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A Discrete Ortho-Lithiated Acetophenone Imine Derivative: Isolation, Characterization, and Synthesis of Group IV Metal Complexes

Tamam I. Baiz and Joseph A. R. Schmidt*

Department of Chemistry, The University of Toledo, 2801 West Bancroft Street, MS 602,
Toledo, Ohio 43606-3390

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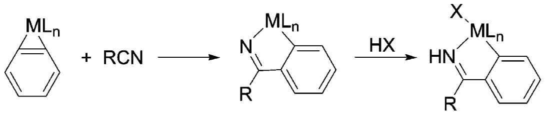
*Summary: The reaction of a 3′,4′-methylenedioxyacetophenone imine (L-H; **1**) with ^{n}BuLi allows for the synthesis and isolation of a discrete ortho-lithiated imine (L-Li; **2**). Through the use of salt metathesis pathways, this monoanionic, chelating N∼C ligand has been employed to produce a series of titanium and zirconium complexes, including L_2MX_2 (M = Ti, X = Cl (**5**); M = Zr, X = Cl (**3**), CH_2SiMe_3 (**4**)) and $L_2Ti{=}N^tBu$ (**6**).*

The use of ortho-metalated ketones in late-metal catalysis has become quite common in recent years. Notably, Crabtree has shown that iridium hydrides supported by ortho-metalated acetophenone ligands function as excellent catalysts for the hydroalkoxylation and hydroamination of alkynes.[1,2] In addition to the use of ortho-metalated ketones, it has been shown that the related imines also support a wide variety of late-metal chemistry.[3−15] Recently, Lai and co-workers reported the use of ortho-metalated imines in iridium-mediated hydroamination of alkenes and alkynes.[15] On the basis of these results, we hypothesized that ortho-metalated imines could likewise function as useful ancillary ligands for *early-metal* organometallic complexes.

Although late-metal complexes have been well investigated, ortho-metalated imine ligands have seen only scant use with highly Lewis acidic early transition metals. In fact, to date there is no direct route for the synthesis of early-metal complexes employing these ligands. In the cases where late metals are used, ortho-metalated imine complexes are readily produced by oxidative addition of the aryl C−H bond following ligation of the imine nitrogen. This direct synthetic route is unavailable for early transition metals, as traditional early-metal starting materials typically contain metal centers in their maximum oxidation states (eliminating the possibility for oxidative addition of the aryl C−H bond). Additionally, due to the redox properties of early metals, the use of starting materials with lower oxidation states generally results in reductive processes, rather than the desired C−H activation of these species.[16,17] To date, the only reported route for the synthesis of early-metal ortho-metalated imine complexes entails the insertion of a cyano group into a metal−benzyne bond, yielding dianionic versions of these ligands; this is a method which has been employed for nitriles,[18−22] cyanophosphines,[23−25] and cyanamides[26] (Scheme 1). One major limitation of this synthetic route is that the nitrogen (anionic following cyano insertion) can only be converted into the parent unsubstituted imine (RC═N$^-$ or RC═NH), eliminating steric and electronic modification of this donor atom.

Scheme 1. Early-Metal Ortho-Metalated Imine Complexes Produced by Cyano Insertion Reactions[a]



[a] M = Ti, Zr, Ta; R = alkyl, aryl, amino, phosphino; HX = weak acid, such as alcohol, amine, thiol.

As a part of our research effort toward the design of new unsymmetrical, bidentate ligand-supported complexes for use in catalytic bond-forming reactions, we present the synthesis and isolation of a newly developed bidentate, monoanionic, ortho-lithiated imine ligand with straightforward steric and electronic tunability. Herein, we detail the synthesis of several group IV metal complexes derived from a 3′,4′-methylenedioxyacetophenone aryl imine. Ultimately, we speculate that

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* To whom correspondence should be addressed. E-mail: Joseph.Schmidt@utoledo.edu.

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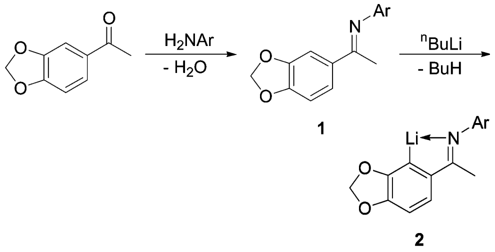
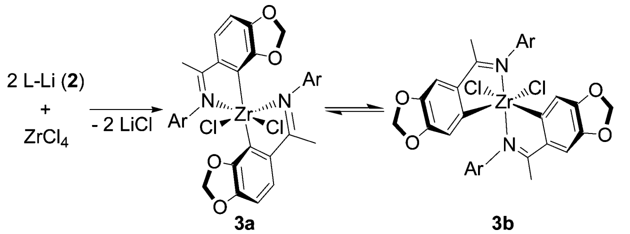
Scheme 2. Synthesis and Lithiation of the Acetophenone Imine Derivative (Ar = 2,6-Et$_2$C$_6$H$_3$)



Scheme 3. Salt Metathesis of the Ortho-Lithiated Imine 2 with ZrCl$_4$ Leading to L$_2$ZrCl$_2$ (3) as an Equilibrium of Two Structural Isomers: 3a and 3b[a]



[a] Ar = 2,6-Et$_2$C$_6$H$_3$.

this ligand platform will allow access to a wide array of complexes yielding new catalytic and stoichiometric reactivity.

The acetophenone imine ligand (L-H; **1**) was readily synthesized by the Schiff-base condensation of 3′,4′-methylenedioxyacetophenone with excess 2,6-diethylaniline in the presence of catalytic *p*-toluenesulfonic acid.[27] The reaction mixture was brought to reflux for 2 days, using a Dean−Stark trap to collect the byproduct water upon formation. After organic extraction, **1** was obtained by vacuum distillation, providing the ligand in 85% yield (Scheme 2). The product could be readily identified by NMR spectroscopy. Notably, a sharp singlet was observed at δ 5.28 in the ^{1}H NMR spectrum of **1**, representative of the $-$OCH_2O$-$ moiety on the phenyl ring.

The reaction of **1** with a stoichiometric amount of ^{n}BuLi in pentane resulted in deprotonation at the 2′-position to yield 1 equiv of butane, with concomitant formation of the ortho-lithiated imine ligand (L-Li; **2**) (Scheme 2). As the reaction was very rapid and exothermic, cooling in an ice bath was used to minimize byproduct formation. Following the reaction, the mixture was slowly warmed to room temperature. The product, an air- and moisture-sensitive yellow solid, was washed liberally with pentane and dried under vacuum, affording **2** in excellent yield. Quenching of the lithiated species with D$_2$O confirmed the regioselective lithiation, with quantitative recovery of 2′-*d*-**1**. The lithiated ligand **2** could also be readily characterized by its NMR spectroscopic data, with the most notable peak again being the $-$OCH_2O$-$ resonance, now appearing as a singlet at δ 4.81.

In order to demonstrate the utility of ortho-metalated imines as ancillary ligands in early-metal organometallic chemistry, a series of group IV metal complexes were targeted, with salt metathesis reactions being the preferred method of synthesis. Two equivalents of **2** were found to react readily with ZrCl$_4$ to form the complex L$_2$ZrCl$_2$ (**3**), where two halide ligands were replaced by two bidentate ortho-metalated imines (Scheme 3). The reaction was carried out at 0 °C and then the mixture was slowly warmed to ambient temperature overnight. The product **3** is insoluble in pentane and diethyl ether and sparingly soluble in toluene, while slowly decomposing in THF and CH$_2$Cl$_2$, preventing efficient isolation from the byproduct LiCl. Liberal washing with pentane was used to remove excess ligand, and drying under vacuum yielded **3** in 85% yield as an orange solid. All attempts to recrystallize this material were unsuccessful, giving only a microcrystalline solid.

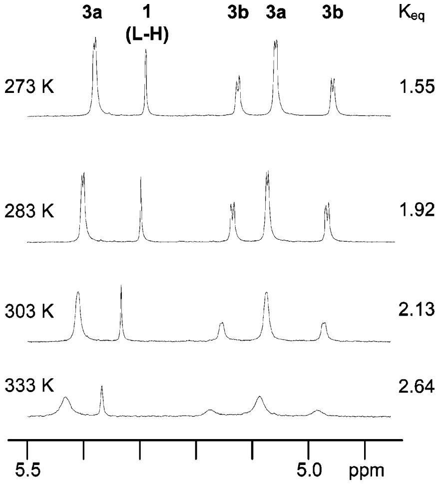


Figure 1. Experimental K_{eq} values and representative ^{1}H NMR spectra of the $-$OCH_2O$-$ region at various temperatures for the equilibrium between **3a** and **3b**. A small amount of ligand **1** (L-H) is present.

The ^{1}H NMR spectrum of **3** indicated the presence of two highly symmetrical species in solution, most readily identified by the distinctive peaks for the $-$OCH_2O$-$ resonances, appearing as two weakly coupled doublets for each isomer. The two distinct sets of peaks observed for the two isomers showed varying ratios, depending on solution temperature (Figure 1). Thus, the presence of two compounds in solution is inferred; there is not just one species with inequivalent ligands. On the basis of the observed symmetry, the empirical formula, and the propensity for six-coordinate zirconium complexes to have cis-chloride ligands, we suggest that the two observed species are the C_2-symmetric L$_2$ZrCl$_2$ isomers **3a**,**b** (Scheme 3). The observed C_2 symmetry necessitates that either the carbons or the nitrogens of the two ligands be arranged in a trans configuration. Variable-temperature (VT) ^{1}H NMR spectroscopy revealed that one isomer (denoted **3a**) was more thermodynamically stable than the other (**3b**) in the temperature range 253−333 K,[28] and the thermodynamic parameters of the equilibrium were investigated. Equilibrium constants (K_{eq}) were calculated throughout the temperature range, according to the equation K_{eq}= [**3a**]/[**3b**], where the relative ratios of the two species were obtained from the integration of the $-$OCH_2O$-$ proton resonances. The standard enthalpy (6.6 kJ mol^{-1}) and entropy changes (28 J mol^{-1} K^{-1}) were estimated from a van't Hoff plot (Figure 2). These small isomerization enthalpy and entropy values support near-equal concentrations of the two isomers at approximately −40 °C.

Compound **3** was further functionalized by reaction with 2 equiv of LiCH$_2$SiMe$_3$ to produce the dialkylated species L$_2$Zr(CH$_2$SiMe$_3$)$_2$ (**4**) (Scheme 4) in moderate yield.[29] Notably, the ^{1}H NMR spectrum of **4** showed the presence of only one isomer in solution, as evidenced by the equivalence of the SiMe_3

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[27] An earlier report details the synthesis of a related aldimine species (3′,4′-methylenedioxybenzaldehyde cyclohexyl imine) and its in situ lithiation, as determined by quenching experiments: Ziegler, F. E.; Fowler, K. W. *J. Org. Chem.* **1976**, *41*, 1564.

[28] The C_2 isomer with ligand carbon donor atoms in a trans orientation was ascribed to the more stable isomer on the basis of the crystal structure of the dialkylated species **4**, detailed below.

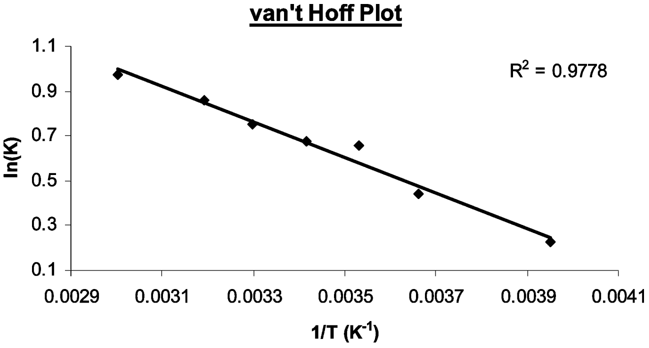
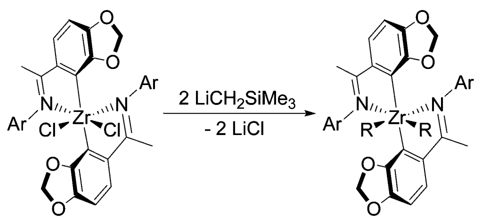


Figure 2. van't Hoff plot for thermodynamic analysis of the equilibrium of **3a** and **3b**.

Scheme 4. Reaction of 3 with $LiCH_2SiMe_3$ Leading to $L_2Zr(CH_2SiMe_3)_2$ (4)[a]



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R = CH_2SiMe_3 (**4**)

[a] Ar = 2,6-$Et_2C_6H_3$.

resonances (*δ* 0.22) as well as the presence of only two weakly coupled doublets for the diastereotopic $-OCH_2O-$ protons. The lack of isomerization in this species can be attributed to the steric demands of the large alkyl groups employed, forcing the complex to adopt the more sterically favored isomer. X-ray-quality crystals of **4** were obtained from diethyl ether at −25 °C, and the crystal structure reveals that the carbons of the two ligands are in a trans orientation, while the two ligand nitrogen atoms and the methylene carbons of the (trimethylsilyl)methyl groups are each oriented in a cis arrangement (Figure 3).[30] The observed Zr−C distances are very similar to those observed in other $Zr-CH_2SiMe_3$ complexes.[31−33] Additionally, a significant intramolecular *π*-stacking interaction is observed between the ortho-metalated imine ligands. The N−Ar and 3′,4′-methylenedioxyphenyl planes are nearly parallel (average deviation ~20°), and the distance between the offset phenyl rings is approximately 3.4 Å, a value indicative of strong *π*-stacking interactions.[34] This contributes to the observed stability of **4** and is also likely an influence on the isomerization process observed for **3**.

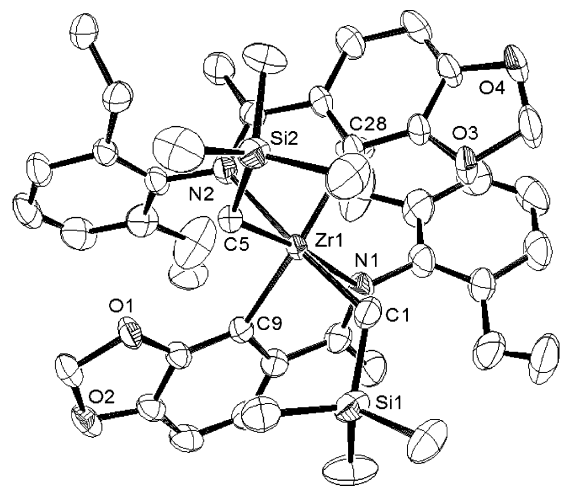

Figure 3. ORTEP diagram (50% probability) of $L_2Zr(CH_2SiMe_3)_2$ (**4**). Disordered methyl groups, hydrogen atoms, and cocrystallized ether have been removed for clarity. Bond lengths (Å) and angles (deg): Zr1−C1 = 2.228(3), Zr1−C5 = 2.223(3), Zr1−C9 = 2.297(3), Zr1−C28 = 2.295(3), Zr1−N1 = 2.540(3), Zr1−N2 = 2.510(2); C1−Zr1−C5 = 90.2(1), C1−Zr1−C9 = 99.9(1), C1−Zr1−C28 = 107.3(1), C1−Zr1−N1 = 87.5(1), C1−Zr1−N2 = 174.8(1), N1−Zr1−N2 = 95.7(1).

Titanium complexes with compositions similar to those of the zirconium species discussed herein were also synthesized. Two equivalents of the lithiated ligand **2** reacted readily with $TiCl_4$ to yield L_2TiCl_2 (**5**). Compound **5** was virtually insoluble in a wide range of organic solvents, making its complete isolation and characterization untenable. In addition to poor solubility, **5** exhibited little or no reactivity with a diverse array of lithium reagents, including MeLi, $LiCH_2SiMe_3$, $LiNEt_2$, and LiNH(2,6-*i*-$Pr_2C_6H_3$). The reactions were invariably slow and proceeded to poor conversion, even with heat and in a variety of solvents. This was somewhat surprising, as titanium was expected to be more reactive than its heavier congener zirconium. Perhaps, since the titanium is smaller, the steric bulk of the ortho-metalated imine ligands is more pronounced in **5**, hindering access to the titanium center. It is also possible that liberated lithium chloride is retained within the metal complex, forming an "ate" salt, which would serve to further reduce the reactivity of these species.[35] Numerous examples in the literature have shown that small alkali-metal salts are often trapped in the coordination sphere of early transition metals, forming "ate" salts of this type.[36−39]

In order to circumvent these solubility issues, we investigated a titanium imido precursor as an entry point for this chemistry. Two equivalents of **2** were found to react readily with $(py)_2Ti(=N^tBu)Cl_2$[40] to form $L_2Ti=N^tBu$ (**6**) (Scheme 5). The red solid that was obtained showed moderate thermal stability (the solid decomposes at 183 °C) and was soluble in most nonpolar solvents. Additionally, it showed no evidence of coordination by a variety of coordinating solvents, supporting its formulation as a five-coordinate titanium imido species. The NMR spectra of **6** indicated the presence of a single, highly symmetrical

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[29] The analogous L_2ZrMe_2 species was synthesized similarly from reaction of **3** with 2 equiv of MeLi. Its solubility was virtually identical with that of **3**, preventing its isolation from unreacted **3**. It could be readily observed spectroscopically: ^1H NMR (C_6D_6, 400 MHz) *δ* 7.14−7.01 (m, 6H), 6.90 (d, 2H, 8 Hz), 6.58 (d, 2H, 8 Hz), 5.32 (s, 4H), 2.59 (s, 6H), 2.56−2.38 (m, 8H), 1.75 (s, 6H), 1.15 (t, 12H, 8 Hz).

[30] Crystal data: $C_{46}H_{62}N_2O_4Si_2Zr\cdot{}^1/_2C_4H_{10}O$, triclinic, $P\bar{1}$, a = 11.4685(6) Å, b = 12.6056(6) Å, c = 18.3425(9) Å, α = 81.983(1)°, β = 77.081(1)°, γ = 65.461(1)°, T = −138 °C, R1 = 0.068, wR2 = 0.199 (all data).

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[35] A flame test indicated the presence of lithium in the sample, but this may be representative of incomplete removal of LiCl from the material on workup. A ^7Li NMR showed only a single resonance at *δ* 0.00 ppm, representative of LiCl. This still does not preclude the presence of "ate" salts within the material, as it has only very low solubility in the NMR solvent (C_6D_6).

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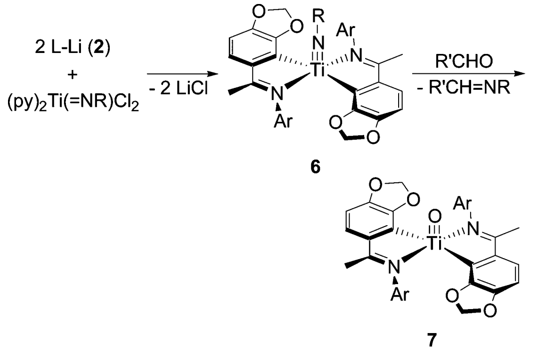
Scheme 5. Synthesis of the Titanium Imido Derivative 6 and Its Subsequent Reactivity with Aldehydes To Form the Analogous Oxo Product 7[a]



[a] Ar = 2,6-Et$_2$C$_6$H$_3$; R = ^{t}Bu; R′ = 3,4-methylenedioxyphenyl.

species, most likely a square-pyramidal complex with the two bidentate ligands in trans basal positions and the imido group occupying the electronically favored axial position, where it functions as a six-electron-donor ligand. Titanium complexes employing bulky bidentate ligands with ^{t}Bu−imido groups are commonly found with five-coordinate pseudo-square-pyramidal coordination geometry,[41−44] whereas bridging imido ligands have generally been limited to lower coordinate titanium species or those with less sterically bulky ligands.[43,45]

As expected, **6** was shown to undergo Wittig-like reactivity by an NMR-scale reaction with an aldehyde (piperonal) to form a metal−oxo product (Scheme 5). The metathesis reactions between metal imido complexes and carbonyl groups have been well documented, generally occurring via a cycloaddition reaction to yield an imine and an oxo product.[46]

In summary, the synthesis of a bidentate, monoanionic, ortho-metalated imine ligand, which can be readily synthesized using a Schiff base condensation and easily activated with ^{n}BuLi to form the corresponding ortho-lithiated compound, has been reported herein. The coordination chemistry of this new ligand with titanium and zirconium precursors has been explored, resulting in the synthesis of unprecedented ortho-metalated titanium and zirconium complexes through salt metathesis routes. We are currently investigating the use of these group IV metal complexes in a broad range of stoichiometric and catalytic applications. Additionally, we will continue to explore the utility of these ortho-metalated imines as supporting ligands for other early-metal centers.

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Supporting Information Available: Text and a table giving experimental procedures and characterization data for **1**−**7**, experimental conditions and K_{eq} values for **3** at various temperatures, and crystallographic procedures and crystal data for **4** and a CIF file giving additional crystallographic data, including bond lengths and angles of compound **4**. This material is available free of charge via the Internet at http://pubs.acs.org.

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