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Nickel-catalyzed decyanation of inert carbon–cyano bonds[†]

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Nickel catalyzed decyanation of aryl and aliphatic cyanides with hydrosilane as the hydride source has been developed. This method is easy to handle, scalable and can be carried out without a glove box. The method has been applied in the cyanide directed functionalization reaction and α -substitution of benzyl cyanide.

Removal of a specific functional group after using its beneficial aspects plays an important role in synthetic chemistry.¹ Although a wide variety of effective approaches now exists for a number of defunctionalization reactions,² some of these have been only recently discovered and need further improvement. Synthetic methodology for the removal of the cyano group can be advantageous due to its *ortho*-directing ability and α -C-H acidity.^{3,4} The electron withdrawing character of a cyano group brings about challenging coupling reactions by making metal-mediated steps *i.e.* oxidative addition and reductive elimination faster than the unsubstituted analogues and thus a decyanation protocol will allow synthetic chemists to take advantage of the cyano group.^{1a,b}

The high bond dissociation energy of the C–CN bond and limited successes of (aryl/alkyl) cyanides as the coupling partner compared to (aryl/alkyl) halides imposes a scientific challenge to develop mild and efficient methods for its reductive cleavage.⁵ Previous decyanation reactions relied on oxidative addition to the silyl hydride and then silicon-assisted carbon–cyano bond cleavage reactions.^{3*a,c,h*} Another powerful approach could be *via* insertion of a transition metal into the C–CN bond and subsequent formation of the decyanated product with a hydride source (Scheme 1). In this context, we note that nickel mediated oxidative addition to the C–CN bond and related transformations are reported in the literature.^{1*a*,6} Herein, we report a general and mild Ni-catalyzed method for reductive cleavage of unactivated C–CN bonds with (Me₂SiH)₂O [tetramethyldisiloxane, TMDSO] as the hydride source.

In order to realize the C-CN bond cleavage, we began our investigation by evaluating a variety of ligand systems for nickel in



Scheme 1 Catalytic decyanation reactions of R-CN.

the presence of various hydride donors such as TMDSO, Et₃SiH, ^{*i*}Pr₃SiH, and Ph₂SiH₂. We studied 2-cyanonaphthalene as the substrate in the presence of various nickel sources including Ni(COD)₂ (COD, 1,5-cyclooctadiene), Ni(acac)₂ (acac, acetylacetonate), NiCl₂, Ni(OAc)₂ *etc.* Use of Lewis acid (AlMe₃) can facilitate oxidative addition into the C–CN bond⁶ and was, therefore, found to be beneficial in terms of substrate scope and yields of the decyanation reactions.

These extensive experimentations showed that the Ni(acac)₂ complex of PCy₃ (or PCy₃·HBF₄ with equimolar K_3PO_4) in combination with TMDSO [(Me₂SiH)₂O] can catalyze the reductive decyanation of R-CN substrates efficiently.

Encouraged by our initial findings, we set out to explore the substrate scope for this Ni(acac)₂ catalyzed reductive decyanation reaction (Table 1). The aryl alkyl ether bonds (Ar–O–R; R = Me, ^{*n*}Bu) were tolerated (**1a**, **1b** and **1j**) under our reaction conditions, thus exhibiting a preference for reductive cleavage of the C–CN bond over Ar–O–R.^{2*b*,*c*,⁷} A monodecyanated product was observed from substrates bearing dicyano groups (**1a** and **1g**). Ester (**1c** and **1h**) and keto (**1i**) groups were also tolerated. Although not essential, presence of an *ortho*-directing group or an *ortho*-substituent was found to be beneficial in achieving better yield of the desired decyanated product.

Having demonstrated the protocol on aryl derivatives, we next focused on heterocyclic cyano compounds. As expected, nickel catalyst can be employed in combination with a hydride source for

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Table 1 Ni-catalyzed reductive decyanation of aryl cyanides



130 °C, 24 h. ^{*a*} R–CN (0.5 mmol), Ni(acac)₂ (15 mol%), PCy₃ (30 mol%), (Me₂SiH)₂O, AlMe₃, toluene. ^{*b*} R–CN (0.5 mmol), Ni(acac)₂ (20 mol%), PCy₃ (40 mol%), (Me₂SiH)₂O, AlMe₃, toluene. ^{*c*} R–CN (0.5 mmol), Ni(acac)₂ (30 mol%), PCy₃ (90 mol%), (Me₂SiH)₂O, AlMe₃, toluene. ^{*d*} 12% Biphenyl.

Table 2 Ni-catalyzed reductive decyanation of heterocycles



130 °C, 24 h. ^{*a*} R–CN (0.5 mmol), Ni(acac)₂ (15 mol%), PCy₃ (30 mol%), (Me₂SiH)₂O, AlMe₃, toluene. ^{*b*} R–CN (0.5 mmol), Ni(acac)₂ (30 mol%), PCy₃ (60–90 mol%), (Me₂SiH)₂O, AlMe₃, toluene.

effective decyanation of heterocyclic cyanides (Table 2). Substrates with two different heteroatoms can be employed successfully (2a, 2b, 2i and 2j) indicating lower Lewis acidity of the nickel catalyst. Notably, reductive decyanation reactions were efficient even with *ortho*-directing groups like pyrazole (2a and 2b), ester (1c) and oxazoline (2i and 2j).

Next we focused on catalytic decyanation of alkyl cyanides since such C–CN bond activations are problematic.⁸ We first tested the ability of the nickel-catalyzed method to transform benzylic C–CN bonds (Table 3) into C–H bonds (**3a–3e**). 2-(4-Hydroxyphenyl)acetonitrile produced the expected product in preparatively useful yields (**3a**). Benzylic cyanide with a long chain alkyl substituent also afforded the corresponding decyanated product (**3c**). Table 3 Ni-catalyzed reductive decyanation of alkyl cyanides



R–CN (0.5 mmol), Ni(acac)₂ (30 mol%), PCy₃ (60–90 mol%), (Me₂SiH)₂O, AlMe₃ in toluene, 130 °C, 24 h. ^{*a*} GC yield. ^{*b*} *m*-Xylene as solvent.



Scheme 2 Deuterium labeling.



Fig. 1 ORTEP diagram of trans-[Ni(PCy₃)₂(CN)₂]. Hydrogen atoms are omitted for clarity.

Synthetic transformations involving alkyl groups ($R_{alkyl}X$) are considered challenging due to their propensity to undergo side reactions from alkyl-metal intermediates to β -hydride elimination.⁸ Consistent with our expectations, aliphatic nitriles (**3f** and **3g**) were successfully decyanated under the present conditions.

Isolation of the deuterated product by using Ph_2SiD_2 indicated that hydrosilane is the source of hydrogen in the resulting decyanated product (Scheme 2). Selective incorporation of the deuterium atom in unbiased arenes can thus easily be done under neutral conditions.

A stable *trans*- $[Ni(PCy_3)_2(CN)_2]$ was isolated and characterized by X-ray crystallography⁹ (Fig. 1) from various decyanation reactions (*e.g.* entries **1f**, **1g**, **1i** and **3f**). Attempted decyanation reactions of 1-cyanonaphthalene by using *trans*- $[Ni(PCy_3)_2(CN)_2]$ as the catalyst [instead of Ni(acac)_2] did not produce any of the desired decyanated product. Therefore, we suspected that the

Table 4 Competition experiment with 2-cyanonaphthalene and 2-X-naphthalene

0.25 mmol	-0.25 mmol	cat. Ni	b CN	s ×
x	Temp (°C)	a (mmol)	b (mmol)	c (mmol)
SMe	90 130	0.29 0.495	0.20	0.005
O- <i>p</i> -tol OMe	130 130	0.18 0.175	0.04 0.06	0.24 0.245



quick formation of this nickel complex, *trans*- $[Ni(PCy_3)_2(CN)_2]$, is possibly contributing to catalyst deactivation.

We next set out to determine the realtive ease of nickel catalyzed defunctionalization reactions with aryl–CN, –SMe, –OMe and –OAr functional groups under the present reaction conditions (Table 4). We have carried out competition experiments with 2-cyanonaphthalene and 2-X-naphthalene (X = OMe, OAr and SMe) where two substrates were reacted in one flask. We observed that reduction of the aromatic C–CN bond occurs faster than ArOAr and ArOMe. Further investigations showed that removal of –SMe is faster than that of the –CN group.^{2a} Thus our present study along with the recent literature^{2a-c,7} enabled us to find a reactivity pattern which is summarized below:

The decyanation reaction proved to be scalable, with 2-(1*H*-pyrrol-1-yl)benzonitrile producing 96% isolated yield of the expected product (Scheme 3, 2d). Benzyl cyanide can be alkylated upon NaH treatment. Subsequent decyanation of the resulting product will therefore allow use of benzyl cyanide as a benzyl anion equivalent (Scheme 3, 4a). A cyano group is also *ortho* directing¹⁰ and therefore direct C–H arylation at the *ortho*-position and successive decyanation would allow efficient synthesis of biaryls (Scheme 3, 1k). These two-step methods (Scheme 3) demonstrate the power of this decyanation strategy to synthesize useful molecules.

In summary, we have developed a general protocol for nickel-mediated decyanation of aryl and alkyl cyanides. A wide range of nitriles with varying electronic and steric substituents were successfully decyanated as well as the substrates with β -hydrogen. Synthetic advantages of the cyano group including *ortho*-directing ability, α -C-H acidity and electron-withdrawing ability can thus temporarily be used. The Ni-catalyzed decyanation reaction is expected to be applicable in synthetic chemistry due to its wide availability and easy to handle protocol. Studies are ongoing in our research group to develop related synthetic transformations and to elucidate mechanistic details for the reductive decyanation of the C-CN bond.

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