

Computational Investigations of Conformational Effects in Organometallic Polymerization Catalysts

by

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Dedication

This thesis is dedicated to my parents for their support and tireless sacrifice.

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Abstract

Computational chemistry is a powerful tool for increasing understanding of known chemistry, discovering new reaction mechanisms, and improving catalyst properties and design. It can provide physical insights that would be difficult or costly to achieve through experiments alone. The insight that can be gained from computational studies, however, can be limited by the accuracy of the models used and often requires an established working knowledge of the chemical system of interest. Below are two examples where computational chemistry is used to provide insight into chemical reactions catalyzed by flexible organometallic catalysts.

Chapter 1 provides a brief overview of computational chemistry fundamentals that are needed to understand reaction landscapes. This introduction includes topics include such as the potential energy surface, molecular dynamics, and transition states. The reaction path finding and transition state finding methods used in this work are also described.

Chapter 2 reveals the interactions between the counteranion and flexible polymer during propagation and termination with the Ti(IV) constrained geometry catalyst. The work studies the dynamic interplay between counteranion and growing polymer chain on ethylene polymerization through conformer sampling and reaction pathway simulations. The results show that the length of the polymer chain substantially influences the counteranion position, where longer polymer chains tend to limit the counteranion's access to the monomer coordination site. Meanwhile, productive insertion and chain termination reaction pathways prefer ion pair orientations where the counteranion is on the opposite side of the Ti catalyst as the ethylene monomer. The effective

activation barriers for insertion and termination reactions calculated from the reaction path ensemble explain the difference in catalytic activity and molecular weight between the two different counteranions observed in experiment.

Chapter 3 elucidates how the differences in ion pair interactions between diastereomers during activation with the Hf(IV)-pyridylamido catalyst influence low active-site counts. Extensive sampling of the ion pair with molecular dynamics simulations reveals distinct preferred counteranion orientations, which are differentiated by the location of the bridgehead substituent. One diastereomer enables the counteranion to slide to favorable staggered orientations suitable for outer sphere coordination, whereas the other diastereomer prefers the counteranion with inner sphere coordination. Ion pair preferences not only affect which conformations are accessible, the ion pair also affects the free energy profile associated with ethylene monomer coordination. The ethylene monomer is shown to coordinate preferentially to one, but not the other, of the two potentially active catalysts. The free energy of these processes are linked to the conformational flexibility of the diastereomers, giving new physical insight into design principles for highly active polymerization catalysts.

The concluding chapter reflects on each study and discusses possible future considerations. Overall, this work highlights accurate models of polymerization catalysts to gain a deeper understanding of organometallic chemistry.

Chapter 1 Introduction

1.1 Molecular Modeling with Computational Chemistry

Computational chemistry is used to study the fundamental properties of molecules and chemical reactions using techniques arising from quantum mechanics, thermodynamics, and kinetics. One purpose of computational methods is to apply these chemical theories and molecular modeling to guide and cooperate with experiment.¹ For experimentally relevant systems, exact quantum mechanical results are not possible to obtain, so approximate methods need to be used. The explosion in computational power and advances in theory and algorithms over the last few decades have made computational modeling with these approximate methods reliable and efficient. Findings from computational analyses make it possible to uncover atomistic details, leading to an understanding of structure-activity relationships, prediction of macroscopic properties, and elucidation of important mechanistic details in chemical reactions.

Nevertheless, the accuracy of a given chemical model obtained from computations can only be established by comparison to experiment. In the laboratory, however, the system is normally an equilibrium mixture of a large number of molecules at a set temperature, which means that measured properties should reflect thermal averaging over multiple discrete states.² Exploring these states depends on the accuracy of the molecular models so care must be taken in comparing theory and experiment. The work presented in the following chapters focus on target systems with particular chemical relevance, where computed properties are motivated by and compared to experimental observations.

1.2 Potential Energy Surface

Two main computable quantities that can be obtained are molecular structures and potential energy surfaces. Determining the best structure from a chemically reasonable guess is a common task in computational chemistry. Except for very small molecules, there are a number of geometries that are accessible and needed to be explored. This is done by characterizing the potential energy surface (PES), which describes the relationship between molecular geometry and energy.³ The PES is a hypersurface defined by the potential energy of a collection of atoms over all possible arrangements. Energy profiles from the PES are useful for detailing thermodynamic equilibrium, determining kinetics, and identifying the minimum-energy reaction paths.⁴

Particular interesting points on the PES include local minima and saddle points. Local minima correspond to optimal molecular structures that are physically stable. Saddle points are the lowest energy barriers on paths connecting local minima, which means that they correspond to transition states. These two types of structures are the accessible states on the PES that are chemically relevant in most experiments at reasonable temperatures.⁵ Complete PESs for polyatomic molecules are hard to visualize because of high dimensionality. Usually, slices through the PES that involve one or two coordinates are taken to show the relevant reduced-dimensionality energy curves (**Figure 1.1**). Points A and C correspond to local minima in the surface defined by two reaction coordinates, where A and C are the reactant and product for the reaction path slice. Point B corresponds to the transition state connecting Points A and C. A further slice gives the energy as a function of one reaction coordinate. Modern computational tools allow for the identification of these stationary states along the PES.

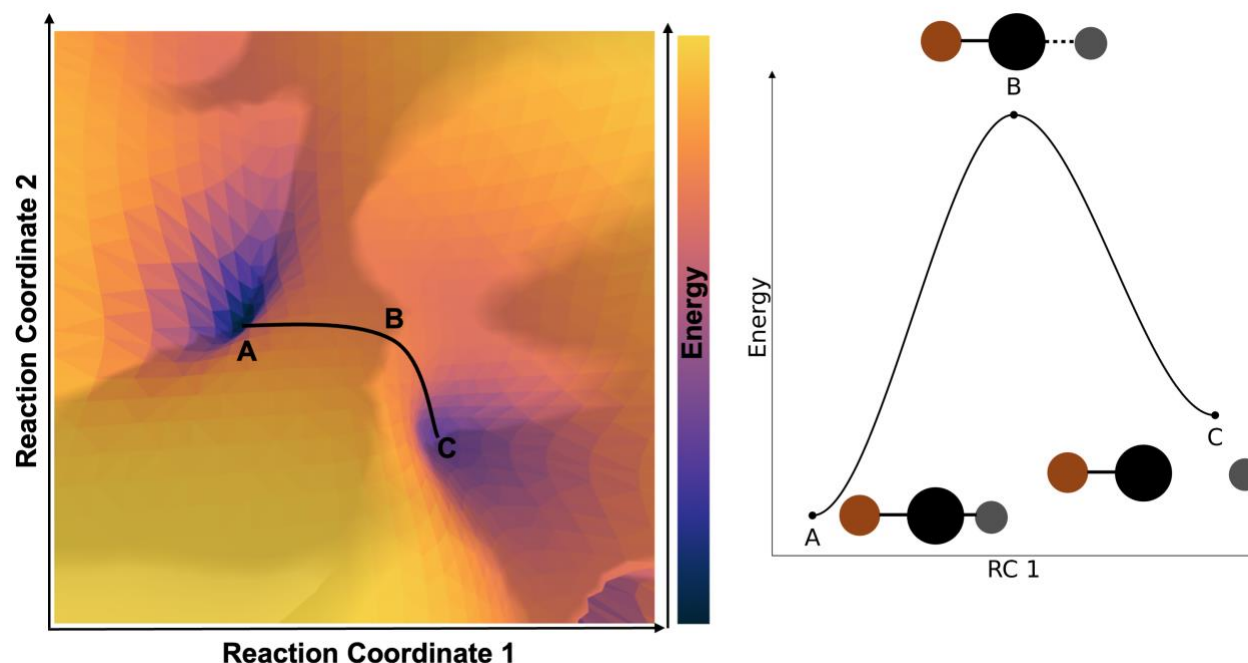


Figure 1.1 PES for a hypothetical molecule. The three-dimensional plot (left) represents a hyperslice through the full PES showing the energy as function of two reaction coordinates (RCs). The slice of this surface (right) gives the energy as a function of the RC 1, where reactant species (A) proceeds through transition state (B) to arrive at product (C).

Thermodynamic and kinetic information can be obtained by computing Gibbs free energies of the relevant minima and transition states. The equilibrium constant, K_{eq} , can be estimated by deriving from free energy differences between minima. In Equation (1.1) K_{eq} can be used to determine equilibrium concentrations of chemical species ($[A]$ and $[C]$) based on the Boltzmann-weighted Gibbs free energy difference at the reaction temperature (T).¹

$$K_{eq} = e^{\left(\frac{-\Delta G}{RT}\right)} = \frac{[A]^{\sigma}}{[C]^{\rho}} \quad (1.1)$$

R is the gas constant the exponents, σ and ρ , correspond to the reaction order of the two species, respectively. With transition-state theory, the kinetics of the chemical system can be described by the transition state.⁵ In Equation (1.2) the reaction rate k is related to the free energy of activation $\Delta^{\ddagger}G$, which is the free energy difference between the transition state and reactant.⁶

$$k = \frac{k_B T}{h} e^{\left(\frac{-\Delta^\ddagger G}{RT}\right)} \quad (1.2)$$

This makes locating TS structures important, since they can be used to predict experimentally observed rates or compare relative rates of competing reactions.

1.3 Levels of Theory

1.3.1 Density Functional Theory

Density functional theory (DFT) has been developed as a valuable tool in computational chemistry as its methods have high chemical accuracy with respect to the required compute cost. DFT is an electronic structure method based on quantum mechanics (QM) that is effective in detailing molecules and chemical reactions at the atomistic level.⁷ It can be used to obtain the geometries and energies of reactants, intermediates, products, and transition states of a reaction path. The energetics from DFT can be used to explain or predict properties obtained from experiment such as selectivity and activity. DFT methods can tackle larger chemical systems compared to wavefunction methods because they use the electron probability density of the system as opposed to the electronic wavefunction. The scaling for DFT is N^3 , where N is the system size, whereas coupled-cluster theory, considered as the gold standard in quantum chemistry, scales at $O(N^7)$.⁸ The lower scaling of DFT makes it viable for static calculations of larger chemical systems.

Accurate modeling with DFT methods requires a careful selection of the appropriate functional to describe electron density. Density functionals take the electron density as input and output a number (an energy). Functionals have been developed by numerous theory groups and improved by using experimental data and chemical databases to parametrize the functional to work with a variety of chemical systems.⁹ Empirical dispersion corrections can be added to a functional

to more accurately capture long range dispersion interactions, which are important in modeling organometallic reactions.¹⁰

1.3.2 Force Fields

Force field (FF) methods differ from *ab initio* and DFT methods since the calculation of the electronic energy is bypassed. Rather, the building blocks in force fields are atoms, where the energy is a parametric function of the nuclear coordinates and parameters are fit to experimental or data from higher levels of theory. Since the quantum aspects are ignored, bonding information is provided explicitly, and atom types are defined to distinguish atoms in different bonding situations. The speed of FF methods towards calculating geometries and energies makes it compelling to use them in long timescale molecular dynamics and extensive conformational search simulations.¹¹

FF methods, also referred to as molecular mechanics (MM) methods, describe molecules by a ball and spring model plus long-range interactions. The force field energy is generally written as a sum of terms as shown below.¹²

$$E_{FF} = E_{bond} + E_{bend} + E_{tors} + E_{vdw} + E_{elec} + \dots \quad (1.3)$$

The first three terms correspond to bonding interactions, where E_{bond} is the energy function for stretching a bond between two atoms, E_{bend} is the energy term for bending a three-atom angle, and E_{tors} is the torsional energy for rotation around a bond described by four atoms. The terms E_{vdw} and E_{elec} describe the nonbonded atom-atom interactions and correspond to van der Waals interactions and electrostatic interactions, respectively.

The quality of the FF depends on the appropriateness of the functional form of the energy expression and accuracy of the parameters for each term. Given a particular form, these components can be limited by the availability of extensive reference data from experimental and

QM methods.¹³ For systems that are well-parametrized, good predictions of geometries and relative energies can be done in a short time.¹⁴ On the other hand, the lack of good parameters is a problem, and this can be especially observed in coordination chemistry. For example, an olefin coordinated to a metal and a cyclopentadiene ligand are not well-defined bonds in FFs.¹² To address these types of problems, more flexible functional forms for the individual energy terms and better parametrization have been developed but the approach varies with each chemical system.¹⁵ Currently, there is no single best universal FF and performance depends on the system of interest.

One particular force field appropriate for organometallic systems is the GFN-FF method, which is a semiclassical force field developed by Grimme et al.¹⁶ It was introduced for the fast calculation of structures and noncovalent interaction energies for molecular systems with elements up to radon (Z (atomic number) = 86). This is advantageous since many classical FFs lack parametrization for many elements such as metals. The total energy expression for GFN-FF is Equation (1.4)

$$E_{GFNFF} = E_{cov} + E_{NCI} \quad (1.4)$$

$$E_{cov} = E_{bond} + E_{bend} + E_{tors} + E_{rep}^{bond} + E_{abc}^{bond} \quad (1.5)$$

$$E_{NCI} = E_{IES} + E_{disp} + E_{HB} + E_{XB} + E_{rep}^{NCI} \quad (1.6)$$

The bonding terms in E_{cov} involve a classical description. The components of noncovalent interactions, E_{NCI} , involve electrostatic and dispersion interactions, hydrogen and halogen bond corrections, and repulsion energy. The electrostatic terms are treated semiclassically with an electronegativity equilibration (EEQ) atomic charges model. Dispersion interactions are treated

with the D4 scheme, where the dispersion coefficients are scaled by atomic charges.¹⁷ GFN-FF exceeded the UFF forcefield and was shown to be as accurate and 3 orders of magnitude faster than GFN2-xTB in transition-metal catalysts (TMG145 dataset).¹⁶ The robustness and generality of GFN-FF makes it applicable for the modeling of organometallic systems.

1.3.3 Semi-empirical Approximate Methods

Semi-empirical quantum mechanical methods (SQM) attempt to bridge the gap between quantum mechanical and force field methods. Within this space, the density functional tight binding (DFTB) approach offers a reduced complexity DFT method.¹⁸ DFTB calculates the total energy of a system by approximating the electron density using a minimal atomic orbital basis set. It uses semiempirical expressions for the electronic interactions, utilizing simplified two-center and three-center integrals. These integral approximations significantly reduce computational demands. Since a QM description of the valence electrons is used in SQM methods, their scope of applications is broader than force fields and they are faster than *ab initio* QM methods by at least 2 orders of magnitude.¹⁹ This made DFTB suitable for investigating the molecular structures of moderately sized metallic and organometallic systems, and simulating dynamics over extended timescales.

However, there are some limitations associated with DFTB. The integral approximations affect accuracy in bond angles and dihedrals, leading to imbalanced descriptions of bonds with different orders. This affects accuracy in energies and vibrational frequencies. Orbital confinement due to the minimal basis set approach underestimates Pauli repulsion forces, which affects non-bonding interactions and molecular polarizabilities.¹⁸ Improvements to DFTB have been made that involve extended parametrization, improved accuracy, and inclusion of dispersion corrections.

1.3.3.1 GFN-xTB Methods

The Grimme group has developed a family of extended semi-empirical DFTB3 variants termed GFN-xTB, which mostly follows a global and element-specific parameters-only strategy and is consistently parametrized for all elements through radon.¹⁷ The purpose of the method is the computation of molecular geometries, vibrational frequencies, and noncovalent interaction energies. This method has been extended by including multipole electrostatic as well as one-center exchange-correlation terms leading to higher accuracy, specifically for noncovalent interactions and conformational energies. Such methods can provide reliable treatment of electronically complicated structures.

The GFN2-xTB method is an accurate and broadly parameterized tight-binding method with multipole electrostatics and density-dependent dispersion contributions.²⁰ The tight-binding energy includes anisotropic electrostatic terms and exchange correlation effects up to the second order of the tight-binding expansion, which allows for a more accurate description of electronic properties compared to traditional DFTB. The parameters are fitted to yield reasonable structures, vibrational frequencies, and noncovalent interactions for molecules across the periodic table. Basis set extrapolated CCSD(T) energies were typically used as reference data for parametrization, while composite PBEh-3c and B97-3c methods were used for forces and structures.²⁰ The method does not include any hydrogen or halogen bond corrections, which are required in other widely used semi-empirical schemes. Parametrization of GFN2-xTB up to radon makes the method especially useful for reactive models of organometallic systems.²¹

1.4 Transition State Finding Methods

1.4.1 Transition State Finding

Finding TS structures can be challenging due to the high dimensionality of the PES and possible limited chemical intuition of the transition state geometries. The saddle point corresponds to the lowest energy barrier on the minimum energy path connecting the reactant and product of an elementary step. In the PES, this requires the saddle point to be a maximum in the direction of the reaction path and a minimum in all other directions. Additionally, due to the high dimensionality of PESs, an exhaustive search of the chemical space is not feasible. Due to these difficulties, many strategies have been proposed and they can be broadly classified into two categories—local and interpolation methods.

Local methods propagate the guess geometry using only information about the function and its first and second derivatives at the current point. Although these methods do not require knowledge of the reactant or product geometries, a good estimate of the TS is required in order to converge. Once the TS is found, the entire reaction path can be located by tracing the steepest intrinsic reaction coordinate. Popular local methods include the Hessian Newton-Raphson approach, the Partitioned Rational Function Optimization (P-RFO), and the Dimer method.²² The main disadvantage with local methods is that they can be computationally intensive if the guess geometry is far from the true TS, which is highly likely when there is lack of information or intuition about the TS structure.

Interpolation methods assume the reactant and product geometries are known and a TS is located between the endpoints. Interpolation methods include one-structure, two-structure, and multistructure approaches. The one-structure approach involves the user selecting one or a few internal reaction coordinates that describe the main difference between reactant and product structures. The selected coordinates are fixed at certain values and the remaining variables are optimized, which maps the energy as a function of the reaction coordinates. The two-structure

approach uses two geometrical structures, corresponding to the reactant and product, and attempts to gradually converge on the TS from both sides. Multistructure approaches, often called chain-of-states methods, use multiple structures or nodes connecting the reactant and product.²² These are important as the relaxation of these structures can lead to the saddle point and an approximation of the whole reaction path, which is represented by the discrete set of nodes.

Two widely used multistructure approaches are the Nudged Elastic Band (NEB) Method and the Growing String Method (GSM). The NEB method defines a target elastic band function as the sum of energies of all nodes and adds a penalty term represented by a spring interaction, with the purpose of distributing the images along a continuous reaction path.²³ One main disadvantage of NEB is the optimal choice of spring constant, where too large of a value can lead to slow convergence and too small leads to a poor description of sections in the reaction path. Typically, the initial guess for the pathway in an NEB calculation is generated using a linear interpolation in Cartesian coordinates between the end points. If this guess is far from the correct path, it can lead to slow convergence or the node may be placed in a high-energy region resulting in overlapping atoms. GSM addresses these problems by gradually adding nodes using internal coordinates from the reactant and product sides, where the string grows from each end of the pathway and converging toward the TS.²⁴ This means that GSM finds the minimum energy path (MEP) without requiring an initial guess for the pathway.

1.4.2 Growing String Method

The Growing String Method (GSM) is a type of interpolation method for TS finding and the method used in the following chapters. GSM can be used to determine reaction pathways and transition states without requiring an initial TS guess. After the string is grown and an approximate reaction path through the TS is found, string optimization is done and the exact TS

can be located using local methods such as eigenvector following.²⁴ During growth, GSM is a two-sided driving coordinate method, where coordinates are driven from the reactant and product side along the GSM reaction tangent direction.²⁵ This double-ended approach requires two input structures representing the starting and ending configurations that are connected by a TS. One advantage of double-ended GSM (DE-GSM) is that it is less prone to exploring undesired regions due to the fixed endpoints, although knowledge of the reactant-product pair is needed.

Driving coordinates can be used instead of the reaction tangent to grow the string. Single-ended GSM (SE-GSM) can locate a reaction path and TS by using a single structure and driving coordinates as inputs.²⁶ Instead of specifying the product structure, the qualitative characteristics of the target reaction can be described by the driving coordinates. These coordinates grow the string to the approximate reaction path, and subsequent string optimizations are done until the reaction path and TS are converged. This is advantageous over other one-structure interpolation methods such as the dimer method because the TS, the product, and the reaction path can be located in a single computation.²⁵ **Figure 1.2** depicts how SE-GSM operates where the driving coordinate involves adding and breaking bonds. One limitation is that the located TS is not guaranteed to be the desired TS for the intended reaction. Nevertheless, the use of driving coordinates allows SE-GSM to be used in automated TS finding and reaction discovery.²⁷

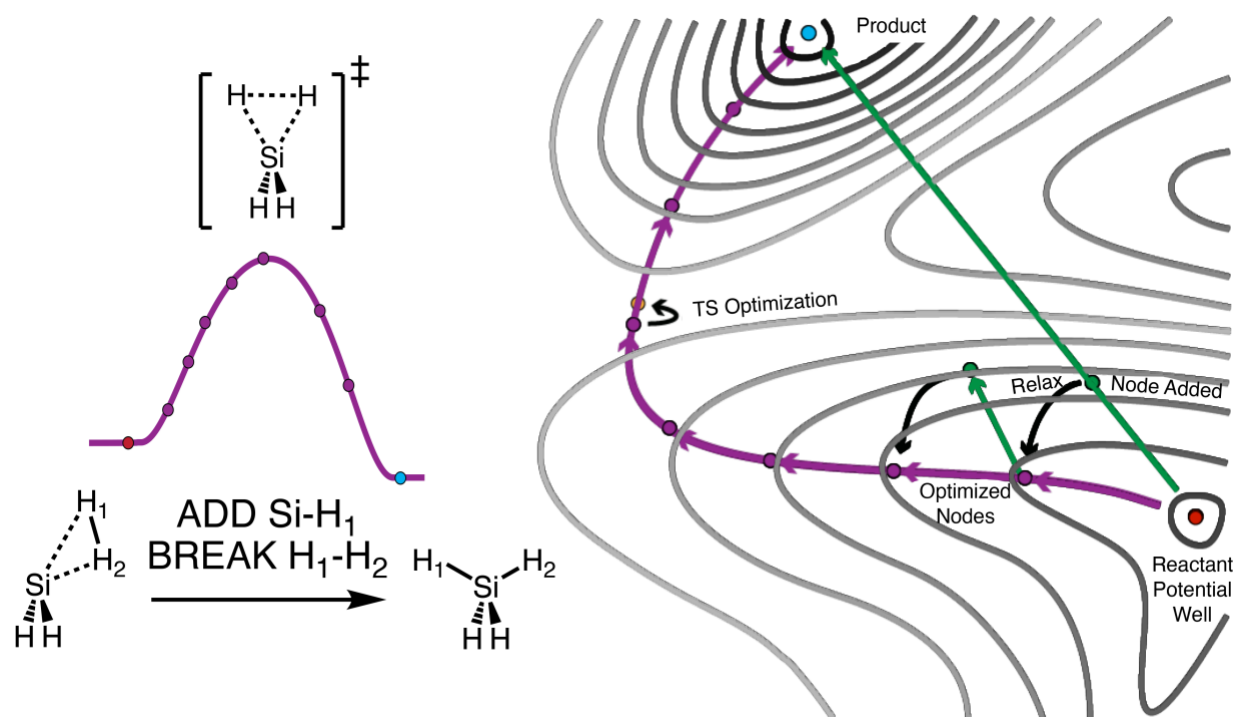


Figure 1.2. Example of single-ended Growing String Method (SE-GSM). The red node represents a reactant geometry at a local minimum on the PES. The green nodes are added along the green vector representing the user-provided driving coordinates. The purple nodes represent the optimized nodes along the reaction path. The blue node represents the product geometry and the yellow node is the optimized transition state geometry.

1.5 Molecular Dynamics

Although GSM can identify reaction paths and transition states, it only reveals energetic and mechanistic details from the set of geometries that the chemist provides. This number may be inadequate for some organometallic complexes, where flexible ligands and additives often allow for a large number of possible conformers for the intermediates that precede a reaction. Molecular dynamics (MD) allows for conformational sampling of the system of interest through the dynamical evolution of the system in time. MD simulations provide a detailed view of the behavior of the system under different conditions (e.g., temperature and solvent) can be used to understand the dynamics surrounding a reaction.²⁸ MD simulations can serve as a complementary tool to GSM, where relevant conformers are used as starting points for studying reaction pathways.

1.5.1 Conditions for Molecular Dynamics Simulations

MD simulations begin with a set of initial conditions: number of particles, potential energy model for interactions between particles, size of the simulation cell, and temperature.²⁹ MD simulations typically use empirical potentials or force fields to describe the potential energy interactions between atoms.¹⁵ Specific initial conditions for the system involve defining the positions and initial velocities for the particles, which are typically atoms. The positions are the Cartesian coordinates of each atom and the initial velocities can be defined according to the Maxwell-Boltzmann distribution at the specified temperature.

During an MD simulation, the system evolves in time according to Newton's equations of motion. The positions and momenta of the particles at the previous timestep are needed to generate the next timestep. The particles move due to the forces exerted by other particles or external fields, which varies depending on the energy model for interactions. Simulation steps are updated at femtosecond timescales since the timestep size is limited by the rate of the fastest process, which is usually the vibration of hydrogen atoms.³⁰ MD simulations are first equilibrated to allow the particles to interact and reach the correct Boltzmann distribution. Since Newton's equations of motion only conserve energy, a thermostat is used for NVT simulations.

The iterative process of calculating forces and updating atom positions based on those forces is done for the duration of the MD simulation. The Verlet algorithm provides a numerical way of solving Newton's equations of motion to update positions by incrementing with a finite timestep. The simulation can be periodically sampled to get statistical estimates for properties of interest, such as the potential and total energies of the system.³¹ Coordinate data are also collected for examination of the dynamical behavior of the particles.

One limitation of MD simulations is the accuracy of the energy interaction model (e.g., force fields) used, which may or may not enable the desired chemical insight. For instance, simulations of complicated chemical systems such as transition metal catalysts require energy models that include dispersion and electrostatic interactions. Fortunately, incorporating different energy models only changes the force calculation. So, appropriate selection of the energy interaction model, which can range from FFs to *ab initio* methods, is necessary. For example, when *ab initio* methods are used for energies, the motion of the atoms are simulated by calculating the interactions from the electronic structure of the system, which is computationally expensive. The high computational cost makes semi-empirical methods such as xTB viable for simulations instead.

1.5.2 Enhanced Sampling

Due to the limitation on the timestep in MD, timescales explored by simulations may not be sufficiently long to describe the reaction or process of interest. Additionally, due to the Boltzmann nature of MD sampling, simulations can be trapped in metastable states where the system must overcome a high potential energy barrier between states.³² To address these limitations, enhanced sampling techniques have been developed to accelerate sampling. Many of these techniques are useful for recovering the equilibrium probability distributions of the system, from which thermodynamic properties can be collected.

One class of methods involves localizing the simulations to well-defined regions of configuration space. Localized sampling within region i can be done with a restraint potential along a chosen reaction coordinate ξ . As shown in Equation (1.7), the most common restraining strategy involves a harmonic potential $U_i^{bias}(\mathbf{x})$ with spring constant k that biases the sampling in region i by confining the reaction coordinate $\xi(\mathbf{x})$ to the equilibrium value $\mathbf{z}_i$.

$$U_i^{bias}(\mathbf{x}) = \frac{k}{2} |\xi(\mathbf{x}) - \mathbf{z}_i|^2 \quad (1.7)$$

Umbrella sampling is the piecewise localized sampling of the energy landscape by implementing multiple biasing potentials at different equilibrium values of the reaction coordinate.³³ Each window sampled by the umbrella potential contains more efficient sampling around the equilibrium of the reaction coordinate. After the window trajectories are collected, their respective probability distributions are stitched to yield a single unbiased probability distribution. The free energies can be calculated through schemes such as the weighted histogram analysis method (WHAM) or multiple Bennett acceptance ratio (MBAR), which allow for an estimation of the free energy landscape.^{34,35} Methods such as umbrella sampling are useful for investigating systems of interest where the reaction coordinate is chemically intuitive or known.

1.5.3 Solvation Models

The chemical research presented in this work intends to simulate a high temperature solution polymerization run typical of that preferred in industry. Thus, incorporating the effect of the solvent environment, is important in the computational models. Methods for involving the solvent effect can be widely classified into two types: explicit and implicit solvation. Explicit solvation describes the solvent in terms of individual solvent molecules where they are included in the model along with the system of interest.¹² Usually, realistic explicit solvation models require up to thousands of solvent molecules, which also call for a sampling of the phase space. Since this is computationally expensive, there is a strong interest in implicit methods that treat the solvent in a less exhaustive fashion.³⁶ Implicit solvation models the solvent as a structure-less continuous medium, where long-range and short-range specific solvation effects are computed or parametrized. Leaving out the explicit solvent reduces the degrees of freedom of a system and

lowers the computational cost for studies such as conformational search. Overall, the solvation (free) energy can be written as a sum of components as shown below:¹²

$$\Delta G_{solvation} = \Delta G_{elec} + \Delta G_{cavity} + \Delta G_{dispersion} + \Delta G_{H-Bond} + \dots \quad (1.8)$$

The long-range effects of solvation are treated by continuum solvation models by considering the solvent as a uniform polarizable medium with a dielectric constant (ϵ), where the solute is placed in a hole in the medium. The dielectric constant ϵ is a parameter that characterizes the electrostatic component of the solvent. The hole in the medium is usually defined as a sphere or an ellipsoid, which allows the electrostatic interaction between solute and the dielectric medium to be calculated analytically. More realistic models use molecular-shaped holes corresponding to the van der Waals surface of the solute, which is then traced out by spherical particles of a given radius corresponding to the solvent. This is defined as the Solvent-Accessible Surface Area (SASA), which is used to compute nonpolar contributions such as solute-solvent cavity and dispersion interactions.³⁶

The polar contribution can be described at higher levels of approximation, which is done by Poisson-Boltzmann and Generalized Born models. Poisson-Boltzmann (PB) methods involve solving differential equations numerically in a grid representation, which give information about the electrostatic potential at any point in space.³⁷ The Poisson equation connects the electrostatic potential to the charge distribution (ρ) and ϵ , where the charge densities of ions (ρ_+ and ρ_-) are given by the Boltzmann distribution. The resulting potential is mapped to the surface of the solute, where regions of interaction with other polar molecules can be described. On the other hand, Generalized Born (GB) models were developed to reproduce the accuracy of PB models without solving for differential equations.³⁸ In GB models, partial atomic charges in a spherical cavity are used to describe charge distribution. Additionally, the Coulomb interaction between the partial

charges depends on the effective Born radii of the atoms, which describe the self-energy contributions of the atoms.³⁶ In practice, PB and GB methods (ΔG_{elec}) are normally combined with SASA (ΔG_{cavity} , $\Delta G_{dispersion}$) to compute the solvation energy.³⁷ The computational studies in the following chapters use these efficient implicit solvation methods.

1.6 Computational Modeling of Transition Metal Catalyzed Olefin Polymerization

1.6.1 Computable Catalyst Properties

The growth and success of metallocenes has led to the development of new organometallic complexes that serve as single-site polymerization catalysts. Although studies have ranged from transition metals to main-group elements, group IV organometallics have seen great use in academic and industrial research for olefin polymerization.³⁹ Development of group IV post-metallocenes, such as *ansa* half-metallocenes and pyridylamido complexes, has involved significant catalyst design, where different ligands and cocatalysts influence catalyst performance and properties of the polymer produced. Understanding the interactions of the ligands and the cocatalyst with the metal center is important for improving the design of new efficient catalysts for olefin polymerization.

Computational studies of olefin polymerization catalysts have focused on steric and electronic properties that give insight into observed catalyst properties. For example, the computed electronic properties of cyclopentadienyl derivatives in zirconium-based complexes showed that the donor ability of the ligands is correlated with the relative stability of the cationic catalyst.⁴⁰ Direct correlations between experimental activity and steric descriptors have also been observed, where descriptors such as ligand cone angle describe the likelihood of monomer uptake. Most

studies use static DFT methods that can provide accurate geometries and energetics to obtain these relationships.

1.6.2 Modeling the Olefin Polymerization Process

The mechanism of the polymerization process with group IV olefin polymerization catalysts are well-established based on extensive research from experimentalists and theoreticians. The primary mechanistic steps (**Figure 1.3**) include activation, initiation, propagation, and termination.⁴¹ Activation of the precatalyst requires a cocatalyst or via a dissociation reaction, resulting in the formation of the catalytic active species. Chain initiation involves olefin coordination into a vacant coordination site at the metal center and first monomer insertion into the metal-alkyl bond. Chain propagation involves consecutive steps consisting of uptake of a free monomer and insertion into the metal-polymer bond, leading to a growth of the polymer chain. Chain termination concludes the polymerization cycle and can occur in various ways. Depending on the catalyst and monomer, polymer growth can involve chain isomerization, which leads to formation of branched structures of the polymer.

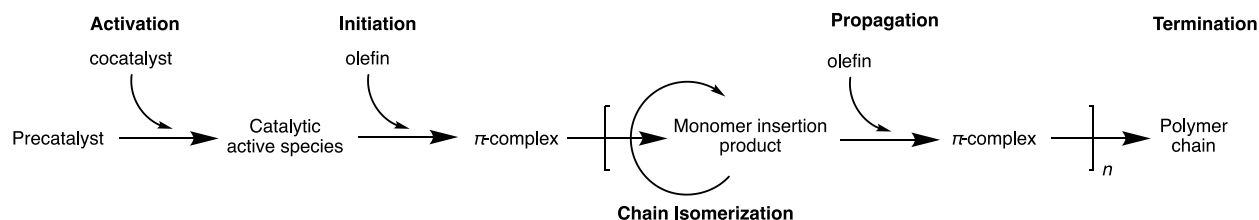


Figure 1.3. Basic steps in the olefin polymerization mechanism.

In activation, the dimethyl precatalyst, $(L)_2M(CH_3)_2$, reacts with a cocatalyst A, which abstracts one of the CH_3 groups to produce $[(L)_2M(CH_3)]^+$, an activated cationic catalyst. Methyl abstraction also generates the anionic form of the cocatalyst, $[A]^-$, where cocatalysts are generally boron-based Lewis acids. Activation leads to the formation of an ion pair, where the anionic counterion or counteranion interacts with the metal center and ligands of the cationic catalyst.

Under standard polymerization conditions, the ion pair is not dissociated. The nature of the ion pair in inert solvent can vary from contact ion pair to olefin-separated ion pair during the polymerization process (**Figure 1.4**; M=transition metal, A=anion, L=ancillary ligand, R=alkyl, S=solvent). The counteranion interacts with the metal through weak electrostatic interactions in inner sphere ion pairs, whereas it interacts with the second coordination sphere in outer sphere ion pairs.

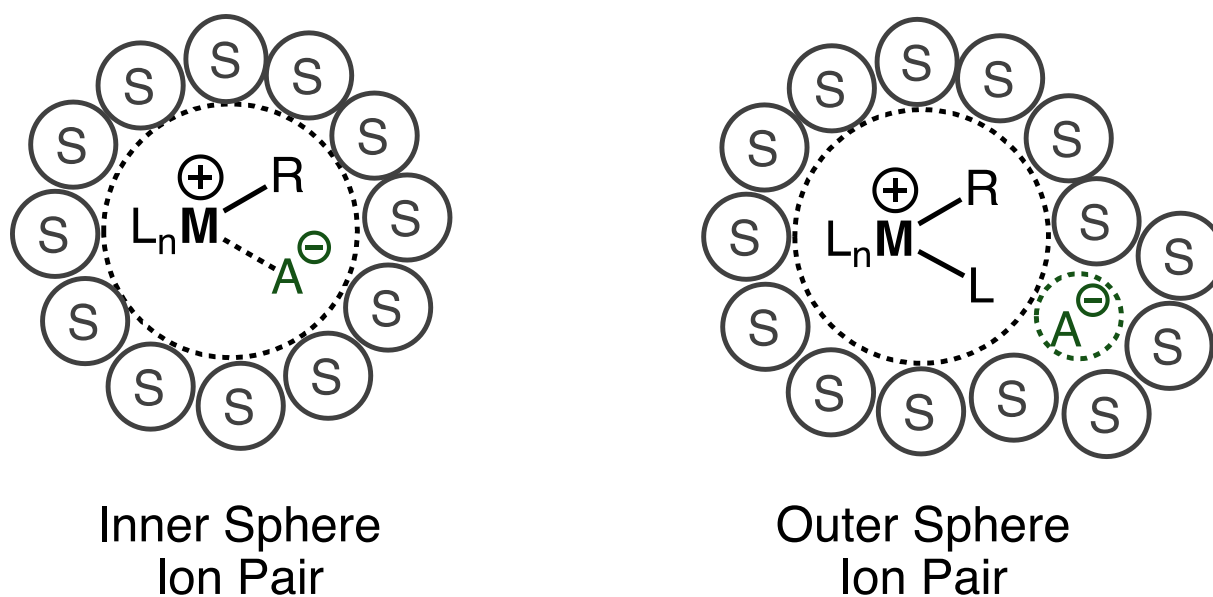


Figure 1.4. Types of contact ion pairs in ionic transition metal complexes.

The type of cocatalyst used has been found to affect catalyst properties such as activity and polymer molecular weight, which indicates that the counteranion plays a role in chain growth. For instance, it is well-established that weakly coordinating counteranions facilitate monomer coordination, resulting in higher catalytic activity. Additionally, replacing phenyl substituents in boron-based cocatalysts with naphthyl rings increases the molecular weight of copolymers produced with group IV metallocenes (e.g., Zr).⁴² Such changes in catalyst performance with varying counteranion require an understanding of their microscopic origin by modeling the steps in the polymerization process involving the ion pair.

However, there are some limitations in molecular modeling of the polymerization steps. In quantum chemical studies, the counteranion is usually ignored in the elementary reactions of the catalytic cycle. The naked cation approximation is not sufficient in mechanistic studies as reaction barriers significantly change with the counteranion present.⁴³ The ion pair is dynamic during polymerization and static studies are by definition not sufficient to tackle ion pairing conformational effects. These limitations are accounted for in the work below. Through simulations, the microscopic effects of ion pair conformations on olefin polymerization reactions are revealed.

1.7 Dissertation Outline

Chapter 1 provided a brief overview of how computational tools are used to inform chemical understanding. Chapter 2 shows how these tools are adapted and combined to fill a gap in the understanding of group IV-catalyzed olefin polymerization. The reactions involved in olefin polymerization at transition metal centers—such as Ti constrained geometry catalysts—have been widely known for some decades, but models that can predict the rate and degree of polymerization are still lacking. This chapter shows that considering the conformational effects from the flexibility of the counteranion and the polymer is necessary to reach qualitatively correct models. Molecular dynamics simulations show that the length of the polymer chain substantially influences the counteranion position, where longer polymer chains have a tendency to limit the counteranion's access to the monomer coordination site. The effective free energy of activation for monomer insertion and chain termination are also affected by ion pair conformations, where the counteranion being on the opposite side of the Ti catalyst as the ethylene monomer are preferred for productive reaction pathways.

Chapter 3 is a conformational investigation of how bridgehead substitution leads to multi-site behavior for olefin polymerization with the Hf-pyridylamido catalyst. The influence of bridgehead substitution in catalyst-cocatalyst ion pair interactions is explored computationally, as the fitting of the ion pair is undoubtedly connected, but poorly understood, with active-site behavior. Molecular dynamics simulations show that specific structural differences between the two cocatalyst-activated diastereomers influence ion pair conformations. The position of the bridgehead substituent in one diastereomer enables the counteranion to slide to favorable staggered orientations suitable for outer sphere coordination, whereas the other diastereomer prefers the counteranion with inner sphere coordination. The use of enhanced sampling simulations informs the path to active site opening and olefin coordination, where it is revealed that ethylene coordinates preferentially to the active site of one, but not the other, of the two diastereomers.

Chapter 4 summarizes the work done above and the significance to modeling olefin polymerization catalysis. Additionally, future directions for the systems studied and sampling workflow are discussed.

Chapter 2 Revealing the Interactions between the Flexible Polymer and Counteranion during Propagation and Termination for Olefin Polymerization with the Ti(IV) Constrained Geometry Catalyst

This chapter is based upon published work:

Punzalan, E.; Froese, R.D.; Zimmerman, P.M. Revealing the Interactions between the Flexible Polymer and Counteranion during Propagation and Termination for Olefin Polymerization with the Ti(IV) Constrained Geometry Catalyst. *Organometallics* **2023**, 42 (22), 3236-3248.

2.1 Abstract

The structure and behavior of counteranions $\text{MeB}(\text{C}_6\text{F}_5)_3^-$ and $\text{B}(\text{C}_6\text{F}_5)_4^-$ interacting with a constrained-geometry Ti olefin polymerization catalyst and its growing polymer chain are examined through conformer sampling and reaction pathway simulations. The results show that the length of the polymer chain substantially influences the counteranion position, where longer polymer chains have a tendency to limit the counteranion's access to the monomer coordination site. Conformations affect not only ion pair preferences, but also the effective free energy of activation for monomer insertion and chain termination. Ion pair orientations of the π -complex where the counteranion is on the opposite side of the Ti catalyst as the ethylene monomer are preferred for productive insertion and chain termination reaction pathways. These result in ion pairs of $\text{B}(\text{C}_6\text{F}_5)_4^-$ having orientations conducive to ethylene insertion as well as chain termination via β -hydrogen transfer, which can explain why $\text{B}(\text{C}_6\text{F}_5)_4^-$ results in lower molecular weight of the polymer.

2.2 Introduction

Olefin polymerization catalysis through single-site, group IV organometallics allows for a high degree of control over the polymer microstructure. Many examples such as metallocenes and *ansa* half-metallocenes have been used in the production of high and low density polyethylene.^{44,45} In particular, constrained-geometry catalysts (CGCs) derived from metallocene *ansa*-bridged compounds have outstanding performance in ethylene polymerization and in copolymerizations with higher α -olefins.^{45–47} Significant research in this area has been carried out on controlling catalytic activity and polymer architectures.^{48,49} One key factor that influences these properties is the cocatalyst, which plays an important role in catalyst activation, chain propagation, molecular weight, and polymer dispersity.^{50,51}

The active catalyst for olefin polymerization consists of an ion pair involving the cationic metal complex and the anionic cocatalyst. Modifications on the anion are known to influence catalyst performance, especially in analogs of tris(pentafluorophenyl)borane ($\text{B}(\text{C}_6\text{F}_5)_3$).⁵² Substantial experimental evidence has indicated that the counteranion affects the catalysts' living character and polymer dispersity.^{53,54} Parveen et al. found that replacing perfluorophenyl substituents in $\text{B}(\text{C}_6\text{F}_5)_4^-$ with naphthyl rings resulted in an increase in molecular weight of the ethylene-propylene copolymer for silicon-bridged bis-indenyl metallocenes.⁴² $\text{B}(\text{C}_6\text{F}_5)_4^-$ was found to lead to higher polymerization activities than $\text{MeB}(\text{C}_6\text{F}_5)_3^-$ under similar conditions (20°C, 1 bar, toluene) for group IV metallocenes.⁵⁵ In CGCs such as *ansa*-cyclopentadienylamido and -fluorenylamido complexes, on the other hand, there is an observed trade-off between catalytic activity and polymer molecular weight (MW) depending on the counteranion identity. Ti-CGC-catalyzed propene polymerization with $\text{B}(\text{C}_6\text{F}_5)_4^-$ was observed to be 10 times more active (-50°C, toluene) than with $\text{MeB}(\text{C}_6\text{F}_5)_3^-$, which indicate higher catalytic activity for $\text{B}(\text{C}_6\text{F}_5)_4^-$.⁵⁴ However,

$\text{B}(\text{C}_6\text{F}_5)_4^-$ was less stable in producing a living polymer, which affected the molecular weight distribution.⁵⁴ These phenomena have been interpreted by invoking interactions between the cation and anion via contact ion pairs in low dielectric constant solvents.^{56,57} These changes in catalyst performance with varying counteranion, however, require a deeper explanation to better understand their microscopic origin.

The abovementioned effects can be qualitatively attributed to the specific interactions involving the active catalyst-cocatalyst ion pair. During polymerization, the physical features of the catalyst-cocatalyst pair can influence monomer coordination, insertion, and chain termination steps.^{15,16} For example, monomer insertion occurs at an open site of the active catalyst, but this site may be occupied by the cocatalyst, which may move between inner sphere and outer sphere coordination as the reaction progresses (**Figure 2.1**).^{60,61} This means that growth of the polymer chain on the active species is controlled not only by insertion barriers but also by the equilibrium concentrations of the inactive and active ion pair structures.³⁹ For the two counteranions under consideration, $\text{MeB}(\text{C}_6\text{F}_5)_3^-$ is believed to prefer inner-sphere ion pairs (ISIP) and $\text{B}(\text{C}_6\text{F}_5)_4^-$ outer-sphere ion pairs (OSIP).^{51,52} Weakly coordinating anions such as the $\text{B}(\text{C}_6\text{F}_5)_4^-$ anion may be argued to facilitate monomer coordination, leading to higher polymerization activities compared to $\text{MeB}(\text{C}_6\text{F}_5)_3^-$. This reasoning suggests that ion pair strength inversely correlates with catalyst activity.^{62–64}

The covalently bound polymer chain also interacts significantly with the metal catalyst, affecting initiation, propagation, and termination steps. In particular, agostic interactions and internal chain rotations may occur along with a variety of chain orientations (in addition to counteranion coordination). Lanza et al. and Ziegler et al. used quantum chemical simulations to examine the first and second olefin monomer insertions into a CGC ($\text{Cp}^*\text{SiMe}_2\text{N}^t\text{Bu}$) TiR^+ ($\text{R} =$

Me, Pr) in the presence of $\text{MeB}(\text{C}_6\text{F}_5)_3^-$.^{65–68} In the first insertion, the monomer coordinates to the metal center to form a π -complex along with counteranion displacement, and the olefin inserts into the metal-carbon bond to yield an agostic complex (Figure 1a). The second and subsequent insertions in chain propagation lead to more complex reaction products since the growing chain can adopt different orientations with or without polymeric H atoms forming agostic interactions (**Figure 2.1b**).⁶⁹ Simulations of the second insertion found that the direct product of insertion can be a γ - or δ -agostic intermediate, which can rearrange through alkyl rotation into a stable β -agostic complex.^{70–72} Nifant'ev et al. compared the effects of $\text{MeB}(\text{C}_6\text{F}_5)_3^-$ and $\text{B}(\text{C}_6\text{F}_5)_4^-$ on ethylene propagation in Cp_2ZrR ($\text{R} = \text{Et, Bu}$) metallocenes and found $\text{B}(\text{C}_6\text{F}_5)_4^-$ forms an OSIP with the cation, leading to a higher fraction of the β -agostic isomer and lower barriers for insertion compared to $\text{MeB}(\text{C}_6\text{F}_5)_3^-$ anion.⁷³ Chain termination is in competition with propagation, where β -hydrogen transfer (βHT) starts from the same OSIP β -agostic olefin π -complex as the insertion path (**Figure 2.1**).^{74,75} The preference of $\text{B}(\text{C}_6\text{F}_5)_4^-$ ion pairs for OSIPs has been suggested to be more conducive to β -agostic interactions that are required for βHT termination, which may explain why $\text{B}(\text{C}_6\text{F}_5)_4^-$ leads to lower MW polymers than $\text{MeB}(\text{C}_6\text{F}_5)_3^-$.^{35,36} The details of the equilibrium between OSIP and ISIP and their connection to insertion and termination steps are therefore critical, but have not been extensively explored so far.

The inner and outer sphere interactions of catalyst, polymer chain, and counteranion all play a role in polymer chain growth, where counteranions influence the relative rates by favoring different equilibrium structures. Agostic interactions in intermediates introduce ion pair separation, and the weak γ - or δ -agostic bonds cannot compensate for the energy cost of this separation.⁷³ Atomistic simulations are therefore critical in identifying stable intermediates that occur through isomerization, polymer chain conformational changes, and/or ion pair

reorganization (**Figure 2.1**).⁷³ Relevant possibilities include changes in polymer chain geometry near the metal center through cleavage or formation of agostic bonds and internal chain rotation, or large amplitude motions of the ion pair.^{76,77} Ion pair reorganizations—between ISIPs and OSIPs—seem to favor different equilibrium states for $\text{MeB}(\text{C}_6\text{F}_5)_3^-$ and $\text{B}(\text{C}_6\text{F}_5)_4^-$, with an unknown dependence on polymer length.³⁹ This is observed via in-situ NMR studies of insertion events in zirconocenes, where the less active $\text{MeB}(\text{C}_6\text{F}_5)_3^-$ anion is inferred to lead to continuous propagation due to the rate difference between recoordination and propagation, where each monomer insertion is followed by counteranion recoordination.^{4,76,78} On the other hand, the catalytically more active $\text{B}(\text{C}_6\text{F}_5)_4^-$ is believed to follow the intermittent propagation mode, where chain growth occurs via successive monomer insertions with occasional interruption by anion recoordination.^{79,80} A balance between ISIP and OSIP states, influenced by favorable cation-anion electrostatic interactions and unfavorable steric constraints, controls the likelihood of these two propagation modes. Additionally, interactions between the counteranion and polymer chain are also likely to be significant, providing another complicating factor that controls the propagation mode.

Despite their critical importance, the specific equilibrium and structural principles that dictate catalyst behavior with changes in polymer conformation and counteranion position have yet to be clearly understood. In the present study, the influence of $\text{MeB}(\text{C}_6\text{F}_5)_3^-$ (methyltris(perfluorophenyl)borate) and $\text{B}(\text{C}_6\text{F}_5)_4^-$ (tetrakis(perfluorophenyl)borate) counteranions on ethylene polymerization catalyzed by a prototypical $[(\text{Cp}^*\text{SiMe}_2\text{N}^t\text{Bu})\text{Ti}-\text{Polymer}]^+$ or CGC (Ti-CGC) is explored. We investigate the microscopic origin of the observed differences in activity and polymer MW between $\text{MeB}(\text{C}_6\text{F}_5)_3^-$ and $\text{B}(\text{C}_6\text{F}_5)_4^-$ through molecular dynamics and reaction path search simulations. Molecular dynamics simulations are used to

explore the range of $[\text{Ti-CGC}]^+[\text{anion}]^-$ ion pair orientations of the resting state and π -complex. The conformational landscape involving a shorter polymer chain will include a wider range of ion pair orientations, whereas the presence of a longer polymer chain leads to ion pair conformers that are more conducive to propagation. The conformer effects arising from different anion orientations influence transition state energies of monomer insertion and chain termination kinetics, with orientations farther from the monomer leading to lower reaction barriers. In total, the simulations of this study will provide a new viewpoint on the impact of counteranion-polymer interactions on insertion and termination reactions involving Ti-CGC catalysts.

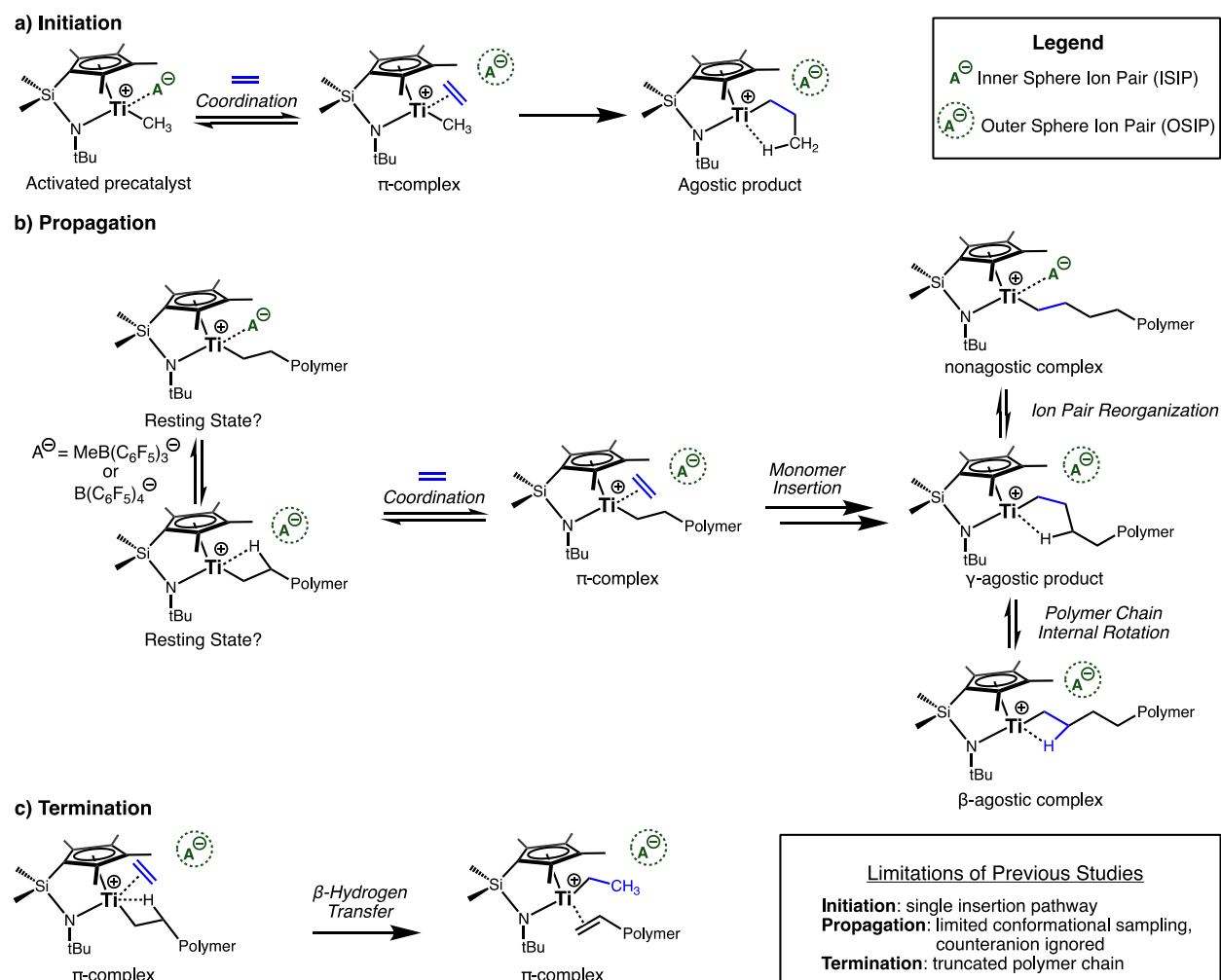


Figure 2.1 Schematic representation of ethylene polymerization by Ti-CGC with counteranion: (a) initiation consisting of first ethylene insertion, (b) propagation to form $[\text{Ti-CGC-C}_n\text{H}_{2n+1}]^+$

with n-meric ethylene polymer chain, and (c) chain termination from the π -complex via β -hydrogen transfer.

2.3 Computational Details

2.3.1 Molecular Dynamics Simulations

2.3.1.1 Model Preparation

Two ion pair (IP) systems were prepared for the MD simulations, which consist of an IP of [Ti-CGC- C_nH_{2n+1}]⁺[anion]⁻ with either MeB(C₆F₅)₃⁻ or B(C₆F₅)₄⁻ (3PFB: MeB(C₆F₅)₃⁻, 4PFB: B(C₆F₅)₄⁻) as the counteranion. With each IP system, the complexes [Ti-CGC- C_nH_{2n+1}]⁺[3PFB/4PFB] (without ethylene) and C₂H₄ [Ti-CGC- C_nH_{2n+1}]⁺[3PFB/4PFB]⁻ (with ethylene) were prepared at two different lengths of the polymer chain ($n = 3, 11$) attached to the metal. The xTB software package was used for molecular dynamics simulations and single-point energy calculations.⁸¹ The GFNFF-xTB force field was used for MD simulations and the GFN2-xTB semiempirical tight-binding method was used for structure optimization.^{21,81,82} The MD simulations were performed in an NVT ensemble at 423.15 K, intended to simulate a higher temperature solution polymerization run (150 °C) typical of that preferred in industry. The NVT-MD simulations were run for 100 ns with a 2 fs time step. From the trajectories, the structures were saved every 1 ps. The ALPB solvation model was used for implicit solvation with toluene as solvent. Harmonic potential restraints were placed on the Ti atom and its distances to the Cp* and Si atoms.

2.3.1.2 Equilibrium Structures of Ion Pairs

To investigate the characteristic change of the ion pair structure, MD trajectories of the [Ti-CGC-polymer]⁺[3PFB/4PFB]⁻ complexes were mapped to distinct regions on the free energy surfaces (FES). To map the FES from the MD trajectories onto two characteristic degrees of freedom, the

interatomic distance r between Ti and B atoms and the Si-Cp*-Ti-B dihedral angle φ formed between the Si-Cp*-Ti and Cp*-Ti-B planes were taken as coordinates (**Figure 2.2**). The centroid of the Cp* ligand is used in calculating φ . The dihedral angle can be envisioned as follows: 0° corresponds to a position below the amido ligand or the polymer chain, 90° corresponds to a position behind the polymer chain, 180° corresponds to a position in front of the catalyst where the titanium and olefin reside, and 270° corresponds to a position on top of the Cp* ligand or below the Ti atom. Calculations were performed by using bins with size (0.05 Å, 2.0°) and the free energy origin (0.0 kcal/mol) is set to the most populated bin.⁵⁷

2.3.2 Reaction Pathways for Insertion and Termination Reactions

2.3.2.1 Transition State Search

For each C₂H₄ [Ti-CGC-polymer]⁺[3PFB/4PFB]⁻ complex, a collection of 10,000-20,000 structures depending on polymer chain length was taken from the MD trajectories and classified into representative configurations using k-medoids clustering on interconformer root mean square deviations (RMSD).⁸³ 100 and 300 medoids were selected for complexes with C₃ and C₁₁ polymer chain lengths, respectively. The optimized medoid structures were used as initial nodes, where the reaction paths and TS structures for insertion and termination reactions were searched for using the Growing String Method.^{24,25,84} The GFN2-xTB method was used to provide energies and gradients with toluene as solvent.⁸⁵ To verify the accuracy of using the GFN2-xTB tight-binding method in the reaction path search, selected TS structures involving the [Ti-CGC-C₁₁H₂₃]⁺[4PFB]⁻ ion pair were compared to QM/MM and DFT methods (**Appendix Table A.1**).

2.3.2.2 Procedure for Effective Free Energy of Activation for Insertion and Termination Reactions

The effective free energy barriers for ethylene insertion and chain termination of the catalysts were computed as a sum of the contributions from possible reaction pathways, while taking into account the populations of the starting π -complexes. Relevant conformers that contribute to monomer insertion and chain termination at the reactant minimum-energy state (RS) and TS were included.⁴⁰ To account for the equilibrium availability of RS conformers on the effective Gibbs energy of activation ($\Delta^\ddagger G_{\text{eff}}$), we follow the procedure from Williams et al.,⁶

$$\exp\left(-\frac{\Delta^\ddagger G_{\text{eff}}}{RT}\right) = \sum_i^{\text{RS}} x_i^{\text{RS}} \exp\left(-\frac{\Delta^\ddagger G_i}{RT}\right) \quad (2.1)$$

This procedure takes the sum of RS-weighted exponential terms involving individual Gibbs energy differences $\Delta^\ddagger G_i$ from each RS conformer to its corresponding TS conformer. Here, each individual Gibbs energy of activation $\Delta^\ddagger G_i$ is for an individual reaction path from RS_i to TS_i . Since MD samples from the Boltzmann distribution, the mole fraction x_i^{RS} of conformer i is expressed as the population ratio of each conformer to the total number of conformers. To estimate the error associated with obtaining the $\Delta^\ddagger G_{\text{eff}}$ value, random sampling of subsets (80%) of the reaction path set was done for 1000 trials. For each subset j , a corresponding $\Delta^\ddagger G_{\text{eff}}^j$ was calculated. The mean and standard deviation of $\Delta^\ddagger G_{\text{eff}}$ are the values reported below.

2.4 Results and Discussion

Extensive sampling of the conformational spaces of Ti-CGC catalyst, counteranion, and polymer chain was carried out with the methods described in the Computational Details section. Following this, reaction pathway searches were used to determine the free energies of reaction. The results are organized as follows. First, the conformational behavior of $[\text{Ti-CGC-polymer}]^+[\text{anion}]^-$ (3PFB: $\text{MeB}(\text{C}_6\text{F}_5)_3^-$, 4PFB: $\text{B}(\text{C}_6\text{F}_5)_4^-$) for representative polymer chains is investigated by considering

equilibrium structures of the ion pairs obtained from MD simulations. Then, a binning procedure is used to examine the characteristic differences between 3PFB and 4PFB ion pair structures with short and long polymer chain lengths. The last section reports on the free energy of activation for ethylene monomer insertion and chain termination at $[\text{Ti-CGC-polymer}]^+[\text{3PFB/4PFB}]^-$ for representative structures arising from the clustering procedure. This analysis will show crucial conformational contributions to the effective free energy barrier for insertion and termination, which align with and explain some experimentally observed differences in catalytic activity and MW as a function of counteranion choice.

2.4.1 Equilibrium Ion Pair Structures with $\text{MeB}(\text{C}_6\text{F}_5)_3^-$ vs $\text{B}(\text{C}_6\text{F}_5)_4^-$ Counteranions

2.4.1.1 Ion Pair Structure for $[\text{Ti-CGC-C}_3\text{H}_7]^+[\text{3PFB/4PFB}]^-$

The first question under examination is the behavior of the ion pair at short polymer chain lengths, which may take on inner sphere (ISIP) and outer sphere (OSIP) ion pair conformations when no monomer is ligated. MD simulations resulted in the FE maps of **Figure 2.2**, which show Ti-CGC with a 3PFB or 4PFB anion and a C_3 (propyl) polymer chain. In the absence of the ethylene monomer, the conformers of $[\text{Ti-CGC-C}_3]^+[\text{3PFB}]^-$ and $[\text{Ti-CGC-C}_3]^+[\text{4PFB}]^-$ show that the anions can be distributed over a range of orientations (φ) along the Si-Cp*-Ti-B dihedral. The states of the complex are distributed in a wide span of $5.5 \text{ \AA} \leq r \leq 9 \text{ \AA}$ and $0^\circ \leq \varphi \leq 360^\circ$. Region B (**Figure 2.2**) is the lowest energy region, representing 42% and 41% of the total conformers for 3PFB and 4PFB ion pairs, respectively. Region B includes ISIP structures, where the counteranion is in front of the Ti center with $\text{Ti} \cdots \text{F}$ interactions (2.3 to 3.8 Å). Region A (**Figure 2.2**) is the next lowest energy region, representing 24 and 25% of total conformers, respectively. This region includes more OSIP structures with longer B-Ti distances ($7 \leq r \leq 9 \text{ \AA}$), where the counteranion takes on a φ orientation to the back of the Ti center (behind the ligand).

The ion pair conformations change significantly when ethylene is bound to the Ti center. The C_2H_4 $[\text{Ti-CGC-C}_3]^+[\text{3PFB/4PFB}]^-$ ethylene π -complex involves OSIPs at $r > 7 \text{ \AA}$, where the anion is displaced to the catalyst's outer coordination sphere. Region A' (**Figure 2.2**), the region analogous to region A after ethylene coordination, is now the most stable region for (3PFB + Et) and (4PFB + Et) complexes, accounting for 46 and 42% of the total structures. The ion pair structure in this region shows the anion displaced from the Ti center, where the ethylene is in the front side and the anion is in the back side of Ti, which allows the anion to be in less congested OSIP orientations. Region B' (which was the most preferred in monomer-less complexes) is less preferred when ethylene is coordinated, accounting for 23% and 26% for (3PFB + Et) and (4PFB + Et), respectively. The ion pair structure in this region shows the displaced anion at a farther r distance located on the same side of the catalyst as ethylene. The φ values in the outlined regions of the FE maps show a change in distribution of states when the ethylene is coordinated, due to the absence of ISIP contact that holds the counteranion in place. Instead, the anion must find other locations with short r values where the ions can maximize their Coulomb binding. For instance, region C' shows a small increase in the structures with top ion pair alignments, where the anion can be below or above the complex and interacting with the Cp^* ligand, accounting for 30 and 31% of the total structures for (3PFB + Et) and (4PFB + Et), respectively. Based on these FE maps, the states of the complex are distributed differently with ethylene monomer since (r, φ) orientations that are conducive to OSIPs are preferred, and ISIP coordination becomes inaccessible. The short C_3 polymer has a minimal effect on these ion pair orientations, but this factor will change with a longer length of the polymer chain.

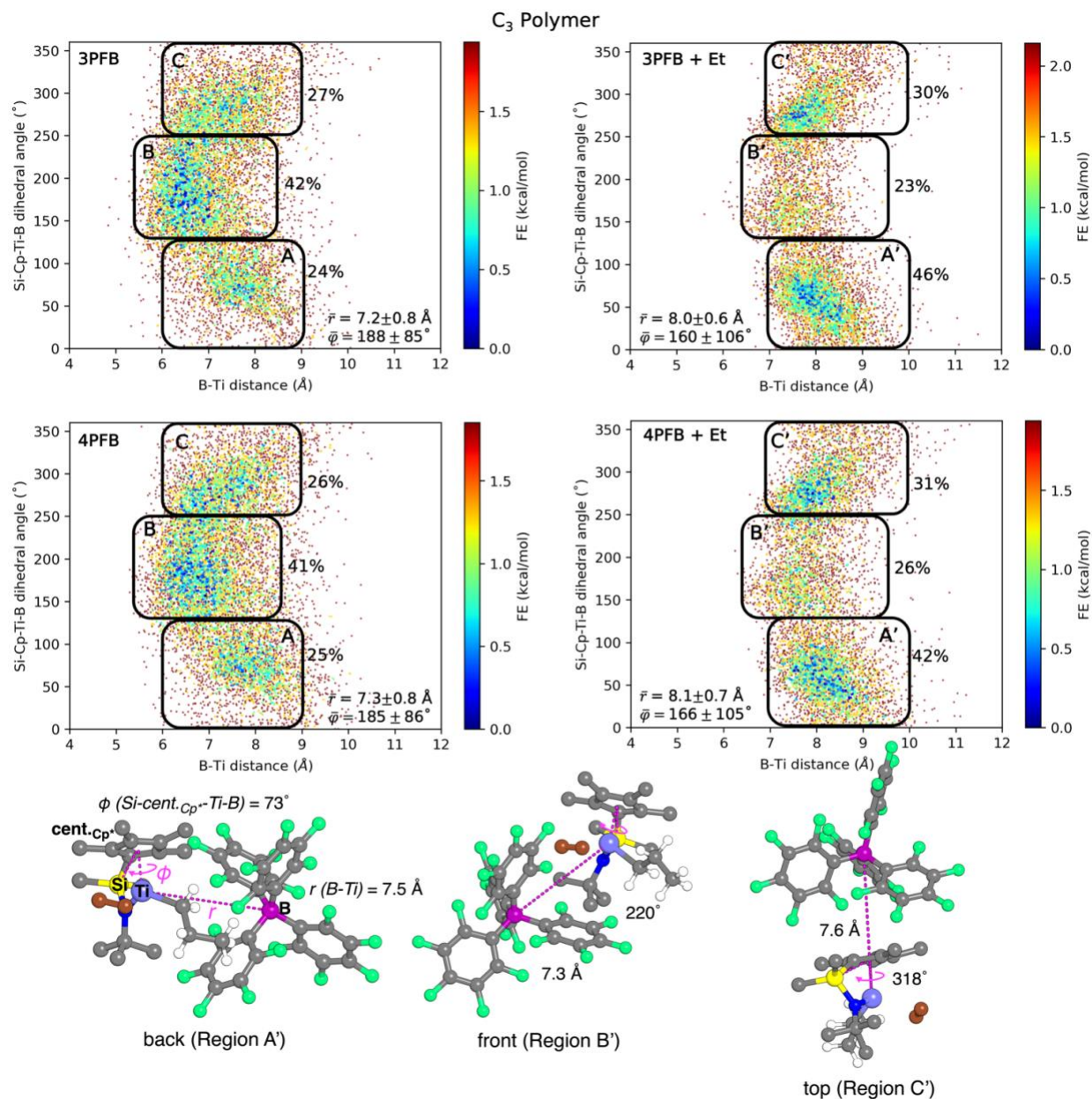


Figure 2.2 Free energy maps with respect to B-Ti distance and Si-Cp*-Ti-B dihedral angle for the [Ti-CGC-C₃H₇]⁺[3PFB/4PFB]⁻ (left) and C₂H₄ [Ti-CGC-C₃H₇]⁺[3PFB/4PFB]⁻ (right) ion pair complexes. (bottom) Representative (4PFB + Et) structures classified by ion pair alignment showing the B-Ti distance and Si-Cp*-Ti-B dihedral angle.

2.4.1.2 Ion Pair Structure for [Ti-CGC-C₁₁H₂₃]⁺[3PFB/4PFB]⁻

As the polymer chain grows, an increased preference for OSIPs is observed in the FES compared to the C₃ chain. **Figure 2.3** shows the FE maps of Ti-CGC with 3PFB or 4PFB anion and a C₁₁ (undecyl) polymer chain (no ethylene). Similar to the C₃ ion pairs, the complexes of [Ti-CGC-

$C_{11}]^+[3PFB]^-$ and $[Ti-CGC-C_{11}]^+[4PFB]^-$ show ISIPs in region B, which remains the lowest energy region and accounts for 56 and 59% of total conformers, respectively. Region B, however, also shows (**Figure 2.3**) that transitions to OSIPs become more prevalent as depicted by higher populations at longer distances ($7 \text{ \AA} \leq r \leq 9 \text{ \AA}$). Region A (**Figure 2.3**), representing 22 and 30% of total conformers for 3PFB and 4PFB, is characterized by OSIPs where the anion cannot interact with the Ti center due to hindrance from the polymer chain. Meanwhile, region C (**Figure 2.3**) includes OSIPs where the anion is below the catalyst and the polymer chain, which account for 13% and 4% of total conformers, respectively. This is in contrast to the higher prevalence of top ion pair alignments in region C observed with the C_3 polymer, where the anion can be located below or above the cation. The preference of 3PFB for regions A and C is comparable, whereas 4PFB prefers region A more. This means that the 3PFB anion could be located in regions A, B, or, C, whereas 4PFB is more likely to settle in between region A and B, with Region B favored for both anions. The change in conformer distribution could be reflective of the size difference between the anions, where the longer polymer chain and the larger 4PFB anion take up more space and restrict the anion from populating region C.

For $C_2H_4 [Ti-CGC-C_{11}]^+[3PFB/4PFB]^-$ complexes with ethylene, the three major regions are similar to those without ethylene, though the distribution of populations changes. Region A' (**Figure 2.3**) is the most stable region in the (3PFB + Et) and (4PFB + Et) complexes, whereas A' and C' were approximately equivalently populated with the C_3 polymer chain. This region contains ~56% of all structures for either anion, where the anion is on the backside of the catalyst opposite to the ethylene coordinated in front of Ti center. Meanwhile, Region B' (which was preferred in monomer-less complexes) is the second lowest energy region and represents ~33% of total structures. This region is characterized by ion pair structures where the anion is on the same side

of the catalyst as ethylene. Region C' was the least preferred region with ~6% of total structures, where the anion is below the catalyst and polymer chain. The low population in Region C' means that equilibrium is strongly biased towards Region A' and B', which contrasts with (3PFB + Et) and (4PFB + Et) complexes with C₃ polymer (**Figure 2.2**) where Region A' and C' were similarly populated. Since the free energy maps of monomer-less and Et complexes show that the anions populate OSIP orientations differently when a longer chain is present, the ion pair orientation in the insertion step, which starts with the ethylene π -complex, becomes important in succeeding insertions.

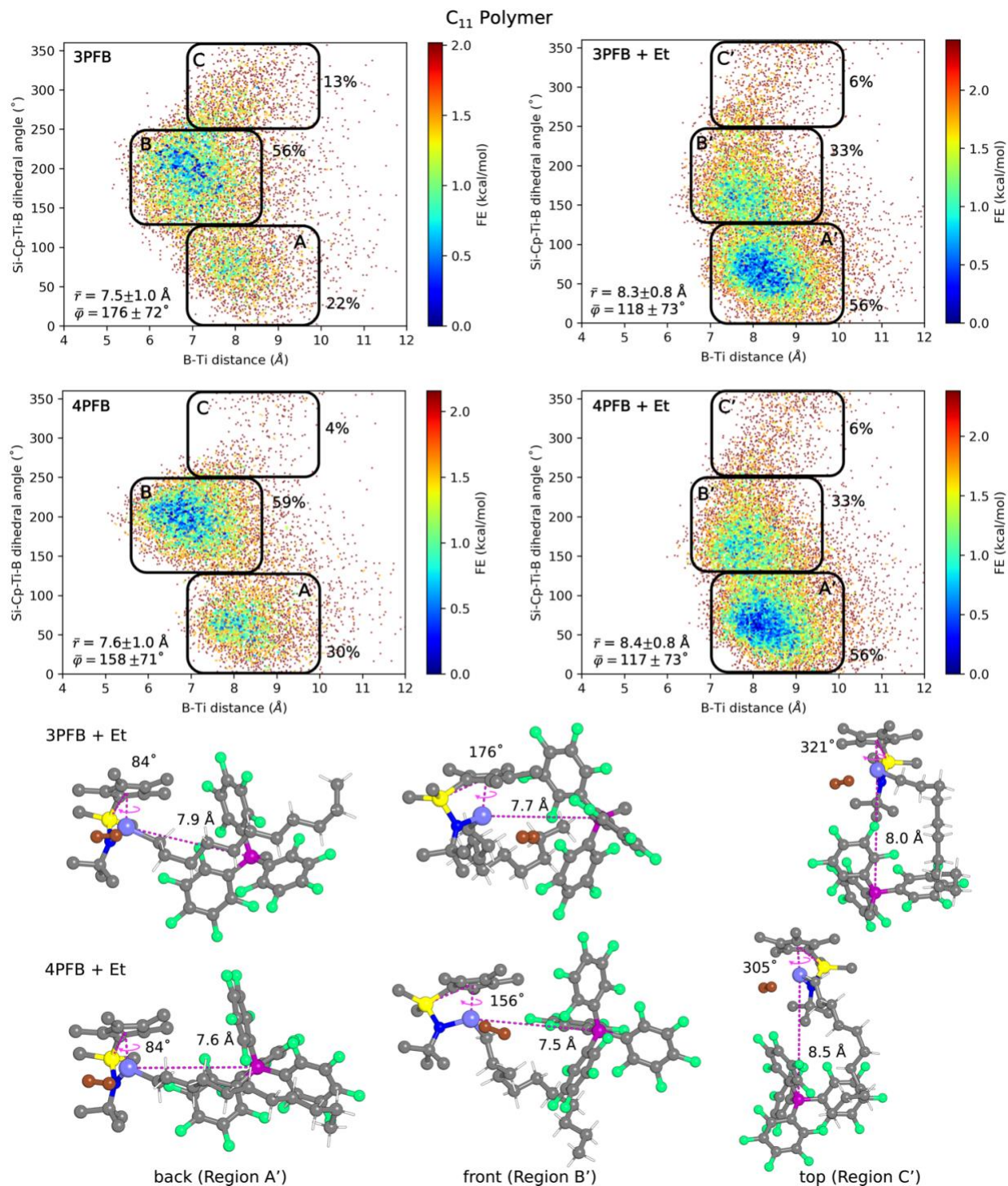


Figure 2.3 Free energy maps with respect to B-Ti distance and Si-Cp*-Ti-B dihedral angle for the $[\text{Ti-CGC-C}_{11}\text{H}_{23}]^+[\text{3PFB/4PFB}]^-$ (left) and $\text{C}_2\text{H}_4[\text{Ti-CGC-C}_{11}\text{H}_{23}]^+[\text{3PFB/4PFB}]^-$ (right) ion pair complexes. (bottom) Representative (3PFB + Et) and (4PFB + Et) structures classified by ion pair alignment showing B-Ti distance and Si-Cp*-Ti-B dihedral angle.

The abovementioned results for $[\text{Ti-CGC-C}_{11}]^+[\text{3PFB/4PFB}]^-$ complexes can be summarized with the help of the representative structures of **Figure 2.4**, which correspond to the labeled regions in **Figure 2.3** (region $A \rightarrow \mathbf{a}$, $B \rightarrow \mathbf{b}$, $C \rightarrow \mathbf{c}$). Without ethylene, structure $\mathbf{b}_{\text{3PFB/4PFB}}$ (**Figure 2.4**) is preferred for both anions. 3PFB can access structures $\mathbf{a}$, $\mathbf{b}$, and $\mathbf{c}$, whereas 4PFB is more likely to prefer structures $\mathbf{a}$ and $\mathbf{b}$. These changes in state are different between the two anions likely because of the size difference due to the additional aryl ring on 4PFB. With the longer C_{11} polymer, the difference between 3PFB and 4PFB can be observed in top ion pair alignments (region C) as the anion is more likely to be below the cation and consequently interact with the polymer and *t*Bu ligand. Meanwhile, when the monomer is present, OSIP structures $\mathbf{a}'_{\text{3PFB/4PFB}}$ and $\mathbf{b}'_{\text{3PFB/4PFB}}$ (**Figure 2.4**) from the corresponding regions A' and B' are significantly stabilized. This means that 4PFB is already at the orientations that are conducive to ethylene monomer coordination, whereas 3PFB can access alternative spaces that are not as viable for ethylene coordination. These differences become more evident with the C_{11} polymer, where the longer chain has an influence on the dominant pair orientations.

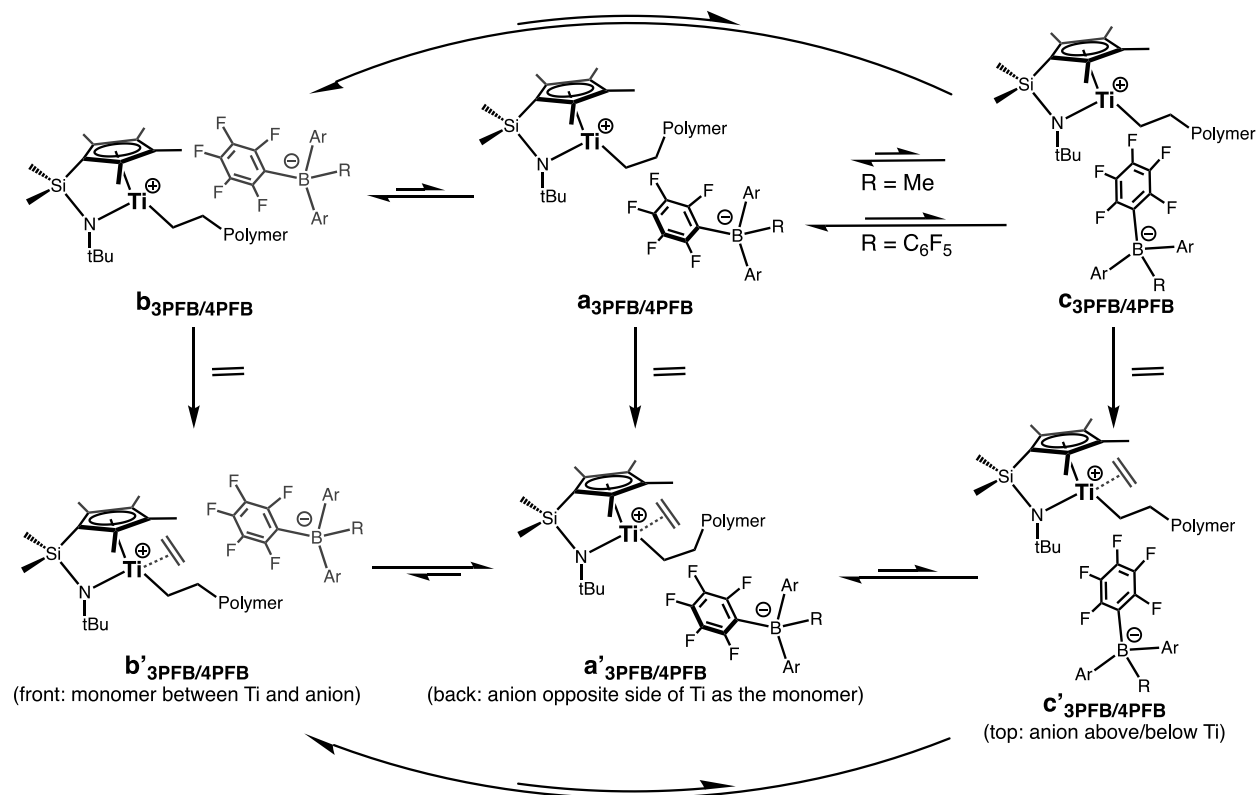


Figure 2.4 Schematic representation of the equilibrium structures of the ion pairs in the ethylene coordination process of the $[\text{Ti-CGC-polymer}]^+[\text{3PFB/4PFB}]^-$ complex. Lowercase labeled structures (a, b, c, a', b', c') correspond to regions A-C and A'-C' in **Figure 2.3**, respectively.

2.4.2 Reaction Pathways of Ethylene Monomer Insertion and β -Hydrogen Transfer in $[\text{Ti-CGC-Polymer}]^+[\text{3PFB/4PFB}]^-$ Ion Pair

The activity of Ti-CGC can be estimated using the free energy of activation for monomer insertion, which in turn provides a propagation rate constant. Moreover, the molecular weight of the polymer produced by Ti-CGC can be estimated using the free energy of activation for β -hydrogen transfer as the chain termination reaction. The effective free energy barriers of insertion and termination depend on an ensemble of accessible insertion and termination pathways, respectively. Determining propagation and termination rates therefore requires the examination of many viable paths, and this ensemble has not been adequately sampled by prior computational studies. Due to the plethora of possible conformers, the free energy of activation must be constructed over many

initial π -complexes as well as TSs. To efficiently assemble this ensemble, a clustering approach was used to identify representative structures. This procedure is described in Computational Details.

2.4.2.1 Ethylene Insertion into $[Ti-CGC-C_3H_7]^+[3PFB/4PFB]^-$

Although the anion is partly displaced in OSIPs during monomer insertion, catalyst-anion interactions can affect whether monomer insertion proceeds or not. At different stages of propagation, there is no established relationship of ion pair orientations that are conducive to or hindering monomer insertion. With the C_3 and C_{11} chain lengths representing a growing polymer chain, each successful pathway involves a π -complex reactant, an insertion TS, and a monomer-inserted product. Based on the preferred ion pair regions outlined in the FE maps previously, the insertion TS structures were labeled (region $A' \rightarrow back$, $B' \rightarrow front$, $C' \rightarrow top$) according to which part of the catalyst the anion is most closely aligned. With the C_3 polymer, successful insertions were found for all alignments. Back and front alignments lead to the highest number of TS structures for 3PFB, whereas back and top alignments lead to the highest number of TS structures for 4PFB (**Figure 2.5a**). From the successful reaction path searches, activation barriers $\Delta^\ddagger G_i$ ranged from 5.3 to 20.0 kcal/mol and from 4.3 to 20.5 kcal/mol for 3PFB and 4PFB (**Figure 2.5a**), respectively, when referencing each TS to its corresponding reactant conformer.

Based on the ensemble of monomer insertion pathways, the effective Gibbs free energies of activation $\Delta^\ddagger G_{eff}^{MI}$ for the 3PFB C_3 and 4PFB C_3 ion pairs are 8.2 ± 0.2 and 7.8 ± 0.4 kcal/mol, respectively. Experimental estimates of the olefin insertion barrier, especially for ethylene and propylene polymerization systems, have been difficult to obtain due to high reactivity and the complex kinetic nature of the systems. Nevertheless, NMR analysis by Erker et al. estimated the intrinsic olefin (propene to 1-hexene series) insertion barrier into the Zr-C bond, relative to the

olefin π -complex of $(\text{MeCp})_2\text{Zr}(\mu\text{-C}_4\text{H}_6\text{-B}(\text{C}_6\text{F}_5)_3^-)$, to be about 10-11 kcal/mol at 15-20 °C, which is comparable to the $\Delta^\ddagger G_{\text{eff}}^{\text{MI}}$ barriers reported here.^{86,87} Meanwhile, DFT calculations provided insertion barrier values of around 7-10 kcal/mol.⁴² Bochmann et al. reported experimental activation barriers for propylene polymerization with $[\text{SBIZrMe}]^+[\text{3PFB/4PFB}]^-$ (SBI = $\text{Me}_2\text{Si}(1\text{-Ind})_2$) of 15.8 kcal/mol and 13.0 kcal/mol for 3PFB and 4PFB, respectively, which involve the overall barrier including both complexation and insertion.⁸⁸ Landis et al. also reported an overall activation barrier of 13.2 kcal/mol for propene polymerization with $[\text{EBIZrMe}]^+[\text{3PFB}]^-$ (EBI = ethylene-1,2-bis(1-indenyl)).⁸⁹ Given the smaller size of ethylene monomer compared to other olefins, the computed effective insertion barrier from the ensemble of reaction paths are in rough agreement with other computational estimates and experimental estimate of the intrinsic olefin insertion barrier.

Further analysis of the conformational ensemble show how anion alignment contributes to the effective insertion barrier. The lowest $\Delta^\ddagger G_i$ for Ti-CGC with 3PFB and 4PFB come from ion pairs with back alignments, which are ~3-4 kcal/mol lower than other alignments. The anion-monomer distance (**Figure 2.5b**), quantified by the Et-B distance, shows that successful insertion, which involves the monomer and α -carbon of C_3 polymer moving closer to each other, can happen regardless of anion distance and orientation from the inserting monomer. So, close proximity of the anion to ethylene, which is more representative of front alignments, does not hinder C-C bond formation and there is no need for additional counteranion displacement for these alignments. This means that the effective insertion barrier at C_3 is not highly sensitive to steric congestion involving the monomer, anion, and chain.

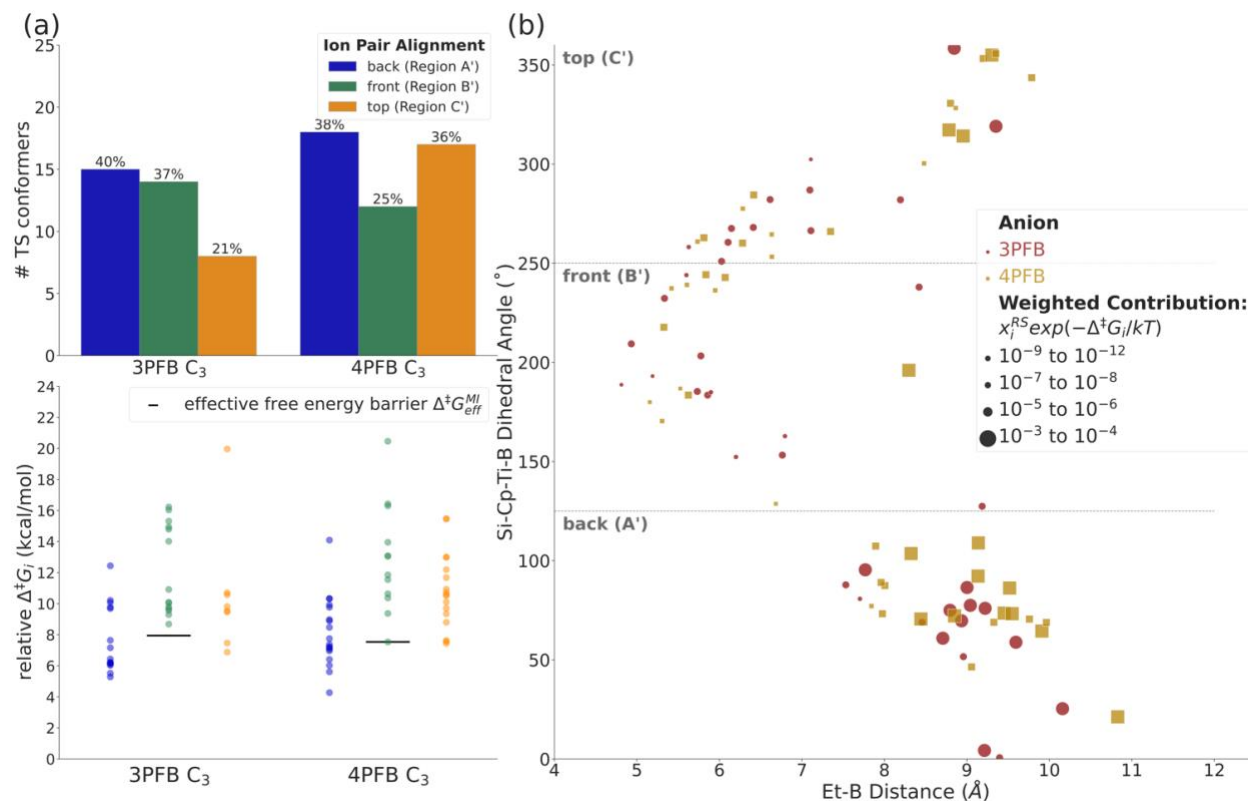


Figure 2.5 Ethylene insertion reaction pathways for each $[\text{Ti-CGC-C}_3\text{H}_7]^+[\text{3PFB/4PFB}]^-$ complex: (a) number of TS conformers and relative activation energies $\Delta^\ddagger G_i$ grouped by ion pair alignment, and effective insertion barrier $\Delta^\ddagger G_{\text{eff}}^{\text{MI}}$ by means of Equation (2.1), (b) orientation of ion pair in TS conformers according to monomer-anion (Et-B) distance and Si-Cp*-Ti-B dihedral angle. Weighted contributions to $\Delta^\ddagger G_{\text{eff}}^{\text{MI}}$ include mole fractions x_i^{RS} and $\Delta^\ddagger G_i$ for an individual reaction path from RS_i to TS_i .

2.4.2.2 Ethylene Insertion into $[\text{Ti-CGC-C}_{11}\text{H}_{23}]^+[\text{3PFB/4PFB}]^-$

When the insertion reaction takes place with the longer C₁₁ chain, the difference in the lowest insertion barriers with respect to ion pair alignments becomes more apparent. For both 3PFB and 4PFB anions, back alignments lead to the highest number of TS structures and the lowest TS energies (**Figure 2.6a**). Front alignments also have productive pathways, but the TS energies are much higher in energy compared to those of the back alignment, with the lowest energy TS for both alignments differing by ~4 kcal/mol. Meanwhile, top alignments barely led to successful insertion pathways. From the successful reaction paths, $\Delta^\ddagger G_i$ ranged from 2.5 to 23.9 kcal/mol and 2.3 to 21.9 kcal/mol for 3PFB and 4PFB, respectively. Averaging over the ensemble of insertion

pathways, the effective activation energies of monomer insertion $\Delta^\ddagger G_{\text{eff}}^{\text{MI}}$ are 6.3 ± 0.5 and 6.7 ± 0.4 kcal/mol for 3PFB and 4PFB ion pairs, respectively. Although $\Delta^\ddagger G_i$ energies for both anions are similar, insertion barriers with the longer C₁₁ polymer are much lower than the C₃ effective insertion barriers.

The prevalence of successful pathways with back ion pair alignments with lower TS energies signifies that insertion pathway contributions to the $\Delta^\ddagger G_{\text{eff}}^{\text{MI}}$ include larger conformer effects when there is a longer polymer chain. Similar to C₃ pathways, many front alignments ($Et-B < 7.5$ Å, $125^\circ < \varphi \leq 250^\circ$) lead to successful insertions, although they are relatively higher in $\Delta^\ddagger G_i$ than other alignments. In contrast to C₃, most of the successful low barrier C₁₁ insertion pathways show the anion is displaced farther from ethylene and at a narrower range of anion orientations ($Et-B > 7.5$ Å, $0^\circ < \varphi \leq 125^\circ$) (**Figure 2.6b**), indicative of back alignments. Since these alignments also belong to the most preferred region in the FE maps discussed above, low TS barriers make these conformers the predominant contributors to the effective insertion barrier. The superposition of the TS conformer ensemble depicts the rotational freedom of the longer polymer chain and the steric effect on anion orientations (**Figure 2.7**). When the C₁₁ polymer chain is present, farther distance of the anion to ethylene indicates a decrease in the activation energy. This indicates that lower $\Delta^\ddagger G_{\text{eff}}^{\text{MI}}$ is influenced by the likelihood of the anion staying at optimal orientations without need for additional displacement at insertion.

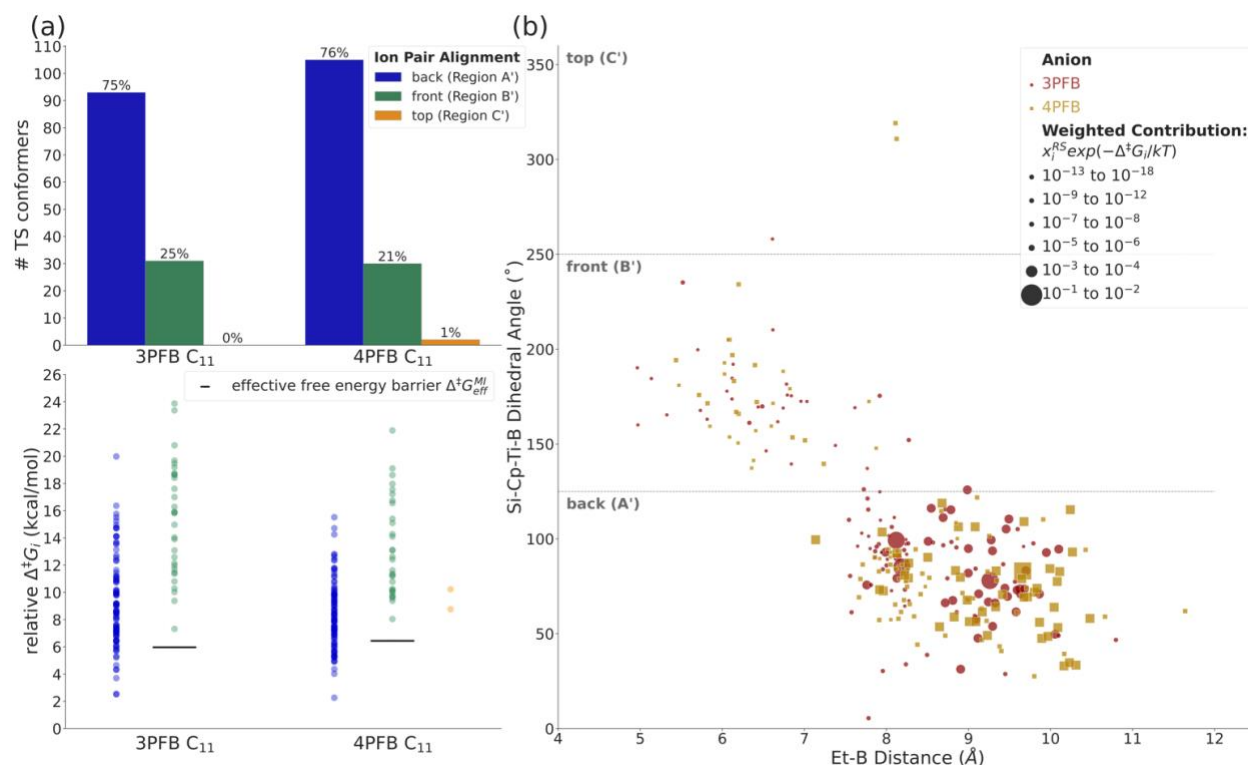


Figure 2.6 Ethylene insertion reaction pathways for each [Ti-CGC-C₁₁H₂₃]⁺[3PFB/4PFB]⁻ complex: (a) number of TS conformers and relative activation energies $\Delta^\ddagger G_i$ grouped by ion pair alignment, and effective insertion barrier $\Delta^\ddagger G_{\text{eff}}^{\text{MI}}$ (b) orientation of ion pair in TS conformers according to monomer-anion (Et-B) distance and Si-Cp*-Ti-B dihedral angle.

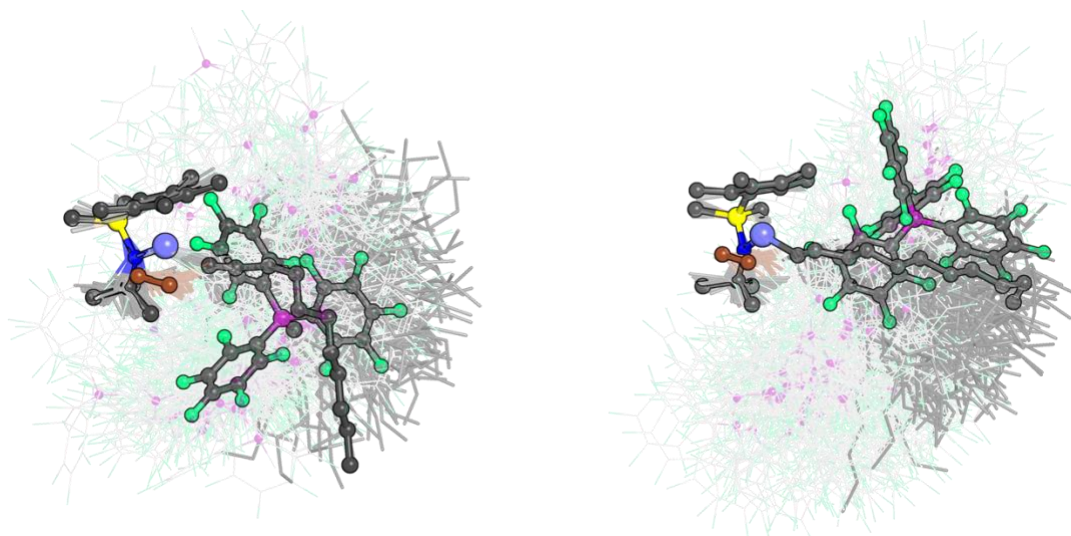


Figure 2.7 Ensemble of ethylene insertion TS conformers for (left) [Ti-CGC-C₁₁H₂₃]⁺[3PFB]⁻ (129 conformers) and (right) [Ti-CGC-C₁₁H₂₃]⁺[4PFB]⁻ (137 conformers). Lowest energy TS conformers and ethylene are shown as ball-and-stick. Superposed conformers are aligned to the lowest energy TS structure with the cyclopentadienyl-amido scaffold (Cp*, Ti, N, Si) as reference. CGC and polymer chain are shown as thick gray wires and the anion is shown as thin gray wires.

(slate: Ti, dark gray: C, brown: ethylene C, gray: C₁₁ polymer, yellow: Si, blue: N, purple: B, lime green: F, light gray: anion C)

2.4.2.3 Chain Termination Via β -Hydrogen Transfer in [Ti-CGC-C₁₁H₂₃]⁺[3PFB/4PFB]⁻

Chain termination is critical to molecular weight control and its rate is anion-dependent in relatively open catalysts such as Ti-CGC.⁵³ In this study, β -hydrogen transfer (β HT) was examined although β -hydride elimination (β HE) is another possible chain termination mechanism. Termination via β HT (**Figure 2.1**) is in competition with chain propagation since the elementary step proceeds from the same olefin π -complex as ethylene insertion. Therefore, β HT pathways were investigated starting from the same ethylene π -complexes that were studied above for polymer growth. $\Delta^\ddagger G_i$ energies varied from 13.3 to 43.1 kcal/mol and 10.0 to 36.6 kcal/mol for 3PFB and 4PFB, respectively (**Figure 2.8a**). Front and back ion pair alignments led to most of the productive and lowest energy pathways, with the back alignment being somewhat preferred over front alignment. Averaging over the ensemble of β HT pathways, the effective activation energies of chain termination $\Delta^\ddagger G_{\text{eff}}^{\beta\text{HT}}$ are 17.3 ± 0.1 and 14.8 ± 0.8 kcal/mol for 3PFB and 4PFB, respectively. Termination barriers are therefore substantially higher than insertion barriers, which confirms that these catalysts will make polyethylene with relatively high MW. At 150°C, the relative rates of insertion compared to termination, computed from $\Delta^\ddagger G_{\text{eff}}^{\text{MI}}$ and $\Delta^\ddagger G_{\text{eff}}^{\beta\text{HT}}$ barriers, are estimated to be 5×10^5 and 10^4 faster for 3PFB and 4PFB, respectively. This indicates that 4PFB will have comparatively more termination and polymers produced with [Ti-CGC]⁺[4PFB]⁻ would have lower MW. These values follow the experimental order of rates for the two anions observed in experiment in similar catalysts.^{88,89}

The observation that 4PFB exhibits a lower effective β HT barrier than 3PFB might be explained by the ion pair orientations of the TS conformer ensemble. Similar to C₁₁ insertion pathways, productive β HT reactions can be found mostly for ion pairs with back and front alignments. This

shows that β HT can occur at a wide range of anion-monomer distances, including shorter anion-monomer distances ($Et-B < 7 \text{ \AA}$) (**Figure 2.8b**). For both 3PFB and 4PFB, the lowest-energy back alignments have lower $\Delta^\ddagger G_i$ than the lowest-energy front alignments, indicating that back alignments are more preferred for β HT. For 4PFB, the back and front structures with the two lowest β HT barriers (**Figure 2.8a**) are further stabilized by shorter agostic Ti-H $_{\beta}$ distances (2.0-2.1 $\text{\AA}$) (**Appendix Figure A.5**). For 3PFB, short Ti-H $_{\beta}$ distances can also be observed for the lowest-energy front structures, but the lowest-energy TS has a back alignment and farther agostic Ti-H $_{\beta}$ distance ($\sim 2.6 \text{ \AA}$). These indicate that ion pair alignment and stronger agostic interactions are each influential factors for β HT. Ion pair orientations such as front ($Et-B < 7.5 \text{ \AA}$, $125^\circ < \varphi \leq 250^\circ$) and top alignments ($\varphi > 250^\circ$) (**Figure 2.8b**) involve closer proximity of the anion to the TS, which modulates the stability of the β -agostic interaction (**Figure 2.9**). On the other hand, back alignments ($Et-B > 7.5 \text{ \AA}$, $0^\circ < \varphi \leq 125^\circ$) benefit from φ orientations with less steric congestion, where the anion is positioned away from the region where the β HT TS occurs. This correspondence may explain why 4PFB has lower $\Delta^\ddagger G_{\text{eff}}^{\beta\text{HT}}$ and is more likely to undergo chain termination (and result in lower MW) compared to 3PFB in Ti-CGC and similar catalysts.

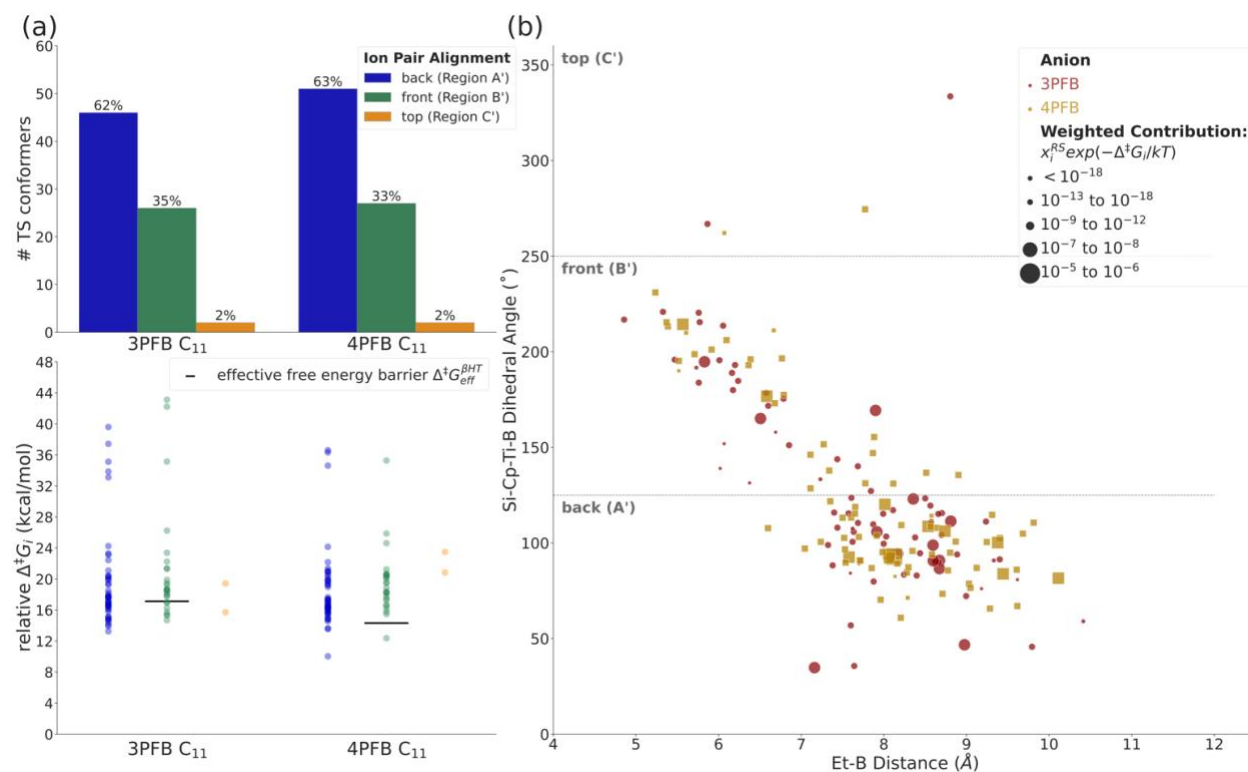


Figure 2.8 β -Hydrogen transfer chain termination reaction pathways for each [Ti-CGC-C₁₁H₂₃]⁺[3PFB/4PFB]⁻ complex: (a) number of TS conformers and relative activation energies $\Delta^\ddagger G_i$ grouped by ion pair alignment, and effective β HT barrier $\Delta^\ddagger G_{\text{eff}}^{\beta\text{HT}}$ (b) orientation of ion pair in TS conformers according to monomer-anion (Et-B) distance and Si-Cp*-Ti-B dihedral angle.

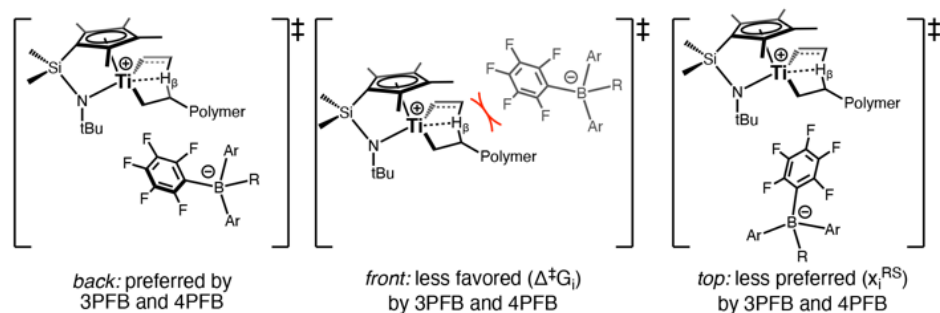


Figure 2.9 Schematic representation of TS conformers from β -hydrogen transfer reaction pathways (Ar = C₆F₅, 3PFB: R = Me, 4PFB: R = C₆F₅). Orientations show optimal back, front, and top alignments that affect anion distance and orientation from the β HT TS.

2.5 Conclusions

The key aspects of ion pair and polymer conformations in Ti-CGC-catalyzed ethylene polymerization were revealed through MD and reaction pathway simulations. Different

preferences of ion pair orientations were shown to influence ethylene insertion and β -hydrogen transfer, which affect propagation and termination, respectively. **Table 2.1** summarizes the key results.

Table 2.1 Summary of Findings from Simulations of [Ti-CGC–Polymer]⁺[3PFB/4PFB][−] Ion Pair.

system	order of favored IP orientations (no Et)	order of favored IP orientations (Et π -complex)	$\Delta^\ddagger G_{\text{eff}}^{\text{MI}}$ (kcal/mol)	$\Delta^\ddagger G_{\text{eff}}^{\text{BHT}}$ (kcal/mol)
[Ti-CGC–C ₃] ⁺ [3PFB] [−]	front > back $\approx$ top	back > top > front	8.2 $\pm$ 0.2	
[Ti-CGC–C ₃] ⁺ [4PFB] [−]	front > back $\approx$ top	back > top > front	7.8 $\pm$ 0.4	
[Ti-CGC–C ₁₁] ⁺ [3PFB] [−]	front > back > top	back > front $\gg$ top	6.3 $\pm$ 0.5	17.3 $\pm$ 0.1
[Ti-CGC–C ₁₁] ⁺ [4PFB] [−]	front > back $\gg$ top	back > front $\gg$ top	6.7 $\pm$ 0.4	14.8 $\pm$ 0.8

The ion pair positions were similar for the two counteranions with a C₃ polymer chain, but differed with the longer chain. For the C₁₁ polymer, though the front counteranion alignment was the most favored in the absence of ethylene, the second preference of the larger 4PFB counteranion was mostly back counteranion alignments, whereas 3PFB was less restricted in position between back and top alignments. In ethylene π -complexes, back alignments were most favored, indicating that 4PFB is more likely than 3PFB to be in orientations conducive to monomer coordination. Although the model did not provide a significant difference in the effective activation barrier of monomer insertion ($\Delta^\ddagger G_{\text{eff}}^{\text{MI}}$) between 3PFB and 4PFB, it did reveal the ion pair alignments that lead to lower ethylene insertion barriers. With a C₃ polymer chain, insertion may occur with any ion pair alignment, although the lowest barriers are those with back alignment. With a C₁₁ chain, lower insertion barriers mainly come from back counteranion alignment compared to front alignment (**Table 2.1**).

Chain termination via β HT showed a bigger difference in effective activation barrier ($\Delta^\ddagger G_{\text{eff}}^{\beta\text{HT}}$) between 3PFB and 4PFB (**Table 2.1**). In this case, back alignments (farther from the ethylene monomer) lead to lower barriers when β -agostic interactions are present, indicating that 4PFB is more likely to undergo β HT compared to 3PFB. These data suggest that the ion pair orientations that are most preferred for insertion and termination are similar, where the reaction pathways favor a displaced anion (OSIP) that involve the growing chain. Insight into the favored ion pair orientations gained in this study increases the understanding of the microscopic origin of contributions to the propagation rate constant and competition between propagation and termination.

Chapter 3 Elucidating the Interactions between Diastereomer and Counteranion during Activation for Olefin Polymerization with the Racemic Hf(IV)-Pyridylamido Catalyst

3.1 Abstract

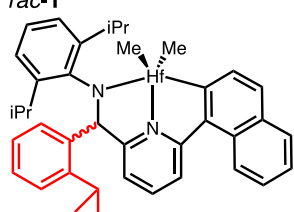
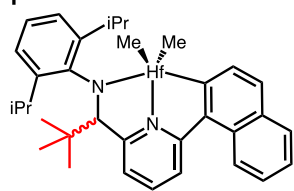
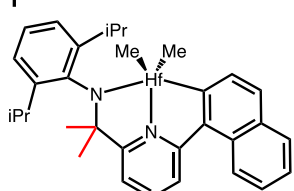
The structure and behavior of the cocatalyst counterion with Hf(IV)-pyridylamido complexes are investigated to elucidate the origin of limited active-site counts observed in olefin polymerization. The catalyst-cocatalyst ion pair interactions will be shown to affect the formation of the catalytically active species, which have different diastereomer structures. Molecular dynamics simulations show that (2-*i*Pr)Ph bridgehead substituent position, which differentiates the two diastereomers, substantially influences the B(C₆F₅)₄⁻ counteranion position. One diastereomer enables the counteranion to slide to favorable staggered orientations suitable for outer sphere coordination, whereas the other diastereomer prefers the counteranion with inner sphere coordination. Ion pair preferences not only affect which conformations are accessible, the ion pair also affects the free energy profile associated with ethylene monomer coordination. When the monomer approaches, the anion dissociates, agostic bonds appear, and the monomer interacts with the ligands. These favorable interactions appear in one diastereomer to form the monomer-metal π -complex, whereas the other diastereomer resists counteranion displacement, preferring with a frontside agostic interaction and monomer outer sphere interactions with the ligands. The differences in conformational flexibility between the two diastereomers provide an explanation the 50% active site counts seen in experiments.

3.2 Introduction

Pyridylamide complexes, such as hafnium-pyridylamido complexes, have shown great promise and use in olefin polymerization catalysis. Hf-pyridylamido complexes have been frequently applied in high-temperature solution production of highly isotactic, high molecular weight polypropylene.^{91,92} These species have also recently been used in high-volume preparation of ethylene/1-octene multiblock copolymers through chain shuttling polymerization.⁹³ This class of catalysts can have higher isoselectivity, activity, thermal stability, and lifetime in olefin polymerizations compared to the more-established metallocene catalysts.^{94,95} The origin of these properties has been attributed to the unconventional structure and specific activation chemistry of these catalysts compared to metallocenes and other postmetallocenes.⁹⁶

One feature of Hf-pyridylamido complexes that differentiates them from conventional catalysts is the possibility for *in situ* ligand modification at the Hf-C_{aryl} bond. The presence of a Hf-C_{aryl} bond with the *ortho*-aryl, cyclometalated ligand offers an alternative reaction site, aside from Hf-C_{alkyl} bonds, where the olefin can insert into the ligand.⁵² Experimental and theoretical studies have shown that the first insertion of monomer into the complex occurs preferentially at the Hf-C_{aryl} bond over the Hf-C_{alkyl} bond.^{97,98} Furthermore, this insertion appears necessary to reach the active catalyst species, and is likely responsible for the high activity and stereoselectivity of these catalysts.⁹⁹—Intriguingly, more than one insertion product is possible depending on the α -olefin, leading to multisite behavior.¹⁰⁰ This effect becomes even more noticeable in the case of ethylene/1-octene copolymerization, where broad molecular weight (MW) distribution (MWD) can be observed, with the high MW polymer fraction being produced by the octene-inserted active species.¹⁰¹ Insertion of olefins into the Hf-C_{aryl} bond therefore has a strong effect on the properties of the active catalyst.

Table 3.1 Hafnium-pyridylamido complexes with different bridgehead substituents and [C(Ph)₃][B(C₆F₅)₄] as cocatalyst activator.

Complex	Bridgehead Substituent	Symmetry	MWD (<i>D</i>) ^a	Activity ^b	Active-Site Counts
<i>rac</i> - 1 	R ₁ = (2- <i>i</i> Pr)Ph R ₂ = H	C ₁	Broad Et: 3.3 1-Oct: 5.1 Et/1-Oct: 3.3	Et: 50,400 Et/1-Oct: 61,200	~ 50% (1-Oct) ~ 75% (Et/1-Oct)
1' 	R ₁ = <i>t</i> Bu R ₂ = H	C ₁	Narrow Et: 1.5-1.7 1-Oct: 1.8	Et: 16,200 Et/1-Oct: 4500-12,000	N/A
1'' 	R ₁ = Me R ₂ = Me	C _s	Narrow Pr: 1.5 ^c	Pr: 1,400	~ 90% (1-Hex)

^a $D = M_w/M_n$. ^b In unit of kg polymer / (mol Hf*h). ^c B(C₆F₅)₃ as cocatalyst.

Hf-pyridylamido complexes also contain another unconventional structural feature: the stereogenic carbon bridging the pyridyl and amido fragments. Depending on the symmetry of substitution at the bridgehead methylene, enantiomers or diastereomers of the catalyst can emerge after activation with a cocatalyst.⁹⁸ The complex **1''** with an achiral dimethyl ligand at the bridgehead (Table 1; $R_1 = R_2$), exhibits living propylene polymerization and narrow MWD with B(C₆F₅)₃ cocatalyst.¹⁰² In contrast, Hf complex *rac*-**1**, (Table 1; $R_1 \neq R_2$), produces broad MWD in ethylene and 1-octene homopolymerization and ethylene/1-octene copolymerization with [C(Ph)₃][B(C₆F₅)₄] cocatalyst (**Table 3.1**). Bimodal MWDs for the same catalyst have also been observed in isotactic polypropylene and 4-methylpentene polymerization, which suggest multiple active sites.^{103,104} These observations can be attributed to multiple diastereomers of the activated

catalyst with different activities, giving polymers with broad MWD.^{105,106} The presence of the chiral bridgehead carbon can therefore lead to multisite behavior of the Hf-pyridylamido complex.

Aside from affecting catalyst symmetry, bridgehead ligands affect properties such as activity, stereocontrol, and active-site counts. The *rac*-**1** complex with the 2-isopropylphenyl ((2-*i*Pr)Ph) group has much higher activity in 4-methylpentene polymerization and higher isoselectivity in propylene polymerization than **1'** and **1''** complexes.¹⁰⁶ For the series of olefins with increasing number of carbons, ethylene to 1-octene, *rac*-**1** also has higher activity than **1'**.¹⁰⁴ The *C*₁-symmetric complexes *rac*-**1** and **1'** can produce highly isotactic polymer ($[m^4] > 99\%$), in 1-hexene and 1-octene polymerization, though **1''** in propylene polymerization is less selective ($[m^4] \sim 85\%$). Active-site counts for chain growth, defined as percentage of catalyst with a metal-bound polymer chain, have been measured in *rac*-**1** and **1''** complexes as well. Hf complex **1''** has 90% active-site counts in 1-hexene polymerization, which means that almost all of the catalyst is active in chain growth.¹⁰⁷ As a function of cocatalyst activator in 1-octene polymerization with *rac*-**1**, Lewis acids that abstract a methyl from the precatalyst, B(C₆F₅)₃ and [C(Ph)₃][B(C₆F₅)₄], had the highest active-site counts at 45% and 51%, respectively.¹⁰⁸ Despite having higher activity than the other two complexes, only ~50% of *rac*-**1** being active suggests that catalyst symmetry, combined with the activation mechanism, are together ineffectively leading to precatalyst activation. This finding raises questions about its origin and the path to active-site generation, which deserves more consideration.

In this work, the stereochemical origin of limited active-site counts in *rac*-**1** is elucidated by investigating the microscopic behavior and interactions of the cationic catalyst with the cocatalyst counteranion. In the activation step, the *rac*-**1** precatalyst forms an ion pair with B(C₆F₅)₄⁻ (tetrakis(perfluorophenyl)borate) counteranion upon cocatalyst activation with the

borate salt, which produces **2a** and **2b** diastereomers (**Figure 3.1**). This is followed by the first insertion of the monomer into the Hf-naphthyl bond to form the catalytically active species. The influence of bridgehead substitution in *rac-1* on $\text{B}(\text{C}_6\text{F}_5)_4^-$ counteranion position in catalyst-cocatalyst ion pair interactions is explored computationally, as the fitting and tightness of the ion pairing are connected with active site opening and formation of the olefin-inserted active species. Molecular dynamics simulations of the two diastereomeric ion pairs are used to explore the range of $[\mathbf{2a}]^+[\text{anion}]^-$ and $[\mathbf{2b}]^+[\text{anion}]^-$ ion pair orientations and reveal distinct preferred counteranion positions for the diastereomers. Umbrella sampling simulations inform the path to active site opening and ethylene coordination, where it is revealed that ethylene coordinates preferentially to the active site of one, but not the other, of the two diastereomers.

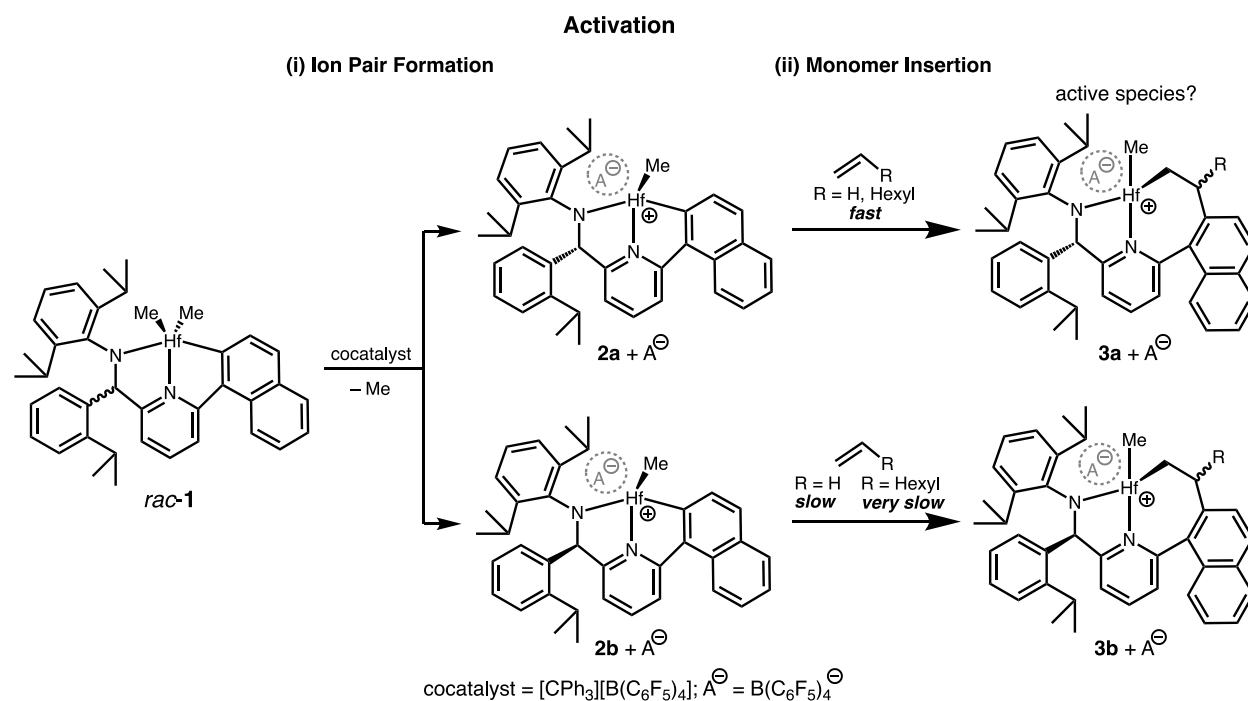


Figure 3.1 Schematic representation of activation of Hf-pyridylamido *rac-1* complex: (i) ion pair formation and (ii) monomer insertion. (i) Two diastereomers, **2a** and **2b**, are produced upon methyl abstraction. (ii) Diastereomers **2a** and **2b** undergo olefin monomer insertion rapidly and slowly, respectively, producing olefin-inserted **3a** and **3b** species.

3.3 Computational Details

3.3.1 Molecular Dynamics Simulations

Four ion pair (IP) atomistic models were prepared for the MD simulations, which consist of **[2a/2b]⁺[anion]⁻** with and without ethylene monomer, with B(C₆F₅)₄⁻ (4PFB) as the counteranion. The xTB software package (ver. 6.4.1) was used for MD simulations and single-point energy calculations.⁸¹ The GFN2-xTB semiempirical tight-binding method was used for single-point calculation, structure optimization and MD simulation.^{21,81,82} The MD simulations (ORCA, ver. 5.0.4) were performed in NVT ensemble at 423.15 K, corresponding to conditions from a higher temperature polymerization (150 °C).¹⁰⁹ The NVT-MD simulations were run for 4 ns with 1 fs timestep. From the trajectories, structures were saved every 100 fs. The ALPB solvation model was used for implicit solvation with toluene as solvent.³⁷ From the trajectories, structures were saved every 100 fs. The ALPB solvation model was used for implicit solvation with toluene as solvent. A spherical harmonic repulsive wall with radius 30 Å was placed around the system. For the ethylene IP systems, constraints were placed on the interatomic distances of the Hf, ethylene, and naphthyl carbon atoms involved in ethylene insertion.

3.3.2 Equilibrium Structures of the Ion Pair

To map free energy surfaces from the MD trajectories onto characteristic degrees of freedom, the interatomic distance r between Hf and B atoms and the B-Hf-N angle φ formed were taken as coordinates (**Figure 3.2**).⁵⁶ Calculations were performed by using bins with size (0.05 Å, 2.0°) and the free energy origin (0.0 kcal/mol) is set to the most populated bin.⁵⁷

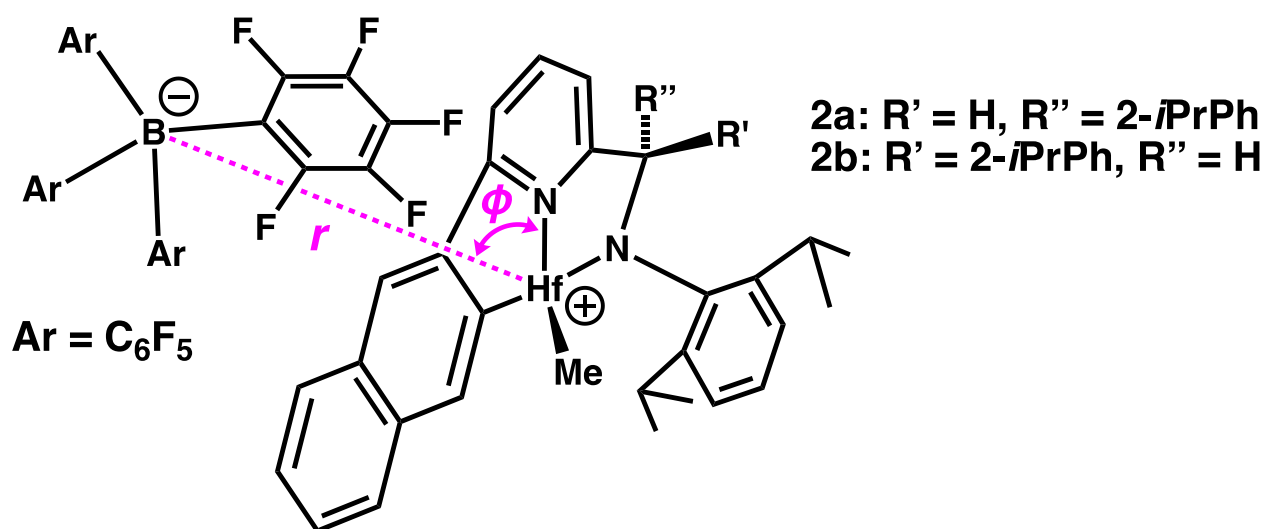


Figure 3.2 Definition of the B-Hf distance (r) and B-Hf-N angle (φ) as descriptors.

3.3.3 Umbrella Sampling Simulations

One-dimensional umbrella sampling simulations were run for [2a]⁺[4PFB][−] and [2b]⁺[4PFB][−] with ethylene present. The coordinate chosen to be restrained with a harmonic potential was the distance of the Hf atom to the center of mass of ethylene (Hf-Et distance). MD simulations (DFTB+ ver. 23.1, PLUMED ver. 2.9) were performed for 200 ps at 423.15 K using a spring constant of 200 kcal/mol/Å² in 25 umbrella windows centered along the Hf-Et distance, which is increased from 2.5 to 5.0 Å at 0.1 Å intervals.^{110,111} For each frame (saved every 50 fs) in each US trajectory, the values of the applied collective variable were evaluated. The multistate Bennett acceptance ratio (MBAR) method was used (pymbar ver. 4.0) to create free energy profiles through kernel density estimation (KDE) based on Hf-Et distance.¹¹² The free energy error was estimated with 50 bootstrapping runs. To understand the mechanism of approach, the Hf-Et distance was varied, and the resulting trajectories revealed that the windows showed sufficient overlap of the chosen coordinate (**Appendix Figure B.1**). Evaluation of the free energy profile convergence showed that a total simulation time of 5 ns was sufficient to reach convergence of the coordinate (**Appendix Figure B.2**).

3.4 Results and Discussion

The present investigation began by considering the hypothesis that bridgehead substitution leads to multi-site behavior for olefin polymerization. As a particular example, we considered *rac*-**1**, where Landis et al. reported approximately equal amounts of the two diastereomers **2a** and **2b** resulted from activation by $[\text{C}(\text{Ph})_3][\text{B}(\text{C}_6\text{F}_5)_4]$. The diastereomers showed different propensities for olefin insertion into the Hf-naphthyl bond, where diastereomer **2a** initiated rapidly and diastereomer **2b** initiated much more slowly (**Figure 3.1**).¹⁰⁷ In the copolymerization of ethylene and 1-octene, however, **2b** could be activated, leading to increased active-site counts of ~75% (**Table 3.1**). This was attributed to faster insertion of ethylene into the Hf-naphthyl bond compared to 1-octene (**Figure 3.1**).¹¹³ These findings led to the conclusion that the diastereomers have reactivity differences toward olefin insertion that lead to the low active-site count phenomena. The following results will provide evidence for specific structural differences between the two activated diastereomers influence the initiation process. To do so, extensive conformer sampling of the diastereomer-anion ion pair is required to reveal the dynamic behavior in the inner and outer coordination spheres.

3.4.1 Equilibrium Ion Pair Structures with **2a** vs **2b**

3.4.1.1 Free Energy Maps of **2a** and **2b** Ion Pair

Molecular dynamics sampling of the conformational spaces of **2a** and **2b** diastereomers were carried out with the methods described in the computational details section. First, the conformational behavior of the ion pairs $[\mathbf{2a}]^+[\text{4PFB}]^-$ and $[\mathbf{2b}]^+[\text{4PFB}]^-$ (4PFB: $\text{B}(\text{C}_6\text{F}_5)_4^-$) were investigated by considering equilibrium structures of the ion pairs. The ion pair conformers of **2a** and **2b** show that the anion position can be distributed over a range of orientations along B-Hf distance (r) and B-Hf-N angle (φ) (**Figure 3.3**) in the free energy maps. The states of the complex

are mostly distributed in a wide span of $4.5 \text{ \AA} \leq r < 8.5 \text{ \AA}$ and $40^\circ \leq \varphi < 150^\circ$. For **2a** and **2b** complexes, Region A is the lowest energy region, representing 51 and 88% of the total conformers, respectively. Region A includes inner-sphere ion pairs (ISIPs) involving short Hf $\cdots$ F interactions (2.4 to 2.6 $\text{\AA}$) and π -stacking interactions between the C₆F₅ ring of the counteranion and the naphthyl ligand of the cation (**Figure 3.3**). These interactions allow the counteranion to be close to the catalyst, where most conformers are located at $4.5 \text{ \AA} \leq r < 6 \text{ \AA}$.

Meanwhile, Region B conformers can be found at slightly farther B-Hf distance ($5 \text{ \AA} \leq r < 6.5 \text{ \AA}$) and higher φ values ($105^\circ \leq \varphi < 150^\circ$). Region B is the second lowest energy region for **2a** and accounts for 36% of the total structures. On the other hand, **2b** does not prefer region B, with only 1% of the total structures. The anion orientation in region B coincides with one C₆F₅ ring interacting with the catalyst via π -stacking and Hf $\cdots$ F interactions. These interaction patterns lead to the anion being in a staggered orientation, where the other C₆F₅ rings are slightly below the catalyst (**Figure 3.3**). With the counteranion and (2-*i*Pr)Ph bridgehead substituent being in a *syn* relationship for **2a**, the interactions between the two lead to a sterically crowded environment. This drives the anion to region B, where most of the anion C₆F₅ rings can find an accessible site below and behind the naphthyl ligand, leading to wider φ orientations. This is in contrast with **2b**, where (2-*i*Pr)Ph and counteranion do not interact because they are on opposite (*anti*) sides of the catalyst. Thus, close contact of the counteranion with the metal center represented by region A is not interrupted by the bridgehead substituent.

Region C mostly consists of outer-sphere ion pairs (OSIPs) depicted by farther B-Hf distances ($6.5 \text{ \AA} \leq r < 8.5 \text{ \AA}$) and wider range of φ orientations ($40^\circ \leq \varphi < 150^\circ$). This region accounts for 12 and 11% for **2a** and **2b**, respectively. The OSIPs are likely stabilized by agostic interactions from either the (2-*i*Pr)Ph or the 2,6-diisopropylaniline (DIPA) ligands, as depicted in

Figure 3.3.¹¹⁴ For **2a**, the Hf center interacts with the *ortho*-H atom of the (2-*i*Pr)Ph ligand with an agostic Hf-H distance of ~ 2.0 Å (**Figure 3.3**). Whereas for **2b**, agostic interactions can occur with the Hf metal and the *ortho*-H atom of (2-*i*Pr)Ph, or the *i*Pr-H atom of the DIPA ligand (**Figure 3.3**). The orientations observed in region C bring importance to the rotations of the (2-*i*Pr)Ph and DIPA rings that bring the H atom closer to the Hf center.

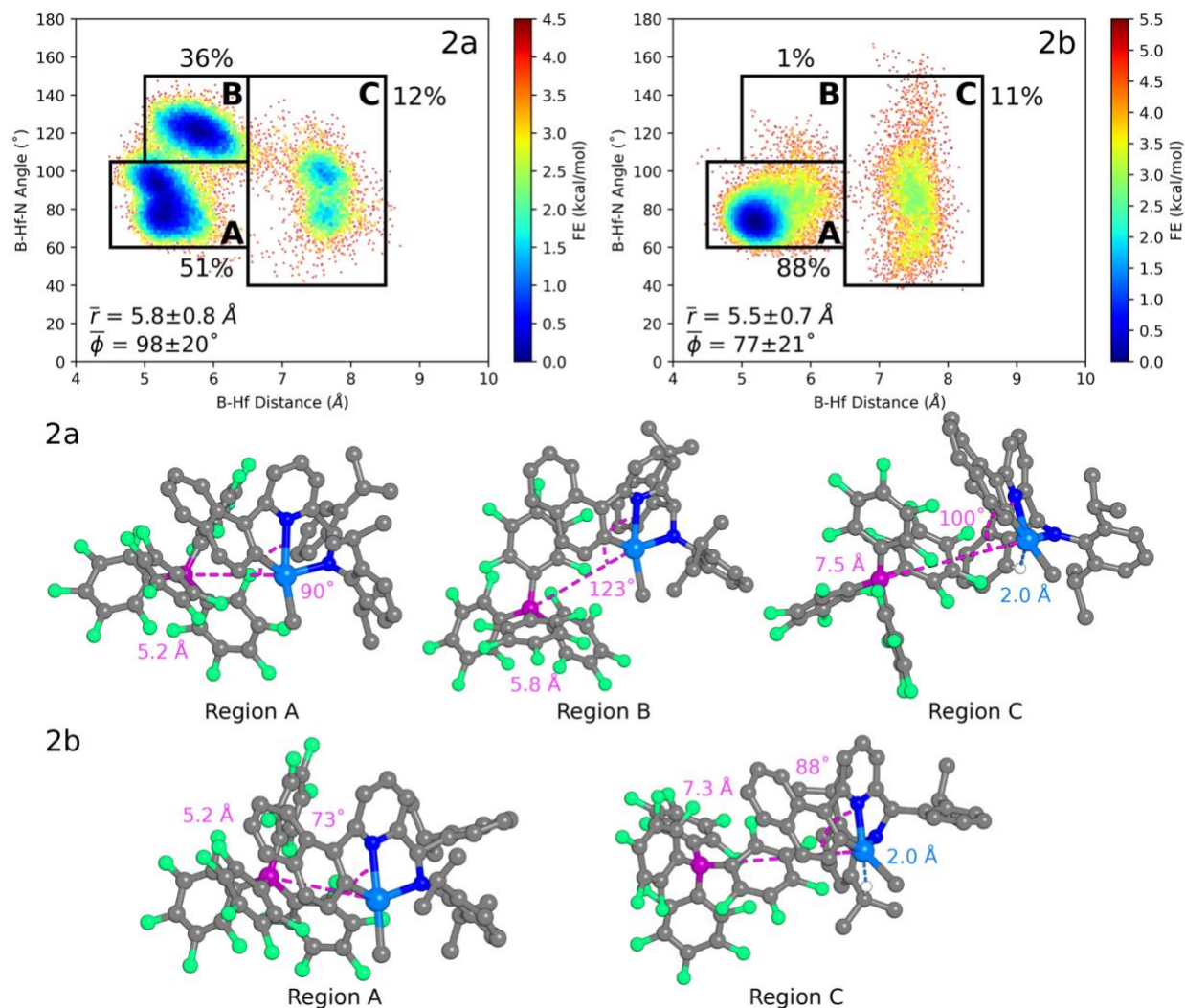


Figure 3.3 Free energy maps with respect to B-Hf distance and B-Hf-N angle for the $[\mathbf{2a}]^+[\mathbf{4PFB}]^-$ (left) and $[\mathbf{2b}]^+[\mathbf{4PFB}]^-$ (right) ion pair complexes. (bottom) Representative **2a** and **2b** ion pair structures classified by region (pink: B-Hf distance and B-Hf-N angle; marine: Hf-H distance).

3.4.1.2 Free Energy Maps of (2a+Et) and (2b+Et) Ion Pair

In order to reach an initial configuration for first monomer insertion into the ion pair, conformational sampling of the ion pair with ethylene was performed. Sampling of the two complexes $\text{C}_2\text{H}_4[\mathbf{2a}]^+[\text{4PFB}]^-$ and $\text{C}_2\text{H}_4[\mathbf{2a}]^+[\text{4PFB}]^-$ involved the 4-membered Cossee ethylene insertion transition state structure.^{70,71} Similar examination of the ion pair structures was done on the free energy maps. In the corresponding (**2a**+Et) and (**2b**+Et) complexes, the outlined regions are similar to those without ethylene, though the distribution of populations changes. Due to the inserting ethylene monomer, OSIPs are preferred as shown by the increase in B-Hf distance ($6.5 \text{ \AA} \leq r < 8.5 \text{ \AA}$). The orientation of the Me group is *trans* to the pyridine N atom. Region A' (which was preferred in the monomer-less complexes) is not observed in (**2a**+Et) and (**2b**+Et) complexes since it mostly consists of ISIPs. Instead, region C' (**Figure 3.4**) is the most preferred region for both (**2a**+Et) and (**2b**+Et), containing 53 and 66% of total structures, respectively. This region is characterized by side structures where the anion is next to the *syn* bridgehead substituent.¹¹⁵ The OSIP side structures are stabilized by π -stacking interactions with the naphthyl ligand.

Meanwhile, Region B' (**Figure 3.4**) is the second lowest energy region and has 45 and 22% of total structures, for **2a** and **2b**, respectively. This region is also characterized by π -stacking interactions and the anion is in a staggered orientation with the C_6F_5 rings below the naphthyl ligand. The (**2a**+Et) complex prefers regions B' and C' to a similar degree, whereas (**2b**+Et) prefers region C' more. These preferences may be due to the bridgehead substituent that is *syn* to the counteranion ((2-*i*Pr)Ph or H atom), which can increase or decrease steric crowding around the anion. This can also be observed in region D', which was the least preferred region with 1 and 11% of total structures, respectively. Region D' (**Figure 3.4**) is characterized by the anion next to the pyridyl ligand and above the Hf center, which corresponds to lower φ values ($40^\circ \leq \varphi < 150^\circ$).

This region is accessible for (**2b**+Et), whereas (**2a**+Et) is more likely to settle between regions B' and C'.

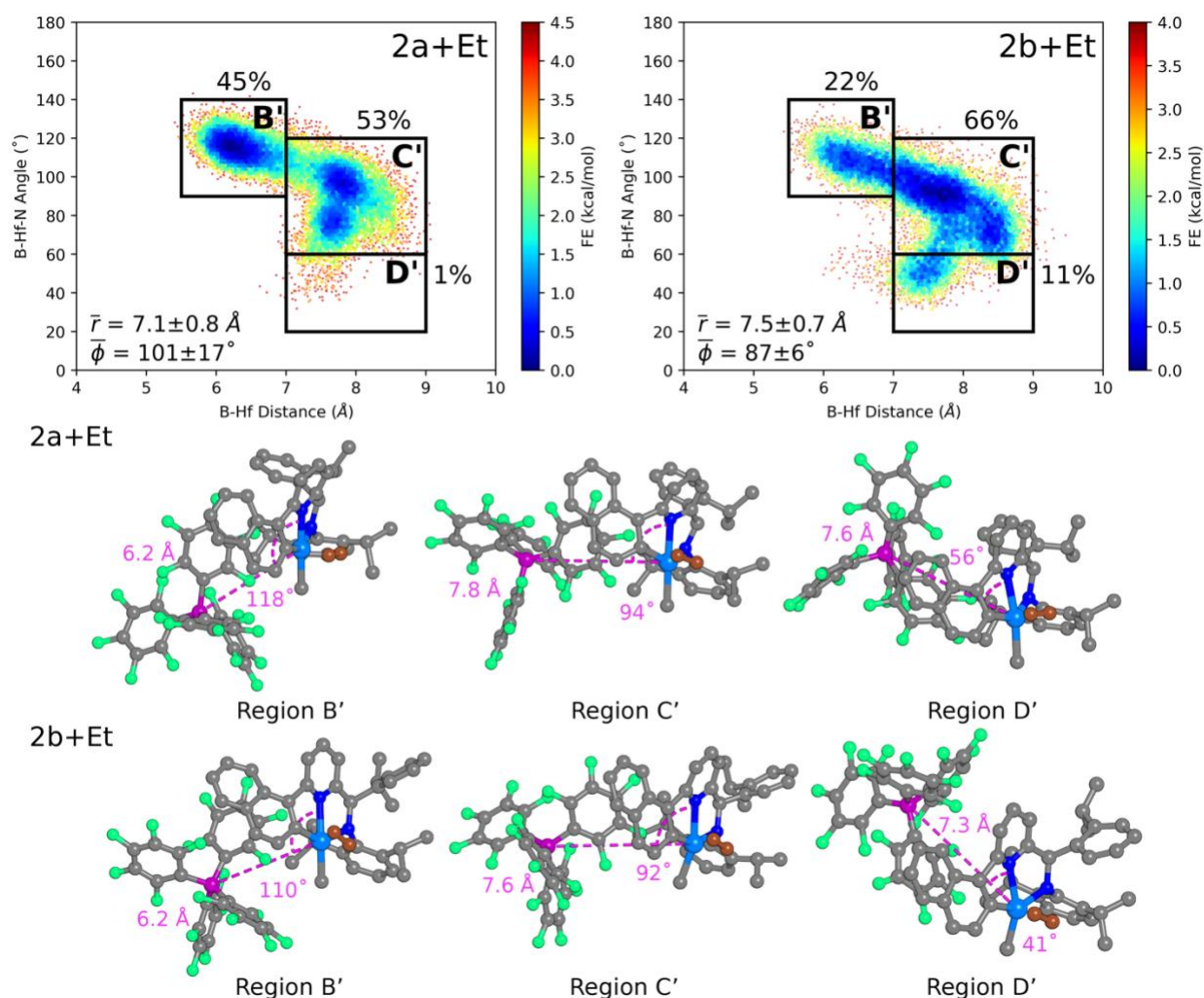


Figure 3.4 Free energy maps with respect to B-Hf distance and B-Hf-N angle for the $\text{C}_2\text{H}_4[\mathbf{2a}]^+[\mathbf{4PFB}]^-$ (left) and $\text{C}_2\text{H}_4[\mathbf{2b}]^+[\mathbf{4PFB}]^-$ (right) ion pair complexes. (bottom) Representative (**2a**+Et) and (**2b**+Et) ion pair structures classified by region (pink: B-Hf distance and B-Hf-N angle)

The results of the conformational sampling can be summarized with the help of the representative structures of **Figure 3.5**, which correspond to the labeled regions in **Figure 3.3** and **Figure 3.4** (region A $\rightarrow$ **a**_{4PFB}, B $\rightarrow$ **b**_{4PFB}, C $\rightarrow$ **c**_{4PFB}, D $\rightarrow$ **d**_{4PFB}). Without ethylene, structure **a**_{4PFB} is preferred for both anions. **2a** can access structures **a**_{4PFB}, **b**_{4PFB}, and **c**_{4PFB}, whereas **2b** is more likely to prefer structures **a**_{4PFB} and **c**_{4PFB}. These changes in state are different between the two

diastereomers likely because of the *syn* and *anti* orientation (**Figure 3.5**) of the counteranion to the (2-*i*Pr)Ph substituent, for **2a** and **2b**, respectively. With the *syn* relationship, the anion is more likely to sterically interact with the bridgehead substituent, so orientations where the anion can move away, such as structure **b**_{4PFB}, are preferred more. The aniline ligand can also stabilize OSIPs with agostic interactions, as observed in the **c**_{4PFB} structure. Meanwhile, when the monomer is present, OSIP structures **b'**_{4PFB} and **c'**_{4PFB} are evidently preferred, which indicates that these are the orientations viable for ethylene coordination. **2a** prefers **b'**_{4PFB} and **c'**_{4PFB} comparably, whereas **2b** prefers structure **c'**_{4PFB} more. The free energy maps with and without ethylene show that **2a** is more likely to be at orientations that are conducive to ethylene monomer coordination, whereas **2b** may be at orientations that are not as viable for coordination.

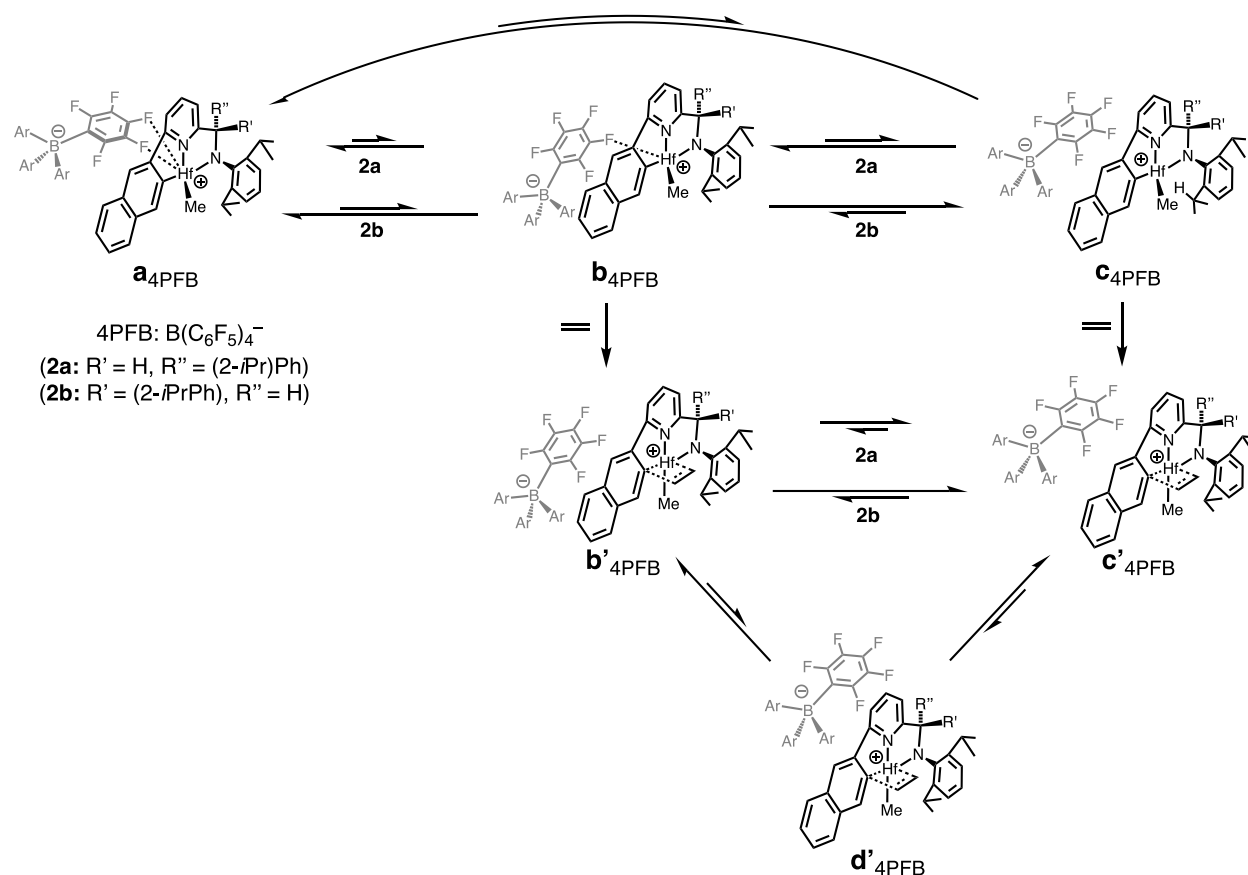


Figure 3.5 Schematic representation of the equilibrium structures of the ion pairs in the ethylene coordination process of **2a** and **2b** with B(C₆F₅)₄⁻ counteranion. Lowercase labeled structures **a**_{4PFB}, **b**_{4PFB}, **c**_{4PFB}, **b'**_{4PFB}, **c'**_{4PFB}, and **d'**_{4PFB} are the representative ion pair structures of regions A-C and B'-D' in Figure 3.2 and Figure 3.3, respectively. Structures **b'**_{4PFB}, **c'**_{4PFB}, and **d'**_{4PFB} involve the 4-membered Cossee ethylene insertion transition state.

3.4.2 Umbrella Sampling Simulations Describe Ethylene Monomer Approach

3.4.2.1 Free Energy Profiles of 2a and 2b

The free energy maps of monomer-less and Et complexes (**Figure 3.3** and **Figure 3.4**) of diastereomers **2a** and **2b** show differences in ion pair positioning in equilibrium configurations. Additional insight can be gained by studying the mechanism and free energy profile for how the monomer approaches the active site. Enhanced sampling molecular dynamics simulations using

umbrella sampling were used to investigate the behavior of the ion pair and the monomer (see Computational Details).

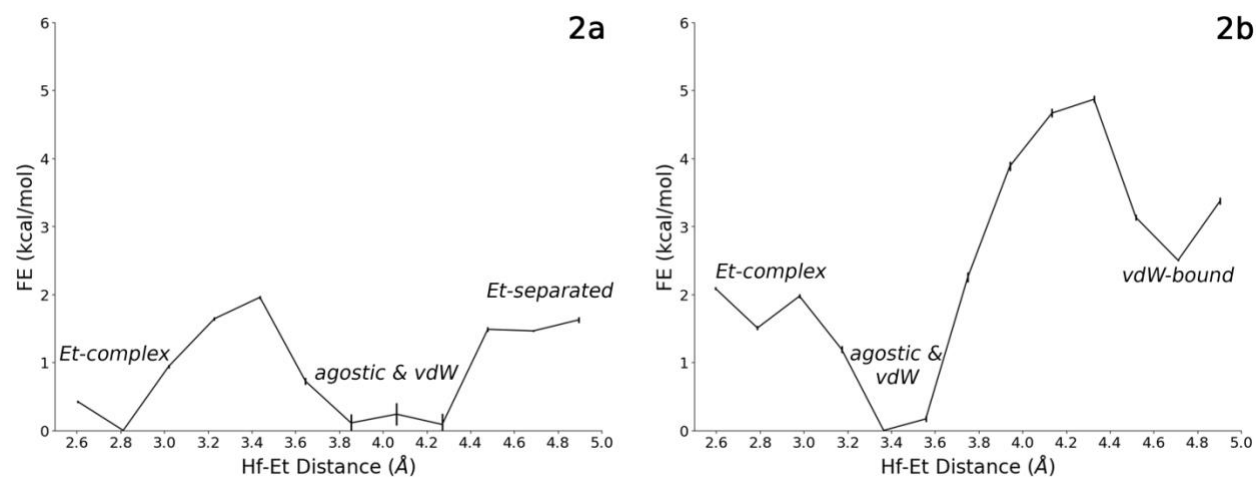


Figure 3.6 Calculated free energy profiles of ethylene approach based on Hf-Et distance for (left) **2a** and (right) **2b** ion pair structures. Error bars represent uncertainty estimate from bootstrapping.

The free energy profiles in **Figure 3.6** depict ethylene approach to the Hf center. Long Hf-Et distances (>4.5 Å) for **2a** indicate the catalyst and ethylene are significantly separated. As the monomer becomes closer (≤ 4.5 Å), two distinct minima appear for **2a**, at regions of ~ 2.8 and ~ 3.8 - 4.2 Å, respectively (**Figure 3.6**). The first is characterized by ethylene coordination forming a relatively stable π -complex with the Hf center (**Figure 3.7**). The minimum around 3.8 - 4.2 Å has a weaker interaction, likely caused by ethylene fitting into a van der Waals pocket near the naphthyl ligand. For **2b**, the free energy profile includes minima at ~ 2.8 , ~ 3.4 , and ~ 4.7 Å, respectively (**Figure 3.6**). The first is characterized by an ethylene π -complex (**Figure 3.7**), but this minimum is not the most stable region in the profile. The (2-*i*Pr)Ph bridgehead substituent of **2b** has a frontside orientation with the approaching monomer, which is the opposite of **2a** and presents differences between the two diastereomers. This can be observed in the minimum around 4.7 Å indicates weaker favorable dispersion interactions between the ethylene and the frontside ligands. As the monomer becomes closer (≤ 4.4 Å), the most stable region is the minimum at

around 3.4 Å. This region involves tighter fitting of the ethylene into the pocket between the (2-*i*Pr)Ph substituent and the naphthyl ligand. Reaching the inner-sphere coordination distance (~2.8 Å) from the van der Waals pocket is easily achieved by **2a**, whereas this approach is uphill with **2b**, due to hindrance of the (2-*i*Pr)Ph group.

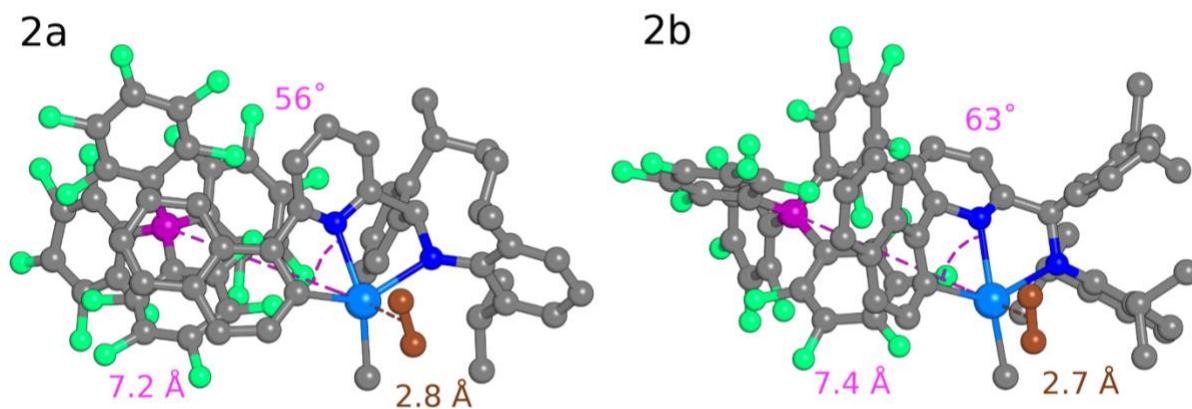


Figure 3.7 Representative structures of **2a** (left) and **2b** (right) ion showing ethylene coordination.

3.4.2.2 Factors for Ethylene Coordination

Further examination of the structures sampled in Figure 6 indicated that agostic interactions appeared as the ethylene approaches. For **2a**, anion displacement to OSIPs can be enabled by the presence of the (2-*i*Pr)Ph, which is on the same side as the anion. With the anion in the outer sphere, the inner sphere is stabilized by the agostic interaction between the *ortho*-H atom of (2-*i*Pr)Ph and the Hf center. For **2a** with ethylene-Hf distances of 3.8 to 4.0 Å, ion pair structures that resemble those from region B' with a slightly staggered anion and a backside agostic interaction are prevalent (**Figure 3.8**). As the monomer becomes closer to the Hf center, such as between 2.7 and 3.4 Å (**Figure 3.8**), the agostic interactions are replaced by the ethylene π -complex. The formation of the π -complex also involves the Me group on the Hf atom in a *trans* relationship with the pyridine N atom. The *syn* position of the (2-*i*Pr)Ph substituent with the counteranion in **2a** leads

to orientations, such as those in region B, that are susceptible to agostic interactions, which can be replaced by stronger ethylene coordination.

Meanwhile, this displacement may be harder for the **2b** diastereomer. Structures from 3.4 to 4.7 Å show ion pair structures with agostic interactions involving the *ortho*-H atom of (2-*i*Pr)Ph (**Figure 3.8**). As the monomer approaches the Hf center, the wider distribution of Hf-H distances indicates likely competition between the agostic interaction and ethylene, as shown in the boxplots of windows 2.7 and 3.4 Å (**Figure 3.8**). Longer Hf-H distances indicate the displacement of the agostic interaction and rotation of the ((2-*i*Pr)Ph ring.¹¹⁶ The preference for the agostic interaction indicates that the ethylene and frontside ((2-*i*Pr)Ph substituent are in an alternative configuration (**Figure 3.8**) that is more favored than the π -complex. This involves the ethylene in the outer coordination sphere between the naphthyl ligand and the Ph ring in (2-*i*Pr)Ph. The presence of the agostic interaction also limits rotation of (2-*i*Pr)Ph, which limits steric hindrance from the ligand. Together, these interactions makes it convenient for the ethylene to stay in the outer sphere.

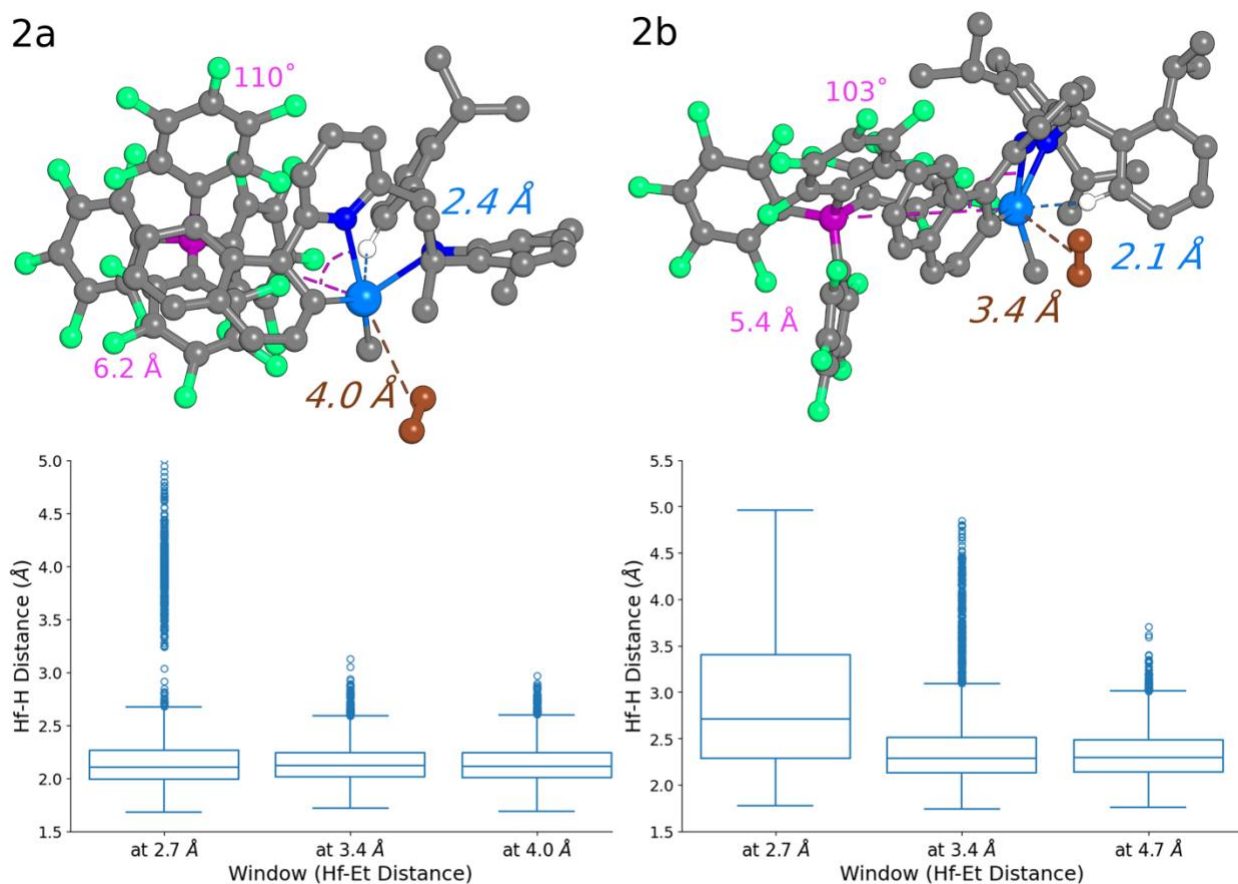


Figure 3.8 (top) Representative structures of **2a** (left) and **2b** (right) from selected windows showing interaction of Hf center to the *ortho*-H atom of (2-*i*Pr)Ph (Hf-H distance) and (bottom) distribution of Hf-H distances from selected windows.

3.5 Conclusions

Atomistic simulation of ethylene polymerization by a Hf(IV)-pyridylamido catalyst was conducted, focusing on the effect of multiple diastereotopic active sites on catalyst activation. Through MD simulations, the free energy maps of the IP structures, each consisting of **2a** or **2b** diastereomer and $[\text{B}(\text{C}_6\text{F}_5)_4]^-$ anion, were examined. Different preferences of IP orientations were shown to influence stabilization of the active site and favorable interactions for monomer coordination. Although both diastereomers mostly prefer ISIPs without the monomer, the **2a** complex can access IP orientations farther from the active site, while the **2b** diastereomer prefers ISIPs. The *syn* relationship of the (2-*i*Pr)Ph bridgehead in **2a** with the counteranion drives the

anion to slide to alternative locations such as region B, whereas the *anti* relationship in **2b** enables the anion to remain in side structures with the cation. When the monomer is coordinated, IP orientations with favorable interactions such as π -stacking are preferred. OSIPs can be further stabilized by agostic interactions of the Hf center with the H atom in DIPA or (2-*i*Pr)Ph. Through umbrella sampling simulations, the monomer coordination process was examined. The free energy profiles showed minima that correspond to an ethylene π -complex and an agostic complex with favorable ethylene-ligand interactions. **2a** facilitates ethylene coordination better than **2b** since monomer approach to the π -complex is unhindered. **2b** prefers the frontside orientation of the agostic interaction, where (2-*i*Pr)Ph is locked with the approaching monomer instead. Insight into the favored ion pair and monomer orientations gained in this study reveals the likely microscopic origin of contributions to low-active site counts in the Hf-pyridylamido catalyst.

Chapter 4 Conclusions

Progress in computing power and computational methods are advancing chemical discovery and broadening chemical knowledge. There is an expanding array of tools available to computational chemists that help create accurate models of complex chemical systems. Development of quantum chemical methods enable efficient potential energy surface exploration, while reaction path finding methods enable the identification of transition states. As computational tools become more accessible, a stronger interplay between experiment and theory emerges.

The efforts in this work have focused on conformational effects resulting from the flexibility in organometallic complexes. Experiment has linked the cation-anion ion pair in group IV olefin polymerization catalysts to performance and polymer properties, but the microscopic behavior of the ion pair and its effects are poorly understood. This is due to the dynamic and flexible nature of the ion pair, where static methods alone are not suitable to tackle the problem. In this work, extensive conformer sampling, enabled by cost-effective quantum chemical methods, was used to reveal the dynamic behavior in the ion pair that affects olefin polymerization. Insights gained from simulations enhance chemical understanding of these organometallic systems by revealing important structure-reactivity relationships, which allows chemists to design effective systems that can exploit these connections. This work should also encourage a more comprehensive evaluation of conformational effects on the reactivity of other transition metal catalysts.

4.1 Research Summary

The work in chapter 2 revealed the interactions between the counteranion and flexible polymer during propagation and termination with the Ti(IV) constrained geometry catalyst. The effects of the counteranion choice and the length of the polymer chain on ethylene polymerization were investigated through conformer sampling and reaction pathway simulations. The dynamic ion pair and flexible polymer together allow for a large number of possible conformers for the intermediates that undergo monomer insertion and chain termination via β -hydrogen transfer. The ion pair prefers different orientations with a short and long polymer chain. Energetic variations found in π -complex conformers give rise to multiple relevant monomer insertion and β HT pathways. The range of TS energies varied widely depending on ion pair orientation, where back ion pair alignments led to the lowest barriers. Analysis of the conformational ensemble of reaction paths reveals relevant contributions to the chain propagation and termination rates. The impact of the counteranion on the reaction mechanism, with a focus on the competition between propagation and termination, highlights how one results in lower molecular weight of the polymer compared to the other.

The work in chapter 3 showed how the differences in ion pair interactions between diastereomers during activation with the Hf(IV)-pyridylamido catalyst influence low active-site counts. The hypothesis that bridgehead substitution leads to multi-site behavior for olefin polymerization was investigated by simulating the microscopic behavior and interactions of the counteranion with the diastereomer. Through molecular dynamics simulations, different preferences of ion orientations for each diastereomer were shown to influence stabilization of the active site and favorable interactions for monomer coordination. The same relationship of the bridgehead substituent with the counteranion in one diastereomer drives the anion to slide to

alternative staggered orientations, whereas the opposite-side relationship in the other diastereomer enables the anion to remain in side orientations with the cation. Through umbrella sampling simulations, the monomer coordination process was examined. The free energy profiles showed minima that correspond to an ethylene π -complex and an agostic complex with favorable ethylene-ligand interactions, where one diastereomer facilitates ethylene approach than the other. Understanding of the favored ion pair and monomer orientations gained in this study reveals the likely microscopic origin of contributions to low-active site counts in the Hf-pyridylamido catalyst.

4.2 Future Considerations

4.2.1 Future Directions for the Systems Studied

Although the simulations contained in this work contribute to an improved understanding of the studied organometallic polymerization reactions, there are open questions and considerations that remain. Chapter 2 showed the microscopic effect of the ion pair on catalyst performance as a function of cocatalyst counteranion choice. Although $\text{B}(\text{C}_6\text{F}_5)_3$ and $[\text{Ph}_3][\text{B}(\text{C}_6\text{F}_5)_4]$ are two widely used cocatalysts, a variety of structural modifications has been designed to modulate their performance.¹¹⁷ Design strategies have consisted of other bulky perfluoroaryl rings, diboranes/diborates, and boranes/borates with non-aryl substituents.⁴² Systematic comparison of these different structural motifs and their behavior with the cation and polymer have not been comprehensively explored thus far. An understanding of how the ancillary ligand with different steric constraints near the active site can impede or enable monomer binding is also of interest. For instance, the cyclopentadienyl ligand with methyl groups substituted with an extended aromatic system is more effective at styrene incorporation. When the cyclopentadienyl ligand is modified with a conformationally flexible pyrrolidine side chain, the CGC has higher activity and copolymer molecular weights than the prototypical catalyst. The

combined approach involving conformer sampling and reaction path simulations in Chapter 2 can be used to investigate the effective activation barriers of reactions resulting from these catalyst modifications.

Nevertheless, there are some limitations that have to be tackled in future studies. The flexible polymer studied in Chapter 2 corresponds to consecutive repetitions of ethylene monomer insertion, resulting in a linear polymer chain. The need to create polymers with new properties leads to increased interest in controlled production of branched polymers with a specific microstructure. Branching in the polyethylene structure can form through chain isomerization or introduction of short-chain α -olefin comonomers.⁴⁰ These should be taken into account if modeling polymerization catalysts that lead to highly branched products.

Chapter 3 described the effect of multiple diastereotopic active sites on catalyst activation with the Hf(IV)-pyridylamido complex. This investigation showed that one diastereomer is more viable for activation through sampling of the ion pair and ethylene coordination process. The monomer-inserted ion pair is established by experiment to be the catalytically active species responsible for polymerization. So, further conformational sampling of the complex, corresponding to initiation and propagation steps, can give insight into the stereochemical differences in the catalytic cycle. If copolymerization with ethylene and 1-octene is considered, then there are more possible products of insertion that can lead to multisite behavior. Hence, competition for ethylene and 1-octene insertion into the Hf-naphthyl bond is an area of consideration.

4.2.2 Future Directions for Computational Approach

With the availability of methods for conformational sampling and reaction path simulations, combining these tools expands the scope of chemical space that can be explored.

Nevertheless, considerations into improving the computational pipeline to reveal chemical insight are required. Conformational sampling, which is not limited to molecular dynamics simulations, can produce large datasets of structures. Identifying representative conformers from these structures requires relevant descriptors of the system of interest. For the catalysts studied above, chemist intuition and visualization were necessary to identify explanatory geometric descriptors, which may not be trivial for larger transition metal complexes. Additionally, reaction path searches using these conformers generate an ensemble of reaction paths, which requires examination for feasible pathways. There is a need for methods that can effectively sample and analyze transition-metal catalyzed reactions ensembles of reactions involving transition metal catalysts, which can inform catalyst design and optimization. With regards to improving the computational pipeline, here are some suggestions:

- 1) An interactive visualization and analysis tool that can facilitate chemist understanding of the relationship between descriptors and reaction paths.
- 2) Methodical approach for assessing relationships between chemical descriptors and energetics
- 3) A systematic strategy to obtain representative structures, such as clustering.
- 4) Low-cost ranking of feasible reaction pathways and determination if energetic refinement with higher level QM methods is needed.

4.3 Final Thoughts

The studies contained in this work demonstrate that advances in computational chemistry can be used to inform experiment and improve chemical understanding. Accurate chemical models of flexible chemical systems can uncover insightful relationships that may otherwise be unseen

with static methods. The studies presented are of particular interest to the organometallic community, especially researchers interested in main group transition metal chemistry, polymerization reactions, and ion pair interactions. The simulation approaches are informative to computational chemists who study conformers and reaction pathways.

Appendices

Appendix A:
**Supporting Information for Chapter 2: Revealing the Interactions between the Flexible
Polymer and Counteranion during Propagation and Termination for Olefin
Polymerization with the Ti(IV) Constrained Geometry Catalyst**

A.1 Details of FE Maps from Trajectories

Two ion pair (IP) atomistic models were prepared for the MD simulations, which consist of $[\text{Ti-CGC-C}_n\text{H}_{2n+1}]^+[\text{anion}]^-$ with $\text{MeB}(\text{C}_6\text{F}_5)_3^-$ or $\text{B}(\text{C}_6\text{F}_5)_4^-$ (3PFB, 4PFB, respectively) as the counteranion. The complexes $[\text{Ti-CGC-C}_n\text{H}_{2n+1}]^+[\text{3PFB/4PFB}]^-$ (without ethylene) and $\text{C}_2\text{H}_4[\text{Ti-CGC-C}_n\text{H}_{2n+1}]^+[\text{3PFB/4PFB}]^-$ (with ethylene) were prepared at different lengths of the polymer chain ($n = 3, 11$) attached to the metal. The xTB software package (ver. 6.4.1) was used for molecular dynamics simulations and single-point energy calculations.⁸¹ The GFNFF-xTB force field was used for MD simulations and the GFN2-xTB semiempirical tight-binding method was used for structure optimization.^{21,81,82} The MD simulations were performed in NVT ensemble at 423.15 K, corresponding to conditions from a higher temperature polymerization (150 °C). The NVT-MD simulations were run for 100 ns with a 2 fs timestep. From the trajectories, structures were saved every 1 ps. The ALPB solvation model was used for implicit solvation with toluene as solvent.³⁷ Harmonic potential restraints were placed on Ti atom and its distances with Cp and Si atoms, in order to fix the ancillary ligand in place during the MD runs.

To map free energy surfaces (FES) from the MD trajectories onto characteristic degrees of freedom, the interatomic distance r between Ti and B atoms and the Si-Cp-Ti-B dihedral angle φ formed between the Si-Cp-Ti and Cp-Ti-B planes were taken as coordinates. The centroid of Cp

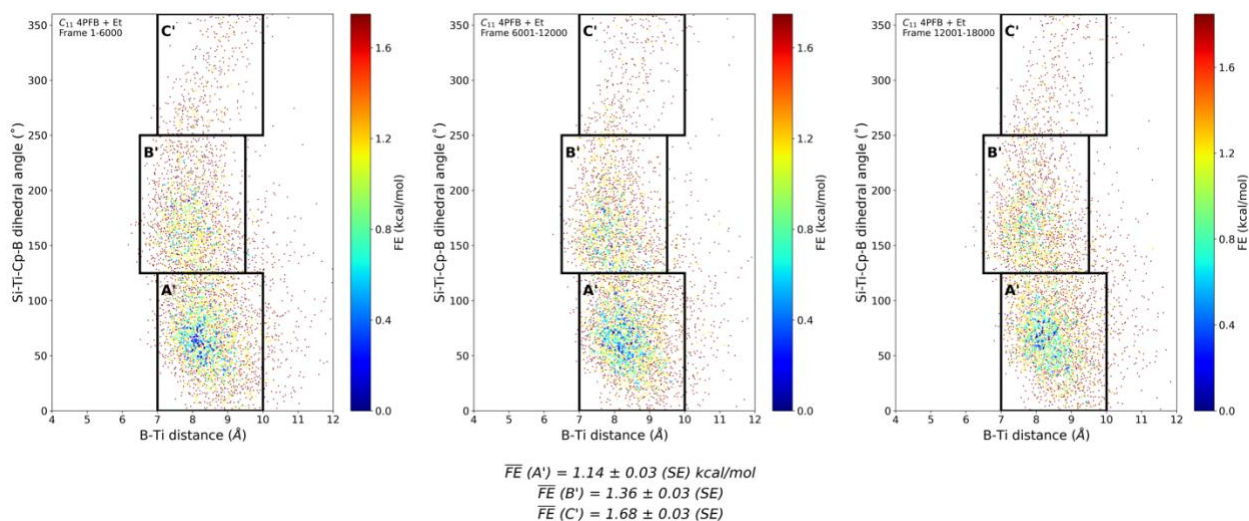
ligand is used in calculating φ . The regions in the FE map were divided into bins with size (0.05 Å, 2.0°).⁵⁷ The fraction of states Z_i in each region i is calculated as,

$$Z_i = \frac{W_i}{\sum_i W_i} \quad (\text{A.1})$$

where W_i corresponds to the number of states in each region. Since the molecular dynamics simulations sample the canonical ensemble, Z_i counts Boltzmann-weighted states. The FE of region i is calculated as,

$$FE = -k_B T \ln(Z_i) \quad (\text{A.2})$$

where the free energy origin (0.0 kcal/mol) is set at the bin with the lowest FE. **Appendix Figure A.1** shows how the sampled ion pair orientations at different frames of the MD trajectories change and converge with respect to r and φ .



Appendix Figure A.1 Free energy maps of $[\text{Ti-CGC-C}_{11}\text{H}_{23}]^+[\text{4PFB}]^-$ from partitions of the trajectory. The standard error (SE) of the free energy for Regions A', B', and C' are reported below.

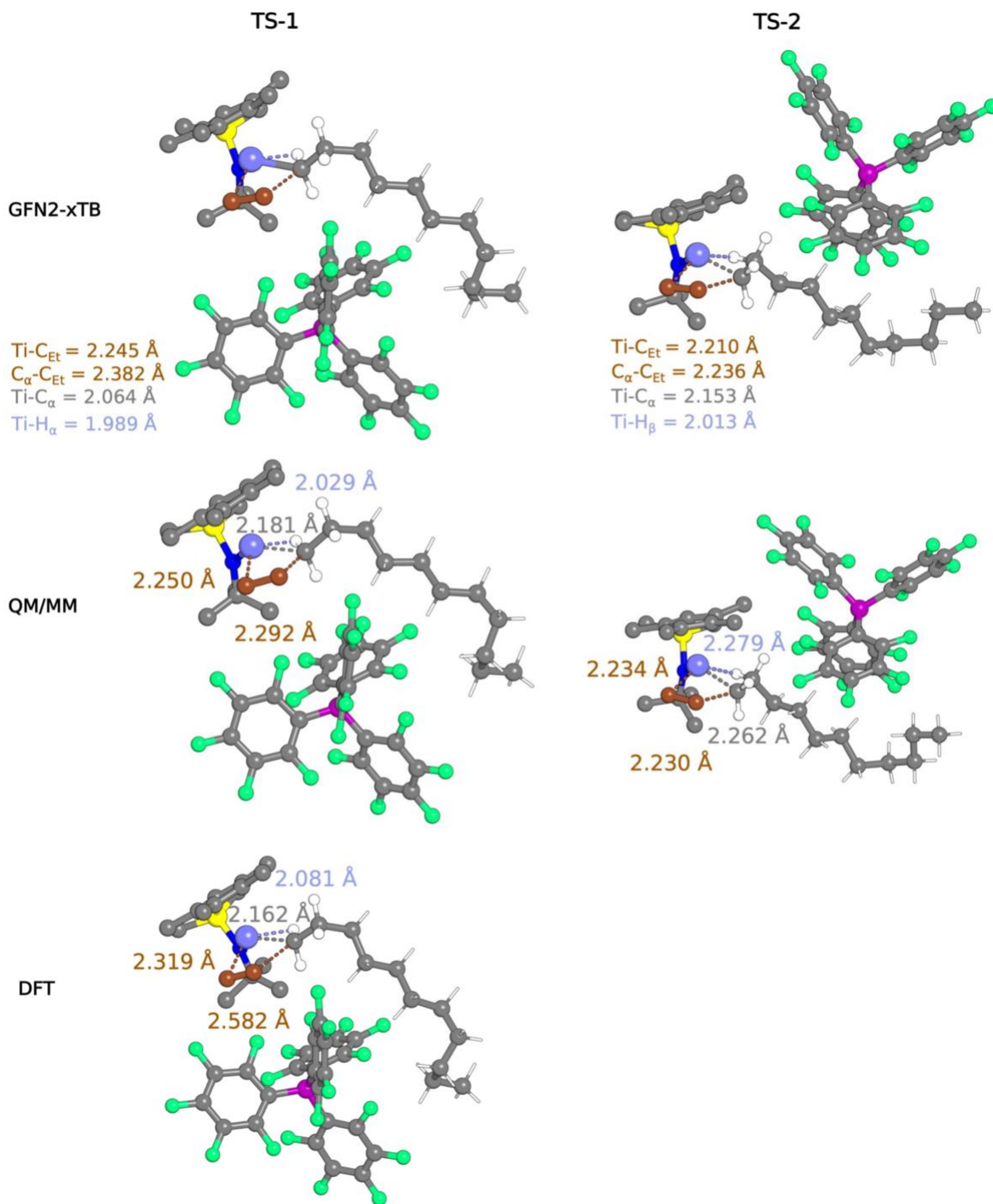
A.2 Details of Catalyst Conformer Ensembles

The k-medoids clustering method was used to identify and obtain representative conformers from MD trajectories. This clustering method finds a set of cluster centers that are themselves data points, i.e. specific structures from the trajectories.^{83,118} The k-medoids clustering method has been shown to be more robust to noise and outliers than k-means, and the choice of distance metric is not limited compared to other clustering methods.¹¹⁸ The method allows for better interpretability of the cluster centers, which can be used as starting structures for downstream reaction path searches. The distance metric used was the root mean square deviation (RMSD) and the full distance matrix was computed between all pairs of data points. The k-medoids method takes in the number of medoids as input instead of minimum RMSD value. 100 and 300 medoids, which correspond to 1-2% of obtained trajectory frames, were selected for complexes with C₃ and C₁₁ polymer chain lengths, respectively.

A.3 Details of Reaction Path Finding Simulations

The single-ended growing string method (GSM) was used for reaction path finding and transition state searching of ethylene insertion and β HT reactions.^{25,84} The GFN2-xTB semiempirical tight-binding method provided energies and gradients. This method was chosen for its balance of cost and accuracy, allowing considerable sampling of the conformational ensemble reaction paths.⁸⁵ The resulting reaction pathways and structures were found to be similar to reaction pathways calculated at the QM level with DFT (B97-D3/6-31G*) and QM/MM level using QM(B97-D3/6-31G*)/MM(OPLS) with electrostatic embedding.^{9,13} **Appendix Table A.1** compares geometric descriptors (**Appendix Figure A.2**) from two ethylene insertion TS structures (TS-1, TS-2) of C₂H₄[Ti-CGC-C₁₁H₂₃]⁺[4PFB]⁻ reactant conformers. **Appendix Table A.2** compares the energetics from GFN2-xTB and DFT reaction paths, with and without the

counteranion. The insertion and β HT TS structures of conformer 1 from the DFT reaction paths are comparable in geometry and energetics to the GFN2-xTB reaction paths (**Appendix Table A.2**). The cation-only approach underestimates the insertion and β HT barriers for both GFN2 and DFT methods (**Appendix Table A.2**).



Appendix Figure A.2 3D renderings of two $[\text{Ti-CGC-C}_{11}\text{H}_{23}]^{+}[\text{4PFB}]^{-}$ ethylene insertion TS structures using GFN2-xTB and QM/MM. H atoms on the ligand were removed to prevent clutter. (slate: Ti, gray: C, brown: ethylene C, yellow: Si, blue: N, white: H, purple: B, lime green: F)

Appendix Table A.1 Comparison of bond lengths from [Ti-CGC-C₁₁H₂₃]⁺[4PFB]⁻ ethylene insertion TS structures.

Key Bond Length (Å)	Method	TS-1	TS-2
Ti-C _{et,1}	GFN2	2.245	2.210
	QM/MM	2.250	2.234
	DFT	2.319	N/A
C _α -C _{et,2}	GFN2	2.382	2.236
	QM/MM	2.292	2.230
	DFT	2.581	N/A
Ti-C _α	GFN2	2.064	2.153
	QM/MM	2.181	2.262
	DFT	2.162	N/A
Ti-H _α (α-agostic)	GFN2	1.989	N/A
	QM/MM	2.029	N/A
	DFT	2.081	N/A
Ti-H _β (β-agostic)	GFN2	N/A	2.013
	QM/MM	N/A	2.279
	DFT	N/A	N/A

Appendix Table A.2 Comparison of energetics from GFN2-xTB and DFT (B97-D3/6-31G*) reaction paths.

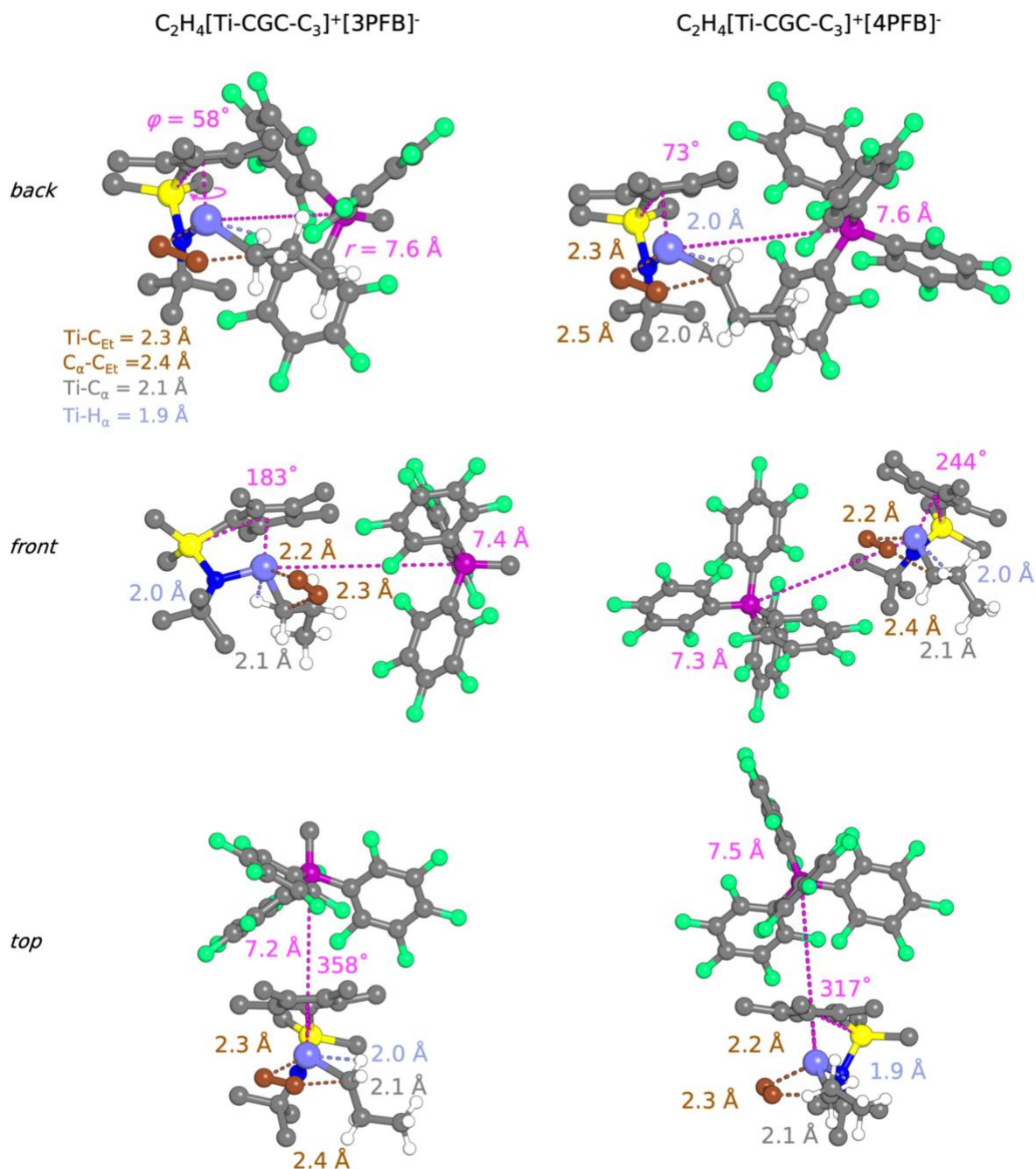
Reaction Path (Conformer 1)	GFN2 Relative TS Energy (kcal/mol)	DFT Relative TS Energy (kcal/mol)
Ethylene Insertion	10.0	7.4
Cation Ethylene Insertion	6.5	1.2
β-Hydrogen Transfer	29.7	26.4
Cation β-Hydrogen Transfer	19.1	14.8

A.4 Visualization of Transition State Structures Organized by Ion Pair Alignment

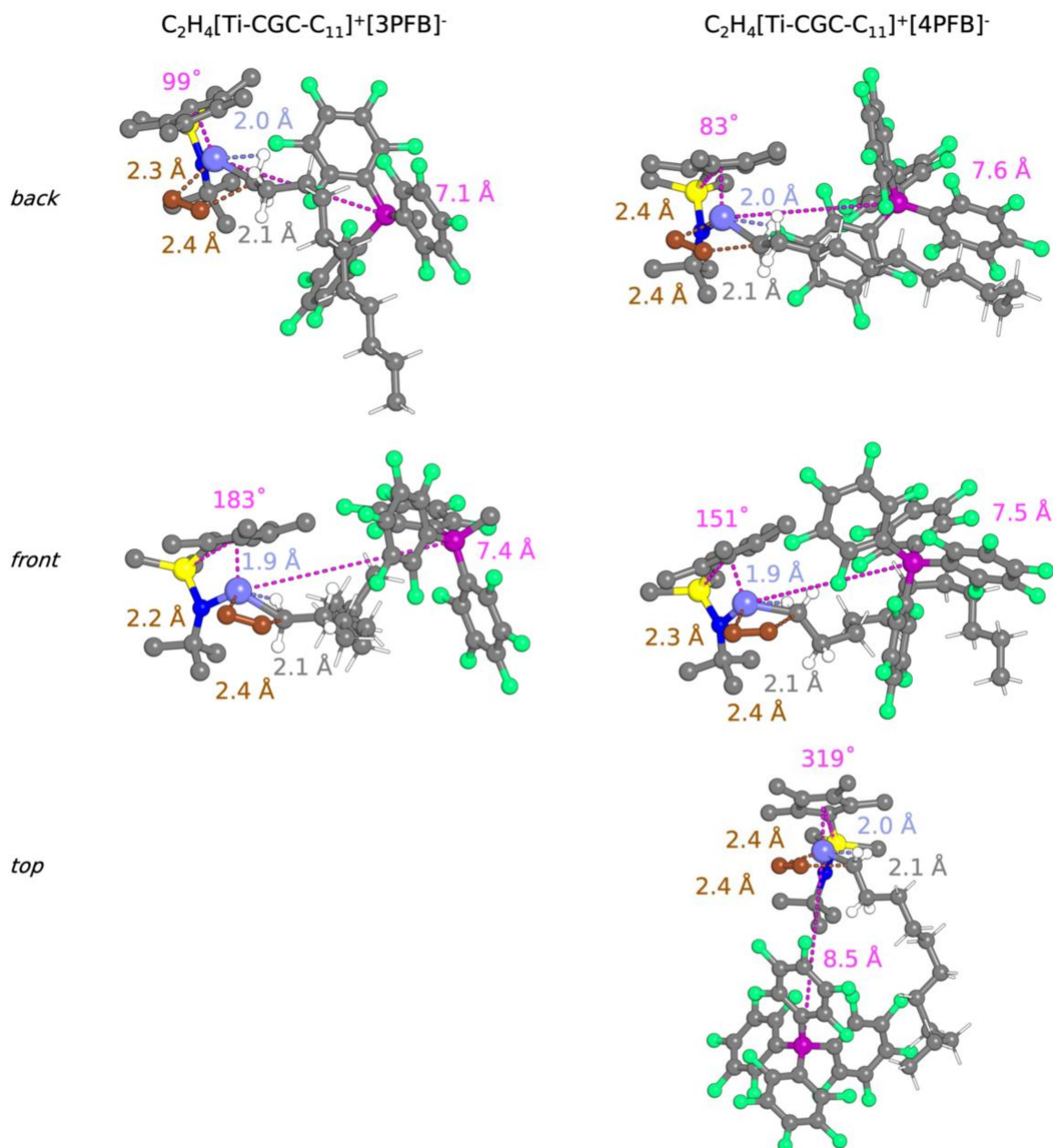
The 3D structures below show representative ethylene insertion and βHT transition state geometries for C₂H₄[Ti-CGC-Polymer]⁺[Anion]⁻ labeled by their ion pair alignment.^{119,120} These structures are some of the top contributors to $\Delta^\ddagger G_{\text{eff}}$ in terms of $x_i^{RS} \exp(-\frac{\Delta^\ddagger G_i}{RT})$. Ti-CGC and anion are shown in ball-and-stick. The hydrogen atoms of the C_α and C_β atoms (and C_γ for [Ti-CGC-C₃])

of the polymer chain are shown in ball-and-stick and the rest are shown as wires. Hydrogen atoms not in the polymer chain are hidden. (slate: Ti, gray: C, brown: ethylene C, yellow: Si, blue: N, white: H, purple: B, lime green: F)

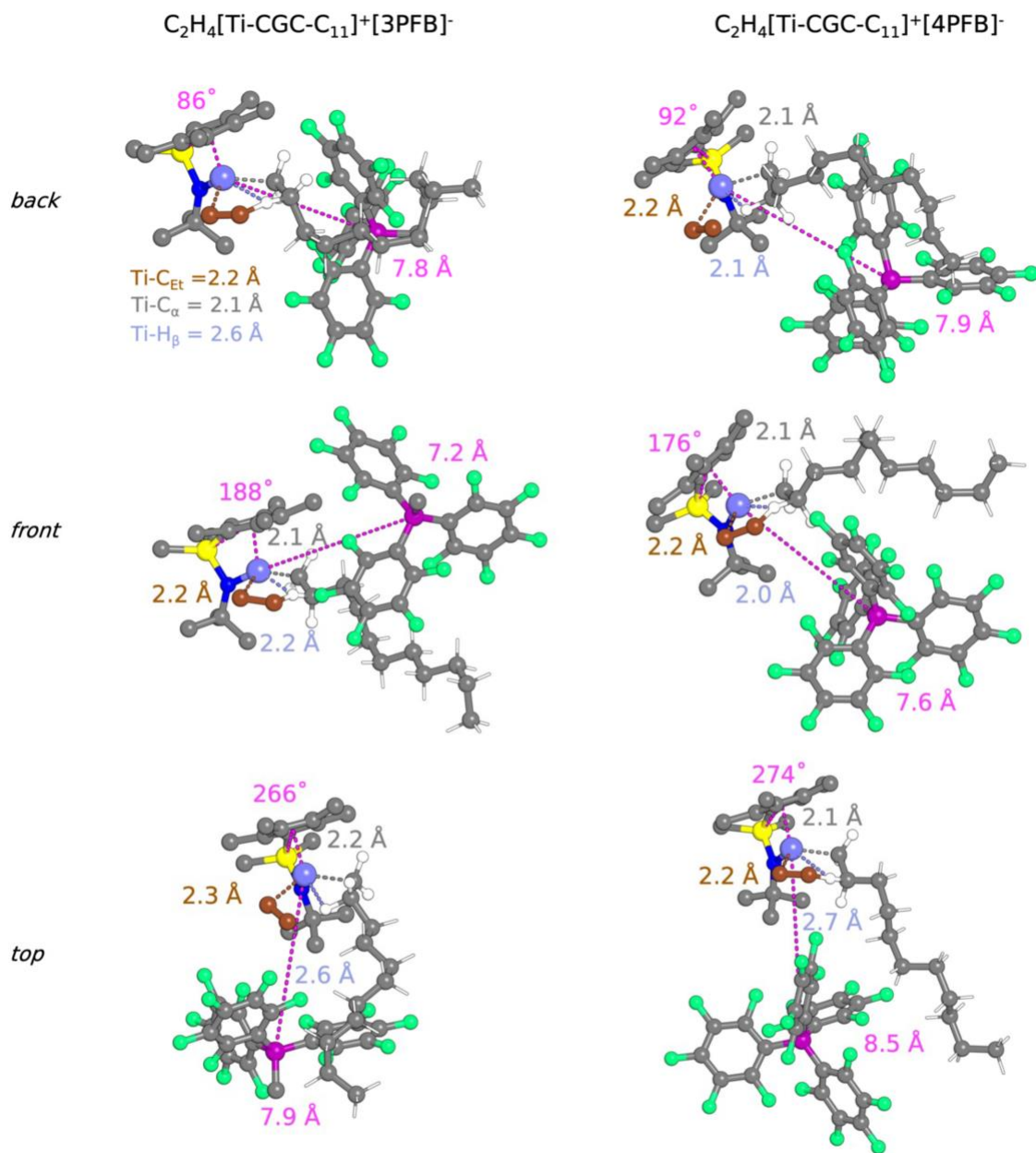
For ethylene insertion TS structures, the following atom-atom distances and dihedral angle are labeled: Ti-B (pink), Ti-C_{et} (brown), C_{et}-C_α (brown), Ti-H_α (slate), and Si-Cp-Ti-B (pink). For βHT TS structures, the following atom-atom distances are labeled: Ti-B (pink), Ti-C_α (gray), Ti-C_{et} (brown), Ti-H_β (slate), and Si-Cp-Ti-B (pink).



Appendix Figure A.3 3D renderings of ethylene insertion TS conformers for each $\text{C}_2\text{H}_4[\text{Ti-CGC-C}_3\text{H}_7]^+[\text{3PFB/4PFB}]^-$ complex classified by ion pair alignment.



Appendix Figure A.4 3D renderings of ethylene insertion TS conformers for each $\text{C}_2\text{H}_4[\text{Ti-CGC-C}_{11}\text{H}_{23}]^+[\text{3PFB/4PFB}]^-$ complex classified by ion pair alignment. (No top structure was classified for $[\text{Ti-CGC-C}_{11}\text{H}_{23}]^+[\text{3PFB}]^-$ complex.)



Appendix Figure A.5 3D renderings of βHT TS conformers for each $\text{C}_2\text{H}_4[\text{Ti-CGC-C}_{11}\text{H}_{23}]^+[\text{3PFB/4PFB}]^-$ complex classified by ion pair alignment.

Appendix B:
Supporting Information for Chapter 3: Elucidating the Interactions between Diastereomer and Counteranion during Activation for Olefin Polymerization with the Racemic Hf(IV)-Pyridylamido Catalyst

B.1 Details of Molecular Dynamics Simulations and Free Energy Maps

Four ion pair (IP) atomistic models were prepared for the MD simulations, which consist of **[2a/2b]⁺[anion]⁻** with and without ethylene monomer, with B(C₆F₅)₄⁻ (4PFB) as the counteranion. The xTB software package (ver. 6.4.1) was used for MD simulations and single-point energy calculations.⁸¹ The GFN2-xTB semiempirical tight-binding method was used for single-point calculation, structure optimization and MD simulation.^{21,81,82} The MD simulations (ORCA, ver. 5.0.4) were performed in NVT ensemble at 423.15 K, corresponding to conditions from a higher temperature polymerization (150 °C). The NVT-MD simulations were run for 4 ns with 1 fs timestep. From the trajectories, structures were saved every 100 fs. The ALPB solvation model was used for implicit solvation with toluene as solvent.³⁷ From the trajectories, structures were saved every 100 fs. The ALPB solvation model was used for implicit solvation with toluene as solvent. A spherical harmonic repulsive wall with radius 30 Å was placed around the system. For the ethylene IP systems, constraints were placed on the interatomic distances of the Hf, ethylene, and naphthyl carbon atoms involved in ethylene insertion.

To map free energy surfaces (FES) from the MD trajectories onto characteristic degrees of freedom, the interatomic distance r between Hf and B atoms and the B-Hf-N angle φ formed were

taken as coordinates. The regions in the FE map were divided into bins with size (0.05 Å, 2.0°).⁵⁷

The fraction of states Z_i in each region i is calculated as,

$$Z_i = \frac{W_i}{\sum_i W_i} \quad (\text{B.3})$$

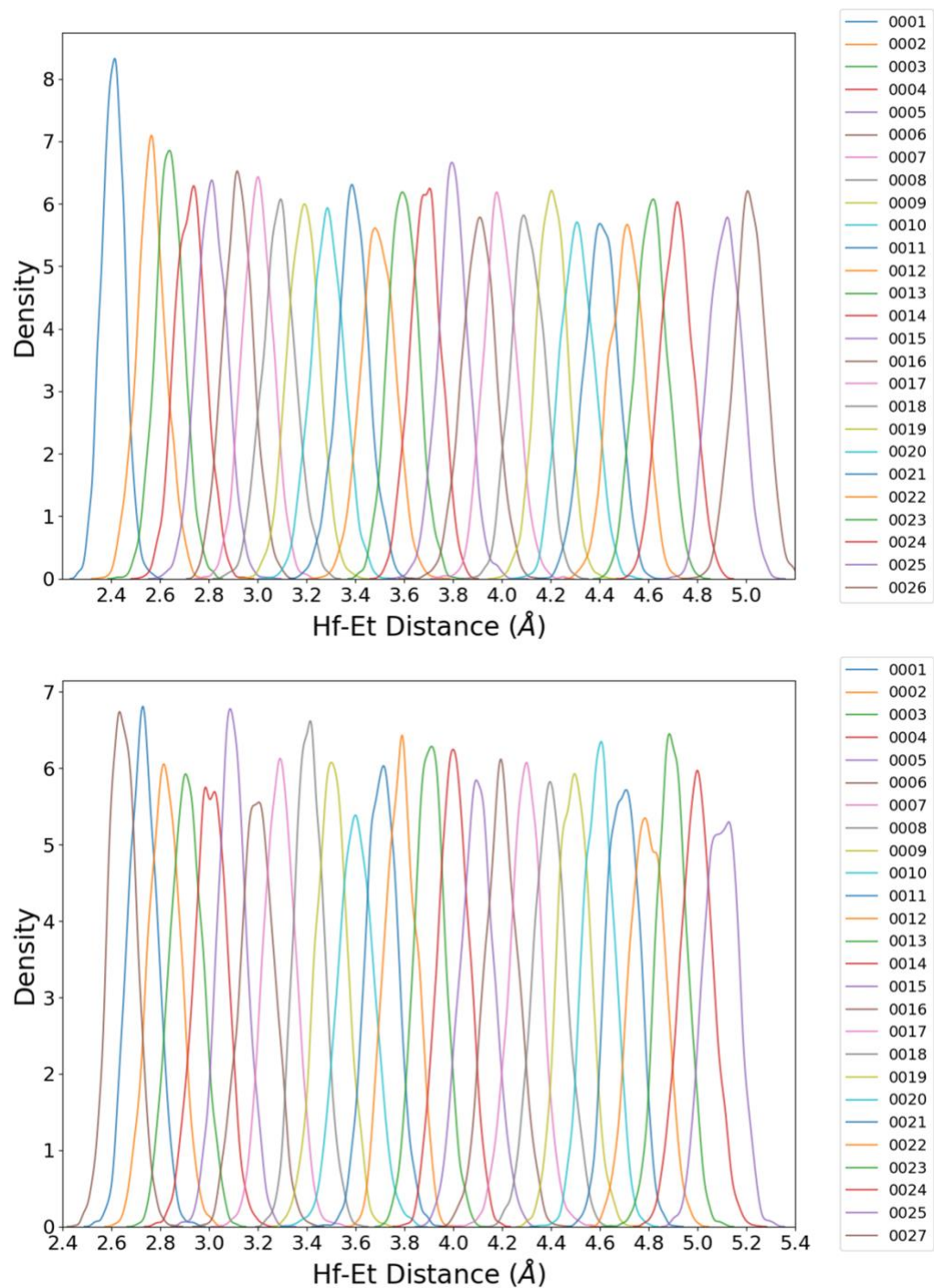
where W_i corresponds to the number of states in each region. Since the molecular dynamics simulations sample the canonical ensemble, Z_i counts Boltzmann-weighted states. The FE of region i is calculated as,

$$FE = -k_B T \ln(Z_i) \quad (\text{B.2})$$

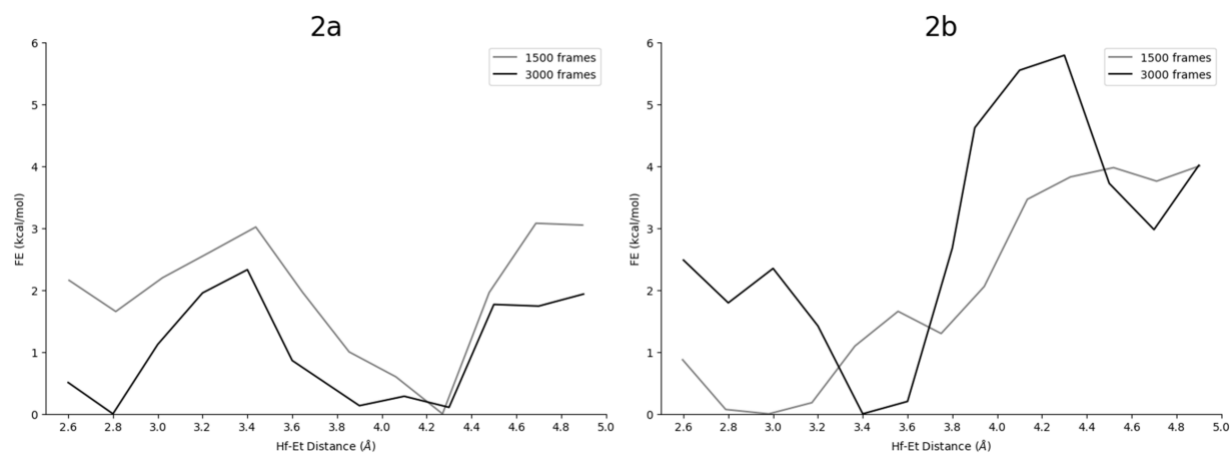
where the free energy origin (0.0 kcal/mol) is set at the bin with the lowest FE.

B.2 Details of Umbrella Sampling Simulations

One-dimensional umbrella sampling simulations were run for **[2a]⁺[4PFB]⁻** and **[2b]⁺[4PFB]⁻** with ethylene present. The reaction coordinate chosen to be restrained with a harmonic potential was the distance of the Hf atom to the center of mass of ethylene (Hf-Et distance). MD simulations (DFTB+ ver. 23.1, PLUMED ver. 2.9) were performed for 200 ps at 423.15 K using a spring constant of 200 kcal/mol/Å² in 25 umbrella windows centered along the Hf-Et distance, which is increased from 2.5 to 5.0 Å at 0.1 Å intervals. For each frame (saved every 50 fs) in each US trajectory, the values of the applied collective variable were evaluated. The multistate Bennett acceptance ratio (MBAR) method was used (pymbar ver. 4.0) to create a FE profile through kernel density estimation (KDE) based on Hf-Et distance. The FE error was calculated with 50 bootstrapping runs. **Appendix Figure B.1** shows the histogram coverage of Hf-Et distance in the umbrella sampling windows for **2a** and **2b**. **Appendix Figure B.2** shows the convergence of the free energy computed with MBAR for **2a** and **2b**, using 1500 and 3000 frames for each window, respectively.



Appendix Figure B.1 Coverage of the collective variable (Hf-Et distance) during umbrella sampling simulations for (top) **2a** and (bottom) **2b** systems.



Appendix Figure B.2 Convergence of MBAR-estimated free energy during umbrella sampling simulations.

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