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H/D Exchange Processes Catalyzed by an Iridium-Pincer Complex

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Supporting Information

ABSTRACT: A PNP-pincer iridium dihydride performs the H/D exchange between aromatic substrates and tertiary hydrosilanes and D_2O or C_6D_6 . Complete incorporation of deuterium into sterically accessible C_{ar} -H and Si-H bonds was observed at a moderate temperature of 80 °C.



The field of transition-metal-catalyzed C–H activation has witnessed major developments¹ since the initial reports on stoichiometric intra- and intermolecular reactions.^{2,3} However, even with this impressive progress, many challenges still remain, especially in being able to predict the activity of a metal complex toward certain substrates.¹ In this respect, isotopic exchange processes are instrumental in evaluating the ability of a particular catalyst to perform difficult C–H activations.^{4,5} From a practical standpoint, selective isotopic labeling offers facile access to deuterium-containing compounds that are useful in medicinal chemistry and in vivo profiling.⁶

Iridium has emerged as one of the most powerful transition metals for the C–H activation of aromatic substrates.⁷ Since the pioneering work of Bergman, who showed that the cyclopentadienyl complex $[Cp*(PMe_3)IrH(CH_2Cl_2)][B-(C_6F_5)_3Me]$ exhibits unprecedented reactivity toward C–H activation and H/D exchange,^{2d,e} the search for reactive systems has focused on catalysts supported by non-cyclopentadienyl ligands.^{7b,c,8} We report herein the efficient and selective H/D exchange between arenes and C_6D_6 or D_2O using the iridium(III) complex (PNP)IrH₂ (1; PNP = bis-(2-(diisopropylphosphino)-4-methylphenyl)amide) as a catalyst.⁹ In addition, related Si–H/D exchanges in tertiary silanes with 1 are also described.

Our initial experiments showed that 1 can be easily converted to $[D_2]$ -1 by heating at 80 °C in C_6D_6 for 1 h (eq 1) and



that the reaction is reversible. The reverse process, converting $[D_2]$ -1 to 1, was achieved by using C_6H_6 under identical conditions (eq 1). Although C_6D_6 is a good source of deuterium, we became interested if the less expensive D_2O could replace it.

Therefore, the reactivity of 1 with H_2O and D_2O was investigated in nonreactive solvents such as cyclohexane and *p*-xylene and it was found that 1 was readily converted to $[D_2]$ -1 in the presence of D_2O and $[D_2]$ -1 to 1 by using H_2O (eq 1). Compound 1 is remarkably stable in the presence of water even at high temperatures (80 °C) for extended periods of time (10 days): no coordination of water to the metal center was observed by NMR spectroscopy, and the only iridium-containing species detected in homogeneous solution was 1 during the entire time.

The H/D exchange with C_6D_6 or D_2O as a deuterium source makes 1 a great candidate for catalytic hydrocarbon deuteration. Toward this end, it was found that benzene and its derivatives undergo H/D exchange with 1 in dry C_6D_6 or with D_2O in cyclohexane- d_{12} (Scheme 1). Thus, benzene (2)





"Reaction conditions: T = 80 °C, t = 3 days, catalyst loading 1%. We assumed complete deuteration when deuterium incorporation exceeded 95%.

Received: October 28, 2011 Published: December 15, 2011 was fully deuterated after 3 days using 1 mol % of the catalyst (80 °C) in both solvent systems. Steric factors played an important role, since toluene was deuterated only at the meta and para positions (3), *o*-xylene in positions 4 and 5 (4), and *m*-xylene only in position 5 (5) and no deuteration was observed for *p*-xylene (6). Deuteration of naphthalene was sluggish and showed that the β position reacted 2 times faster than the α position (7; Scheme 1).

Heteroaromatic substrates were also tested (Scheme 1). Both furan (8) and thiophene (9) were converted to the corresponding isotopologues with 92% and 90% deuterium incorporation, respectively. In contrast, pyridine (10) deactivated the catalyst by coordinating to the metal center (as assessed by ¹H NMR spectroscopy; see the Supporting Information for details). Since Milstein and Leitner reported that aliphatic H/D exchange can be facilitated in 2,5dimethylfuran (11) via precoordination of this substrate to the metal center,^{4d} we decided to verify if such a process is operative with 1 as well and subjected 11 to our standard reaction conditions. Addition of 2,5-dimethylfuran to an orange solution of 1 in C₆D₆ at room temperature led to a deep crimson solution; this transformation was not observed with unsubstituted furan or other substrates. While the orange color reappeared upon heating, the degree of deuterium incorporation into 11 was marginal (Scheme 1), presumably due to substrate coordination to the iridium center and to steric effects highlighted earlier. Likewise, switching to the D_2O/C_6D_{12} solvent system did not improve the amount of incorporated deuterium (Scheme 1). These data suggest that the oxidative addition of aromatic C-H bonds to 1 is strongly preferred over the addition of aliphatic C-H bonds.⁹

Encouraged by these results, we became interested in extending the substrate scope of H/D exchange to tertiary silanes, since only a few systems are known to perform their Si–H/D exchange.¹⁰ Moreover, a report on olefin hydrosilylation with 1^{11} indicated that such a process is viable. Table 1 presents the experimental details.

Table 1. Si–H/D Exchange of Tertiary Silanes Catalyzed by 1 in D_2O/C_6D_6 at 80 °C

$R_{3}Si-H \xrightarrow{1, D_{2}O/C_{6}D_{6}, 80 \ ^{\circ}C, t} \longrightarrow R_{3}Si-D$				
entry	silane	amt of $1 \pmod{\%}$	<i>t</i> (h)	amt of D (%)
1	Et ₃ SiH	1	65	>95
		1	65	51 ^a
2	<i>i</i> -Pr ₃ SiH	2.5	24	>95
3	$(C_6H_5CH_2)_3SiH^b$	5	132	>95
4	(Me ₃ Si) ₃ SiH	5	90	>90
5	PhSiHMe ₂	2	60	<5
6	<i>i</i> -Pr ₂ Si(Cl)H	2	60	<5
^a Reaction conducted in C ₆ D ₆ instead of D ₂ O/C ₆ D ₆ . ^b See text.				

Since we observed that the deuteration of triethylsilane in the presence of C_6D_6 saturated with D_2O exhibits approximately a 2-fold rate acceleration as compared to using dry benzene (Table 1, entry 1), this solvent system was employed as a practical deuterium source for the other silanes as well. Thus, more than 95% deuteration was achieved with triethyl-, triisopropyl-, and tribenzylsilanes (entries 1–3, Table 1) with a 1–5 mol % catalyst loading. In agreement with the preference of 1 for aromatic C–H bonds, no benzylic exchange occurred for tribenzylsilane, as the ²H NMR spectrum of deuterated

tribenzylsilane only shows aromatic peaks with a $C_{ar}D$ to SiD ratio of 0.9:1. Additionally, the ortho position incorporated the highest amount of deuterium, presumably because of the vicinity of the metal center during Si-H/D exchange. Remarkably, even the very bulky substrate (Me₃Si)₃SiH was almost completely deuterated with 1, as assessed by FT-IR spectroscopy (entry 4). Finally, substrates containing Ph–Si and Cl–Si bonds were inactive (entries 5 and 6, Table 1).

In terms of the reaction mechanism, we propose that 1 first reacts with D_2O to form the intermediate iridium complex 1- D_2O (Scheme 2), as the product of the O–D oxidative





^aFor simplicity all the steps are shown as irreversible.

addition. Subsequent reductive elimination of HOD from 1-D₂O generates [D]-1. An analogous process is expected when C_6D_6 is used as a deuterium source. As exemplified for C_6H_6 , [D]-1 may then oxidatively add the C–H (or Si–H) bond of a substrate to generate [D]-1- C_6H_6 , which subsequently regenerates 1 by reductive elimination. We propose that the intermediates 1-D₂O and 1- C_6H_6 may be formulated either as Ir(V) trihydride complexes or as Ir(III) monohydrides bearing a dihydrogen ligand.^{8h}

A mercury test was conducted during the deuteration of triethylsilane or furan, and no decrease in rate was observed, thus indicating that deuterium incorporation occurs homogeneously.¹² Apparent exchange rates were also measured for these substrates using 5 mol % of 1 in dry C_6D_6 at 80 °C: the rate for triethylsilane was determined to be 2.7×10^{-3} min⁻¹, while those for furan were $6.8 \times 10^{-3} \text{ min}^{-1}$ (α position) and $5.4 \times 10^{-3} \text{ min}^{-1}$ (β position). These observed reaction rates follow first-order kinetics and are in agreement with the other experimental observations presented earlier. Given the strength of the Si-O bond, the absence of hydrolysis products during SiH/D exchanges with D2O is particularly noteworthy and strongly supports the proposed mechanism.^{11b} The catalyst deactivation pathway may involve dehydrogenation of iridium species such as 1-D₂O and [D]-1-C₆H₆ (Scheme 2), as was observed by Tilley for a number of tertiary silane substrates.¹¹

In conclusion, we have shown that a noncyclopentadienyl iridium(III) dihydride complex can perform H/D exchange under mild conditions using D_2O as an inexpensive deuterium source. The process was applied to aromatic hydrocarbons as well as to tertiary hydrosilanes, and full deuterium incorporation into sterically accessible aromatic C–H and Si–H bonds was illustrated. Our results indicate that 1 efficiently mediates

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difficult C–H activation reactions and its activity is comparable to that of other reported systems.

ASSOCIATED CONTENT

Supporting Information

Text, a table, and figures giving detailed experimental procedures and characterization data for new compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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ACKNOWLEDGMENTS

Generous financial support of this research was provided by BP $(MC^2 \text{ initiative})$. A.F. thanks the Swiss National Science Foundation for a postdoctoral fellowship.

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NOTE ADDED AFTER ASAP PUBLICATION

In the version of this paper that was published on December 15, 2011, two footnotes were inadvertently left out of Table 1. The version that appears as of December 20, 2011, is correct.