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Rhodium-Catalyzed Reductive Cleavage of Carbon−Cyano Bonds with Hydrosilane: A Catalytic Protocol for Removal of Cyano Groups

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Synthetic methodologies for removing functional groups from organic molecules have long played a profitable role in organic synthesis, as exemplified by the widespread use of Barton−McCombie deoxygenation,[1a] Krapcho decarboxylation in acetoacetic and malonic ester syntheses,[1b] Tsuji−Wilkinson decarbonylation,[1c] and many others.[1d,e] In this context, the methods that transform organic nitriles into their parent alkanes or arenes should find utility, since such processes enable the temporary use of the beneficial features of a cyano functionality, such as α-C−H acidity[2] and the ortho-directing effect.[3] Methods for the reductive cleavage of a C−CN bond are less common, however, and generally suffer from the use of strong reducing agents (Na/NH_3, K, or $LiAlH_4$) and from a limited scope.[4] Herein, we report a general catalytic protocol for the reduction of C−CN bonds using hydrosilane as a reducing agent (eq 1).

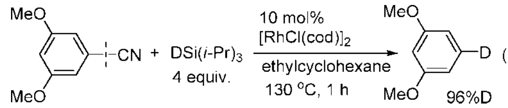
$$\text{R}\text{–}\text{CN} + \text{HSi}(i\text{-Pr})_3 \xrightarrow[\text{cat. P(OR')}_3]{\text{cat. [RhCl(cod)]}_2} \text{R–H} \quad (1)$$

$$\boxed{\text{R = aryl, 1°, 2°, 3° alkyl}}$$

Previously, we have reported that C−CN bonds of aryl and alkenyl cyanides can be cleaved and silylated with disilanes in the presence of a rhodium catalyst[5] via a unique silicon-assisted mechanism.[6] We envisaged the use of hydrosilane in place of disilane resulting in a reductive cleavage of the C−CN bond in view of Nakazawa's reports on the photoinduced reductive decyanation of nitriles with hydrosilanes catalyzed by iron complexes.[6d−f] Our initial experiments focused on the reaction of 2-cyanonaphthalene with hydrosilane in the presence of a rhodium catalyst. After a series of optimization studies,[7] we found that the use of triisopropylsilane (**1**) as a reducing agent and $P(OBu)_3$ as a ligand afforded the desired decyanated product quantitatively (entry 1 in Table 1).

As shown in Table 1, a wide array of aryl cyanides can be reduced to the corresponding arenes under these catalytic conditions. Functional groups, such as ethers (entries 2, 7, 8, and 12), amines (entry 3), amides (entry 4), esters (entries 5 and 12), boronic esters (entry 6), and heteroaryls (entry 13), can be tolerated. Benzonitriles bearing an ortho substituent were successfully applied to this catalysis (entries 8−9). Notably, highly congested nitriles, 2,6-disubstituted benzonitrile (entry 10) and antracene-9-carbonitrile (entry 11), were efficiently decyanated.

A cyano group can be replaced with a deuterium atom by using deuteriosilane (eq 2). This method should be broadly applicable to the regiospecific synthesis of deuterium-labeled arenes under neutral conditions.



In addition to aromatic cyanides, benzylic C−CN bonds can also be efficiently transformed into C−H bonds under these catalytic conditions (entries 1−4, Table 2). In the reactions of these substrates, the use of $P(O\text{-}i\text{-}Pr)_3$ as a ligand generally resulted in better yields than those obtained using $P(OBu)_3$. Nitriles bearing their cyano groups at primary (entry 1) and secondary (entry 2) benzylic positions afforded the corresponding decyanated products in good yields. Notably, substrates containing tertiary benzylic C−CN bonds, such as trityl cyanide (entry 3) and a cyanoacetate derivative (entry 4), can react. Motivated by the successful results with benzylic substrates, we next turned our attention to the applicability of simple alkyl cyanides. The catalytic methods for the activation of C−CN bonds in alkyl cyanides, especially those containing a β-hydrogen atom, are particularly rare, due, in part, to the facile β-hydride elimination of the resultant metal σ-alkyl intermediates.[8] We were pleased to find that the catalytic reaction of tridecanenitrile afforded the reduced product, dodecane, in 78% yield (entry 5). In addition, catalytic decyanation of 3-phenylpropionitrile, which is prone to affording styrene via β-hydrogen elimination, proceeded smoothly to furnish ethylbenzene quantitatively (entry 6). Introduction of a bulky substituent at the α-position of primary alkyl cyanides did not deteriorate the efficiency of the reaction (entry 7). Importantly, catalytic reductive decyanation proved to be applicable to secondary alkyl cyanides

Table 1. Rh-Catalyzed Reductive Decyanation of Aromatic Nitriles[a]

$$\text{Ar–CN} + \underset{\textbf{1}\ \text{(2 equiv.)}}{\text{H–Si}(i\text{-Pr})_3} \xrightarrow[\substack{\text{ethylcyclohexane}\\ 130\ ^{\circ}\text{C, 15 h}}]{\substack{\text{[RhCl(cod)]}_2\ \text{(5 mol\%)}\\ \text{P(OBu)}_3\ \text{(10 mol\%)}}} \text{Ar–H}$$

entry	Ar	yield (%)[b]	entry	Ar	yield (%)[b]
1	2-naphthyl	99[c]	8	$(2\text{-PhO})C_6H_4$	95
2	$(4\text{-MeO})C_6H_4$	74[c]	9	$(2\text{-Ph})C_6H_4$	89
3	$(4\text{-Me}_2N)C_6H_4$	76[c]	10[e]	$(2,4,6\text{-tri-Me})C_6H_2$	81
4	$(4\text{-AcMeN})C_6H_4$	85	11[e,f]	9-anthracenyl	94
5	$(4\text{-EtO}_2C)C_6H_4$	84	12	$(2\text{-MeO-5-MeO}_2C)C_6H_3$	77
6[d]	$(4\text{-Bpin})C_6H_4$	94	13[g]	1-Ts-3-indolyl	81
7	$(3\text{-MeO})C_6H_4$	64[c]			

[a] Reaction conditions: aryl cyanide (0.5 mmol), **1** (1.0 mmol), $[RhCl(cod)]_2$ (0.025 mmol), $P(OBu)_3$ (0.05 mmol) in ethylcyclohexane (0.25 mL) at 130 °C for 15 h. [b] Isolated yields are based on aryl cyanides unless otherwise noted. [c] Determined by GC due to the volatility of the product. [d] Pin = pinacolate. [e] Run at 160 °C using $[RhCl(cod)]_2$ (0.05 mmol) in the presence of $P(O\text{-}i\text{-}Pr)_3$ (0.10 mmol). [f] Toluene was used as a solvent. [g] Run at 100 °C in the absence of $P(OBu)_3$.

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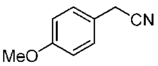
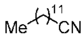
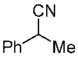
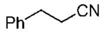
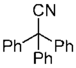
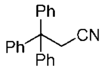
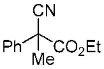
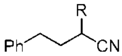
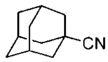
Table 2. Rh-Catalyzed Reductive Decyanation of Aliphatic Nitriles[a]

$$\text{R-CN} + \text{H-Si}(i\text{-Pr})_3 \xrightarrow[\text{ethylcyclohexane, } 160\ ^{\circ}\text{C, } 15\ \text{h}]{[\text{RhCl(cod)}]_2\ (10\ \text{mol\%}),\ \text{P(O-}i\text{-Pr)}_3\ (20\ \text{mol\%})} \text{R-H}$$

1 (2 equiv.)

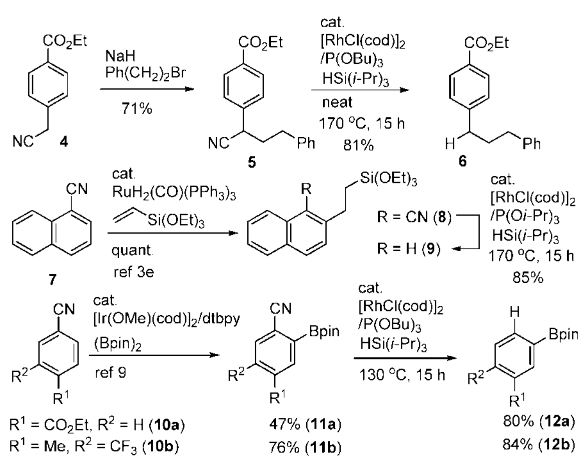
entry	R−CN	yield (%)[b]	entry	R−CN	yield (%)[b]
1[c,d]		75	5		78[e]
2[c]		90[e]	6		99[e]
3		91	7		95
4[f]		91	8		98 (R = Me)[e]
			9[g]		93 (R = Et)
			10		43[e]

[a] Reaction conditions: alkyl cyanide (0.5 mmol), **1** (1.0 mmol), $[\text{RhCl(cod)}]_2$ (0.05 mmol), and $\text{P(O-}i\text{-Pr)}_3$ (0.10 mmol) in ethylcyclohexane (0.25 mL) at 160 °C, 15 h. [b] Isolated yields based on alkyl cyanides unless otherwise noted. [c] Run at 130 °C. [d] Run in the absence of $\text{P(O-}i\text{-Pr)}_3$. [e] Determined by GC due to the volatility of the product. [f] Run using **1** (2.0 mmol), $[\text{RhCl(cod)}]_2$ (0.10 mmol) at 80 °C in the absence of $\text{P(O-}i\text{-Pr)}_3$. [g] Run at 170 °C using **1** (2.5 mmol) in the absence of solvent.

(entries 8 and 9). The reaction of 2-methyl-4-phenylbutanenitrile afforded the corresponding decyanated product uneventfully (entry 8). On the other hand, nitrile bearing a slightly bulkier group resulted in the formation of pentylbenzene (64%) along with a β-hydrogen elimination product (*E*-pent-1-enylbenzene, 28%) under the same conditions, indicating the sensitivity of this reaction toward a steric effect. However, increasing the amount of hydrosilane completely suppressed the undesired β-hydrogen elimination and afforded pentylbenzene in excellent yield (entry 9). In cases where β-hydrogen elimination is not allowed for geometric reasons, even tertiary alkyl cyanides can be applied to catalytic decyanation (entry 10).

Rhodium-catalyzed reductive decyanation provides diverse opportunities for application to organic synthesis (Scheme 1). For example, α-alkylation of benzyl cyanide **4**, followed by the treatment of the obtained **5** with hydrosilane **1** in the presence of $[\text{RhCl(cod)}]_2$ and P(OBu)_3, afforded alkylarene **6** in 81% yield. This protocol opens up the utility of benzyl cyanides as a benzyl anion equivalent. Also, our catalytic reductive decyanation reaction enables the use of a cyano group as a *removable* ortho-directing group in some catalytic C−H bond functionalization reactions. A ruthenium-catalyzed reaction of nitrile **7** with vinylsilane furnishes an alkylated product **8** in a regioselective manner.[3e] The cyano group in **8** can be removed by treatment with hydrosilane under rhodium catalysis to afford **9** in 85% yield. A catalytic C−H bond borylation of benzonitrile derivatives **10** proceeded to form arylboronic esters **11** regioselectively due to the steric directive effect of a cyano group.[9] Subsequent decyanation afforded borylated arenes **12**, which are difficult to access by direct borylation of the corresponding arenes.

Scheme 1. Synthetic Applications



In summary, we have established a general catalytic protocol for the removal of a cyano group using hydrosilane as a mild reducing agent. A notable aspect of the present rhodium-catalyzed reductive decyanation reaction is its wide scope of substrates, including aromatic, β-hydrogen-containing primary and secondary, and some tertiary alkyl cyanides bearing a variety of functional groups. In this respect, the present silicon-assisted C−CN bond cleavage strategy is advantageous over C−CN bond cleavage via oxidative addition, which normally accompanies β-hydrogen elimination when applied to alkyl cyanides.[8] The utility of this decyanation protocol was also demonstrated in the α-substitution of benzyl cyanides and cyano-directed C−H bond functionalization reactions. Future studies will continue to explore additional catalytic reactions involving silicon-assisted C−CN bond cleavage.

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Supporting Information Available: Detailed experimental procedures, characterization of products, and a possible mechanism. This material is available free of charge via the Internet at http://pubs.acs.org.

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