

DFT Virtual Screening Identifies Rhodium–Amidinate Complexes As Potential Homogeneous Catalysts for Methane-to-Methanol Oxidation

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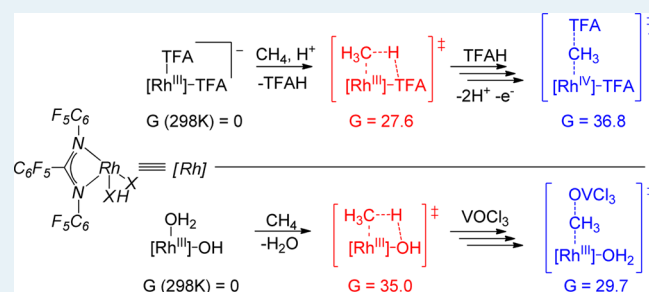
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Supporting Information

ABSTRACT: In the search for new organometallic catalysts for low-temperature selective conversion of CH_4 to CH_3OH , we apply quantum mechanical virtual screening to select the optimum combination of ligand and solvent on rhodium to achieve low barriers for CH_4 activation and functionalization to recommend for experimental validation. Here, we considered Rh because its lower electronegativity compared with Pt and Pd may allow it to avoid poisoning by coordinating media. We report quantum mechanical predictions (including implicit and explicit solvation) of the mechanisms for $\text{Rh}^{\text{III}}(\text{NN})$ and $\text{Rh}^{\text{III}}(\text{NN}^{\text{F}})$ complexes [where (NN) = bis(*N*-phenyl)-benzylamidinate and (NN^F) = bis(*N*-pentafluorophenyl)pentamethylimidate] to catalytically activate and functionalize methane using trifluoroacetic acid (TFAH) or water as a solvent. In particular, we designed the (NN^F) ligand as a more electrophilic analogue to the (NN) ligand, and our results predict the lowest transition state barrier ($\Delta G^\ddagger = 27.6$ kcal/mol) for methane activation in TFAH from a pool of four different classes of ligands. To close the catalytic cycle, the functionalization of methylrhodium intermediates was also investigated, involving carbon–oxygen bond formation via $\text{S}_{\text{N}}2$ attack by solvent, or $\text{S}_{\text{R}}2$ attack by a vanadium oxo. Activation barriers for the functionalization of methylrhodium intermediates via nucleophilic attack are lower when the solvent is water, but CH_4 activation barriers are higher. In addition, we have found a correlation between CH_4 activation barriers and rhodium–methyl bond energies that allow us to predict the activation transition state energies for future ligands, as well.

KEYWORDS: rhodium, catalysis, quantum mechanical screening, C–H activation, methane functionalization, amidinate, fluorinated ligands



INTRODUCTION

The facile, selective, and direct conversion of methane into methanol has long been a goal of industrial chemists.¹ Methane, the chief component of natural gas, is typically found in abundant quantities wherever petroleum deposits are found. However, due to its difficulty in liquefaction (its boiling point being only 110 K) and its relative paucity of demand as compared with other hydrocarbons, it is often not economical to harvest this gas, which is essentially a byproduct or coproduct of petroleum recovery, and to transport it to market. Since methane is also a potent greenhouse gas, with a global warming potential 72 times more powerful than that of carbon dioxide,² it cannot simply be released. Hence, it is often flared, a process that is both intrinsically wasteful and which results in a large amount of heat pollution.

One potential solution is to convert these vast quantities of methane into methanol. Because methanol is liquid at room

temperature and pressure, it is much more easily transported and stored. Methanol can be used as a fuel in flex fuel vehicles, blended with gasoline, or converted to gasoline or diesel fuel. In addition, it has many applications as an industrial solvent and chemical feedstock. Because methanol is both more easily processed and in greater demand than methane, the efficient conversion from the former to the latter has the potential to be both environmentally friendly and economically favorable.

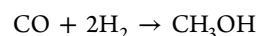
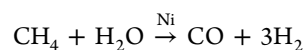
Although the reaction $\text{CH}_4 + 1/2 \text{O}_2 \rightarrow \text{CH}_3\text{OH}$ is exoenergetic by 30 kcal/mol, efficient catalysis is hampered by the fact that the C–H bond dissociation energy (BDE) of methane is 104 kcal/mol, whereas the C–H BDE of methanol is only 95 kcal/mol. Hence, overoxidation is a major problem. In fact,

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potential methods for direct conversion of methane to methanol that involve radicals have a theoretical maximum yield of only 5%, even with perfect conversion.³ Hence, the currently favored industry-scale conversion of methane to methanol involves an indirect pathway via syngas:¹



However, this pathway suffers from a difficult first step that is highly endergonic, requiring very high temperatures and pressures (700–1100 °C, 40 atm). Hence, this state-of-the-art pathway requires large inputs of energy and very expensive production facilities, despite the significantly exothermic nature of the overall reaction. An alternative mechanism that does not require such extreme conditions would thus be highly desirable.

Molecular compounds in solution have long been investigated as potential catalysts for this transformation, as they are typically well-defined, easy to characterize and model, and operate under relatively mild conditions. Whereas much previous work has been done on Pt and Pd catalysts,^{3,4} we focus here on rhodium due to its well-documented nature as an effective C–H activating metal⁵ and whose lower electronegativity may allow it to avoid poisoning by coordinating media.

Our initial calculations found that using neutral tridentate pincer ligands (L_3) resulted in neutral $L_3\text{Rh}(\text{TFA})_3$ resting states. For such complexes to activate methane, a TFA ligand must be both protonated and removed to create an open coordination site. The frequent result was that the overall methane activation energy (i.e., energy of the transition state minus energy of the resting state) was too high to be feasible. Thus, to provide the best candidates for experiments, we shifted our attention to bidentate and monoanionic ligands, which are expected to favor Rh^{III} states that would incorporate a labile, protonated TFAH solvent molecule, thus removing the extra energy penalty for protonation. Bidentate and tridentate ligands were chosen to facilitate redox processes, which interconvert square-planar and octahedral coordination environments. Thus, we examined four classes of ligands that we thought might prove effective while likely not too hard to synthesize:

- bis(*N*-phenyl)benzylamidinate (NN)
- (*N*-phenyl)acetaldiminyl quinolate (ONN)
- bis(pyridyl)methanesulfonate (DPMS)
- bis(pyrryl)quinolinyl phosphine (PN)

and two solvents: water and trifluoroacetic acid, due to their pH range and oxidative stability. We then embarked on quantum mechanical (QM) virtual screening to select the optimum combinations of ligand and solvent to recommend for experimental validation. Here, we used density functional theory (DFT) at the B3LYP and M06 levels, including both implicit and explicit solvation, for systematic searches over possible reactions mechanisms for CH_4 activation and for functionalization.

We found that rhodium complexed with the bidentate bis(*N*-phenyl) benzylamidinate (NN) ligand was the most promising in our initial screen. We then designed a new ligand bis(*N*-pentafluorophenyl)pentafluorobenzylamidinate (NN^{F}), essentially an electron-poor version of (NN), that we find to be even more promising. Here, increased electron-withdrawing character lowers both activation barriers (but with decreased stability).

Our efforts culminated in two complexes,

- $\text{Rh}^{\text{III}}[\text{bis}(\textit{N}\text{-phenyl})\text{benzylamidinate}]$, denoted as $\text{Rh}^{\text{III}}(\text{NN})$, and

- $\text{Rh}^{\text{III}}[\text{bis}(\textit{N}\text{-pentafluorophenyl})\text{pentafluorobenzylamidinate}]$, denoted as $\text{Rh}^{\text{III}}(\text{NN}^{\text{F}})$

that are predicted to catalytically activate and functionalize methane using TFAH or water as a solvent. The second case leads to a transition state barrier of $\Delta G^\ddagger = 27.6$ kcal/mol at 298 K for methane activation in TFAH (35.0 kcal/mol in water), the lowest we have found using Rh^{III} . The barrier for functionalization is $\Delta G^\ddagger = 36.8$ kcal/mol for TFAH and 29.7 kcal/mol in water. In particular, for Rh^{III} complexes, we find that increasing the electron-withdrawing nature of the ligands decreases barriers for both activation and functionalization. Thus, the only condition opposing even less donating ligands (i.e., lower barriers) is catalyst stability. Furthermore, we have found a correlation between methane activation barriers and $\text{Rh}\text{--}\text{CH}_3$ bond energy that allows us to predict the activation barriers of additional new complexes without searching for transition states.

This publication should be of great interest to experimentalists who can now focus on these two ligands in TFAH and water to validate and further optimize these systems.

■ MATERIALS AND METHODS

All quantum mechanical calculations were carried out using the Jaguar software version 7.6 developed by Schrödinger Inc.⁶ Geometry optimizations were carried out on initial guess structures, and vibrational frequencies were gathered to confirm the optimized geometries as intermediates or transition states and to construct a free energy profile. Solvation energies were calculated using the PBF Poisson–Boltzmann implicit continuum solvation model⁷ in Jaguar, with a dielectric constant of 8.55 and a probe radius of 2.451 Å for TFAH and 80.37 and 1.40 Å for water. Explicit waters were added into the calculations of aqueous $\text{Rh}(\text{NN}^{\text{F}})$ (two explicit waters per aqua ligand) for more accurate solvation modeling.

Geometry optimization and vibrational data were calculated using the B3LYP density functional⁸ with a smaller basis set, whereas single-point gas-phase and solvated energies were calculated using the M06 functional⁹ and a larger basis set. Here the “smaller basis set” consists of a modified double- ζ Los Alamos basis set and pseudopotential¹⁰ that includes *f* functions for rhodium,¹¹ and the 6-31G** basis set¹² for the other atoms; whereas the “larger basis set” consists of the triple- ζ Los Alamos basis set and pseudopotential (LACV3P**++) modified to include *f* functions and diffuse functions for rhodium, and the 6-311G**++ basis set¹³ for the other atoms. For orbital analysis, the Pipek–Mezey localization procedure was used.¹⁴

Rather than specify a particular chemical oxidant, we adopted a consistent electrostatic potential for electrons to determine the free energy changes of redox reactions. A value of 1.23 V vs SHE, the standard potential for the reduction of oxygen at pH = 0 and 25 °C ($\text{O}_2(\text{g}) + 4\text{H}^+(\text{aq}) + 4\text{e}^-(\text{aq}) \rightarrow 2\text{H}_2\text{O}(\text{l})$), was adopted for models in trifluoroacetic acid. For water, the pH was taken as 7 and the potential thus reduced to 0.817 V; these voltages correspond to electron free energies of –127.1 and –117.5 kcal/mol, respectively.¹⁵ The free energy of the proton was taken as –260.0 kcal/mol in TFAH and –279.8 kcal/mol in pH = 7 water.¹⁶ The free energy for each molecular species in solution was calculated using the formula

$$G = E_{\text{gas}} + \Delta G_{\text{solv}} + \text{ZPE} + H_{\text{vib}} + 6kT - T[S_{\text{vib}} + 0.54(S_{\text{trans}} + S_{\text{rot}} - 14.3\text{e.u.}) + 7.98\text{e.u.}]$$

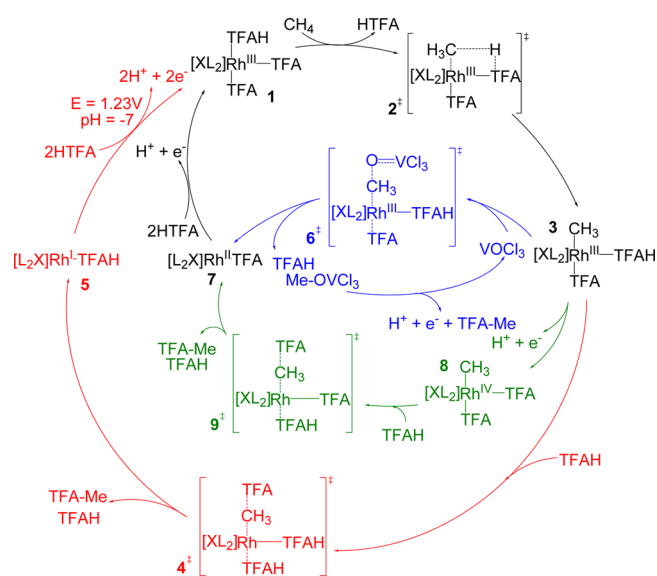


Figure 1. Hypothetical catalytic cycles for the activation and functionalization of methane. This shows several potential routes, including III–I (red), III–II (blue), and III–IV–II (green), which are further described in the text. [L₂X] may represent a three-coordinate L₂X ligand; a two-coordinate LX ligand and TFAH; or a two-coordinate L₂ ligand and TFA.

where the last term is an empirical approximation for the change in the translational and rotational entropy of the molecule between the gas phase and the solution phase (due to the finite librational frequencies) derived from Wertz.¹⁷ For gas phase molecules (methane; methanol at 498.15 K; and for the purposes of this publication, methyl trifluoroacetate), we assumed that equilibration between the dissolved gas and the headspace occurred at a much faster time scale than the reactions in question, leading to $\Delta G_{\text{gas} \rightarrow \text{sol}} = 0$. Thus, the free energy of such gas molecules can be simply calculated using the formula

$$G = G_{\text{gas}} = E_{\text{gas}} + \text{ZPE} + H_{\text{tot}} - TS_{\text{tot}}$$

We simulated methanol in the gas phase at 498.15 K and the solution phase at room temperature by adding the empirical hydration free energy of -3.2 kcal/mol¹⁸ to the gas phase free energy.

For pure liquids (e.g., trifluoroacetic acid and water), the Gibbs free energy was calculated using the formula

$$G_{\text{liquid}} = E_{\text{gas}} + \text{ZPE} + H_{\text{tot}} - TS_{\text{tot}} + \Delta G_{\text{gas} \rightarrow \text{liquid}}$$

where $\Delta G_{\text{gas} \rightarrow \text{liquid}} = G_{\text{liquid}} - G_{\text{gas}} (1 \text{ atm})$ is the free energy of condensation to liquid from 1 atm gas.¹⁵

The S_R2 attack involving OV^VCl₃ converts two singlets to two doublets, and hence, the transition states feature spin contamination ($S^2 > 0$) while representing an overall singlet. Structures that did not feature such spin contamination were considered to be transition states for an alternative S_N2 attack that forms MeOV^{III}Cl₃[−] and a Rh^I species, all of which were higher in energy.

RESULTS

The most common oxidation state of rhodium is III, but oxidation states from 0 to VI have been observed.¹⁹ Although previous work has focused on the C–H activation ability of Rh^I,^{4b} our current results center on a Rh^{III} resting state. This is due to the requirement that the desired process operate above the CH₄/CH₃OH redox couple (0.59 V vs SHE at pH = 0) and below the reduction potential of O₂ in the reaction conditions, which favor higher oxidation states.

Figure 1 shows hypothetical catalytic cycles for the activation and functionalization of methane. Starting from an inorganic Rh^{III} resting state (1), we investigated the C–H activation of methane following the displacement of a TFAH solvent molecule (2[‡]) to form a Rh^{III}–methyl organometallic species (3). Starting with 3, there are several pathways to functionalization:

1. III–I: S_N2 attack (4[‡]) by the conjugate base of the solvent to form methyl trifluoroacetate and a Rh^I species (5), which is reoxidized to the inorganic Rh^{III} resting state (1). In all cases investigated, we found that this S_N2 attack occurs on a five-coordinate Rh complex, with the neutral solvent trans to the methyl group dissociated in the transition state. This is consistent with previous work by Goldberg et al. implicating five-coordinate platinum intermediates;²⁰
2. III–II: S_R2 attack (6[‡]) by a metal–oxo species to form a metal–methoxy species and a Rh^{II} species (7) via methyl radical transfer. Both of these are then reoxidized by one electron to the metal–oxo species and methanol and to the inorganic Rh^{III} resting state (1), respectively. Here,

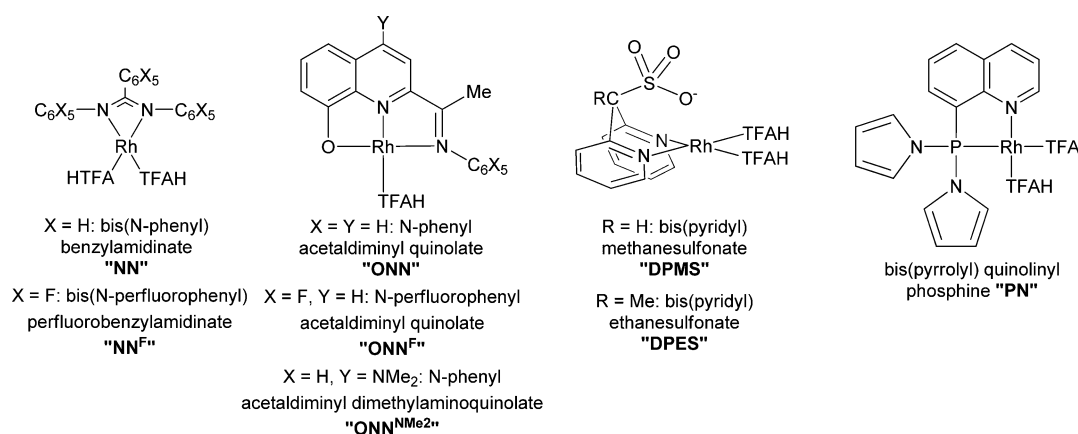


Figure 2. Rhodium complexes screened. For each complex, the Rh^I form in TFAH is shown here, but full catalytic cycles were computed. The best kinetics were predicted for the Rh(NN) and Rh(NN^F) complexes.

Table 1. Lowest Activation and Functionalization Energies for Each Series of Rh–Ligand Complexes in TFAH^a

TS type		Rh(NN)	Rh(NN ^F)	Rh(ONN)	Rh(ONN ^F)
activation	Rh ^{III} + CH ₄ ^{ax}	32.6/34.8	27.6/29.6	37.2/39.8	35.8/37.8
	Rh ^{III} + CH ₄ ^{eq}	38.3/40.4	33.7/36.3	37.9/40.7	38.1/40.1
functionalization	Rh ^{III–I} + TFA	54.8/60.3	42.7/48.2	44.2/49.3	41.7/45.8
	Rh ^{III–II} + VOCl ₃	43.2/44.2	38.1/40.0	40.4/42.5	39.1/40.8
	Rh ^{III–IV–II} + TFA	42.2/48.6	36.8/43.6	N/A	N/A
TS type		Rh(ONN ^{NMe₃})	Rh(DPMS)	Rh(DPES)	Rh(PN)
activation	Rh ^{III} + CH ₄ ^{ax}	38.7/41.2	38.0/40.2	41.0/44.0	40.1/43.0
	Rh ^{III} + CH ₄ ^{eq}	40.0/42.9	33.9/36.2	35.6/38.4	35.0/37.7
functionalization	Rh ^{III–I} + TFA	46.7/52.6	46.6/51.3	53.8/59.3	38.3/43.8
	Rh ^{III–II} + VOCl ₃	41.4/43.4	41.0/41.6	45.5/47.4	47.7/56.9
	Rh ^{III–IV–II} + TFA	N/A	49.3/56.3	49.9/57.1	N/A

^aCycles containing the key intermediates and transition states for the (NN^x) family of ligands are found in Figures 3 and 5. Detailed cycles for all ligands are found in SI Figures S1–S10. For each entry, the first number is at 298 K, and the second, at 498 K. Not all III–IV–II transition states were calculated. All free energies in kcal/mol.

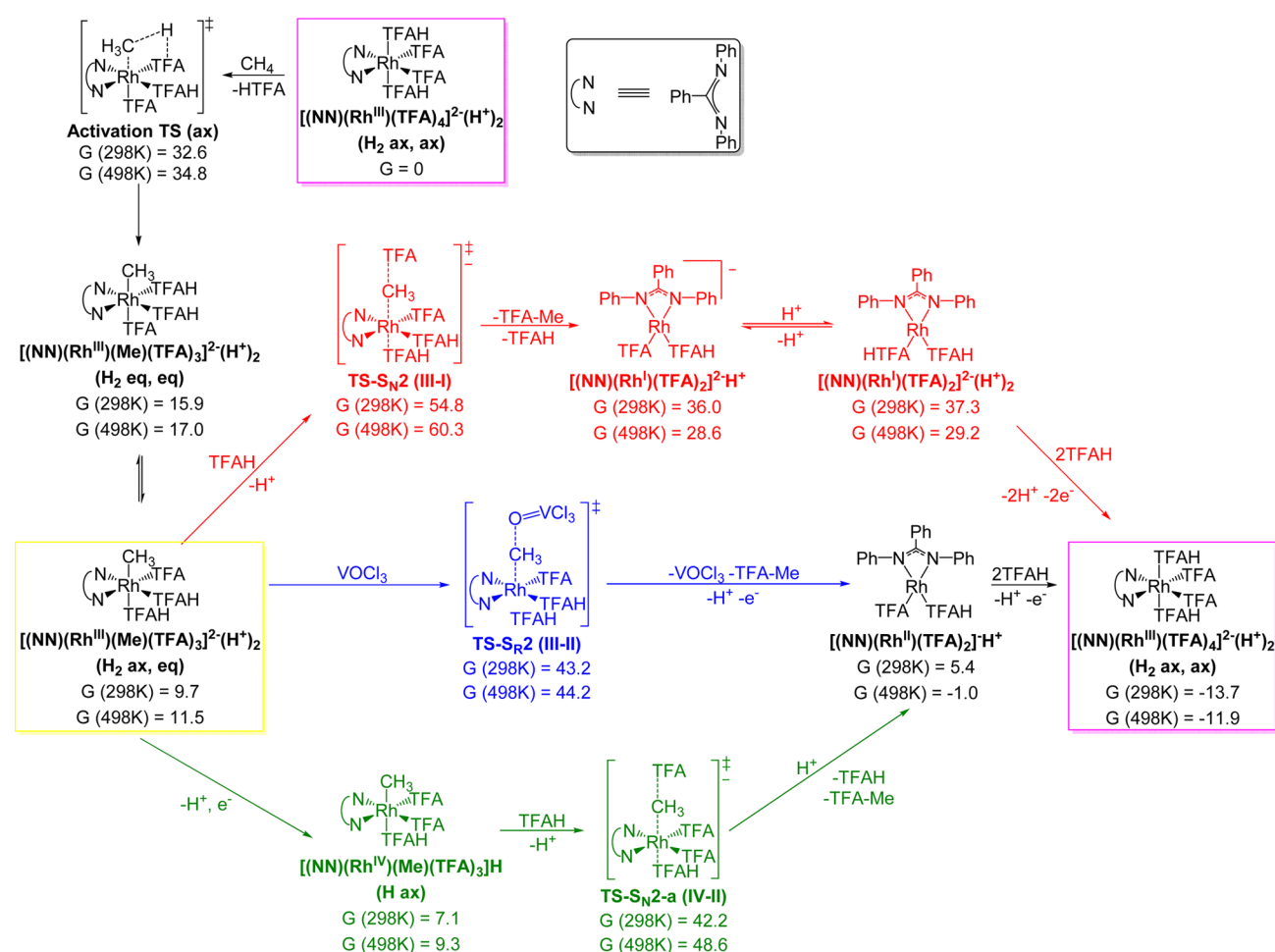


Figure 3. Activation of methane and its subsequent functionalization using Rh(NN) complexes in TFAH. Red denotes the III–I functionalization pathway; blue, the III–II pathway; and green, the III–IV–II pathway. Free energies (kcal/mol) are referenced to the resting state, $[(\text{NN})(\text{Rh}^{\text{III}})(\text{TFA})_4]^{2-}(\text{H}^{\text{ax}})_2$. The resting state is highlighted by a purple box, and the key methyl intermediate, $[(\text{NN})(\text{Rh}^{\text{III}})(\text{Me})(\text{TFA})_3]^{2-}(\text{H}^{\text{ax}})(\text{H}^{\text{eq}})$, is highlighted by a yellow box. A more detailed version of this figure, showing additional isomers and protonation states, is provided in SI Figure S1.

OVCl₃ was used as a model metal–oxo capable of one-electron reduction, even though it would likely hydrolyze in these solvents.²¹ We are developing stable metal–oxo reagents optimized for this reaction mechanism and use OVCl₃ here as a computationally simple model. The S_R2 transition state for Rh(NN) involves a five-coordinate Rh

complex, as well. For the Rh(NN^F) case, the transition states retain weak interactions with the neutral trans ligand, with an elongated Rh–O bond distance of 2.472 Å for TFAH and 2.228 Å for water. This is presumably due to the increased electrophilicity of the metal center in the Rh(NN^F) complexes.

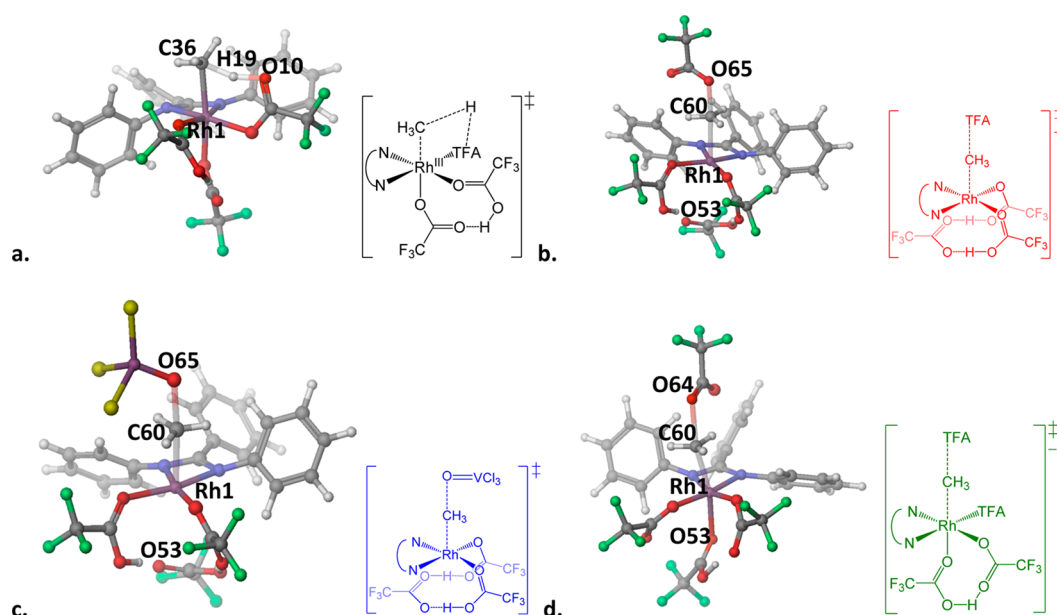


Figure 4. Rh(NN) transition state structures. (a) Methane activation: Rh1–C36 2.273 Å, C36–H19 1.365 Å, H19–O10 1.321 Å, Rh1–C36–H19 64.624°, C36–H19–O10 155.492°. (b) Rh^{III–I} S_{N2} attack: Rh1–C60 2.431 Å, C60–O65 1.936 Å, Rh1–C60–O65 176.680°, Rh1–O53 3.473 Å. (c) Rh^{III–II} S_{R2} attack: Rh1–C60 2.368 Å, C60–O65 1.995 Å, Rh1–C60–O65 175.541°, Rh1–O53 3.171 Å. (d) Rh^{III–IV–II} S_{N2} attack: Rh1–C60 2.138 Å, C60–O64 2.263 Å, Rh1–O53 2.377 Å, Rh1–C60–O64 168.802°, C60–Rh1–O53 164.984°.

3. III–IV–II: Oxidation to a Rh^{IV} species (8) followed by S_{N2} attack (9[‡]), generating a Rh^{II} species (7), which is then further oxidized back to the Rh^{III} resting state (1). In all cases investigated, we found that this S_{N2} attack occurs on a six-coordinate Rh complex, presumably due to the increased electrophilicity of the Rh^{IV} center. The six-coordinate Rh complexes have elongated Rh–O bond distances to the neutral trans ligand (2.377 Å for Rh(NN), 2.379 Å for Rh(NN^F), and 2.255 Å for Rh(NN^F) in water).

In all cases, the energy of oxidation (i.e., Rh^I and Rh^{II} to Rh^{III} species; Rh^{III} to Rh^{IV} species) was calculated assuming a potential of 1.23 V vs SHE, that is, with O₂ as the terminal oxidant. However, in practice, it may be necessary to use intermediate oxidants as well, although that is beyond the scope of this study.

A system that can proceed around any of these cycles with a global activation barrier below ~36 kcal/mol at 200 °C is of academic interest because transition state theory gives a turnover frequency (TOF) of roughly 1 h⁻¹ at 1 atm CH₄ for such a process. Achieving an industrially relevant TOF on the order of 1 s⁻¹ requires a global barrier of 29 kcal/mol, although greater pressures of CH₄ would increase this limit.²²

We screened complexes of rhodium with the following ligands, as depicted in Figure 2:

- The bis(*N*-phenyl)benzylamidinate (NN) ligand and its fluorinated analogue (NN^F).
- The (*N*-phenyl)acetaldiminyl quinolate (ONN) ligand and its related (ONN^F) and (ONN^{NMe₂}) ligands.
- The bis(pyridyl)methanesulfonate (DPMS) and bis(pyridyl) ethanesulfonate (DPES) ligands.
- The bis(pyrrrolyl)quinolinyl phosphine (PN) ligand.

For each of these ligands complexed with rhodium, we generated catalytic cycles in the template of Figure 1. For the (DPMS), (DPES), (PN), and (ONN^F) family of ligands, we found that both the methane activation energy and the methyl functionalization energy were too high for effective catalysis (Table 1); however,

we found lower numbers for the (NN^F) family of ligands, on which we have decided to focus our discussion.

The Rh(NN) Complexes in TFAH. Figure 3 shows the calculated free energies of key Rh(NN) complexes in trifluoroacetic acid solvent. Note that all free energies are referenced to the resting state, [(NN)(Rh^{III})(TFA)₄]²⁻(H_{ax}⁺)₂, which is highlighted by a purple box. Hence, although the resting complex is regenerated at the end of the catalytic cycle, the new free energy is –13.7 kcal/mol at 298 K because this is the energy change of the overall equation CH₄ + TFAH → TFA–Me + 2H⁺ + 2e⁻; thus, all energies at the second cycle would be –13.7 kcal/mol lower.

Oxidation of the inorganic Rh^I species to inorganic Rh^{III} species is highly favorable, from 40 to 50 kcal/mol downhill, depending on the temperature and the charge of the species. We conclude that the III–I S_{N2} attack pathway is not likely. Indeed, the activation barrier for this is a prohibitively high 54.8 kcal/mol at room temperature (Figure 4b).

All the remaining viable pathways involve methane activation by the inorganic Rh^{III}(NN) complex to form a Rh^{III}(NN)–Me species. We were initially gratified to see that thermodynamically the methyl species is not very endergonic. We were even more intrigued to find that the methane activation transition state barrier is only 32.6 kcal/mol at 298 K (Figure 4a), making it the most accessible barrier that we had found for Rh^{III} complexes in TFAH (Table 1).

In contrast, neither the III–II (Figure 4c) nor the III–IV–II (Figure 4d) functionalization pathways seemed as promising. Although further oxidation to a Rh^{IV}(NN)–Me species was roughly thermoneutral, the barrier to reductive functionalization was 42.2 kcal/mol. The oxidation from Rh^{III} to Rh^{IV} was effective in lowering the global S_{N2} barrier from 54.8 to 42.2 kcal/mol. To explain the high functionalization barrier for S_{N2} attack, we note that this may be due to the high energy or low chemical activity of trifluoroacetate ion in solution. Since TFA is necessary as the attacking nucleophile, a higher pH may be

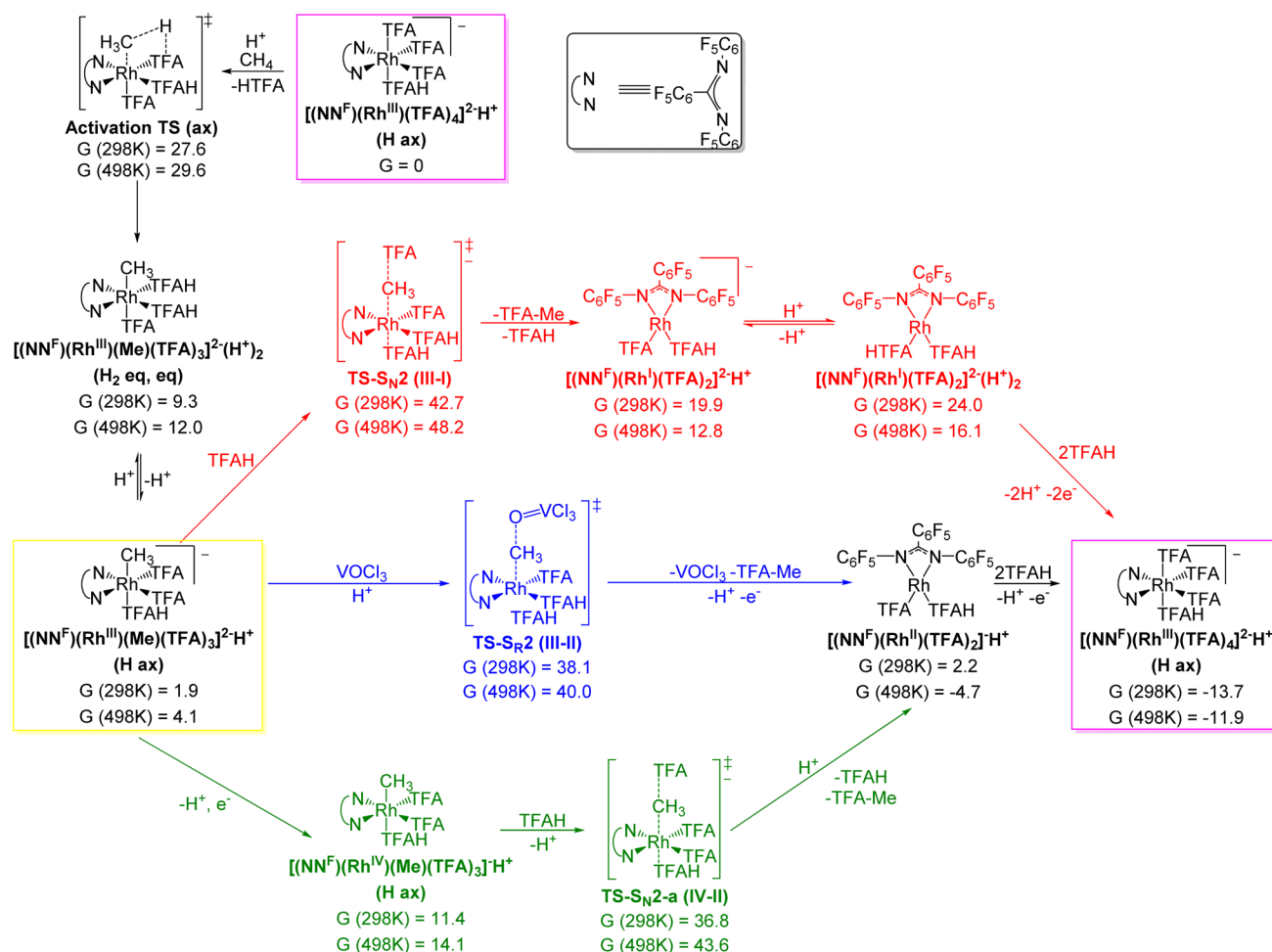


Figure 5. Activation of methane and its subsequent functionalization using Rh(NN^F) complexes in TFAH. Red denotes the III–I functionalization pathway; blue, the III–II pathway; and green, the III–IV–II pathway. Free energies (kcal/mol) are referenced to the resting state, $[(\text{NN}^{\text{F}})(\text{Rh}^{\text{III}})(\text{TFA})_4]^{2-}(\text{H}^+_{\text{ax}})$. The resting state is highlighted by a purple box, and the key methyl intermediate, $[(\text{NN}^{\text{F}})(\text{Rh}^{\text{III}})(\text{Me})(\text{TFA})_3]^{2-}(\text{H}^+_{\text{ax}})$, is highlighted by a yellow box. A more detailed version of this figure, showing additional species, is provided in SI Figure S2.

employed to lower this barrier before a deprotonated intermediate becomes the new resting state.

Because of the unusually low barrier for methane activation, we did not want to dismiss this ligand framework; rather, our efforts focused on how potential modifications on the (NN) ligand might lower the functionalization barrier. Reasoning that a more electronegative ligand may inductively increase the electrophilicity of the Rh–methyl and make nucleophilic attack more likely, we decided to investigate Rh complexes with the fluorinated analogue bis(*N*-pentafluorophenyl)pentafluorobenzylamidinate (NN^F) ligand.

The Rh(NN^F) Complexes in TFAH. Compared with the analogous Rh(NN) complexes, the fluorinated Rh(NN^F) complexes (Figure 5) show some marked differences in free energies. Many of these differences can be attributed to the much higher electron-withdrawing character of the (NN^F) ligand. For instance, the Rh^I(NN^F) species is 13.3 kcal/mol more stable to oxidation than the corresponding Rh^I(NN) species. In the same way, the S_N2 functionalization barrier on the III–I path is 12.1 kcal/mol lower. This is due to the highly electron-withdrawing (NN^F) ligand, which stabilizes lower oxidation states.²³ Unfortunately, this effect is not sufficiently large for us to consider the III–I pathway. Other thermodynamic effects of fluorine atom substitution include increased

acidity of all the complexes (i.e., stabilization of the anionic species by 4–8 kcal/mol), an increased stabilization of the Rh^{III}–Me species (by ~8 kcal/mol), and a decreased stabilization of the Rh^{IV}–Me species (by ~10 kcal/mol relative to Rh^{III}–Me.) Dimerization of the Rh^{III} resting state is not favored because of entropic reasons (SI Figure S2).

The barrier for methane activation, already relatively low for the Rh(NN) case, was even lower for the Rh(NN^F) case, at only 28.7 kcal/mol at 298 K (Figure 6a); however, the real test of the utility of the (NN^F) ligand is its effectiveness in aiding the functionalization step. It lowers the global III–I barrier from 54.8 to 42.7 kcal/mol and the isolated S_N2 barrier (from the Rh^{III}–CH₃ intermediate) from 45.1 to 40.8 kcal/mol (Figure 6b). It raises the neutral III–IV–II S_N2 barrier by raising the Rh^{IV} intermediate energy (SI Figure S2). Hence, we put our hopes into the (NN^F) ligand lowering the barrier for a net anionic III–IV–II S_N2 or a III–II S_R2 attack (Figure 6c,d), and indeed, it does: the new global S_N2 and S_R2 barriers of 36.8 and 38.1 kcal/mol, respectively, approach the target values.

The Rh(NN^F) Complexes in Water. Another method that may lower transition state barriers is switching the solvent (and therefore the nucleophile) to water. This has the practical advantage that any commercialized process will have greater simplicity if carried out in water as opposed to a strong acid;

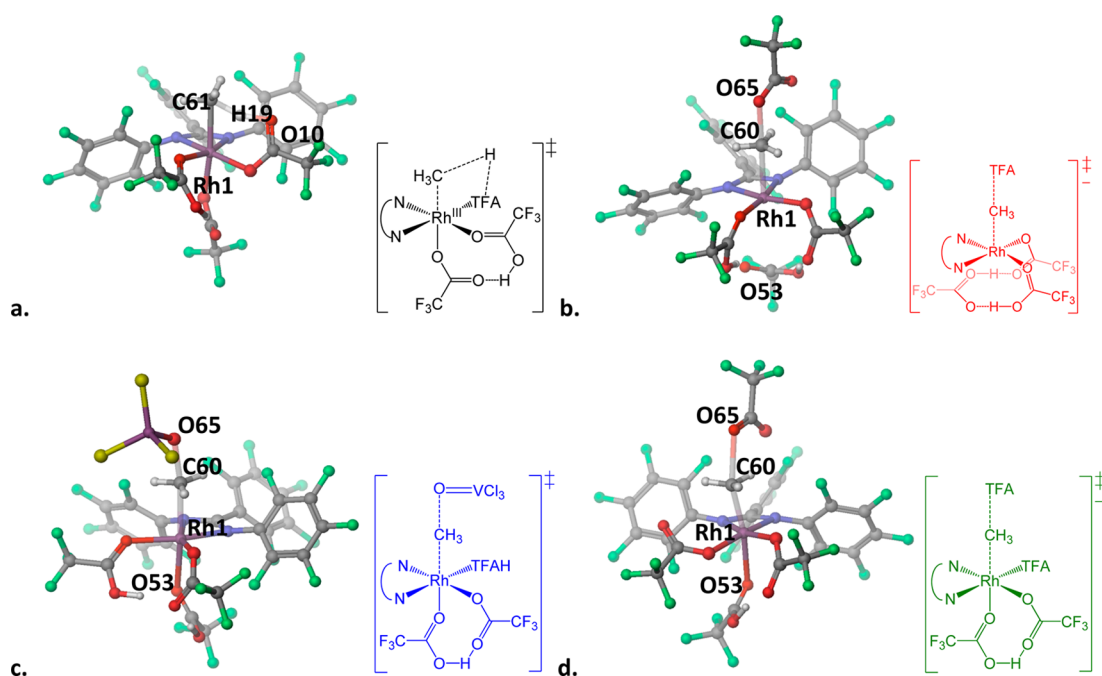


Figure 6. Rh(NN^F) transition state structures. (a) Methane activation: Rh1–C61 2.267 Å, C61–H19 1.365 Å, H19–O10 1.321 Å, Rh1–C61–H19 63.875°, C61–H19–O10 157.549°. (b) Rh^{III–I} S_N2 attack: Rh1–C60 2.368 Å, C60–O65 2.021 Å, Rh1–C60–O65 176.330°, Rh1–O53 3.265 Å. (c) Rh^{III–II} S_R2 attack: Rh1–C60 2.399 Å, C60–O65 1.935 Å, Rh1–O53 2.472 Å, Rh1–C60–O65 172.164°, C60–Rh1–O53 168.496°. (d) Rh^{III–V–II} S_N2 attack: Rh1–C60 2.259 Å, C60–O64 2.156 Å, Rh1–O53 2.379 Å, Rh1–C60–O64 159.539°, C60–Rh1–O53 169.220°.

however, it may also provide additional challenges in the prevention of overoxidation due to reaction with methanol product (*vide infra*). We investigated the same Rh(NN^F) complexes in water to see if the energetics may be advantageous.

The thermodynamic profile for key Rh(NN^F) complexes in water is given in Figure 7 and in greater detail in SI Figure S11. The Rh^{III}(NN^F)–methyl, Rh^{IV}(NN^F)–methyl, and Rh^{II}(NN^F) species are all stabilized relative to the inorganic Rh^{III}(NN^F) reference state. Hence, whereas for the TFAH solvent case, a thermodynamic barrier must be climbed in each catalytic step, in water, each step is either thermodynamically downhill or approximately neutral.

In Figure 7, all energies are referenced to the lowest inorganic Rh^{III} state, [(NN^F)(Rh^{III})(OH)₄]^{2–}(H_{ax}⁺)(H_{eq}⁺), which is highlighted by a purple box. This is to keep consistent with the practices in Figures 3 and 5, where the lowest inorganic Rh^{III} state is also the resting state. However, in this case, the organometallic Rh^{III}(NN^F)–methyl complexes are stabilized to such an extent that [(NN^F)(Rh^{III})(Me_{eq})(OH)₃]^{2–}(H_{ax}⁺)₂, which is highlighted by a yellow box and is analogous to the key methyl intermediate referenced in Figures 3 and 5, is slightly lower in energy by 2.0 kcal/mol at 298 K. However, because the rate-determining step is methane activation, the lowest inorganic Rh^{III} state [(NN^F)(Rh^{III})(OH)₄]^{2–}(H_{ax}⁺)(H_{eq}⁺) (in a purple box) is still the resting state. The practical consequence is that the barrier to CH₄ activation is properly referenced to the resting Rh^{III} state, whereas the barrier to methyl group functionalization ought to be referenced to the lowest Rh^{III}–CH₃ state.

An in-depth analysis of the barriers for activation and functionalization of Rh(NN^F) complexes in water is given in the Supporting Information. The activation and functionalization processes themselves are given in SI Figures S12 and S14–16, respectively, and the transition state structures, in SI Figure S13. We conclude from these figures that for the Rh(NN^F) catalytic

system in water, both III–IV–II S_N2 and III–II S_R2 are viable pathways for functionalization, whereas the III–I S_N2 pathway is still too high in energy. This is similar to the case in TFAH, except that the relative ease of activation vis-à-vis functionalization has now been reversed. However, the question of whether the Rh(NN^F) system is more advantageous in water or TFAH will depend on their product protection ability, which will be discussed in the following section.

Product Protection and CH Activation. As mentioned in the Introduction, a major hurdle that any putative methane to methanol catalytic scheme must overcome arises because the C–H bond dissociation energy of methanol is 9 kcal/mol weaker than that of methane. Preventing the overoxidation of the product is thus a challenge and is the reason we elected to investigate electrophilic metal centers in acidic solvent. Because the transition state of an electrophilic activation involves donation of electron density from the methane C–H σ bond to the metal, a highly electron-withdrawing trifluoroacetate substituent that decreases this σ bond electron density is expected to increase the transition state energy. Thus, the highly electronegative trifluoroacetate group of methyl trifluoroacetate withdraws electron density from the methyl C–H bonds, thereby decreasing their ability to donate into the Rh center and raising activation barriers.^{24,25} Indeed, we see this effect in explicit calculations with both the (NN) and (NN^F) ligand sets. SI Figures S17 and S18 show the various isomeric transition states for the activation of both methane and methyl trifluoroacetate, for Rh(NN) and Rh(NN^F) complexes, respectively. At 298 K, each transition state for the activation of methane was 3–10 kcal/mol lower than the corresponding transition state for the activation of methyl trifluoroacetate (1 atm reference for both).

The first two rows of Figure 8 shows only the lowest energy isomer of each activation, and thus, an overall $\Delta\Delta G^\ddagger$ (lowest CH₃TFA transition state minus lowest CH₄ transition state) of

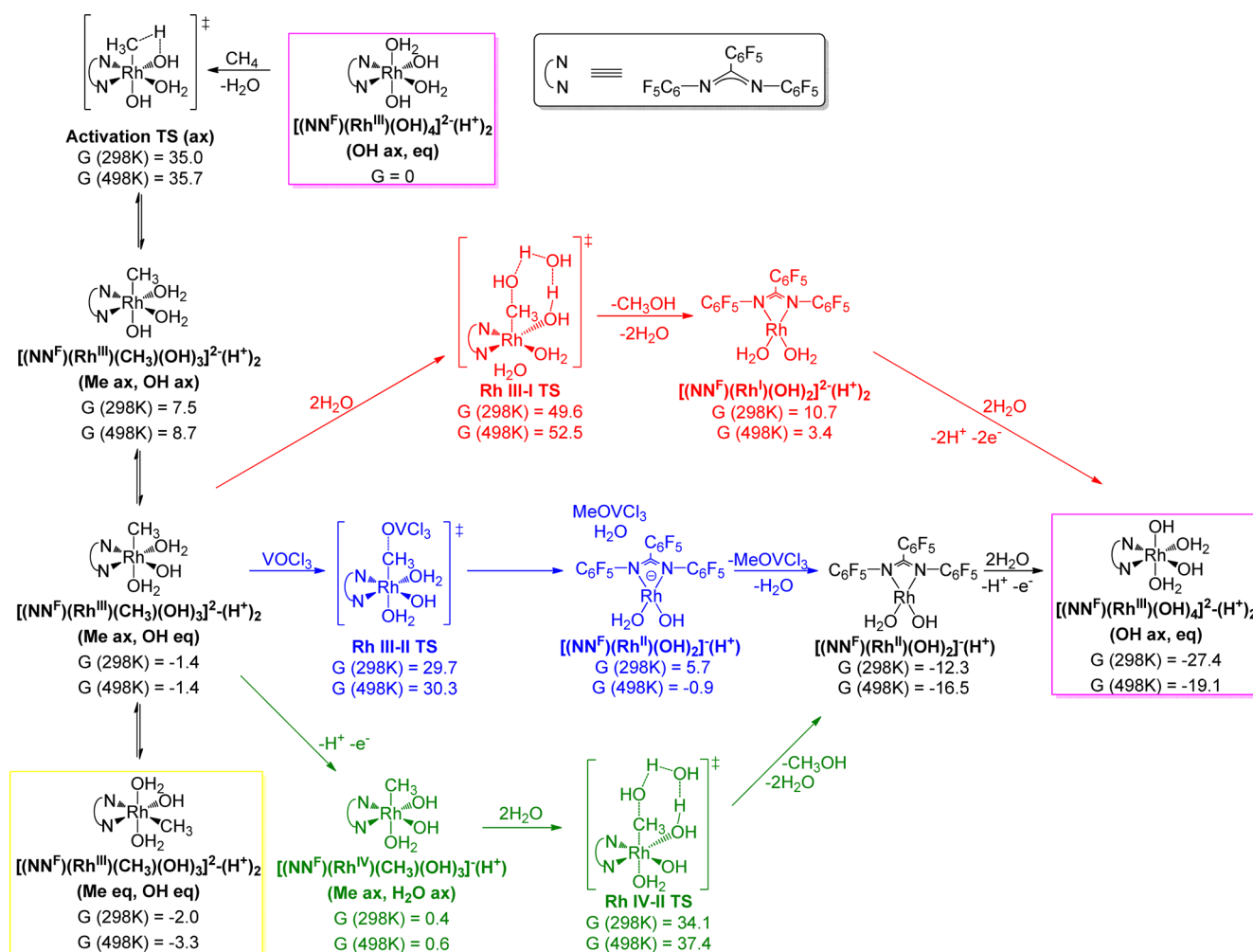


Figure 7. Thermodynamic profile for the activation and functionalization of methane using Rh(NN^F) complexes in water. This figure shows only the key species; a more detailed version is given in SI Figure S11. Red denotes the III–I functionalization pathway; blue, the III–II; and green, the III–IV–II pathway. All free energies (kcal/mol) at pH = 7 and referenced to the resting Rh^{III} state, $[(\text{NN}^{\text{F}})(\text{Rh}^{\text{III}})(\text{OH})_4]^{2-}(\text{H}^+)_2$, highlighted by a purple box, whereas the key methyl intermediate, $[(\text{NN}^{\text{F}})(\text{Rh}^{\text{III}})(\text{Me}_{\text{eq}})(\text{OH})_3]^{2-}(\text{H}^+)_2$, is highlighted by a yellow box.

2.7 kcal/mol is found for (NN) and 5.5 kcal/mol for (NN^F). In contrast, activation of methanol (1 M reference state) was even lower than that of methane: by 0.3 or 1.8 kcal/mol at 298 K when comparing the lowest CH₃OH transition state and the lowest CH₄ transition state in TFAH (Figure 8, first and second rows); for (NN^F) in water, this gap is larger at 2–3 kcal/mol (Figure 8, third row). We can explain this by noting that the hydroxyl group in methanol has electron-donating properties, and hence, the donation effect of the C–H σ orbital into the electrophilic metal center is increased, leading to a decreased transition state barrier; however, these numbers are lower than the 9 kcal/mol simple BDE difference between the C–H bonds in methane and methanol and comparable to work done by Owen et al.²⁶

Because the ease of activation decreases as CH₃OH > CH₄ > CH₃TFA, it is important to consider the relative chemical potential of CH₃OH and CH₃TFA in solution. As we have found that the equilibrium CH₃TFA(g) + H₂O(soln) \rightleftharpoons CH₃OH(g) + TFAH(l) is exergonic by 1.3 kcal/mol at 298 K, it is predicted that this catalyst would be selective for methane oxidation only in the absence of water.

In comparison with previous work, we note that Ahlquist et al.²⁷ showed that the reason why the Catalytica-Periana bipyrimidine Pt catalyst²⁸ was able to achieve high selectivity

is that the barrier to activate the CH₃–OSO₃H product is 14 kcal/mol higher than for CH₄ or CH₃OH, and the acidity of the medium drives the protection of methyl products via esterification. Although the Catalytica-Periana system distinguishes between methane and the methyl ester more than the rhodium complexes, we note that a key advantage to our system is the volatility of CH₃OH and CH₃TFA (boiling points at 64.7 and 43 °C, respectively) relative to the nonvolatile CH₃OSO₃H. Thus, increasing selectivity beyond what is provided by the electrophilicity of the metal and esterification is still an important area of research. The addition of nonpolar ligand side chains may decrease the propensity of methanol coordination to the metal relative to methane coordination.

DISCUSSION

Because our ligands have poor electron-donating ability and Rh^{III}-centered cycles, we expect the metal center to be electrophilic with reactions proceeding along an electrophilic route.^{5h} We can rule out oxidative addition due to the high oxidation state of our metal and the nature of our ligands; hence, we expected that the most likely C–H activation pathway is through a base-mediated electrophilic mechanism (Figure 9).

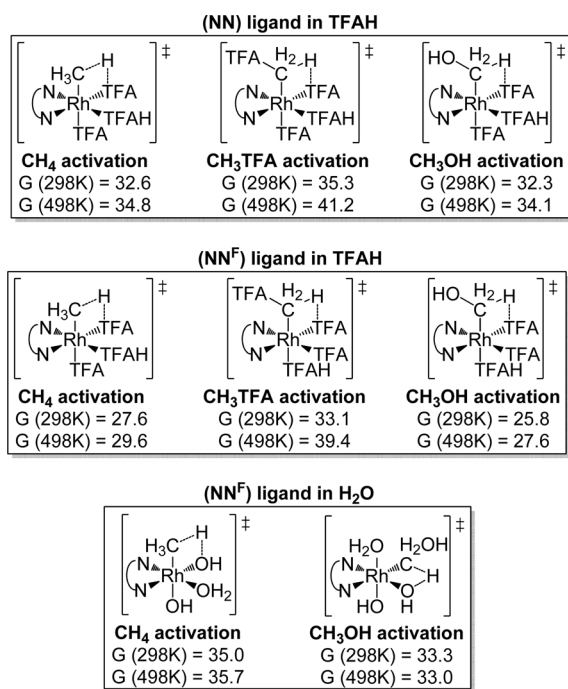


Figure 8. In each row, the leftmost structure is the lowest-energy activation transition state for methane (1 atm), the center structure is the lowest-energy transition state for the activation of MeTFA (1 atm, not applicable for the H₂O case), and the rightmost structure is the lowest-energy transition state for the activation of MeOH (1 atm). All numbers are in kcal/mol and relative to the lowest energy inorganic state (i.e., right before methane activation). Other isomeric transition states for CH₄, MeTFA, and MeOH activation are shown in SI Figures S17, S18, and S19.

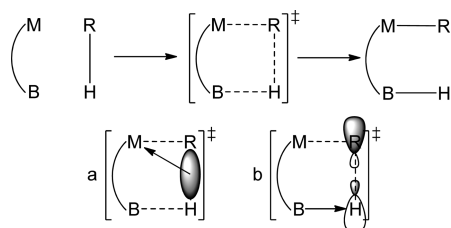


Figure 9. A schematic diagram showing the metal activation of an R–H bond, for example, methane. Activation occurs via ligand donation to the electrophilic metal center (a) and basic abstraction of the hydrogen (b).

Similar internal electrophilic substitution processes have been reported.²⁹

Because we propose an electrophilic pathway for the methane activation step [4h], we expect there to be a relationship between the activation transition state energy and some aspect of the metal's electropositivity. To estimate the electropositivity, we initially used the calculated energy of the rhodium 4s core orbital in the Rh^{III} resting state, which we compared with the corresponding methane activation energies (Figure 10a). We found that there is approximately a positive correlation between increasing electropositivity (as measured by negative numbers closer to zero) and increase overall transition state barriers. We explain this by noting that decreasing the metal's electropositivity increases its electrophilicity and thus encourages sigma donation of the Me–H bond.

In the hopes that a more directional aspect of a given rhodium–ligand's electron density might give us a better

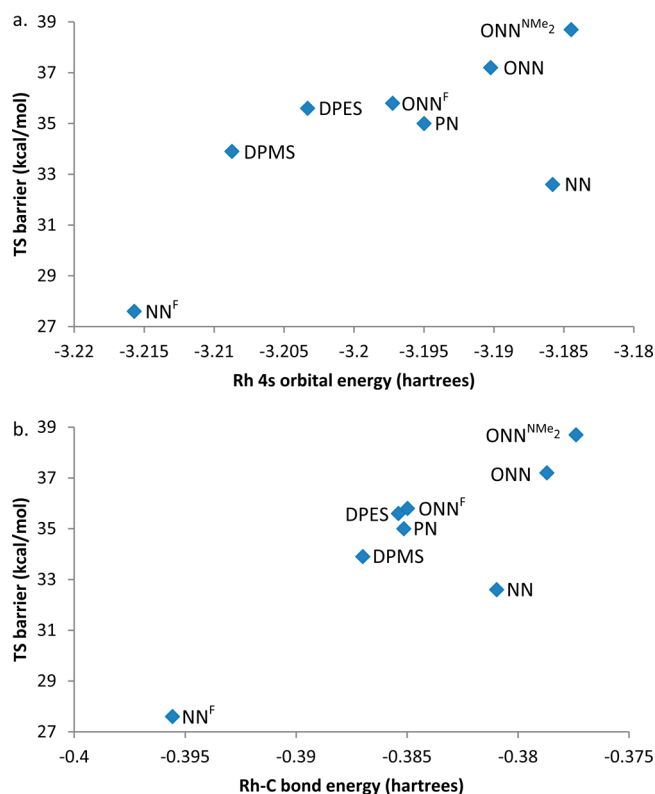


Figure 10. Graphs of rhodium orbital energies with TS barriers for the various Rh^{III}–ligand complexes. In all cases, the lowest transition state was used; this involves an axial Rh–Me being formed in the cases of the (NN^{*}) and (ONN^{*}) ligand families and an equatorial Rh–Me being formed in the (DPMS), (DPES), and (PN) cases. (a) A graph of the methane activation energy of the various rhodium complexes versus the 4s orbital energy of the rhodium in their resting states. This calculated value is a proxy for the relative overall electropositivity of the specific rhodium–ligand complexes. (b) A graph of the methane activation energy of the various rhodium complexes versus the Rh–Me bond energy as localized by the Pipek–Mezey method¹⁴ of the lowest-energy Rh–Me complex. This calculated value is a proxy for the relative directional electropositivity of the specific rhodium–ligand complexes toward the methyl bond being formed. These graphs were based on data from SI Table S2; details may be found in the Supporting Information.

correlation with the transition state barrier, we then plotted the methane activation energies with the energies of the Rh–C bond in the resultant Rh–methyl intermediate (Figure 10b). These Rh–C bond energies were obtained by performing a Pipek–Mezey orbital localization procedure on the Rh–methyl complex's electronic wave function.¹⁴ We found that the correlation is much better, with increasingly negative Rh–C bond energies being correlated with decreasing transition state barriers. This may be due to the increasing favorability of forming the Rh–methyl bond. We give the caveat that again, the only outlier is the Rh(NN) ligand complex, but we note that our trend represents only an overestimation and, therefore, does not include false positives. In addition, there is a definite positive correlation within a ligand family (i.e., Rh(NN) versus Rh(NN^F); Rh(ONN^F) versus Rh(ONN) versus Rh(ONN^{NMe₂})). We conclude from this relationship that (a) given a Rh–ligand complex that already shows some promise, we can further fine-tune its properties with additional modifications on the ligand to further lower the transition state barriers of interest, and (b) given a new Rh–ligand complex, by calculating the Rh–methyl

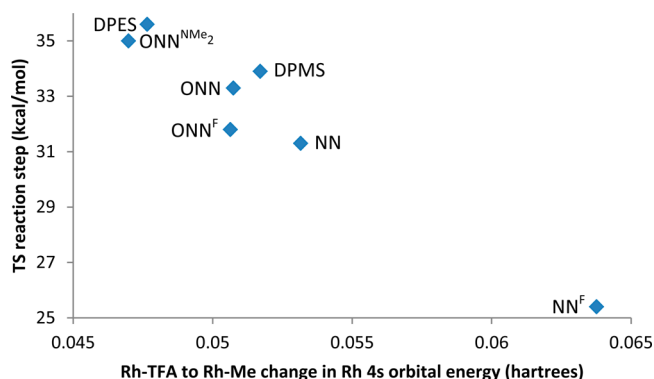


Figure 11. A graph of the Rh–TFA to Rh–Me change in the 4s orbital energy, a measure of the Rh atom’s softness, versus the adjusted TS barrier (see text). Note that the ONN^F data point is an estimated value, which may explain its deviation from the monotonicity. In all cases, the lowest transition state was used. This involves an axial Rh–Me being formed in the cases of the (NN^x) and (ONN^x) ligand families, and an equatorial Rh–Me being formed in the (DPMS), (DPES), and (PN) cases. This graph is based on data from SI Table S2; details may be found in the Supporting Information.

intermediates and extracting the Rh–C bond energy, we can get an estimate of the expected methane activation transition state barrier for that ligand set and thus gauge its worthiness for further investigation.

We also wished to see if there was a correlation between the transition state barrier and the rhodium center’s hardness as modified by its ligand. Because the hardness of an atom or molecule is defined as the polarizability of its electron cloud,³⁰ we measured the difference in the Rh 4s orbital energy going from the inorganic resting state to the Rh–methyl as a proxy for hardness. Although we did not find a correlation with the overall transition state barrier of activation, we did find a negative correlation with the “adjusted” TS barrier, that is, the free energy change of the actual transition state itself (Figure 11). In other words, the activation transition state [Rh⋯CH₄][‡] is derived from the replacement of a TFAH ligand with CH₄, but the immediate Rh–TFAH precursor is not the resting state, but differs slightly in its axial/equatorial arrangement of TFAH/TFA ligands and is a few kilocalories per mole higher in energy. Taking this out gives us our correlation. Hence, we see that increased polarizability or softness, as measured by the amount of energy increase in the Rh–ligand system when a TFA ligand is exchanged for a methyl, correlates with a lower activation barrier.

The result of our fine-tuning has yielded the (NN^F) ligand set with a methane activation energy of 27.6 kcal/mol at 298 K, which compares favorably with other homogeneous systems. Indeed, an effective activation barrier of 33.5 kcal/mol is derived from the turnover frequency of the Catalytica–Periana catalyst (bpym)PtCl₂ in H₂SO₄.³¹ Specifically, C–H activation by (*η*³-6-phenyl-2,2′-bipyridine)Ir^{III}(TFA)(C₂H₄)(C₂H₅) is shown to catalyze H/D exchange between CH₄ and TFAD with a turnover frequency of 2.12 × 10⁻² s⁻¹ at 180 °C (SI Figure S25). From the turnover frequency, an apparent free energy barrier of 33.5 kcal/mol can be calculated using transition state theory.³²

In the course of these studies, we found that it was more difficult to find effective routes of Rh–methyl functionalization than to find low methane activation barriers. We found that the III–II pathway (S_{R2} attack with OVCl₃) typically gives the lowest barriers, whereas the III–IV–II pathway (S_{N2} attack on Rh^{IV}) is typically more favorable thermodynamically.

We found that Rh(NN^F) complexes in water led to a flatter thermodynamic profile than in TFAH, increased transition state energies for methane activation, and decreased transition state energies for functionalization. We can understand these changes in the thermodynamics by noting that hydroxo ligands’ lone pairs stabilize higher oxidation states of rhodium. Overall, these changes are favorable for activity because the functionalization energy is lowered to 31.7 kcal/mol while the methane activation energy of 35.0 kcal/mol remains acceptable. Unfortunately, aqueous solution is predicted to offer no product protection, a result consistent with the reactivity of platinum diimine catalysts.²⁸

We can understand the decreased barrier for S_{N2} methane functionalization (III–I, III–IV–II) in terms of several factors: the increased stability of the Rh^{IV} starting material in water, the greater thermodynamic activity of water in aqueous solution (at 55 M) as opposed to the TFA anion in TFAH, and the fact that the transition state involves a concerted reaction featuring simultaneous formation of a C–O bond, deprotonation to form neutral methanol, and protonation of a hydroxo ligand on the Rh complex. However, we remain unclear about the reason behind the decreased S_{R2} functionalization barrier for III–II.

The most important hurdle that must be cleared experimentally for us to have a viable catalytic system is catalyst stability. The trend we have observed, that Rh^{III} complexes with less-electron-donating ligands, tend to have lower activation and functionalization barriers, must be balanced with the consideration that a ligand that is too electron-poor may not have sufficient binding strength for a stable complex with rhodium to be made. The next logical step of our investigation is the experimental synthesis and stability study of the Rh^{III}(NN^F) complexes. However, even if we fail to see good robustness for this particular complex, our more valuable contribution is that we have undertaken the most detailed ab initio study of the requirements of a Rh methane activation catalyst to date.

CONCLUSIONS

In our QM virtual screening of potential methane to methanol catalysts, we identified the Rh(NN^F) complex as a highly promising candidate. Features of the Rh(NN^F) complex include

- Transition state barriers at 298 K for methane activation of 27.6 (TFAH) and 35.0 kcal/mol (water) and
- Transition state barriers for functionalization at 298 K of 36.8 (TFAH) or 31.7 kcal/mol (water),

which are better than any other Rh^{III} complex we have investigated.

Moreover, we provide a rational accounting for the role that ligand design plays in the effectiveness of this promising catalyst. In particular, for Rh^{III} complexes, increased electron-withdrawing ligands leads to lower barriers for both activation and functionalization. We can estimate the overall transition state barrier by simply calculating the Rh–methyl species and extracting the Rh–C bond energies. Thus, the only condition opposing even less-donating ligands (i.e., lower barriers) is catalyst stability. These results from QM virtual screening are now ready for experimental testing, validation, and improvement.

ASSOCIATED CONTENT

Supporting Information

Computational details, catalytic cycles, further experimental results, additional references, Cartesian coordinates, and tables of thermodynamic values. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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Notes

The authors declare no competing financial interest.

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