Doctoral Dissertation

Studies on Nickel and Rhodium-Catalyzed Direct Transformation of C-O and C-N Bonds

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January 2016

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Preface and Acknowledgements

The findings reported in this thesis were obtained under the direction of Professor Naoto Chatani of the Department of Applied Chemistry, Faculty of Engineering, Osaka University between April 2010 and March 2016. The thesis is concerned with the transition metal-catalyzed transformation of phenol and aniline derivatives via the cleavage of carbon-oxygen and carbon-nitrogen bonds.

I would not have been able to complete this thesis without the help, advice, and support from many people and I wish to express my sincerest appreciation to all of them.

First of all, I would like to express my utmost gratitude to Professor Naoto Chatani for the guidance and suggestions he provided throughout this work. His enthusiasm for chemistry has always motivated me. I respect him not only for his interest in chemistry but also for his personality.

I would like to make a most cordial acknowledgment of Dr. Mamoru Tobisu for his invaluable advice and support. He always presented logical and ingenious suggestions regarding my research efforts during the course of my studies. He always took the time to develop an appropriate mood for our laboratory. It is a great honor to have had the opportunity to function as a member of his team.

I would also like to thank Dr. Yoshiya Fukumoto for his instructive and pertinent advice and for his great interest in chemistry.

I thank the secretaries in our laboratory, including Ms. Mayuko Nakamura, Ms. Yoshimi Shinomiya and Ms. Junko Ohmagari for their kind assistance.

I would like to express my special thanks to the past and present members of the Chatani Group. Since I joined this group in 2010, Dr. Isao Hyodo consistently responded to my requests for advice. I am really proud of that I had the opportunity to have studied with him.

I also acknowledge the marvelous senior members of the group, including Mr. Takeshi Uemura, Dr. Yusuke Ano, Dr. Masahiro Onoe (he likes pro wrestling), Mr. Keika Koh, Mr. Hirotaka Shiota, Mr. Takuya Tsuruta, Mr. Tomohiko Yasunaga, and Mr. Ken Yamakawa, Dr. Hirotaka Kinuta, Dr. Katsuaki Baba, Mr. Motohiro Shiratani, Ms. Nao Hasegawa, Mr. Masato Daijo and Ms. Tian Xu. I learned many things, such as experimental techniquea and how to enjoy chemical research, from them.

I would also thank my unique classmates, including Dr. Yoshinori Aihara (*Aihara-kun*), Mr. Akihiro Ohmae (*Ohmae-san*), Mr. Junya Hasegawa (*Hasegawa-kun*) and Yasunori Soga (*Soga-cchi*). They kept my spirits up and made me happy, and the many drinking parties and travels with them are irreplaceable memories for me.

I also wish to thank to the junior members of the Chatani group, including Mr. Kaname Shibata, Mr. Hiroto Shimizu, Mr. Takayuki Furukawa (I often played the video games with him), Ms. Ayaka Yasutome, Ms. Miki Iyanaga, Ms. Aya Tashiro, Mr. Masaya Hirano, Mr. Toshifumi Morioka, Ms. Ayana Yokota, Mr. Motonobu Kamiya, Mr. Tsuyoshi Takahira, Mr. Yuto Tamura, Ms. Moe Noguchi, Mr. Yoshihiro Masuya (only he and I are smokers in my laboratory), Mr. Takuya Igarashi, Mr. Teruhiko Kubo, Mr. Jiangning Zhao(*Cho-kun*), Ms. Natsuki Okazaki, Mr. Yuta Seo, Mr. Kosuke Yasui (a beloved pupil), Mr. Takuma Yamaguchi, Ms. Mao Yamaguchi, Mr. Sodai Yamada, Mr. Yasuaki Iyori, Mr. Atsushi Obata, Ms. Satoko Natsui, Mr. Akihiro Nishizawa and Mr. Kosuke Yanagisawa.

Furthermore, I express my appreciation to Dr. Rebecca Reguillo Carmona, Dr. Valentine Charra, Ms. Yoonjoo Kim, Mr. Melih Kus, Dr. Guy Rouquet, Mr. Ho Jordan Sun, Dr. Luis Carlos Misal Castro, Mr. Jendrik Wuelbern, Dr Yadagiri Kommagalla (everyone call him *Giri-san*) and Dr. Akimichi Ohtsuki who worked in the Chatani laboratory as visiting fellows or postdoctoral fellows.

I also acknowledge financial support that I received from JCIA in the form of a scholarship during my doctorial term.

I would also like to express my deepest gratitude to my parents, Mr. Kiyoshi Nakamura and Ms. Keiko Nakamura and my sister, Ms. Ayumi Nakamura. They provided consistent support for me not only financially but also mentally.

Finally, I also thank to Ms. Asako Nakagawa (*Asako-chan*) specially. I couldn't have overcomed the problems I was faced with in my everyday life, without her encouragement.

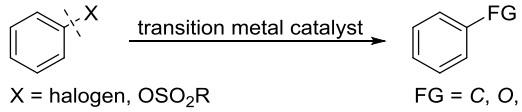
Suita, Osaka
January 2016

Keisuke Nakamura

Contents

General Introduction

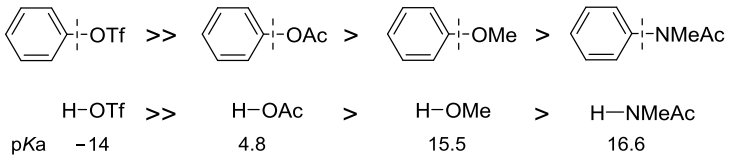
Transition metal-catalyzed transformations of aryl halides, such as Suzuki-Miyaura cross-coupling, [1] are well accepted, powerful methods that can be used to synthesize a variety of valuable organic molecules, including pharmaceuticals and organic materials. These processes permit a wide range of functional groups to be introduced in a molecule by forming carbon-carbon, carbon-oxygen,[2] carbon-nitrogen,[3] and carbon-silicon,[4] bonds via the activation of a carbon-halogen bond (eq 1).



(1)

In contrast, functionalizing carbon-oxygen or carbon-nitrogen bonds in phenol or aniline derivatives remains a challenge, except for cases of highly reactive aryl sulfonates, using common catalysts for the transformation of aryl halides. Not surprisingly, the difficulty in developing catalytic methods for the transformation of C(aryl)-O and C(aryl)-N bonds can be attributed to the inertness of these chemical bonds compared with C(aryl)-X bonds. The relative reactivity of phenol and aniline derivatives can be estimated based on the p*K*a values for the conjugate acids of the leaving groups (Scheme 1). For example, in the case of phenyl triflate, which is highly reactive and commonly used in transition metal-catalyzed reactions, the p*K*a value of TfOH is as low as -14, thus exemplifying the extraordinary ability of a OTf group as a leaving group. On the other hand, the higher p*K*a value of 4.8 for AcOH indicates the much lower reactivity of phenyl acetate compared to triflates. Indeed, no palladium catalysts for promoting the oxidative addition of C(aryl)-O bonds in aryl esters have yet been reported. Similarly, it would be expected that anisoles and anilides would be even much less reactive than esters, on the basis of the much higher p*K*a values for MeOH and AcNHMe by a factor of three.

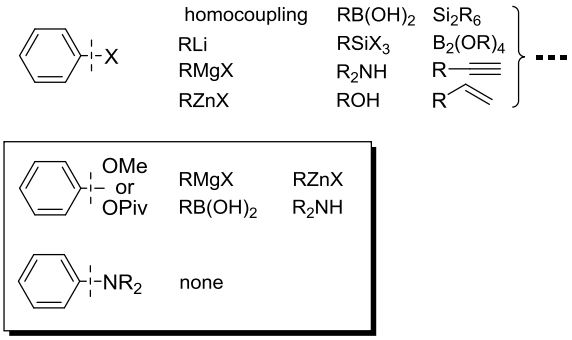
Scheme 1. Estimated Reactivity Order of Aryl Electrophiles



When this thesis study was initiated in 2010, a myriad of reactions using aryl halides had been established, encompassing cross-coupling with organometallic reagents and addition to unsaturated bonds (Scheme 2).

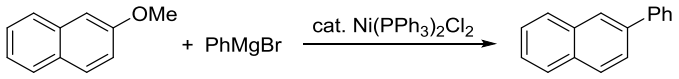
In contrast, catalytic transformations of unactivated phenol or aniline derivatives were much less explored.

Scheme 2. Applicable Coupling Partners as of 2010



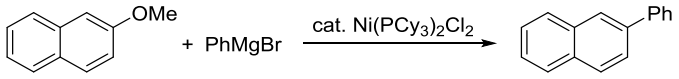
Recently, it has come to light that low valent nickel species possess exceptionally high levels of reactivity towards C(aryl)-O bonds, and nickel catalysis have been actively investigated in this context.

In 1979, Wenkert et al. reported the first examples of reactions of C(sp2)-OMe bonds in vinyl ethers and aryl ethers with Grignard reagents (eq 2).[5]



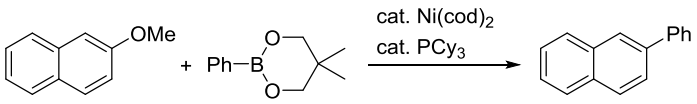
(2)

In 2004, Dankwardt developed the nickel-catalyzed reaction of an aryl ether with an aryl Grignard reagent by using tricyclohexylphosphine (PCy_3) as a ligand (eq 3).[6] The combination of a nickel with a PCy_3 was found to be effective for the activation of inert C(aryl)-O bonds.



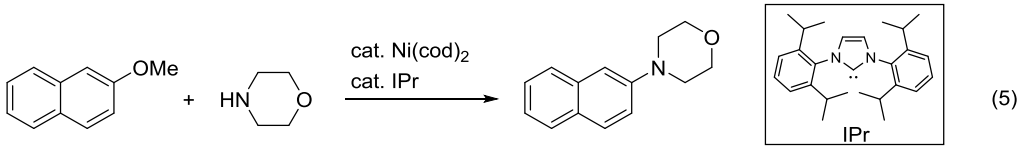
(3)

In 2008, Chatani et al. reported the first Suzuki-Miyaura type cross-coupling reaction of methoxyarene derivatives by using Ni/PCy_3 catalytic system (eq 4).[7]



(4)

In 2009, Chatani et al. also reported on the development of the amination of an aryl methyl ether (eq 5).[8] In that reaction, $Ni(cod)_2$ and a 1,3-bis(2,6-diisopropylphenyl)imidazole-2-ylidene (IPr) ligand resulted in efficient performance.



(5)

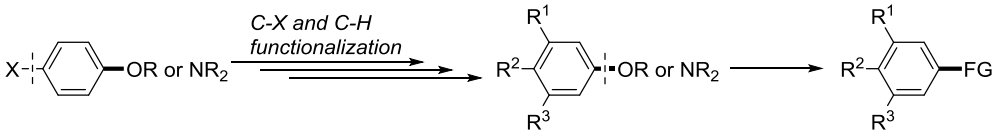
As shown in eqs 2-5, the catalytic transformation of methoxyarenes were limited to cross-coupling with organomagnesium or organoboron reagents and amination. Similarly, the diversity of the nucleophiles available for the cross-coupling of aromatic esters and

carbamates are also limited to cross-coupling with organomagnesium,[9] organoboron[10] and organozinc reagents,[11] and amination reaction[12] as of 2010.

No reports have yet appeared regarding the catalytic transformation of a C(aryl)-N bond in simple aniline derivatives.

The purpose of this study was to expand the diversity of reagents in catalytic C(aryl)-O bond transformations and to react simple aniline derivatives via C(aryl)-N bond cleavage by using a transition metal-catalyst. The development of diverse methods for C(aryl)-O bond transformation and unprecedented C(aryl)-N bond cleavage would allow these bonds to be used as a reactive site in organic synthesis. Furthermore, the selective transformation of these inert bonds would provide a new synthetic strategy, for example for tandem cross-coupling or the late-stage functionalization of C(aryl)-O or C(aryl)-N bonds in phenol or aniline derivatives (Scheme 3). For this reason, catalytic transformations using phenol or aniline derivatives would be highly desirable. These circumstances motivated us to study the transition metal-catalyzed direct transformation of inert C(aryl)-O and C(aryl)-N bonds, which is the subject of this thesis.

Scheme 3. Late-Stage Functionalization of the Inert C-O and C-N Bonds



Chapter 1 discusses the rhodium-catalyzed cross-coupling reaction of aryl carbamates with organoboronic esters.

Chtapter 2 deals with the nickel-catalyzed formal homocoupling reaction of anisole derivatives. The reaction involves the cleavage of C(aryl)-OMe bonds.

Chapter 3 is concerned with the nickel-catalyzed reduction and borylation of aniline derivatives via the cleavage of C(aryl)-N bonds in non-activated aniline derivatives.

Finally, the findings are summarized in the conclusion section.

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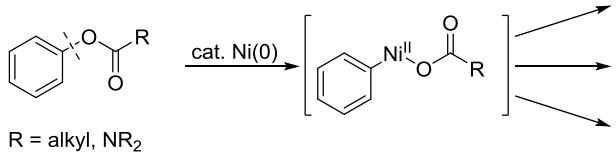
Chapter 1

Rhodium-Catalyzed Cross-Coupling of Aryl Carbamates with Organoboron Reagents

1.1 Introduction

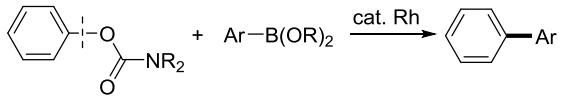
As described in general introduction, C(aryl)-O bonds in aromatic esters and carbamates were stable, and could not be activated under conventional palladium-catalyzed conditions.[1] The use of nickel catalysts allowed for the cross-coupling of simple unactivated phenol derivatives such as esters,[2] and carbamates[3] (Scheme 1). The success of these reactions indicated that low valent nickel species possess exceptionally high levels of reactivity towards C(aryl)-O bonds.

Scheme 1. Ni(0)-Catalyzed C-O Bond Transformation of Aryl Esters and Carbamates



From a fundamental perspective, it would be intriguing to know whether transition metals other than nickel could be used to promote the transformation of such unactivated phenol derivatives. It has also been reported that the C(aryl)-O bonds of aryl esters and pivalates can be activated by iron[4] and cobalt[5] catalysts, although these reactions require the addition of more than a stoichiometric amount of Grignard reagents.[6,7] Furthermore, these catalysts cannot be used to affect cross-coupling reactions with organoboron reagents. Our group recently found that the rhodium-catalyzed reaction of aryl pivalates with a diboron reagent resulted in the formation of borylated products.[8] The use of a diboron reagent in this reaction was found to be essential to promote the cleavage of the C(aryl)-O bond of aryl pivalates under these rhodium-catalyzed conditions (i.e., $[RhCl(cod)]_2/P(4\text{-}MeOC_6H_4)_3$), and the catalyst system was therefore only applicable to carbon-boron bond-forming reactions. Based on these results, it was envisaged that the C(aryl)-O bond transformation of inert phenol derivatives could be realized by identifying an appropriate rhodium catalyst system. Ozerov et al.[9] reported that a rhodium complex bearing a PNP-pincer ligand could be used to mediate the oxidative addition of phenyl pivalate and carbamate, and this observation also encouraged us to investigate the development of a new rhodium-catalyzed reaction. Pleasingly, our investigative efforts in this area culminated in the development of a rhodium-catalyzed cross-coupling of aryl carbamates with arylboronic esters, which we report herein (Scheme 2).

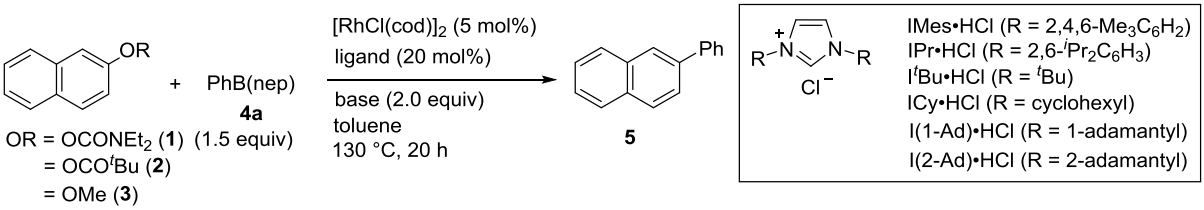
Scheme 2. This Work



1.2 Results and Discussion

At the outset of our studies, we decided to investigate the reaction of 2-naphthyl carbamates **1** with boronic ester **4a** (nep = neopentylglycolate) in the presence of $[RhCl(cod)]_2$ as a catalyst and NaOEt as a base (Table 1). However, virtually none of the desired cross-coupling product **5** was formed in the absence of a ligand (Entry 1) and in the presence of phosphine ligands, such as PPh_3 (Entry 2) and PCy_3 (Entry 3). Based on our experience of nickel-catalyzed C(aryl)-O bond activation processes[10] as well as related reports from others[11] it was assumed that a stronger σ-donor would provide a better ligand candidate, and we therefore preceded to examine a series of NHC ligands. As expected, the use of IMes as a ligand led to the formation of **5** in 25% yield (Entry 4). Although the use of an NHC ligand bearing bulkier aryl groups (i.e., IPr) inhibited the arylation (Entry 5), the use of a ^{t}Bu-substituted NHC ligand (I^{t}Bu) led to a significant increase in the yield of **5** to 77% (Entry 6). Furthermore, the use of an NHC ligand bearing adamantyl groups led to even higher catalytic activity, with the 2-adamantyl derivative I(2-Ad) (Entry 9) performing much more effectively than the 1-adamantyl isomer I(1-Ad) (Entry 8). In terms of the base, NaOEt could be replaced with CsF, although this led to a slight decrease in the yield of **5** from 98 to 74% (Entry 10). The boronic acid $PhB(OH)_2$ could also be used as an arylating reagent under these conditions, without any discernible decrease in the efficiency of the reaction (Entry 11), whereas the use of the bulkier PhB(pin) resulted in a much lower yield of **5** (Entry 12). The cross-coupling of aryl pivalate **2** with **4a** did not occur under these conditions, but resulted instead in the exclusive formation of a hydrolyzed naphthol product (Entry 13). Aryl methyl ether **3** was found to be completely unreactive under the current conditions (Entry 14).

Table 1. Optimization Studies[a]



Entry	Substrate	Ligand	Base	Yield/%[b]	Entry	Substrate	Ligand	Base	Yield/%[b]
1	**1**	none	NaOEt	8	8	**1**	I(1-Ad)•HCl	NaOEt	54
2	**1**	PPh_3	NaOEt	0	9	**1**	I(2-Ad)•HCl	NaOEt	94
3	**1**	PCy_3	NaOEt	0	10	**1**	I(2-Ad)•HCl	CsF	74
4	**1**	IMes•HCl	NaOEt	25	11[c]	**1**	I(2-Ad)•HCl	NaOEt	73
5	**1**	IPr•HCl	NaOEt	3	12[d]	**1**	I(2-Ad)•HCl	NaOEt	16
6	**1**	I^tBu•HCl	NaOEt	77	13	**2**	I(2-Ad)•HCl	NaOEt	3
7	**1**	ICy•HCl	NaOEt	5	14	**3**	I(2-Ad)•HCl	NaOEt	0

[a] Reaction conditions: substrate (0.30 mmol), **4a** (0.45 mmol), $[RhCl(cod)]_2$ (0.015 mmol), ligand (0.060 mmol), and base (0.60 mmol) in toluene (1.0mL) at 130 °C for 20 h in a sealed tube. [b] GC yield of **5** based on the substrate. [c] *p*-TolylB$(OH)_2$ was used instead of **4a**. [d] *p*-TolylB(pin) was used instead of **4a**.

Having identified I(2-Ad) as the optimal ligand for the reaction (Table 1, Entry 9), we preceded to examine the scope of aryl carbamates. Although 2-naphthyl carbamate **1** underwent the cross-coupling with **4a** to form **5** in excellent yield, use of less reactive substrates led to a significant reduction in the yield. For example, phenyl carbamate **6** underwent the cross-coupling with **4a** to afford **8** in only 38% yield, with the hydrolyzed compound **9** being formed as the major product in 56% yield (Scheme 3). This undesired hydrolysis could be suppressed completely by increasing the steric bulk of the carbamate moiety, as exemplified by the use of an $OCON^iPr_2$ group, which delivered **8** in 86% yield. Based on these results, the bulky diisopropyl carbamate group ($-OCON^iPr_2$) was selected as the best group for further exploration. It is noteworthy that this carbamate moiety can be readily introduced at a phenolic hydroxyl group by the reaction of the appropriate phenol with $ClCON^iPr_2$, which is commercially available (See Experimental Section for details).

Scheme 3. Effect of Substituent of the Carbamoyl Group

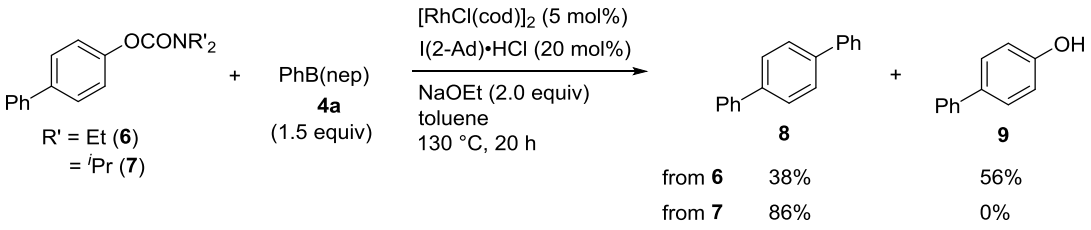
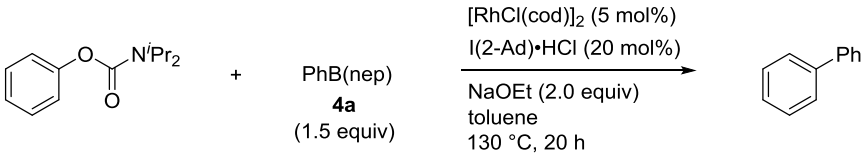
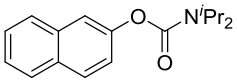
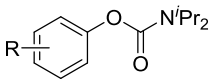
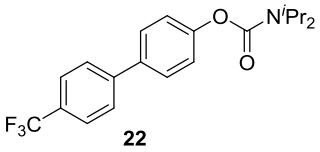
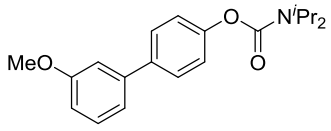
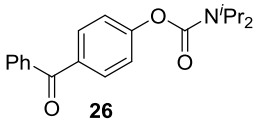
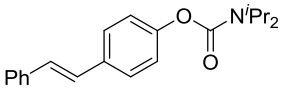
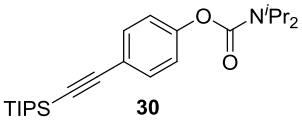
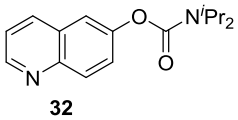
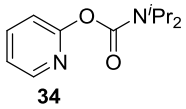
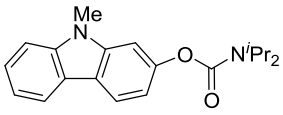


Table 2. Rh(I)/NHC-Catalyzed Cross-Coupling of Aryl Carbamates with **4a**[a]



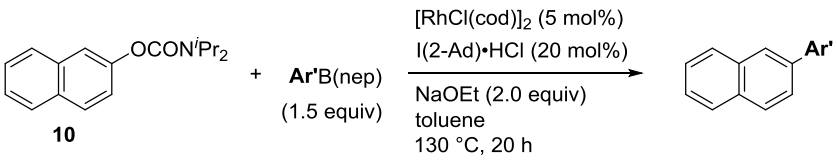
Entry	Aryl carbamate	Product	Yield/%[b]
1	 **10**	**11**	80
2	 R = *p*-^{t}Bu **12**	**13**	18
3	R = *p*-Ph **14**	**15**	86
4	R = *m*-Ph **16**	**17**	82
5	R = *o*-Ph **18**	**19**	0
6	R = *p*-CF_3 **20**	**21**	79
7[c]	 **22**	**23**	97
8[c]	 **24**	**25**	61
9[c]	 **26**	**27**	31
10[c]	 **28**	**29**	44
11	 **30**	**31**	57
12[c]	 **32**	**33**	63
13	 **34**	**35**	40
14	 **36**	**37**	90

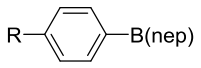
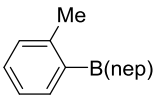
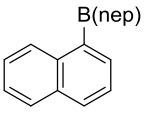
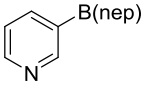
[a] Reaction conditions: aryl carbamates (0.30 mmol), **4a** (0.45 mmol), $[RhCl(cod)]_2$ (0.015 mmol), I(2-Ad)•HCl (0.060 mmol), and NaOEt (0.60 mmol) in toluene (1.0mL) at 130 °C for 20 h in a sealed tube. [b] Isolated yield after column chromatography. [c] Toluene (1.5 mL) was used.

The scope of the rhodium/I(2-Ad)-catalyzed cross-coupling of aryl carbamates with boronic ester **4a** is shown in Table 2. Phenyl carbamate **12** (Entry 2) proved to be significantly less reactive than the naphthyl substrate **10** (Entry 1), as is often observed in nickel-catalyzed C(aryl)-O bond activation reactions.[12] Interestingly, the introduction of a phenyl group to the substrate led to a significant improvement in the yield of the product, as evidenced by biphenyl carbamates **14** (Entry 3) and **16** (Entry 4), which reacted successfully under the optimized conditions to give **15** and **17** in 86 and 82% yields, respectively. Several biaryl derivatives bearing CF_3 and MeO groups also performed effectively as substrates for the coupling reactions (Entries 7 and 8), whereas the *o*-phenyl-substituted substrate **18** (Entry

5) was found to be completely unreactive, most likely because of its steric bulk. Given the minor inductive effect of a phenyl group (σ_p =0.05, σ_m =0.05),[13] the significant enhancement observed in the reactivity of the biaryl carbamates could be attributed to the extension of their π-conjugation. Indeed, stryrenyl (Entry 10) and alkynyl (Entry 11) groups also exerted a positive effect on the efficiency of the reaction and exhibited higher levels of reactivity compared with the simple alkyl-substituted substrate **12** (Entry 2). Inductive effects can also have an important impact on this cross-coupling, as exemplified by the electron-deficient aryl carbamate **20** with no extended π-system, which gave rise to the arylated product **21** in 79% yield (Entry 6). Notably, several heteroaromatic substrates, including π-deficient quinoline (Entry 12) and pyridine (Entry 13) rings and a π-rich carbazole (Entry 14), all reacted smoothly to provide the corresponding phenylated products. Aryl bromides and chlorides were found to be incompatible with these conditions and reacted instead to give the arylated products.[14]

Table 3. Scope of the Boronic Ester in the Rh(I)/NHC-Catalyzed Cross-Coupling of **10**[a]



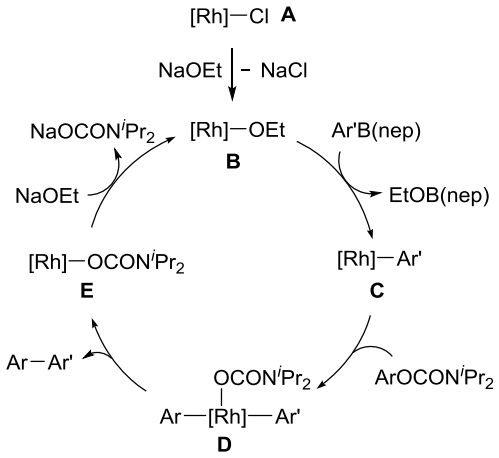
Entry	Boronic ester		Product	Yield/%[b]	Entry	Boronic ester	Product	Yield/%[b]
					6	 **4g**	**43**	81
1	R = Me	**4b**	**38**	98				
2	R = NMe_2	**4c**	**39**	81	7	 **4h**	**44**	79
3	R = OMe	**4d**	**40**	82				
4	R = CF_3	**4e**	**41**	17	8	 **4i**	**45**	49
5	R = CO_2Et	**4f**	**42**	62				

[a] Reaction conditions: **10** (0.30 mmol), arylboronic ester (0.45 mmol), $[RhCl(cod)]_2$ (0.015 mmol), I(2-Ad)•HCl (0.060 mmol), and NaOEt (0.60 mmol) in toluene (1.0 mL) at 130 °C for 20 h in a sealed tube. [b] Isolated yield after column chromatography.

The scope with respect to boronic esters is shown in Table 3. The electronic nature of the aryl group in the boronic ester was found to have a profound impact on the outcome of the reaction. Arylboronic esters bearing an electron-donating group, such as a Me (Entry 1),

NMe_2 (Entry 2) or an OMe (Entry 3) group, performed as excellent aryl donors to efficiently form the corresponding biaryl derivatives. In contrast, arylboronic esters bearing an electron-deficient CF_3 group on its phenyl ring, i.e., **4e** reacted poorly to afford the desired biaryl product in only 17% yield (Entry 4). The presence of an ester group was also well tolerated under these rhodium/I(2-Ad)-catalyzed conditions (Entry 5). The sterically hindered o-tolylboronic ester **4g** (Entry 6) and 1-naphthylboronic ester **4h** (Entry 7) also reacted smoothly with **10** to form the corresponding congested biaryl frameworks. Heteroarylboronic esters, including those containing a pyridine ring, could also be used in this arylation, although the product was formed in a relatively low yield (Entry 8).

Scheme 4. Possible Mechanism



Based on the results reported by Ozerov,[9] we have proposed a mechanism for the current rhodium-catalyzed cross-coupling of aryl carbamates with aryl boronic esters, which is depicted in Scheme 4 The catalyst precursor **A** would initially react with NaOEt to give the catalytically competent rhodium ethoxide complex **B**, which would subsequently undergo transmetalation with an aryl boronic ester Ar'$B(OR)_2$ to give the arylrhodium species **C**. The oxidative addition of a carbamate substrate to the arylrhodium **C** would activate the C(aryl)-O bond of the carbamate, leading to the formation of a rhodium(III) intermediate **D**, which would release an arylated product through reductive elimination. The resulting rhodium carbamate **E** would then be converted to rhodium ethoxide **B** via ligand exchange with NaOEt. A direct transmetalation pathway from **E** to **C** was considered to be unlikely because the use of excess NaOEt was essential for an efficient cross-coupling under these conditions.[15] The key to achieving the difficult oxidative addition of the C(aryl)-O bond of the aryl carbamate (i.e., **C→D**) could be attributed to the electron-rich nature of the rhodium center generated through the addition of the I(2-Ad) ligand. The electronic effects observed for the boronic

ester most likely originated from the electronic effect of the oxidative addition step (**C→D**) rather than the effect of the transmetalation step (**B→C**), because it is well known that the latter of these two steps can proceed with a wide range of electronically different organoboron compounds.[16] The use of electron-deficient boronic esters would lead to a decrease in the electron density of the rhodium center in **C**, which would in turn lead to reduction in the efficiency of the oxidative addition.[17]

1.3 Conclusion

In summary, we have developed a new rhodium-catalyzed cross-coupling reaction of aryl carbamates with organoboron reagents, which involves the cleavage of a relatively inert C(aryl)-O bond. Although C(aryl)-O bonds of this type can be activated using nickel-based catalysts, the reaction described herein represents the first use of a rhodium-based catalyst in a Suzuki-Miyaura type reaction. The choice of an appropriate ligand was found to be essential for efficient catalysis, and an NHC ligand bearing a 2-adamantyl group was found to be optimal. It is envisaged that this rhodium-mediated C(aryl)-O bond activation reaction could be applied to a range of other catalytic transformations, when considering a diverse reactivity of organorhodium intermediates, such as C-H activation. Studies aimed at developing a better understanding of the scope and limitations of this rhodium-mediated C(aryl)-O bond activation strategy are currently underway in our laboratory.

1.4 Experimental Section

General Information.

^{1}H NMR and ^{13}C NMR spectra were recorded on a JEOL JMTC-400/54/ss spectrometer in $CDCl_3$ with tetramethylsilane as an internal standard. Data have been reported as follows: chemical shift in ppm (δ), multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, and m = multiplet), coupling constant (Hz), and integration. Infrared spectra (IR) were obtained on a JASCO FT/IR-4000; absorptions have been reported in reciprocal centimeters with the following relative intensities: s (strong), m (medium), or w (weak). Mass spectra were recorded on a Shimadzu GCMS-QP 2010 instrument with an ionization voltage of 70 eV. Melting points were determined using a Yamato melting point apparatus. Column chromatography was performed with SiO2 [Merck SilicaGel 60 (230-400 mesh) or Silycycle Silica Flash F60 (230-400 mesh)]. Gel permeation chromatography (GPC) was performed using LC-9210NEXT HPLC or LC9225NEXT HPLC system. All of the reactions were carried out in 10 mL sample vials with Teflon-sealed screw caps. All of the chemicals used in the current study were manipulated in a glovebox filled with nitrogen.

Materials.

I(1-Ad)•HCl were purchased from Strem Chemicals and used as received. NaOtBu, NaOEt, IMes•HCl, IPr•HCl and diisopropylcarbamoyl chloride were purchased from TCI and used as received. Toluene (for Organic Synthesis), $[RhCl(cod)]_2$, PPh_3, **4a**, **4b** and **4j** [845885-86-1] were purchased from Wako Chemicals and used as received. PCy_3 and CsF were purchased from Aldrich and used as received. NaH was purchased from nacalai tesque and used as received. Compounds **10** [61912-15-0],[18] **12** [1203709-69-6],[19] **16** [885012-28-2],[20] **34** [1225288-38-9],[21] **4c** [95752-87-7],[10e] **4d** [213596-33-9],[22] **4e** [501374-30-7],[10e] **4f** [1192765-24-4],[23] **4g** [1632250-03-3],[10e] **4h** [91994-11-5],[10e] **4i** [22871-77-8][10e] and **4k** [916518-57-5][24] were synthesized according to the reported procedures.

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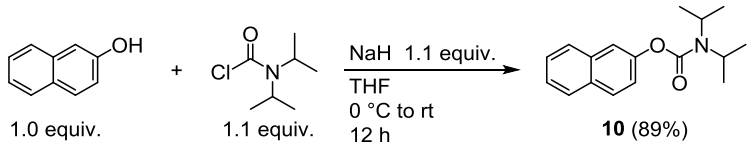
General Procedure for the Preparation of Starting Materials.

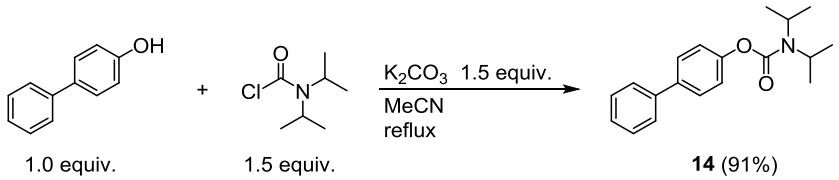


A solution of naphthalen-2-ol (4.3 g, 30 mmol) in dry THF (15 mmol) was added dropwise to a suspension of NaH (60% oil dispersion, 1.3 g, 33 mmol) in dry THF (15 mL) at 0 °C, and the resulting mixture was stirred at room temperature for 10 min. Diisopropylcarbamoyl chloride (5.4 g, 33 mmol) was then added to he reaction, and the resulting mixture was stirred at room temperature for 12 h. The reaction mixture was then cooled to 0 °C and quenched by the addition of EtOH. The solvent was removed in vacuo to give a residue, which was dissolved in EtOAc and filtered through a pad of silica gel. The filtrate was then concentrated in vacuo to give the crude product, which was purified by flash column chromatography over silica gel (eluent: hexane/EtOAc = 10/1) to give naphthalen-2-yl diisopropylcarbamate (**10**, 7.3g, 89%) as a white solid.

^{1}H NMR ($CDCl_3$, 400 MHz): 1.32 (bs, 6H), 1.39 (bs, 6H), 4.00 (bs, 1H), 4.15 (bs, 1H), 7.29 (dd, J = 2.2, 8.6 Hz, 1H), 7.41-7.49 (m, 2H), 7.58 (d, J = 2.4 Hz, 1H), 7.78-7.84 (m, 3H).

^{13}C NMR ($CDCl_3$, 100 MHz): 20.4, 21.5, 46.0, 46.9, 118.3, 121.7, 125.1, 126.2, 127.4, 127.6, 129.0, 131.0, 133.8, 149.0, 153.9.

[1,1'-Biphenyl]-4-yl diisopropylcarbamate (14).



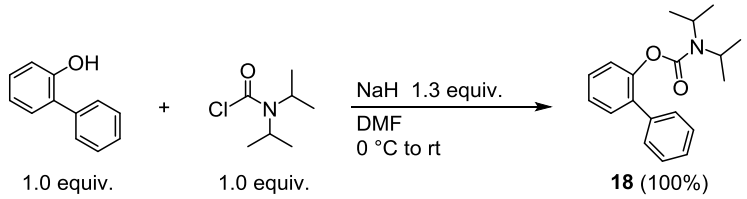
[1,1'-Biphenyl]-4-ol (1.7 g, 10 mmol), diisopropylcarbamic chloride (2.5 g, 15 mmol) and K_2CO_3 (2.1 g, 15 mmol) were refluxed in MeCN for 12 h. The resulting mixture was cooled to room temperature, and the solvent was removed in vacuo. The purification by flash column chromatography over silica gel (hexane/EtOAc = 2/1) gave the product as a white solid (**14**, 2.7 g, 91%). Rf = 0.67 (hexane/EtOAc = 3/1). Mp 76 °C.

^{1}H NMR ($CDCl_3$, 400 MHz): 1.31 (bs, 6H), 1.36 (bs, 6H), 3.97 (bs, 1H), 4.13 (bs, 1H), 7.20 (d, J = 8.8 Hz, 2H), 7.34 (t, J = 7.4 H, 1H), 7.43 (t, J = 7.8 Hz, 2H), 7.56-7.58 (m, 4H).

^{13}C NMR ($CDCl_3$, 150 MHz): 20.4, 21.5, 46.0, 46.8, 122.0, 126.97, 127.01, 127.9, 128.6, 138.0, 140.6, 150.8, 153.7.

HRMS (FAB): Calcd for $C_{19}H_{23}NO_2$+H^+ 298.1802, Found 298.1801.

[1,1'-Biphenyl]-2-yl diisopropylcarbamate (18).



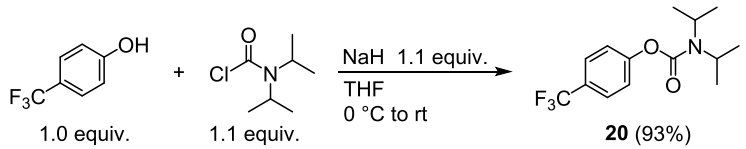
A solution of [1,1'-biphenyl]-2-ol (1.7 g, 10 mmol) in dry THF (5 mL) was added dropwise at 0°C to a suspension of NaH (60% oil dispersion, 520 mg, 13 mmol) in dry THF (5 mL). The resulting mixture was stirred at room temperature for 10 min, diisopropylcarbamoyl chloride (1.6 g, 10 mmol) was then added, and the mixture was stirred at room temperature for 12 h. The purification described in the general method, gave colorless oil (**18**, 3.0 g, 100%). Rf = 0.57 (hexane/EtOAc = 3/1).

^{1}H NMR ($CDCl_3$, 400 MHz): 1.05 (d, 6.0 Hz, 6H), 1.17 (d, J = 5.6 Hz, 6H), 3.78 (bs, 1 H), 3.94 (bs, 1H), 7.18 (d, J = 8.0 Hz, 1H), 7.24-7.42 (m, 8H).

^{13}C NMR ($CDCl_3$, 100 MHz): 20.2, 20.8, 46.0, 46.4, 123.3, 125.3, 127.0, 127.9, 128.2, 129.0, 130.5, 135.4, 138.1, 148.3, 153.1.

HRMS (FAB): Calcd for $C_{19}H_{23}NO_2$+H^+ 298.1802, Found 298.1807.

4-(Trifluoromethyl)phenyl diisopropylcarbamate (20).



Compound **20** was prepared according to the general procedure.

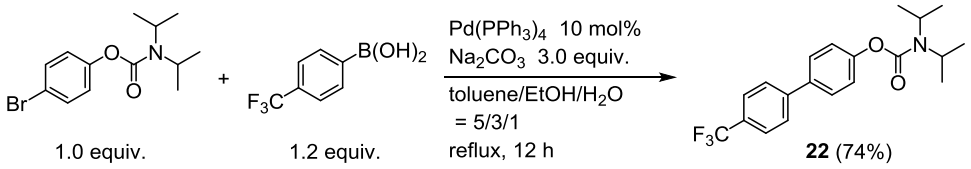
Colorless oil (**20**, 2.7 g, 93%). Rf = 0.49 (hexane/EtOAc = 5/1).

^{1}H NMR ($CDCl_3$, 400 MHz): 1.30 (bs, 6H), 1.33 (bs, 6H), 3.98 (bs, 1H), 4.09 (bs, 1H), 7.24 (d, J = 8.8 Hz, 2H), 7.62 (d, J = 8.8 Hz, 2H).

^{13}C NMR ($CDCl_3$, 100 MHz): 19.7, 20.8, 45.9, 46.5, 121.8, 123.8 (q, J = 270.2 Hz), 126.0, 126.5 (q, J = 32.5 Hz), 152.4, 153.8.

HRMS (APCI): Calcd for $C_{14}H_{18}F_3NO_2$+H^+ 290.1362, Found 290.1362.

4'-(Trifluoromethyl)-[1,1'-biphenyl]-4-yl diisopropylcarbamate (22).



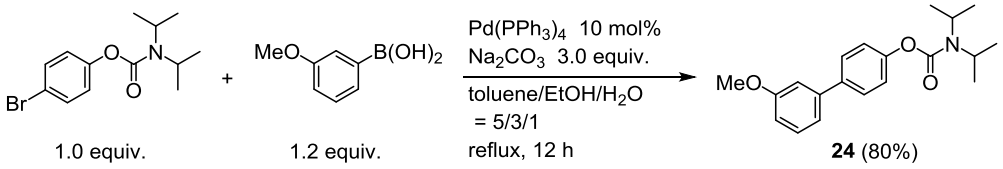
An oven-dried two-necked flask was charged with 4-bromophenyl diisopropylcarbamate (3.0 g, 10 mmol), which was synthesized from *p*-bromophenol accordintg to the general procedure, (4-(trifluoromethyl)phenyl)boronic acid (2.3 g, 12 mmol), $Pd(PPh_3)_4$ (1.2 g, 1.0 mmol) and Na_2CO_3 (3.2 g, 30 mmol), toluene (25 mL), EtOH (15 mL) and H_2O (5 mL), and the mixture was refluxed for 12 h. The resulting mixture was cooled to room temperature. The solvent was removed in vacuo. The residual solid was dissolved in EtOAc and filtrated through a pad of silica gel. The crude product was obtained after evaporation of the solvent under reduced pressure. The purification by flash column chromatography over silica gel (hexane/EtOAc = 10/1) gave the product as a white solid (**22**, 2.7 g, 74%). Rf = 0.49 (hexane/EtOAc = 5/1). Mp 65-69 °C.

^{1}H NMR ($CDCl_3$, 400 MHz): 1.31 (bs, 6H), 1.36 (bs, 6H) 3.99 (bs, 1H), 4.12 (bs, 1H), 7.21-7.25 (m, 2H), 7.56-7.60 (m, 2H), 7.65-7.70 (m, 4H).

^{13}C NMR ($CDCl_3$, 100 MHz): 20.3, 21.5, 46.1, 46.9, 122.4, 124.2 (q, J = 270.5 Hz), 125.6 (q, J = 3.80 Hz), 127.2, 128.1, 129.1 (q, J = 32.1 Hz), 136.5, 144.0, 151.5, 153.6.

HRMS (EI): Calcd for $C_{20}H_{22}F_3NO_2$ 365.1603, Found 365.1604.

3'-Methoxy-[1,1'-biphenyl]-4-yl diisopropylcarbamate (24).



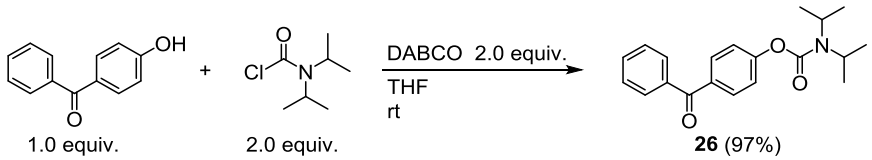
An oven-dried two-necked flask was charged with 4-bromophenyl diisopropylcarbamate (3.0 g, 10 mmol) and (3-methoxyphenyl)boronic acid (1.8 g, 12 mmol), $Pd(PPh_3)_4$ (1.2 g, 1.0 mmol) and Na_2CO_3 (3.2 g, 30 mmol), toluene (25 mL), EtOH (15 mL) and H_2O (5 mL), and the mixture was refluxed for 12 h. The resulting mixture was cooled to room temperature. The solvent was removed in vacuo. The residual solid was dissolved by EtOAc, and filtrated through a pad of silica gel. The crude product was obtained after evaporation of the solvent under reduced pressure. The purification by flash column chromatography over silica gel (hexane/EtOAc = 10/1) gave the product as a colorless oil (**24**, 2.6 g, 80%). Rf = 0.37 (hexane/EtOAc = 5/1).

^{1}H NMR ($CDCl_3$, 400 MHz): 1.31(bs, 6H), 1.34 (bs, 6H), 3.85 (s, 3H) , 3.97 (bs, 1H), 4.12 (bs, 1H), 6.90 (dd, *J* = 2.8, 8.4 Hz, 1H), 7.09 (s, 1H), 7.14-7.20 (m, 3H), 7.34 (t, *J* = 7.8 Hz, 1H), 7.56 (d, *J* = 8.4 Hz, 2H).

^{13}C NMR ($CDCl_3$, 100 MHz): 20.4, 21.5, 46.0, 46.9, 55.2, 112.4, 112.8, 119.5, 122.0, 128.0, 129.7, 137.9, 142.1, 150.8, 153.7, 159.8.

HRMS (FAB): Calcd for $C_{20}H_{25}NO_3+H^+$ 328.1907, Found 328.1908.

4-Benzoylphenyl diisopropylcarbamate (26).



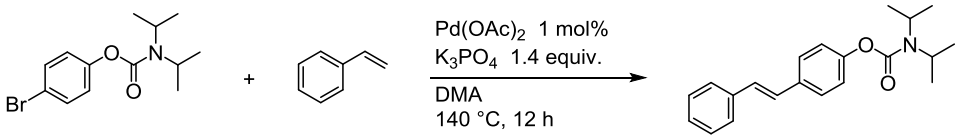
A mixture of (4-hydroxyphenyl)(phenyl)methanone (2.0 g, 10 mmol), was treated with diisopropylcarbamic chloride (2.5 g, 15 mmol) and DABCO (2.2 g, 20 mmol) were refluxed in THF (50 mL) for 12 h. The solvent was removed in vacuo. The purification by flash column chromatography on silica gel (hexane/EtOAc = 10/1) gave the product as a white solid (**26**, 3.1 g, 97%). Rf = 0.32 (hexane/EtOAc = 5/1), White solid. Mp 70 °C.

^{1}H NMR ($CDCl_3$, 400 MHz): 1.32 (bs, 6H), 1.35 (bs, 6H), 4.00 (bs, 1H), 4.11 (bs, 1H), 7.24-7.26 (m, 2H), 7.48 (t, *J* = 5.2 Hz, 2H), 7.59 (t, *J* = 4.8 Hz, 1H), 7.79-7.86 (m, 4H).

^{13}C NMR ($CDCl_3$, 100 MHz): 20.3, 21.4, 46.2, 46.9, 121.5, 128.1, 129.8, 131.4, 132.2, 134.0, 137.5, 152.8, 154.7, 195.6.

HRMS (EI): Calcd for $C_{20}H_{23}NO_3$ 325.1678, Found 325.1679.

(E)-4-Styrylphenyl diisopropylcarbamate (28).



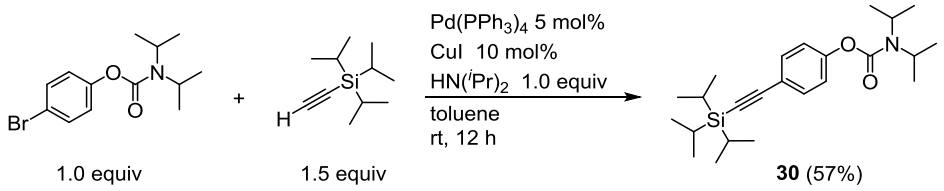
An oven-dried two-necked flask was charged with 4-bromophenyl diisopropylcarbamate (3.0 g, 10 mmol), styrene (1.3 g, 12 mmol), $Pd(OAc)_2$ (48 mg, 0.1 mmol) and K_3PO_4 (3.0 g, 14 mmol) and DMA (10 mL), and the mixture was heated for 12 h at 140 °C. The resulting mixture was cooled to rom temperture. The solvent was removed in vacuo. The residual solid was dissolved in EtOAc, and filtrated through a pad of silica gel. The crude product was obtained after evaporation of the solvent under reduced pressure. The purification by flash column chromatography over silica gel (hexane/EtOAc = 10/1) gave the product as a white solid (**28**, 1.9 g, 59%). Rf = 0.42 (hexane/EtOAc = 5/1). Mp 109 °C.

^{1}H NMR ($CDCl_3$, 400 MHz): 1.30 (bs, 6H), 1.34(bs, 6H), 3.95 (bs, 1H), 4.13 (bs, 1H), 7.02-7.13 (m, 4H), 7.25-7.27 (m, 1H), 7.34-7.38 (m, 2H), 7.49-7.52 (m, 4H).

^{13}C NMR ($CDCl_3$, 100 MHz): 20.4, 21.5, 46.0, 46.9, 122.0, 126.4, 127.2, 127.5, 127.9, 128.3, 128.6, 134.2, 137.2, 150.8, 153.7.

HRMS (FAB): Calcd for $C_{21}H_{25}NO_2+H^+$ 324.1958, Found 324.1963.

4-((Triisopropylsilyl)ethynyl)phenyl diisopropylcarbamate (30).

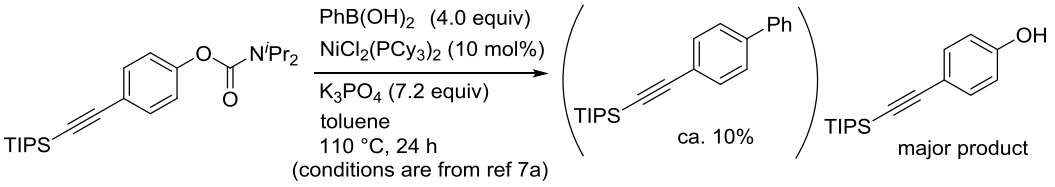


A toluene solution (20 mL) of a mixture of 4-bromophenyl diisopropylcarbamate (3.0 g, 10 mmol), ethynyltriisopropylsilane (2.7 g, 15 mmol), $Pd(PPh_3)_4$ (580 mg, 0.5 mmol), and CuI (190 mg, 1.0 mmol) was subjected to freeze-to-thaw cycles 3 times. Then, ^{i}Pr$_2$NH (1.0 g, 10 mmol) was added, and the mixture was stirred for 12 h at 25 °C. The resulting mixture was cooled to rt. The solvent was removed in vacuo. The residual solid was dissolved in EtOAc, and filtrated through a pad of silica gel. The crude product was obtained after evaporation of the solvent under reduced pressure. The purification by flash column chromatography over silica gel (hexane/EtOAc = 10/1) gave the product as a white solid (**30**, 2.3 g, 57%). Rf = 0.56 (hexane/EtOAc = 5/1). Mp 61-62 °C.

^{1}H NMR ($CDCl_3$, 400 MHz): 1.12 (s, 21H), 1.29 (bs, 6H), 1.32 (bs, 6H), 3.94 (bs, 1H), 4.11 (bs, 1H), 7.06 (dt, J = 0.6, 2.2 Hz, 2H), 7.44-7.48 (dt, J = 0.6, 2.2 Hz, 2H).

^{13}C NMR ($CDCl_3$, 100 MHz): 11.3, 18.6, 20.4, 21.5, 46.0, 46.9, 90.0, 106.6, 120.2, 121.7, 133.0, 151.2, 153.3.

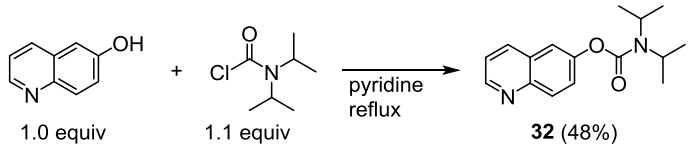
HRMS (FAB): Calcd for $C_{24}H_{39}NO_2Si+H^+$ 402.2823, Found 402.2825.



cf. under our optimized conditions: 82%

This carbamate **30** could not be arylated under the previously reported nickel-catalyzed conditions.[3a]

Quinolin-6-yl diisopropylcarbamate (32).



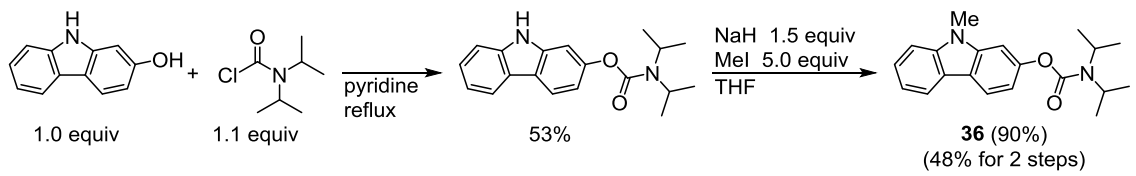
Quinolin-6-ol (1.5 g, 10 mmol) and diisopropylcarbamic chloride (1.8 g, 11 mmol) were refluxed in pyridine (30 mL) for 12 h. The resulting mixture was cooled to room temperature, and the solvent was removed in vacuo. The purification by flash column chromatography on silica gel (hexane/EtOAc = 2/1) gave the product as a white solid (**32**, 1.3 g, 48%). Rf = 0.19 (hexane/EtOAc = 2/1). Mp 114 °C.

^{1}H NMR ($CDCl_3$, 400 MHz): 1.33 (bs, 6H), 1.39 (bs, 6H), 4.02 (bs, 1H), 4.14 (bs,1H), 7.40 (dd, *J* = 4.0, 8.0 Hz, 1H), 7.52 (dd, *J* = 2.8, 9.2 Hz, 1H), 7.60 (d, *J* = 2.4 Hz, 1H), 8.09-8.13 (m, 2H), 8.88 (dd, *J* = 1.2, 4.2 Hz, 1H).

^{13}C NMR ($CDCl_3$, 100 MHz): 20.3, 21.5, 46.1, 46.9, 118.1, 121.2, 125.2, 128.5, 130.5, 135.5, 145.9, 149.1, 149.7, 153.4.

HRMS (FAB): Calcd for $C_{16}H_{20}N_2O_2+H^+$ 273.1598, Found 273.1602.

9-Methyl-9H-carbazol-2-yl diisopropylcarbamate (36).



9*H*-Carbazol-2-ol (3.7 g, 20 mmol) and diisopropylcarbamic chloride (3.6 g, 22 mmol) were refluxed in pyridine (50 mL) for 12 h. The resulting mixture was cooled to rt and the solvent

was removed in vacuo. The purification by flash column chromatography on silica gel (hexane/EtOAc = 2/1, Rf = 0.61) gave 9*H*-carbazol-2-yl diisopropylcarbamate as a white solid (3.3 g, 53%).

9*H*-Carbazol-2-yl diisopropylcarbamate (2.1 g, 6.6 mmol) in dry THF (10 ml) was added dropwise at 0 °C to a suspension of NaH (60 wt% oil dispersion, 400 mg, 9.9 mmol) in dry THF (10 mL). The resulting mixture was stirred at room temperature for 10 min, MeI (2 mL) was then added, and the mixture was stirred at room temperature for 16 h. The mixture was then cooled to 0 °C and quenched by the addition of water (10 mL). The THF was removed in vacuo to give an aqueous residue, which was extracted with ether (10 mL x 3). The combined extracts were then washed with brine, dried over Na_2SO_4 and evaporated in vacuo to give the crude product, which was purified by recrystallization from $CHCl_3$-hexane to give **36** as a white solid (1.9 g, 90 %, 48% for 2 steps). Rf = 0.47 (hexane/EtOAc = 5/1), white solid. Mp = 117-118 °C.

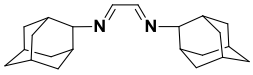
^{1}H NMR ($CDCl_3$, 400 MHz): 1.32 (bs, 6H), 1.41 (bs, 6H), 3.83 (s, 3H), 4.00 (bs, 1H), 4.17 (bs, 1H), 6.98 (dd, J = 2.0, 8.6 Hz, 1H), 7.20-7.25 (m, 2H), 7.39 (d, J = 8.0 Hz, 1H), 7.46 (t, J = 8.4 Hz, 1H), 8.04 (t, J = 8.2 Hz, 2H).

^{13}C NMR ($CDCl_3$, 150 MHz): 20.5, 21.6, 29.2 46.0, 46.9, 102.1, 108.3, 113.2, 119.0, 119.99, 120.02, 120.5, 122.6, 125.2, 141.4, 141.5, 150.0, 154.3.

HRMS (EI): Calcd for $C_{20}H_{24}N_2O_2$ 324.1838, Found 324.1848.

Preparation of I(2-Ad)·HCl

***N, N'*-Bis(adamantan-2-yl)ethane-1,2-diimine.**



2-Adamantanamine hydrochloride (14 g, 75 mmol), Et_2O (200 mL) and a saturated aqueous solution of K_2CO_3 (300 mL) was added to 500 mL flask, and the mixture was stirred for 1 h. The mixture was then partitioned between Et_2O and water. The organic layer was washed with water, dried ($MgSO_4$) and concentrated *in vacuo* to give 2-adamantanamine as a white solid (11 g, 98%).

The resulting 2-adamantanamine (11 g, 73 mmol) and an aqueous solution of glyoxal (8.8 M, 4.0 mL, 35 mmol) were dissolved in THF (100 mL), and the mixture was stirred at room temperature for 12 h. The resulting mixture was partitioned between Et_2O and a saturated aqueous solution of $NaHCO_3$. The organic layer was washed with a saturated aqueous solution of $NaHCO_3$ and water, dried ($MgSO_4$) and concentrated *in vacuo* to give the title compound as a white solid (12 g, 100%).

White solid. Rf 0.83 (NH Silica, Et_2O). Mp: 159 -162 °C.

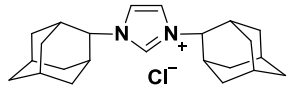
^{1}H NMR ($CDCl_3$, 400 MHz): 8.02 (s, 2H), 3.41 (s, 2H), 2.23 (d, J = 12.0 Hz, 4H), 1.89-1.75 (m, 22H), 1.52 (s, 2H).

^{13}C NMR ($CDCl_3$, 100 MHz): 160.6, 74.5, 38.1, 37.4, 35.2, 31.9, 28.2, 27.5.

IR (ATR): 2901 s, 2849 s, 2823 m, 1633 m, 1467 w, 1449 m, 1364 w, 1336 w, 1288 w, 1101 m, 1049 w, 1011 w, 966 w, 930 m, 902 w, 877 w, 809 w, 669 w.

HRMS (EI): Calcd for $C_{22}H_{32}N_2$ 324.2565, Found 324.2566.

1,3-Bis(adamantan-2-yl)imidazolin-2-yliden chloride (I(2-Ad)•HCl).



N, N, N', N'-tetramethyldiaminomethane (6.6 mL, 5.0 g, 49 mmol) and CH_2Cl_2 (60 mL) was added to a dry 500 mL three-necked flask, and the mixture was degassed before cooling to 0 °C. Acetyl chloride (3.7 mL, 4.1 g, 52 mmol) was added dropwise to the reaction mixture over 20 min, and resulting mixture was stirred at 0 °C for 1 h. The solution of *N, N'*-bis(adamantan-2-yl)ethane-1,2-diimine (12 g, 37 mmol) in CH_2Cl_2 (60 mL) was added dropwise to the reaction mixture over 30 min at -78 ^{o}C. The reaction mixture was then warmed to room temperature and stirred for 14 h. Et_2O (400 mL) was added to the resulting white suspension, and a white precipitate was collected by filtration. The precipitate was purified by recrystallization (H_2O) to give the title compound as a white powder (9.0 g, 65%).

White powder. Mp: 318 -320 °C.

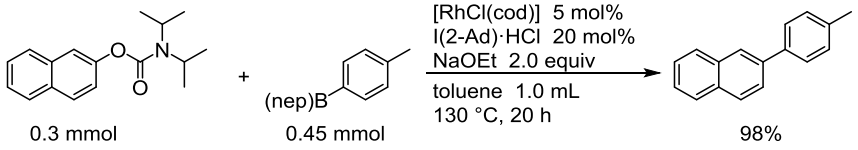
^{1}H NMR ($CDCl_3$, 400 MHz): 10.5 (s, 1 H), 7.36 (t, J = 1.4 Hz, 2 H), 4.60 (s, 2H), 2.83 (s, 4 H), 2.07-1.98 (m, 10 H), 1.95-1.85 (m, 2 H), 1.79-1.74 (m, 8 H), 1.68-1.63 (m, 4 H).

^{13}C NMR ($CDCl_3$, 100 MHz): 137.7, 119.4, 64.2, 37.0, 36.8, 31.3, 31.2, 26.78, 26.72.

IR (ATR): 3298 w, 3091 w, 3039 m, 2920 s, 2901 s, 2855 m,1736 w, 1544 m, 1470 w, 1449 m, 1390 w, 1372 m, 1342 m, 1282 w, 1244 w, 1188 w, 1159 s, 1106 m, 1075 w, 964 m, 864 s, 821 m, 792 w, 782 w, 765 w, 704 m.

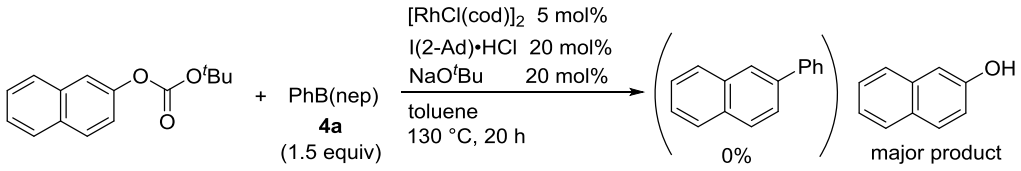
HRMS (FAB): Calcd for $C_{23}H_{33}N_2^+$ 337.2644, Found 337.2642.

Typical Procedure for Rh-catalyzed Cross-coupling of Aryl Carbamates (Entry 1 in Table 3).



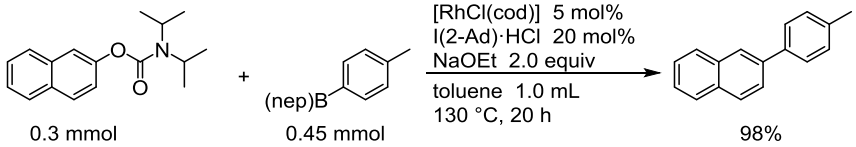
[RhCl(cod)]$_2$ (7.4 mg, 0.015 mmol), I(2-Ad)·HCl (22 mg, 0.060 mmol), NaOEt (41 mg, 0.60 mmol) and toluene (0.40 mL) were added to a 10 mL sample vial with a Teflon sealed screwcap in a glovebox filled with nitrogen, and the resulting mixture was stirred for 10 min. Naphthalen-2-yl diisopropylcarbamate (**10**, 81 mg, 0.30 mmol), 5,5-dimethyl-2-(p-tolyl)-1,3,2-dioxaborinane (**4b**, 92 mg, 0.45 mmol) and toluene (0.60 mL) were then added to the vial, and the resulting mixture was sealed in the vessel and heated at 130 °C for 20 h on an aluminum block. The mixture was then cooled to room temperature and purified directly by flash column chromatography over silica gel (eluent: hexane/EtOAc = 10:1) to give 2-(p-tolyl)naphthalene (**38**, 64 mg, 98%) as a white solid.

Rh-catalyzed Cross-coupling of *tert*-Butyl Naphthalen-2-yl Carbonate with Arylboron Reagent.



[RhCl(cod)]$_2$ (7.4 mg, 0.015 mmol), I(2-Ad)·HCl (22 mg, 0.060 mmol), NaO^{t}Bu (5.8 mg, 0.060 mmol) and toluene (0.40 mL) were added to a 10 mL sample vial with a Teflon sealed screwcap in a glovebox filled with nitrogen, and the resulting mixture was stirred for 10 min. *tert*-Butyl naphthalen-2-yl carbonate (73 mg, 0.30 mmol), 5,5-dimethyl-2-phenyl-1,3,2-dioxaborinane (**4a**, 86 mg, 0.45 mmol) and toluene (0.60 mL) were then added to the vial, and the resulting mixture was sealed in the vessel and heated at 130 °C for 20 h on an aluminum block. The mixture was then cooled to room temperature and analyzed by GC. Starting carbonate was completely consumed and 2-naphthol was ditected as a only one product.

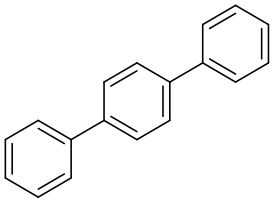
Typical Procedure for Rh-catalyzed Cross-Coupling of Aryl Carbamates.



[RhCl(cod)]2 (7.4 mg, 0.015 mmol), I(2-Ad)·HCl (22 mg, 0.060 mmol), NaOEt (41 mg, 0.60 mmol) and toluene (0.40 mL) were added to a 10 mL sample vial with a Teflon sealed screwcap in a glovebox filled with nitrogen, and the resulting mixture was stirred for 10 min. Naphthalen-2-yl diisopropylcarbamate (**10**, 81 mg, 0.30 mmol), 5,5-dimethyl-2-(p-tolyl)-1,3,2-dioxaborinane (4b, 92 mg, 0.45 mmol) and toluene (0.60 mL) were then added to the vial, and the resulting mixture was sealed in the vessel and heated at 130 °C for 20 h on an

aluminum block. The mixture was then cooled to room temperature and purified directly by flash column chromatography over silica gel (eluent: hexane/EtOAc = 10:1) to give 2-(p-tolyl)naphthalene (**38**, 64 mg, 98%) as a white solid.

1,1':4',1''-Terphenyl (15) [CAS: 92-94-4].



General procedure was followed, except that **14** was used instead of **10**.

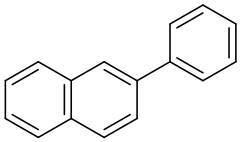
Rf = 0.75 (hexane/EtOAc = 3/1). White solid (59 mg, 86%).

^{1}H NMR ($CDCl_3$, 400 MHz): 7.37 (t, J = 7.4 Hz, 2H), 7.47 (t, J = 7.4 Hz, 4H), 7.65 (d, J = 7.6 Hz, 4H), 7.68 (s, 4H).

^{13}C NMR ($CDCl_3$, 100 MHz): 127.0, 127.3, 127.5, 128.8, 140.0, 140.7.

HRMS (EI): Calcd for $C_{18}H_{14}$ 230.1096, Found 230.1089.

2-Phenylnaphthalene (11) [CAS:612-94-2].



General procedure was followed.

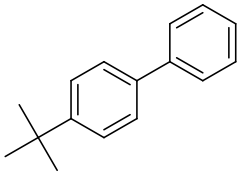
Rf = 0.66 (hexane/EtOAc = 3/1). White solid (49 mg, 80%).

^{1}H NMR ($CDCl_3$, 400 MHz): 7.39 (t, J = 7.8 Hz, 1H), 7.48-7.53 (m, 4H), 7.72-7.77 (m, 3H), 7.87-7.94 (m, 3H), 8.05 (s, 1H).

^{13}C NMR ($CDCl_3$, 100 MHz): 125.6, 125.8, 125.9, 126.3, 127.3, 127.4, 127.6, 128.2, 128.4, 128.8, 132.6, 133.6, 138.5, 141.1.

HRMS (APCI): Calcd for $C_{16}H_{12}$+H^+ 205.1012, Found 205.1047.

4-(*tert*-Butyl)-1,1'-biphenyl (13) [CAS: 1625-92-9].



General procedure was followed, except that **12** was used instead of **10**.

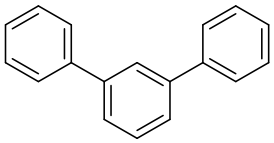
Rf = 0.71 (hexane/EtOAc = 3/1). White solid (11 mg, 18%).

^{1}H NMR ($CDCl_3$, 400 MHz): 1.37 (s, 9H), 7.33 (t, J = 4.9 Hz, 1H), 7.41-7.48 (m, 4H), 7.54 (d, J = 8.0 Hz, 2H), 7.59 (d, J = 8.0 Hz, 2H).

^{13}C NMR ($CDCl_3$, 100 MHz): 31.4, 34.5, 125.7, 126.8, 127.0, 127.0, 128.7, 128.3, 141.0, 150.2.

HRMS (FAB): Calcd for $C_{16}H_{18}$ 210.1409, Found 210.1407.

1,1':3',1''-Terphenyl (17) [CAS: 92-06-8].



General procedure was followed, except that **16** was used instead of **10**.

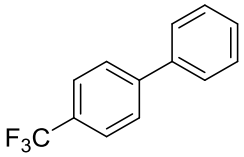
Rf = 0.60 (hexane/EtOAc = 3/1). White solid (57 mg, 82%).

^{1}H NMR ($CDCl_3$, 400 MHz): 7.32-7.40 (m, 2H), 7.42-7.48 (m, 4H), 7.50-7.52 (m, 1H), 7.56-7.60 (m, 2H), 7.63-7.69 (m, 4H), 7.80 (s, 1H).

^{13}C NMR ($CDCl_3$, 100 MHz): 126.1, 126.1, 127.2, 127.4, 128.8, 129.2, 141.1, 141.7.

HRMS (EI): Calcd for $C_{18}H_{14}$ 230.1096, Found 230.1087

4-(Trifluoromethyl)-1,1'-biphenyl (21) [CAS:398-36-7].



General procedure was followed, except that **20** was used instead of **10**.

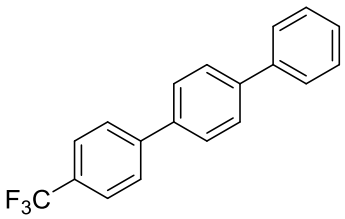
Rf = 0.63 (hexane/EtOAc = 5/1). White solid (53 mg, 79%).

^{1}H NMR ($CDCl_3$, 400 MHz): 7.39-7.50 (m, 3H), 7.60 (d, J = 8.0 Hz, 2H), 7.70 (s, 4H).

^{13}C NMR ($CDCl_3$, 100 MHz): 124.3 (q, J = 272.2 Hz), 127.3, 127.4, 128.2, 128.7, 129.0, 129.3 (q, J = 32.4 Hz), 139.7, 144.7.

HRMS (APCI): Calcd for $C_{13}H_9F_3$+H^+ 223.0729, Found 223.0738.

4-(Trifluoromethyl)-1,1':4',1''-terphenyl (23) [CAS:72864-00-7].



General procedure was followed, except that **22** was used instead of **10**.

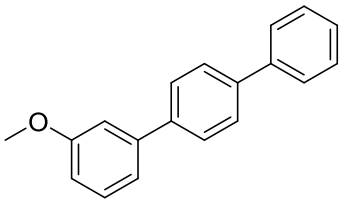
Rf = 0.57 (hexane / EtOAc = 5 / 1). White solid (87 mg, 97%).

^{1}H NMR ($CDCl_3$, 400 MHz): 7.39 (t, *J* =3.2 Hz, 1H), 7.48 (t, *J* = 3.4 Hz, 2H), 7.64-7.76 (m, 10H).

^{13}C NMR ($CDCl_3$, 100 MHz): 124.3 (q, *J* = 270.7 Hz), 125.8 (q, *J* = 2.8 Hz), 127.1, 127.2, 127.58, 127.62, 127.7, 128.9, 129.3 (q, *J* =32.4 Hz), 138.5, 140.3, 141.0, 144.2.

HRMS (APCI): Calcd for $C_{19}H_{13}F_3$+H^+ 299.1042, Found 299.1041.

3-Methoxy-1,1':4',1''-terphenyl (25) [CAS:908297-75-6].



General procedure was followed, except that **24** was used instead of **10**.

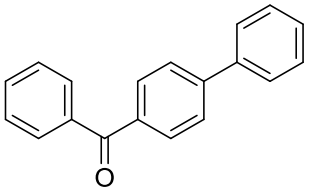
Rf = 0.54 (hexane / EtOAc = 5/ 1). White solid (48 mg, 61%).

^{1}H NMR ($CDCl_3$, 400 MHz): 3.86 (s, 3H), 6.91 (dd, *J* = 2.4, 7.8 Hz, 1H), 7.17 (s, 1H), 7.23 (d, *J* = 6.8 Hz, 1H), 7.34-7.39 (m, 2H), 7.45 (t, *J* = 7.8 Hz, 2H), 7.62-7.66 (m, 6H).

^{13}C NMR ($CDCl_3$, 100 MHz): 55.4, 112.8, 112.9, 119.7, 127.2, 127.5, 127.6, 127.7, 128.9, 129.9, 140.1, 140.4, 140.8, 140.3, 160.1.

HRMS (APCI): Calcd for $C_{19}H_{16}O$+H^+ 261.1274, Found 261.1278.

[1,1'-Biphenyl]-4-yl(phenyl)methanone (27) [CAS:2128-93-0].



General procedure was followed, except that **26** was used instead of **10**.

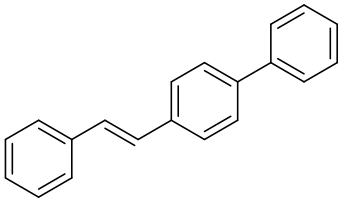
Rf = 0.49 (hexane/EtOAc = 5/1). White solid (24 mg, 31%).

^{1}H NMR ($CDCl_3$, 400 MHz): 7.41 (t, *J* = 7.4 Hz, 1H), 7.50 (d, *J* = 7.5 Hz, 4H), 7.61 (t, 7.4 Hz, 1H), 7.65-7.67 (m, 2H), 7.70-7.72 (m, 2H), 7.84 (d, *J* = 7.2 Hz, 2H), 7.90 (dd, *J* = 2.0, 6.4 Hz, 2H).

^{13}C NMR ($CDCl_3$, 100 MHz): 127.0, 127.3, 128.2, 128.3, 129.0, 130.0, 130.7, 132.4, 136.2, 137.7, 139.9, 145.2, 196.4,

HRMS (APCI): Calcd for $C_{19}H_{14}O$+H^+ 259.1117, Found 259.1118.

(*E*)-4-Styryl-1,1'-biphenyl (29) [CAS:2039-69-2].



General procedure was followed, except that **28** was used instead of **10**.

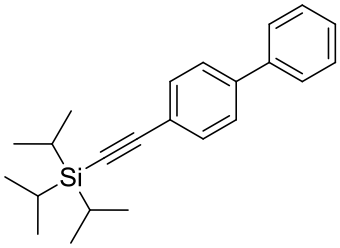
Rf = 0.54 (hexane/EtOAc = 5/1). White solid (34 mg, 44%).

^{1}H NMR ($CDCl_3$, 400 MHz): 7.16 (s, 2H), 7.28 (d, *J* = 7.2 Hz, 1H), 7.34-7.40 (m, 3H), 7.46 (t, *J* = 7.6 Hz, 2H), 7.54 (d, *J* = 7.2 Hz, 2H), 7.61-7.64 (m, 6H).

^{13}C NMR ($CDCl_3$, 150 MHz): 126.5, 126.90, 126.92, 127.31, 127.34, 127.6, 128.2, 128.69, 128.74, 128.8, 136.4, 137.3, 140.3, 140.7.

HRMS (APCI): Calcd for $C_{20}H_{16}+H^+$ 257.1325, Found 257.1326.

([1,1'-Biphenyl]-4-ylethynyl)triisopropylsilane (31).[10d]



General procedure was followed, except that **30** was used instead of **10**.

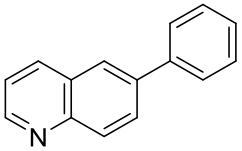
Rf = 0.69 (hexane/EtOAc = 5/1). White solid (57 mg, 57%).

^{1}H NMR ($CDCl_3$, 400 MHz): 0.95-1.00 (m, 3H), 1.12-1.19 (m, 18H), 7.36 (t, *J* = 7.4 Hz, 2H), 7.45 (t, *J* = 7.6 Hz, 2H), 7.54-7.60 (m, 5H).

^{13}C NMR ($CDCl_3$, 100 MHz): 11.4, 18.8, 91.4, 107.0, 122.5, 126.8, 127.0, 127.7, 128.9, 132.6, 140.5, 141.1.

HRMS (APCI): Calcd for $C_{23}H_{30}Si+H^+$ 335.2190, Found 335.2199.

6-Phenylquinoline (33) [CAS: 612-95-3].



General procedure was followed, except that **32** was used instead of **10**.

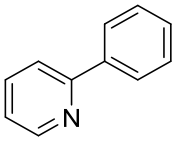
Rf = 0.43 (hexane/EtOAc = 5/1). Pale yellow solid (39 g, 63%).

^{1}H NMR ($CDCl_3$, 400 MHz): 7.40-7.43(m, 2H), 7.50 (t, *J* = 7.4 Hz, 2H), 7.71 (d, *J* = 8.4 Hz, 2H), 7.98 (d, *J* = 8.4 Hz, 2H), 8.18 (dd, *J* = 8.4, 13.2 Hz, 2H), 8.91 (d, *J* = 4.0 Hz, 1H).

^{13}C NMR ($CDCl_3$, 100 MHz): 121.6, 125.6, 127.6, 127.9, 128.6, 129.1, 129.4, 130.0, 136.4, 139.4, 140.4, 147.8, 150.5.

HRMS (APCI): Calcd for $C_{15}H_{11}N+H^+$ 206.0964, Found 206.0973.

2-Phenylpyridine (35) [CAS:1008-89-5].



General procedure was followed, except that **34** was used instead of **10**.

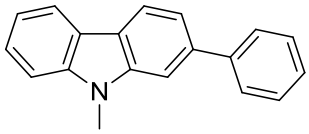
Rf = 0.21 (hexane/EtOAc = 2/1). Pale yellow oil (19 mg, 40%).

^{1}H NMR ($CDCl_3$, 400 MHz): 7.22-7.25 (m, 1H), 7.40-7.51 (m, 3H), 7.72-7.78 (m, 2H), 7.98-8.01 (m, 2H), 8.69-8.71 (m, 1H).

^{13}C NMR ($CDCl_3$, 100 MHz): 120.2, 121.8, 126.6, 128.5, 128.7, 136.4, 139.1, 140.3, 157.0.

HRMS (APCI): Calcd for $C_{11}H_9N+H^+$ 156.0808, Found 156.0837.

9-Methyl-2-phenyl-4a,9a-dihydro-9H-carbazole (37) [CAS:884847-90-9].



General procedure was followed, except that **36** was used instead of **10**.

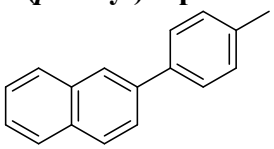
Rf = 0.59 (hexane/EtOAc = 5/1). White solid (69 mg, 90%).

^{1}H NMR ($CDCl_3$, 400 MHz): 3.89 (s, 3H), 7.27 (t, *J* = 7.8 Hz, 1H), 7.38-7.43 (m, 2H), 7.49-7.53 (m, 4H), 7.60 (s, 1H), 7.75 (d, *J* = 8.0 Hz, 2H), 8.14 (dd, *J* = 8.0, 11.2 Hz, 2H).

^{13}C NMR ($CDCl_3$, 100 MHz): 29.2, 107.2, 108.6, 118.7, 119.1, 120.5, 120.6, 122.1, 122.6, 125.8, 127.2, 127.7, 128.7, 128.9, 139.3, 141.6, 142.3.

HRMS (APCI): Calcd for $C_{19}H_{15}N+H^+$ 258.1277, Found 258.1278.

2-(*p*-Tolyl)naphthalene (38) [CAS: 59115-49-0].



General procedure was followed.

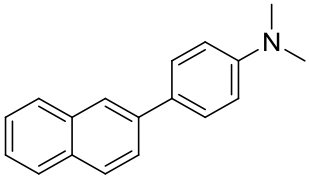
Rf = 0.74 (hexane/EtOAc = 3/1). White solid (67 mg, 98%).

^{1}H NMR ($CDCl_3$, 400 MHz): 2.43 (s, 3H), 7.30 (d, *J* = 8.0 Hz, 2H), 7.45-7.53 (m, 2H), 7.63 (d, *J* = 8.4 Hz, 2H), 7.74 (d, *J* = 8.4 Hz, 1H), 7.85-7.95 (m, 3H), 8.03 (s, 1H).

^{13}C NMR ($CDCl_3$, 100 MHz): 21.1, 125.4, 125.5, 125.8, 126.2, 127.2, 127.6, 128.1, 128.3, 129.6, 132.5, 133.7, 137.2, 138.2, 138.4.

HRMS (EI): Calcd for $C_{17}H_{14}$ 218.1096, Found 218.1095.

N,N-Dimethyl-4-(naphthalen-2-yl)aniline (39) [CAS:359653-43-3].



General procedure was followed, except that **4c** was used instead of **4b**.

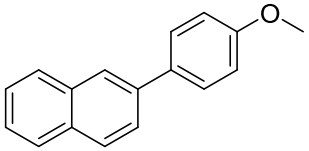
Rf = 0.60 (hexane/EtOAc = 3/1). White solid (66 mg, 81%).

^{1}H NMR ($CDCl_3$, 400 MHz): 3.01 (s, 6H), 6.84-6.86 (m, 2H), 7.41-7.49 (m, 2H), 7.63-7.65 (m, 2H), 7.74 (dd, *J* = 1.6, 8.8 Hz, 1H), 7.82-7.87 (m, 3H), 7.98 (s, 1H).

^{13}C NMR ($CDCl_3$, 100 MHz): 38.8, 110.1, 122.3, 123.4, 123.5, 124.2, 125.7, 126.1, 126.3, 127.1, 130.2, 132.0, 136.7, 148.2.

HRMS (EI): Calcd for $C_{18}H_{17}N$ 247.1361, Found 247.1360.

2-(4-Methoxyphenyl)naphthalene (40) [CAS: 59115-45-6].



General procedure was followed, except that **4d** was used instead of **4b**.

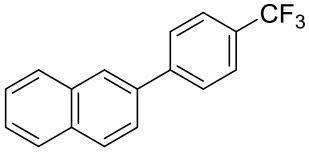
Rf = 0.42 (hexane/EtOAc = 3/1). White solid (58 mg, 82%).

^{1}H NMR ($CDCl_3$, 400 MHz): 3.88 (s, 3H), 7.02-7.05 (m, 2H), 7.45-7.52 (m, 2H), 7.66-7.69 (m, 2H), 7.73 (dd, *J* = 1.6, 8.8 Hz, 1H), 7.85-7.91 (m, 3H), 8.00 (d, *J* = 1.6 Hz, 1H).

^{13}C NMR ($CDCl_3$, 150 MHz): 55.4, 114.3, 125.0, 125.4, 125.6, 126.2, 127.6, 128.0, 128.3, 128.4, 132.3, 133.6, 133.7, 138.2, 159.2.

HRMS (EI): Calcd for $C_{17}H_{14}O$ 234.1045, Found 234.1047

2-(4-(Trifluoromethyl)phenyl)naphthalene (41) [CAS: 460743-71-9].



General procedure was followed, except that **4e** was used instead of **4b**.

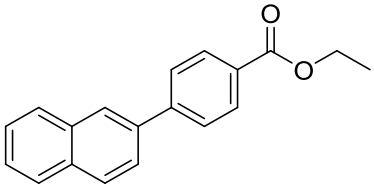
Rf = 0.83 (hexane/EtOAc = 3/1). White solid (15 mg, 17%).

^{1}H NMR ($CDCl_3$, 400 MHz): 7.51-7.56 (m, 2H), 7.73-7.79 (m, 3H), 7.83 (d, *J* = 8.0 Hz, 2H), 7.88-7.96 (m, 3H), 8.06 (s, 1H).

^{13}C NMR ($CDCl_3$, 100 MHz): 178.3 (q, *J* = 270.8 Hz), 125.1, 125.7 (q, *J* = 3.33 Hz), 126.3, 126.5, 126.6, 127.6, 127.7, 128.3, 128.7, 129.3 (q, *J* = 32.4 Hz), 132.9, 133.5, 136.9, 144.5.

HRMS (EI): Calcd for $C_{17}H_{11}F_3$ 272.0813, Found 272.0814

Ethyl 4-(naphthalen-2-yl)benzoate (42) [CAS: 119999-21-2].



General procedure was followed, except that **4f** was used instead of **4b**.

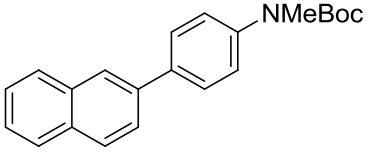
Rf = 0.56 (hexane/EtOAc = 3/1). White solid (51 mg, 62%).

^{1}H NMR ($CDCl_3$, 400 MHz): 1.43 (t, *J* = 7.0 Hz, 3H), 4.42 (q, *J* = 7.2 Hz, 2H), 7.50-7.55 (m, 2H), 7.76-7.81 (m, 3H), 7.87-7.96 (m, 3H), 8.10 (s, 1H), 8.16 (d, *J* = 8.4 Hz, 2H).

^{13}C NMR ($CDCl_3$, 100 MHz): 14.4, 61.0, 125.2, 126.3, 126.4, 126.5, 127.2, 127.6, 128.3, 128.6, 129.2, 130.0, 132.9, 133.5, 137.3, 145.4, 166.5.

HRMS (APCI): Calcd for $C_{19}H_{16}O_2$+H^+ 277.1223, Found 277.1223.

tert-butyl methyl(4-(naphthalen-2-yl)phenyl)carbamate (43).



General procedure was followed, except that **4g** was used instead of **4b**.

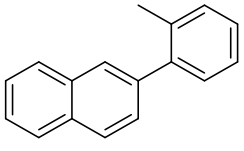
Rf = 0.36 (hexane/EtOAc = 5/1). White solid (73 mg, 73%).

^{1}H NMR ($CDCl_3$, 400 MHz): 1.49 (s, 9H), 3.33 (s, 3H), 7.36 (d, *J* = 8.4 Hz, 2H), 7.46-7.53. (m, 2H), 7.68 (dt, *J* = 2.2, 8.8 Hz, 2H), 7.74 (dd, *J* = 1.6, 8.8 Hz, 1H), 7.85-7.93 (m 3H), 8.03 (s, 1H).

^{13}C NMR ($CDCl_3$, 100 MHz): 28.3, 37.2, 80.4, 125.4, 125.5, 125.6, 125.9, 126.3, 127.4, 127.6, 128.1, 128.4, 132.5, 133.6, 137.8, 137.9, 143.1, 154.7.

HRMS (APCI): Calcd for $C_{22}H_{23}NO_2$+H^+ 334.1800, Found 334.1802.

2-(*o*-Tolyl)naphthalene (44) [CAS: 66778-24-3].



General procedure was followed, except that **4h** was used instead of **4b**.

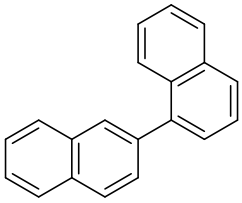
Rf = 0.53 (hexane/EtOAc = 3/1). White solid (56 mg, 81%).

^{1}H NMR ($CDCl_3$, 400 MHz): 2.33 (s, 3H), 7.28-7.35 (m, 4H), 7.48-7.54 (m, 3H), 7.79 (d, *J* = 0.8 Hz, 1H), 7.86-7.90 (m, 3H).

^{13}C NMR ($CDCl_3$, 150 MHz): 20.5, 125.8, 126.1, 127.3, 127.5, 127.65, 127.71, 127.8, 127.9, 128.0, 130.0, 130.3, 132.2, 133.3, 135.5, 139.5, 141.8.

HRMS (EI): Calcd for $C_{17}H_{14}O$ 218.1096, Found 218.1099.

1,2'-Binaphthalene (45) [CAS: 4325-74-0].



General procedure was followed, except that **4i** was used instead of **4b**.

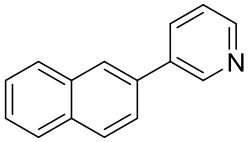
Rf = 0.67 (hexane/EtOAc = 3/1). White solid (60 mg, 79%).

^{1}H NMR ($CDCl_3$, 400 MHz): 7.40-7.44 (m, 1H), 7.48-7.57 (m, 5H), 7.63 (dd, *J* = 1.6, 8.4Hz, 1H), 7.88-7.95 (m, 7H).

^{13}C NMR ($CDCl_3$, 100 MHz): 125.4, 125.8, 126.0, 126.1, 126.1, 126.3, 127.2, 127.6, 127.7, 128.0, 128.3, 128.5, 128.7, 131.7, 132.5, 133.4, 133.8, 138.3, 140.1.

HRMS (EI): Calcd for $C_{20}H_{14}$ 254.1096, Found 254.1088.

3-(Naphthalen-2-yl)pyridine (46) [CAS: 92497-48-8].



General procedure was followed, except that **4j** was used instead of **4b**.

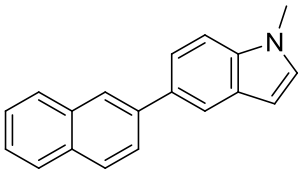
Rf = 0.14 (hexane/EtOAc = 3/1). White solid (30 mg, 49%).

^{1}H NMR ($CDCl_3$, 400 MHz): 7.42 (q, *J* = 4.3 Hz, 1H), 7.53-7.55 (m, 2H), 7.73 (dd, *J* = 2.0, 8.4 Hz, 1H), 7.89-8.03 (m, 4H), 8.06 (s, 1H), 8.64 (dd, *J* = 2.0, 2.4 Hz, 1H), 8.99 (d, *J* = 2.0 Hz, 1H).

^{13}C NMR ($CDCl_3$, 100 MHz): 123.6, 125.0, 126.2, 126.4, 126.6, 127.7, 128.2, 128.9, 132.8, 133.6, 134.6, 135.1, 136.6, 148.5, 148.6.

HRMS (FAB): Calcd for $C_{15}H_{11}N+H^{+}$ 206.0964, Found 206.0974.

1-methyl-5-(naphthalen-2-yl)-1H-indole (47) [CAS: 1648784-58-0].



General procedure was followed, except that **4k** was used instead of **4b**.

Rf = 0.35 (hexane/EtOAc = 5/1). White solid (72 mg, 93%).

^{1}H NMR ($CDCl_3$, 400 MHz): 3.85 (s, 3H), 6.57 (d, *J* = 2.8 Hz, 1H), 7.11 (d, *J* = 2.4 Hz, 1H), 7.43-7.52 (m, 3H), 7.62 (dd, *J* = 2.0, 8.4 Hz, 1H), 7.83-7.93 (m, 4H), 7.98 (d, *J* = 2.0 Hz, 1H), 8.09 (s, 1H).

^{13}C NMR ($CDCl_3$, 100 MHz): 33.0, 101.3, 109.5, 119.7, 121.6, 125.4, 125.5, 126.1, 126.3, 127.6, 128.0, 128.1, 129.0, 129.5, 132.1, 132.6, 133.8, 136.3, 139.9.

HRMS (APCI): Calcd for $C_{19}H_{15}N+H^+$ 258.1278, Found 258.1277.

1.5 References and Notes

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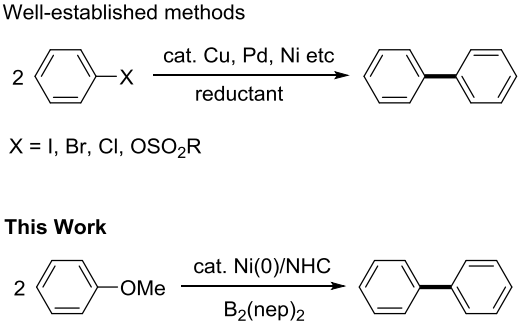
Chapter 2

Nickel-Catalyzed Formal Homocoupling of Methoxyarenes for the Synthesis of Symmetrical Biaryls via C-O Bond Cleavage

2.1 Introduction

Given the numerous applications of biaryl substructure across a broad range of fields, including pharmaceuticals and organic materials, development of catalytic methods for their efficient synthesis has turned into an intense area of research.[1] Despite the outstanding progress made in metal-catalyzed cross-coupling technologies during the past few decades, the homocoupling reactions of aryl halides and their equivalents continue to serve as powerful methods for the synthesis of symmetrical biaryl compounds.[2] Since Ullman reported the first homocoupling of aryl halides using stoichiometric copper salts,[3] a variety of advanced procedures have been developed for this transformation, which have culminated in the a widespread use of homocoupling methods, as exemplified by the syntheses of natural products[4] and conjugated polymers.[5] In terms of the scope of the aryl electrophiles used in the catalytic homocoupling reactions reported to date, aryl halides and sulfonates have been used extensively. Herein, we report the first catalytic homocoupling of aryl ethers via the nickel-catalyzed activation of strong C(aryl)-O bonds.[6,7] In addition to the ready availability and low toxicity of aryl ether substrates, the use of an inert methoxy group as a handle for homocoupling would allow for the rapid extension of the π-system through sequential cross-/homo-coupling processes.

Scheme 1. Catalytic Homocoupling of Aryl Electrophiles Leading to Biaryls

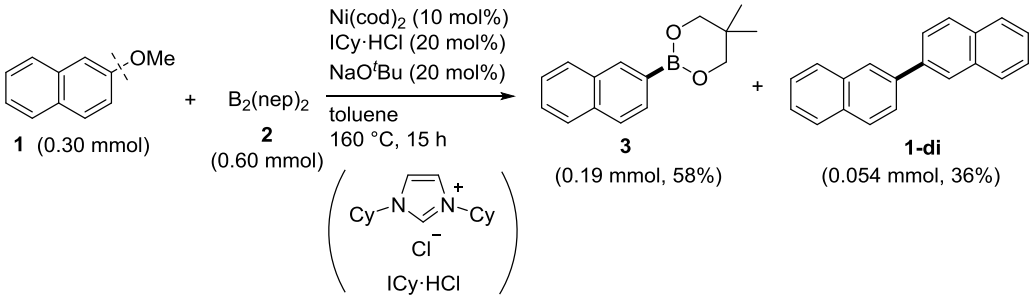


2.2 Results and Discussion

Our ongoing interest in the catalytic transformation of aryl ethers[7b,8] led us to investigate the borylation of **1** using a diboron reagent **2**. When $Ni(cod)_2$ was used as a catalyst in conjunction with 1,3-dicyclohexylimidazol-2-ylidene (ICy),[9] the expected borylated product **3**

was obtained in 58% yield. Interestingly, however, we also obtained the homocoupling product **1-di** in 36% yield. Although we were unable to obtain **3** selectively using the $Ni(cod)_2$/ICy system, we developed a keen interest in the optimization of this reaction for the selective formation of **1-di**. We were especially interested in the novelty of this transformation as a means of satisfying the growing demands for new homocoupling methodologies from the synthetic chemistry community.[4,5] It is noteworthy that Martin and coworkers recently reported the successful development of a nickel-catalyzed C-O borylation of aryl ethers using a $Ni(cod)_2/PCy_3$ system.[10] Interestingly, no homocoupling product was formed under the $Ni(cod)_2/PCy_3$ conditions, highlighting the profound effect of the ligand on the product selectivity of this process.

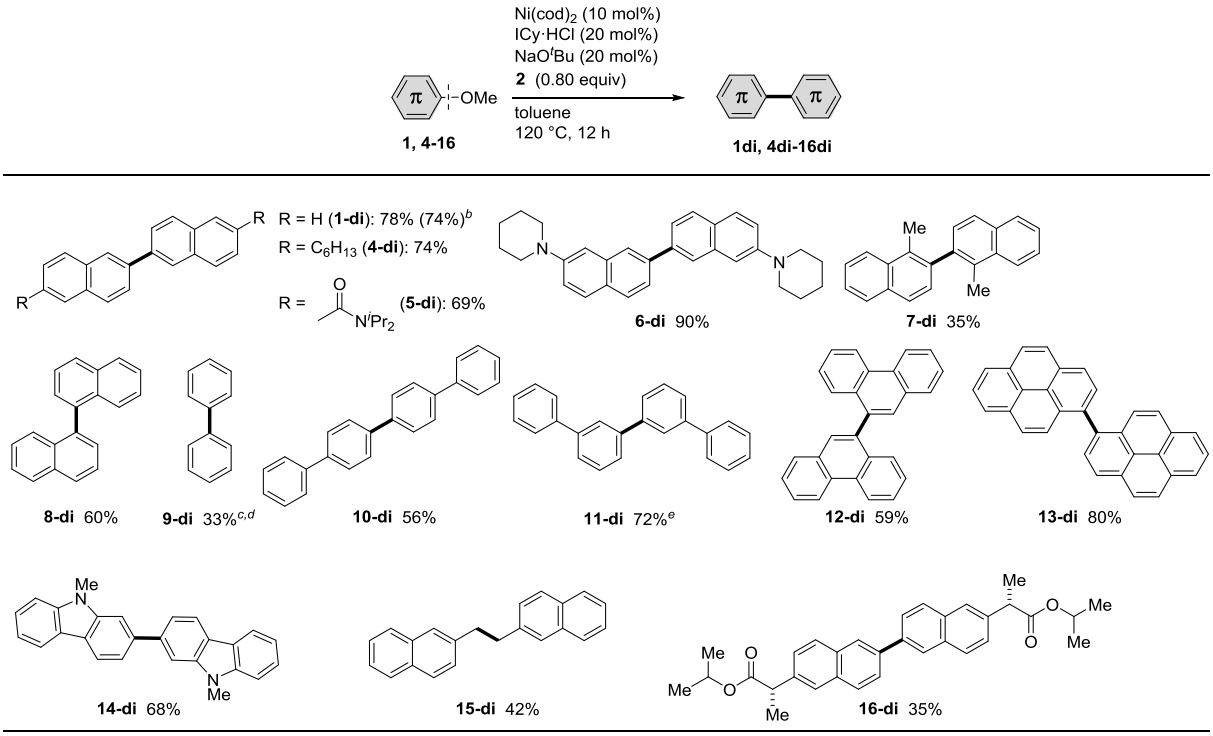
Scheme 2. Ni-Catalyzed Reaction of **1** with **2**



After a series of screening experiments, we found that decreasing the amount of **2** to 0.80 equiv relative to the aryl ether substrate led to the selective formation of a homocoupling product.[11] For example, aryl ether **1** formed **1-di** in 90% yield by NMR (78% isolated yield) under these nickel-catalyzed conditions with neither **3** nor **1** being observed by GC analysis of the crude reaction mixture (Table 1). A series of 2,2'-binaphthalene derivatives, including those bearing alkyl (**4-di**), amide (**5-di**) and amine (**6-di**) groups, were successfully synthesized under these conditions. This catalytic homocoupling was found to be sensitive to the steric environment of the aryl ether substrates, since increase in the steric hindrance of the substrate leads to a two-fold increase in the steric hindrance developed in the transition state for the C-C bond-forming event (e.g., **7-di**). Nevertheless, this method allowed for the synthesis of the sterically demanding 1,1'-binaphthalene system, as in **8-di**. The extent of the π-conjugation in the substrate had a significant impact on its reactivity towards this homocoupling reaction. For example, anisole afforded a homocoupling product **9-di** in 33% yield under these conditions, along with PhB(nep) (16%) and **9** (41%). These results indicate that the C-O bond activation of anisole is less efficient than naphthalene derivatives, which is

consistent with the reactivity trend observed in the nickel-catalyzed cross-coupling reactions of aryl ethers with relatively less nucleophilic reagents.[7b] Methoxybiphenyls were determined to be suitable substrates for this nickel-catalyzed homocoupling process, providing quaterphenyls **10-di** and **11-di**. Further π-extended methoxyarenes such as phenanthrene **12** and pyrene **13** also homocoupled under these conditions, allowing facile access to much larger aromatic molecules. This homocoupling method also worked well for heteroarenes, as exemplified by the formation of **14-di**. Importantly, 2-naphthylmethyl methyl ether (**15**) also afforded a dimerized product via the activation of its C(sp^3)-O bond.[9a,10] This method was also found to be suitable for the homocoupling of biologically active methoxyarenes. For example, the dimeric derivative of naproxen (**16**) was successfully synthesized using our homocoupling protocol.

Table 1. Ni/ICy-Catalyzed Homocoupling of Aryl Ethers[a]

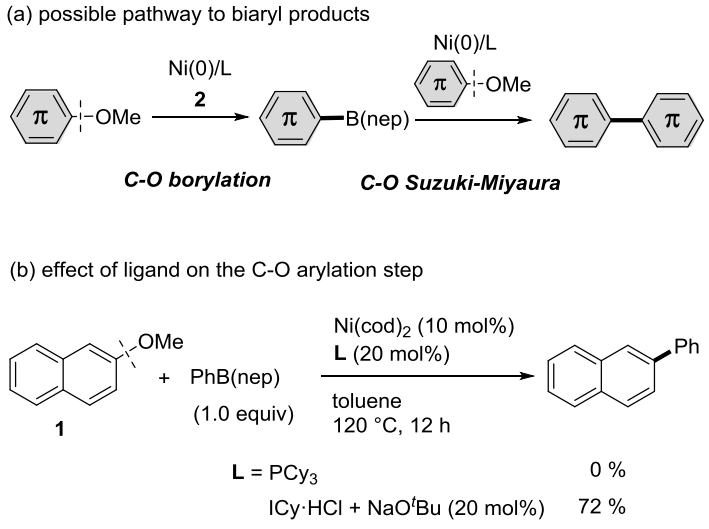


[a] Reaction conditions: aryl ether (0.50 mmol), **2** (0.40 mmol), $Ni(cod)_2$ (0.050 mmol), ICy•HCl (0.10 mmol) and NaO^{t}Bu (0.10 mmol) in toluene (1.5 mL) at 120 °C for 12 h. [b] Isolated yield on a 10 mmol scale using 5.0 mol% catalyst. [c] Yield determined by GC because of the volatility of the product. [d] PhB(nep) (16%) and anisole (41%) were also observed. [e] **2** (0.50 mmol) was used.

Of all the additives evaluated in the current study, only a diboron reagent **2** produced a homocoupling product.[11] The yield of the homocoupling product reached its highest level

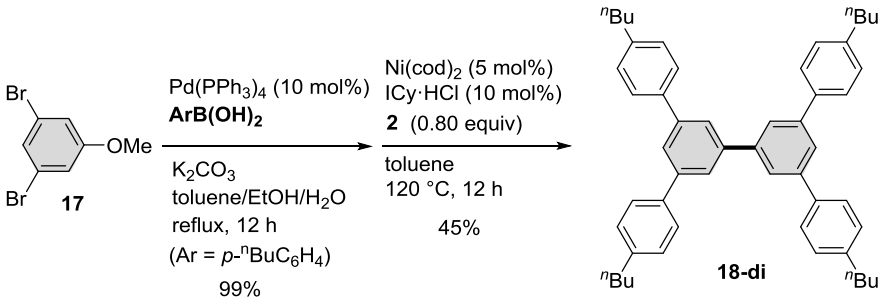
when 0.80 equiv of **2** relative to the methoxyarene substrate was added to the reaction, with the use of excess **2** leading to the formation of the C-O borylated product (Scheme 2). Taken together, all of these observations suggested that the homocoupling product was being formed through two sequential nickel-catalyzed C-O activation reactions, including the borylation of methoxyarene with **2**,[10] followed by the cross-coupling of the borylated arene with the starting methoxyarene (Scheme 3a).[9a] The catalytic homocoupling of aryl halides via a similar pathway has been reported previously.[12] This mechanistic hypothesis led us to question why the use of PCy_3 as a ligand instead of ICy failed to provide any of the desired homocoupling product, even though PCy_3 and ICy are capable of promoting the borylation[10] and Suzuki-Miyaura-type cross-coupling reactions of methoxynaphthalenes.[9a,13] To develop a deeper understanding of the differences between these two ligands, we investigated the cross-coupling of **1** with phenylboronic ester (Scheme 3b). When PCy_3 was used as the ligand in the absence of an extra base, we found that none of the arylated product was formed, which was consistent with the results of our previous study.[13] In contrast, the use of ICy as the ligand for this reaction led to cross-coupling product in good yield, even in the absence of a stoichiometric base.[14,15] These results therefore provide a clear explanation for the unique activity of ICy towards the nickel-catalyzed homocoupling of methoxyarenes. It is noteworthy that the superior activity of ICy towards the activation of C(aryl)-OMe bonds allowed for the successful reaction of the less reactive non-naphthalene substrates **9**, **10** and **11**, which did not react with the Ni/PCy_3 system.[9a]

Scheme 3. Possible Pathway and Ligand Effect



The robust nature of the methoxy group under the conditions commonly used for organic synthesis allows for this homocoupling to be conducted at the later stage of synthesis. For example, the rapid assembly of highly π-extended molecules was achieved by implementing sequential cross/homo coupling processes with halogenated methoxyarenes (Scheme 4).

Scheme 4. Rapid Expansion of π-Systems via the Sequential Cross/Homo Coupling Reactions of Halogenated Aryl Ethers



2.3 Conclusion

In summary, we have developed a nickel-catalyzed homocoupling of methoxyarenes using the diboron reagent **2**. The homocoupling most likely proceeds through sequential nickel-catalyzed C-O borylation and C-O/C-B cross-coupling. The use of ICy as a ligand was found to be critical to the success of this homocoupling because of its ability to promote the C-O/C-B cross-coupling process in the absence of a stoichiometric amount of base. This new homocoupling protocol is distinct from the classical homocoupling methods in the sense that it involves the cleavage of an inert C-O bond. Based on its unique features, it is envisioned that this method will find numerous applications in organic synthesis, especially for π-conjugated molecules. Further studies towards the development of new catalytic methods involving the transformation of inert C-O bonds are currently underway in our laboratories.

2.4 Experimental Section

General Information.

^{1}H NMR and ^{13}C NMR spectra were recorded on a JEOL JMTC-400/54/ss spectrometer or a VARIAN UNITY INOVA-600 spectrometer in $CDCl_3$ with tetramethylsilane as an internal standard. Data have been reported as follows: chemical shift in ppm (δ), multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, and m = multiplet), coupling constant (Hz), and integration. Mass spectra were recorded on a Shimadzu GCMS-QP 2010 instrument with an ionization voltage of 70 eV. High resolution mass spectra (HRMS) were obtained on a JEOL

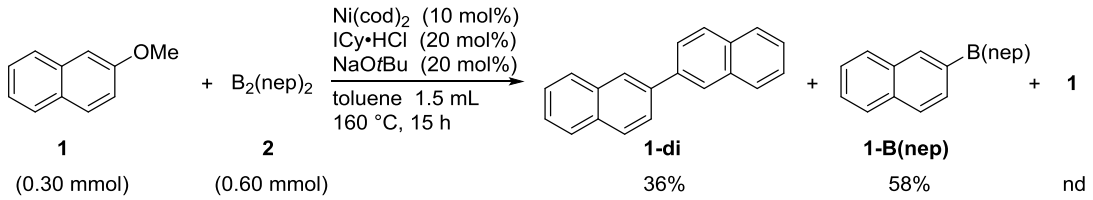
JMS-700 spectrometer and BRUKER micrOTOF II. Melting points were determined using a Yamato melting point apparatus. Column chromatography was performed with SiO_2 [Merck SilicaGel 60 (230-400 mesh) or Silycycle Silica Flash F60 (230-400 mesh)]. Gel permeation chromatography (GPC) was performed using LC-9210NEXT HPLC or LC9225NEXT HPLC system. All of the reactions were carried out in 10 mL sample vials with Teflon-sealed screw caps. All of the chemicals used in the current study were manipulated in a glovebox filled with nitrogen.

Materials.

$Ni(cod)_2$ [1295-35-8] and **2** [201733-56-4] were purchased from Strem Chemicals and used as received. NaO^{t}Bu [865-48-5], ICy•HCl [181422-72-0], PhB(nep) [5123-13-7], 4-butylboronic acid [4426-47-5], **1** [93-04-9], **9** [100-66-3], and **10** [613-37-6] were purchased from TCI and used as received. Toluene (for Organic Synthesis) were purchased from Wako Chemicals and used as received. PCy_3 [2622-14-2], CsF [13400-13-0], $Pd(PPh_3)_4$ [14221-01-3] and **8** [2216-69-5] were purchased from Aldrich and used as received. K_2CO_3 [584-08-7] was purchased from nacalai tesque and used as received. Compounds **4** [188774-60-9],[16] **5** [108711-00-8],[17] **6** [1228374-26-2],[18] **7** [1130-80-9],[19] **11** [2113-56-6],[20] **12** [5085-74-5],[21] **13** [34246-96-3],[22] **14** [39027-93-5],[23] **15** [42101-92-8][24] and **16** [156967-24-7][25] were synthesized according to the reported procedures.

Optimization Studies.

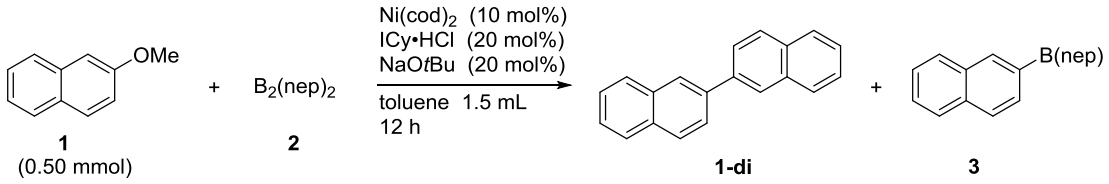
Ni-Catalyzed Reaction of 2-Methoxynaphthalene with $B_2(nep)_2$ (Scheme 2).



$Ni(cod)_2$ (8.3 mg, 0.03 mmol), ICy·HCl (16 mg, 0.06 mmol), NaO^{t}Bu (5.8 mg, 0.06 mmol) and toluene (0.50 mL) were added to a 10 mL sample vial with a Teflon sealed screwcap in a glovebox filled with nitrogen, and the resulting mixture was stirred for 10 min. 2-Methoxynaphthalene (**1**, 47 mg, 0.30 mmol), bis(neopentyl glycolato)diboron (**2**, 140 mg, 0.60 mmol) and toluene (1.0 mL) were then added to the vial, and the resulting mixture was sealed in the vessel and heated at 160 °C for 15 h on an aluminum block. The mixture was then cooled to room temperature and purified directly by flash column chromatography over

silica gel (eluent: hexane/EtOAc = 20/1) to give 2,2'-binaphthalene (**1-di**, 14 mg, 36%) as a white solid and 5,5-dimethyl-2-(naphthalene
-2-yl)-1,3,2-dioxaborinane (**1-B(nep)**, 42 mg, 58%) as a white solid.

Optimization of Reaction Conditions for the Reaction of 1 with 2.

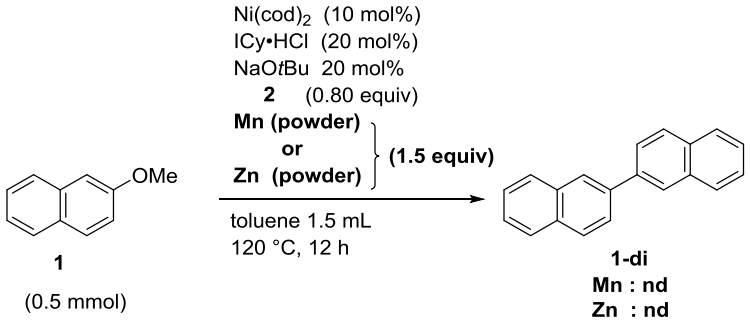


1 (0.50 mmol) **2** **1-di** **3**

Entry	**2** (equiv)	temp. (°C)	NMR yields (%)			Entry	**2** (equiv)	temp. (°C)	NMR yields (%)		
			1-di	**3**	**1**				**1-di**	**3**	**1**
1	0.50	160	40	nd	44	7	0.60	120	60	nd	21
2[a]	0.50	160	6	nd	68	8	0.70	120	72	nd	10
3	1.0	160	68	15	nd	**9**	**0.80**	**120**	**90(78)[b]**	**nd**	**nd**
4	0.50	140	76	16	nd	10	0.90	120	80	17	nd
5	0.50	120	82	14	nd	11[c]	0.80	120	6	29	52
6	0.50	100	68	23	6	12[a, c]	0.80	120	trace	8	78

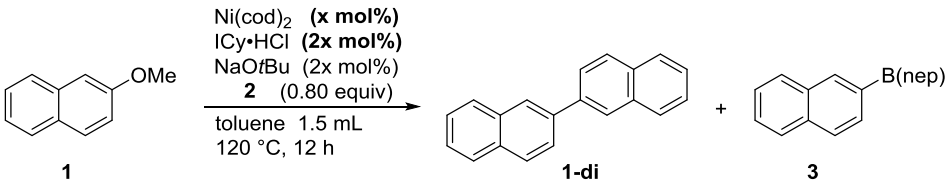
[a] CsF (2.0 equiv) was added as a base. [b] Number in parenthesis is isolated yield. [c] PCy_3 was used instead of ICy•HCl and NaO^{t}Bu.

Ni-Catalyzed Reductive Homocoupling Reaction of 1 in Presence of Metal Reducing Reagents.



1 (0.5 mmol) **1-di** **Mn : nd** **Zn : nd**

Effect of Catalyst Loading and Scale-up Experiment for Homocoupling of 1.

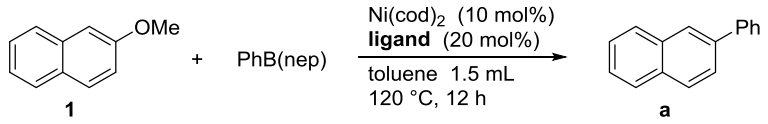


1 (0.50 mmol) **1-di** **3**

entry	x	NMR yields (%)		
		1-di	**3**	**1**
1[a]	10	90(78)	nd	nd
2	5	99	9	nd
3	2	nd	trace	>99
4	1	nd	nd	>99
5[a,b]	**5**	**(74)**	**(7)**	**nd**

[a] The number of parenthesis is isolated yield. [b] The reaction was conducted by usin 10 mmol of **1** in 4 mL of toluene.

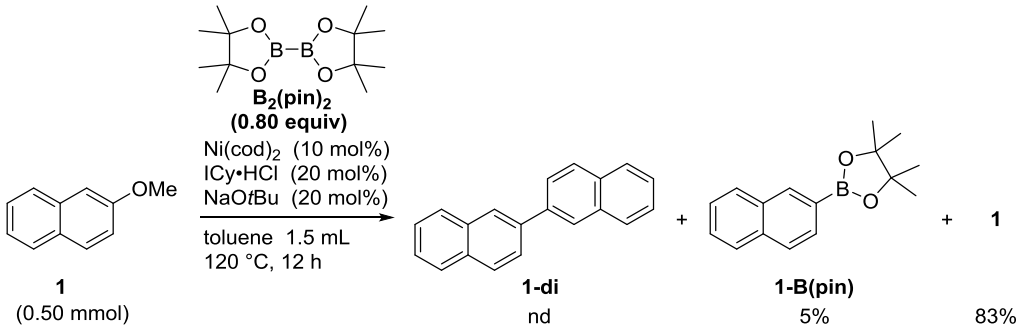
Effect of the Ligand (Scheme 4b).



1 (0.30 mmol) (0.30 mmol) **a**

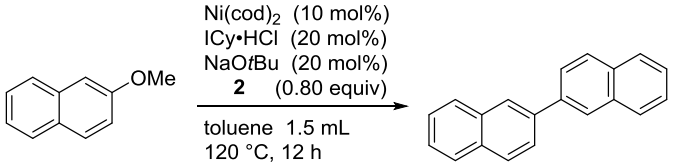
entry	**ligand**	NMR yields (%) **a**	**1**
1	ICy•HCl + NaO*t*Bu (20 mol%)	72	14
2	PCy_3	nd	>99
3	PCy_3 + NaO*t*Bu (20 mol%)	19	91

Reaction of 1 with $B_2(pin)_2$ Instead of 2.



1 (0.50 mmol) **1-di** nd **1-B(pin)** 5% 83%

Typical Procedure for Ni-catalyzed Homocoupling of Methoxyarenes.

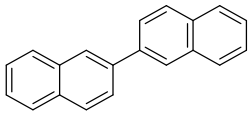


1 (0.50 mmol) **1-di** 78%

$Ni(cod)_2$ (14 mg, 0.05 mmol), ICy·HCl (27 mg, 0.1 mmol), NaO*t*Bu (10 mg, 0.1 mmol) and toluene (0.50 mL) were added to a 10 mL sample vial with a Teflon sealed screwcap in a glovebox filled with nitrogen, and the resulting mixture was stirred for 10 min. 2-Methoxynaphthalene (**1**, 79 mg, 0.50 mmol), bis(neopentyl glycolato)diboron (**2**, 90 mg, 0.40 mmol) and toluene (1.0 mL) were then added to the vial, and the resulting mixture was sealed in the vessel and heated at 120 °C for 12 h on an aluminum block. The mixture was

then cooled to room temperature and purified directly by flash column chromatography over silica gel (eluent: hexane/EtOAc = 50/1) to give 2,2'-binaphthalene (**1-di**, 50 mg, 78%) as a white solid.

2,2'-Binaphthalene (1-di) [CAS: 612-78-2].



General procedure was followed.

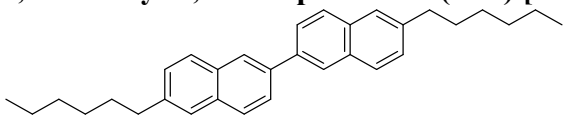
Rf = 0.55 (hexane/EtOAc = 5/1). White solid (99 mg, 78%).

^{1}H NMR ($CDCl_3$, 400 MHz): 7.48-7.55 (m, 4H), 7.88-7.98 (m, 8H), 8.18 (s, 2H).

^{13}C NMR ($CDCl_3$, 100 MHz): 125.7, 126.0, 126.1, 126.3, 127.7, 128.2, 128.5, 132.7, 133.7, 138.4.

HRMS (EI): Calcd for $C_{20}H_{14}$ 254.1096, Found 254.1095.

6,6'-Dihexyl-2,2'-binaphthalene (4-di) [CAS: 100808-00-2].



General procedure was followed, except that **4** was used instead of **1**.

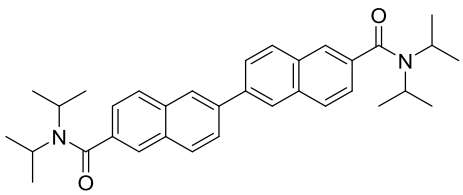
Rf = 0.74 (hexane/EtOAc = 5/1). White solid (78 mg, 74%).

^{1}H NMR ($CDCl_3$, 400 MHz): 0.89 (t, J = 6.9 Hz, 6H), 1.25-1.40 (m, 12H), 1.68-1.75 (m, 4H), 2.78 (t, J = 7.6 Hz, 4H), 7.36 (dd, J =1.4 Hz, 8.2 Hz, 2H), 7.64 (s, 2H), 7.82-7.88 (m, 6H), 8.11 (s, 2H).

^{13}C NMR ($CDCl_3$, 100 MHz): 14.1, 22.6, 29.0, 31.3, 31.8, 36.2, 125.7 (two overlapping peaks), 126.1, 127.9, 127.95, 128.03, 132.2, 132.8, 137.7, 140.6.

HRMS (EI): Calcd for $C_{32}H_{38}$ 422.2974, Found 422.2967.

***N*,*N*,*N*,*N*-Tetraisopropyl-[2,2'-binaphthalene]-6,6'-dicarboxamide (5-di).**



General procedure was followed, except that **5** was used instead of **1**. Reduced byproduct (*N*,*N*-diisopropyl-2-naphthamide, 19%) was also formed .

Rf = 0.04 (hexane/EtOAc = 5/1). White solid (88 mg, 69%). Mp = 246 °C.

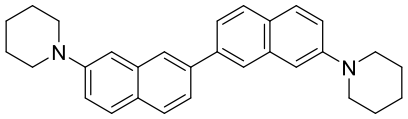
^{1}H NMR ($CDCl_3$, 400 MHz): 1.26 (bs, 12H), 1.56 (bs, 12H), 3.65 (bs, 2H), 3.99 (bs, 2H), 7.47 (d, *J* = 8.7 Hz, 2H), 7.84 (d, *J* = 8.3 Hz, 2H), 7.90-7.99 (m, 6H), 8.17 (s, 2H).

^{13}C NMR ($CDCl_3$, 100 MHz): 20.8, 46.0 (br), 51.0 (br), 124.1, 124.7, 126.0, 126.4, 128.6, 129.0, 132.2, 133.4, 136.5, 138.9, 170.9.

HRMS (EI): Calcd for $C_{34}H_{40}N_2O_2$ 508.3090, Found 508.3092.

IR (ATR): 2969 w, 2933 w, 1621 s, 1474 m, 1439 m, 1370 m, 1332 s, 1211 w, 1157 w, 1036 m, 888 m, 808 m, 747 s.

7,7'-Di(piperidin-1-yl)-2,2'-binaphthalene (6-di).



General procedure was followed, except that **6** was used instead of **1**.

Rf = 0.43 (hexane/EtOAc = 5/1). White solid (95 mg, 90%). Mp = 170 °C.

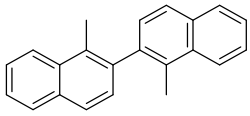
^{1}H NMR ($CDCl_3$, 400 MHz): 1.59-1.64 (m, 4H), 1.74-1.80 (m, 8H), 3.27 (t, *J* = 5.5 Hz, 8H), 7.22 (s, 2H), 7.28 (dd, *J* = 2.3 Hz, 9.2 Hz, 2H), 7.65 (dd, *J* = 1.6 Hz, 8.5 Hz, 2H), 7.72 (d, *J* = 8.7 Hz, 2H), 7.78 (d, *J* = 8.2 Hz, 2H), 7.99 (s, 2H).

^{13}C NMR ($CDCl_3$, 100 MHz): 24.3, 25.8, 51.0, 110.7, 120.1, 123.1, 124.9, 127.5, 127.8, 128.2, 135.0, 139.0, 150.2.

HRMS (EI): Calcd for $C_{30}H_{32}N_2$ 420.2565, Found 420.2561.

IR (ATR): 2930 m, 2851 w, 2801 w, 1622 s, 1600 m, 1507 m, 1449 m, 1386 m, 1210 s, 1122 s, 1026 w, 957 m, 880 m, 829 s, 751 s.

1,1'-Dimethyl-2,2'-binaphthalene (7-di) [CAS: 50418-13-8].



General procedure was followed, except that **7** was used instead of **1**. Starting material (**7**,12%) was recovered.

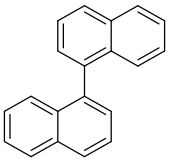
Rf = 0.70 (hexane/EtOAc = 5/1). White solid (25 mg, 35%).

^{1}H NMR ($CDCl_3$, 400 MHz): 2.43 (s, 6H), 7.33 (d, *J* = 8.7 Hz, 2H), 7.51-7.61 (m, 4H), 7.77 (d, *J* = 8.2 Hz, 2H), 7.91 (d, *J* = 7.8 Hz, 2H), 8.11 (d, *J* = 8.2 Hz, 2H).

^{13}C NMR ($CDCl_3$, 100 MHz): 15.9, 124.4, 125.4, 125.7, 126.2, 128.2, 128.5, 131.5, 132.76, 132.78, 139.2.

HRMS (EI): Calcd for $C_{22}H_{18}$ 282.1409, Found 282.1413.

1,1'-Binaphthalene (8-di) [CAS:604-53-5].



General procedure was followed, except that **8** was used instead of **1**. Only trace amount of starting material was recovered, but produce of reduced byproduct (naphthalene) was confirmed by GC analysis (not quantitative).

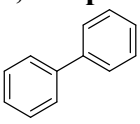
Rf = 0.60 (hexane / EtOAc = 5 / 1). White solid (38 mg, 60%).

^{1}H NMR ($CDCl_3$, 400 MHz): 7.26-7.30 (m, 2H), 7.39 (d, J = 8.2 Hz, 2H), 7.45-7.50 (m, 4H), 7.59 (dd, J = 7.34 Hz, 8.3 Hz, 2H), 7.95 (dd, J = 3.7 Hz, 8.2 Hz, 4H).

^{13}C NMR ($CDCl_3$, 100 MHz): 125.4, 125.8, 126.0, 126.5, 127.8, 127.9, 128.1, 132.8, 133.5, 138.4.

HRMS (EI): Calcd for $C_{20}H_{14}$ 254.1096, Found 254.1097.

1,1'-biphenyl (9-di) [CAS: 92-52-4].



General procedure was followed, except that **9** was used instead of **1**. Yield was determined by GC using icosane as an internal standard because of the volatility of the product.

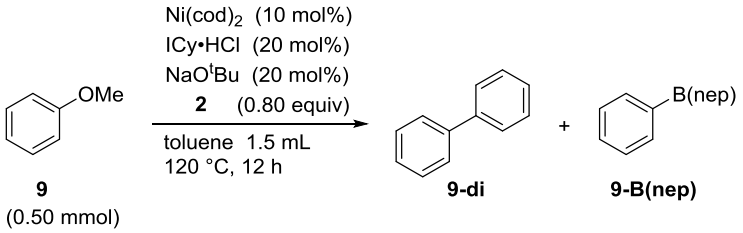
Rf = 0.77 (hexane/EtOAc = 5/1). White solid.

^{1}H NMR ($CDCl_3$, 400 MHz): 7.58-7.61 (m, 4 H), 7.42-7.46 (m, 4 H), 7.32-7.36 (m, 2 H).

^{13}C NMR ($CDCl_3$, 100 MHz): 127.1, 127.2, 128.7, 141.2.

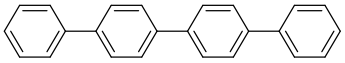
HRMS (EI): Calcd for C12H10 154.0783, Found 154.0783.

All the attempts to increase the yield of **9-di** failed (see below).



entry	variety of condition	GC yields (%)		
		9-di	**9-B(nep)**	**9**
1	none	33	16	41
2	140 °C	20	15	42
3	$B_2(nep)_2$ = 1.0 equiv	24	22	51
4	CsF (1equiv.) was added	13	nd	57
5	$Ni(cod)_2$ (0.050 mmol) ICy•HCl (0.10 mmol) NaO*t*Bu (0.050 mmol)	25	nd	48

1,1':4',1'':4'',1'''-Quaterphenyl (10-di) [CAS: 137-70-6].



General procedure was followed, except that **10** was used instead of **1**. The resulting mixture was cooled to room temperature, insoluble material was filtered off, and the solid was washed with $CHCl_3$, giving 1,1':4',1'':4'',1'''-quaterphenyl as a white solid (**11-di**, 31 mg, 40%). The filtrate was purified by flash column chromatography over silica gel (eluent: hexane/EtOAc = 50/1) to give an additional amount of **10-di** (12 mg, 16%) as a white solid. Starting material (**10**, 11%) was recovered.

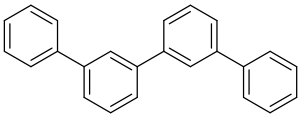
Rf = 0.55 (hexane/EtOAc = 5/1). White solid (43 mg, 56%).

^{1}H NMR ($CDCl_3$, 400 MHz): 7.37 (t, *J* = 7.3Hz, 2H), 7.47 (t, *J* = 7.6 Hz, 4H), 7.65-7.75 (m, 12H).

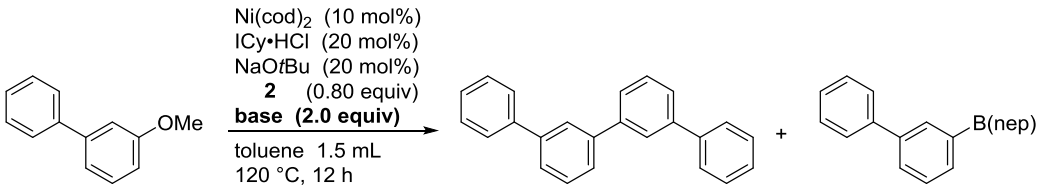
^{13}C NMR ($CDCl_3$, 100 MHz): 127.0, 127.4 (two overlapping peaks), 127.5, 128.8, 139.6, 140.2, 140.7.

HRMS (EI): Calcd for $C_{24}H_{18}$ 306.1409, Found 306.1406.

1,1':3',1'':3'',1'''-Quaterphenyl (11-di) [CAS: 1166-18-3].



The reaction of **11** under the general conditions afforded **11-di** in 58% isolated yield with **11** being recovered in 32%. A brief re-optimization of the reaction conditions revealed that the use of 2 equiv of 2 increased the yield of **11-di** to 72%.



11 (0.50 mmol) **11-di** **11-B(nep)**

entry	base	NMR yields (%)		
		11-di	**11-B(nep)**	**11**
1	none	58	nd	32
2	Na_2CO_3	62	nd	24
3	NaOH	nd	nd	96
4	DABCO	61	nd	24
5[a, b]	**none**	**81(72)**	**16(17)**	**7(8)**
6[a, c]	none	56	28	nd

[a] $B_2(nep)_2$ (1.0 equiv) was used. [b] Numbers in parentheses are isolated yields. [c] $Ni(cod)_2$ (0.05 mmol) and ICy•Cl (0.10 mmol) was used.

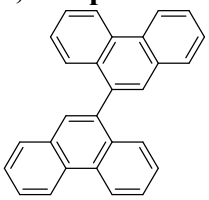
Rf = 0.57 (hexane/EtOAc = 5/1). White solid (55 mg, 72%).

^{1}H NMR ($CDCl_3$, 400 MHz): 7.35-7.67 (m, 16H), 7.86 (s, 2H).

^{13}C NMR ($CDCl_3$, 100 MHz): 126.20, 126.24, 126.3, 127.3, 127.4, 128.8, 129.2, 141.1, 141.7, 141.9.

HRMS (EI): Calcd for $C_{24}H_{18}$ 306.1409, Found 306.1411.

9,9'-Biphenanthrene (12-di) [CAS: 20532-03-0].



General procedure was followed, except that **12** was used instead of **1**. Reduced byproduct (phenanthrene, 36%) was also formed .

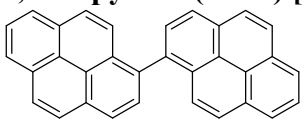
Rf = 0.47 (hexane/CH_2Cl_2 = 5/1). White solid (52 mg, 59%).

^{1}H NMR ($CDCl_3$, 400 MHz): 7.36-7.40 (m, 2H), 7.51 (d, *J* = 8.3 Hz, 2H), 7.63-7.75 (m, 6H), 7.86 (s, 2H), 7.92 (d, *J* = 7.8 Hz, 2H), 8.82 (t, *J* = 7.1 Hz, 4H).

^{13}C NMR ($CDCl_3$, 100 MHz): 122.6, 122.8, 126.5, 126.6, 126.8, 126.9, 127.5, 128.5, 128.7, 130.29, 130.31, 131.7, 132.2, 137.1.

HRMS (EI): Calcd for $C_{28}H_{18}$ 354.1409, Found 354.1411.

1,1'-Bipyrene (13-di) [CAS: 5101-26-8].



General procedure was followed, except that **13** was used instead of **1**. The resulting mixture was cooled to room temperature, an insoluble material was flirted off, and the solid was washed with $CHCl_3$, giving 1,1'-bipyrene as a pale green solid (**13-di**, 73 mg, 73%). The filtrate was purified by flash column chromatography over silica gel (eluent: hexane/EtOAc = 50/1) to give an additional amount of **13-di** (6.6 mg, 7%) as a pale green solid.

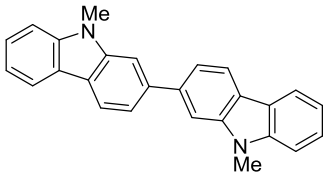
Rf = 0.55 (hexane/EtOAc = 5/1). Pale green solid (80 g, 80%).

^{1}H NMR ($CDCl_3$, 400 MHz): 7.67 (d, *J* = 9.6 Hz, 2H), 7.89 (d, *J* = 8.8 Hz, 2H), 8.04 (t, *J* = 7.8 Hz, 2H), 8.15-8.27 (m, 10H), 8.36 (d, *J* = 7.8Hz, 2H).

^{13}C NMR ($CDCl_3$, 100 MHz): 124.5, 124.8, 125.1, 125.3, 125.8, 126.1, 127.5, 127.59, 127.61 (two overlapping peaks), 128.8, 130.1, 130.9, 131.0, 131.5, 136.3.

HRMS (EI): Calcd for $C_{32}H_{18}$ 402.1409, Found 402.1409.

9,9'-Dimethyl-9*H*,9'*H*-2,2'-bicarbazole (14-di).



General procedure was followed, except that **14** was used at 140°C instead of **1** at 120°C. Reduced byproduct (*N*-methylcarbazole) and starting material (**14**) were detected by GC analysis (not quantitative).

Rf = 0.45 (hexane/EtOAc = 5/1). White solid (61 mg, 68%). Mp = 282 °C.

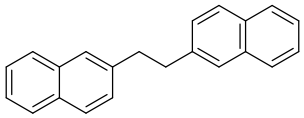
^{1}H NMR ($CDCl_3$, 400 MHz): 3.95 (s, 6H), 7.25-7.29 (m, 2H), 7.44 (d, J = 7.8 Hz, 2H), 7.50 (t, J = 7.6 Hz, 2H), 7.63 (dd, J = 1.1 Hz, 8.0 Hz, 2H), 7.73 (s, 2H), 8.14 (d, J = 7.8 Hz, 2H), 8.19 (d, J = 7.8 Hz, 2H).

^{13}C NMR ($CDCl_3$, 100 MHz): 29.2, 107.4, 108.4, 119.0, 119.1, 120.3, 120.5, 121.9, 122.7, 125.6, 140.2, 141.5, 141.6.

HRMS (EI): Calcd for $C_{26}H_{20}N_2$ 360.1626, Found 360.1625.

IR (ATR): 2925 w, 2364 w, 1596 m, 1475 m, 1449 m, 1421 m, 1322 m, 1254 m, 1123 w, 838 m, 804 m, 745 s, 723 m.

1,2-Di(naphthalen-2-yl)ethane (15-di) [CAS:21969-45-9].



General procedure was followed, except that **15** was used instead of **1**. Reduced byproduct (2-methylnaphthalene, 10%) and starting material (**15**, 2%) was obtained.

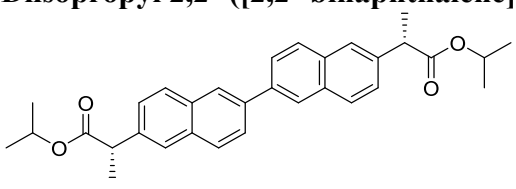
Rf = 0.63 (hexane/EtOAc = 5/1). White solid (30 mg, 42%).

^{1}H NMR ($CDCl_3$, 400 MHz): 3.19 (s, 4H), 7.37 (dd, J = 1.8 Hz, 8.2 Hz, 2 H), 7.41-7.47 (m, 4H), 7.66 (s, 2H), 7.76-7.83 (m, 6H).

^{13}C NMR ($CDCl_3$, 100 MHz): 38.0, 125.2, 125.9, 126.5, 127.3, 127.5, 127.6, 127.9, 132.0, 133.6, 139.3.

HRMS (EI): Calcd for $C_{22}H_{18}$ 282.1409, Found 282.1410.

Diisopropyl 2,2'-([2,2'-binaphthalene]-6,6'-diyl)(2*S*,2'*S*)-dipropionate (16-di).



General procedure was followed, except that **16** was used instead of **1**. Aside from **16-di**, borylated product (isopropyl (S)-2-(6-(5,5-dimethyl-1,3,2-dioxaborinan-2-yl) naphthalen-2-yl)propanoate, 14%), reduced product (isopropyl (S)-2-(naphthalen-2-yl) propanoate, 12%) and starting material (**16**, 28%) were olso obtained.

Rf = 0.39 (hexane/EtOAc = 5/1). White solid (42 mg, 35%). Mp = 125°C.

^{1}H NMR ($CDCl_3$, 400 MHz): 1.14 (d, *J* = 5.9 Hz, 6H), 1.24 (d, *J* = 6.0 Hz, 6H), 1.59 (d, *J* = 7.3 Hz, 6H), 3.86 (q, *J* = 7.2 Hz, 2H), 5.00-5.06 (m, 2H), 7.49 (dd, *J* = 1.6 Hz, 8.5 Hz, 2H), 7.78 (s, 2H), 7.84-7.93 (m, 6H), 8.13 (s, 2H).

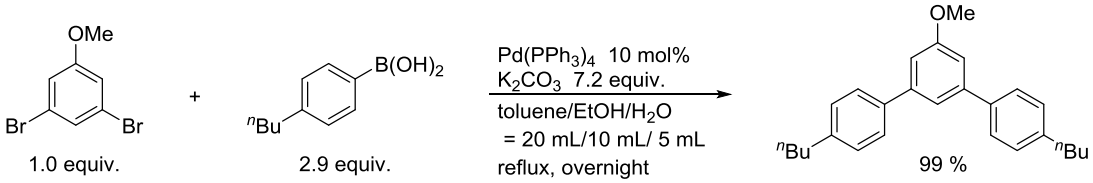
^{13}C NMR ($CDCl_3$, 100 MHz): 18.5, 21.6, 21.7, 45.9, 68.1, 125.7, 125.8, 125.9, 126.3, 128.4, 128.5, 132.7, 132.8, 138.2, 138.5, 174.0.

HRMS (EI): Calcd for $C_{32}H_{34}O_4$ 482.2457, Found 482.2458.

IR (ATR): 2979 w, 1724 s, 1629 w, 1599 w, 1452 w, 1375 m, 1318 m, 1191 s, 1106 s, 1070 m, 928 w, 882 m, 806 m, 753 s.

Sequential Cross/Homo Coupling Reactions of 17.

4,4''-Dibutyl-5'-methoxy-1,1':3',1''-terphenyl (18).



An oven-dried two-necked flask was charged with 3,5-dibromoanisole (2.7 g, 10 mmol), 4-butylboronic acid (5.2 g, 29 mmol), $Pd(PPh_3)_4$ (1.2 g, 1.0 mmol) and K_2CO_3 (10 g, 72 mmol), toluene (20 mL), EtOH (10 mL) and H_2O (5 mL), and the mixture was refluxed for overnight. The resulting mixture was cooled to room temperature. The solvent was removed in vacuo. The residual solid was dissolved in EtOAc and filtrated through a pad of silica gel. The crude product was obtained after evaporation of the solvent under reduced pressure. The purification by flash column chromatography over silica gel (hexane/EtOAc = 100/1) gave the product as a colorless oil (**18**, 3.7 g, 99%). Rf = 0.69 (hexane/EtOAc = 5/1).

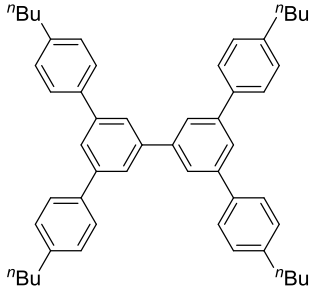
^{1}H NMR ($CDCl_3$, 400 MHz): 0.95 (t, *J* = 7.6 Hz, 6H), 1.35-1.44 (m, 4H), 1.60-1.68 (m, 4H), 2.66 (t, *J* = 7.8 Hz, 4H), 3.90 (s, 3H), 7.08 (d, *J* = 1.4 Hz, 2H), 7.26 (d, *J* = 8.2 Hz, 4H), 7.38 (d, *J* = 1.4 Hz, 1H), 7.55 (d, *J* = 8.2 Hz, 4H).

^{13}C NMR ($CDCl_3$, 100 MHz): 14.0, 22.4, 33.6, 35.3, 55.4, 111.3, 118.6, 127.1, 128.8, 138.5, 142.4, 143.0, 160.2.

HRMS (EI): Calcd for $C_{27}H_{32}O$ 372.2453, Found 372.2451.

IR (ATR): 2955 m, 2928 m, 2857 w, 1591 s, 1514 m, 1453 m, 1394 w, 1345 m, 1246 w, 1206 s, 1173 m, 1072 m, 1035 m, 1017 m, 824 s.

4,4'''-Dibutyl-5',5''-bis(4-butylphenyl)-1,1':3',1'':3'',1'''-quaterphenyl (18-di).



General procedure was followed, except that **18** was used instead of **1**. Aside from **18-di**, reduced product (4,4"-dibutyl-1,1':3',1"-terphenyl, 14%) and starting material (**18**, 18%) were olso obtained.

Rf = 0.69 (hexane/EtOAc = 5/1). White solid (77 mg, 45%). Mp = 139 °C.

^{1}H NMR ($CDCl_3$, 400 MHz): 0.95 (t, *J* = 7.3 Hz, 12H), 1.36-1.45 (m, 8H), 1.62-1.69 (m, 8H), 2.67 (t, *J* = 7.8 Hz, 8H), 7.29 (d, *J* = 8.3 Hz, 8H), 7.62 (d, *J* = 8.2 Hz, 8H), 7.80 (t, *J* = 1.6 Hz, 2H), 7.84 (d, *J* = 1.8 Hz, 4H).

^{13}C NMR ($CDCl_3$, 100 MHz):14.0, 22.4, 33.7, 35.3, 124.9, 125.0, 127.2, 128.9, 138.5, 142.25, 142.30, 142.4.

HRMS (EI): Calcd for $C_{52}H_{58}$ 682.4539, Found 682.4540.

IR (ATR): 2955 m, 2926 m, 2856 w, 1591 m, 1511 m, 1461 w, 1390 w, 1017 w, 873 w, 825 s, 706 m.

2.5 References and Notes

(1) Selected reviews on biaryl synthesis: (a) Hassan, J.; Sévignon, M.; Gozzi, C.; Schulz, E.; Lemaire, M. *Chem. Rev.* **2002**, *102*, 1359. (b) Chan, T. L.; Wu, Y.; Choy, P. Y.; Kwong, F. Y. *Chem.–Eur. J.* **2013**, *19*, 15802. (c) Hussain, I.; Singh, T. *Adv. Synth. Catal.* **2014**, *356*, 1661. (d) Aldemir, H.; Richarz, R.; Gulder, T. A. M. *Angew. Chem., Int. Ed.* **2014**, *53*, 8286.

(2) Nelson, T. D.; Crouch, R. D. *Org. React.* **2004**, *63*, 265.

(3) Ullmann, F.; Bielecki, J. *Chem. Ber.* **1901**, *34*, 2174.

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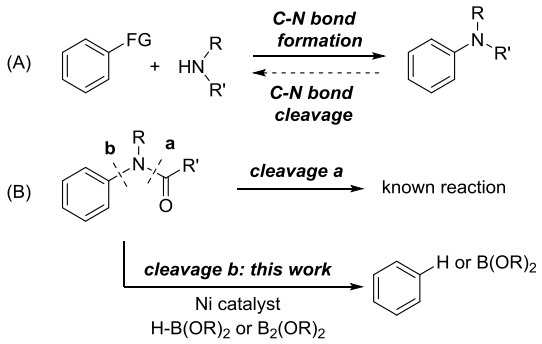
Chapter 3

Nickel-Catalyzed Reductive and Borylative Cleavage of Aromatic Carbon-Nitrogen Bonds in N-Aryl Amides and Carbamates

3.1 Introduction

Over the course of the past decade, there has been substantial progress in the development of metal-catalyzed C(aryl)-N bond forming reactions for the construction of aryl amine derivatives (Scheme 1A, forward).[1] In contrast, a research towards the reverse process involving the catalytic cleavage of C(aryl)-N bonds has been scarce (Scheme 1A, reverse).[2] The cleavage of the C(aryl)-N bonds of aniline derivatives has traditionally been accomplished using highly reactive cationic intermediates such as diazonium[3] and ammonium[4] salts, wherein the C(aryl)-N bond cleavage process is facilitated by the elimination of electronically neutral molecules, i.e., dinitrogen and an amine, respectively.[5] Kakiuchi et al. reported the development of a notable ruthenium-catalyzed C(aryl)-N bond activation reaction for electronically neutral aniline derivatives, but the process was limited to substrates bearing an ortho directing group.[6] Herein, we report the first catalytic C(aryl)-N bond cleavage reactions of electronically neutral and structurally simple aryl amine derivatives via the nickel-catalyzed reduction and borylation of N-aryl amides. These reactions therefore enable a new mode of bond disconnection for amide derivatives (Scheme 1B, cleavage b) and represent a valuable addition to the normal C(acyl)-N cleavage methods (Scheme 1B, cleavage a).

Scheme 1. Cleavage of Aromatic Carbon-Nitrogen Bonds

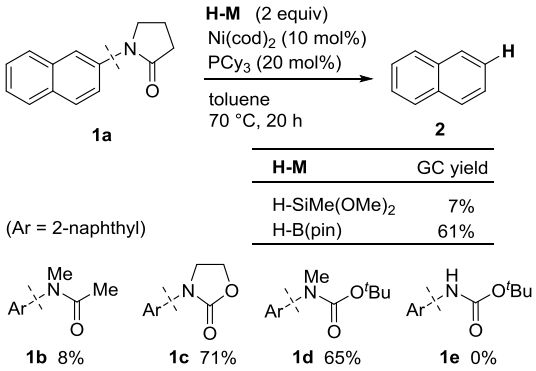


3.2 Results and Discussion

We initiated our study by examining the reaction of amide **1a** with a variety of different coupling partners in the presence of a wide range of transition metal catalysts. The results of

these preliminary screening experiments revealed that the use of $HSiMe(OMe)_2$ in conjunction with a $Ni(cod)_2/PCy_3$ catalyst allowed for the successful conversion of **1a** to naphthalene (**2**) via the reductive cleavage of the C(aryl)-N bond,[7] although the yield for this transformation was very low at 7% (Scheme 2). Unfortunately, further changes to the catalyst, ligand, substituents on the silicon, solvent and reaction temperature did not result in any discernible improvement (see Experimental Section for details). However, the use of HB(pin) as a reductant led to an increase in the yield of **2** to 61%. Several other reducing agents were also screened against the reaction, including $BH_3•Me_2S$, KBH_4 and DIBALH, but these reagents led exclusively to the formation of 1-(naphthalen-2-yl)pyrrolidine via the reduction of the carbonyl group, with no **2** being detected. The nature of the C(aryl)-N bond structure had a profound effect on the outcome of the current C(aryl)-N bond cleavage reaction. For example, the acyclic amide **1b** did not react under the current conditions, whereas the cyclic and acyclic carbamates **1c** and **1d** successfully underwent the nickel-catalyzed reductive cleavage to give **2** in good yields. It is noteworthy that the current cleavage process could be readily applied to the Boc-protected aryl amine **1d**, which represents a common structural motif in synthetic chemistry, despite the substantial steric bulk of the Boc group. Furthermore, the presence of an unprotected N-H group on the carbamate, as in **1e**, was determined to be detrimental to the catalytic process.

Scheme 2. Nickel-Catalyzed Reductive Cleavage of C(aryl)-N Bonds: The Effect of the Reductant and Different N-Substituents[a]

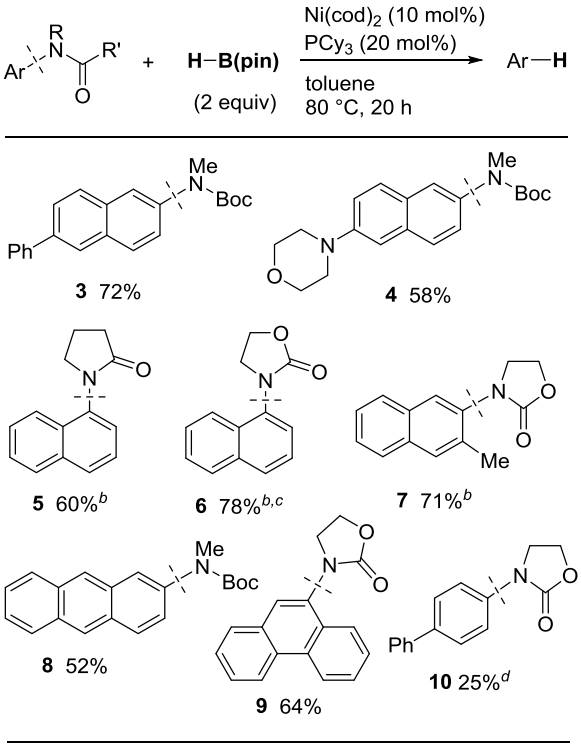


[a]Reaction conditions: **1** (0.50 mmol), reductant (1.0 mmol), $Ni(cod)_2$ (0.050 mmol), and PCy_3 (0.10 mmol) in toluene (1.5 mL) at 70 °C for 20 h. The yields were determined by GC analysis versus a calibrated internal standard because of the volatility of the product.

As shown in Table 1, the current nickel-catalyzed reductive cleavage reaction could be successfully applied to a variety of different aromatic amides and carbamates. Under these

conditions, the C-N bonds of amines remained intact, whereas those of amides and carbamates were substituted with hydrogen in a chemoselective manner (i.e., **4**).

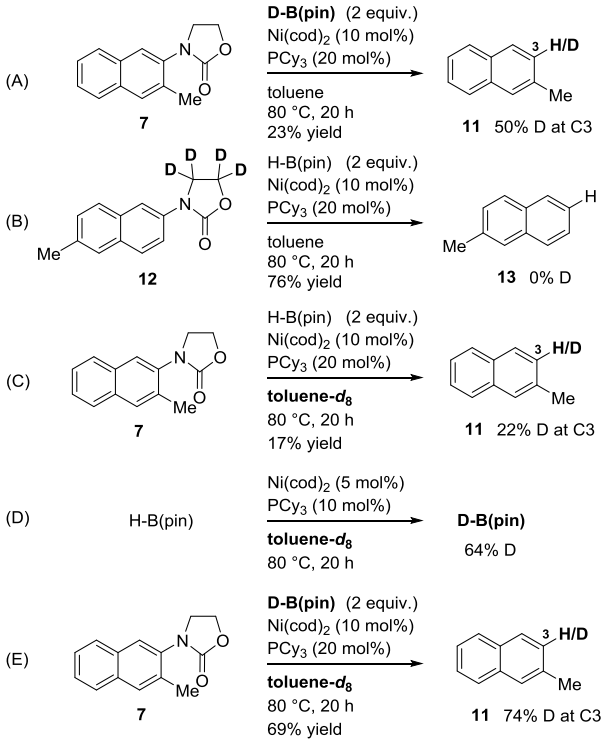
Table 1. Nickel-Catalyzed Reductive Cleavage of C(aryl)-N Bonds: Evaluation of the Substrate Scope[a]



[a] Reaction conditions: Amide or carbamate (0.50 mmol), HB(pin) (1.0 mmol), $Ni(cod)_2$ (0.050 mmol), and PCy_3 (0.10 mmol) in toluene (1.5 mL) at 70 °C for 20 h. Isolated yield is shown unless otherwise noted. [b] GC yield because of the volatility of the product. [c] Reaction time of 48 h. [d] Reaction conducted at 120 °C using IMes instead of PCy_3. 71% of **10** was recovered.

Sterically demanding substrates bearing a C-N bond at the 1-position of the naphthalene, such as **5** and **6**, as well as those containing an ortho substituent, such as **7**, underwent the reductive cleavage reaction to give the corresponding reduction products. Several other fused aromatic systems, including anthracene **8** and phenanthrene **9**, also proceeded smoothly under the optimized condition to give the corresponding reduction products, whereas benzene derivatives, such as **10**, were found to be much less reactive. The trend in reactivity observed in the current transformation is similar to that reported previously for the nickel-catalyzed cleavage of inert C-O bonds.[8]

Scheme 3. Labeling Studies

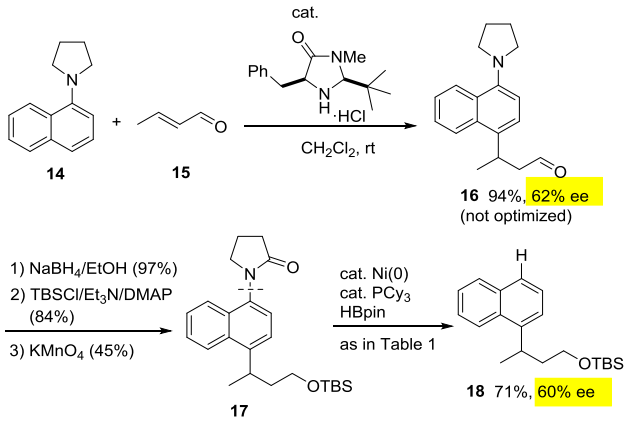


We next conducted a series of labeling experiments to develop a deeper understanding of the reaction mechanism in terms of the origin of the hydrogen atom incorporated in the final product.[9] The use of DB(pin) afforded the reduction product **11** with only 50% deuterium incorporation at the 3-position. This result suggested that the hydrogen atom in the reduction product was not derived exclusively from hydroborane, and that some other source of hydrogen must be present in the system (Scheme 3A). The deuterium labeling the methylene groups of the oxazolidinone ring in compound **12** followed by reduction under the standard conditions delivered the anticipated reduction product, but with no deuterium incorporation (Scheme 3B). In contrast, 22% deuterium incorporated was observed at the 3-position when deuterium labelled toluene was used as the reaction solvent (Scheme 3C), which indicated that a H/D exchange reaction was occurring between the HB(pin) and the toluene solvent. This possibility was confirmed to be true by a simple experiment, where the exposure of HB(pin) to the nickel-catalyzed conditions in toluene-d_8 led to the formation of DB(pin) (Scheme 3D).[10] When the reaction was run with DB(pin) in toluene-d_8, deuterium incorporation at the 3-position of the product increased to 74% (Scheme 3E). The hydrogen incorporation (26%) in this experiment was attributed to a decrease in the deuterium content of the DB(pin) reductant resulting from the H/D exchange reaction of the C-H bonds in the naphthalene rings of the products and the starting carbamates with the deuterium of the

DB(pin).[11] Although the rapidity of the hydrogen exchange reactions between DB(pin) and the aromatic C-H bonds may have complicated the outcome of the labelling studies, the experimental observations collectively indicate that the C-N bonds were substituted by the hydride derived from HB(pin).

The potential utility of this C-N bond cleavage reaction is demonstrated in Scheme 4. Thus, the 1,4-addition of **14** to enal **15** using Macmillan's amine catalyst afforded **16**, where the pyrrolidine group was essential both in terms of the reactivity and regiochemical outcome of the reaction.[12] Subsequent removal of the pyrrolidine group was enabled by the α-oxidation of the pyrrolidine followed by the cleavage of the resulting amide **17** using our newly developed nickel-catalyzed C-N bond cleavage, which gave the corresponding reduced product **18** in good yield. This C-N bond cleavage process was accomplished without having any discernible impact on the stereochemical integrity of the benzylic stereocenter. In this way, the amino groups on an aromatic ring can now be used as a removable activating and directing groups in electrophilic aromatic substitutions.

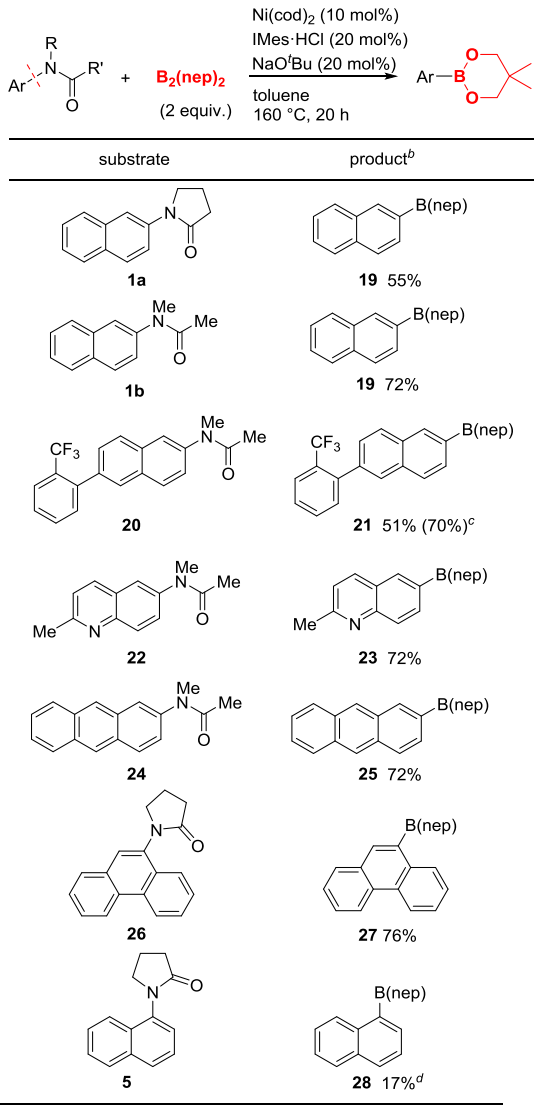
Scheme 4. Synthetic Application



Importantly, we also found that the use of diboron reagents instead of hydroborane resulted in the formation of the borylated product via the cleavage of the C-N bond (Table 2). Following a brief period of optimization, IMes was determined to be the optimal ligand for this nickel-catalyzed borylation reaction (see Experimental Section for details). This borylation process was found to be amenable to both acyclic and cyclic amides. In the case of acyclic amide **1b**, the deacylated material *N*-methyl-2-naphthylamine was also formed as a minor product. The application of the nickel-catalyzed reaction conditions to *N*-methyl-2-naphthylamine, however, did not provide **19**, which precluded its involvement as an intermediate in the catalytic borylation of **1b**. Fluoride **20** and quinoline **22** were compatible with the conditions and gave the corresponding borylated products in good yields. Once again, polyaromatic substrates, including naphthalenes, quinolines, anthracenes and

phenanthrenes were shown to exhibit significantly higher levels of reactivity towards the borylative cleavage of their C-N bonds under these conditions than the corresponding benzanilides.[13] Unlike the reductive cleavage reaction using HB(pin), the borylation reaction was found to be relatively sensitive to the steric environment of the substrate, as indicated by the decreased yield with 1-substituted amide **5**.

Table 2. Nickel-Catalyzed Borylation of C(aryl)-N Bonds[a]



[a] Reaction conditions: Amide (0.50 mmol), $B_2(nep)_2$ (1.0 mmol), $Ni(cod)_2$ (0.050 mmol), IMes•HCl (0.10 mmol), and NaO^{t}Bu (0.10 mmol) in toluene (1.5 mL) at 160 °C for 20 h. [b] Isolated yield. [c] NMR yield. [d] 61% of **5** was recovered.

Although several experiments have been conducted with the aim of establishing the mechanism of this novel nickel-mediated C-N bond cleavage reaction, very little is known

about the precise nature of the catalyst. To address this issue, we investigated the effect of adding mercury to the reaction. When the nickel-catalyzed reductive cleavage reaction was conducted with HB(pin) in the presence of an excess of mercury the reaction was completely suppressed, whereas the addition of an excess of mercury to the borylation reaction involving diboron still proceeded, albeit to a lesser extent.[14] Interestingly, the reductive cleavage reaction with HB(pin) continued to proceed even after the reaction mixture was filtered following 5 hours and the filtrate subsequently reheated.[15] Although these data do not provide a definitive understanding as to whether the catalysis is homogeneous or heterogeneous,[16,17] it is likely that the reactions described in the current study were mediated by soluble or nano-sized (~10 nm) nickel species,[18] rather than larger-sized nickel aggregates.

3.3 Conclusion

In summary, we have developed a nickel-catalyzed C(aryl)-N bond cleavage reaction for the cleavage of amides and carbamates in the absence of an ortho directing group. In the current transformation, the C-N bonds were converted into C-H and C-B bonds with hydroborane and diboron reagents, respectively. Although further studies will be required to develop a greater understanding of the scope and efficiency of the these reactions, this work clearly demonstrates that the current C(aryl)-N bond cleavage reaction represents a viable disconnection process capable of enabling a nonconventional synthetic strategy. The application of this strategy to other C-N bonds as well as computational studies aimed at revealing the mechanism of the reaction are currently being investigated in our laboratory.

3.4 Experimental Section

General Information.

^{1}H NMR and ^{13}C NMR spectra were recorded on a JEOL JMTC-400/54/ss spectrometer in $CDCl_3$ with tetramethylsilane as an internal standard. Data have been reported as follows: chemical shift in ppm (δ), multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, and m = multiplet), coupling constant (Hz), and integration. Infrared spectra (IR) were obtained on a JASCO TF/IR-4000; absorptions have been reported in reciprocal centimeters with the following relative intensities: s (strong), m (medium), or w (weak). Mass spectra were recorded on a Shimadzu GCMS-QP 2010 instrument with an ionization voltage of 70 eV. High resolution mass spectra (HRMS) were obtained on a JEOL JMS-700 spectrometer. Melting points were determined using a Yamato melting point apparatus. Column chromatography was performed with SiO_2 [Merck SilicaGel 60 (230-400 mesh) or Silycycle Silica Flash F60 (230-400 mesh)]. Gel permeation chromatography (GPC) was performed

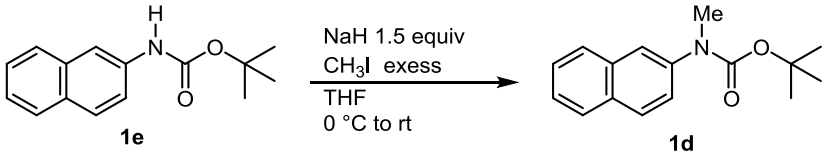
using LC-908 HPLC or LC9210NEXT HPLC system. All of the reduction and borylation reactions were carried out in 10 mL sample vials with Teflon-sealed screw caps. All of the chemicals used in the current study were manipulated in a glovebox filled with nitrogen.

Materials.

$Ni(cod)_2$, and bis(neopentylglycolato)diboron were purchased from Strem Chemicals and used as received. NaO^{t}Bu [865-48-5], IMes·HCl, 4,4,5,5-tetramethyl-1,3,2-dioxaborolane, $HSiMe(OMe)_2$ were purchased from TCI and used as received. Toluene (for Organic Synthesis) was purchased from Wako Chemicals and used as received. PCy_3 was purchased from Aldrich and used as received. Compounds **1a** [38348-86-6],[19] **1b** [100712-92-3],[19] **1c** [38348-86-6],[20] **1e** [454713-45-2],[21] **5** [6831-28-3],[22] **6** [90052-63-4],[23] **10** [360580-21-8],[24] **14** [82238-92-4],[25] were synthesized according to the reported procedures.

Synthesis of Starting Materials.

***tert*-Butyl methyl(naphthalen-2-yl)carbamates (1d).**



A solution of carbamate **1e**[21] (2.9 g, 12 mmol) in dry THF (30 ml) was added dropwise at 0 °C to a suspension of NaH (60 wt% oil dispersion, 1.5 g, 35 mmol) in dry THF (10 mL). The resulting mixture was stirred at rt for 10 min, MeI (12 mL) was then added, and the mixture was stirred at rt for 16 h. The mixture was then cooled to 0 °C and quenched by by the addition of water (10 mL). The THF was removed in vacuo to give an aqueous residue, which was extracted with ether (10 mL x 3). The combined extracts were then washed with brine, dried over Na_2SO_4 and evaporated in vacuo to give the crude product, which was purified by recrystallization from $CHCl_3$-hexane to give **1d** as a white solid (2.5 g, 81 %).

Rf 0.42 (hexane/CH_2Cl_2 = 1/1). Mp = 69 °C.

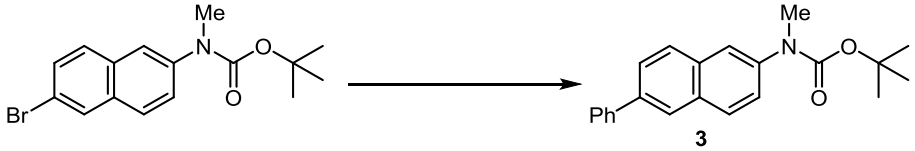
^{1}H NMR (400 MHz, $CDCl_3$): 1.46 (s, 9H), 3.37 (s, 3H), 7.41-7.49 (m, 3H), 7.63 (d, J = 1.6 Hz, 1H), 7.77-7.82 (m, 3H).

^{13}C NMR ($CDCl_3$, 100 MHz): 28.3, 37.5, 80.4, 122.4, 125.1, 125.5, 126.1, 127.5, 127.6, 128.0, 131.2, 133.4, 141.4, 154.8

IR (ATR): 2975 w, 2361 w, 2314 w, 1697 s, 1475 w, 1438 w, 1369 m, 1331 m, 1150 s, 857 w.

HRMS (EI): Calcd for $C_{16}H_{19}NO_2$ 257.1416, Found 257.1415.

***tert*-Butyl methyl(6-phenylnaphthalen-2-yl)carbamate (3).**



3

An oven-dried two-necked flask was charged with *tert*-Butyl (6-bromonaphthalen-2-yl)-(methyl)carbamate ([1388628-76-9], 3.4 g, 10 mmol),[26] phenylboronic acid (1.5 g, 12 mmol), K_2CO_3 (2.8 g, 20 mmol), $Pd(PPh_3)_4$ (580 mg, 0.50 mmol), and dioxane (10 mL), and the mixture was heated for 3 h at 90 °C. The resulting mixture was filtrated through a pad of Celite, and the filtrate was concentrated. The residue was purified by flash column chromatography on silica gel (hexane/EtOAc = 3:1) to provide **3** as a white solid (1.7 g, 50% yield).

Rf 0.38 (hexane/ CH_2Cl_2 = 1/1). Mp = 121-122 °C.

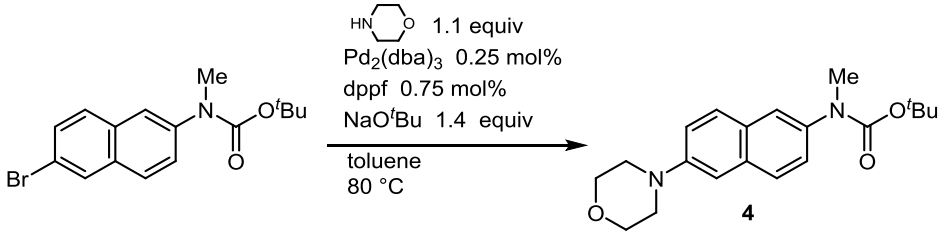
^{1}H NMR (400 MHz, $CDCl_3$): 8.01 (s, 1H), 7.85 (t, *J* = 8.0 Hz, 2H), 7.71-7.75 (m, 3H), 7.65 (s, 1H), 7.38-7.51 (m, 4H), 3.38 (s, 3H), 1.48 (s, 9H).

^{13}C NMR ($CDCl_3$, 100 MHz): 28.3, 37.5, 80.4, 122.1, 125.4, 125.5, 125.9, 127.3, 128.1, 128.3, 128.8, 129.8, 131.4, 132.6, 138.2, 140.9, 141.5, 154.8.

IR (ATR): 2975 w, 2930 w, 2365 w, 2315 w, 1694 s, 1601 w, 1496 m, 1450 w, 1354 m, 1323 m, 1254 w, 1147 s, 1099 m, 1890 m, 813 w.

HRMS (EI): Calcd for $C_{22}H_{23}NO_2$ 333.1729, Found 333.1727.

***tert*-Butyl methyl(6-morpholinonaphthalen-2-yl)carbamate (4).**



4

$Pd_2(dba)_3$ (12 mg, 0.013 mmol), dppf (21 mg, 0.038 mmol), NaO^tBu (680 mg, 7.0 mmol) and morpholine (0.48 mL, 5.5 mmol) were added to a solution of tert-butyl (6-bromonaphthalen-2-yl)(methyl)carbamate[26] (1.7 g, 5.0 mmol) in toluene (10 mL) under an atmosphere of nitrogen, and the resulting mixture was heated at 80 °C for 16 h. The mixture was filtrated through a pad of Celite, and the filtrate was concentrated in vacuo. The residue was purified by column chromatography on silica gel (CH_2Cl_2/EtOAc = 10:1) to give **4** as a white solid (1.2 g, 70%).

Rf 0.41 (CH_2Cl_2/EtOAc = 5/1). Mp = 141-142 °C.

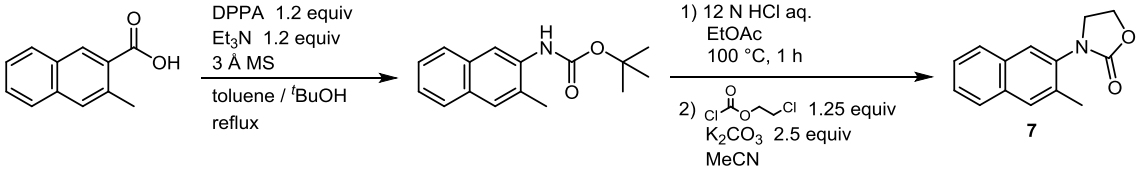
^{1}H NMR (400 MHz, $CDCl_3$): 7.63-7.70 (m, 2H), 7.52 (s, 1H), 7.33 (d, J = 8.0 Hz, 1H), 7.23-7.26 (m, 1H), 7.10 (d, J = 2.4 Hz, 1H), 3.92 (t, J = 4.8 Hz, 4H), 3.33 (s, 3H), 3.26 (t, J = 4.8 Hz, 4H), 1.45 (s, 9H).

^{13}C NMR ($CDCl_3$, 100 MHz): 28.3, 37.6, 49.8, 66.9, 80.2, 109.8, 119.2, 122.5, 125.7, 126.9, 128.49, 128.53, 132.3, 139.5, 149.0, 155.0.

IR (ATR): 2971 m, 2823 w, 2373 w, 2349 w, 2314 w, 1739 w, 1685 s, 1604 m, 1478 w, 1449 w, 1429 m, 1389 m, 1360 s, 1332 w, 1263 m, 1208 m, 1146 s, 1120 s, 1101 s, 942 m, 868 m, 811 w, 768 w.

HRMS (EI): Calcd for $C_{20}H_{26}N_2O_3$ 342.1943, Found 342.1942.

3-(3-Methylnaphthalen-2-yl)oxazolidin-2-one (7).



Et_3N (2.5 mL, 18 mmol), 3 Å molecular sieves (10 g) and diphenyl phosphorylazide (3.9 mL, 18 mmol) were added sequentially to a solution of 3-methyl-2-naphthoic acid[27] (3.0 g, 16 mmol) in *t*-BuOH (50 mL) and toluene (50 mL), and the resulting mixture was refluxed for 24 h. The reaction mixture was then cooled to room temperature and filtered through a pad of Celite. The filtrate was concentrated in vacuo to give a residue, which was purified by column chromatography (SiO_2, hexane/CH_2Cl_2 = 1:1) to afford *tert*-butyl (3-methylnaphthalen-2-yl) carbamate as a pale yellow solid (3.0 g, 74%).

Thus obtained tert-butyl (3-methylnaphthalen-2-yl)carbamate (1.5 g, 6.2 mmol) was dissolved in a solution of HCl in EtOAc (12 M, 50 mL), and the resulting mixture was refluxed for 1 h. The reaction mixture was then cooled to room temperature and basified (pH ~12) with an aqueous solution of NaOH (3 M), before being extracted with EtOAc. The EtOAc layer was then washed with brine, dried over Na_2SO_4 and filtrated. Concentration of the filtrate afforded 3-methylnaphthalene-2-amine, which was used directly in the next step.

2-Chloroethyl chloroformate (180 mg, 1.3 mmol) was added to a stirred mixture of 3-methylnaphthalene-2-amine (230 mg, 1.5 mmol) and K_2CO_3 (350 mg, 2.5 mmol) in MeCN (2.0 mL), and the resulting mixture was stirred for 1 h at rt, before being refluxed for 16 h. The mixture was then cooled to rt and filtered through a pad of Celite. The filtrate was concentrated in vacuo to give a residue, which was purified by column chromatography on silica gel (CH_2Cl_2/EtOAc = 5:1) to give **7** as a white solid (100 mg, 31%).

Rf 0.68 (CH_2Cl_2/EtOAc = 3/1). Mp = 135-136 °C.

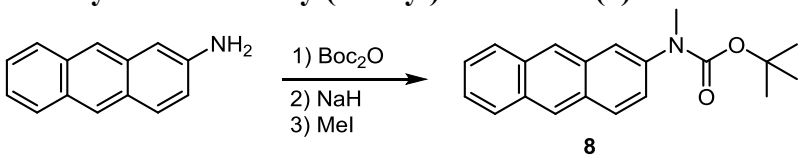
^{1}H NMR (400 MHz, $CDCl_3$): 7.74-7.78 (m, 4H), 7.41-7.49 (m, 2H), 4.57 (dd, *J* = 8.8, 7.4Hz, 2H), 4.03 (dd, *J* = 8.4, 7.0 Hz, 2H), 2.48 (s, 3H).

^{13}C NMR ($CDCl_3$, 100 MHz): 18.2, 48.4, 62.3, 125.5, 125.8, 126.6, 127.0, 127.4, 129.7, 132.3, 133.1, 133.6, 134.9, 157.0

IR (ATR): 2970 w, 2372 w, 2350 w, 2314 w, 1739 s, 1599 w, 1486 w, 1415 m, 1293 w, 1229 m, 1136 w, 1092 m, 1034 m, 986 w, 944 w, 888 m, 756 m.

HRMS (EI): Calcd for $C_{14}H_{13}NO_2$ 227.0946, Found 227.0947.

***tert*-Butyl anthracen-2-yl(methyl)carbamate (8).**



8

A mixture of 2-aminoanthracene (500 mg, 2.6 mmol), Boc_2O (710 mL, 3.1 mmol), and K_2CO_3 (720 mg, 5.2 mmol) in THF (5.0 mL) and H_2O (5.0 mL) was stirred at 80 °C for 8 h. After removing THF in vacuo, the residue was extracted with EtOAc. The extract was concentrated in vacuo, and the residue was triturated with Et_2O to give 2-BocNH-anthracene as a pale yellow powder (540 mg). A solution of the 2-BocNH-anthracene in DMF (5 mL) was added dropwise at 0 °C to a suspension of NaH (60 wt% oil dispersion, 110 mg, ca. 2.7 mmol) in DMF (5.0 mL). After the mixture was stirred at rt for 0.5 h, MeI (340 □L, 5.4 mmol) was added. The mixture was then stirred at rt for 16 h. The mixture was partitioned between EtOAc and saturated aqueous solution of NH_4Cl. The organic layer was washed with brine, dried ($MgSO_4$) and concentrated in vacuo. The residue was purified by recrystallization (hexane/Et_2O = 30:1) to give **8** as a pale yellow powder (330 mg, 41% for 2 steps).

Rf 0.49 (hexane/EtOAc = 3/1).

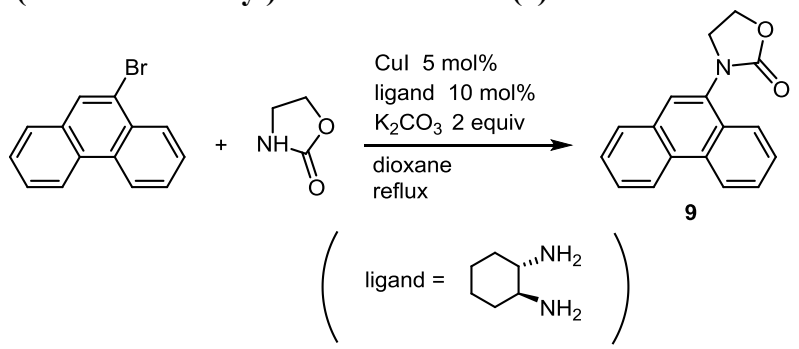
^{1}H NMR ($CDCl_3$, 400 MHz): 1.49 (s, 9H), 3.41 (s, 3H), 7.43-7.47 (m, 3H), 7.75 (d, *J* = 1.8 Hz, 1H), 7.93-8.00 (m, 3H), 8.35 (bs, 1H), 8.39 (bs, 1H).

^{13}C NMR ($CDCl_3$, 100 MHz): 28.4, 37.5, 80.6, 121.6, 125.2, 125.4, 125.5, 125.7, 125.9, 127.9, 128.2, 128.3, 129.6, 131.47, 131.54, 131.9, 140.9, 154.8.

IR (ATR): 2925 m, 2359 m, 2329 w, 1703 s, 1556 w, 1509 w, 1458 w, 1369 m, 1335 w, 1284 w, 1153 m, 1093 w, 895 w, 870 w.

HRMS (EI): Calcd for $C_{20}H_{21}NO_2$ 307.1572, Found 307.1570.

3-(Phenanthren-9-yl)oxazolidin-2-one (9).



An oven-dried flask was charged with 2-bromophenanthrene (purchased from TCI, 2.6 g, 10 mmol), oxazolidin-2-one (880 mg, 10 mmol), K_2CO_3 (2.8 g, 20 mmol), CuI (97 mg, 0.51 mmol), (±)-*trans*-cyclohexane-1,2-diamine (0.12 mL, 1.0 mmol) and 1,4-dioxane (5.0 mL). The flask was refluxed for 15 h. The reaction mixture was then cooled to room temperature, diluted with CH_2Cl_2 and filtered through a pad of silica gel (CH_2Cl_2/EtOAc = 1:1). The filtrate was concentrated *in vacuo* to give a crude material as a solid, which was recrystallized (hexane/$CHCl_3$) to give **9** as a white solid (2.3 g, 87%).

Rf 0.57 (CH_2Cl_2/EtOAc = 10/1). Mp = 137 °C.

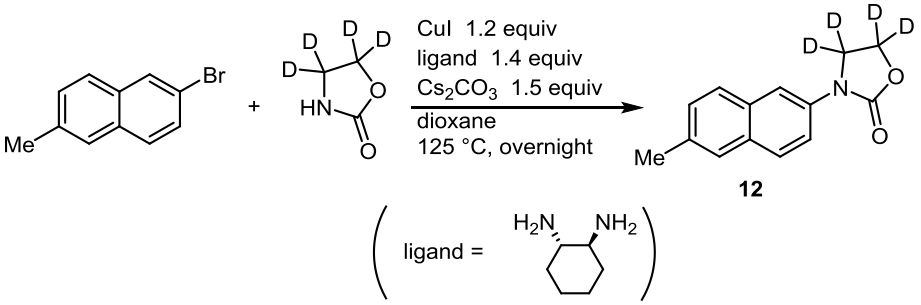
^{1}H NMR (400 MHz, $CDCl_3$): 8.75 (d, J = 8.0 Hz, 1H), 8.69 (d, J = 8.4 Hz, 1H), 7.97 (dd, J = 1.4, 7.8 Hz, 1H), 7.88 (d, J = 8.2 Hz, 1H) 7.81 (s, 1H), 7.60-7.75 (m, 4H), 4.69 (t, J = 7.8 Hz, 2H), 4.15 (t, J = 7.8 Hz, 2H).

^{13}C NMR ($CDCl_3$, 100 MHz): 49.0, 62.5, 122.5, 122.9, 123.3, 125.8, 127.0, 127.15, 127.24, 127.4, 128.4, 128.7, 130.1, 131.2, 131.5, 132.4, 157.6.

IR (ATR): 3010 w, 2913 w, 2371 w, 2315 w, 1737 s, 1601 w, 1478 w, 1452 w, 1409 m, 1324 w, 1228 m, 1104 w, 1073 m, 1033 m, 977 w, 913 w, 890 w.

HRMS (EI): Calcd for $C_{17}H_{13}NO_2$ 263.0946, Found 263.0948.

3-(6-Methylnaphthalen-2-yl)oxazolidin-2-one-d_4 (12).



An oven-dried flask was charged with 2-bromo-6-methylnaphthalene (this known compound [37796-78-4] was prepared from (6-bromonaphthalen-2-yl)methanol[28] by tosylation and $LiAlH_4$ reduction;[29] 1.4 g, 6.2 mmol), oxazolidin-2-one-d_4 (prepared from ethylene carbonate

and 2-aminoethan-1,1,2,2-d_4-1-ol by following a reported procedure,[30] 270 mg, 3.0 mmol), Cs_2CO_3 (1.5 g, 4.5 mmol), CuI (690 mg, 3.6 mmol), 1,4-dioxane (20 mL) and (±)-*trans*-cyclohexane-1,2-diamine (0.50 mL, 4.2 mmol) and the resulting mixture was refluxed for 16 h. The mixture was then cooled to rt, diluted with CH_2Cl_2, filtered through a pad of silica gel (CH_2Cl_2/EtOAc = 1:1). The filtrate was concentrated *in vacuo* to give a crude material, which was purified by flash chromatography on silica gel (CH_2Cl_2/EtOAc = 2:1) to give **12** as a white solid (0.80 mg, 99%).

Rf 0.14 (hexane/EtOAc = 2/1). Mp = 182 °C.

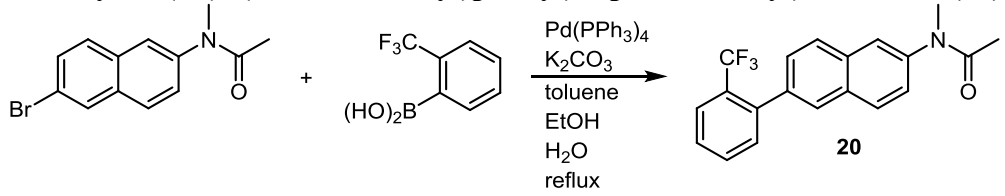
^{1}H NMR (400 MHz, $CDCl_3$): 7.91 (dd, *J* = 2.4, 8.8 Hz, 1H), 7.76 (d, *J* = 9.2 Hz, 1H), 7.67-7.71 (m, 2H), 7.58 (s, 1H), 7.32 (dd, *J* = 1.4, 8.4 Hz, 1H), 2.50 (s, 3H).

^{13}C NMR ($CDCl_3$, 100 MHz): 21.7, 44.5-44.9 (m), 60.4-60.9 (m), 114.8, 118.4, 126.6, 127.4, 128.4, 129.1, 130.6, 131.7, 135.0, 135.3, 155.5.

IR (ATR): 2919 w, 2375 w, 2349 w, 2313 w, 1729 s, 1603 m, 1503 w, 1485 w, 1388 m, 1356 s, 1334 s, 1269 m, 1239 m, 1196 m, 1168 w, 1093 w, 1040 s, 961 m, 880 m, 858 m.

HRMS (EI): Calcd for $C_{14}H_9D_4NO_2$ 231.1197, Found 231.1195.

***N*-Methyl-*N*-(6-(2-(trifluoromethyl)phenyl)naphthalen-2-yl)acetamide (20).**



A 200-mL round-bottom flask was charged with N-(6-bromonaphthalen-2-yl)-N-methylacetamide[26] (1.4 g, 5.0 mmol), 2-trifluoromethylboronic acid (1.2 g, 6.5 mmol), K_2CO_3 (2.8 g, 20 mmol), $Pd(PPh_3)_4$ (510 mg, 0.44 mmol), toluene (30 mL), EtOH (20 mL) and H_2O (10 mL). The mixture was refluxed for 3 h. The reaction mixture was purified by flash chromatography on silica gel (hexane/EtOAc = 1:1), GPC and recrystallization (hexane) to give **20** as a white solid (1.1 g, 61%).

Rf 0.34 (hexane/EtOAc = 1/2). Mp. 80-81 °C.

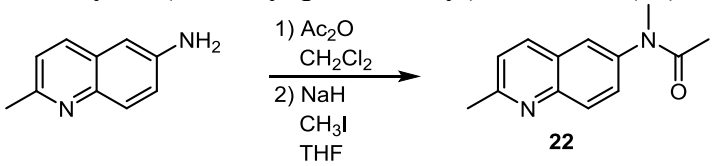
^{1}H NMR (400 MHz, $CDCl_3$): 7.80-7.94 (m, 4H), 7.71 (d *J* = 2.0 Hz, 1H), 7.62 (t, *J* = 7.2 Hz, 1H), 7.52-7.55 (m, 2H), 7.41 (d, *J* = 7.2 Hz, 1H), 7.35 (dd, *J* = 1.8, 8.6 Hz, 1H), 3.37 (s, 3H), 1.96 (s, 3H).

^{13}C NMR ($CDCl_3$, 100 MHz): 22.6, 37.3, 124.0 (q, *J* = 272.7 Hz), 125.2, 125.5, 126.0 (q, *J* = 5.4 Hz), 127.1, 127.56, 127.60, 128.1, 128.4 (q, *J* = 29.5 Hz), 130.0, 131.3, 131.5, 132.0, 132.6, 138.1, 140.6, 142.1, 170.5.

IR (ATR): 3031 w, 1372 w, 2349 w, 2314 w, 1745 w, 1661 s, 1631 w, 1601 m, 1577 w, 1494 w, 1418 m, 1385 m, 1313 s, 1264 w, 1168 s, 1123 s, 1108 s, 1068 m, 1034 m, 979 w, 901 w, 819 w.

HRMS (EI): Calcd for $C_{20}H_{16}F_3NO$ 343.1184, Found 343.1186.

***N*-Methyl-*N*-(2-methylquinolin-6-yl)acetamide (22).**



Ac_2O (0.36 mL, 3.8 mmol) was added to a solution of 2-methylquinolin-6-amine (purchased from TCI, 510 g, 3.2 mmol) in CH_2Cl_2 (40 mL), and the resulting mixture was stirred at rt for 7 h for 16 h. The mixture was washed with aqueous solution of $NaHCO_3$, and the organic extract was dried over Na_2SO_4, filtrated and concentrated. The residue (ca. 530 mg) was dissolved in THF (5.0 mL), and the solution was added dropwise at 0 °C to a suspension of NaH (ca. 60% oil dispersion, 180 mg, 4.5 mmmol) in THF (10 mL). The mixture was stirred at room temperature for 0.5 h and cooled to 0 °C. MeI (1.5 mL) was added to the reaction mixture at 0 °C, and the mixture was stirred at room temperature for 7 h. After water was added, the mixture was extracted with Et_2O. The organic extracts were washed with brine, dried (Na_2SO_4) and concentrated. Recrystallization (hexane/$CHCl_3$) of the residue afforded **22** as a beige solid (320 mg, 46% yield).

Rf 0.2 (hexane/EtOAc = 1/1). Mp = 94-95 °C.

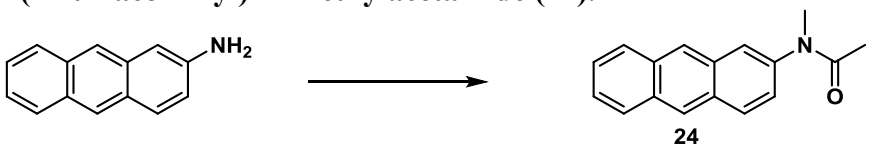
^{1}H NMR (400 MHz, $CDCl_3$): 8.05-8.09 (m, 2H), 7.61 (s, 1H), 7.51 (d, J = 7.8 Hz, 1H), 7.36 (d, J = 8.4 Hz, 1H), 3.36 (s, 3H), 2.78 (s, 3H), 1.93 (s, 3H)

^{13}C NMR ($CDCl_3$, 100 MHz): 22.5, 25.4, 37.2, 122.9, 125.0, 126.6, 128.6, 130.6, 135.9, 141.6, 146.7, 160.0, 170.5.

IR (ATR): 3043 w, 2925 w, 1657 s, 1599 m, 1495 m, 1427 m, 1377 s, 1284 m, 1128 w, 1080 w, 976 m, 926 w, 820 m.

HRMS (EI): Calcd for $C_{13}H_{14}N_2O$ 214.1106, Found 214.1108.

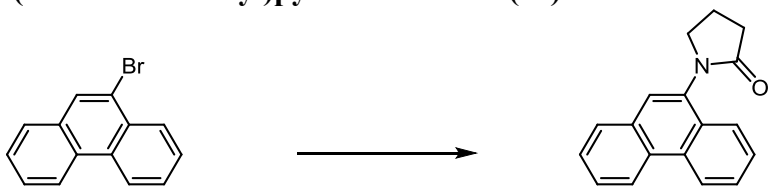
***N*-(Anthracen-2-yl)-*N*-methylacetamide (24).**



Ac_2O (290 μL, 3.1 mmol) was added to a solution of 2-aminoanthracene (500 mg, 2.6 mmol) in CH_2Cl_2 (10 mL), and the resulting mixture was stirred at room temperature for 16 h. After

removing CH_2Cl_2 in vacuo, the residue was triturated with Et_2O, and the precipitate was collected by filtration. The resultant pale yellow powder (560 mg) was dissolved in DMF (10 mL), and the solution was added dropwise at 0 °C to a suspension of NaH (60% oil dispersion, 110 mg, ca. 2.9 mmol) in DMF (10 mL). After the mixture was stirred at room temperature for 0.5 h, MeI (300 μL, 4.8 mmol) was added. The mixture was then stirred at room temperature for 16 h. The mixture was partitioned between EtOAc and 1M aqueous solution of HCl. The organic layer was washed with brine, dried ($MgSO_4$) and concentrated in vacuo. The residue was purified by column chromatography on silica gel (hexane/EtOAc = 1:3) and then by washing with Et_2O to give **24** as a pale yellow powder (530 mg, 82% for 2 steps).
Rf 0.30 (hexane/EtOAc = 1/2). Mp = 135-136 °C.
^{1}H NMR ($CDCl_3$, 400 MHz): 1.98 (s, 3H), 3.39 (s, 3H), 7.26-7.29 (m, 1H), 7.50-7.52 (m, 2H), 7.80 (d, J = 1.8 Hz, 1H), 8.01-8.08 (m, 3H), 8.42 (bs, 1H), 8.46 (bs, 1H).
^{13}C NMR ($CDCl_3$, 100 MHz): 22.8, 37.3, 125.0, 125.5, 126.1, 126.2, 126.6 (2C), 128.2, 128.4, 130.4, 130.5, 131.4, 132.2, 132.3, 141.3, 171.0.
IR (ATR): 3053 w, 3016 w, 2937 w, 1676 s, 1628 m, 1581 w, 1477 w, 1459 w, 1411 w, 1383 m, 1350 w, 1335 w, 1309 w, 1286 w, 1240 w, 1136 w, 1070 w, 1039 w, 978 w, 903 m.
HRMS (EI): Calcd for $C_{17}H_{15}NO$ 249.1154, Found 249.1157.

1-(Phenanthren-9-yl)pyrrolidin-2-one (26).



26

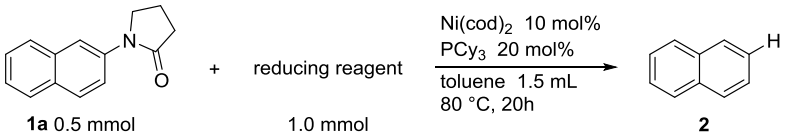
An oven-dried 50 mL two-necked flask was charged with 2-bromophenanthrene (purchased from TCI, 2.6 g, 10 mmol), pyrrolidin-2-one (0.93 mL, 12 mmol), Cs_2CO_3 (4.6 g, 14 mmol), Xantphos (88 mg, 0.15 mmol), $Pd_2(dba)_3$ (47 mg, 0.050 mmol) and 1,4-dioxane (10 mL) under nitrogen atmosphere, and the mixture was refluxed for 18 h. The mixture was filtrated through a pad of Celite, and the filtrate was concentrated in vacuo. The residue was purified by flash column chromatography on silica gel (CH_2Cl_2/EtOAc = 10:1) and then by recrystallization (hexane/$CHCl_3$) to give **26** as a white solid (1.9 g, 73%).
Rf 0.34 (CH_2Cl_2/EtOAc = 10/1). Mp = 162-163 °C.
^{1}H NMR (400 MHz, $CDCl_3$): 8.74 (d, J = 8.0 Hz, 1H), 8.68 (d, J = 8.4 Hz, 1H), 7.82-7.87 (m, 2H), 7.60-7.71 (m, 5H), 3.93 (t, J = 7.0 Hz, 2H), 2.77 (t, J = 8.4 Hz, 2H), 2.35-2.43 (m, 2 H)
^{13}C NMR ($CDCl_3$, 100 MHz): 19.3, 31.5, 51.8, 122.6, 123.2, 123.3, 125.7, 126.9, 127.07, 127.11, 127.2, 128.3, 128.6, 130.1, 131.4, 131.5, 134.0, 175.6.

IR (ATR): 2973 w, 2375 w, 2349 w, 2313 w, 1744 w, 1680 s, 1602 w, 1485 w, 1452 m, 1412 m, 1320 m, 1272 m, 1240 m, 1144 w, 1103 w, 1058 w, 1038 w, 1018 w, 918 w, 895 w, 860 w, 821 w.

HRMS (EI): Calcd for $C_{18}H_{15}NO$ 261.1154, Found 261.1152.

Optimization Studies for the Reductive Cleavage of C(aryl)-N Bonds.

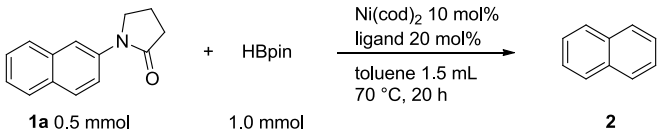
1. Screening of Reducing Reagents



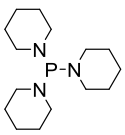
entry	reducing reagent	**2** (%)
1	HBpin	61
2	$HSiMe(OMe)_2$	7
3	BH_3·DMS	0[a]
4	KBH_4	0
5	DIBAL	0[b]
6	H_2 (1 atm)	0

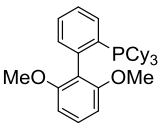
a) 1-(Naphthalen-2-yl)pyrrolidine was formed (52%)
b) **1a** was completely consumed, but no identifiable products were observed.

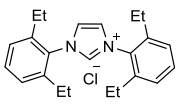
2. Screening of Ligand



entry	ligand	results (%)		entry	ligand	results (%)	
		2	**1a**			**2**	**1a**
1	PCy_3	61	21	10	ligand 2	nd	74
2	$PCyp_3$	9	35	11[a]	IMes	30	32
3	ligand 1	nd	43	12[b]	IMes	20	48
4	PMe_3	nd	>99	13[c]	IMes	26	42
5	P^tBu_3	nd	83	14	IPr	nd	27
6	PMe^tBu_2	8	66	15	ligand 3	29	42
7	PPh_3	nd	>99	16	IAd	trace	62
8	PMe_2Ph	nd	53	17	SIMes	trace	48
9	$P(OPh)_3$	nd	31				

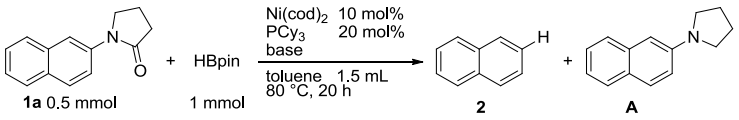
ligand 1= 

ligand 2= 

ligand 3= 

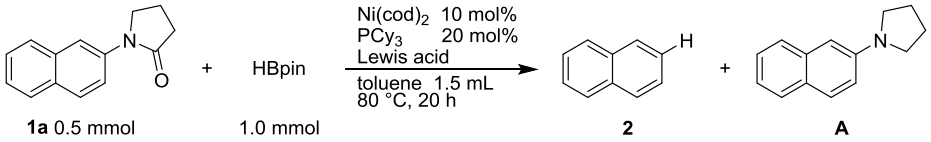
[a] =temp. 80 °C
[b] =temp. 100 °C
[c] =temp. 120 °C

3. Effect of Added Base



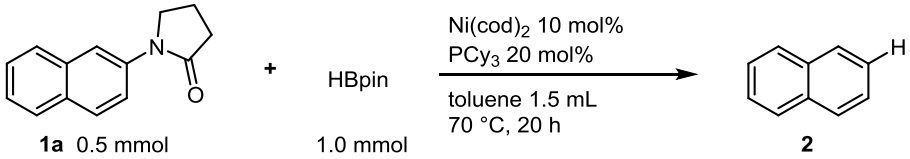
entry	base (mol%)	results (%)			entry	base (mol%)	results (%)		
		2	A	1a			2	A	1a
0	none	61	2	14	5	K_2CO_3 (200)	24	2	87
1	KF(50)	69	6	18	6	Cs_2CO_3 (200)	8	11	>99
2	KF (200)	52	8	36	7	CsOAc (200)	34	8	72
3	CsF (200)	4	34	41	8	CF_3CO_2Ag (200)	nd	nd	>99
4	KO^{t}Bu (100)	trace	39	trace					

4. Scope of Added Lewis Acid



entry	Lewis acid (mol%)	result (%)			entry	Lewis acid (mol%)	results (%)		
		2	A	1a			2	A	1a
0	none	61	2	14	10	AlF_3 (20)	37	5	53
1	$AlMe_3$ (200)	nd	41	2	11	FeF_3 (80)	13	8	92
2	MAD (200)	nd	41	48	12	GaF_3 (80)	35	6	48
3	BPh_3 (200)	nd	25	11	13	CeF_3 (80)	46	6	34
4	$B(OPh)_3$ (200)	nd	nd	92	14	TiF_3 (80)	3	8	>99
5	$B(OEt)_3$ (200)	nd	31	37	15	TiF_4 (50)	7	10	75
6	MgF_2 (100)	47	8	43	16	$ZrCl_4$ (50)	nd	45	10
7	$MgBr_2$ (100)	nd	4	7	17	$AgBF_4$ (50)	nd	14	87
8	MnF_2 (100)	49	4	36	18	ZrF_4 (50)	35	8	30
9	ZnF_2 (100)	53	4	29					

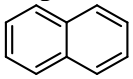
A General Procedure for the Reductive Cleavage of C(aryl)-N bonds (Scheme 2).



An oven-dried 10 mL screw-capped vial was charged with 2-*N*-(2-naphthyl)pyrrolidin-2-one (**1a**, 110 mg, 0.50 mmol), HBpin (130mg, 1.0 mmol), $Ni(cod)_2$ (14 mg, 0.050 mmol), PCy_3 (28 mg, 0.10 mmol) and toluene (1.5 mL) in a glovebox filled with nitrogen, and the resulting mixture was sealed and heated at 80 °C for 20 h on an aluminum. The mixture was then cooled to room temperature and purified directly by flash column chromatography on silica gel (hexane/EtOAc = 50:1) to give naphthalene (**2**, 60 mg, 55%) as a white solid.

Spectroscopic Data of the Reductive Cleavage Products.

Naphthalene (2) [CAS: 91-20-3].



The general procedure was followed.

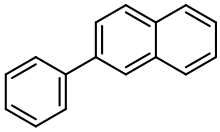
Rf 0.84 (hexane/EtOAc = 5/1). White solid.

^{1}H NMR ($CDCl_3$, 399.78 MHz): 7.83-7.87 (m, 4H), 7.46-7.50 (m, 4H).

^{13}C NMR ($CDCl_3$, 100.53 MHz): 125.8, 127.8.

HRMS (EI): Calcd for $C_{10}H_8$ 128.0626, Found 128.0627.

2-Phenylnaphthalene [CAS: 612-94-2].



The general procedure was followed, except that **3** was used instead of **1a**.

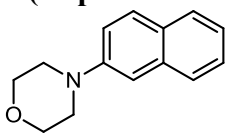
Rf 0.53 (hexane / EtOAc = 10/1). White solid. Mp = 105 °C.

^{1}H NMR ($CDCl_3$, 399.78 MHz): 8.04 (d, *J* = 0.8 Hz, 1H), 7.84-7.92 (m, 3H), 7.71-7.73 (m, 3H), 7.46-7.51 (m, 4H), 7.35-7.39 (m, 1H).

^{13}C NMR ($CDCl_3$, 100.53 MHz): 125.6, 125.8, 125.9, 126.3, 127.3, 127.4, 127.6, 128.2, 128.4, 128.8, 132.6, 133.7, 138.5, 141.1.

HRMS (EI): Calcd for $C_{16}H_{12}$ 204.0939, Found 204.0938.

4-(Naphthalene-2-yl)morpholine [CAS: 7508-21-6].



The general procedure was followed except that **4** was used instead of **1a**.

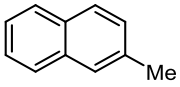
Rf 0.49 (CH_2Cl_2/EtOAc = 10/1). White solid = 87-90 °C.

^{1}H NMR ($CDCl_3$, 399.78 MHz): 7.69-7.76 (m, 3H), 7.41 (t, *J* = 7.6 Hz, 1H), 7.25-7.33 (m, 2H), 7.13 (s, 1H), 3.92 (t, *J* = 4.6 Hz, 4H), 3.27 (t, *J* = 4.8 Hz, 4H).

^{13}C NMR ($CDCl_3$, 100.53 MHz): 49.8, 67.0, 110.1, 118.9, 123.5, 126.3, 126.8, 127.4, 128.7, 128.8, 134.5, 149.1.

HRMS (EI): Calcd for $C_{14}H_{15}NO$ 213.1154, Found 213.1155.

2-Methylnaphthalene [CAS: 91-57-6].



The general procedure was followed, except that **7** was used instead of **1a**.

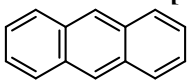
Rf 0.86 (hexane/EtOAc = 5/1). White solid. Mp. = 32-36 °C.

^{1}H NMR ($CDCl_3$, 399.78 MHz): 7.74-7.79 (m, 3H), 7.62 (s, 1H), 7.38-7.45 (m, 2H), 7.32 (dd, *J* = 1.8, 8.6 Hz, 1H), 2.52 (s, 3H).

^{13}C NMR ($CDCl_3$, 100.53 MHz): 21.7, 124.9, 125.8, 126.8, 127.2, 127.5, 127.6, 128.1, 131.6, 133.6, 135.4.

HRMS (EI): Calcd for $C_{11}H_{10}$ 142.0783, Found 142.0782.

Anthracene [CAS: 120-12-7].



The general procedure was followed, except that **8** was used instead of **1a**.

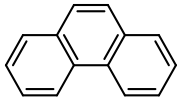
Rf 0.66 (hexane/EtOAc = 5/1). White solid. Mp. = 215 °C.

^{1}H NMR ($CDCl_3$, 399.78 MHz): 8.44 (s, 2H), 7.99-8.04 (m, 4H), 7.45-7.49 (m, 4H).

^{13}C NMR ($CDCl_3$, 100.53 MHz): 125.3, 126.2, 128.1, 131.6.

HRMS (EI): Calcd for $C_{14}H_{10}$ 178.0783, Found 178.0782.

Phenanthrene [CAS: 85-01-8].



The general procedure was followed, except that **9** was used instead of **1a**.

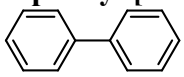
Rf 0.71 (hexane/EtOAc = 5/1). White solid. Mp. = 97-101.

^{1}H NMR ($CDCl_3$, 399.78 MHz): 8.69 (d, J = 8.4 Hz, 2 H), 7.89 (dd, J = 1.2, 7.6 Hz, 2H), 7.74 (s, 2H), 7.25-7.66 (m, 4H).

^{13}C NMR ($CDCl_3$, 100.53 MHz): 122.6, 126.5 (2C), 126.9, 128.5, 130.2, 132.0.

HRMS (EI): Calcd for $C_{14}H_{10}$ 178.0783, Found 178.0782.

Biphenyl [CAS: 92-52-4].



The general procedure was followed except that **10** was used instead of **1a**.

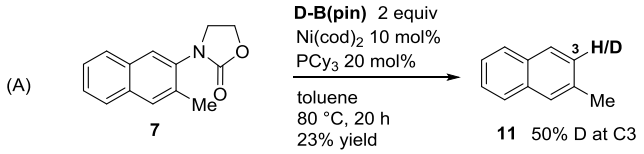
Rf 0.77 (hexane/EtOAc = 5/1). White solid. Mp. = 69-71.

^{1}H NMR ($CDCl_3$, 399.78 MHz): 7.58-7.61 (m, 4 H), 7.42-7.46 (m, 4 H), 7.32-7.36 (m, 2 H).

^{13}C NMR ($CDCl_3$, 100.53 MHz): 127.1, 127.2, 128.7, 141.2.

HRMS (EI): Calcd for $C_{12}H_{10}$ 154.0783, Found 154.0783.

Labelling Studies for Reductive Cleavage Reaction (Scheme 3).



An oven-dried 10-mL screw-capped vial was charged with **7** (120 mg, 0.50 mmol), DBpin[31] (97% D, 130 mg, 1.0 mmol), $Ni(cod)_2$ (14 mg, 0.050 mmol), PCy_3 (28 mg, 0.10 mmol) and toluene (1.5 mL) in a glovebox filled with nitrogen, and the resulting mixture was sealed and heated at 80 °C for 20 h on an aluminum block. GC analysis of the reaction mixture indicated that the yield was 23%. The mixture was purified directly by flash column chromatography on silica gel (hexane/EtOAc = 50:1) to give **11** as a white solid. The deuterium content at the 3-position was determined to be 50% by NMR spectroscopy (Figure S1). The other positions were also deuterated slightly (see below).

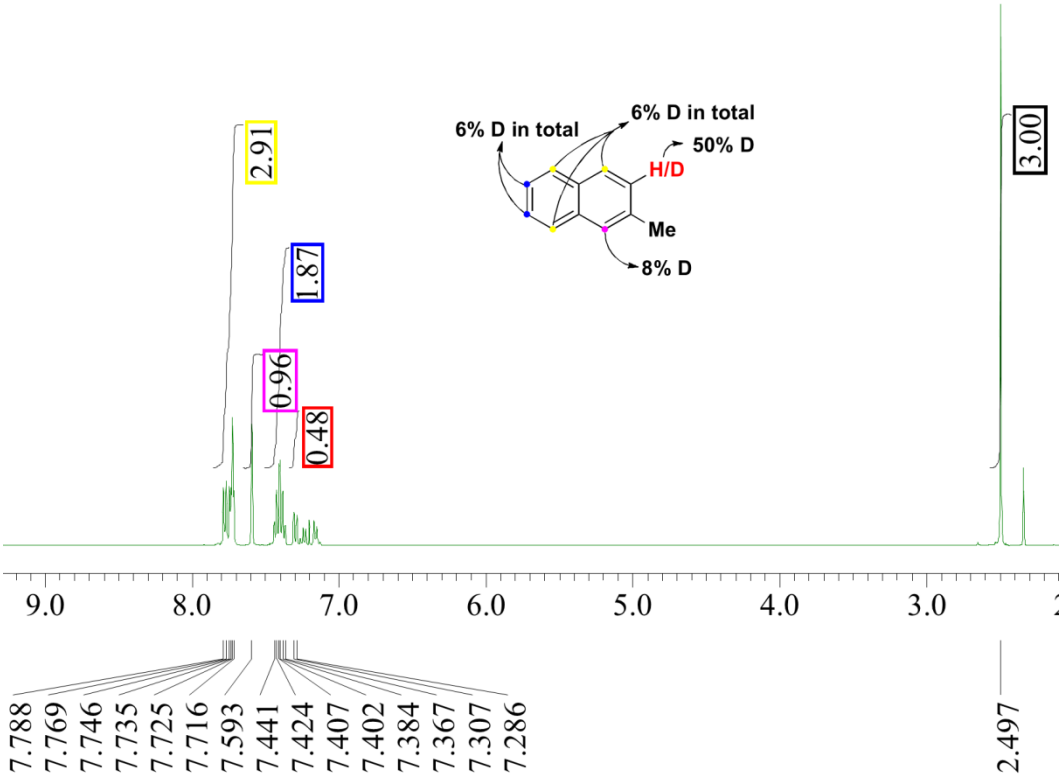
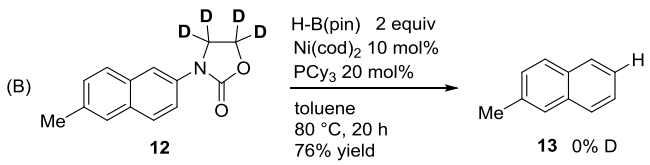


Figure S1. NMR spectra for **11** obtained from the reaction shown in Scheme 3A.



An oven-dried 10 mL screw-capped vial was charged with **12** (130 mg, 0.54 mmol), HBpin (130 mg, 1.0 mmol), $Ni(cod)_2$ (14 mg, 0.050 mmol), PCy_3 (28 mg, 0.10 mmol) and toluene

(1.5 mL) in a glovebox filled with nitrogen, and the resulting mixture was sealed and heated at 80 °C for 20 h on an aluminum block. GC analysis of the reaction mixture indicated that the yield was 76%. The mixture was purified directly by flash column chromatography on silica gel (hexane/EtOAc = 50:1) to give **13** as a white solid. The deuterium content at the 3-position was determined to be 0% by NMR spectroscopy (Figure S2).

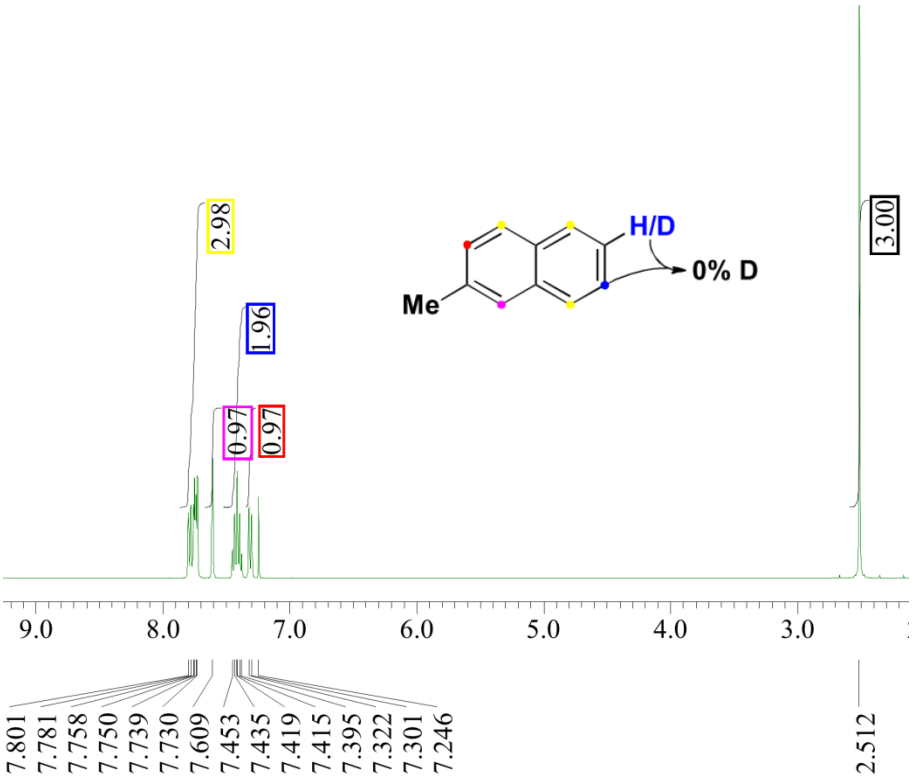
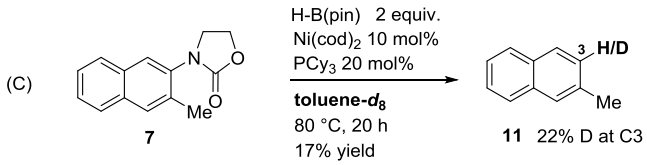


Figure S2. NMR spectra for **13**



An oven-dried 10 mL screw-capped vial was charged with **7** (110 mg, 0.49 mmol), HBpin (130 mg, 1.0 mmol), $Ni(cod)_2$ (14 mg, 0.050 mmol), PCy_3 (28 mg, 0.10 mmol) and toluene-d_8 (1.5 mL) in a glovebox filled with nitrogen, and the resulting mixture was sealed and heated at 80 °C for 20 h on an aluminum block. GC analysis of the reaction mixture indicated that the yield was 17%. The mixture was purified directly by flash column chromatography on silica gel (hexane/EtOAc = 50:1) to give **11** as a white solid. The deuterium content at the 3-position was determined to be 22% by NMR spectroscopy (Figure S3).

The other positions are also deuterated slightly (see below).

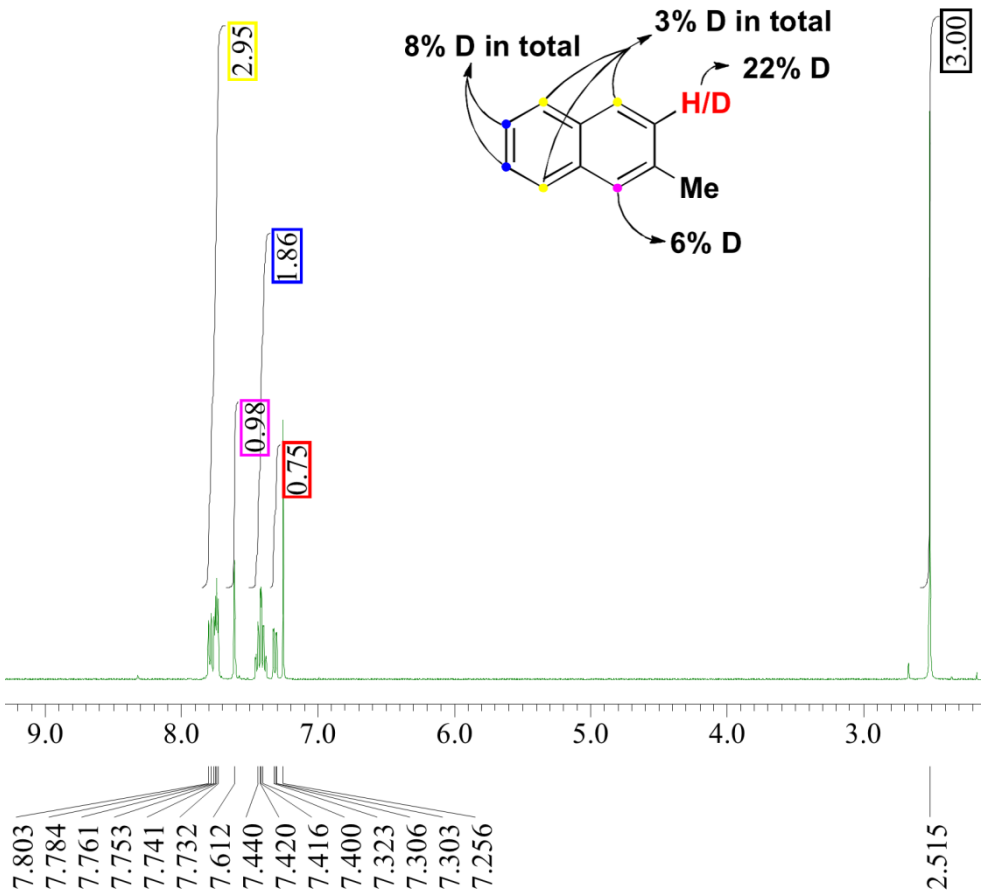
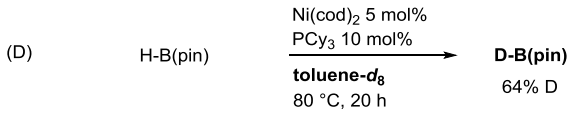
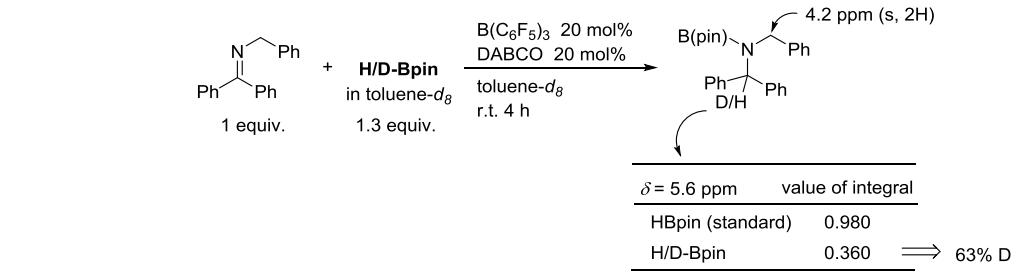


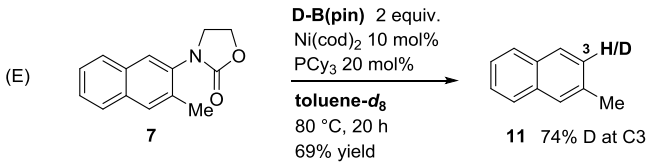
Figure S3. NMR spectra for **11** obtained from the reaction shown in Scheme 3C



An oven-dried 10 mL screw-capped vial was charged with HBpin (130 mg, 1.0 mmol), $Ni(cod)_2$ (14 mg, 0.050 mmol), PCy_3 (28 mg, 0.10 mmol) and toluene-d_8 (1.5 mL) in a glovebox filled with nitrogen, and the resulting mixture was sealed and heated at 80 °C for 20 h on an aluminum block. ^{11}B NMR analysis of the mixture showed a *singlet* peak at 28.4 ppm (^{11}B NMR spectra of HBpin showed a *doublet* peak at 28.4 ppm, J = 172 Hz), indicating that deuterium was incorporated. Deuterium content was determined by ^{1}H NMR analysis of a hydroborated compound using the resultant H/D-Bpin.[32] Thus, a separate oven-dried 10 mL screw-capped vial was charged with $B(C_6F_5)_3$ (100 mg, 0.20 mmol), DABCO (23 mg, 0.20 mmol) and toluene-d_8 (0.5 mL), and the resulting solution was stirred for 3 min at room temperature. The solution obtained from the H/D scrambling experiment described above was then added to this screw-capped vial, and the resulting mixture was stirred for 5 min. N-(Diphenylmethylene)-1-phenylmethanamine[32] (330 mg, 1.2 mmol) was then added to the reaction, and the resulting mixture was stirred at room temperature for 4 h. ^{1}H NMR analysis

of the reaction mixture revealed the level of deuterium incorporation to be 63% based on the integration value of the resonance signal appeared at 5.6 ppm (see below).





An oven-dried 10 mL screw-capped vial was charged with **7** (120 mg, 0.51 mmol), DBpin[31] (97%D, 130 mg, 1.0 mmol), $Ni(cod)_2$ (14 mg, 0.050 mmol), PCy_3 (28 mg, 0.10 mmol) and toluene-d_8 (1.5 mL) in a glovebox filled with nitrogen, and the resulting mixture was sealed and heated at 80 °C for 20 h on an aluminum block. GC analysis of the reaction mixture indicated that the yield was 69%. The mixture was purified directly by flash column chromatography on silica gel (hexane/EtOAc = 50:1) to give **11** as a white solid. The deuterium content at the 3-position was determined to be 74% by NMR spectroscopy (Figure S4).

The other positions are also deuterated slightly (see below).

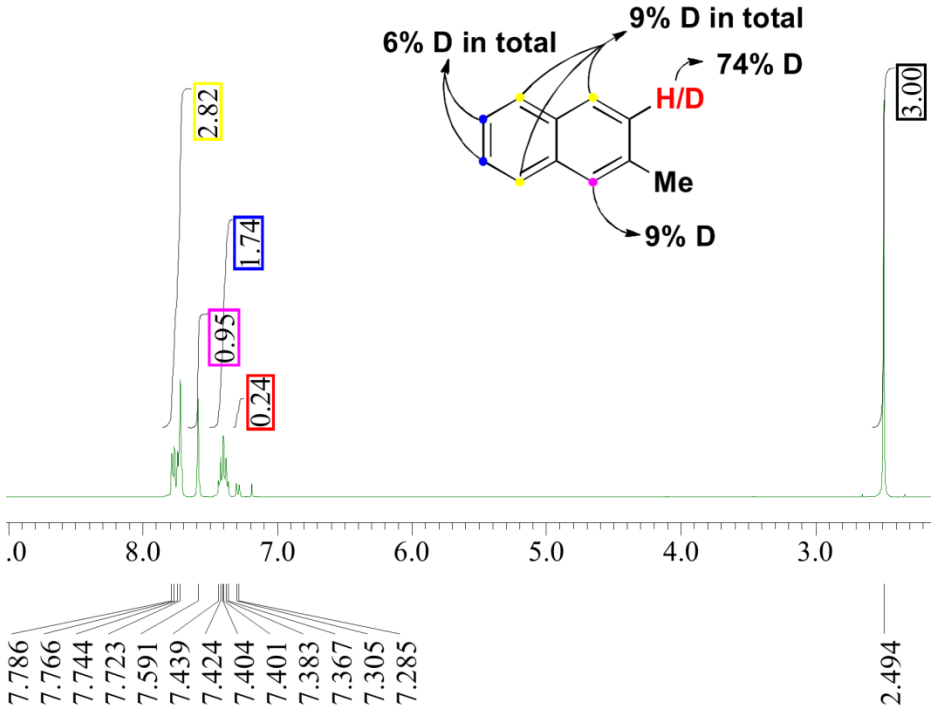
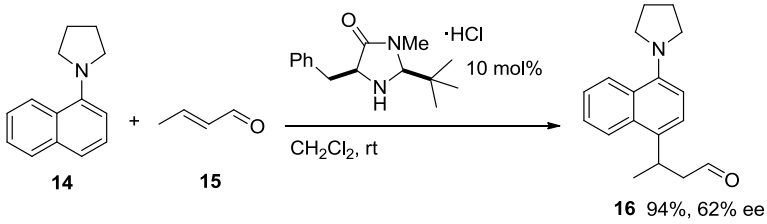


Figure S4. NMR spectra for **11** obtained from the reaction shown in Scheme 3E

Synthetic Application (Scheme 4).

3-(4-(Pyrrolidin-1-yl)naphthalen-1-yl)butanal (16).[33]



An oven-dried 10-mL screw-capped vial was charged with **14**[34] (110 mg, 0.53 mmol), (2*S*,5*S*)-5-benzyl-2-tert-butyl-3-methylimidazolidin-4-one (purchased from Aldrich, 13 mg, 0.050 mmol), 4M solution of HCl in dioxane (13 μL, 0.050 mmol) and CH_2Cl_2 (1 mL), and the resulting mixture was stirred at room temperature for 5 min. Aldehyde **15** (84 μL, 1.0 mmol) was then added to the reaction, and the resulting mixture was stirred at room temperature for 120 h. The mixture was purified directly by flash column chromatography on silica gel (hexane/EtOAc = 10:1) to give **16** (130 mg, 94%) as a pale yellow oil. The enantiomeric ratio of the product was determined to be 62% ee by HPLC analysis of the corresponding alcohol (obtained by $NaBH_4$ reduction, see below) using a Chiracel IA and IA guard column (0.5% EtOH/hexane, 1.0 mL/min); t_1 = 34.7 min, t_2 = 37.9 min.

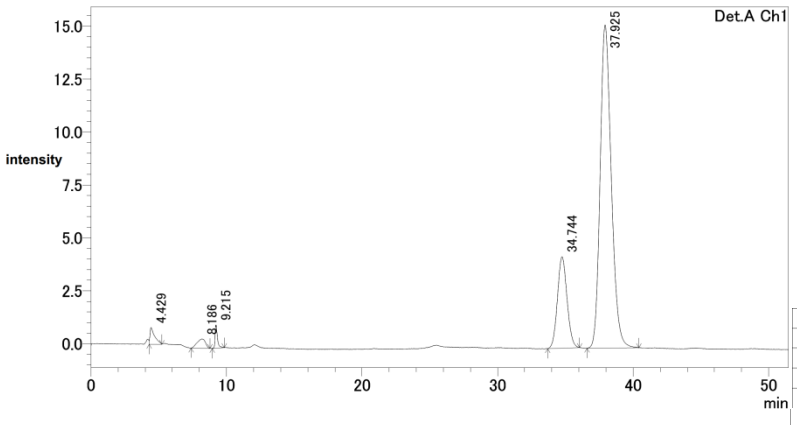
Rf 0.70 (hexane/EtOAc = 10/1).

^{1}H NMR (400 MHz, $CDCl_3$): 9.79 (s, 1H), 8.57 (d, *J* = 7.6 Hz, 1H), 8.41 (d, *J* = 8.4 Hz, 1H), 8.23-8.38(m, 1H), 7.48-7.55 (m, 2H), 7.20 (d, *J* = 6.4 Hz, 1H), 6.92-7.09 (m, 1H), 4.16 (m, 1H), 3.18-3.47 (m, 4H), 2.74-2.95 (m, 2H), 1.93-2.14 (m, 4H), 1.43 (d, *J* = 6.8 Hz, 3H).

^{3}C NMR ($CDCl_3$, 100 MHz): 21.5, 24.6, 28.1, 51.3, 52.8, 111.5, 122.7, 122.9, 124.1, 125.5, 125.9, 128.8, 132.1, 134.1, 146.5, 202.3.

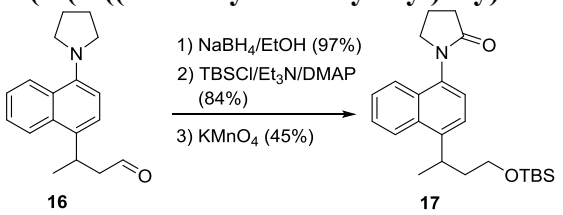
IR (ATR): 2964 m, 2874 w, 2816 w, 2721 w, 2371 w, 2349 w, 2315 w, 1721 s, 1578 m, 1514 w, 1458 m, 1393 m, 1320 m, 1193 w, 1129 w, 1076 w, 1036 w, 961 w, 902 w, 825 w.

HRMS (EI): Calcd for $C_{24}H_{37}NOSi$ 383.2644, Found 383.2642.



peak#	retention time	area
1	4.429	19150
2	8.186	18642
3	9.215	13235
4	34.744	211900
5	37.925	871703

1-(4-(4-((*tert*-Butyldimethylsilyl)oxy)butan-2-yl)naphthalen-1-yl)pyrrolidin-2-one (**17**).



An oven-dried 10 mL screw-capped vial was charged with $NaBH_4$ (32 mg, 0.85 mmol) and EtOH (1.7 mL). Aldehyde **16** (220 mg, 0.81 mmol) was then added dropwise at 0 °C, and the resulting mixture was stirred for 15 min at room temperature. The reaction was then quenched by the addition of an aqueous solution of $NaHCO_3$, and the resulting mixture was extracted with CH_2Cl_2. The organic extract was then washed sequentially with an aqueous solution of $NaHCO_3$ and brine, before being dried over Na_2SO_4 and filtrated The filtrate was concentrated to give 3-(4-(pyrrolidin-1-yl)naphthalen-1-yl)butan-1-ol as a pale yellow oil (210 mg, 97% yield, 62% ee). HPLC analysis of the alcohol was conducted using a Chiracel IA and IA guard column (0.5% EtOH/hexane, 1.0 mL/min); t_1 = 42.7 min, t_2 = 47.2 min.

An oven-dried 10 mL screw-capped vial was charged with *tert*-$BuMe_2SiCl$ (250 mg, 1.7 mmol), DMAP (8.5 mg, 0.070 mmol), Et_3N (0.25 mL, 1.8 mmol) and CH_2Cl_2 and the resulting mixture was stirred for 1 min at room temperature. 3-(4-(Pyrrolidin-1-yl)naphthalen-1-yl)butan-1-ol (210 mg, 0.78 mmol) was then added to the reaction, and the resulting mixture was stirred for 12 h at room temperature. The mixture was then purified directly by flash column chromatography on silica gel (hexane/EtOAc = 10:1) to give 1-(4-(4-((tert-butyl-dimethylsilyl)oxy)butan-2-yl)naphthalen-1-yl)pyrrolidine as a pale yellow oil (250 mg, 81% yield).

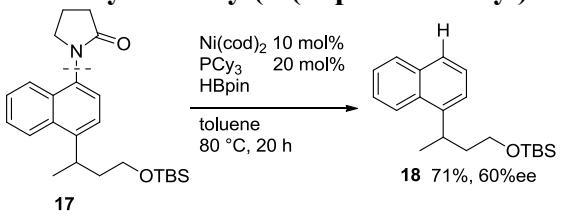
A 50-mL round-bottom flask was charged with 1-(4-(4-((tert-butyldimethyl-silyl)oxy)butan-2-yl)naphthalen-1-yl)pyrrolidine (970 mg, 2.5 mmol), $KMnO_4$ (3.5 g, 22 mmol), $BnNEt_3Cl$ (5.7 g, 25 mmol) and CH_2Cl_2 (25 mL), and the resulting mixture was refluxed for 5 h.[35] The mixture was quenched by the addition of an aqueous solution of $NaHSO_3$ and extracted with CH_2Cl_2. The organic extract was then washed with water, dried (Na_2SO_4) and filtered. The filtrate was concentratedin vacuo to give residue, which was purified by flash column chromatography on silica gel (CH_2Cl_2/EtOAc = 10:1) and then by GPC to give **17** as a colorless oil (450 mg, 45% yield). Rf 0.33 (CH_2Cl_2/EtOAc = 10/1).
^{1}H NMR (400 MHz, $CDCl_3$): 8.26-8.30 (m, 1H), 7.75-7.78 (m, 1H), 7.50-7.54 (m, 2H), 7.42 (d, J = 8.0 Hz, 1H), 7.35 (d, J = 8.0 Hz, 1H), 3.81-3.88 (m, 3H), 3.63-3.73 (m, 2H), 2.73 (t, J = 8.0Hz, 2H), 2.32-2.36 (m, 2H), 2.04-2.09 (m, 1H), 1.79-1.81 (m, 1H), 1.39 (d, J = 6.8 Hz, 3H), 0.91 (s, 9H), 0.02 (d, J = 6.8 Hz, 6H)

^{13}C NMR ($CDCl_3$, 100 MHz): -5.44, -5.35, 18.2, 19.2, 21.0, 25.9, 29.7, 31.5, 41.0, 52.0, 61.0, 122.4, 123.1, 124.2, 124.4, 126.1, 126.2, 129.8, 132.7, 133.4, 144.3, 175.5.

IR (ATR): 2953 m, 2928 m, 2857 w, 2361 m, 2339 w, 1696 s, 1597 w, 1465 m, 1409 m, 1298 m, 1252 m, 1091 s, 1007 w, 984 w, 912 m, 833 s.

HRMS (EI): Calcd for $C_{24}H_{35}NO_2Si$ 397.2437, Found 397.2435.

***tert*-Butyldimethyl(3-(naphthalen-1-yl)butoxy)silane (18).**



17 **18** 71%, 60%ee

An oven-dried 10 mL screw-capped vial was charged with **17** (95 mg, 0.24 mmol), HBpin (64 mg, 0.50 mmol), $Ni(cod)_2$ (6.9 mg, 0.025 mmol), PCy_3 (14 mg, 0.050 mmol) and toluene (1 mL) in a glovebox filled with nitrogen, and the resulting mixture was sealed in the vessel and heated at 80 °C for 20 h on an aluminum block. The mixture was then cooled and purified directly by flash column chromatography on silica gel (hexane/EtOAc = 50:1) to give **18** (54 mg, 71% yield) as a colorless oil. Rf 0.61 (hexane/EtOAc = 0.61).

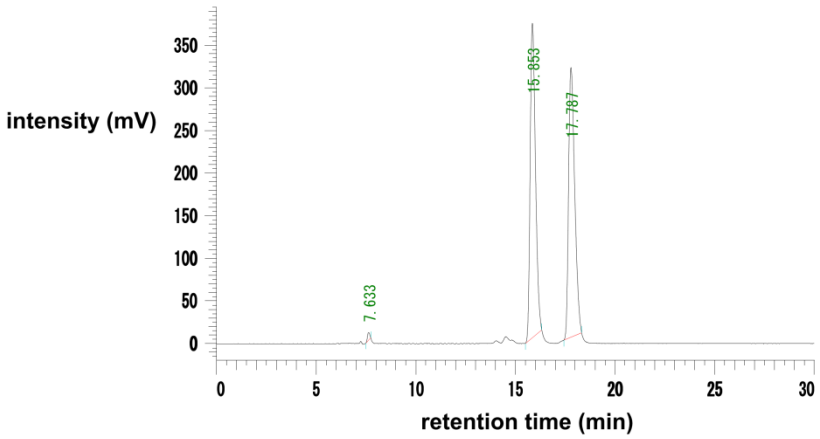
The enantiomeric ratio of the product was determined by HPLC analysis of the corresponding alcohol (obtained by deprotection of the TBS ether with TBAF) using a Chiracel IB and IB guard column (10% ^{i}PrOH/hexane, 1.0 mL/min); t_1 = 15.8 min, t_2 = 17.6 min.

^{1}H NMR (400 MHz, $CDCl_3$): 8.23 (d, J = 8.4 Hz, 1 H), 7.86 (dd, J = 2.4, 7.2 Hz, 1 H), 7.71 (d, J = 8.4 Hz, 1 H), 7.40-7.53 (m, 4 H), 3.84 (m, 1 H), 3.62-3.72 (m, 2 H), 2.05-2.12 (m, 1 H), 1.82-1.89 (m, 1 H), 1.41 (d, J = 6.8 Hz, 3 H), 0.92 (s, 9 H), 0.01 (d, J = 6.0 Hz, 6 H).

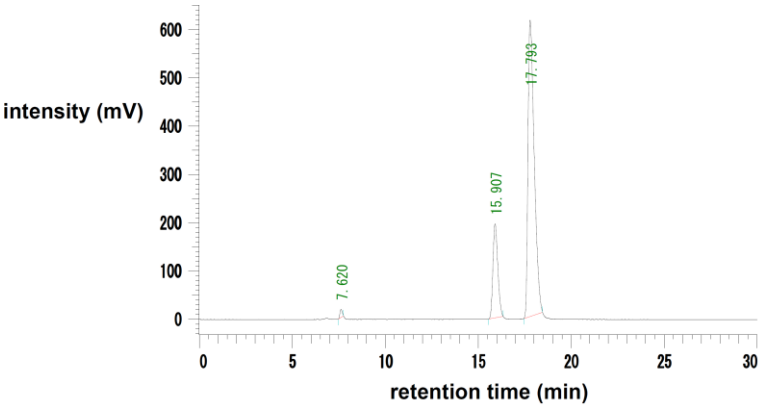
^{13}C NMR ($CDCl_3$, 100 MHz): -5.5, -5.3, 18.3, 21.2, 26.0, 29.6, 41.0, 61.1, 122.4, 123.5, 125.2, 125.5, 125.6, 126.3, 128.8, 131.7, 133.9, 143.5.

IR (ATR): 3047 w, 2954 w, 2929 w, 2857 w, 2361 w, 1597 w, 1511 w, 1467 w, 1389 w, 1254 m, 1093 s, 1007 w, 986 w, 910 m, 832 s.

HRMS (EI): Calcd for $C_{20}H_{30}OSi$ 314.2066 Found 314.2065.



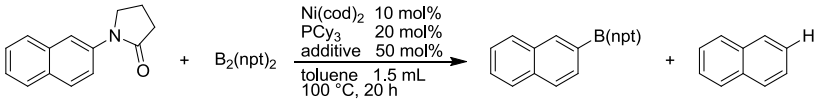
NO	RT	area	retio	BC
1	7.633	65851	0.488	BB
2	15.853	6742892	49.949	BB
3	17.787	6690764	49.563	BB
		13499507	100.000	



NO	RT	area	retio	BC
1	7.620	138235	0.775	BB
2	15.907	3500958	19.637	BB
3	17.793	14189436	79.588	BB
		17828629	100.000	

Optimization Studies for the Borylative Cleavage of C(aryl)-N Bonds.

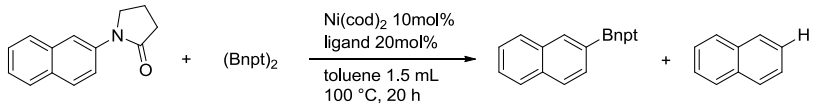
1. Effect of Additives



1a 0.5 mmol 1 mmol **19** **2**

entry	additive	results (%) 19	2	1a	entry	additive	results (%) 19	2	1a
0	none	35	7	32	5	NaO^{t}Bu	10	1	30
1	DABCO	19	13	45	6	KF	28	6	34
2	CsF	22	6	19	7	ZrF_4	9	31	38
3	TBAF	nd	7	66	8	TiF_4	nd	6	35
4	DBU	nd	2	64					

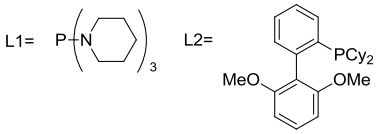
2. Screening of Ligands



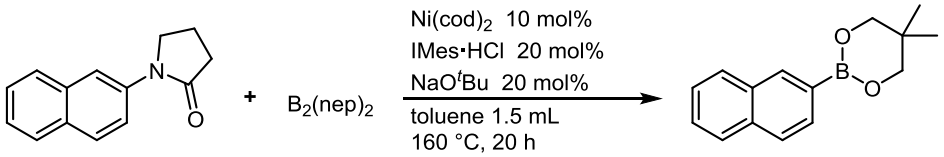
1a 0.5 mmol 1.0 mmol **19** **2**

entry	ligand	result (%) 19	2	1a	entry	ligand	result (%) 19	2	1a
1	PCy_3	35	7	32	8	L2	nd	nd	83
2[a]	PCy_3	trace	nd	48	9	dppf	nd	nd	72
3[b]	PCy_3	2	13	64	10	SIMes	nd	nd	45
4	P^iPr_3	15	26	53	11	IMes	36	5	56
5	$PCyp_3$	9	6	21	12[c]	IMes	55	10	15
6	PMe_3	nd	nd	77	13[c]	IPr	trace	nd	57
7	L1	nd	nd	86					

a) NaO^{t}Bu (1 equiv.) was added and toluene / DME (= 1 : 1) was used as a solvent.
b) K_3PO_4 (1 equiv.) was added and toluene / DME (= 1 : 1) was used as a solvent.
c) NaO^{t}Bu (25 mol%) was used for prepare NHC ligand in situ and reaction temperature is 160 °C



A General Procedure for the Borylative Cleavage of C(aryl)-N bonds (Table 2).

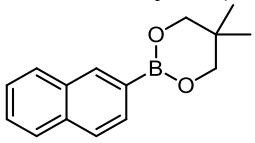


1a 0.5 mmol 1 mmol **19**

An oven-dried 10 mL screw-capped vial was charged with $Ni(cod)_2$ (14 mg, 0.050 mmol), IMes·HCl (34 mg, 0.10 mmol), NaO^{t}Bu (9.6 mg, 0.10 mmol) and toluene (0.50 mL) in a globvebox filled with nitrogen, and the resulting mixture was stirred for 10 min. 2-*N*-(2-Naphthyl)pyrrolidin-2-one (**1a**, 110 mg, 0.50 mmol), bis(neopentylglycolato)diboron (230 mg, 1.0 mmol), and toluene (1.0 mL) were then added to the vial, and the resulting mixture was sealed in the vessel and heated at 160 °C for 20 h on an aluminum block. The mixture was then cooled to room temperature and purified directly by flash column chromatography on silica gel (hexane/EtOAc = 5:1) to give 5,5-dimethyl-2-(2-naphthyl)-1,3,2-dioxaborinane (**19**, 66 mg, 55%) as a white solid.

Spectroscopic Data of the Borylative Cleavage Products.

5,5-Dimethyl-2-(naphthalen-2-yl)-1,3,2-dioxaborinane (19) [CAS: 627906-96-1].



General procedure was followed.

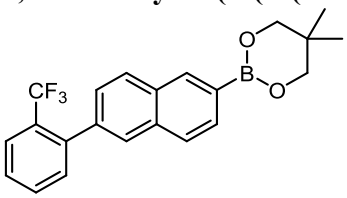
Rf 0.27 (hexane/EtOAc = 3/1). White solid.

^{1}H NMR ($CDCl_3$, 400 MHz): 8.35 (s, 1 H), 7.80-7.89 (m, 4 H), 7.44-7.51 (m, 2 H), 3.84 (s, 4 H), 1.06 (s, 6 H).

^{13}C NMR ($CDCl_3$, 100 MHz): 21.9, 31.9, 72.4, 125.6, 126.6, 126.8, 127.6, 128.6, 129.9, 132.9, 134.8, 135.0.

HRMS (EI): Calcd for $C_{15}H_{17}O_2B$ 240.1322, Found 240.1323.

5,5-Dimethyl-2-(6-(2-(trifluoromethyl)phenyl)naphthalen-2-yl)-1,3,2-dioxaborinane (21).



General procedure was followed, except that **20** was used instead of **1b**.

Rf 0.43 (hexane/EtOAc = 5/1). Pale yellow solid.

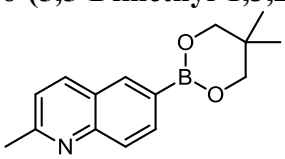
^{1}H NMR ($CDCl_3$, 400 MHz): 8.40 (s, 1 H), 7.78-7.92 (m, 5 H), 7.43-7.60 (m, 4 H), 3.85 (s, 4 H), 1.07 (s, 6 H).

^{13}C NMR ($CDCl_3$, 100 MHz): 21.9, 31.9, 72.4, 126.1 (q, J = 5.1 Hz), 126.87 (q, J = 272.2 Hz), 126.94, 127.0, 127.4, 127.7, 128.0, 128.6 (q, J = 29.6 Hz), 130.4, 131.3, 132.0, 132.2, 134.2, 134.8, 138.1, 141.4.

IR (ATR):3027 w, 2962 w, 2931 w, 2361 w, 2338 w, 1738 w, 1631 w, 1604 w, 1576 w, 1476 m, 1447 w, 1419 m, 1379 m, 1306 s, 1250 m, 1226 m, 1172 m, 1121 s, 1069 m, 1035 m, 985 w, 912 m, 823 w.

HRMS (EI): Calcd for $C_{22}H_{20}F_3O_2B$ 384.1508, Found 384.1510.

6-(5,5-Dimethyl-1,3,2-dioxaborinan-2-yl)-2-methylquinoline (23) [CAS: 1352304-55-2].



General procedure was followed, except that **22** was used instead of **1b**.

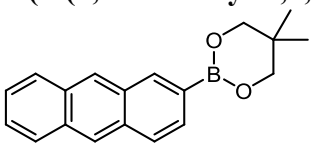
Rf 0.43 (hexane/EtOAc = 1/1). Pale yellow solid.

^{1}H NMR ($CDCl_3$, 400 MHz): 8.27 (s, 1 H), 8.05-8.09 (m, 2 H), 7.98 (d, J = 8.0 Hz, 1 H), 7.27 (d, J = 8.0 Hz, 1 H), 3.83 (s, 4 H), 2.75 (s, 3 H), 1.05 (s, 6 H).

^{13}C NMR ($CDCl_3$, 100 MHz): 22.1, 25.4, 31.9, 72.4, 121.8, 125.8, 127.4, 133.8, 134.6, 136.8, 149.2, 159.7.

HRMS (EI): Calcd for $C_{15}H_{18}NO_2B$ 255.1431, Found 255.1433.

4-(6-(5,5-Dimethyl-1,3,2-dioxaborinan-2-yl)naphthalen-2-yl)-N,N-dimethylaniline (25).



General procedure was followed, except that **24** was used instead of **1b**.

Rf 0.29 (hexane/EtOAc = 3/1). Pale yellow solid. Mp = 185-187 °C

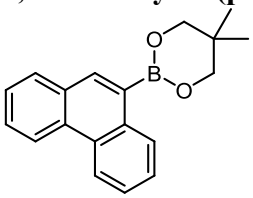
^{1}H NMR ($CDCl_3$, 400 MHz): 8.54 (s, 1 H), 8.47 (s, 1 H), 8.40 (s, 1 H), 7.96-8.03 (m, 3 H), 7.81 (d, *J* = 8.4 Hz, 1 H), 7.45-7.47 (m, 2 H), 3.86 (s, 4 H), 1.08 (s, 6 H).

^{13}C NMR ($CDCl_3$, 100 MHz): 21.9, 32.0, 72.4, 125.1, 125.6, 125.8, 126.9, 127.3, 128.1, 128.4, 128.8, 131.2, 131.5, 132.2, 132.7, 136.0.

IR (ATR): 2957 w, 2931 w, 2898 w, 1622 w, 1579 w, 1480 m, 1428 m, 1411 m, 1375 m, 1344 m, 1314 s, 1288 s, 1248 s, 1184 m, 1155 m, 1124 s, 1004 w, 984 w, 950 w, 918 w, 900m, 872 m, 814 w.

HRMS (EI): Calcd for $C_{19}H_{19}O_2B$ 290.1478, Found 290.1476.

5,5-Dimethyl-2-(phenanthren-9-yl)-1,3,2-dioxaborinane (27)[CAS: 1416371-19-1].



General procedure was followed, except that **26** was used instead of **1b**.

Rf 0.57 (hexane/EtOAc = 5/1). Pale yellow solid.

^{1}H NMR ($CDCl_3$, 400 MHz): 8.79-8.82 (m, 1 H), 8.66-8.72 (m, 2 H), 8.34 (s, 1 H), 7.92 (d, *J* = 8.0 Hz, 1 H), 7.55-7.68 (m, 4 H), 3.93 (s, 4 H), 1.13 (s, 6 H).

^{13}C NMR ($CDCl_3$, 100 MHz): 21.9, 31.8, 72.5, 122.4, 122.6, 125.9, 126.3, 126.4, 127.4, 129.0, 129.2, 130.0, 131.1, 131.6, 134.5, 136.6.

HRMS (EI): Calcd for $C_{19}H_{19}O_2B$ 290.1478, Found 290.1480.

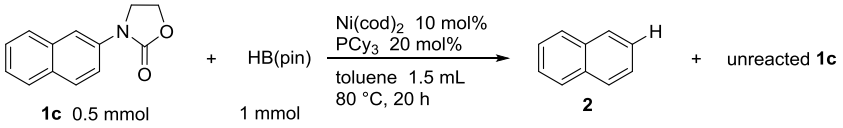
Mechanistic Studies.

Mercury poisoning and filtration tests were conducted to develop a greater understanding of the heterogeneity of the catalysis.[36]

Mercury Poisoning Test.

The nickel-catalyzed reductive cleavage of **1c** was conducted in the presence of mercury. Thus, an oven-dried 10 mL screw-capped vial was charged with **1c** (110 mg, 0.50 mmol), HBpin (130 mg, 1.0 mmol), $Ni(cod)_2$ (14 mg, 0.050 mmol), PCy_3 (28 mg, 0.10 mmol), C20

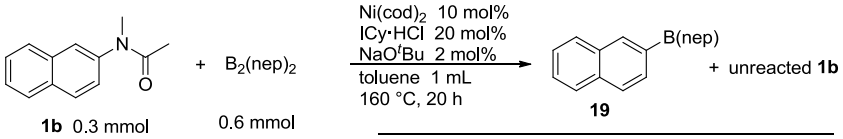
(internal standard, 18 mg) and toluene (1.5 mL) in a glovebox filled with nitrogen, and the resulting mixture was sealed in the vial and heated at 80 °C for 20 h on an aluminum block. GC analysis of the crude reaction mixture using eicosane as an internal standard revealed that none of the reductive cleavage product was formed under these conditions.



1c 0.5 mmol

	GC yields (%)	
	2	**1c**
with Hg (ca. 25 equiv.)	n.d.	69
standard condition (no Hg)	83	6

The effect of adding mercury to the borylative cleavage of the C-N bond of **1b** was also examined. Thus, an oven-dried 10 mL screw-capped vial was charged with $Ni(cod)_2$ (8.3 mg, 0.030 mmol), IMes·HCl (21 mg, 0.60 mmol), NaO^{t}Bu (5.8 mg, 0.60 mmol), eicosane (internal standard, 12 mg) and toluene (0.40 mL) in a globvebox filled with nitrogen, and the resulting mixture was stirred for 10 min. *N*-Methyl-*N*-(naphthalen-2-yl)acetamide (**1b**, 50 mg, 0.30 mmol), bis(neopentylglycolato)- diboron (140 mg, 0.60 mmol), and toluene (0.60 mL) were then added to the vial, and the resulting mixture was sealed to the vial and heated at 160 °C for 20 h on an aluminum block. GC analysis of the crude reaction mixture revealed that the borylated product **19** was formed in 19% yield. Although the yield for this reaction was significantly lower than that observed in the reaction conducted in the absence of mercury (72% isolated yield), these results indicated that a homogeneous species was responsible for the catalysis, even if it was not the only competent species present in the catalytic system.



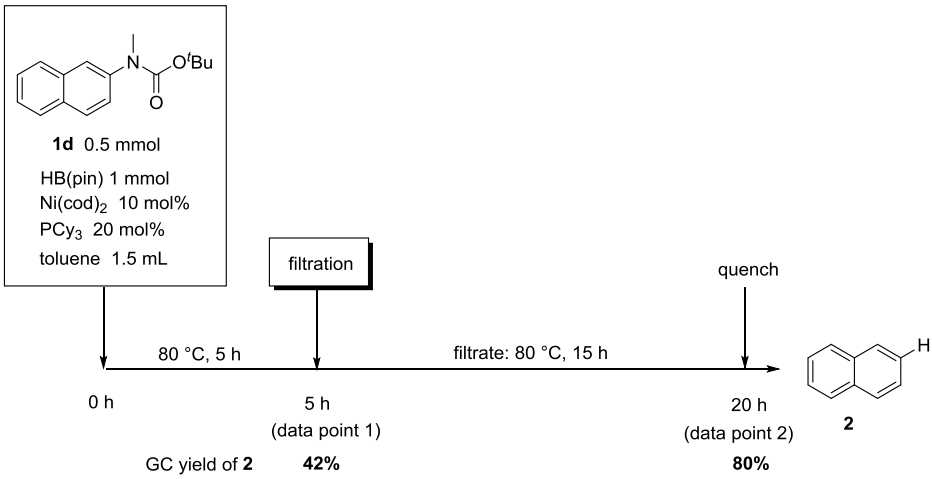
1b 0.3 mmol

	GC yields (%)	
	19	**1b**
with Hg (ca. 25 equiv.)	19	67
standard condition (no Hg)	72(isolated)	n.d.

Filtration Test.

An oven-dried 10 mL screw-capped vial was charged with **1d** (130 mg, 0.50 mmol), HBpin (130 mg, 1.0 mmol), $Ni(cod)_2$ (14 mg, 0.050 mmol), PCy_3 (28 mg, 0.10 mmol), eicosane (internal standard, 29 mg) and toluene (1.5 mL) in a glovebox filled with nitrogen and the resulting mixture was sealed to the vial and heated at 80 °C for 5 h on an aluminum block. The mixture was then filtered through a pad of Al_2O_3 (neutral, activity I, purchased from

Wako) in a glovebox. An aliquot of the filtrate was analyzed by GC, which revealed that the yield of **2** to be 42%. The rest of the filtrate was transferred to another 10 mL screw-capped vial, and the mixture was sealed to the vial and heated at 80 °C for 15 h on an aluminum block. GC analysis of the mixture revealed that the yields of **2** increased to 80%. These results therefore indicated that the nickel species in the filtrate was responsible for the catalysis.



To further examine the nature of the catalytically active species, the filtrate was examined by dynamic light scattering analysis. The result of this analysis revealed that there were no particles greater than 20 nm in size (Figure S5).

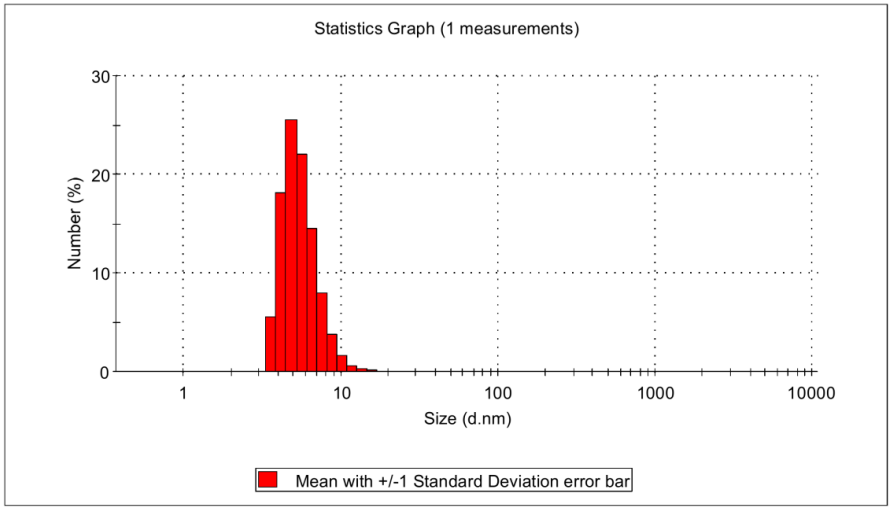
(a)

Size d.nm	Mean Number %	Std Dev Number %
0.4000	0.0	
0.4632	0.0	
0.5365	0.0	
0.6213	0.0	
0.7195	0.0	
0.8332	0.0	
0.9649	0.0	
1.117	0.0	
1.294	0.0	
1.499	0.0	
1.736	0.0	
2.010	0.0	
2.328	0.0	
2.696	0.0	
3.122	0.0	
3.615	5.5	
4.187	18.1	
4.849	25.5	

Size d.nm	Mean Number %	Std Dev Number %
5.615	22.0	
6.503	14.5	
7.531	7.9	
8.721	3.8	
10.10	1.7	
11.70	0.6	
13.54	0.2	
15.69	0.1	
18.17	0.0	
21.04	0.0	
24.36	0.0	
28.21	0.0	
32.67	0.0	
37.84	0.0	
43.82	0.0	
50.75	0.0	
58.77	0.0	
68.06	0.0	

Size d.nm	Mean Number %	Std Dev Number %
78.82	0.0	
91.28	0.0	
105.7	0.0	
122.4	0.0	
141.8	0.0	
164.2	0.0	
190.1	0.0	
220.2	0.0	
255.0	0.0	
295.3	0.0	
342.0	0.0	
396.1	0.0	
458.7	0.0	
531.2	0.0	
615.1	0.0	
712.4	0.0	
825.0	0.0	
955.4	0.0	

Size d.nm	Mean Number %	Std Dev Number %
1106	0.0	
1281	0.0	
1484	0.0	
1718	0.0	
1990	0.0	
2305	0.0	
2669	0.0	
3091	0.0	
3580	0.0	
4145	0.0	
4801	0.0	
5560	0.0	
6439	0.0	
7456	0.0	
8635	0.0	
1.000e4	0.0	



(b)

Size d.nm	Mean Number %	Std Dev Number %
0.4000	0.0	
0.4632	0.0	
0.5365	0.0	
0.6213	0.0	
0.7195	0.0	
0.8332	0.0	
0.9649	0.0	
1.117	0.0	
1.294	0.0	
1.499	0.0	
1.736	0.0	
2.010	0.0	
2.328	0.0	
2.696	0.0	
3.122	0.0	
3.615	0.0	
4.187	5.8	
4.849	19.9	

Size d.nm	Mean Number %	Std Dev Number %
5.615	28.6	
6.503	23.8	
7.531	13.6	
8.721	5.9	
10.10	2.0	
11.70	0.5	
13.54	0.1	
15.69	0.0	
18.17	0.0	
21.04	0.0	
24.36	0.0	
28.21	0.0	
32.67	0.0	
37.84	0.0	
43.82	0.0	
50.75	0.0	
58.77	0.0	
68.06	0.0	

Size d.nm	Mean Number %	Std Dev Number %
78.82	0.0	
91.28	0.0	
105.7	0.0	
122.4	0.0	
141.8	0.0	
164.2	0.0	
190.1	0.0	
220.2	0.0	
255.0	0.0	
295.3	0.0	
342.0	0.0	
396.1	0.0	
458.7	0.0	
531.2	0.0	
615.1	0.0	
712.4	0.0	
825.0	0.0	
955.4	0.0	

Size d.nm	Mean Number %	Std Dev Number %
1106	0.0	
1281	0.0	
1484	0.0	
1718	0.0	
1990	0.0	
2305	0.0	
2669	0.0	
3091	0.0	
3580	0.0	
4145	0.0	
4801	0.0	
5560	0.0	
6439	0.0	
7456	0.0	
8635	0.0	
1.000e4	0.0	

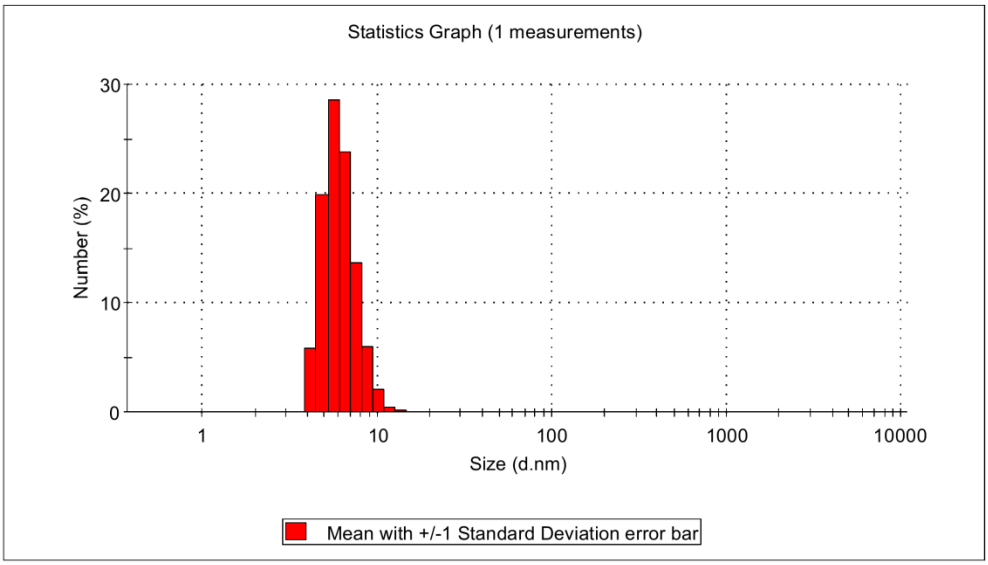


Figure S5. The result of DLS analysis for the reaction mixtures (a) before heating and (b) after heating (80 °C, 20 h)

3.5 References and Notes

(1) Reviews: (a) Surry, D. S.; Buchwald, S. L. *Angew. Chem., Int. Ed.* **2008**, *47*, 6338. (b) Hartwig, J. F. *Acc. Chem. Res.* **2008**, *41*, 1534.

(2) Catalytic C(sp^3)-N bond cleavage is also an interesting subject. Geng, W.; Zhang, W.-X.; Hao, W.; Xi, Z. *J. Am. Chem. Soc.* **2012**, *134*, 20230 and references therein.

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Conclusion

The direct nickel and rhodium-catalyzed transformation of inert C(aryl)-O and C(aryl)-N bonds was developed in this study. The scope of the C(aryl)-O bond activation process was expanded by identifying a new rhodium-based catalyst and a new nickel/NHC system. Moreover, the first catalytic process that involves the activation of C(aryl)-N bonds in electronically neutral simple aniline derivatives was developed.

In Chapter 1, a rhodium-catalyzed Suzuki-Miyaura type cross-coupling reaction of aryl carbamates with organoboronic esters is described. The reaction proceeds through the cleavage of a carbon-oxygen bond by a combination of a Rh(I) catalyst with an electron donating NHC ligand. These studies demonstrate that the oxidative addition of an inert C(aryl)-O bond to the Rh(I) center can be used for designing the catalytic transformations of unactivated phenol derivatives.

Chapter 2 deals with a nickel-catalyzed homocoupling reaction involving C(aryl)-OMe bonds in anisole derivatives. The conclusion is that not only aryl halides, but also methoxyarenes can be considered as substrates for the homocoupling reaction. The rapid expansion of π-systems was enabled by combining it with the conventional palladium–catalyzed cross-coupling reaction.

Chapter 3 is concerned with the nickel-catalyzed reduction and borylation of C(aryl)-N bonds in simple aniline derivatives. This is the first example of a catalytic C-N bond transformation involving unactivated, electronically neutral aniline derivatives without the need for a directing group.

In the past, catalytic transformations of inert C(aryl)-O bonds in phenol derivatives required the use of a Ni/PCy_3 catalyst, which limits the substrate scope and the diversity of the coupling partners. The findings presented herein demonstrate that new catalyst systems, i.e., Ni/NHC and Rh/NHC, can be used for the activation of inert C(aryl)-O bonds, thus permitting the expanded scope of substrates and new reaction designs based on the completely different catalytic intermediates to be achieved. In addition, the catalytic C(aryl)-N activation of simple anilides was demonstrated to be viable using a suitable nickel catalyst. These studies enable synthetic strategies that involve the use of inert phenol and aniline derivatives as synthetic intermediates. The described strategies are distinctly different from the conventional organic synthesis methodology based on the transformation of reactive functionalities. These results provide a good starting point for the further diversification of chemical bonds that can be used for organic synthesis.

List of Publications

(1) Nickel-Catalyzed Reductive and Borylative Cleavage of Aromatic Carbon-Nitrogen Bonds in N-Aryl Amides and Carbamates
Mamoru Tobisu, Keisuke Nakamura and Naoto Chatani
J. Am. Chem. Soc. **2014**, *136*, 5587.

(2) Rhodium-Catalyzed Cross-coupling of Aryl Carbamates with Arylboron Reagents
Keisuke Nakamura, Kosuke Yasui, Mamoru Tobisu and Naoto Chatani
Tetrahedron **2015**, *71*, 4484.

(3) Nickel-Catalyzed Formal Homocoupling of Methoxyarenes for the Synthesis of Symmetrical Biaryls
Keisuke Nakamura, Mamoru Tobisu and Naoto Chatani
Org. Lett. **2015**, *17*, 6142.

Supplementary List of Publications

(1) 1,3-Dicyclohexylimidazol-2-ylidene as a Superior Ligand for the Nickel-Catalyzed Cross-Couplings of Aryl and Benzyl Methyl Ethers with Organoboron Reagents
Mamoru Tobisu, Ayaka Yasutome, Hirotaka Kinuta, Keisuke Nakamura and Naoto Chatani
Org. Lett. **2014***, 16,* 5572.

(2) Nickel-Catalyzed Cross-coupling of Anisole Derivatives with Trimethylaluminum through the Cleavage of Carbon–Oxygen Bonds
Toshifumi Morioka, Akihiro Nishizawa, Keisuke Nakamura, Mamoru Tobisu and Naoto Chatani
Chem. Lett. **2015**, *44*, 1729.