

# Direct Ortho-Metallation of Aryl Substituted Heteroaromatic Ligands with $\text{TiCl}_4$ and $\text{ZrCl}_4$ - An Experimental and DFT Study with 2-Phenyl Indole as the Ligand.

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**ABSTRACT:**  $\text{TiCl}_4$  and  $\text{ZrCl}_4$  each react with aryl substituted heteroaromatic ligands such as 2-Phenyl-1H-indole, to thermally undergo one-pot direct orthometallations, and yield new types of cyclometallated complexes.  $\text{TiCl}_4$  coordinates at ambient temperature to form the indole complex (**1**), which undergoes isomerization to the indolenine (**2**). DFT calculations indicate that complex (**2**) is more stable than (**1**) by 6.4 kcal/mol. Upon warming to about 105°C, extrusion of HCl takes place with simultaneous orthometallation (**3**), yielding a metallacyclic complex (**4**). The mechanism of the orthometallation has been investigated by DFT, and the transition state confirmed by IRC. At the elevated temperature the transition state (**3**) involves the synchronous transformation of four atoms, Ti, ortho C, H, and the apical Cl. The ortho C of the phenyl group acquires a partial positive charge through conjugation, forming a  $(\text{C-H})\delta^+ \dots \text{Cl}\delta^-$  interaction, with a simultaneous elongation and breaking of the Ti-Cl bond, resulting in the formation of a Ti-C bond. The latter bond is created at the same time a Ti-Cl bond is breaking, and an HCl is being formed, as illustrated in transition state (**3**). This HCl is retained in the crystal structure of the final product (**4**), by electrostatic interaction with one of the chloride ligands. The reaction sequence may be repeated with  $\text{ZrCl}_4$  in place of  $\text{TiCl}_4$ . Complex (**4**) has been isolated and characterized by solid state  $^{13}\text{C}$  NMR CPMAS/DDMAS spectra, X-ray photoelectron spectroscopy (XPS), infrared and analytical data. The intermediate structures (**1** through **4**), as well as the sequence of ligand transformations to produce the ortho-metallated complex are supported by DFT calculations. The new cyclometallated complexes are thermally stable, unlike several other complexes featuring a Ti-C bond. They may have important applications, such as in  $\alpha$ -olefin polymerization catalysis, and as building blocks in metalodrugs for cancer therapy.

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## INTRODUCTION

Addition compounds of titanium tetrachloride with various amines have been widely used in synthetic organic chemistry (1). Similarly, aromatic amines such as carbazole, complexed with  $\text{ZrCl}_4$ , have found applications as catalysts in Ziegler-Natta polymerizations (2). Furthermore, Pt complexes of 2-phenyl indole derivatives have been tested as cytotoxic agents against human breast adenocarcinoma cell lines (3).

Direct  $\text{C}_{\text{aryl}}$  metallation with Ti or Zr compounds has been very rare so far, although directed orthometallation (DOM) by a regiospecific ortholithiation with  $\text{RLi}$  (4) and subsequent transmetallation is the technique commonly being followed to achieve cyclometallation. In fact, the

prevailing assumption up to now has been that "Early transition metals like titanium and zirconium are unable to undergo the necessary C-H activation step to form the orthometallated complex" (5). Others have shared similar views (6), although some examples of direct cyclometallation using titanium and zirconium tetra alkyls (7), or using tetrachlorides, but not involving aromatic carbons (8), have been reported. We have been able to determine by DFT studies that in the titanium and zirconium complexes we have studied, metal-hydrogen interactions are weak, as indicated by the metal-ortho hydrogen distance, and do not lead to ortho metallation by C-H insertion of the metal. See below. However, ortho metallation does occur by an HCl elimination mechanism.

We now report the direct cyclometallation of 2-phenyl indole with  $\text{TiCl}_4$  or  $\text{ZrCl}_4$ , as an efficient one-pot reaction. This reaction runs over a series of suggested intermediates (**1** through **3**), until the formation of the final product (**4**) at elevated temperature (up to  $105^\circ\text{C}$ ). DFT studies suggest that this orthometallation takes place via an ortho phenyl hydrogen abstraction by the chloride ligand, facilitated by being adjacent to a cationic center. This unexpected reaction was discovered during our investigations on the commercial Amoco CD catalyst for propylene polymerization (**9**), through the introduction of 2-phenyl indole as a new internal catalyst modifier.

The reaction sequence in the orthometallation was studied computationally with density functional theory (DFT), and the EDF2 functional was used because it works well with transition metals and is optimized for calculating spectra. In the course of this work, the EDF2 method was validated for its ability to reproduce agostic interactions.

Each intermediate in the reaction sequence shown in the abstract was modeled to understand its structure and the mechanism for its formation. Each geometry was confirmed to be a thermodynamically stable species, and spectra were calculated to guide and corroborate the interpretation of the experimental spectra. The calculated energies provide an indication of how accessible each intermediate is thermodynamically, and what the driving force is for each reaction step.

The Ti/Zr orthometallation/cyclometallation reaction may not be restricted to 2-phenyl indole, but it may be applied to a great variety of heteroaromatic ligands with a pendant aromatic ring in the 2-position from the heteroatom, N, O, P or S.

These novel cyclometallated complexes, besides their application in polymerization catalysis (**10**), may have application in organic synthesis through the insertion reaction of several small molecules into the metal- $\text{C}_{\text{aryl}}$  bond (CO,  $\text{CO}_2$ , etc.), including nitrogen fixation (**11**), or by the insertion of certain unsaturated compounds such as olefins. Their pharmacological potency as anticancer agents may also be re-visited (**12**).

The new complexes may undergo several other types of reactions such as reduction/alkylation with aluminum alkyls, yielding new mixed-metal complexes. The reaction of the cyclotitanated 2-phenyl indole with triethyl aluminum has been carried out, and data were recorded. See discussion. Furthermore, we may project that **4** or **7** (the Zr equivalent of **4**) may show a reactive profile similar to  $\text{Cp}_2\text{TiCl}_2$ , like in the Petasis reaction, reacting with MeLi or MeMgCl.

## RESULTS AND DISCUSSION

**Cyclotitanation of 2-Phenyl Indole with  $\text{TiCl}_4$ .**  $\text{TiCl}_4$  is a strong Lewis acid, forming 1:2 addition compounds with aromatic amines (**13**), and 1:1 with imidazole, and several other diamines like 2,2'-bipyridine and dabco (**14**).

Upon mixing of  $\text{TiCl}_4$  and 2-phenyl indole at ambient temperature, the five-coordinated complex (**1**) forms, which isomerizes readily to the more stable indolenine

tautomeric form (**2**), with a shift of the double bond from the 2,3- to the 1,2-position, and a simultaneous hydrogen migration from the 1- to the 3-position. For these two complexes we considered an alternative coordination structure via an additional  $\eta^6$ -phenyl bond to Ti, but this possibility was eliminated by DFT calculations. At ambient temperature, the solution of the mixture is light yellow-orange. Upon slow (within 30 min) warming, starting at about  $80^\circ\text{C}$  and up to  $105^\circ\text{C}$ , the solution darkens to red-burgundy, with rapid formation of burgundy crystals. During this time, orthometallation of the phenyl group takes place, with a bathochromic color shift due to the newly created  $\pi$ -conjugation, described also in other heteroaromatic systems (**15**). The proposed structure of the crystalline product (**4**) is corroborated by elemental analysis, solid  $^{13}\text{C}$  NMR, infrared (including far infrared) spectra, X-ray photoelectron spectroscopy (XPS), and supported by DFT calculations. The experimental results will be discussed along with the DFT study, under "orthometallated Product **4**", below.

In the reaction sequence, the HCl produced by the orthometallation of the phenyl group is retained in the structure **4**, even in the presence of excess 2-phenyl indole, which is not basic enough to remove the HCl from the complex. DFT calculations indicate that the  $\Delta G^\circ$  of a reaction for the removal of the HCl from **4** with 2-phenyl indole is slightly endothermic by 0.59 kcal/mol. Therefore, there is no driving force for 2-phenyl indole to neutralize HCl, in preference to the product **4** formed by the orthometallation.

The oxidation state of Ti in **4** has been confirmed with X-ray photoelectron spectroscopy (XPS). The binding energy (BE) of Ti  $2p_{3/2}$  photoelectrons in the complex was found to be 458 eV from the XPS data. This value of BE compared with the literature data on other Ti compounds suggests a +4 oxidation state for Ti. The XPS analysis also provided approximate quantitative data on elemental atomic ratios. For the three key elements Ti, N and Cl, the atomic ratios were determined to be 1:0.8:2.7, a reasonable approximation to 1:1:3. These data indicate that the fourth Cl is not "bound" directly to Ti.

**Zirconium Chloride 2-Phenyl Indole Complex.** The methodology described above was followed for the preparation and characterization of the reaction product between  $\text{ZrCl}_4$  and 2-phenyl indole. The IR and solid state CPMAS and DDMAS  $^{13}\text{C}$  NMR spectra of the complex were recorded. The significant features of the spectra were very similar to those from the Ti 2-phenyl indole complex. Details are discussed under Zr complex **7**, DFT study.

A key functional difference between the cyclometallated class of polymerization catalysts like **4**, and other catalytic complexes (metallocenes, FI catalysts (**16**) etc.) is the insertion reaction into the metal- $\text{C}_{\text{aryl}}$  bond. Small molecules such as  $\text{O}_2$ , CO,  $\text{CO}_2$ ,  $\text{CS}_2$ , COS,  $\text{SO}_2$ , are capable of inserting, as well as multiple compounds with functional groups, and of course alkenes and alkynes (**17**). The insertion reaction

provides a platform for the discovery of new advanced catalysts from cyclometallated complexes.

### Density Functional Study of the Ortho-Metallation of 2-Phenyl Indole.

**Addition Compound 1.** The first step in this synthesis, is the addition of  $\text{TiCl}_4$  to 2-phenyl-1H-indole. This is expected to first complex by electron donation from the lone pair of electrons on the nitrogen, to form intermediate **1**. The structure of **1** was found by DFT with EDF2/6-31G\* to have the indole nitrogen occupying a fifth coordination site on Ti, as an equatorial ligand in a roughly trigonal bipyramidal coordination sphere, with a Ti-N bond distance of 2.39 Å. The aromatic rings are nearly coplanar, with a C-C-C-N dihedral angle of only 4.7°. See Figure 1a.

Titanium was not found to also form an  $\eta^6$  bond to the phenyl ring of phenyl indole and adopt an octahedral configuration. To do so would twist the phenyl group perpendicular to the plane of the indole ring, and interrupt the extended conjugation of the two aromatic pi systems. Instead, the two rings are coplanar in the ground state, and the Highest Occupied Molecular Orbital (HOMO) was found to be delocalized over both rings, extending the conjugation.

The EDF2 result was checked with BLYP and MP2 calculations, neither of which found Ti coordinating to the phenyl ring. The MP2 calculation did give a slightly different minimum energy geometry from the two DFT calculations, with a Ti-N distance of 2.56 Å and the rings partly twisted (with a C-C-C-N dihedral of 40.8°), but the HOMO still shows extended conjugation with delocalization over both rings.

At a lower level of theory, a semiempirical PM3 calculation did find an  $\eta^6$ -phenyl bonding geometry, but when this starting geometry was refined by EDF2, BLYP, or MP2 it was found to be a false minimum, and quickly flattened out to the structure with extended conjugation shown in Figure 1a.

This vinyl C-H would appear at 116.0 ppm in the  $^{13}\text{C}$  NMR (See Figure 2a) and at 7.20 ppm in the  $^1\text{H}$  NMR. The phenyl substituted indole C next to N (position 2) is at 149.4 ppm in the  $^{13}\text{C}$  NMR. The UV-Vis spectrum is calculated to have electronic transitions in the visible range, 437-675 nm, but with low absorbance intensities: below 0.007.

**Tautomerized Complex 2.** Next, the indolenine tautomer arising from a 1,3 H-shift from N to C in the indole 5-membered ring was modeled by DFT with EDF2/6-31G\*, and its energy calculated. See Table 1. Tautomer **2** is found to be lower in energy than **1** by 6.9 kcal/mol ( $\Delta\text{H}^\circ = -6.9$  kcal/mol,  $\Delta\text{G}^\circ = -7.1$  kcal/mol). So this 1,3 H-shift should occur spontaneously. Interestingly, the ring geometry is slightly different: although a metastable geometry with the two aromatic rings coplanar can be found, the lowest energy conformation actually has the phenyl group rotated by

37° to bring the ortho hydrogen within 2.89 Å of the titanium, see Fig. 1b. This is evidence of an agostic type interaction. (The EDF2 method was validated for describing agostic interactions, and is described in the supplemental material.) The Ti-N distance in **2** is slightly shorter than in **1**, at 2.23 Å. The Ti is still roughly trigonal bipyramidal, with the N in an equatorial position. The agostic bonded geometry, **2**, is 2.0 kcal more stable than the alternative geometry, in which the phenyl is perpendicular to the indole.

The strong 408 and 440  $\text{cm}^{-1}$  Ti-Cl absorbances dominate the calculated IR of **2**, as they did in **1**. But the 5-membered ring, no longer aromatic, is now characterized by having methylene C-H's that appear as a weak symmetric stretch at 2943  $\text{cm}^{-1}$ , instead of the N-H stretch in **1**. The lack of a 3347  $\text{cm}^{-1}$  peak in the experimental IR confirms that tautomerization has taken place. The mono substituted phenyl still has the 5 C-H's absorbing at 684  $\text{cm}^{-1}$ , and the 4 adjacent C-H's of the indole ring at 751  $\text{cm}^{-1}$ .

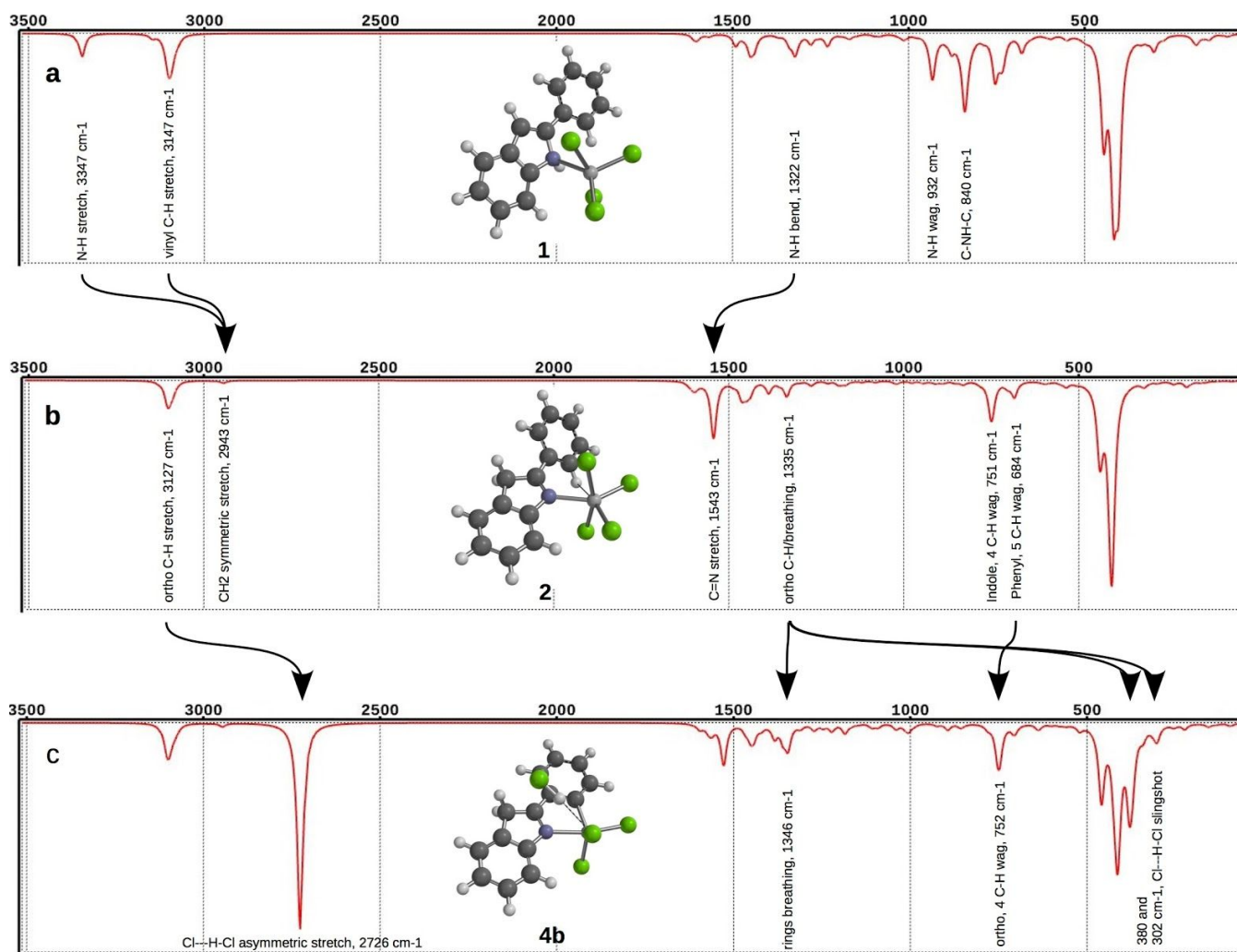
The methylene H's are calculated to appear at 3.95 and 4.44 ppm in the  $^1\text{H}$  NMR, and the C at 41.4 ppm in the  $^{13}\text{C}$  NMR. See Figure 2b. The ortho carbon with the agostic hydrogen is still at 128.3 ppm, but the bridge C next to N (indole position 7a) is at 151.7 ppm. The electronic, UV-Vis, transitions are now mostly below the visible region, 375-461 nm, and have absorption intensities all below 0.009, so there would be little observable color at this stage of the reaction sequence.

**Transition State 3.** Ti ultimately metallated the phenyl ring, replacing the ortho hydrogen in **2**. Although initially close to the Ti in **2**, the ortho H does not transfer to the Ti and then insert into a Ti-Cl bond before eliminating HCl. Instead, it has been found to transfer to the neighboring, axial Cl ligand on Ti by way of 4-membered cyclic transition state **3**, shown in Figure 3.

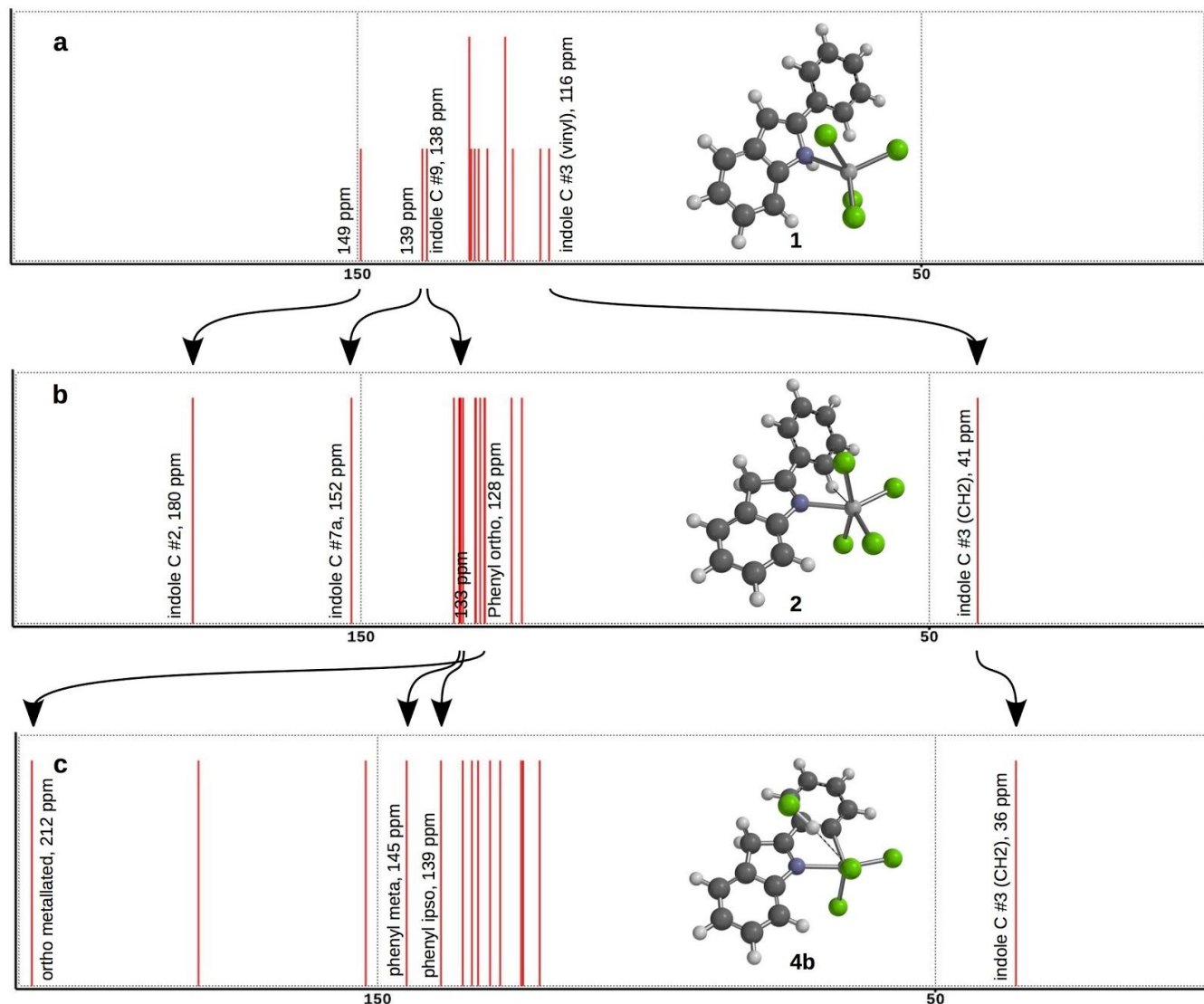
Attempts to find an intermediate step with transfer of H to Ti failed to find a stable geometry by DFT. They either spontaneously eliminated  $\text{Cl}_2$ , chlorinated the phenyl ring, or collapsed back to **2**. But the transition state, **3**, was found with the ortho H halfway between the C and the Cl: with C-H 1.58 Å and H-Cl 1.42 Å. This was confirmed to be a true transition state for this reaction, being a minimum in energy with respect to all degrees of freedom except for along the reaction coordinate, which leads directly back to reactant, **2**, and forward to the ortho-metallated product, **4a**. This was verified by an Intrinsic Reaction Coordinate search. A four-membered cyclic transition state for metallation of an aromatic ring is consistent with the observation of cyclic transition states for intermolecular C-H bond metallation-deprotonation (18) and specifically with four-membered cyclic transition states proposed for [Ru-OH] and [Ir-OMe] complexes (19).

In transition state **3** the two rings are once again nearly coplanar, with a C-C-C-N dihedral angle of 8.1°. The Ti-N distance is still 2.23 Å. The Ti at this stage has become roughly octahedral, with the Ti-C bond being formed occupying one coordination site at a distance of 2.24 Å.





**Figure 1.** Calculated IR spectra of Ti complexes, highlighting differentiation between (a) initial donor complex **1**, (b) tautomerized complex with agostic contacts **2**, and (c) orthometallated complex **4b**, with associated HCl above plane.

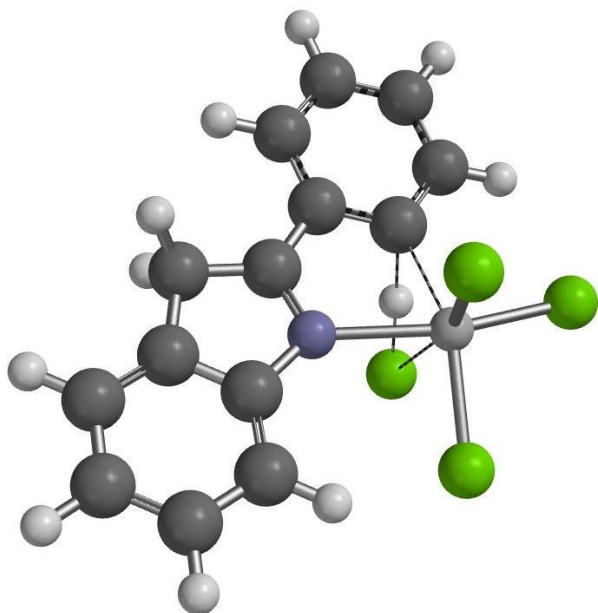


**Figure 2.** Calculated  $^{13}\text{C}$  NMR spectra highlighting differentiation between (a) initial donor complex 1, (b) tautomerized complex with agostic contact 2, and (c) orthometallated complex 3, with HCl above plane.

**Table 1. EDF2/6-31G\* Energies and Geometries**

Molecule	H <sup>o</sup> , au	G <sup>o</sup> , au	Dipole Moment, D	C-C-C-N Dihedral, °	M-N, Å	M-C, Å
Ti adduct, <b>1</b>	-3284.84982	-3284.90990	6.05	4.7	2.39	3.79
Ti tautomer, <b>2</b>	-3284.86087	-3284.92125	8.30	37.3	2.23	3.39
TS, <b>3</b>	-3284.80606	-3284.86682	8.77	8.1	2.23	2.24
Titanacycle, <b>4a</b>	-3284.81851	-3284.88048	10.43	-0.3	2.20	2.12
HCl above, <b>4b</b>	-3284.81989	-3284.88134	6.69	-0.6	2.20	2.11
Zr adduct, <b>5</b>	-2481.93700	-2481.99760	6.89	6.4	2.49	3.84
Zr tautomer, <b>6</b>	-2481.94874	-2482.00969	9.36	36.5	2.36	3.33
Zirconacycle, <b>7</b>	-2481.89575	-2481.95850	10.82	0.42	2.33	2.27

An appreciable activation energy is calculated for this reaction, however, with **3** being 34.4 kcal/mol higher in energy than **2**, see Table 2. This is in line with calculations by Goddard's group (20), which calculated an activation energy of 39.8 kcal/mol for the 4-membered ring transition state for intermolecular metallation of benzene by an iridium hydroxide complex.



**Figure 3.** Cyclic transition state, **3**, for orthometallation.

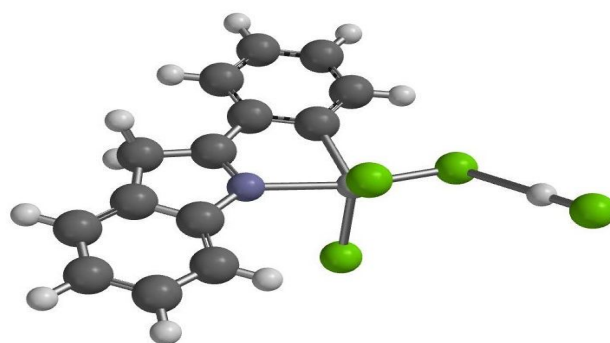
**Table 2. Reaction Sequence Thermodynamics**

Step	$\Delta H^\circ(\text{rxn})$ , kcal/mol	$\Delta G^\circ(\text{rxn})$ , kcal/mol
<b>1</b> $\rightarrow$ <b>2</b>	-6.93	-7.12
<b>2</b> $\rightarrow$ [ <b>3</b> ]	34.39	34.16
<b>2</b> $\rightarrow$ <b>4b</b>	25.72	34.16
<b>5</b> $\rightarrow$ <b>6</b>	-7.37	-7.59
<b>6</b> $\rightarrow$ <b>7</b>	33.25	32.12

**Orthometallated Product 4.** The Intrinsic Reaction Coordinate (IRC) search from transition state, **3**, leads directly to formation of a Ti-C bond at the ortho position of the phenyl group, with elimination of an HCl molecule. In the absence of polar solvation, HCl remains paired up with the Ti-phenyl indole complex, forming a bimolecular complex: the partially positive H being attracted to one of the electronegative Cl ligands on titanium. Several orientations of the HCl around the orthometallated, phenyl indole complex were found by DFT to be nearly equivalent energetically, but the initially formed structure from transition state **3**, has the HCl projecting out from the in-plane Cl, and angles a little up from the plane: structure **4a** in Figure 4.

The Ti in **4a** has returned to a trigonal bipyramid, with the N and the H-bonded Cl occupying the axial positions. The rings are coplanar with a dihedral angle of  $0.3^\circ$ , the Ti-N bond is 2.20 Å, and the Ti-C bond is 2.12 Å. The Cl H-bond distance is 2.44 Å. These bond distances are virtually unchanged in the slightly more stable (by 0.9 kcal/mol) lowest energy orientation, **4b**, with the HCl above the plane of the rings and oriented with the H toward an equatorial Cl on Ti.

The Cl—H—Cl structure is calculated to have a very strong IR vibration (back and forth between the Cl's in **4b**) at  $2726\text{ cm}^{-1}$ . It also has a pair of weak side-to-side vibrations at  $309$  and  $249\text{ cm}^{-1}$  in **4a**: side-to-side and up and down vibrations at  $380$  and  $302\text{ cm}^{-1}$  in **4b**.



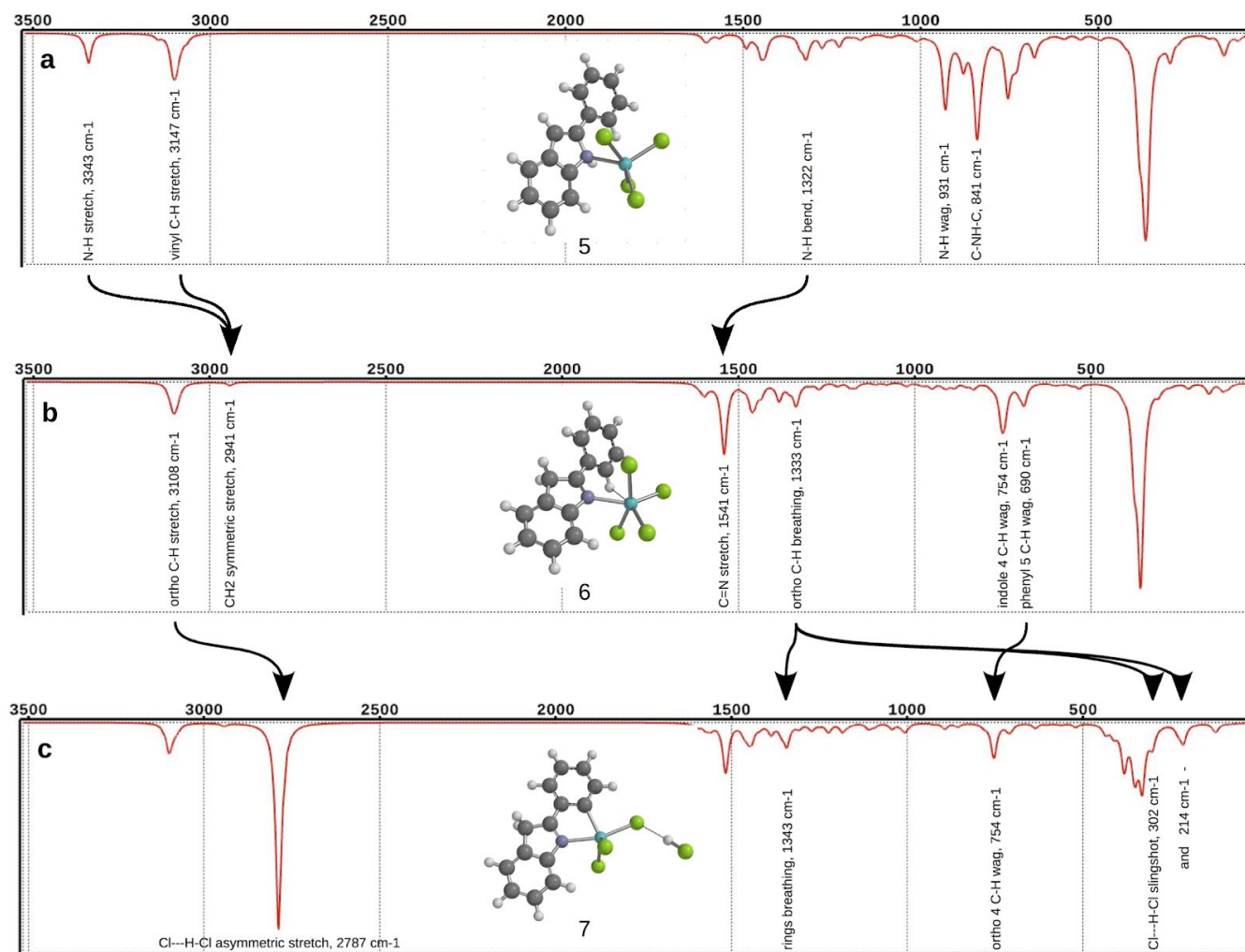
**Figure 4.** Initial bimolecular complex of HCl and orthometallated phenyl indole, **4a**.

The calculated HCl/[HCl<sub>2</sub>]<sup>-</sup> IR absorbance is ambiguous, due to the variety of equivalent orientations the HCl can adopt around the orthometallated complex. Although the H-bonded Cl-H-Cl structure is in a linear configuration, it is in a significantly different environment than the free HCl<sub>2</sub><sup>-</sup> ion: either in the gas phase, or in the ionic solids studied by Ward et. al. (21). One of the chlorines is chemically bonded to another molecule and there is not a net negative charge, so the Cl-H distances are not equal, and any Cl-H vibrational mode will be strongly coupled to the rest of the system. Ward has reported IR absorbances for HCl<sub>2</sub><sup>-</sup> in ionic solids at 200, 1080-1210, and an overtone band at 1525-1660  $\text{cm}^{-1}$ . The experimentally observed 1595 and 1566  $\text{cm}^{-1}$  bands would be consistent with an [HCl<sub>2</sub>]<sup>-</sup>, but were not found by DFT, because overtones are not calculated.

The experimentally observed 2723 and 2680  $\text{cm}^{-1}$  bands are consistent with the calculated 2726  $\text{cm}^{-1}$  in-line H vibration in **4b**, and the medium 203  $\text{cm}^{-1}$  band is consistent with the side-to-side vibration calculated at 249  $\text{cm}^{-1}$  in **4a**. Calculated IR absorbances at 1183 and 1091  $\text{cm}^{-1}$  (for **4b**) are near the observed 1195 and 1079  $\text{cm}^{-1}$ , but these are CH<sub>2</sub> wag and in-plane aromatic C-H bending vibrations, respectively.



The Ti-Cl vibrations are complex modes, with frequencies of 371, 380, and 413  $\text{cm}^{-1}$  that dominate the IR, as they did in **2**. These compare with the experimentally observed strong absorptions at 383, 394, and 419  $\text{cm}^{-1}$ .



**Figure 5.** Calculated IR spectra of Zr complexes, highlighting differentiation between (a) initial donor complex **5**, (b) automerized complex.. with agostic contact **6**, and (c) orthometallated complex **7**, with associated HCl

The 5 C-H wag of the phenyl group at  $684\text{ cm}^{-1}$  is gone, replaced by a  $747\text{ cm}^{-1}$  absorbance for 4 adjacent C-H's in ortho substituted rings, overlapping the  $752\text{ cm}^{-1}$  absorbance of the indole's 4 adjacent C-H's serving as an indicator for orthometallation. The corresponding observed strong absorption is at  $728\text{ cm}^{-1}$ .

The HCl hydrogen in **4b** is calculated to appear at 2.01 ppm in the  $^1\text{H}$  NMR, but presumably this will be highly dependent on the solvent. The 5-membered ring methylene group should show up at 3.98 and 4.36 ppm in the  $^1\text{H}$  NMR and at 35.6 ppm in the  $^{13}\text{C}$  NMR. The experimentally observed is at 42 ppm.

Solid state  $^{13}\text{C}$  NMR cross-polarization with magic angle spinning (CPMAS) was used to investigate the shift changes in the Ti complex **4** in order to confirm the Ti-C<sub>aryl</sub> bond. A dipolar dephasing spectrum DDMAS (containing the expected five peaks from quaternary carbons only) showed shifts at 183, 140, 132, 128 and

126 ppm. The 183 ppm shift has been assigned to the phenyl 2-position bonded to Ti, and the other four to the existing quaternary carbons in the complex (phenyl to indole bonded C, indole C next to N, C in indole 2 position, and indole ring fused C between 3 and 4 positions, respectively). The corresponding four shifts of quaternary carbons in free indole are 135.8, 137.1, 137.6, and 128.2 ppm, in relatively good agreement.

The DFT calculated quaternary carbon shifts of complex **4b** were at 212.0, 182.1, 152.1, 138.7, and 133.1 ppm, following the same order. Here we do not have good agreement between the calculated and the experimental values. This could be attributed to a number of reasons, like our calculations were made for gas phase, and we are dealing with a solid, with possible strong intermolecular interactions. Also, the effect of HCl in shielding or deshielding certain carbon centers could be substantial (21).



There may be some other indications that the experimental 183 ppm may indeed belong to the metallated phenyl carbon. First, it is the one extra quarternary shift appearing upfield after the ortho-metallation of 2-phenyl indole. The reaction of **4** with  $\text{AlEt}_3$  produces a Ti (III) bimetallic complex which shows the peak now at 196 ppm. Finally, in the Zr complex **7** the fifth quarternary peak is at 181.8 ppm, similar to the shift in **4**.

The remaining peaks, at 144.8, 134.7, 132.0, 129.9, 128.0, 124.3, 123.9, and 121.0 ppm, are all within the experimentally observed envelope for the protonated carbons, from 146 to 115 ppm.

The electronic transitions are calculated to absorb more strongly in the UV, with intensities up to 0.04, and to extend into the visible region: 379-518 nm. Absorbing the violet, blue, and green colors would leave the red end of the spectrum, and is consistent with the observed burgundy color of the reaction product.

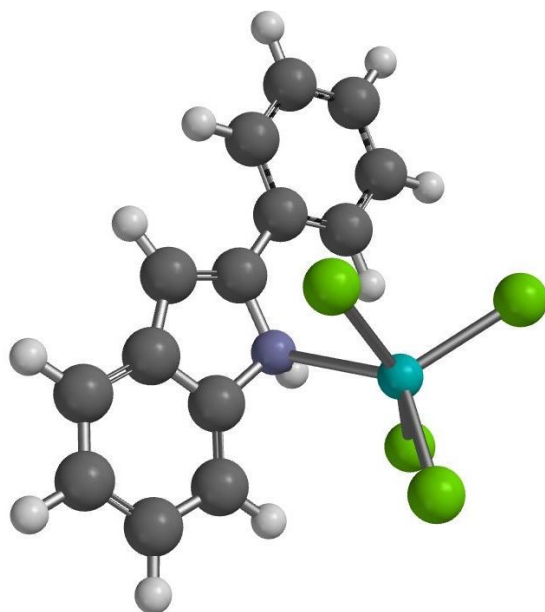
Two other orientations for HCl in the bimolecular complex were found to be very close in energy. In one the HCl is still oriented toward the axial Cl, but projects up from the plane of the rings, **4a**. In another, the HCl lies above the ring, with the H oriented toward an equatorial Cl, **4b**. This latter is the most stable bimolecular pair, being 1.0 kcal lower in energy than **4a**. The stability is due, in part, to the reduced charge separation by having HCl's dipole aligned to oppose the dipole of the organometallic complex. While this is the preferred geometry, these energy differences are small, and may be within the accuracy of the calculation. The more so, because density functional methods typically do poorly for intermolecular interactions, so the bimolecular complex relative energies may be less accurate than the other calculations reported here.

The calculated spectra of **4a** and **4b** have similar absorbances for the Cl-H-Cl modes: **4a** should have a strong  $2770\text{ cm}^{-1}$  in-line stretch and weak  $309$  and  $209\text{ cm}^{-1}$  side-to-side modes, and **4b** should have a strong  $2726\text{ cm}^{-1}$  in-line stretch and weak  $380$  and  $302\text{ cm}^{-1}$  side-to-side modes.

Molecule pair **4b**, the lowest energy configuration, is calculated to be  $8.7\text{ kcal/mol}$  lower in energy than transition state, **3**, but is still  $26\text{ kcal/mol}$  higher in energy than **2**. See Table 2. So this reaction would not proceed spontaneously. But experimentally, the product precipitates out of solution, which drives the reaction.

These reactions were carried out experimentally in nonpolar solvents, such as toluene. Each intermediate, however, is calculated to have a significant dipole, which changes throughout the reaction sequence. See Table 1. So a polar solvent should shift the thermodynamics, by stabilizing the more polar intermediates more than the less polar ones. In particular, the dipole moment is calculated to be a maximum for the transition state, **3**, and for the initially formed molecule pair, **4**. Therefore, a polar solvent should lower the activation energy for formation of **4** and **5**.

**Zirconium Adduct 5.** Zirconium was found experimentally to behave similarly to titanium in the same synthetic sequence, so it was examined with EDF2/6-31G\* calculations, also. The Zr analogue of **1** was first modeled by DFT, to study the corresponding  $\text{ZrCl}_4$  adduct, **5**, shown in Figure 6.

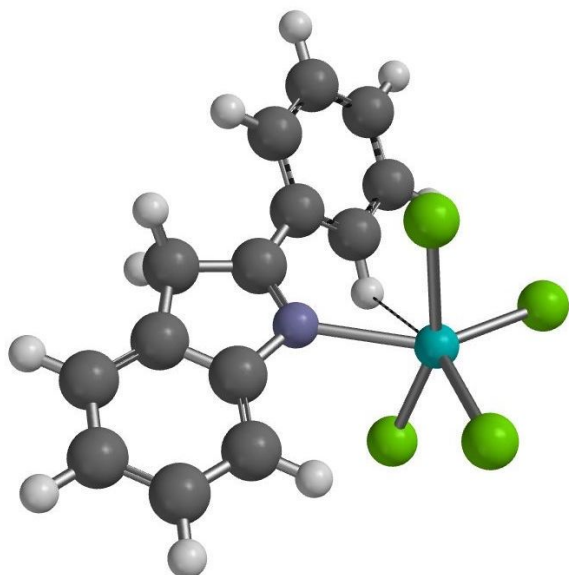


**Figure 6.** Zirconium adduct **5**, Zr analogue of **1**.

In **5** the Zr is roughly a trigonal bipyramid with N equatorial, as was the case with titanium. The Zr-Cl IR vibrations at  $362\text{-}384\text{ cm}^{-1}$  dominate, and aromatic ring breathing vibrations absorb at  $1600$  and  $1567\text{ cm}^{-1}$ . The N-H vibration is at  $3343\text{ cm}^{-1}$  and the vinyl C-H stretch is a shoulder at  $3147\text{ cm}^{-1}$ .

**Zirconium Tautomer 6.** A 1,3 H-shift from N to C in the 5-membered ring to give the indolenine tautomer analogue of **2** with Zr gives **6**, shown in Figure 7. Once again, as in the case with Ti, there appears to be an agostic interaction with the phenyl's ortho hydrogen. The Zr in **6** is more nearly trigonal bipyramidal, however, rather than octahedral, and the N is equatorial. The Zr-Cl vibrations are at  $358$  to  $377\text{ cm}^{-1}$ , the iminium C=N stretch is a strong absorbance at  $1541\text{ cm}^{-1}$ , and the characteristic 5 C-H wag of the mono substituted phenyl is at  $745\text{ cm}^{-1}$ . The UV-Vis transitions absorb up to  $345\text{ nm}$  with a maximum intensity of 0.2. **6** is  $7.4\text{ kcal/mol}$  lower in energy than **5**, so this tautomerization should proceed spontaneously, as was the case with Ti. See Table 2.

**Orthometallated Zirconium Complex 7.** The orthometallated zirconium analogue of **4a** was modeled, and again found to be a stable molecule pair with HCl. See Figure 8. The Zr is roughly a trigonal bipyramid, with the N axial, the Zr-C distance  $2.27\text{ \AA}$ , Zr-N  $2.33\text{ \AA}$ , Cl-HCl  $2.43\text{ \AA}$ , and H-Cl  $1.30\text{ \AA}$ .



**Figure 7.** Zirconium tautomer, **6**, Zr analogue of **2**.

The calculated IR shows a Cl-H-Cl absorbance at  $2787\text{ cm}^{-1}$ , which compares favorably with the observed at  $2750\text{ cm}^{-1}$ . The phenyl 5 C-H absorbance is gone, replaced by a 4 C-H wag at  $754\text{ cm}^{-1}$ , coalesced with the indole 4 C-H wag. This is consistent with the observed strong  $792\text{ cm}^{-1}$  indicating orthometallation in **7**. The calculated Zr-Cl sym stretch is at  $355\text{ cm}^{-1}$  and the asym at  $383\text{ cm}^{-1}$ . They compare with the observed  $366\text{ cm}^{-1}$  and  $386\text{ cm}^{-1}$  strong absorptions. The calculated asym/sym absorptions for the Zr-Cl...HCl are at  $331/350\text{ cm}^{-1}$ , vs the observed  $301/341\text{ cm}^{-1}$ .

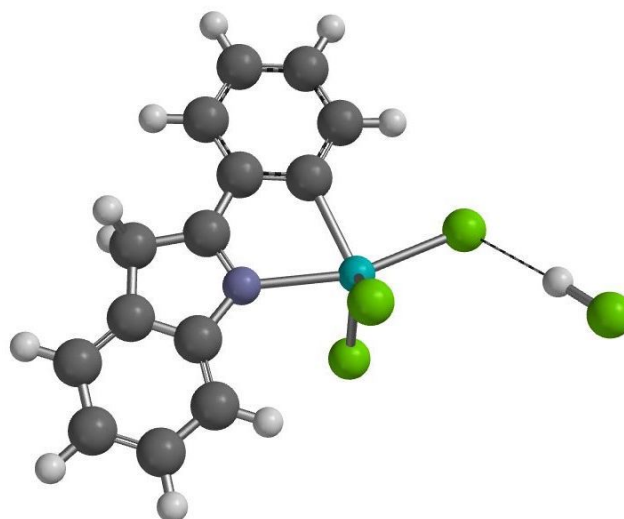
From the solid state CPMAS study, the five  $^{13}\text{C}$  NMR shifts experimentally recorded for this complex were 124.4, 132.0 140.9, 141.6, and 181.8 ppm, the latter attributed to the Zr-C bond. Analogous DFT values could not be calculated.

**Thermal Stability of Complexes 4 and 7.** Compounds with a Ti-C bond are in general thermally unstable, unless structural conditions or the lower oxidation state of Ti, contributes to their stability. Tetraphenyl Ti prepared at  $-78^\circ\text{C}$ , decomposes at  $-10^\circ\text{C}$  to form a room temperature stable (but pyrophoric in air) Ti (II) compound  $\text{Ti}(\text{C}_6\text{H}_5)_2$  (22). In  $\text{R}_n\text{TiX}_{4-n}$  compounds stability increases with increasing electronegativity of R: butyl < methyl < acetylenyl < p-anisyl < phenyl < a-naphthyl < indenyl (23). Derivatives of  $\text{Cp}_2\text{TiX}_2$  are more stable, in the order of  $\text{x}=\text{C}_6\text{H}_5 < \text{CH}_3 < \text{C}_6\text{F}_5$  (22). Complexes **4** and **7** exhibit remarkable thermal stability, perhaps higher than any known Ti organometallic derivative. They are formed at the high temperature of  $105^\circ\text{C}$ , and they remain unchanged at room temperature under Nitrogen. The reason for their stability is the coordination with a donor-N (24), but also the pi-conjugating system of the indole ligand, This stability is an important characteristic of **4** and **7** in applications as reagents.

## CONCLUSIONS

Cyclometallated complexes of titanium and zirconium with 2-phenyl indole, promising olefin polymerization catalysts when activated with TEA, have been described for the first time. They may represent a new class of materials with diverse applications, as catalysts in general, in cancer therapy, photoluminescence (3b), and as starting materials in synthetic organic chemistry, through insertion reactions into the metal- $\text{C}_{\text{aryl}}$  bond, and reactions with aluminum alkyls, among others.

This type of thermal orthometallation may not be restricted to 2-phenyl-indole, but could be expanded to



**Figure 8.** Zirconium bimolecular complex **7**, Zr analogue of **4**.

several other ligand types, capable of undergoing ortho-metallation, as for example, tetraphenyl cyclopentadienone (25).

The Density Functional calculations with the EDF2 functional and the 6-31G\* basis set were found to support the proposed mechanism shown in the abstract for the formation of a phenyl indole complexed titanium catalyst. The tautomerization step would proceed spontaneously, based on the thermodynamic analysis. A 4-membered cyclic transition state was found for ortho-metallation, but the elimination of HCl to complete the reaction needs to be driven, since it is calculated to be endothermic. Excess phenyl indole is insufficiently basic to remove the HCl. More polar solvents may lower the activation energy, due to the increased polarity of the transition state. Zirconium was found to give similar intermediates.

## COMPUTATIONAL METHODS

All calculations were carried out with the Spartan program (Spartan'14, Wavefunction, Inc. Irvine, CA) (25), using the

EDF2 functional with the 6-31G\* basis set. In some instances, additional calculations were carried out with the MP2 post-Hartree Fock method, also with the 6-31G\* basis set, to check the Density Functional results. All structures were fully optimized, and characterized by vibrational analysis to confirm that they were in fact stationary points: reactants, intermediates, complexes, or transition states. When necessary, the default convergence criteria were tightened up to a TOLG=0.00006, to eliminate any negative frequencies. Zero-point (vibrational) energies (ZPEs) and IR absorbances were also calculated, and Thermodynamic values derived: enthalpy (H°), entropy (S°), and Gibbs free energy (G°). NMR spectra were calculated with the GIAO method, and select 6-31G\* calculations were repeated with the 6-31G+G\*\* basis set, to confirm their accuracy.

## EXPERIMENTAL SECTION

Materials were used as received. Solvents (toluene, hexane) were dried using standard procedures. Experiments were carried-out in a dry-box, under dry, purified nitrogen.

Cross-polarization with magic angle spinning (CPMAS) solid state <sup>13</sup>C NMR technique was used for all cyclometallated complexes. The samples were packed into MAS rotors in dry box, and dry nitrogen was used for sample spinning to prevent exposure to air and moisture. Typical CPMAS experimental conditions used were: external magnet = 2.35 tesla: CP contact time = 2 milliseconds; proton spin-lock radio-frequency field = 40 KHz; recycle delay = 3 seconds. Dipolar dephasing (DDMAS) technique, with 40 microseconds dephasing time, was used to obtain quaternary (and methyl) carbons only spectra, to aid in spectral assignment.

**Preparation of the 2-phenyl indole/TiCl<sub>4</sub> cyclometallated complex.** Inside a dry box, 25 ml of 1.0 molar solution of 2-phenyl indole in toluene was added slowly within 30 minutes to 25 ml of a 1.0 molar toluene solution of TiCl<sub>4</sub>, under magnetic agitation, at ambient temperature. After the addition, the temperature was raised gradually to 105°C over a period of 30 minutes, and a toluene insoluble, crystalline dark orange-burgundy product formed. The temperature was maintained at 105°C for another five minutes. Heating was turned-off, the supernatant decanted, and the product was washed four times with toluene. It was further washed three times with hexane, and dried in vacuum. Yield 91% based on TiCl<sub>4</sub>. Spectroscopic evidence indicates that the product may be about 97% pure, the rest being hexane that could not be removed by the vacuum.

Analytical: Calculated for C<sub>14</sub>H<sub>11</sub>NTiCl<sub>4</sub>: C, 43.91%; H, 2.90%; N, 3.66%; Ti, 12.5%; Cl, 37.03%. Found: C, 43.04%; H, 3.07%; N, 3.4%; Ti, 13.1%; Cl, 37.2%.

## ASSOCIATED CONTENT

### Supporting Information

The Supporting Information is available free of charge on the ACS Publications website.

Additional calculations of indole-HCl affinity and validating EDF2/6-31G\* for agostic interactions (PDF)

A text file of all computed molecule Cartesian coordinates in .xyz format for convenient visualization (XYZ)

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### Notes

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Naresh K. Sethi conducted the solid <sup>13</sup>C NMR study and interpreted the data.

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