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Rh(CAAC)-Catalyzed Arene Hydrogenation: Evidence for Nanocatalysis and Sterically Controlled Site-Selective Hydrogenation

Ba L. Tran, John L. Fulton, John C. Linehan, Johannes A. Lercher, and R. Morris Bullock*

Institute for Integrated Catalysis, Pacific Northwest National Laboratory, Richland, WA 99352, United States

ABSTRACT: We report arene hydrogenation of ethers, amides, and esters at room temperature and low hydrogen pressure, starting from [(CAAC)Rh(COD)Cl] (CAAC = cyclic alkyl amino carbene). Kinetic, mechanistic, and Rh K-edge XAFS studies showed formation of Rh nanoparticles from [(CAAC)Rh(COD)Cl], in contrast to a previous report of [(CAAC)Rh(COD)Cl] functioning as a homogeneous catalyst for arene hydrogenation. We determined that the site-selective arene hydrogenation catalyzed by this system is under steric control, as shown by detailed competition experiments with derivatives of ethers, amides, and esters bearing different aromatic rings of varying electronic and steric influence. This work illustrates the potential of CAAC ligands in the formation and stabilization of a colloidal dispersion of stable nanoparticle catalysts.

Keywords: rhodium, nanocatalysis, arene hydrogenation, site selectivity, XAFS

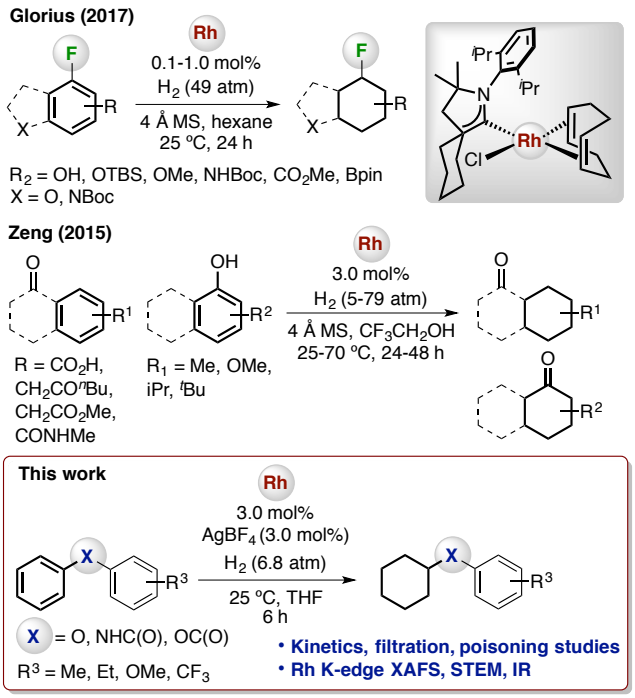
Introduction

Metal-catalyzed hydrogenations constitute crucially important transformations in the production of commodity and specialty chemicals, pharmaceuticals and bio-renewable formulations.[1] Within that broad scope, hydrogenation of olefins,[2] aldehydes,[3] ketones[3a, 3b] esters,[4] amides,[5] carboxylic acids,[6] imines,[3a, 7] nitriles,[8] and nitro[9] groups have been studied extensively. In contrast, arene hydrogenation, despite its longstanding importance,[10] has been less explored; the variety of catalysts is limited, and high reaction temperatures (>200 °C) are typically required. The utility of arene hydrogenations is largely confined to petroleum feedstocks, as sufficient selectivity in the presence of functional groups is difficult to achieve. A prominent application of arene hydrogenation is the conversion of benzene to cyclohexane to produce Nylon, solvents, and plasticizers.[11]

Traditional arene hydrogenations use heterogeneous catalysts (e.g., Ni, Pd, Ru, Rh, Pt) supported on a material to stabilize the nanoparticles (NPs).[12] Intense efforts seek to achieve reproducible synthesis of colloidal materials.[13] *N*-Heterocyclic carbenes (NHCs)[14] have been established as a new stabilizing agents for colloidal catalysts.[15] Applications of ionic liquids containing NHC stabilize colloidal metals not only on the basis of electrostatic interactions,[16] but also stabilize colloidal metals by covalent metal-carbene ligation.[17]

These insights have led to interest in NHCs for modification of nanoparticles catalysts [15a, 18] and functional materials; the steric and electronic profiles of NHCs are readily tunable.[19] The combination of chiral NHCs and Pd-Fe_2O_3 catalyzes, for example, enantioselective α-arylation reactions.[20] There is also growing evidence of electronic and steric effects of NHCs on the stability of metal particles[15a, 21] and the activity of heterogeneous systems such as Ni-catalyzed C-H borylation of arenes and heteroarenes,[22] Buchwald-Hartwig C-N cross couplings,[23] and electrocatalytic reduction of CO_2 to CO.[24] These developments illustrate the potential for a bottom-up approach to translate systematic ligand design, which has been the key to success in transition metal catalysis, to the colloidal chemistry, reproducibly generating hybrid nanomaterials from well-defined molecular precursors.[15a]

Scheme 1. Catalytic arene hydrogenations by Rh(CAAC) systems.



Herein, we report studies with Rh(CAAC) (CAAC = cyclic alkyl amino carbene)[25] for the chemoselective hydrogenation of aryl groups of ethers, amides, and esters at room temperature

under low pressure of H_2. While Rh(CAAC) complexes have been reported for chemoselective arene hydrogenations of aryl carbonyls[26] and aryl fluorides[27] (Scheme 1), the nature of the active Rh catalysts have not been thoroughly examined. These Rh(CAAC) complexes can potentially catalyze difficult, selective arene hydrogenations under mild conditions. We report a combined study of kinetic, mechanistic, spectroscopic, and microscopic experiments that determine the nature of the active Rh species for arene hydrogenation as Rh nanoparticles (Rh NPs). In addition, we perform competition experiments to understand the site-selective hydrogenation of ethers, amides, and esters by this Rh system.

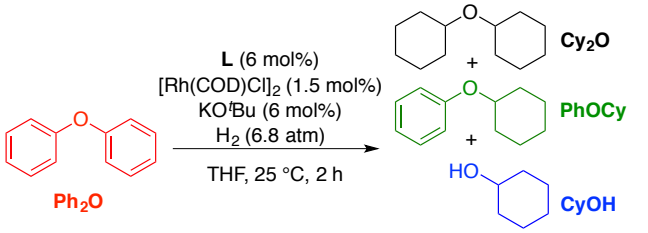
Results and Discussion

Reaction Development. We initially studied arene hydrogenation by evaluating the reaction of diphenyl ether (Ph_2O) at 25 ºC with $[Rh(COD)Cl]_2$, a series of NHCs, and KO^{t}Bu in THF under H_2 (6.8 atm). Results of the Rh-catalyzed hydrogenation of Ph_2O are presented in Table 1. No conversion of Ph_2O at 2 h was observed from the combination of several NHCs,[28] $[Rh(COD)Cl]_2$, and KO^{t}Bu in THF (Table 1, entry 1). Attempts to stabilize the Rh with the bidentate NHC [bis(1-mesityl-3-imidazol-3-yl)methane] or the tridentate NHC [2,6-bis[(3-mesityl)imidazolium]pyridine] ligand (Table 1, entry 2) also led to no conversion of Ph_2O after 24 h. The lack of catalytic activity using the tridentate NHC is readily understood, since the isolated Rh(I) complex is inert towards the oxidative addition of H_2.[29]

We next explored cyclic alkyl amino carbenes (CAACs), which are more electron-donating than NHCs[25, 30] and which confer a different spatial orientation around the metal center because of their asymmetric characteristics, compared to symmetrical NHCs.[14a, 14b, 25, 31] Treating $[Rh(COD)Cl]_2$ with **L1** (4 equiv) and KO^{t}Bu (4 equiv) under H_2 (6.8 atm) provided quantitative conversion of Ph_2O to dicyclohexyl ether (Cy_2O, 70%) and cyclohexanol (CyOH, 30%) in 2 h (Table 1, entry 3).

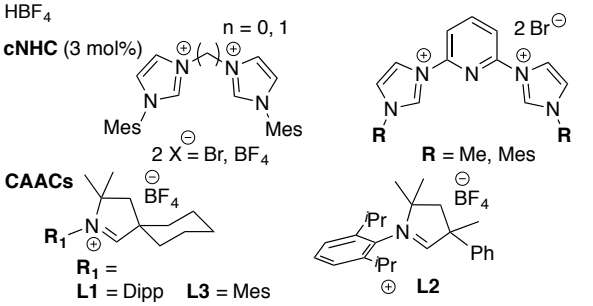
To elucidate the structure-activity relationship of CAACs on Rh-catalyzed arene hydrogenations, we prepared a series of CAAC derivatives (**L2**, **L3**, **L4**, **L5**) of varying steric influence and substitution pattern at the nitrogen atom and the quaternary carbon center. The Rh-catalyzed hydrogenations using **L2**-**L5** (Table 1, entries 4-7) exhibited no activity to moderate activity compared to **L1**. The structure-activity studies showed that the cyclohexyl group at the quaternary carbon is crucial for high activity, as replacing the cyclohexyl group with a phenyl and a methyl in **L2** thwarted catalysis (Table 1, entry 4). A smaller mesityl group at the nitrogen (**L3**), compared to 2,6-diisopropylphenyl (**L1**), reduces catalytic activity to give Cy_2O (8%), PhOCy (50%), and CyOH (20%) at 78% conversion (Table 1, entry 5). Increasing the steric demand at the aniline (i.e., 2,6-bis(diphenylmethyl)-4-methylaniline) (**L4**) dramatically reduced activity, giving 29% conversion (Table 1, entry 6). Introducing a cyclohexyl group at the nitrogen (**L5**) completely shuts down catalysis (Table 1, entry 7). Lastly, no conversion was observed under the conditions used here [Ph_2O (0.5 mM) under 6.8 atm H_2 at 25 ºC] for 2 h in the presence of $[Rh(COD)Cl]_2$ without **L1**, or without $[Rh(COD)Cl]_2$ (Table 1, entry 11-12). These results indicate that the combination of ligand and rhodium is required to effectively generate the catalyst.

Table 1. Reaction development for arene hydrogenation



Entry	Ligand	mol% Ligand	Conv.[a]	Cy_2O %	PhOCy %	CyOH %[a]
1	NHC	3 to 6	0			
2	cNHC	3	0			
3	**L1**	6	100	70	0	30
4	**L2**	6	0			
5	**L3**	6	78	20	50	8
6	**L4**	6	29	24	0	5
7	**L5**	6	0			
8[b]	**L1**	6	35	10	22	3
9[c]	**L1**	1.8	93	45	34	14
10[d]	**L1**	6	0			
11[e]	**L1**	6	0			
12	none	none	0			

Conditions: 0.5 mmol Ph_2O in 1 mL THF. [a]Conversion and yields were determined by GC analysis with dodecane as the internal standard. [b]H_2 (1 atm), 24 h. [c]0.30 mol% $[Rh(COD)Cl]_2$, 1.2 mol% L1, neat Ph_2O, 24 h. [d]1-2 equiv. MO^{t}Bu (M = Na, K) to Ph_2O. [e]no $[Rh(COD)Cl]_2$.
Ligands: **NHC** = IMes-HCl, IPr-HCl, IPr*-HCl, IPr-HBF$_4$, SIPr-HBF$_4$, ICy-HBF$_4$



Dipp = 2,6-diisopropylphenyl
Dipp* = 2,6-bis(diphenylmethyl)4-methylphenyl

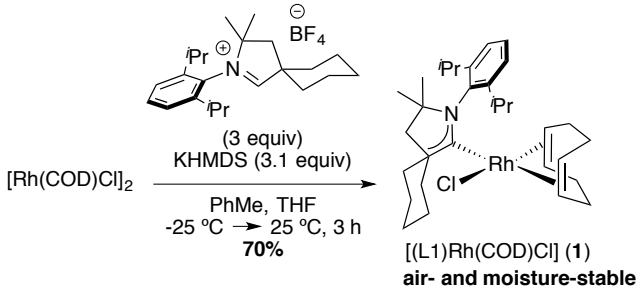
Hydrogenation of Ph_2O at lower H_2 pressure and low loading of $[Rh(COD)Cl]_2$ led to products, albeit with modest activity and extended reaction time. Only 35% conversion was achieved when the reaction was performed with $[Rh(COD)Cl]_2$ and **L1** at 1 atm of H_2 for 24 h (Table 1, entry 8). Performing the catalysis at 0.3 mol% of $[Rh(COD)Cl]_2$ and **L1** at 6.8 atm H_2 for 24 h led to 93% conversion (Table 1, entry 9). The pressure of hydrogen clearly has a greater impact on the activity than low loading of Rh and ligand.

We also investigated the effect of different bases on our catalytic hydrogenations. Alkoxide bases (i.e., NaO^{t}Bu and KO^{t}Bu) provided the best hydrogenation results compared to $NaN(SiMe)_2$, $KN(SiMe)_2$, $LiN(SiMe)_2$, or LiN^{i}Pr$_2$ (see Supporting Information).[14b, 14c, 31a, 32] We studied the effect of stoichiometric base to promote C-O cleavage without arene hydrogenation. Hartwig, Chatani and their co-workers have demonstrated that excess NaO^{t}Bu in NHC-Ni systems led to selective cleavage of C-O bonds.[33] Accordingly, we performed catalysis with MO^{t}Bu (M = Na, K) (1-2 equiv) with respect to Ph_2O (Table 1, entry 10). No conversion of Ph_2O was found when using excess MO^{t}Bu. We hypothesize that the excess base prevents formation of the Rh catalyst, as homogeneity of the reaction mix-

ture was observed, in contrast to the appearance of black precipitates when catalysis occurred. Observation of black precipitates during catalysis prompted the isolation of well-defined Rh complexes to thoroughly investigate the identity of the active Rh species for arene hydrogenation.

Speciation of Rhodium Complexes. The reaction of $[Rh(COD)Cl]_2$, **L1**, and KHMDS $[KN(SiMe_3)_2]$ in THF/toluene produced pure [(L1)Rh(COD)Cl] (**1**; 70%) (Scheme 2) after recrystallization from hexanes. Key to the easy purification of **1**, without the need for column chromatography previously reported,[26] is the use of excess ligand for complete consumption of $[Rh(COD)Cl]_2$.

Scheme 2. Synthesis of (L1)Rh(COD)Cl (1)



To determine if **1** is an active pre-catalyst, we monitored the time-dependence of hydrogenation of Ph_2O. Conversion of Ph_2O was not observed after 24 hours (Figure 1). **1** was recovered (80%) and its identity confirmed by comparison to an authentic sample by ^1H NMR spectroscopy. We hypothesized that a cationic Rh species is the pre-catalyst, given the extensive literature on olefin hydrogenation with cationic Rh.[1b] In addition, **1** is a square-planar Rh complex that needs a vacant site for the binding and activation of H_2.

Accordingly, addition of $AgBF_4$ (3 mol%) to **1** (3 mol%) produced Cy_2O (8%) and PhOCy (27%) in 2 h, and 80% Cy_2O and 20% CyOH in 6 h. The reaction profile for the conversion of Ph_2O revealed buildup of the PhOCy intermediate (22%) after an induction period, with slower formation of Cy_2O (6%) and CyOH (3%) at 2 h (Figure 1). The concurrent onset of formation of Cy_2O and CyOH, and the higher concentration of PhOCy to Cy_2O at 2 h with respect to Cy_2O, suggests the C-O cleavage to form CyOH derives from PhOCy, or possibly from Ph_2O, but not from Cy_2O. This observation was corroborated by the absence of CyOH formation when Cy_2O was subjected to our hydrogenation conditions. The formation of cyclohexane was detected by GC in these catalysis experiments, but its quantification was not attempted because of its position near the solvent peak.

Lastly, as the concentration of PhOCy reached its peak between the interval of 2 h and 3 h, there is a dramatic switch in the rate of hydrogenation toward Cy_2O relative to the steady formation of CyOH. The reason for this behavior can be twofold: (1) PhOCy accumulates as an intermediate and (2) more catalytically active species for arene hydrogenation are formed over time from the slow hydrogenation of COD to COA from complex **1**. Detailed control experiments ruled out the possibility of a CAAC-Ag complex or CAAC-free cationic Rh as the pre-catalyst (see Supporting Information).

Significant accumulation of the PhOCy intermediate during catalysis led us to question whether CyOH may form by reductive hydrolytic C-O cleavage due to adventitious moisture.[34] Accordingly, we performed the reaction of Ph_2O in water. The major products remained Cy_2O (79%) and CyOH (14%). Moreover, starting from PhOCy also yielded a similar ratio of Cy_2O:CyOH. These results and literature precedent strongly suggest that C-O hydrogenolysis formed the CyOH in this system.[33a, 35]

Kinetic studies showed that the end of the induction period coincided with appearance of black particulate. We hypothesize that the catalyst is a nanoparticle, in contrast to a recent report attributing catalytic activity for arene hydrogenation of aryl carbonyls and phenols by **1** to homogeneous catalysis.[26] Considering the controversy of homogeneous vs. heterogeneous catalysts for arene hydrogenation,[12c] coupled with the reported observations, further studies were undertaken to understand the nature of the active Rh species using filtration tests, controlled poisoning experiments, and X-ray absorption fine structure (XAFS) measurements.[12b, 12c, 36]

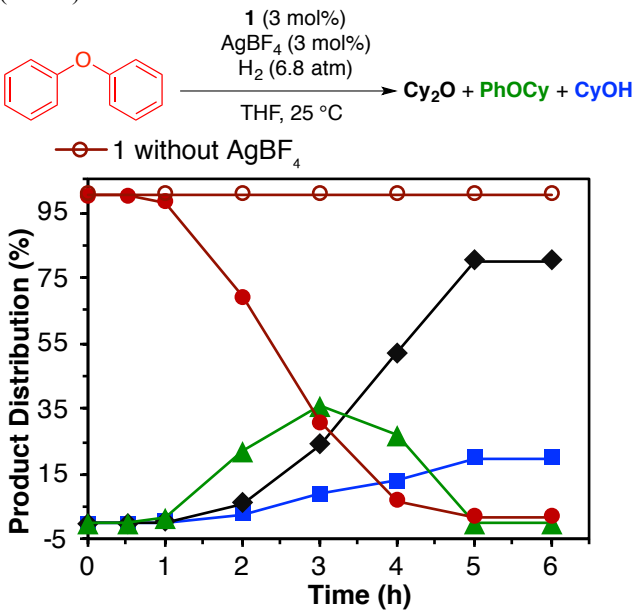
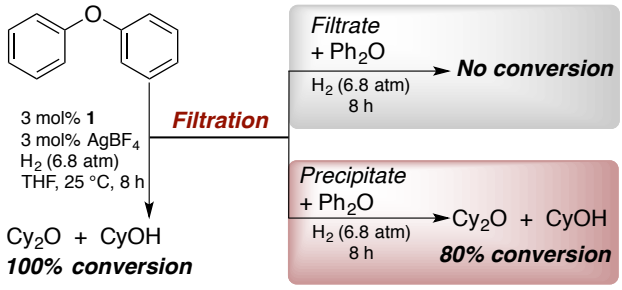


Figure 1. Reaction profile for hydrogenation of Ph_2O by **1** with $AgBF_4$, and without $AgBF_4$, to form Cy_2O and CyOH. Color codes in the plot are the same as the colors in the equation. No catalysis is observed without $AgBF_4$.

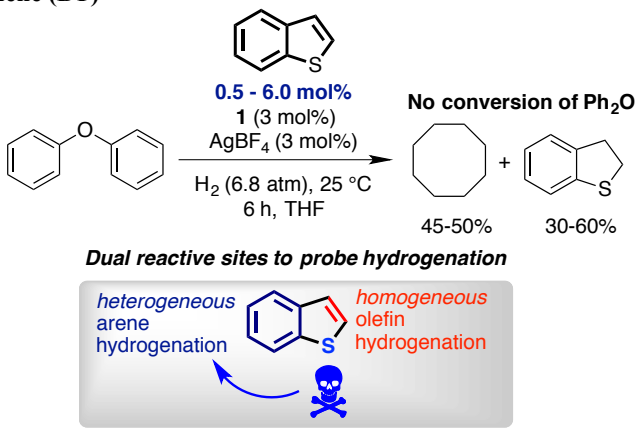
Understanding the Identity of the Rh Catalyst by Filtration, Poisoning, and XAFS Studies. To probe for soluble Rh species, the reaction was filtered after complete consumption of **1** and Ph_2O. The precipitate was removed under N_2, and fresh Ph_2O was added to the filtrate. The precipitate was added to a separate reaction vessel with fresh Ph_2O and THF. The reaction mixtures were again subjected to the same catalytic conditions. Analysis of the reaction with the filtrate and fresh Ph_2O revealed no conversion of Ph_2O (Scheme 3). Conversely, the reaction with the precipitate and fresh Ph_2O gave 80% conversion of Ph_2O after 8 h. These results provide evidence against soluble catalysts for arene hydrogenation. We cannot entirely rule out the possibility of a soluble Rh species leaching from the bulk heterogeneous Rh, becoming active under catalytic conditions.[37]

Scheme 3. Filtration experiments to probe for soluble Rh species



We turned to poisoning experiments to understand the dynamics of *homogeneous* and *heterogeneous* Rh species during catalysis. Benzothiophene (BT) was used for fractional poisoning studies, as it offers several attractive features: (1) there are two reactive sites, an olefin and aryl, that undergo distinctive reactivity; (2) the sulfur atom of BT does not bind tightly to molecular Rh, hence it should not interfere with H_2 activation for the formation of Rh NPs for arene hydrogenation; (3) sulfur-containing heterocycles are known to poison *heterogeneous* hydrogenation catalysts,[38] but are tolerated in *homogeneous* hydrogenations.[39] The rationale for the fractional poisoning studies with BT is that if **1** aggregates toward the catalytically active heterogeneous species, then the number of active Rh sites on the surface will decrease, hence some Rh centers of larger particles must be inaccessible.[12b] Therefore, small amounts of BT can poison an aggregated Rh species.

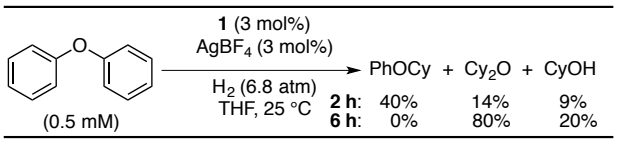
Scheme 4. Controlled poisoning studies with benzothiophene (BT)



Fractional poisoning studies were performed for the reaction of **1**, $AgBF_4$, and Ph_2O at different loadings of BT (0.5, 1.5, 2.0, 3.0, 6.0 mol% with respect to **1**). The results of the poisoning studies are summarized in Scheme 4. No conversion of Ph_2O occurred at any loading of BT. As expected, BT did not interfere with H_2 activation, as evidenced by the hydrogenation of COD and BT to cyclooctane (COA) and 2,3-dihydrobenzo[b]thiophene (DHBT) in 45-50% and 30-60% yields, respectively. Importantly, olefin hydrogenation of COD and BT indicates *homogeneous* hydrogenation occurred under these conditions, while arene hydrogenation of Ph_2O or BT did not. This observation suggests that the active species for arene hydrogenation is rapidly deactivated by BT or DHBT. Additional support for the generation of the active species for arene hydrogenation is that the conversion of COD to COA in the presence of BT is similar to the hydrogenation of Ph_2O to Cy_2O and CyOH without BT.

It might be argued that the stable interaction of Rh with BT or DHBT, compared to that of Ph_2O, leads to no conversion, and that *homogeneous* catalysis is possible. If *homogeneous* arene hydrogenation were operational, then Ph_2O hydrogenation should be observed under conditions of low concentrations of BT or DHBT that cannot have 1 BT/DHBT : 1 Rh stoichiometry. However, our results clearly indicate that arene hydrogenation of Ph_2O does not occur at low concentrations of BT, in which the stoichiometry is 6 Rh : 1 BT.

For a direct study of the evolution of Rh, we turned to Rh K-edge XAFS. These measurements were performed on Ph_2O hydrogenations with **1** and $AgBF_4$ to determine if Rh nanoparticles, Rh clusters, or single-site Rh complexes are present. The XAFS data were collected at intervals of 2 h and 6 h (Figure 2). The transformation of the catalytic Rh species from the mixture is compared to **1** and a Rh foil. At 2 h, 63% Ph_2O was converted to PhOCy (40%), Cy_2O (14%), and CyOH (9%). At 6 h, Ph_2O was fully converted to Cy_2O (80%) and CyOH (20%).



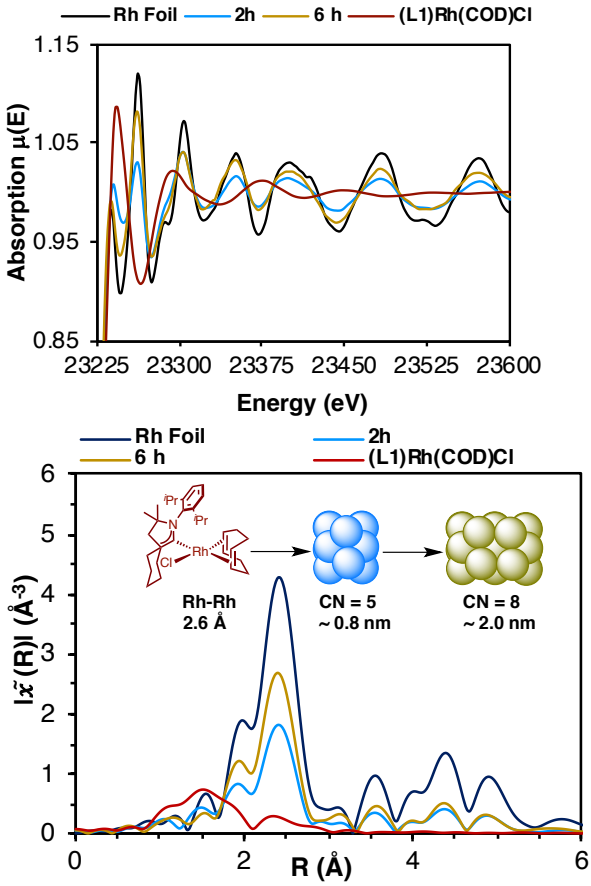


Figure 2. Rh K-edge XAFS plot of energy vs. absorption (top); Rh K-edge XAFS radial structure plot represents transformation of the active Rh species for Ph_2O hydrogenation, compared to **1** and Rh foil (bottom). The graphical scheme shows the evolution of **1** to Rh NPs of different size as a function of time.

At 2 h, the Rh catalyst for arene hydrogenation is active, and has no resemblance to **1**, as evidenced by the growing Rh-Rh feature at ~2.6 Å that corresponds to the Rh-Rh distance in the Rh metal foil, indicating the formation of Rh NPs (Figure 2, bottom). The time-dependence of the change in magnitude at ~ 2.6 Å indicates that the Rh NPs are growing. The size of these Rh NPs, which can be estimated from the Rh-Rh coordination numbers (CNs), yields approximately 0.8 nm (CN = 5) at 2 h and 2.0 nm (CN = 8) at 6 h.[40] Moreover, the disproportionately higher amplitude of higher neighboring shells, in the range from 3.5-5.5 Å, indicates the presence of a fraction of much larger Rh NPs. Therefore, the Rh K-edge XAFS results provide direct evidence for the evolution of Rh NPs of different sizes from **1** under catalytic conditions, which is consistent with the increasing rate of hydrogenation of Ph_2O in the kinetic studies (see above). Lastly, analysis of the radial structure plot (Figure 2, bottom) does not support the presence of $Rh_{4\text{-}6}$ clusters for arene hydrogenation, which would contain a feature at ~2.71-2.73 Å.[36a, 36c]

Detection of Rh NPs in the reaction mixture by Rh K-edge XAFS prompted further characterization of these nanoparticles with scanning transmission electron microscopy (STEM) to determine the size of the Rh NPs, and IR spectroscopy to detect the presence of organic ligands decorating the Rh NPs. STEM analysis of the reaction mixture for Ph_2O hydrogenation with **1** and $AgBF_4$ after 6 h showed the presence of Rh NPs of 5 nm particle size (see Supporting Information). Additionally, the insoluble Rh nanoparticles were collected and washed thoroughly with THF to remove unreacted Ph_2O and hydrogenated products. Analysis of the isolated Rh NPs by IR spectroscopy[15a, 24] showed bands characteristic of **L1**, suggesting that the Rh NPs are stabilized by **L1** (see Supporting Information). The formation of nanoparticles stabilized by imidazolium salts from well-defined metal complexes ligated by NHC ligands has been reported.[41] Loss of the NHC ligand from a metal center to form nanoparticles has been proposed to occur by C-H coupling of the NHC and hydride ligands bound to the same metal center.[41a, 42] Thus, the combination of kinetic studies, filtration tests, poisoning experiments, XAFS measurements, and STEM characterization provide conclusive evidence that the aromatic groups of Ph_2O are hydrogenated by Rh NPs derived from **1** and $AgBF_4$ under the reaction conditions (Figure 3).

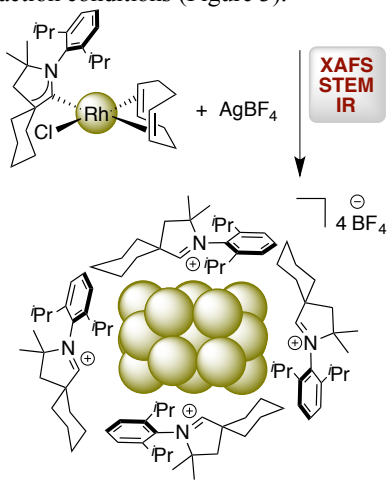
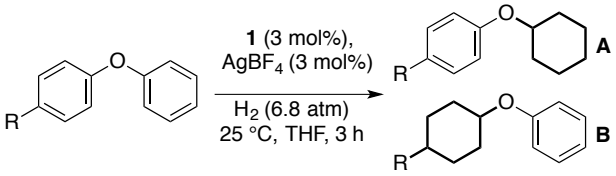


Figure 3. Formation of Rh NPs stabilized by **L1** from **1** and $AgBF_4$ is supported by the results of XAFS, STEM, and IR spectroscopy

Understanding Site Selectivity of Rh-Catalyzed Arene Hydrogenation and Hydrogenolysis of the C-O Bond of Ethers, Amides, and Esters. We determined the site selectivity of arene hydrogenation with sterically and electronically unsymmetrical aryl ethers, amides, and esters. We first examined a series of *para*-substituted diphenyl ethers containing an ethyl, methoxy, or trifluoromethyl group, as well as *ortho*- and *meta*-methoxy substituted diphenyl ethers (Table 2). All derivatives of Ph_2O showed faster hydrogenation at the unsubstituted arenes than at the substituted arenes, with a ratio of 9-25 : 1, regardless of the electronic properties of the substituent (OMe or CF_3) or the position of the substituents on the ring. These results clearly indicate that steric effects dominate over electronic effects in the hydrogenation of unsymmetrical diphenyl ethers.

The selectivity for C-O hydrogenolysis of diphenyl ether derivatives is similar to that of arene hydrogenation, with C-O cleavage occurring at the less hindered arene (see Supporting Information). Arene hydrogenation and C-O hydrogenolysis appear to share a common preference for the interaction of Rh with the less hindered arene.[43] This preference is tentatively attributed to the preferred adsorption of the less hindered arene to Rh. Lastly, the influence of steric effects on the selectivity of C-O hydrogenolysis of diphenyl ether derivatives of this Rh(CAAC) catalyst is complementary to the electronic effect of Ni(NHC)-catalyzed C-O hydrogenolysis, which favors C-O bond cleavage at the electron-deficient arene.[33a]

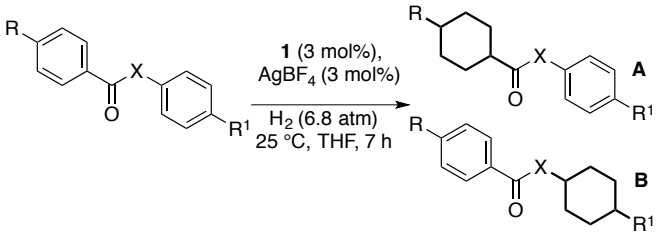
Table 2. Site-selective arene hydrogenation of usymmetrical diphenyl ethers



Entry	R	% Conversion[a]	Ratio A/B (A+B%)
1	Et	63	11/1 (50%)
2	OMe	57	10/1 (52%)
3	CF_3	86	25/1 (80%)
4	*o*-Me	55	9/1 (40%)
5	*m*-Me	60	8.7/1 (45%)

[a] Conversions and yields were determined by GC analysis with dodecane as internal standard. The remaining mass balance is fully hydrogenated and hydrogenolysis products.

Table 3. Site-selective arene hydrogenation of usymmetrical diphenyl amides and esters



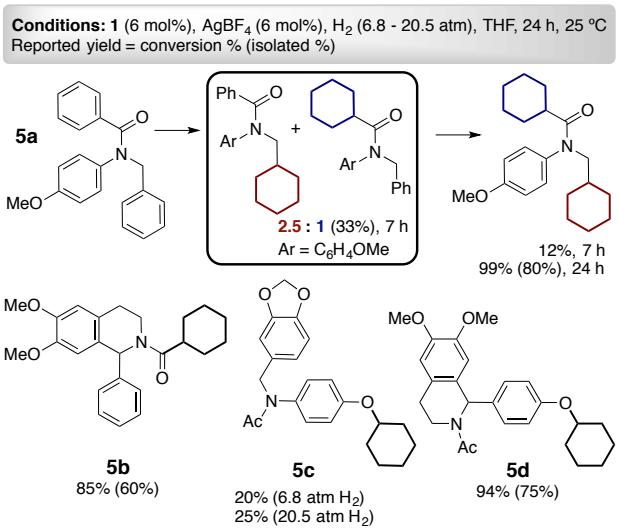
Entry	X	R	R_1	% Conversion[a]	Ratio A/B (A+B%)
1	NH	H	H	94	1.7/1.0 (52%)
2	NH	CF_3	H	99[b]	B (90%)
3	NH	H	OMe	44	A (44%)
4	NH	H	*o*-OMe	35	A (35%)
5	NH	H	*m*-OMe	42	A (42%)
6	O	CF_3	H	100[b]	B (93%)
7	O	H	OMe	48	A (48%)

[a] Conversions and yields were determined by GC analysis with dodecane as internal standard. The remaining mass balance is fully hydrogenated products. [b] 24 h.

To study the site-selective arene hydrogenation of esters and amides, we first examined *N*-phenylbenzamide, because the two aryl groups have a similar steric environments, yet their electronic properties differ because of the amide linkage (Table 3, entry 1). Hydrogenation of *N*-phenylbenzamide formed *N*-phenylcyclohexanecarboxamide and *N*-cyclohexylbenzamide in a ratio of 1.7 : 1.0, for a combined yield of 52% at 94% conversion. The remaining mass balance is the fully hydrogenated product, *N*-cyclohexyl-cyclohexanecarboxamide, and unreacted starting material (Table 3, entry 12). In the hydrogenation of *N*-phenylbenzamide, despite having equally accessible arenes for hydrogenation, we observed faster hydrogenation at the electron-poor arene adjacent to the carbonyl relative to the electron-rich arene bonded to the nitrogen.

We also investigated the effects of *para*-, *ortho*-, and *-meta* substitution for amides and esters, to compare to the diphenyl ether derivatives (Table 3, entries 2-7). As found for the diphenyl ether derivatives, unsubstituted arenes undergo faster hydrogenation than the substituted arenes for all amides and esters in our studies. These combined results for diphenyl ethers, amides, and esters reinforce the conclusion of the dominant steric effect on arene hydrogenation, in which less hindered arenes are hydrogenated faster than more hindered arenes.

Scheme 5. Site selectivity for Rh-catalyzed hydrogenation of small molecules



The insight that the arene hydrogenation is under steric control prompted us to investigate the site selectivity in small molecules with more than two reactive sites. The results for the Rh-catalyzed arene hydrogenations of small molecules are summarized in Scheme 5. In the hydrogenation of **5a**, the two reactive phenyl groups have a similar steric environment; however, the electronic effect and flexibility are different. At 7 h, hydrogenation of the benzyl group occurs faster than that of the acyl phenyl group, with a ratio of 2.5 :1, at 45% conversion. This observation suggests that in addition to steric effects, flexible aryl groups undergo faster hydrogenation between two similarly accessible arenes. At 24 h, quantitative hydrogenation of both aryl groups has occurred, giving *N*-(cyclohexylmethyl)-*N*-(4-methoxyphenyl)cyclohexane-carboxamide (80% isolated yield). For **5b**, hydrogenation of the acyl phenyl is preferred over the unsubstituted phenyl, which is explained by the steric congestion resulting from the adjacent proximity of the dimethoxy-substituted arene to the phenyl, thus rendering the acyl phenyl group as more sterically accessible for arene hydrogenation. In **5c** and **5d**, arene hydrogenation occurs exclusively at the sterically accessible and unsubstituted phenyl group in the diphenyl ether fragment, giving a single product and unreacted starting material at 20-25% for **5c**, but with good conversion (94%) and an isolated yield of 75% for **5d**. The identity of all hydrogenated products has been confirmed by independent synthesis (see Supporting Information).

Conclusions

Metal nanoparticles have been prepared from a small library of carbene ligands in combination with $[Rh(COD)Cl]_2$ for arene hydrogenation at low H_2 pressure and room temperature. We have identified Rh-CAAC nanoparticles to be the active species for arene hydrogenation under our experimental conditions. This conclusion is supported by the induction period by kinetic studies, mechanistic studies involving a filtration test, fractional poisoning experiments, XAFS measurements, STEM characterization, and infrared spectroscopy. From site-selective studies for the arene hydrogenation of ethers, amides, and esters with different electronic and steric effects, we conclude that the site selectivity for arene hydrogenation in this system markedly depends on steric factors. We speculate that the high activity is

related to the presence of CAAC on the surface of the catalytically active particles. Ongoing characterization of such catalysts under operating conditions is expected to lead to new generations of catalysts at the interface between homogeneous and heterogeneous catalysis.

ASSOCIATED CONTENT

Supporting Information

Additional experimental data, synthetic procedures, characterization of compounds, and spectroscopic data are included in the Supporting Information. The Supporting Information is available free of charge on the ACS Publications website.

AUTHOR INFORMATION

Corresponding Author

morris.bullock@pnnl.gov

Author Contributions

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Notes

The authors declare no competing financial interest.

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