Rhodium-Catalyzed Intramolecular Silylation of Unactivated C(sp³)—H Bonds

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The treatment of a variety of hydrosilanes, each incorporating a benzylic $C(sp^3)$ -H bond, with a rhodium catalyst resulted in intramolecular dehydrogenative silylation. This silylation reaction was found to occur at typically unreactive $C(sp^3)$ -H bonds located at terminal positions on alkyl chains. Interestingly, the rhodium catalyst also promoted regioselective silylation at a site internal to an alkyl chain.

C–H bond functionalization is one of the most useful and most versatile techniques for the synthesis of organic molecules. As a result of the significant amount of research recently applied to this aspect of synthetic chemistry, the number of potential C–H bond transformations has increased dramatically, especially in the case of $C(sp^2)$ –H bonds.¹ In contrast, examples of transformations via $C(sp^3)$ –H bond activation are still rare.¹ While there have been several reports concerning $C(sp^3)$ –H bond transformations at benzylic² and allylic³ C–H bonds and at C–H bonds adjacent to a heteroatom,⁴ it is typically difficult to achieve the functionalization of unactivated $C(sp^3)$ –H bonds.⁵ Such functionalizations are challenging partly because the $C(sp^3)$ –H bond is particularly strong and also since it is difficult to control the regioselectivity of the process. The few reports of successful functionalization include the selective borylation of alkanes at terminal carbons,⁶ transformations of $C(sp^3)$ –H bonds adjacent to quaternary carbon centers,⁷ $C(sp^3)$ –H bond functionalizations using a bidentate directing group,⁸ and others.⁹

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We have recently reported the rhodium-catalyzed synthesis of silafluorene derivatives via Si-H and $C(sp^2)-H$ bond activation.¹⁰ On reacting a biphenylhydrosilane bearing a methyl group at the *ortho*-position of the phenyl group (A in Figure 1), the desired intramolecular $C(sp^2)$ -H bond silvlation proceeded and the corresponding silafluorene derivative **B** was formed in low yield. Interestingly, silvlation also proceeded at the $C(sp^3)$ -H bond of the methyl group, and 5.6-dihydrodibenzolb.d|silane C was obtained in 47% yield as the major product (Figure 1). This result encouraged us to investigate benzylic $C(sp^3)$ -H bond silvlation employing rhodium catalysis. We report herein the rhodium-catalyzed silvlation of a benzylic $C(sp^3)$ -H bond. This work further demonstrated that this catalytic rhodium system can also promote the regioselective silvlation of unactivated terminal and internal $C(sp^3)$ -H bonds.



Figure 1. Rhodium-catalyzed silylation of aromatic $C(sp^2)$ -H and benzylic $C(sp^3)$ -H bonds.

Compared with the biphenylhydrosilane **A**, the silyl moiety of (2-methylbenzyl)hydrosilane (**1a** in eq 1) possesses significantly more freedom of motion. We therefore anticipated that the transformation of **1a** would be more difficult for entropic reasons. Indeed, treatment of **1a** with a catalytic amount of a rhodium complex, $[RhCl(PPh_3)_3]$, gave the desired benzylic $C(sp^3)$ -H silylation (resulting in

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the formation of 2,3-dihydro-1*H*-benzo[*b*]silole, **2a**) in only 8% yield. However, on changing the catalyst to a mixture of catalytic amounts of a rhodium complex, $[RhCl(cod)]_2$, and 1,3-bis(diphenylphosphino)propane (dppp), the yield of **2a** increased dramatically and this product was obtained in 61% yield (eq 1).^{11,12}

We next investigated the variety of substrates to which this reaction is applicable (Table 1). Usually, functionalization of an unactivated $C(sp^3)$ -H bond in tertiary alkyl groups is readily accomplished, compared with primary and secondary alkyl positions.⁷ Similarly, the silylation reaction of the tertiary $C(sp^3)$ -H bond of **1b** proceeded efficiently when applying our catalytic system, and the





^{*a*} 1.0 M. ^{*b*} Isolated yield. ^{*c*} 1,2-Bis(diphenylphosphino)benzene (4.5 mol %) was added as a phosphine ligand. ^{*d*} 4 h. ^{*e*} [RhCI(cod)]₂ (2.5 mol %), 1,2-bis(diphenylphosphino)benzene (7.5 mol %). ^{*f*} GC yield. ^{*g*} 0.08 M, [RhCI(cod)]₂ (6.0 mol %), 1,2-bis(diphenylphosphino)benzene (18 mol %), and 3,3-dimethyl-1-butene (2.0 equiv) were added as a phosphine ligand and hydrogen acceptor.

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corresponding five-membered compound 2b was provided in 80% yield (entry 1). Treatment of (2-ethylphenyl)dimethylsilane (1c) with catalytic amounts of [RhCl(cod)]₂ and dppp gave 1,1-dimethyl-2,3-dihydro-1H-benzo[b]silole (2c) in 66% yield (entry 2).^{13–17} This result shows that the silvlation of primary unactivated alkyl C(sp³)-H bonds can also be achieved. The silvlation reaction also proceeded when using 1d, a hydrosilane with two phenyl groups on the silicon atom (entry 3). When employing substrates bearing a methoxy group on the aromatic ring or a naphthalene moiety as the aromatic ring, the corresponding silvlated products 2e and 2f were obtained in reasonable yields (entries 4 and 5). In the above syntheses, the aromatic ring can be considered to play an important role by fixing the relative conformational positions of the hydrosilyl and $C(sp^3)$ -H reactive sites. However, our results demonstrate that this intramolecular silvlation reaction also proceeded without the presence of aromatic rings. The silacyclopentane (2g) was produced in 43% yield when tributylsilane (1g) was treated with a catalytic amount of the rhodium catalyst (entry 6).¹⁸⁻²⁰ Interestingly, the silvlation reaction also proceeded at the internal aliphatic position of 1h, and the corresponding dihydrobenzosilole 2h was obtained in 37% yield (entry 7). This result is important because many previous reactions proceeded only at the terminal aliphatic positions. It is worthy of special mention that, in entry 7, the regioselectivity was controlled completely.²¹

(12) There have been several reports on silulation of benzylic C-H bonds. See: Mita, T.; Michigami, K.; Sato, Y. *Org. Lett.* **2012**, *14*, 3462. See also ref 2d.

(13) The structure of **2c** was determined by comparison of its ¹H and ¹³C NMR and GC-MS spectra with those of the same compound prepared by another method. See: Benkeser, R. A.; Mozdzen, E. C.; Muench, W. C.; Roche, R. T.; Siklosi, M. P. *J. Org. Chem.* **1979**, *44*, 1370.

(14) RhCl(PPh₃)₃ (3.0 mol %), 22%; [Rh(cod)]BF₄ (3.0 mol %) + dppp (9.0 mol %), 25%; (1,4-dioxane, 180 °C, 24 h); [IrCl(cod)]₂ (1.5 mol %) + dppp (4.5 mol %), 16%; Pd(PPh₃)₄ (3.0 mol %, 150 °C), 9%; Pd₂(dba)₃ (1.5 mol %), 0%. Product **2c** was not obtained: Pd/C, Pd/CaCO₃, RhH-(CO)(PPh₃)₃, Rh₄(CO)₁₂, Ru₃(CO)₁₂, Ir₄(CO)₁₂, Re₂(CO)₁₀.

(15) Investigation of several combinations of catalytic amounts of $[RhCl(cod)]_2$ and several phosphine (and amine) ligands: 1,2-bis-(diphenylphosphino)ethane (dppe), 50%; 1,2-bis(diphenylphosphine)ethane, (dppb), 16%; 1,2-bis[di(pentafluorophenyl)phosphine]ethane, 56%; 1,1'-bis(diphenylphosphine)ferrocene (dppf), 44%; 1,2-bis-(diphenylphosphino)benzene, 66%; bis(2-biphenylyl)phenylphosphine, 19%; BINAP, 38%; TMEDA, 7%; 1,10-phenanthroline, 21%.

(16) Investigation of several solvents: cyclopentylmethylether (CPME), 68%; dibutylether, 15%; toluene, 65%; *p*-xylene, 29%; mesi-tylene, 28%; octane, 5%; neat, 10%. Product **2c** was not obtained: 1,1,2-trichloroethane, DMF.

(17) Investigation of reaction temperature: 150 °C, 5%; 135 °C, 4%.
(18) The structure of 2g was determined by comparison of its ¹H and ¹³C NMR and GC-MS spectra with those of the same compound prepared by another method. See ref 10.

(19) For an example of intramolecular dehydrogenative silvlation at the terminal position of the alkyl chain, see: Tsukada, N.; Hartwig, J. F. *J. Am. Chem. Soc.* **2005**, *127*, 5022.

(20) During our investigation, Hartwig's group reported iridiumcatalyzed intramolecular silylation at the terminal positions of alkyl chains. See: Simmons, E. M.; Hartwig, J. F. *Nature* **2012**, *483*, 70.

(21) The obtained silapentane derivatives are precursors of 1,4-diols by oxidation. See: Reference 20. See also: Kuznetsov, A.; Gevorgyan, V. *Org. Lett.* **2012**, *14*, 914.

The proposed mechanism for aliphatic $C(sp^3)$ -H bond silylation is presented in Scheme 1. In step (1), the oxidative addition of the Si-H bond of 1 to a rhodium center takes place, resulting in Si-H bond activation. After the formation of intermediate **D**, there are two possible pathways. One possible route (2) involves σ -bond metathesis between the Rh-H and C-H bonds of intermediate **D** via the elimination of H₂ to give intermediate **E**. The alternate pathway (3) consists of the oxidative addition of the $C(sp^3)$ -H bond of the alkyl chain (C-H bond activation) followed by reductive elimination (4) to produce intermediate **E** with the formation of H₂. After the formation of intermediate **E**, reductive elimination (5) occurs to give product **2** and regenerate the rhodium catalyst.





In summary, we have succeeded in the rhodium-catalyzed silylation of a benzylic $C(sp^3)$ —H bond. In addition, we have demonstrated the regioselective intramolecular silylation of unactivated terminal and internal $C(sp^3)$ —H bonds using this rhodium-based catalytic system. Since it is usually difficult to functionalize an unactivated $C(sp^3)$ —H bond regioselectively, especially at internal positions along an alkyl chain, these results are important. In addition, this is the first example of regioselective silylation of a $C(sp^3)$ —H bond at a location internal to an alkyl chain. It is our hope that these novel silylation reactions will provide useful insights into the future possibilities of this aspect of synthetic organic chemistry.

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Supporting Information Available. General experimental procedures and characterization data for $C(sp^3)$ -H silylated products 2. This material is available free of charge via the Internet at http://pubs.acs.org.

⁽¹¹⁾ Investigation of several hydrogen acceptors: norbornene, 59%; cyclohexene, 49%; 3,3-dimethyl-1-butene, 44%; methyl acrylate, 0%. In this reaction, the yield of 2a decreased by adding a hydrogen acceptor.

The authors declare no competing financial interest.