Appendix A

C–H activation using Rh¹ complexes supported by bis-nitrogen chelating ligands

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A.1 Abstract

Rhodium (I) complexes $(DAB^F)Rh(COE)(TFA)$ **1** and (BOZO)Rh(COE)(TFA) **2** $((DAB^F) = N, N$ bis(pentafluorophenyl)-2,3-dimethyl-1,4-diaza-1,3-butadiene, (COE) = cyclooctene, (TFA) = trifluoroacetate, <math>(BOZO) = bis(2-oxazolin-2-yl) have been synthesized. Complexes **1** and **2** are catalyst precursors for the efficient C–H bond activation of arenes with TFA–D. DFT calculations determined that H/D exchange is possible through reversible oxidative addition of benzene onto the Rh^I complex. Catalyst **1** is reported to have a TOF of 227.5 h⁻¹ and is the most active H/D exchange catalyst reported to date.

A.2 Introduction

In the search for a rhodium analogue to the Shilov cycle catalyst, putative rhodium complexes are often first experimentally tested for their C–H activation ability by investigating their ability to catalyze the exchange of hydrogen and deuterium atoms on various aliphatic and aromatic substrates. towards this end, Kloek, Heinekey, and Goldberg have reported an example of a rhodium complex containing a (PNP) pincer ligand that catalyzes the H/D exchange of benzene with D₂O with a turnover frequency (TOF) of 0.1 h⁻¹ [1]. Goldberg and Jones et al. have also reported H/D exchange with deuterated trifluoroacetic acid (TFA–D) and benzene with a pendant acetate rhodium complex, which had a TOF of 1.6 h⁻¹ [2]. Despite the success of these rhodium catalysts for the C–H activation of arenes, the rates of reaction as determined by turnover frequency have been significantly slower, e.g., by an order of magnitude, than comparable results for Pd and Pt based catalysts [3]. Bidentate nitrogen chelating ligands have been used successfully for H/D exchange with these Pd and Pt systems. In this chapter we report the reactivity and computational study of two new rhodium complexes with bidentate nitrogen chelating ligands which have rates of arene H/D exchange comparable to platinum/palladium systems.

A.3 Materials and methods

Experimentally, complexes $(DAB^{F})Rh(COE)(TFA)$ **1** and (BOZO)Rh(COE)(TFA) **2** $((DAB^{F}) = N, N$ -bis(pentafluorophenyl)-2,3-dimethyl-1,4-diaza-1,3-butadiene, (COE) = cyclooctene, (TFA) = trifluoroacetate, (BOZO) = bis(2-oxazolin-2-yl)) (Scheme A.1) were synthesized by reaction of $[(COE)_{2}Rh(TFA)]_{2}$ dimer with 1 equivalent of ligand in THF at room temperature for 1 hour to afford **1** and **2** as purple solids in 58% and 73% yield, respectively. Both of these complexes were characterized by ¹H, ¹³C, and ¹⁹F NMR spectroscopy, and elemental analysis.

Computational investigations were made as described in Section 3.3.

A.4 Results and discussion

A.4.1 Experimental results

We screened these rhodium complexes for C–H activation by monitoring H/D exchange between d_1 -trifluoroacetic acid and benzene. Under our conditions (1.6 mol % Rh, 1 equiv. C₆H₆ in 17.5 equiv. of d_1 -trifluoroacetic acid, 2 hours, 800 psi Ar, at 130°C), both complexes **1** and **2** showed rapid H/D exchange with turnover numbers of 89 ± 13 and 90 ± 11 , respectively, resulting in turnover frequencies (TOFs) of 0.01 s⁻¹ over the 2 hour period for both catalysts, as determined by GC-MS. Minimal turnovers were detected for the reaction of just [(COE)₂Rh(TFA)]₂ in trifluoroacetic acid



Scheme A.1. Synthesis of rhodium H/D exchange catalysts $(DAB^F)Rh(COE)(TFA)$ 1 and (BOZO)Rh(COE)(TFA) 2.

under our conditions.

Measuring the effect of temperature on catalysis (Figure A.1) shows that highest turnovers at 2 hours occur at 150°C. TON decreases at temperatures above 150°C, most likely due to catalyst decomposition. Complex **2** has the highest TON when the temperature is 130°C, with a decrease in turnovers at higher temperatures.

Figure A.1. Temperature dependence vs. turnover numbers for complexes 1 and 2. Reactions were performed using 1.6 mol % Rh, 1 equiv. C_6H_6 in 17.5 equiv. d_1 -trifluoroacetic acid, for 2 hours, under 800 psi Ar.



To determine the optimal solvent for catalysis, H/D exchange of benzene was then examined with other deuterated solvents at the optimized temperature. However, no significant measurable H/D exchange of benzene above the background reactions was observed for D_2O , CD_3OD , D_3PO_4 , D_2SO_4 , or CD_3COOD for either 1 or 2.

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We then sought to determine the dependence on catalyst concentration. By lowering the catalyst loading to 0.4% relative to benzene, a large increase in TON was observed (Figure A.2). After 2 hours at 150°C, complex 1 showed 456 TON to give a TOF of 228 h^{-1} .





The selectivity of the reaction mechanism was determined by examining the H/D exchange of toluene in trifluoroacetic acid at each catalyst's respective optimal temperature. The *ortho:meta:para* selectivity is 6.87 : 1 : 6.39 and 5.68 : 1 : 5.24 for **1** and **2**, respectively. No clear deuteration of the methyl fragment of toluene was seen.

A crucial aspect of catalysis is the recyclability of the catalyst. To study this, each complex was run and sampled, and then the contents of the reaction were evaporated off, leaving behind the catalyst. Fresh trifluoroacetic acid and benzene were added to the reaction vessel and the experiment was run again. For complex 1, this was successfully done over four times for a period of over 72 hours, with H/D exchange observed each time.

An interesting question is the role of cyclooctene in the mechanism. The addition of cyclooctene to the experiment showed a clear decrease in turnover number for complex **2**. We hypothesized that this is due to COE binding to the rhodium metal competitively to slow down catalysis. However, upon careful consideration of the ¹H and ¹³C NMR spectra, clear peaks for the trifluoroacetate adduct of cyclooctene can be seen. Indeed, a report from Nordlander indicates that cyclooctene in trifluoroacetic acid funnels to a cyclooctyl trifluoroacetate complex [4]. Attempts to synthesize either complex with a trifluoroacetic acid ligand instead of cyclooctene were unsuccessful.

Attempts to extend this reactivity to substrates other than aromatics were investigated. H/D exchange was attempted with methane under a variety of pressures and temperatures; however, no

deuterated methane species was observed by GC-MS. In addition, H/D exchange of benzene sp^2 C-H bonds with cyclohexane was also attempted, but no deuteration was observed after 2 hours at the optimal conditions for each catalyst.

A.4.2 Computational results

We have also undertaken a computational investigation for the mechanism of H/D exchange by complexes 1 and 2. We set our reference complex to (L)Rh(TFA)(TFAH) (3 and 4 for $L = (DAB^F)$ or (BOZO), respectively); these being the presumed species after the (COE) ligand is hydrotrifluoroacetylated off from the base (L)Rh(TFA)(COE) species. We hypothesized that C-H activation of benzene could proceed through one of two routes. The first route is by direct oxidative addition to (L)Rh^I(TFA)(TFAH) to form (L)Rh^{III}(TFA)(TFAH)(Ph)(H). H/D exchange could then occur because the Rh^{III}(H) bond can be reversibly reductively deprotonated: Rh^{III}(TFA)(H) \rightleftharpoons Rh^I(TFAH). The second is by an internal protonation (L)Rh^I(TFA)(TFAH) \longrightarrow (L)Rh^{III}(TFA)₂(H), followed by either benzene coordination and deprotonation by TFA *via* a six-membered ring transition state, or direct hydrogen exchange with the Rh^{III}(H) hydride. We found that, in both the (DAB^F) and (BOZO) ligands, the first scenario (direct oxidative addition) was more likely, with lower transition states.

Direct oxidative addition of benzene by **3** or **4** is shown in Scheme A.2. The lowest barrier found for **3** is 22.2 kcal/mol at 298 K and 23.7 kcal/mol at 498 K. In contrast, the lowest barrier found for **4** is 18.5 kcal/mol at 298 K and 19.5 kcal/mol at 498 K. All of these values imply accessible benzene oxidative addition at the reaction temperatures investigated. The increased activity of **3** compared to **4** is most likely simply due to the increased temperature that H/D exchange with catalyst **1** can be run without decomposition. A comparison of direct oxidative addition and benzene coordination/deprotonation is shown in Scheme A.3 for complex **3** and Scheme A.4 for complex **4**.



Scheme A.2. Oxidative addition of benzene by $Rh(DAB^F)$ and Rh(BOZO) complexes 3 and 4. H/D exchange most likely proceeds through these transition states. All free energies in kcal/mol.

Methane activation by complex 3, in a manner analogous to benzene activation, was also in-



Scheme A.3. The $Rh(DAB^F)$ complex 3 activates benzene with a barrier of 22.2 kcal/mol at 298 K and 23.7 kcal/mol at 498 K. Top row: direct oxidative addition of benzene by Rh^I . Elsewhere: internal oxidative addition of 3 followed by benzene coordination. All free energies in kcal/mol.



Scheme A.4. The Rh(BOZO) complex **4** activates benzene with a barrier of 18.5 kcal/mol at 298 K and 19.5 kcal/mol at 498 K. Bottom row, first and second TSs: Direct oxidative addition of benzene by Rh^I. Elsewhere: internal oxidative addition followed by benzene coordination. All free energies in kcal/mol.

vestigated, with the results shown in Scheme A.5. The Rh(Me) intermediates and transition states were approximately 7-19 kcal/mol higher in energy than their Rh(Ph) counterparts. In particular, the direct oxidative addition of methane has in its lowest transition state a barrier of 32.4 kcal/mol at 298 K and 37.6 kcal/mol at 498 K, which is prohibitively high under reaction conditions. This is consistent with the lack of experimentally observed methane activation by complex **1**.



Scheme A.5. Activation of methane by the $Rh(DAB^F)$ complex 3 in a manner analogous to the oxidative addition of benzene (see Scheme A.3). The lowest transition state found has a barrier of 32.4 kcal/mol at 298 K and 37.6 kcal/mol at 498 K, rendering methane activation inaccessible. All free energies in kcal/mol.

A.5 Conclusions

This work has demonstrated two efficient rhodium catalysts for H/D exchange between benzene and TFAD. To the best of our knowledge, catalyst 1 is the most active rhodium catalyst yet discovered for benzene H/D exchange. These results demonstrate TOFs similar to platinum and palladium systems. In addition, these rhodium complexes were studied under catalytically relevant conditions for industrial C-H activation and functionalization.

A.6 References

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