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Synthesis of new zirconium diketiminate complexes and catalytic applications

Par

Ibrahim El-Zoghbi

Département de chimie

Faculté des arts et des sciences

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Synthesis of new zirconium diketiminate complexes and catalytic applications

Présenté par:

Ibrahim El-Zoghbi

A été évaluée par un jury composé des personnes suivantes :

Davit Zargarian, président rapporteur

Frank Schaper, directeur de recherche

Helene Lebel, membre de jury

Scott Collins, examinateur externe

Jean-Yves Lapointe, représentant du doyen de la Faculté

Résumé

Dans le but de préparer des complexes de Zr pour la catalyse homogène de la polymérisation des lactides et de l'hydroamination des olefines, l'elaboration et l'optimisation d'une méthode systématique et efficace de synthèse des ligands dikétimines ayant différents substituants alkyles (R) à la position *N,N'* a été realisée. Des dikétimines (*nacnac*^{R}H) symétriques ont été obtenus avec une pureté de plus de 95 % et un rendement de 65 % lorsque R = Me et des rendements allant de 80 à 95 % lorsque le groupe R = *n*-Pr, *i*-Pr, *i*-Bu, Bu, Cy et (+)-CH(Me)Ph. La synthèse des dikétimines ayant des substituants *N*-alkyls différents, dite asymétriques, donne toujours un mélange statistique de trois ligands: *nacnac*$^{R,R'}$H, *nacnac*^{R,R}H et *nacnac*$^{R',R'}$H qui n'ont pu être separés. Seuls les dikétimines asymétriques avec un substituant *N*-alkyl et un autre *N*-aryl (*nacnac*^{R,Ar}H) ont été obtenus avec des rendements plus élevés que celui du mélange statistique.

Par la suite, la complexation de ces ligands bidentés au Zr, la caractérisation de ces complexes et l'investigation de la réactivité ont été étudiés. Les complexes de Zr de type (*nacnac*^{R})$_2$ZrCl$_2$ ont été obtenus par deux voies de synthèse principales: la première consiste à traiter le sel de lithium du ligand avec le ZrCl$_4$. La seconde est la réaction du ligand avec les complexes neutres d'alkyl-zirconium(IV) par protonation de l'alkyle coordonné. En solution, les complexes obtenus de (*nacnac*^{R})$_2$ZrX$_2$ possèdent un comportement dynamique via un « Bailar-twist » et les paramètres d'activation de cette isomérisation ont été calculés. Le complexe octaèdrique (*nacnac*^{Bn})$_2$ZrCl$_2$ n'est pas réactif dans la carbozirconation et son alkylation n'était pas possible par l'échange des chlorures

avec les alkyles. L'analogue diméthylé (*nacnac*^{Bn})$_2$ZrMe$_2$ peut être préparé par alkylation du $ZrCl_4$ avant la complexation du ligand. On a également observé que ce dernier n'est pas réactif dans la carbozirconation. L'analogue diéthoxyde (*nacnac*^{Bn})$_2$Zr(OEt)$_2$ est obtenu par échange des diméthyles avec les éthoxydes. La polymérisation du lactide avec celui-ci en tant que précurseur est relativement lente et ne peut être effectuée que dans le monomère fondu.

Par conséquent, pour résoudre les problèmes rencontrés avec les complexes de zirconium (dikétiminates non-pontés), un ligand dikétimines pontés par le diaminocyclohexane, (±)-C_6H_{10}(*nacnac*^{Xyl}H)$_2$, LH_2, (Xyl = 2,6-diméthylphényle) a été préparé. La complexation de ce ligand tetradenté au metal a été réalisée par deux voies de synthèse; la première est la réaction du sel de lithium de ce ligand avec le $ZrCl_4(THF)_2$. La deuxième est la déprotonation du ligand neutre avec le $Zr(NMe_2)_4$ et l'élimination du diméthylamine. Des complexes du type: (±)-C_6H_{10}(*nacnac*^{Xyl}H)$_2$ZrX$_2$ avec X = Cl, NMe_2 ont été obtenus. Les ligands de chlorure sont dans ce cas facilement remplaçables par des éthoxydes ou des méthyles.

On a observé l'activité la plus élevée jamais observée pour un complexe d'un métal du groupe 4 avec le complexe de (±)-C_6H_{10}(*nacnac*^{Xyl}H)$_2$Zr(OEt)$_2$ dans la polymérisation de lactide. L'étude cinétique a montré que la loi de vitesse est du premier ordre en catalyseur et en monomère et la constante de vitesse est k = 14 (1) L mol^{-1} s^{-1}. L'analyse des polymères a montré l'obtention de masses moléculaires faibles et l'abscence de stéréocontrôle.

La réaction de (±)-C_6H_{10}(*nacnac*^{Xyl}H)$_2$ZrCl$_2$ avec le triflate d'argent donne le (±)-C_6H_{10}(*nacnac*^{Xyl}H)$_2$Zr(OTf)$_2$. Le complexe bis-triflate obtenu possède une activité

catalytique elevée pour les additions du type aza-Michael. L'utilisation du *R,R*-C_6H_{10}(*nacnac*^{Xyl}H)$_2$Zr(OTf)$_2$ énantiopur comme catalyseur, dans les additions du type aza-Michael asymétriques donne le produit desiré avec un excès énantiomérique de 19%.

Mots-clés : Zirconium, complexes de *nacnac*, complexes β-dikétiminate, « Bailar-twist », polymérisation des lactides, aza-Michael, bis triflates.

Abstract

In order to prepare the complexes of Zr targeted for homogeneous catalysis in polymerization of lactides and hydroamination of activated olefins, we focused on the elaboration and the optimization of a systematic and efficient method for the synthesis of diketimines ligands with a variety of substituted alkyl (R) on their position *N,N′*. Symmetrical diketimines (*nacnac*^{R}H) were obtained with a greater than 95% purity and a yield of 65% when R = Me and yields ranging from 80 to 95% when R = *n*Pr, *i*Pr, *i*Bu, Bn, and Cy (+)-CH (Me) Ph. The Synthesis of diketimines with different *N*-alkyl substituents, called asymmetric, always gives a statistical mixture of three ligands: *nacnac*$^{R,R'}$H *nacnac*^{R,R}H and *nacnac*$^{R',R'}$H that made their isolation problematic. Yields greater than statistical mixtures were obtained only with asymmetric diketimines bearing N-alky and N-aryl substituents (*nacnac*^{R,Ar}H).

Subsequently, we studied the complexation of these bidentate ligands with Zr, the characterization of these complexes and investigation of their reactivity. Zr complexes of type (*nacnac*^{R}H)$_2$ZrCl$_2$ were obtained via two main synthetic routes: the first consists in treatment of the lithium salt of the ligand with $ZrCl_4$. The second is the reaction of the ligand with neutral complexes of alkyl-zirconium (IV) by protonation of the alkyl coordinated. In solution, the obtained complexes (*nacnac*^{R})$_2$ZrX$_2$ showed dynamic behavior via a "Bailar-twist" isomerization and the activation parameters of the isomerization were calculated. Octahedral complex (*nacnac*^{Bn})$_2$ZrCl$_2$, showed no reactivity in alkylation and carbozirconation was not possible by the exchange of alkyl with chlorides. The dimethyl

analogue $(nacnac^{Bn})_2ZrMe_2$, can be prepared by alkylation of $ZrCl_4$ before ligand complexing. The diethoxide analogue $(nacnac^{Bn})_2Zr(OEt)_2$ is obtained by exchange of dimethyls with ethoxides. The latter had slow reactivity in lactide polymerization under melt conditions.

Consequently, to address the problems encountered with unbridged (diketiminate) zirconium complexes, a cyclohexanediyl-bridged diketiminate ligand, (±)-$C_6H_{10}(nacnac^{Xyl}H)_2$, LH_2, (Xyl = 2,6-dimethylphenyl) is prepared. Complexation of the tetradentate ligand is realized via two synthetic routes; The first is reaction of the lithium salt of the ligand with $ZrCl_4(THF)_2$. The second is deprotonation of the neutral ligand with $Zr(NMe_2)_4$ and elimination of dimethylamine. Complexes of the type: (±)-$C_6H_{10}(nacnac^{Xyl}H)_2ZrX_2$ with X = Cl, NMe_2 are obtained. The chloride ligands are in this case readily replaceable with ethoxides or methyls.

The (±)-$C_6H_{10}(nacnac^{Xyl}H)_2Zr(OEt)_2$ complex showed the highest activity ever observed for any group 4 metal complex in lactide polymerization. The kinetic study showed that the rate law is first order in catalyst and monomer and the rate constant is $k = 14(1)$ L mol^{-1} s^{-1}. Analysis of the obtained polymer showed low molecular weight with no-stereocontrol.

Reaction of the (±)-$C_6H_{10}(nacnac^{Xyl}H)_2ZrCl_2$ with silver triflates yielded the (±)-$C_6H_{10}(nacnac^{Xyl}H)_2Zr(OTf)_2$. The obtained bis-triflate complex showed to be a highly active catalyst for aza-Michael additions. The use of the enatiopure *R,R*-$C_6H_{10}(nacnac^{Xyl})_2Zr(OTf)_2$ as catalyst for asymmetric aza-Michael additions of activated olefines gave the desired product with an enantiomeric excess of 19%.

Key words: Zirconium, *nacnac* complexes, β-diketiminate complexes, Bailar-twist, lactide polymerization, aza-Michael addition, bis triflates.

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Ar	Aryl
BINOL	[1,1'-binaphthalene]-2,2'-diol
*i*Bu	*iso*-butyl
*n*Bu	*n*-butyl
*t*Bu	*tert*-butyl
bp	boiling point
bs	broad (singlet)

bm	broad (multiplet)
Bn	benzyl
Cp	cyclopentadienyl (η^5-C_5H_5)
Cy	cyclohexyl
d	distance
Dipp	2,6-diisopropylphenyl
d	doublet
dd	doublet of doublets
equiv.	equivalents
Et	ethyl
GC	Gas chromatography
Ind	Indenyl
MS	mass spectrometry
Me	methyl
MW	molecular weight
m	multiplet (spectral)
M	Metal
nacnac	β-Diketiminate
NMR	nuclear magnetic resonance
OTf	triflate
PDI	polydispersity
ppm	part per milliom

Ph	phenyl
PLA	polylactide
P_m	probability of obtaining meso diads
P_r	probability of obtaining racemic diads
*i*Pr	*iso*-propyl
*n*Pr	*n*-propyl
PS	polystyrene
q	quartet (NMR)
rac	racemic
ROP	ring opening polymerization
R	alkyl group
sbc	steroblock copolymer
s	singlet
TADDOL	(α,α,α,α-tetraaryl-1,3-dioxolane-4,5- dimethanol)
THF	Tetrahydroforan
TsOH	*para*-toluene sulfonic acid
t	triplet
vdW	van der waals
Xyl	2,6-dimethylphenyl

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CHAPTER 1

Introduction

1.1 β-Diketimine ligands

Since their appearance in 1968[1] as bidentate ligands with first row transition metals, diketiminates have attracted considerable attention in the metal coordination chemistry.[2,3] The success of these ligands stems from their electronic and steric tunability along with their accessibility via different synthetic pathways. Their recent popularity can be attributed to Brookhart's phenomenal work in the mid 1990's on α-diketiminate Ni(II) and Pd(II) based catalysts for the preparation of high molar mass olefin polymers.[4] Since then, *β*-diketiminates, their anionic analogues, with bulky *N*-aryl substituents have attracted considerable attention while those with *N*-alkyl substituents were only timidly explored.

1.1.1 Properties of β-diketimines

β-Diketiminate ligands also, known as "*nacnac*", are bidentate ligands that derive from the condensation of a β-diketone and two equivalents of amine.[3,5] The facile modification of this ligand, the presence of nitrogen coordination sites and the ease of synthetic access allowed extensive exploration of electronic and steric properties.

Variable coordination modes: While the most common coordination mode for this ligand is a *N,N′*-κ^2-coordination, higher hapticities such as "η^5-like" or a κ^2,η^2-coordinations involving more than the nitrogen atoms of the ligand framework were observed, in most cases causing the ligand backbone to deform from planarity (Fig.1.1). The diversity of bonding to metal centers allows the ligand to increase its electron donation from 4 to 8, especially in cases of electron deficiency.[3,6] Other coordination modes were rarely encountered and involved binding two metals to the same ligand (*N,N′*-κ^2- and κ-C_β).[7]

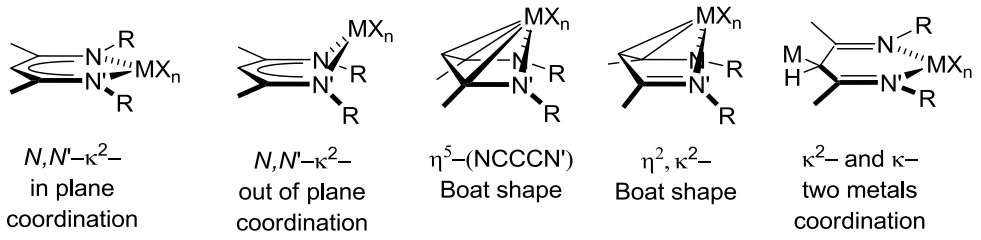


Fig. 1.1: Coordination modes of diketiminates ligands.

Tunable steric and electronic properties: Perhaps the most important characteristic of this ligand is the ease of varying its electronic and steric properties. This can be achieved mainly during the ligand synthesis by incorporation of different *N,N′*-substituents or by substitution on the backbone.[2,8] While changing the nitrogen substituents influences both reactivity and geometry of the metal coordination surrounding, substituting the H in position β with a nucleophile/electrophile is used only for electronic purposes without having a steric impact on the metal coordination geometry (Fig.1.2). In our case we were interested in diketimines with *N*-alkyl substituents, since replacing an *N*-aryl substituent with an *N*-alkyl should allow access to geometries which cannot be realized with *N*-aryl substituents.

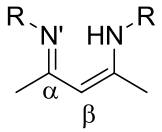


Fig. 1.2: β-Diketimine ligand.

Bridged β-diketiminates: Ligands composed of two β-diketiminate units have received small attention in the literature.[9-11] In bridged diketiminates, the bridge can be found either between the C_β atom of the two diketiminates or by use of a diamine, thus bridging the

nitrogen atoms of two diketiminates. Lappert *et al.*[3] reported a binucleating ligand consisting of two β-diketiminates units linked through the backbone by a CH_2-bridge in β position. Vitanova *et al.* reported a mononucleating bisdiketiminate ligand using a longer and more flexible bridge linking the nitrogens of each diketiminate unit.[10] The obtained lanthanide complexes displayed good to moderate catalytic activity in asymmetric hydroamination of aminoalkenes and in epoxide/CO_2-copolymerization.[11]. Vitanova showed that the arrangement of the nitrogen substituents of the bis-diketiminate ligands depends significantly on the bridging unit. While a *cisoid* arrangement of the *N,N′*-substituents having both *N*-Ar pointing towards the ancillary ligand (X) was observed with an ethylene bridge, a cyclohexylene bridge resulted in a *transoid* arrangement having one *N*-Ar pointing towards the X and one *N′*-Ar pointing away from X.[10]

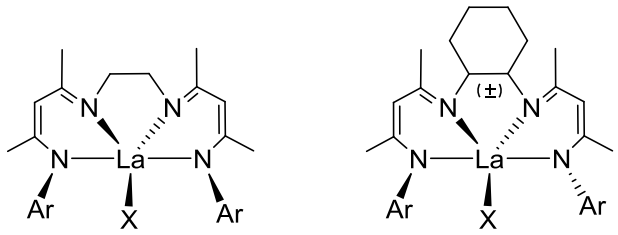


Fig. 1.3: *Cisoid* and *transoid* orientations of the *N*-substituents in bridged diketiminate complexes.[10]

Good spectator ligands: β-Diketiminate ligand proves to be a robust ancillary species due to the chelating coordination of the nitrogen atoms to the metal, and only in very rare cases it does undergo some transformations. Lappert *et al.,* while working with sterically hindered lanthanoid complexes, reported the "self-deprotonation" of the β-diketiminate

ligand (Fig.1.4a).[12] Another example is oxidative degradation of the diketiminate under aerobic conditions to give the diimine ketone (Fig.1.4b).[13]

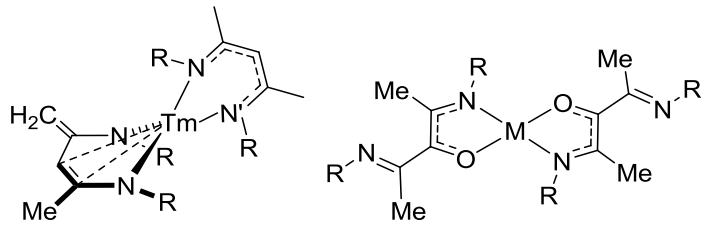


Fig. 1.4: (a) "Self deprotonation" and (b) "oxidative degradation" of the diketiminate ligand.

Coordination to metals with unusual oxidation states. Almost all metals of the periodic table can coordinate to diketiminates, but one of the best characteristics of the β-diketiminate ligand is its ability to host a wide variety of oxidation states of the metal centers.[2,3] Cui *et al.*[14] used the crowded *N,N'*- dipp-diketiminate ligand (dipp = 2,6-iPr$_2$C$_6$H$_3$) to prepare the first monomeric species of Al(I) as a stable analogue of carbene. Using the same dipp-diketiminate a thermostable dimeric species of Mg(I) was reported in the work of Bonyhady *et al.*[15] Also supported by the same dipp-diketiminate ligand, *Hill et al.* presented a series of heteroleptic Be(I) complexes.[16] Holland *et al.* used the (2,2,6,6-tetramethyl-3,5-bis(2,6-diisopropylphenylimido)hept-4-yl ligand to stabilize Fe(I).[17,18] They also used the same ligand and reported unsaturated three-coordinate complexes of Fe(II), Co(II), and Ni(II). Recently Holland presented the first examples of Iron(I) sulfide complexes stabilized by the presence of alkali-metals and, as in all previous examples, by steric hindrance from the ligand.[19] These diketiminate complexes serve as powerful reducing agents and as electron reservoirs.

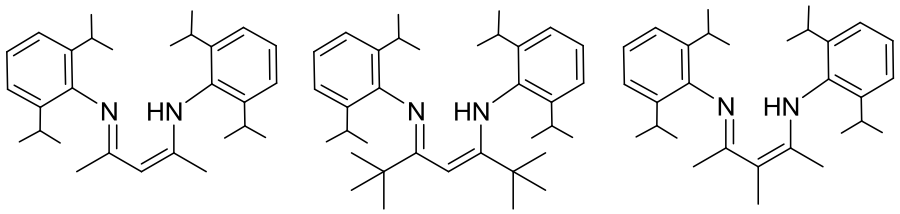


Fig. 1.5: β-Diketimine ligands used for stabilization of low oxidation states.

1.2 Zirconium (IV) chemistry

Zirconium compounds are ranking twentieth in the earth's crust with a relative high abundance of 0.016%.[20] Although the separation of Zr from other contaminants such as Hf is problematic, it is still considered one of the least expensive transition metals. In most cases, Zr compounds are easy to handle under air and moisture and have low toxicity.[21] While the most common oxidation state of Zirconium compounds is IV, a significant number of Zr(II) compounds exists, whereas Zr(III) compounds are few and Zr(I) compounds are even fewer.[21] The high charge to size ratio (q^2/r) of Zr^{4+} 22.22 e^2m^{-10} compared to most of metal ions (Li^+, Co^{2+}, Cu^{2+}, Mg^{2+}, Bi^{3+}, In^{3+}, Sc^{3+}) favors a strong Lewis-acid behavior of Zirconium(IV) compounds.[22]

The chemistry of Zr(IV) for organic transformations started in the early seventies due to the discovery of hydrozirconation by Wailes and Weigold.[23] In the mid seventies Schwartz pioneered the application of organozirconium chemistry in organic applications through a systematic development of alkene and alkyne hydrozirconations.[24] It was not until the late seventies that this chemistry expanded to the C-C formation with the extensive works of Negishi who used Zr(IV) in catalyzed carboalumination of alkynes.[25] Since then Zr(IV)

compounds (mainly zirconocenes) have found many applications in organic synthesis, particularly in Lewis-acid catalysis.[26]

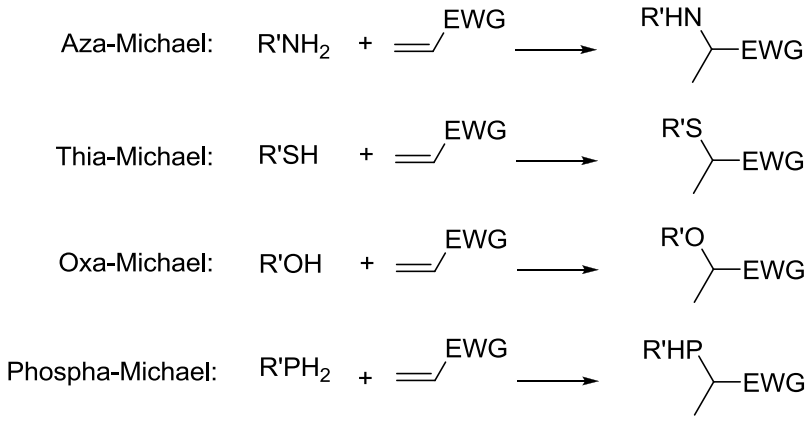
1.2.1 Lewis-acid catalyzed reactions of Zirconium(IV) compounds

Catalysis is one of the most intensively studied subjects in chemistry. Definitely, the use of catalysts is essential for environmental management and to overcome economic challenges. Lewis acid catalysts are usually metal halide salts like aluminum chloride, ferric chloride, antimony fluoride, titanium chloride, and tin chloride mostly used in catalysis for organic transformations. During these reactions, the metal forms adduct with the substrate which allows activation of the latter towards nucleophilic attack, heterolytic bond cleavage or other applications in organic chemistry.[21] One major problem that arises from Lewis acid catalysis is the need for the catalyst to be hydrolyzed at the end of the catalytic process after which it cannot be recovered. Rising environmental awareness and the need for efficient and low cost Lewis-acid catalysts for various useful organic reactions increased the interest in zirconium and its compounds in last decade.

A large variety of organic reactions, such as additions (Michael-addition, Aldol-addition, carbometalation, cycloaddition), reductions (Nitro-, Azido and Carbonyl-compounds), cyclizations (synthesis of THF, γ-lactone…), substitutions, ring opening reactions and rearrangements (Ferrier, Bckman, Pinacol), were accomplished using Zr-based Lewis acids.[22] In the following, I present two examples for the applications of zirconium catalysis in organic synthesis.

1.2.2 Michael addition

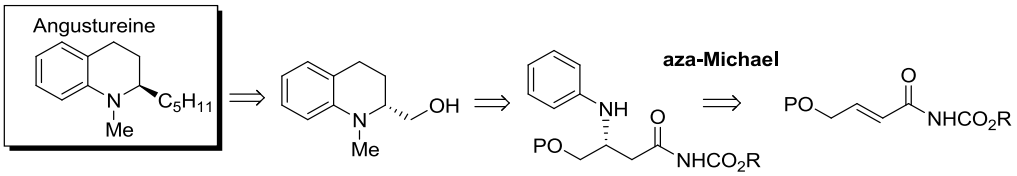
Michael addition is one of the most important breakthroughs in organic synthesis which appeared first in literature in 1887.[27] Promoted by an alkaline reagent, the reaction originally involved the addition of a nucleophilic carbon to electron-poor activated alkenes and formation of a C-C bond. The scope of this reaction was then extended to other bonds such as C-N, C-S, C-O and C-P using appropriate nucleophiles and is known as aza-Michael (C-N), thia-Michael (C-S), oxa-Michael (C-O) or phospha-Michael (C-P) additions.[28,29]



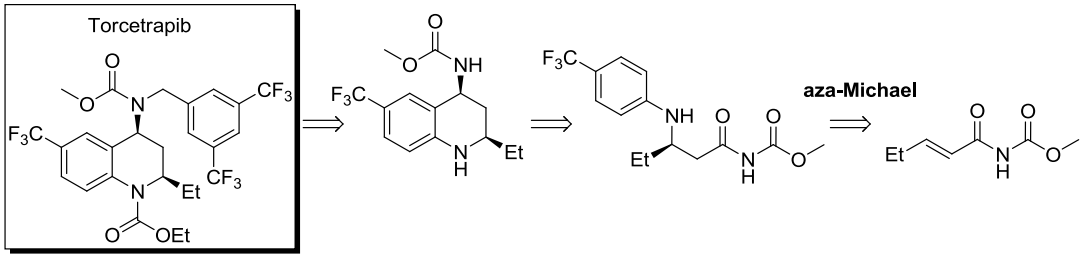
Scheme 1.1: Michael additions

1.2.2.1 Aza -Michael Addition

Hydroamination of activated alkenes also known as Aza-Michael addition is the direct reaction of alkene and alkynes with N–H bonds. This addition is very important not just for the formation of C-N bonds but also attractive to the pharmaceutical industry for the preparation of many compounds or intermediates that are biologically active since the reaction is waste free due to the absence of any by-products.[30]

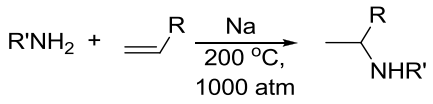


Scheme 1.2: Retrosynthetic scheme for Angusturein, a natural and anti-malaria product.[31]



Scheme 1.3: Retrosynthetic scheme for Torcetrapib, "one of the most important drugs of our generation" used for the treatment of CHD (coronary heart diseases).[32]

The first example of olefin hydroamination appeared in literature back in 1954,[33] the reaction between primary amines and olefins in presence of Na under harsh conditions (200 ºC and 1000 atm) gave the hydroamination product in poor yields next to polymeric side-products.[34]



Scheme 1.4: Hydroamination under harsh conditions

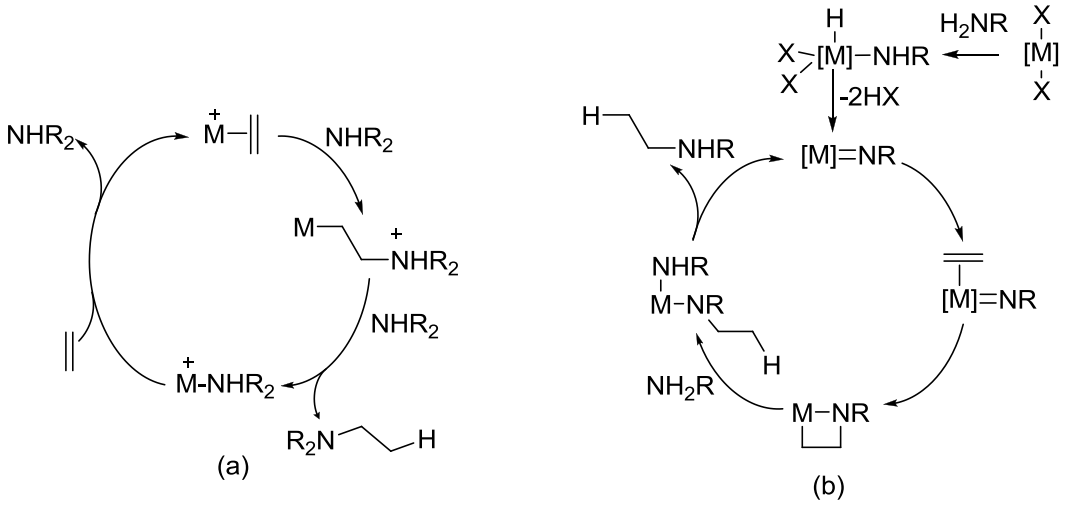
Basic conditions or acid catalysis to promote aza-Michael reactions showed in some cases to be detrimental to the desired products and were often accompanied by side reactions.[35,36] To overcome such disadvantages, a wide variety of active catalysts have been reported in the literature, in particular various Lewis acid catalysts starting from expensive metal salts such as $Yb(OTf)_3$[37] and $InCl_3$,[38] through metal complexes of Rh(II),[39] Pd(II)[40] and Ir(III),[41] to cheaper metal complexes or metals salts of Ni(II),[42] Cu(II), Cu(I), $Y(NO_3)_3$,[43] $FeCl_2$,

$CrCl_3$, $AlCl_3$,$TiCl_4$ and $SnCl_4$.[44] Despite their usefulness, the aza-Michael reaction is still not generalized as most of these catalysts fail in the addition of aromatic as well as heterocyclic amines to various activated alkenes. As a result, many of these catalysts require prolonged reaction times (>12 hours to reach completion), harsh reaction conditions and in some cases stoichiometric amounts of the catalyst. During the last decade, other strategies like organocatalysis have been developed for aza-Michael additions; molecules such as acetic acid,[45] polyvinyl pyridine,[46] Borax[47a] and β-cyclodextrines[47b] promote addition of aromatic amines to a wide range of activated alkenes. More recently, a variety of enantiopure organocatalytic molecules featuring different activation modes were used in asymmetric aza-Michael addition. The use of enantiopure secondary amines such as L-proline, prolinol derivatives, bipyrrolidine derivatives[48a] and imidazolidinone derivatives[48b] or of chiral Bronsted acids such as Binol-derived phosphoric acid diester and chiral thiourea catalysts gave high enantioenrriched products but in most cases reactions required organocatalyst loading of at least 15-30 % apparantely due to otherwise long reaction times.

1.2.2.2 Group 4 catalysts for aza-Michael additions

Generally, early transition metal-based catalysts like titanium and zirconium are more employed in hydroamination reactions with alkynes and allenes especially bisamido or the alkyl amido Zr/Ti-complexes.[49] Extensive mechanistic studies showed that in most cases the active catalytic species is the imido intermediate [M]=NR which in turn favors the formation of azametallacyclobutene/butane intermediates.[50] There are several regioselective catalysts for hydroamination of internal or terminal alkynes that are readily available, such as Cp_2TiMe_2 or Ind_2TiMe_2. Their regioselectivity towards Markovnikov addition generally

increased with increasing size of the amine.[50] In the case of activated olefins (with an electron-withdrawing group) the regioselectivity is directed towards anti-Markownikov addition. Alternatively, cationic Zr and Ti complexes catalyze hydroamination of alkenes with both primary and secondary amines by C=C activation. It is recognized that metal activation of either the olefinic bond or the amine is generally required as a preliminary step in catalytic hydroamination.[51]



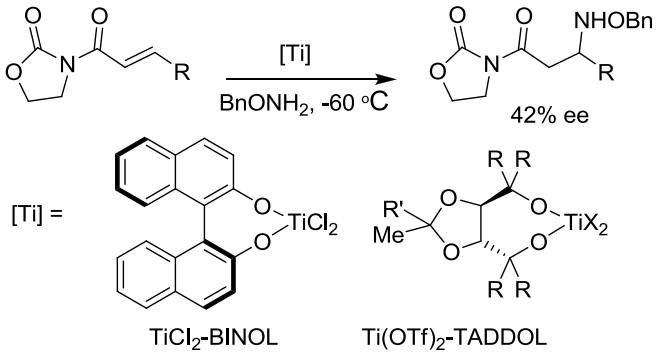
Scheme 1.5: Hydroamination mechanistic pathways catalyzed by a metal complex [M]: (a) C=C activation and (b) N-H activation

In both mechanisms, the tolerance of various functional groups limits their use as a general method. Many research groups have paid attention to applications of zirconium compounds as catalysts for this reaction.[52] In most cases, simple zirconium salts such as $ZrCl_4$ or derivatives have been used. An example is $ZrOCl_2 \cdot 8H_2O$ as a highly efficient and moisture-tolerant Lewis-acid.[53a,53b] In contrast, group 4 metal systems have been extensively explored for inter- and intra-molecular hydroamination of non-activated olefins.

In particular, Zr/Ti-amido complexes with tethered/non-tethered chiral bis-amidates ligands have been shown to be efficient for asymmetric hydroamination.[50, 53c, 53d]

1.2.2.3 Zr and Ti asymmetric aza-Michael addition

In the last decade, the asymmetric aza-Michael reaction has been recognized as a powerful synthetic tool to obtain chiral compounds,[48,54] but enantioselective aza-Michael additions is still a major challenge in organic synthesis. There are two possibilities for chiral induction in aza-Michael additions: Using chiral amines in stoichiometric amounts or by using a chiral controller in catalytical amounts. There is no doubt that the latter is more elegant and economical. For group 4 catalysts, only a limited number of studies reported their use for aza-Michael additions. Jørgensen *et al*.[55] reported the use of the enantioselective aza-Michael addition of hydroxylamine to an acyl pyrolidine with the chiral catalysts (BINOL)$TiCl_2$, (TADDOL)$Ti(OTf)_2$, and obtained moderate ee (29-40%).

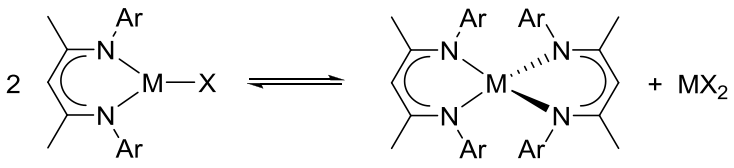


Scheme 1.6: Asymetric aza-Michael addition with Ti-complexes

1.2.2.4 Diketiminate ligands in asymmetric hydroamination

One of the best examples for the use of diketiminates in enantioselective hydroamination/cyclization of aminoalkenes and aminoalkynes is the one reported by Hill

et al.[56] that used a *β*-diketiminato calcium amido complex. Although some reactions occured under prolonged reaction time, chiral induction reached in some cases up to 99% ee. One limiting factor was the observation of a facile ligand redistribution reaction (Schlenk equilibrium) and formation of the homoleptic bis(β-diketiminato) and diamido species resulting in catalyst deactivation.



Scheme 1.7. Ligand redistribution reaction (Schlenk equilibrium)

1.2.3 Lactide Polymerization

Polylactide or polylactic acid (PLA) is synthetic polyester from lactic acid. Lately, researchers have been paying increasing attention to biomass-based polymers, namely polylactide (PLA) as it is sustainable and biodegradable.[57] The fermentation of glucose, harvested from sugar beets or corn, produces lactic acid which is dehydrated to yield the lactide monomer. The hydrolysis of PLA, on the other hand, gives lactic acid which is easily metabolized in the environment.[58] PLA production is currently around 180,000 tons per year. With increasing emphasis on the use of renewable raw materials, the PLA production is expected to hit 1 million tons by the year 2020.[59] Currently, 70% of the PLA demand is accounted for by food and beverage packaging, since its physical properties makes PLA a green alternative to non-biodegradable polystyrene (PS) packaging. In a recent report, the Nova-institute for Ecology and Innovation showed that production of PLA when compared to that of PS has beneficial consequences at the ecological and

economical level: Production of greenhouse gases and depletion of non-renewable fossil fuels are reduced almost to a half.[60]

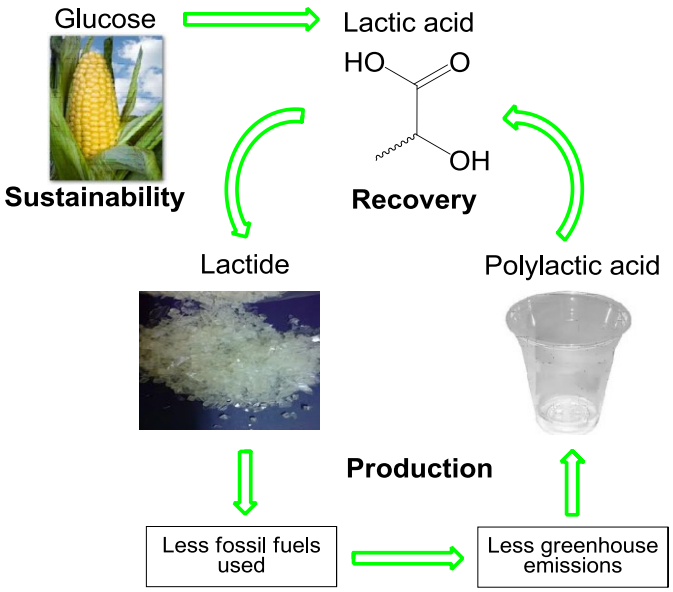


Fig. 1.6: Lactide cycle

The crystallinity of PLA depends on the stereochemistry of the polymer. Atactic PLA is an amorphous material with a glass transition temperature T_g below 50 ^oC, undesirable for industrial application. Isotactic PLLA (Poly-L-Lactic acid) is a solid crystalline with a glass transition temperature T_g of 60 ^oC and a high melting point ranging between 160 to 180 ^oC. The melting point can be easily increased up to 200 ^oC by blending D-lactide (monomer) with L-lactide (monomer) forming a **steroblock** copolymer (sbc) material with high cristallinity or up to 230 ^oC by preparing a **stereocomplex** polymer by blending both PLLA (Poly-L-Lactic acid) with PDLA (Poly-D-Lactic acid).[58,61] Thus stereochemical control is of high importance in polymerization of rac-lactide.

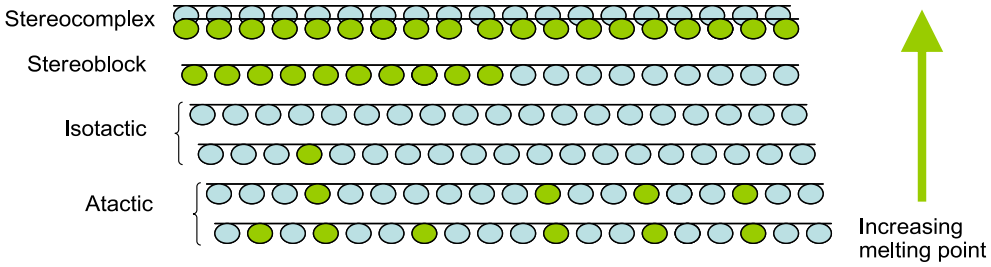
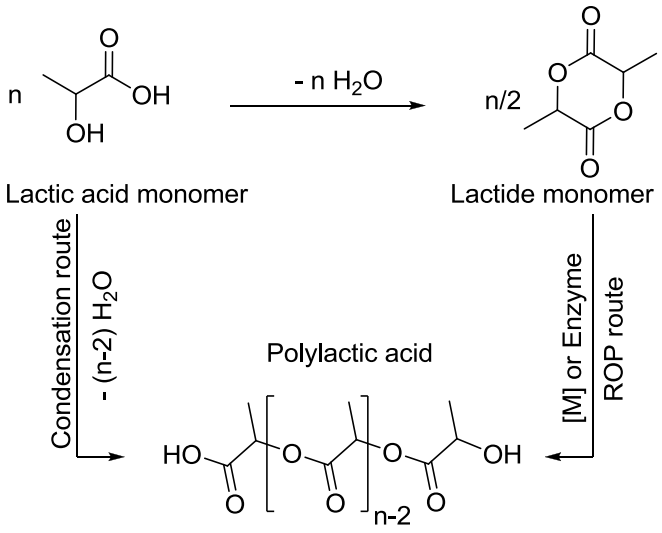


Fig. 1.7: Effect of stereocontrol on the melting point of PLA

1.2.3.1 Polymerization

While the condensation of lactic acid seems to be an easy and cheap route for the synthesis of PLA, the use of coupling agents, the need for controlling the esterification equilibrium and the lack of polymer molecular weight control limit its use for commercial production. The method mainly adopted in commercial production of PLA is the ring opening polymerization (ROP) of lactide. This can be performed either by using metal-complex catalysts (initiators), organocatalysts or enzymes.

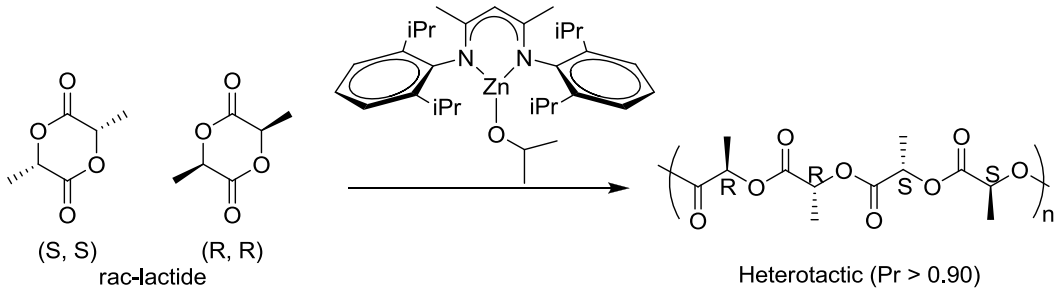


Scheme 1.8: Different routes for polylactic acid polymer

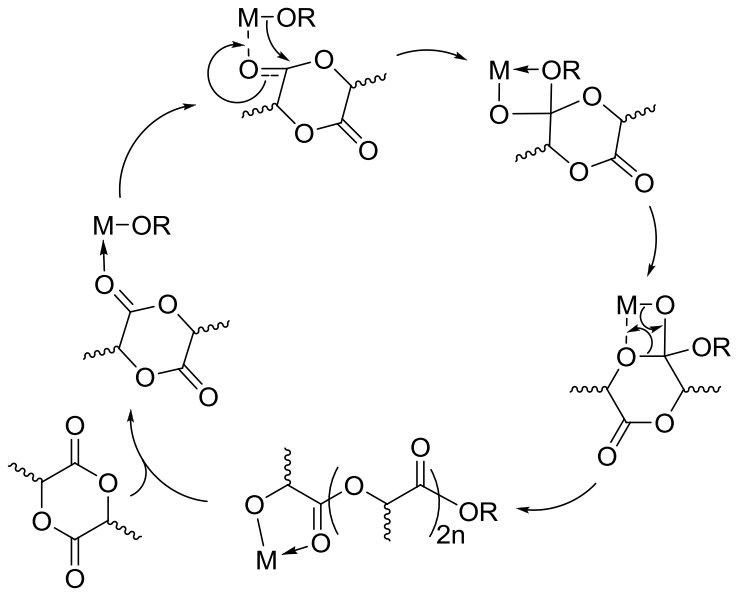
The use of metal catalysts is highly desirable in the PLA industry. The properties of the metal initiator control the quality of the resulting polymer. Therefore, the design and development of a suitable metal catalyst needs to meet the industrial conditions: (a) Stereocontrol to yield isotactic PLA. (b) Well defined polymer molecular weight with a narrow polydispersity (PDI). (c) High activity. (d) Chemical robustness under harsh conditions is an asset. The most common initiators for the lactide polymerization are ionic or covalent metal alkoxy coordination compounds ([M]OR).

1.2.3.2 Diketiminates in lactide polymerization

β-Diketiminate complexes have received considerable attraction due to the phenomenal work of Coates *et al.* who reported in 2001 the use of β-diketiminate magnesium and zinc complexes for lactide polymerization (Scheme 1.8). In particular with isopropoxide as the initiating group, these complexes showed excellent activities, high preference for heterotactic polymers in *rac*-lactide polymerization and gave predictable M_n and/or narrow PDI.[62] Since then, the interest in preparing new catalysts bearing diketiminate ligands increased, but the focus remained on diketiminates with *N*-aromatic substituents.[63,64] Our group has been lately interested in preparing *β*-diketimine ligands with aliphatic *N*-substituents for catalytic applications. The interest in such ligands is the ease of introduction of C_2-symmetry around the metal center which in absence of epimerization can induce stereopreference towards isotactic polymers.



Scheme 1.9 β-diketiminate zinc complex for lactide polymerization.[62]



Scheme 1.10: Coordination-insertion mechanism of lactide polymerization using metal catalysts**.**

1.2.3.3 Zr in lactide polymerization

There are many examples of catalysts for this process based on group 4 metals, most of them are octahedral complexes with Ti and Zr metal centers.[65] In general, most of the conducted studies were interested in the activity of the catalyst in the polymerization of L-lactide; polymerizations are slow and in most cases are performed at high temperature or in

molten monomer. Most *rac*-lactide polymerizations showed heterotactic preferences of the catalysts, and only few gave isotactic PLA acids with P_m values reaching 0.73.[64g,64h]

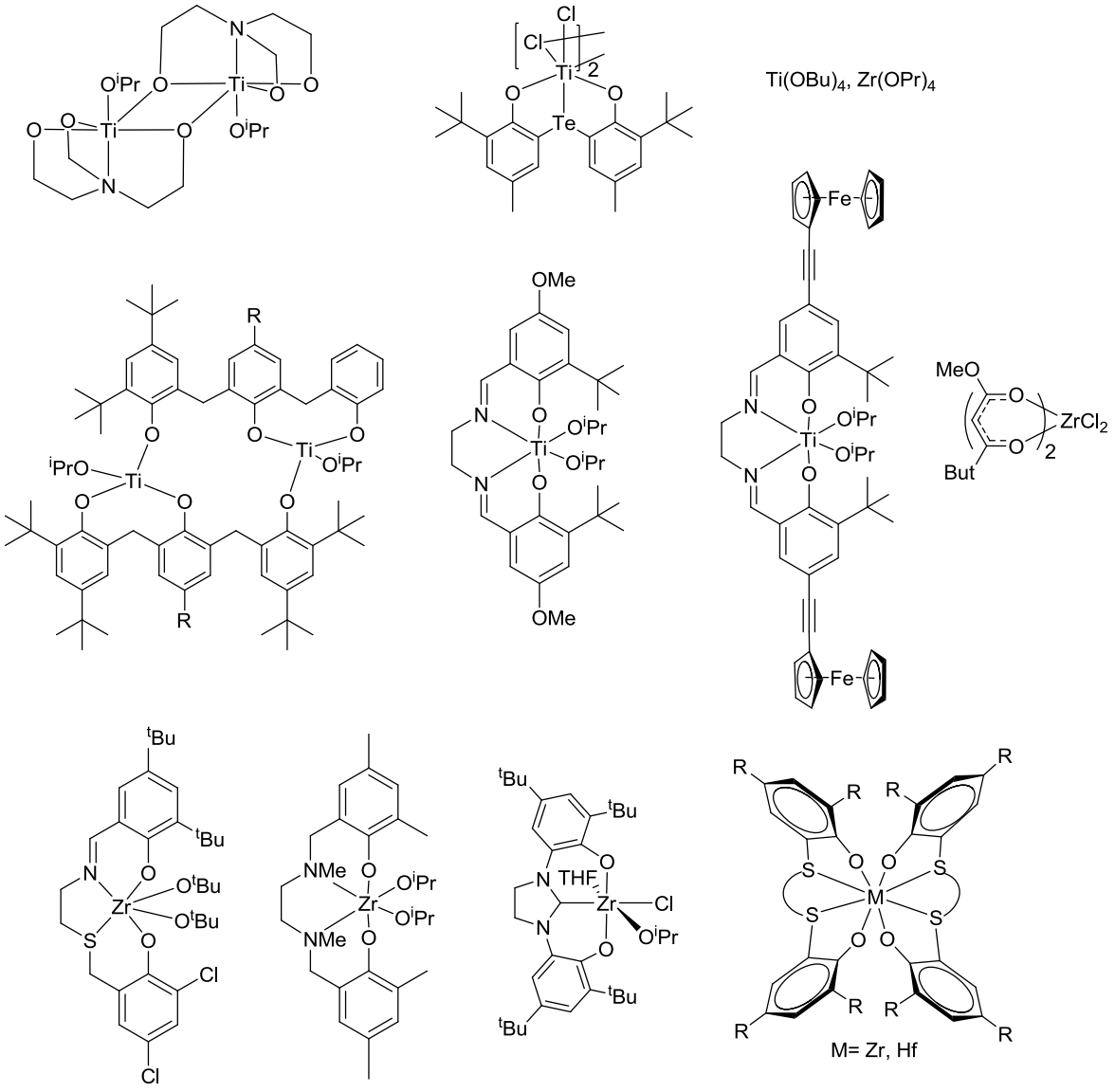


Fig. 1.8: Octahedral zirconium complexes for lactide polymerization

Although octahedral zirconium bisdiketiminate complexes bearing *N*-aromatic substituents are active catalysts for olefin, notably ethylene, polymerization,[66,67] they have never been reported for rac-lactide polymerization.

1.3 Aims of the thesis

Octahedral zirconium bisdiketiminate complexes bearing *N*-aliphatic substituents would be attractive targets for a variety of catalytic transformations for several reasons. First, the presence of a robust ligand like diketiminate with κ^2-coordination provides a well defined structure. Second, the *N*-alkyl substituents will favor *cis*-C_2 symmetry around the Zr center, forcing the two reactive sites to be in a *cis* geometry ideal for coordination-insertion reactions and for coordination-addition reactions. Third, a chiral octahedral Zr complex might exert stereocontrol on the catalyzed reaction.

The objective of this project is to explore the chemistry of octahedral *N*-alkyl β-diketiminates with zirconium as the metal center.

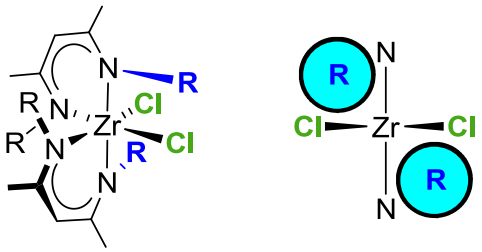


Fig. 1.9: Idealized eclipsed *cis* octahedral geometry for zirconium bis(diketiminate) complexes.

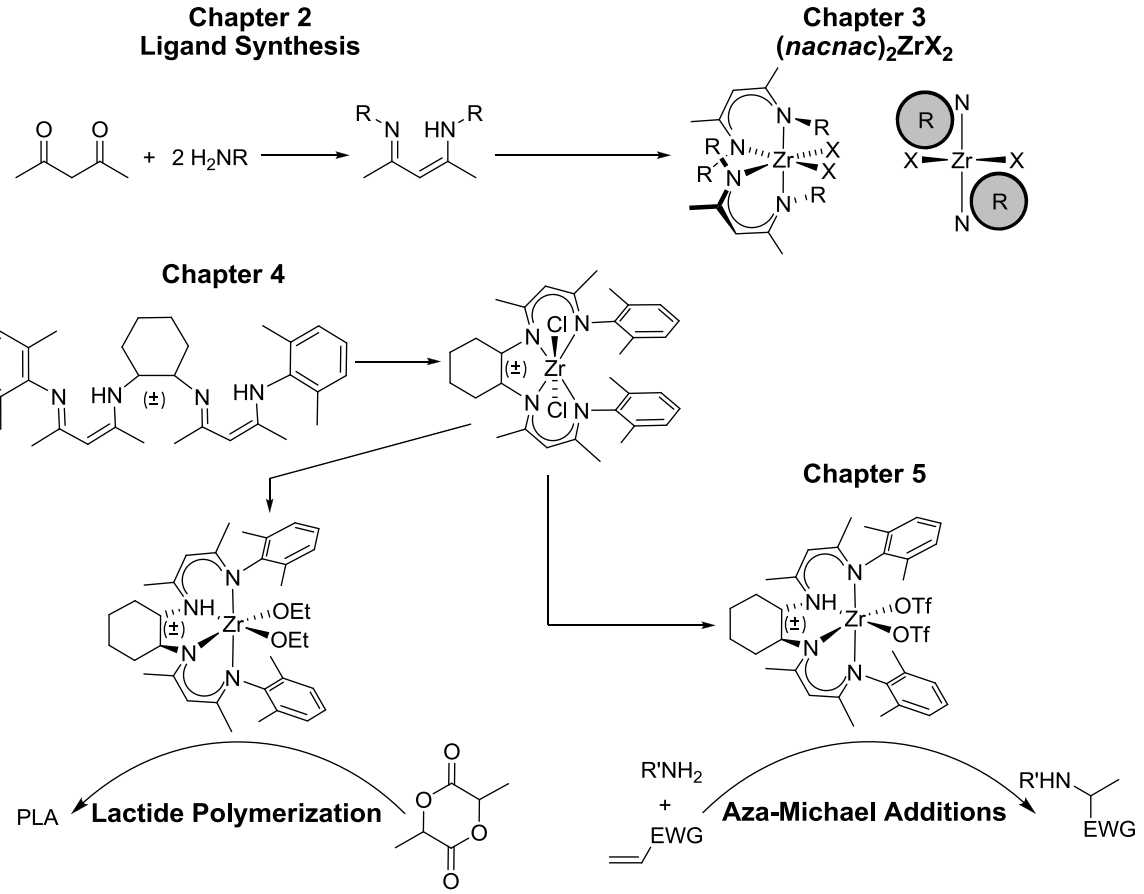
Chapter 2 describes the preparation of symmetric *N*-alkyl diketimines and the optimization of a simple one-pot synthesis from 1 equiv. of acetylacetone and 2 equiv. of amine. (Scheme 1.9)

In chapter 3, the syntheses of zirconium bis(diketiminate) complexes with *N*-alkyl substituents such as Bn, Cy, and (+)-CH(Me)Ph, is described. Investigation of their solid

state structures and their fluxional behavior in solution are detailed in this chapter in order to explain their low reactivity and lack of chiral induction.

In chapter 4, a cyclohexylene bridge between the two diketiminate ligands is introduced to address the problems encountered in chapter 3, i.e. to increase reactivity at the ancillary sites, as well as to prevent the epimerization of the metal center. The bisethoxide complex obtained is used in lactide polymerization.

In chapter 5, a cationic version of this complex is used in aza-Michael additions.



Scheme 1.11 Chapters content's

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CHAPTER 2

One-pot Synthesis of β-Diketimine Ligands

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Ibrahim El-Zoghbi, Aysha Ased, Paul O. Oguadinma, Ekou Tchirioua and

Frank Schaper

Département de chimie, Université de Montréal, Montréal, Québec, H3C 3J7, Canada.

2.1 Abstract

Symmetrical *N*,*N*'-dialkyl-2-amino-4-imino-pent-2-enes (*nacnac*^{R}H) can be prepared in high yields in a simple one-pot reaction from acetylacetone and 2 equiv. of amine. Optimized conditions involve the azeotropic removal of water, use of a minimum amount of solvent and of 1 equiv of acid. Either *para*-toluenesulfonic acid, hydrochloric acid or a mixture of both can be employed, with the latter being most advantageous. Symmetrical *nacnac*^{R}H are thus obtained in higher than 95% purity and with 65% yield for R = Me and 80-95% yields for R = Me, *n*Pr, *i*Pr, *i*Bu, Bn, Cy and (+)-CH(Me)Ph.

On peut préparer les *N*,*N*'-dialkyl-2-amino-4-iminopent-2-ènes (*nacnac*^{R}H) avec des rendements élevés en réalisant la réaction monotope de l'acétylacétone avec deux équivalents d'amine. Les conditions optimisées nécessitent l'élimination azéotropique de l'eau, l'utilisation d'une quantité minimale de solvant et un équivalent d'acide qui peut être l'acide *para*-toluènesulfonique, l'acide chlorhydrique ou un mélange des deux; ce dernier est le plus avantageux. Des *nacnac*^{R}H symétriques peuvent ainsi être obtenus avec une pureté de plus de 95 % et un rendement de 65 % lorsque R = Me et des rendements allant de 80 à 95 % lorsque le groupe R = *n*Pr, *i*Pr, *i*Bu, Bn, Cy et (+)-CH(Me)Ph.

KEYWORDS: diketimines, one-pot reaction

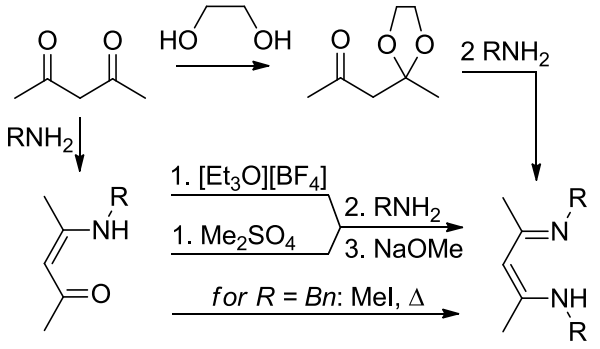
MOTS CLÉS: dicétimines, synthèse monotope.

2.2 Introduction

Preparation of β-diketimines ("*nacnac*" ligands), based on diimine analogues of acetylacetone, was described already in 1950,[1] and their first metal complexes in 1968.[2, 3] They played only a marginal role in coordination chemistry until the introduction of *nacnac*^{dipp} (dipp = 2,6-diisopropylphenyl) as a spectator ligand in the late '90s.[4] Since then, β-diketiminate ligands have become some of the most widely used bidentate *N*-donor ligands in coordination chemistry.[5] Interest in diketiminate ligands concentrated mostly on their *N*-aryl derivatives and *N*-alkyl substituted diketimines were used only rarely, mostly as low molecular weight ligands for chemical vapour deposition and atomic layer deposition applications.[6] We recently started to investigate the coordination chemistry of diketiminate ligands with aliphatic *N*-substituents.[7-11] For these investigations we required a simple, efficient and economic access to these compounds.

The most efficient and versatile preparation of 2-amino-4-imino-pent-2-enes is through condensation of acetylacetone with amines. While condensation of the first amine proceeds readily, the resulting enaminoketone has to be activated for the second condensation.[2, 5] The reasons for this is not clearly understood. A possible explanation involves increased steric bulk after 1st condensation. However, even reactions with methyl amine require activation. A more likely reason is the reduced electrophilicity. The activation for the second condensation might be achieved by transformation into the ketal, and the ethylene glycol monoketal has been used successfully as starting material for the synthesis of *nacnac*^{Bn}H and some macrocyclic diketimines (Scheme 2.1).[12, 13] Alternatively, in the case of aryl *N*-substituents, reaction in ethanolic HCl yielded the desired dicondensation product, probably

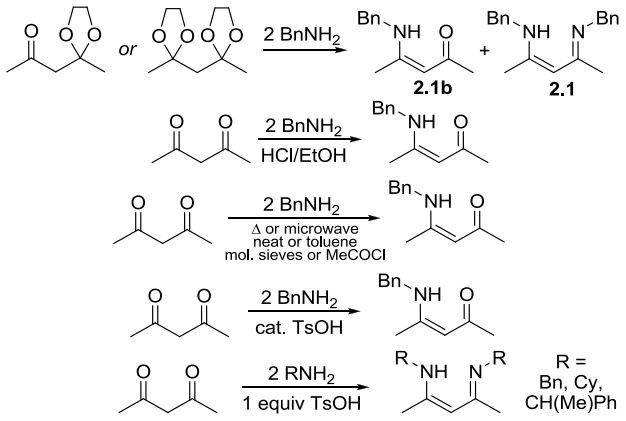
by intermediate formation of the diethyoxyketal.[3] For the diketimines with *N*-alkyl substituents of interest here, alkylation of the enaminoketone obtained after the first condensation with Meerwein salt and subsequent reaction with a second equivalent of amine is the most commonly employed method.[2] In an isolated report, *nacnac*^{Bn}H, **2.1**, has been obtained by refluxing the monocondensation product *acnac*^{Bn}H, **2.1b**, in methyl iodide (scheme 2.1).[14] The mechanism of this reaction (no second equivalent of amine was added) remains unclear. Recently, Bradley et al. showed that Meerwein's salt can be replaced by the less toxic and more economical methyl sulphate as alkylating agent (Scheme 2.1).[15] The latter, to our knowledge, is the most efficient synthesis described and diketimines were obtained in yields of 46 – 87% starting from the enaminoketone intermediate after distillation. Diketimines with aliphatic substituents are thus accessible, but their synthesis still requires a two step reaction, often distillation of the obtained product for purification, exclusion of moisture and the use of toxic alkylating reagents. In the following we describe a one-step preparation of these compounds, which avoids these drawbacks.



Scheme 2.1

2.3 Results and Discussion

Initial explorations. We repeated the preparation of *nacnac*^{Bn}H, **2.1**, described by Dorman[12] using either acetylacetone ethylene glycol mono- or diketal as starting material. We found, however, the reaction to give varying yields of diketimine product and to be highly dependent on reaction conditions (Scheme 2.2). If the reaction is carried out in diluted toluene solutions, only the monocondensation product **2.1b** was obtained. Reaction of acetylacetone with two equiv. of benzylamine in ethanolic HCl, following the procedure described by Parks and Holm[3] and Feldman et al.[16] for *N*-aryl substituted diketimines, also yielded only **2.1b**. Direct condensation of acetylacetone and benzylamine (no solvent, T > 100 °C, in the presence of molecular sieves or thionyl chloride), under microwave heating (neat or in toluene solution, without or with addition of molecular sieves or acetyl chloride), or under azeotropic removal of water (toluene solution, catalytic quantities of *para*-toluenesulfonic acid, several days) yielded either **2.1b** or decomposition products and at best traces (< 10%) of the desired **2.1**.



Scheme 2.2

While aryl-substituted diketimines have been obtained sometimes under typical "Dean-Stark-conditions", i. e. catalytic amounts of acid and azeotropic removal of water, yields have been generally low to moderate. Budzelaar et al. reported the synthesis of *nacnac*^{Xyl}H, **2.2**, (Xyl = 2,6-dimethylphenyl) in 75% yield in the presence of stoichiometric amounts of acid. Applying this protocol, we had previously obtained *nacnac*^{Bn}H,[8] *nacnac*^{Cy}H,[10] and *nacnac*$^{CH(Me)Ph}$H[7] in 67-82% yield. The initially obtained tosylate salt can be neutralized using a variety of bases of which aqueous potassium hydroxide proved to be the most convenient. (Aqueous $NaHCO_3$ failed in some cases to deprotonate the tosylate salt). Azeotropic water removal is required and reaction of $BnNH_2$ (or *i*$BuNH_2$), acetylacetone and 1 equiv TsOH either in toluene or without solvent only yielded the monocondensation product **2.1b**.

Optimization of the reaction conditions. Attempts to widen the scope of the above synthesis to diketimines bearing simple alkyl substituents such as Me, *i*Pr, *n*Pr and *i*Bu yielded, even after prolonged heating, only mixtures of bis- and monocondensation products with less than 60% of the desired diketimine by to NMR analysis. Use of more than one equiv. of TsOH proved to be of no advantage, and in some instances had detrimental influence on product yields. While it has never been understood why reactions proceed differently when catalytic or stoichiometric amounts of acid are used, we find it reasonable to assume that alkylation of the intermediate enaminoketone is in competition by its (reversible) protonation and that the latter requires amounts of acid which are equal or slightly higher than those of the amine. In agreement with this putative mechanism, presence of excess amine reduced the yield of the diketimine when not compensated with

excess TsOH (Table 2.1). Since the presence of excess amine and TsOH in equimolar amounts did not increase the yield when compared to the stoichiometric reaction (Table 2.1), loss of the low-boiling amine seems not to be responsible for the low yields obtained.

Table 2.1. Influence of excess base in the preparation of *nacnac*^{iBu}H

*i*BuNH$_2$ / acacH	TsOH / acacH	Reaction time	% *nacnac*^{iBu}H [a]	% *acnac*^{iBu}H [a]
2	1.1	24 h	60	30
3	1.1	24 h	5	70
3	1.5	20 h	15	30
3	2.2	18 h – 54 h	60	30

[a] determined by ^{1}H NMR from the crude product after basic workup.

Inspired by the decrease in yields in the reaction of acetylacetone ketal with amines on dilution, we found that concentration of the reaction mixture reduced drastically the amounts of monocondensation product and impurities formed (Table 2.2). Best results were obtained when the minimum amount of toluene necessary to operate the Dean-Stark-aparatus was employed.

Table 2.2. Influence of concentration in the preparation of *nacnac*^{nPr}H[a]

[acacH]	Reaction time	*nacnac*^{iBu}H [b]	*acnac*^{iBu}H [b]
48 mM	68 h	62%	18%
1.2 M	68 h	80%	traces
4 M	16 h	90%	traces

[a] acacH/*n*PrNH$_2$/TsOH = 1:2:1, toluene solution, azeotropic removal of water. [b] determined via ^{1}H NMR from the crude product after washing with aqueous KOH.

Reactions with other primary and secondary amines showed that concentration of the solution in general improved product yields and in most cases shortened reaction times to less than one day (Table 2.3). The low isolated yields for *nacnac*^{Me}H are related to its high volatility and its high sensitivity towards hydrolysis.[15] Reactions with isopropyl amine and isobutyl amine, however, did not show conversions above 30% even under these conditions. Substituting *p*-toluenesulfonic acid with sulphuric acid led to strongly decreased yields. The use of concentrated hydrochloric acid, on the other hand, increased the yields to 85-95% for R = *i*Pr and *i*Bu, respectively. In addition, use of conc. HCl prevented the formation of impurities observed in reactions with TsOH, and diketimines were obtained analytically pure for R = *i*Bu, *i*Pr and *n*Pr without need of further purification. Diketimines with R = Bn or CH(Me)Ph were obtained with >90% purity according to NMR (the main contamination being the monocondensation product), which is in most cases sufficient for their use in subsequent reactions. Analytically pure compounds

were obtained by recrystallisation from ethanol. For methylamine and cyclohexylamine, yields were drastically reduced by replacing *para*-toluenesulfonic acid with HCl. In both cases, the formation of an insoluble precipitate even at reflux temperature indicated that this might be related to the insolubility of the respective ammonium chloride salt. Consequently, use of an equimolar mixture of HCl/TsOH restored the yields observed for TsOH in these two cases, but did not otherwise affect reactions for other amines (Table 2.3).

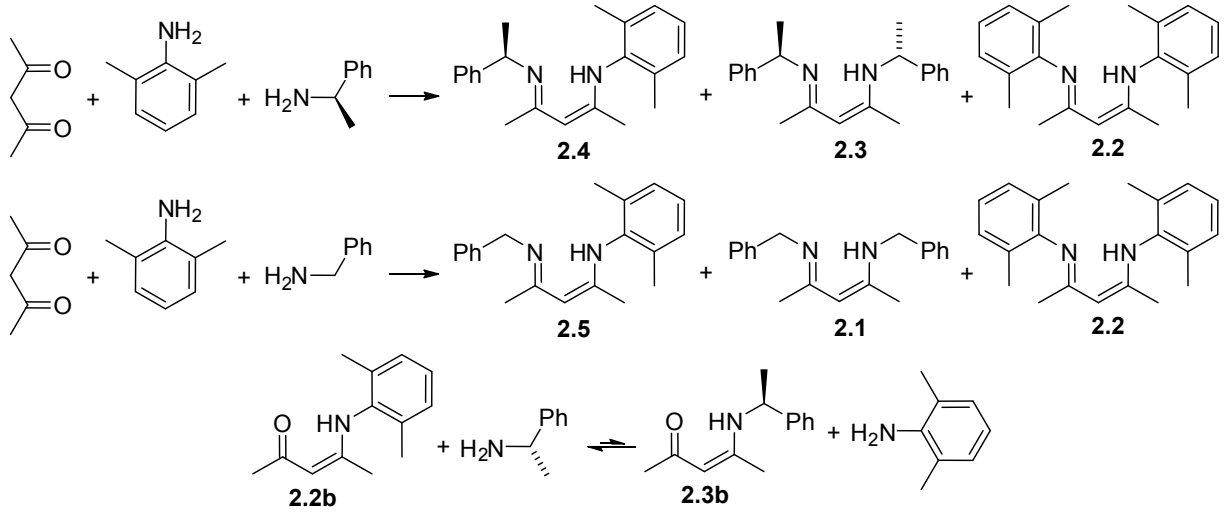
Table 2.3. Yields in diketimine synthesis for different combinations of amines and acids (Purity is given in parentheses). [a]

R	TsOH (c_{acacH} < 1 M)	TsOH	HCl	HCl/TsOH	Reaction time
*n*Pr	50% (EA)	80% (90%)	90% (EA)		72 h
Bn	82% (EA) [b]	80% (>95%)	75% (>95%)		24 h
CH(Me)Ph	70% (EA) [c]	80% (90%)	80% (90%)	80% (90%)	5 d
*i*Bu	35% (EA)	30%	95% (EA)		18 h
*i*Pr	23% (90%) [d]	30% (>95%)	85% (EA)	95% (EA)	24 h
Cy	69% (EA) [e]	90% (>95%)	0%	90% (90 %)	72 h
Me	60% (50%)	50% (95%)	5%	65% (>95%)	18 h

[a] Purity estimated by ^{1}H NMR, EA indicates correct elemental analysis. Reaction conditions: acacH/RNH_2/acid = 1:2:1, minimum amount of toluene used, with exception of the first column. [b] c_{acacH} = 0.5 M.[8] [c] c_{acacH} = 0.1 M, 5 d.[7] [d] c_{acacH} = 0.2 M, 3 d.[9] [e] c_{acacH} = 0.1 M, 3 d.[10]

Non-symmetrical diketimines. Synthesis of non-symmetrically substituted diketimines with different substituents on N and N' is a challenge and step-wise reaction using alkylating reagents such as Meerwein salt led to product mixtures.[17, 18] We thus explored if non-symmetric diketimines can be obtained using the one-pot procedure established above. Reactions of acetylacetone with 1 equiv 2,6-dimethylaniline and 1 equiv of either (+)-methylbenzylamine or benzylamine, yielded product mixtures containing the non-

symmetric diketimines **2.4** or **2.5** in higher than statistical amounts, but always accompanied by the two symmetric diketimines (Scheme 2.3).



Scheme 2.3 Synthesis of non-symmetrically substituted β-diketimine ligands

The preferred formation of the non-symmetric diketimine can be rationalized by the trapping of the more reactive 2,6-dimethylaniline in the monocondensation product, which diminishes its concentration in solution. Following reactions between *acnac*^{Xyl}H, **2.2b**, with methylbenzylamine, and *vice versa* of *acnac*$^{CH(Me)Ph}$H, **2.3b**, with 2,6-dimethylaniline by NMR showed that scrambling between the monocondensation products and free amines was observed already before significant amounts of diketimine were obtained (Scheme 2.3). In all cases, *acnac*^{Xyl}H was obtained preferentially. In particular at the beginning of the reaction, diketimines were thus formed from the two species present in the highest concentrations, i. e. *acnac*^{Xyl}H and either methylbenzylamine or benzylamine. As was previously observed by others, separation of non-symmetrical substituted diketimines from their symmetric counterparts is nearly impossible.[18] Despite their disproportionally high

amount in the obtained product mixtures, **2.4** and **2.5** were not separated from the symmetric diketimines **2.1**-**2.3** by recrystallisation, sublimation or column chromatography (extensive hydrolysis in the latter case). For **2.5**, diketimine **2.1** could be separated by recrystallisation and **2.5** was obtained in 30% yield and 90% purity, still contaminated by 10% of **2.2**.

2.4 Summary and Conclusions

β-Diketimines with aliphatic substituents on nitrogen can be obtained in simple one-pot condensation reactions between acetylacetone and primary or secondary amine, provided that water is removed azeotropically and that one equivalent of acid is present. Under optimized reaction conditions, we employed an equimolar mixture of hydrochloric and *para*-toluenesulfonic acid and the amount of solvent was kept to the minimum required for water removal. Symmetric diketimines can thus be obtained very economically, without the need of toxic alkylating reagents or moisture-free conditions.

For non-symmetric diketimines, the fast scrambling between free amine and monocondensation products makes the proposed protocol less efficient. Although they are obtained in higher than statistic ratio, their separation from the symmetric diketimines, invariably formed as side products, was not possible and the synthetically more demanding routes proposed by Park et al.[18, 19] are still more advantageous.

2.5 Experimental Section

All chemicals were obtained from commercial suppliers and used as received. Elemental analyses were performed at the Laboratoire d'Analyse Élémentaire (Université de Montréal). NMR spectra were recorded on a Bruker ARX 400 MHz spectrometer and referenced to residual solvent ($CHCl_3$: δ 7.26).

General procedure for the synthesis of symmetric diketimines. Acetylacetone and 1 equiv of the desired acid or acid mixture (see Table 2.3) were combined in a minimum volume of toluene, usually equal to the combined volumes of all reactants. The mixture was stirred for 10 min and 2 equiv of the desired amine were added to give a white suspension, which was allowed to stir for appr. 20 min. The reaction mixture was then refluxed for the required time (Table 2.3) with azeotropic removal of water (Dean-Stark-aparatus). The brown precipitate formed after cooling to room temperature and standing for 3 - 4 h was isolated by decantation. Ether (50 mL) and aqueous KOH (11.2 g, 0.2 mol, 50 mL) were added and the mixture stirred for 15 min. The ether phase was separated, dried over Na_2SO_4 and the solvent evaporated. Yields and purities of the obtained products, estimated from ^{1}H NMR, are given in Table 2.3. Characterization data and quantities are given below for selected experiments.

***nacnac*^{Bn}H, 2.1**.[2, 14, 15] Acetylacetone (2.00 g, 20 mmol), HCl (12.1 M, 1.65 mL, 20 mmol) and benzylamine (4.28 g, 40 mmol) in toluene (7 mL) gave a red brown solid (2.90 g, 75%, > 95% purity). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 11.49 (bs, 1H, NH), 7.22-7.30 (m, 10H, Ph), 4.64 (s, 1H, $CH(C{=}N)_2$), 4.46 (s, 4H, CH_2), 1.95 (s, 6H, Me). Recrystallisation from a

saturated ethanol solution at –20°C gave: Anal. Calcd. for $C_{21}H_{26}N_2$: C, 81.97; H, 7.97; N, 10.06. Found: C, 81.75; H, 8.19; N, 10.05.

***nacnac*$^{\mathbf{CH(Me)Ph}}$H, 2.3**.[7, 20] Acetylacetone (1.00 g, 10 mmol), HCl (12.1 M, 0.82 mL, 10 mmol) and (+)-phenylethylamine (2.42 g, 20 mmol) in toluene (6 mL) gave a red brown oil (2.45 g, 80%, 92% purity). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 11.89 (bs, 1H, NH), 7.20-7.35 (m, 10H, Ph), 4.68 (q, 2H, J = 7 Hz, C*H*(Me)Ph), 4.48 (s, 1H, CH(C=N)$_2$), 1.82 (s, 6H, Me(C=N)), 1.49 (d, 6H, J = 7 Hz CH(*Me*)Ph). Recrystallisation from a saturated ethanol solution at –20°C gave: Anal. Calcd. for $C_{21}H_{26}N_2$: C, 82.31; H, 8.55; N, 9.15. Found: C, 81.75; H, 8.52; N, 9.06.

***nacnac*$^{n\mathbf{Pr}}$H.**[15] Acetylacetone (2.00 g, 20 mmol), HCl (12.1 M, 1.65 mL, 20 mmol) and *n*-propylamine (2.36 g, 40 mmol) in toluene (5 mL) gave a dark brown oil (3.3 g, 90%). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 10.04 (bs, 1H, NH), 4.47 (s, 1H, CH(C=N)$_2$), 3.17 (t, J = 9 Hz, 4H, NCH_2), 1.87 (s, 6H, Me(C=N)), 1.61 (m, 4H, $CH_2CH_2CH_3$), 0.97 (t, J = 9 Hz, 6H, CH_2CH_3). Anal. Calcd for $C_{11}H_{22}N_2$: C, 72.47; H, 12.16; N, 15.37; Found C, 72.41; H, 11.81; N, 15.39

***nacnac*$^{i\mathbf{Pr}}$H.**[2] Acetylacetone (2.00 g, 20 mmol), HCl (12.1 M, 1.65 mL, 20 mmol) and isopropylamine (2.36 g, 40 mmol) in toluene (5 mL). To eliminate monocondensation product, the oil obtained after decantation of toluene was treated with excess saturated aqueous $NaHCO_3$ and ether (20 mL). Ether and water phase were decanted from the remaining oil. Ether (50 mL) and aqueous KOH (11.2 g, 0.2 mol, 50 mL) were added and the mixture stirred. The ether phase was separated, dried over Na_2SO_4 and evaporated to dryness to give a dark-red oil (3.4 g, 85%). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 11.43 (bs, 1H,

NH), 4.38 (s, 1H, CH(C=N)$_2$), 3.06 (hept., *J*= 6 Hz, 2H, C*H*(CH$_3$)$_2$), 1.89 (s, 6H, CH$_3$(C=N)), 1.16 (d, *J* = 6 Hz, 12H, CH(C*H*$_3$)$_2$). Anal. Calcd for $C_{11}H_{22}N_2$: C, 72.47; H, 12.16; N, 15.37; Found C, 72.06; H, 12.08; N, 15.15.

***nacnac*$^{i\mathbf{Bu}}$H**.[15, 21] Acetylacetone (2.00 g, 20 mmol), HCl (12.1 M, 1.65 mL, 20 mmol) and isobutylamine (2.92 g, 40 mmol) in toluene (5 mL) gave a brown oil (4.3 g, 95%). ^{1}H NMR (CDCl$_3$, 400 MHz): δ 11.07 (bs, 1H, NH), 4.48 (s, 1H, CH(C=N)$_2$), 3.05 (d, *J* = 9 Hz, 4H, CH$_2$), 1.88 (m, 2H, C*H*(CH$_3$)$_2$), 1.86 (s, 6H, CH$_3$(C=N)), 0.96 (d, *J* = 9 Hz, 12H, CH(C*H*$_3$)$_2$). Anal. Calcd for $C_{13}H_{26}N_2$: C, 74.23; H, 12.46; N, 13.32; Found C, 74.06; H, 13.03; N, 12.99.

***nacnac*$^{\mathbf{Cy}}$H**.[22] Acetylacetone (2.00 g, 20 mmol), HCl (12.1 M, 0.82 mL, 10 mmol), *p*-toluenesulfonic acid monohydrate (2.00 g, 11 mmol) and cyclohexylamine (3.98 g, 40 mmol) in toluene (15 mL) gave a colorless oil that crystallizes into colorless crystals upon standing for 2-3 hours (4.75 g, 90%). ^{1}H NMR (CDCl$_3$, 400 MHz): δ 11.72 (bs, 1H, NH), 4.44 (s, 1H, CH(C=N)$_2$), 3.32-3.35 (m, 2H, Cy CH), 1.90 (s, 6H, Me(C=N)), 1.80-1.35 (m, 20H, Cy). Anal. Calcd for $C_{13}H_{26}N_2$: C, 77.80; H, 11.52; N, 10.64; Found C, 77.44; H, 11.57; N, 10.67.

***nacnac*$^{\mathbf{Me}}$H.**[2] Acetylacetone (3.00 g, 30 mmol), HCl (12.1 M, 1.24 mL, 15 mmol), *p*-toluenesulfonic acid monohydrate (2.99 g, 16 mmol) and methylamine (40%, 4.65 g, 0.06 mol) in toluene (6 mL). The aqueous phase was re-extracted with ether (3 x 300 mL), the combined organic phases were dried over Na_2SO_4 and evaporated to dryness. The dark-yellow oil obtained solidifies to an orange precipitate that darkens upon standing to room temperature (2.5 g, 65%). ^{1}H NMR (CDCl$_3$, 400 MHz): δ 10.04 (bs, 1H, NH), 5.2 (s, 1H,

$CH(C{=}N)_2$), 2.99 (s, 6H, NMe), 1.86 (s, 6H, $CH_3(C{=}N)$). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 400 MHz): δ 162.1 (C=N), 93.9 ($CH(C{=}N)_2$), 33.3 (Me), 19.0 ($CH_3(C{=}N)$). Elemental analysis unsatisfactory due to easy decomposition.[15]

***nacnac*^{Xyl,Bn}H, 2.5**. Acetylacetone (3.00 g, 30 mmol), HCl (12.1 M, 2.5 mL, 30 mmol) and 2,6-dimethylaniline (3.63 g, 30 mmol) in toluene (12 mL) were refluxed for appr. 2 h. To the obtained yellow suspension benzylamine (3.27 g, 30 mmol) was added and allowed to reflux for 3 days under azeotropic removal of water in a Dean-Stark-aparatus. After cooling to room temperature and decantation of toluene, the brown oil obtained was treated with ether (50 mL) and aqueous KOH (16.8 g, 0.3 mol, 50 mL). The ether phase was separated and evaporated to dryness. The obtained red-brown oil was dissolved in a minimum amount of ethanol and kept at –20°C for several days. Crystals of *nacnac*^{Bn}H formed were removed by filtration and the remaining ethanol solution evaporated to dryness to yield a brown oil (2.62 g, 30%, in 90% purity containing 10% **2.2**). Further recrystallisations in MeOH or in EtOH as well as sublimation still yielded product mixtures. ^1H NMR ($CDCl_3$, 400 MHz) δ 11.18 (bs, 1H, NH), 7.22-7.30 (m, 8H, Ph), 4.45 (s, 1H, $CH(C{=}N)_2$), 4.43 (s, 2H, CH_2), 2.07 (s, 6H, Ar Me), 1.90 (s, 3H, Me(C=N)), 1.63 (s, 3H, Me(C=N)). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 400 MHz) δ 160.1 (C=N), 140.1 (C=N), 128.4, 128.3, 127.6, 127.5, 127.2, 127.0, 126.7, 126.3 (all Ph), 93.9 ($CH(C{=}N)_2$), 46.5 (CH_2), 21.2 (*Me*(C=N)), 19.1 (*Me*(C=N)), 18.3 (Me_2Ph). EI-HRMS (m/z): Calcd for $C_{20}H_{25}N_2$ $[M+H]^+$: 293.2012; Found: 293.2013.

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CHAPTER 3

Zirconium Complexes of Symmetric and of Chiral Diketiminate Ligands – Synthesis, Crystal Structures and Reactivities

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Ibrahim El-Zoghbi, Saïda Latreche and Frank Schaper

Département de chimie, Université de Montréal, Montréal, Québec, H3C 3J7, Canada.

3.1 Abstract

Reaction of *N*,*N*-dialkyl-2-amino-4-imino-pent-2-enes (*nacnac*^{R}H; R = Bn (**3.1a**), Cy (**3.1b**), *R*-CH(Me)Ph (**3.1c**)) with *n*BuLi afforded the lithium salts *nacnac*^{R}Li(THF), **3.2a-c**. Further reaction with $ZrCl_4$ or $ZrCl_4(THF)_2$ yielded the *cis*-dichloride complexes *nacnac*$^{R}{}_2ZrCl_2$, **3.3a-c**. As a side reaction in the synthesis of **3.3c**, CH-activation of CH(Me)Ph under formal HCl elimination was observed. Complex **3.3a** could also be obtained by reaction of *nacnac*^{Bn}H with *n*Bu_2ZrCl_2. *Nacnac*$^{Bn}{}_2ZrMe_2$, **3.5**, was formed in reactions of **3.3a** with MeLi in the presence of excess $AlMe_3$ and was isolated from the reaction of Me_2ZrCl_2 with **3.2a**. Complex **3.5** reacts with aluminum chloride compounds, but not with lithium chloride, to form the dichloride complex **3.3a** and with ethanol to form *nacnac*$^{Bn}{}_2Zr(OEt)_2$, **3.6**. X-ray diffraction studies have been performed for **3.3a-c**, **3.5** and **3.6**.

3.2 Introduction

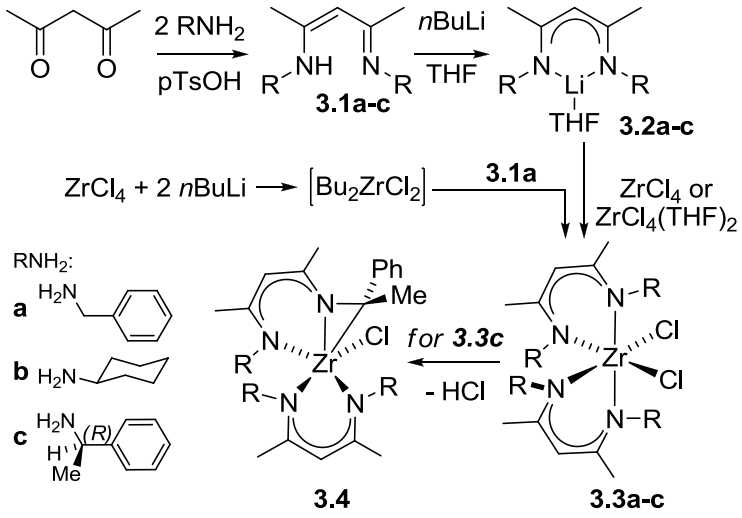
β-Diketiminate ("*nacnac*") ligands have gained increasing popularity since the mid '90s due to their suitability as spectator ligands.[1] Zirconium complexes with diketiminate ligands (based on 2,4-diiminopentane)[2, 3] appeared in the literature in 1994 by the work of Lappert and coworkers,[4] followed by more extensive work in the groups of Collins,[5, 6] Smith,[7, 8] Novak,[9] and others.[10-16] Interest in these complexes was focused mostly on their application in olefin, notably ethylene, polymerization[5, 9-11] or on investigations of the ligand coordination mode,[4, 6-8, 15, 16] which varies between in-plane κ^2-coordination and out-

of-plane $\eta^{4/5}$-coordination. With a single exception,[12] ligands with aryl substituents on nitrogen were employed, as is the case in most diketiminate metal complexes. Variations in the ligand framework were limited by the fact that ortho-substitution of both *N*-aryl substituents impedes the coordination of a second diketiminate ligand to zirconium,[6-8] although the use of unsymmetrical ligands allowed the substitution of at least one phenyl ring.[11] Complexation of the bulky bis(trimethylsilyl) diketiminate (*nacnac*^{TMS}) to Zr, resulted in a rearrangement of one *nacnac*^{TMS} ligand.[10] Coordination of two diketiminate ligands to a ZrX_2 fragment should favor the formation of C_2-symmetric *cis*-complexes, with two homotopic Zr-X sites, whose environment is strongly influenced by the substituent on nitrogen. We present in the following the syntheses of zirconium bis(diketiminate) complexes with aliphatic substituents on nitrogen, which increase the possibilities of steric variations in these complexes and allow easy introduction of chirality, the investigation of their solid state and solution structures and (attempted) applications in catalysis.

3.3 Results and Discussion

***nacnac*$_2$ZrCl$_2$ complexes**. Diketimine ligands **3.1a-c** were obtained from condensation of acetylacetone and the corresponding amine in the presence of stoichiometric amounts of *para*-toluenesulfonic acid. Synthesis of **3.1a** and **3.1c** by this method has been previously described.[17, 18] Ligand **3.1b** has been prepared previously using $TiCl_4$ as an activator in 29% yield.[19] Deprotonation with *n*BuLi in THF yielded the THF coordinated lithium salts **3.2a-c**, which were used without further purification (Scheme 3.1). Reaction of **3.2a-c** with

$ZrCl_4$ or $ZrCl_4(THF)_2$ in toluene afforded the respective bis(diketiminate) complexes *nacnac*$^{Bn}{}_2ZrCl_2$, **3.3a**, *nacnac*$^{Cy}{}_2ZrCl_2$, **3.3b**, and (*R*,*R*-*nacnac*^{MeBn})$_2ZrCl_2$, **3.3c**, in moderate yields (Scheme 3.1). The choice of zirconium starting material or the solvent (toluene, THF) did not seem to influence reaction yields. Following an alternative synthetic route,[20] reaction of *n*Bu_2ZrCl_2, generated in situ by reaction of *n*BuLi with $ZrCl_4$, with the neutral ligand **3.1a** in toluene at 90 °C improved the yield of **3.3a** from 35% to 75%. Similar reactions with **3.1b** and **3.1c** in toluene or hexane at various temperatures and reaction times led only to unidentified product mixtures, which did not contain **3.3b** or **3.3c** in significant amounts. Reactions of diketiminate ligands with secondary alkyl substituents on nitrogen seem to be too slow with respect to the instability of *n*Bu_2ZrCl_2.



Scheme 3.1

X-ray diffractions studies of complexes **3.3a-c** (Figure 3.1 & 3.2, Table 3.1) show distorted octahedral coordination geometries around the zirconium center (X-Zr-X angles

of 78-107°). In all cases the expected *cis*-geometry of the $ZrCl_2$ fragment is found. Complexes **3.3a** & **3.3b** contain a crystallographic C_2-axis, while chiral complex **3.3c** crystallizes with two diastereomers in the asymmetric unit, which, however, approach C_2-symmetry. The structural features of **3.3a-c** seem to be governed by steric interactions between the alkyl substituent on nitrogen and the atoms coordinated to the metal center. The complex distorts in a way that places the *N*-substituent in the space above the mid-point of two Zr-Cl bonds (or between chloride and nitrogen) instead of the eclipsed placement expected from an idealized geometry. Similar distortions were observed, sometimes to a lesser extent, in related octahedral bis(diketiminato) zirconium complexes,[6, 7, 12] while they are mostly absent in zirconium complexes with two aminoketone (*acnac*) ligands, where the oxygen atom occupies the position *trans* to the chloride (or amide) ligands.[7, 12, 21] For all complexes, the *N*-alkyl substituents are oriented away from the chloride ligands, indicating stronger steric interactions of the alkyl substituent with the chloride ligand than with the methyl group in the ligand backbone.

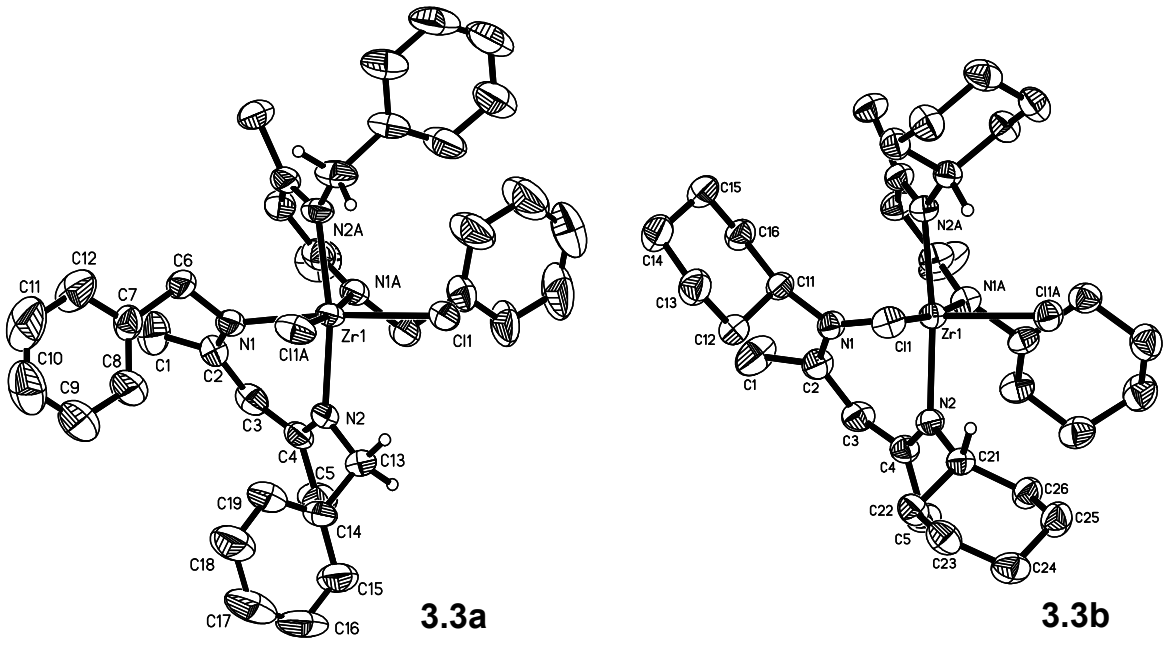


Figure 3.1. Crystal Structures of **3.3a** & **3.3b**. Thermal ellipsoids are drawn at the 50% probability level. Most hydrogen atoms are omitted for clarity.

Table 3.1 Selected bond distances [Å] and bond angles [deg] for **3.3a** - **3.3c**, **3.5** and **3.6**. [a]

	3.3a	**3.3b**	**Λ-3.3c**	**Δ-3.3c**	**3.5**	**3.6**
Zr-N1 [b]	2.201(3)	2.235(2)	2.181(2) & 2.205(2)	2.177(3) & 2.183(2)	2.203(3) & 2.217(3)	2.288(2) - 2.305(2)
Zr-N2 [c]	2.190(2)	2.197(2)	2.213(3) & 2.246(3)	2.221(3) & 2.247(3)	2.289(3) & 2.295(3)	2.225(2) - 2.232(2)
Zr-X [d]	2.455(1)	2.483(1)	2.499(1) & 2.516(1)	2.483(1) & 2.487(1)	2.290(4) & 2.297(4)	1.939(2) - 1.954(2)
N1-C2 / N2-C4	1.325(4) & 1.339(4)	1.339(3) & 1.331(2)	1.321(4) - 1.357(4)	1.328(4) - 1.348(4)	1.328(5)- 1.338(5)	1.314(3) - 1.336(3)
C2-C3 / C3-C4	1.410(5) & 1.388(5)	1.397(3) & 1.410(3)	1.394(5) - 1.408(4)	1.398(4) - 1.413(4)	1.380(6)- 1.403(5)	1.388(4) - 1.416(4)
Complex bending [e]	37	34	47-49	36-42	31	32-34
N1-Zr-N2 [f]	78.06(9)	80.52(6)	83.71(9) & 85.46(9)	82.28(9) & 82.44(9)	74.56(11) & 74.81(11)	76.65(7)- 77.52(8)
N-Zr-N [g]	86.71(13)- 87.28(9)	86.7(1)- 89.2(1)	91.32(9) - 106.81(9)	91.31(9) - 98.60(9)	77.31(11)- 127.20(12)	83.20(7)- 87.37(8)
X1-Zr-X2	93.58(5)	93.36(3)	88.52(3)	90.59(3)	116.36(15)	97.12(7) & 98.72(7)
N-Zr-X [d]	90.11(7) - 97.54(7)	90.07(5)- 95.48(4)	83.53(6) - 92.51(7)	88.95(7) - 91.41(7)	78.34(13) - 94.59(12)	87.78(7) - 102.55(8)

[a] Atom numbering according to **3.3a**. Values were provided for analogous atoms in other structures, *independent of the numbering in the respective complex*. [b] Nitrogen atoms *trans* to Cl, numbering differs between complexes. [c] Nitrogen atoms *trans* to N, numbering differs between complexes. [d] X = Cl (**3.3a** - **3.3c**), C (**3.5**), O (**3.6**). [e] Angle(s) between the least-square planes defined by N1,N2,C2-C4 and Zr1,N1,N2 in **3.3a** or respective atoms in other complexes. [f] *Cis*-angle(s) between nitrogen atoms of the same ligand. [g] *Cis*-angle(s) between nitrogen atoms of different ligands.

The diastereomeric Δ- and Λ-isomers of **3.3c** can both be found in the asymmetric unit. Changes in the Δ/Λ conformation of the complex are accompanied by changes in the conformation of the diketiminate ligand. In the Δ-isomer, the diketiminate ligands retain a C_2-symmetric conformation with the phenyl substituents *anti* towards each other. In the Λ-isomer, rotation around the N1-C20 and N4-C50 bonds places the phenyl rings of each diketiminate in a *syn*-orientation, comparable to the C_s-symmetric ligand conformation observed in **3.3a** (Figure 3.1). Consequently, methyl groups C27 and C57 instead of hydrogen atoms are oriented towards the Zr center, causing an increased distortion from octahedral geometry, increased Zr1-Cl distances and a reduced Cl1-Zr1-Cl2 angle in Λ-**3.3c** compared to Δ-**3.3c** (Table 3.1).

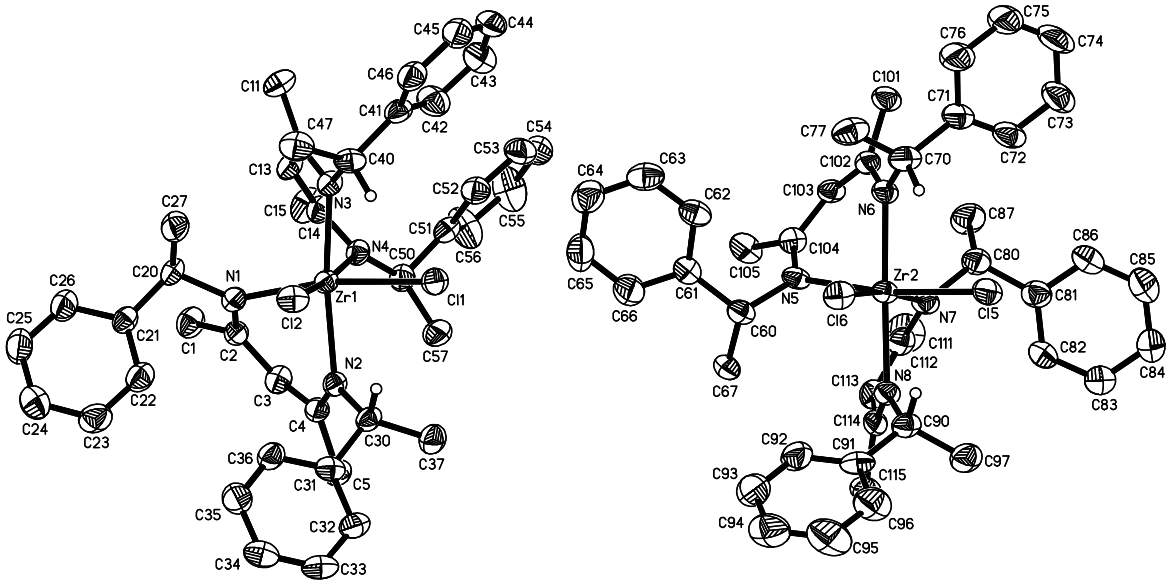


Figure 3.2. Crystal Structures of Λ-**3.3c** (left) and Δ-**3.3c** (right), both found in the same asymmetric unit. Thermal ellipsoids are drawn at the 50% probability level. Most hydrogen atoms are omitted for clarity.

The zirconium atom in **3.3a-c** is bent significantly out of the mean plane of the *nacnac* ligand (bending angles of 34-49°, Table 3.1), as commonly observed in sterically encumbered diketiminate complexes.[1] Since the nitrogen atoms retain their planar geometry (e.g. for **3.3a**: Σ(X-N1-Y) = 359°, Σ(X-N2-Y) = 359°), the alkyl substituents on N are displaced out of the ligand mean plane (Figure 3.3). In all cases, the remaining ligand framework adopts a boat-like conformation, which reduces the distance between the electron-rich central carbon atom of the ligand back-bone and the zirconium center.[4] In diketiminate Zr complexes with a $\eta^{4/5}$-coordinated *nacnac* ligand, distances of the metal center to the central carbon atom are below 2.8 Å.[5-7, 13, 16] The rather longer respective

distances in **3.3a-c** (3.1-3.3 Å) indicate, as expected for octahedral coordinated Zr complexes, the absence of significant coordinative interactions between Zr and the central carbon atom (C3 in figure 3.3). Similar ligand conformations in *nacnac* Sc complexes have likewise been ascribed to steric origins.[22] Leaving aside potential p_N-d donation, diketiminate ligands in **3.3a-c** thus act as κ^2-coordinated, 4 e^--donor ligands.

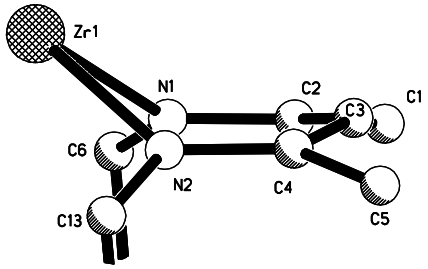


Figure 3.3. Boat-like conformation of the diketiminate ligand in **3.3a**.

Yellow crystals of **3.3c** were consistently contaminated with a minor amount of red crystalline material, which could not be isolated in sufficient quantity for characterization. X-ray analysis identified the contamination as the CH-activation product **3.4** (Scheme 3.1, Figure 3.4). The complex is non-symmetric and its geometry can be best described as distorted square pyramidal with N1 and C27 sharing the apical position (X-Zr-X angles (X = Cl1, N2-N4) = 84-89°, X-Zr-Y angles (Y = centroid N1/C27) = 96-112°). The two *nacnac* ligands are coordinated differently. The CH-activated ligand is planar with an anti-orientation of the phenyl rings and the Zr atom coordinated in the ligand mean plane. In the second ligand, Zr is found to be bent quite severely (62°) out of the mean ligand plane. Zr-C distances to the ligand backbone are shorter than those in **3.3c** (**3.4**: 2.8-2.9 Å, **3.3c**: 3.0-3.3 Å), but still noticeably longer than those observed in $\eta^{4/5}$-coordinated *nacnac* ligands

(2.5-2.8 Å).[5-7, 13, 16] The shortened Zr-C_{nacnac} distances are thus most likely due to steric reasons, i. e. the increased out-of-plane bending of the Zr atom.

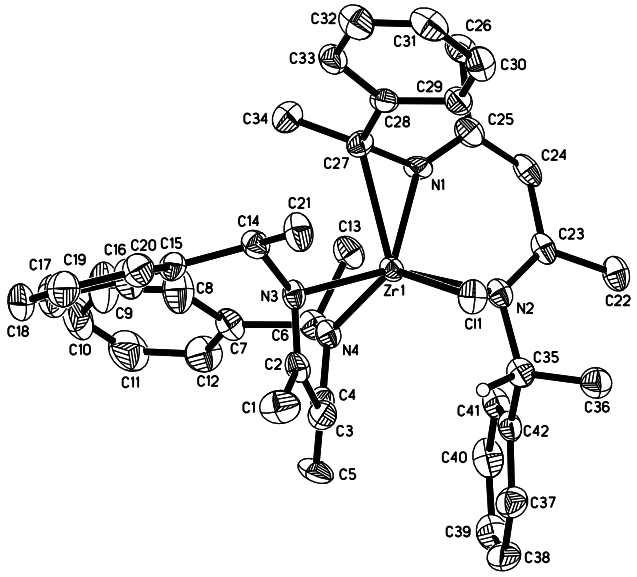


Figure 3.4. Crystal structure of complex **3.4** with 50% probability thermal ellipsoids depicted. Hydrogen atoms, other than H35, omitted for clarity.

Table 3.2. Selected bond distances [Å] and bond angles [deg] for **3.4**.

Zr1-Cl1	2.477(1)	N1-C25	1.330(6)
Zr1-N1	2.031(3)	C24-C25	1.366(8)
Zr1-N2	2.318(4)	C23-C24	1.437(7)
Zr1-N3	2.230(3)	N2-C23	1.323(6)
Zr1-N4	2.196(4)	N1-Zr1-N2	76.6(2)
Zr1-C27	2.305(5)	N3-Zr1-N4	83.5(1)
N1-C27	1.410(7)	N1-Zr1-N4	109.1(2)

The formation of **3.4** as a result of formal HCl elimination was surprising and only observed as a side reaction during the preparation of **3.3c**. Treatment of complexes **3.3a-c** with excess (1-2 equiv) of bases such as NaO*t*Bu, NEt_3, pyridine, $Na(NSiMe_3)_2$ or *n*BuLi showed no reaction (or decomposition upon heating).

Dynamic behaviour in solution. NMR spectra of complexes **3.3a-c** indicate that the complexes do not retain their conformation in solution. The ^{1}H NMR spectrum of **3.3a** in $CDCl_3$ at room temperature displays two doublets for diastereotopic hydrogen atoms of the benzyl CH_2 groups, one singlet for the CH groups in the ligand backbone and one singlet for the ligand methyl groups. Below –50 °C, four doublets for benzyl CH_2, two singlets for the methyl groups, but still only one sharp singlet for the backbone CH groups are obtained (Figure 3.5). The low temperature spectrum is thus in agreement with the observed solid state structure: a symmetric complex, in which unsymmetrically coordinated *nacnac* ligands are connected by a C_2-axis. The observed spectral changes on heating can be explained with an isomerization between the Δ- and Λ-enantiomer, which at the same time exchanges *trans* chloride and *trans* nitrogen sites (Scheme 3.2). Rahim et al. proposed a Bailar-twist mechanism for a similar fluxional behaviour in $nacnac^{Ph}{}_2ZrCl_2$.[6] That two doublets are observed for the benzyl CH_2 group even at higher temperatures, indicates that the C_s-symmetric isomer with *trans* chloride ligands is not obtained, even as a short-lived intermediate at high temperatures.

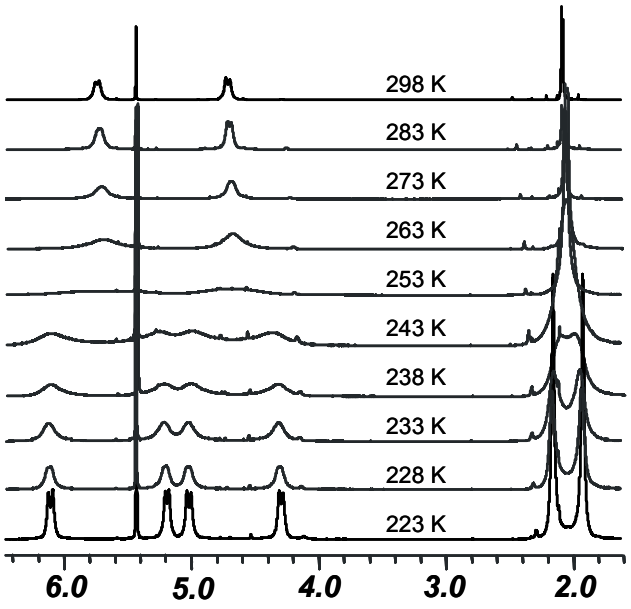
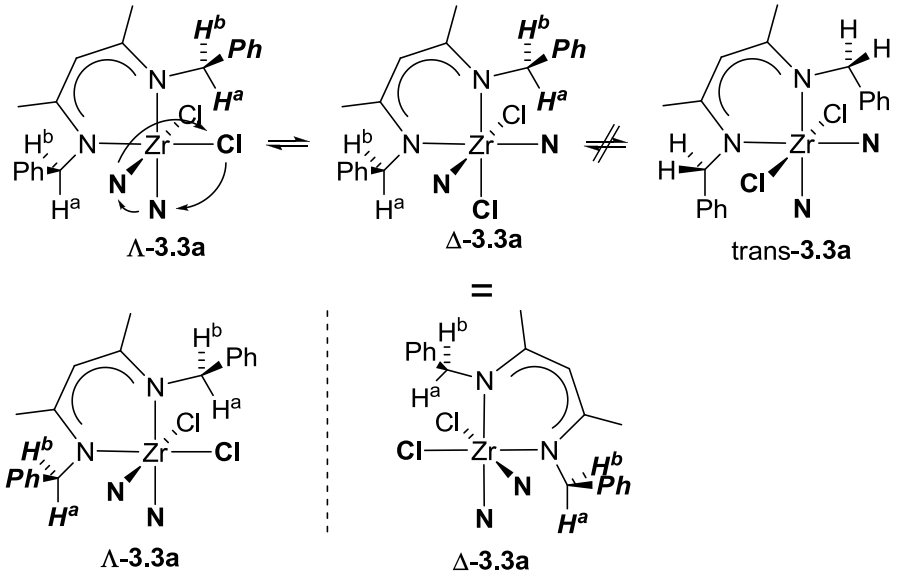


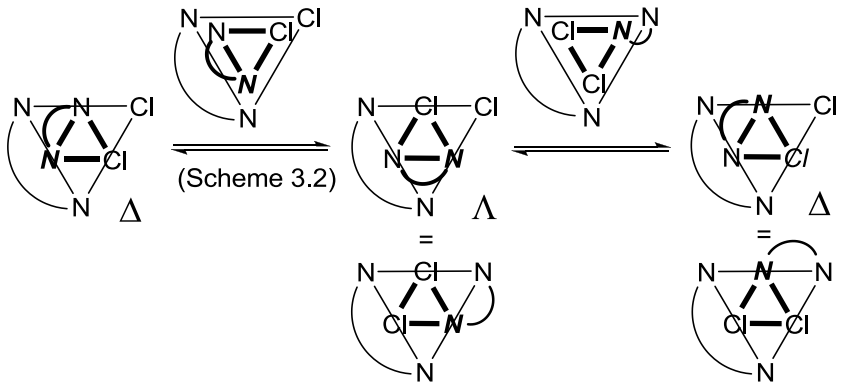
Figure 3.5. Variable temperature ^{1}H NMR spectra of **3.3a**.



Scheme 3.2

The Bailar-twist is significantly slower for cyclohexyl substituted **3.3b**, resulting in exchange-broadened peaks close to coalescence at room temperature. The presence of six signals for the cyclohexyl ring in ^{13}C spectra of **3.3b** at higher temperatures again indicates that isomerisation occurs between Δ- and Λ-enantiomers, but not between *cis*- and *trans*-isomers. The isomerisation is even slower in **3.3c**. Resonances in ^{1}H and ^{13}C spectra are broadened by exchange, but show the presence of two diastereomeric complexes. Cooling of a $CDCl_3$ solution below 0 °C resulted in two signal sets in a 2:1 ratio for Δ-(*R*,*R*-*nacnac*^{MeBn})$ZrCl_2$, Δ-**3.3c**, and Λ-(*R*,*R*-*nacnac*^{MeBn})$ZrCl_2$, Λ-**3.3c**. A spectrum in the fast exchange region was not obtained in $CDCl_3$ or even in toluene-d_8 at 100 °C. In contrast to **3.3a** and **3.3b**, coalescence into fully symmetric spectra requires two different Bailar-twists for **3.3c**. The mechanism depicted in Scheme 3.2 will exchange groups *trans* to N in the Δ-isomer (short: Δ-N, Scheme 3.3) with groups *trans* to Cl in the Λ-isomer (short: Λ-Cl). Since the pairs Δ-N/Λ-Cl and Λ-N/Δ-Cl are enantiomeric in **3.3a** and **3.3b**, only one resonance is observed for these groups. This is not the case for diastereomeric Δ-**3.3c** and Λ-**3.3c**, and a second Bailar-twist mechanism is required to exchange Δ-N with Δ-Cl (or Λ-N with Λ-Cl, respectively). Since this requires one diketiminate ligand to bridge the two trigonal faces of the prismatic transition state (Scheme 3.3), the latter is probably of higher energy.[23] The presence of two, eventually overlapping exchange processes might explain the lack of coalescence even at higher temperatures. The presence of four C*H*(Me)Ph resonances in the ^{1}H NMR spectrum of **3.3c** at room temperature and two H*C*(=N)$_2$ resonances in its ^{13}C spectrum, indicate that even the first Bailar-twist, which leads to Δ-Λ-

isomerisation, is slow on the NMR time scale at room temperature and that activation parameters in table 3.3 thus describe comparable processes. Nevertheless, the chiral diketiminate complex **3.3c** does not have the configurational stability exhibited, for example, by the chiral "IAN amino" zirconium complexes of Johnston and coworkers,[3] since, in contrast to those, Δ-Λ-isomerisation in **3.3c** does not require ligand enantiomerisation.



Scheme 3.3. Exchange of Δ-Cl first with Λ-N, then with Δ-N.

Simulation of the line-shape of selected peaks in the ^{1}H NMR spectra of **3.3a-c** allowed the determination of exchange rates (k_{obs}) at different temperatures (see Exp. section). Activation parameters were obtained from Eyring plots of these rate constants (Figure 3.6, Table 3.3). While satisfactory linear plots and identical values from different pairs of exchanging nuclei were obtained for **3.3a** and **3.3b**, a smaller temperature window and difficulties in the determination of exchange constants made the determination rather unreliable for **3.3c**. Activation enthalpies for **3.3a** and **3.3b** (Table 3.3) are slightly higher than that of *nacnac*$^{Ph}{}_2ZrCl_2$ (38 kJ/mol),[6] but comparable to those in other *nac(n)ac*$_2ZrX_2$

complexes (36-57 kJ/mol),[7, 12] which undergo the same exchange process. The activation entropy of 18(3) J/(mol·K) for **3.3a** is significantly more positive than those previously observed (–39 to –56 J/(mol·K))[6, 7, 12] and might be indicative for a dissociation/re-coordination mechanism instead of a Bailar-twist mechanism for **3.3a**. However, a negative activation entropy is obtained for **3.3b**, although its crystal structure indicates increased steric interactions in the presence of a cyclohexyl substituent on nitrogen and **3.3b** would be expected to be even more prone to follow a dissociation/re-coordination mechanism than **3.3a**. In addition, as will be discussed below, alkylation of **3.3a** can be aided by partial dissociation of diketimine. The inactivity of **3.3a-c** towards alkylation (*vide infra*) indicates that a five-coordinated intermediate is not present with sufficient lifetime to allow chloride-alkyl exchange. While a dissociation mechanism for **3.3a** can thus not be excluded, it seems incompatible with additional data. An alternative explanation would involve a less restricted rotation around the N-CH_2 bond in the prismatic transition state, which is blocked in the Δ/Λ-ground state. In agreement with this, the activation entropy obtained for **3.3b**, which has only one hydrogen on the secondary alkyl substituent and no other accessible rotamers, is comparable to those in *N*-aryl substituted complexes.

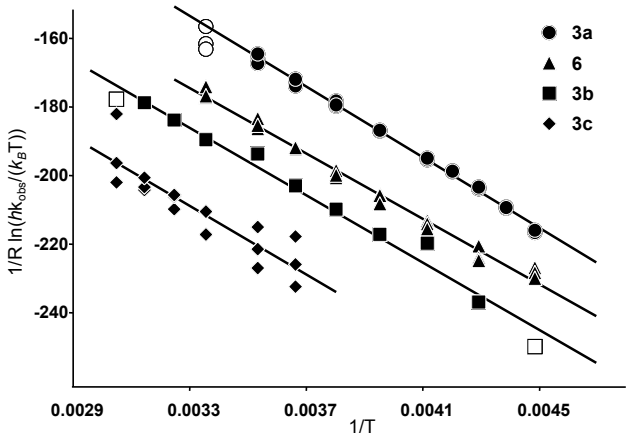


Figure 3.6. Eyring plots of the exchange rates for isomerizations of **3.3a-c** and **3.6**. (Hollow data points not used in linear regression analysis.)

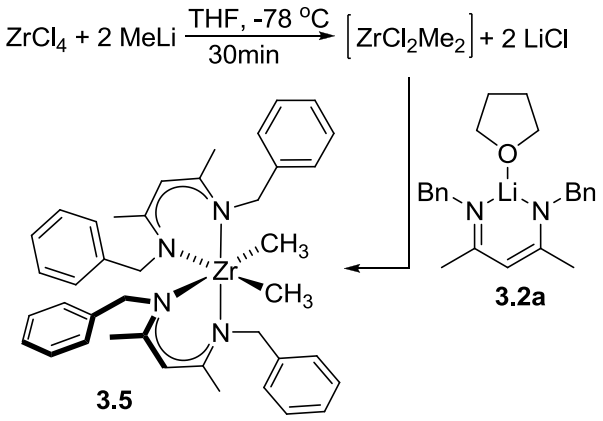
Table 3.3. Activation parameters determined from Eyring plots of k_{obs} for the isomerisation of $nacnac^{R}{}_{2}ZrX_{2}$.

Complex	R/X	$\Delta H^{\ddagger}$ [kJ·mol^{-1}]	$\Delta S^{\ddagger}$ [J·mol^{-1}·K^{-1}]	k_{298K} [x 10^{3} s^{-1}]
3.3a	Bn/Cl	51(1)	18(3)	60
3.3b	Cy/Cl	48(2)	–27(9)	1
3.6	Bn/OEt	48(1)	–16(6)	3

Temperature range used for determination of $\Delta H^{\ddagger}$ and $\Delta S^{\ddagger}$: 223-283 K (**3.3a**), 233-318 K (**3.3b**), 223-298 K (**3.6**).

***Nacnac*$_2$ZrMe$_2$ Complexes**. Attempts to prepare alkyl derivatives of **3.3a-c** using alkylating agents such as MeLi, MeMgBr, BnMgBr, $ZnEt_2$, *t*BuLi or *n*BuLi in a variety of solvents and reaction conditions did not meet with success. NMR spectra of reaction products showed only the presence of starting material or – under forcing conditions such

as prolonged heating – decomposition products. Since alkylation seemed not possible after complexation of the *nacnac* ligand, we decided to introduce the methyl group prior to complexation.[24] Indeed, the dimethyl analogue **3.5** was obtained in moderate yield (60%) by reaction of $ZrCl_4$ first with 2 equiv MeLi and then with the lithium salt **3.2a** (Scheme 3.4). Only **3.5** was accessible by this pathway. As observed for the synthesis of the dichloride complexes, ligands with secondary alkyls on N, i. e. **3.2b** and **3.2c**, did not react fast enough to compete with the decomposition of the zirconium alkyl chloride complex.



Scheme 3.4

The solid state structure of **3.5** shows the octahedral *cis*-geometry previously observed (Figure 3.7), but with a significantly more pronounced deviation from ideal geometry (N-Zr-N/X angles of 75-127°), while the bending angle of 31° is the smallest observed (Table 3.1). A possible reason for the increased deviation might lie in the shorter Zr-Me distance in **3.5** (2.290(4) & 2.297(4) Å), when compared to Zr-Cl in **3.3a** (2.454(1) Å). The closer distance to the benzyl CH_2 group (C30 & C50, Figure 3.7) results in a widening of the X-

Zr-X angle by 23° (**3.3a**, Cl1-Zr1-Cl1: 93.6(1)°; **3.5**, C16-Zr1-C17: 116.4(2)°) and subsequent distortion of the octahedral geometry.

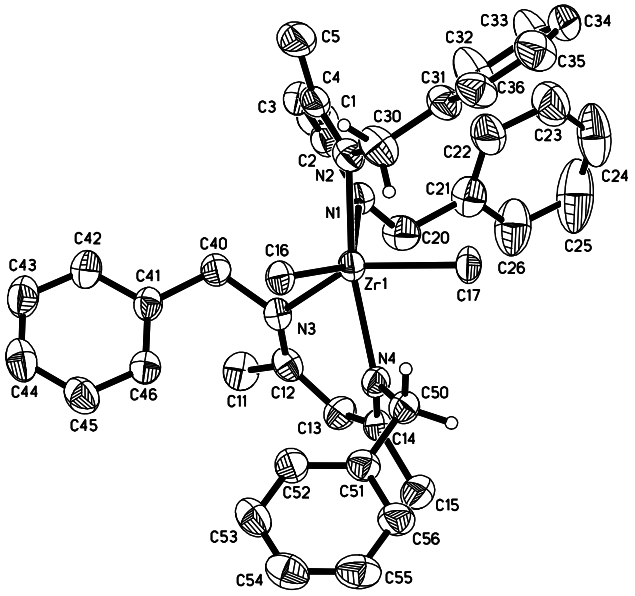


Figure 3.7. Crystal structure of complex **3.5**. Thermal ellipsoids are drawn at the 50% probability level and most H-atoms were omitted for clarity.

Reactions of styrene with **3.3a-c**/$AlCl_{3-x}Me_x$ (x = 1-3),[25] **3.3a**/$AlMe_3$/H_2O,[26] **3.5**/$AlCl_{3-x}Me_x$ (x = 0-3), or **3.5**/$B(C_6F_5)_3$,[27] in polar or apolar solvents, at room temperature or upon heating, showed no evidence for insertion of the olefin into the Zr-Me bond (NMR, GC-MS). No insertion was likewise observed in reactions of **3.5**/$B(C_6F_5)_3$ with diphenylacetylene or benzaldehyde. Surprisingly with regard to the failed attempts to exchange chloride against alkyl ligands, **3.5** reacted fast with $AlCl_{3-x}Me_x$ (x = 0-2) in C_6D_6 solution to yield the dichloride complex **3.3a**. To investigate this further, a C_6D_6 solution of **3.5** was titrated with $AlMe_3$ (0-1.8 equiv). ^1H NMR spectra, recorded after each addition,

showed no change in the diketiminate ligand resonances, but only one averaged resonance for Zr- as well as Al-bound methyl groups, which shifted from 0.32 (Al/Zr = 0) to –0.23 ppm (Al/Zr = 1.8) as the concentration of $AlMe_3$ increased (Figure 3.8). Interpolation of the linear regression line yielded a reasonable value of δ –0.36 ppm for pure $AlMe_3$ in C_6D_6. Exchange of methyl groups between Al and Zr centers is thus occurring fast on the NMR time scale, in contradiction with the problems encountered in the alkylation of these complexes. This might indicate that alkylation of **3.3a-c** is a thermodynamic, rather than a kinetic problem. Alternatively, interaction of $AlMe_3$ with a diketiminate ligand might loosen its coordination to zirconium, rendering the methyl ligands in **3.5** more accessible for exchange processes (Scheme 3.5). Additional experiments support the latter explanation: Reaction of C_6D_6 solutions of **3.5** with excess LiCl did not lead to the formation of the dichloride complex **3.3a** and methyl against chloride exchange is thus no more feasible than chloride against methyl.[28] On the other hand, when C_6D_6 solutions of the dichloride complex **3.3a** were reacted with methyl lithium in the presence of 10 equiv $AlMe_3$, the obtained reaction mixtures contained up to 90% of the dimethyl complex **3.5** (Scheme 3.5). Ligand exchange between **3.3a** and **3.5** is thus most likely aided by a loosening of the diketiminate coordination with $AlMe_3$.

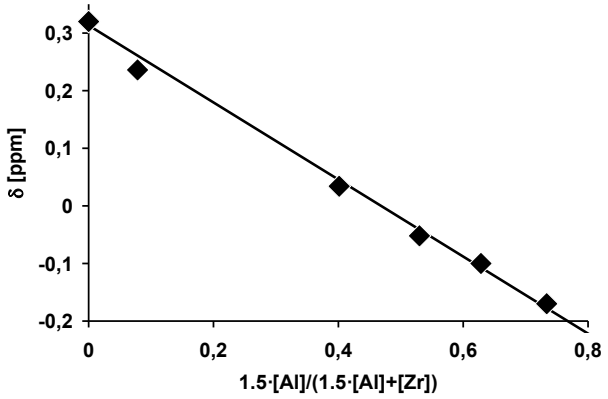
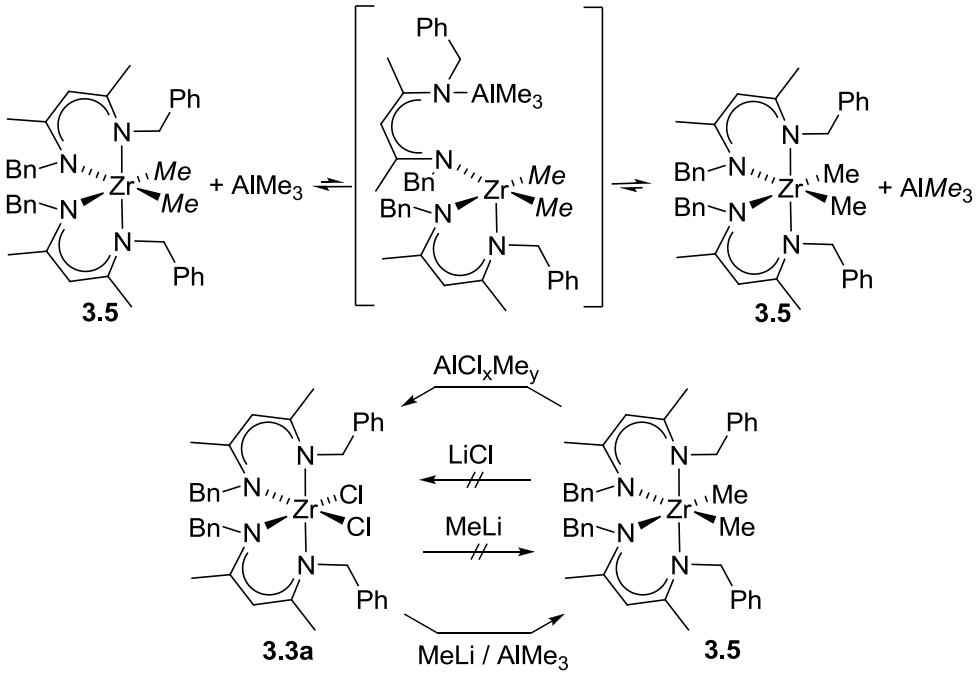


Figure 3.8. Chemical displacement of the averaged methyl resonance in **3.5**/$AlMe_3$ mixtures in C_6D_6.



Scheme 3.5

While **3.3a** did not undergo ligand exchange with NaOEt, reaction of **3.5** with 2 equiv ethanol afforded the dialkoxide complex *nacnac*$^{Bn}_2$Zr(OEt)$_2$, **3.6**.[29] Despite Zr-O distances even shorter (1.939(2)-1.954(2) Å) than Zr-Me in **3.5** (2.290(4) & 2.297(4) Å), its crystal structure (Figure 3.9) is again very similar to that of the dichloride complex **3.3a**, with a O-Zr-O angles of 97.12(7)° & 98.72(7)° and a slightly distorted octahedral coordination environment (Table 3.1). This might be related to the smaller vdW-radius of oxygen compared to chloride and methyl, which can accommodate a shorter Zr-O distance: shortest distances between a benzyl hydrogen and the Zr-X ligand (**3.3a**, *d*(H-Cl) = 2.9 Å; **3.5**, *d*(H-C) = 2.8 Å; **3.6**, *d*(H-O) = 2.5 Å) are in all three complexes only slightly shorter than the sum of their vdW-radii (H-Cl: 3.0 Å, H-C: 2.9 Å, H-O: 2.7 Å). Again, a fluxional process was observed by NMR. In addition to the changes observed for **3.3a** and **3.5**, the quartet of the CH_2O group splits into two multiplets of equal intensity at –50 °C, confirming again that the fluxional process is associated with a racemisation of the complex. Activation parameters yielded an activation enthalpy comparable to **3.3a**, but an activation entropy lower by 34 J/(mol·K) ($\Delta S^{\ddagger}$ = –16(6) J/(mol·K), Table 3.3), which might indicate reduced rotational freedom of the ethoxy substituents in the transition state.

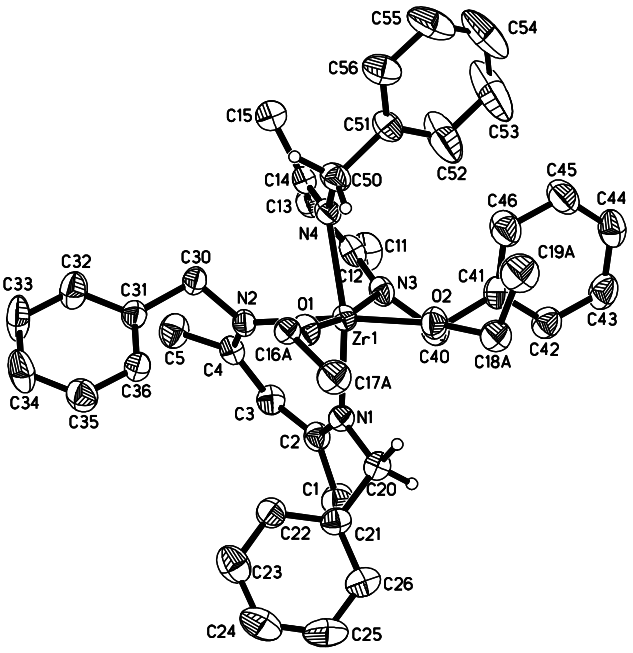


Figure 3.9. Crystal structure of **3.6**. Only one of two independent molecules is shown. Thermal ellipsoids are drawn at the 50% probability level. The minor occupied positions of the disordered ethyl groups and most H-atoms were omitted for clarity.

3.4 Conclusions

While not accessible with ortho-substituted *N*-aryl diketiminate ligands, β-diketiminates with aliphatic *N*-alkyl substituents readily form bis(diketiminate) zirconium complexes, even with bulky secondary alkyls, and offer access to an easy modification of the steric environment. Steric crowding caused by the *N*-substituent seems the most likely cause for the inactivity of the dichloride complexes towards ligand exchange. It does not impede fast complex racemisation, however, most probably by a Bailar-twist mechanism. While structural analyses confirm the targeted proximity of the alkyl substituent and the reactive

coordination sites and the potential utility of the ligand framework in catalysis, the dimethyl complex **3.5** does not insert styrene, diphenylacetylene or benzaldehyde when activated with $AlMe_{3-x}Cl_x$ or $B(C_6F_5)_3$, which might be due again to steric crowding or a too low Lewis acidity of the metal center. Complex racemisation proved to be too fast to impart selectivity in lactide polymerizations. We are currently investigating the effects of interligand bridging to control complex racemisation and to improve the reactivity of this class of compounds.

3.5 Experimental Section

All reactions, except ligand synthesis, were carried out under an inert atmosphere using Schlenk and glove box techniques under nitrogen atmosphere. *Nacnac*^{Bn}H (**3.1a**),[18] *R,R-nacnac*^{MeBn}H (**3.1c**),[17] and $ZrCl_4(THF)_2$[30] were prepared according to literature procedures. All others chemicals were purchased from common commercial suppliers and used without further purification. THF was distilled from sodium/benzophenone, all others solvents were dried by passage through activated aluminum oxide (MBrown SPS) and de-oxygenated by repeated extraction with nitrogen. C_6D_6 was dried over sodium, $CDCl_3$ was dried over CaH_2 and both were distilled under reduced pressure, and then degassed by three freeze-pump-thaw cycles. Styrene and ethanol were evacuated under vacuum and dried over 4A molecular sieves. ^1H and ^{13}C NMR spectra were acquired on a Bruker AMX 300 or Bruker AV 400 spectrometer. ^{19}F NMR spectra were acquired on a Bruker Avance 300. Chemical shifts were referenced to the residual signals of the deuterated solvents (C_6D_6: ^1H: δ 7.16 ppm, ^{13}C: δ 128.38 ppm; $CDCl_3$: ^1H: δ 7.26 ppm, ^{13}C: δ 77.00 ppm and C_7D_8: ^1H: δ 2.09

ppm, ^{13}C: δ 20.40 ppm). Low-temperature NMR spectra were recorded using a Bruker AV 500 spectrometer. NMR data at low or high temperatures are given in the supporting information. Exchange rates were obtained by comparison of experimental and simulated spectra with the WINDNMR program.[31] Elemental analyses were performed by the Laboratoire d'analyse élémentaire (Université de Montréal).

2-Cyclohexylamino-4-cyclohexylimino-pent-2-ene, *nacnac*^{Cy}H, 3.1b.[19] Acetylacetone (1.00 g, 10 mmol), *para*-toluenesulfonic acid monohydrate (1.9 g, 10 mmol) and cyclohexylamine (1.0 g, 10 mmol) were combined with toluene (100 mL). The resulting white suspension was refluxed for 3 h with the help of Dean-Stark apparatus to afford a colorless solution. After cooling to room temperature, a second equivalent of cyclohexylamine (1.0 g, 10 mmol) was added and the reaction mixture was refluxed for 3 days. A colorless precipitate appeared upon cooling to room temperature, which was separated by filtration and combined with 100 mL ether and 100 mL of an aqueous solution of KOH (5.6 g, 100 mmol). Phases were separated and the aqueous phase was extracted with ether. The combined phases were dried over Na_2SO_4, filtered and the solvent evaporated. The obtained yellow liquid was allowed to cool down slowly to room temperature to yield colorless crystals (1.8 g, 69%). The crude product contained ca. 5% impurities according to NMR, but was used without further purification in subsequent reactions. Recrystallization from ethanol afforded analytically pure compound.

^1H NMR ($CDCl_3$, 400 MHz, 298 K): δ 11. 72 (bs, 1H, NH), 4.44 (s, 1H, $CH(C=N)_2$), 3.32-3.35 (m, 2H,CH(Cy)), 1.90 (s, 6H, Me(C=N)), 1.80-1.35 (m, 20H, Cy). $^{13}C\{^1H\}$ NMR

($CDCl_3$, 101 MHz, 298 K): δ 158.4 (*C*=N), 93.7(*C*H(C=N)$_2$), 54.1 (*C*H$_{Cy}$), 34.6 (*C*H$_{2a}$), 25.7 (*C*H$_{2b}$), 25.7 (*C*H$_{2c}$), 18.8 (*C*H$_3$). Anal. Calcd for $C_{17}H_{30}N_2$: C, 77.80; H, 11.52; N, 10.62. Found: C, 77.60; H, 11.24; N, 10.85.

***Nacnac*^{Bn}Li(THF), 3.2a.** A hexane solution of *n*BuLi (1.36 mL, 2.9 M, 3.95 mmol) was added over 25 minutes at room temperature to a yellow THF solution of **3.1a** (1.0 g, 3.6 mmol). The yellow orange solution was allowed to stir for 4 hrs. The volatiles were removed and the remaining solid was washed with 2 x 5 mL of hexane. The solid was dried under reduced pressure to yield a colorless powder (1.25 g, 90%) and used without further purification.

^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.22-7.30 (m, 10H, Ph), 4.54 (s, 1H, C*H*(C=N)$_2$), 4.42 (s, 4H, C*H*$_2$Ph), 3.74 (m, 4H, THF), 1.93 (s, 6H, *Me*(C=N)), 1.83 (m, 4H, THF). ^{1}H NMR (C_6D_6, 400 MHz): δ 7.00-7.30 (m, 10H, Ph), 4.82 (s, 1H, C*H*(C=N)$_2$), 4.60 (s, 4H, C*H*$_2$Ph), 2.86 (m, 4H, THF), 2.09 (s, 6H, *Me*(C=N)), 0.98 (m, 4H, THF). ^{13}C{^{1}H} NMR ($CDCl_3$, 101 MHz): δ 161.0 (C=N), 140.9 (*ipso* Ph) 128.3 (*ortho* Ph), 127.2 (*para* Ph), 126 (*meta* Ph), 95.1 (*C*H(C=N)$_2$), 67.9 (THF**)**, 50.7 (*C*H$_2$(Ph)), 25.6 (THF), 19.6 (*Me*(C=N)). ^{13}C{^{1}H} NMR (C_6D_6, 101 MHz): δ 165.8 (C=N), 145.4 (*ipso* Ph) 128.5 (*ortho* Ph), 127.5 (*para* Ph), 126.0 (*meta* Ph), 93.8 (*C*H(C=N)$_2$), 67.5 (THF**)**, 50.7 (*C*H$_2$(Ph)), 25.1 (THF), 22.0 (*Me*(C=N)).

***Nacnac*^{Cy}Li(THF), 3.2b.** To a yellow THF solution of **3.1b** (1.5 g, 5.8 mmol), a hexane solution of *n*BuLi (2 mL, 2.9 M, 5.8 mmol) was added gradually at room temperature. After 4 hours of stirring the solution turned orange. The volatiles were removed under

reduced pressure to yield **3.2b** as a yellow solid (1.9 g, 96%), which was used without further purification.

^{1}H NMR (C_6D_6, 400 MHz, 298 K): δ 4.56 (s, 1 H, C*H*(C=N)$_2$), 3.40-3.44 (m, 6 H, Cy C*H* & CH_2O), 2.16 (s, 6 H, CH_3), 1.77-1.3 (m, 24 H, THF & Cy CH_2). ^{13}C{^{1}H} NMR (C_6D_6, 101 MHz, 298 K): δ 158.0 (*C*=N), 95.0 (*C*H(C=N)$_2$), 54.6 (THF), 54.4 (Cy *C*H), 34.6 (*C*H$_{2a}$), 25.7 (*C*H$_{2b}$), 25.7 (*C*H$_{2c}$), 24.5 (THF), 18.8 (*C*H$_3$).

***R,R-Nacnac*$^{\mathbf{MeBn}}$Li(THF), 3.2c.** A solution of *n*BuLi in hexane (2.9 M, 0.9 mmol) was added gradually over 10 minutes to a yellow THF solution of **3.1c** (0.25 g, 0.82 mmol). The yellow/orange solution was allowed to stir for 4 hours at room temperature, volatiles were evaporated and a brown oil is obtained (0.30 g, 92%), which was used without further purification.

^{1}H NMR (400 MHz, C_6D_6): δ 7.16-7.42 (m, 10H, *Ph*), 4.81 (q, 2H, *J* = 7 Hz, C*H*(Me)Ph), 4.71 (s, 1H, C*H*(C=N)$_2$), 3.00(m, 4H, THF), 2.07 (s, 6H, *Me*(C=N)), 1.44 (d, 6H, *J* = 7 Hz, CH(*Me*)Ph), 0.97 (m, 4H, THF). ^{13}C{^{1}H} NMR (C_6D_6, 101 MHz): δ 161.0 (C=N), 150.2 (*ipso* Ph), 128.4 (*ortho* Ph), 126.6 (*para Ph*), 125.8 (*meta* Ph), 93.7 (*C*H(C=N)$_2$), 67.6 (*C*H(Me)Ph), 57.2 (THF), 25.5 (THF), 24.6 (CH(*Me*)Ph), 22.3 (*Me*(C=N)).

***Nacnac*$^{\mathbf{Bn}}_{\mathbf{2}}$ZrCl$_2$, 3.3a.** *Method A*. In a dry Schlenk tube, $ZrCl_4$ (0.34 g, 1.4 mmol) and **3.2a** (1.0 g, 2.8 mmol) were mixed. Toluene (10 mL) was added under stirring. After 24 hours at room temperature, the obtained orange mixture was filtered. The yellow filtrate was concentrated to half its volume and the desired product was precipitated by addition of

15 mL of hexane. The yellow precipitate was separated by filtration and dried at a vacuum line to yield **3.3a** (0.35 g, 0.50 mmol, 35%).

Method B. A hexane solution of *n*BuLi (2.9 M, 5.4 mmol) was added to a toluene suspension of $ZrCl_4$ (0.62 g, 2.7 mmol) at –78°C. The mixture was allowed to warm to room temperature and then stirred for another 12 h. To the obtained brown mixture, 15 mL of a toluene solution of **3.1a** (5.4 mmol, 1.5 g) were gradually added. The mixture was stirred for 2 days at 90˚C during which it turned yellow. After cooling to room temperature, 20 mL of dichloromethane were added and the mixture was filtered. The combined volatiles were removed under vacuum, yielding **3.3a** as a yellow powder (1.5 g, 75%). Crystals suitable for X-ray diffraction studies were obtained by slow diffusion of hexane into a THF solution of the complex at 25 °C.

^{1}H NMR ($CDCl_3$, 400 MHz, 298 K): δ 7.20-7.30 (m, 20H, Ph), 5.65 (bs, 2H, C*H*$_2$Ph), 5.62 (bs, 2H, C*H*$_2$Ph), 5.32 (s, 2H, C*H*(C=N)$_2$), 4.61(bs, 2H, C*H*$_2$Ph), 4.56 (bs, 2H, C*H*$_2$Ph), 1.92 (s,12H, *Me*(C=N)). ^{13}C{^{1}H} NMR ($CDCl_3$, 101 MHz**,** 298 K): δ 167.1 (C=N), 139.5 (*ipso* Ph), 128.2 (*ortho* Ph), 127.2 (*para* Ph), 126.5 (*meta* Ph), 108.1 (*C*H(C=N)$_2$), 54.9 (*C*H$_2$Ph), 23.2 (*Me*(C=N)). Anal. Calcd for $C_{38}H_{42}ZrN_4Cl_2$: C, 63.66; H, 5.91; N, 7.82. Found: C, 63.00; H, 6.19; N, 7.69.

***Nacnac*$^{Cy}_2$ZrCl$_2$, 3.3b.** In a dry Schlenk, $ZrCl_4$ (0.34 g, 1.5 mmol) and **3.2b** (1.0 g, 3.0 mmol) were mixed and toluene (10 mL) was added under stirring. After 24 hours of stirring at room temperature the obtained orange mixture was filtered. The red filtrate was concentrated to half its volume and the desired product was precipitated by addition of 15

mL of hexane. The white precipitate separated by filtration was dried at a vacuum line to yield **3.3b** (0.35 g, 35%). Crystals suitable for X-ray diffraction studies were obtained by slow diffusion of hexane into a THF solution of the complex at 25 °C.

^{1}H NMR ($CDCl_3$, 500 MHz, 298 K): δ 5.15 (s, 2H, C*H*(C=N)$_2$), 4.25 (bm, 4H, Cy C*H*), 1.91 (bs, 12H, CH_3), 2.16-1.19 (m, 40 H, Cy CH_2). ^{13}C{^{1}H} NMR ($CDCl_3$, 75 MHz**,** 298 K): Peaks severely broadened. For low and high temperature spectra see the supp. inform. Anal. Calcd for $C_{34}H_{58}ZrN_4Cl_2$: C, 59.62; H, 8.53; N, 8.18. Found: C, 58.98; H, 8.75; N, 7.71.

***R,R-nacnac*$^{\mathbf{MeBn}}$$_2$$\mathbf{ZrCl_2}$, 3.3c.** To a mixture of $ZrCl_4(THF)_2$ (0.77 g, 2.04 mmol) and **3.2c** (1.57 g, 4.08 mmol), toluene was added under stirring. The obtained orange mixture was allowed to react for 3 d at room temperature. The mixture was filtered, the orange filtrate concentrated to half its volume and the desired product precipitated by addition of 15 mL of hexane. Recrystallization by slow diffusion of hexane into a saturated toluene solution gave yellow crystals of **3.3c** (1.1 g, 65%), contaminated with isolated red crystals of **3.4** (insufficient quantity for full characterization), which were separated by hand.

^{1}H NMR ($CDCl_3$, 400 MHz, 298 K): (Peaks severely broadened. For low temperature spectra of both diastereomers, see supp. inform.) δ 7.08-7.4 (m, 20H, *Ph*), 6.74 (bm, 2H, *b* C*H*(Me)Ph), 6.64 (bm, 2H, *a* C*H*(Me)Ph), 6.14 (bm, 2H, *a* C*H*(Me)Ph), 5.26 (bs, *a*+*b* C*H*(C=N)$_2$), 4.48 (bm, 2H, *b* C*H*(Me)Ph), 2.15-1.63 (m, 24H, Me). ^{13}C{^{1}H} NMR ($CDCl_3$, 75 MHz, 298 K): (Peaks severely broadened, many not observed or overlapping. For low temperature spectra of both diastereomers, see supp. inform.) δ 168.1 (C=N), 167 (C=N),

162.9 (C=N), 143.9 (*ipso* Ph), 143.4 (*ipso* Ph), 110.8 (*C*H(C=N)$_2$), 104.3 (*C*H(C=N)$_2$), 62 (*C*H(Me)Ph), 59.4 (*C*H(Me)Ph), 57.6 (*C*H(Me)Ph), 27.2 (CH(*Me*)Ph), 25.3 (CH(*Me*)Ph), 19.8 (*Me*(C=N)), 18.2 (*Me*(C=N)), 17 (*Me*(C=N)). Anal. Calcd. for $C_{42}H_{50}N_2ZrCl_2$: C, 65.26; H, 6.52; N, 7.01. Found: C, 64.93; H, 6.70 ; N, 7.13.

***Nacnac*$^{Bn}_2$ZrMe$_2$, 3.5.** $ZrCl_4$ (0.42 g, 1.8 mmol) was dissolved in THF (60 mL). An ether solution of MeLi (2.5 mL, 1.6 M, 4.0 mmol) was added at –78 °C under exclusion of light. The obtained white suspension was allowed to stir for 30 min in order to generate Me_2ZrCl_2. To the obtained mixture **3.2a** (1.28 g, 3.6 mmol) was added, affording a yellow suspension. The mixture was allowed to warm up to room temperature during 18 h, upon which it turned red. The volatiles were evaporated under reduced pressure to give an orange solid film. The product was extracted with CH_2Cl_2 (20 mL) and the resulting red solution was evaporated to dryness to yield **3.5** as a yellow powder (0.70 g, 63%). Crystals suitable for X-ray diffraction analysis were obtained by slow diffusion of hexane into a saturated toluene solution at –20˚C.

^{1}H NMR (C_6D_6, 400 MHz, 298 K): δ 7.60-7.06 (m, 20 H, Ph), 4.94 (s, 2H, CH(C=N)$_2$), 4.77 (bs, 8 H, CH_2), 1.76 (s, 12 H, Me(C=N)), 0.32 (s, 6H, Me-Zr). ^{13}C{^{1}H} NMR (C_6D_6, 101 MHz, 298 K): δ 163.5 (C=N), 140.2 (*ipso* Ph), 128.1 (*ortho* Ph), 126.6 (*para* Ph), 126.1 (*meta* Ph), 100.5 (*C*H(C=N)), 52.1 (*C*H$_2$Ph), 41.2 (Me-Zr), 21.4 (*Me*(C=N)). Anal. Calcd for $C_{40}H_{48}N_4Zr$: C, 71.06; H, 7.16; N, 8.29. Found: C, 71.59; H, 7.28; N, 8.29.

Reaction of 3.5 with B(C$_6$F$_5$)$_3$. To a C_6D_6 solution of $B(C_6F_5)_3$ (7.5 mg, 0.0148 mmol) in a J. Young NMR tube, 0.5 mL of a yellow C_6D_6 solution of **3.5** (2.96 10^{-3} M, 0.0148

mmol) was added in portions of 0.1 mL every 5 min to give [*Nacnac*$^{Bn}_2$ZrMe][MeB(C_6F_5)$_3$]. A red oil separates from the solution upon standing.

^{1}H NMR (C_6D_6, 400 MHz, 298 K): δ 7.37-7.06 (m, 20 H, Ph), 4.89 (bs, 2 H, CH(C=N)$_2$), 4.54 (bs, 8 H, CH_2), 1.77 (bs, 12 H, Me(C=N)), 0.43 (s, 3H, MeB), 0.19 (s, 3H, MeZr). ^{13}C{^{1}H} NMR (C_6D_6, 101 MHz, 298 K): δ 191.0 (C=N), 136.9 (*ipso* Ph), 129.3 (B(C_6F_5)$_3$) 128.3 (B(C_6F_5)$_3$), 128.1 (*ortho* Ph*),* 128.05 (*para* Ph), 127.9 (*meta* Ph), 126.9 (B(C_6F_5)$_3$), 93.2 (*C*H(C=N)), 31.9 (*C*H_2Ph), 23.0 (MeB), 21.4 (*Me*(C=N)), 14.4 (MeZr).

***Nacnac*$^{Bn}_2$Zr(OEt)$_2$, 3.6**. Ethanol (37.5 mg, 0.81 mmol) was added to a yellow ether solution of **3.5** (250 mg, 0.37 mmol), upon which gas formation (CH_4) was observed. The yellow solution was evaporated to dryness and the obtained yellow solid was extracted with 15 mL of hexane. Evaporation of the volatiles yielded a colorless powder, which contained mostly **3.6** and the free ligand **3.1a**. Recrystallization from a saturated ethanol solution at –20˚C gave colorless crystals of **3.6** (136 mg, 50%).

^{1}H NMR ($CDCl_3$, 400 MHz, 298 K): δ 7.30-7.06 (m, 20H, Ph), 5.10 (bs, 4 H, CH_2), 4.86 (s, 2H, CH(C=N)$_2$), 4.54 (bs, 4H, CH_2), 3.69 (q, 4H, CH_2O), 1.83 (bs, 12H, Me(C=N)), 0.72 (t, 6H, *Me*CH_2O). ^{13}C{^{1}H} NMR (C_6D_6, 400 MHz, 298 K): δ 163.5 (C=N), 142.1 (*ipso* Ph), 127.9 (*ortho* Ph), 127.2 (*para* Ph), 125.8 (*meta* Ph), 102.7 (*C*H(C=N)), 64.7 (CH_2O), 53.6 (*C*H_2Ph), 22.2 (*Me*CH_2O), 19.8 (*Me*(C=N)). Anal. Calcd for $C_{42}H_{48}N_4O_2Zr$: C, 68.53; H, 7.12; N, 7.61. Found: C, 68.13; H, 7.45; N, 7.68.

Variable temperature NMR measurements. Variable temperature NMR spectra were recorded using a Bruker AV 500 spectrometer with $CDCl_3$ solutions of complexes **3.3a-c**

and **3.6**. NMR data at low or high temperatures are given in the supporting information. Exchange rates were obtained by simulation of the experimental spectra with the WINDNMR program.[31] Temperature range, exchange simulated: **3.3a**, 223 – 298 K, *Me*(CN) and both diastereotopic NC*H*$_2$Ph; **3.3b**, 223 – 328 K, N-C*H*=(CH$_2$)$_5$; **3.3c**, 223 – 328 K, *Me*(CN) and both diastereotopic C*H*(Me)Ph; **3.6**, 223 – 298 K, *Me*(CN) and both diastereotopic MeC*H*$_2$O.

X-ray diffraction studies. Diffraction data for complexes **3.3a** was recorded on a Bruker Smart APEXII (Mo radiation) diffractometer, for complex **3.4** on a Bruker Smart 6000 (Cu rotating anode) and for all others on a Bruker Proteum X8/Microstar (Cu radiation), using the APEX2 software package.[32] Data reduction was performed with SAINT,[33] absorption corrections with SADABS.[34] Structures were solved with direct methods (SHELXS97).[35] All non-hydrogen atoms were refined anisotropically using full-matrix least-squares on F^2 and hydrogen atoms refined with fixed isotropic U using a riding model (SHELXL97).[35] For **3.3b,** the co-crystallized solvent was identified as a disordered hexane (in agreement with NMR data), but could not be resolved and thus suppressed by application of SQUEEZE.[36] For further details see table 3.4 and the supporting information.

Table 3.4. Details of X-ray Diffraction Studies

	3.3a	**3.3b**	**3.3c**	**3.4**	**3.5**	**3.6**
Formula	$C_{38}H_{42}Cl_2N_4Zr$	$C_{34}H_{58}Cl_2N_4Zr$	$C_{42}H_{50}Cl_2N_4Zr$	$C_{42}H_{49}ClN_4Zr$	$C_{40}H_{48}N_4Zr$	$C_{42}H_{52}N_4O_2Zr$
M_w (g/mol); F(000)	716.88; 1488	684.96; 1456	772.98; 1616	736.52; 772	676.04; 1424	736.10; 3104
Crystal color and form	yellow block	colorless block	yellow fragment	red plate	yellow plate	colorless plate
Crystal size (mm)	0.12x0.06x0.03	0.60x0.28x0.10	0.10x0.08x0.04	0.06x0.06x0.04	0.06x0.05x0.02	0.06x0.04x0.02
T (K); wavelength	200; 0.71073	150; 1.54178	150; 1.54178	150; 1.54178	150; 1.54178	150; 1.54178
Crystal System	Tetragonal	Monoclinic	Monoclinic	Monoclinic	Monoclinic	Orthorhombic
Space Group	$P4_32_12$	C2/c	$P2_1$	$P2_1$	$P2_1/n$	$P2_12_12_1$
Unit Cell: a (Å)	8.7244(5)	20.2320(8)	13.6460(3)	13.5011(18)	15.2045(13)	11.6079(9)
b (Å)	8.7244(5)	9.0276(4)	20.5189(5)	9.1289(11)	9.6321(8)	15.7760(12)
c (Å)	47.453(6)	22.539(1)	14.4588(4)	15.1108(18)	24.0981(19)	42.516(3)
β (°)	90	91.250(2)	108.891(1)	95.413(7)	97.213(4)	90
V (Å^3); Z; $d_{calcd.}$ (g/cm^3)	3611.9(6); 4;1.318	4115.7(3); 4; 1.105 [a]	3830.41(16);4; 1.340	1854.1(4); 2; 1.319	3501.3(5); 4; 1.283	7785.8(10); 8; 1.256
θ range (°); completeness	1.7-27.6; 1.0	3.9-72.3; 0.99	3.2-58.0; 0.99	2.9-68.1; 0.98	3.3-67.5; 1.0	2.1-67.9; 1.0
collected reflections; R_σ	99235; 0.070	53603; 0.021	60497; 0.025	27516; 0.082	54484; 0.063	137856; 0.027
unique reflections; R_{int}	4177; 0.144	4013; 0.036	10532; 0.046	6510; 0.079	6282; 0.116	14075; 0.060
μ (mm^{-1}); Abs. Corr.	0.484; multi-scan	3.554; multi-scan	3.893; multi-scan	3.348; multi-scan	2.813; multi-scan	2.611; multi-scan
R1(F); wR(F^2) ($I > 2\sigma(I)$)	0.039; 0.069	0.034; 0.098	0.025; 0.064	0.050; 0.127	0.045; 0.101	0.027; 0.072
R1(F); wR(F^2) (all data)	0.075; 0.078	0.034; 0.098	0.027; 0.065	0.058; 0.131	0.076; 0.117	0.029; 0.073
GoF(F^2)	0.920	1.113	1.029	0.793	1.013	1.026
Residual electron density	0.28 e$^-$/Å^3	0.40 e$^-$/Å^3	0.53 e$^-$/Å^3	1.28 e$^-$/Å^3	0.88 e$^-$/Å^3	0.31 e$^-$/Å^3

[a] co-crystallized solvent removed with SQUEEZE

3.6 Acknowledgement.

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Supporting Information. Variable temperature NMR data. Crystallographic Information Files (CIF).

3.7 References

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(23) For **3.3a**, the second Bailar-twist would lead to an exchange of H_a and H_b (Scheme 3.2). That two doublets are observed for the diastereotopic CH_2 hydrogens of **3.3a** at room temperature is in agreement with a higher activation barrier for this isomerisation.

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(27) Reaction of **3.5** with $B(C_6F_5)_3$ in C_6D_6 solution yielded NMR spectra in agreement with the formation of the ion pair $[(nacnac^{Bn})_2ZrMe][MeB(C_6F_5)_3]$: only one peak each is observed for all CH_2, CH, or Me groups of the diketiminate ligands in ^1H and ^{13}C spectra, while the former $ZrMe_2$ group splits into two signals. The ion-pair is only meta-stable in solution and rapidly separates as a red oil.

(28) Minor amounts of **3.3a** (ca. 5%) were attributed to the presence of traces of water and excess LiCl. These amounts increased if aged LiCl, not kept from moisture, is used.

(29) Complex **3.6** can be employed as initiator for the polymerisation of *rac*-lactide in molten monomer (Zr/lactide = 1/200, 130 °C, 98% conversion in 0.5 h), but yielded essentially atactic polymer ($P_r = 0.6$).

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Supporting Information

Zirconium Complexes of Symmetric and of Chiral Bisdiketiminate Ligands – Synthesis, Crystal Structures and Reactivities

Variable temperature NMR data and NMR data in various solvents:

Complex 3.3a

Low temperature spectra: ^{1}H NMR ($CDCl_3$, 500 MHz, 223 K): δ 7.20-7.30 (m, 20H, *Ph,*), 6.06 (bd, 2H, H_a), 5.37 (s, 2H, C*H*(C=N)$_2$), 5.14 (bd, 2H, H_b), 4.96 (bd, 2H, H_c), 4.23 (bd, 2H, H_d), 2.05 (s, 6H, *Me*(C=N)), 1.80 (s, 6H, *Me*(C=N)).

^{13}C{^{1}H} NMR ($CDCl_3$, 126 MHz, 223 K): δ 168.0 (*C*=N), 165.5 (*C*=N), 139.4 (*ipso* Ph), 135.1 (*ipso* Ph), 128.8 (*ortho* Ph), 128.4 (*ortho* Ph), 128.1 (*para* Ph), 127.3 (*para* Ph), 126.8 (*meta* Ph), 126.4 (*meta* Ph), 108.3 (*C*H(C=N)$_2$), 54.3 (*C*H$_2$Ph), 24.4 (*C*H$_2$Ph), 22.7 (*Me*(C=N)), 22.3 (*Me*(C=N)).

Complex 3.3b

^{1}H NMR (C_6D_6, 300 MHz, 298 K): δ 5.16 (bm, 2H, Cy C*H*), 4.95 (s, 2H, C*H*(C=N)$_2$), 4.05 (bm, 2H, Cy C*H*), 2.75 - 1.01 (m, 52H, CH_3 & Cy).

^{1}H NMR (Toluene-d_8, 400 MHz, 298 K): δ 4.96 (s, 2H, C*H*(C=N)$_2$), 4,48 (bm, 4H, Cy C*H*), 1.89 (bs, 12H, CH_3), 1.78- 1.30 (m, 40 H, Cy CH_2).

High temperature spectra: ^{1}H NMR (C_6D_6, 300 MHz, 343 K): δ 4.94 (s, 2H, C*H*(C=N)$_2$), 4. 53 (bm, 4H, Cy C*H*), 2.75 - 1.01 (m, 52H, CH_3 & Cy).

^{1}H NMR (Toluene-d_8, 400 MHz, 383 K): δ 4.98 (s, 2H, C*H*(C=N)$_2$), 4,49 (bm, 4H, Cy C*H*), 1.92 (bs, 12H, CH_3**)**, 1.76- 1.30 (m, 40 H, Cy CH_2).

^{13}C{^{1}H} NMR (C_6D_6,76 MHz**,** 343 K): δ 160.0 (C=N)), 108.0 (*C*H(C=N)$_2$), 59.3 (Cy *C*H), 30.6, 29.6, 25.1, 24.2, 22.5 (Cy *C*H_2), 23.6 (CH_3).

Low temperature spectra: ^{1}H NMR ($CDCl_3$, 500 MHz, 223 K): δ 5.11 (s, 2H, C*H*(C=N)$_2$), 4.70 (bm, 2H,CH_{Cy}), 3.70 (bm, 2H,CH_{Cy}), 2.16 (bs, 6H, CH_{3b}**)**, 1.91(bs, H, CH_{3a}**)**, 1.89-1.57 (m, 40 H, Cy).

^{13}C{^{1}H} NMR ($CDCl_3$, 126 MHz, 223 K): δ 162.7 (C=N)), 162.0(C=N)), 112.4 (*C*H(C=N)$_2$), 61.6, 59.9 (Cy *C*H), 34.8, 33.8, 32.2, 31.2, 30.7 (Cy *C*H_2), 27.5 (*Me*(C=N)), 27.1, 26.4, 25.9, 25.6, 25.1 (Cy CH_2), 24.0 (*Me*(C=N)). (tentative assignment)

Complex 3.3c

^{1}H NMR (C_6D_6, 400 MHz, 298 K): δ 7.08-7.4 (m, 20H, *Ph*), 6.45-6.43 (bm, 2H, C*H*(Me)Ph), 4.88 (bs, 2H, C*H*(C=N)$_2$), 4.74 (bm, 2H, C*H*(Me)Ph), 2.07-1.42 (m, 24H, Me).

^{1}H NMR (toluene-d_8, 400 MHz, 298 K): δ 7.08-7.8 (m, 20H, *Ph*), 6.37 (bm, 1H, C*H*(Me)Ph), 6.28 (bm, 1H, C*H*(Me)Ph), 4.79 (bs, 2H, CH(C=N)$_2$), 4.68 (bm, 2H, C*H*(Me)Ph), 2.05-1.44 (m, 24H, Me).

Low temperature spectra: ^{1}H NMR (500 MHz, $CDCl_3$, 223 K), two isomers, *a* & *b* in a ratio of 2:1: δ 7.85-7.07 (m, 20H, *a*&*b* Ph), 6.74 (q, *J* = 7 Hz, 2H, *b* C*H*(Me)Ph), 6.65 (q, *J* = 7 Hz, 2H, *a* C*H*(Me)Ph,), 6.12 (q, *J* = 7 Hz, 2H, *a* C*H*(Me)Ph), 5.29 (s, 2H, *a* C*H*(C=N)$_2$), 5.28 (s, 2H, *b* C*H*(C=N)$_2$), 4.83 (q, *J* = 7 Hz, 2H, *b* C*H*(Me)Ph), 2.15 (d, *J* = 7 Hz, 6H, *b* CH(*Me*)Ph), 2.01 (s, 6H, *b* Me(C=N), 1.92 (d, *J* = 7 Hz, 6H, *a* CH(*Me*)Ph,), 1.77 (s, 6H, *a* Me(C=N), 1.90 (s, 6H, *b* Me(C=N), 1.80 (d, *J* = 7 Hz, 6H, *b* CH(*Me*)Ph), 1.69 (s, 6H, *a* Me(C=N), 1.61 (d, *J* = 7 Hz, 6H, *a* CH(*Me*)Ph).

^{13}C{^{1}H} NMR ($CDCl_3$, 126 MHz, 223 K) for both *a* and *b*: 168.2, 167.1, 162.2 (C=N), 146.8, 143.9, 143.6, 143.2 (ispo Ph), 128.4, 127.9, 127.7, 127.5, 126.9, 126.8, 126.5, 126.3, 126.2, 126.1, 126.0, 125.9 (Ph), 111.1, 104.2 (*C*H(C=N)$_2$), 62.33, 59.5, 59.2, 57.5 (*C*H(Me)Ph), 27.3, 26.7, 25.6, 25.3, 25.2, 19.5, 17.9, 17.1 (Me). (one C=N resonance missing or overlapping)

High temperature spectra: ^{1}H NMR (toluene-d_8, 400 MHz, 373 K): δ 6.96-7.41 (m, 20H, *Ph*), 6.38 (bm, 4H, C*H*(Me)Ph), 4.79 (bs, 2H, C*H*(C=N)$_2$), 1.80 (bs, 12H, Me), 1.59 (bs, 12H, Me).

^{1}H NMR (500 MHz, $CDCl_3$, 328 K): δ 8.07-6.85 (m, 20H, Ph), 6.4 (bs, 4H, C*H*(Me)Ph), 5.25 (s, 2H, C*H*(C=N)$_2$), 1.89 (bs, 12H, CH(*Me*)Ph,), 1.79 (bs, 12H, Me(C=N).

Complex 3.6

^{1}H NMR ($CDCl_3$, 400 MHz, 223 K): δ 7.30-7.06 (m, 20H, Ph), 5.30 (bd, *J* = 7 Hz, 2H, C*H*$_2$), 4.87 (bd, *J* = 7 Hz, 2H, CH_2), 4.86 (s, 1H, CH(C=N)$_2$), 4.75 (bd, *J* = 7 Hz, 2H, CH_2),

4.23 (bd, J = 7 Hz, 2H, CH_2), 3.80 (m, 2H, CH_2O), 3.60 (m, 2H, CH_2O), 1.99 (bs, 12H, Me(C=N)), 1.68 (bs, 12H, Me(C=N)), 0.72 (t, J = 7 Hz, 6H, *Me*CH_2O).

CHAPTER 4

Exceptionally high lactide polymerization activity of zirconium complexes with bridged diketiminate ligands

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Ibrahim El-Zoghbi, Todd J. J. Whitehorne and Frank Schaper

Département de chimie, Université de Montréal, Montréal, Québec, H3C 3J7, Canada.

4.1 Abstract

A cyclohexanediyl-bridged, bis(*N*-xylyl) diketiminate ligand, (±)-C_6H_{10}(*nacnac*^{Xyl}H)$_2$, LH_2, (Xyl = 2,6-dimethylphenyl) was obtained from reaction of [(2,6-dimethylphenyl)amino]-pent-3-en-2-one first with Meerwein salt, then with (±)-cyclohexanediamine. Reaction of the ligand with $Zr(NMe_2)_4$ yielded $LZr(NMe_2)_2$. Protonation of the remaining diamide ligands with EtOH or $[H_2NMe_2]Cl$ yielded $LZr(OEt)_2$ and $LZrCl_2$, respectively. The latter complex was also obtained by reaction of LH_2 first with *n*BuLi and then with $ZrCl_4(THF)_2$. The dichloride complex yielded $LZr(OEt)_2$ and $LZrMe_2$ upon reaction with NaOEt or MeLi/$AlMe_3$, respectively. X-ray diffraction studies showed a *trans*-configuration of the ancillary ligands in $LZrCl_2$ and $LZrMe_2$, and a *cis*-configuration in $LZr(NMe_2)_2$ and $LZr(OEt)_2$. $LZr(OEt)_2$ was tested as catalyst for the polymerization of *rac*-lactide. Kinetic investigations yielded a rate law first order in catalyst and monomer and a rate constant k = 14(1) L/(mol·s), the latter being orders of magnitude higher than typical activities for group 4 complexes in lactide polymerization. Analyses of the obtained polymer revealed an atactic polymer and broad polymer molecular weight distributions with sizeable fractions of cyclic oligomers. The influence of contaminants on the polymerization activity was examined: While lactic acid deactivates the catalyst, addition of up to 1 equiv of water or *para*-toluenesulfonic acid revitalized catalysts not showing maximum activity.

4.2 Introduction

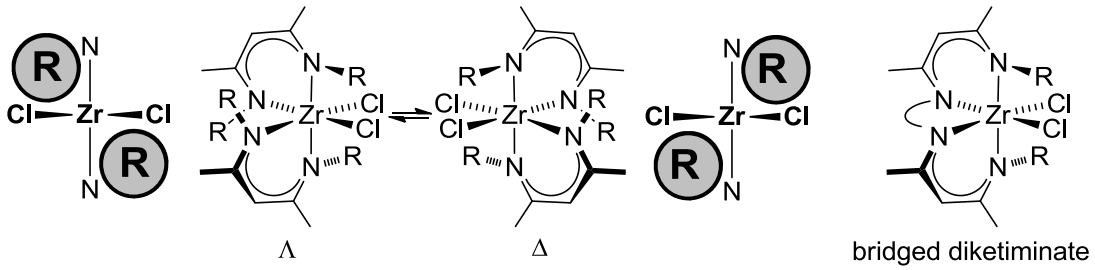
The increased popularity of β-diketiminate ("*nacnac*") ligands led to several investigations of their coordination chemistry with zirconium in the last two decades. The

obtained complexes can be summarized in three types: *nacnac*ZrX_3L_{0-1},[1-10] pseudo-tetrahedral Cp^R(*nacnac*)ZrX_2,[3, 5, 10-19] and octahedral *nacnac*$_2ZrX_2$.[3-5, 20-23] The coordination mode of the diketiminate ligand in all of these complexes can vary between a simple *N*,*N*'-κ^2-coordination and higher coordination modes such as "η^5-like" or a κ^2,η^2-coordination.[19, 24] Octahedral zirconium bisdiketiminate complexes, *nacnac*$_2ZrX_2$, or their respective cations, [*nacnac*$_2$ZrX]$^+$, are very attractive targets as catalysts for coordination-insertion polymerization or related reactions: (i) They show the least variation in diketiminate binding modes (in nearly all complexes a simple κ^2-coordination is observed). (ii) They contain two reactive sites, which are forced in a *cis*-position with each other, since the *N*-substituents disfavour an assembly of all nitrogen atoms in the same plane.[23] (iii) The fixed C_2-symmetry of the chiral metal complex renders the coordination sites homotopic and allows stereoselectivity for the catalysed reaction. (iv) Last but not least, the *N*-substituents in an idealized *cis*-octahedral structure are ideally placed to exert control on the reaction (Scheme 4.1). Unfortunately, *ortho*-substituted *N*-aryl diketimines are sterically too demanding to form bisdiketiminate complexes and *nacnac*$^{Ar}{}_2ZrX_2$ complexes were limited to ligands where at least one *N*-substituent lacks *ortho*-substituents.[3-5, 21]

We recently reported that diketimines with *N*-alkyl substituents form the desired C_2-symmetric bisdiketiminate complexes, *nacnac*$^R{}_2ZrX_2$, even with sterically demanding *N*-alkyl substituents such as cyclohexyl or α-methylbenzyl.[23] Application of these compounds in catalytic reactions has been, however, prevented by the high steric crowding, which shielded the active sites from further reactions. Thus, *nacnac*$^R{}_2ZrCl_2$ (R = benzyl, cyclohexyl, α-methylbenzyl) failed to react either with a variety of alkylating reagents such

as MeLi, *n*BuLi, $AlMe_3$, MeMgX, or $ZnEt_2$, or with sodium ethoxide. The corresponding dimethyl complex *nacnac*$^{Bn}{}_2ZrMe_2$ reacted with $B(C_6F_5)_3$, but the obtained cationic zirconium methyl complex reacted neither with diphenylacetylene nor benzaldehyde, most likely due to steric blocking of the metal center.[23] In addition to the low reactivity at the "active coordination sites", the configuration of the complexes was not stable. As observed for *N*-aryl complexes,[3-5] Bailar-Twist isomerisation led to fast interconversion between Δ- and Λ-enantiomers at room temperature on the NMR time scale (Scheme 4.1), which could not be prevented even by use of a chiral *N*-substituent.[23]

To address both of the above problems, we decided to connect the two diketiminate ligands by a cyclohexanediyl bridge (Scheme 4.1). The smaller bite angle enforced by the C_2-bridge should provide easier access to the reactive sites, while its axial chirality should prevent the Δ-Λ-isomerisation. Similar bisdiketiminate ligands with achiral $(CH_2)_n$-bridges (n = 2, 3) were previously employed by Gong *et al.*, but the respective zirconium complexes still showed fast Δ- Λ-isomerisation in solution.[22] Herein we report the preparation and structural analysis of C_6H_{10}(*nacnac*^{Xyl})$_2ZrX_2$ complexes (Xyl = 2,6-dimethylphenyl), their reactivity compared to unbridged analogues and in *rac*-lactide polymerization.

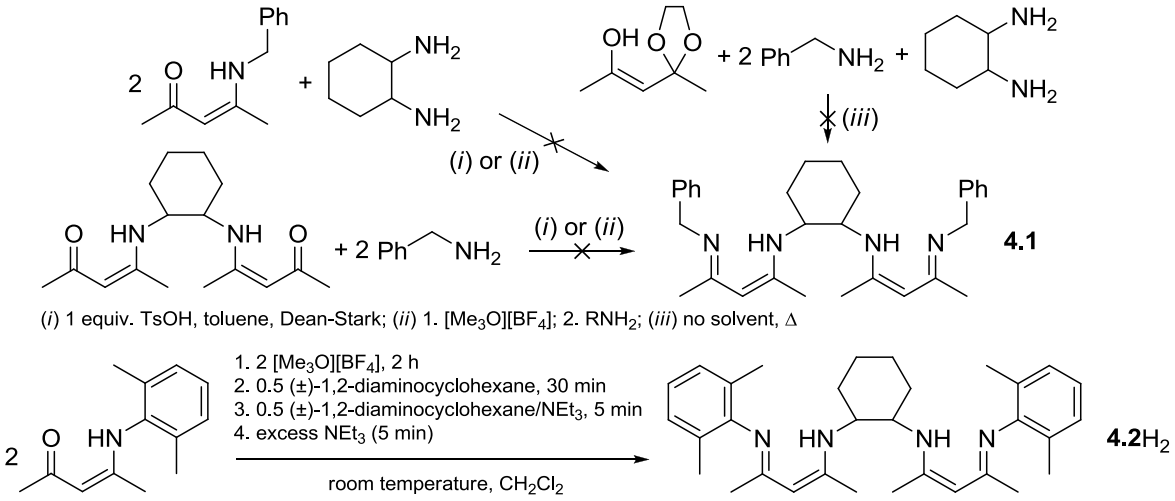


Scheme 4.1

4.3 Results and Discussion

Ligand synthesis. As a close analogue to the *N*-alkyl bisdiketiminate complexes studied before,[23] we attempted to prepare the bridged ligand **4.1** with *N*-benzyl substituents (Scheme 4.2). However, independent of the starting point of the reaction or the synthetic path used (acid-catalysed water elimination, alkylation with Meerwein salt, use of ethyleneketal), either no reaction occurred or inseparable product mixtures were obtained. This was in agreement with previous observations in our group: while several non-symmetrically substituted *N*-aryl diketimines have been reported, we were unable to isolate a mixed *N*-alkyl diketimine. Closer investigations indicated that attack at the imine group was faster than attack at the keto group, leading to scrambling of the *N*-substituents and – in the best cases – to statistical product mixtures.[25] However, due to the favoured formation of *N*-aryl imines over *N*-alkyl imines, a more than statistical yield of a mixed diketimine was obtained, when acetylacetone was reacted with mixtures of aniline and amine.[25] We thus decided to employ *N*-xylyl substituents and obtained the bridged ligand $C_6H_{10}(nacnac^{Xyl})_2H_2$, **4.2**$H_2$, in 76% yield (Scheme 4.2). Reaction conditions were chosen to disfavour *N*-substituent scrambling. Thus, acetylacetone was first reacted with aniline to form the respective enamine. Instead of the acid-catalysed condensation we normally

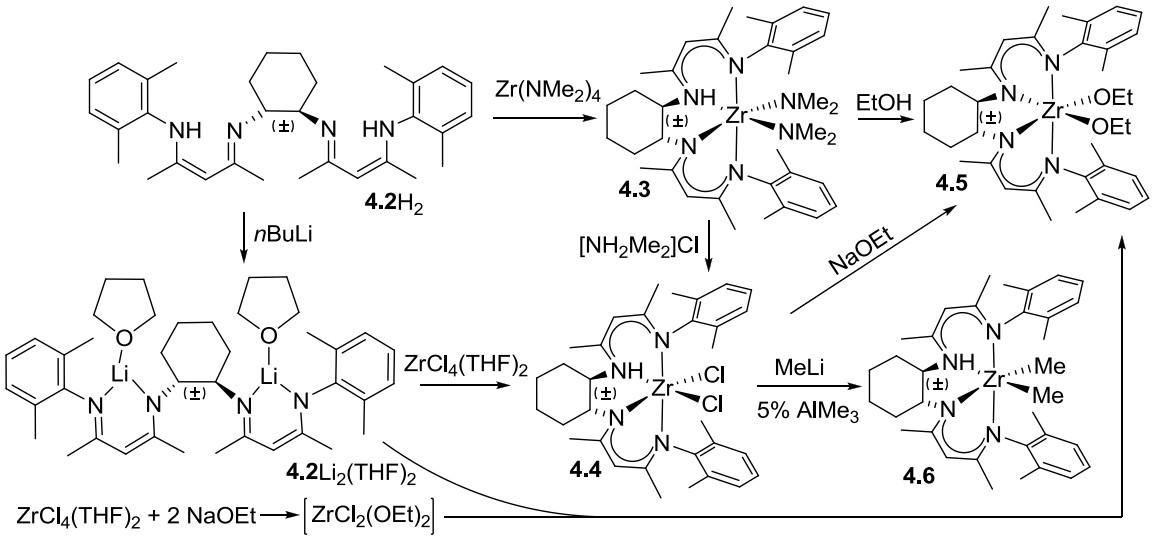
employ for symmetric *N*-alkyl diketimines and which requires long reaction times,[25] we followed a synthetic protocol used for closely related ligands[26-28] and used Meerwein salt to activate the enamine ($[Me_3O][BF_4]$ worked slightly better than the respective ethyl salt in our hands). Nevertheless, the reaction outcome was very sensitive to the reaction times involving amines. Either addition of NEt_3 directly with the amine or prolonged reaction times (steps 2-4, Scheme 4.2), drastically reduced isolated yields of **4.2**H_2.



Scheme 4.2

Complex syntheses. Reactions of ligand **4.2**H_2 with $ZrBn_4$ under various conditions did not yield an isolable product. $Zr(NMe_2)_4$ proved to be more reactive and yielded 50% conversion in solution (C_6D_6, 60 °C). Reaction in the absence of solvent at 120 °C then afforded the diamido complex **4.3** (Scheme 4.3) in 71% crystallized yield. The latter complex reacted with dimethylammonium chloride or ethanol to the respective dichloride and diethoxide complexes **4.4** and **4.5** (Scheme 4.3). The protonation reaction, however, was unselective and in both cases protonation of the bisdiketiminate ligand occurred in

significant amounts (up to 50%). Complex **4.4** was obtained, however, in good yields following a salt metathesis route: Deprotonation of bisdiketimine ligand **4.2**H_2 with *n*BuLi in THF yielded the ligand dilithium salt **4.2**$Li_2(THF)_2$ (Scheme 4.3). Spectroscopic data and combustion analysis suggest the coordination of one THF molecule per lithium atom, as usually observed for diketiminate lithium salts containing coordinated THF or diethyl ether. Further reaction between **4.2**$Li_2(THF)_2$ and $ZrCl_4(THF)_2$ yielded the zirconium dichloride complex **4.4** in 80% yield (Scheme 4.3). Contrary to the unbridged bis(diketiminate) zirconium complexes, *nacnac*$^R{}_2ZrCl_2$, which did not react with MeLi even at higher temperatures,[23] reaction of dichloride complex **4.4** with MeLi at room temperature in C_6D_6 afforded complete conversion of the dichloride to the respective dimethyl complex **4.6** (contaminated with significant amounts (35%) of the monomethylation product) in less than 5 min (Scheme 4.3). Constraining the ligand by introduction of a cyclohexanediyl bridge thus indeed resulted in the intended increase of reactivity. Analytically pure dimethyl complex **4.6** was isolated from large-scale reactions employing MeLi and a catalytic amount of $AlMe_3$ in 36% yield. Dichloride **4.4** also proved to be more reactive than unbridged bisdiketiminate complexes towards NaOEt[23] and cleanly yielded the diethoxy complex **4.5** (Scheme 4.3), albeit under harsher reaction conditions (3 d, 110 °C). Complex **4.5** can be prepared directly from $ZrCl_4(THF)_2$ under milder conditions (12 h, 80 °C) and with identical yields, if $ZrCl_4(THF)_2$ is first reacted with $NaOEt_2$ and then with **4.2**$Li_2(THF)_2$. Formation of a putative $ZrCl_2(OEt)_2$ intermediate is crucial. The direct reaction of $ZrCl_4$ with a mixture of NaOEt and **4.2**$Li_2(THF)_2$ still yielded **4.5**, but again required 3 d of reaction time.



Scheme 4.3

Solid state and solution structures. The solid state structures of complexes **4.3-4.6** are shown in figures 4.1-4.4. Compared to unbridged bisdiketiminate zirconium complexes, the constraint introduced by bridging the diketiminate ligands results in a severe distortion of the octahedral geometry. The bridgehead nitrogen atoms (N1 and N3) are severely tilted out of the ZrX_2 plane (38-49° in *cis*-C_2-bridged, 8±5° in unbridged complexes, Table 4.1). The reduced bite-angle enforced by the bridge (N1-Zr-N3 = 70-73° in C_2-bridged, 89±3° in unbridged complexes) further results in a widening of the ZrX_2 angles of the atoms *trans* to the bridgehead nitrogen atoms (117-138° in *cis*-C_2-bridged, 91±3° in unbridged complexes) and slightly elongated (≈0.01 Å) Zr-N distances for the non-bridgehead nitrogen atoms. A structural effect of bridging favourable for potential applications is a slight change in the position of the xylyl substituents. While the *N*-substituents in unbridged diketiminate complexes were positioned between the $ZrCl_2$-fragment (C-N-Zr-Cl torsion angles >27°,

Table 4.1), they are eclipsed with one Zr-X bond in bridged complexes (C-N-Zr-X torsion angles <14°).

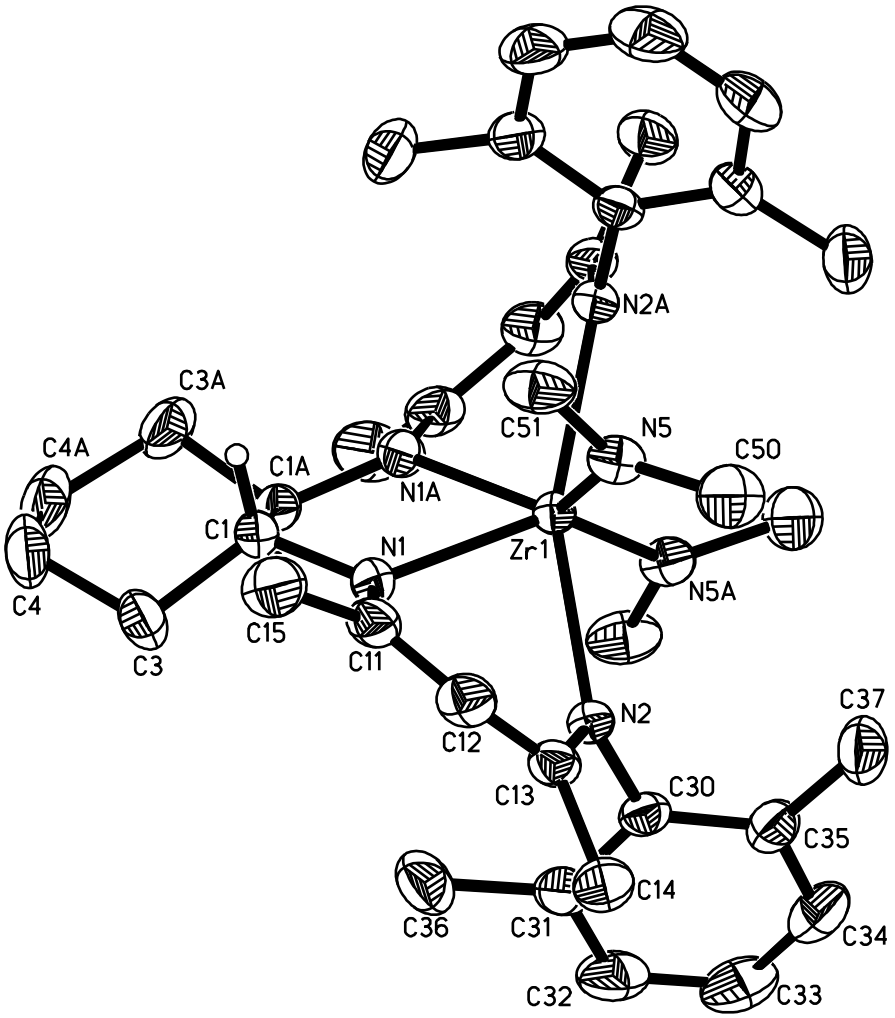


Fig. 4.1. X-ray structure of **4.3**. Thermal ellipsoids are drawn at the 50% probability level. Most hydrogen atoms were omitted for clarity.

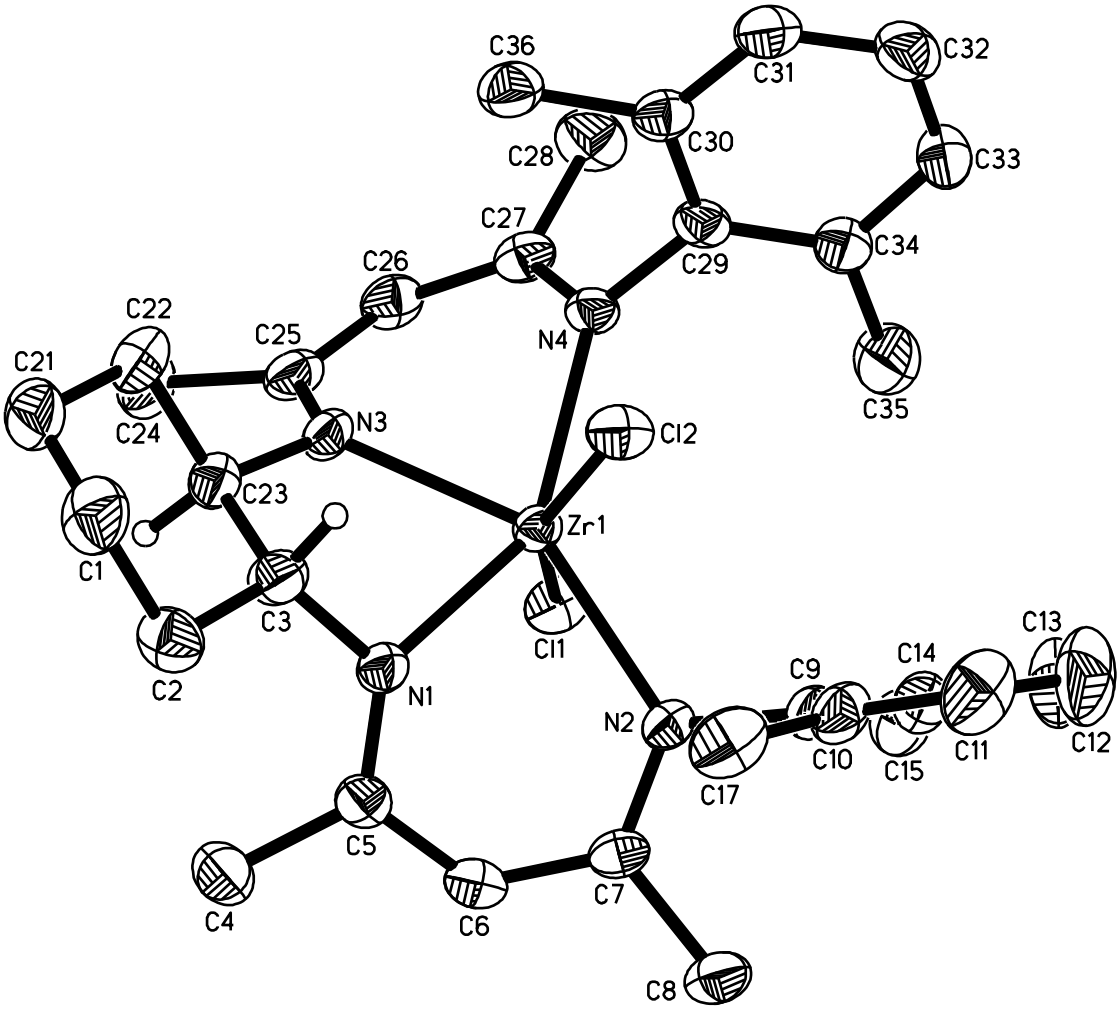


Fig. 4.2. X-ray structure of **4.4**. Thermal ellipsoids are drawn at the 50% probability level. Most hydrogen atoms and co-crystallized benzene were omitted for clarity.

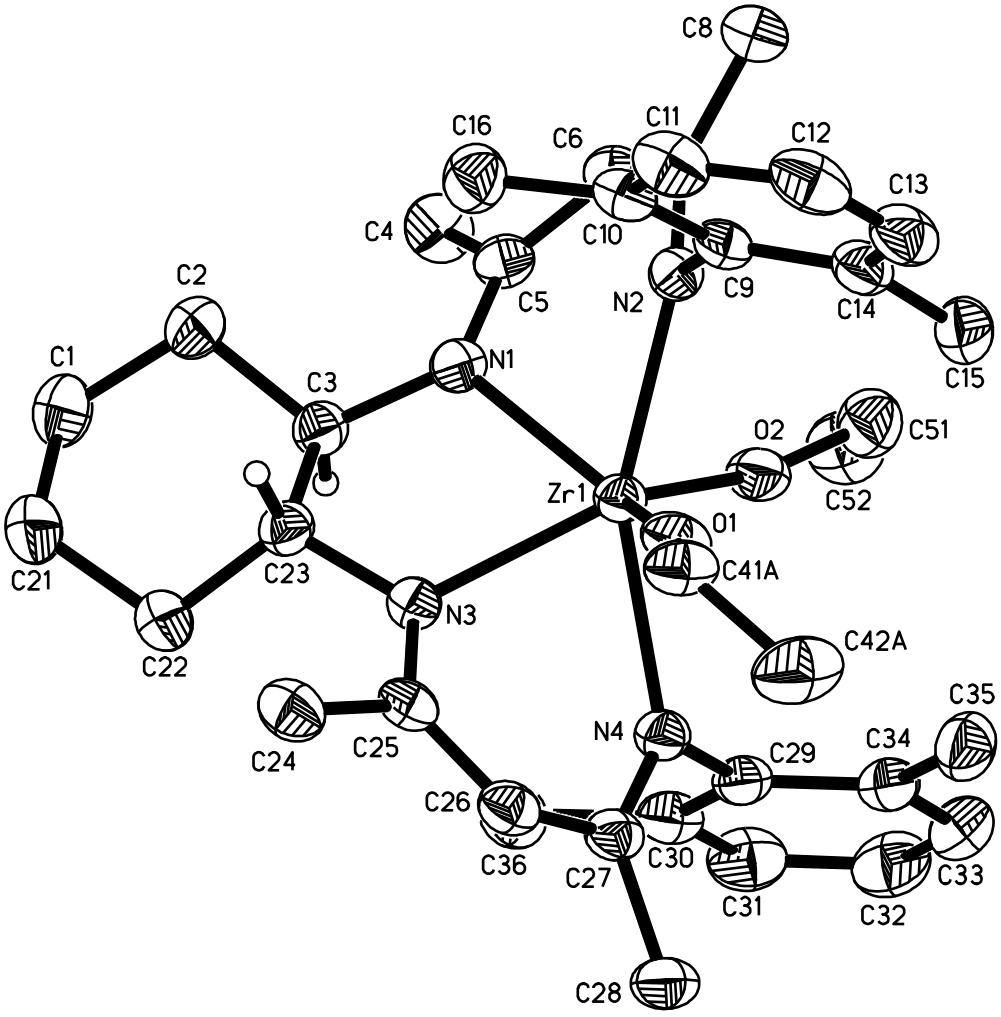


Fig. 4.3. X-ray structure of **4.5**. Thermal ellipsoids are drawn at the 50% probability level. Most hydrogen atoms and the disorder of one OEt group were omitted for clarity.

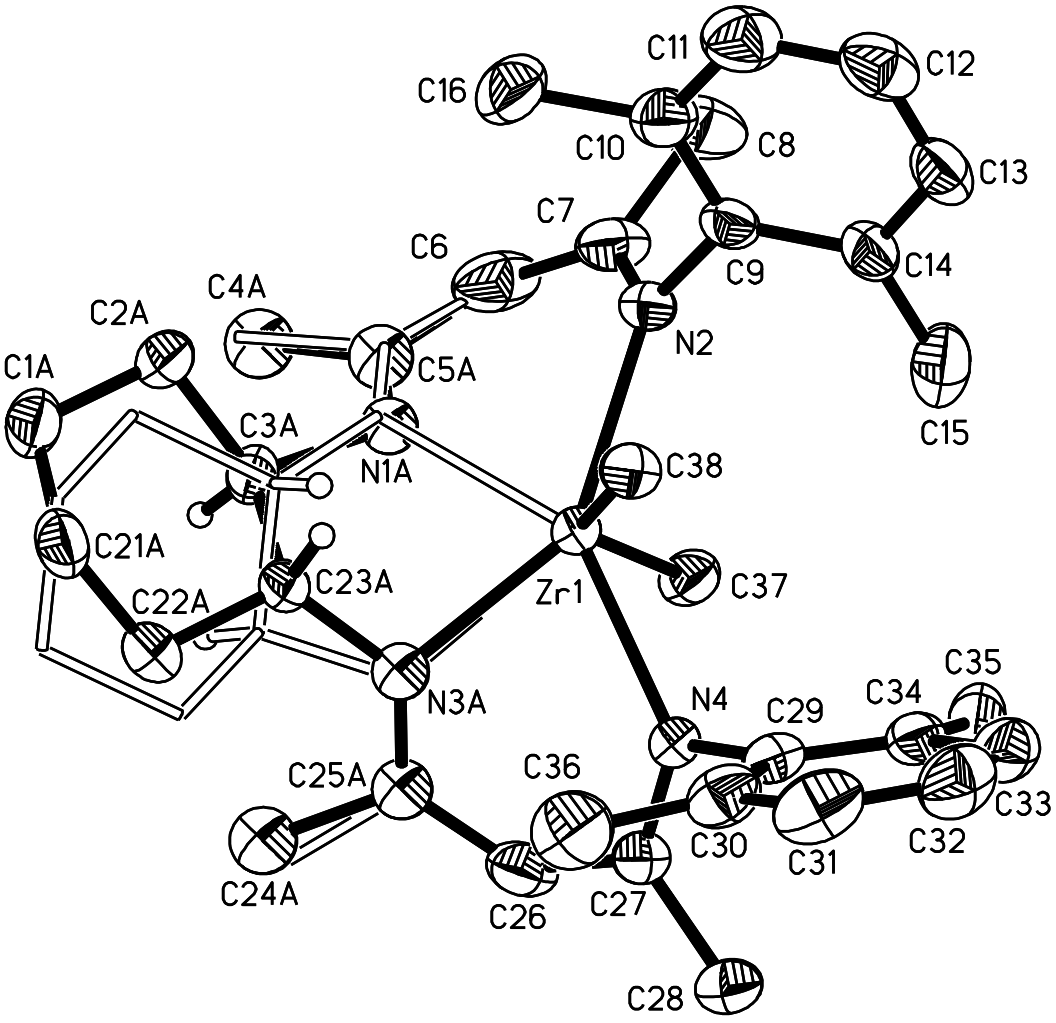


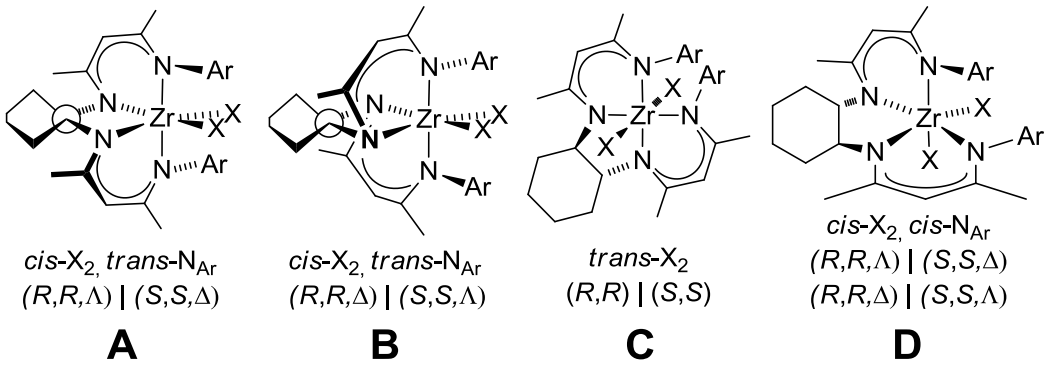
Fig. 4.4. X-ray structure of **4.6**. Thermal ellipsoids are drawn at the 50% probability level. Most hydrogen atoms were omitted for clarity. The smaller fraction of the disordered cyclohexanediamine bridge is shown in open lines without thermal ellipsoids or labelling.

Table 4.1 Bond distances [Å] and bond angles [°] in the crystal structures of **4.3**-**4.6**.

	4.3	**4.4**	**4.5**	**4.6**	*nacnac*$^{R}_{2}ZrCl_2$ [a]	C_2H_4(*nacnac*^{dipp})$_2$ $ZrCl_2$ [b]
Zr-N1/N3	2.252(1)	2.183(2), 2.211(2)	2.256(2), 2.226(2)	2.190(5) - 2.250(7)	2.23±0,05	2.175(3)
Zr-N2/N4	2.374(1)	2.285(2), 2.277(2)	2.307(2), 2.344(2)	2.315(3), 2.344(3)	2.22±0,05	2.318(4)
Zr-X [c]	2.068(1)	2.425(1), 2.438(1)	1.937(2), 1.941(2)	2.265(4), 2.283(3)	2.45±0,06	2.422(2)
N1-Zr-N3 [d]	71.92(7)	72.26(8)	72.32(7)	70.1(2), 72.0(2)	89±3	72.68(11)
N2-Zr-N4 [d]	159.47(7)	133.18(8)	156.14(7)	138.4(1)	165±13	160.03(10)
N1-Zr-N2	74.36(5)	77.97(8)	76.41(7)	75.5(1), 75.9(2)		
N3-Zr-N4		77.85(8)	74.82(7)	75.0(1), 76.2(2)		
X-Zr-X [c]	124.93(8)	156.24(3)	121.13(8)	138.0(1)	91±3	117.40(4)
(Zr/N1/N3)-(Zr/X1/X2) [c,d]	49	80	49	80, 81	8±5	38
(Zr/N1/N3)-(Zr/N2/N4) [c]	44	12	44	9, 10	83±7	53
C-N2/4-Zr-X [e]	13	-	1, 10	-	37±10	3, 6

[a] Taken from ref. [23]. [b] Taken from ref. [22]. [c] **4.4** : X = Cl1, Cl2; **4.3** : X = N5, N5A; **4.5** : X = O1, O2; **4.6** : X = C37, C38. [d] for **4.3** : N3 = N1A, N4 = N2A. for **4.6** : N1 = N1A/B, N3 = N3A/B. [e] Torsion angle between the *N*-substituent and the ancillary ligand on Zr.

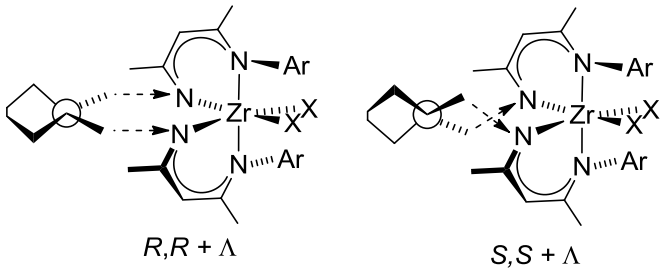
Of the possible structural isomers of $C_6H_{10}(nacnac^{Xyl})_2ZrX_2$ complexes, only C_2-symmetric isomers **A** and **C** were observed in the solid state (Scheme 4.4). Complexes **4.3** and **4.5** show a *cis*-X_2 configuration[22] in the solid state, as was observed for all other bisdiketiminate zirconium complexes reported (X-Zr-X angle = 89-117°).[3, 4, 20-23] In both cases, the *S*,*S*,Δ/*R*,*R*,Λ-isomer (**A**, Scheme 4.4) was observed, while the *S*,*S*,Λ/*R*,*R*,Δ-isomer (**B**, Scheme 4.4) was absent. Complexes **4.4** and **4.6** crystallize as the *trans*-isomer (**C**, Scheme 4.4). While variable temperature NMR investigations have shown that for unbridged diketiminate complexes a *trans*-Cl configuration is not obtained even as a short-lived intermediate at elevated temperatures,[23] the decreased N1-Zr-N3 angle in **4.4** and **4.6**, caused by the cyclohexanediyl bridge, enables the placement of all four nitrogen atoms in the equatorial plane. The preference for the *trans*-arrangement of the chloride atoms in **4.4** is nevertheless surprising, since structures of *cis*-**4.3** and *cis*-**4.5** are nearly superposable with *cis*-$C_2H_4(nacnac^{dipp})_2ZrCl_2$ (dipp = 2,6-diisopropylphenyl, see also Fig. 4.5b),[22] indicating that neither the cyclohexanediyl bridge nor the chloride ligands should prevent formation of a *cis*-Cl complex. Most likely, the *trans*-configuration is sterically slightly more favourable, but only for small ligands, such as chloride or methyl. Space-filling diagrams of **4.4** and **4.6** indicate that increased steric demand, either of the ancillary ligand (as in **4.3** or **4.5**) or of the *ortho*-substituents on the phenyl ring (as in $C_2H_4(nacnac^{dipp})_2ZrCl_2$), would destabilize the *trans*-configuration. Additionally, π-donation from the OEt or the NMe_2 substituents in **4.3** and **4.5** might further favor a *cis*-geometry for these complexes.



Scheme 4.4

The preference of *cis*-complexes **4.3** and **4.5** to form the *S*,*S*,Δ/*R*,*R*,Λ-isomer (**A**, Scheme 4.4) seems intuitively correct on a first glance. Since the diketiminate bite-angle of 74-78° (Table 4.1) is significantly smaller than the ideal octahedral angle, nitrogen atoms N1 and N3 *trans* to the ancillary ligands are slightly displaced out of the ZrX_2 plane (Fig. 4.1 & 4.3). In the case of the Λ-isomer, an *R*,*R*-cyclohexanediyl bridge seems to accommodate this deformation more readily than the *S*,*S*-configuration (Scheme 4.5). To investigate in more detail this simplistic explanation, which neglects the strong deviation from octahedral geometry observed in **4.3** and **4.5**, as well as the typical distortion of the diketiminate ligand into a boat-like conformation,[19, 24] an idealized *S*,*S*-cyclohexanediyl bridge was fitted into the crystal structure of Λ-**4.5** (Fig. 4.5a). The change of configuration in the cyclohexanediyl bridge requires a higher bending of the N-C3/C23 bond out of the diketiminate mean plane (52° in the hypothetical *S*,*S*,Λ-isomer depicted in Fig. 4.5a, 24±3° for the *R*,*R*,Λ-isomers **4.3** and **4.5**). This latter value is very close to the out-of-plane bending of the *N*-substituent in unbridged *N*-alkyl bisdiketiminate complexes (16-24°)[23]

and in C_2H_4- and C_3H_6-bridged bisdiketiminate complexes (24-33°).[22] In fact, crystal structures of **4.5** and the C_2H_4-bridged complex C_2H_4(*nacnac*^{dipp})$_2$ZrCl$_2$[22] are nearly superposable (Fig. 4.5b), indicating the correct stereochemical match between an *R*,*R*-configured cyclohexanediyl bridge and a Λ-configuration at the metal center.



Scheme 4.5

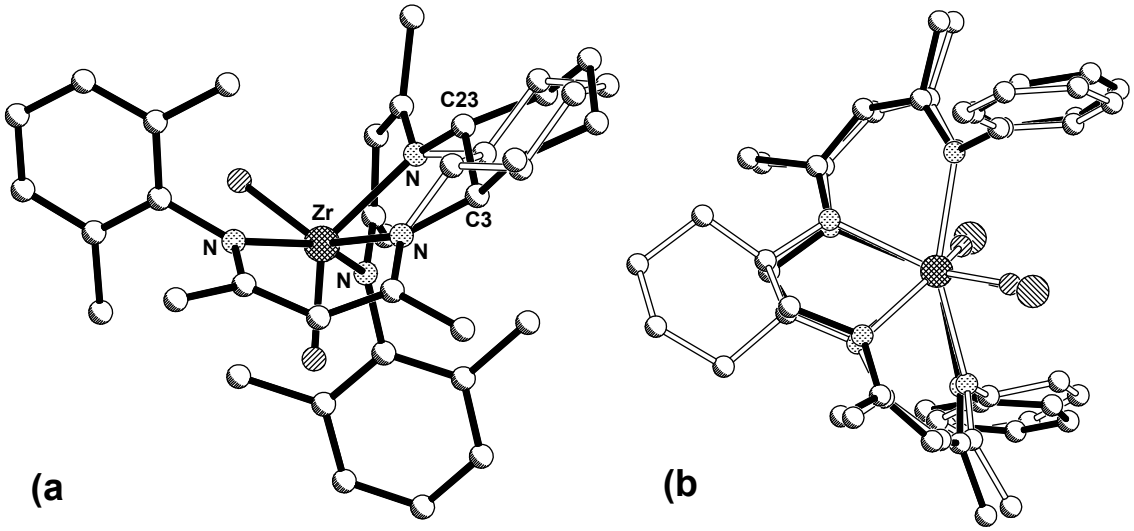


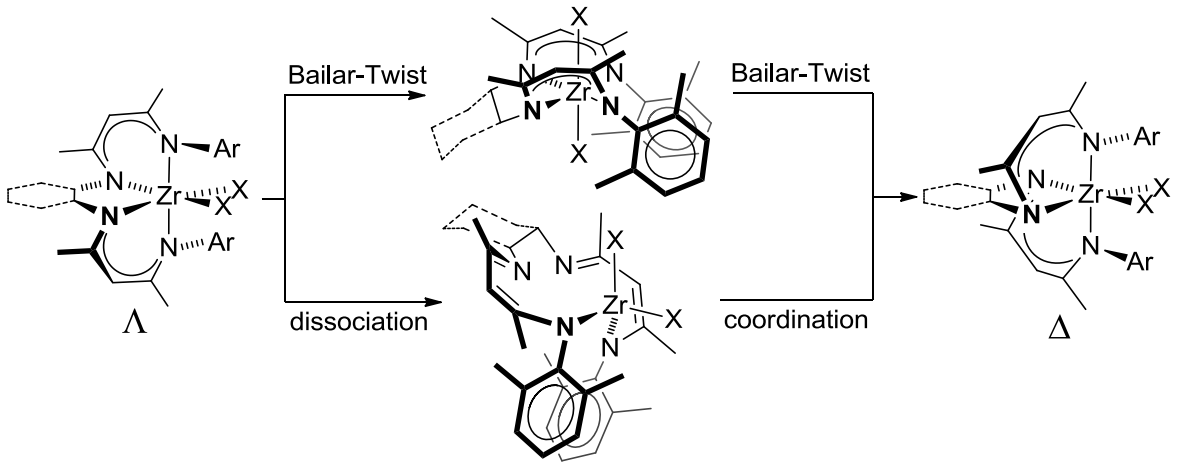
Fig. 4.5 (a) X-ray structure of (*R*,*R*,Λ)- **4.5** with an idealized *S*,*S*-cyclohexanediamine fitted into the structure (hollow lines). (b) Best fit overlay of C_2H_4(*nacnac*^{dipp})$_2$ZrCl$_2$[22] and **4.5**. Ethyl groups, aryl substituents and hydrogen atoms were omitted for clarity.

In solution, proton NMR spectra of **4.3**-**4.6** show one signal for the methine protons of the cyclohexane ring, one signal for the central CH resonance of the diketiminate ligand, two signals for the diketiminate methyl groups and two signals for the xylyl methyl groups. The C_2-symmetry of the ligand is thus preserved in the complex (either by symmetry or fast isomerisation). The presence of two xylyl methyl resonances, of three aromatic resonances in proton NMR spectra of **4.3**-**4.6**, as well as of four resonances for the aromatic ring in carbon NMR spectra of **4.3**-**4.6**, and the fact that two xylyl methyl resonances were observed also for lithium complex **4.2**$Li_2(THF)_2$ and the free ligand **4.2**H_2 (see exp. section), all indicate that *N*-aryl rotation is slow on the NMR time scale. In agreement with hindered *N*-aryl rotation, NMR spectra of **4.5** did not indicate any coalescence of the xylyl methyl groups up to 70 °C.

Unbridged diketiminate complexes have shown evidence for fast Δ-Λ-isomerisation in solution (**A**↔**B**, Scheme 4.4) by a Bailar-Twist mechanism.[3-5, 23] Despite the introduction of a bridging group, the same fast isomerisation was observed by Dong *et al.* in C_2H_4- or C_3H_6-bridged complexes: coalescence of the CH_2 protons in the bridge yielded averaged C_{2v}-symmetric NMR spectra,[22] in the case of a C_2H_4-bridge even at –70 °C. NMR spectra of **4.3**-**4.6** do not contain any group which would coalesce in case of a fast Δ-Λ-isomerisation and thus no straightforward way to establish the absence or presence of Δ-Λ-isomerisation. However, while spectra of C_2H_4(*nacnac*^{Xyl})$_2ZrCl_2$ displayed only one resonance for the xylyl methyl group even at low temperatures,[22] two xylyl methyl resonances were observed in spectra of **4.3**-**4.6**. In the absence of *N*-xylyl rotation (*vide supra*), the equivalence of the xylyl methyl groups in C_2H_4(*nacnac*^{Xyl})$_2ZrCl_2$ has to be

caused by passage through a C_{2v}-symmetric intermediate associated with the Δ-Λ-isomerisation. Direct Δ-Λ-isomerisation of bridged bisdiketiminate complexes by a Bailar-Twist would result in an isomer with the bridgehead nitrogen atoms in an impossible *trans*-configuration. Contrary to unbridged $nacnac^{R}{}_2ZrX_2$ complexes, Δ-Λ-isomerisation via a Bailar-Twist mechanism thus has to pass by a *trans*-X_2 complex (Scheme 4.6). Alternatively, based on the fact that isomerisation is faster for C_2H_4- than for C_3H_6-bridged complexes, Dong *et al.* had proposed that Δ-Λ-isomerisation in bridged bisdiketiminate complexes proceeds by dissociation of the bridging nitrogen atoms and through a tetrahedral intermediate rather than via a Bailar-Twist mechanism (Scheme 4.6).[22] Although only two structurally characterized examples of κ^1-coordinated diketiminate ligands were reported,[29, 30] such an intermediate does not seem unreasonable, in particular considering the steric strain introduced by the bridge. In the case of C_2H_4-bridged complexes, the *trans*-X_2 complex as well as the four-coordinated intermediate easily achieve apparent C_{2v}-symmetry by a ring inversion of the metallacycle(s) and Δ-Λ-isomerisation would thus lead to the observed equalization of the xylyl methyl groups for C_2H_4-bridged complexes (Scheme 6). In **4.3**-**4.6**, even fast inversion of the metallacycle(s) of the same intermediates results only in apparent C_2-symmetry and the inequivalence of the xylyl methyl groups is preserved. (In fact, if **4.4** and **4.6** retain the C_1-symmetric *trans*-X geometry observed in the solid state, fast ring inversion has to be present to result in the observed (apparent) C_2-symmetry of the NMR spectra.) While the equivalence of the xylyl methyl resonances is thus a further indication of fast isomerisation

of the complex geometry, the existence of two distinct xylyl methyl peaks in **4.3**-**4.6** unfortunately does not indicate the absence of these isomerisations.



Scheme **4.**6

To further investigate the possibility of a fast isomerisation, proton NMR spectra of **4.5** were recorded at variable temperatures down to –50 °C. While no splitting of resonances was observed, significant broadening of all resonances occurred below –20 °C, indicative of a dynamic process (Fig. 4.6 and supp. inform.). In summary, while there is thus no clear evidence for dynamic processes in **4.3**-**4.6**, the available data indicates that a fast isomerisation is indeed present. Given that isomers **A** and **C** were observed in the solid state, it seems reasonable to presume that the complexes retain the geometry observed in the solid state and that a *cis*-*trans* isomerisation is responsible for the peak broadening at low temperatures, without necessarily forming the wrong stereomatch **B** or C_1-symmetric species **D**.

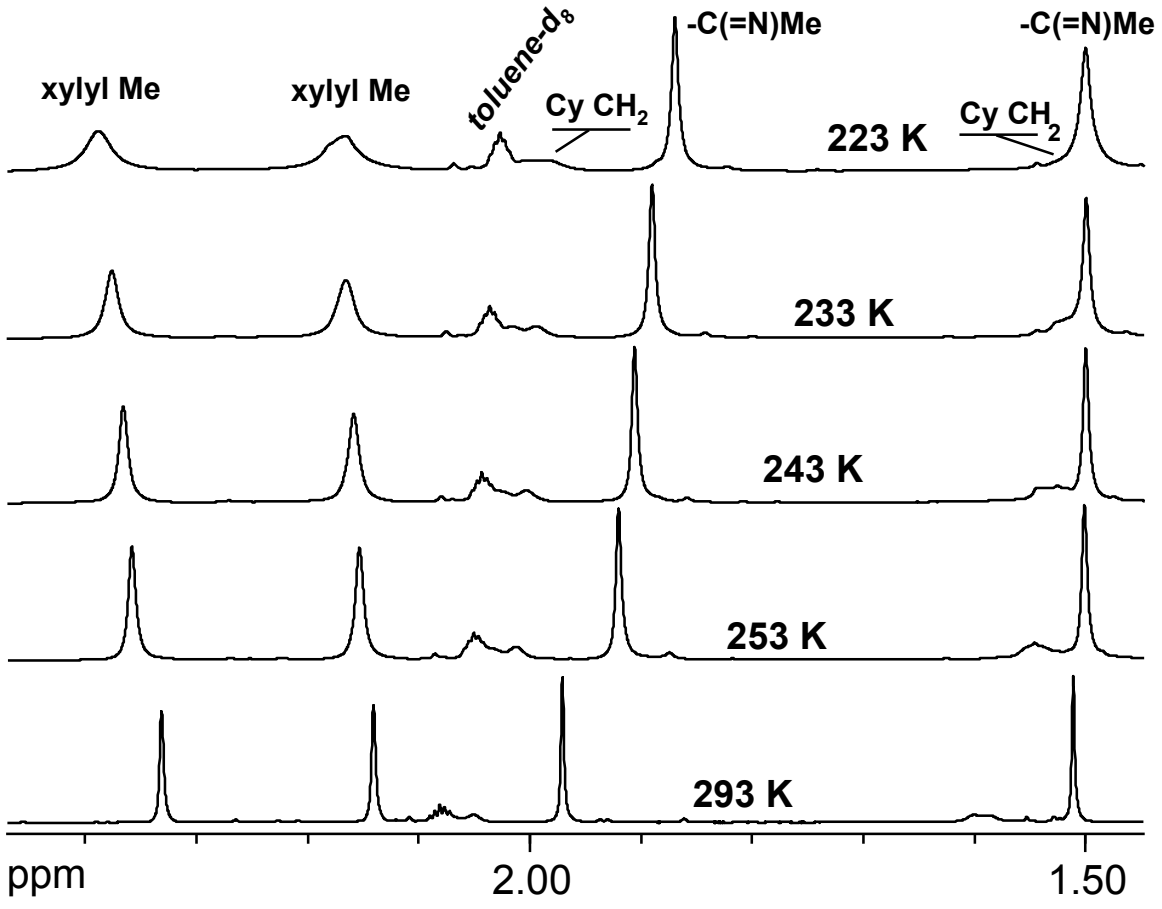


Fig. 4.6. ^{1}H NMR spectra (aliphatic region) of **4.5** at different temperatures. See supp. inform. for complete spectra.

Lactide polymerization. Attempts to obtain a cationic alkoxide complex $[C_6H_{10}(nacnac^{Xyl})_2ZrOEt]^+$, which would be an attractive catalyst for lactide polymerization, from reaction of **4.5** with either *para*-toluenesulfonic acid, triflic acid or $[PhN(H)Me_2][OTf]$ under a variety of conditions yielded only complex product mixtures, in which protonated ligand was the most prevalent species. Reaction of **4.4** with one equiv of AgOTf, followed by reaction with NaOEt likewise did not afford the desired cationic

complex. We thus investigated octahedral coordinated **4.5** directly as catalyst for lactide polymerization. While six-coordinate zirconium alkoxide complexes have been shown to be active for lactide polymerization, they typically display only moderate activity, requiring several hours at temperatures of >70 °C in solution[31-34] or polymerization in molten polymer,[35-37] which is not surprising for a sterically saturated octahedral complex. We were thus surprised to note that *rac*-lactide polymerization with **4.5** at room temperature in dichloromethane solution reached 40% conversion already after one minute. Conversion did not exceed 50%, however, indicative of catalyst decomposition in this solvent (see. supp. inform.). Better catalyst stability was obtained in toluene or diethyl ether, but the lactide monomer has only limited solubility in these solvents. Polymerization in THF finally led to fast and complete (95%) conversion of monomer in five minutes (see supp. Inform.). For comparison: the unbridged bisdiketiminate complex *nacnac*$^{Bn}_2$Zr(OEt)$_2$ was only reactive in molten monomer at 130 °C and still required 30 min to reach >95% conversion.[23] As observed for the substitution of chloride ligands in **4.4**, bridging of the diketiminates thus drastically increased the reactivity of the complex.

More detailed investigations of the reaction kinetics showed the expected first-order dependence in monomer concentration (Fig. 4.7). Reactions typically reached completion in less than 5 min, but conversions did not exceed ≈95%. Incomplete conversion is typical for lactide polymerizations and attributed to a reversible polymerization.[38, 39] Apparent rate constants at catalyst concentrations of 0.5-2 mM show a linear dependence on catalyst concentration (Fig. 4.8), yielding a second-order rate constant at room temperature of $k_{298\ K}$ = 14(1) L/(mol·s). To the best of our knowledge, this is the highest activity, by several

orders of magnitude, reported for any zirconium or other group 4 complex in lactide polymerization. Highly active Zr catalysts include a salalen Zr complex, described as "*incredibly active*" and which reached 99% conversion in 6 h ($k_{298\ K} \approx 5 \cdot 10^{-2}$ L/(mol·s)),[40] a carbene Zr complex (95% after 15 h, $k_{298\ K} \approx 5 \cdot 10^{-3}$ L/(mol·s)),[41] a sulfonamide Zr complex (5 h at 60 °C to reach completion, $k_{333\ K} \approx 1 \cdot 10^{-2}$ L/(mol·s)),[42a] and a dithiodiolate Hf complex reported in 2010 to show the "*highest activity of any group 4 metal catalyst*", which reached complete conversion in 1 min in molten monomer ($k_{403\ K} \approx 4$ L/(mol·s)).[42b]

While **4.5** thus displays an extremely high activity for group 4 complexes and compares well with the most active catalyst systems reported so far for the polymerization of lactide, its remaining characteristics, such as stereoselectivity, complex stability and polymer molecular weight control, are much less desirable.

Stereoselectivity: All obtained polymers are essentially atactic with a slight heterotactic bias (P_r = 0.56-0.64). The lack of isoselectivity imposed by the C_2-symmetric complex might be due to thermodynamic, kinetic or mechanistic reasons: (i) In the crystal structure of **4.3** and **4.5** we note that the introduction of the bridge forces the central atom of the diketiminate ligand (**4.3**: Fig. 4.1, C12; **4.5**: Fig. 4.3, C6/C36) towards the ancillary ligands, occupying the "empty" part of the catalytic pocket. (ii) The observed dynamic process in the NMR might prevent stereochemical stability of the catalytic site. (iii) The active species might not be a C_2-symmetric *cis*-isomer, but rather a species for which less stereocontrol by the chiral bridge would be expected, such as the *trans*-isomer or a tetracoordinated species (Scheme 4.6).

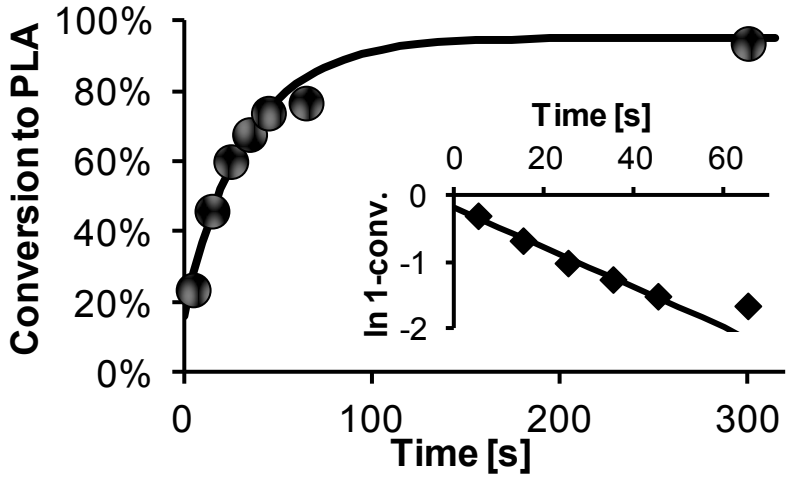


Fig. 4.7. PLA concentration vs. time for *rac*-lactide polymerization with **4.5**: [Lactide] = 0.6 M; [**4.5**] = 2 mM; THF; ambient temperature. The inset shows the linearised plot of monomer consumption assuming a first-order rate law; $k_{obs} = 0.030\ s^{-1}$.

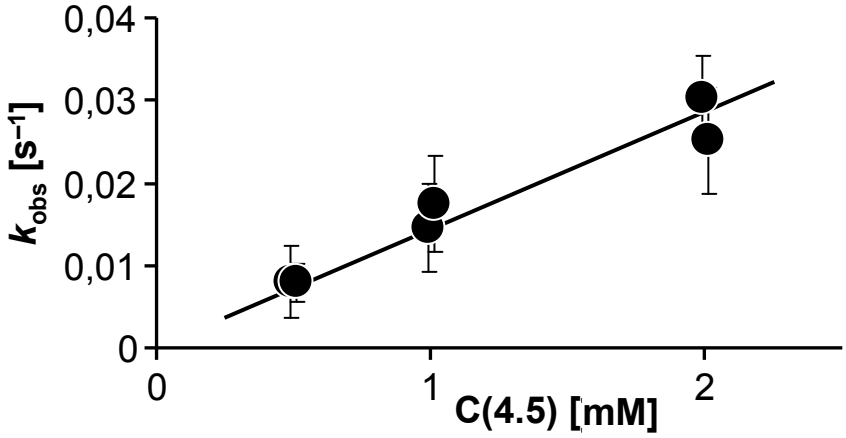


Fig. 4.8. Dependence of apparent rate constants k_{obs} on catalyst concentration; k = 14(1) L/(mol·s).

Complex stability: Despite rigorous drying of solvents and repeated recrystallisation of lactide, the stability of **4.5** under polymerization conditions is limited. All kinetic analyses

show slight deviations from first order behaviour, which can be described to catalyst decomposition. No further polymerization is observed, when a second portion of lactide is added after 15 min polymerization time. In fact, polymerizations either reached completion in less than 5 minutes or, in case of lower activities, such as with catalyst concentrations below 0.5 mM, did not reach completion at all.

Polymer molecular weight: Resulting polymers showed broad, sometimes bimodal polymer molecular weight distributions with polymer molecular weights much lower than expected even for two chains produced per zirconium center and despite high conversions of >90%. Polymerizations in solvents other than THF or at different lactide:Zr ratios yielded the same results (see supp. inform.). The obtained polymers contained a sizeable fraction of oligomers with polymerization degrees lower than 10. Maldi-MS analysis of the oligomeric fraction showed a series of peaks with m/z ratios of $n \cdot 72+m(Na^+)$ (Fig. 4.9). Combined with the overall to high number of polymer chains per catalyst, this indicates that intramolecular transesterification leads to the formation of cyclic oligomers next to linear polymers.

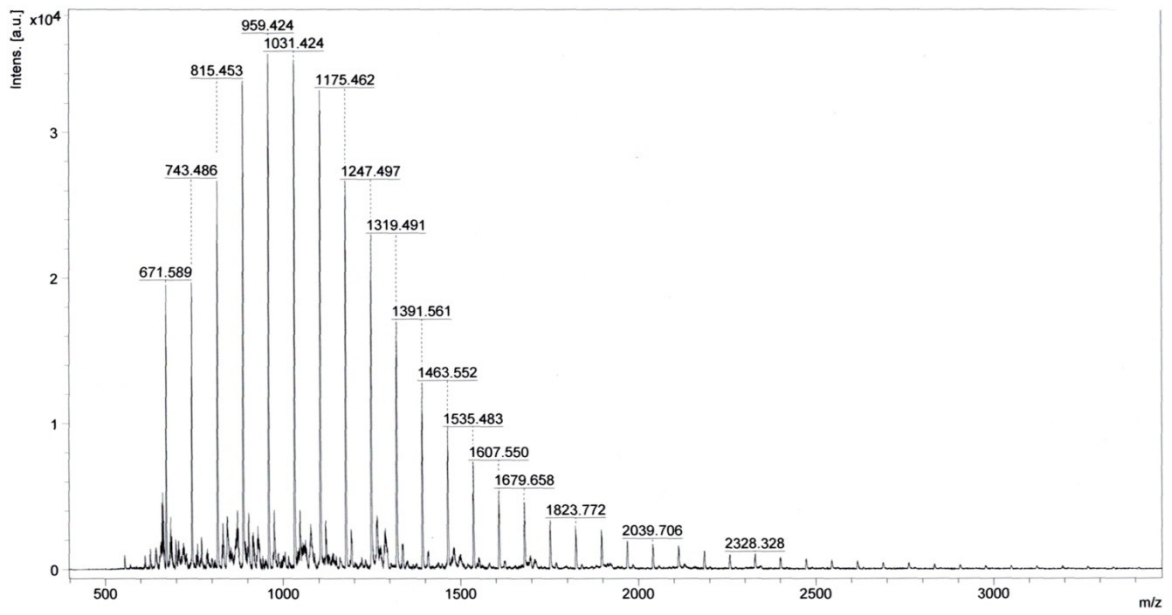


Fig. 4.9. Maldi-mass spectrum of the oligomeric fraction of PLA obtained from **4.5** (2 mM, THF, [lactide]/[**4.5**]=100/1).

Intrigued by the variations of activity on aging of catalyst stock solutions, as well as by the unusually high activity of **4.5** in general, we investigated the effects of potential contaminants on polymerization activity. Due to the possibility of fast alkoxide exchange, the observed polymer molecular weights do not exclude that small quantities of a highly active species are responsible for the observed polymerization activity. Polymerizations using possible contaminants from the catalyst preparation, i. e. free ligand **4.2**H_2, sodium ethoxide, $ZrCl_4(THF)_2$ or combinations thereof, as initiator did not result in any activity of the same order of magnitude as the activity observed for **4.5** (see supp. inform.). Although these polymerizations were not investigated in detail, it should be noted that sodium ethoxide in the presence of free ligand **4.2**H_2 showed surprisingly high activities (94% conversion in 1 h at ambient temperature).

In an alternative approach, we added selected contaminants to *rac*-lactide polymerizations with **4.5** (slow), i. e. stock solutions of **4.5** which showed less than the normally observed activity (approximately 20-35% of the maximum activity observed, c.f. Table S4.3). Surprisingly, addition of protic contaminants, such as water or *para*-toluenesulfonic acid, slightly *increased* the polymerization activity of **4.5** (slow), albeit never surpassing the maximum activity observed for **4.5**. Addition of lactic acid quenched the polymerization (Table S4.3). While the slight rate-enhancing effect of water remains unexplained at the moment, it seems improbable that activation by protic substances is responsible for the high activities observed (see supporting information). Water (or TsOH) might rather be involved in the re-activation of deactivated species, for example after reaction with lactic acid impurities, although no mechanism for this can be proposed at the moment.

4.4 Conclusion

Bridging of two diketiminate ligands by a cyclohexanediyl bridge increased, as intended, the reactivity of bisdiketiminate zirconium complexes, which are now able to undergo ligand exchange and show vastly higher activities in lactide polymerization. The chiral bridge also shows a clear stereochemical impact on the conformation at the metal center. Unfortunately, the steric constraints introduced permit the formation of undesired *trans*-X_2 species and variable temperature NMR spectra showed evidence for a dynamic process, which is most likely a fast isomerisation between *cis*- and *trans*-X_2 complexes. In lactide polymerization, the unprecedented high activity of diethoxy complex **4.5** provides valuable starting points in optimizing group 4-based lactide polymerization catalysts. Its poor

stereoselectivity, its low stability under polymerization conditions, and the formation of notable amounts of cyclic oligomers drastically reduces its value as catalyst for cyclic ester polymerizations, however. We are currently investigating other applications of the chiral $C_6H_{10}(nacnac^{Xyl})_2ZrX_2$ system, in particular hydroamination and carbozirconation reactions.

4.5 Experimental Section

All reactions, except ligand synthesis, were carried out using Schlenk and glove box techniques under nitrogen atmosphere. $ZrCl_4(THF)_2$,[43] $Zr(NMe_2)_4$,[44] and 4-[(2,6-dimethylphenyl)amino]-pent-3-en-2-one[45] were prepared according to literature procedures. $ZrCl_4$, NaOEt, $LiNMe_2$ and other chemicals were purchased from common commercial suppliers. ^1H and ^{13}C NMR spectra were acquired on a Bruker AMX 400 or Bruker AV 400 spectrometer. ^{19}F NMR spectra were acquired on a Bruker AV 400 spectrometer. Chemical shifts were referenced to the residual signals of the deuterated solvents (C_6D_6: ^1H: δ 7.16 ppm, ^{13}C: δ 128.38 ppm; $CDCl_3$: ^1H: δ 7.26 ppm, ^{13}C: δ 77.00 ppm). Solvents were dried by passage through activated aluminum oxide (MBraun SPS) and de-oxygenated by repeated extraction with nitrogen. Polymerization solvents were additionally passed through a column of activated molecular sieves. C_6D_6 was dried over sodium, $CDCl_3$ was dried over CaH_2 and both were distilled under reduced pressure, and then degassed by three freeze-pump-thaw cycles. Racemic lactide was sublimed and recrystallized twice from dry ethyl acetate. Elemental analyses were performed by the Laboratoire d'analyse élémentaire (Université de Montréal).

X-ray diffraction studies. Diffraction data were collected on a Bruker Smart 6000 with Helios MX mirror optics and Cu Kα radiation (rotating anode), using the APEX2 software package.[46] Data reduction was performed with SAINT,[47] absorption corrections with SADABS.[48] Structures were solved with direct methods (SHELXS97).[49] All non-hydrogen atoms were refined anisotropic using full-matrix least-squares on F^2 and hydrogen atoms refined with fixed isotropic U using a riding model (SHELXL97).[49] One ethyl group in **4.5** was disordered and refined anisotropic with refined occupation factors of 0.73 and 0.27. The cyclohexanediamine bridge in **4.6** was found to be disordered and was refined, partially isotropic, with appropriate restraints. For further details, please see Table 4.2 or the supporting information.

Table 4.2 Details of X-ray Diffraction Studies

	4.3	**4.4**	**4.5**	**4.6**
Formula	$C_{36}H_{54}N_6Zr$	$C_{32}H_{42}Cl_2N_4Zr \cdot C_6H_6$	$C_{36}H_{52}N_4O_2Zr$	$C_{34}H_{48}N_4Zr$
M_w (g/mol); $d_{calcd.}$ (g/cm^3)	662.07; 1.27	722.92; 1.33	664.04; 1.27	603.98; 1.26
Crystal size (mm)	0.14x0.14x0.18	0.03x0.03x0.08	0.08x0.08x0.08	0.1x0.1x0.3
T (K); F(000)	200; 1408	150; 756	150; 704	150; 1280
Crystal System	monoclinic	triclinic	triclinic	monoclinic
Space Group	*C*2/c	*P*-1	*P*-1	$P2_1/n$
Unit Cell: a (Å)	18.5065(3)	9.7217(4)	10.9326(11)	11.4759(9)
b (Å)	11.7278(2)	11.9708(5)	11.2187(12)	14.9142(12)
c (Å)	17.2506(4)	16.5433(7)	16.3787(16)	18.6288(14)
α (°)		100.423(2)	82.459(5)	
β (°)	112.842(1)	104.614(2)	71.522(5)	91.042(3)
γ (°)		96.408(2)	65.213(5)	
V (Å^3); Z	3450.5(1); 4	1807.0(1); 2	1729.7(3); 2	3187.9(4); 4
θ range (°); completeness	4.6 – 72.6; 0.99	2.8 – 69.6; 0.97	2.8 – 69.7; 0.98	3.8 – 69.8; 1.00
collected reflections; R_σ	22047; 0.014	25219; 0.060	66389; 0.032	116139; 0.024
unique reflections; R_{int}	3393; 0.031	6640; 0.049	6426; 0.084	5989; 0.083
μ (mm^{-1}); Abs. Corr.	2.85; multi-scan	4.09; multi-scan	2.88; multi-scan	3.02; multi-scan
R1(F); wR(F^2) ($I > 2\sigma(I)$)	0.027; 0.073	0.033; 0.070	0.037; 0.096	0.045; 0.117
R1(F); wR(F^2) (all data)	0.027; 0.073	0.047; 0.073	0.039; 0.102	0.047; 0.118
GoF(F^2)	1.098	0.915	1.107	1.156
Residual electron density	0.36, -0.41	0.58, -0.34	0.97; -0.58	1.39; -0.68

(±)-C_6H_{10}(*nacnac*^{Xyl})$_2H_2$, 4.2H_2. [Me_3O][BF_4] (1.08 g, 7.3 mmol) was added to a yellow dichloromethane solution of 4-[(2,6-dimethylphenyl)amino]-pent-3-en-2-one (1.49 g, 7.3 mmol, 10 mL). The resulting suspension was stirred for approximately 2 h until complete dissolution of [Me_3O][BF_4]. A dichloromethane solution of (±)-*trans*-cyclohexane-1,2-diamine (0.21 g, 1.8 mmol, 1.0 mL) was added, after which stirring was continued for 30 minutes to yield an orange solution. A mixture of (±)-*trans*-cyclohexane-1,2-diamine (0.24 mL, 1.8 mmol) and triethylamine (0.76 mL, 5.4 mmol) was added. After short additional stirring (5 min), the volatiles were removed *in vacuo*. Diethyl ether (100 mL) was added to the residue. The obtained suspension was treated with excess of Et_3N (0.11 mol, 15 mL) and stirred for 5 min. From the yellow phase separated by decantation, solvents were removed *in vacuo* and the residual yellow solid was crystallized from ethanol at -20 ºC to afford 1.35 g (76%) of yellow crystals.

^{1}H NMR ($CDCl_3$, 400 MHz): δ 10.94 (bs, 2H, NH), 7.01 (d, J = 2 Hz , 4H, *meta* Ar), 6.85 (t, J = 2 Hz, 2H, *para* Ar), 4.56 (bs, 2H, CH(C=N)), 3.14 (m, 2H, Cy C*H*), 2.17 (s, 6H, *Me*$_2$Ar), 2.04 (s, 6H, *Me*$_2$Ar), 2.02 (s, 6H, Me(C=N)), 1.95- 1.86 (m, 8H, CH_2), 1.59 (s, 6H, Me(C=N)). ^{13}C{^{1}H} NMR ($CDCl_3$, 101 MHz): δ 165.9 (Me*C*=N), 155.2 (Me*C*=N) , 149.5 (*ipso* Ar), 128.1 (Ar), 127.7 (Ar), 127.6 (Ar), 127.5 (Ar), 121.7 (*para* Ar), 92.6 (*C*H(C=N)), 58.0 (Cy CH), 33.5 (Cy CH_2), 24.7 (Cy CH_2), 21.2 (*Me*C=N), 19.6 (*Me*C=N), 18.5 (*Me*$_2$Ar), 18.2 (*Me*$_2$Ar). ^{1}H NMR (C_6D_6, 400 MHz): δ 11.09 (bs, 2H, NH), 7.10 (d, J = 2 Hz , 4H, *meta* Ar), 6.96 (t, J = 2 Hz, 2H, *para* Ar), 4.61 (bs, 2H, CH(C=N)), 2.90 (m, 2H, Cy C*H*), 2.20 (s, 6H, *Me*$_2$Ar), 2.17 (s, 6H, *Me*$_2$Ar), 1.87 (s, 6H, Me(C=N)), 1.67 (m, 2H, Cy C*H*$_2$), 1.58 (s, 6H, Me(C=N)) 1.3- 0.80 (m, 6H, Cy C*H*$_2$). ^{13}C{^{1}H} NMR (C_6D_6, 101

MHz): δ166.2 (Me*C*=N), 155.2 (Me*C*=N), 150.3 (*ipso* Ar), 128.3 (Ar), 128.2 (Ar), 128.1 (Ar), 127.9 (Ar), 122.5 (*para* Ar), 93.6 (*C*H(C=N)), 58.2 (Cy CH), 33.6 (Cy CH_2), 24.6 (Cy CH_2), 21.3 (*Me*C=N), 19.7 (*Me*C=N), 18.8 (*Me*$_2$Ar), 18.7 (*Me*$_2$Ar). Anal. Calcd. for: $C_{13}H_{26}N_2$: C, 79.29; H, 9.15; N, 11.56; Found C, 79.05; H, 9.18; N, 11.56;

(±)-C_6H_{10}(*nacnac*^{Xyl}Li(THF))$_2$·0.5 THF, 4.2Li$_2$(THF)$_2$·0.5 THF. To a yellow THF solution of Ligand **4.1a** (0.3 g, 0.63 mmol), *n*BuLi (2.9 M, 0.43 mL, 0. 13 mmol) was added gradually at room temperature. The obtained orange solution was stirred for 5 min. All volatiles were removed *in vacuo* to give orange oil. Addition of hexanes (5 mL) gave an off-white precipitate, which was isolated by decantation and dried under vacuum to yield an off-white powder (0.32 g, 80%).

^{1}H NMR (C_6D_6, 400 MHz): δ7.10 (d, *J* = 2 Hz, 2H, *meta* Ar), 7.03 (d, *J* = 2 Hz, 2H, *meta* Ar), 6.90 (t, *J* = 2 Hz, 2H, *para* Ar), 4.67 (bs, 2H, CH(C=N)), 3.40 (m, 10H, THF), 3.29 (m, 2H, Cy CH), 2.32 (s, 6H, *Me*$_2$Ar), 2.17 (s, 6H, *Me*$_2$Ar), 2.12 (m, 2H, Cy CH_2), 1.99 (s, 6H, Me(C=N)), 1.78 (s, 6H, Me(C=N)), 1.40 – 1.32 (m, 6H, Cy CH_2), 1.14 (m, 10H, THF). ^{13}C{^{1}H} NMR (C_6D_6, 101 MHz): δ164.5 (Me*C*=N), 161.8 (Me*C*=N) , 153.6 (*ipso* Ar), 131.2 (*ortho* Ar), 130.7 (*ortho* Ar), 128.13 (*meta* Ar), 127.8 (*meta* Ar), 121.4 (*para* Ar), 93.5 (CH(*C*=N)), 68.3 (THF), 65.9 (Cy CH), 35.9, 19.6 (Cy CH_2), 26.5, 23.0 (*Me*C=N), 25.2 (THF), 19.6 (*Me*$_2$Ar), 19.0 (*Me*$_2$Ar). Anal. Calcd for $C_{40}H_{58}Li_2N_4O_2$·0.5 C_4H_8O; C, 74.53; H, 9.23; N, 8.28; Found C, 74.14; H, 9.22; N, 8.68. (NMR shows presence of 2.5 THF).

(±)-C_6H_{10}(*nacnac*^{Xyl})$_2$Zr(NMe$_2$)$_2$, 4.3. Zr(NMe$_2$)$_4$ (0.14 g, 0.53 mmol) and ligand **4.2**H_2 (0.25 g, 0.53 mmol) were mixed and heated, in absence of solvent, to 120 ºC under N_2

atmosphere for 1 h. The obtained brown oil was dissolved in toluene (1 mL) and crystallized by slow evaporation at room temperature (0.25 g, 71%).

^{1}H NMR (C_6D_6, 400 MHz): δ 7.10 (d, J = 2 Hz, 2H, *meta* Ar), 7.00 (d, J = 2 Hz, 2H, *meta* Ar), 6.93 (t, J = 2 Hz, 2H, *p*-Ar), 5.04 (bs, 2H, CH(C=N)), 3.79 (m, 2H, Cy CH), 2.80 (s, 6H, NMe_2), 2.50 (s, 6H, Me_2Ar), 2.13 (m, 2H, Cy CH_2), 2.09 (s, 6H, Me_2Ar), 1.90 (s, 6H, Me(C=N)), 1.77 (s, 6H, NMe_2), 1.58 (s, 2H, Cy CH_2), 1.56 (s, 6H, Me(C=N)), 1.29 – 1.25 (m, 4H, Cy CH_2). ^{13}C {^{1}H} NMR (C_6D_6, 101 MHz): δ 166.1 (Me(*C*=N)), 163.0 (Me(*C*=N)), 153.7 (*ipso* Ar), 132.1 (*ortho* Ar), 131.9 (*ortho* Ar), 128.7 (*meta* Ar), 127.7 (*meta* Ar) , 123.7 (*para* Ar), 105.7 (*C*H(C=N)), 70.2 (Cy CH), 43.2 (Cy CH_2), 41.5 (Cy CH_2), 35.3 (NMe_2), 25.7 (NMe_2), 24.8 (*Me*(C=N)), 22.6 (*Me*(C=N)), 21.3 (Me_2Ar), 18.9 (Me_2Ar). Anal. Calcd for $C_{36}H_{54}N_6Zr$: C, 65.31; H, 8.22; N, 12.69; Found C, 64.68; H, 8.86; N, 12.42

(±)-C_6H_{10}(*nacnac*^{Xyl})$_2$$ZrCl_2$, 4.4. A suspension of $ZrCl_4(THF)_2$ (0.50 g , 1.34 mmol) in toluene (10 mL) was added drop by drop to a of **4.2**$Li_2(THF)_2$·0.5 THF (0.86 g, 1.34 mmol) in toluene (10 mL) while stirring. After 10 min at room temperature, the yellow suspension obtained was filtered and the remaining residue extracted with toluene (5 mL). The toluene solution was evaporated to dryness yielding a yellow powder (0.69 g, 80%). Crystals suitable for elemental analysis and X-ray structure determination were obtained by slow evaporation of C_6D_6.

^{1}H NMR ($CDCl_3$, 400 MHz): δ 6.94-6.85 (m, 6H, Ar), 5.45 (bs, 2H, CH(C=N)), 4.19 (m, 2H, Cy CH), 2.18(s, 6H Me(C=N)), 2.14 (s, 6H, Me_2Ar), 2.11 (m, 2H, Cy CH_2), 2.06 (s, 6H, Me_2Ar), 1.87-1.72 (m, 4H, Cy CH_2), 1.64 (s, 6H, Me(C=N)), 1.41 (m, 2H, Cy CH_2).

^{1}H NMR (C_6D_6, 400 MHz): δ 6.95-6.84 (m, 6H, Ar), 5.39 (bs, 2H, CH(C=N)), 4.19 (m, 2H, Cy CH), 2.37 (s, 6H, *Me*$_2$Ar), 2.29 (s, 6H, *Me*$_2$Ar), 1.86 (m, 2H, Cy CH_2), 1.83 (s, 6H, Me(C=N)), 1.56 (s, 6H, Me(C=N)), 1.53 - 1.46 (m, 4H, Cy CH_2), 1.03 (m, 2H, Cy CH_2). ^{13}C{^{1}H} NMR (C_6D_6, 101 MHz): δ166.2 (Me*C*=N), 161.2 (Me*C*=N), 133.1 (*ortho* Ar), 132.6 (*ortho* Ar), 128.5 (*ipso* Ar), 128.4 (*meta* Ar), 128.3 (*meta* Ar), 125.1 (*para* Ar), 105.7 (*C*H(C=N)), 69.0 (Cy CH), 32.6 (Cy CH_2), 25.3 (*Me*C=N), 23.3 (*Me*C=N), 22.5 (*Me*$_2$Ar), 19.6 (*Me*$_2$Ar), 19.53 (Cy CH_2). Anal. Calcd for $C_{32}H_{42}N_4ZrCl_2 \cdot C_6D_6$: C, 62.61; H, 6.64; N, 7.69; Found C, 62.79; H, 6.94; N, 7.57 (X-ray structure shows presence of one C_6D_6).

(±)-C_6H_{10}(*nacnac*^{Xyl})$_2$Zr(OEt)$_2$, 4.5. Method A: A yellow solution of **4.4** (0.32 g, 0.50 mmol) in toluene (10 mL) was added drop by drop to a suspension of NaOEt (0.86 g, 1.34 mmol) in toluene (5 mL). The obtained red suspension was refluxed for 3 days. The suspension was filtered while hot and the obtained filtrate was evaporated to dryness to yield a red oil (0.30 g, 91%, 90% purity determined by NMR). Addition of hexane (2 mL) gave a red solution which yielded orange crystals separated upon standing (200 mg, 60%).

Method B: To a suspension of $ZrCl_4(THF)_2$ (222 mg, 0.59 mmol) in toluene (5 mL) was added a suspension of NaOEt (80 mg, 1.2 mmol) in toluene (20 mL). The suspension was heated for 3 h at 80°C. The resulting mixture was added to a solution of **4.2**Li_2THF_2 (400 mg; 0.59 mmol) in toluene (10 mL). The orange suspension was heated overnight at 80 °C, then filtered. Recrystallisation of the residue yielded **4.5** as orange crystals (55%).

^{1}H NMR (C_6D_6, 400 MHz): δ 7.06 (d, J = 8 Hz, 2H, *meta* Ar), 7.04 (d, J = 8 Hz, 2H, *meta* Ar), 6.93 (t, J = 8 Hz, 2H, *para* Ar), 5.10 (bs, 2H, CH(C=N)), 3.75 (m, 2H, Cy C*H*), 3.20 (m, 4H, OCH_2), 2.37 (s, 6H, *Me*$_2$Ar), 2.20 (s, 6H, *Me*$_2$Ar), 2.07 (m, 2H, Cy CH_2),

1.96 (s, 6H, Me(C=N)), 1.55 - 1.48 (m, 8H, Cy CH & Me(C=N)), 1.30 (m, 4H, Cy CH_2), 0.77 (t, *J*=7 Hz, 6H, OCH_2*Me*). ^{13}C {^1H} NMR (C_6D_6, 101 MHz): δ163.8 (Me*C*=N), 162.8 (Me*C*=N), 152.8 (*ipso* Ar), 132.6 (*ortho* Ar), 130.9 (*ortho* Ar), 128.6 (*meta* Ar), 127.9 (*meta* Ar), 123.9 (*para* Ar), 104.1 (*C*H(C=N)), 68.8 (Cy CH), 63.8 (O*C*H_2Me), 34.8 (Cy CH_2), 25.8 (OCH_2*Me*) 22.7 (*Me*$_2$Ar), 22.3 (Cy CH_2), 19.7 (*Me*$_2$Ar), 19.2 (*Me*(C=N)), 19.0 (*Me*(C=N)). Anal. Calcd for $C_{36}H_{52}N_4O_2Zr$· C, 65.11; H, 7.89; N, 8.44; Found C, 64.92; H, 8.04; N, 8.14.

(±)-C_6H_{10}(*nacnac*^{Xyl})$_2$$ZrMe_2$·0.5 toluene, 4.6. A mixture of MeLi (10 mg, 0.45 mmol) in toluene (2 mL) and $AlMe_3$ in hexane (0.20 M, 0.12 mL, 0.024 mmol) was gradually added at -78 ºC to a solution of **4.4** (150 mg, 0.23 mmol) in toluene (10 mL) and stirred for 5 min. The cold bath was removed and stirring was completed for another 5 min. The obtained yellow suspension was filtered cold and the remaining residue was extracted with toluene (5 mL). The combined toluene filtrates were concentrated to 2 mL. Slow diffusion of hexane into toluene solution of **4.6** at -35 ºC gave yellow crystals (50 mg, 36%). ^1H NMR of the obtained crystals showed presence of 0.5 equiv of toluene.

^1H NMR (C_6D_6, 400 MHz): δ7.10 - 6.93 (m, 6H, Ar), 5.27 (bs, 2H, CH(C=N)), 3.69 (m, 2H, Cy CH), 2.34 (s, 6H, *Me*$_2$Ar), 2.29 (s, 6H, *Me*$_2$Ar), 2.07-1.93 (m, 4H, Cy CH_2), 1.86 (s, 6H, Me(C=N)), 1.66 (s, 6H, Me(C=N)), 1.50 (m, 2H, Cy CH_2), 1.04 (m, 2H, Cy CH_2), -0.06 (s, 6H, ZrMe).^{13}C NMR (C_6D_6, 101 MHz): δ164.0, 156.2 (Me(*C*=N)), 153.1 (*ipso* Ar), 132.2 (*ortho* Ar), 131.7 (*ortho* Ar), 129.6 (*meta* Ar), 128.8 (*meta* Ar), 124.7 (*para* Ar), 103.8 (*C*H(C=N)), 67.4 (Cy CH), 57.7 , 33.9 (Cy CH_2), 26.0 (*Me*$_2$Ar), 23.9 (*Me*$_2$Ar), 22.7

(*Me*(C=N)), 19.9 (*Me*(C=N)), 19.8 (ZrMe). Anal. Calcd. for $C_{34}H_{48}N_4Zr \cdot \frac{1}{2}C_7H_8$. C, 69.29; H, 8.06; N, 8.62; Found C, 68.87; H, 8.22; N, 8.26.

***rac*-Lactide polymerization.** In a well closed vial, a toluene solution of **4.5** (200 μl, 10 mM, 2.0 mmol) was added to a THF solution of *rac*-lactide (87 mg, 0.60 mmol, 0.8 ml). Reaction mixtures were quenched at the desired polymerization time by addition of a dichloromethane solution of acetic acid (5 mM). Samples for kinetic investigations were taken at the desired intervals and added to vials already containing a dichloromethane solution of acetic acid (5 mM). In both cases, volatiles were immediately evaporated afterwards. Solid polymer samples were stored at -80 °C. Conversion was determined from ^{1}H NMR in $CDCl_3$ by comparison to remaining lactide. P_r values were determined from homodecoupled 1H NMR spectra. Molecular weight analyses were performed on a Waters 1525 gel permeation chromatograph equipped with three Phenomenex columns and a refractive index detector at 35 °C. THF was used as the eluent at a flow rate of 1.0 mL·min^{-1} and polystyrene standards (Sigma–Aldrich, 1.5 mg·mL^{-1}, prepared and filtered (0.2 mm) directly prior to injection) were used for calibration. Obtained molecular weights were corrected by a Mark-Houwink factor of 0.58.[50] Mass spectroscopic analyses were performed on a MALDI TOF/TOF Ultraflextreme mass spectrometer equipped with SmartBeam II Nd:YAG/355 nm laser operating at 1 kHz and providing a laser focus down to 20 μm in diameter for the "minimum" focus setting (Bruker Daltonics, Billerica, MA). The matrix used contained 10 mg/ml of 2, 5-dihydroxybenzoic acid (DHB) in MeOH: deionised water (1:1).

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Supporting Information. Tables S4.1-4.6, investigations regarding variations in catalyst activity, variable temperature NMR data, details of polymerization experiments, Crystallographic Information Files (CIF).

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Supporting information

Exceptionally high lactide polymerization activity of zirconium complexes with bridged diketiminate ligands

Ibrahim El-Zoghbi, Todd J. J. Whitehorne and Frank Schaper

Table S4.1. Polymerization in different solvents

Solvent	[lactide]/ [4.5]	Conversion , 1 min (%)	Conversion (%)	Time (min)	P_r	GPC appearance	M_n (g/mol)	expected M_n (g/mol)
DCM	300		44	18				
DCM	300	37	44	30	0.56			
DCM	300		38	22	0.61	broad	3900	8200
DCM	100	60	82	30	0.64	broad	2700	5900
Ether	100	34	90	30	0.54	broad	2100	6500
Toluene	300	54	69	30	0.54	broad	10 000	14 900
Toluene	100	79	96	30	0.62	broad	2300	6900
Toluene	100		80	1.5				
Toluene	100		82	1.5				
Toluene	100		55	0.5	0.60			
THF	300	82	91	30	0.60	bimodal	6400, 500	19 700
THF	300	86	86	1	0.59	bimodal	7500, 500	18 600
THF	100	92	91	30	0.64	broad	600	6600

Conditions: ambient temperature, [**4.5**] = 2 mM. P_r is the probability of obtaining an *r*-dyad by insertion, determined from homodecoupled proton NMR. Polymerizations in toluene and ether were suspensions at least part of the time.

Table S4.2. Polymerization kinetics at different concentrations of **4.5**

[4.5] (mM)	k_{obs} (s^{-1})	Final conversion (%)	Expected M_n (g/mol)	M_n (g/mol)	GPC appearance
0.5	0.008(4)	87	18 800	6 400	bimodal
0.5	0.008(2)	88			
1	0.015(5)	91			
1	0.017(6)	94			
2	0.030(5)	94			
2	0.025(6)	91	19 700	8 400	bimodal
2	0.029(9)	95			

Conditions : THF, ambient temperature, Lactide:Zr = 300:1.

Comments on variations in catalyst activity

The sensitivity of the catalyst also affected the kinetic analyses. While reproducible results have been obtained in experiments conducted with the same batch of catalyst stock solution in a limited time (such as those discussed above), use of different catalyst stock solutions or aging of said solutions might lead to variations in the observed polymerization activities. For most catalyst stock solutions (and for all which showed the maximum activity reported above), activities declined notably on aging over several weeks, trivially explained by catalyst decomposition. Curiously however, some catalyst stock solutions which already showed less than the maximum activity directly after preparation, showed over two to three weeks first increasing, then decreasing activities, without ever reaching the activity reported in the manuscript.

In an alternative approach, we added selected contaminants to *rac*-lactide polymerizations with **4.5**(slow), i. e. stock solutions of **4.5** which showed less than the normally observed activity (approximately 20-35% of the maximum activity observed, c.f. Table S4.3). Addition of 1 equiv of *para*-toluenesulfonic acid slightly increased polymerization activity (Table S4.3). Analogously, addition of water slightly *increased* the polymerization activity of **4.5**(slow), albeit never surpassing the maximum activity observed for **4.5** (Table S4.3).

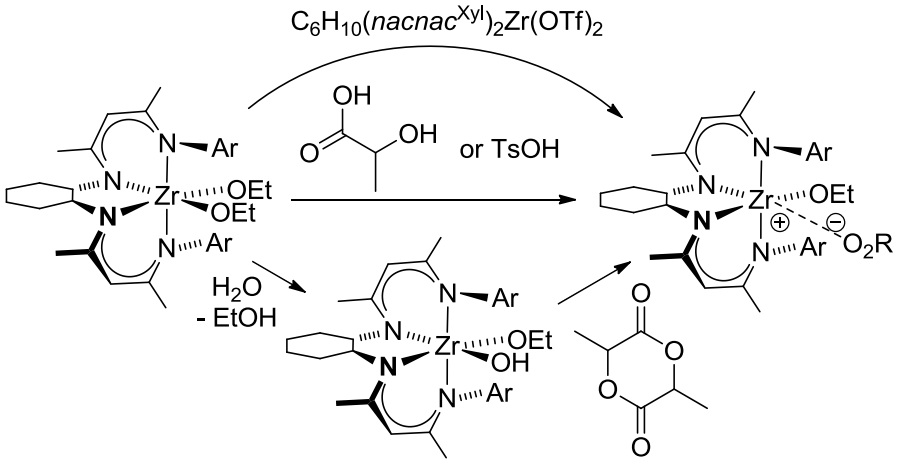
Table S4.3 Effects of contaminants upon polymerization activity using batches of **4.5**(slow), i. e. catalyst stock solutions showing less than the normally observed activity (k_{obs}(2 mM) = 0.03 s^{-1}).

	Equiv. added	Conversion after 1 min	GPC appearance	M_n [g/mol]	Expected M_n [g/mol] [a]
4.5 [b]		77–92%	bimodal	7500, 600 [c]	20 300 [c]
4.5(slow) [c]		25%	bimodal	9600, 900	9900 [c]
4.5(slow)		26%	broad	800	2000
4.5(slow)/TsOH	1	55%	broad	700	5000
4.5(slow)/water	0.5	72%	bimodal	9000, 800	5800
4.5(slow)/water	1	64%	broad	900	5300
4.5(slow)/water	2 or 3	0%			
4.5(slow)/lactic acid	1	0%			
4.5(slow)/(**4.2**)Zr(OTf)$_2$	1	0%			
4.5(slow) [d]		13%			
4.5(slow)/TsOH [d]	1	29%			
4.5(slow)/water [d]	1	46%			
4.5(slow)/(**4.2**)Zr(OTf)$_2$ [d]	1	0%			

Conditions: lactide: **4.5** = 100:1 (unless otherwise stated), THF, [**4.5**] = 2 mM, ambient temperature. [a] assuming two polymer chains per Zr. [b] For comparison: polymerizations using several stock solutions showing maximum activity. [c] lactide: **4.5** = 300:1. [d] different catalyst batch and stock solution.

Not surprisingly, reactions of **4.5** with water in the absence of lactide yielded only the free ligand **4.2**H_2, but in the presence of monomer and given the observed increase in activity, the role of water is less clear. The high activity observed at a H_2O:Zr ratio of 1:1, followed by its drop to zero at H_2O:Zr at ratios above 1:1 (Table S4.3), excludes the formation of oxo-bridged zirconium complexes as active species. Alternatively, a [Zr]OH species, formed initially by protonation of an ethoxide ligand, might react with lactide to form an ion pair [C_6H_{10}(*nacnac*^{Xyl})$_2$ZrOEt][bislactate] (Scheme S4.1). Thus slow reaction of

[Zr]OH with lactide would generate a cationic species, while polymerization is still initiated at Zr[OEt]. A similar species would have been obtained in the presence of one equiv *para*-toluenesulfonic acid, even though we were not able to obtain this complex synthetically (*vide supra*). However, in contradiction to this mechanistic proposal, addition of either one equiv. of lactic acid or one equiv. of a bis(triflate) complex bearing the same ligand, (**4.2**)$Zr(OTf)_2$, which both should yield comparable active species (Scheme S4.1), completely quenched activity (Table S4.3). Also, NMR analysis of catalyst stock solutions yielding the most active polymerizations displayed after evaporation and redissolution only resonances of **4.5** (>90%) and free ligand **4.2**H_2 (<10%).



Scheme S4.1

Alternatively, polymerization might not occur at an octahedral zirconium complex, but rather via the four-coordinated intermediate proposed by Dong *et al.* (Scheme 4.6), which would be in agreement with the exceptionally high activities observed. Partial dissociation of the ligand might be favoured by (partial) protonation of the ligand by water or acids. To test this hypothesis, we undertook polymerizations with in *in-situ* mixtures of **4.2**H_2,

$ZrCl_4(THF)_2$, and 2 equiv of NaOEt. However, no polymerization activity was observed. Given that the slight rate-enhancing effect of water was only observed for stock solutions not showing the highest activity and that the activity increase was relatively minor (2-3 fold), it seems improbable that activation by protic substances in general is responsible for the high activities observed.

Table S4.4. Effect of the [lactide]:[**4.5**] ratio and of catalyst source on polymer molecular weight distribution.

Catalyst batch	**[Lactide]: [4.5]**	**Conversion (%)**	**Time (min)**	**GPC appearance**	M_n **(g/mol)**	**Expected** M_n **(g/mol)**	M_w/M_n
#1	300	≈90	7	bimodal	8300, 300	19 400	2.2
#1	100	≈90	7	broad	700	6 400	2.4
#1	50	≈90	7	broad	500	3 300	1.5
#2	300	90	32	broad	1 600	19 400	3.1
#2	100	89	17	broad	1 500	6 400	3.0
#2	100	90	34	broad	1 600	6 500	3.1
#2	50	91	17	broad	300	3 300	2.4

Conditions: ambient temperature, [**4.5**] = 2 mM, THF, polymerization times not optimized.

Table S4.5. Polymerizations using possible contaminants from catalyst preparation

[$ZrCl_4(THF)_2$]	[NaOEt]	[**4.2**H_2]	[Lactide]	Conversion (%)	Time (min)	GPC appearance	M_n (g/mol)	Expected M_n (g/mol)
2 mM	6 mM		0.6 M	13	120	broad	600	2 800
	4 mM		0.2 M	94	170	broad	2 200	6 800
	8 mM		0.2 M	92	170	bimodal	3600, 300	6 600
	4 mM	2 mM	0.2 M	89	120			
	8 mM	2 mM	0.2 M	94	60			

Conditions: ambient temperature, THF.

Table S4.6. Polymerizations with catalyst stock solutions showing less than the normally observed activity (k_{obs}(2 mM) = 0.03 s^{-1}).

Catalyst batch	Equiv. contaminant	[Lact]/ [**4.5**]	Conversion, 1 min (%)	k (s^{-1})	Final conversion	Time (min)	GPC remark	M_n (g/mol)	Expected M_n (g/mol)
#1	-	300	33	0.007	46	120	bimodal	9600, 900	9900
#1	-	100	26	0.005	28	120	broad	800	2000
#1	1 TsOH	100	55	0.013	70	50	broad	700	5000
#1	0.5 water	100	72	0.021	81	90	bimodal	9000, 800	5800
#1	1 water	100	64	0.017	73	180	broad	900	5300
#1	2 or 3 water	100	0		0	120			
#1	1 lactic acid	100	0		0	120			
#1	1(**4.2**)$Zr(OTf)_2$	100	0		0	120			
#2	-	100	13	0.002	83	120			
#2	1 TsOH	100	29	0.006	78	47			
#2	1 water	100	46	0.010	83	47			
#2	1 (**4.2**)$Zr(OTf)_2$	100	0		12	47			

Conditions: ambient temperature, THF, [**4.5**] = 2 mM, rate constants estimated from 1 min conversion.

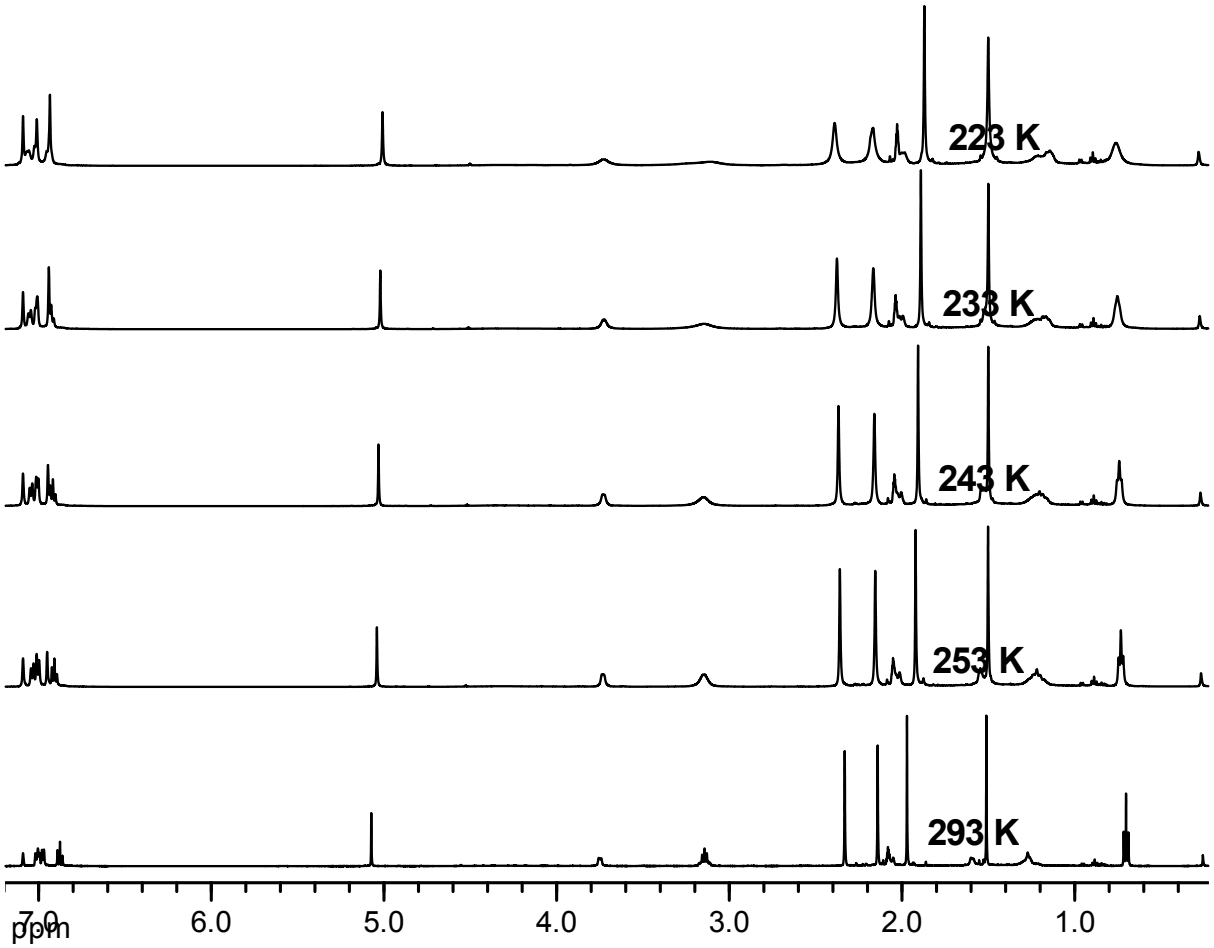


Figure S4.1. Low temperature spectra of **4.5**, full spectra.

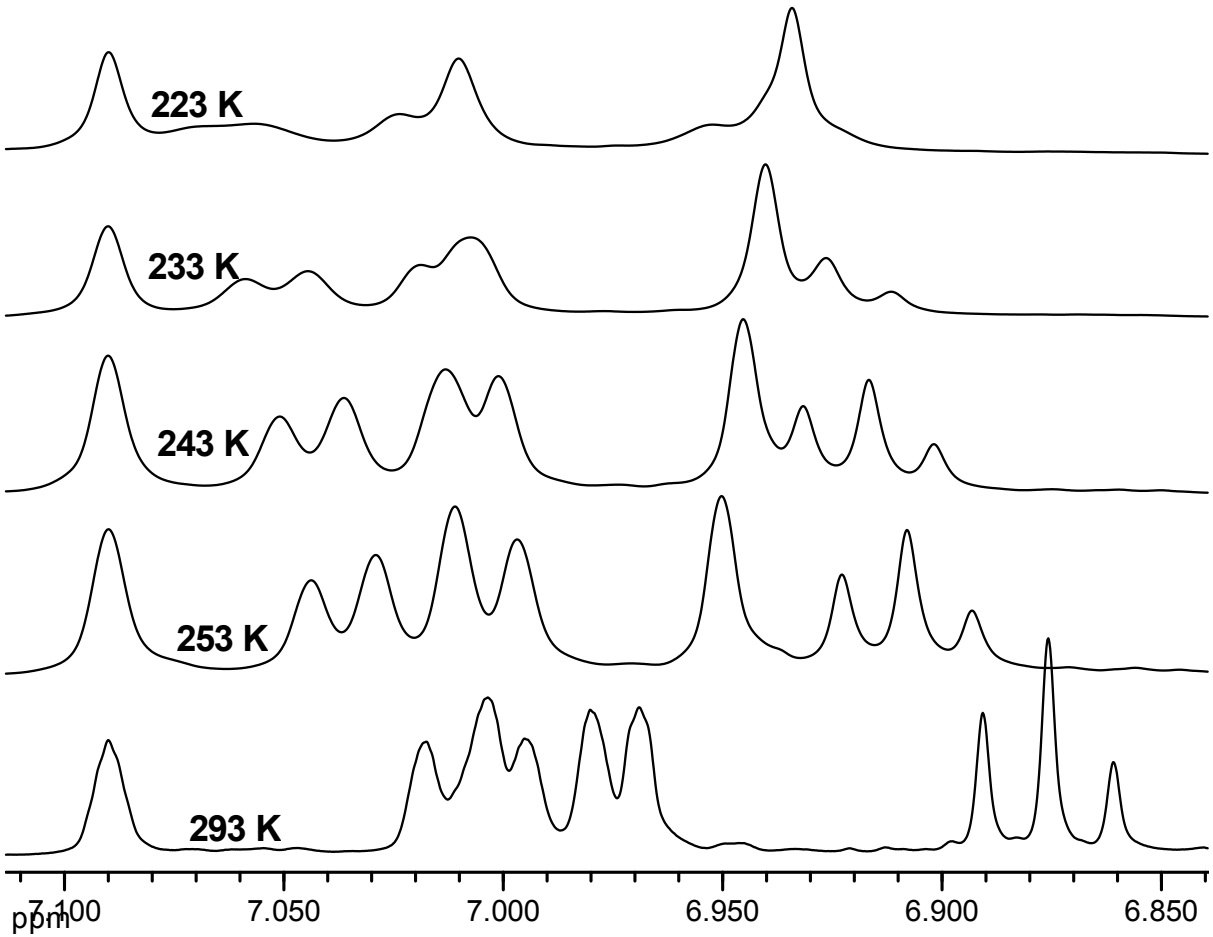


Figure S4.2. Low temperature spectra of **4.5**, aromatic region.

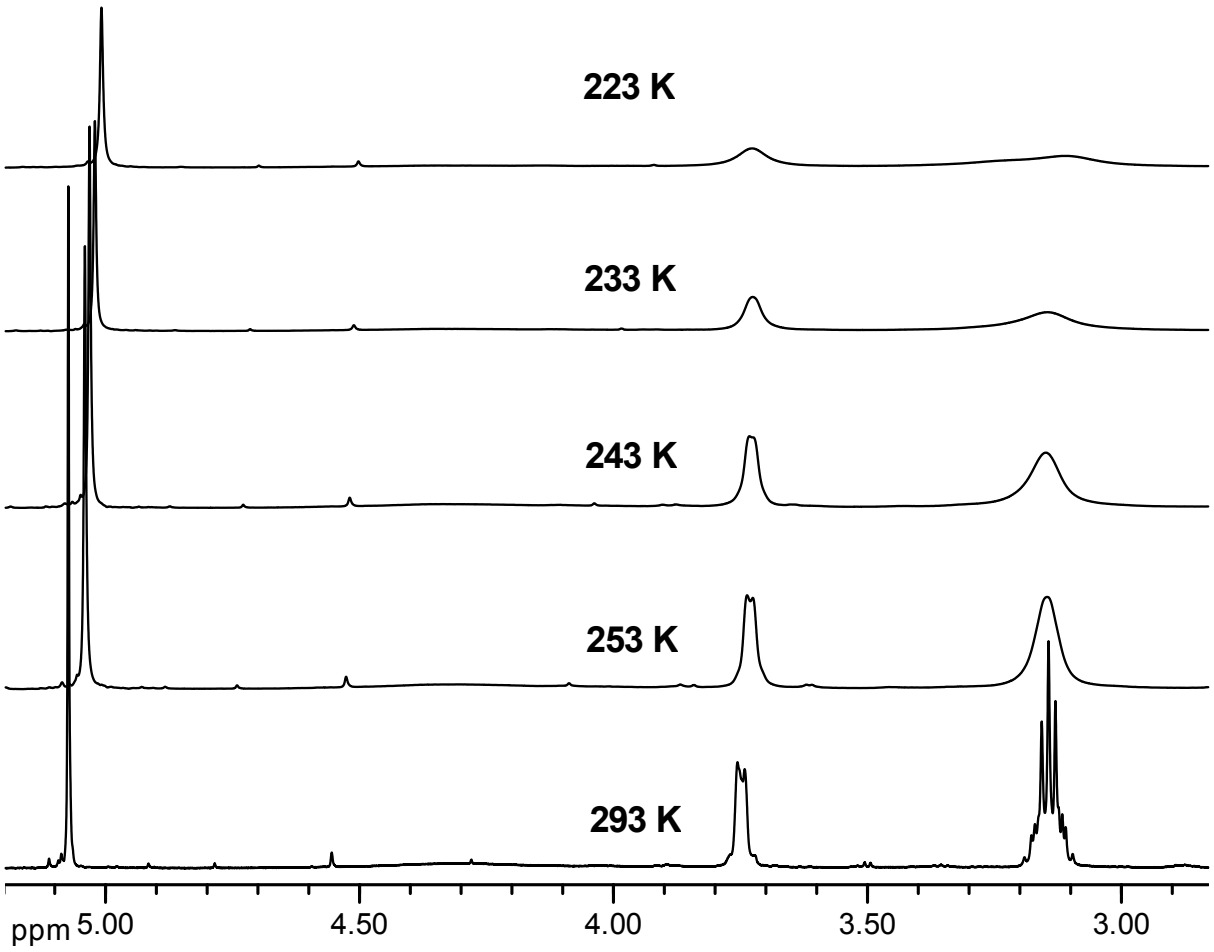


Figure S4.3. Low temperature spectra of **4.5**, CH, Cyc C(H)N, OCH_2.

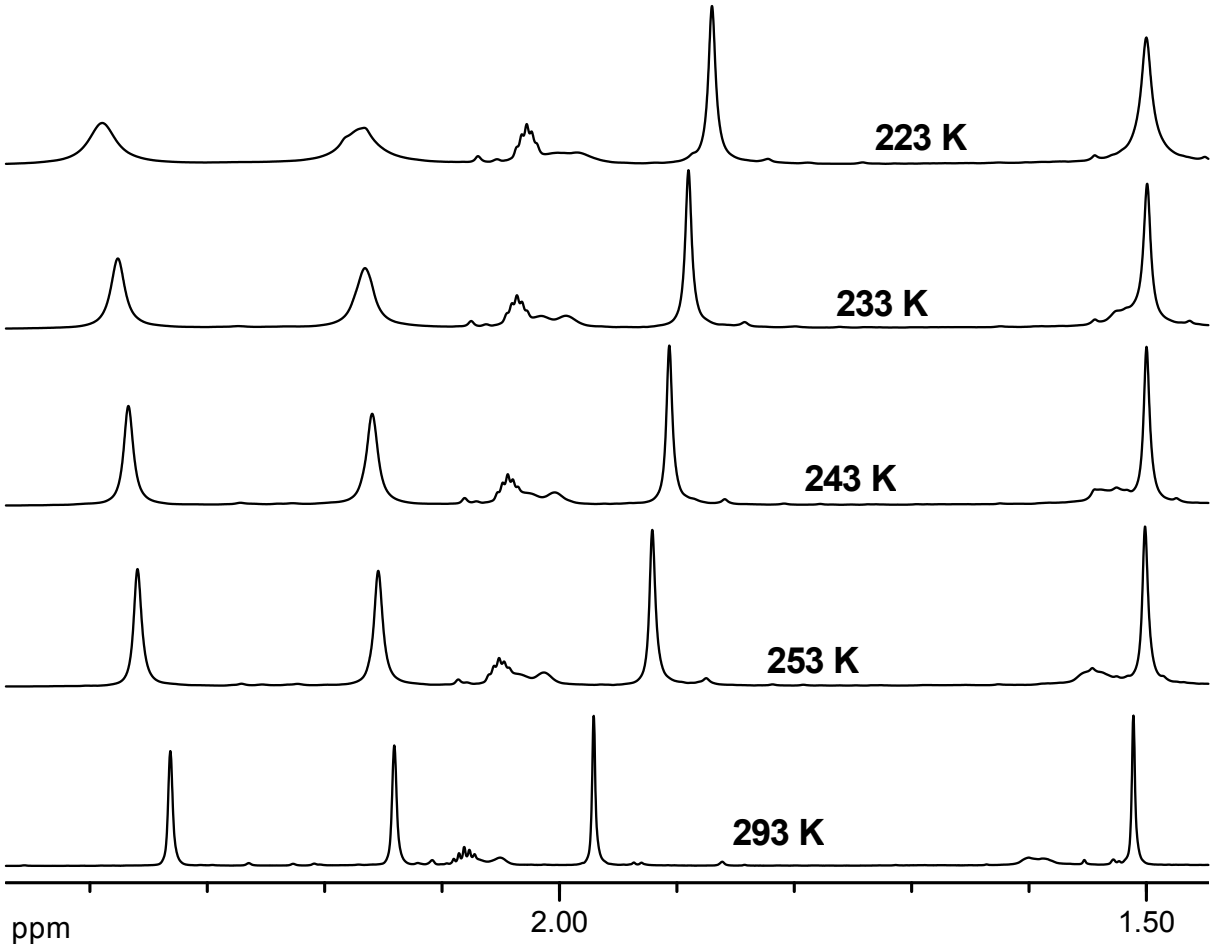


Figure S4.4. Low temperature spectra of **4.5**, aliphatic region.

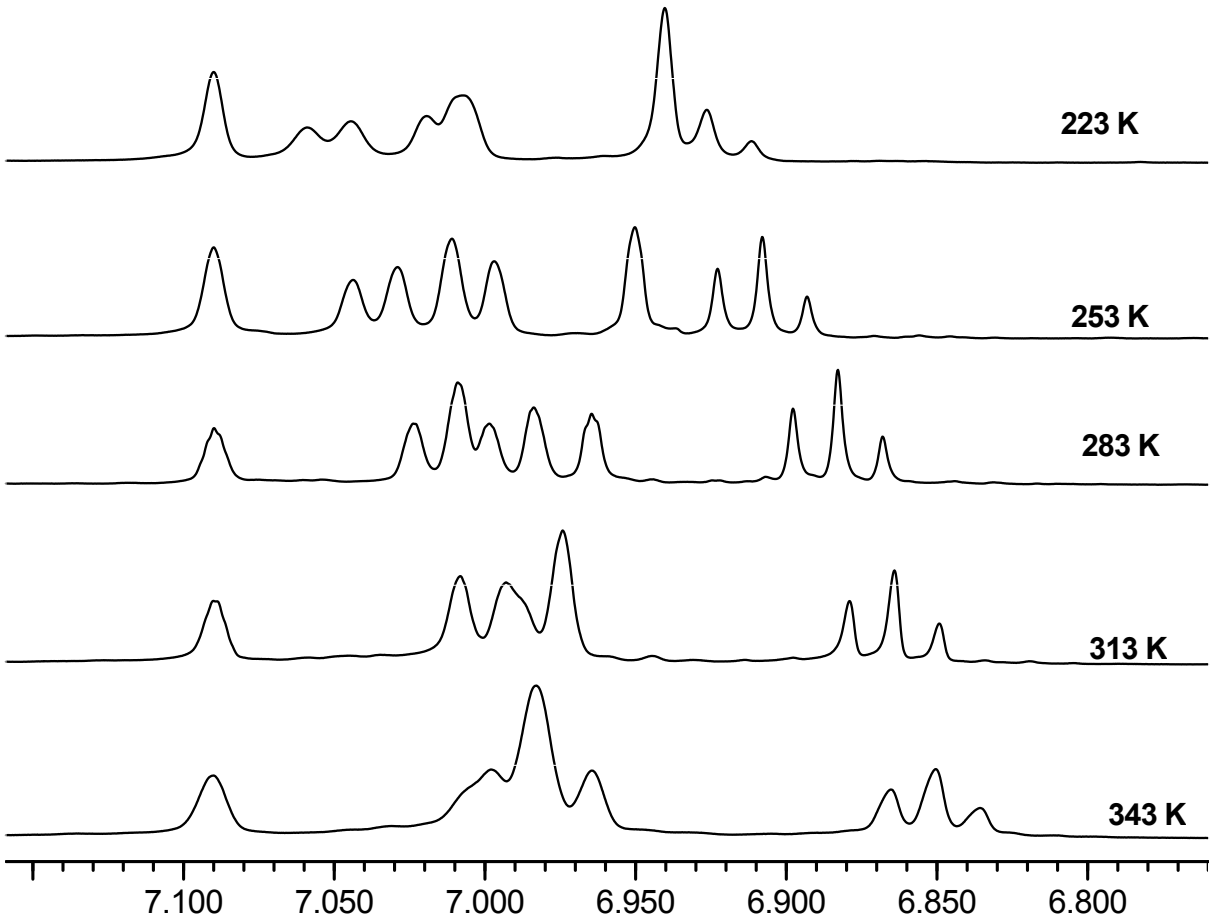


Figure S4.5. VT NMR spectra of **4.5**. Aromatic region.

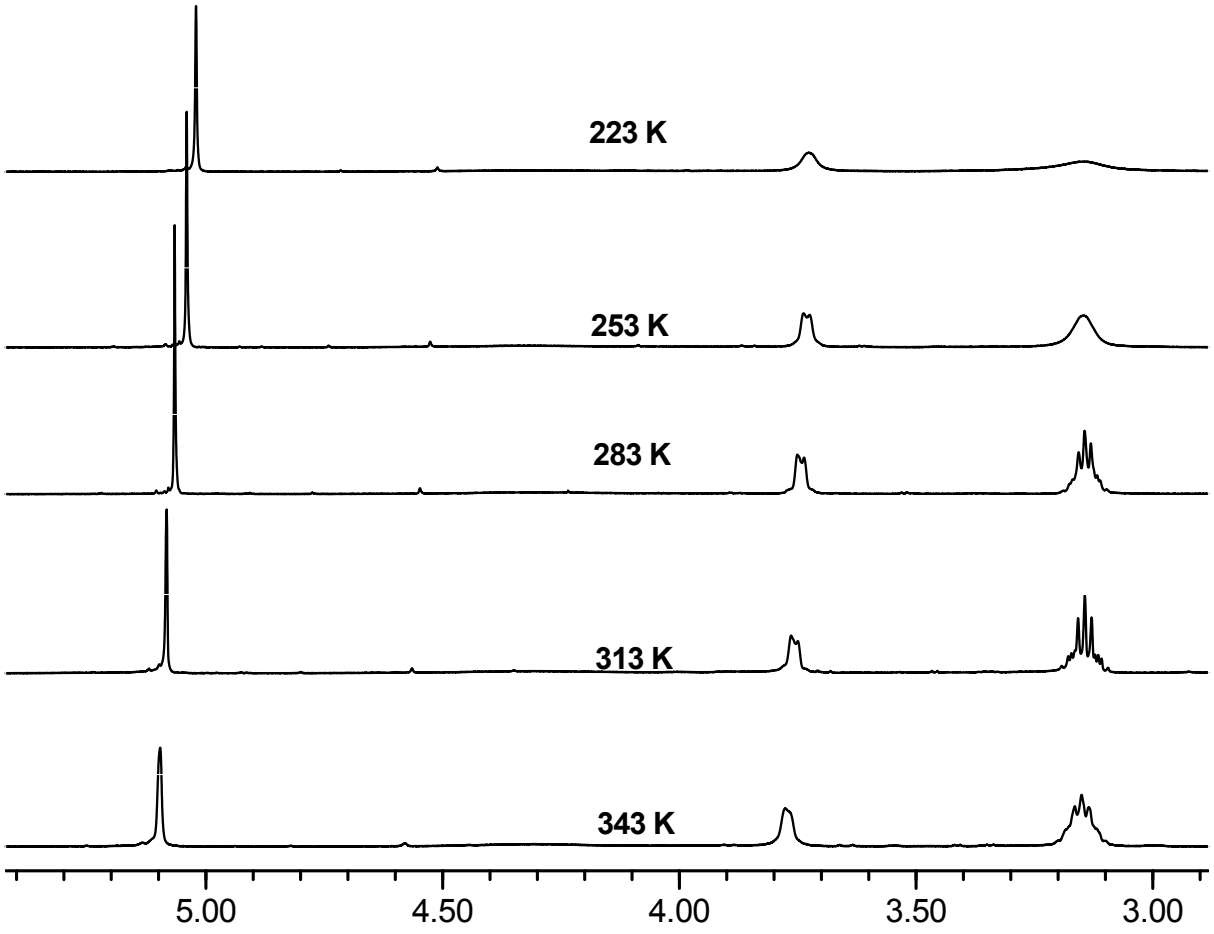


Figure S4.6. VT NMR spectra of **4.5**, CH, Cyc C(H)N, OCH_2.

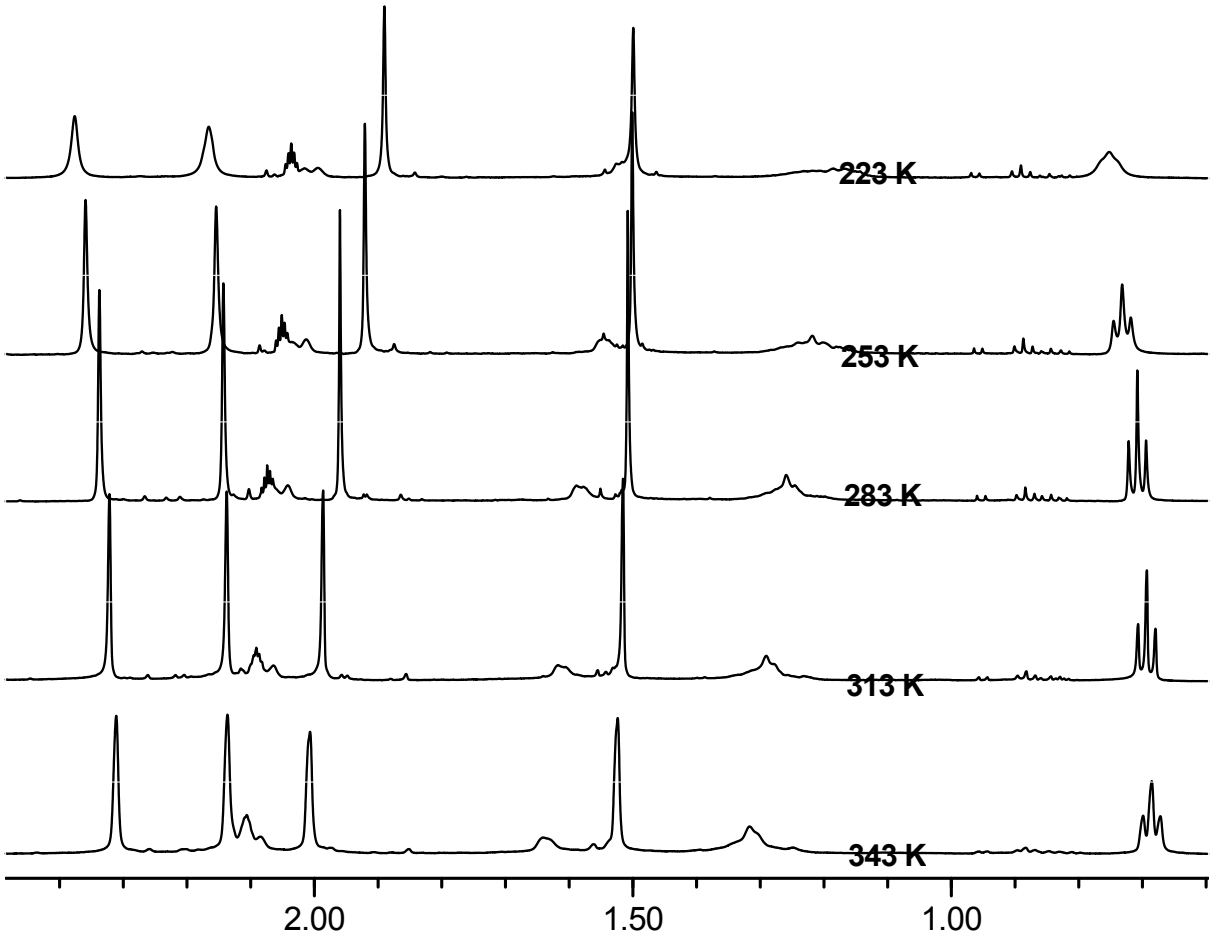


Figure S4.7. VT NMR spectra of **4.5**, aliphatic region.

CHAPTER 5

Selective and Non-selective Aza-Michael Additions Catalyzed by a Chiral Zirconium Bisdiketiminate Complex

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Ibrahim El-Zoghbi, Todd J. J. Whitehorne and Frank Schaper

Département de chimie, Université de Montréal, Montréal, Québec, H3C 3J7, Canada.

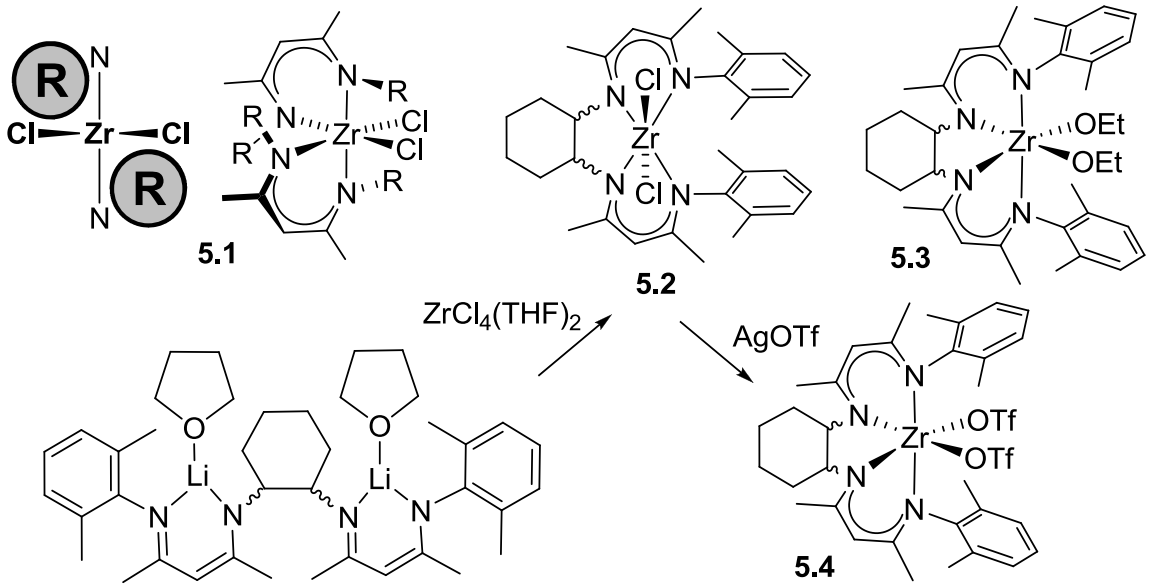
5.1 Abstract

Reaction of the chiral bisdiketiminate complex *rac*- or *R,R*-C_6H_{10}(*nacnac*^{Xyl})$_2$$ZrCl_2$ with AgOTf yielded the corresponding bistriflate complex. Complex geometry changes from distorted octahedral in the dichloride complex to a pseudo-tetrahedral coordination involving π-coordination of the diketiminate ligands. The bistriflate complex is highly active for aza-Michael additions with turn-over frequencies of 20 000/h for the addition of morpholine to acrylonitrile and 1000/h for the addition of morpholine to methacrylonitrile. The enantioselectivities of the latter reaction in various solvents were low, never surpassing 19% ee. The reaction is first-order in olefin concentration and second order in amine concentration, which is explained by its participation as a base in the reaction mechanism. The presence of catalytic amounts of triethylamine slightly increases the observed rate constants and reduces the reaction order in amine to first order. Other activated alkenes, such as methacrylonitrile, crotonitrile, methyl acrylate, or cyclohexenone can be employed, but no reactivity is observed towards styrene or vinyl ethers. Primary amines, secondary amines and anilines can be employed as nucleophiles with activities correlating with their nucleophilicity, but the catalyst is unstable in the presence of alcohols.

5.2 Introduction

We recently investigated bisdiketiminate zirconium complexes as potential catalysts for organic transformations. The attraction of complexes of the type *nacnac*$^{R}_{2}ZrX_2$, **5.1** (Scheme 5.1), as precatalysts is based on the presence of a chiral metal center with close proximity of the *N*-R substituents to the reactive coordination sites in *cis*-position. Initial explorations showed that bisdiketiminate complexes with *N*-alkyl substituents indeed showed the desired complex geometry.[1] Their application, however, was impeded by a fast epimerization of the metal center as well as a very low reactivity, presumably due to steric crowding: dichloride complexes showed no reactivity towards exchange of the chloride ligands and the cationic methyl derivative [*nacnac*$^{Bn}_{2}$ZrMe][MeB(C_6F_5)$_3$] did not undergo insertion reactions with styrene, diphenylacetylene or benzaldehyde.[1]

To increase reactivity at the ancillary coordination sites, as well as to prevent the epimerization of the metal center, we introduced a cyclohexane diamine bridge between the two diketiminate ligands to yield (±)-C_6H_{10}(*nacnac*^{Xyl})$_2ZrX_2$ (Xyl = 2,6-dimethylphenyl, *trans*-geometry: X = Cl (**5.2**), Me; *cis*-geometry: X = OEt (**5.3**), NMe_2; Scheme 5.1).[2] The deformation caused by the cyclohexane diamine bridge increased the reactivity of the ancillary zirconium substituents significantly and now allowed easy ligand exchange. The corresponding bisethoxide complex **5.3** (Scheme 5.1) proved to be highly active in lactide polymerization, surpassing the activity of any other group 4 catalyst by several orders of magnitude.[2] Here we report the synthesis of the Lewis-acidic chiral bistriflate complex **5.4** (Scheme 5.1) employing the same ligand.



Scheme 5.1

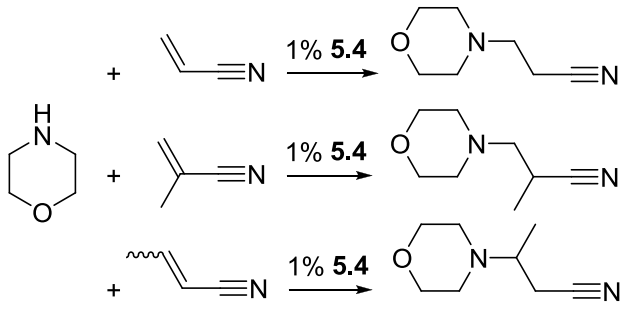
For group 4 compounds, only a limited number of studies have reported their use as catalysts for aza-Michael additions, in most cases as simple zirconium salts such as $ZrCl_4$ or derivatives.[3] We found it thus of interest to test the chiral Lewis acid **5.4** in aza-Michael additions of amines to activated olefins, such as acrylonitrile and acrylate. Enantioselective aza-Michael additions are an even more challenging target[4] and we are not aware of any applications of group 4 metal catalysts in asymmetric aza-Michael additions, although titanium complexes are of course widely employed in asymmetric hydroamination reactions.[4b, 4c] Complex **5.4** was thus tested in enantioselective aza-Michael additions and structural reasons for its rather disappointing performance will be discussed.

5.3 Results and discussion

Attempts to prepare mono- or bistriflate complexes by reaction of bisethoxide complex **5.3** with triflic acid or $[PhN(H)Me_2][OTf]$ at different temperatures and reaction conditions

yielded reaction mixtures in which the main product was the protonated ligand (±)-C_6H_{10}(*nacnac*^{Xyl})$_2H_2$. Reaction of dichloride complex **5.2** with two equivalents of AgOTf, on the other hand, cleanly yielded the bistriflate complex (±)-C_6H_{10}(*nacnac*^{Xyl})$_2$Zr(OTf)$_2$, **5.4** (Scheme 5.1). First and second chloride are exchanged with similar reactivity and reactions with one equivalent of AgOTf yielded mixtures of **5.2**, **5.4** and very small amounts of a product putatively assigned as (±)-C_6H_{10}(*nacnac*^{Xyl})$_2$Zr(Cl)(OTf).

Aza-Michael additions. Initial screening of the performance of **5.4** as catalyst for aza-Michael additions was undertaken for the addition of morpholine to acrylonitrile, methacrylonitrile and crotonitrile (Scheme 5.2, Table 5.1). GC/MS and NMR analysis of all reaction mixtures showed only the presence of the anti-Markownikoff product and – in the case of incomplete reactions – starting material. With a catalyst loading of 1%, **5.4** proved to be highly efficient for the addition of morpholine to acrylonitrile in benzene-d_6, the reaction reaching full conversion in less than 5 min. As expected, the sterically hindered alkenes methacrylonitrile and crotonitrile were less reactive. Addition of 1 equiv (per morpholine) of NEt_3 significantly reduced reactivity. When substance concentrations were raised from 0.25 M to 1.0 M, all three olefins displayed conversions of >90% after 5 min of reaction at room temperature (Table 5.1, #6-8). Under the same conditions, the non-catalyzed reaction of morpholine with acrylonitrile proceeded slowly with 40% conversion after 80 min, while the more hindered alkenes did not react in the absence of catalyst (#9-11).



Scheme 5.2

Table 5.1. Aza-Michael addition of morpholine to unsaturated nitriles

Entry	Alkene	Concentration/M	Reaction time/min	conversion
1	Acrylonitrile	0.25	5	100%
2	Methacrylonitrile	0.25	40	50%
3	E/Z-Crotonitrile	0.25	80	40%
4	Methacrylonitrile	0.50	5	95%
5	E/Z-Crotonitrile	0.50	10	60%
6	Acrylonitrile	1.0	5	100%
7	Methacrylonitrile	1.0	5	95%
8	E/Z-Crotonitrile	1.0	5	90%
9	Acrylonitrile [a]	1.0	80	40% [a]
10	Methacrylonitrile [a]	1.0	80	0% [a]
11	E/Z-Crotonitrile [a]	1.0	80	0% [a]

Reaction conditions: C_6D_6, ambient temperature, [Morpholine]:[Alkene]:[**5.4**] = 100:100:1, yield determined by NMR. [a] Control experiments without addition of **5.4**.

To test catalyst efficiency, reactions of acrylonitrile with morpholine were run at reduced catalyst concentrations. Efficient catalysis was still observed at 500 ppm of catalyst loading (Table 5.2, #3, 70% after 5 min, reaction did not surpass 90% conversion, probably due to

catalyst decomposition). Below this concentration, reactions turned sluggish and did not reach completion even at prolonged reaction times, consistent with catalyst poisoning by impurities in the reaction mixture. The obtained turn-over frequency of appr. 300/min at 500 ppm catalyst loading should thus be considered a lower estimate of catalyst activity. It is likely that a notable fraction of the catalyst was deactivated by impurities already at this concentration.

Table 5.2. Aza-Michael addition of morpholine to acrylonitrile at different catalyst concentrations

[Zr]:[Acrylonitrile]	Reaction time/min	conversion	TOF [a]
1%	5	100%	>20
0.1%	5	100%	>200
0.05%	5 / 40	70% / 90%	≈300
0.02%	45	9%	≈10

Reaction conditions: C_6D_6, ambient temperature, [morpholine] = [acrylonitrile] = 1 M. [a] mol alkene/(mol **5.4** · min)

The scope of the reaction with regard to the nucleophile was investigated with 1% **5.4**. In all cases, NMR and GC-MS analysis confirmed that hydroamination yielded the expected anti-Markownikoff product and that the uncatalyzed reaction yielded less than 5% yield in 3 to 24 hours of reaction time (Table S5.1). Benzylamine proved to be likewise highly reactive and reactions with acrylonitrile reached completion in 5 min at room temperature (Table 5.3, #1). In the presence of two equivalents of alkene (#2), the second

hydroamination was significantly slower and only 10% of bishydroamination product was observed when all starting amine was consumed. Reactions with methacrylonitrile proved again to be more difficult, but still proceeded reasonably fast. Higher conversions were reached at longer reaction times, but did not always reach completion, most likely due to catalyst decomposition (#3,#4). In line with this, no bishydroamination product was observed if two equivalents of methacrylonitrile were reacted with benzylamine (#4). To verify the reactivity of non-cyclic secondary amines, diethylamine was reacted with methacrylonitrile, yielding complete conversion in 5 min. Cyclic and non-cyclic secondary amines are thus more reactive than primary amines. Reactions of aniline with acrylonitrile proceeded more slowly than those of primary and secondary amines. High conversions could be achieved at longer reaction times (#7) or at elevated temperatures (#9). As observed for morpholine, presence of NEt_3 impeded the reaction (#8). Methacrylonitrile and crotonitrile showed low or no reactivity towards aniline at the conditions investigated (#10). With acrylonitrile, 4-methoxyaniline proved to be more reactive, 4-chloroaniline to be less reactive than unsubstituted aniline. Thus reactivity declines in the order: secondary amines > primary amines > 4-methoxyaniline > aniline > 4-chloroaniline, in parallel with the nucleophilicity of the amine employed.

Table 5.3. Aza-Michael addition of different nucleophiles [a]

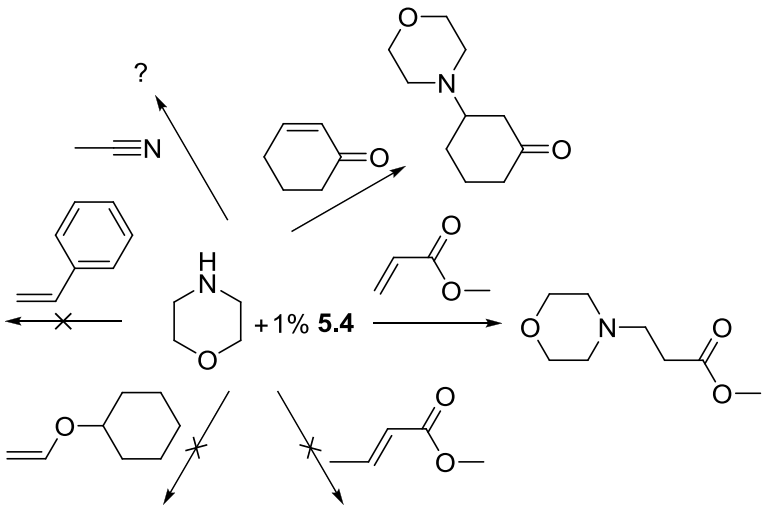
Entry	Nucleophile	Alkene	Reaction time / min	Conversion
1	Benzylamine	Acrylonitrile	5	97%
2	Benzylamine [b]	Acrylonitrile	5	90% [b]
3	Benzylamine	Methacrylonitrile	5	20%
4	Benzylamine [c]	Methacrylonitrile	10 / 24 h	52% / 70% [c,d]
5	Diethylamine	Methacrylonitrile	5	100%
6	Aniline	Acrylonitrile	5 / 60	35% / 80%
7	Aniline [c]	Acrylonitrile	24 h	100% [c]
8	Aniline + NEt_3 [e]	Acrylonitrile	5	5% [e]
9	Aniline, 60°C [f]	Acrylonitrile	5	63% [f]
10	Aniline [c]	Methacrylonitrile	5 / 24 h	<1% / 9% [c]
11	4-methoxyaniline	Acrylonitrile	5	80%
12	4-chloroaniline	Acrylonitrile	5	12%
13	4-Methoxyphenol	Acrylonitrile	24 h	0%
14	4-Methylphenol	Acrylonitrile	24 h	0%
15	4-Chlorophenol	Acrylonitrile	24 h	0%
16	Ethanol	Acrylonitrile	24 h	0%
17	Ethanolamine	Acrylonitrile	24 h	0%

[a] Reaction conditions: C_6D_6, ambient temperature, [Amine]:[Alkene]:[**5.4**] = 1 M : 1 M : 0.01 M, yield determined by NMR. [b] [Alkene]=2 M, 10% bishydroamination product after 10 min. [c] [Alkene]=2 M, only monohydroamination product was observed. [d] Lab scale reaction, isolated yield 52%. [e] in the presence of NEt_3, 1 M. [f] Reaction at 60 °C.

As typically observed for aza-Michael reactions, benzylamine and anilines yielded either only the monohydroamination product (#4, #7, #10) or a mixture of mono- and

bishydroamination products which favours the former (#2). Given that the monohydroamination products should be more nucleophilic than the starting amines, the reason for their low reactivity to undergo further hydroamination is unclear at the moment. Based on the higher reactivity of secondary aliphatic amines compared to primary aliphatic amines, simple steric reasons can be excluded as explanation for the reduced reactivity. Neither did any of the observed kinetics (vide infra) indicate the possibility of product poisoning. No reactivity was observed when phenols or ethanol were used as nucleophile (Table 5.3, #13-#16). The presence of free bisdiketimine in the NMR spectra indicates that the impeding factor is not the nucleophilicity of the alcohols, but protonation of the bisdiketiminate ligand. Consequently, ethanolamine likewise did not yield any hydroamination product (#17). Complex **5.4** is thus not stable in the presence of alcohols.

To further test the scope of the catalytic reaction and to gain first insights in a probable reaction mechanism, amines were reacted with alkenes other than conjugated nitriles (Scheme 5.3, Table 5.4). Cyclohexenone and methyl acrylate, but not methyl crotonate, reacted readily with morpholine or diethylamine. Benzylamine and aniline were less reactive, but still reached conversion above 75% at prolonged reaction times. (Yields of the uncatalyzed reaction were below 5% after 24 h reaction time, Table S5.1.) In all cases, NMR and GC/MS-analysis confirmed the formation of 1,4-addition products. Non-activated alkenes, such as cyclohexyl vinyl ether or styrene, did not show any reactivity, in support of a Lewis-acid mechanism. Reactions with acetonitrile proceeded sluggishly and yielded an (unidentified) mixture of products in low yields.



Scheme 5.3

Table 5.4. Aza-Michael addition to alkenes other than unsaturated nitriles

Entry	Nucleophile	Alkene	Reaction time/min	Conversion
1	Morpholine	Methyl acrylate	5	81%
2	Diethylamine	Methyl acrylate	5 / 60	29% / 68%
3	Benzylamine	Methyl acrylate	5 / 24 h	16% / 84%
4	Aniline	Methyl acrylate	5 / 60	23% / 75%
5	Morpholine	Methyl crotonate	60	0%
6	Diethylamine	Methyl crotonate	60	0%
7	Morpholine	Cyclohexenone	60	80%
8	Morpholine	Cyclohexylvinylether	60	0%
9	Morpholine	Styrene	24 h	0%
10	Morpholine	Acetonitrile	48 h	20% [a]

Reaction conditions: C_6D_6, ambient temperature, [Amine]:[Alkene]:[**5.4**] = 1 M:1 M:0.01 M, yield determined by NMR. [a] Conversion of starting material, a mixture of products was observed.

Reaction kinetics and mechanism. The two main mechanisms for hydroamination of alkenes with early transition metals involve either insertion of the olefin into a metal amide bond or Lewis-acid activation of the alkene and outer-sphere attack of the neutral nucleophile. In the case of **5.4**, its inactivity towards non-activated alkenes and the relationship between reactivity and amine nucleophilicity argue for a Lewis-acid mechanism in this case. NMR spectra of equimolar mixtures of **5.4** with acrylonitrile, morpholine or both did not show any notable displacement of the catalyst resonances. In 2:1 mixtures of **5.4** and acrylonitrile, a very slight displacement of the acrylonitrile chemical shifts was observed (^{13}C: 1 ppm downfield for the terminal carbon atom and the CN group, 0.5 ppm upfield for the internal carbon atom. ^{1}H: slight downfield shift (< 0.05 ppm) for all protons). These are in agreement with a fast, incomplete and reversible *N*-coordination of acrylonitrile to **5.4**.[5] No effects were observed on morpholine resonances, even with excess **5.4**.

The kinetics of the reaction of methacrylonitrile with diethylamine was investigated in detail. Under pseudo-first order conditions (10-fold excess of amine), the reaction showed first-order dependence on methacrylonitrile concentration (Fig. 5.1, Table 5.5). Reactions in the presence of excess methacrylonitrile, on the other hand, failed to give linear ln(conversion) vs. time plots and first-order rate constants determined at different methacrylonitrile starting concentrations were inconsistent (Fig. 5.2). On the other hand, 1/[$NHEt_2$] vs. time plots were highly linear and yielded rate constants independent from starting concentrations (Fig. 5.2, Table 5.5). The reaction is thus second order with respect to amine. Consequently, linear $1/c^2$ vs time plots were obtained with equal initial

concentrations of methacrylonitrile and diethylamine (Fig. S5.1), confirming a combined reaction order of three for the nucleophile and the olefin. Assuming a first-order dependence on catalyst concentration, the overall rate law is thus $v = k \cdot [NEt_2H]^2 \cdot [\text{methacrylonitrile}][\mathbf{5.4}]$ and we obtain from kinetics under equal concentrations, excess amine, or excess olefin values for k of 25(1), 38(5), and 25(4) $\text{min}^{-1} \cdot \text{M}^{-3}$, respectively, which are identical within the margin of error (Table 5.5).

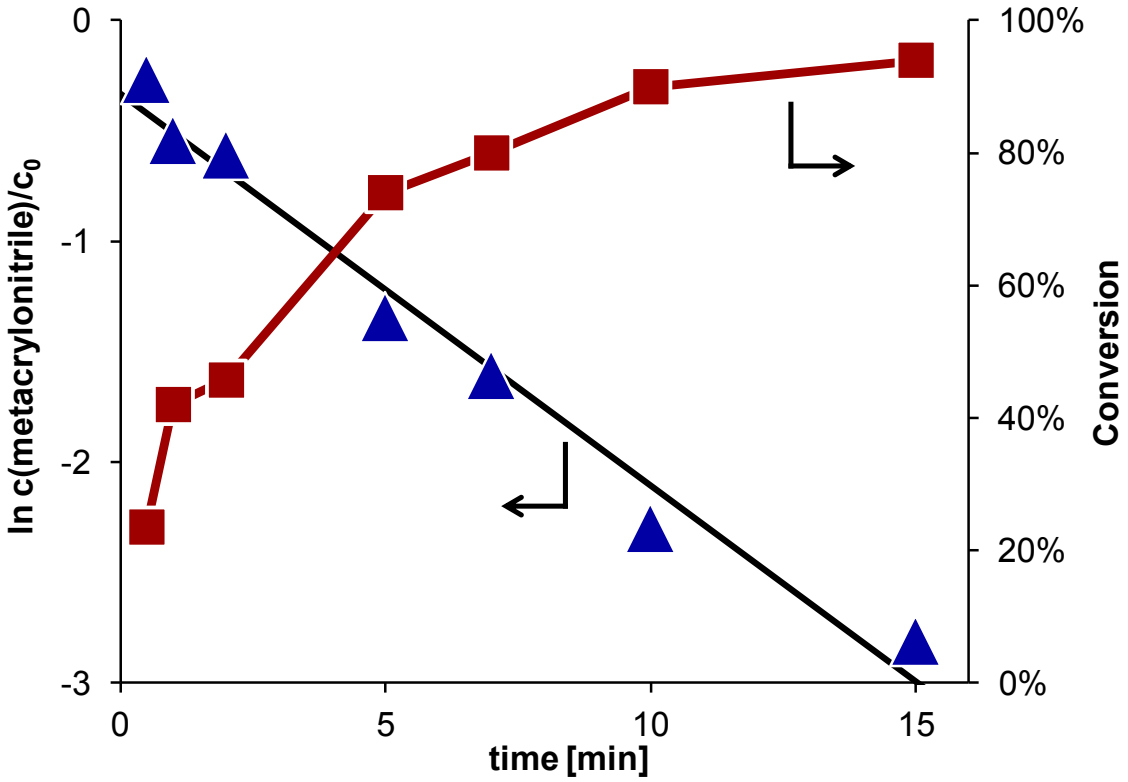


Fig. 5.1. Conversion vs. time (squares) and the corresponding linearised plot ln c/c_0 vs. time (triangles) under pseudo-first order conditions: C_6D_6, ambient temperature, $[NEt_2H]_0$ = 1.3 M, $[\text{methacrylonitrile}]_0$ = 0.13 M, [**5.4**] = 3.1 mM (2.4%).

Table 5.5. Observed rate constants obtained under different conditions.

$[NEt_2H]_0$ / M	$[C_4H_5N]_0$ / M	[**5.4**] / mM	Conversion range	Rate law	k_{obs}	k [a] $\cdot(min \cdot M^3)$
1.3	0.13	3.1	24 – 94%	$v = k_{obs}[A]$	0.18(1) min^{-1}	
1.3	0.13	3.1	46 – 99%	$v = k_{obs}[A]$	0.23(5) min^{-1}	38(5)
0.50	4.8	5.0	58 – 93%	$v = k_{obs}[A]^2$	0.37(1) $M^{-1} \cdot min^{-1}$	
0.50	4.8	5.0	43 – 99%	$v = k_{obs}[A]^2$	0.72(4) $M^{-1} \cdot min^{-1}$	
0.50	4.8	5.0	27 – 83%	$v = k_{obs}[A]^2$	0.61(4) $M^{-1} \cdot min^{-1}$	
0.50	4.8	5.0	13 – 76%	$v = k_{obs}[A]^2$	0.54(3) $M^{-1} \cdot min^{-1}$	
1.0	4.8	5.0	71 – 97%	$v = k_{obs}[A]^2$	0.49(7) $M^{-1} \cdot min^{-1}$	23(4)
1.0	1.0	10	53 – 83%	$v = k_{obs}[A]^3$	0.25(1) $M^{-2} \cdot min^{-1}$	25(1)

[a] For rate law: $v = k \cdot [NEt_2H]^2 \cdot$[methacrylonitrile][**5.4**]. Errors estimated from the standard deviation of the mean or from the linear regression analysis.

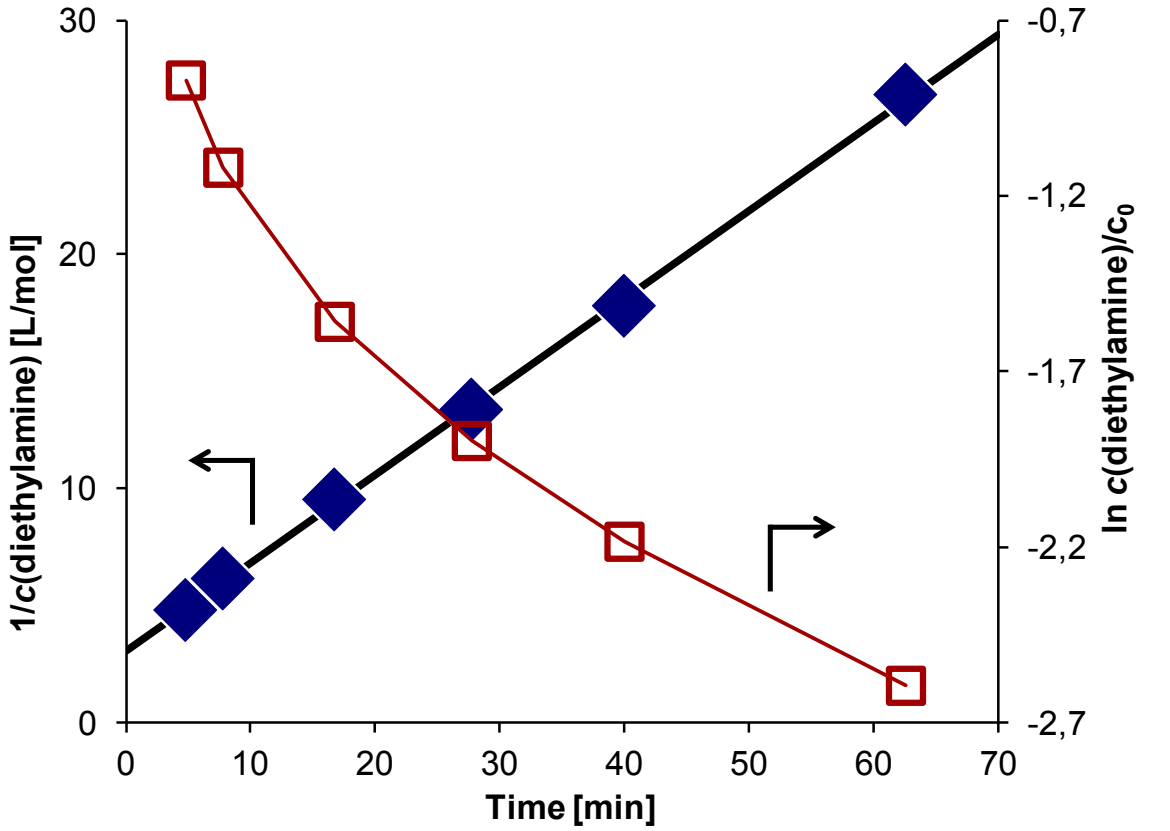


Fig. 5.2. Linearised first-order (squares) and second-order (diamonds) concentration-time profiles in the presence of excess methacrylonitrile: C_6D_6, ambient temperature, $[NEt_2H]_0$ = 0.50 M, [methacrylonitrile]$_0$ = 4.8 M, [**5.4**] = 5.0 mM (1%).

Dependence on amine as well as olefin concentration indicates either that coordination of methacrylonitrile to zirconium is rate-limiting, followed by fast addition of amine in competition with dissociation, or that amine addition is rate-limiting and methacrylonitrile coordination is in a fast pre-equilibrium far from saturation. The latter would be in agreement with the observed slight displacements of acrylonitrile resonances observed in ^{1}H NMR, but the former cannot be ruled out from the available data. A second-order dependence on amine was slightly puzzling. The most likely activating role of a second

amine would be to act as a base which aids in the proton transfer from *N* to *C*, constistent with the notion that the rate-limiting step is amine addition to a zirconium-coordinated substrate. However, addition of a non-reactive amine such as triethylamine was observed to lead to de-activation (vide supra). Closer inspection of the role of triethylamine under pseudo-first order conditions (excess olefin) revealed that its presence has a slight activating effect on the reaction if added in catalytic amounts only. In the presence of < 0,1 M triethylamine, conversions reached 50% in 0.5 to 1 min (Table 5.6, #2-#8). In its absence, 3 to 5 min was required (#1). Under the reaction conditions examined, maximum activity was observed around [NEt_3] = 25 mM, i. e. 10-times the concentration of the catalyst (Fig. 5.3). Higher triethylamine concentrations slowly led to reduced activities (#9-#12), probably due to deactivation of the catalyst by amine coordination to zirconium, although catalyst poisoning by impurities cannot be excluded or due to trapping the catalytical species by the addition of triethylamine to the activated acrylonitrile. While the increase in reactivity with triethylamine was slight, its presence provided additional information on the reaction mechanism. Investigation of the initial reaction rates in the presence of NEt_3 (5 mM) showed a first-order dependence on diethylamine concentration (#2-#4, slope of 1.2 in log-log plots). This is in contrast to the second-order dependence observed in the absence of triethylamine and confirms that diethylamine acts as a base in the absence of triethylamine. The reaction mechanism outlined in Scheme 5.4 is proposed to explain the kinetic results. The fast coordination equilibrium between 5.4 and acrylonitrile observed in NMR experiments indicates that **A** is likely formed in a fast, unfavourable pre-equilibrium. Assuming that **A** to **B** is likewise reversible and that the

amine is involved in the proton transfer from **B** to **D**, a second-order dependence on amine concentration originates from the competition of the equilibrium backreaction (k_{BA}) and the proton transfer ($k_{Bc}[HNEt_2]$) for **B**. The kinetic data only indicate a second amine is involved somewhere in the reaction mechanism, but this is not necessarily the step with the highest activation barrier. While participation in the proton transfer is in our opinion, the most likely explanation, any other mechanism which involves two amines between the rate-determining intermediate and the rate-determining transition state in the catalytic cycle[19] is in agreement as well with the observed kinetics.

Table 5.6. Conversions and observed first-order rate constants for the addition of diethylamine to methacrylonitrile in the presence of triethylamine.

Entry	[NEt_3] / M	Conversion after 1 min	k_{obs} · min [a]	[Et_2NH] / M	$v_{initial}$ · min/M
1	-	35%	0.30(5) [b]	0.50	
2	0.0050	48%	0.60(2)	0.50	0.58
3	0.0049	60%	0.71(3)	1.0	1.1
4	0.0048	56%	0.78(13)	1.5	2.1
5	0.010	61%	0.75(7)	0.50	
6	0.024	48%	0.87(6)	0.50	
7	0.050	59%	0.67(7)	0.50	
8	0.10	53%	0.77(5)	0.50	
9	0.24	38%	0.36(5)	0.50	
10	0.48	48%	0.30(4)	0.50	
11	1.0	34%	0.39(7)	0.50	
12	2.0	19%	0.094(5)	0.50	

C_6D_6, ambient temperature, $[\text{methacrylonitrile}]_0$ = 4.6 M, [**5.4**] = 5.0 mM (1%). [a] Obtained from $\ln c/c_0 = -kt$. [b] Second-order reaction. Conversions < 30% were fitted using a first-order rate law.

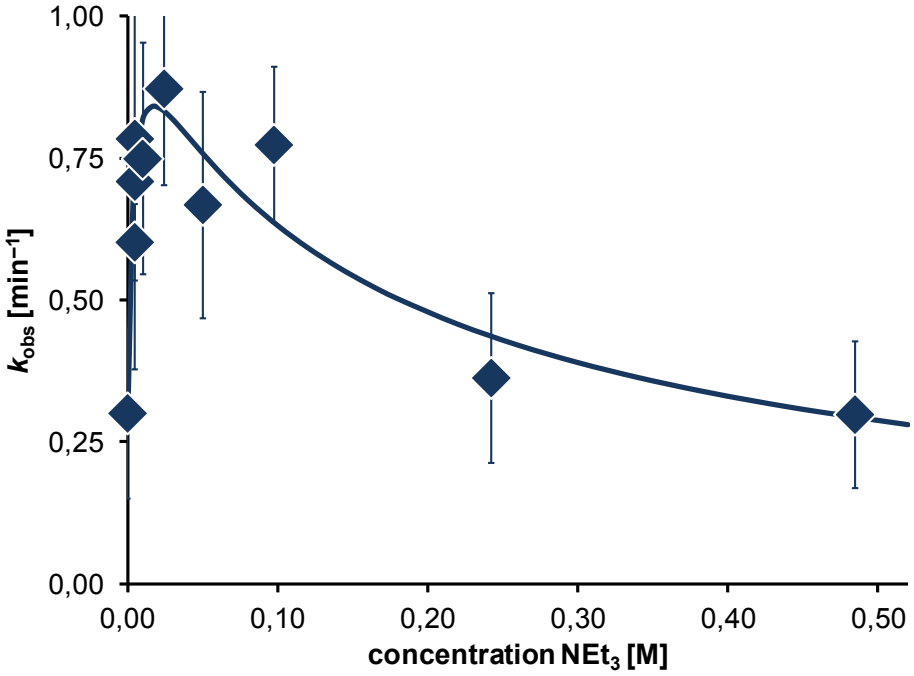
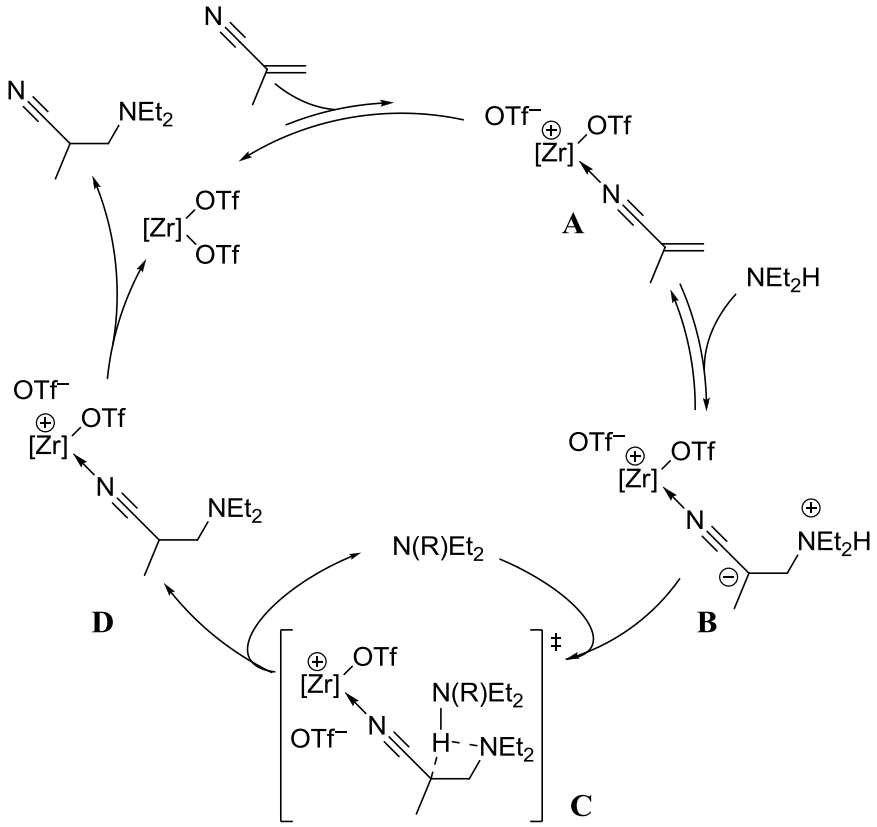


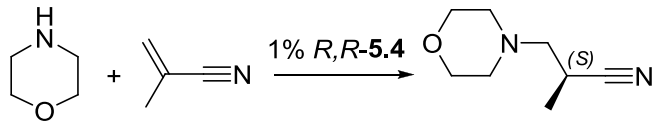
Fig. 5.3. Pseudo-first-order rate constants in the presence of triethylamine: C_6D_6, ambient temperature, $[NEt_2H]_0$ = 0.5 M, [methacrylonitrile]$_0$ = 5 M, [**5.4**] = 5 mM (1%).



Scheme 5.4

Enantioselective reactions. Enantiopure complex *R,R*-**5.4** was prepared in a simplified procedure starting from *R,R*-diaminocyclohexane *L*-tartrate and tested in the enantioselective aza-Michael addition of morpholine to methacrylonitrile. Several attempts to determine the obtained ee using NMR shift reagents ((+)-Eu(tfc)$_3$, (+)-Eu(hfc)$_3$, or (+)-Yb(hfc)$_3$, tfc/hfc = 3-trifluoromethyl- or 3-heptafluoropropyl hydroxymethylene camphorate) were unsuccessful. Use of chiral GC yielded the expected ee = 0% for the product obtained with *rac*-**5.4**, while 2-*S*-methyl-3-morpholino-proprionitrile was obtained in low ee of 19% with *R,R*-**5.4** (Scheme 5.5). Variation of catalyst concentration or solvent (Table 5.7) failed to improve the obtained enantioselectivity. In strongly coordinating

solvents, such as THF and acetonitrile, activity was drastically reduced. Diethyl ether, dichloromethane and toluene led to complete conversion in 1 h at reagent concentrations of 0.5 M. Dilution led to the expected decrease in activity (increased catalyst poisoning is also suspected for dichloromethane). Enantioselectivities, however, were unaffected either by choice of solvent or dilution and remained between 10 – 19%. Reactions at low temperatures led to incomplete conversion even at prolonged reaction times and were not investigated further. While **5.4** is sufficiently stable at room temperature to convert most substrates to high conversions, its stability is limited at low catalyst concentrations or low temperatures where significantly longer reactions times are required and it seems unlikely that reaction conditions can be found which would significantly increase the observed enantioselectivities. It should be noted that Vitanova et al. obtained enantioselectivities up to 72% ee for the intramolecular hydroamination of non-activated olefins with similar bisdiketiminate lanthanide complexes.[6] The reaction mechanism in this case, however, is based on olefin insertion into a lanthanide amide bond, distinctly different from the Lewis-acid activation mechanism proposed for **5.4** (*vide supra*).



Scheme 5.5

Table 5.7. Enantioselective aza-Michael additions with *R,R*-**5.4**.

Solvent	[NEt_2H] = [methacrylonitrile]	Conversion (after 1 h)	ee
C_6D_6	0.50 M	95% (2 min)	19%
THF	0.50 M	20%	13%
MeCN	0.50 M	12%	1%
Et_2O	0.50 M	100%	17%
	0.25 M	85%	19%
	0.125 M	72%	16%
	0.050 M	30%	15%
CH_2Cl_2	0.50 M	100%	13%
	0.25 M	70%	13%
	0.125 M	33%	10%
	0.050 M	17%	3%
Toluene	0.50 M	100%	16%
	0.25 M	84%	10%
	0.125 M	70%	10%
	0.050 M	24%	10%
Et_2O, -78 °C	0.50 M	30% [a]	n. d.

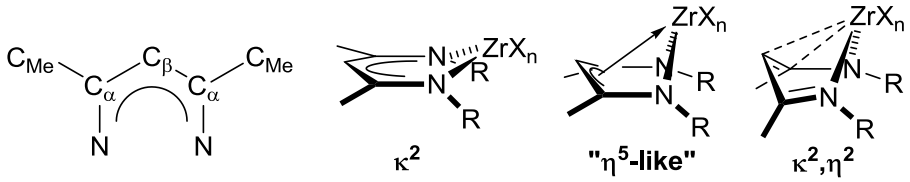
Reaction conditions: ambient temperature, 1 h reaction time, 1 mol% **5.4**. [a] The observed conversion did not increase at prolonged reaction times.

Solution and solid state structure of 5.4. A possible explanation for the unsatisfactory performance of **5.4** in asymmetric reactions might be derived from the loss of C_2-symmetry. Previously reported (±)-$C_6H_{10}(nacnac^{Xyl})_2ZrX_2$ complexes (X = Cl, Me, NMe_2,

OEt) displayed C_2-symmetric ^{1}H and ^{13}C NMR spectra, with one resonance for the ligand methine group, one resonance for the methine proton of the cyclohexyl bridge, two methyl diketiminate methyl resonances and two resonances for the xylyl methyl groups.[2] Their solid state structures also displayed C_2 point symmetry, either in a *cis*- (X = NMe_2, OEt) or *trans*-geometry (X = Cl, Me). In ^{1}H NMR spectra of **5.4**, however, C_2-symmetry was lost and two different signal sets were observed for the two diketiminate moieties, as well as four resonances for the xylyl methyl group and two resonances for the methine group in the chiral bridge. The fluorine NMR spectrum displayed two signals at –76.6 and –77.5 ppm, indicating chemically different triflate anions. It was tempting to assign these to coordinated and non-coordinated triflate anions. However, lack of symmetry in the ^{1}H NMR spectrum would require either a configurationally stable five-coordinated $[C_6H_{10}(nacnac^{Xyl})_2Zr(OTf)]^+$ cation or a stable, unsymmetric bridging coordination of the triflate anion, both of which seem unlikely. Also, a higher downfield shift would be expected for free triflate. Both triflate resonances still fall in the range observed for coordinated triflate anions in octahedral Zr complexes (–73 and –79 ppm),[7] while uncoordinated triflate anions are expected around –80 ppm (e. g. $[NBu_4][OTf]$: –78.8 ppm,[8] $[(Ph_3P)_2N][OTf]$: –80.5 ppm).[9]

Crystals of **5.4** suitable for an X-ray diffraction study were obtained by diffusion of hexane into a toluene solution. Two independent molecules are found in the asymmetric unit, which show a non-crystallographic pseudo-symmetry (glide plane perpendicular to z; x+0.25, y, -z) broken only by slightly different orientations of the triflate ligands and the xylyl substituents. Presence of pseudosymmetry resulted in relatively low quality of the

structural data, despite sufficient crystal quality. Nevertheless, the obtained structure clearly revealed a coordination of both triflate anions to the zirconium center in the solid state and an involvement of the diketiminate π-system in metal-ligand bonding (Figure 5.4, Table 5.8). Zirconium diketiminate complexes typically show three distinct coordination modes. Most typically observed is κ^2-coordination of the two nitrogen atoms (Scheme 5.5).[10] The other two bonding modes involve coordination of the ligand π-system to the zirconium center and are commonly observed either for electron-deficient zirconium centers or if the second ligand is an η^5-ligand such as cyclopentadienyl. Coordination of the π-system might occur symmetrically to yield an "η^5-like"-coordination of the diketiminate or in form of an unsymmetrical κ^2,η^2-coordination (Scheme 5.6).[10]



d Zr-C_β	> 3.2 Å	< 2.8 Å	< 2.8 Å
angle (N,N,Zr)/(N,C_α,C_α,N)	< 35°	> 40°	> 40°
Δd Zr-C_α		< 0.1 Å	> 0.2 Å
Δangle Zr-C_α-C_{Me}		< 15°	> 25°
angle N-C_α-C_α-N		< 10°	> 15°

Scheme 5.6

In **5.4**, short bond distances of Zr to the central carbon atom C_β of the diketiminate ligands (Zr-C3/C23/C43/C63 = 2.6 – 2.8 Å, Table 5.8) and a high bending of Zr atom out of the ligands' mean planes (≈70°), clearly indicate that the diketiminate π-system is involved in the ligand-metal bonding, contrary to previous C_6H_{10}(*nacnac*^{Xyl})$_2$ZrX_2

complexes, such as **5.2** and **5.3** (Scheme 5.1), which showed bis-κ^2-coordination.[2] Despite some variation introduced by the bridging of two diketiminate ligands, the coordination of one diketiminate can be clearly assigned as symmetric "η^5-like"-coordination with comparable Zr-C_α distances ($\Delta < 0.1$ Å) and Zr-C_α-C_{Me} angles ($\Delta < 5°$, Table 5.1).[10] The coordination of the second diketiminate fragment is best described as κ^2,η^2-coordination, evidenced by larger differences in Zr-C_α distances and Zr-C_α-C_{Me} angles (≈ 0.2 Å and $> 20°$).[10] While a non-symmetric coordination of the bis-diketiminate ligand would explain the C_1-symmetric NMR spectra, neither steric nor electronic reasons would suggest a substantive activation barrier for interconversion between κ^2,η^2- and the symmetric "η^5-like"-coordination (zirconium complexes with κ^2,η^2-coordinated diketiminate ligands generally display symmetrical NMR spectra). The non-symmetric NMR spectra of **5.4** is thus unlikely to be caused by the non-symmetric κ^2,η^2-/"η^5-like"-coordination of the bisdiketiminate ligand, which we would expect to interconvert rapidly in solution.

Table 5.8. Selected bond distances (Å) and angles (°) for **5.4**.

	N1,N2,C1-5	**N11,N12,C41-45**	**N3,N4,C21-45**	**N13,N14,C61-C65**
Coordination	κ^2,η^2	κ^2,η^2	"η^5-like"	"η^5-like"
Zr-N	2.307(10), 2.124(10)	2.271(9), 2.167(8)	2.166(9), 2.162(9)	2.169(8), 2.185(8)
(Zr,N,N)/(N,N,C_α,C_α) [a]	68°	72°	68°	68°
Zr-C_β	2.626(11)	2.656(11)	2.776(13)	2.805(11)
Zr-C_α	2.782(11), 2.596(12)	2.852(11), 2.660(11)	2.828(11), 2.748(13)	2.822(10), 2.770(10)
N-C_α-C_{Me}	161, 143	168. 145	157. 153	154, 154
Zr-O6/O9/O3/O12	2.197(8)	2.179(7)	2.235(8)	2.263(7)

C_α = C2, C4, C22, C24, C42, C44, C62, C64. C_β = C3, C23, C43, C63. [a] Bending of Zr out of the mean ligand plane, defined by the nitrogen and C_α atoms.

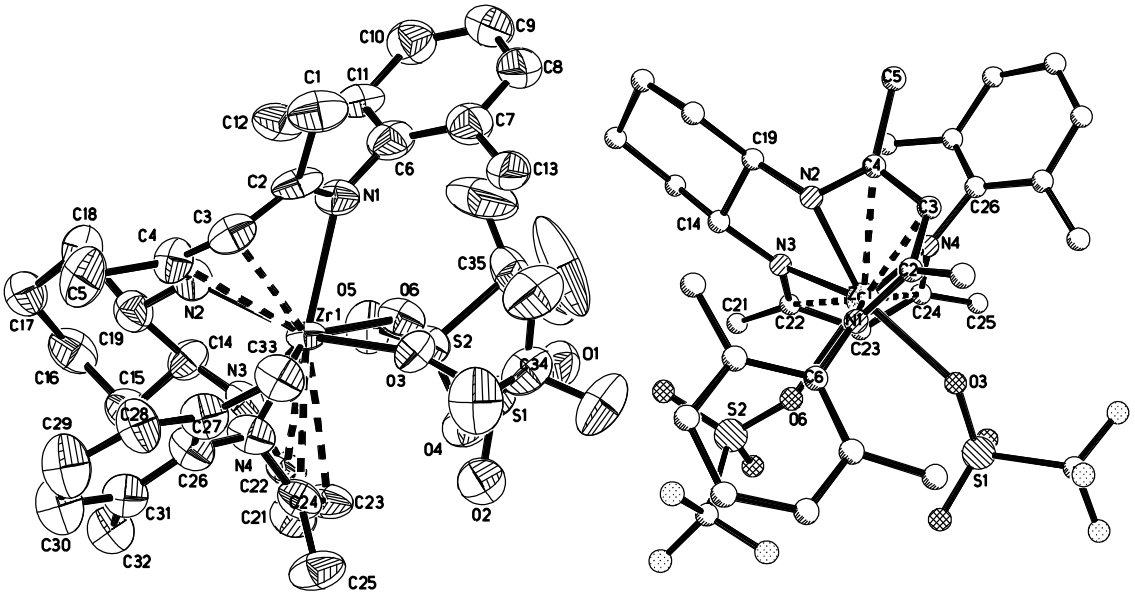


Fig. 5.4. X-ray structure of **5.4**. Hydrogen atoms and the second, independent molecule of identical geometry omitted for clarity. Thermal ellipsoids are presented with a 50%-probability cut-off.

π-Coordination of the bisdiketiminate ligand also caused a change in the general coordination geometry around Zr. Previous $C_6H_{10}(nacnac^{Xyl})_2ZrX_2$ complexes with X = Cl, Me, NMe_2, OEt displayed distorted octahedral geometries, as expected for a bis-κ^2-coordinated ligand. Due to the steric constraints introduced by the cyclohexyldiamine bridge (bite angle of 72°), the structures are strongly distorted with widened X-Zr-X angles of 121-125° for *cis*-X_2 complexes (X = NMe_2, OEt).[2] The structure of **5.4**, however, is best described as pseudo-tetrahedral (O3-Zr1-O6 = 83.2(3)°, O9-Zr2-O12 = 82.9(3), Z-Zr-Z = 138-140°, Zr-Z ≈ 2.1 Å, Z = centroid of the diketiminate ligand), comparable to $(nacnac^{Ar})(Cp)ZrCl_2$ or $(nacnac^{Ar})(Ind)ZrCl_2$ complexes, also showing π-coordination of the diketiminate ligand (Cl-Zr-Cl = 84-90°, Z-Zr-Z = 136-141°, Zr-Z_{nacnac} ≈ 2.1 Å, Z =

centroid of the diketiminate, Cp or Ind ligand).[11] Comparable to substituted *ansa*-zirconocenes with triatomic bridges (such as C_3H_6-, Me_2SiOMe_2Si- or ferrocenyl-brigded indenyl or cyclopentadienyl complexes),[12] the structure of **5.4** deviates from C_2-symmetry by placing the bridge to one side of the complex (Fig. 5.4). As a consequence, one Cp- or *N*-substituent is eclipsed with the ZrX_2 fragment while the other is oriented to the side of the complex away from the ZrX_2 fragment. In the resulting C_1-symmetric structure, the two triflate ligands have a clearly different chemical environment, further evidenced by differences in Zr-O distances of 0.04-0.08 Å (Table 5.8). For the *ansa*-metallocenes mentioned above, NMR spectra showed apparent C_2-symmetry, explained by a fast rotation of the ZrX_2 fragment. Nevertheless, it is reasonable to assume that the latter is more difficult in **5.4**, given the more rigid nature of the cyclohexyl diamine bridge and the higher steric demands of xylyl and triflate substituents. The observed C_1-symmetric, pseudo-tetrahedral structure is thus most likely preserved in solution and responsible for the lack of symmetry in NMR spectra, resulting in different coordination environments for the triflate ligands and in poor enantioselectivities.

5.4 Conclusions

Lewis-acidic **5.4** proved to be highly active for the addition of amines to activated olefins with a maximum turnover frequency of 20 000/h for the addition of morpholine to acrylonitrile at ambient temperature. For sterically more hindered substrates, a turn-over-frequency of 1000/h for the addition of morpholine to methacrylonitrile compares favourably to those obtained with di- and triphosphine Ni(II) (1/h – 3/h),[13] bisphosphine-NHC Pd(II) (1/h),[14] bis(NHC) Pd(II) (3/h at 90 °C),[15] and Ni(II) pincer complexes (30/h –

1000/h).[16] Enantiopure *R,R*-**5.4** showed only low enantioselectivity (ee < 20%) for the addition of morpholine to methacrylonitrile. For the same reaction, Togni reported Ni(II) and Pd(II) complexes with chiral phosphine ligands which showed notably higher enantioselectivities of 32 – 69% ee.[13-14] The change of coordination mode from C_2-symmetric octahedral bis-κ^2-coordination to C_1-symmetric pseudo-tetragonal π-coordination of the bisdiketiminate ligand in **5.4** is most likely responsible for the low enantioselectivities obtained. The pseudo-tetragonal structure does not only show a less clear distinction between "up" and "down"-sides of the $Zr(OTf)_2$-plane, but the two coordination sites are chemically inequivalent with different, if any, stereoselectivity. The overall reaction order of 4 (assuming a first-order dependence on catalyst concentration in agreement with the values in Table 5.6) underlines the importance to work under high concentrations or even without solvent to achieve high turn-over-frequencies. Since the nucleophile also participates as a base in the reaction mechanism, resulting in a partial reaction order of two in amine concentration, it seems advantageous to conduct hydroaminations under slight excess of amine whenever no external base is added.

5.5 Experimental section

General. All reactions were carried out under an inert atmosphere using Schlenk and glove box techniques under a purified N_2 atmosphere. Complex **5.2** was prepared as described elsewhere,[2] all others chemicals were purchased from common commercial suppliers. ^1H and ^{13}C NMR spectra were acquired on a Bruker AMX 400 or Bruker AV 400 spectrometer. ^{19}F NMR spectra were acquired on a Bruker AV 400 spectrometer. Chemical shifts were referenced to the residual signals of the deuterated solvents (C_6D_6: ^1H: δ 7.16

ppm, ^{13}C: δ 128.38 ppm; $CDCl_3$: ^{1}H: δ 7.26 ppm, ^{13}C: δ 77.00 ppm). Solvents were dried by passage through activated aluminum oxide (MBraun SPS) and de-oxygenated by repeated extraction with nitrogen. C_6D_6 was dried over sodium and degassed by three freeze-pump-thaw cycles. Acrylonitrile, methacrylonitrile, (Z/E)-crotonitrile, 2-cyclohexeneone, benzylamine, morpholine, aniline, and diethylamine were distilled under reduced pressure and dried over 4A molecular sieves. Elemental analyses were performed by the Laboratoire d'analyse élémentaire (Université de Montréal). GC/MS analyses were obtained using an Agilent 6890 N spectrometer. Enantiomeric excess (ee) was determined by chiral GC (HP 6890 Series, *β-dex*120 (30 m x 0.25 mm x0.25 μm, isothermal mode at 90^{o} C).

Diffraction data for **5.4** was recorded on a Bruker APEXII/Microsource diffractometer (Cu Kα radiation) at 100 K using the APEX2 software package. Data reduction was performed with SAINT, the structure was solved with direct methods (SHELXS97).[17] All non-hydrogen atoms were refined anisotropically using full-matrix least-squares on F^2 and hydrogen atoms refined with fixed isotropic U using a riding model (SHELXL97).[17] For further details see supporting information and Table 5.9.

Table 5.9. Details of the X-ray diffraction study of **5.4**.

Formula	$C_{34}H_{42}F_6N_4O_6S_2Zr$	Z; $d_{calcd.}$ (g/cm^3)	8; 1.561
M_w (g/mol); F(000)	872.05; 3584	θ range (°); completeness	2.3 – 71.9; 1.0
Crystal color and form	colorless fragment	collected reflections; R_σ	103102; 5.8%
Crystal size (mm)	0.08 x 0.06 x 0.06	unique reflections; R_{int}	14451; 9.5%
Crystal System	Orthorhombic	μ (mm^{-1}); Abs. Corr.	4.2; multiscan
Space Group	$Pna2_1$	R1(F); wR(F^2) ($I > 2\sigma(I)$)	7.3%; 18.8%
Unit Cell: a (Å)	38.0942(10)	R1(F); wR(F^2) (all data)	8.5%; 20.2%
b (Å)	11.4367(4)	GoF(F^2)	1.034
c (Å)	17.0337(5)	Flack-x	0.32(2)
V (Å^3)	7421.1(4)	Residual electron density	3.45

(±)-C_6H_{10}(*nacnac*^{Xyl})$_2$Zr(OTf)$_2$, 5.4. A toluene solution of silver triflate (77 mg, 0.30 mmol, 5.0 mL) was gradually added to a toluene solution of **5.2** (100 mg, 0.15 mmol, 10 mL) at room temperature. The precipitated AgCl was removed by filtration. The obtained yellow filtrate was concentrated and diffusion of hexane into the solution yielded yellow crystals (74 mg, 75%).

^{1}H NMR (C_6D_6, 400 MHz): δ 7.05 - 6.64 (m, 6H, Ar), 5.65 (s, 1H, *C*H(C=N)), 5.02 (m, 1H, Cy CH), 4.37 (s, 1H, CH(C=N)), 3.11 (m, 1H, Cy CH), 2.61 (s, 3H,(C*H*$_3$)$_2$Ar), 2.49 (s, 3H,(C*H*$_3$)$_2$Ar), 2.38 (m, 1H, Cy CH_2), 2.16 (s, 3H, CH_3(C=N)), 1.90 (s, 3H, CH_3(C=N)), 1.71 (s, 3H, CH_3(C=N)), 1.38 - 1.43 (m, 5H, Cy CH_2), 1.32 (s, 3H, CH_3(C=N)), 1.17 (s, 3H,(C*H*$_3$)$_2$Ar), 1.05 (s, 3H,(C*H*$_3$)$_2$Ar), 0.88 (m, 3H, Cy CH_2). ^{13}C {^{1}H} NMR (C_6D_6, 101 MHz): δ 164.3, 163.9, 162.4, 161.5 (CH_3*C*=N), 145.5, 144. 3 (CF_3SO_3), 134.4, 133.7, 132.6, 132.1 (*ortho* $(CH_3)_2$*Ar*), 129.3, 129.1 (*ipso* $(CH_3)_2$*Ar*), 129.0, 128.9, 128.1, 127.9 (*meta* $(CH_3)_2$*Ar*) 126.7, 126.6 (*para* $(CH_3)_2$*Ar*), 102.6, 98.4 (CH(*C*=N)), 73.0, 67.9 (Cy

CH), 32.4, 31.2 (Cy CH_2), 25.0 ((CH_3)$_2$Ar), 24.7 (Cy CH_2), 24.6, 23.5, 22.1((CH_3)$_2$Ar), 20.6 (CH_3C=N), 20.3 (Cy CH_2), 20.1, 19.2, 17.3 (CH_3C=N). ^{19}F {^{1}H} NMR (C_6D_6, 400 MHz): -76.6 (s, 3F), -77.5 (s, 3F). Anal. Calcd for $C_{34}H_{42}F_6N_4O_6S_2Zr$: C, 46.83; H, 4.85; N, 6.42; S, 7.35. Found C, 47.01; H, 5.34; N, 6.38; S, 7.06.

***R,R*-C_6H_{10}(*nacnac*^{Xyl})$_2$Zr(OTf)$_2$, *R,R*-5.4.** A solution of NaOH (2.2 g, 55 mmol) in a mixture of water (5 mL) and brine (5 mL) was added dropwise to a suspension of (1*R*,2*R*)-(+)-1,2-cyclohexane *L*-tartrate (2.00 g, 7.58 mmol) in CH_2Cl_2 (50 mL). The resulting mixture was allowed to stir overnight. The organic layer was separated and the aqueous layer was extracted with CH_2Cl_2 (4 x 20 mL). The combined organic phases were dried over $MgSO_4$, filtered, and concentrated to yield 0.60 g of *R,R*-cyclohexyldiamine as a white solid, which was used without further purification. Preparation of the ligand, dichloride and bistriflate complex followed the described procedures for the racemic complex, with similar yields and identical spectroscopic properties (final yield of the bistriflate complex: 80 mg, 77%). An analytically pure sample was obtained from C_6D_6 solution. Anal. Calcd for $C_{34}H_{42}F_6N_4O_6S_2Zr \cdot C_6D_6$: C, 50.24; H, 5.69; N, 5.86; S, 6.71. Found C, 50.19; H, 5.67; N, 5.49; S, 6.57.

General procedure for catalytic hydroamination reactions. In a glove box, the olefin and a stock solution with the desired amount of **5.4** was combined in a J. Young NMR tube. The desired amount of amine was added, followed by C_6D_6 to complete the volume to 500 μL. Reactions were monitored by ^{1}H NMR to determine conversion. The obtained products were identified by ^{1}H NMR and GC/MS.

2-Methyl-3-morpholino-propanenitrile. Methacrylonitrile (5.0 mmol, 0.42 mL) was added to a C_6D_6 solution of rac-**5.4** or *R,R*-**5.4** (0.050 mmol, 1.82 mL, 0.0274 M). Morpholine (5.0 mmol, 0.43 mL) was added to the obtained yellow solution. The reaction mixture was followed by ^{1}H NMR for conversion determination, poured into a vial containing wet hexane and purified by flash chromatography to yield a colorless oil (650 mg, 85%).

^{1}H NMR (CDCl3, 400 MHz): δ3.67 (t, J = 6, $(CH_2)_2O$), 2.69 – 2.20 (m, 1H, MeC*H*), 2.6 (dd, J = 17, 1 H, CH_2), 2.48 (t, J = 6, $(CH_2)_2N$), 2.38 (dd, J = 7, 1 H, CH_2), 1.31 (d, J = 8, 3H, *Me*CH). GC(β *dex*; 90^o, isothermal): t_R (min) 139 (*R*), 142 (*S*, major product with *R,R*-**5.4**) (assigned by comparison to literature).[18]

3-Benzylamino-2-methyl-propanenitrile. Reaction as described above (methacrylonitrile, 5.0 mmol, 0.42 mL; **5.4**, 0.05 mmol, 1.82 mL, 0.0274 M; benzylamine, 5.0 mmol, 0.55 mL; 24 h) yielded a colorless oil (530 mg, 55%).

^{1}H NMR (CDCl3, 400 MHz): δ7.23—7.34 (m, 5H, Ar), 3.85 (s, 2H, CH_2-Bn), 2.49- 2.90 (m, 3H, CH_2 & MeC*H*), 1.31 (d, J = 6, 3H, *Me*CH).

Determination of reaction kinetics. For slow reactions, the required amount of diethylamine, methacrylonitrile and triethylamine (either directly or from C_6D_6 stock solutions) were combined with C_6D_6 in a J. Young tube inside a glove box. A stock solution with the required amount of **5.4** was added last, yielding a total reaction volume of 500 µL in most of the cases. In several cases, hexamethyldisiloxane served as an internal standard. Conversion was monitored by ^{1}H NMR spectroscopy at the required intervals. For faster reactions, reagents were combined in a small vial and agitated. Samples were

taken at the desired intervals and added to vials containing wet $CDCl_3$ for NMR analysis (Control experiments confirmed that no further reaction took place in wet $CDCl_3$.)

5.6 Acknowledgements. Myriam Kebdani's contributions to these studies during her internship are gratefully acknowledged. We thank J. Bartholomeus, C. Trudel and Prof. H. Lebel for chiral GC analyses, B. B. Mougang Djanteng, A. B. Salah and Prof. D. Zargarian for access to GC-MS and F. Bélanger for support with X-ray diffraction studies. Funding was provided by NSERC, Centre en chimie verte et catalyse (CCVC) and FQRNT (Ph. D. stipend for I. E-Z. and T. W.).

Supporting Information. Table S5.1 and Figure S5.1. Single-crystal diffraction data (CIF).

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Supporting Information

Selective and Non-selective Aza-Michael Additions Catalyzed by a Chiral Zirconium Bisdiketiminate Complex

Given the problems of integrating small peaks in crowded NMR spectra, the accuracy of the provided conversions should be considered to be less than ±5%. There is thus no meaningful distinction between low yields of 5% and no reaction (0%).

Table S5.1. Blank reactions in the absence of catalyst

Nucleophile	**Alkene**	**Reaction time/min**	**Conversion**
Benzylamine	Acrylonitrile	24 h	6%
Aniline	Acrylonitrile	24 h	0%
4-methoxyaniline	Acrylonitrile	150	5%
4-chloroaniline	Acrylonitrile	150	4%
Benzylamine	Metacrylonitrile	24 h	5%
Diethylamine	Metacrylonitrile	24 h	4%
Aniline	Methyl acrylate	24 h	4%
Benzylamine	Methyl acrylate	24 h	5%
Diethylamine	Methyl acrylate	24 h	0%
Morpholine	Methyl crotonate	5 h	0%
Diethylamine	Methyl crotonate	5 h	0%
Benzylamine	Methyl crotonate	5 h	0%
Aniline	Methyl crotonate	5 h	0%

Reaction conditions: C_6D_6, ambient temperature, [Amine]:[Alkene]:[**4**] = 1 M:1 M:0.01 M, yield determined by NMR.

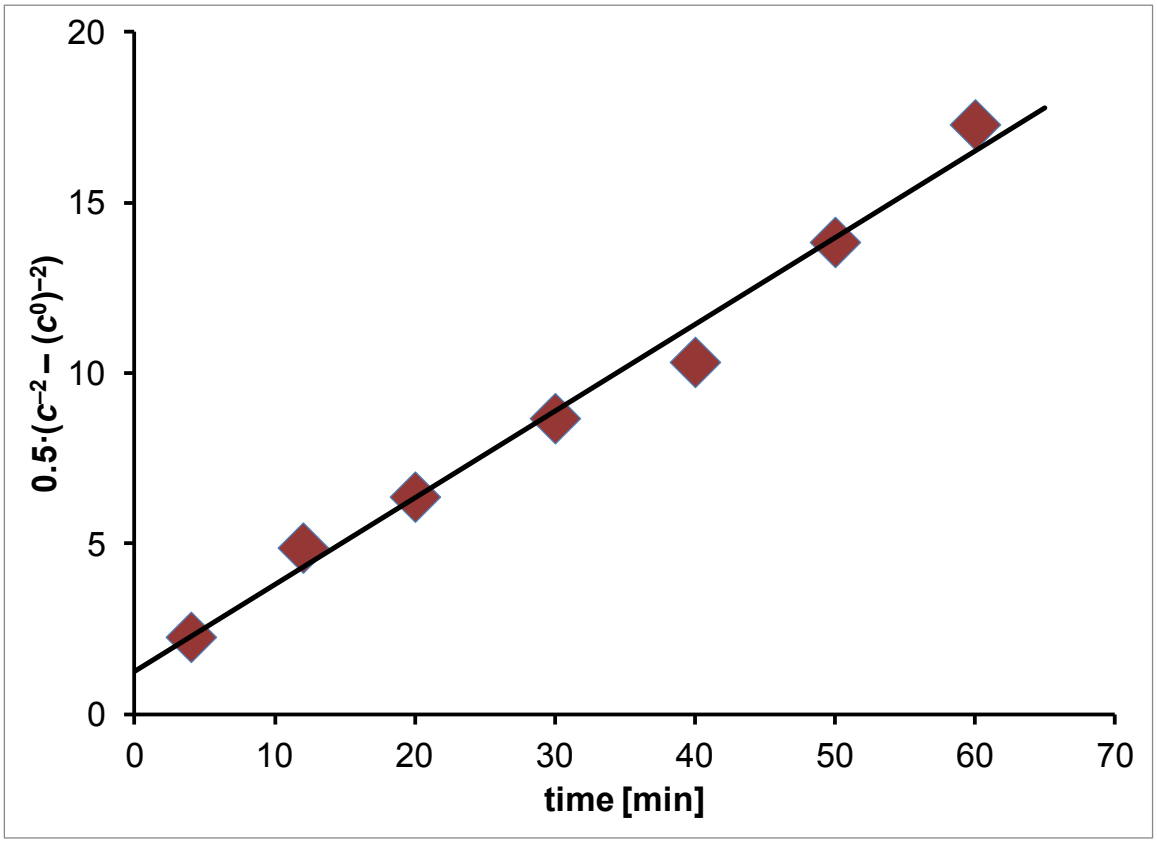


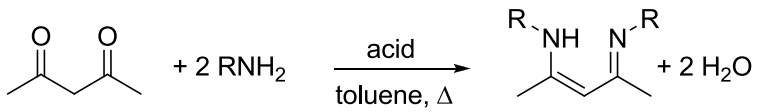
Figure S5.1. Linearized concentration time profile. C_6D_6, ambient temperature, $[NEt_2H]_0$ = [metacrylonitrile]$_0$ = 1.0 M, [**4**] = 10 mM (1.0%). y = 0.25(1)x + 1.3(5)

CHAPTER 6

Conclusion and Perspectives

6.1 Ligand synthesis

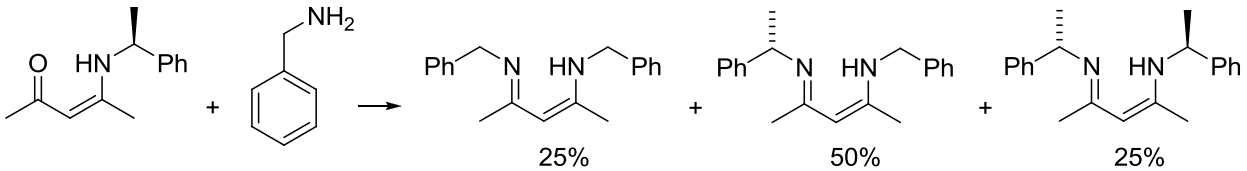
6.1.1 Symmetric *N*-alkyl *β*-diketimines (*nacnac*^{R}H) are now economically accessible through a simple one-pot reaction from condensation of acetylacetone with the appropriate primary or secondary amine. High yields of *N*-alkyl *β*-diketimines are obtained under the following optimized conditions (Scheme 6.1): (1) The presence of one equiv. of TsOH and/or HCl as activating agent(s) for the substitution of the second alkyl amine. Their use is advantageous when compared to other activating agents such as Meerwein salts that are toxic, expensive and difficult to handle ambient atmosphere. (2) The use of minimum amount of solvent. (3) Azeotropic removal of water.



R= nPr, Bn, CH(Me)Ph, iBu, iPr, Cy & Me

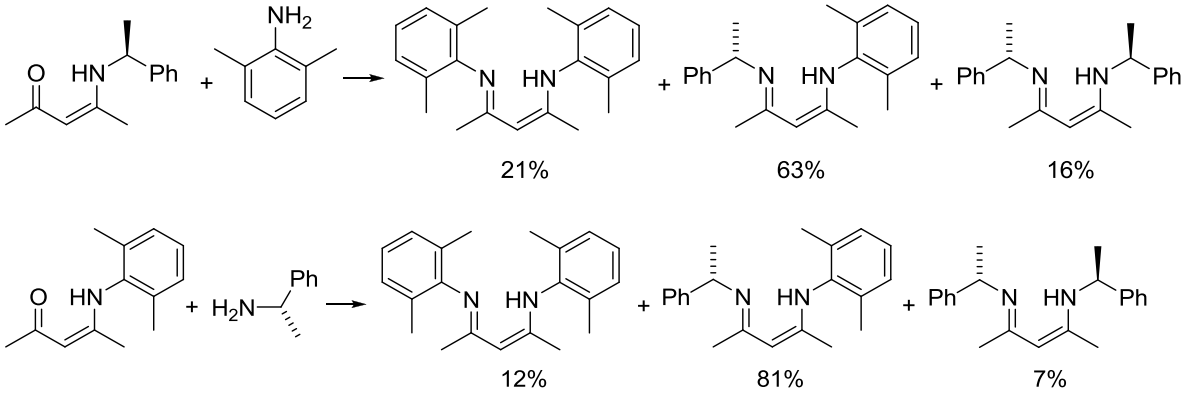
Scheme 6.1

6.1.2 Non-symmetric *β*-diketimines (*nacnac*$^{R,R'}$H): The condensation of acetylacetone with two different alkyl amines, under the same optimized conditions, gave a statistical mixture of the desired non-symmetric product and the symmetric diketimines of each of the alkyl amines used. A detailed study showed that the fast scrambling between the amines is responsible for the low efficiency of this method.



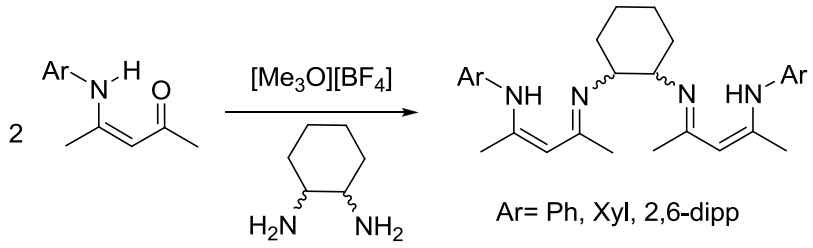
Scheme 6.2

Condensation of acetylacetone with a mixture of an aliphatic amine and an aromatic amine favours the formation of the monocondensation product having an aromatic substituent, independent from the starting material used, followed by condensation of the aliphatic amine. Although the mixed diketimine is obtained in higher than statistic ratio, isolation was not possible.



Scheme 6.3

Preparing a bridged diketiminate using an alkyl bridge and alkyl substituents was neither possible using our optimized synthesis for the *N*-symmetric diketimines nor using activating agents such as Meerwein salt or Me_2SO_4. However using aniline in combination with an alkyl bridge after activation with Meerwein salt, three ligands with cyclohexylene bridge and *N*-aryl substituents (phenyl, bis-diisopropylphenyl and xylyl) were prepared (Scheme 6.4).

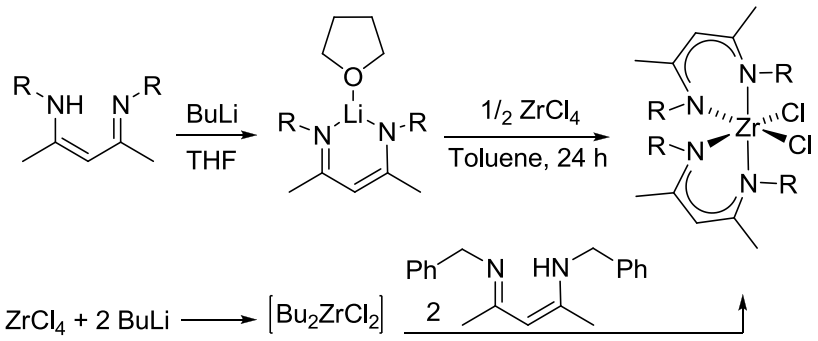


Scheme 6.4

In conclusion, symmetrical diketimine ligands are readily accessible and suitable for large scale applications. The use of cheap starting materials and activators, low solvent quantities and of non-toxic materials under ambient conditions are amenable to use in industry and concur with the principles of green chemistry. On the other hand, the preparation of bridged ligands is possible only with the use of Meerwein salt. While this method raised the cost of preparation, the main cost factor in enantiopure diketimine will nevertheless remain the enantiopure amine.

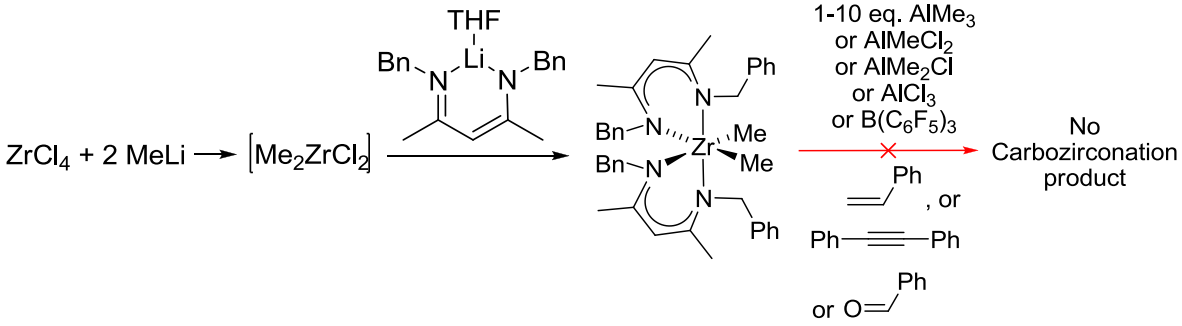
6.2 *Bis (N*-alkyl substituted β-diketiminates) zirconium complexes

While the preparation of bis(diketiminate) zirconium complexes with *N*-aryl substituent was impeded by the presence of *ortho*-substitution on at least one of the two ligands, bis(diketiminate) zirconium complexes with *N*-alkyl substituents are readily accessible, not just with primary alkyls such as benzyl, but even with bulkier secondary alkyls, such as cyclohexyl or the *R*,*R*-methylbenzyl. The preparation of these complexes is achieved in a one pot-synthesis via two main routes (Scheme 6.5); (1) The lithiation of the ligand followed by reaction with $ZrCl_4$, (2) The *in situ* preparation of $n Bu_2ZrCl_2$ followed by protonation of the butyl groups with the free ligand. Although yields are higher in the latter method, it is limited to the preparation of the complexes with primary alkyls, mainly due to a competition with the decomposition side reaction of $n Bu_2ZrCl_2$. In the obtained *cis*-octahedral complexes, it is noteworthy that diketiminate ligands with aliphatic *N*-substituents coordinate in a κ^2-coordination mode, while in sterically hindered complexes a κ^2, η^2-coordination mode seems to be a general mode for at least one of the two diketiminate ligands.



Scheme 6.5

The steric crowding caused by the *N*-substituents complicated the exchange of the chlorides with alkyls for targeted applications in organic catalysis. Methylation of the dichloride complexes finally met success using a MeLi/$AlMe_3$ mixture, probably aided by $AlMe_3$-assisted ligand dissociation. Alternatively the dimethyl complexes were prepared by methylation of $ZrCl_4$, followed by a salt metathesis reaction with the lithiated ligand. However due to the decrease in the Lewis acidity of the metal with *N*-alkyl substituents or, more likely, due to steric crowding, the dimethyl complex did not insert alkenes, alkynes, or even aldehydes after activation with AlX_3 or borane (Scheme 6.6).



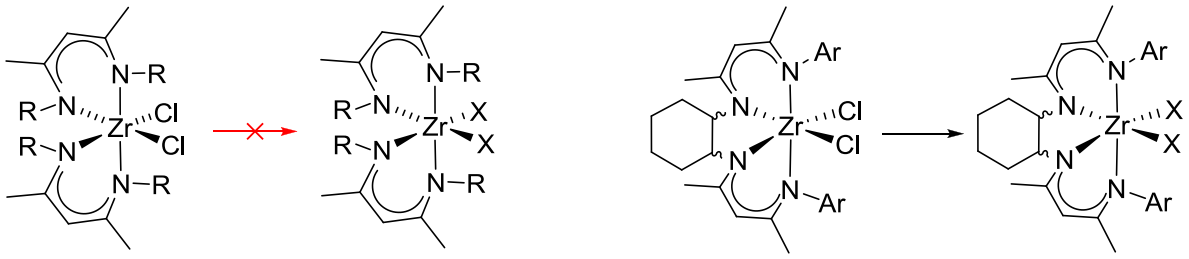
Scheme 6.6

Unfortunately all of the obtained complexes showed fast isomerisation at room temperature and activation parameters are in agreement with a Bailar-Twist mechanism.

Despite the simplicity of their synthesis, unbridged bis(diketiminate) zirconium complexes seem not to be suitable active precursors since even with *N*-benzyl substituents, steric crowding prevented simple reactions at the coordination sites. It seems unlikely that this reactivity will increase with any simple changes made to the ligand and the introduction of a cyclohexylene bridge seemed to be crucial to prevent epimerization and to allow access to coordination sites for reaction.

6.3 Bridged diketiminate complex

The chloride ligands are in this case readily replaceable with ethoxide or methyl (Scheme 6.7). Although there is no indication for epimerization taking place, some indications for a fluxional behaviour are seen in the variable temperature NMR spectrum. It is possible that the degree of fluxionality of the obtained complexes is not just bridge/*N*-substituent dependent but could also be backbone dependent.



Scheme 6.7

6.3.1 Bridged diketiminate complex in lactide polymerization:

In lactide polymerization, the bridged (diketiminate) zirconium diethoxide complex showed the highest activity ever observed for any group 4 metal complex. Unfortunately the zirconium complex showed only very limited stability under polymerization conditions, showed no stereospecifity and catalyzed intramolecular transesterification.

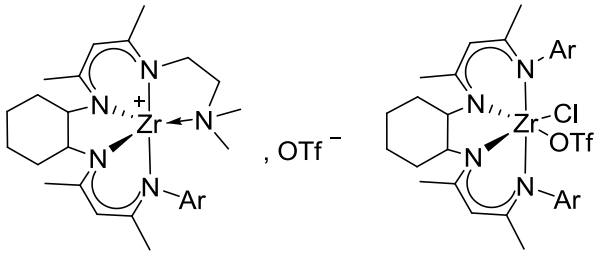
Given the low stability of the bridged (diketiminate) zirconium diethoxide complex under polymerization conditions and an activity several orders of magnitude above other octahedral zirconium complexes for lactide polymerization, it is very doubtful that minor modifications of the diketiminate ligand would yield a suitable catalyst. Instead, modifications should be oriented towards alternative geometries such as tetrahedral zirconium complexes.

6.3.2 Bridged diketiminates in aza-Michael additions

The study of chiral *R,R*-C_6H_{10}(*nacnac*^{Xyl})$_2$Zr(OTf)$_2$ as catalyst for aza-Michael additions showed to be highly active for the addition of primary amines, secondary amines and anilines to activated acylonitriles, acrylates or cylcohexenone with activities correlating to the nucleophilicity of the employed amine and to the steric hindrance of the alkene used.

The surprising change of geometry of the triflate compound towards pseudo-tetrahedral is probably responsible for the low enantioselectivities observed during aza-Michael additions. With the obtained C_1 symmetry and two reactive coordination sites, substrates for aza-Michael additions have the possibility to coordinate on two diastereotopic sites. It will not be possible to improve the selectivity (ee) of this catalyst without blocking one of the two different ancillary sites, e.g. in a five coordinated cationic compound. Considering

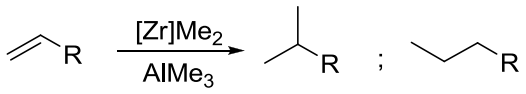
the pseudo-tetrahedral geometry of the bis-triflate complex in the solid state, only one of the two ligand backbones is pointing towards the metal center, therefore providing dangling lewis base substituents that could coordinate to the metal center will probably stabilize a five coordinated compound. Another possibility would be to isolate the bridged bis-diketiminate zirconium monochloro monotriflate complex (Scheme 6.9)



Scheme 6.8.

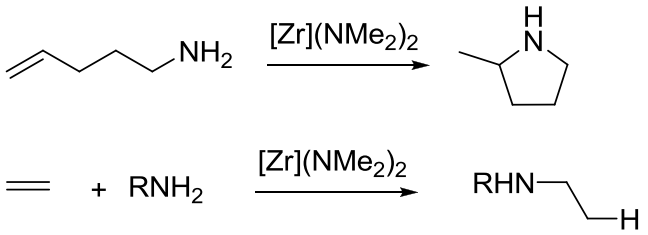
In general, bridging of two diketiminate ligands by a cyclohexylene bridge increased, as intended, the reactivity of bisdiketiminate zirconium complexes, which are now able to undergo ligand exchange and show vastly higher activities in lactide polymerization and in aza-Michael additions. The high sensitivity of these catalysts towards protic solvents or substrates limits their use to dry conditions, however.

Bridging the diketiminates also allowed the formation of the dimethyl complex of which its reactivity remained unexplored. It would be of high interest to use the dimethyl complex as a catalyst for carbozirconation reactions (Scheme 6.9) since this could introduce a new alkyl group as well as a functional group on a non-activated olefin.[1]



Scheme 6.9. Zr-Catalyzed carboalumination of non-activated olefins

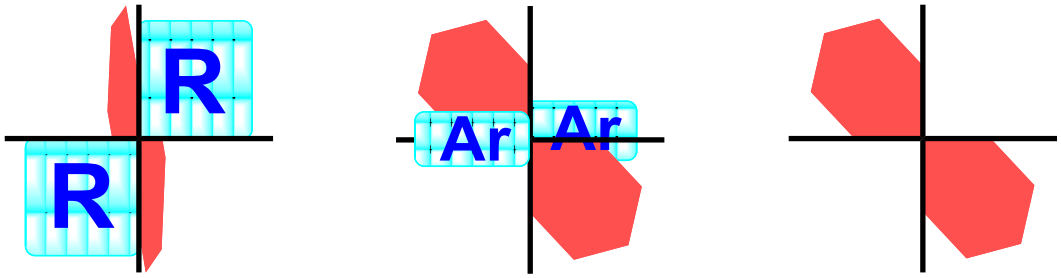
The obtained bridged bis-diketiminate zirconium diamido complex could also be used as catalyst for enantioselective inter- and intra-hydroamination of non-activated olefin following an N-H activation mechanism.[2]



Scheme 6.10. Intra- and inter-hydroamination of non-activated olefin

Contrary to the unbridged bis-diketiminate *cis* octahedral zirconium complexes, the structures of the bridged ones depend on the size of the ancillary ligand X. While *trans* configurations of the bridged complexes are obtained with chlorides and methyls ancillary ligands, *cis* configurations resulted from steric hindrance of ancillary ligands such as ethoxides and dimethylamides (X= Et_2O and NMe_2). As a matter of fact, the tethering via a cylohexylene unit of two diketiminates placed the *N,N′*-aryl substituents in an eclipsed manner, in the *cis* adduct, having an aryl substituent above one ancillary ligand and another aryl substituent below the second one; on the other hand, the two backbone compartments of the bridged ligand are placed between the two ancillary sites or between a nitrogen and a chloride instead of being eclipsed along the two apical axes. This acute deformation of the

eclipsed octahedral geometry is still responsible for steric hindrance around the metal center even if it is less pronounced when compared to the unbridged systems.



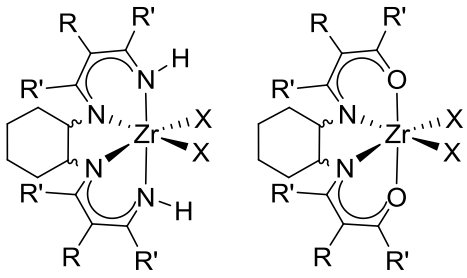
Unbridged bis-diketiminates

Cyclohexyldiamine bridged bis-diketiminates with aromatic *N*-substituents

Cyclohexyldiamine bridged bis-diketiminates without aromatic *N*-substituents

Scheme 6.11

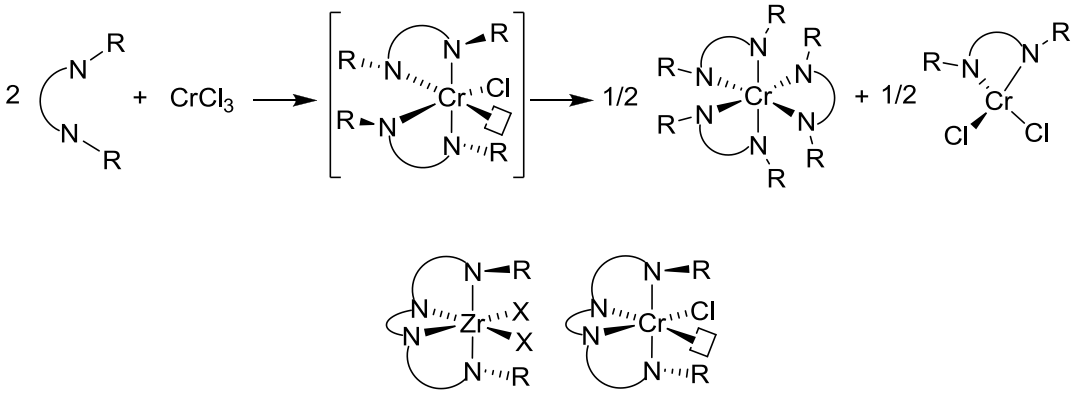
It seems that the main drawback of these complexes relies on their structural stability under catalytic conditions. Therefore stabilizing an eclipsed *Cis* C_2-octahedral geometry in solution necessitates the use of bridged diketiminates with less steric demanding *N*-substituents or the use of bridged *N*-acetylacetonates both ligands having more bulk on the backbone to prevent their interactions with the metal.



Scheme 6.12

A further modification of this system could be inspired from the works of my collegue Saida Latreche, who conducted research on the preparation of $(nacnac^{Bn})_2CrCl$ containing a free coordination site and thus providing easier access to the chloride ligand. Instead, she

obtained a mixture of mono and tris diketiminate chromium complexes suggesting the formation of the bisdiketiminate as an intermediate, which rearranges afterwards into the mono and tris diketiminate complexes.[3] It would be of interest to employ the cyclohexylene bridged diketiminate with Cr(III) (Scheme 6.8). Use of a bridged ligand would prevent ligand redistribution. The resulting 5-coordinate Cr(III) complex offers easy access to the ancillary coordination sites and avoid the ambiguity of two identical reactive groups. This could lead to higher ee in asymmetric aza-Michael additions and more stereocontrol in lactide polymerization.



Scheme 6.13

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