Group 4 hydroxides and their multimetallic assemblies for ring opening polymerization (ROMP) of rac-lactide without solvent

Prabhuodeyara M. Gurubasavaraj* and Jasmith S. Charantimath

Department of Chemistry, Rani Channamma University, NH-4, Vidyasangama, Belagavi 596156, India

*Corresponding author; Tel : (+91) 9538083102; E-mail : pmg@rcub.ac.in

Abstract

In this work, we report the synthesis, structural characterization of Group 4 mono and bis-hydroxides and their derivatives and their catalytic properties in the Ring Opening Polymerization (ROP) of *rac-Lactide*. The hydroxides, and their multimetallic assemblies were characterized, using ^{1}H NMR, 2D NMR, Elemental Analysis, and Single crystal XRD. These complexes were used as catalysts for ring opening polymerization of rac-Lactide. All complexes exhibit varied activity in the polymerization but produce heterotactic polylactide in high yield. These polymers were further characterized by ^{13}C NMR. A tendency toward formation of heterotactic polylactide was observed in the bulk polymerizations. Copyright © 2017 VBRI Press.

Keywords: Rac-Lactide, heterotactic, biodegradable, heterobimetallic, 2D NMR.

Introduction

Heterometallic complexes in general have enormous potential to revolutionize homogeneous catalytic processes. They can simultaneously activate both components of a bimolecular reaction, overcome entropy barriers associated with bringing the two reagents together, and minimize the energy barrier that arises from solvent–shell rearrangements during the reaction by virtue of the cooperative interaction between the two different metal centers [**1**]. In this way a very important area of "tandem catalysis" has burgeoned in recent years in which one site produces a specific type of polymer that is immediately incorporated into another type of polymer produced by the other proximate metal center [**2-6**].

Multimetallic systems of various main group and transition metals bridged by oxygen, carbon, nitrogen and halides have been reported [**7**]. Properties such as multifunctionality and cooperative effects have been studied [**8**]. Nevertheless, the problems found to meet the different coordination environments of both metals in close proximity could be as great as the expectations, and thus synthetic strategies leading to new complexes are highly desirable. The synthesis and characterization of heterobimetallic oxides, which are used as polyfunctional catalysts and precursors for the preparation of bi- and polymetallic heterogeneous catalysts, have been the topic of various academic and industrial studies [**9,10**] since the discovery of the catalytic olefin polymerization by Ziegler and Natta. These heterogeneous catalysts have complicated structural features and are insoluble in solvents advantageous for polymerization reactions. Subsequent years have witnessed tremendous advances in the design and application of organometallic complexes as olefin polymerization catalysts.

In this contribution, we report a facile route for the preparation of hydroxides and their heterobimetallic and trimetallic derivative Zr-O-Ti and Zr-O-Hf-O-Zr complexes and their use in ring opening polymerization (ROP). The complexes are characterized using 2D NMR, single crystal X-ray studies and used as a catalysts in the ring opening polymerization of rac-lactide. The heterometallic Complexes exhibit high activity and produce heterotactic polylactic acid (PLA).

Results and discussion

Group four elements interact strongly with oxygen and are therefore obvious choices for stable inorganic cornerstones in combination with oxygen containing linkers. Group 4 hydroxides have been the subject of study since two decades because they produce interesting and unprecedented intermediates.

The controlled hydrolysis of Cp*$_2$ZrMe$_2$ with one equivalent of water resulted in the formation of Cp*$_2$ZrMe(OH) (1) in high yield with the elimination of methane (**Scheme 1**) [**11**]. However, even with one equivalent of water, Cp*$_2$HfMe$_2$ produces dihydroxide,

$Cp*_2Hf(OH)_2$. An Effort to isolate the monohydroxide analogue for 1 was unsuccessful. However, It was reported [12] that the reaction of water with $Cp*_2HfH_2$, in 1:1 stoichiometry produces $Cp*_2HfH(OH)$ with the evolution of hydrogen but surprisingly its congener, $Cp*_2HfMe(OH)$ was not observed even at low temperature. Moreover, the bimetallic oxide bridged complex of $Cp*_2HHfOHfHCp*_2$ was also observed during the course but $Cp*_2MeHfOHfMeCp*_2$ was never observed in our case.

Compound 2 is the first structurally characterized Hafnium compound which is bonded to two OH groups at the same hafnium atom **(Scheme 1)**. Interestingly, 2 is monomeric in the solid state and OH groups are not involved in any kind of hydrogen bonding as shown by X-ray structural analysis and IR spectroscopy. ^{1}H NMR studies at low temperature to find out the possible formation of monohydroxide did not show any methyl peaks ruling out the formation of $Cp*_2HfMe(OH)$. It is interesting to note that group 4 metallocenes react in different proportion with water. Titanium forms bis-aqua as well as hydroxyl aqua complexes [12], while zirconium forms both mono and bis- hydroxides and hafnium produces bis-hydroxide complex only. Furthermore, the reaction of 2 with one equivalent of $Cp*HfMe_2$ did not occur. This may be due to the fact that the hafnium center is surrounded by sterically bulky Cp* ligands, which restrict complex 2 from dimerising with loss of water.

Scheme 1. Preparation of Group 4 hydroxides.

Fig. 1. Molecular structures of 2 [$Cp*_2Zr(Me)OH$] and 3 [$Cp*_2Hf(OH)_2$]. Hydrogen atoms (except for OH group) are omitted for clarity.

To the best of our knowledge compound 2 is the first structurally characterized hafnium hydroxide. The X-ray quality single crystals were obtained from *n*-hexane by cooling 2 at −20 °C. Molecular structure of 2 is shown in **Fig. 2**. Compound 2 crystallizes in the orthorhombic space group *P*212121. The Hf center is bonded to two Cp* groups and to two ancillary ligands (OH) adopting a

distorted tetrahedral geometry around the metal. The O(1)–Hf(1)–O(2) bond angle (93.3º) and the angle involving the centroids of the Cp* rings (138.7º) **(Table 1)** are in good agreement with the corresponding $Cp*_2Zr(OH)_2$ [11] (O–Zr–O, av 98.9(2)º and Cp* angle av 137.7(5)º) The Hf(1)-O(1) and Hf(2)-O(2) bond lengths are similar to each other (2.345(3) and 2.351(3) Å) but are longer when compared to those (Hf–O, av 1.943 Å), in the homobimetallic compound (Cp_2ClHf (μ-O)$HfClCp_2$).[11]

Table 1. Selected Bond angles (deg) and Bond length (Å) parameters for compounds 1 and 2.

Compound 1			
Zr(1)-O(1)	2.040(4)	O(1)-Zr(1)-C(21)	95.5(2)
Zr(1)-C(21)	2.302(7)	X_{Cp*1}-Zr-X_{Cp*2}	137.6
Compound 2			
Hf(1)-O(1)	2.345(3)	O(1)-Hf(1)-O(2)	93.3^0
Hf(1)-O(2)	2.351(3)	X_{Cp*1}-Hf-X_{Cp*2}	131.7

X_{Cp*} = Centroid of cyclopentadienyl ring

Complex 1 reacts cleanly with $Cp*TiMe3$ at room temperature under elimination of methane to form the heterobimetallic compound 2 with a Zr-O-Ti moiety **(Scheme 2)** in good yield.

Scheme 2. Synthesis of $Cp*_2MeZr$ (μ-O) $TiCp*Me_2$ and $Cp*_2MeZr$ (μ-O) $Ti(NMe_2)_3$

Scheme 3. Synthesis of $Cp*_2MeZr$ (μ-O) $Hf(NMe_2)_3$ and $Cp*2MeZr$ (μ-O)$Hf(NMe_2)_2$ (μ-O)$ZrMeCp*_2$

2D NMR characterization of complexes 4 and 6

To understand the interaction of atoms in complex molecules of 4 and 6 in solution state, 2D ([1]H[1]H NOESY) NMR experiments were carried out. The experiments

reveal that 4 and 6 are indeed heterometallic complexes. The 2D spectrum of Cp*$_2$MeZr(μ-O)Ti(NMe$_2$)$_3$ (4) exhibits the methyl resonances from the Zr-(CH$_3$)$_2$ (δ 0.01 ppm) and Ti-N(CH$_3$)$_2$ (δ 3.14 ppm) moieties have cross-peaks, and also the methyl signals on Cp* (δ 1.89 ppm) and methyl signals on Ti-N(CH$_3$)$_2$ (δ 3.14 ppm) shows the cross peaks which can be expected considering the bulky Cp* ligands. This data indicates that the Zr and Ti moieties are present within the same molecule **(Fig. 2)** The crystal structure data for all complexes (1 to 6) but 2 were reported [**11**]. The ^{1}H,^{1}H NOESY spectrum for complex 6 is shown in **Fig. 2**. The spectrum is similar to that of 4 exhibiting the cross peaks between the methyl resonances of Zr-CH$_3$ (δ - 0.05 ppm) and methyl resonances of Hf-N(CH$_3$)$_2$ (δ 1.99 ppm). The cross peaks between methyl signals of Hf-N(CH$_3$)$_2$ (δ 1.99 ppm) and methyl signals of C(CH$_3$)$_5$ [(Cp*) (δ 1.92 ppm)] has also been seen indicating the presence of Zr and Hf in the same molecule. In both 2D spectra of compounds 4 and 6 the cross peaks between corresponding methyl resonances of Zr-Me (δ 0.01 ppm, for 4, and δ -0.05 ppm for 6) and methyl resonances of C(CH$_3$)$_5$ (Cp*) (δ 1.89 ppm for 4, and δ 1.92 ppm for 6) has been observed. This may be attributed to the steric interaction between the methyl-methyl groups of the bulky Cp* ligands.
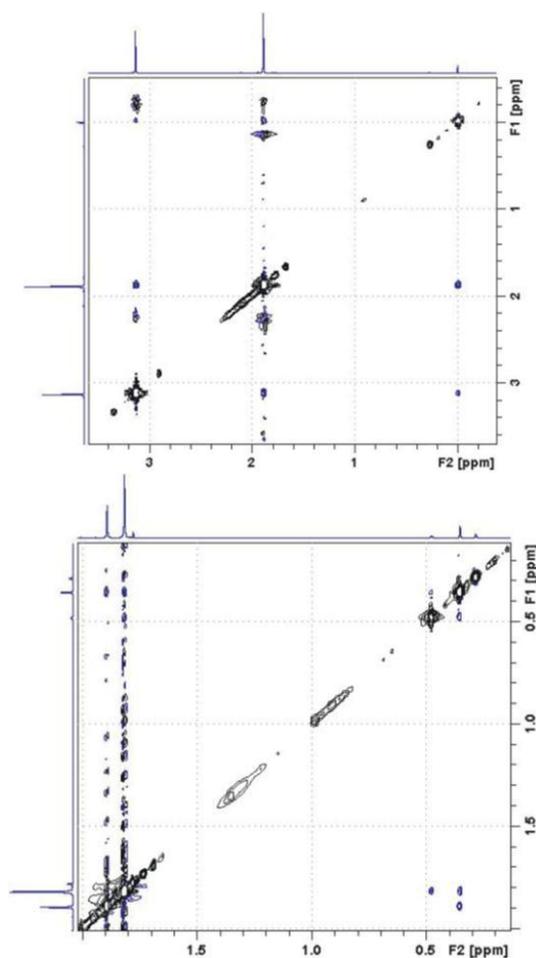
Fig. 2. 2D (^{1}H,^{1}H NOESY) spectrum of Cp*$_2$MeZr(μ-O)Ti(NMe$_2$)$_3$ (4) and Cp*$_2$MeZr(μ-O)Hf(NMe$_2$)$_2$(μ-O)ZrMeCp*$_2$ (6).

Bulk polymerisation of rac-lactide (rac-LA)

Due to their unique properties, biodegradable polymers have long been considered as alternative environmentally friendly polymers. The most important synthetic biocompatible and biodegradable polymer known is polylactide (PLA) which has wide range of biomedical, pharmaceutical, agricultural, and packing applications. PLA is conventionally synthesised through the ring opening polymerisation (ROP) of lactide (LA) [**13**]. The mechanical, physical, and degradation properties are closely related to the stereochemistry of PLA, so stereocontrol of PLA homopolymers or copolymers is of utmost importance to achieve the desired features for applications.

In recent times the study of ring-opening polymerisation (ROP) of cyclic esters such as rac-lactide (LA) with metal complexes has been intensively reported. Various types of metal alkoxides such as tin, aluminium, zinc, magnesium, iron, lanthanide, and lithium [**14**] organometallic complexes have been found to be active LA polymerisation catalysts, and many afford materials with controlled molecular weights and narrow molecular weight distributions. Despite the fact that some excellent initiators have been reported for the polymerisation of LA, the search for new catalysts that generate well-defined polylactides remains of keen interest. The roles of the structure of metal alkoxide complexes in determining molecular weights and molecular weight distributions, as well as the polymerisation pathway, are significant current research issues.

Preliminary results on the use of catalysts 3-6 for the bulk polymerisation of rac-LA are summarised and are presented in **Table 2**. Polymerisations were performed at 130 °C with the [LA]/ [Ti] ratio fixed at 300. This table reveals that all the compounds catalyse LA polymerisation. Moreover, it appears that compound 6 significantly decreases the polydispersity index and polymer yield. However, some transesterification probably occurred during the polymerisation reaction since the polydispersity indices of both PLA products were somewhat higher than expected for a controlled polymerisation.

These bimetallic complexes exhibit high activity and produce polylactide with high molecular weight and lower polydispersity. The preference for heterotacticity in our poly(rac-LA) are comparatively stronger for bimetallic complexes than their mononuclear precursor compounds [**12**] and are similar to the previous reports by Kasperczyk et al [**15**]. This may be due to the initiating oxide/amide group which dissociate relatively easily from the metal center in bimetallic complexes than the monometallic precursors in the early stage of polymerisation so that it can be utilised to initiate LA polymerisation and provide a means of controlling the molecular weight by functioning as an end group.

Scheme 4.

Heterotactic Polymer
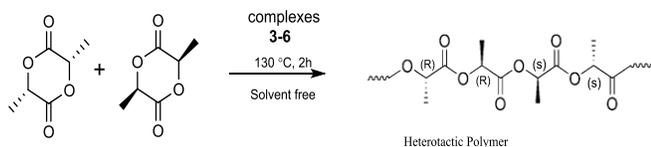
The bimetallic complexes show similar trend in the activity, while trimetallic complex (6) shows lower activity with broader molecular distribution. Complexes with amide ligand (4 and 5) show higher activity and lower polydispersity that may be attributed to the less steric bulkiness of amide ligands compared to Cp* ligand. It can also be noted that amide ligands are better initiators in catalytic reactions. The lower activity of complex 6 can be attributed to its instability in polymerization process.

It appears that the initiating group is the highly oxide (in 3) or *amides* (4 and 6) group in bimetallic, similar to the observation made by Verkade et al. [14] But the scenario in trimetallic complex (6) is complicated. We assume that the initiating group may be similar to the mononuclear complexes, although the insertion of lactide into M-O (Zr, Ti or Hf) of the oxide arm or amide arm cannot be ruled out.

Table 2. Data for bulk solvent-free ring opening polymerisation (ROP) of rac-Lactide Data for Complexes. 3-6^a [3: Cp*$_2$MeZr(μ-O)TiMe$_2$Cp*; 4: Cp*$_2$MeZr(μ-O)Ti(NMe$_2$)$_3$; 5: Cp*$_2$MeZr(μ-O)Hf(NMe$_2$)$_3$; 6: Cp*$_2$MeZr(μ-O)Hf(NMe$_2$)$_2$(μ-O)ZrMeCp*$_2$]

run	complex	Polymer (g)	Yield (%)	M_w^{b}	M_n^{b}	M_w/M_n^{c}
1	**3**	1.82	88	39420	20373	1.44
2	**4**	1.68	98	43131	22890	1.40
3	**5**	1.76	95	41109	41306	1.22
4	**6**	1.80	74	21577	16564	2.11

^{a}LA (2.027 g) LA/Ti = 150, polymerisation temperature = 130 °C, time = 20 min. ^{b}The weight average molecular weight (M_w), the number average molecular weight (M_n), and the polydispersity index (PDI) M_w/M_n) were determined by GPC.

Experimental

General procedures

All experimental manipulations were carried out under an atmosphere of dry nitrogen using standard Schlenk techniques or using a Vacuum Atmospheres dry box unless otherwise specified. All chemicals used were of reagent grades and were purified by standard purification procedures.

All ^{1}H spectra were recorded on a JEOL JNMLA 400 spectrometer (399.65 MHz for ^{1}H, 100.626 MHz for ^{13}C). All deuterated NMR solvents were stored over molecular sieves under a nitrogen atmosphere in the dry box, and all chemical shifts are given in ppm and referenced to SiMe$_4$ (TMS). All spectra were obtained in the solvent indicated at 25 °C unless otherwise specified. Elemental analyses were performed by using PE2400II Series (Perkin-Elmer Co.).

Synthesis of complexes 1-4

Complexes 1 to 4 were synthesized by the procedure reported earlier [11].

Crystallographic analysis

All measurements were made on a Rigaku RAXIS-RAPID imaging plate diffractometer with graphite-monochromated Mo Kα radiation. All structures were solved by direct methods and expanded using Fourier techniques, [15]and the non-hydrogen atoms were refined anisotropically. Hydrogen atoms were included but not refined. All calculations for complex 2 were performed using the crystal structure crystallographic software package [16]. Selected crystal collection parameters are summarised in **Table S1**, and the detailed structure reports including their CIF files were shown in the Supporting Information.

Procedure for rac-lactide polymerisation

LA bulk polymerisations were carried out by charging a stirring bar, 2.00 g of LA, and then the appropriate amount of catalyst precursor to a 10 mL Schlenk flask. The flask was then immersed in an oil bath at 130 °C, and after the appropriate time, the reaction was terminated by the addition of 5 mL of methanol. The precipitated polymers were dissolved in a minimum amount of methylene chloride, and then, excess methanol was added. The resulting re-precipitated polymers were collected, washed with 50 mL of methanol, and dried in vacuum at 50 °C for 12 h.

Conclusion

In conclusion, we succeeded in synthesizing the mono and bis-hydroxide complexes of all the group 4 elements. Hafnium produces only bis-hydroxide compound. Series of bimetallic derivatives were prepared using metallocenes and amides. All the complexes were thoroughly characterized. Because of their high basicity, steric hindrance, and high activity at low temperature, bimetallic oxides exhibit excellent stereocontrol for the ROP of *rac*-lactide.

The bimetallic complexes showed high activity with uniform molecular distribution. Complex 6 showed lower activity in polymerization process. It may be attributed to the low stability of 6 in solution. Further investigations are underway in our laboratory.

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