Doctoral Dissertation

Studies on the Nickel-Mediated Cleavage of C−O, C−C and C−N Bonds Involving Elimination of C1 Fragment

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Preface and Acknowledgements

The research presented in this thesis was carried out under the direction of Professor Naoto Chatani of the Department of Applied Chemistry, Faculty of Engineering, Osaka University from Aplil 2012 to March 2018. This thesis is concerned with transformations of inert σ-bonds using nickel complexes as catalysts.

This thesis would not have been possible without the support of many amazing people around me. I wish to express my sincerest appreciation to all them.

First and foremost, I wish to express my utmost gratitude to Professor Naoto Chatani. He gave me the opportunity of a lifetime and I can't possibly thank him enough for his help. I will never forget what he taught me and my experiences in the Chatani laboratory.

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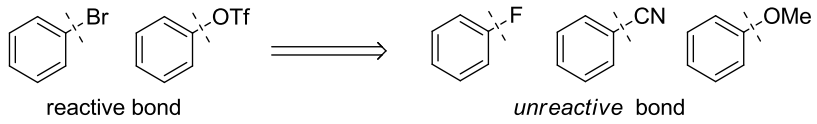
Contents

General Introduction

Substitution reactions of aryl halides, as exemplified by cross-coupling, are among the most important class of reactions enabled by transition-metal catalysts. Concerning substrates, activated phenol derivatives such as triflates can also be employed as electrophiles in the traditional cross-coupling reactions. Meanwhile, arenes having poor leaving groups such as fluoride, cyano and methoxy groups have emerged as viable substrates in catalytic substitution reactions over the past decade.[1] For example, Suzuki-Miyaura cross-coupling via the cleavage of these inert σ-bonds have been reported by several groups (Scheme 1).[2]

Scheme 1. Substrates for Catalytic Aromatic Substitution



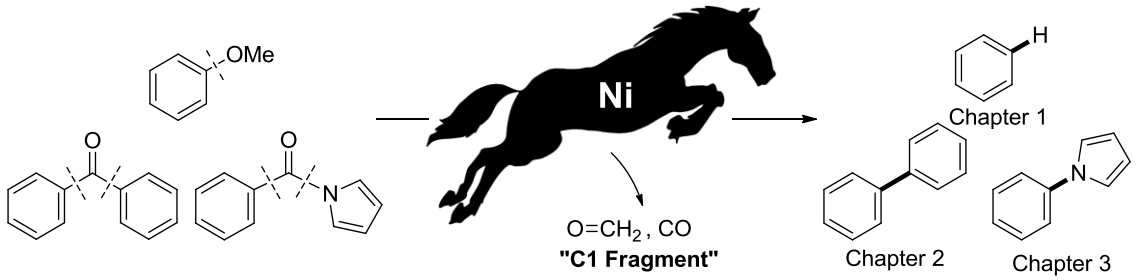
While the transformations of aryl halides and triflates involve the use of palladium catalysts, low valent nickel complexes are much more effective for the catalytic conversion of inert σ-bonds. The basic characteristics of nickel and palladium are distinctly different even though both metals are located in 10th group of the periodic table (Table 1). A particularly notable difference is the lower ionization energy of nickel compared to that for palladium. Nickel is relatively more electron positive than palladium as evidenced by electronegativity values. Based on these characteristics, nickel promotes oxidative addition reactions, which involves in the loss of electron density around the metal, in a more efficient way than palladium.[3] However, nickel is often referred as the *Spirited Horse*[4] because it is difficult to control; therefore, the formation of stable but reactive nickel species coordinated by a ligand is the key to the success of developing nickel-mediated processes.

Table 1. Comparison of Basic Characteristics of Nickel and Palladium

	electron configuration	atomic radius (Å)	ionization potential (kJ mol^{-1})	Pauling's electronegativity
Palladium	[Kr] 10(4d)	1.28	first: 804 second: 1874 third: 3177	2.20
Nickel	[Ar] 8(3d) 2(4s)	1.15	first: 737 second: 1752 third: 3489	1.91

Based on these considerations, transformations of inert σ-bonds using nickel and appropriate ligands have been examined. Specifically, it was found that nickel complexes activated carbon-oxygen bonds in anisoles,

carbon-carbon bonds in ketones and carbon-nitrogen bonds in amides. These reactions proceed through a formal intramolecular coupling accompanied by the release of formaldehyde and carbon monoxide.



In Chapter 1, the nickel-catalyzed reduction of inert carbon-oxygen bonds in anisole derivatives is discussed. Our newly developed NHC ligand promotes the reductive cleavage of carbon-methoxy bond, even without the need for external reducing agents.

In Chapter 2, the nickel-catalyzed methylation of anisole derivatives with $AlMe_3$ is discussed. In these reactions, organoaluminum reagents could be used as nucleophiles in cross-coupling reactions of aryl ethers.

In Chapter 3, the nickel-mediated decarbonylation of simple aromatic ketones is discussed. This is the first example of the decarbonylation of simple ketones mediated by transition metals other than rhodium complexes.

In Chapter 4, the nickel-mediated decarbonylation of *N*-acylpyrrole derivatives is discussed. This reaction can also be applied to amides derived from azaindole and phenoxazine instead of pyrrole to give the corresponding *N*-arylated product.

References

(1) Reviews on catalytic reactions involving the cleavage of carbon-fluoride, carbon-cyano and carbon-oxygen bonds: (a) Yang, S.-D. In *Homogeneous Catalysis for Unreactive Bond Activation*; Shi, Z.-J., Ed.; John Wiley & Sons Ltd.: Chichester, U.K., 2014; p 203. (b) Wem, Q.; Lu, P.; Wang, Y. *RSC Adv.* **2014**, *4*, 47806. (c) Cornella, J.; Zarate, C.; Martin, R. *Chem. Soc. Rev.* **2014**, *43*, 8081. (d) Tobisu, M.; Chatani, N. *Acc. Chem. Res.* **2015**, *48*, 1717. (e) Zeng, H.; Qiu, Z.; Domínguez-Huerta, A.; Hearne, Z.; Chen, Z.; Li, C.-L. *ACS Catal.* **2017**, *7*, 510.

(2) Selected examples: (a) Tobisu, M.; Shimasaki, T.; Chatani, N. *Angew. Chem. Int. Ed.* **2008**, *47*, 4866. (b) Yu, D.-G.; Yu, M.; Guan, B.-T.; Li, B.-J.; Zheng, Y.; Wu, Z.-H.; Shi, Z.-J. *Org. Lett.* **2009**, *11*, 3374. (c) Tobisu, M.; Xu, T.; Shimasaki, T.; Chatani, N. *J. Am. Chem. Soc.* **2011**, *133*, 19505.

(3) Tasker, S, Z.; Standley, E. A.; Jamison, T. F. *Nature* **2014**, *509*, 299.

(4) (a) Sabatier, P. *Catalysis in Organic Chemistry*; D. Van Nostrand Company: New York, 1922; p 15. (b) Ananikov, V. P. *ACS Catal.* **2015**, *5*, 1964.

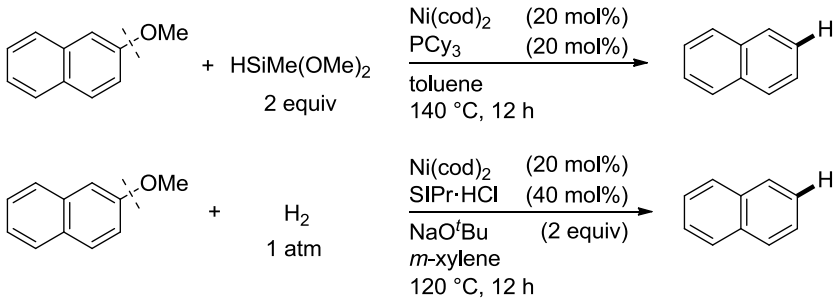
Chapter 1

Nickel-Catalyzed Reductive Cleavage of Anisole Derivatives in the Absence of an External Reductant

1.1 Introduction

As described in the general introduction, recent progress in nickel-catalyzed reactions via C-O bond activation[1] has enabled unactivated phenol derivatives to be directly used in these reactions, while traditional C-O bond activation reactions involve converting them to reactive sulfonates such as triflates. One of the most notable achievements in this area has been the catalytic reduction of inert aryl ethers to the parent arenes. This reaction not only allows the use of readily available anisoles in reductive deoxygenation reactions, but also provides a platform for the conversion of aryl ether-containing biomasses to alternative sources of fuel and chemicals, including the depolymerization of lignin.[2] However, these nickel-catalyzed reductive cleavage of aryl ethers only proceed in the presence of a stoichiometric amount of an external reductant such as hydrosilane[3] and hydrogen[4] (Scheme 1). Herein, the first nickel system capable of promoting reductive cleavage reaction of aryl alkyl ethers in the absence of an external reductant is reported.

Scheme 1. Nickel-Catalyzed Reductive Cleavage Reactions of Anisole in the Presence of External Reductants

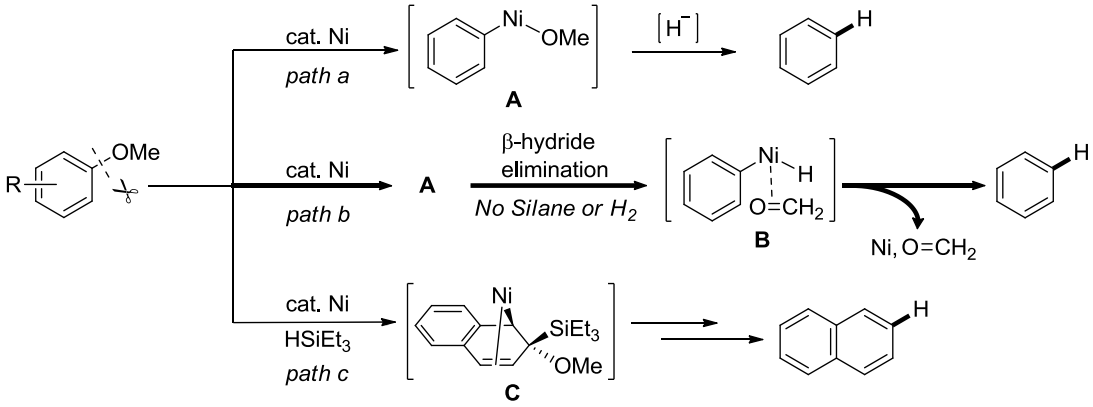


1.2 Results and Discussion

One possible mechanism for the conversion of aryl methyl ethers to parent arenes with an external hydride reagent involves oxidative addition of the C-O bond to form nickel(II)-methoxide **A**, followed by reduction of an aryl-nickel bond (Scheme 2, path a). Although this mechanism seems plausible when considering the mechanism of conventional cross-coupling reactions, the key oxidative addition step has never been verified experimentally.[5] It was envisaged that if oxidative addition of the C-O bond takes place to form intermediate **A**, β-hydrogen elimination would lead to the formation of the same reduced product via intermediate **B** (Scheme 2, path b). Although Agapie[6] and Martin[3c] have already suggested the β-hydrogen elimination from intermediate **A**, catalytic conversion of aryl ethers into parent arenes in the absence of an external reductant has not been reported.

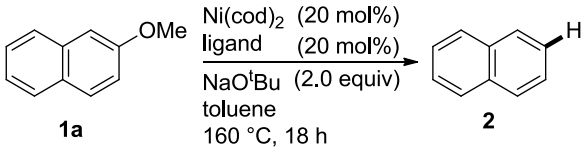
Meanwhile, another mechanism for the nickel-catalyzed reductive cleavage of aryl ethers in the presence of hydrosilane was reported by Martin (Scheme 2, path c),[3c] who suggested that silylnickel(I) species generated in situ mediate C-OMe bond cleavage via migratory insertion of an arene to form benzylnickel species **C**, followed by concerted elimination of $MeOSiR_3$.

Scheme 2. Mechanistic Diversity of Reductive Cleavage of Aryl Methyl Ether



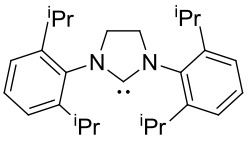
In an attempt to realize our working hypothesis, the effect of ligands was initially evaluated in the nickel-catalyzed reduction of 2-methoxynaphthalene **1a** (Table 1). As previously reported, the addition of PCy_3 and SIPr, which are effective for the reductive deoxygenation of **1a** with hydrosilane[3] and hydrogen,[4] respectively, did not lead to the formation of appreciable amounts of the reduced product **2** in the absence of an external reductant (Table 1, entries 1 and 2). Systematic screening of several other NHC-based ligands showed that a new NHC ligand containing 2-adamantyl groups on its imidazole nitrogen atom [I(2-Ad)] produced high yield of desired product (Table 1, entries 9). The yield of the reductive cleavage product was unaffected by the addition of excess mercury; therefore it was suggested that the soluble nickel species is responsible for the catalysis. Interestingly, I(1-Ad) which has a similar chemical structure to I(2-Ad) was found to be less effective under current conditions (Table 1, entries 8).

Table 1. Effect of Ligands[a]

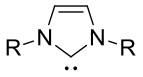


1a **2**

entry	ligand	GC yield of **2** (%)
1	PCy_3	0
2	SIPr·HCl	5
3	IPr·HCl	31
4	IMes·HCl	38
5	I^iPr·HCl	2
6	I^tBu·HCl	3
7	ICy·HCl	50
8	I(1-Ad)·HCl	45
9	I(2-Ad)·HCl	84



SIPr·HCl



IPr (R = 2,6-^{i}Pr$_2$C$_6$H$_3$)
IMes (R = 2,4,6-Me$_3$C$_6$H$_2$)
I^iPr (R = ^{i}Pr)
I^tBu (R = ^{t}Bu)
ICy (R = cyclohexyl)
I(1-Ad) (R = R = 1-adamantyl)
I(2-Ad) (R = R = 2-adamantyl)

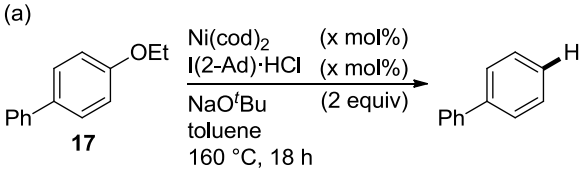
[a] Reaction conditions: **1a** (0.25 mmol), $Ni(cod)_2$ (0.050 mmol), ligand (0.050 mmol), NaO^tBu (0.50 mmol) in toluene (0.5 mL) at 160 °C for 18 h.

The optimization of reaction conditions was carried out (Scheme 3). The catalyst loading can be reduced to 10 mol% without a significant decrease in the yield of the reduced product when ethyl ether **17** was used as the substrate (Scheme 3a). However, the decrease in the yield was significant in the case of methyl ethers, such as **1a** (Scheme 3b). The amount of the base was also examined (Scheme 3c). The reaction proceeded when the amount of NaO^tBu was reduced to a catalytic amount (25 mol%), although the yield of the product was slightly decreased. Therefore, 20 mol% and 2 equivalents were set as the standard amount of Ni/I(2-Ad) and NaO^tBu respectively to maximize the yield of the product.

To gain further insight into the role of NaO^tBu, the reaction in the absence of NaO^tBu was conducted using pure IMes (pure I(2-Ad) was unable to be used for this experiment due to its unstability). As a result, the reaction proceeded in the absence of NaO^tBu (Scheme 3d). These results suggest that the key elementary steps involved in this reaction, *i.e.*, oxidative addition of the C-OMe bond and β-hydrogen elimination of Ni-OMe, can basically proceed in the absence of NaO^tBu. Slight improvement in yield by the presence of NaO^tBu is due to the accelerating effect of these elementary steps and/or the assistance of the catalyst turnover.

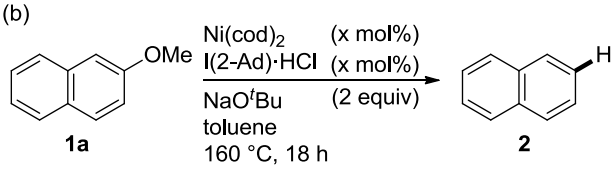
Scheme 3. Optimization of Reaction Conditions

(a)



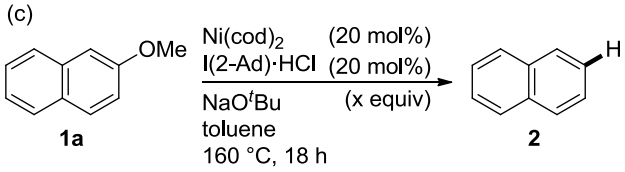
x (mol%)	GC yield of **2** (%)
10	69
20	78

(b)



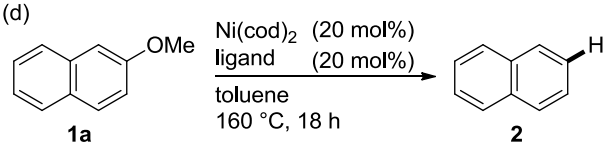
x (mol%)	GC yield of **2** (%)
10	52
20	84

(c)



x (mol%)	GC yield of **2** (%)
25	63
50	80
200	84

(d)

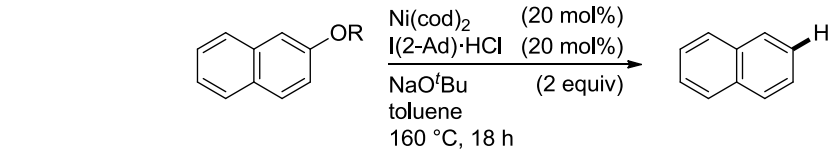


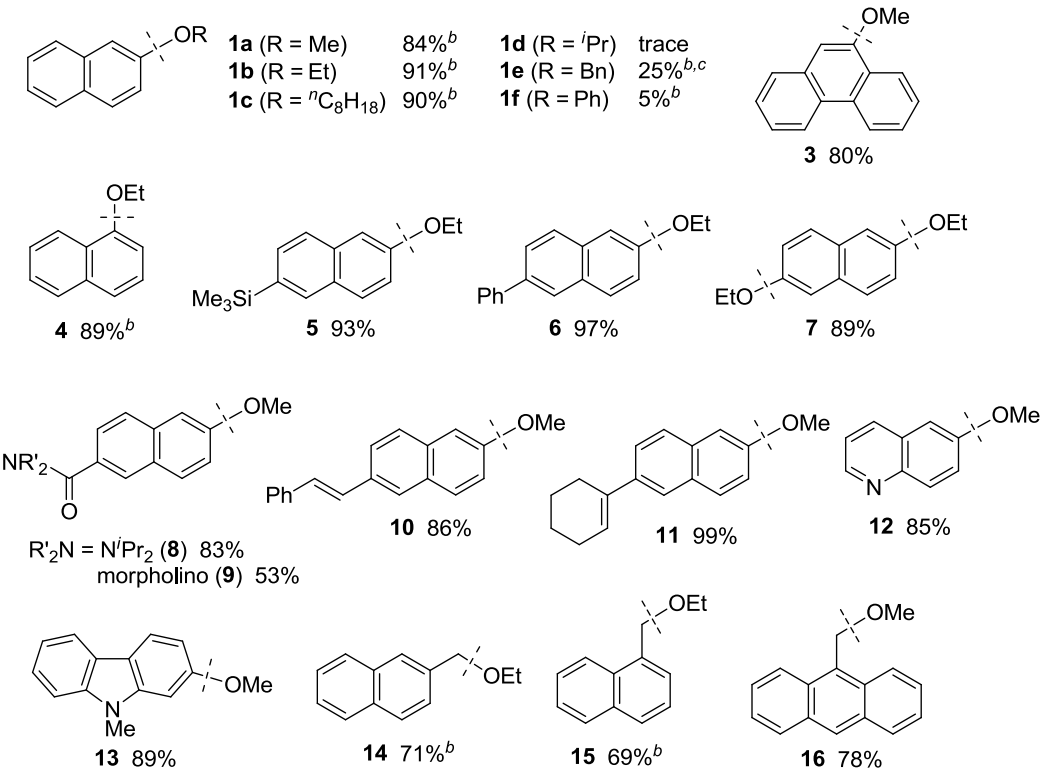
ligand	GC yield of **2** (%)
IMes	22
IMes·HCl[a]	38

[a] NaO^{t}Bu (2 equiv) was used.

These newly developed conditions using I(2-Ad) ligand were then applied to the reductive cleavage of other aryl alkyl ethers (Table 2). Primary alkoxy groups, including EtO (**1b**) and the longer ^{n}C$_8$H$_{17}$O groups (**1c**), were efficiently removed under these condition, but the bulkier ^{i}PrO group (**1d**) was completely unreactive. When a substrate bearing a PhCH$_2$O group **(1e**) was employed, reductive cleavage of benzylic C-O bond was also observed. A PhO group (**1f**) did not produce any of the reduced products, which is consistent with our proposed mechanism (Scheme 2, path c). Alkoxy groups on polyaromatic scaffolds such as naphthalenes (**4**-**11**) and phenanthrene (**3**) successfully underwent nickel-catalyzed reductive cleavage under these conditions to provide the parent arenes. Functional groups such as silyl (**5**), and amide (**8** and **9**) were compatible. Notably, a pendant alkene moiety (**10** and **11**), which was reduced under the previously reported conditions using hydrogen,[4] remained intact under the current conditions. Heteroarenes, such as the electron-deficient quinolone (**12**) and electron-rich carbazole (**13**), were also good substrates. In addition, benzyl ethers **14**-**16** were also applicable in this reaction.

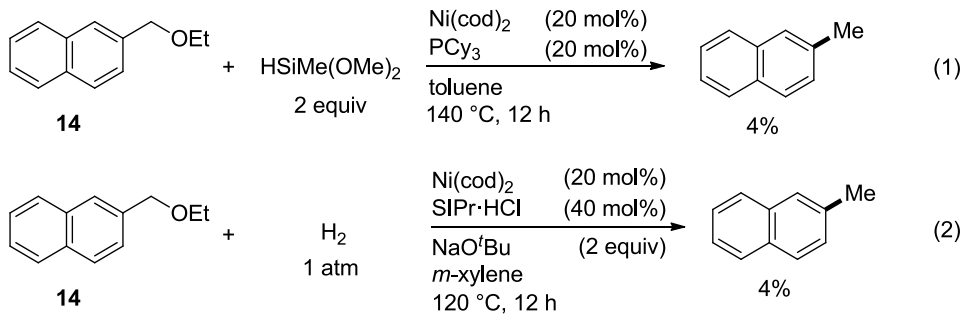
Table 2. Ni/I(2-Ad)-Catalyzed Reductive Deoxygenation of Naphthyl Alkyl Ethers[a]



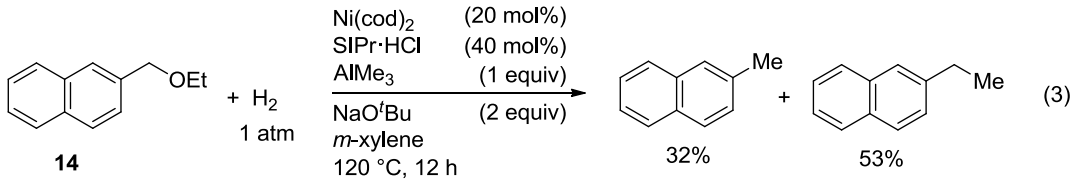


[a] Reaction conditions: Aryl or benzyl ether (0.25 mmol), $Ni(cod)_2$ (0.050 mmol), I(2-Ad)·HCl (0.050 mmol), NaO^tBu (0.50 mmol) in toluene (0.50 mL) at 160 °C for 18 h. Yields shown are the isolated yields, unless otherwise noted. [b] Yield was determined by GC analysis because of the volatility of the product. [c] 2-Naphthol was obtained in 16%.

In contrast, when the previously reported catalytic conditions using hydrosilane[3] was directly applied to benzyl ether **14**, the reduced product was formed in only 4% yield (eq. 1). The reported conditions using hydrogen[4] could not promote the reductive cleavage of **14**, either (eq. 2).

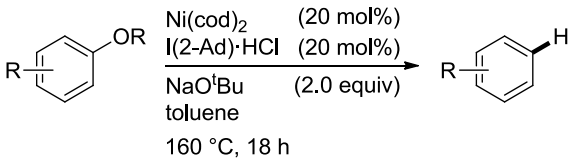


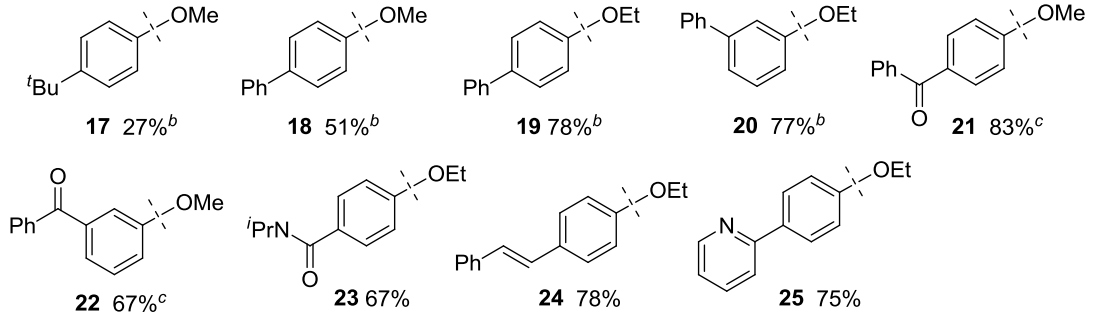
The other conditions using stoichiometric $AlMe_3$, which was also reported by Hartwig,[4] was also tested for the reaction of **14** and the product was obtained in 32% yield, and 53% of a methylated product was also formed (eq. 3). This result indicated that organoaluminum reagents can be used for cross-coupling of aryl and benzyl ethers and studies along this line are described in Chapter 2.



Substrates lacking a fused aromatic ring were also examined under the current conditions (Table 3). 4-tert-Butylanisole (**17**) was found to be much less reactive; however, the introduction of a phenyl group (**18**) instead of tert-butyl group promoted the reductive cleavage reaction. Note that compound **18** is completely unreactive under previously reported nickel-catalyzed reductive cleavage conditions using hydrosilane.[3] The efficiency of this catalysis was further improved by replacing the methoxy group with an ethoxy group, as described in Scheme 3. Ethoxybenzenes bearing a phenyl group at the para (**19**) and meta positions (**20**), respectively, afforded the corresponding reduction products in good yields. The anisole derivatives bearing ketone functionality (**21** and **22**) underwent the selective reductions of C-O bonds, whereas a pedant ketone moiety is reduced under previous methods using an external reductant. The current nickel catalyst system also enables the selective conversion of aryl ethers bearing amide (**23**), alkene (**24**), and pyridine (**25**) groups to the corresponding arenes.

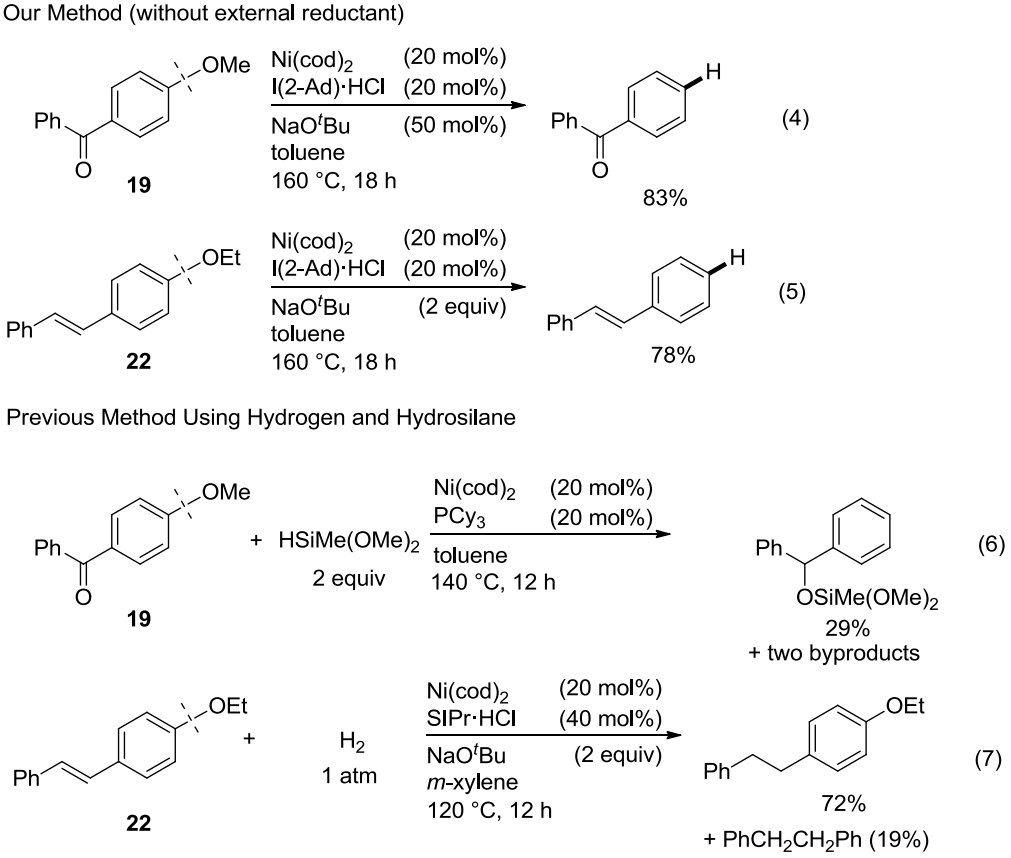
Table 3. Ni/I(2-Ad)-Catalyzed Reductive Deoxygenation of Anisole Derivatives[a]



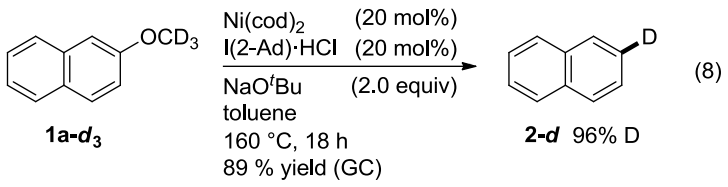


[a] Reaction conditions: aryl or benzyl ether (0.25 mmol), $Ni(cod)_2$ (0.050 mmol), I(2-Ad)·HCl (0.050 mmol), NaO^{t}Bu (0.50 mmol) in toluene (0.50 mL) at 160 °C for 18 h. Yields shown are the isolated yields, unless otherwise noted. [b] Yield was determined by GC analysis because of the volatility of the product. [c] NaO^{t}Bu (0.13 mmol) was used.

The method using an external reductant[3, 4] cannot be applied to substrates bearing reducible functionalities, such as alkenes and keotones, however, this limitation was overcome under our nickel catalyst system which enables the selective reduction of aryl ethers to parent arenes. (eq. 4 and 5).



To elucidate the source of hydrogen of a reduced product, an isotopic labeling experiment was performed with the labeled substrate 2-CD_3O-naphthalene (**1a-*d*3**). The result of this experiment revealed that the hydrogen delivered to the reduced product was primarily derived from the methoxy group of the substrate (eq 8). This result supports our proposed mechanism shown in Scheme 2.



The key to a successful reaction is the use of a new NHC ligand I(2-Ad). The electronic and steric properties of I(2-Ad) were investigated to gain insights that will help in the future design of better ligands for catalytic C-O bond activation processes (Table 4). In terms of the electronic properties, the Tolman electronic parameter (TEP)[7] for the new I(2-Ad) ligand was determined to be 2049.4, by synthesizing [IrCl(I(2-Ad))$(CO)_2$]. This value is similar to the TEP values obtained for ICy and I(1-Ad), and I(2-Ad) is a significantly stronger σ-donor than PCy_3, the commonest ligand used in nickel-mediated C-O bond activation.[1] The steric properties were determined by

calculating the buried volume (%V_{bur}),[8] based on the crystal structure of [IrCl(I(2-Ad))(cod)]. The %V_{bur} of I(2-Ad) (33.4) was found to be close to that for IMes (33.8), exerting a significantly larger steric demand than ICy, but not as large as those of I(1-Ad) and IPr. The catalytic activity in this study clearly cannot be explained solely by these two static parameters, and other factors such as dynamic behavior of the substituents[9] should be considered for a complete understanding of the structure-activity relationships.

Table 4. TEP[7] and %V_{bur}[8] Values for Selected NHCs Used in This Study

entry	ligand	TEP[a]	%V_{bur}[b]
1	PCy_3	2060	(35.7)[d]
2	IMes	2050.7	33.8
3	IPr	2051.5	36.9
4	ICy	2049.6	28.1
5	I(1-Ad)	2048.3	37.3
6	I(2-Ad)	2049.4[c]	33.4

[a] Tolman electronic parameter. Values are taken from ref 10 unless otherwise noted. [b] Buried volume. Values are calculated based on crystal structures of the corresponding [IrCl(NHC)(cod)] unless otherwise noted. See 1.4.8 for details. [c] Determined by synthesizing [IrCl(I(2-Ad))$(CO)_2$]. See 1.4.8 for details. [d] Calculated based on the crystal structure of [Ir(PCy_3)(cod)(pyridine)]PF_6.

1.3 Conclusion

In conclusion, the first nickel system capable of promoting reductive deoxygenation of aryl ethers is described. This new reaction proceeds in the absence of an external stoichiometric reductant via a mechanism involving oxidative addition of the C-O bond followed by β-hydrogen elimination, which has not previously been unexploited in a catalytic setting. The result of an isotopic labeling experiment shows that the elusive oxidative addition of a C-OMe bond which has never verified experimentally is a reliable elementary step in nickel-catalyzed C-O bond transformations of aryl ethers, particularly when an NHC-based ligand is used.

1.4 Experimental Section

1.4.1 General Information

^1H and ^{13}C NMR spectra were recorded on a JEOL ECS-400 spectrometer (JEOL, Tokyo, Japan) or VARIAN UNITY INOVA-600 spectrometer in $CDCl_3$ with tetramethylsilane as an internal reference standard. NMR data have been reported as follows: chemical shift (δ) in ppm, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, and m = multiplet), coupling constant (*J*) in Hz, and integration. Infrared spectra (IR) were obtained on a JASCO FT/IR-4000 spectrometer, and the absorptions have been reported in reciprocal centimeters with the following relative intensities: s (strong), m (medium), or w (weak). Mass spectra were obtained on a Shimadzu

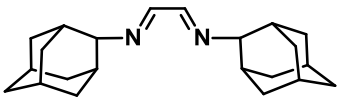
GCMS-QP 5000 or GCMS-QP 2010 instrument with an ionization voltage of 70 eV. High resolution mass spectra (HRMS) were obtained on a JEOL JMS-DX303. Analytical gas chromatography (GC) was carried out on Shimadzu GC-2014, equipped with a flame ionization detector. Melting points were determined using a Yamato melting point apparatus. Column chromatography was performed over SiO_2 (Silycycle Silica Flash F60 (230-400 mesh)) and NH Silica (Silica Gel 60 (spherical) NH_2 (40-50 μm)). Some of the compounds were purified by LC-908 HPLC (GPC).

1.4.2 Materials

Toluene (for Organic Synth.) was purchased from Wako Chemicals and used as received. $Ni(cod)_2$ was purchased from Strem Chemicals and used as received. PCy_3 (Sigma-Aldrich), SIPr·HCl (TCI), IPr·HCl (TCI), IMes·HCl (TCI), I^{i}Pr·HCl (TCI), I(1-Ad)·HCl (Sigma-Aldrich), ICy·HBF_4 (TCI) and NaO^{t}Bu (TCI) were purchased from commercial suppliers and used as received. I^{t}Bu[11] and ICy·HCl[12] were prepared according to the literature procedures. Aryl ethers **1a** (TCI), **1b** (TCI), **14** (TCI), **19** (TCI), **20** (TCI) were purchased from commercial suppliers and purified by distillation over CaH_2 prior to being used. Aryl ethers **1a-*d*$_3$** (CAS 97073-37-5),[13] **1c** (CAS 70617-42-4),[14] **1d** (CAS 15052-09-2),[15] **1e** (CAS 613-62-7),[16] **1f** (CAS 19420-29-2),[17] **3** (CAS 5085-74-5),[18] **4** (CAS 5328-01-8),[19] **14** (CAS 93359-83-2),[20] **18** (CAS 2584-79-4),[21] **19** (CAS 613-40-1),[22] and **20** (CAS 54852-73-2)[23] were prepared from the corresponding phenols or alcohols by treatment with NaH followed by the addition of an alkyl halide. Ethers **6** (CAS 858458-42-1),[24] **8** (CAS 6297-10-5),[25] **10** (CAS 123871-53-4),[26] **21** (CAS 611-94-9),[27] **22** (CAS 6136-7-0)[28] and **25** (CAS 4357-28-2)[29] were prepared according to the literature procedures. All spectrum data of starting materials are cited in original paper.[30]

1.4.3 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) were added to a 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%).

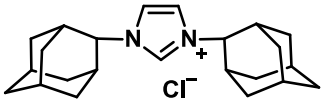
White solid (12 g, 98 %). Rf 0.83 (NH Silica, Et_2O). Mp: 159−162 °C.

^{1}H NMR ($CDCl_3$, 399.78 MHz): 1.54 (s, 2H), 1.90-1.77 (m, 22H), 2.24 (d, J = 12.0 Hz, 4H), 3.42 (s, 2H), 8.04 (s, 2H).

^{13}C NMR ($CDCl_3$, 100.53 MHz): 27.3, 28.0, 31.8, 35.0, 37.2, 37.9, 74.3, 160.5. 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.

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

1,3-Bis(adamantan-2-yl)imidazolin-2-ylidene chloride [I(2-Ad) ·HCl].



N,N,N',N'-Tetramethyldiaminomethane (6.6 mL, 5.0 g, 49 mmol) and CH_2Cl_2 (60 mL) were added to a dry 500 mL three-necked flask; 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 the resulting mixture was stirred at 0 °C for 1 h.

A 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 °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 the 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 (9.0 g, 65%). Mp: 318−320 °C.

^{1}H NMR ($CDCl_3$, 399.78 MHz): 1.69-1.64 (m, 4H), 1.80-1.77 (m, 8H), 1.89 (bs, 2H), 2.08-2.00 (m, 10H), 2.85 (s, 4H), 4.60 (s, 2H), 7.37 (t, J = 1.4 Hz, 2 H), 10.53 (s, 1H).

^{13}C NMR ($CDCl_3$, 100.53 MHz): 26.56, 26.62, 30.99, 31.10, 36.6, 36.9, 64.0, 119.2, 137.5. 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.

Exact Mass (FAB) Calcd for $C_{23}H_{33}N_2$ ([M-Cl]$^+$): 337.2644. Found: 337.2642.

1.4.4 Typical Procedure for Ni/I(2-Ad)-Catalyzed Reductive Cleavage of Aryl Methyl Ethers

$Ni(cod)_2$ (14 mg, 0.050 mmol), I(2-Ad)·HCl (13 mg, 0.050 mmol), NaO^{t}Bu (48 mg, 0.50 mmol) and toluene (0.25 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 at room temperature for 3 min. An aryl methyl ether (0.25 mmol) in toluene (0.25 mL) was then added to the vial and the cap was closed. The contents of the vial were stirred at 160 °C for 18 h. The reaction mixture was cooled to room temperature, and the crude mixture was filtered through a pad of silica gel,

and then analyzed by GC. The filtrate was concentrated *in vacuo* to give a residue, which was purified by flash column chromatography over silica gel.

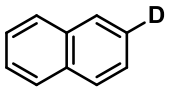
1.4.5 Typical Procedure for Ni/ICy-Catalyzed Methylation of Aryl Methyl Ethers

$Ni(cod)_2$ (6.9 mg, 0.050 mmol), ICy·HBF_4 (8.0 mg, 0.050 mmol), NaO^{t}Bu (48 mg, 0.50 mmol) and toluene (0.5 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 at room temperature for 3 min. An aryl methyl ether (0.25 mmol) in toluene (0.50 mL) and $AlMe_3$ (1.8 M in toluene solution, 0.14 mL, 0.25 mmol) were then added to the vial and the cap was closed. The contents of the vial were stirred at 80 °C for 6 or 18 h. The reaction mixture was cooled to room temperature, and the crude mixture was then treated with EtOH. The resulting mixture was filtered through a pad of silica gel, and then analyzed by GC. The filtrate was concentrated *in vacuo* to give a residue, which was purified by flash column chromatography over silica gel.

1.4.6 Labeling Studies

Compound **1a-*d*$_3$** was subjected to the typical reaction conditions described in section 1.2 (eq 8). The yield of **2-*d*** was determined by GC (90%). The deuterium content of **2-*d*** obtained under these conditions was determined to be 96% by ^{1}H NMR spectroscopy.

2-Deuteronaphthalene (2-*d*). [CAS: 2430-34-4]



2-*d*

White solid (90%). Rf 0.66 (SiO_2, hexane/EtOAc = 20/1).

^{1}H NMR ($CDCl_3$, 399.78 MHz) δ: 7.50-7.48 (s, 3H), 7.87-7.85 (m, 4H).

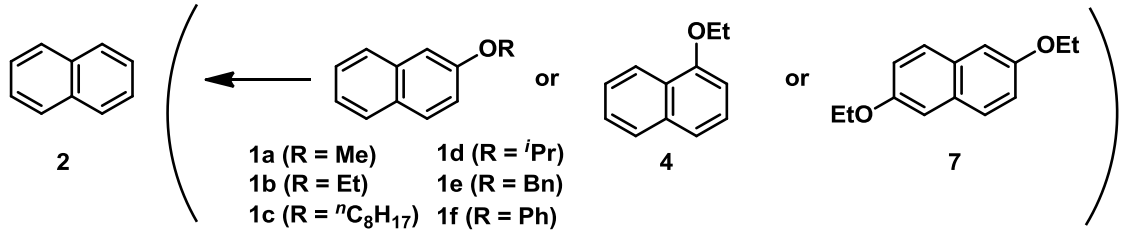
^{13}C NMR ($CDCl_3$, 100.53 MHz) δ: 125.7, 125.8, 127.7, 127.9, 133.4.

^{2}D NMR (acetone-d_6, 399.78 MHz) δ: 7.44.

Exact Mass (EI) Calcd for $C_{10}H_7D$: 129.0689. Found: 129.0687.

1.4.7 Spectroscopic Data of Products

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



The product was obtained from either **1a**-**1f**, **4** or **7** under the typical conditions. The yield for this compound was determined by GC, because of its volatility. The GC and ^{1}H NMR spectra of the compound were in agreement with those determined for an authentic sample.

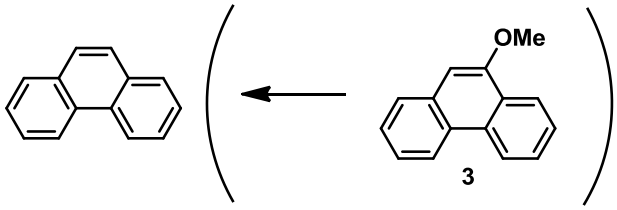
White solid. Rf 0.63 (Hexane/EtOAc = 50/1).

^{1}H NMR ($CDCl_3$, 399.78 MHz) δ: 7.55-7.51 (m, 4H), 7.90-7.87 (m, 4H).

^{13}C NMR ($CDCl_3$, 100.53 MHz) δ: 125.8, 127.8, 133.4.

Exact Mass (EI) Calcd for $C_{10}H_8$: 128.0626. Found: 128.0624.

Phenanthrene [CAS: 85-01-8].



The typical procedure was followed using **3** as the substrate.

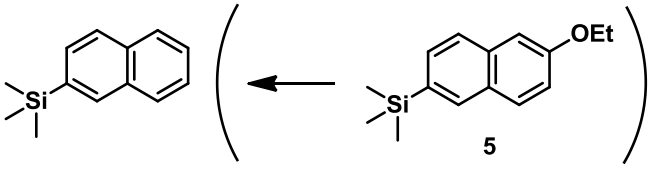
White solid (35.6 mg, 80%). Rf 0.43 (SiO_2, hexane/EtOAc = 50/1).

^{1}H NMR ($CDCl_3$, 399.78 MHz) δ: 7.61 (dd, *J* = 6.9, 7.8 Hz, 2H), 7.67 (dd, *J* = 6.9, 8.2 Hz, 2H), 7.76 (s, 2H), 7.91 (d, *J* = 8.2 Hz, 2H), 8.71 (d, *J* = 7.8 Hz, 2H).

^{13}C NMR ($CDCl_3$, 100.53 MHz) δ: 122.6, 126.54, 125.55, 126.9, 128.5, 130.3, 132.0.

Exact Mass (EI) Calcd for $C_{14}H_{10}$: 178.07825. Found: 178.0785.

Trimethyl(naphthalen-2-yl)silane [CAS: 18052-85-2].



The typical procedure was followed using **5** as the substrate.

White solid (46.6 mg, 93%). Rf 0.63 (SiO_2, hexane/EtOAc = 20/1).

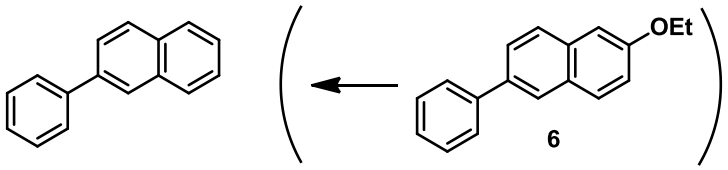
^{1}H NMR ($CDCl_3$, 399.78 MHz) δ: 0.38 (s, 9H), 7.50 (dd, *J* = 6.0, 6.8 Hz, 2H), 7.64 (d, *J* = 8.2 Hz, 1H), 7.86-7.83

(m, 3H), 8.03 (s, 1H).

^{13}C NMR ($CDCl_3$, 100.53 MHz) δ: −1.1, 125.8, 126.2, 126.9, 127.7, 128.0, 129.8, 132.9, 133.6, 133.7, 137.9.

Exact Mass (EI) Calcd for $C_{13}H_{16}Si$: 200.1021. Found: 200.1020.

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



The typical procedure was followed using **6** as the substrate.

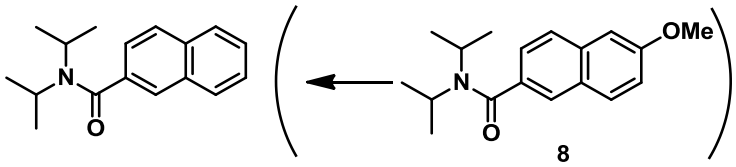
White solid (49.5 mg, 97%). Rf 0.51 (SiO_2, hexane/EtOAc = 20/1).

^{1}H NMR ($CDCl_3$, 399.78 MHz) δ: 7.43 (d, *J* = 7.8 Hz, 1H), 7.57-7.51 (m, 4H), 7.80-7.76 (m, 3H), 7.97-7.90 (m, 3H), 8.09 (s, 1H).

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

Exact Mass (EI) Calcd for $C_{11}H_{10}$: 204.0939. Found: 204.0941.

***N*,*N*-Diisopropyl-6-methoxy-2-naphthamide [CAS: 31609-22-0].**



The typical procedure was followed using **8** as the substrate.

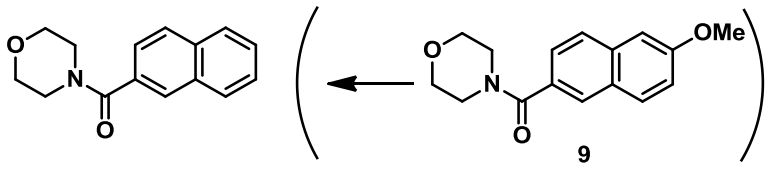
White solid (53.0 mg, 83%). Rf 0.2 (NH Silica, hexane/EtOAc = 10/1).

^{1}H NMR ($CDCl_3$, 399.78 MHz) δ: 1.56-1.18 (m, 12H), 3.87-3.60 (m, 2H), 7.42 (d, *J* = 8.2 Hz, 1H), 7.53-7.49 (m, 2H), 7.80 (s, 1H), 7.87-7.83 (m, 3H).

^{13}C NMR ($CDCl_3$, 100.53 MHz) δ: 20.7, 46.0 (bs), 50.9 (bs), 123.4, 124.8, 126.50, 126.51, 127.7, 128.20, 128.25, 132.9, 133.1, 136.2, 171.0.

Exact Mass (EI) Calcd for $C_{17}H_{21}NO$: 255.1623. Found: 255.1625.

Morpholino(naphthalen-2-yl)methanone [CAS: 26162-88-9].



The typical procedure was followed using **9** as the substrate.

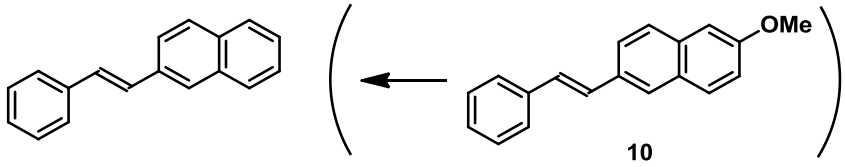
White solid (41.0 mg, 53%). Rf 0.40 (NH Silica, hexane/EtOAc = 5/1).

^{1}H NMR ($CDCl_3$, 399.78 MHz) δ: 3.79-3.53 (m, 8H), 7.49 (d, *J* = 8.2 Hz, 1H), 7.57-7.52 (m, 2H), 7.91-7.85 (m, 4H).

^{13}C NMR ($CDCl_3$, 100.53 MHz) δ: 42.7 (bs), 48.3 (bs), 66.9, 124.2, 126.7, 127.0, 127.2, 127.8, 128.37, 128.42, 132.5, 132.6, 133.7, 170.5.

Exact Mass (EI) Calcd for $C_{15}H_{15}NO_2$: 241.1101. Found: 241.1100.

(*E*)-2-Styrylnaphthalene [CAS: 2039-70-5].



10

The typical procedure was followed using **10** as the substrate.

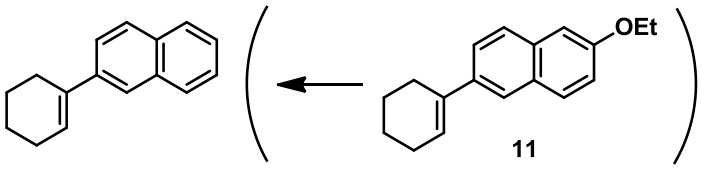
White solid (49.5 mg, 86%). Rf 0.40 (SiO_2, hexane/EtOAc = 50/1).

^{1}H NMR ($CDCl_3$, 399.78 MHz) δ: 7.36-7.28 (m, 3H), 7.44 (dd, *J* = 7.3, 7.8 Hz, 2H), 7.51 (dd, *J* = 6.9, 7.8 Hz, 2H), 7.62 (d, *J* = 7.3 Hz, 2H), 7.79 (d, *J* = 8.7 Hz, 1H), 7.90-7.84 (m, 4H).

^{13}C NMR ($CDCl_3$, 100.53 MHz) δ: 123.5, 125.9, 126.3, 126.5, 126.6, 127.6, 127.7, 128.0, 128.3, 128.7, 128.7, 129.0, 133.0, 133.7, 134.8, 137.3.

Exact Mass (EI) Calcd for $C_{18}H_{14}$: 230.1096. Found: 230.1094.

2-(Cyclohex-1-en-1-yl)naphthalene. [CAS: 54607-03-3]



11

The typical procedure was followed using **11** as the substrate.

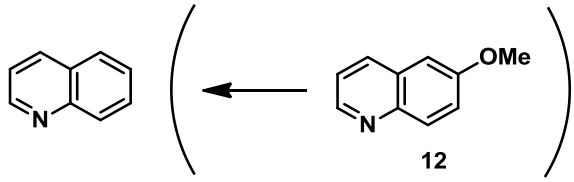
White solid (51.6 mg, 99%). Rf 0.57 (SiO_2, hexane/EtOAc = 100/1).

^{1}H NMR ($CDCl_3$, 399.78 MHz) δ: 1.76-1.72 (m, 2H). 1.90-1.84 (m, 2H), 2.32-2.28 (m, 2H), 2.59-2.55 (m, 2H), 6.33-6.31 (m, 1H), 7.43 (dd, *J* = 6.9, 7.4 Hz, 1H), 7.47 (dd, *J* = 6.9, 7.8 Hz, 1H), 7.62 (d, *J* = 8.7 Hz, 1H), 7.84-7.78 (m, 4H).

^{13}C NMR ($CDCl_3$, 100.53 MHz) δ: 22.2, 23.1, 26.0, 27.3, 123.1, 123.8, 125.3, 125.5, 125.9, 127.4, 127.5, 128.0, 132.4, 133.5, 136.3, 139.7.

Exact Mass (EI) Calcd for $C_{16}H_{16}$: 208.1252. Found: 208.1253.

Quinoline [CAS: 91-22-5].



12

The typical procedure was followed using **12** as the substrate.

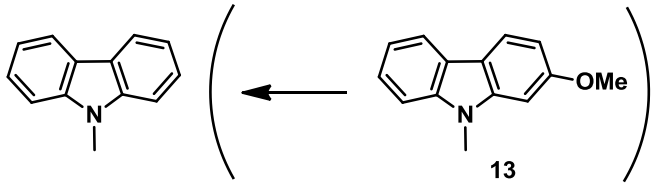
Colorless oil (85%). Rf 0.11 (SiO_2, hexane/EtOAc = 20/1).

^{1}H NMR ($CDCl_3$, 399.78 MHz) δ: 7.31 (dd, *J* = 4.1, 8.2 Hz, 1H), 7.49 (dd, *J* = 6.9, 8.2 Hz, 1H), 7.66 (dd, *J* = 6.9, 8.2 Hz, 1H), 7.75 (d, *J* = 8.2 Hz, 1H), 8.13 (d, *J* = 8.2 Hz, 2H), 8.88 (d, *J* = 4.1 Hz, 1H).

^{13}C NMR ($CDCl_3$, 100.53 MHz) δ: 120.9, 126.4, 127.6, 128.1, 129.29, 129.32, 135.9, 148.1, 150.2.

Exact Mass (EI) Calcd for C_9H_7N: 129.0579. Found: 129.0579.

9-Methyl-9H-carbazolel [CAS: 1484-12-4].



13

The typical procedure was followed using **13** as the substrate.

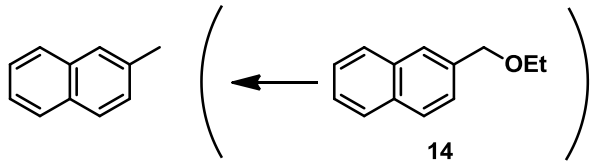
White solid (40.3 mg, 89%). Rf 0.26 (NH Silica, hexane/EtOAc = 50/1).

^{1}H NMR ($CDCl_3$, 399.78 MHz) δ: 3.86 (s, 3H), 7.27 (dd, *J* = 7.3 Hz, 7.8 Hz, 2H), 7.42 (d, *J* = 8.2 Hz, 2H), 7.52 (dd, *J* = 7.3, 8.2 Hz, 2H), 8.14 (d, *J* = 7.82 Hz, 2H).

^{13}C NMR ($CDCl_3$, 100.53 MHz) δ: 29.0, 108.4, 118.8, 120.3, 122.7, 125.6, 140.9.

Exact Mass (EI) Calcd for $C_{11}H_{10}$: 181.0892. Found: 181.0894.

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



14

The typical procedure was followed using **14** as the substrate.

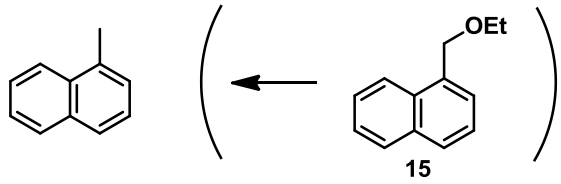
Colorless oil (71%). Rf 0.74 (SiO_2, hexane/EtOAc = 20/1).

^{1}H NMR ($CDCl_3$, 399.78 MHz) δ: 2.53 (s, 3H), 7.33 (d, *J* = 8.3 Hz, 1H), 7.41 (dd, *J* = 7.3, 7.3 Hz, 1H), 7.44 (dd, *J* = 7.3, 7.8 Hz, 1H), 7.65 (s, 1H), 7.75 (d, *J* = 7.8 Hz, 1H), 7.77 (d, *J* = 8.3 Hz, 1H), 7.81 (d, *J* = 7.8 Hz, 1H).

^{13}C NMR ($CDCl_3$, 100.53 MHz) δ: 27.7, 124.9, 125.8, 126.8, 127.2, 127.6, 127.6, 128.1, 131.6, 133.6, 135.4.

Exact Mass (EI) Calcd for $C_{11}H_{10}$: 142.07825. Found: 142.0782.

1-Methylnaphthalene [CAS: 90-12-0].



15

The typical procedure was followed using **15** as the substrate.

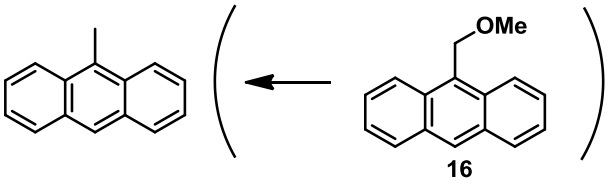
Colorless oil (69%). Rf 0.49 (SiO_2, hexane/EtOAc = 50/1).

^{1}H NMR ($CDCl_3$, 399.78 MHz) δ: 2.73 (s, 3H), 7.35 (d, *J* = 6.9 Hz, 1H), 7.41 (dd, *J* = 6.8, 7.8 Hz, 1H), 7.51 (dd, *J* = 6.8, 7.8 Hz, 1H), 7.55 (dd, *J* = 6.9, 8.2 Hz, 1H), 7.74 (d, *J* = 7.8 Hz, 1H), 7.88 (d, *J* = 7.8 Hz, 1H), 8.03 (d, *J* = 8.2 Hz, 1H).

^{13}C NMR ($CDCl_3$, 100.53 MHz) δ: 19.4, 124.1, 125.50, 125.54, 125.7, 126.3, 126.5, 128.5, 132.5, 133.4, 134.2.

Exact Mass (EI) Calcd for $C_{11}H_{10}$: 142.07825. Found: 142.0783.

9-Methylanthracene [CAS: 779-02-2].



16

The typical procedure was followed using **16** as the substrate.

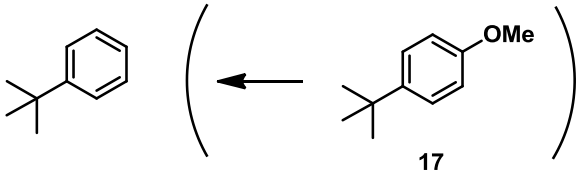
White solid (37.5 mg, 78%). Rf 0.60 (SiO_2, hexane/EtOAc = 20/1).

^{1}H NMR ($CDCl_3$, 399.78 MHz) δ: 3.12 (s, 3H), 7.50 (dd, *J* = 6.9, 8.2 Hz, 2H), 7.54 (dd, *J* = 6.9, 8.7 Hz, 2H), 8.03 (d, *J* = 8.2 Hz, 2H), 8.32 (d, *J* = 8.7 Hz, 2H), 8.36 (s, 1H).

^{13}C NMR ($CDCl_3$, 100.53 MHz) δ: 13.9, 124.7, 124.8, 125.20, 125.25, 129.0, 130.0, 130.1, 131.4.

Exact Mass (EI) Calcd for $C_{15}H_{12}$: 192.09390. Found: 192.0940.

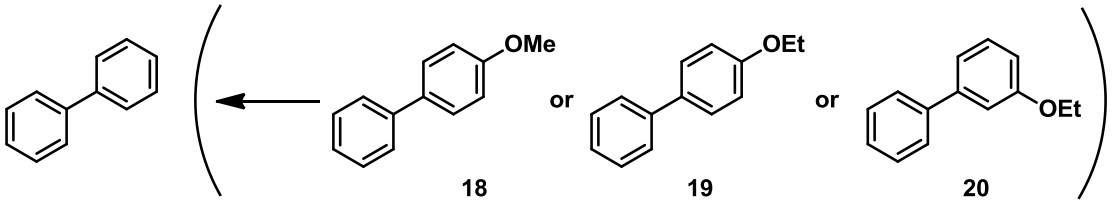
tert-Butylbenzene [CAS: 98-06-6].



17

The modified procedure was followed using **17** as the substrate. The yield was determined by GC analysis using an authentic sample (27%).

Biphenyl [CAS: 92-52-4].



The product was obtained from either **18**, **19** or **20** under the typical conditions. The yield for this compound was determined by GC, because of its volatility. The GC and ^{1}H NMR spectra were in agreement with those determined for an authentic sample.

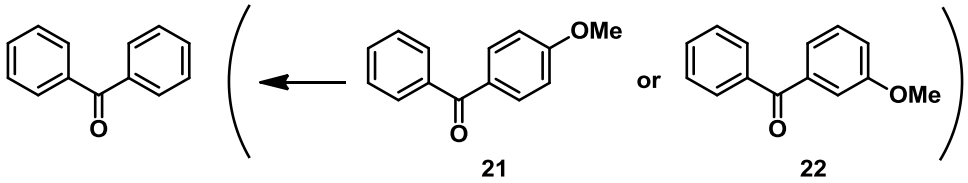
White solid. Rf 0.60 (SiO_2, hexane/EtOAc = 50/1).

^{1}H NMR ($CDCl_3$, 399.78 MHz) δ: 7.37 (d, *J* = 7.3, 2H), 7.47 (dd, *J* = 7.3, 7.9 Hz, 4H), 7.62 (d, *J* = 7.9 Hz, 4H).

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

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

Benzophenone [CAS: 119-61-9].



The product was obtained from either **21** or **22** under the typical conditions.

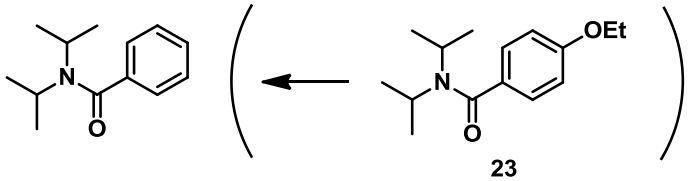
White solid. Rf 0.77 (NH Silica, hexane/EtOAc = 20/1).

^{1}H NMR ($CDCl_3$, 399.78 MHz) δ: 7.48 (dd, *J* = 6.9, 7.8 Hz, 4H), 7.60 (dd, *J* = 7.8, 7.8 Hz, 2H), 7.80 (d, *J* = 6.9 Hz, 4H).

^{13}C NMR ($CDCl_3$, 100.53 MHz) δ: 128.22, 128.23, 130.0, 132.38, 132.39, 137.5, 196.7.

Exact Mass (EI) Calcd for $C_{13}H_{10}O$: 182.0732. Found: 182.0730.

N,N-Diisopropylbenzamide [CAS: 20383-28-2].



The typical procedure was followed using **23** as the substrate.

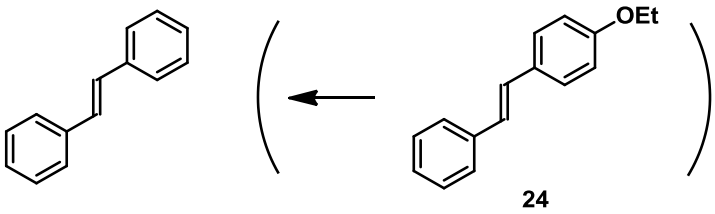
White solid (34.9 mg, 67%). Rf 0.34 (NH Silica, hexane/EtOAc = 5/1).

^{1}H NMR ($CDCl_3$, 399.78 MHz) δ: 1.53-1.14 (m, 12H), 3.82-3.52 (m, 2H), 7.30 (dd, *J* = 5.5, 6.9 Hz, 2H), 7.38-7.34 (m, 3H).

^{13}C NMR ($CDCl_3$, 100.53 MHz) δ: 20.7, 45.7 (bs), 50.8 (bs), 125.5, 128.4, 128.6, 138.9, 171.0.

Exact Mass (EI) Calcd for $C_{17}H_{21}NO$: 255.1623. Found: 255.1625.

(E)-1,2-Diphenylethene [CAS: 103-30-0].



24

The typical procedure was followed using **24** as the substrate.

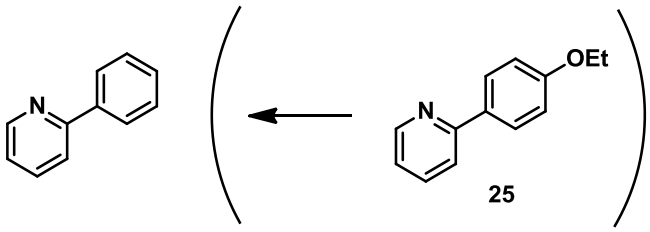
White solid (35 mg, 78%). Rf 0.69 (SiO_2, hexane/EtOAc = 20/1).

^{1}H NMR ($CDCl_3$, 399.78 MHz) δ: 7.12 (s, 2H), 7.26 (dd, *J* = 8.4 Hz, 2H), 7.37 (dd, *J* = 7.3, 8.4 Hz, 4H), 7.52 (d, *J* = 7.3 Hz, 4H).

^{13}C NMR ($CDCl_3$, 100.53 MHz) δ: 126.5, 127.6, 128.65, 128.66, 137.3.

Exact Mass (EI) Calcd for $C_{14}H_{12}$: 180.0939. Found: 180.0980.

2-Phenylpyridine [CAS: 1008-89-5].



25

The typical procedure was followed using **25** as the substrate.

White solid (29.1 mg, 75%). Rf 0.14 (SiO_2, hexane/EtOAc = 20/1).

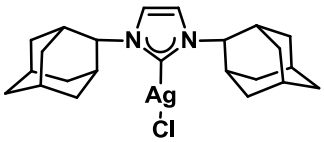
^{1}H NMR ($CDCl_3$, 399.78 MHz) δ: 7.21-7.23 (m, 1H), 7.43 (d, *J* = 6.0 Hz, 1H), 7.49 (dd, *J* = 6.0, 8.2 Hz, 2H), 7.78-7.73 (m, 2H), 8.00 (d, *J* = 8.2 Hz, 2H), 8.71 (d, *J* = 5.2 Hz, 1H).

^{13}C NMR ($CDCl_3$, 100.53 MHz) δ: 120.6, 122.1, 126.9, 128.8, 129.0, 136.9, 139.2, 149.6, 157.4.

Exact Mass (EI) Calcd for $C_{11}H_9N$: 155.0735. Found: 155.0737.

1.4.8 Determination of Tolman Electronic Parameter and Buried Volume of [Ir(I(2-Ad))$(CO)_2$Cl]

Chloro[1,3-bis(adamantan-2-yl)imidazolin-2-yliden]silver (I) ([I(2-Ad)]AgCl).[31]



1,3-Bis(adamantan-2-yl)imidazolin-2-ylidene chloride [I(2-Ad)·HCl, 310 mg, 0.80 mmol] and Ag_2O (220 mg, 0.95

mmol) were dissolved in CH_2Cl_2 (45 mL). The reaction mixture was refluxed under an atmosphere of nitrogen for 12 h, and then filtered through a Celite pad; the filtrate volume was reduced to about 2 mL by evaporation. The reaction mixture was cooled to 0 °C, and then hexane was slowly added to this solution until white precipitate appeared. The solid was filtered, washed with cold hexane, and dried *in vacuo* to give title compound as a white solid (340 mg, 86%). This compound was used for the subsequent reaction without further purification.

White solid (340 mg, 86%). Rf 0.00 (SiO_2, CH_2Cl_2). Mp: 252−255 °C.

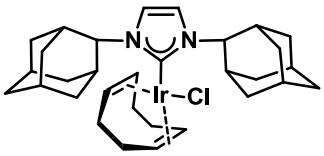
^{1}H NMR ($CDCl_3$, 399.78 MHz) δ: 1.74-1.70 (m, 4H), 1.80 (s, 4H), 2.00-1.87 (m, 16H), 2.70 (s, 4H), 4.43 (s, 2H), 7.31 (s, 2H).

^{13}C NMR ($CDCl_3$, 100.53 MHz) δ: 27.01, 27.07, 31.4, 33.3, 37.3, 37.9, 65.4, 118.3.

IR (ATR): 2915 s, 2888 s, 2853 m, 2361 m, 2336 m, 1554 w, 1467 w, 1451 m, 1425 w, 1382 w, 1353 w, 1306 w, 1232 w, 1200 m, 1172 w, 1127 w, 1102 w, 1071 w, 1054 w, 1028 w, 980 w, 956 w, 907 w, 822 w, 792 w, 767 w, 719 s, 668 w.

Exact Mass (FAB^+) Calcd for $C_{23}H_{32}N_2ClAg$ (M-HCl): 443.1616. Found: 443.1617.

Chloro(η^4-1,5-cyclooctadiene)[1,3-bis(adamantan-2-yl)-imidazolin-2-ylidene]iridium(I) ([I(2-Ad)]Ir(COD)Cl).[32]



[I(2-Ad)]AgCl (230 mg, 0.47 mmol) and $[Ir(COD)Cl]_2$ (160 mg, 0.24 mmol) were dissolved in CH_2Cl_2 (13 mL). The reaction mixture was stirred under an atmosphere of nitrogen for 2.5 h, and then filtered through a Celite pad; the filtrate volume was reduced to about 1 mL by evaporation. The reaction mixture was cooled to 0 °C, and then Et_2O was slowly added to the solution until a white precipitate appeared. The solid was filtered, and the residue was concentrated *in vacuo* to give the title compound as a yellow powder (310 mg, 94%). This compound was used for the subsequent reaction without further purification.

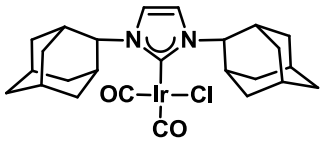
Yellow powder 310 mg, 94%). Rf 0.66 (SiO_2, CH_2Cl_2).

^{1}H NMR ($CDCl_3$, 399.78 MHz) δ: 1.80-1.56 (m, 12H), 2.08-1.93 (m, 14H), 2.18-2.15 (m, 6H), 2.32 (bs, 2H), 2.78 (bs, 2H), 2.91-2.90 (m, 2H), 4.55 (t, J = 2.8 Hz, 2H), 5.67 (br, 2H), 7.30 (s, 2H).

^{13}C NMR ($CDCl_3$, 100.53 MHz) δ: 27.1, 27.6, 29.7, 30.9, 32.3, 33.40, 33.48, 33.90, 38.0, 38.8, 39.4, 50.6, 65.2, 81.8, 118.7, 181.1. IR (ATR): 2906 s, 2850 m, 2825 w, 2360 s, 2339 w, 2057 w, 2975 w, 1736 w, 1650 w, 1554 w, 1541 w, 1517 w, 1474 w, 1455 w, 1432 w, 1404 w, 1353 w, 1336 w, 1246 w, 1215 w, 1192 m, 1098 w, 1068 w, 1026 w, 959 w, 904 w, 883 w, 864 w, 810 m, 708 s, 669 m.

Exact Mass (FAB^+) Calcd for $C_{31}H_{44}N_2ClIr$: 672.2822. Found: 672.2794.

Dicarbonylchloro[1,3-bis(adamantan-2-yl)-imidazolin-2-ylidene]iridium(I) [I(2-Ad)]Ir(CO)$_2$Cl[33]



A CH_2Cl_2 (5 mL) solution of [I(2-Ad)]Ir(COD)Cl (220 mg, 0.33 mmol) was placed under 1 atm of CO. The reaction mixture was stirred for 2 h. The color of the solution was changed from yellow-brown to pale yellow. The solvent was removed under reduced pressure. Hexane (5 mL) was added, and the collected precipitate was washed with Et_2O (0.5 mL) and pentane (2 mL X 3), and dried under vacuum to give the title compound as a yellow powder (170 mg, 84%).

Yellow powder (170 mg, 84%). R_f 0.83 (SiO_2, CH_2Cl_2).

^{1}H NMR ($CDCl_3$, 399.78 MHz) δ: 1.81-1.71 (m, 8H), 2.05-1.93 (m, 16H), 2.71 (s, 4H), 5.11 (s, 2H), 7.40 (s, 2H).

^{13}C NMR ($CDCl_3$, 100.53 MHz) δ: 27.1, 27.3, 31.46, 31.51, 33.1, 38.0, 38.2, 38.3, 65.5, 119.3, 168.1, 174.6, 181.1.

IR (ATR): 3155 w, 3014 w, 2970 w, 2911 m, 2855 m, 2361 w, 2339 w, 2055 s, 1964 s, 1739 s, 1561 w, 1542 w, 1452 m, 1416 m, 1366 s, 1215 s, 1173 m, 1097 w, 1058 w, 1028 w, 982 w, 958 w, 904 w, 810 w, 727 m, 703 m, 667 w.

Exact Mass (FAB$^+$) Calcd for $C_{25}H_{32}O_2N_2ClIr$: 620.1782. Found: 620.1776.

The infrared carbonyl stretching frequencies of [Ir(I(2-Ad))(CO)$_2$Cl] (ν_{co}^{Ir}) in CH_2Cl_2 appeared at 2062.50 and 1980.54 cm^{-1}. The average of the frequencies for the iridium complex ($\nu_{co}^{av/Ir}$) is therefore 2021.52. The TEP value for I(2-Ad) was determined to be 2049.4, using the following equation:[34]

$$TEP = 0.8475\ \nu_{co}^{av/Ir} + 336.2$$

The buried volume, $\%V_{bur}$, was calculated with SambV_{ca}, using the crystal structures of [Ir(I(2-Ad))(cod)Cl] (data are shown in the next section), [Ir(I(1-Ad)(cod)Cl] (CSD Refcode: QIWMEP), [Ir(ICy)(cod)Cl] (CSD Refcode: QIWLVE), [Ir(IMes)(cod)Cl] (CSD Refcode: CIVNOL), [Ir(IPr)(cod)Cl] (CSD Refcode: QIWMAL), and [Ir(PCy_3)(COD)(pyridine)PF_6] (CSD Refcode: JAFFOL) deposited with the Cambridge Structural Database (CSD). The parameters used for the SambV_{ca} calculations were as follows:[35] 3.5 Å was selected as the value for the sphere radius, 2.00 Å was used as the distance between the coordinated atom center of the ligand and the metal atom center, hydrogen atoms were included, and Bondi radii scaled by 1.17 were used. These parameters applied are identical to those in literature examples[36] allowing a direct comparison with the calculated values.

1.4.9 X-Ray Crystallographic Structure Analysis of [Ir(I(2-Ad))$(CO)_2$Cl]

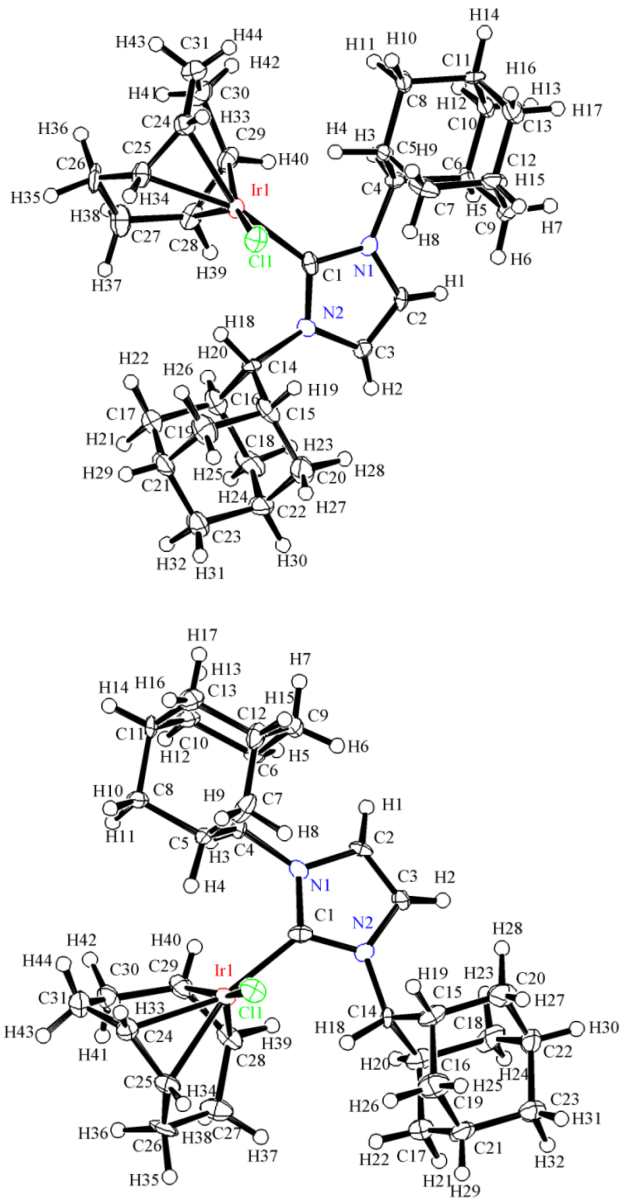


Table S1. Crystal Data and structure refinement for compound [Ir(I(2-Ad))$(CO)_2$Cl]

Empirical Formula	$C_{31}H_{44}N_2ClIr$
Formula Weight	672.37
Crystal Color, Habit	yellow, platelet
Crystal Dimensions	0.150 X 0.100 X 0.010 mm
Crystal System	monoclinic
Lattice Type	Primitive
Lattice Parameters	a = 10.4452(2) Å
	b = 7.3064(2) Å

	c = 34.6675(7) Å
	β = 91.7266(7) ^{o}
	V = 2644.52(9) Å^3
Space Group	$P2_1/n$ (#14)
Z value	4
D_{calc}	1.689 g/cm^3
F000	1352.00
μ(CuKα)	106.429 cm^{-1}
Diffractometer	R-AXIS RAPID
Radiation	CuKα (λ = 1.54187 Å)
	graphite monochromated
Voltage, Current	50kV, 100mA
Temperature	-150.0^{o}C
Detector Aperture	460 x 256 mm
Data Images	60 exposures
ω oscillation Range (χ=54.0, ϕ=0.0)	80.0 - 260.0^{o}
Exposure Rate	135.0 sec./^{o}
ω oscillation Range (χ=54.0, ϕ=60.0)	80.0 - 260.0^{o}
Exposure Rate	135.0 sec./^{o}
ω oscillation Range (χ=54.0, ϕ=120.0)	80.0 - 260.0^{o}
Exposure Rate	135.0 sec./^{o}
ω oscillation Range (χ=54.0, ϕ=180.0)	80.0 - 260.0^{o}
Exposure Rate	135.0 sec./^{o}
ω oscillation Range (χ=54.0, ϕ=240.0)	80.0 - 260.0^{o}
Exposure Rate	135.0 sec./^{o}
Detector Position	127.40 mm
Pixel Size	0.100 mm
$2\theta_{max}$	136.4^{o}
No. of Reflections Measured	Total: 27352
	Unique: 4831 (R_{int} = 0.0891)
Corrections	Lorentz-polarization
	Absorption
	(trans. factors: 0.704 - 0.899)

1.5 References

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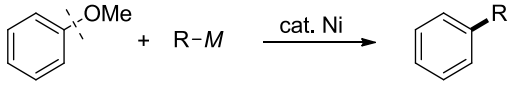
Chapter 2

Nickel-catalyzed Cross-Coupling of Anisoles with Trimethylaluminum through the Cleavage of Carbon–Oxygen Bonds

2.1 Introduction

Ni-catalyzed cross-coupling reactions involving the cleavage of C(aryl)-OMe bonds have been actively studied (Scheme 1).[1] Wenkert demonstrated the nickel-catalyzed cross-coupling of methoxyarenes with Grignard reagents as early as 1979. In 2008, nearly 20 years after Wenkert's report, the first application of the Wenkert reaction to organoboron cross-coupling was reported by our laboratory. To date, the nucleophiles that can be used for the substitution of methoxyarenes include Grignard,[2] organolithium,[3] organoboron,[4] organozinc,[5] hydride (described in Chapter1), amine,[6] and boron[7] reagents. It has been reported that the scope of aryl ether substrates is strongly dependent on the nature of the nucleophile, probably because it influences the mechanism of the key C-O bond cleavage process, as indicated by several theoretical studies.[8] Therefore, the systematic exploration of the various nucleophiles used in nickel-catalyzed crosscoupling of aryl ethers is of fundamental importance in terms of understanding the nickel-mediated activation of inert C-O bonds. We report herein on the first cross-coupling of anisole derivatives with trimethylaluminum ($AlMe_3$).

Scheme 1. Ni-Catalyzed C-C Bond Formation via C-OMe Bond Cleavage



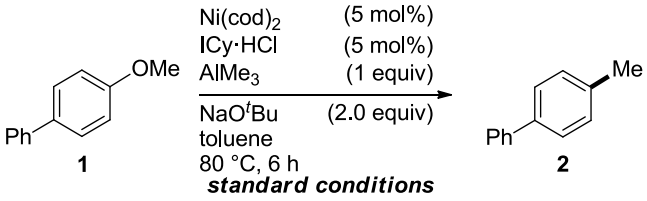
M = Mg: Wenkert (1979), Dankwardt (2004) and others
B: Our group (2008, 2014)
Zn: Wang and Uchiyama (2012)
Li: Rueping (2014), Hornillos and Feringa (2016)
Al: *This work*

2.2 Results and Discussion

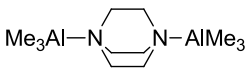
First, the nickel-catalyzed methylation of 4-methoxybiphenyl (**1**) with $AlMe_3$ was examined (Table 1). After screening various conditions, it was found that the reaction of **1** (0.25 mmol) with $AlMe_3$ (0.25 mmol, 1.8 M solution in toluene) in the presence of $Ni(cod)_2$ (5 mol%) and ICy·HCl (5 mol %) in toluene at 80 °C for 18 h gave 4-methylbiphenyl (**2**) in 97% yield according to GC analysis (entry 1). This reaction did not proceed in the absence of a nickel catalyst, which excludes a pathway via the S_NAr mechanism (entry 2).[9] Replacing the ICy ligand with PCy_3[1] (entry 4) or other NHCs (entries 5-7) led to a substantial decrease in the yield of **2**, highlighting the prominent ability of ICy to activate C-OMe bonds.[4c] Methylation occurred much less efficiently when $Ni(acac)_2$ or

$Ni(OAc)_2$ was used as the catalyst precursor instead of $Ni(cod)_2$ (entries 8 and 9). Air-stable $DABCO{\cdot}2AlMe_3$[10] (entry 10) did not provide the corresponding cross-coupling product under these conditions. The use of $Al(OEt)Me_2$ (1.66 M in toluene solution) in place of $AlMe_3$ afforded **2** in 93% yield (entry 11), although the yield decreased to 48% when 0.33 equiv of $AlMe_3$ was used (entry 12). The amount of base added is critical, as evidenced by the fact that no methylated product **2** was formed when the amount of NaO^tBu was decreased to 10 mol % (entry 13).

Table 1. Optimization of Reaction Conditions[a]



entry	variation from the "standard conditions"	GC yields/% 2	1
1	none	97	0
2	without $Ni(cod)_2$, ICy·HCl	0	85
3	without ICy·HCl	3	56
4	PCy_3 instead of ICy·HCl	5	60
5	IPr·HCl instead of ICy·HCl	39	43
6	IMes·HCl instead of ICy·HCl	14	15
7	I^{t}Bu·HCl instead of ICy·HCl	6	50
8	$Ni(acac)_2$instead of $Ni(cod)_2$	10	68
9	$Ni(OAc)_2$ instead of $Ni(cod)_2$	8	65
10	DABAL-2$AlMe_3$ instead of $AlMe_3$	23	66
11	$Al(OEt)Me_2$ instead of $AlMe_3$	93	0
12	$AlMe_3$ 0.33 equiv instead of 1.0 equiv	48	32
13	NaO^tBu (10 mol%) instead of 2 equiv.	0	88
14	$ICy{\cdot}HBF_4$ instead of ICy·HCl	>99 (99[b])	0



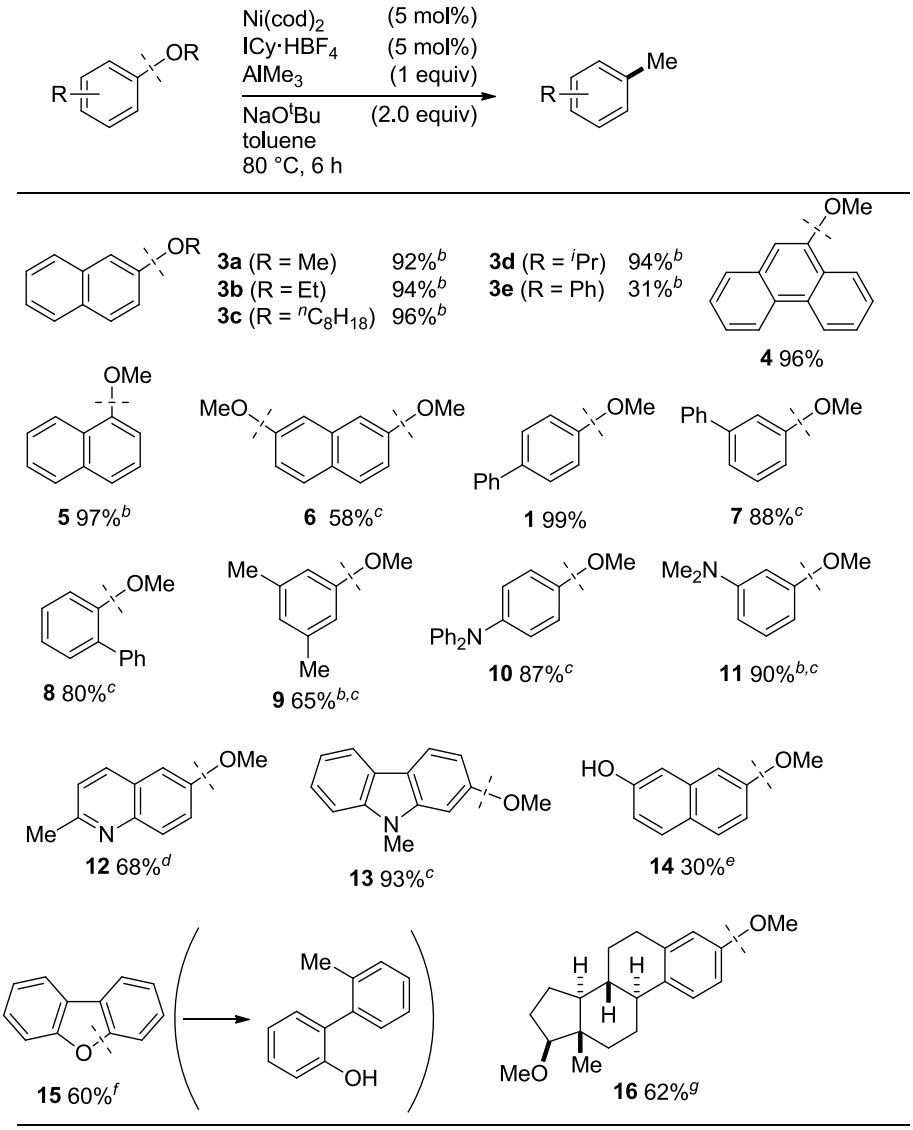
DABAL-2$AlMe_3$

[a] Reaction conditions: **1** (0.25 mmol), $AlMe_3$ (0.25 mmol), $Ni(cod)_2$ (0.013 mmol), ligand (0.013 mmol), NaO^tBu (0.50 mmol) in toluene (1.0 mL) for 6 h at 80 °C. [b] For 6 h instead of 18 h, and the yield shown is an isolated yield.

The scope of this nickel-catalyzed methylation using a series of aryl methyl ethers was next investigated (Table 2). Primary alkoxy groups, including EtO (**3b**) and the longer $^nC_8H_{17}O$ groups (**3c**), were efficiently methylated under current conditions. Notably, the bulkier ^{i}PrO group also underwent this methylation efficiently (**3d**), whereas the PhO group was less reactive under the current conditions (**3e**). Alkoxy groups on polyaromatic scaffolds such as phenanthrene (**4**) successfully underwent to provide the corresponding methylated arene. This reaction also exhibited a high level of tolerance toward substrates bearing a bulky ortho substituent (**8**). Less reactive electron-rich anisoles (**9**-**11**) also underwent cross-coupling to provide the corresponding methylated products.

Heteroarenes such as electron-deficient quinolone (**12**) and electron-rich carbazole (**13**) were also good substrates. This methylation method was also applicable to dibenzofuran (**15**), the reaction of which led to a ring-opened product. Methylation of estradiol derivative (**16)** also proceeded to form the corresponding methylated product.

Table 2. Scope of Substrate[a]

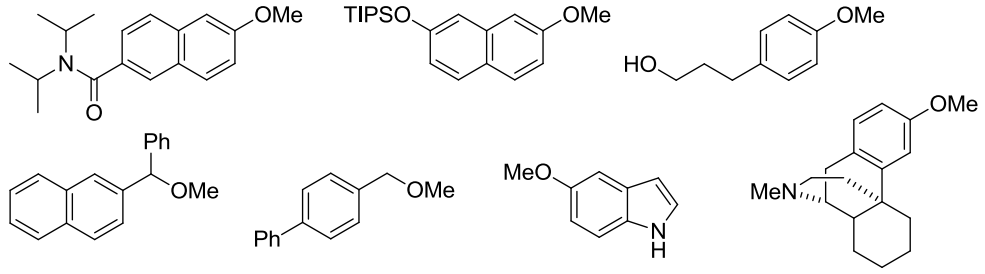


[a] Reaction conditions: Aryl ether (0.25 mmol), $AlMe_3$ (0.25 mmol), $Ni(cod)_2$ (0.013 mmol), ICy·HBF_4 (0.013 mmol), NaO^tBu (0.50 mmol) in toluene (1.0 mL) at 80 °C for 6 h. [b] Yield was determined by GC analysis because of the volatility of the product. [c] $Ni(cod)_2$ (0.025 mmol), ICy·HBF_4 (0.025 mmol) at 100 °C for 6 h. [d] $Ni(cod)_2$ (0.025 mmol), ICy·HBF_4 (0.025 mmol) at 80 °C for 6 h. [e] $AlMe_3$ (0.50 mmol), $Ni(cod)_2$ (0.025 mmol), ICy·HBF_4 (0.025 mmol), NaO^tBu (0.75 mmol) at 120 °C for 6 h. [f] $Ni(cod)_2$ (0.025 mmol), ICy·HBF_4 (0.025 mmol) at 80 °C for 18 h. [g] $Ni(cod)_2$ (0.038 mmol), ICy·HBF_4 (0.038 mmol) at 80 °C for 18 h.

Ineffective substrates under current conditions are shown in Table 3. Secondary benzylic ether and benzyl ether

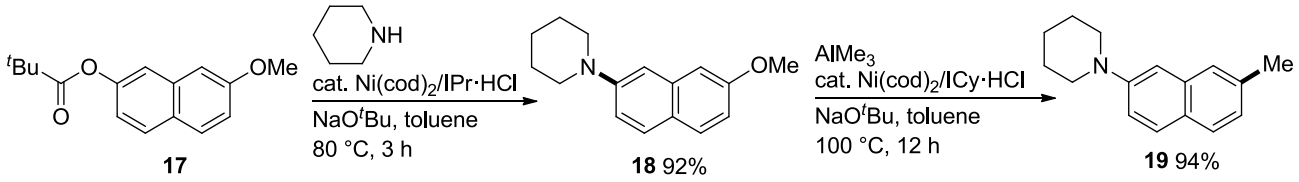
lacking a fused aromatic ring were found to be less reactive.

Table 3. Ineffective Substrates

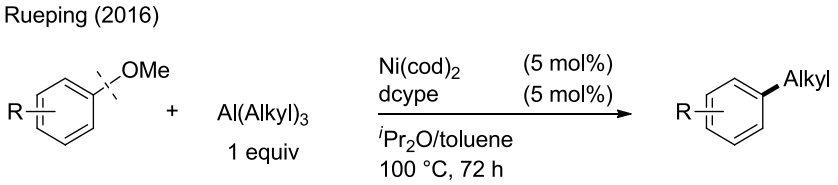


The difference in reactivity between aryl methyl ethers and aryl carboxylates in nickel-catalyzed C-O bond functionalization allows rapid sequential functionalization of aromatic frameworks (Scheme 2). The pivalate group in **17** could be aminated through our previously reported cross-coupling reaction using an IPr ligand without affecting the methoxy group.[11] The methoxy group in **18** was subsequently methylated under our developed condition to form **19**.

Scheme 2. Sequential Functionalization of Two Different Inert C-O Bonds



An independent work on the nickel-catalyzed alkylation of aryl methyl ethers with trialkylaluminium was reported by Rueping.[12]



2.3 Conclusion

In conclusion, a nickel-catalyzed methylation of anisole derivatives using $AlMe_3$ was developed. This reaction represents the first cross-coupling of aryl ethers with an organoaluminum reagent. Given the profound effects of a methyl group in drug discovery processes,[13] expanding the repertoire of methylation methods by our development reported here will benefit synthetic chemists.

2.4 Experimental Section

2.4.1 General Information

^{1}H and ^{13}C NMR spectra were recorded on a JEOL ECS-400 spectrometer (JEOL, Tokyo, Japan) or VARIAN UNITY INOVA-600 spectrometer in $CDCl_3$ with tetramethylsilane as an internal reference standard. NMR data have been reported as follows: chemical shift (δ) in ppm, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, and m = multiplet), coupling constant (*J*) in Hz, and integration. Infrared spectra (IR) were obtained on a JASCO FT/IR-4000 spectrometer, and the absorptions have been reported in reciprocal centimeters with the following relative intensities: s (strong), m (medium), or w (weak). Mass spectra were obtained on a Shimadzu GCMS-QP 5000 or GCMS-QP 2010 instrument with an ionization voltage of 70 eV. High resolution mass spectra (HRMS) were obtained on a JEOL JMS-DX303. Analytical gas chromatography (GC) was carried out on Shimadzu GC-2014, equipped with a flame ionization detector. Melting points were determined using a Yamato melting point apparatus. Column chromatography was performed over SiO_2 (Silycycle Silica Flash F60 (230-400 mesh)) and NH Silica (Silica Gel 60 (spherical) NH_2 (40-50 μm)). Some of the compounds were purified by LC-908 HPLC (GPC).

2.4.2 Materials

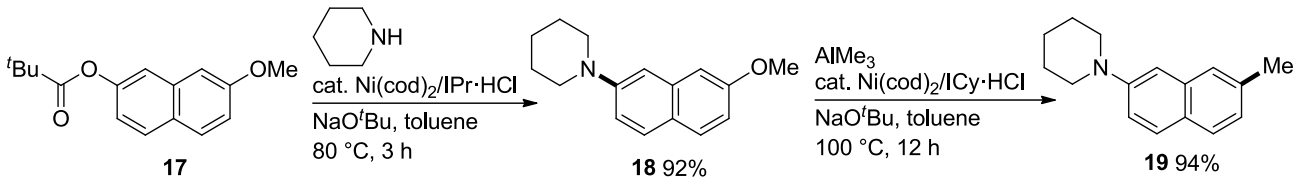
Toluene (for Organic Synth.) was purchased from Wako Chemicals and used as received. $Ni(cod)_2$ was purchased from Strem Chemicals and used as received. $AlMe_3$ (1.8 M in toluene solution) was purchased from TCI and used as received. $Al(OEt)Me_2$ (1.66 M in touene solution) was prepared according to the literature procedure.[14] PCy_3 (Sigma-Aldrich), IPr·HCl (TCI), IMes·HCl (TCI), ICy·HBF_4 (TCI) and NaO^{t}Bu (TCI) were purchased from commercial suppliers and used as received. ICy·HCl[15] and I^{t}Bu[16] were prepared according to the literature procedures. Aryl ethers **1** (Wako), **3a** (TCI), **3b** (TCI), **5** (TCI), **6** (TCI), **7** (TCI), **8** (TCI), **9** (TCI), **10** (Sigma-Aldrich), **11** (TCI), **12** (TCI), **14** (Sigma-Aldrich), **15** (TCI) were purchased from commercial suppliers and purified by distillation over CaH_2 prior to use. Aryl ethers **3c** (CAS 70617-42-4),[17] **3d** (CAS 15052-09-2),[18] **3e** (CAS 19420-29-2),[19] **4** (CAS 5085-74-5)[20] and **16** (CAS 4954-14-7)[21] were prepared from the corresponding phenols or alcohols by treatment with NaH followed by the addition of the corresponding alkyl halide. Ethers **13** (CAS 39027-93-5)[22] and **17** (CAS 1228374-26-2)[23] were prepared according to the literature procedures.

2.4.3 Typical Procedure for Ni/ICy-Catalyzed Methylation of Anisoles

$Ni(cod)_2$ (3.4 mg, 0.025 mmol), ICy·HBF_4 (4 mg, 0.025 mmol), NaO^{t}Bu (48 mg, 0.50 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 at room temperature for 3 min. An aryl methyl ether (0.25 mmol) in toluene (0.50 mL) and $AlMe_3$ (1.8 M in toluene solution, 0.14 mL, 0.25 mmol) were then added to the vial and the cap was closed.

The contents of the vial were stirred at 80 °C for 6 or 18 h. The reaction mixture was cooled to room temperature, and the crude mixture was then treated with EtOH. The resulting mixture was filtered through a pad of silica gel, and then analyzed by GC. The filtrate was concentrated *in vacuo* to give a residue, which was purified by flash column chromatography over silica gel.

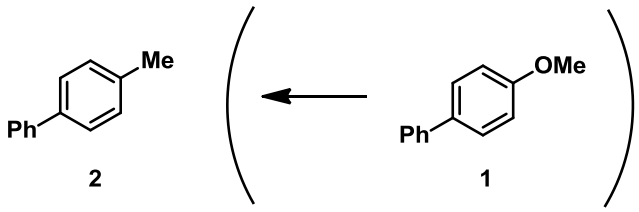
2.4.4 A Procedure for Nickel-Catalyzed Tandem C−O Bond Functionalization



1-(7-Methoxynaphthalen-2-yl)piperidine (**18**) was prepared according to the previously reported literature procedure.[1] $Ni(cod)_2$ (6.8 mg, 0.050 mmol), $ICy{\cdot}HBF_4$ (8 mg, 0.050 mmol), NaO^tBu (48 mg, 0.50 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 at room temperature for 3 min. **18** (0.25 mmol) in toluene (0.50 mL) and $AlMe_3$ (1.8 M in toluene solution, 0.14 mL, 0.25 mmol) was then added to the vial and the cap was closed. The contents of the vial were stirred at 100 °C for 12 h. The reaction mixture was cooled to room temperature, and the crude mixture was then treated with EtOH. The resulting mixture was filtered through a pad of silica gel, and then analyzed by GC. The filtrate was concentrated *in vacuo* to give a residue, which was purified by flash column chromatography over silica gel (hexane/EtOAc = 100/1) to give **19** as a white solid (59.0 mg, 94%).

2.4.5 Spectroscopic Data of Products

4-Methyl-1,1'-biphenyl (2) [CAS: 644-08-6].



The typical procedure was followed using **2** as the substrate.

White solid (41.6 mg, 80%). Rf 0.74 (SiO_2, hexane/EtOAc = 20/1).

^{1}H NMR ($CDCl_3$, 399.78 MHz) δ: 2.43 (s, 3H), 7.28 (d, J = 7.8 Hz, 2H), 7.35 (dd, J = 7.4, 7.4 Hz, 1H), 7.45 (dd, J = 7.4, 7.8 Hz, 2H), 7.52 (d, J = 8.2 Hz, 2H), 7.61 (d, J = 8.2 Hz, 2H).

^{13}C NMR ($CDCl_3$, 100.53 MHz) δ: 21.1, 126.95 (2C, overlapped peaks), 126.97, 128.7, 129.4, 137.0, 138.3, 141.1.

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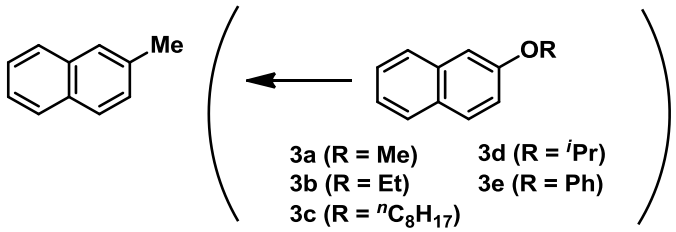
[1] Shimasaki, T.; Tobisu, M.; Chatani, N. *Angew. Chem., Int. Ed.*, **2010**, *49*, 2929.

Exact Mass (EI) Calcd for $C_{13}H_{12}$: 168.0939. Found: 168.0939.

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



The product was obtained from **3a**-**3e** under the typical conditions. The yield for this compound was determined by GC, because of its sublimability. The GC and ^{1}H NMR spectra of the compound were in agreement with those determined for an authentic sample.

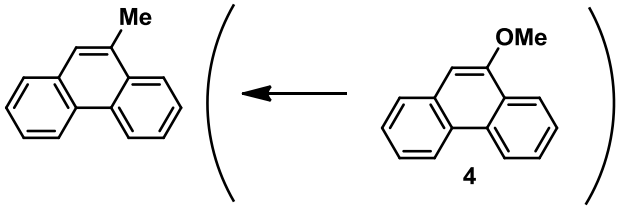
White solid. Rf 0.60 (Hexane/EtOAc = 20/1).

^{1}H NMR ($CDCl_3$, 399.78 MHz) δ: 2.53 (s, 3H), 7.33 (d, *J* = 8.2 Hz, 1H), 7.44 (dd, *J* = 7.8, 8.2 Hz, 2H), 7.60 (d, *J* = 8.2 Hz, 1H), 7.63 (s, 1H), 7.77 (d, *J* = 7.8 Hz, 1H), 7.81 (d, *J* = 7.8 Hz, 1H).

^{13}C NMR ($CDCl_3$, 100.53 MHz) δ: 21.7, 124.9, 125.8, 126.8, 127.2, 127.6, 127.7, 128.0, 131.7, 133.6, 135.4.

Exact Mass (EI) Calcd for $C_{11}H_{10}$: 142.0783. Found: 142.0783.

9-Methylphenanthrene [CAS: 883-20-5].



The typical procedure was followed using **4** as the substrate.

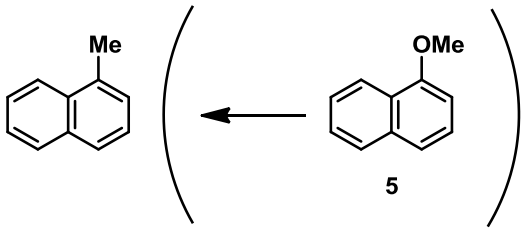
White solid (46.1 mg, 96%). Rf 0.46 (SiO_2, hexane/EtOAc = 20/1).

^{1}H NMR ($CDCl_3$, 399.78 MHz) δ: 2.75 (s, 3H), 7.61-7.57 (m, 3H), 7.69-7.66 (m, 2H), 7.82 (d, *J* = 7.3 Hz, 1H), 8.08 (d, *J* = 9.2 Hz, 1H), 8.66 (d, *J* = 7.8 Hz, 1H), 8.74 (d, *J* = 6.9 Hz, 1H).

^{13}C NMR ($CDCl_3$, 100.53 MHz) δ: 20.0, 122.4, 123.0, 124.6, 125.8, 126.2, 126.5, 126.6, 126.7, 127.8, 129.6, 130.4, 132.0, 132.1, 132.5.

Exact Mass (EI) Calcd for $C_{15}H_{12}$: 192.0939. Found: 192.0939.

1-Methylnaphthalene [CAS: 90-12-0].

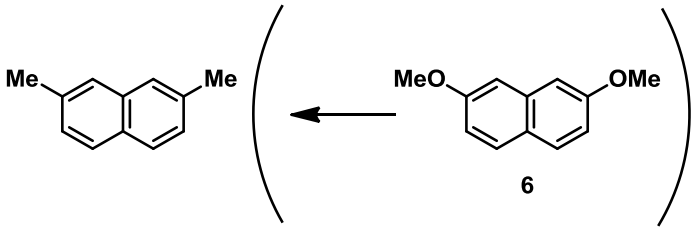


The product was obtained from **5** under the typical conditions. The yield for this compound was determined by GC, because of its volatility. The GC and ^{1}H NMR spectra of the compound were in agreement with those determined for an authentic sample.

Colorless oil. Rf 0.60 (Hexane/EtOAc = 100/1). ^{1}H NMR ($CDCl_3$, 399.78 MHz) δ: 2.73 (s, 3H), 7.34 (d, *J* = 7.3 Hz, 1H), 7.40 (dd, *J* = 7.3, 8.2 Hz, 1H), 7.53 (dd, *J* = 6.9, 8.2 Hz, 2H), 7.73 (d, *J* = 8.2 Hz, 1H), 7.87 (d, *J* = 7.8 Hz, 1H), 8.03 (d, *J* = 8.2 Hz, 1H). ^{13}C NMR ($CDCl_3$, 100.53 MHz) δ: 19.4, 124.1, 125.5, 125.6, 125.7, 126.3, 126.5, 128.5, 132.6, 133.5, 134.2.

Exact Mass (EI) Calcd for $C_{11}H_{10}$: 142.0783. Found: 142.0786.

2,7-Dimethylnaphthalene [CAS: 582-16-1].



The typical procedure was followed using **6** as the substrate except that 10 mol% of $Ni(cod)_2$ and 10 mol% of $ICy{\cdot}HBF_4$ were used, and the reaction was run at 100 °C for 6 h.

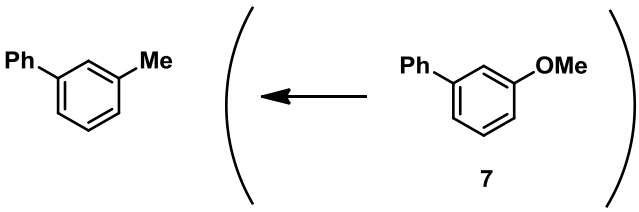
White solid (22.7 mg, 58%). Rf 0.46 (Hexane/EtOAc = 20/1).

^{1}H NMR ($CDCl_3$, 399.78 MHz) δ: 2.52 (s, 6H), 7.27 (d, *J* = 8.2 Hz, 2H), 7.54 (s, 2H), 7.71 (d, *J* = 8.2 Hz, 2H).

^{13}C NMR ($CDCl_3$, 100.53 MHz) δ: 21.7, 126.2, 127.2, 127.4, 129.9, 133.9, 135.4.

Exact Mass (EI) Calcd for $C_{12}H_{12}$: 156.0939. Found: 156.0938.

3-Methyl-1,1'-biphenyl [CAS: 643-93-6].



The typical procedure was followed using **7** as the substrate except that 10 mol% of $Ni(cod)_2$ and 10 mol% of

ICy·HBF_4 were used, and the reaction was run at 100 °C for 6 h.

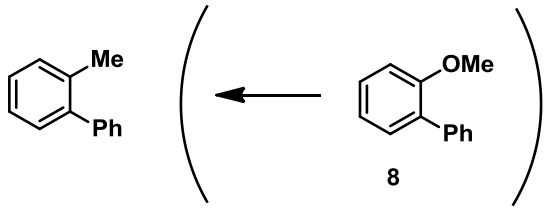
Colorless oil (37.0 mg, 88%). Rf 0.54 (SiO_2, hexane/EtOAc = 100/1).

^{1}H NMR ($CDCl_3$, 399.78 MHz) δ: 2.44 (s, 3H), 7.18 (d, *J* = 7.4, 1H), 7.35 (dd, *J* = 7.3, 7.3 Hz, 2H), 7.46-7.40 (m, 4H), 7.61 (dd, *J* = 7.3, 8.7 Hz, 2H).

^{13}C NMR ($CDCl_3$, 100.53 MHz) δ: 21.5, 124.3, 127.2 (2C, overlapped peaks), 127.96, 127.97, 128.64, 128.67, 138.3, 141.2, 141.3.

Exact Mass (EI) Calcd for $C_{13}H_{12}$: 168.0939. Found: 168.0940.

2-Methyl-1,1'-biphenyl [CAS: 643-58-3].



8

The typical procedure was followed using **8** as the substrate except that 10 mol% of $Ni(cod)_2$ and 10 mol% of ICy·HBF_4 were used, and the reaction was run at 100 °C for 6 h.

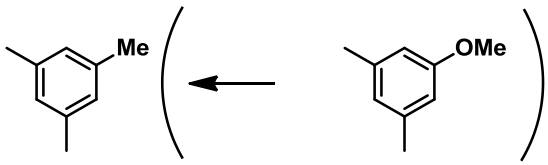
Colorless oil (33.6 mg, 80%). Rf 0.68 (SiO_2, hexane/EtOAc = 20/1).

^{1}H NMR ($CDCl_3$, 399.78 MHz) δ: 2.28 (s, 3H), 7.27-7.24 (m, 4H), 7.36-7.31 (m, 3H), 7.41 (dd, *J* = 7.8, 8.7 Hz, 2H).

^{13}C NMR ($CDCl_3$, 100.53 MHz) δ: 20.5, 125.7, 126.7, 127.2, 128.0, 129.2, 129.8, 130.3, 135.3, 141.9, 141.9.

Exact Mass (EI) Calcd for $C_{13}H_{12}$: 168.0939. Found: 168.0937.

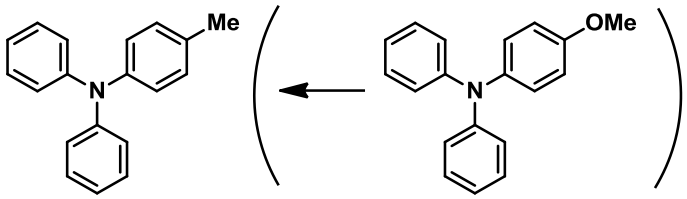
Mesitylene [CAS: 108-67-8].



9

The typical procedure was followed using **9** as the substrate except that 10 mol% of $Ni(cod)_2$ and 10 mol% of ICy·HBF_4 were used, and the reaction was run at 100 °C for 6 h. The yield was determined by GC analysis using an authentic sample (65%).

4-Methyl-*N*,*N*-diphenylaniline [CAS: 4316-53-4].



10

The typical procedure was followed using **10** as the substrate except that 10 mol% of $Ni(cod)_2$ and 10 mol% of $ICy{\cdot}HBF_4$ were used, and the reaction was run at 100 °C for 6 h.

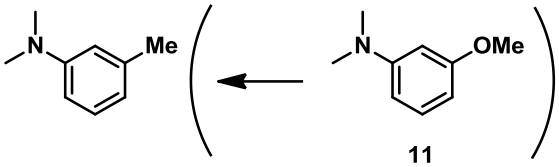
White solid (56.4 mg, 87%). Rf 0.37 (SiO_2, hexane/EtOAc = 20/1).

^1H NMR ($CDCl_3$, 399.78 MHz) δ: 2.38 (s, 3H), 7.08-7.01 (m, 4H), 7.16-7.11 (m, 6H), 7.28 (dd, *J* = 7.3, 8.2 Hz, 4H).

^{13}C NMR ($CDCl_3$, 100.53 MHz) δ: 20.8, 122.2, 123.6, 124.9, 129.1, 129.9, 132.7, 145.2, 148.0.

Exact Mass (EI) Calcd for $C_{19}H_{17}N$: 259.1361. Found: 259.1364.

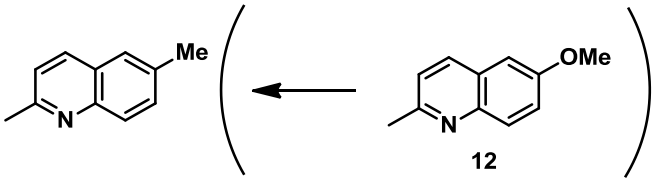
***N*,*N*,3-Trimethylaniline [CAS: 121-72-2].**



11

The typical procedure was followed using **11** as the substrate except that 10 mol% of $Ni(cod)_2$ and 10 mol% of $ICy{\cdot}HBF_4$ were used, and the reaction was run at 100 °C for 6 h. The yield was determined by GC analysis using an authentic sample (90%).

2,6-Dimethylquinoline [CAS: 877-43-0].



12

The typical procedure was followed using **12** as the substrate except that 10 mol% of $Ni(cod)_2$ and 10 mol% of $ICy{\cdot}HBF_4$ were used, and the reaction was run at 80 °C for 6 h.

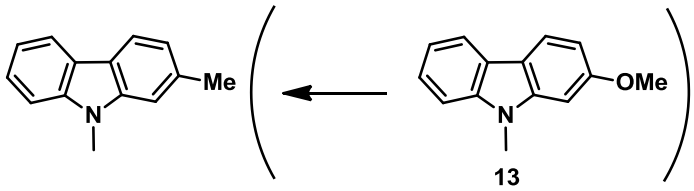
White solid (68%). Rf 0.05 (SiO_2, hexane/EtOAc = 20/1).

^1H NMR ($CDCl_3$, 399.78 MHz) δ: 2.51 (s, 3H), 2.72 (s, 3H), 7.24 (d, *J* = 8.7 Hz, 1H), 7.52-7.49 (m, 2H), 7.90 (d, *J* = 8.7 Hz, 1H), 7.95 (d, *J* = 8.7 Hz, 1H).

^{13}C NMR ($CDCl_3$, 100.53 MHz) δ: 21.4, 25.2, 121.9, 126.4, 126.5, 128.3, 131.6, 135.4, 135.5, 146.4, 158.0.

Exact Mass (EI) Calcd for $C_{11}H_{11}N$: 157.0892. Found: 157.0892.

2,9-Dimethyl-9H-carbazole [CAS: 24075-47-6].



13

The typical procedure was followed using **13** as the substrate except that 10 mol% of $Ni(cod)_2$ and 10 mol% of $ICy{\cdot}HBF_4$ were used, and the reaction was run at 100 °C for 6 h.

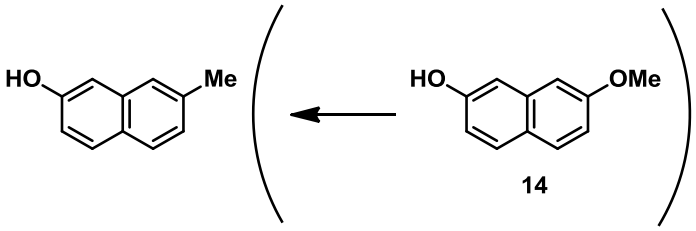
White solid (45.4 mg, 93%). Rf 0.48 (SiO_2, hexane/EtOAc = 100/1).

^1H NMR ($CDCl_3$, 399.78 MHz) δ: 2.60 (s, 3H), 3.81 (s, 3H), 7.08 (d, J = 7.8 Hz, 1H), 7.26-7.21 (m, 2H), 7.387 (d, J = 8.2 Hz, 1H), 7.47 (dd, J = 6.8, 8.2 Hz, 1H), 7.99 (d, J = 7.8 Hz, 1H), 8.07 (d, J = 7.8 Hz, 1H).

^{13}C NMR ($CDCl_3$, 100.53 MHz) δ: 22.2, 28.9, 108.3, 108.6, 118.7, 119.91, 119.93, 120.3, 120.4, 122.8, 125.0, 135.8, 141.0, 141.4.

Exact Mass (EI) Calcd for $C_{14}H_{13}N$: 195.1048. Found: 195.1050.

7-Methylnaphthalen-2-ol [CAS: 26593-50-0].



14

The typical procedure was followed using **14** as the substrate except that 0.50 mmol of $AlMe_3$, 10 mol% of $Ni(cod)_2$, 10 mol% of $ICy{\cdot}HBF_4$ and 0.75 mmol of NaO^tBu were used, and the reaction was run at 100 °C for 6 h. The mixture was then cooled to room temperature and treated with a saturated aqueous solution of NH_4Cl, and the resulting mixture was extracted with EtOAc. The combined extracts were then washed with brine, dried ($MgSO_4$) and concentrated to give a residue, which was purified by column chromatography (hexane/EtOAc = 20/1) to give a white solid, which was further purified by GPC.

White solid (21.4 mg, 54%). Mp 111.4-112.4 °C. Rf 0.06 (SiO_2, Hexane/EtOAc = 20/1).

^1H NMR ($CDCl_3$, 399.78 MHz) δ: 2.49 (s, 3H), 5.09 (s, 1H), 7.06-7.02 (m, 2H), 7.17 (d, J = 8.2 Hz, 1H), 7.45 (s, 1H), 7.67 (d, J = 8.7 Hz, 1H), 7.70 (d, J = 8.2 Hz, 1H).

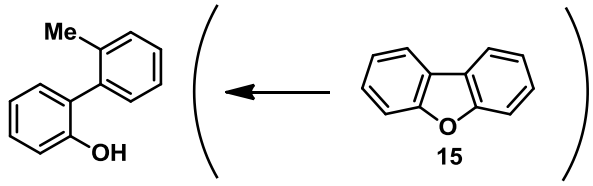
^{13}C NMR ($CDCl_3$, 100.53 MHz) δ: 21.7, 108.9, 116.7, 125.4, 125.9, 127.2, 127.5, 129.5, 134.8, 136.2, 153.4.

IR (ATR): 3271 s, 3048 s, 2909 w, 1904 w, 1636 m, 1607 m, 1512 m, 1485 w, 1469 w, 1431 m, 1398 w, 1351 m, 1316 w, 1244 m, 1211 m, 1184 m, 1164 m, 1123 w, 958 m, 895 m, 830 s, 784 w, 743 w, 691 w.

MS, *m/z* (relative intensity, %): 158 (100), 157 (53), 128 (13).

Exact Mass (EI) Calcd for $C_{11}H_{10}O$: 158.0732. Found: 158.0732.

2'-Methyl-[1,1'-biphenyl]-2-ol [CAS: 77897-02-0].



The typical procedure was followed using **15** as the substrate except that 10 mol% of $Ni(cod)_2$ and 10 mol% of $ICy{\cdot}HBF_4$ were used, and the reaction was run at 80 °C for 18 h. The mixture was then cooled to room temperature and treated with a saturated aqueous solution of NH_4Cl, and the resulting mixture was extracted with EtOAc. The combined extracts were then washed with brine, dried ($MgSO_4$) and concentrated to give a residue, which was purified by column chromatography (hexane/EtOAc = 20/1).

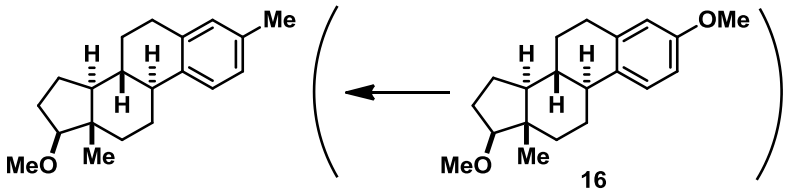
Colorless oil (27.6 mg, 60%). Rf 0.11 (SiO_2, hexane/EtOAc = 20/1).

^{1}H NMR ($CDCl_3$, 399.78 MHz) δ: 2.18 (s, 3H), 4.80 (s, 1H), 6.98 (dd, *J* = 7.3 Hz, 8.2 Hz, 2H), 7.12 (d, *J* = 7.3 Hz, 1H), 7.35-7.24 (m, 6H).

^{13}C NMR ($CDCl_3$, 100.53 MHz) δ: 19.7, 115.3, 120.4, 126.4, 127.7, 128.5, 129.1, 130.1, 130.5, 130.7, 135.7, 137.4, 152.5.

Exact Mass (EI) Calcd for $C_{13}H_{12}O$: 184.0888. Found: 184.0885.

(8R,9S,13S,14S,17S)-17-Methoxy-3,13-dimethyl-7,8,9,11,12,13,14,15,16,17-decahydro-6H-cyclopenta[a]phenanthrene



The typical procedure was followed using **16** as the substrate except that 15 mol% of $Ni(cod)_2$ and 15 mol% of $ICy{\cdot}HBF_4$ were used, and the reaction was run at 80 °C for 18 h. A residue was purified by column chromatography (hexane/EtOAc = 20/1) to give a white solid, which was further purified by GPC.

White solid (44.1 mg, 62%). Mp 142.7-143.5 °C. Rf 0.34 (SiO_2, hexane/EtOAc = 20/1).

^{1}H NMR ($CDCl_3$, 399.78 MHz) δ: 0.79 (s, 3H), 1.60-1.18 (m, 7H), 1.74-1.66 (m, 1H), 1.92-1.86 (m, 1H), 2.14-2.03 (m, 2H), 2.35-2.19 (m, 5H), 2.91-2.81 (m, 2H), 3.33 (t, *J* = 8.3 Hz, 1H), 3.39 (s, 3H), 6.92 (s, 1H), 6.97 (d, *J* = 8.0 Hz, 1H), 7.19 (d, *J* = 8.0 Hz, 1H).

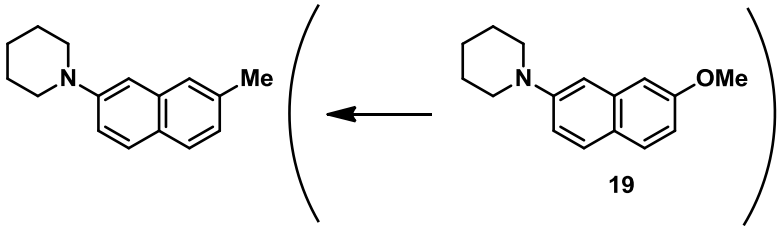
^{13}C NMR ($CDCl_3$, 100.53 MHz) δ: 11.5, 20.8, 23.0, 26.3, 27.2, 27.7, 29.5, 38.1, 38.5, 43.2, 44.2, 50.4, 57.9, 90.8, 125.3, 126.3, 129.6, 135.0, 136.5, 137.3.

IR (ATR): 2963 m, 2931 s, 2915 s, 2871 m, 2854 m, 2817 m, 1640 w, 1608 w, 1515 m, 1449 m, 1384 m, 1333 w, 1263 w, 1216 m, 1193 m, 1167 m, 1120 m, 1104 s, 1014 w, 993 w, 962 w, 912 m, 880 w.

MS, *m/z* (relative intensity, %): 285 (18), 284 (82), 212 (20), 211 (100), 158 (33), 157 (19), 156 (13), 143 (14).

Exact Mass (EI) Calcd for $C_{20}H_{28}O$: 284.2140. Found: 284.2142.

1-(7-Methylnaphthalen-2-yl)piperidine



The typical procedure was followed using **19** as the substrate except that 0.25 mmol of $AlMe_3$, 10 mol% of $Ni(cod)_2$, 10 mol% of $ICy{\cdot}HBF_4$ and 0.50 mmol of NaO^tBu were used, and the reaction was run at 100 °C for 12 h.

White solid (59.0 mg, 94%). Mp 82.5-83.7 °C. Rf 0.49 (NH Silica, Hexane/EtOAc = 20/1).

^{1}H NMR ($CDCl_3$, 399.78 MHz) δ: 1.68-1.63 (m, 2H), 1.83-1.77 (m, 4H), 2.51 (s, 3H), 3.27 (t, *J* = 5.7 Hz, 4H), 7.09 (s, 1H), 7.14 (d, *J* = 8.2 Hz, 1H), 7.24 (d, *J* = 8.7 Hz, 1H), 7.50 (s, 1H), 7.64 (d, *J* = 8.2 Hz, 1H), 7.69 (d, *J* = 8.7 Hz, 1H) .

^{13}C NMR ($CDCl_3$, 100.53 MHz) δ: 21.7, 24.4, 25.9, 51.0, 109.9, 119.3, 125.3, 125.8, 126.5, 127.2, 128.2, 134.9, 135.6, 150.2.

IR (ATR): 2933 m , 2852 w, 2796 w, 1629 s, 1605 m, 1572 w, 1512 w, 1449 m, 1388 m, 1353 w, 1317 w, 1253 m, 1204 s, 1154 w, 1121 s, 1070 w, 1029 m, 958 m, 915 w, 888 m, 862 m, 827 s, 739 w, 681 w, 655 w.

MS, *m/z* (relative intensity, %): 226 (17), 225 (100), 224 (71), 169 (16), 141 (16).

Exact Mass (EI) Calcd for $C_{16}H_{19}N$: 225.1518. Found: 255.1516.

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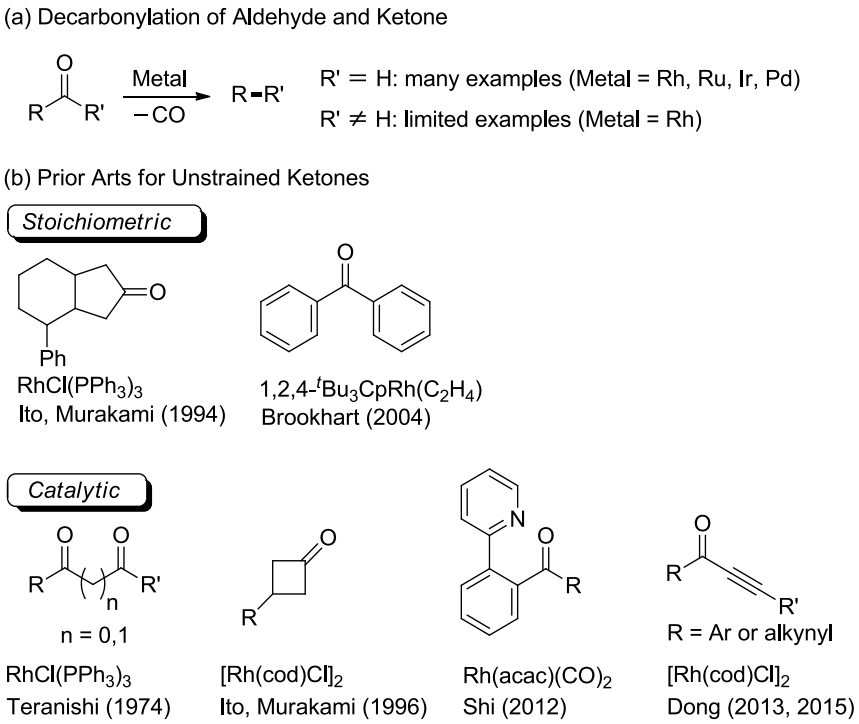
Chapter 3

Nickel-Mediated Decarbonylation of Simple Unstrained Ketones through the Cleavage of Carbon−Carbon Bonds

3.1 Introduction

The transition metal-mediated decarbonylation of aldehydes, known as the Tsuji−Wilkinson decarbonylation, is widely used in organic synthesis.[1] In contrast, the decarbonylation of ketones is a much more difficult process because it requires the cleavage of two carbon-carbon bonds, which are both kinetically and thermodynamically more stable than the carbon-hydrogen bond of a formyl group (Scheme 1a).[2] In fact, there are only two examples of the decarbonylation of simple ketones (Scheme 1b). A pioneering work regarding the decarbonylation of strained and unstrained cyclic aliphatic ketone was reported by Ito and Murakami, in which a stoichiometric amount of Wilkinson's complex was used.[3] Brookhart then reported on the decarbonylation of aromatic ketones using a stoichiometric amount of a rhodium complex bearing a bulky cyclopentadienyl ligand.[4] Catalytic reactions have also been reported. However, applicable substrates are limited to diketones,[5] strained ketones,[6] ketones containing a directing group[7] and alkynyl ketones.[8] Therefore, rhodium complexes are essential for all of the decarbonylation reactions of ketones that have been reported to date. The first example of a nickel system capable of mediating the decarbonylation of simple diaryl ketones is described herein.

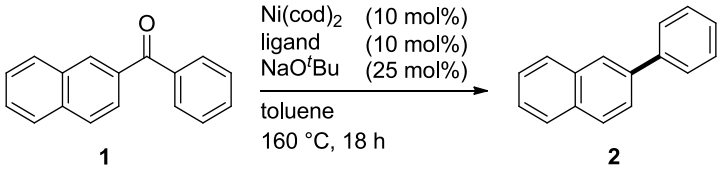
Scheme 1. Metal Complex-Mediated Decarbonylation of Unstrained Aldehydes and Ketones



3.2 Results and Discussion

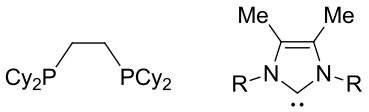
The effect of ligands was initially evaluated in the nickel-catalyzed decarbonylation of aromatic ketone **1** (Table 1). The addition of phosphine ligands such as PCy_3 and dcype did not lead to the formation of decarbonylated product **2** (Table 1, entries 1 and 2). Relatively electron-rich *N*-heterocyclic carbene ligands (NHC) were then tested to facilitate the required C-C bond activation process. Among the NHC ligands examined, $IMes^{Me}$ was found to be the most effective ligand, providing the desired decarbonylation product in 21% yield, and 72% of the starting ketone was recovered under the catalytic conditions (Table 1, entry 6). The yield increased to 63% when the amount of nickel and ligand were increased to one equivalent relative to the ketone substrate (Table 1, entry 9). It is noteworthy that no byproducts were formed in this reaction, and that the starting ketone **1** was recovered in 38% yield.

Table 1. Effect of Ligands[a]



1 **2**

entry	ligand	GC yields (%) **2**	**1**
1	PCy_3 (no NaO^tBu, 120 °C)	0	93
2	dcype (no NaO^tBu)	0	79
3	ICy·HCl	0	97
4	ICy^{Me}·HCl	4	89
5	IMes·HCl	8	96
6	$IMes^{Me}$·HCl	21	72
7	IPr·HCl	10	90
8	IPr^{Me}·HCl	0	94
9[b]	$IMes^{Me}$·HCl	63 (59)[c]	38



dcype

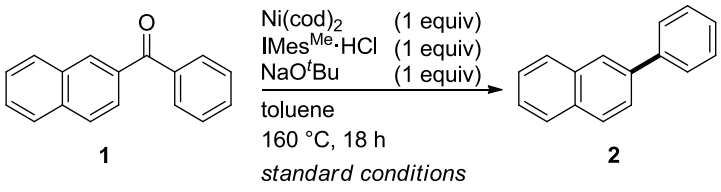
ICy^{Me} (R = cyclohexyl)
$IMes^{Me}$ (R = 2,4,6-$Me_3C_6H_2$)
IPr^{Me} (R = 2,6-$^iPr_2C_6H_3$)

[a] Reaction conditions: **1** (0.25 mmol), $Ni(cod)_2$ (0.025 mmol), ligand (0.025 mmol), NaO^tBu (0.06 mmol) in toluene (0.5 mL) for 18 h at 160 °C. [b] Reaction conditions: 1 (0.25 mmol), $Ni(cod)_2$ (0.25 mmol), $IMes^{Me}$·HCl (0.25 mmol), NaO^tBu (0.25 mmol) in toluene (1.0 mL) for 18 h at 160 °C. [c] Isolated yields.

The optimization of reaction conditions was carried out (Table 2). Changing the ratio of Ni/NHC from 1:1 to 1:2 did not increase the yield of **2** (entry 1 vs. 3). Increasing the amount of nickel/NHC complex to 2 equiv did not lead to any improvement in yield of **2** (entry 4). We also conducted the reaction using a free $IMes^{Me}$ ligand in the

absence of NaO^{t}Bu and found that the yield of the decarbonylated product was comparable to that using IMes^{Me}·HCl/NaO^{t}Bu (entry 1 vs entry 5). Thus, the role of NaO^{t}Bu in this reaction is simply to serve as a base to abstract proton from the carbene precursor.

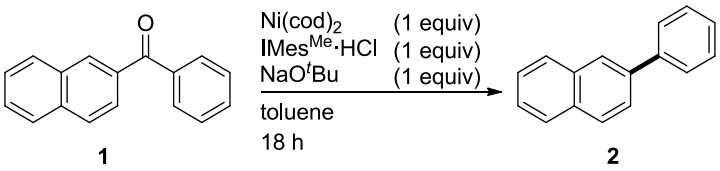
Table 2. Optimization of Reaction Conditions



entry	variation from the "standard conditions"	GC yields/%	
		2	**1**
1	none	63(59[a])	38
2	mesitylene instead of toluene	42	39
3	IMes^{Me}·HCl, NaO^{t}Bu 2 equiv	59	28
4	Ni(cod)$_2$, IMes^{Me}·HCl, NaO^{t}Bu 2 equivv	62	19
5	IMes^{Me} (no NaO^{t}Bu) instead of IMes^{Me}·HCl	64	22
6	in two-necked flask using mesitylene	13	11

As shown in the Table 3, this decarbonylation reaction basically requires heating at 160 °C to obtain a maximum yield. Therefore, all the reaction was conducted at 160 °C in the scope and limitation studies.

Table 3. Effect of the Reaction Temperature

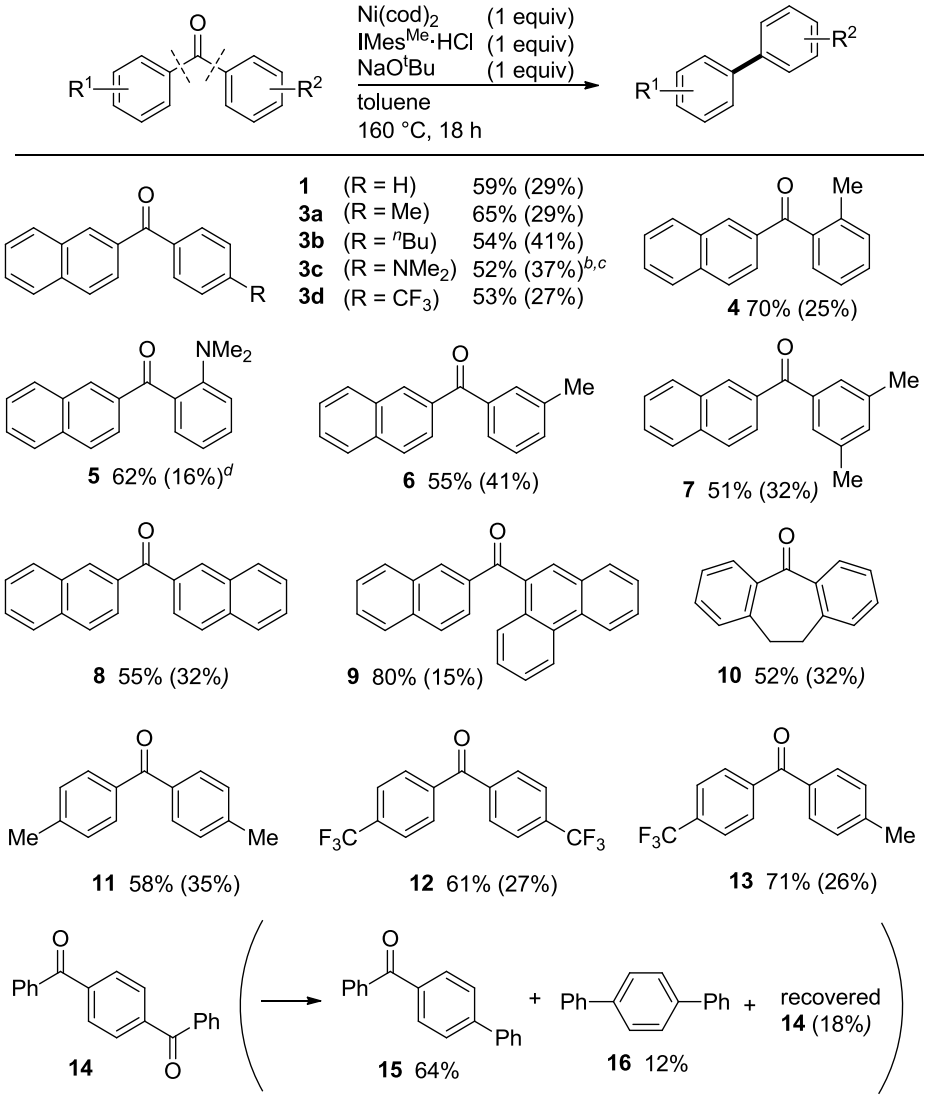


entry	temprature (°C)	GC yields (%)		note
		2	**1**	
1	120	39	39	
2	140	47	36	
3	160	63	29	
4	180	57	33	in mesitylene

The scope of this nickel-mediated decarbonylation using a series of simple diaryl ketones was next investigated (Table 4). The effects of different substituents on the performance of the decarbonylation reaction were evaluated initially. An electron-donating substituent such as methyl (**3a**), butyl (**3b**) or dimethylamino (**3c**) group was well tolerated at the para-position of the phenyl ring. A substrate having an electron-deficient trifluoromethyl group (**3d**) at the same position also successfully underwent decarbonylation. This reaction exhibited a high level of tolerance

toward substrates bearing an ortho substituent on the phenyl ring, such as ketones **4** and **5**. Polyaromatic ketone **9** bearing a phenanthrene group reacted smoothly under current conditions to give the decarbonylation product. Cyclic ketone **10** was also a good substrate to give 9,10-dihydrophenanthrene. Several benzophenone derivatives (**11**-**13**) were also decarbonylated under our newly developed conditions to form the corresponding substituted biphenyls. A substrate bearing two benzoyl groups (**14**) preferentially afforded the mono-decarbonylated product **15** in 64% yield, along with the corresponding di-decarbonylated product (**16**, 12%).

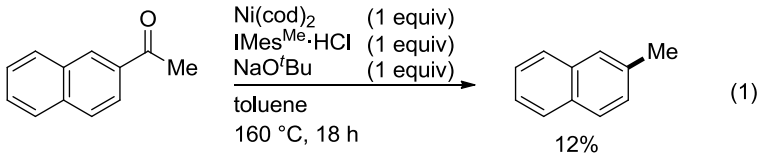
Table 4. Substrate Scope[a]



[a] Reaction conditions: Ketone (0.25 mmol), $Ni(cod)_2$ (0.25 mmol), $IMes^{Me}$·HCl (0.25 mmol), NaO^{t}Bu (0.25 mmol) in toluene (1.0 mL) for 18 h at 160 °C. Isolated yields are shown unless otherwise noted. Numbers in the parentheses refer to the yield of the recovered starting ketone. [b] NMR yield. [c] Ketone **1** was formed as a byproduct

(4% GC yield). [d] Ketone **1** was formed as a byproduct (9% GC yield).

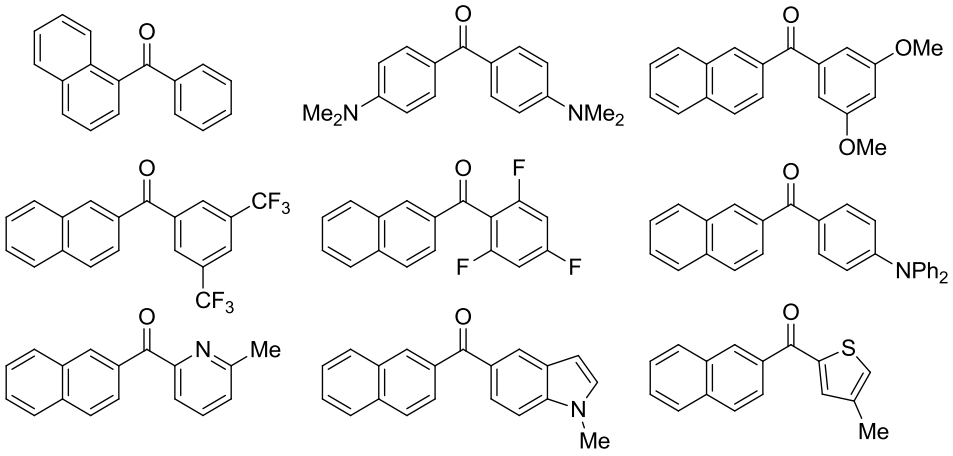
Enolizable ketones generally failed to form the decarbonylation products, but rather led to the formation of a complicated mixture. For example, the nickel-mediated reaction of 2-acetylnaphthalene afforded the decarbonylation product in only 12%, although the conversion of the ketone substrate was 81% (eq. 1).



(1)

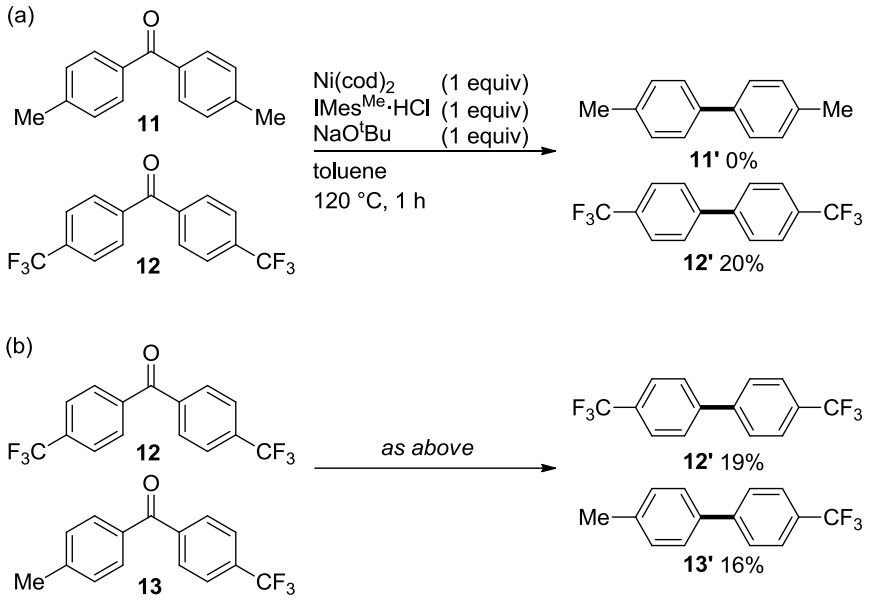
The other ineffective substrates are shown in Table 5. Functional groups such as amine, methoxy and fluoride were cleaved much more easily under current conditions.

Table 5. Ineffective Substrates



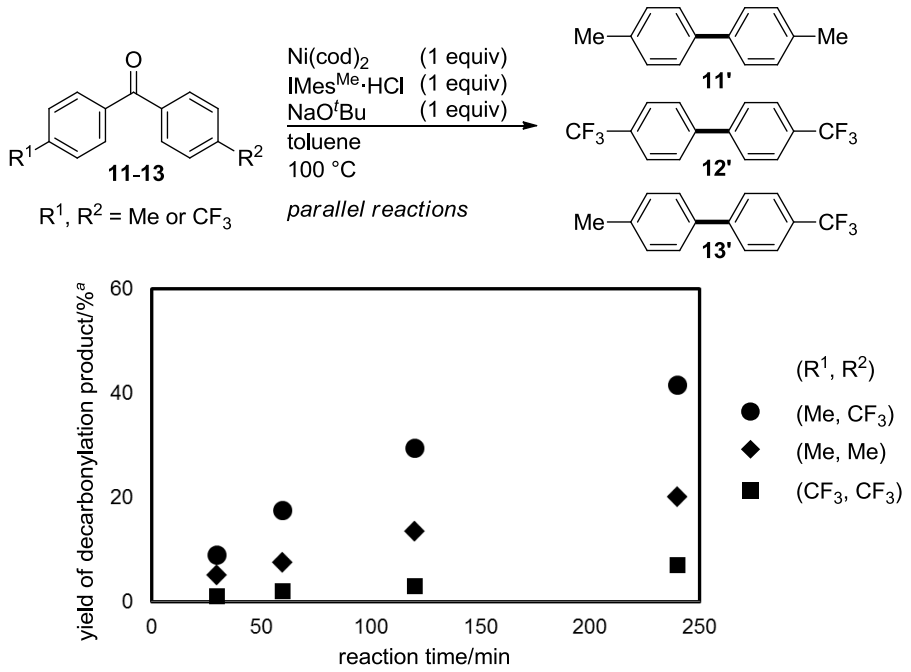
A series of competition experiments were subsequently conducted to gain a deeper insight into the effect of the electronic properties of the diaryl rings on the outcome of the decarbonylation reaction. Intermolecular competitive experiments were performed using 4,4'-disubstituted benzophenones bearing different substituents at the para-positions of their phenyl rings (**11**-**13**). These reactions were conducted under milder conditions than those described above with shorter reactions times (Scheme 2). While the electron-deficient ketone **12** is reacted faster than the electron-rich analogue **11** under these conditions (Scheme 2a), ketones **12** (bis-CF_3-substituted) and **13** (methyl and CF_3 substituted) reacted at similar rates (Scheme 2b). It is noteworthy that no crossover products were observed, indicating that this process occurs through an intramolecular mechanism.

Scheme 2. Intermolecular Competition Experiments



To examine the substituent effect, a series of parallel reactions using substrates **11**-**13** were conducted to compare their initial rates of decarbonylation (Figure 1). Interestingly, ketone **13**, which contains both electron-donating and electron-withdrawing groups, underwent the decarbonylation reaction at a higher initial rate than other ketones bearing two electron-donating groups (**11**) or two electron-withdrawing groups (**12**).

Figure 1. Measurements of the Initial Rates of the Decarbonylation of Electronically Different Ketones

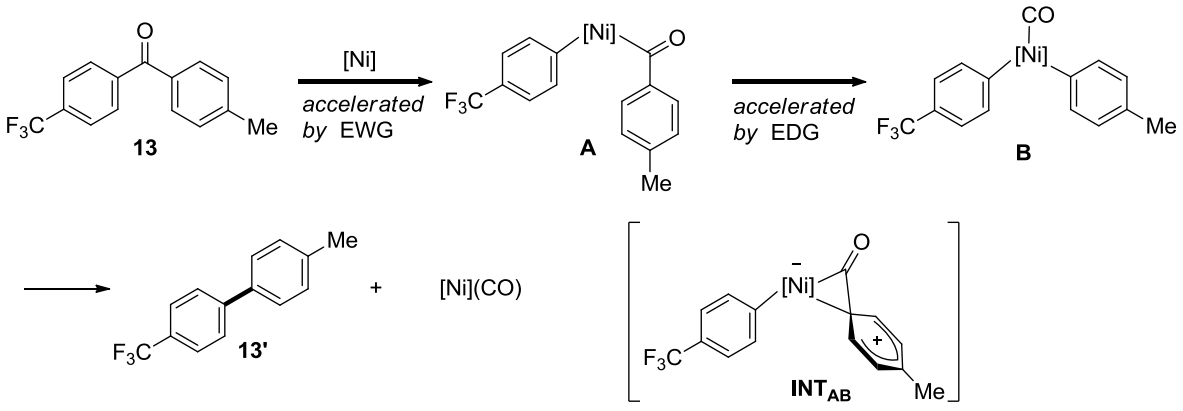


[a] Data are the average of two independent experiments.

A mechanistic detail to account for the unique electronic effects observed is shown in Scheme 3. The initial oxidative addition of one of the C(aryl)-C(=O) bonds to nickel(0) species would lead to the formation of aroylnickel(II) intermediate **A**, which would undergo a decarbonylation reaction to form diarylnickel complex **B**. Finally, reductive elimination from **B** would afford the desired biaryl product, along with a nickel carbonyl species, which would be unable to undergo an oxidative addition of the C(aryl)-C(=O) bond. The formation of nickel carbonyl species was observed by FTIR (1980 cm^{-1}, See 3.4.7 for details.).

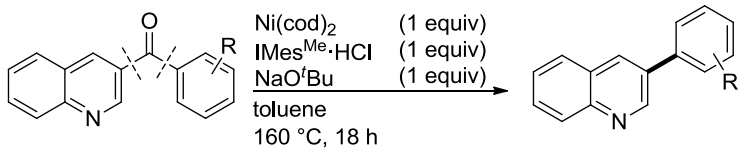
Based on the observed substituent effect, the initial oxidative addition is expected to be accelerated by an electron-withdrawing group. In contrast, the author currently believes that the second decarbonylation is accelerated by electron-donating group, which can explain why push/pull groups accelerated the reaction. The second decarbonylation is expected to proceeds through the intermediate $\mathbf{INT_{AB}}$, where the electrophilic nickel(II) attacks the aromatic ring of the acyl ligand electrophilically. A similar S_EAr type transition state is also proposed for a related decarboxylation of a palladium benzoate derivative.[9] In agreement with S_EAr mechanism, an electron-rich phenyl group is essential for this decarboxylation reaction. This mechanistic model can therefore account for the unique electronic effect observed in the current decarbonylation reaction.

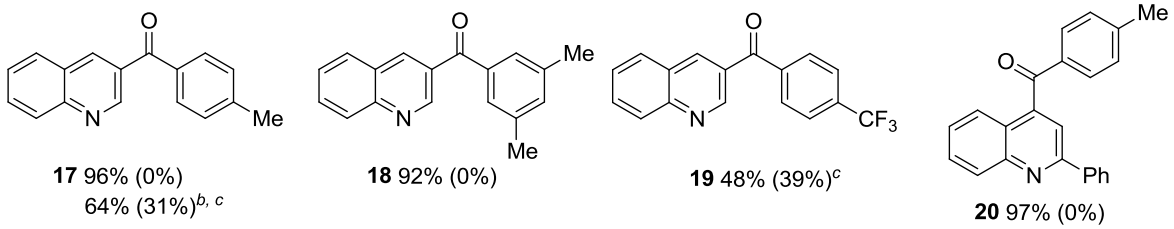
Scheme 3. Possible Mechanism



Based on this unique positive effect by the push/pull groups, several other ketones bearing push and pull groups were next examined (Table 6). 3-Quinolyl ketones bearing a relatively electron-rich aryl group, such as **17** and **18**, were found to be exceptionally reactive under these nickel-mediated conditions. In consistent with our hypothesis, a quinoline substrate bearing an electron-withdrawing group (**19**) was less reactive. A similar trend was also observed for the 4-quinolyl ketone **20** bearing an electron-rich phenyl ring.

Table 6. Decarbonylation of Quinolinyl Ketones[a]





17 96% (0%)
64% (31%)[b, c]

18 92% (0%)

19 48% (39%)[c]

20 97% (0%)

[a] Reaction conditions: Ketone (0.25 mmol), $Ni(cod)_2$ (0.25 mmol), $IMes^{Me}$·HCl (0.25 mmol), NaO^{t}Bu (0.25 mmol) in toluene (1.0 mL) for 18 h at 160 °C. Isolated yields are shown unless otherwise noted. Numbers in the parentheses refer to the yield of the recovered starting ketone. [b] $Ni(cod)_2$ (20 mol%), $IMes^{Me}$·HCl (20 mol%). [c] NMR yield.

3.3 Conclusion

In conclusion, the first nickel system capable of mediating decarbonylation of simple aromatic ketones through the cleavage of two carbon-carbon bonds is described. This is the first example of decarbonylation of simple ketones mediated by nickel complex. Notably, this new reactivity of nickel complexes such as unique electronic effect of substituents could provide valuable insights for the development of new organometallic reactions. Studies aimed at expanding this new reactivity of nickel complexes to catalytic transformations are ongoing in our laboratories.

3.4 Experimental Section

3.4.1 General Information

^1H and ^{13}C NMR spectra were recorded on a JEOL ECS-400 spectrometer (JEOL, Tokyo, Japan) or VARIAN UNITY INOVA-600 spectrometer in $CDCl_3$ with tetramethylsilane as an internal reference standard. NMR data have been reported as follows: chemical shift (δ) in ppm, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, and m = multiplet), coupling constant (*J*) in Hz, and integration. Infrared spectra (IR) were obtained on a JASCO FT/IR-4000 spectrometer, and the absorptions have been reported in reciprocal centimeters with the following relative intensities: s (strong), m (medium), or w (weak). Mass spectra were obtained on a Shimadzu GCMS-QP 5000 or GCMS-QP 2010 instrument with an ionization voltage of 70 eV. High resolution mass spectra (HRMS) were obtained on a JEOL JMS-DX303. Analytical gas chromatography (GC) was carried out on Shimadzu GC-2014, equipped with a flame ionization detector. Melting points were determined using a Yamato melting point apparatus. Column chromatography was performed over SiO_2 (Silycycle Silica Flash F60 (230-400

mesh)) and NH Silica (Silica Gel 60 (spherical) NH_2 (40-50 μm)). Some of the compounds were purified by LC-908 HPLC (GPC).

3.4.2 Materials

Toluene (for Organic Synth.) was purchased from Wako Chemicals and used as received. $Ni(cod)_2$ was purchased from Strem Chemicals and used as received. PCy_3 (Sigma-Aldrich), dcype (Sigma-Aldrich), IPr·HCl (TCI), IMes·HCl (TCI), ICy·HCl (TCI) and NaO^{t}Bu (TCI) were purchased from commercial suppliers and used as received. IMes^{Me}·HCl[10] was prepared according to the literature procedures. Diaryl ketones **1** (TCI), **10** (TCI), **11** (TCI) and **14** (TCI) were purchased from commercial suppliers and purified by recrystallization or distillation over CaH_2 prior to use. Diaryl ketones **3a** (CAS 136935-71-2),[11] **5** (CAS 1314779-58-2),[12] **8** (CAS 613-56-9),[13] **12** (CAS 21221-91-0),[14] **13** (CAS 34328-30-8),[15] **17** (CAS 1182441-50-4)[16] and **19** (CAS 1207847-74-2)[17] were prepared by the reactions between the corresponding Weinreb amides and Grignard reagents.

3.4.3 General Procedure for Synthesis of Starting Materials

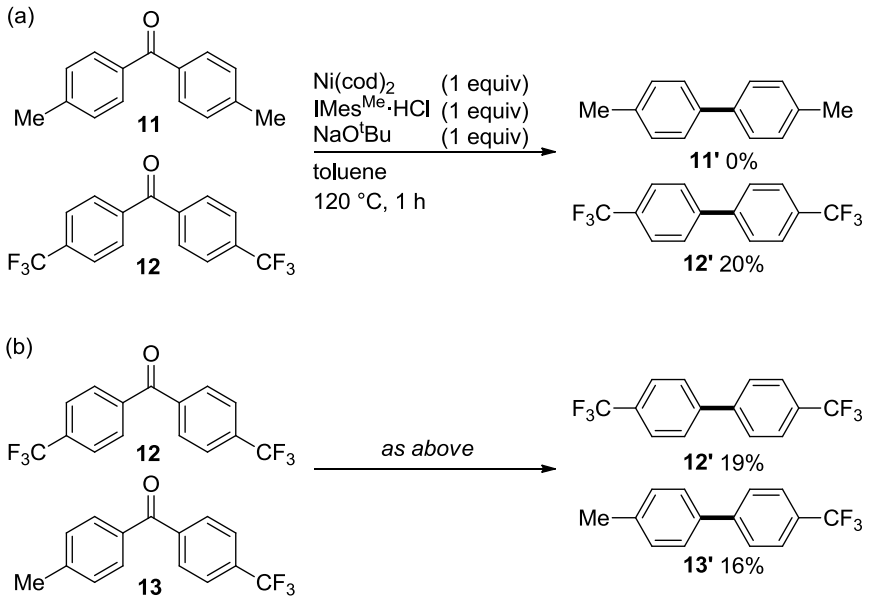
A solution of aryl bromide (12 mmol) in 12 mL of THF was added to magnesium turnings (36 mmol) in a dropwise manner at room temperature. After addition was completed, the reaction mixture was stirred at 60 °C for 2 hour. Thereafter the mixture was cooled to room temperature, and then added to the solution of *N*-methoxy-*N*-methyl-2-naphthamide (CAS 113443-62-2)[18] (2.15 g, 10 mmol) in THF (30 mL) in a dropwise manner at 0 °C. The resulting mixture was stirred at 0 °C until the starting naphthyl amide was disappeared by TLC. The reaction was quenched by the addition of saturated aqueous solution of NH_4Cl, and the resulting mixture was extracted with EtOAc. The combined extracts were washed with brine, dried ($MgSO_4$), and concentrated to give a residue, which was purified by column chromatography to give a desired ketone.

3.4.4 Typical Procedure for the Ni/IMes^{Me}-Mediated Decarbonylation of Diaryl Ketones

$Ni(cod)_2$ (69 mg, 0.25 mmol), IMes^{Me}·HCl (92 mg, 0.25 mmol), NaO^{t}Bu (24 mg, 0.25 mmol) and toluene (0.5 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 at room temperature for 3 min. A diaryl ketone (0.25 mmol) in toluene (0.5 mL) was then added to the vial and the cap was closed. The contents of the vial were then stirred at 160 °C for 18 h. The reaction was cooled to room temperature, and the crude mixture was filtered through a pad of silica gel before being analyzed by GC. The filtrate was then concentrated *in vacuo* to give a residue, which was purified by flash column chromatography over silica gel. All spectrum data of starting materials are cited in original paper.[19]

3.4.5 Intermolecular Competition Reactions for the Ni/IMes^{Me}-Mediated Decarbonylation of Diaryl Ketones

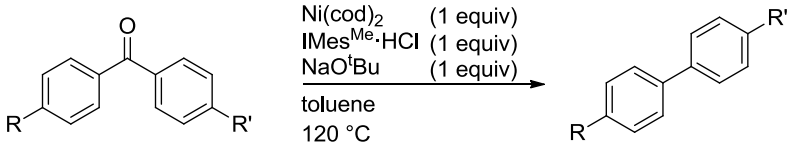
$Ni(cod)_2$ (69 mg, 0.25 mmol), IMes^{Me}·HCl (92 mg, 0.25 mmol), NaO^{t}Bu (24 mg, 0.25 mmol) and toluene (0.5 mL) were added to a 10 mL-sample vial with a Teflon-sealed screwcap in a glovebox filled with nitrogen, and the resulting mixture was stirred at room temperature for 3 min. Two diaryl ketones (0.25 mmol each) in toluene (0.5 mL) were then added to the vial and the cap was closed. The contents of the vial were then stirred at 120 °C for 1 h. The reaction was cooled to room temperature, and the crude mixture was filtered through a pad of silica gel before being analyzed by GC. The yields for these compounds were determined by GC using undecane as an internal standard.



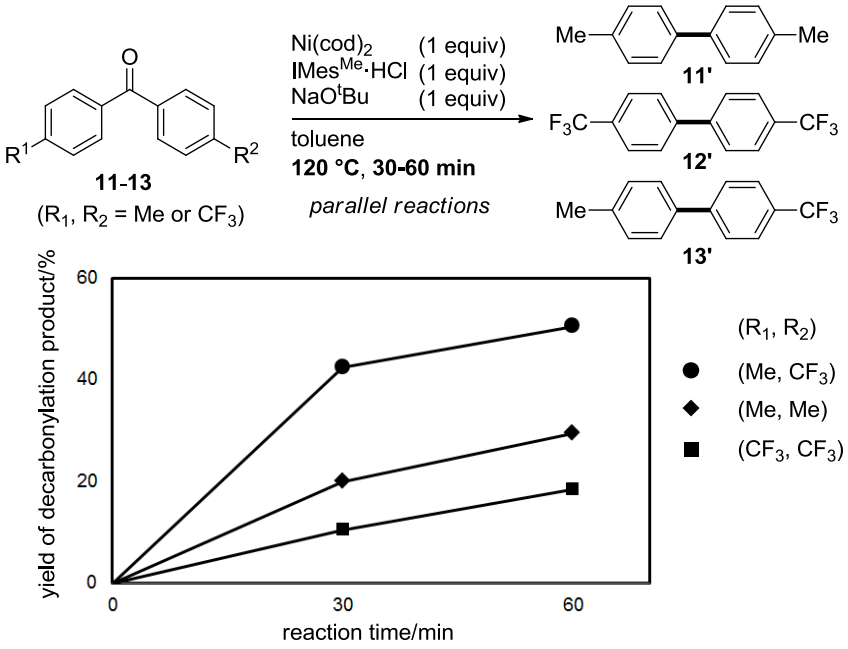
3.4.6 Initial Rate Studies

Although we conducted the reaction at 160 °C for our scope and limitation studies, milder conditions (100-120 °C) were employed for initial rate studies to make a clear comparison. The experimental procedure is as follows:

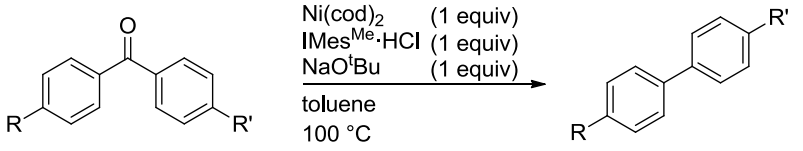
$Ni(cod)_2$ (69 mg, 0.25 mmol), IMes^{Me}·HCl (92 mg, 0.25 mmol), NaO^{t}Bu (24 mg, 0.25 mmol) and toluene (0.5 mL) were added to a 10 mL-sample vial with a Teflon-sealed screwcap in a glovebox filled with nitrogen, and the resulting mixture was stirred at room temperature for 3 min. Diaryl ketone (0.25 mmol) in toluene (0.5 mL) were then added to the vial and the cap was closed. The contents of the vial were then stirred at 120 °C for 30 min. The reaction was cooled to room temperature, and the crude mixture was filtered through a pad of silica gel before being analyzed by GC. The yield of the decarbonylation product was determined by GC using undecane as an internal standard. The yield was obtained from the two independent experiments. The same experiments were conducted by extending the reaction time of 60 min. As revealed by the table and graph below, the reactivity order is as follows: **13** > **11** > **12**.



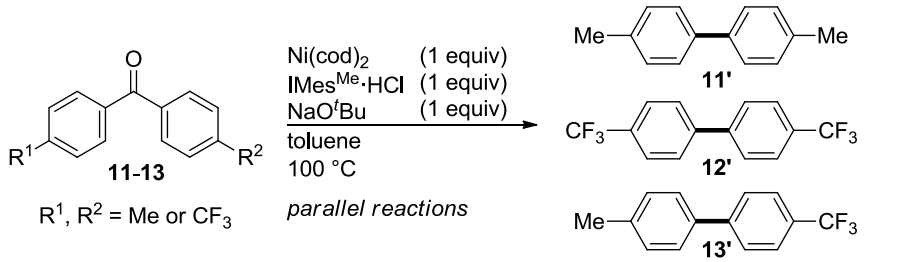
(R, R')		30 min	60 min
11 (Me, Me)	1st run	18% (SM 73%)	27% (SM 62%)
	2nd run	22% (SM 71%)	32% (SM 55%)
12 (CF_3, CF_3)	1st run	10% (SM 96%)	15% (SM 70%)
	2nd run	11% (SM 92%)	22% (SM 68%)
13 (Me, CF_3)	1st run	42% (SM 61%)	50% (SM 55%)
	2nd run	43% (SM 61%)	51% (SM 50%)

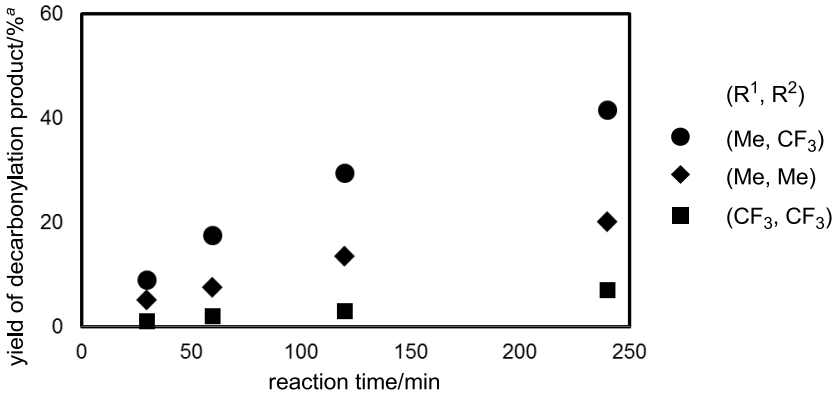


The same experiments were conducted at 100 °C during 30-240 min, which also showed the same reactivity order at 120 °C.

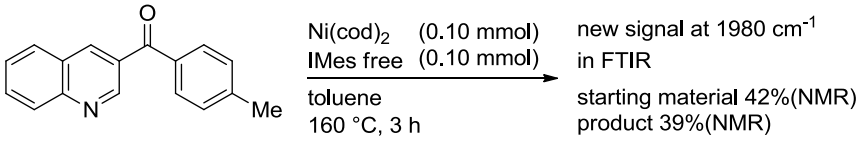


(R, R')		30 min	60 min	120 min	240 min
11 (Me, Me)	1st run	6%	6%	15%	23%
	2nd run	4%	9%	12%	17%
12 (CF_3, CF_3)	1st run	1%	2%	3%	7%
	2nd run	1%	2%	3%	7%
13 (Me, CF_3)	1st run	13%	18%	33%	41%
	2nd run	5%	17%	26%	42%



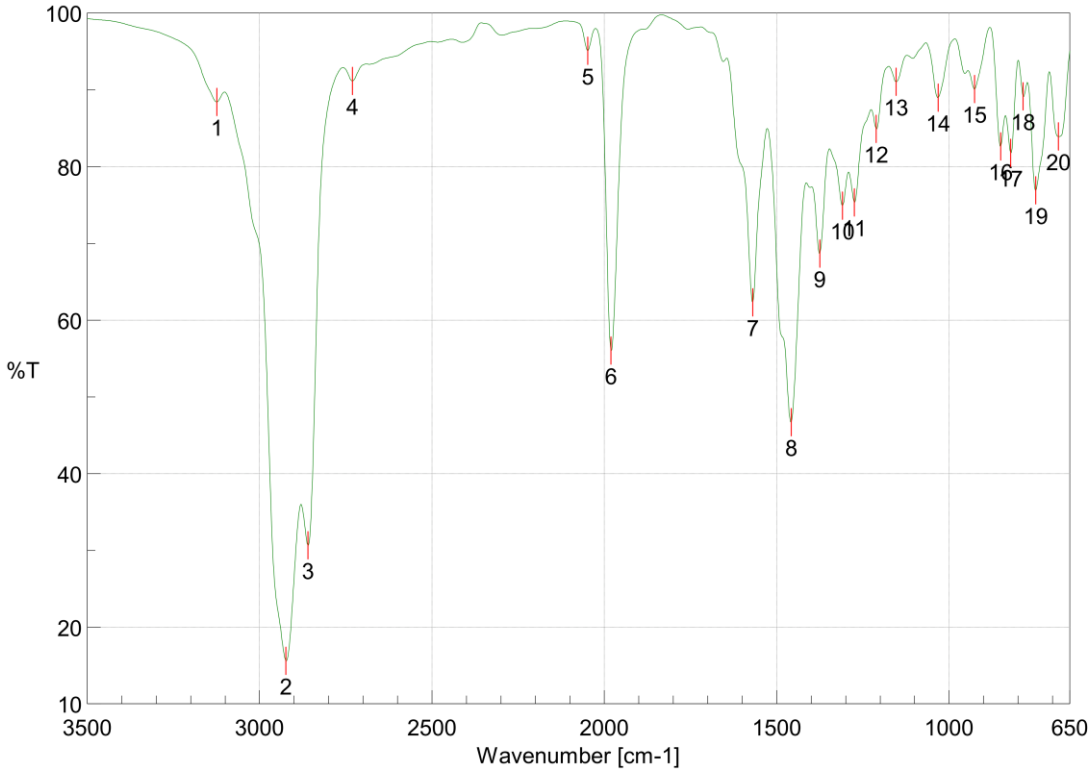


3.4.7. Observation of Nickel Carbonyl Species



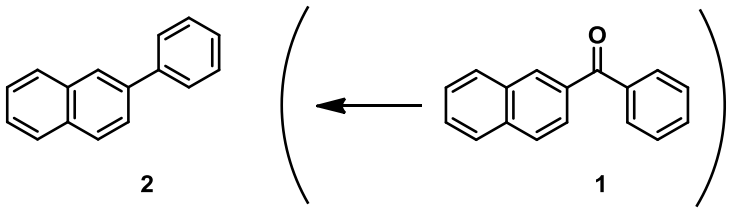
To a 10 mL-sample vial with a Teflon-sealed screwcap, $Ni(cod)_2$ (28 mg, 0.10 mmol), free IMes (30 mg, 0.10 mmol), ketone (25 mg, 0.10 mmol) and toluene (0.4 mL) were added in a glovebox filled with nitrogen. The cap was applied to seal and the mixture was heated at 160 °C for 3h outside the glove box. Again the vial was moved inside the glove box and an aliquot of the mixture was taken for IR analysis. The aliquot was dried in vacuo and

paraffin oil was added. The paste was put between two KBr windows and analyzed by FTIR. FTIR analysis showed a new peak at 1980 cm^{-1} which is assignable to ν_{CO} for a carbonyl ligand on nickel (see the following spectrum). NMR analysis revealed that 42% of the starting ketone was remained and 39% of the target product was produced.



3.4.8 Spectroscopic Data of Products

2-phenylnaphthalene (2) [CAS: 612-94-2].



The typical procedure was followed using **1** as the substrate. The starting ketone was recovered in 29% yield.

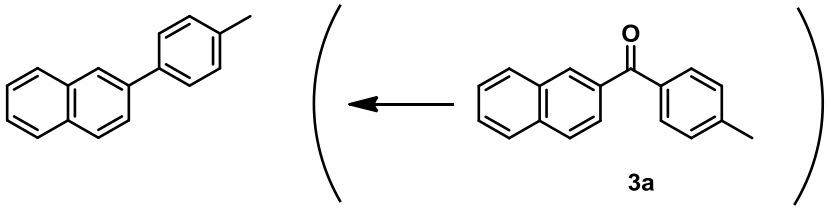
White solid (30.1 mg, 59%). Rf 0.23 (SiO_2, hexane only).

^{1}H NMR ($CDCl_3$, 399.78 MHz) δ: 7.40 (d, J = 7.3 Hz, 1H), 7.51-7.47 (m, 4H), 7.76-7.72 (m, 3H), 7.93-7.86 (m, 3H), 8.04 (s, 1H).

^{13}C NMR ($CDCl_3$, 100.53 MHz) δ: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.

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

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



The typical procedure was followed using **3a** as the substrate. The starting ketone was recovered in 29% yield.

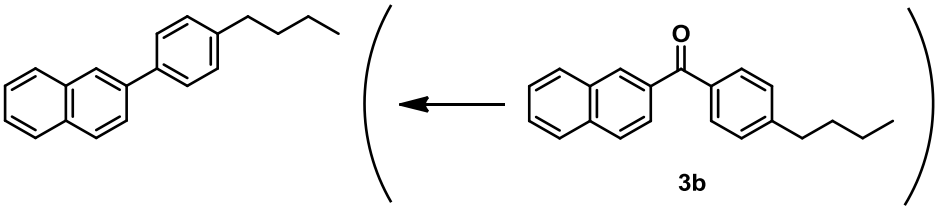
White solid (35.5 mg, 65%). Rf 0.74 (SiO_2, hexane/EtOAc = 20/1).

^{1}H NMR ($CDCl_3$, 399.78 MHz) δ: 2.43 (s, 3H), 7.31 (d, *J* = 8.2 Hz, 2H), 7.49 (dd, *J* = 9.6 Hz, 9.6 Hz, 2H), 7.64 (d, *J* = 8.2 Hz, 2H), 7.75 (d, *J* = 8.7 Hz, 1H), 7.92-7.86 (m, 3H), 8.04 (s, 1H).

^{13}C NMR ($CDCl_3$, 100.53 MHz) δ: 21.1, 125.4, 125.5, 125.8, 126.2, 127.2, 127.6, 128.1, 128.3, 129.6, 132.5, 133.7, 137.1, 138.2, 138.5.

Exact Mass (EI) Calcd for $C_{17}H_{14}$: 218.1096. Found: 218.1097.

2-(4-Butylphenyl)naphthalene [CAS: 1075754-29-8].



The typical procedure was followed using **3b** as the substrate. The yield of the recovered substrate was determined by NMR (41%).

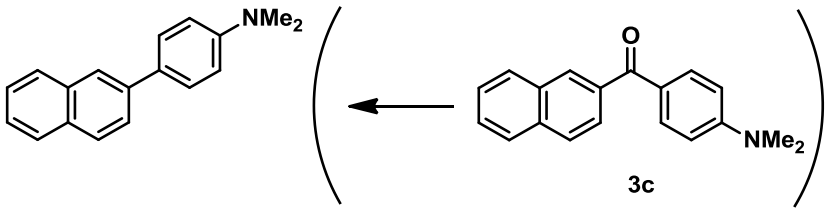
White solid (35.1 mg, 54%). Rf 0.74 (SiO_2, hexane/EtOAc = 20/1).

^{1}H NMR ($CDCl_3$, 399.78 MHz) δ: 0.97 (t, *J* = 7.3 Hz, 3H), 1.42 (tq, *J* = 7.3, 7.4 Hz, 2H), 1.68 (tt, *J* = 7.3 Hz, 7.4 Hz, 2H), 2.69 (t, *J* = 7.3 Hz, 2H), 7.30 (d, *J* = 8.0 Hz, 2H), 7.53-7.46 (m, 2H), 7.66 (d, *J* = 8.0 Hz, 2H), 7.76 (d, *J* = 8.7 Hz, 1H), 7.93-7.86 (m, 3H), 8.04 (s, 1H).

^{13}C NMR ($CDCl_3$, 100.53 MHz) δ: 14.0, 22.4, 33.7, 35.3, 125.4, 125.6, 125.7, 126.2, 127.2, 127.6, 128.1, 128.3, 128.9, 132.5, 133.7, 138.4, 138.5, 142.2.

Exact Mass (EI) Calcd for $C_{20}H_{20}$: 260.1565. Found: 260.1567.

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



The typical procedure was followed using **3c** as the substrate. Purification by column chromatography allowed us to separate a pure recovered starting material (37%) and a mixture of the desired product, a deaminated product (i.e., 2-naphthyl phenyl ketone, 4% yield by CG analysis), and unidentified byproduct(s). The latter mixture was further purified by another column chromatography. The first fraction contained the pure desired product (17 mg, 28%), and the second fraction was a mixture of the desired product, deaminated product and unidentified byproducts. The yield of the desired product in the second fraction was determined to be 24% by NMR spectroscopy. Therefore, the total yield of the decarbonylation product is estimated to be 52%.

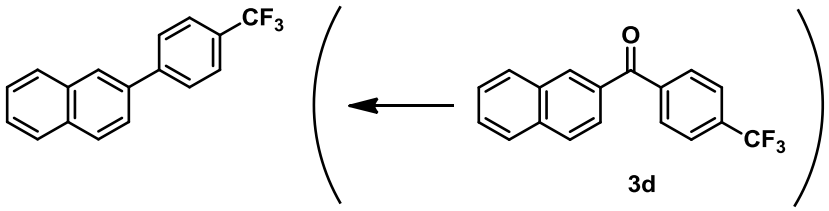
White solid (17 mg, 28%). Rf 0.37 (SiO_2, hexane/EtOAc = 20/1).

^{1}H NMR ($CDCl_3$, 399.78 MHz) δ: 3.02 (s, 6H), 6.86 (d, J = 8.9 Hz, 2H), 7.50-7.42 (m, 2H), 7.65 (d, J = 8.9 Hz, 2H), 7.75 (d, J = 8.2 Hz, 1H), 7.89-7.83 (m, 3H), 7.99 (s, 1H).

^{13}C NMR ($CDCl_3$, 100.53 MHz) δ: 40.6, 112.8, 124.2, 125.2, 125.3, 126.0, 127.6, 127.9, 128.2, 128.98, 128.99, 132.0, 133.9, 138.5, 150.0.

Exact Mass (EI) Calcd for $C_{18}H_{17}N$: 247.1361. Found: 247.1359.

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



The typical procedure was followed using **3d** as the substrate. The starting ketone was recovered in 27% yield.

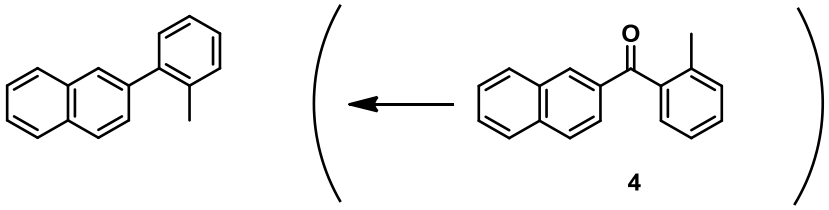
White solid (36.1 mg, 53%). Rf 0.77 (SiO_2, hexane/EtOAc = 20/1).

^{1}H NMR ($CDCl_3$, 399.78 MHz) δ: 7.56-7.51 (m, 2H), 7.75-7.73 (m, 3H), 7.82 (d, J = 8.2 Hz, 2H), 7.96-7.88 (m, 3H), 8.07 (s, 1H).

^{13}C NMR ($CDCl_3$, 100.53 MHz) δ: 123.0, 125.2, 125.8 (q, J_{CF} = 3.8 Hz), 126.3, 126.5, 126.6, 127.6, 127.7, 128.3, 128.8, 129.4 (q, J_{CF} = 32.6 Hz), 133.0, 133.5, 137.0, 144.6.

Exact Mass (EI) Calcd for $C_{17}H_{11}F_3$: 272.0813. Found: 272.0813.

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



The typical procedure was followed using **4** as the substrate. The yield of the recovered substrate was determined by NMR (25%).

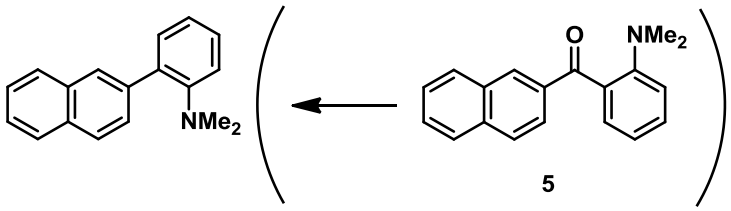
Colorless oil (38.2 mg, 70%). Rf 0.63 (SiO_2, hexane/EtOAc = 20/1).

^{1}H NMR ($CDCl_3$, 399.78 MHz) δ: 2.35 (s, 3H), 7.37-7.31 (m, 4H), 7.54-7.49 (m, 3H), 7.81 (s, 1H), 7.92-7.88 (m, 3H).

^{13}C NMR ($CDCl_3$, 100.53 MHz) δ: 20.5, 125.80, 125.82, 126.1, 127.4, 127.5, 127.67, 127.72, 127.77, 127.98, 130.0, 130.3, 132.3, 133.3, 135.6, 139.5, 141.8.

Exact Mass (EI) Calcd for $C_{17}H_{14}$: 218.1096. Found: 218.1092.

***N*,*N*-Dimethyl-2-(naphthalen-2-yl)anilin [CAS: 101733-49-7].**



The typical procedure was followed using **5** as the substrate. A deaminated product (i.e., 2-naphthyl phenyl ketone) was also formed as a byproduct (9% GC yield). The yield of the recovered substrate was determined by NMR (16%).

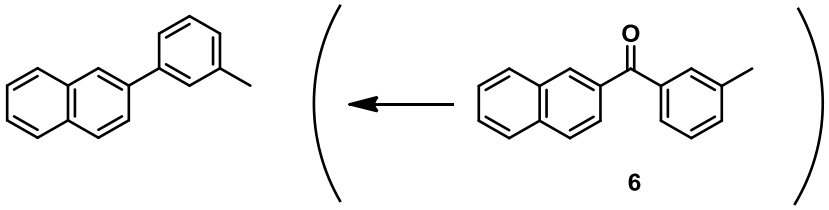
Colorless oil (38.3 mg, 62%). Rf 0.0.57 (SiO_2, hexane/EtOAc = 20/1).

^{1}H NMR ($CDCl_3$, 399.78 MHz) δ: 2.59 (s, 6H), 7.08 (dd, J = 6.4 Hz, 7.8 Hz, 2H), 7.35 (dd, J = 6.4 Hz, 7.8 Hz, 2H), 7.50-7.49 (m, 2H), 7.89-7.84 (m, 4H), 7.98 (s, 1H).

^{13}C NMR ($CDCl_3$, 100.53 MHz) δ: 43.4, 117.6, 121.5, 125.6, 125.8, 126.8, 127.4, 127.5, 127.6, 128.0, 128.2, 132.0, 132.3, 133.8, 133.9, 139.9, 151.4.

Exact Mass (EI) Calcd for $C_{18}H_{17}N$: 247.1361. Found: 247.1357.

2-(*m*-Tolyl)naphthalene [CAS: 36821-15-5].



6

The typical procedure was followed using **6** as the substrate. The yield of recovered substrate was determined by NMR (41%).

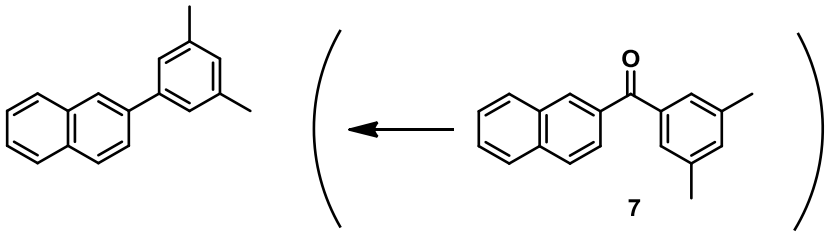
Colorless oil (30.0 mg, 55%). Rf 0.65 (SiO_2, hexane/EtOAc = 20/1).

^{1}H NMR ($CDCl_3$, 399.78 MHz) δ: 2.49 (s, 3H), 7.22 (d, *J* = 7.8 Hz, 1H), 7.40 (dd, *J* = 7.4 Hz, 7.8 Hz, 1H), 7.57-7.48 (m, 4H), 7.77 (d, *J* = 8.7 Hz, 1H), 7.94-7.87 (m, 3H), 8.06 (s, 1H).

^{13}C NMR ($CDCl_3$, 100.53 MHz) δ: 21.6, 124.5, 125.6, 125.7, 125.8, 126.2, 127.6, 128.07, 128.15, 128.18, 128.3, 128.7, 132.6, 133.6, 138.4, 138.6, 141.1.

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

2-(3,5-Dimethylphenyl)naphthalene [CAS: 13183-56-7].



7

The typical procedure was followed using **7** as the substrate. The starting ketone was recovered in 32% yield.

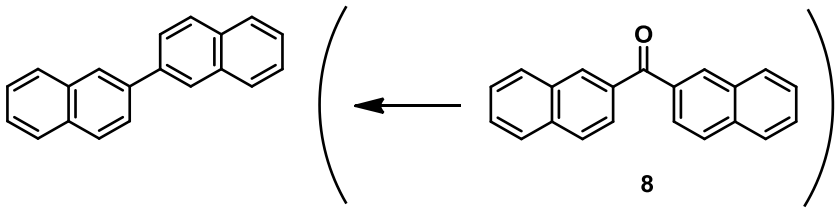
White solid (29.6 mg, 51%). Rf 0.57 (SiO_2, hexane/EtOAc = 20/1).

^{1}H NMR ($CDCl_3$, 399.78 MHz) δ: 2.44 (s, 6H), 7.05 (s, 1H), 7.37 (s, 2H), 7.51 (dd, *J* = 7.4, 8.2 Hz, 2H), 7.76 (d, *J* = 8.4 Hz, 1H), 7.93-7.87 (m, 3H), 8.05 (s, 1H).

^{13}C NMR ($CDCl_3$, 100.53 MHz) δ: 21.4, 125.3, 125.68, 125.72, 125.75, 126.1, 127.6, 128.1, 128.2, 129.0, 132.5, 133.7, 138.3, 138.8, 141.1.

Exact Mass (EI) Calcd for $C_{17}H_{14}$: 232.1252. Found: 232.1249.

2,2'-Binaphthalene [CAS: 612-78-2].



8

The typical procedure was followed using **8** as the substrate. The starting ketone was recovered in 32% yield.

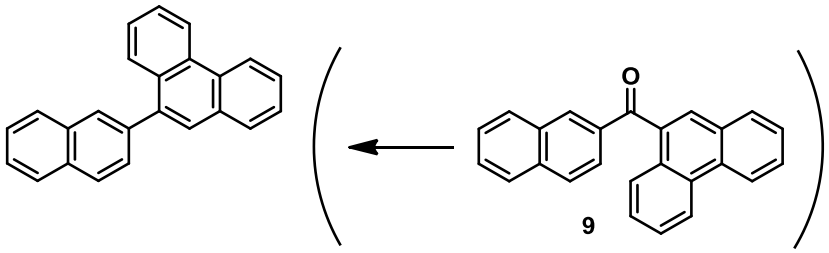
White solid (35.0 mg, 55%). Rf 0.29 (SiO_2, hexane only).

^{1}H NMR ($CDCl_3$, 399.78 MHz) δ: 7.55-7.48 (m, 4H), 7.98-7.88 (m, 8H), 8.18 (s, 2H).

^{13}C NMR ($CDCl_3$, 100.53 MHz) δ: 125.7, 126.0, 126.1, 126.4, 127.7, 128.2, 128.5, 132.7, 133.7, 138.4.

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

9-(Naphthalen-2-yl)phenanthrene [CAS: 119925-46-1].



The typical procedure was followed using **9** as the substrate. The yield of recovered substrate was determined by NMR (15%).

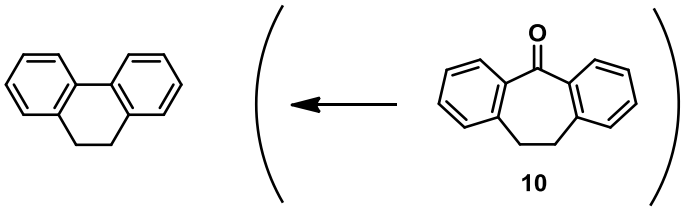
White solid (60.9 mg, 80%). Rf 0.54 (SiO_2, hexane/EtOAc = 20/1).

^{1}H NMR ($CDCl_3$, 399.78 MHz) δ: 7.57-7.53 (m, 3H), 7.71-7.62 (m, 4H), 7.79 (s, 1H), 8.03-7.92 (m, 6H), 8.75 (d, *J* = 8.2 Hz, 1H), 8.81 (d, *J* = 8.2 Hz, 1H).

^{13}C NMR ($CDCl_3$, 150.92 MHz) δ: 122.5, 122.93, 126.1, 126.3, 126.47, 126.53, 126.6, 126.9, 127.0, 127.6, 127.75, 127.83, 128.0, 128.4, 128.7, 130.0, 130.6, 131.2, 131.6, 132.6, 133.4, 138.4, 138.6 (2C, overlapped peaks).

Exact Mass (EI) Calcd for $C_{24}H_{16}$: 304.1252. Found: 304.1248.

9,10-Dihydrophenanthrene [CAS: 776-35-2].



The typical procedure was followed using **10** as the substrate. The starting ketone was recovered in 32% yield.

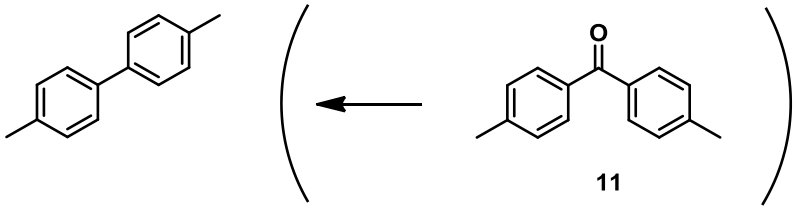
White solid (23.4 mg, 52%). Rf 0.74 (SiO_2, hexane/EtOAc = 50/1).

^{1}H NMR ($CDCl_3$, 399.78 MHz) δ: 2.89 (s, 4H), 7.30-7.22 (m, 4H), 7.34-7.29 (m, 2H), 7.77 (d, *J* = 7.8 Hz, 2 H).

^{13}C NMR ($CDCl_3$, 100.53 MHz) δ: 29.0, 123.7, 126.9, 127.35, 127.36, 128.1, 134.5, 137.4.

Exact Mass (EI) Calcd for $C_{14}H_{12}$: 180.0939. Found: 180.0939.

4,4'-Dimethyl-1,1'-biphenyl [CAS: 613-33-2].



The typical procedure was followed using **11** as the substrate. The starting ketone was recovered in 35% yield.

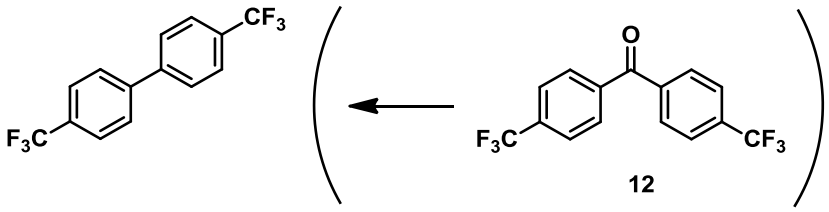
White solid (26.4 mg, 58%). Rf 0.71 (SiO_2, hexane/EtOAc = 20/1).

^{1}H NMR ($CDCl_3$, 399.78 MHz) δ: 2.40 (s, 6H), 7.25 (d, J = 8.0 Hz, 4H), 7.49 (d, J = 8.0 Hz, 4H).

^{13}C NMR ($CDCl_3$, 100.53 MHz) δ: 21.1, 126.8, 129.4, 136.7, 138.3.

Exact Mass (EI) Calcd for $C_{14}H_{14}$: 182.1096. Found: 182.1096.

4,4'-Bis(trifluoromethyl)-1,1'-biphenyl [CAS: 581-80-6].



The typical procedure was followed using **12** as the substrate. The yield of recovered substrate was determined by GC (27%).

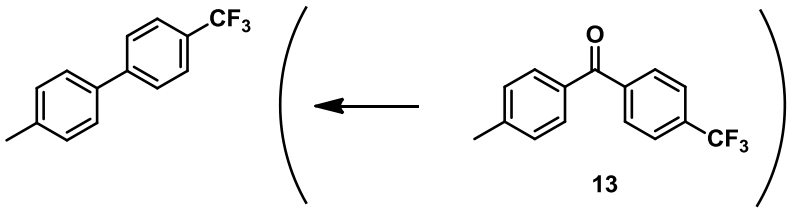
White solid (44.3 mg, 61%). Rf 0.69 (SiO_2, hexane/EtOAc = 20/1).

^{1}H NMR ($CDCl_3$, 399.78 MHz) δ: 7.75-7.69 (m, 8H).

^{13}C NMR ($CDCl_3$, 100.53 MHz) δ: 124.10 (q, J_{CF} = 272.2 Hz), 125.9 (q, J_{CF} = 3.8 Hz), 127.6, 130.3 (q, J_{CF} = 32.6 Hz), 143.2.

Exact Mass (EI) Calcd for $C_{14}H_8F_6$: 290.0530. Found: 290.0529.

4-Methyl-4'-(trifluoromethyl)-1,1'-biphenyl [CAS: 97067-18-0].



The typical procedure was followed using **13** as the substrate. The yield of recovered substrate was determined by NMR (26%).

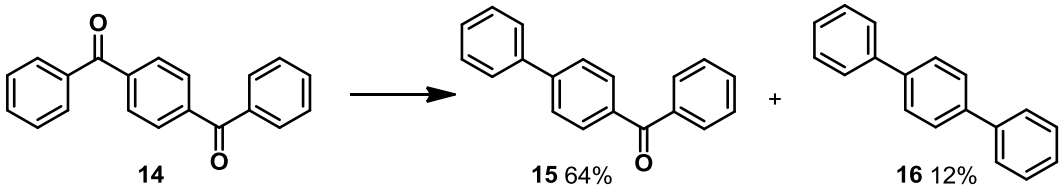
White solid (41.9 mg, 71%). Rf 0.89 (SiO_2, hexane/EtOAc = 100/1).

^{1}H NMR ($CDCl_3$, 399.78 MHz) δ: 2.42 (s, 3H), 7.28 (d, J = 8.2 Hz, 2H), 7.51 (dd, J = 8.2 Hz, 2H), 7.68 (m, 4H).

^{13}C NMR ($CDCl_3$, 100.53 MHz) δ: 21.1, 123.0, 125.6 (q, J_{CF} = 3.8 Hz), 127.1, 127.2, 129.0 (q, J_{CF} = 31.6 Hz), 129.7, 136.9, 138.1, 144.6.

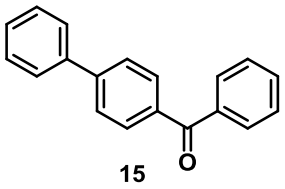
Exact Mass (EI) Calcd for $C_{14}H_{11}F_3$: 236.0813. Found: 236.0811.

Decarbonylation of diketone 14.



The typical procedure was followed using **14** as the substrate. The starting diketone was recovered in 18% yield.

[1,1'-Biphenyl]-4-yl(phenyl)methanone (15) [CAS: 2128-93-0].



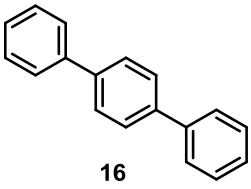
White solid (41.3 mg, 64%). Rf 0.48 (SiO_2, hexane/EtOAc = 20/1).

^{1}H NMR ($CDCl_3$, 399.78 MHz) δ: 7.41 (d, J = 7.3 Hz, 1H), 7.50 (dd, J = 7.3, 8.2 Hz, 4H), 7.67-7.59 (m, 3H), 7.71 (d, J = 8.2 Hz, 2H), 7.85 (d, J = 8.2 Hz, 2H), 7.90 (d, J = 8.2 Hz, 2H).

^{13}C NMR ($CDCl_3$, 100.53 MHz) δ: 127.0, 127.3, 128.1, 128.3, 129.0, 130.0, 130.7, 132.4, 136.2, 137.7, 140.0, 142.2, 196.3.

Exact Mass (EI) Calcd for $C_{19}H_{14}O$: 258.1045. Found: 258.1044.

1,1':4',1''-Terphenyl (16) [CAS: 92-94-4].



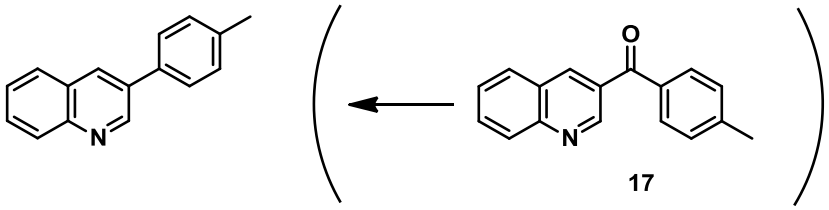
White solid (6.9 mg, 12%). Rf 0.57 (SiO_2, hexane/EtOAc = 20/1).

^{1}H NMR ($CDCl_3$, 399.78 MHz) δ: 7.37 (d, J = 7.3 Hz, 2H), 7.46 (dd, J = 7.3 Hz, 7.8 Hz, 4H), 7.68-7.64 (m, 8H).

^{13}C NMR ($CDCl_3$, 100.53 MHz) δ: 127.0, 127.3, 127.5, 128.8, 140.1, 140.7.

Exact Mass (EI) Calcd for $C_{18}H_{14}$: 230.1096. Found: 230.1092.

3-(*p*-Tolyl)quinoline [CAS: 42925-09-7].



17

The typical procedure was followed using **17** as the substrate. Chromatography was performed using NH silica.

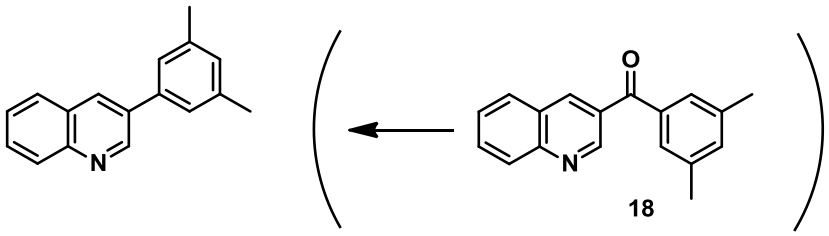
White solid (50.1 mg, 93%). Rf 0.20 (NH silica, hexane only).

^{1}H NMR ($CDCl_3$, 399.78 MHz) δ: 2.44 (s, 3H), 7.33 (d, *J* = 8.2 Hz, 2H), 7.56 (dd, *J* = 7.3, 7.6 Hz, 1H), 7.62 (d, *J* = 8.2 Hz, 2H), 7.71 (dd, *J* = 7.3, 8.7 Hz, 1H), 7.86 (d, *J* = 7.8 Hz, 1H), 8.14 (d, *J* = 8.7 Hz, 1H), 8.27 (s, 1H), 9.18 (s, 1H).

^{13}C NMR ($CDCl_3$, 100.53 MHz) δ: 21.1, 126.9, 127.2, 127.9, 128.0, 129.15, 129.16, 129.9, 132.8, 133.7, 134.9, 138.0, 147.2, 149.9.

Exact Mass (EI) Calcd for $C_{16}H_{13}N_1$: 219.1048. Found: 219.1045.

3-(3,5-Dimethylphenyl)quinoline [CAS: 1100255-26-2].



18

The typical procedure was followed using **18** as the substrate.

Colorless oil (53.7 mg, 92%). Rf 0.14 (SiO_2, hexane/EtOAc = 20/1).

^{1}H NMR ($CDCl_3$, 399.78 MHz) δ: 2.44 (s, 6H), 7.01 (s, 1H), 7.33 (s, 2H), 7.58 (dd, *J* = 6.9, 8.2 Hz, 1H), 7.72 (dd, *J* = 6.9, 8.7 Hz, 1H), 7.88 (d, *J* = 8.2 Hz, 1H), 8.15 (d, *J* = 8.7 Hz, 1H), 8.30 (s, 1H), 9.17 (s, 1H).

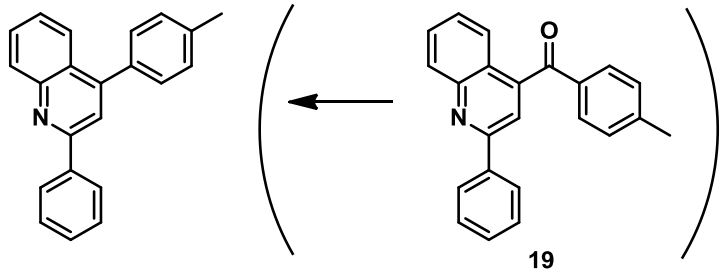
^{13}C NMR ($CDCl_3$, 100.53 MHz) δ: 21.4, 125.2, 126.9, 127.9, 128.0, 129.1, 129.2, 129.7, 133.1, 134.0, 137.8, 138.7, 147.2, 150.0.

IR (ATR): 2984 w, 1736 s, 1602 w, 1568 w, 1492 w, 1460 w, 1373 m, 1302 w, 1236 s, 1097 w, 1044 s, 938 w, 916 w, 848 m, 786 w, 753 w, 700 w.

MS, *m/z* (relative intensity, %): 234 (16), 233 (M^+, 100), 232 (21), 218 (26), 217 (24).

Exact Mass (EI) Calcd for $C_{17}H_{15}N$: 233.1205. Found: 233.1205.

2-Phenyl-4-(*p*-tolyl)quinoline [CAS: 73402-87-6].



19

The typical procedure was followed using **19** as the substrate.

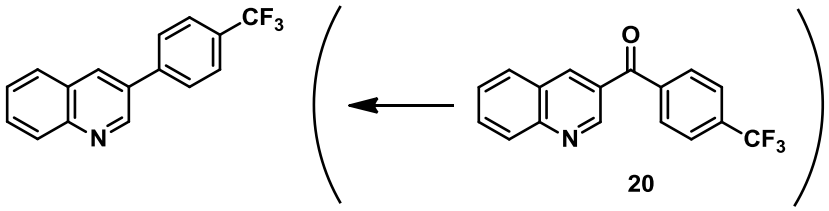
Colorless oil (71.6 mg, 97%). Rf 0.29 (SiO_2, hexane/EtOAc = 20/1).

^{1}H NMR ($CDCl_3$, 399.78 MHz) δ: 2.49 (s, 3H), 7.37 (d, *J* = 8.2 Hz, 2H), 7.50-7.45 (m, 4H), 7.56-7.7.52 (m, 2H), 7.74 (dd, *J* =6.8, 8.2 Hz, 1H), 7.82 (s, 1H), 7.94 (d, *J* = 8.3 Hz, 1H), 8.21-8.19 (m, 2H), 8.25 (d, *J* = 8.3 Hz, 1H).

^{13}C NMR ($CDCl_3$, 100.53 MHz) δ:14.3, 112.3, 118.7, 118.8, 119.2, 120.6, 121.8, 122.3, 122.44, 122.45, 123.06, 123.07, 128.4, 131.3, 132.7, 141.8, 142.2, 149.9.

Exact Mass (EI) Calcd for $C_{22}H_{17}N$: 295.1361. Found: 295.1362.

3-(4-(Trifluoromethyl)phenyl)quinoline [CAS: 1134099-67-4].



20

The typical procedure was followed using **20** as the substrate. The yield was determined by NMR spectroscopy because the product was inseparable from the unreacted starting ketone (product: 48%; unreacted **20**: 39%). Analytically pure product was obtained by purification by GPC (15.0 mg, 22%).

White solid (15.0 mg, 22%). Rf 0.23 (SiO_2, hexane/EtOAc = 6/1).

^{1}H NMR ($CDCl_3$, 399.78 MHz) δ: 7.61 (dd, *J* = 6.9 8.2 Hz, 1H), 7.85-7.76 (m, 5H), 7.93 (d, *J* = 6.9, 1H), 8.18 (d, *J* = 8.2, 1H), 8.35 (s, 1H), 9.20 (s, 1H).

^{13}C NMR ($CDCl_3$, 100.53 MHz) δ: 124.1 (q, J_{CF} = 272.2 Hz), 126.1 (q, J_{CF} = 2.9 Hz), 127.35, 127.36, 127.7, 128.2, 129.3, 130.0, 130.3, 132.5 (q, J_{CF} = 36.4 Hz), 133.8, 141.4, 147.7, 149.3.

Exact Mass (EI) Calcd for $C_{16}H_{10}F_3N$: 273.0765. Found: 273.0764.

3.5 References

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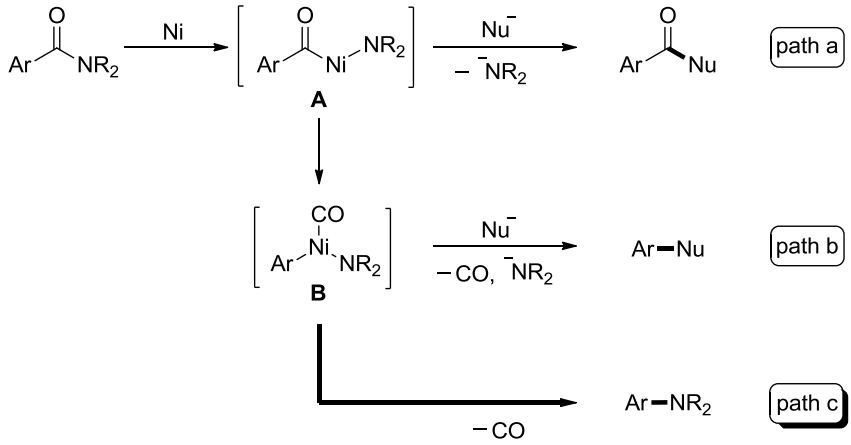
Chapter 4

Nickel-Mediated Decarbonylation of *N*-Acylpyrrole Derivatives

4.1 Introduction

Based on the results for the nickel mediated decarbonylation of ketones described in Chapter 3, the author became interested in extending this decarbonylation reaction to other carbonyl compounds. The nickel-catalyzed cross-coupling of amides through the cleavage of carbon-nitrogen bond has been a subject of recent, active study. Garg reported a pioneering work on the catalytic conversion of amides into esters. One mechanism for the conversion of amide involves the oxidative addition of the C-N bond to form an aroylnickel(II) intermediate **A** (Scheme 1, path a),[1] which undergoes transmetallation with external nucleophiles to form coupling products. The decarbonylative coupling of amides accompanied by the release of carbon monoxide from intermediate **A** was also reported (Scheme 1, path b).[2] Despite these advances, the decarbonylation of amides to give the corresponding amines via the formation of an arylnickel(II) intermediate **B** has not been reported (Scheme 1, path c), except for 2-picolinamide substrates.[3] In contrast to traditional cross-coupling reactions of amides, the amine moiety can be used as an internal nucleophile. Herein, the first nickel system for promoting the decarbonylation of *N*-acylpyrrole derivatives through carbon-nitrogen bond cleavage is described.

Scheme 1. Metal-Mediated Transformation of Aromatic Amides

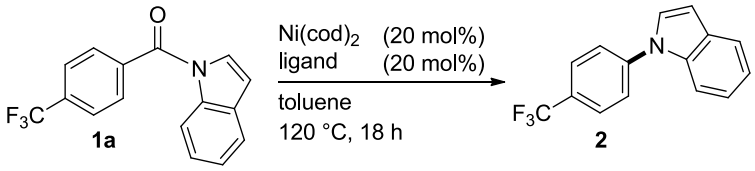


4.2 Results and Discussion

The effect of ligands in the nickel-catalyzed decarbonylation of *N*-acylindole **1a** was initially examined (Table 1). The addition of the $IMes^{Me}$ ligand, which is effective for the nickel-mediated decarbonylation of ketones as described in Chapter 3, and other NHC ligands resulted in the decomposition of the starting material (Table 1, entries 1-4). Meanwhile, PCy_3 and dcype were found to suppress amide decomposition, leading to the formation of

the decarbonylated product **2** in modest yield, respectively (Table 1, entries 6 and 7). Further optimization revealed that the use of a stoichiometric amount of nickel and PCy_3 provided the desired product in 88% isolated yield, even when the reaction was carried out at low temperatures (Table 1, entry 8). In the case of dcype, product yield increased to 84% when the temperature was increased to 180 °C (Table 1, entry 9).

Table 1. Effect of Ligands[a]

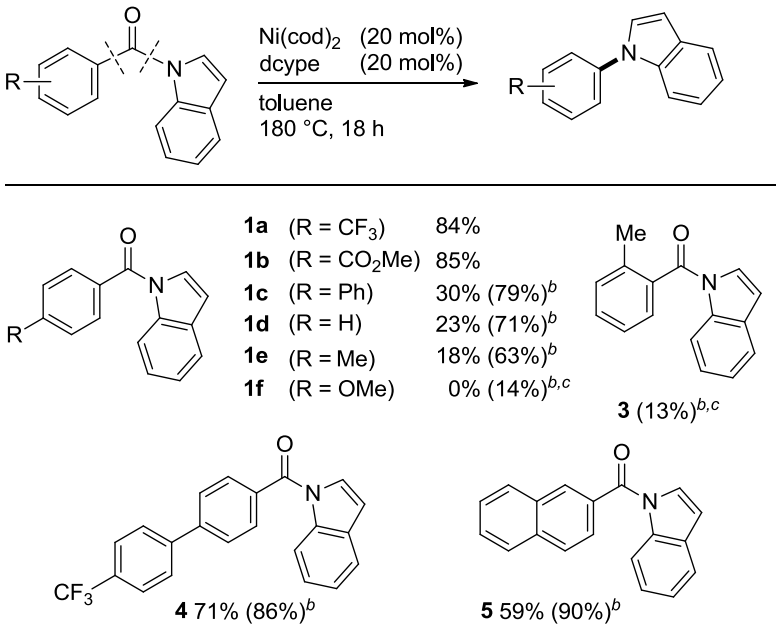


entry	ligand	GC yields (%)	
		2	**1**
1[b]	IPr·HCl	12	25
2[b]	IMes·HCl	28	29
3[b]	$IMes^{Me}$·HCl	27	27
4[b]	ICy·HCl	0	46
5	PPh_3	0	71
6	PCy_3	31	60
7	dcype	16	52
8[c]	PCy_3	>99 (88)[e]	0
9[d]	dcype	93 (84)[e]	0

[a] Reaction conditions: **1a** (0.25 mmol), $Ni(cod)_2$ (0.050 mmol), ligand (0.050 mmol) in toluene (1.0 mL) for 18 h at 120 °C. [b] NaO^{t}Bu (0.063 mmol) was used to generate carbene. [c] $Ni(cod)_2$ (0.25 mmol), ligand (0.25 mmol) at 80 °C. [d] At 180 °C. [e] Isolated yields.

These newly developed conditions using PCy_3 and the dcype ligand were then applied to other amides (Table 2). In initial experiments, dcype was used to examine the effects of different substituents on the progress of the decarbonylation reaction. Electron-withdrawing substituents such as CF_3 (**1a**) and CO_2Me (**1b**) promoted the decarbonylation, with the desired products being produced in good yield. When phenyl (**1c**), hydrogen (**1d**) and Me (**1e)** groups were introduced at the same position instead of an electron-withdrawing substituent, the starting amide was recovered in ca. 40% yield. When the decarbonylation was performed using a stoichiometric amount of PCy_3 instead of dcype, the yields of these amides were improved dramatically. An electron-donating OMe group (**1f**) could not be used under our developed conditions with either PCy_3 or the dcype ligand. This reaction is sensitive to steric effects, as evidenced by the decreased yield for amide **3**.

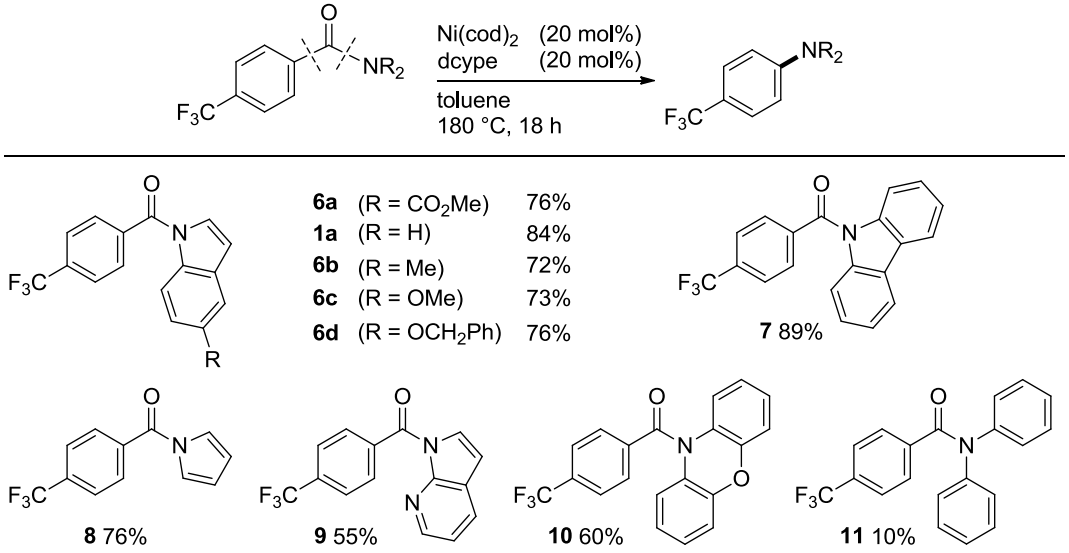
Table 2. Scope of Substrates[a]



[a] Reaction conditions: Amide (0.25 mmol), $Ni(cod)_2$ (0.050 mmol), dcype (0.050 mmol) in toluene (1.0 mL) for 18 h at 180 °C. Isolated yields. [b] $Ni(cod)_2$ (0.25 mmol), PCy_3 (0.25 mmol) at 80 °C. [c] NMR yield.

The scope of the amine moiety of the amide group using dcype as a ligand was next evaluated (Table 3). Methoxy (**6c**) and benzyloxy groups (**6d**), which are known to be cleaved in nickel-catalyzed reactions,[4] remained intact under the current conditions. Carbazole (**7**) and pyrrole (**8**) derivatives instead of indole were also found to be good substrates. The present catalytic system was also applicable to amides bearing azaindole (**9**) and phenoxazine (**10**) as an amine moiety. *N*,*N*-Diphenylamine derivative **11**, which is more basic than indole (p*K*a of indole: 21.0; p*K*a of Ph_2NH: 25.0), was found to be less reactive under the current conditions.

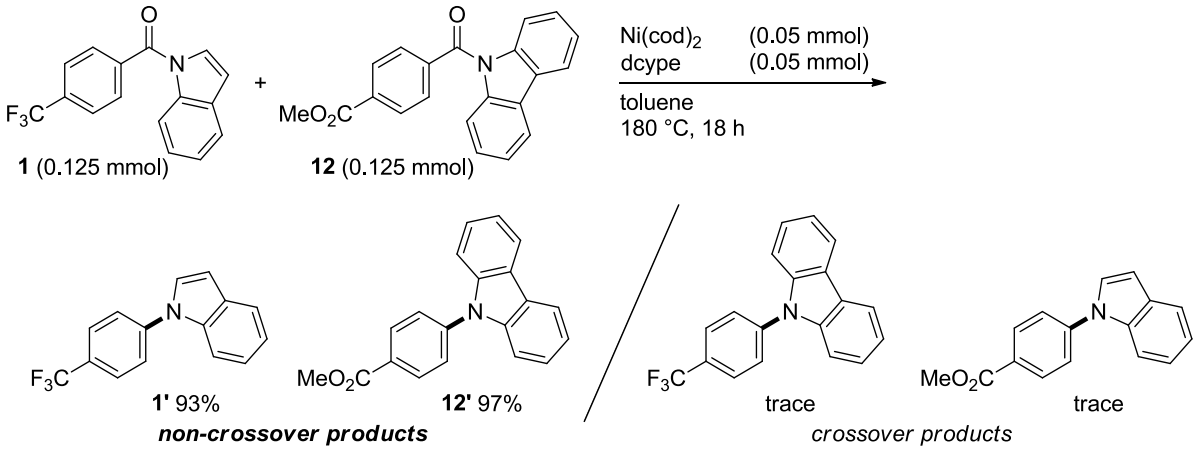
Table 3. Scope of Substrates[a]



[a] Reaction conditions: Amides (0.25 mmol), $Ni(cod)_2$ (0.050 mmol), dcype (0.050 mmol) in toluene (1.0 mL) for 18 h at 180 °C. Isolated yields.

A crossover experiment was performed using two amides that have different substituents (Scheme 2). As a result, no crossover products were obtained. The result of this experiment revealed that the present decarbonylation reaction proceeds in an intramolecular fashion.

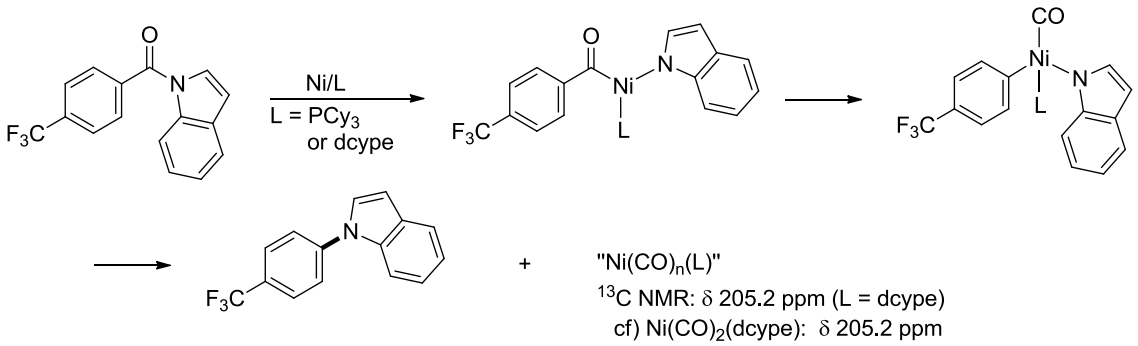
Scheme 2. Crossover Experiment



A plausible mechanism for the reaction is shown in Scheme 3. Similar to the decarbonylation of diaryl ketones described in Chapter 3, the oxidative addition of the C-N bond in amides would occur, followed by decarbonylation. Finally, reductive elimination would afford the desired amine product, along with a nickel carbonyl species. A ^{13}C NMR analysis showed that the $Ni(CO)_2$(dcype) complex was formed after the reaction when dcype was used as a

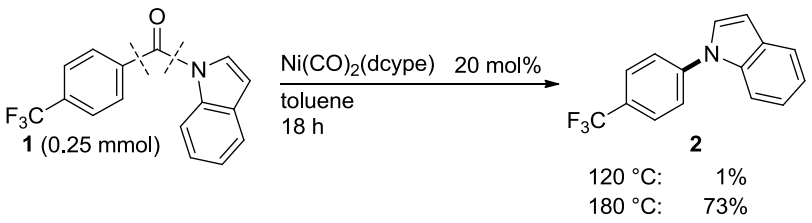
ligand.

Scheme 3. Possible Mechanism



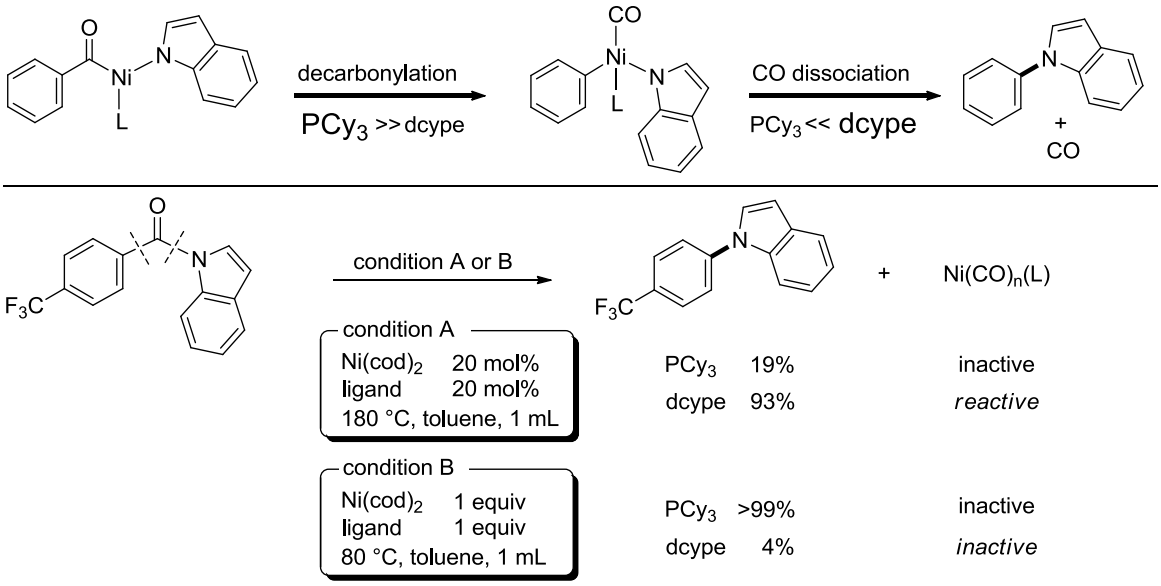
The decarbonylation of amides using $Ni(CO)_2$(dcype) as a catalyst was then investigated (Scheme 4). Although the desired product was not formed at 120 °C, the yield increased to 73% when the temperature was increased to 180 °C. This result indicates that the use of a high temperature assisted in the regeneration of the nickel catalyst by dissociation of the CO ligand from the nickel center.

Scheme 4. Temperature Dependence

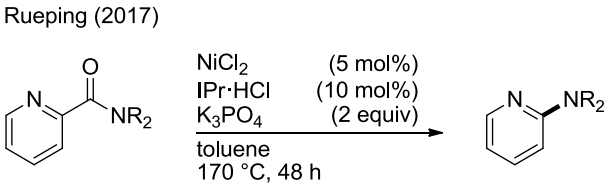


A mechanistic rationale for the difference in reactivities between PCy_3 and dcype is shown in Scheme 5. In the case of PCy_3, the amount of decarbonylated product was the same as that for the nickel complex used (20 mol% Ni → 19% yield; 1 equiv Ni → >99% yield). These results indicate that, although the PCy_3 complex exerts high activity with respect to the decarbonylation reaction, nickel carbonyl species that are generated in situ are unable to participate in the oxidative addition of the C-N bond. In the case of dcype, a small amount of the desired product was obtained at 80 °C, which can be attributed to its lower activity for decarbonylation than PCy_3. In contrast, the reaction proceeds effectively at 180 °C, indicating that the dcype complex promotes the dissociation of the CO ligand from the nickel center to recover the catalytic activity. In fact, similar ligand effects of PCy_3 and dcype have been reported in the cross-coupling of phenyl ester based on DFT calculations.[5]

Scheme 5. Effect of the Ligand: PCy_3 vs Dcype



An independent work on the nickel-catalyzed decarbonylation of 2-picolinamide substrates was reported by Rueping.[3]



4.3 Conclusion

In conclusion, the first nickel system capable of promoting the decarbonylation of amides via the cleavage of carbon–nitrogen bonds is described. *N*-Acylpyrrole derivatives are particularly reactive with this catalyst system, affording the corresponding *N*-arylated products. The successful use of the dcype ligand promoted the decarbonylation step, which is considered to be difficult when mono-phosphine ligands or NHC ligands are used. Studies aimed at expanding this new type of reactivity of nickel complexes, although further investigations will be required for a full understanding of the mechanism to be revealed.

4.4 Experimental Section

4.4.1 General Information

^1H and ^{13}C NMR spectra were recorded on a JEOL ECS-400 spectrometer (JEOL, Tokyo, Japan) or VARIAN UNITY INOVA-600 spectrometer in $CDCl_3$ with tetramethylsilane as an internal reference standard. NMR data have been reported as follows: chemical shift (δ) in ppm, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, and m = multiplet), coupling constant (*J*) in Hz, and integration. Infrared spectra (IR) were obtained on a

JASCO FT/IR-4000 spectrometer, and the absorptions have been reported in reciprocal centimeters with the following relative intensities: s (strong), m (medium), or w (weak). Mass spectra were obtained on a Shimadzu GCMS-QP 5000 or GCMS-QP 2010 instrument with an ionization voltage of 70 eV. High resolution mass spectra (HRMS) were obtained on a JEOL JMS-T100LP AccuTOF LC-plus in direct analysis real time (DART) method using PEG as the internal standard. Analytical gas chromatography (GC) was carried out on Shimadzu GC-2014, equipped with a flame ionization detector. Melting points were determined using a Yamato melting point apparatus. Column chromatography was performed over SiO_2 (Silycycle Silica Flash F60 (230-400 mesh)) and NH Silica (Silica Gel 60 (spherical) NH_2 (40-50 μm)). Some of the compounds were purified by LC-908 HPLC (GPC).

4.4.2 Materials

Toluene (for Organic Synth.) was purchased from Wako Chemicals and used as received. $Ni(cod)_2$ was purchased from Strem Chemicals and used as received. PCy_3 (Sigma-Aldrich), dcype (Sigma-Aldrich), IPr·HCl (TCI), IMes·HCl (TCI), ICy·HCl (TCI) and PPh_3 (TCI) were purchased from commercial suppliers and used as received. $IMes^{Me}$·HCl[6] was prepared according to the literature procedures.

4.4.3 General Procedure for Synthesis of Starting Materials

Aroyl chloride (20 mmol) was partially added to a solution of pyrrole (20 mmol), Et_3N (1 equiv) and *N*,*N*-dimethyl-4-aminopyridine (0.4 mmol) in 20 mL of CH_2Cl_2 at 0 °C. After addition was completed, the reaction mixture was stirred at room temperature for 12 hour. The reaction was quenched by the addition of H_2O, and the resulting mixture was extracted with CH_2Cl_2. The combined extracts were washed with brine, dried ($MgSO_4$), and concentrated to give a residue, which was purified by recrystallization or column chromatography to give a desired *N*-acylpyrrole derivative. All spectrum data of starting materials are cited in original paper.[7]

4.4.4 Typical Procedure for the Ni-Mediated Decarbonylation of *N*-Acylpyrrole Derivatives

Condition A: Procedure for the Ni/Dcype-Catalyzed Decarbonylation of *N*-Acylpyrrole Derivatives

$Ni(cod)_2$ (13.8 mg, 0.050 mmol), dcype (21.1 mg, 0.050 mmol), *N*-acylpyrrole derivatives and toluene (1 mL) were added to a 10 mL-sample vial with a Teflon-sealed screwcap in a glovebox filled with nitrogen. The resulting mixture was stirred at room temperature for 3 min and the cap was closed. The contents of the vial were then stirred at 180 °C for 18 h. The reaction was cooled to room temperature, and the crude mixture was filtered through a pad of silica gel before being analyzed by GC. The filtrate was then concentrated *in vacuo* to give a residue, which was purified by flash column chromatography over silica gel.

Condition B: Procedure for the Ni/PCy_3-Mediated Decarbonylation of *N*-Acylpyrrole Derivatives

$Ni(cod)_2$ (68.8 mg, 0.25 mmol), PCy_3 (70.1 mg, 0.25 mmol), *N*-acylpyrrole derivatives and toluene (1 mL) were added to a 10 mL-sample vial with a Teflon-sealed screwcap in a glovebox filled with nitrogen. The resulting mixture was stirred at room temperature for 3 min and the cap was closed. The contents of the vial were then stirred at 80 °C for 18 h. The reaction was cooled to room temperature, and the crude mixture was filtered through a pad of silica gel before being analyzed by GC. The filtrate was then concentrated *in vacuo* to give a residue, which was purified by flash column chromatography over silica gel.

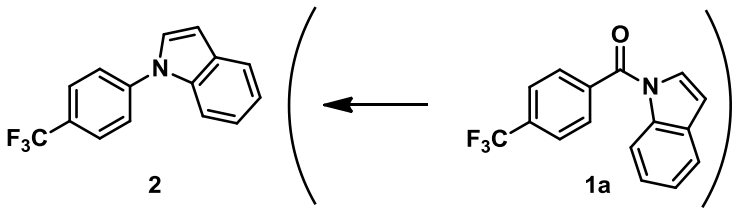
4.4.5 Intermolecular Competition Reactions for the Ni-Mediated Decarbonylation of Amides

$Ni(cod)_2$ (13.8 mg, 0.050 mmol), dcype (21.1 mg, 0.050 mmol), two amides (0.13 mmol each) and toluene (1 mL) were added to a 10 mL-sample vial with a Teflon-sealed screwcap in a glovebox filled with nitrogen. The resulting mixture was stirred at room temperature for 3 min and the cap was closed. The contents of the vial were then stirred at 180 °C for 18 h. The reaction was cooled to room temperature, and the crude mixture was filtered through a pad of silica gel before being analyzed by GC. The filtrate was then concentrated *in vacuo* to give a residue, which was purified by flash column chromatography over silica gel.

4.4.6 Spectroscopic Data of Products

4.4.6 Spectroscopic Data of Products

1-(4-(Trifluoromethyl)phenyl)-1*H*-indole [CAS: 174621-55-7].



The typical procedure (Condition A) was followed using **1a** as the substrate.

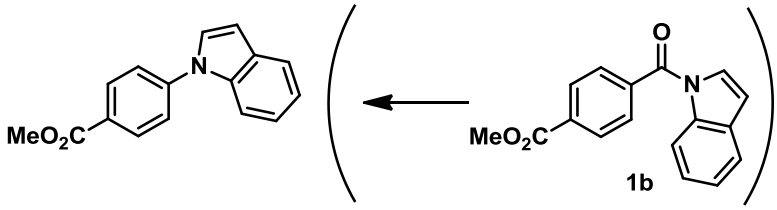
White solid (54.9 mg, 84%). Rf 0.57 (SiO_2, hexane/EtOAc = 20/1).

^1H NMR ($CDCl_3$, 399.78 MHz) δ: 6.76 (d, J = 3.2 Hz, 1H), 7.23 (dd, J = 6.9, 7.8 Hz, 1H), 7.29 (dd, J = 6.8, 8.2 Hz, 1H), 7.37 (d, J = 3.2 Hz, 1H), 7.66-7.61 (m, 3H), 7.72 (d, J = 7.8 Hz, 1H), 7.80 (d, J = 8.7 Hz, 1H).

^{13}C NMR ($CDCl_3$, 100.53 MHz) δ: 104.9, 110.3, 121.0, 121.4, 122.9, 123.9, 124.0 (q, J_{CF} = 272.6 Hz), 126.9 (q, J_{CF} = 4.1 Hz), 127.4, 128.2 (q, J_{CF} = 28.0 Hz), 129.7, 135.5, 142.8.

HRMS calcd for $C_{15}H_{10}F_3N$ ([M+H^+]): 262.0838. Found: 262.0839.

Methyl 4-(1*H*-indol-1-yl)benzoate [CAS: 212382-74-6].



The typical procedure (Condition A) was followed using **1b** as the substrate.

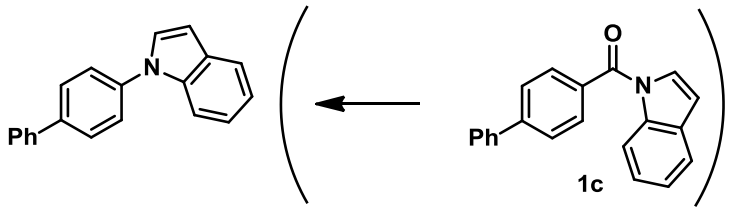
Colorless oil (53.4 mg, 85%). Rf 0.23 (SiO_2, hexane/EtOAc = 20/1).

^{1}H NMR ($CDCl_3$, 399.78 MHz) δ: 3.96 (s, 3H), 6.73 (d, *J* = 3.6 Hz, 1H), 7.21 (dd, *J* = 7.3, 7.8 Hz, 1H), 7.27 (dd, *J* = 7.3, 8.2 Hz, 1H), 7.38 (d, *J* = 3.6 Hz, 1H), 7.60 (d, *J* = 8.7 Hz, 2H), 7.64 (d, *J* = 8.2 Hz, 1H), 7.70 (d, *J* = 7.8 Hz, 1H), 8.20 (d, *J* = 8.7 Hz, 2H).

^{13}C NMR ($CDCl_3$, 100.53 MHz) δ: 52.2, 104.9, 110.5, 120.9, 121.4, 122.9, 123.2, 127.4, 127.6, 129.8, 131.2, 135.4, 143.7, 166.4.

HRMS calcd for $C_{16}H_{13}NO_2$ ([M+H$^+$]): 252.1019. Found: 252.1017.

1-([1,1'-Biphenyl]-4-yl)-1*H*-indole [CAS: 174621-51-3].



The typical procedure (Condition A and B) was followed using **1c** as the substrate.

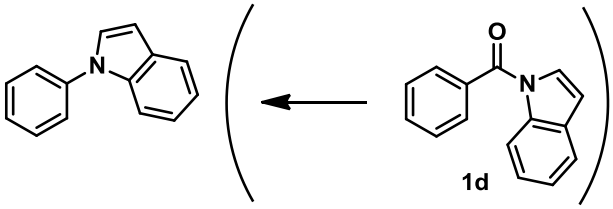
White solid (53.2 mg, 79%). Rf 0.57 (SiO_2, hexane/EtOAc = 20/1).

^{1}H NMR ($CDCl_3$, 399.78 MHz) δ: 6.75 (d, *J* = 3.2 Hz, 1H), 7.22 (dd, *J* = 6.8, 7.3 Hz, 1H), 7.29 (dd, *J* = 7.3, 8.2 Hz, 1H), 7.44-7.39 (m, 2H), 7.54-7.49 (m, 2H), 7.62-7.59 (m, 2H), 7.70-7.66 (m, 3H), 7.78-7.34 (m, 3H).

^{13}C NMR ($CDCl_3$, 100.53 MHz) δ: 103.7, 110.6, 120.4, 121.2, 122.4, 124.5, 127.0, 127.5, 127.8, 128.2, 128.9, 129.4, 135.8, 138.9, 139.3, 140.2.

HRMS calcd for $C_{20}H_{15}N$ ([M+H$^+$]): 270.1277. Found: 270.1274.

1-Phenyl-1*H*-indole [CAS: 16096-33-6].



The typical procedure (Condition A and B) was followed using **1d** as the substrate.

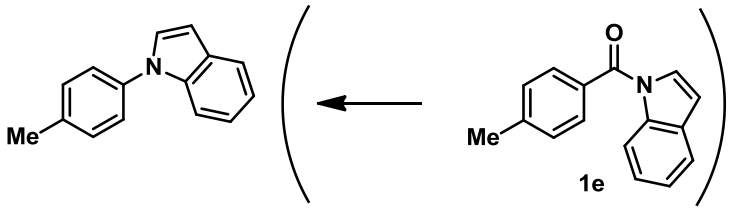
White solid (34.3 mg, 71%). Rf 0.49 (SiO_2, hexane/EtOAc = 10/1).

^{1}H NMR ($CDCl_3$, 399.78 MHz) δ: 6.70 (d, *J* = 3.2 Hz, 1H), 7.19 (dd, *J* = 6.9, 7.3 Hz, 1H), 7.24 (dd, *J* = 7.3, 8.2 Hz, 1H), 7.39-7.35 (m, 2H), 7.54-7.52 (m, 4H), 7.59 (d, *J* = 6.8 Hz, 1H), 7.71 (d, *J* = 8.2 Hz, 1H).

^{13}C NMR ($CDCl_3$, 100.53 MHz) δ: 103.5, 110.5, 120.3, 121.1, 122.3, 124.4, 126.4, 127.9, 129.3, 129.6, 135.8, 139.8.

HRMS calcd for $C_{14}H_{11}N$ ([M+H$^+$]): 194.0964. Found: 194.0974.

1-(*p*-Tolyl)-1*H*-indole [CAS: 167283-32-1].



The typical procedure (Condition A and B) was followed using **1e** as the substrate.

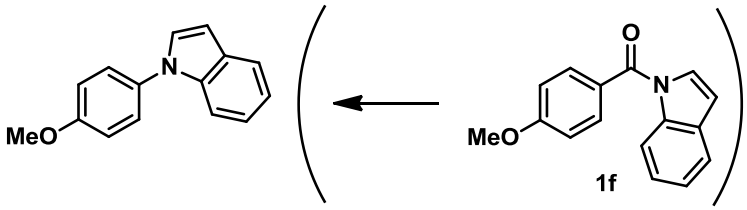
Colorless oil (32.6 mg, 63%). Rf 0.49 (SiO_2, hexane/EtOAc = 10/1).

^{1}H NMR ($CDCl_3$, 399.78 MHz) δ: 2.44 (s, 3H), 6.67 (d, *J* = 3.2 Hz, 1H), 7.17 (dd, *J* = 6.9, 7.8 Hz, 1H), 7.21 (dd, *J* = 6.9, 8.3 Hz, 1H), 7.33-7.31 (m, 3H), 7.40 (d, *J* = 8.3 Hz, 2H), 7.54 (d, *J* = 8.3 Hz, 1H), 7.54 (d, *J* = 7.8 Hz, 1H).

^{13}C NMR ($CDCl_3$, 100.53 MHz) δ: 21.0, 103.2, 110.5, 120.1, 121.0, 122.2, 124.3, 128.0, 129.1, 130.1, 136.0, 136.3, 137.3.

HRMS calcd for $C_{15}H_{13}N$ ([M+H$^+$]): 208.1121. Found: 208.1122.

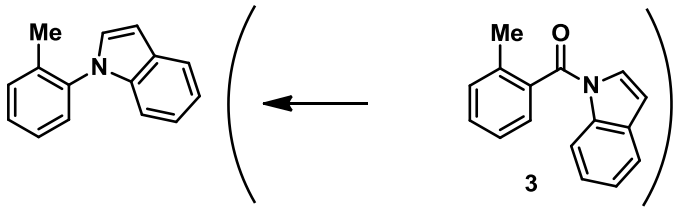
1-(4-Methoxyphenyl)-1*H*-indole [CAS: 93597-01-4].



The typical procedure (Condition B) was followed using **1f** as the substrate. The yield was determined by NMR analysis using 1,1,2,2-tetrachloroethane as an internal standard (14%).

HRMS calcd for $C_{15}H_{13}NO$ ([M+H$^+$]): 224.1070. Found: 224.1077.

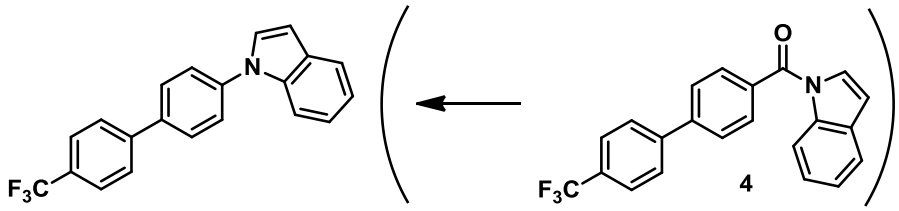
1-(*o*-Tolyl)-1*H*-indole [CAS: 210162-61-1].



The typical procedure (Condition B) was followed using **3** as the substrate. The yield was determined by NMR analysis using 1,1,2,2-tetrachloroethane as an internal standard (13%).

HRMS calcd for $C_{15}H_{13}N$ ([M+H$^+$]): 208.1121. Found: 208.1121.

1-(4'-(Trifluoromethyl)-[1,1'-biphenyl]-4-yl)-1*H*-indole.



The typical procedure (Condition A and B) was followed using **4** as the substrate.

White solid (72.7 mg, 86%). Mp 133.3-133.8 °C. Rf 0.23 (SiO_2, hexane/EtOAc = 20/1).

^{1}H NMR ($CDCl_3$, 399.78 MHz) δ: 6.74 (d, *J* = 3.3 Hz, 1H), 7.21 (dd, *J* = 6.9, 7.2 Hz, 1H), 7.27 (dd, *J* = 7.1, 8.2 Hz, 1H), 7.40 (d, *J* = 3.3 Hz, 1H), 7.66-7.62 (m, 3H), 7.79-7.72 (m, 7H).

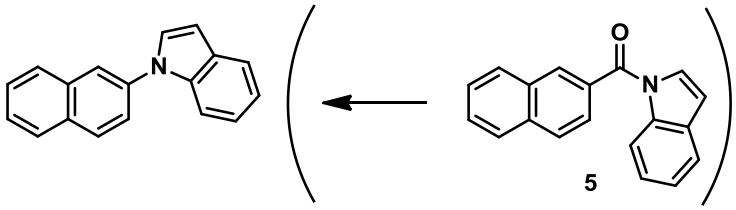
^{13}C NMR ($CDCl_3$, 100.53 MHz) δ: 104.1, 110.5, 120.6, 121.3, 122.6, 124.2 (q, J_{CF} = 272.2 Hz), 124.6, 125.9 (q, J_{CF} = 2.9 Hz), 127.3, 127.7, 128.4, 129.5, 129.6 (q, J_{CF} = 32.6 Hz), 135.7, 137.7, 139.8, 143.7.

IR (ATR): 2942 w, 2865 w, 1713 m, 1616 w, 1526w, 1473 m, 1379 w, 1324 s, 1263 m, 1217 w, 1163 m, 1124 m, 1069 m, 1016 w, 958 w, 883 w, 848 w, 830 w, 803 w, 770 w, 743 w, 718 w, 696 w, 677 w.

MS, *m/z* (relative intensity, %): 338 (23), 337 (M$^+$, 100), 89 (13).

HRMS calcd for $C_{21}H_{14}F_3N$ ([M+H$^+$]): 338.1151. Found: 338.1149.

1-(Naphthalen-2-yl)-1*H*-indole [CAS: 348111-49-9].



The typical procedure (Condition A and B) was followed using **5** as the substrate.

Colorless oil (54.7 mg, 90%). Rf 0.40 (SiO_2, hexane/EtOAc = 20/1).

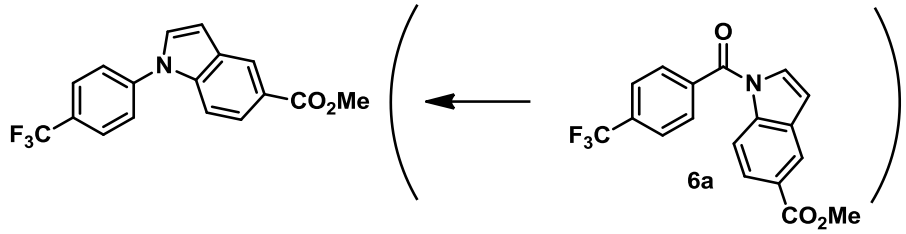
^{1}H NMR ($CDCl_3$, 399.78 MHz) δ: 6.77 (d, *J* = 3.2 Hz, 1H), 7.30-7.21 (m, 2H), 7.49-7.47 (m, 1H), 7.60-7.53 (m,

3H), 7.71-7.67 (m, 2H), 7.76 (d, J = 7.8 Hz, 1H), 7.96-7.90 (m, 3H), 8.01 (d, J = 8.7 Hz, 1H)

^{13}C NMR ($CDCl_3$, 100.53 MHz) δ: 103.8, 110.5, 120.5, 121.2, 121.9, 122.4, 123.2, 126.0, 126.9, 127.7, 127.8, 128.1, 129.4, 129.6, 131.8, 133.8, 136.0, 137.3.

HRMS calcd for $C_{18}H_{13}N$ ([M+H$^+$]): 244.1121. Found: 244.1135.

Methyl 1-(4-(trifluoromethyl)phenyl)-1*H*-indole-5-carboxylate [CAS: 1373525-79-1].



The typical procedure (Condition A) was followed using **6a** as the substrate.

White solid (60.6 mg, 76%). Mp 141.8-142.1 °C. Rf 0.18 (SiO_2, hexane/EtOAc = 20/1).

^{1}H NMR ($CDCl_3$, 399.78 MHz) δ: 3.95 (s, 3H), 6.81 (d, J = 3.2 Hz, 1H), 7.41 (d, J = 3.2 Hz, 1H), 7.57 (d, J = 8.8 Hz, 1H), 7.63 (d, J = 8.3 Hz, 2H), 7.81 (d, J = 8.4 Hz, 2H), 7.95 (d, J = 8.8 Hz, 1H), 8.45 (s, 1H).

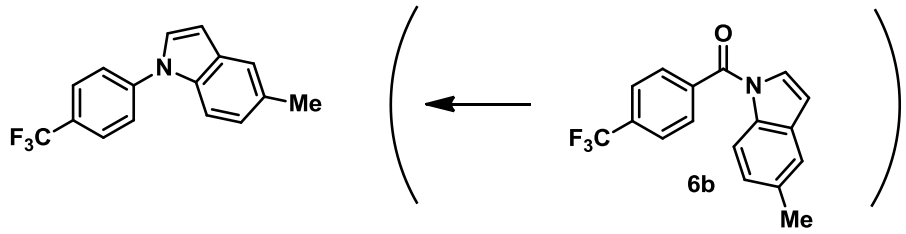
^{13}C NMR ($CDCl_3$, 100.53 MHz) δ: 52.0, 105.96, 105.97, 110.0, 123.0, 123.8 (q, J_{CF} = 272.2 Hz), 124.2, 127.0 (q, J_{CF} = 3.8 Hz), 128.8 (q, J_{CF} = 15.3 Hz), 128.9, 129.2, 137.90, 137.92, 142.2, 167.7.

IR (ATR): 2951 w, 1712 m, 1610 m, 1526 w, 1475 w, 1436 w, 1377 w, 1359 w, 1324 s, 1272 m, 1228 m, 1198 m, 1166 m, 1123 mm, 1087 w, 1066 m, 1016 w, 987 w, 954 w, 909 w, 848 w, 754 m, 718 w, 667 w.

MS, *m/z* (relative intensity, %): 320 (17), 319 (M$^+$, 89), 289 (18), 288 (100), 260 (28), 240 (13), 191 (30), 144 (16).

HRMS calcd for $C_{17}H_{12}F_3NO_2$ ([M+H$^+$]): 320.0893. Found: 320.0881.

5-Methyl-1-(4-(trifluoromethyl)phenyl)-1*H*-indole.



The typical procedure (Condition A) was followed using **6b** as the substrate.

White solid (49.5 mg, 72%). Mp 60.5-60.9 °C. Rf 0.45 (SiO_2, hexane/EtOAc = 20/1).

^{1}H NMR ($CDCl_3$, 399.78 MHz) δ: 2.48 (s, 3H), 6.66 (d, J = 3.2 Hz, 1H), 7.10 (d, J = 8.6 Hz, 1H), 7.32 (d, J = 3.2 Hz, 1H), 7.52-7.49 (m, 2H), 7.62 (d, J = 8.4 Hz, 2H), 7.77 (d, J = 8.4 Hz, 2H).

^{13}C NMR ($CDCl_3$, 100.53 MHz) δ: 21.3, 104.5, 110.0, 121.1, 123.6, 124.0, 124.5, 126.8, 127.4, 127.9, 130.0, 130.3, 133.8, 142.9.

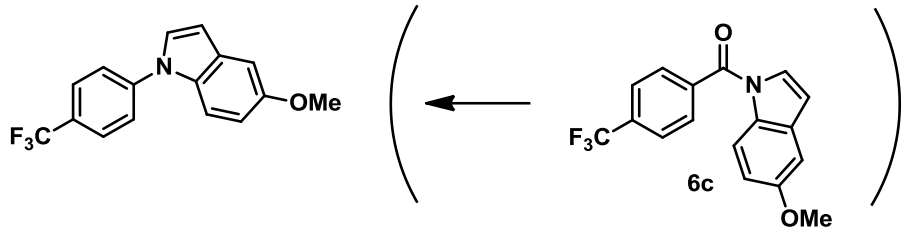
IR (ATR): 2941 w, 2865 w, 2156 w, 1712 w, 1616 w, 1525 w, 1473 m, 1451 w, 1378 w, 1323 s, 1260 m, 1218 w,

1162 m, 1122 m, 1066 m, 1015 w, 958 w, 913 w, 882 w, 846 w, 800 w, 770 w, 751 w, 717 w, 696 w, 677 w.

MS, *m/z* (relative intensity, %): 276 (17), 275 (M^+, 100), 274 (65), 77 (12).

HRMS calcd for $C_{16}H_{12}F_3N$ ([M+H^+]): 276.0995. Found: 276.0987.

5-methoxy-1-(4-(trifluoromethyl)phenyl)-1*H*-indole.



The typical procedure (Condition A) was followed using **6c** as the substrate.

White solid (53.1 mg, 73%). Mp 84.8-85.1 °C. Rf 0.38 (SiO_2, hexane/EtOAc = 20/1).

^{1}H NMR ($CDCl_3$, 399.78 MHz) δ: 3.89 (s, 3H), 6.66 (d, *J* = 3.2 Hz, 1H), 6.92 (d, *J* = 2.3, 9.2 Hz, 1H), 7.15 (d, *J* = 2.3 Hz, 1H), 7.33 (d, *J* = 3.2 Hz, 1H), 7.51 (d, *J* = 9.2 Hz, 1H), 7.61 (d, *J* = 8.4 Hz, 2H), 7.77 (d, *J* = 8.4 Hz, 2H).

^{13}C NMR ($CDCl_3$, 100.53 MHz) δ: 55.8, 103.0, 104.6, 111.2, 112.9, 123.5, 124.0 (q, J_{CF} = 271.8 Hz), 126.9 (q, J_{CF} = 3.7 Hz), 127.7 (q, J_{CF} = 32.7 Hz), 127.8, 130.3, 130.5, 142.8, 154.9.

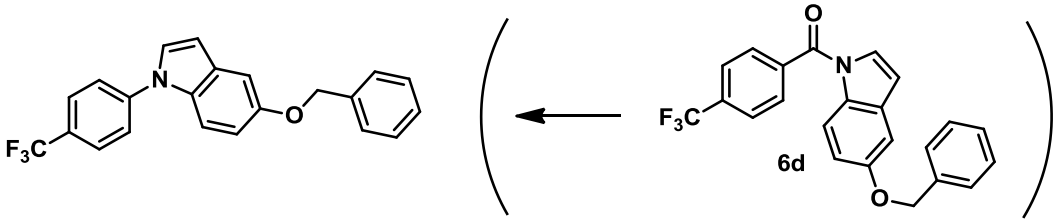
IR (ATR): 2941 w, 1712 w, 1616 w, 1524 w, 1476 m, 1449 w, 1378 w, 1323 s, 1262 m, 1217 w, 1159 m, 1120 m, 1066 m, 1033 w, 1016 w, 957 w, 846 w, 803 w, 771 w, 754 w, 717 w.

MS, *m/z* (relative intensity, %): 292 (18), 291 (M^+, 100), 277 (12), 276 (70), 248 (42).

Exact Mass (EI) Calcd for $C_{16}H_{12}F_3NO$: 291.08710. Found:

HRMS calcd for $C_{16}H_{12}F_3NO$ ([M+H^+]): 292.0944. Found: 292.0937.

5-(Benzyloxy)-1-(4-(trifluoromethyl)phenyl)-1*H*-indole [CAS: 161460-21-5].



The typical procedure (Condition A) was followed using **6d** as the substrate.

White solid (69.8 mg, 76%). Mp 104.3-104.8 °C. Rf 0.34 (SiO_2, hexane/EtOAc = 10/1).

^{1}H NMR ($CDCl_3$, 399.78 MHz) δ: 5.14 (s, 2H), 6.65 (d, *J* = 3.2 Hz, 1H), 7.00 (dd, *J* = 2.8, 8.7 Hz, 1H), 7.23 (d, *J* = 2.8 Hz, 1H), 7.34-7.32 (m, 2H), 7.42-7.39 (m, 2H), 7.52-7.646 (m, 3H), 7.61 (d, *J* = 8.3 Hz, 2H), 7.77 (d, *J* = 8.3 Hz, 2H).

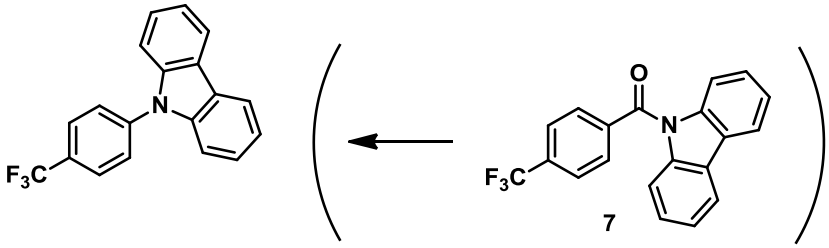
^{13}C NMR ($CDCl_3$, 100.53 MHz) δ: 70.7, 104.5, 104.6, 111.2, 113.6, 123.5, 123.9 (q, J_{CF} = 272.6 Hz), 126.9 (q, J_{CF} = 3.1 Hz), 127.5, 127.8, 127.9 (q, J_{CF} = 32.1 Hz), 128.5, 128.6, 130.3, 130.7, 137.4, 142.8, 154.0.

IR (ATR): 3033 w, 2863 w, 1708 w, 1616 m, 1572 w, 1524 m, 1472 m, 1450 m, 1424 w, 1379 w, 1322 s, 1258 m, 1217 w, 1159 s, 1115 s, 1065 m, 1015 m, 957 w, 911 w, 845 m, 802 w, 737 m, 717 m, 697 m.

MS, *m/z* (relative intensity, %): 367 (M^+, 39), 277 (18), 276 (100), 248 (27), 91 (65).

HRMS calcd for $C_{22}H_{16}F_3NO$ ([M+H^+]): 368.1257. Found: 368.1251.

9-(4-(Trifluoromethyl)phenyl)-9*H*-carbazole [CAS: 204066-03-5].



7

The typical procedure (Condition A) was followed using **7** as the substrate.

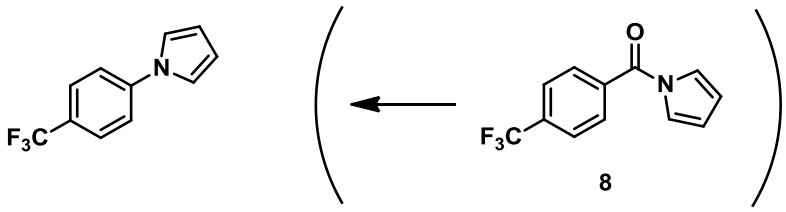
White solid (69.3 mg, 89%). Rf 0.43 (SiO_2, hexane/EtOAc = 10/1).

^{1}H NMR ($CDCl_3$, 399.78 MHz) δ: 7.34-7.31 (m, 2H), 7.45-7.41 (m, 4H), 7.73 (d, *J* = 8.2 Hz, 2H), 7.88 (d, *J* = 8.2 Hz, 2H), 8.15 (d, *J* = 8.9 Hz, 2H).

^{13}C NMR ($CDCl_3$, 100.53 MHz) δ: 109.5, 120.45, 120.56, 123.7, 123.9 (q, J_{CF} = 272.6 Hz), 126.2, 127.0, 127.1 (q, J_{CF} = 3.2 Hz), 129.1 (q, J_{CF} = 33.2 Hz), 140.2, 140.1.

HRMS calcd for $C_{19}H_{12}F_3N$ ([M+H^+]): 312.0995. Found: 312.0991.

1-(4-(Trifluoromethyl)phenyl)-1*H*-pyrrole [CAS: 92636-38-9].



8

The typical procedure (Condition A) was followed using **8** as the substrate.

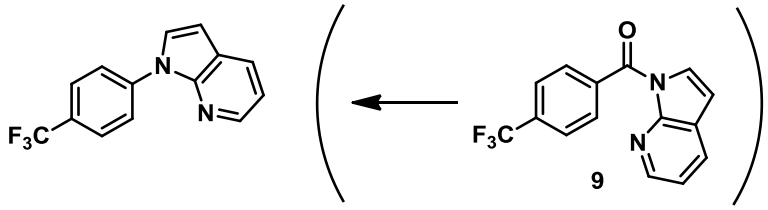
White solid (40.1 mg, 76%). Rf 0.40 (SiO_2, hexane/EtOAc = 20/1).

^{1}H NMR ($CDCl_3$, 399.78 MHz) δ: 6.39 (d, *J* = 3.7 Hz, 2H), 7.13 (d, *J* = 3.7 Hz, 2H), 7.49 (d, *J* = 8.8, 2H), 7.68 (d, *J* = 8.8 Hz, 2H).

^{13}C NMR ($CDCl_3$, 100.53 MHz) δ: 111.5, 119.1, 112.0, 124.0 (q, J_{CF} = 271.6 Hz), 126.9 (q, J_{CF} = 3.1 Hz), 127.4 (q, J_{CF} = 33.2 Hz), 143.2.

HRMS calcd for $C_{11}H_8F_3N$ ([M+H^+]): 212.0682. Found: 212.0688.

1-(4-(Trifluoromethyl)phenyl)-1*H*-pyrrolo[2,3-*b*]pyridine [CAS: 1797430-69-3].



The typical procedure (Condition A) was followed using **9** as the substrate.

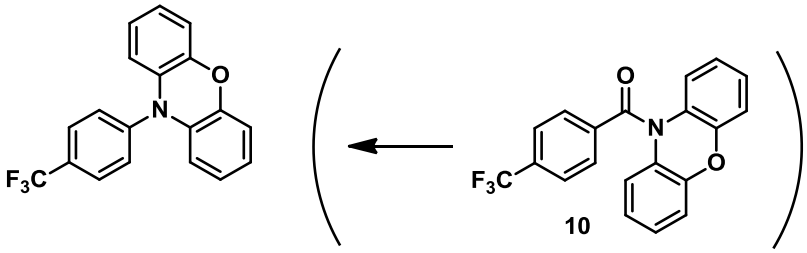
White solid (36.1 mg, 55%). Rf 0.34 (SiO_2, hexane/EtOAc = 10/1).

^{1}H NMR ($CDCl_3$, 399.78 MHz) δ: 6.99 (d, *J* = 3.7 Hz, 1H), 7.18 (dd, *J* = 4.8, 7.8 Hz, 1H), 7.55 (d, *J* = 3.7 Hz, 1H), 7.78 (d, *J* = 8.5 Hz, 2H), 8.00-7.97 (m, 3H), 8.39 (d, *J* = 4.8 Hz, 1H).

^{13}C NMR ($CDCl_3$, 100.53 MHz) δ: 102.9, 117.3, 121.9, 123.3, 124.0 (q, J_{CF} = 271.6 Hz), 126.6 (q, J_{CF} = 3.2 Hz), 127.0, 127.8 (q, J_{CF} = 33.2 Hz), 129.4, 141.4, 143.8, 137.4.

HRMS calcd for $C_{14}H_9F_3N_2$ ([M+H$^+$]): 263.0791. Found: 263.0796.

10-(4-(Trifluoromethyl)phenyl)-10*H*-phenoxazine [CAS: 58736-86-0].



The typical procedure (Condition A) was followed using **10** as the substrate.

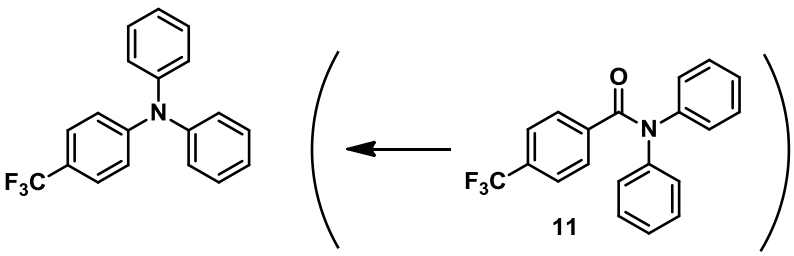
White solid (49.1 mg, 60%). Rf 0.54 (SiO_2, hexane/EtOAc = 20/1).

^{1}H NMR ($CDCl_3$, 399.78 MHz) δ: 5.90 (d, *J* = 7.8 Hz, 2H), 6.61 (dd, *J* = 7.3, 7.8 Hz, 2H), 6.74-6.67 (m, 4H), 7.51 (d, *J* = 8.0 Hz, 2H), 7.87 (d, *J* = 8.2 Hz, 2H).

^{13}C NMR ($CDCl_3$, 100.53 MHz) δ: 113.2, 115.7, 121.9, 123.3, 123.8 (q, J_{CF} = 272.6 Hz), 128.2 (q, J_{CF} = 4.1 Hz), 130.6 (q, J_{CF} = 32.1 Hz), 131.5, 133.7, 142.5, 143.9.

HRMS calcd for $C_{19}H_{12}F_3NO$ ([M+H$^+$]): 328.0944. Found: 328.0944.

***N*,*N*-diphenyl-4-(trifluoromethyl)aniline [CAS: 36809-32-2].**



The typical procedure (Condition A) was followed using **11** as the substrate.

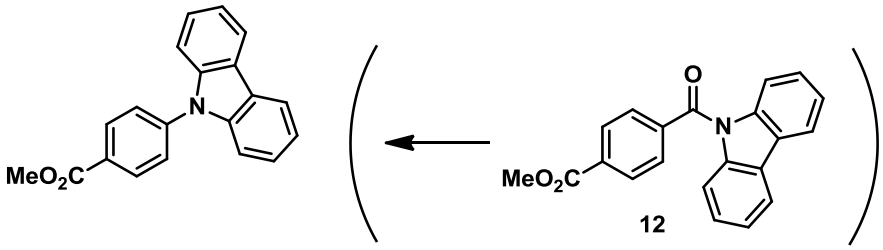
White solid (7.8 mg, 10%). Rf 0.63 (SiO_2, hexane/EtOAc = 10/1).

^{1}H NMR ($CDCl_3$, 399.78 MHz) δ: 7.05 (d, J = 8.3 Hz, 2H), 7.14-7.10 (m, 6H), 7.32-7.28 (m, 4H), 7.41 (d, J = 8.7 Hz, 2H).

^{13}C NMR ($CDCl_3$, 100.53 MHz) δ:121.0, 122.7 (q, J_{CF} = 33.2 Hz), 124.2, 123.3 (q, J_{CF} = 300.0 Hz), 125.4, 126.2 (q, J_{CF} = 4.1 Hz), 129.5, 146.8, 150.8.

HRMS calcd for $C_{19}H_{14}F_3N$ ([M+H$^+$]): 314.1151. Found: 314.1149.

Methyl 4-(9*H*-carbazol-9-yl)benzoate [CAS: 57103-16-9].



The typical procedure (Condition A) was followed using **12** as the substrate.

White solid (70.8 mg, 94%). Rf 0.23 (SiO_2, hexane/EtOAc = 10/1).

^{1}H NMR ($CDCl_3$, 399.78 MHz) δ: 4.00 (s, 3H), 7.32 (dd, J = 6.9, 7.8 Hz, 2H), 7.43 (dd, J = 6.9, 8.2 Hz, 2H), 7.47 (d, J = 8.2 Hz, 2H), 7.69 (d, J = 8.2 Hz, 2H), 8.16 (d, J = 7.8 Hz, 2H), 8.29 (d, J = 8.2 Hz, 2H).

^{13}C NMR ($CDCl_3$, 100.53 MHz) δ: 52.3, 109.7, 120.4, 120.5, 123.8, 126.2, 126.4, 128.6, 131.3, 140.2, 142.0, 166.4.

Exact Mass (EI) Calcd for $C_{20}H_{15}NO_2$: 301.11028. Found:

HRMS calcd for $C_{20}H_{15}NO_2$ ([M+H$^+$]): 302.1176. Found: 302.1172.

4.5 References

(1) Reviews on C−N amide cross-coupling: (a) Meng, G.; Shi, S.; Szostak, M. *Synlett* **2016**, *27*, 2530. (b) Liu, C.; Szostak, M. *Chem. Eur. J*. **2017**, *23*, 7157. (c) Dander, J. E.; Garg, N. K. *ACS Catal*. **2017**, *7*, 1413. (d) Takise, R.; Muto, K.; Yamaguchi, J. *Chem. Soc. Rev*. **2017**, *46*, 5864.

(2) (a) Meng, G.; Szostak, M. *Angew. Chem., Int. Ed*. **2015**, *54*, 14518. (b) Shi, S.; Meng, G.; Szostak, M. *Angew. Chem., Int. Ed*. **2016**, *55*, 6959. (c) Meng, G.; Szostak, M. *Org. Lett*. **2016**, *18*, 796. (d) Liu, C.; Meng, G.; Szostak, M. *J. Org. Chem*. **2016**, *81*, 12023. (e) Hu, J.; Zhao, Y.; Liu, J.; Zhang, Y.; Shi, Z. *Angew. Chem., Int. Ed*. **2016**, *55*, 8718. (f) Wu, H.; Liu, T.; Cui, M.; Li, Y.; Jian, J.; Wang, H.; Zeng, Z. *Org. Biomol. Chem*. **2017**, *15*, 536. (g) Dey, A.; Sasmal, S.; Seth, K.; Lahiri, G. K.; Maiti, D. *ACS Catal*. **2017**, *7*, 433. (h) Srimontree, W.; Chatupheeraphat, A.; Liao, H.-H.; Rueping, M. *Org. Lett*. **2017**, *19*, 3091. (i) Shi, S.; Szostak, M. *Org. Lett*. **2017**, *19*, 3095.

(3) Nickel-catalyzed decarbonylation of 2-pyridinecarboxamides: Liu,X.; Yue, H.; Jia, J.; Guo, L.; Rueping, M.

Chem. Eur. J. **2017**, *23*, 11771.

(4) Tobisu, M.; Yasutome, A.; Kinuta, H.; Nakamura, K.; Chatani, N. *Org. Lett.* **2014**, *16*, 5572.

(5) Hong, X.; Liang, Y.; Houk, K. N. *J. Am. Chem. Soc*. **2014**, *136*, 2017.

(6) Kinuta, H.; Tobisu, M.; Chatani, N. *J. Am. Chem. Soc*. **2015**, *137*, 159.

(7) Morioka, T.; Sakamoto, Y.; Tobisu, M.; Chatani, N. *Manuscript in preparation*.

Conclusion

The research reported in this dissertation was directed at the nickel-mediated transformation of inert σ-bonds such as C-O, C-C and C-N bonds in anisoles, ketones and amides, respectively.

In Chapter 1, the nickel-catalyzed reduction of inert carbon-oxygen bond in anisole derivatives is discussed. Our newly developed NHC ligand promotes the reductive cleavage of carbon-methoxy bonds, even in the absence of an external reductant. Anisole derivatives bearing a ketone functionality were also applicable under the current conditions, although it is known that ketone groups can be reduced using previously reported methods using an external reductant. The result of an isotopic labeling experiment revealed that the hydrogen delivered to the reduced product was primarily derived from the methoxy group of the substrate.

In Chapter 2, the nickel-catalyzed methylation of anisole derivatives with $AlMe_3$ as a nucleophile is discussed. Organoaluminum reagents were found to be used as nucleophiles in cross-coupling reaction of aryl ethers.

In Chapter 3, the nickel-mediated decarbonylation of simple aromatic ketones is discussed. Based on the substituent effect of ketone derivatives, both electron-donating and electron-withdrawing groups accelerated the decarbonylation reaction at a higher initial rate. This is the first example of the decarbonylation of simple ketones mediated by transition metals other than rhodium complexes.

In Chapter 4, the nickel-mediated decarbonylation of *N*-acylpyrrole derivatives is discussed. A crossover experiment revealed that the decarbonylation of amides proceeds through the formal intramolecular coupling, since an amine moiety derived from the amide group functions as a nucleophile. This reaction can also be applied to amides derived from azaindole and phenoxazine instead of pyrrole to give the corresponding *N*-arylated product.

These reactions presented herein, except for Chapter 2, proceed through a formal intramolecular coupling accompanied by the release of formaldehyde and carbon monoxide. The findings of this study may contribute to the further development of transformations of inert σ-bonds and provide new synthetic methodology that is currently considered to be difficult to achieve in traditional cross-coupling reactions.

List of Publications

(1) Nickel-Catalyzed Reductive Cleavage of Aryl Alkyl Ethers to Arenes in Absence of External Reductant
Mamoru Tobisu, Toshifumi Morioka, Akimichi Ohtsuki, Naoto Chatani.
Chem. Sci. **2015**, *6*, 3410.

(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, Naoto Chatani.
Chem. Lett. **2015**, *44*, 1729-1731.

(3) Nickel-Mediated Decarbonylation of Simple Unstrained Ketones through the Cleavage of Carbon-Carbon Bonds
Toshifumi Morioka, Akihiro Nishizawa, Takayuki Furukawa, Mamoru Tobisu, Naoto Chatani.
J. Am. Chem. Soc. **2017**, *139*, 1416.

(4) Nickel-Mediated Decarbonylation of Amides Leading to *N*-Arylated Heteroarenes
Toshifumi Morioka, Yuki Sakamoto, Mamoru Tobisu, Naoto Chatani.
In preparation.

Supplementary List of Publications

(1) Synthesis of Six-membered Silacycles by Intramolecular Nucleophilic Substitution at Silicon Involving the Cleavage of CarbonSilicon Bonds
Masahiro Onoe, Toshifumi Morioka, Mamoru Tobisu, Naoto Chatani.
Chem. Lett. **2013**, *42*, 238.

(2) Nickel-Catalyzed Alkylative Cross-Coupling of Anisoles with Grignard reagents via C-O Bond Activation
Mamoru Tobisu, Tsuyoshi Takahira, Toshifumi Morioka, Naoto Chatani.
J. Am. Chem. Soc. **2016**, *138*, 6711.