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C-H Silylation

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Revealing Silylation of Csp^2/sp^3-H Bonds in Arylphosphines by Ruthenium Catalysis

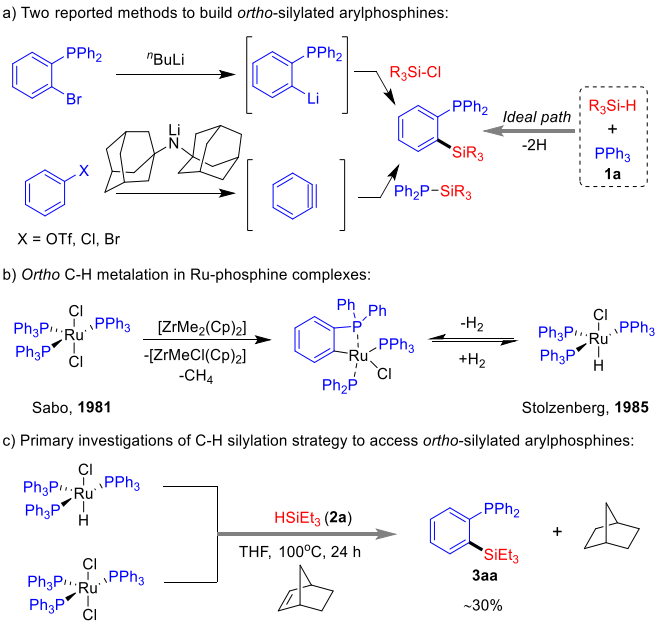
Jian Wen[+], *Ben Dong*[+], *Jinjun Zhu, Yue Zhao, and Zhuangzhi Shi**

Dedicated to the 100th anniversary of the School of Chemistry and Chemical Engineering, Nanjing University

Abstract: *The first aromatic C–H silylation between arylphosphines and hydrosilanes enabled by ruthenium complex has been developed. The excellent ortho-selectivity is resulted from a four-membered metallacyclic intermediate involving phosphorus chelation. The developed system can be extended to benzylic C–H silylation of arylphosphines. Diverse silylated arylphosphines are produced, exhibiting broad functional group compatibility. Further functionalization of the products under mild conditions renders the formed compounds useful building blocks.*

Silicon-containing compounds exhibit great interest in the fields of medicinal chemistry, advanced materials and complex molecule synthesis.[1] O*rtho*-silylated arylphosphines possess intriguing properties, which have been widely used for ligand design and diverse chemical transformation.[2] Although the modern organic synthesis has evolved rapidly, only two practical routes for the construction of these compounds have been explored so far, from the classic way on substitution of silicon electrophiles with lithiated arylphosphines formed in-situ[2] to a more recent method by lithium-di-1-adamantylamide-mediated aryne insertion into Si−P reagents (Scheme 1a).[3] Both approaches are useful, but they are often limited in scope and require pre-installation of functional groups such as halides into substrates and the use of large amounts of sensitive organometallic species. Therefore, the development of a simple and general approach to synthesize these compounds with excellent atom and step economy is still in high demand.

Coordiantion of arylphosphines with transition metals have been found to form the strained *ortho*-metallated rings.[4] In 1981, the Sabo group first reported that a $Ph_2P(o\text{-}C_6H_4)Ru$ complex could be generated by treatment of $[RuCl_2(PPh_3)_3]$ and $[ZrMe_2(Cp)_2]$ (Scheme 1b).[5] Later, Stolzenberg and coworkers also demonstrated the formation of the same complex from $RuHCl(PPh_3)_3$ and olefin.[6] Inspired by these previous results, we considered whether such metallated



Scheme 1. Synthesis of *ortho*-silylated arylphosphines.

species could further react with silicon reagents to form *ortho*-silylation products. To evaluate this hypothesis, we primary conducted these reactions with equimolar amounts of $[RuCl_2(PPh_3)_3]$ or $RuHCl(PPh_3)_3$ complex and hydrosilane **2a** in THF at 100°C (Scheme 1c). To our delight, these reactions afforded the desired silylation product **3aa** in trace amounts, as detected by GC-MS. Considering that the transformations proceed with formal loss of hydrogen, norbornene (NBE) was added as a hydrogen acceptor to the above systems. Both of the reactions conducted with NBE indeed led to a higher, but modest yield (~30%) of product **3aa**. Based on the results, a catalytic C-H silylation process was considered to access the o*rtho*-silylated arylphosphines.[7] Here, we report a Ru-catalyzed dehydrogenative silylation between arylphosphines and hydrosilanes chelation assisted by phosphorus atom.[8]

We started our studies by treatment of PPh_3 (**1a**) and Et_3SiH (**2a**) as the model substrates (Table 1). After systematic screening, we found that using 5.0 mol% of $[RuCl_2(p\text{-cymene})]_2$,[9] 5.0 equiv of norbornene as the hydrogen acceptor and 3.0 equiv of $CyNH_2$ as an base at 100 °C under an argon atmosphere in THF (0.5 M) provided the best results, affording product **3aa** in 79% yield (entry 1). Ruthenium complexes such as $(PPh_3)_3RuCl_2$ and $(PPh_3)_3RuHCl$ showed better results for this reaction (entries 2-3). However, they are not suitable as catalysts because mixed products could form when using other arylphosphines as substrates. Rhodium and iridium catalysts failed to promote this transformation (entries 4-5). Other

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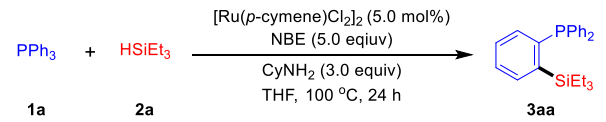
Table 1. Optimization of reaction conditions.[a]



1a 2a 3aa

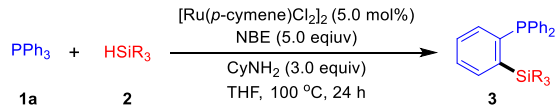
Entry	Variation from the standard conditions	Yield of **3aa** (%)[b]
1	none	79
2	$(PPh_3)_3RuCl_2$ instead of $[RuCl_2(p\text{-cymene})]_2$	82
3	$(PPh_3)_3RuHCl$ instead of $[RuCl_2(p\text{-cymene})]_2$	85
4	$[Rh(cod)Cl]_2$ instead of $[RuCl_2(p\text{-cymene})]_2$	trace
5	$[Ir(OMe)cod]_2$ instead of $[RuCl_2(p\text{-cymene})]_2$	0
6	Using cyclohexene instead of NBE	63
7	Without $CyNH_2$	22
8	Et_3N instead of $CyNH_2$	55

[a]Reaction conditions: cat [TM] (10 mol %), **1a** (0.3 mmol), **2a** (1.5 mmol), NBE (1.5 mmol) and $CyNH_2$ (0.9 mmol) in THF (0.6 mL) at 100 °C for 24 h, under argon. [b]Isolated yields.

hydrogen acceptors, such as cyclohexene, were also effective, albeit with a slightly lower yield (entry 6). It was confirmed that the reaction became sluggish without the addition of the base $CyNH_2$ (entry 7). Finally, when the reaction was conducted with other organic bases, such as Et_3N, the desired product **3aa** was formed in a much lower yield (entry 8).

We first investigated a range of hydrosilane **2** with phosphine **1a** (Table 2). Hydrosilanes, including tributylsilane (**2b**), trihexylsilane (**2c**), diethylmethylsilane (**2d**) and cyclohexyldimethylsilane (**2e**), could form the corresponding silylation products **3ab**-**3ae** in 51-72% yields. Among them, the structure of **3ae** was confirmed by X-ray diffraction analysis. The sterically hindered silane $HSiMe(OTMS)_2$ (**2j**) has been applied in aromatic C–H silylation to achieve excellent remote steric control using rhodium catalysis.[10] This bulky hydrosilane did not hinder the phosphorus-directed *ortho*-selective C-H silylation, affording desired product **3aj** in 67% yield in the absence of the base.[11]

Table 2. Substrate scope of hydrosilanes.[a]



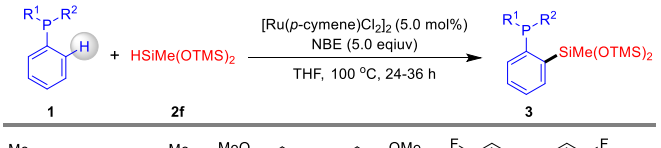
1a 2 3

H-SiEt$_3$ (**2a**)	**3aa**, 79%	
H-Si(^{n}Bu)$_3$ (**2b**)	**3ab**, 72%	
H-Si(^{n}Hex)$_3$ (**2c**)	**3ac**, 63%	
H-SiMeEt$_2$ (**2d**)	**3ad**, 51%	
H-SiMe$_2$Cy (**2e**)	**3ae**, 55%	X-ray of **3ae**
H-SiMe(OTMS)$_2$ (**2f**)	**3af**, 75%[b]	CCDC 1981299

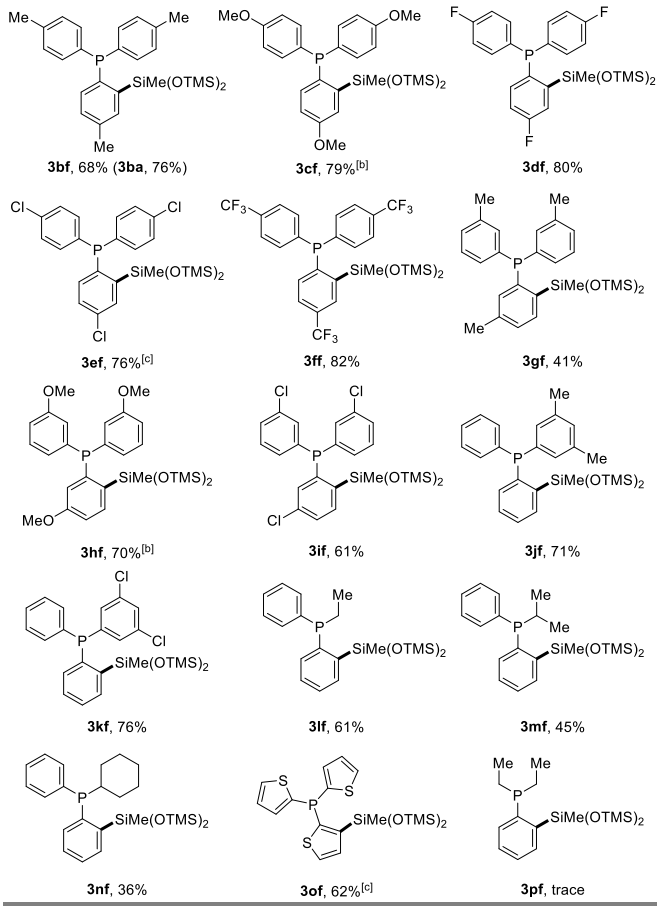
[a]Reaction conditions: $[Ru(p\text{-cymene})Cl_2]_2$ (5.0 mol %), **1a** (0.3 mmol), **2** (5.0 eqiuv), NBE (1.5 mmol) and $CyNH_2$ (1.5 mmol) in THF (0.6 mL) at 100 °C for 24 hours under argon; isolated yields. [b]Without $CyNH_2$, in THF (0.1 mL).

Given that the formed Ar-$SiMe(OTMS)_2$ motif can be easily functionalized under mild conditions, we next subjected various phosphines **1** with hydrosilane **2f** (Table 3). Aryl moieties in triarylphosphines **1b-1f**, with methyl (**1b**), methoxy (**1c**), F (**1d**), Cl (**1e**), and CF_3 (**1g**) groups at the *para* position, were compatiable, and the desired products **3bf-3ff** were generated in moderate to good yields. Treatment of *meta*-substituted triarylphosphines **1g-1i** in our catlytic system, C-H silylation only occured at the less hindered C-H bonds. Phosphines **1j** and **1k**, containing two different aryls for C-H silylation, showed excellent selectivity for reaction of the sterically more hindered ones. Diarylalkylphosphines bearing primary (**1l**) and secondary (**1m**, **1n**) aliphatic substituents, exhibited the sole selectivity at the aromatic C-H bonds. In addition, heteroaromatic phosphines such as **1o** could also be used for such transformation. However, phosphine **1p** with two ethyl substituents displayed very low reactivity under the current reaction conditions.

Table 3. Substrate scope of arylphosphines.[a]



1 2f 3



[a]Reaction conditions: $[Ru(p\text{-cymene})Cl_2]_2$ (5.0 mol %), **1** (0.3 mmol), **2f** (1.5 mmol), NBE (1.5 mmol) in THF (0.1 mL) at 100 °C for 24 hours under argon; isolated yields. [b]36 h. [c]THF (0.6 mL) was used.

The developed system was also found to display good reactivity for Csp^3–H bonds (Table 4).[12] Emplyment of phosphine **1q** bearing an *ortho*-methyl group with Et_3SiH (**2a**)

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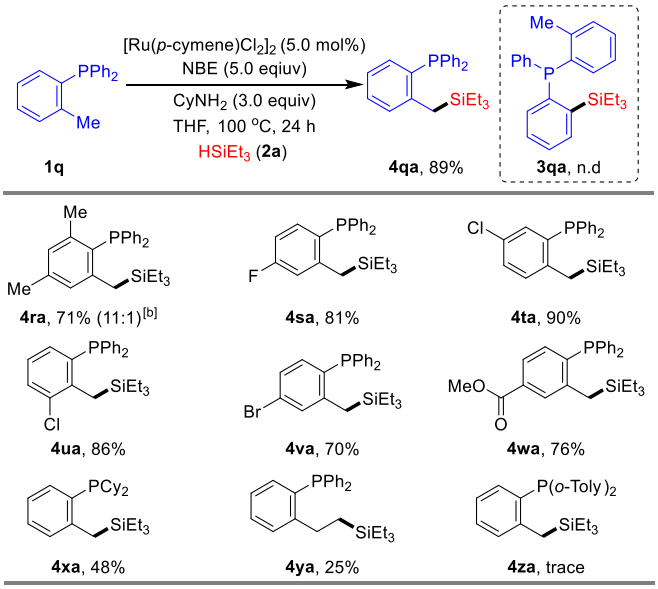
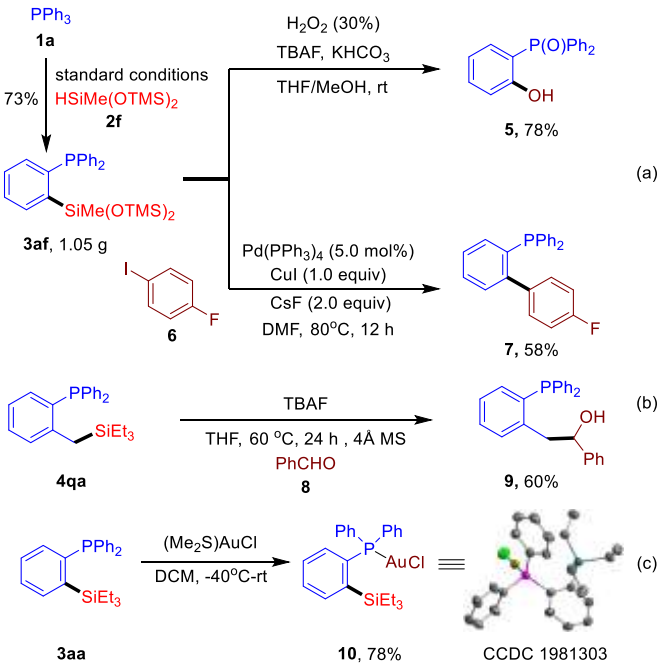
in our catalytic system, benzylic C-H silylation occurred preferentially to afford **4qa** in excellent yield. Upon reaction of phosphine **1r** with a bulky mesityl group, the mono-substituted product **4ra** was obtained with a small amount of disilylation product **4ra'** (**4ra**:**4ra'** = 11:1). Other triarylphosphines **1s-1w** with different substituents, including F (**1s**), Cl (**1t-1u**), Br (**1v**) and COOMe (**1w**), underwent facile benzylic C-H silylation. In the case of phosphine **1y** with an ethyl group, the silylation occured exclusively at the methyl group. Further investigation showed that phosphine **1z** containing three *o*-tolyl moieties could only transfer into the desired product **4za** in trace amounts.

Table 4. Ru-catalyzed Csp^3–H silylation in arylphosphines.[a]



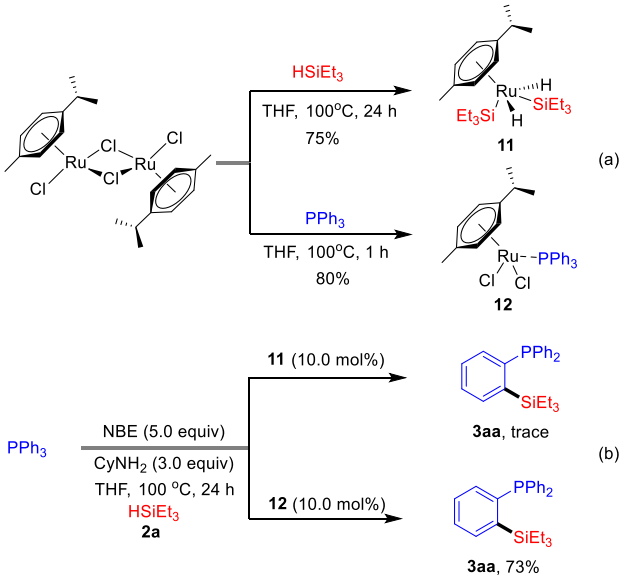
[a]Reaction conditions: [Ru(*p*-cymene)Cl_2]$_2$ (5.0 mol %), **1** (0.3 mmol), **2a** (1.5 mmol), NBE (1.5 mmol) and $CyNH_2$ (3.0 equiv) in THF (0.5 mL) at 100 °C for 24 hours under argon; isolated yields. [b]Determined by ^{1}H NMR.

To showcase the practical utility of this C-H silylation process, further investigations were conducted (Scheme 2). This silylation reaction was viable on the gram scale. To demonstrate this potential, 3.0 mmol of phosphine **1a** was silylated with $HSiMe(OTMS)_2$ (**2j**) under our established conditions, affording product **3af** in 73% yield, consistent with the small-scale trial. With compound **3af** in hand, some synthetic transformations were also demonstrated (Scheme 2a). Treatment of **3af** with H_2O_2 (30%) generated a hydroxylation product **5** in 78% yield. Pd-catalyzed Hiyama cross-coupling of **3af** with iodoarene **6** furnished Buchwald-type phosphine **7** in moderate yield. The silyl moiety at the benzylic position of phosphines can also be further functionalized under mild conditions (Scheme 2b). For example, the reaction of product **4qa** with benzaldehyde (**8**) and TBAF could produce alcohol **9** in 60% yield. Moreover, *ortho*-silylated arylphosphines have some special properties as ligands with transition metals. For instance, coordination of *ortho*-silylated arylphosphine **3aa** with a gold salt could form complex **10** in good yield (Scheme 2c).[13]



Scheme 2. Synthetic applications.

When stoichiometric amout of [$RuCl_2$(*p*-cymene)]$_2$ was allowed to react with Et_3SiH (**2a**) or PPh_3 (**1a**) in THF at100 °C, two complexes, **11**[14] and **12**[15], were obtained respectively (Scheme 3a). Further investigation demonstrated that product **3aa** could be generated by a catalytic amount of complex **12** (Scheme 3b). These results indicate that the catalyst [$RuCl_2$(*p*-cymene)]$_2$ first coordinates with phosphine to form complex **12**, which can undergo dehydrogenative silylation with $HSiEt_3$ (**2a**) using NBE as the hydrogen acceptor[16] through the key four-membered ring intermediate.



Scheme 3. Investigation of the possible intermediates.

In summary, we have demonstrated an important advance which could considerably broaden the *ortho*-selective C–H silylation process to arylphosphines. [$RuCl_2$(*p*-cymene)]$_2$ can serve as a unique catalyst in this transformation for the silylation of Csp^2 and Csp^3-H bonds with hydrosilanes. This

method shows excellent atom and step economy, greatly simplifying the construction the library of *ortho*-silylated arylphosphines for research in chemistry. Diverse C-H functionalization of arylphosphines and detailed mechanistic investigation of this C-H silylation process are currently being carried out in our group.

Acknowledgments

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Keywords: phosphorus ·C-H activation ·silylation ·site-selectivity ·coordination

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C-H Silylation

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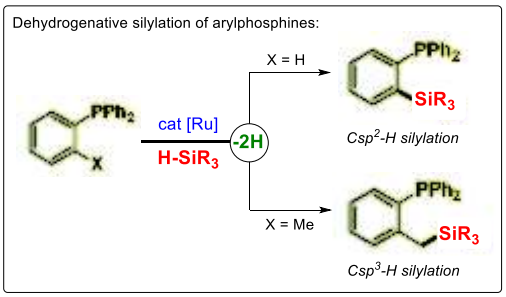
Revealing Silylation of Csp^2/sp^3-H Bonds in Arylphosphines by Ruthenium Catalysis



SiRuP: An efficient Ru-catalyzed system has been uncovered for *ortho*-selective aromatic C-H silylation of arylphosphines with hydrosilanes chelation assisted by phosphorus atom. When the arylphosphine contains an *ortho*-methyl group, silylation takes place preferentially at the benzylic C–H bond.