

A Cationic Rh(III) Complex That Efficiently Catalyzes Hydrogen Isotope Exchange in Hydrosilanes

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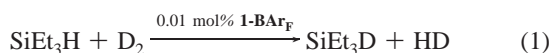
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Abstract: The synthesis and structural characterization of a mixed-sandwich ($\eta^5\text{-C}_5\text{Me}_5$)Rh(III) complex of the cyclometalated phosphine PMeXyl_2 (Xyl = 2,6- $\text{C}_6\text{H}_3\text{Me}_2$) with unusual $\kappa^4\text{-P,C,C',C''}$ coordination (compound **1-BAr_F**; $\text{BAr}_F = \text{B}(3,5\text{-C}_6\text{H}_3(\text{CF}_3)_2)_4$) are reported. A reversible κ^4 to κ^2 change in the binding of the chelating phosphine in cation **1⁺** induced by dihydrogen and hydrosilanes triggers a highly efficient Si–H/Si–D (or Si–T) exchange applicable to a wide range of hydrosilanes. Catalysis can be carried out in an organic solvent solution or without solvent, with catalyst loadings as low as 0.001 mol %, and the catalyst may be recycled a number of times.

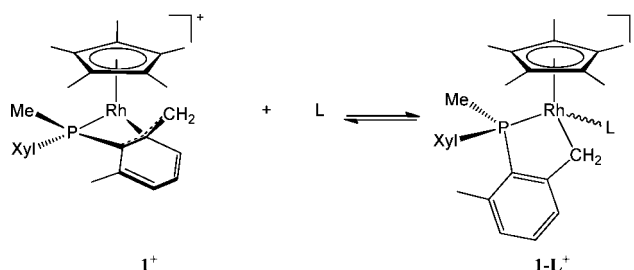
There is increased demand for isotopically labeled compounds as internal standards for mass spectrometric studies, as well as for other modern technologies that include agrochemical, biological, and pharmaceutical investigations of the interaction of small molecules with receptors, enzymes, and other biomolecules.¹ Compounds labeled with both stable and radioactive isotopes are critical to the drug development process and have become essential in many clinical studies.^{2,3}

Labeling organic molecules with deuterium (D) and tritium (T) is a common, important practice for the pharmaceutical industry.^{4,5} Hydrosilanes, $\text{SiR}_{4-n}\text{H}_n$ ($n = 1\text{--}3$), provide one of the most powerful tools in synthetic organic chemistry⁶ and are able to add catalytically to C–C, C–N, and C–O multiple bonds in the wide-scope hydrosilylation reaction^{7–9} and to reduce, also catalytically, carbon–halogen bonds,¹⁰ including unreactive C–F bonds.^{11–13} Therefore, they are ideal reagents for D and T labeling procedures. Herein we describe the synthesis and properties of the cationic Rh(III) complex **1⁺** (Scheme 1) that catalyzes with high efficacy hydrogen isotope exchange (H/D/T) in a wide range of hydrosilanes (see eq 1 and Table 1 for selected H/D exchanges), employing D_2 or T_2 as the hydrogen isotope source.



In the search for analogues of the unusual iridium and rhodium cations $[(\eta^5\text{-C}_5\text{Me}_5)\text{M}(\text{Me})(\text{PMe}_3)(\text{ClCH}_2\text{Cl})]^+$,^{14,15} we have focused on rhodium precursor **1-Cl** that contains a metalated PMeXyl_2 ligand. A preliminary report on the synthesis and reactivity of the iridium analogue has appeared recently.^{16a} Since the reaction between $[(\eta^5\text{-C}_5\text{Me}_5)\text{RhCl}_2]_2$ and PMeXyl_2 gives a mixture of complexes that

Scheme 1



contains less than 50% of **1-Cl**, the latter compound is best obtained by chlorination (CH_2Cl_2 or CHCl_3) of hydride **1-H** (Scheme 2), which in turn results from the stepwise reaction of $[\text{RhCl}(\text{C}_2\text{H}_4)_2]_2$ with PMeXyl_2 and $\text{Zn}(\text{C}_5\text{Me}_5)_2$.¹⁶ Characterization by spectroscopy and X-ray studies has been achieved. A CH_2Cl_2 solution of **1-Cl** reacts with NaBAr_F ($\text{BAr}_F = \text{B}(3,5\text{-C}_6\text{H}_3(\text{CF}_3)_2)_4$) and acetonitrile (or other Lewis bases, L, like for example NH_3 , PMe_3 , or CO) with formation of the corresponding adducts (isolated as BAr_F salts), whereas, in the absence of L, **1-BAr_F** is the only isolable product. Consequently, for poorly coordinating CH_2Cl_2 the equilibrium of Scheme 1 shifts to the left and the unusual $\kappa^4\text{-P,C,C',C''}$ structure prevails over CH_2Cl_2 adduct formation, which might be expected on the basis of previous reports^{14,15} for related cationic rhodium and iridium compounds. Moreover cations **1⁺** and **1-L⁺** feature characteristic $^{31}\text{P}\{^1\text{H}\}$ NMR signals with chemical shifts δ of -14.7 and *ca.* $37\text{--}43$ ppm, respectively. Hence, equilibria between **1⁺** and adducts **1-L⁺** can be readily ascertained by $^{31}\text{P}\{^1\text{H}\}$ NMR spectroscopy (for **1-L⁺** two

Table 1. H/D Exchange in Hydrosilanes Catalyzed by **1-BAr_F**^a

Entry	Silane	Cat. (mol %)	Solvent ^b	Temp (°C)	T (h)	D incorp. (%)
1	SiEt_3H	1	A	25	3	≥ 99
2	SiEt_3H	0.01	B	50	24	≥ 99
3	SiEt_3H	0.001	B	60	48	89
4	SiPh_3H	0.1	A	50	5	≥ 99
5	SiPh_2H_2	0.1	A	50	5	≥ 99
6	SiPhH_3	0.1	A	50	5	≥ 99
7	$\text{Si}(\text{SiMe}_3)_3\text{H}^d$	2	A	50	16	98
8	$\text{Si}^d\text{Pr}_3\text{H}^d$	1	A	25	16	80
9	PMHS^e	0.1	A	25	5	≥ 99
10	$1,2\text{-C}_6\text{H}_4(\text{SiMe}_2\text{H}_2)$	1	A	25	16	90
11	SiEt_2H_2	0.1	A	50	5	≥ 99
12	$\text{Si}(\text{EtO})_3\text{H}$	1	A	25	5	≥ 99

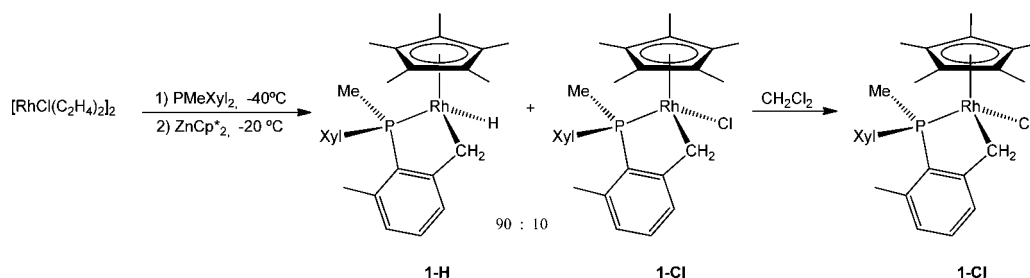
^a To ensure full deuteration three D_2 loadings are routinely employed, each consisting of cooling $0^\circ\text{C}/\text{vacuum}$ (0.1 bar)/0.5 bar of D_2 .

^b Solvent: A, CD_2Cl_2 (0.6 mL); B, neat silane. ^c Determined by IR and NMR (^1H and ^{29}Si) spectroscopy. ^d Catalyst decomposition occurs. ^e Polymethylhydrosiloxane.

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Scheme 2



diastereomers are commonly observed). Cation $\mathbf{1}^+$ exhibits fluxional behavior in solution, to be described in due course. It is, however, appropriate mentioning at this stage that the solution dynamics of $\mathbf{1}^+$ implies exchange of the roles of the metalated and nonmetalated xylyl rings. Theoretical calculations support this degenerate exchange to occur through agostic intermediate **A** (Figure 1), with an energy of only 7.4 kcal·mol⁻¹ above $\mathbf{1}^+$. Indeed, this rearrangement seems to be crucial for the chemical reactivity to be described below.

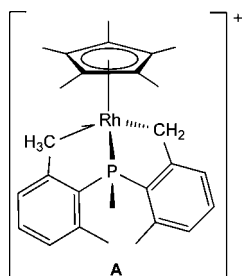


Figure 1. Agostic intermediate proposed for the exchange of the two xylyl rings of the phosphine moiety.

Figure 2 compares the X-ray structures of $\mathbf{1}^+$ and $\mathbf{1-CO}^+$. The coordinated atoms of the metalated phosphine ligand of $\mathbf{1}^+$, that is, P(1), C(17), C(12), and C(11), form an essentially planar arrangement which is nearly parallel to the C₅Me₅ ring plane (dihedral angle 7.3°). Accordingly, the Rh–C distances to C(11), 2.135(5) Å; C(12), 2.200(5) Å; and C(17), 2.254(4) Å are clearly bonding, while for $\mathbf{1-CO}^+$ only the Rh–C(11) distance of 2.124(2) Å is bonding. In this compound the Rh–C(12) and Rh–C(17) separations are 3.112 and 3.290 Å, respectively. Despite the simplicity of the metalated ligand in $\mathbf{1}^+$, the mixed-sandwich structure of the cation is unique. AIM analysis of its DFT-optimized structure shows the expected (3, -1) Bond Critical Points (BCPs) between Rh–P(1) and Rh–C(11). Furthermore, a third BCP¹⁷ has been located between Rh and C(17), but not between Rh and C(12), in spite of the short experimental (2.200(5) Å) and calculated (2.245 Å) distances found for this linkage. Instead, two (3, +1) ring critical points have been found roughly at the centroids of the Rh–P(1)–C(17) and Rh–C(17)–C(12) triangles.

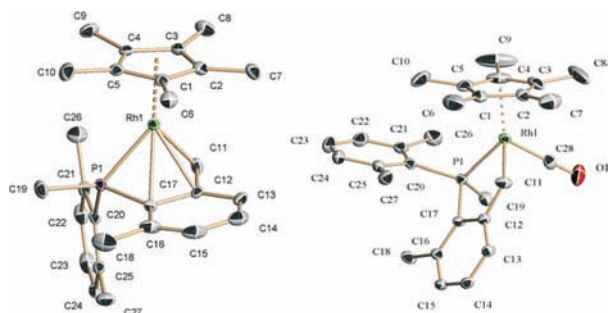
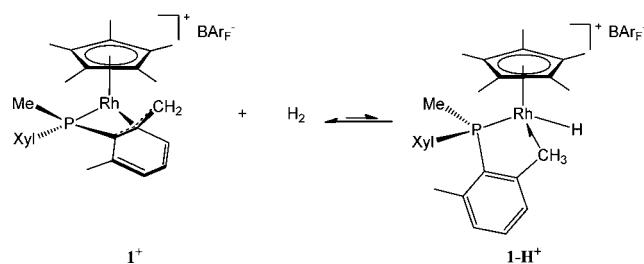


Figure 2. X-ray molecular structures of $\mathbf{1-SbF}_6^+$ and $[\mathbf{1-CO}]^+\text{BARF}_4^-$, with H atoms and anions omitted for clarity.

Studying the reactivity of $\mathbf{1}^+$ toward molecules like dihydrogen and hydrosilanes that have only σ -bonded electrons^{18,19} was of evident interest. At room temperature there is no observable reaction between $\mathbf{1}^+$ and either type of molecule. However, exposure of solutions of $\mathbf{1}^+$ to D₂ yields $\mathbf{1(D_{11})}^+$ almost instantly, due to fast H/D exchange of all sp³-hybridized C–H bonds of the phosphine xylyl units. Low-temperature (–90 °C) NMR monitoring of the reaction of $\mathbf{1}^+$ and H₂ does not provide experimental evidence for the formation of a σ -H₂ complex but unveils the existence of a cationic agostic hydride $\mathbf{1-H}^+$ ($\mathbf{1}^+:\mathbf{1-H}^+$ ratio of ca. 85:15) that is in equilibrium with $\mathbf{1}^+$ (Scheme 3). Examination of its ¹H NMR spectrum shows a doublet of doublet resonance at –9.43 ppm due to the hydride ligand (with spin–lattice relaxation time T₁ = 300 ms) that undergoes exchange with a signal with δ –0.02 ppm attributed to the agostic methyl protons. A corresponding ³¹P{¹H} signal at 29.8 ppm can be observed in the range of –90 to –70 °C but disappears above the latter temperature, although cooling at –90 °C restores the original spectrum. Cation $\mathbf{1}^+$ also undergoes exchange with SiEt₃D yielding $\mathbf{1(D_{11})}^+$, but for this system neither a σ -silane complex nor an agostic silyl related to $\mathbf{1-H}^+$ can be detected by NMR spectroscopy. Nevertheless, DFT calculations reveal that both σ -H₂ and σ -HSiEt₃ complexes are key intermediates in these reactions.

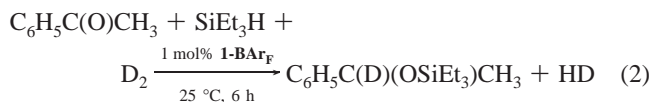
Scheme 3



The H/D exchange between $\mathbf{1}^+$ and D₂ or SiEt₃D suggests that a catalytic synthesis of deuterated silanes can be developed (eq 1). This is an important target as it can lead to labeling procedures that are alternative to current practices.^{20,21} Although catalytic Si–H/Si–D exchange is known,^{22–25} present information is scarce and to our knowledge an efficient catalytic process for the synthesis of labeled hydrosilanes, SiR_{4–n}D_n (n = 1–3), has not yet been developed. Table 1 presents a summary of the Si–H/Si–D exchanges catalyzed by $\mathbf{1-BARF}$ that have been investigated.

Deuteration of hydrosilanes may be carried out in CH₂Cl₂ solution or in the neat silane, using D₂ (0.5 bar) as the source of deuterium, at room temperature or above (40–60 °C), and with catalyst loadings between 1 and 0.001 mol %. Deuteration is equally effective for secondary and tertiary silanes (entries 5, 6, and 11). Polymethylhydrosiloxane (PMHS, entry 9), an inexpensive, non-toxic, and environmentally benign reagent,²⁶ becomes deuterated under similar conditions. As revealed by NMR studies, compound

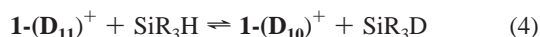
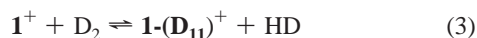
1-BAR_F is recovered unaltered after the catalytic runs (see entries 7 and 8 in Table 1 for exceptions). Furthermore, the catalyst can be recycled at least eight times (tested for deuteration of SiEt₃H) without loss of efficacy. These and other data that include the Hg test are indicative of a homogeneous process. Since compound **1-BAR_F** is also an efficient catalyst for hydrosilylation of carbon–oxygen and carbon–nitrogen multiple bonds, direct one-flask addition of a Si–D bond to these functionalities (for some examples, see eq 2 and Supporting Information) can be achieved.



Tritiated silanes are convenient tritiation reagents,⁵ but their synthesis requires treatment of the corresponding chlorosilanes with LiT or complex metal hydrides.²⁷ Catalyst **1**⁺ allows facile tritium incorporation into hydrosilanes and overcomes many of the disadvantages of commonly used tritiation methods.²⁸ A catalytic procedure similar to that described for deuterium exchanges may be utilized. However to avoid frequent use of tritium gas, which is a dangerous and difficult substance to manipulate,²⁸ complex **1**⁺ may be used as a tritium carrier for low specific activity tritium labeling. Thus, exposure of CH₂Cl₂ solutions of **1**⁺ (200 mg; 148 μmol) to 1 Ci (18 μmol) of T₂ permits T-incorporation (≥85%) into the CH₂ and CH₃(xylyl) sites of the catalyst to yield **1(T_n)**⁺, which can be stored safely. Then, heating for example 1 mg (0.74 μmol, 4.5 mCi) of the tritiated rhodium complex with an excess of SiEt₃H (1.2 mL, 7.5 mmol; 50 °C, 5 days) permits T transfer to the silane that can be separated from the catalyst by trap-to-trap distillation; the resulting tritiated silane features a specific activity of 0.5 mCi/mmol.

Competition experiments with different silanes show that SiEt₃H, SiPh₃H, and Si(OEt)₃H undergo deuteration with comparable rates. However, Si–H/Si–D exchange for SiEt₃H is ca. 500 times faster than that for SiⁱPr₃H or Si(SiMe₃)₃H. The rate of incorporation of D into phenyl silanes qualitatively follows the order SiPh₃H > SiPh₂H₂ > SiPh₃H. It thus seems that steric effects may be responsible for the observed differences.

Mechanistic studies on the Si–H/Si–D exchange are underway and will be reported in due course. The exchange may require the operation of eqs 3 and 4 that have been demonstrated experimentally. In accord with theoretical calculations these reactions imply, as already mentioned, participation of reactive σ-H₂ and σ-silane complex intermediates.^{18,19,29} In view of the lability of the agostic interaction in **1-H**⁺, it is also plausible that a σ-silane complex may result from coordination of the silane to **1-H**⁺. However present data indicate that such species is kinetically unstable toward dissociation into **1-H**⁺ and silane. Regardless of the precise mechanism, our catalytic Si–H/Si–D exchange constitutes a new example of metal–ligand cooperation³⁰ that implies reversible Rh–C bond cleavage and formation by action of dihydrogen and hydrosilanes.



In conclusion, a very productive catalytic procedure for hydrogen isotope exchange in hydrosilanes has been developed. Catalysis can

be carried out in an organic solvent solution or in a solvent-free manner, and the catalyst may be recycled a number of times. The catalyst is also effective for hydrosilylation of C–O and C–N multiple bonds and permits D or T incorporation into a wide class of organic molecules employing one-flask procedures. All these properties make the new method an environmentally benign, technically robust, short, and atom-efficient technology for incorporation of deuterium and tritium into organic molecules.

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Supporting Information Available: Experimental methods; synthesis and structural characterization of new compounds; X-ray structure analysis of complexes **1**⁺, **1-CO**⁺, and **1-NCMe**⁺; catalytic Si–H/D/T exchanges procedures; and computational details are included in the Supporting Information. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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