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Nickel-Catalyzed Reductive Cleavage of Carbon-Oxygen Bonds in Anisole Derivatives Using Diisopropylaminoborane

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ABSTRACT: The catalytic removal of a methoxy group on an aromatic ring allows this group to be used as a traceless activating and directing group for aromatic functionalization reactions. Although several catalytic methods for the reductive cleavage of anisole derivatives have been reported, all are applicable only to π-extended aryl ethers, such as naphthyl and biphenyl ethers, while monocyclic aryl ethers cannot be reduced. Herein, we report a nickel-catalyzed reductive cleavage reaction of C-O bonds in aryl ethers using diisopropylaminoborane as the reducing agent. Unlike previously reported methods, this reducing reagent allows effective C-O bond reduction in a much wider range of aryl ether substrates, including monocyclic and heterocyclic ethers bearing various functional groups.

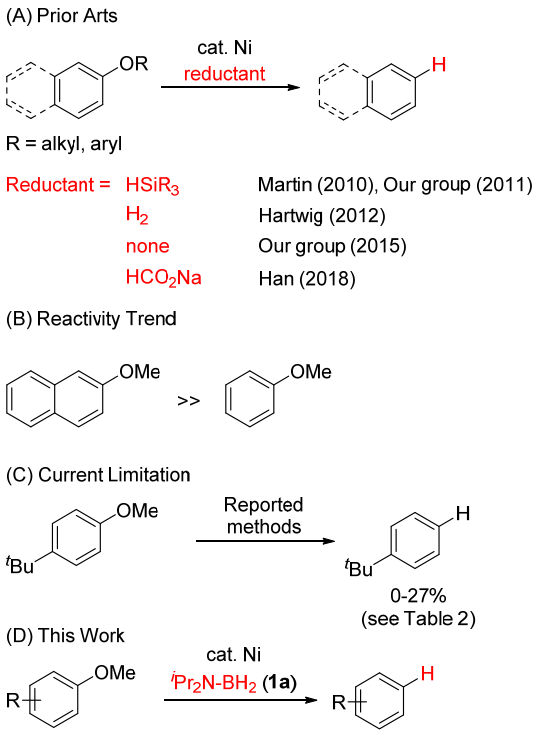
KEYWORDS: nickel catalyst, carbon-oxygen bond cleavage, reduction, aminoborane, anisole

Introduction

The introduction and interconversion of functional groups are central issues in organic synthesis. However, functional group removal also plays a key role, allowing electronic, steric, and coordinating properties that are unique to the functional group to be used in a traceless manner. For example, the Krapcho decarboxylation allows carbanions of β-keto esters to serve as more accessible equivalents to simpler ketone enolates by temporarily using the ester group to increase the acidity of an α-C-H bond.[1] Another example involves the Barton-McCombie deoxygenation, in which a hydroxyl group is converted into an alkyl chain, which is widely used for the construction of elaborate architectures in combination with carbonyl addition reactions.[2] Methoxy groups are common functionalities that exert a significant electronic perturbation when connected to aromatic rings. This activates the aromatic ring toward S_EAr reactions with controlled ortho and para selectivity.[3] Furthermore, a methoxy group on an aromatic ring can be used as an ortho-directing group in lithiation[4] and transition metal-catalyzed reactions,[5] as well as a para-directing group in other aromatic substitution processes.[6,7] Therefore, a method for removing a methoxy group on an aromatic ring to temporarily employ its unique features would be a valuable synthetic tool. However, the inert nature of C(aryl)-O bonds in anisole derivatives makes reductive cleavage of this bond challenging. A classical procedure for accomplishing this transformation involves a three-step sequence, as follows: (i) Demethylation with BBr_3 to form phenol, (ii) treatment with Tf_2O to form the aryl trifluoromethane sulfonate (triflate), and (iii) catalytic reduction of the resulting aryl triflate.[8] In the past decade, low valent nickel complexes have emerged as powerful catalysts for activating the C(aryl)-O bond of inert phenol derivatives, including anisoles.[9] Meanwhile, several one-step catalytic methods for the reductive cleavage of C(aryl)-O bonds in anisole derivatives have been developed (Scheme 1A).[10-14] In 2010, Martin reported a nickel-catalyzed reductive cleavage reaction of aryl ethers using $(HSiMe_2)_2O$ as a reductant.[10a] Our group independently reported an almost identical reaction using $HSiMe(OMe)_2$.[10b] Furthermore, Hartwig demonstrated that hydrogen can function as an effective reducing agent in the nickel-catalyzed deoxygenation of aryl ethers.[10c] Our group has also reported that the nickel-catalyzed reduction of aryl ethers can even occur in the absence of an external reductant.[10d] This reaction is likely to proceed through oxidative addition of a C(aryl)-O bond to form an Ar-Ni-OMe species, followed by β-hydrogen elimination. Therefore, the methoxy group itself serves as the internal reductant. Despite these significant advances, all reported reactions have the common problem that the reactivity is highly dependent on the degree of π-conjugation in the substrate, with simple anisole derivatives being much less reactive than extended naphthyl or polyaromatic methyl ethers (Scheme 1B). In fact, we confirmed for ourselves that application of the reported nickel-catalyzed methods to 4-tert-butylanisole resulted in the formation of the desired reduced product only in yields of only 0-27% (Scheme 1C). Quite recently, Han reported that sodium formate can also serve as a reductant in the nickel-catalyzed reduction of aryl ethers, although the substrates that can be used are limited to fused aromatics and π-acetylanisole.[10f] Although a heterogeneous iron system was reported to catalyze the reductive cleavage of resorcinol dimethyl ether and 4-methoxyphenol, the method requires $LiAlH_4$ as a reducing agent, which severely limits the scope of substrates.[13b]

Borane (BH_3) is a reducing agent commonly used in synthetic organic chemistry. A number of borane derivatives, such as $NaBH_4$ and pinacol borane, have been developed, which allows tuning of the reactivity and selectivity in both direct and catalytic hydride transfer reactions.[15] Among them, (dialkylamino)boranes, $(R^1R^2N)BH_2$, were first reported in the 1960s, although their extensive use in organic synthesis was limited until the 2000s because these compounds readily form mixtures of cyclic and linear oligomers.[16] In 2003, Alcaraz and coworkers reported that diisopropylaminoborane (**1a**) can be synthesized easily in two steps from diisopropylamine and $NaBH_4$, and isolated in a monomeric form as a distillable and

non-pyrophoric liquid.[17] The group also used **1a** as a borylating reagent in a palladium-catalyzed reaction of aryl halides. Subsequently, several studies using **1a** for the catalytic borylation of aryl halides have been reported.[18] Our group previously demonstrated that **1a** can be used in a catalytic diborylation reaction for the synthesis of cyclic organoboron compounds,[19] and in the C-H borylation of arenes and heteroarenes.[20] Despite these advances, the synthetic utility of **1a** has yet to be well explored compared with other widely used boron reagents, such as pinacol borane. Herein, we report that **1a** serves as an extremely efficient reducing agent for the nickel-catalyzed reductive cleavage of C-O bonds, enabling the reduction of anisole derivatives with poor reactivity in previously reported methods (Scheme 1D).



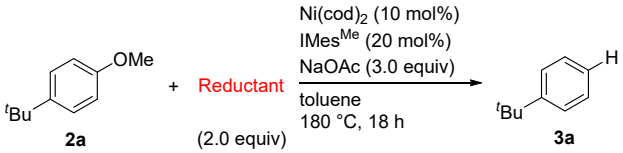
Scheme 1. **Nickel-Catalyzed Reductive Cleavage of Carbon-Oxygen Bonds in Aryl Ethers**

Results and Discussion

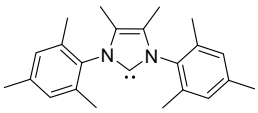
We initially examined the effect of reductants on the reaction of 4-tert-butylanisole (**2a**) in the presence of $Ni(cod)_2$, $IMes^{Me}$, and NaOAc (Table 1a). As previously reported, the addition of hydrosilane reagents (entries 1 and 2), which are effective reductants for the reductive deoxygenation of polycyclic aryl ethers,[10a,b] did not afford reduction product **3a**. The reaction also failed to proceed, when hydrogen was used as a reductant (entry 3). The catalytic conditions in the absence of an external reductant[10d] afforded **3a** in only 11% yield (entry 4). We next examined a series of boron-based reductants, expecting that substrate activation by the Lewis acidic boron atom would facilitate the difficult oxidative addition of C(aryl)-O bonds.[21] Reductive deoxygenation did not proceed when common hydroboranes, such as HBcat (entry 5), 9-BBN (entry 6), HBpin (entry 7) and BH_3 (entry 8), were used. In contrast, using diisopropylaminoborane (**1a**) achieved the formation of **3a** in 79% yield (entry 9). The yield of **3a** was further improved to 93% by increasing the amount of **1a** to 2.5 equiv (entry 10). The use of excess **1a** was required for an

Table 1. **Optimization of Nickel-Catalyzed Reductive Cleavage of 2a**

a) Effect of reductants

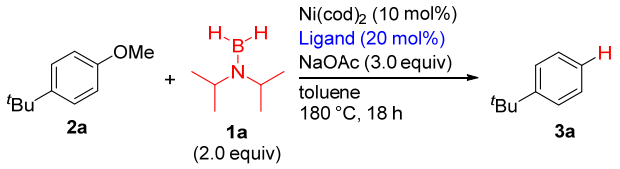


entry	reductant	GC yields (%)	
		3a	**2a**
1	$HSiMe(OMe)_2$	0	>99
2	$HSiEt_3$	0	95
3	H_2 (1 atm)	1	96
4	none	11	88
5	HBcat	0	98
6	9-BBN dimer	0	99
7	HBpin	13	85
8	$BH_3 \cdot {}^iPr_2NH$	0	91
9	**1a**	79	17
10	**1a** (2.5 equiv)	93	6

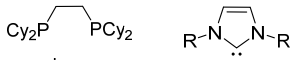


$IMes^{Me}$

b) Effect of ligands

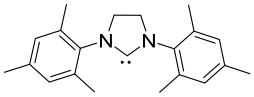


entry	ligand	GC yields (%)	
		3a	**2a**
1	PCy_3	0	75
2	PPh_3	0	92
3	dcype	0	>99
4	ICy	0	>99
5	IPr	36	64
6	IMes	0	58
7	SIMes	0	>99
8	$IMes^{Me}$	79	17
9	$IMes^{Me}$ (10 mol%)	4	92
10	$IMes^{Me}$ (without NaOAc)	51	7



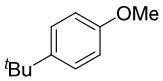
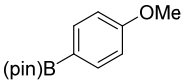
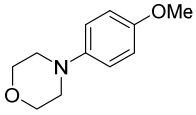
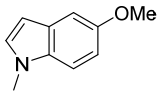
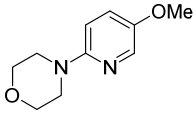
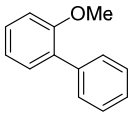
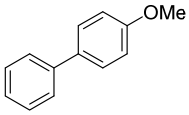
dcype

ICy (R = cyclohexyl)
IPr (R = 2,6-^{i}Pr$_2$C$_6$H$_3$)
IMes (R = 2,4,6-Me$_3$C$_6$H$_2$)



SIMes

Table 2. **Comparison with Reported Catalytic Methods**[a]

substrate	yield of reduced product [%] (yield of recovered substrate [%])			
Method/	**A (This work)**	B	C	D
 **2a**	**93** (6)	1 (78)	13 (87)	27 (-)
 **2b**	**77** (0)	4 (96)	1 (1)	0 (6)
 **2c**	**77** (5)	0 (>99)	5 (89)	13 (37)
 **2d**	**56** (0)	3 (97)	0 (95)	24 (72)
 **2e**	**77** (0)	0 (>99)	0 (0)	0 (80)
 **2f**	**80** (16)	0 (>99)	0 (97)	13 (87)
 **2g**[b]	**88** (0)	0 (93)	0 (76)	0 (>99)

[a]Conditions: Method A: **1a** with Ni(cod)$_2$/IMes^{Me}/NaOAc; Method B: HSiMe(OMe)$_2$ with Ni(cod)$_2$/PCy$_3$[10b]; Method C: H_2 with Ni(cod)$_2$/SIPr/NaO^{t}Bu/AlMe$_3$[10c]; Method D: no external reductant with Ni(cod)$_2$/I(2-Ad)/NaO^{t}Bu[10d]. [b]Reactions were conducted at 60 °C.

efficient reaction because a significant amount of **1a** was consumed by undesired C(aryl)-H borylation of solvent toluene (ca. 55% based on **1a**). Although other solvents were explored to avoid C-H borylation, such as 1,4-dioxane and ^{n}octane, using excess **1a** in toluene gave the highest yield of **3a** (see the Supporting Information for details (Table S2)).

We next turned our attention to exploring the effect of the ligand. Among the ligands reported to be effective for C-O bond cleavage, IMes^{Me} was found to be the best ligand for reductive cleavage using **1a** (Table 1b). When the amount of IMes^{Me} was reduced to 10 mol%, the yield of **3a** decreased to 4% (entry 9). The yield of the reductive deoxygenation also decreased in the absence of NaOAc (entry 10) (see the Supporting Information for the details of additive screening (Table S1)).

To evaluate the superiority of our catalytic system, the reductive cleavage of several demanding substrates was performed under our conditions (Method A) and previously reported conditions (Methods B-D) (Table 2). Method B used HSiMe(OMe)$_2$ as reductant,[10b] Method C involved reduction under H_2 atmosphere in the presence of AlMe$_3$,[10c] and Method D represents the conditions with the absence of an external reductant.[10d] Anisole **2a**, which has no fused aromatic ring, did not undergo reductive cleavage reaction efficiently using Methods B-D, highlighting the outstanding effectiveness of Method A. Method A was advantageous in terms of functional group compatibility, as evidenced by the reductive cleavage of anisole bearing a boryl group (**2b**). Methods C and D required more than a stoichiometric amount of NaO^{t}Bu, which limited their application to substrates bearing base-sensitive functional groups. In contrast, Method A allowed reductive cleavage to occur under virtually neutral conditions, which made the boryl group compatible. Electron-rich anisoles are among the most difficult substrates to reduce, with Methods B-D found to be ineffective at reducing this type of substrate (**2c**). However, to our delight, Method A was able to reduce electron-rich anisoles successfully. Heteroaromatic substrates are another chal-

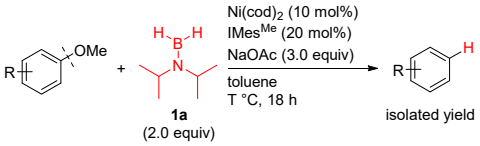
lenging class of compounds for which Methods B-D were also ineffective (**2d** and **2e**). For pyridine derivative **2e**, the pyridine ring was hydrogenated under a H_2 atmosphere (Method C). Substrates **2d** and **2e** were successfully reduced by Method A, demonstrating its robustness toward heteroaromatic systems. Furthermore, unlike other methods, Method A was uniquely tolerant of steric hindrance, as exemplified by the reaction of 2-methoxybiphenyl (**2f**). Method A performed better than reported methods, even in the case of relatively reactive biphenyl substrate **2g**, which underwent reductive cleavage at a low temperature of 60 °C, while Methods B-D did not form any desired product at this temperature.

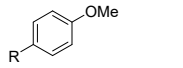
Having established the exceptional reactivity of aminoborane **1a** in the reductive cleavage of aryl ethers (Table 2), we next examined the scope of this reaction in more detail (Table 3). The reaction was successfully applied to substrates bearing a series of functional groups, including silyl (**2i**), boryl (**2b**, **2s**, **2v**, **2aj**), ester (**2p**, **2at**), amide (**2j**, **2k**, **2aa**), and amino groups (**2c**, **2e**, **2l**, **2m**, **2n**, **2t**, **2ae, 2af**). In particular, the applicability of highly electron-rich para-amino-substituted anisoles (**2c, 2e, 2l-2n**) was notable. Although amide groups can be reduced by mild reducing agents in the presence of transition metal catalysts,[22] aryl ethers bearing both secondary (**2j**) and tertiary (**2k**, **2aa**) amides were compatible. Although ketones were reduced by **1a** under these conditions, such substrates could be used by protecting as acetals (**2o**). Similarly, the incompatibility of hydroxyl groups was addressed by using the corresponding silyl ethers (**2q**). This reaction was also applied to naphthyl ethers (**2w-2ac**), which underwent reductive cleavage at 100 °C. Regarding the scope of alkoxy substituents, methoxy (**2w**), ethoxy (**2x**), isopropoxy (**2y**), and phenoxy (**2z**) groups were all cleaved under identical conditions. Biphenyl compounds (**2f**, **2g**, **2ad**) were also suitable substrates, undergoing reductive cleavage at 100 °C. Although the reductive cleavage of relatively reactive polyaromatic substrates were routinely performed at 100 °C, some reacted efficiently even at 60 °C (**2g** in Table 2). Methoxy groups located at sterically demanding positions, such as those in **2f, 2ac, 2af** and **2ag**, were removed under these conditions to form corresponding reduction products. The tolerance of this catalytic method toward steric hindrance was further highlighted by the successful reduction of an anisole derivative bearing two ortho methyl groups (**2ag**). The reaction of 4,4'-diethoxy-1,1'-biphenyl (**2ai**) with 2.0 equiv of **1a** gave a mixture of biphenyl and 4-ethoxy-1,1'-biphenyl. Selective formation of 4-ethoxy-1,1'-biphenyl was difficult because 4-ethoxy-1,1'-biphenyl is less electron-rich, and therefore more reactive, than the starting **2ai**. The two ethoxy groups in **2ai** were completely cleaved by increasing the amount of **1a** to 3.0 equiv. In contrast, the selective removal of one of two methoxy groups was possible when less reactive 1,3-dimethoxybenzene derivative **2aj** was used. This reaction was also applicable to a variety of *N*-heteroaromatic compounds, including pyridines (**2e**), quinolines (**2ak**, **2al**), indoles (**2d**), and carbazoles (**2am**), which are common motifs in medicinal and materials chemistry. A methoxy group at the benzylic position can be reduced under these conditions, forming the corresponding alkylarenes. Furthermore, primary (**2an**, **2ar**) and secondary (**2ao-2aq**) benzylic ethers underwent reductive cleavage. A competition experiment between **2a** and 1-(tert-butyl)-4-(methoxymethyl)benzene (**2a'**) using 2.0 equiv of **1a** under the standard conditions led to the exclusive formation of **3a** with the complete recovery of **2a'**, indicating that C(benzyl)-O bonds are less reactive than C(aryl)-O bonds under these conditions (see the Supporting Information for details). Interestingly, the reaction of 2-(2-methoxyethyl)naphthalene (**2as**) under the standard reaction conditions afforded 2-ethylnaphthalene in 93% yield, demonstrating the potential utility of this method for the reductive cleavage of non-benzylic C(sp^3)-O bonds.[23] Similarly, 4-(2-methoxyethyl)-1,1'-biphenyl and (2-methoxyethyl)benzene can be applied to this reaction (see the Supporting Information for details (Table S6)). Methoxyarenes are common substructures found in various natural and unnatural biologically active compounds. Deoxygenated analogues of such compounds can readily be accessed using our protocol. For example, the removal of a methoxy group from naproxen (**2at**), estradiol (**2au**), and harmine (**2av**) derivatives was possible in one step under these nickel-catalyzed conditions using **1a**.

To gain insight into the unique reactivity of **1a** in this reductive cleavage of C(aryl)-O bonds, the reactivities of several common hydride reagents with **1a** in the reduction of benzophenone **4** were compared (Table 4). $HSiMe(OMe)_2$, HBcat and HBpin did not react with **4** in the absence of catalyst. In contrast, **1a** reduced **4** to give **5** in 76% yield at room temperature. This clearly indicated that the Lewis acidity of **1a** was higher than those of $HSiMe(OMe)_2$, HBcat, and HBpin, which allowed stronger interaction with the carbonyl oxygen atom of **4**, thereby facilitating the reduction.[15] The relatively high Lewis acidity of **1a** was further confirmed by ^{11}B NMR spectroscopy, which showed that the chemical shift of **1a** appeared down field of the others (**1a**, 35.5 ppm; HBcat, 28.7 ppm; HBpin, 28.3 ppm). Based on these results, the Lewis acid nature of **1a** probably played a key role in the reductive cleavage of aryl ethers. Although these observations indicated the relatively high Lewis acidity of **1a**, we were unable to obtain any direct evidence of interaction between **1a** and aryl ether **2a** or ketone **4** by ^1H and ^{11}B NMR, probably due to the equilibrium favoring their uncomplexed forms.

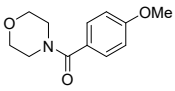
We next conducted a series of deuterium labeling experiments to clarify the origin of hydride incorporated into the reduced product (Scheme 2). The nickel-catalyzed reaction of labeled substrate 4-CD_3O-biphenyl **2aw** with **1a** afforded deoxygenated product **3aw** without deuterium incorporation. This result suggested that, unlike our previously reported method,[10d] β-hydrogen elimination from the oxidative addition complex (Ar-Ni-OMe) was not a major pathway in this catalytic system (Scheme 2A). We next conducted the reductive cleavage of **2ax** using a labeled aminoborane **1b** (75%D) and again found no deuterium incorporated into product **3ax** (Scheme 2B). In contrast, 97% deuterium was found to be incorporated at the *ipso* position of the product when the same reaction using **1b** was conducted in toluene-d_8 (Scheme 2C). Furthermore, 91% deuterium was incorporated into the product when the reaction of non-labelled **2ax** and **1a** was conducted in toluene-d_8 (Scheme 2D). These results indicated that an H/D exchange reaction was occurring between the reduced product and toluene solvent in the presence of **1a**.[24] Owing to this H/D exchange reaction, deuterium was also incorporated into other aromatic C-H bonds in **3ax** (Scheme 2C). To avoid H/D exchange with the solvent, we conducted the reaction of **2ax** with **1b** in 1,4-dioxane. However, H/D scrambling between the aromatic C-H bonds in **2ax** and **3ax** still hampered probing of the origin of incorporated hydride (Scheme 2E). Although rapid H/D exchange between **1b** and aromatic C-H bonds complicated the results of this labeling study, the source

Table 3. **Substrate Scope**

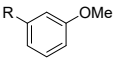




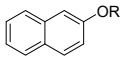
		T (°C)	
1	R = ^{t}Bu (**2a**)	180	93[a,b]
2	^{t}Oct (**2h**)	180	85[a]
3	$SiMe_3$ (**2i**)	180	99[a]
4	B(pin) (**2b**)	180	74
5	CONH^{t}Bu (**2j**)	180	58



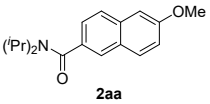
6	**2k**	180	78
7	**2c**	180	75
8	**2l**	180	51[c]
9	**2m**	180	66
10	**2n**	180	57
11	**2o**	180	52
12	**2p**	180	53
13	**2q**	180	83



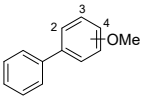
14	R = ^{n}pentadecanyl (**2r**)	180	87
15	B(pin) (**2s**)	180	65
16	NMe_2 (**2t**)	180	55[a]
17	**2u**	180	67[a]
18	**2v**	180	70



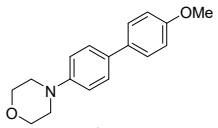
		T (°C)	
19	R = Me (**2w**)	100	98[a]
20	Et (**2x**)	100	76[a]
21	^{i}Pr (**2y**)	100	50[a]
22	Ph (**2z**)	100	82[a,d]



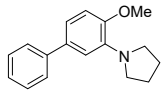
23	**2aa**	100	87
24	**2ab**	180	89[a]
25	**2ac**	180	91



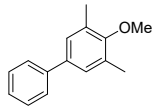
26	2-OMe (**2f**)	100	80[a]
27	3-OMe (**2ad**)	100	97[a]
28	4-OMe (**2g**)	100	90[a]



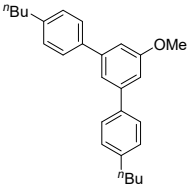
29	**2ae**	100	67



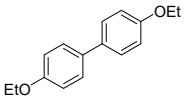
30	**2af**	100	59



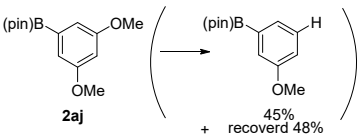
31	**2ag**	180	56



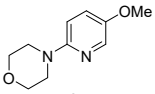
32	**2ah**	100	92



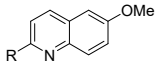
33	**2ai**	100	68[a,e]



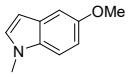
34	**2aj**		



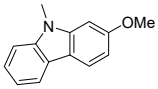
		T (°C)	
35	**2e**	180	77



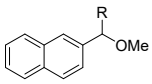
36	R = H (**2ak**)	180	57
37	Me (**2al**)	180	55



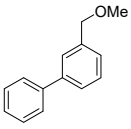
38	**2d**	180	56



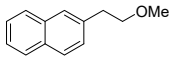
39	**2am**	180	91



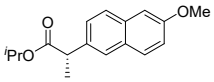
40	R = H (**2an**)	180	82[a]
41	Me (**2ao**)	180	97[a]
42	^{t}Bu (**2ap**)	180	46
43	Ph (**2aq**)	180	86



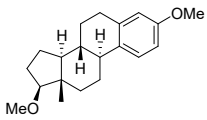
44	**2ar**	180	59[a]



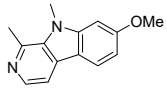
45	**2as**	180	93[a,c]



46	**2at**	100	66[f]



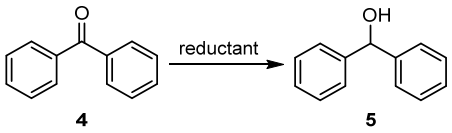
47	**2au**	180	75



48	**2av**	180	70

[a]Yields determined by GC analysis owing to product volatility. [b]**1a** (0.75 mmol) was used. [c]$Ni(cod)_2$ (0.060 mmol) and IMes^{Me} (0.12 mmol) were used. [d]Phenol was obtained in 75% GC yield. [e]**1a** (0.90 mmol) was used. The yield refers to that for biphenyl. [f]NaOAc was not added.

Table 4. **Reduction of 4 by Using Hydrosilane or Hydroboranes[a]**

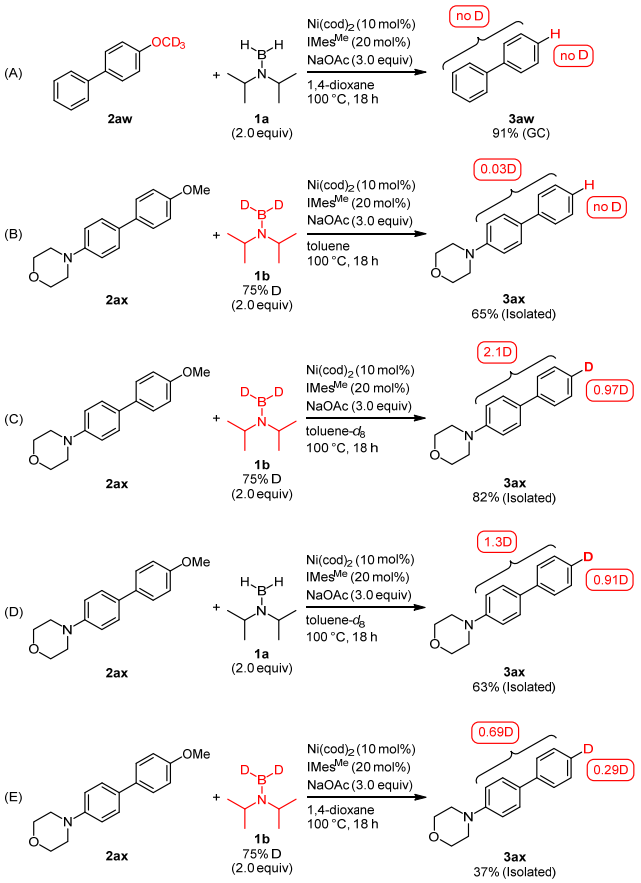


reductant	yield (%)[b]	δ (ppm)[c]
$HSiMe(OMe)_2$	0	-
HBcat	0	28.7
HBpin	0	28.3
1a	76	35.5

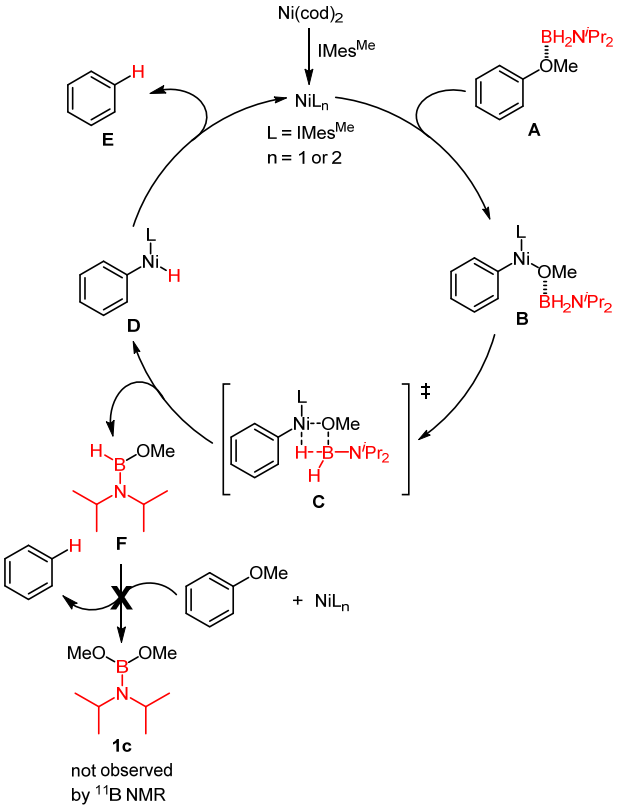
[a]Reaction conditions: **4** (0.30 mmol), hydrosilane or hydroborane (0.60 mmol), and THF (5.0 mL) at room temperature for 15 h. [b]Isolated yield is shown. [c]Chemical shifts in ^{11}B NMR using toluene-d_8.

of hydride for the deoxygenation of C(aryl)-O bonds was most likely to be **1a**.

A possible mechanism is shown in Scheme 3. Given that using **1a** as the reducing agent is essential for the reaction to occur and that **1a** can reduce ketones in the absence of catalyst, coordination of the oxygen atom of anisole with the boron atom of **1a** to generate complex **A** was likely key for reductive cleavage. The formation of **A** should reduce the electron density of the C(aryl)-O bond of anisole, thereby facilitating oxidative addition of the C-O bond to $Ni(IMes^{Me})_n$ (n = 1 or 2) to form intermediate **B**. Subsequent hydride migration from



Scheme 2. Deuterium Labeling Experiments



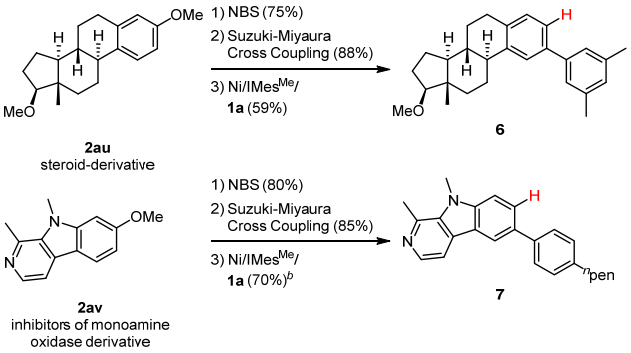
Scheme 3. **Proposed Mechanism**

boron to nickel, presumably occurring in an intramolecular manner through **C**, provides a nickel hydride **D**, which finally forms deoxygenated product **E** by reductive elimination accompanied by regeneration of the nickel catalyst. To investigate the fate of the boron residue, we analyzed the crude reaction mixture using ^{11}B NMR. Signals were observed at 38, 32, and 30 ppm in toluene-d_8. Dimethoxyaminoborane **1c** was not thought to be generated in this reaction, as the chemical shift corresponding to **1c** was confirmed to appear at 19 ppm by synthesizing **1c** separately. These results indicated that monohydride **F** was incapable of reducing anisole and that only one of the two B-H bonds in **1a** reacted in the deoxygenation reaction. Pathways involving nickel-hydride[25] or boryl nickel intermediate[26] cannot be completely excluded at this stage. However, these pathways require Ni(IV) or a dearomatized intermediate, which we currently believe to be unlikely. Several reductive cleavage reactions are proposed to proceed through heterogeneous catalysis, even though soluble metal complexes are used as catalyst precursors.[13] Therefore, we conducted a mercury test[27] for the nickel-catalyzed reaction of **2a** with **1a**. However, no significant decrease in the yield of **3a** was observed with the addition of mercury (79% without Hg vs 71% with Hg (23 equiv)), which suggested that this reaction was catalyzed by a homogeneous catalytic species.

The potential utility of this reductive cleavage reaction of anisoles in the site-selective functionalization of biologically active phenol derivatives is demonstrated in Scheme 4. A methoxy group can activate an aromatic ring toward S_EAr and direct the reaction to occur at the ortho position. After serving as an activating group, a methoxy group can be removed using our method. Overall, a methoxy group can be used as a traceless ortho-directing group. This strategy allows C2 functionalization of steroidal architecture **2au** and regioselective func-

tionalization of **2av**, a derivative of harmine (a reversible inhibitor of monoamine oxidase type-A).

Scheme 4. **Synthetic Applications**[a]



[a]Reaction Conditions: (1) NBS, CCl_4, rt. (2) cat. $Pd(P^tBu_3)_2$, Na_2CO_3, boryl compound, toluene/H_2O, reflux. (3) aryl ether (0.30 mmol), **1a** (0.60 mmol), $Ni(cod)_2$ (0.030 mmol), $IMes^{Me}$ (0.060 mmol), NaOAc (0.90 mmol), toluene (1.0 mL) at 180 °C for 18 h. [b]**1a** (1.2 mmol) was used.

Conclusions

In summary, we have developed a nickel-catalyzed reductive cleavage reaction of C(aryl)-O bonds using **1a** as reductant. This reaction enabled the deoxygenation of simple anisole derivatives that were difficult to reduce using previously reported methods. Reductant **1a** was shown to exhibit higher Lewis acidity than commonly used $HSiMe(OMe)_2$ and HBipn reagents, which accounted for the unique effectiveness of **1a** in this reductive cleavage reaction. This reaction allows methoxy groups to be used as removable directing groups, which will provide numerous opportunities for the late-stage functionalization of common methoxyarene motifs. The dramatically decreased reactivity of mono-cyclic arenes compared with π-extended analogues, such as naphthyl or polyaromatic derivatives, is a prevalent problem encountered throughout nickel-catalyzed cross-coupling reactions using inert aromatic electrophiles, including aryl fluorides, aryl amides, aryl esters, and phenols.[9g] The present study indicates that using Lewis acidic reagents that can electrophilically activate substrates is a viable approach to solving this problem. Research into the development of new reactions using aminoborane reagents are ongoing in our laboratories.

ASSOCIATED CONTENT

Supporting Information. Detailed experimental procedures and characterization of new compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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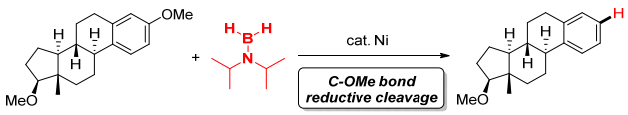
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