect to initiator for $Zr_2(\mathbf{1})_2(O^iPr)_2$, $Zr_2(\mathbf{3})_2(O^iPr)_2$ and the C_3-symmetric analogue (toluene-d_8, 353 K, $[LA]_0$ = 0.50 M, [M]/[I] = 50, 100, (150), 200, 400).

of the methylene bridges are no longer observed. This is attributed to dissociation of the dimer species due to coordination of THF to the metal centre.† Furthermore, whilst heating to 333 K appeared to disrupt the AX spin system, upon cooling the system was not re-established suggesting, for $Zr_2(\mathbf{1})_2(O^iPr)_2$ at least, a barrier to both coordination and reformation of the dimer. The ROP of lactide *via* a coordination-insertion method requires the initial coordination of the lactide to the metal centre. We therefore suggest that the ROP-active form of these dimer complexes is a discreet monomeric five-coordinate complex, akin to that observed for the C_3-symmetric analogue.

Implications for reactivity and stereochemistry

The high heteroselectivity previously reported for the C_3-symmetric Zr(IV) amine tris(phenolate) complex has been attributed to dynamic enantiomorphic site control due to "flipping" of the propeller geometry about the C_3 axis.[19,28,29] $Zr_2(\mathbf{1})_2(O^iPr)_2$ offers an active species that removes the C_3-symmetry yet maintains considerable steric bulk about the metal centre. A significant drop in selectivity is observed with this removal of C_3-symmetry, whilst further removal of steric bulk has no significant further effect on the stereoselectivity {$Zr_2(\mathbf{1})_2(O^iPr)_2$ *vs.* $Zr_2(\mathbf{3})_2(O^iPr)_2$}. These observations provide further support for the origin of stereoselectivity in ROP of lactide by C_3-symmetric complexes. The lack of higher stereoselectivity for $Zr_2(\mathbf{1})_2(O^iPr)_2$ and $Zr_2(\mathbf{3})_2(O^iPr)_2$ at a lower temperature in solution suggests the preferable enantiomeric pairing of the *P*/*M* axial chirality and *RR*/*SS* chain-end stereochemistry as previously presented in the literature[29] is not present for these unsymmetrical analogues.

Polymeric material produced through the ROP of *rac*-LA initiated by $Zr_2(\mathbf{1–3})_2(O^iPr)_2$ has a higher polydispersity than that observed for the C_3-symmetric analogue. It is proposed that this is a combination of the reduced steric bulk about the metal centre allowing for an increased rate in undesirable transesterification[15] reactions and a potentially slower initiation step of the polymerisation due to the requirement for the dimer to dissociate into the active monomeric species.

It is also possible that removal of the steric bulk for these amine tris(phenolate) complexes would increase the rate of polymerisation due to the greater ease of coordination of lactide.[15,30] Whilst this is the case for $Zr_2(\mathbf{1})_2(O^iPr)_2$ it is not the case for $Zr_2(\mathbf{2–3})_2(O^iPr)_2$ as activity is reduced. Half order dependency has been previously reported by Mountford *et al.* for a dimeric zinc species and attributed to aggregation a catalytically active monomeric species during the ROP of ε-caprolactone.[31] Whilst for the previously published zinc species, the dimer–monomer equilibrium is caused by the benzyl alcohol co-initiator, herein we propose that dissociation is caused by the coordination of the lactide monomer. For both $Zr_2(\mathbf{1})_2(O^iPr)_2$ and $Zr_2(\mathbf{3})_2(O^iPr)_2$, the dimer is disrupted and a propagating lactidyl alkoxide species generated; the less-sterically hindered $Zr_2(\mathbf{3})_2(O^iPr)_2$ can aggregate back to a ROP-inactive dimer whilst $Zr_2(\mathbf{1})_2(O^iPr)_2$ does not. The observed trend in kinetics can be attributed to the relative reduction in steric bulk in close proximity to the metal centre (C_3-symm. Zr → $Zr_2(\mathbf{1})_2(O^iPr)_2$) coupled with the potential of the propagating species to aggregate ($Zr_2(\mathbf{1})_2(O^iPr)_2$ → $Zr_2(\mathbf{3})_2(O^iPr)_2$).

Conclusions

In summary we present a novel step-wise synthesis for the production of unsymmetrical amine tris(phenolate) ligands that when coordinated to Zr(IV) centres form dimeric complexes. Whilst interesting in their own right, they have been shown to be active for the ROP of lactide and have provided insight into the highly heterotactic selectivity previously published for a C_3-symmetric Zr(IV) amine tris(phenolate).[19] The investigation of reaction order with respect to initiator provides an interesting case study of the need to understand the potential nature and behaviour of ROP-active species when considering relative rates of polymerisation. Work is underway to utilise the step-wise ligand synthesis methodology to access Zr(IV) amine tris(phenolate) complexes that disrupt the C_3-symmetry *via* the increase in steric bulk of the phenolate substituents.

Acknowledgements

We wish to thank the EPSRC (EP/G03768X/1) for funding.

Notes and references

1 R. Auras, B. Harte and S. Selke, *Macromol. Biosci.*, 2004, **4**, 835–864.
2 M. Vert, *Biomacromolecules*, 2005, **6**, 538–546.
3 O. Dechy-Cabaret, B. Martin-Vaca and D. Bourissou, *Chem. Rev.*, 2004, **104**, 6147–6176.
4 C. K. Williams and M. A. Hillmyer, *Polym. Rev.*, 2008, **48**, 1–10.
5 N. Ajellal, J.-F. Carpentier, C. Guillaume, S. M. Guillaume, M. Helou, V. Poirier, Y. Sarazin and A. Trifonov, *Dalton Trans.*, 2010, **39**, 8363–8376.

6 R. J. Pounder and A. P. Dove, *Polym. Chem.*, 2010, **1**, 260–271.
7 A.-C. Albertsson and I. K. Varma, *Biomacromolecules*, 2003, **4**, 1466–1486.
8 J. Börner, U. Flörke, A. Döring, D. Kuckling, M. D. Jones, M. Steiner, M. Breuning and S. Herres-Pawlis, *Inorg. Chem. Commun.*, 2010, **13**, 369–371.
9 B. M. Chamberlain, M. Cheng, D. R. Moore, T. M. Ovitt, E. B. Lobkovsky and G. W. Coates, *J. Am. Chem. Soc.*, 2001, **123**, 3229–3238.
10 M. H. Chisholm, J. C. Gallucci and K. Phomphrai, *Inorg. Chem.*, 2004, **43**, 6717–6725.
11 R. A. Collins, J. Unruangsri and P. Mountford, *Dalton Trans.*, 2013, **42**, 759–769.
12 S. L. Hancock, M. D. Jones, C. J. Langridge and M. F. Mahon, *New J. Chem.*, 2012, **36**, 1891–1896.
13 P. Hormnirun, E. L. Marshall, V. C. Gibson, A. J. P. White and D. J. Williams, *J. Am. Chem. Soc.*, 2004, **126**, 2688–2689.
14 J. Okuda and J. C. Buffet, *Chem. Commun.*, 2011, **47**, 4796–4798.
15 E. L. Whitelaw, M. G. Davidson and M. D. Jones, *Chem. Commun.*, 2011, **47**, 10004–10006.
16 C. Bakewell, T.-P.-A. Cao, N. Long, X. F. Le Goff, A. Auffrant and C. K. Williams, *J. Am. Chem. Soc.*, 2012, **134**, 20577–20580.
17 A. Stopper, J. Okuda and M. Kol, *Macromolecules*, 2012, **45**, 698–704.
18 A. Sauer, A. Kapelski, C. Fliedel, S. Dagorne, M. Kol and J. Okuda, *Dalton Trans.*, 2013, **42**, 9007–9023.
19 A. J. Chmura, M. G. Davidson, C. J. Frankis, M. D. Jones and M. D. Lunn, *Chem. Commun.*, 2008, 1293–1295.
20 Y. Kim, G. K. Jnaneshwara and J. G. Verkade, *Inorg. Chem.*, 2003, **42**, 1437–1447.
21 M. Kol, M. Shamis, I. Goldberg, Z. Goldschmidt, S. Alfi and E. Hayut-Salant, *Inorg. Chem. Commun.*, 2001, **4**, 177–179.
22 S. Gendler, S. Segal, I. Goldberg, Z. Goldschmidt and M. Kol, *Inorg. Chem.*, 2006, **45**, 4783–4790.
23 M. G. Davidson, C. L. Doherty, A. L. Johnson and M. F. Mahon, *Chem. Commun.*, 2003, 1832–1833.
24 S. Groysman, I. Goldberg, Z. Goldschmidt and M. Kol, *Inorg. Chem.*, 2005, **44**, 5073–5080.
25 S. Groysman, I. Goldberg, M. Kol, E. Genizi and Z. Goldschmidt, *Adv. Synth. Catal.*, 2005, **347**, 409–415.
26 G. Licini, M. Mba and C. Zonta, *Dalton Trans.*, 2009, 5265–5277.
27 C. K. Williams, *Chem. Soc. Rev.*, 2007, **36**, 1573–1580.
28 H. Ma, T. P. Spaniol and J. Okuda, *Angew. Chem., Int. Ed.*, 2006, **45**, 7818–7821.
29 A. J. Chmura, C. J. Chuck, M. G. Davidson, M. D. Jones, M. D. Lunn, S. D. Bull and M. F. Mahon, *Angew. Chem., Int. Ed.*, 2007, **46**, 2280–2283.
30 E. L. Whitelaw, M. D. Jones and M. F. Mahon, *Inorg. Chem.*, 2010, **49**, 7176–7181.
31 Y. Huang, W. Wang, C.-C. Lin, M. P. Blake, L. Clark, A. D. Schwarz and P. Mountford, *Dalton Trans.*, 2013, **42**, 9313–9324.