Suzuki-Miyaura Reactions Catalyzed by C₂-Symmetric Pd-Multi-Dentate N-Heterocyclic Carbene Complexes

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Abstract: Suzuki-Miyaura coupling reactions are promoted by Pd complexes ligated with C₂-symmetric multi-dentate N-heterocyclic carbene derived in situ from Pd(OAc)₂ and imidazolium salts. Good to excellent yields were obtained for aryl bromides as substrates. Turnover numbers of up to $10^5$ could be achieved with $5 \times 10^{-4}$ mol% of Pd(OAc)₂/1 $\times 10^{-3}$ mol% NHC precatalyst in 24 h.

Keywords: imidazolium salt; N-heterocyclic carbene; palladium; Suzuki-Miyaura coupling; catalysis

1. Introduction

The formation of C-C bonds catalyzed by transition metal complexes represents one of the most powerful tools in organic synthesis [1–3] and has found important applications in the synthesis of organic molecules such as pharmaceuticals [4], natural products [5], and polymers [6]. The Suzuki-Miyaura reaction, the C-C cross-coupling reaction between aryl halides and arylboronic acids, is an example of this kind of reaction [7–9]. As is well known, many Pd-phosphine complexes have been employed as the catalysts for this transformation [10,11], but most phosphine ligands, especially those displaying good catalytic properties, are expensive, toxic and air-sensitive. Accordingly, Pd-complexes overcoming these limitations are highly desirable. N-Heterocyclic carbene (NHCs) have
received increasing attention after the isolation of free NHC by Arduengo and co-workers in 1991 [12], and Herrmann’s seminal work demonstrating the catalysis of coupling reactions using Pd-NHC complexes [13]. The excellent σ-donor and lower π-acceptor characteristics of NHC, in combination with their good stability towards air and moisture, make them attractive as ligands in catalytic reactions [14–16]. Furthermore, substituents attached to the NHC framework could be easily modulated to tune their electronic as well as the steric properties. These results have shown NHCs to be an alternative for conventional phosphine ligands in homogeneous catalysis including olefin metathesis [17], hydrosilylation [18,19], hydrogenation [20,21], C-C coupling reactions, etc. [22].

Suzuki-Miyaura coupling reactions promoted by Pd-NHC complexes were initiated by Herrmann’s report in 1998 [23]. Since then, Pd-NHC complexes have been found as efficient catalysts for this kind of coupling reaction [24–30], and new NHCs or their precursors have been synthesized to confer more efficient catalytic properties or ease of operation [31–34]. Among these catalysts, most of them are derived from monodentated NHCs, and some are bidentate anionic ligands [26,27]. The chelating NHC ligands predominantly consist of two NHC moieties linked by a chain or a ring, e.g., Shi’s cis-chelating, bidentate NHC derived from binaphthyl-2,2′-diamine [35], and more importantly, hybrid NHC ligands. Typical examples of the hybrid NHC ligands used in palladium-catalyzed reactions include NHC,P chelating ligands derived from 1 and 2, and NHC,N chelating ligands in complexes 3, 4 and 5 (Figure 1) [36–39]. Nonetheless, little attention has been paid to hybrid NHC chelating ligands bearing weakly-coordinating O-atom as a potential coordination atom until now [40–42].

The fact that Pd complexes containing both NHC and phosphine ligands, show higher activity than those with phosphine as the only ligand or Pd(NHC)₂X₂, was reasoned to be due to the strong Pd-NHC bond and relatively weak Pd-P bond, which results in the stabilization of Pd, easy dissociation of phosphine ligand and favorable oxidative addition of aryl halides to Pd. In metal-NHC complexes promoted reactions, metal complexes with both NHC and phosphine structural motif generally exhibit better activity and selectivity than those only with monodentate NHC ligands. Therefore, a second, relatively weak coordination atom in the chelating metal-NHC complex might be beneficial for improving the catalytic performance.

We have an interest in the applications of multidentate, C₂-symmetric NHCs with one chelating carbene and two O-atoms as ligands in catalytic reactions, for which there have been few precedents. We envisioned that the coordinative ability of the heteroatom can be adjusted by changing its bonding. Previously, we have synthesized tridentate C₂-symmetric imidazolinium salts 6 (Figure 2) and their NHC precursors, which have two oxygen atoms in the arms, and found that their copper complexes could catalyze the asymmetric conjugate addition of Et₂Zn to cycloalkenones efficiently [43].
continue this work, we designed 7, the unsaturated counterpart of 6, to explore their applications in Suzuki-Miyaura coupling reactions, as it has been reported that Pd coordinated with unsaturated NHCs show higher reactivity than those with saturated NHCs [44]. Herein, we wish to report the preparation and catalytic properties of the novel $C_2$-symmetric tridentate imidazolium salts 7 in the Suzuki-Miyaura coupling reaction.

**Figure 2.** The structure of tridentate $C_2$-symmetric imidazol(in)ium salts 6 and 7.

2. Results and Discussion

The synthesis of the NHC precursor imidazolium salts 7a–f in 22-30% overall yield is shown in Scheme 1. The synthetic route to the NHC precursor imidazolium salts 7a–f started from (S)-ethyl lactate or (S)-ethyl mandelate by etherification with phenol or substituted phenols. The $\alpha$-aryloxycarboxylates 8a–f were next reduced, yielding $\beta$-aryloxyalcohols 9a–f. Then the alcohol were converted into halides 11a–f, and reacted with imidazole giving imidazolium salts 7a–f, which contain $\beta$-aryloxy groups in the side chains. They are quite stable towards air and moisture.

**Scheme 1.** Synthesis of the NHC precursor imidazolium salts 7a–f.

Reagents and Conditions: (a) PPh$_3$, DEAD, CH$_2$Cl$_2$; (b) NaBH$_4$, THF-MeOH; (c) TsCl, pyridine; (d) LiBr, LiCO$_3$, acetone; (e) imidazole, K$_2$CO$_3$, DMF.

The imidazolium salts 7c–f synthesized from (S)-ethyl lactate were optically pure. This can be deduced from the fact that only one set of NMR signals was observed in both $^1$H-NMR and $^{13}$C-NMR spectra of these compounds. Reaction of racemic bromides 11c–f with imidazole would yield racemic $C_2$-symmetric (R,R), (S,S)-isomers of 7c–f, and Cs-symmetric meso-(R,S)-isomer of 7c–f. Even though the (R,R), (S,S)-isomers could not be distinguished by NMR, the signals of the racemic isomers and meso-isomer should be different. Therefore, the sets of NMR signals of 7 could be used to judge whether the products are optically pure.

On the other hand, use of (S)-ethyl mandelate yielded 7a and 7b as a mixture of diastereomers, since $^1$H-NMR and $^{13}$C-NMR signals for two sets or more than one set were observed. This indicates
that racemization occurs using (S)-ethyl mandelate as the starting material, whose α-H is more acidic than that in ethyl lactate.

The catalytic activities of the Pd-complexes of the NHCs derived from imidazolium salts 7 in Suzuki-Miyaura coupling reactions were screened, using catalysts generated in situ from a mixture in a solvent of 7, Pd(OAc)$_2$, and a base.

The reaction conditions were optimized on a model reaction between phenyl bromide and phenylboronic acid. First, the effect of solvents was examined using the catalyst generated from imidazolium salt 7a and Pd(OAc)$_2$. The product biphenyl 12a was obtained in 95% yield in either toluene or DMF. Addition of H$_2$O to DMF (V/V = 1:2) accelerated the reaction but no increase in the yield was observed. The reaction was completed in 1.5 h using toluene as the solvent. Moderate to low yields were obtained when polar solvents, including 1,4-dioxane, THF and EtOH, were used, even though 1,4-dioxane and EtOH have been reported in the literature as good solvents for this kind of reaction.

Using toluene as the solvent, bases were then optimized, and the results are shown in Table 1. Although Cs$_2$CO$_3$ is generally efficient for the Suzuki-Miyaura coupling reactions catalyzed by Pd-NHC or palladium-phosphine complexes, in our case, only a 32% yield of 12a was observed, whereas the use of K$_2$CO$_3$ resulted in an excellent yield (entry 2). With other bases like NaOH, KF and K$_3$PO$_4$, the reaction also proceeded well, but somewhat more slowly. Then the temperature was optimized. Phenyl bromide was quantitatively converted to 12a in 0.5 h at 110 °C, much faster than at 90 °C. At lower temperature, the reaction is very slow. Only a 53% yield of 12a was obtained after 21 h at 70 °C. Therefore, subsequent reactions were carried out using K$_2$CO$_3$ as the base and toluene as the solvent at 110 °C.

Table 1. Influence of the base on the Suzuki-Miyaura reaction catalyzed by Pd(OAc)$_2$/7a $^a$.

| Entry | Base       | Time (h) | Yield $^b$(%) |
|-------|------------|----------|---------------|
| 1     | Na$_2$CO$_3$ | 24       | 12            |
| 2     | K$_2$CO$_3$ | 1.5      | 95            |
| 3     | Cs$_2$CO$_3$ | 24       | 32            |
| 4     | NaOH       | 24       | 86            |
| 5     | KF         | 24       | 75            |
| 6     | K$_3$PO$_4$ | 24       | 82            |
| 7     | CH$_3$COONa | 24       | 4             |

$^a$Reaction conditions: 0.5 mmol phenyl bromide, 0.75 mmol phenylboronic acid, 1.5 mmol base, 0.5 mol% Pd(OAc)$_2$, 1 mol% 7a, 3.0 mL toluene, 90 °C. $^b$GC yield.

Next, the catalytic abilities of 7a analogues were evaluated and the results are shown in Table 2. The most efficient catalyst was derived from 7a (entry 1). A comparable yield was obtained with the methyl substituted analogue 7c (entry 3). Introduction of a nitro group to the aryloxy substituent results in a ligand-Pd complex generating a lower yield of the coupling product (entry 4), which shows that reduction of the electron density of the phenyl ring and the resultant decrease in the coordination ability of the O-atom reduced the catalytic ability of 7. The presence of a 4-methyl group in the
aryloxy substituent also led to a lower yield (entry 5), but higher than that using 7d. Yields of 86–87% were generated when the (substituted)-phenoxy substituent was changed to a 2-naphthoxy group (entries 2 and 6), which is more steric demanding and resulted in the O-atom being less coordinative. Two typical imidazolium salts IMes·HCl (IMes = 1,3-bis(2,4,6-trimethylphenyl)-imidazol-2-ylidene) and IPr·HCl (IPr = 1,3-bis(2,6-diisopropylphenyl)-imidazol-2-ylidene) catalyze the coupling reaction giving inferior results (entries 7, 8). In the absence of imidazolium salt or other ligand, a 72% yield of 12a was obtained in 1h using Pd(OAc)₂ as the catalyst (entry 9). These results demonstrate that the ligand derived from imidazolium salts 7 which contains two potentially chelated oxygen atoms is more efficient than simple NHC ligands, e.g., IPr and IMes in the coupling reactions. This might be due to the presence of a NHC moiety and oxygen atoms in the hybrid NHC ligands. The strong coordinating of NHC can prevent the dissociate of ligand from palladium complex, and therefore, stablize the catalytically active palladium species. In the meanwhile, the weak coordinative oxygen atom(s) can easily dissociate from palladium complex and generate a coordination-unsaturated palladium species. This favors the oxidation of aryl halides or arylboronic acids toward the coordination-unsaturated palladium species and catalytic cycle. Indeed, formation of palladium balck, which is catalytic inert to the Suzuki reaction and an indication of ligands dissociate from palladium completely, is rarely observed in the coupling reaction using 7. The coupling reaction of phenylboric acid with phenyl bromide could be performed in air with a slightly reduced yield (78%).

Table 2. Evaluation of the NHCs from 7a–f in the Suzuki-Miyaura reaction a.

| Entry | Imidazolium salt | Time (h) | Yield b (%) |
|-------|------------------|----------|-------------|
| 1     | 7a               | 0.5      | 99          |
| 2     | 7b               | 1        | 87          |
| 3     | 7c               | 1        | 96          |
| 4     | 7d               | 1        | 85          |
| 5     | 7e               | 1        | 90          |
| 6     | 7f               | 1        | 86          |
| 7     | IPr·HCl          | 1        | 75          |
| 8     | IMes·HCl         | 1        | 70          |
| 9     | -                | 1        | 72          |

a Reaction conditions: 0.5 mmol phenyl bromide, 0.75 mmol phenylboronic acid, 1.5 mmol K₂CO₃, 0.5 mol% Pd(OAc)₂, 1 mol% 7, 3.0 mL toluene, 110 °C. b GC yield.

The reactions of various aryl halides with phenylboronic acids were then investigated under the optimized conditions, and the results are summarized in Table 3. Only 5 minutes were needed for the complete reactions of 4-nitrophenyl bromide and 4-acetophenyl bromide, which are electron-deficient and more reactive in this kind of reaction.
Table 3. Suzuki-Miyaura reaction of aryl halides (benzyl halides) with phenylboronic acid catalyzed by Pd(OAc)$_2$/7a.

| Entry | ArX or BnX | R | Time | Product | Yield $^\circ$ (%) |
|-------|------------|---|------|---------|-------------------|
| 1     |             | H | 5 min| 12b     | 95               |
| 2     |             | H | 5 min| 12c     | 98               |
| 3     |             | H | 1 h  | 12d     | 98               |
| 4     |             | H | 0.5 h| 12e     | 99               |
| 5     |             | H | 0.5 h| 12f     | 96               |
| 6     |             | H | 1 h  | 12g     | 93               |
| 7     |             | H | 0.5 h| 12h     | 95               |
| 8     |             | H | 1 h  | 12i     | 92               |
| 9     |             | H | 0.5 h| 12j     | 91               |
| 10    |             | H | 1 h  | 12k     | 85               |
| 11    |             | H | 1 h  | 12l     | 90               |
| 12    |             | H | 1 h  | 12m     | 96               |
| 13    |             | H | 1 h  | 12n     | 97               |
| 14    |             | H | 3 h  | 12o     | 90               |
| 15    |             | H | 24 h | 12a     | 35               |
| 16    |             | H | 24 h | 12b     | 70               |
| 17    |             | H | 10 h | 12o     | 71               |
| 18    | 3-Me       | H | 0.5 h| 12p     | 93               |
Table 3. Cont.

| Entry | ArX or BnX | R     | Time | Product | Yield a (%) |
|-------|------------|-------|------|---------|-------------|
| 19    | Br         | 4-Me  | 0.5 h| 12j     | 85          |
| 20    | Br         | 2-Me  | 2.5 h| 12k     | 93          |
| 21    | -O2C       | 4-MeO2C | 24 h| 12q     | 86          |
| 22    | Br         | 2-Me  | 1 h  | 12r     | 21 b        |
| 23    | Br         | 2-Me  | 11.5 h| 12r   | 56 b,c      |

a Isolated yield except noted. b GC yield. c Using 0.05 mol% Pd(OAc)$_2$, 0.1 mol% imidazolium salt 7a.

For those aryl halides with electron-donating groups (entries 7, 10, 13) or sterically hindered aryl bromides (entry 11), longer reaction times were needed. Generally, almost quantitative yields of coupling products could be obtained in 1 h. It is worth to note that 4-hydroxylphenyl bromide, which is very electron-rich in the phenyl ring and the C-Br bond, is highly reactive to coupling. As expected, a wide range of functional groups including keto, nitro, cyano, ester, amide, hydroxy and ether, were tolerated. The coupling reactions could be extended to benzyl bromide which contains a sp$^3$-C atom bearing the halide, and therefore, a C-C coupling product between a sp$^3$-C and a sp$^3$-C was achieved (entry 14). The reaction of 4-chlorophenyl bromide gave 4-chlorobiphenyl as the only coupling product in high yield, and demonstrated the inertness of C-Cl in the presence of C-Br (entry 6). When phenyl chloride was used, only a 35% yield of biphenyl was obtained (entry 15). Introduction of an acetyl group to phenyl chloride led to an increase in the activity, and a 70% yield of the coupling product was achieved (entry 16). Gratifyingly, benzyl chloride also gave a reasonable yield of coupling product (entry 17), although in lower yield than that obtained with benzyl bromide. Palladium black was only observed unremarkably in reactions performed at 110 °C and after long reaction times.

In addition, reactions of various arylboronic acids with substituted phenyl bromides were performed. The reactions proceed smoothly in high yield using 2-tolyboronic acid. In contrast to aryl halides, the presence of an electron-withdrawing group results in a low coupling yield which may be attributed to the tendency of hydrolysis of the electron deficient arylboronic acids (Table 3, entry 21) [45]. Even though the presence of an ortho-Me group in either the aryl halide or the arylboronic acid did not affect the coupling yield, it was still difficult to obtain tri-ortho substituted biphenyl in high yields, a challenging reaction in literature, due to the large hindrance for our catalyst system. In the case of a very sterically hindered reaction (entry 22), the less bulky 2,2'-dimethylbiphenyl (the homocoupling product of two arylboronic acid molecules), was formed in preference to the more bulky 2,6,2'-trimethylbiphenyl product derived from the expected Suzuki-Miyaura coupling when 0.5 mol% of Pd catalyst was employed. This indicated the relative inertness of the 2,6-dimethylphenyl bromide. Therefore, the amount of the Pd salt was decreased to 0.05 mol% to depress the relative faster coupling reaction between the aryl groups in the boronic acid. In this case, the yield of the trimethylbiphenyl increased to 56% as judged by gas chromatography over a prolonged reaction time (entry 23). Similar
results were observed for the reaction of 4-bromoacetophenone with phenylboronic acid (entries 1, 2 in Table 4 vs. entry 1 in Table 3).

**Table 4.** The activities of Pd(OAc)$_2$/7a with variation of loading.

| Entry | R   | Pd (mol%) | Time (h) | Product | Yield $^a$ (%) | TON   |
|-------|-----|-----------|----------|---------|----------------|-------|
| 1     | COMe | 0.05      | 1        | 12b     | 100            | 2000  |
| 2     | COMe | 0.005     | 4        | 12b     | 100            | 20000 |
| 3     | COMe | 0.0005    | 24       | 12b     | 50             | 100000|
| 4     | H    | 0.05      | 2        | 12a     | 95             | 1900  |
| 5     | H    | 0.005     | 2        | 12a     | 38             | 7600  |
| 6     | Me   | 0.05      | 1.5      | 12j     | 100            | 2000  |
| 7     | Me   | 0.005     | 4        | 12j     | 95             | 19000 |

$^a$ GC yield using diethylene glycol di-n-butyl ether as an internal standard.

The efficiencies of Pd(OAc)$_2$/7a were further tested with different catalyst loadings, and the results are summarized in Table 4. 4-Acetylphenyl bromide could be completely converted to the coupling product using $5 \times 10^{-2}$ mol% in 1 h and $5 \times 10^{-3}$ mol% of Pd catalyst in 4 h, respectively (entries 1 and 2). The turnover numbers (TON) reached $2 \times 10^4$. Furthermore, a maximum TON of $10^5$ was obtained at $5 \times 10^{-4}$ mol% of catalyst loading in 24 h (entry 3), and the turnover frequency (TOF) is ca. $4.17 \times 10^3$ h$^{-1}$. A TON of up to 7,600 was recorded for the reaction of phenyl bromide (entry 5). Interestingly, for the less active 4-bromotoluene, TON and TOF values up to $1.9 \times 10^4$ and $4.75 \times 10^3$ h$^{-1}$, respectively, could be achieved with $5 \times 10^{-3}$ mol% Pd catalyst in 4 h (entry 7), which was better than the case of phenyl bromide. Details of the progress of reactions with different amount of catalyst and substrates are given in Figures 3 and 4.

**Figure 3.** Reaction profiles for Suzuki-Miyaura reaction between 4-acetylphenyl bromide and phenylboronic acid catalyzed by different Pd/7a loading: 0.05 mol% (■), 0.005 mol% (○), 0.0005 mol% (▲).
Figure 4. Reaction profiles for Suzuki-Miyaura reaction of 4-methylphenyl bromide catalyzed by Pd/7a 0.05 mol% (●), 0.005 mol% (○), and phenyl bromide catalyzed by Pd/7a 0.05 mol% (▲), 0.0005 mol% (△).

3. Experimental

3.1. General

All chemicals were purchased from Alfa Aesar Co., Ltd. (Tianjin, China) and Accela ChemBio Co., Ltd. (Shanghai, China), except arylboronic acids which were products of Ally Chemical Ltd. (Dalian, China). The solvents were freshly distilled prior to use. NMR spectra were recorded on a Varian 400 MHz spectrometer or on a Bruker DRX500 spectrometer, using TMS as an internal standard. IR spectra were recorded on a Nicolet 550 spectrometer. MS spectra were measured on a Hewlett-Packard HP-6890/5973 gas chromatography-mass spectrometer. HRMS were recorded on a Micromass UPLC/Q-Tof Micro spectrometer. The reaction mixtures were analyzed by gas chromatography (Shimadzu GC-2010, capillary column SE-54, 30 m × 0.32 mm × 4 μm; FID detector; N2 gas). Column chromatography was performed with silica gel (200–300 mesh).

3.2. Synthesis of Imidazolium Salts 7a–f (Exemplified by the Synthesis of 7f)

3.2.1. Ethyl 2-(2-Naphthoxy)propanoate (8f)

β-Naphthol (1.586 g, 11.00 mmol), PPh3 (3.148 g, 12.00 mmol) and dichloromethane (10 mL) were added to a round-bottom flask, and the mixture was stirred for 5 min. (S)-Ethyl lactate (1.182 g, 10.00 mmol) was added to the flask, then the flask was cooled with an ice-water bath. DEAD (1.742 g, 10.00 mmol) was added slowly. The mixture was stirred for 30 min at 0 °C, and then 6 h at room temperature. After removal of the colorless precipitate by filtration, the filtrate was concentrated in vacuo. 8f (2.230 g, 91.2% yield) was isolated by column chromatography as colorless oil. Rf = 0.57 (EA: PE = 10: 90), [α]D25 = +12.1 (c 1.46, EtOH). 1H-NMR (400 MHz, CDCl3) δ 7.72 (d, J = 9.0 Hz, 2H, Ar-H), 7.67 (d, J = 8.2 Hz, 1H, Ar-H), 7.40 (ddd, J = 8.2, 6.9, 1.2 Hz, 1H, Ar-H), 7.31 (ddd, J = 8.1, 6.9, 1.2 Hz, 1H, Ar-H), 7.19 (dd, J = 8.9, 2.6 Hz, 1H, Ar-H), 7.04 (d, J = 2.5 Hz, 1H, Ar-H),
4.87 (q, J = 6.8 Hz, 1H, CH), 4.27–4.13 (m, 2H, CH₂), 1.66 (d, J = 6.8 Hz, 3H, CH₃(CH), 1.21 (t, J = 7.1 Hz, 3H, CH₃CH₂). ¹³C-NMR (101 MHz, CDCl₃) δ 171.99 (C=O), 155.44, 134.21, 129.55, 129.22, 127.52, 126.74, 126.31, 123.85, 118.78, 107.60 (Ar-C), 72.51 (CH), 61.10 (CH₂), 18.40 (CH₃CH), 13.99 (CH₃CH₂).

3.2.2. 2-(2-Naphthoxyl)propan-1-ol (9f)

To an ice-water cooled round-bottom flask containing a solution of 8f (1.243 g, 5.09 mmol) in THF (10.0 mL) was added NaBH₄ (0.380 g, 10 mmol) in portions, and the mixture was stirred for 30 min at 0 °C. Then the temperature was recovered to room temperature slowly, and the mixture was stirred at room temperature for 6 h. The volatiles were removed by evaporation in vacuo. Water was added to the residue, and the aqueous phase was extracted with dichloromethane. The combined organic phase was dried with Na₂SO₄ and purified by column chromatography, yielding 9f (0.85 g, 84.2% yield) as colorless oily liquid. Rf = 0.14 (EA:PE = 10:90), [α]₂₅° = −14.5 (c 1.11, EtOH). ¹H-NMR (400 MHz, CDCl₃) δ 7.75–7.61 (m, 3H, Ar-H), 7.39 (dd, J = 8.1, 7.0 Hz, 1H, Ar-H), 7.30 (dd, J = 8.0, 7.0 Hz, 1H, Ar-H), 7.15 (d, J = 2.1 Hz, 1H, Ar-H), 7.11 (dd, J = 8.9, 2.4 Hz, 1H, Ar-H), 4.61–4.51 (m, 1H, CH), 3.77–3.69 (m, 2H, CH₂), 2.88 (s, 1H, OH), 1.25 (d, J = 6.2 Hz, 3H, CH₃). ¹³C-NMR (101 MHz, CDCl₃) δ 155.50, 134.51, 129.61, 129.13, 127.64, 126.78, 126.42, 123.83, 119.51, 108.98 (Ar-C), 74.75 (CH), 66.11 (CH₂), 15.73 (CH₃).

3.2.3. 2-(2-Naphthoxyl)propyl 4-methylbenzenesulfonate (10f)

To a round-bottom flask, 9f (0.850 g, 3.93 mmol) and dichloromethane (15 mL) was added, followed by tolylsulfonyl chloride (0.964 g, 5.06 mmol) and pyridine (0.396 g, 5.01 mmol). The mixture was stirred at room temperature for 24 h, and quenched by the addition of water. After phases separation and general workup, oily 10f (1.104 g, 73.8% yield) was isolated. Rf = 0.28 (EA:PE = 20:80), [α]₂₅° = +70.27 (c 1.04, CHCl₃). ¹H-NMR (400 MHz, CDCl₃) δ 7.73 (t, J = 7.1 Hz, 3H, Ar-H), 7.65 (dd, J = 13.7, 8.6 Hz, 2H, Ar-H), 7.41 (t, J = 7.5 Hz, 1H, Ar-H), 7.31 (t, J = 7.5 Hz, 1H, Ar-H), 7.19 (d, J = 8.0 Hz, 2H, Ar-H), 7.01 (s, 1H, Ar-H), 6.98 (dd, J = 8.9, 2.4 Hz, 1H, Ar-H), 4.72–4.63 (m, 1H, CH), 4.20 (dd, J = 10.6, 5.8 Hz, 1H, CH-H), 4.14 (dd, J = 10.6, 4.4 Hz, 1H, CH-H), 2.31 (s, 3H, Ph-CH₃), 1.33 (d, J = 6.3 Hz, 3H, CH₃(CH)). ¹³C-NMR (101 MHz, CDCl₃) δ 154.95, 144.93, 134.36, 132.82, 129.84, 129.58, 129.21, 127.90, 127.63, 126.81, 126.47, 123.98, 119.34, 108.76 (Ar-C), 71.74 (CH), 71.23 (CH₂), 21.55 (Ph-CH₃), 16.44 (CH₃(CH)).

3.2.4. 1-Bromo-2-(2-naphthoxyl)propane (11f)

Compound 10f (1.10 g, 2.97 mmol), acetone (15 mL), LiBr (0.348 g, 4.01 mmol) and Li₂CO₃ (0.030 g, 0.45 mmol) were added to a flask in sequence. The mixture was refluxed for 48 h. After cooled to room temperature, the solvent was removed by evaporation in vacuo. The residue was separated by column chromatography, affording oily 11f (0.654 g, 82.6% yield). Rf = 0.69 (EA:PE = 20:80), [α]₂₅° = −41.86 (c 1.01, CHCl₃). ¹H-NMR (400 MHz, CDCl₃) δ 7.76 (dd, J = 8.3, 2.9 Hz, 2H, Ar-H), 7.72 (d, J = 8.3 Hz, 1H, Ar-H), 7.44 (ddd, J = 8.2, 6.9, 1.3 Hz, 1H, Ar-H), 7.35 (ddd, J = 8.1, 6.9, 1.2 Hz, 1H, Ar-H), 7.20–7.12 (m, 2H, Ar-H), 4.77–4.66 (m, 1H, CH), 3.62 (dd, J = 10.4,
4.8 Hz, 1H, CH-H), 3.48 (dd, J = 10.4, 6.2 Hz, 1H, CH-H), 1.52 (d, J = 6.1 Hz, 3H, CH3). 13C-NMR (101 MHz, CDCl3) δ 155.16, 134.50, 129.83, 129.38, 127.74, 126.89, 126.56, 124.08, 119.60, 109.17 (Ar-C), 73.50 (CH), 35.43 (CH2), 18.84 (CH3).

3.2.5. 1,3-Bis-[2-(naphthoxy)propyl]imidazolium Bromide (7f)

To a flask, 11f (0.653 g, 2.46 mmol), DMF (10 mL), imidazole (0.0816 g, 1.20 mmol) and K2CO3 (0.653 g, 2.46 mmol), 7a were similarly prepared and characterized. 1H-NMR (400 MHz, CDCl3) δ 10.78 (s, 1H, N-C-H-N), 10.77 (s, 1H, N-C′H=N), 7.51–7.45 (m, 8H, Ar-H), 7.38 (d, J = 1.5 Hz, 2H, N-C′H), 7.34 (d, J = 1.5 Hz, 2H, N-C′H′), 7.33–7.27 (m, 12H, Ar-H), 7.18–7.10 (m, 8H, Ar-H), 6.92–6.86 (m, 4H, Ar-H), 6.78–6.77 7a (m, 8H, Ar-H), 5.72 (dd, J = 8.6, 2.8 Hz, 1H, O-C-H), 5.64 (dd, J = 8.4, 2.8 Hz, 1H, O-C′H′), 4.93 (dd, J = 14.3, 2.9 Hz, 1H, NCH-H), 4.92 (dd, J = 14.2, 2.9 Hz, 1H, NCH-H′), 4.51 (dd, J = 14.3, 8.2 Hz, 2H, NCH-H), 4.49 (dd, J = 14.2, 8.4 Hz, 2H, NCH-H′). 13C-NMR (101 MHz, CDCl3) δ 156.53 (N=CH=N), 156.49 (N=CH=N), 138.98 (N=CH=CH), 138.78 (N=CH=CH), 135.85, 135.72, 129.65, 129.64, 129.21, 129.05, 129.02, 126.29, 126.17, 122.55, 122.50, 122.02, 122.00, 115.82, 115.72 (Ar-C), 78.03 (O-CH), 77.91 (O-CH), 55.51 (CH2). HRMS: m/z 461.2222 (calcd. 461.2229 for C29H29N2O2). Two sets of NMR signals indicated the racemization of 7a.
561.2527 (calcd. 561.2542 for C$_{39}$H$_{33}$N$_{2}$O$_{2}$). More than one set of NMR signals indicated the racemization of 7b.

1,3-Bis-(2-phenoxypropyl)imidazolium Bromide (7c). Total yield 21.8%. Yellow oil. [α]$_{25}^{20}$ = −20.55 (c 0.69, CHCl$_3$). IR: $\nu_{C-N}$ 1602 cm$^{-1}$, $\nu_{C-O}$ 1172 cm$^{-1}$. $^1$H-NMR (400 MHz, CDCl$_3$) δ 10.26 (s, 1H, N-C$_{6}$H$_{5}$=N), 7.63 (s, 2H, N-C$_{6}$H$_{5}$), 7.21 (t, J = 7.7 Hz, 4H, Ph-H), 6.94 (t, J = 7.2 Hz, 2H, Ph-H), 6.82 (d, J = 8.1 Hz, 4H, Ph-H), 4.89 (d, J = 14.0 Hz, 2H, N-CH$_2$-H), 4.85–4.79 (m, 2H, O-CH$_2$), 4.44 (dd, J = 14.0, 7.7 Hz, 2H, N-CH$_2$-H), 1.35 (d, J = 6.1 Hz, 6H, C$_3$H$_6$). 13C-NMR (101 MHz, CDCl$_3$) δ 156.07 (N-C$_{6}$H$_{5}$=N), 137.16 (N-C$_{6}$H$_{5}$=CH), 129.43, 122.86, 121.57, 115.68 (Ph-C$_{6}$H), 72.17 (O-CH$_2$), 53.83 (CH$_2$), 16.42 (C$_3$H$_6$). HRMS: m/z 337.1920 (calcd. 337.1916 for C$_{21}$H$_{25}$N$_{2}$O$_{2}$).

1,3-Bis[2-(4-nitrophenoxy)propyl]imidazolium Bromide (7d). Total yield 23.2%. Yellow oil. [α]$_{25}^{25}$ = −10.99 (c 0.56, CHCl$_3$). IR: $\nu_{C-N}$ 1602 cm$^{-1}$, $\nu_{C-O}$ 1172 cm$^{-1}$, $\nu_{NO_2}$ 1508 cm$^{-1}$. 1H-NMR (400 MHz, CD$_3$OD) δ 9.58 (s, 1H, N-C$_{6}$H$_{5}$=N), 8.07 (d, J = 2.1 Hz, 2H, N-C$_{6}$H$_{5}$), 8.05 (d, J = 2.0 Hz, 2H, Ph-H), 7.98 (d, J = 1.5 Hz, 2H, Ph-H), 7.16 (d, J = 2.1 Hz, 2H, Ph-H), 7.14 (d, J = 2.0 Hz, 2H, Ph-H), 5.23–5.15 (m, 2H, O-CH$_2$), 4.91 (dd, J = 14.3, 2.6 Hz, 2H, N-CH$_2$-H), 4.74 (dd, J = 14.4, 8.4 Hz, 2H, N-CH$_2$-H), 1.55 (d, J = 6.1 Hz, 6H, C$_3$H$_6$). 13C-NMR (101 MHz, CD$_3$OD) δ 163.13 (N-C$_{6}$H$_{5}$=N), 142.48 (Ph-C$_{6}$H), 138.54 (N-C$_{6}$H$_{5}$=CH), 126.69, 124.49, 116.50 (Ph-C$_{6}$H), 74.37 (O-CH$_2$), 54.80 (CH$_2$), 16.76 (C$_3$H$_6$). HRMS: m/z 427.1630 (calcd. 427.1618 for C$_{21}$H$_{23}$N$_{4}$O$_{6}$).

1,3-Bis[2-(4-methylphenoxy)propyl]imidazolium Bromide (7e). Total yield 22.7%. Yellow oil. [α]$_{25}^{20}$ = −15.12 (c 1.025, CHCl$_3$). IR: $\nu_{C-N}$ 1616 cm$^{-1}$, $\nu_{C-O}$ 1092 cm$^{-1}$. 1H-NMR (400 MHz, CDCl$_3$) δ 10.04 (s, 1H, N-C$_{6}$H$_{5}$=N), 7.83 (d, J = 0.9 Hz, 2H, N-C$_{6}$H$_{5}$), 6.96 (d, J = 8.4 Hz, 4H, Ph-H), 6.71 (t, J = 5.9 Hz, 4H, Ph-H), 4.91 (dd, J = 13.8, 2.0 Hz, 2H, NCH$_2$-H), 4.77–4.70 (m, 2H, O-CH$_2$), 4.47 (dd, J = 13.9, 7.9 Hz, 2H, NCH$_2$-H), 2.22 (s, 6H, Ph-CH$_3$), 1.33 (d, J = 6.2 Hz, 6H, CH-CH$_3$). 13C-NMR (101 MHz, CDCl$_3$) δ 153.54 (N-C$_{6}$H$_{5}$=N), 136.59 (N-C$_{6}$H$_{5}$=CH), 130.31, 129.33, 122.40, 115.28 (Ph-C$_{6}$H), 72.02 (O-CH$_2$), 53.31 (CH$_2$), 19.68 (CH-CH$_3$), 15.95 (Ph-CH$_3$). HRMS: m/z 365.2228 (calcd. 365.2229 for C$_{23}$H$_{29}$N$_{2}$O$_{2}$).

3.3. General Procedure for the Suzuki-Miyaura Coupling Reactions

Under an Ar atmosphere, Pd(OAc)$_2$ (0.6 mg, 0.0025 mmol, 0.5 mol%), imidazolium salt (0.005 mmol, 1 mol%), arylboronic acid (0.75 mmol), aryl halide (0.5 mmol), K$_2$CO$_3$ (207.30 mg, 1.5 mmol), and toluene (3.0 mL) were added to a dried Schlenk tube in sequence. The mixture was stirred at 110 °C and the progress of the reaction was monitored by TLC and gas chromatography. Upon the consumption of aryl halide, the mixture was cooled to room temperature, and H$_2$O (3.0 mL) was added to quench the reaction. The organic layer was separated, and the aqueous layer was back-extracted with CH$_2$Cl$_2$ (3.0 mL × 3). The organic phases were combined, dried over Na$_2$SO$_4$ and concentrated. The product was isolated by column chromatography with petroleum ether-ethyl acetate as the eluents or analyzed by gas chromatography using diethylene glycol dinit-butyl ether as an internal standard. The structures of the coupling products were confirmed by comparison of $^1$H-NMR, $^{13}$C-NMR with those reported in literature. All products, 12a–q, showed molecular ionic peak in MS spectra.
Biphenyl (12a): colorless solid, m.p. 69–70 °C (lit. [46], m.p. 69–70 °C). \(^1\)H-NMR (400 MHz, CDCl\(_3\)) \(\delta\) 7.62–7.56 (m, 2H), 7.48–7.40 (m, 2H), 7.40–7.29 (m, 1H) ppm. \(^13\)C-NMR (101 MHz, CDCl\(_3\)) \(\delta\) 141.37, 128.89, 127.38, 127.30 ppm. The NMR data were in agreement with those reported in literature [46].

4-Acetyl biphenyl (12b): colorless solid, m.p. 122–124 °C (lit. [46], m.p. 120–121 °C). \(^1\)H-NMR (400 MHz, CDCl\(_3\)) \(\delta\) 8.04 (d, \(J = 8.3\) Hz, 2H), 7.69 (d, \(J = 8.3\) Hz, 2H), 7.65–7.60 (m, 2H), 7.48 (t, \(J = 7.2\) Hz, 1H), 2.64 (s, 3H) ppm. \(^13\)C-NMR (101 MHz, CDCl\(_3\)) \(\delta\) 197.62, 145.69, 139.82, 135.87, 128.96, 128.91, 128.24, 127.24, 127.17, 26.60 ppm. The NMR spectral data matched literature data [46,47].

4-Nitrobiphenyl (12c): yellow solid, m.p. 112–113 °C (lit. [46], m.p. 112–114 °C). \(^1\)H-NMR (400 MHz, CDCl\(_3\)) \(\delta\) 8.29 (d, \(J = 8.7\) Hz, 2H), 7.73 (d, \(J = 8.7\) Hz, 2H), 7.63 (d, \(J = 7.3\) Hz, 2H), 7.49 (dt, \(J = 13.6, 7.0\) Hz, 3H) ppm. \(^13\)C-NMR (101 MHz, CDCl\(_3\)) \(\delta\) 147.62, 147.06, 138.74, 129.21, 128.99, 127.82, 127.42, 124.14 ppm. The NMR spectral data matched literature data [46,47].

4-Cyanobiphenyl (12d): colorless solid, m.p. 86–87 °C (lit. [46], m.p. 85–86 °C). \(^1\)H-NMR (400 MHz, CDCl\(_3\)) \(\delta\) 7.73–7.60 (m, 4H), 7.59–7.52 (m, 2H), 7.50–7.33 (m, 3H) ppm. \(^13\)C-NMR (101 MHz, CDCl\(_3\)) \(\delta\) 145.55, 139.05, 132.55, 129.10, 128.66, 127.67, 127.18, 118.95, 110.81 ppm. The NMR spectral data matched literature data [46,47].

Methyl biphenyl-4-carboxylate (12e): colorless solid, m.p. 119–120 °C (lit. [46], m.p. 115–116 °C). \(^1\)H-NMR (400 MHz, CDCl\(_3\)) \(\delta\) 8.13 (d, \(J = 8.3\) Hz, 2H), 7.65 (dd, \(J = 14.4, 7.8\) Hz, 4H), 7.44 (dt, \(J = 26.9, 7.2\) Hz, 3H), 3.95 (s, 3H) ppm. \(^13\)C-NMR (101 MHz, CDCl\(_3\)) \(\delta\) 166.96, 145.58, 139.94, 130.12, 128.94, 128.87, 128.16, 127.27, 127.03, 52.13 ppm. The NMR data are in agreement to those in literature [46,47].

N-Acetyl-4-aminobiphenyl (12f): colorless solid, m.p. 172–174 °C (lit. [46], m.p. 171–172 °C). \(^1\)H-NMR (400 MHz, CD\(_3\)OD) \(\delta\) 7.65–7.50 (m, 6H), 7.39 (t, \(J = 7.6\) Hz, 2H), 7.39 (t, \(J = 7.3\) Hz, 1H), 2.13 (s, 3H) ppm. \(^13\)C-NMR (101 MHz, CD\(_3\)OD) \(\delta\) 171.60, 141.81, 139.21, 138.13, 129.80, 128.80, 128.20, 128.04, 127.64, 121.41, 23.84 ppm. The NMR spectral data matched literature data [46,47].

4-Chlorobiphenyl (12g): colorless solid, m.p. 77–78 °C (lit. [46], m.p. 78–79 °C, lit. [49], m.p. 75–78 °C). \(^1\)H-NMR (400 MHz, CDCl\(_3\)) \(\delta\) 7.56 (dd, \(J = 14.8, 7.9\) Hz, 4H), 7.50–7.35 (m, 5H) ppm. \(^13\)C-NMR (101 MHz, CDCl\(_3\)) \(\delta\) 171.60, 141.81, 139.21, 138.13, 129.80, 128.20, 128.04, 127.64, 121.41, 23.84 ppm. The NMR spectral data matched literature data [46,48].

4-Phenylphenol (12h): colorless solid, m.p. 164–166 °C (lit. [50], m.p. 162–164 °C, lit. [51], m.p. 167.2–168.0 °C). \(^1\)H-NMR (400 MHz, CD\(_3\)OD) \(\delta\) 7.48 (dd, \(J = 8.2, 1.0\) Hz, 2H), 7.45–7.37 (m, 2H), 7.32 (t, \(J = 7.7\) Hz, 2H), 7.24–7.16 (m, 1H), 6.92–6.83 (m, 2H) ppm. \(^13\)C-NMR (101 MHz, CD\(_3\)OD) \(\delta\) 157.93, 142.18, 133.74, 129.60, 128.96, 127.30, 127.28, 116.53, 49.43, 49.21, 49.00, 48.79, 48.57 ppm. The NMR spectral data matched literature data [50,51]. MS (EI): \(m/z = 170\) [M\(^+\)].

2-Butyoxyl-5-tert-butylbiphenyl (12i): colorless oil. \(^1\)H-NMR (400 MHz, CDCl\(_3\)) \(\delta\) 7.70–7.65 (m, 2H), 7.53–7.46 (m, 3H), 7.44–7.38 (m, 2H), 7.02 (d, \(J = 8.6\) Hz, 1H), 4.04 (t, \(J = 6.4\) Hz, 2H), 1.79 (dt,
Molecules 2012, 17 12134

J = 14.3, 6.5 Hz, 2H), 1.52 (dd, J = 14.9, 7.5 Hz, 2H), 1.45 (s, 9H), 1.01 (t, J = 7.4 Hz, 3H) ppm.

$^{13}$C-NMR (101 MHz, CDCl$_3$) δ 154.00, 143.45, 139.37, 130.46, 129.80, 128.24, 127.90, 126.74, 125.24, 112.30, 77.48, 77.16, 76.84, 68.35, 34.28, 31.71, 31.50, 19.45, 13.91 ppm.

4-Methylbiphenyl (12j): colorless solid, m.p. 42–44 °C (lit. [52], m.p. 41–42 °C). $^1$H-NMR (400 MHz, CDCl$_3$) δ 7.70–7.65 (m, 2H), 7.59 (d, J = 8.1 Hz, 2H), 7.51 (t, J = 7.6 Hz, 2H), 7.41 (dd, J = 11.6, 4.3 Hz, 1H), 7.33 (d, J = 7.9 Hz, 2H), 2.48 (s, 3H) ppm. $^{13}$C-NMR (101 MHz, CDCl$_3$) δ 141.30, 138.50, 137.11, 129.60, 128.33, 127.12, 127.09, 21.22 ppm. The NMR spectral data matched literature data [52,53].

2-Methylbiphenyl (12k): colorless oil. $^1$H-NMR (400 MHz, CDCl$_3$) δ 7.53–7.47 (m, 2H), 7.42 (d, J = 7.2 Hz, 3H), 7.39–7.30 (m, 4H), 2.37 (s, 3H) ppm. $^{13}$C-NMR (101 MHz, CDCl$_3$) δ 142.06, 142.04, 135.44, 130.42, 129.91, 129.30, 128.18, 127.36, 125.88, 20.61 ppm. The NMR spectral data matched literature data [52,54].

2,5-Dimethylbiphenyl (12l): colorless solid, m.p. 68–70 °C. $^1$H-NMR (400 MHz, CDCl$_3$) δ 7.40–7.35 (m, 2H), 7.30 (d, J = 7.1 Hz, 3H), 7.15 (d, J = 7.9 Hz, 1H), 7.06 (d, J = 6.7 Hz, 2H), 2.33 (s, 3H), 2.22 (s, 3H) ppm. $^{13}$C-NMR (101 MHz, CDCl$_3$) δ 142.21, 141.87, 135.28, 132.27, 130.66, 130.37, 129.29, 128.14, 128.06, 126.80, 21.06, 20.10 ppm. The NMR spectral data matched literature data [55,56].

2,6-Dimethylbiphenyl (12m): colorless oil. $^1$H-NMR (400 MHz, CDCl$_3$) δ 7.37 (t, J = 7.5 Hz, 2H), 7.28 (t, J = 7.3 Hz, 1H), 7.15–7.03 (m, 5H), 1.99 (s, 6H) ppm. $^{13}$C-NMR (101 MHz, CDCl$_3$) δ 142.01, 141.25, 136.17, 129.16, 128.54, 127.41, 127.15, 126.73, 20.97 ppm. The NMR spectral data matched literature data [52,57].

3,5-Di-tert-butylbiphenyl (12n): colorless solid, m.p. 63–64 °C (lit. [58], m.p. 62–63 °C). $^1$H-NMR (400 MHz, CDCl$_3$) δ 7.69–7.64 (m, 2H), 7.55–7.45 (m, 5H), 7.40 (dd, J = 6.9, 1.1 Hz, 1H), 1.45 (d, J = 2.3 Hz, 18H) ppm. $^{13}$C-NMR (101 MHz, CDCl$_3$) δ 151.25, 142.70, 140.87, 128.77, 127.62, 127.09, 121.87, 121.53, 35.14, 31.71 ppm. The NMR spectral data matched literature data [58].

Diphenylmethane (12o): colorless solid, m.p. 20–22 °C (lit. [59], m.p. 21–24 °C). $^1$H-NMR (400 MHz, CDCl$_3$) δ 7.27 (d, J = 7.2 Hz, 4H), 7.18 (d, J = 6.5 Hz, 6H), 3.98 (s, 2H) ppm. $^{13}$C-NMR (101 MHz, CDCl$_3$) δ 141.24, 129.06, 128.58, 126.19, 42.07 ppm. The NMR spectral data matched literature data [59,60].

3-Methylbiphenyl (12p): colorless oil. $^1$H-NMR (400 MHz, CDCl$_3$) δ 7.48 (d, J = 7.2 Hz, 2H), 7.31 (t, J = 10.4 Hz, 4H), 7.22 (t, J = 7.1 Hz, 2H), 7.06 (d, J = 7.1 Hz, 1H), 2.31 (s, 3H) ppm. $^{13}$C-NMR (101 MHz, CDCl$_3$) δ 141.46, 141.34, 138.42, 128.81, 128.79, 128.12, 128.09, 127.29, 124.39, 21.68 ppm. The NMR spectral data matched literature data [61].

Methyl 1-(4′-acetyl-biphenyl-4-yl)-carboxylate (12q): colorless solid, m.p. 165–168 °C (lit. [62], m.p. 164.5–166 °C). $^1$H-NMR (400 MHz, CDCl$_3$) δ 8.14 (d, J = 8.4 Hz, 2H), 8.05 (d, J = 8.4 Hz, 2H), 7.71 (t, J = 8.8 Hz, 4H), 3.95 (s, 3H), 2.65 (s, 3H) ppm. $^{13}$C-NMR (101 MHz, CDCl$_3$) δ 197.68, 166.87, 144.57, 144.32, 136.65, 130.34, 129.91, 129.10, 127.56, 127.35, 52.34, 26.80 ppm. The NMR spectral data matched literature data [62,63].
4. Conclusions

In conclusion, we have synthesized a range of novel $C_2$-symmetric NHC precursor imidazolium salts containing side arms substituted with aryloxyl groups. The Suzuki-Miyaura coupling reaction could be catalyzed remarkably by the Pd/NHC catalysts formed in situ. Various functionalized and sterically hindered aryl halides and arylboronic acids could be used. TON of up to $10^5$ was achieved with $5 \times 10^{-4}$ mol% Pd catalyst.

Supplementary Materials

Supplementary materials can be accessed at: http://www.mdpi.com/1420-3049/17/10/12121/s1.

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Conflict of Interest

The authors declare no conflict of interest.

References

1. Suzuki, A. Recent advances in the cross-coupling reactions of organoboron derivatives with organic electrophiles, 1995–1998. J. Organomet. Chem. 1999, 576, 147–168.
2. Nicolaou, K.C.; Bulger, P.G.; Sarlah, D. Palladium-catalyzed cross-coupling reactions in total synthesis. Angew. Chem. Int. Ed. 2005, 44, 4442–4489.
3. Phan, N.T.S.; Sluys, M.V.D.; Jones, C.W. On the nature of the active species in palladium catalyzed Mizoroki-Heck and Suzuki-Miyaura couplings-homogeneous or heterogeneous catalysis, a critical review. Adv. Synth. Catal. 2006, 348, 609–679.
4. Nicolaou, K.C.; Ramanjulu, J.M.; Natarajan, S.; Bräse, S.; Rübsam, F. A Suzuki coupling-macrolactamization approach to the AB-COD bicyclic system of vancomycin. Chem. Commun. 1997, 1899–1900.
5. Baudoin, O.; Cesario, M.; Guénard, D.; Guéritte, F. Application of the palladium-catalyzed borylation/Suzuki coupling (BSC) reaction to the synthesis of biologically active biaryl lactams. J. Org. Chem. 2002, 67, 1199–1207.
6. Sandee, A.J.; Williams, C.K.; Evans, N.R.; Davies, J.E.; Boothby, C.E.; Köhler, A.; Friend, R.H.; Holmes, A.B. Solution-processible conjugated electrophosphorescent polymers. J. Am. Chem. Soc. 2004, 126, 7041–7048.
7. Miyaura, N.; Suzuki, A. Stereoselective synthesis of arylated (E)-alkenes by the reaction of alk-1-enylboranes with aryl halides in the presence of palladium catalyst. J. Chem. Soc. Chem. Commun. 1979, 866–867.
8. Miyaura, N.; Yanagi, T.; Suzuki, A. The palladium-catalyzed cross-coupling reaction of phenylboronic acid with haloarenes in the presence of bases. Synth. Commun. 1981, 11, 513–519.
9. Miyaura, N.; Suzuki, A. Palladium-catalyzed cross-coupling reactions of organoboron compounds. *Chem. Rev.* 1995, 95, 2457–2483.

10. Netherton, M.R.; Dai, C.; Neuschütz, K.; Fu, G.C. Room-temperature alkyl–alkyl Suzuki cross-coupling of alkyl bromides that possess β-hydrogens. *J. Am. Chem. Soc.* 2002, doi:10.1002/chin.200205050.

11. Stambuli, J.P.; Kuwano, R.; Hartwig, J.F. Unparalleled rates for the activation of aryl chlorides and bromides: Coupling with amines and boronic acids in minutes at room temperature. *Angew. Chem. Int. Ed.* 2002, 41, 4746–4748.

12. Arduengo, A.J., III; Harlow, R.L.; Kline, M. A stable crystalline carbene. *J. Am. Chem. Soc.* 1991, 113, 361–363.

13. Herrmann, W.A.; Elison, M.; Fischer, J.; Köcher, C.; Artus, G.R.J. Metal complexes of N-heterocyclic carbenes—a new structural principle for catalysts in homogeneous catalysis. *Angew. Chem. Int. Ed. Engl.* 1995, 34, 2371–2374.

14. Herrmann, W.A. N-heterocyclic carbenes: A new concept in organometallic catalysis. *Angew. Chem. Int. Ed.* 2002, 41, 1290–1309.

15. Scott, N.M.; Clavier, H.; Mahjoor, P.; Stevens, E.D.; Nolan, S.P. Synthetic, structural, and thermochemical studies of N-heterocyclic carbene (NHC) and tertiary phosphine ligands in the [(L)2Ni(CO)2] (L = PR3, NHC) system. *Organometallics* 2008, 27, 3181–3186.

16. Lee, M.-T.; Hu, C.-H. Density functional study of N-heterocyclic and diamino carbene complexes: Comparison with phosphines. *Organometallics* 2004, 23, 976–983.

17. Colacino, E.; Martinez, J.; Lamaty, F. Preparation of NHC-ruthenium complexes and their catalytic activity in metathesis reaction. *Coord. Chem. Rev.* 2007, 251, 726–764.

18. Gade, L.H.; César, V.; Bellemin-Laponnaz, S. A modular assembly of chiral oxazolinylcarbene-rhodium complexes: Efficient phosphane-free catalysts for the asymmetric hydrosilylation of dialkyl ketones. *Angew. Chem. Int. Ed.* 2004, 43, 1014–1017.

19. Song, C.; Ma, C.; Ma, Y.; Feng, W.; Ma, S.; Chai, Q.; Andrus, M.B. Bis-paracyclophane N-heterocyclic carbene-ruthenium catalyzed asymmetric ketone hydrosilylation. *Tetrahedron Lett.* 2005, 46, 3241–3244.

20. Powell, M.T.; Hou, D.-R.; Perry, M.C.; Cui, X.; Burgess, K. Chiral imidazolylidine ligands for asymmetric hydrogenation of aryl alkenes. *J. Am. Chem. Soc.* 2001, 123, 8878–8879.

21. César, V.; Bellemin-Laponnaz, S.; Gade, L.H. Chiral N-heterocyclic carbenes as stereodirecting ligands in asymmetric catalysis. *Chem. Soc. Rev.* 2004, 33, 619–636.

22. Alonso, F.; Belekskaya, I.P.; Yus, M. Non-conventional methodologies for transition-metal catalysed carbon-carbon coupling: A critical overview. Part 2: The Suzuki reaction. *Tetrahedron* 2008, 64, 3047–3101.

23. Herrmann, W.A.; Reisinger, C.P.; Spiegler, M. Chelating N-heterocyclic carbene ligands in palladium-catalyzed Heck-type reactions. *J. Organomet. Chem.* 1998, 557, 93–96.

24. Kim, J.-H.; Kim, J.-W.; Shokouhimehr, M.; Lee, Y.-S. Polymer-supported N-heterocyclic carbene-palladium complex for heterogeneous Suzuki cross-coupling reaction. *J. Org. Chem.* 2005, 70, 6714–6720.

25. Schneider, S.K.; Herrmann, W.A.; Herdtweck, E. Active catalysts for the Suzuki coupling: Palladium complexes of tetrahydropyrimid-2-ylidenes. *J. Mol. Catal. A Chem.* 2006, 245, 248–254.
26. Navarro, O.; Kelly, R.A.; Nolan, S.P. A general method for the Suzuki-Miyaura cross-coupling of sterically hindered aryl chlorides: Synthesis of di- and tri-ortho-substituted biaryls in 2-propanol at room temperature. *J. Am. Chem. Soc.* 2003, 125, 16194–16195.

27. Marion, N.; Navarro, O.; Mei, J.; Stevens, E.D.; Scott, N.M.; Nolan, S.P. Modified (NHC)Pd(allyl)Cl (NHC=N-heterocyclic carbene) complexes for room-temperature Suzuki-Miyaura and Buchwald-Hartwig reactions. *J. Am. Chem. Soc.* 2006, 128, 4101–4111.

28. Kantchev, E.A.B.; ÓBrien, C.J.; Organ, M.G. Palladium complexes of N-heterocyclic carbenes as catalysts for cross-coupling reactions—a synthetic chemist’s perspective. *Angew. Chem. Int. Ed.* 2007, 46, 2768–2813.

29. Marion, N.; Nolan, S.P. Well-defined N-heterocyclic carbenes-palladium(II) precatalysts for cross-coupling reactions. *Acc. Chem. Res.* 2008, 41, 1440–1449.

30. Jiang, L.; Li, Z.N.; Zhao, D.F. Progress in the Heck reaction and Suzuki reaction catalyzed by Pd-N-heterocyclic carbene complexes. *Chin. J. Org. Chem.* 2010, 30, 200–210.

31. Türkmen, H.; Pelit, L.; Çetinkaya, B. Water-soluble cis-[(NHC)PdBr₂(TPPTS)] catalysts and their applications in Suzuki-Miyaura coupling of aryl chlorides. *J. Mol. Catal. A Chem.* 2011, 348, 88–93.

32. Godoy, F.; Segarra, C.; Poyatos, M.; Peris, E. Palladium catalysts with sulfonate-functionalized-NHC ligands for Suzuki-Miyaura cross-coupling reactions in water. *Organometallics* 2011, 30, 684–688.

33. Dible, B.R.; Cowley, R.E.; Holland, P.L. Remote substitution on N-heterocyclic carbenes heightens the catalytic reactivity of their palladium complexes. *Organometallics* 2011, 30, 5123–5132.

34. Xu, X.; Xu, B.; Li, Y.; Hong, S.H. Abnormal N-heterocyclic carbene promoted Suzuki-Miyaura coupling reaction: A comparative study. *Organometallics* 2010, 29, 6343–6349.

35. Xu, Q.; Duan, W.-L.; Lei, Z.-Y.; Zhu, Z.B.; Shi, M. A novel cis-chelated Pd(II)-NHC complex for catalyzing Suzuki and Heck-type cross-coupling reactions. *Tetrahedron* 2005, 61, 11225–11229.

36. Shi, J.-C.; Yang, P.-Y.; Tong, Q.; Wu, Y.; Peng, Y. Highly efficient and stable palladium/imidazolium salt-phosphine catalysts for Suzuki-Miyaura cross-coupling of aryl bromides. *J. Mol. Catal. A Chem.* 2006, 259, 7–10.

37. Tulloch, A.A.D.; Danopoulos, A.A.; Tooze, R.P.; Cafferkey, S.M.; Kleinhenz, S.; Hursthouse, M.B. Pyridine functionaized N-heterocyclic carbene complexes of palladium. *Chem. Commun.* 2000, 1247–1248.

38. Netland, K.A.; Krivokapic, A.; Schröder, M.; Boldt, K.; Lundvall, F.; Tilset, M. Synthesis, X-ray structures, and catalytic applications of palladium(II) complexes bearing N-heterocyclic iminocarbene ligands. *J. Organomet. Chem.* 2008, 693, 3703–3710.

39. Yang, C.; Lee, H.M.; Nolan, S.P. Highly efficient Heck reactions of aryl bromides with n-butyl acrylate mediated by a palladium/phosphine-imidazolium salt system. *Org. Lett.* 2001, 3, 1511–1514.

40. Wang, J.-W.; Meng, F.-H.; Zhang, L.-F. Suzuki coupling reaction of aryl halides catalyzed by an N-heterocyclic carbene-PdCl₂ species based on a porphyrin at room temperature. *Organometallics* 2009, 28, 2334–2337.

41. Zhang, X.; Qiu, Y.; Rao, B.; Luo, M. Palladium(II)–N-heterocyclic carbene metallacrown ether complexes: Synthesis, structure, and catalytic activity in the Suzuki-Miyaura reaction. *Organometallics* 2009, 28, 3093–3099.
42. Yuan, D.; Huynh, H.V. Dinuclear and tetranuclear palladium(II) complexes of a thiolato-functionalized, benzannulated N-heterocyclic carbene ligand and their activities toward Suzuki-Miyaura coupling. *Organometallics* **2010**, *29*, 6020–6027.

43. Shan, F.J.; Jiang, L.; Li, Z.N.; Zhao, D.F. Asymmetric conjugate addition to cyclic enone catalyzed by Cu-NHC complexes with C$_2$ symmetry. *Chin. J. Chem.* **2011**, *29*, 973–977.

44. Navarro, O.; Kaur, H.; Mahjoor, P.; Nolan, S.P. Cross-coupling and dehalogenation reactions catalyzed by (N-heterocyclic carbene)Pd(allyl)Cl complexes. *J. Org. Chem.* **2004**, *69*, 3173–3180.

45. Watanabe, T.; Miyaura, N.; Suzuki, A. Synthesis of sterically hindered biaryls via the palladium-catalyzed cross-coupling reaction of arylboronic acids or their esters with haloarenes. *Synlett* **1992**, *3*, 207–210.

46. Zhou, W.-J.; Wang, K.-H.; Wang, J.-X. Atom-efficient, palladium-catalyzed Stille coupling reactions of tetraphenyldistannane with aryl iodides or aryl bromides in polyethylene glycol 400 (PEG-400). *Adv. Synth. Catal.* **2009**, *351*, 1378–1382.

47. Zhou, W.-J.; Wang, K.-H.; Wang, J.-X. Pd(PPh$_3$)$_3$-PEG 400 catalyzed protocol for the atom-efficient Stille cross-coupling reaction of organotin with aryl bromides. *J. Org. Chem.* **2009**, *74*, 5599–5602.

48. Percec, V.; Golding, G.M.; Smidrkal, J.; Weichold, O. NiCl$_2$(dppe)-catalyzed cross-coupling of aryl mesylates, arenesulfonates, and halides with arylboronic acids. *J. Org. Chem.* **2004**, *69*, 3447–3452.

49. Kylmälä, T.; Kuuloja, N.; Xu, Y.; Rissanen, K.; Franzén, R. Synthesis of chlorinated biphenyls by Suzuki cross-coupling using diamine or diimine-palladium complexes. *Eur. J. Org. Chem.* **2010**, *6*, 1021–1025.

50. Schmidt, B.; Hölter, F. Suzuki-Miyaura cross coupling reactions with phenoldiazonium salts. *Org. Biomol. Chem.* **2011**, *9*, 4914–4920.

51. Hanada, S.; Yuasa, A.; Kuroiwa, H.; Motoyama, Y.; Nagashima, H. Hydrosilanes are not always reducing agents for carbonyl compounds, II: ruthenium-catalyzed deprotection of tert-butyl groups in carbamates, carbonates, esters, and ethers. *Eur. J. Org. Chem.* **2010**, *6*, 1021–1025.

52. Fan, X.-H.; Yang, L.-M. Ni$^{II}$-(σ-Aryl) complex catalyzed Suzuki reaction of aryl tosylates with arylboronic acids. *Eur. J. Org. Chem.* **2010**, *13*, 2457–2460.

53. Diebolt, O.; Braunstein, P.; Nolan, S.P.; Cazin, C.S.J. Room-temperature activation of aryl chlorides in Suzuki–Miyaura coupling using a [Pd(l-Cl)Cl(NHC)$_2$] complex (NHC = N-heterocyclic carbene). *Chem. Commun.* **2008**, *3190–3192.

54. Firouzabadi, H.; Iranpoor, N.; Gholinejad, M. 2-Aminophenyl diphenylphosphinite as an easily accessible ligand for heterogeneous palladium-catalyzed Suzuki-Miyaura reaction in water in the absence of any organic co-solvent. *J. Organomet. Chem.* **2010**, *695*, 2093–2097.

55. Kawai, H.; Kobayashi, Y.; Oi, S.; Inoue, Y. Direct C–H bond arylation of arenes with aryltin reagents catalysed by palladium complexes. *Chem. Commun.* **2008**, *1464–1466.

56. Liu, D.; Gao, W.; Dai, Q.; Zhang, X. Triazole-based monophosphines for Suzuki-Miyaura coupling and amination reactions of aryl chlorides. *Org. Lett.* **2005**, *7*, 4907–4910.

57. Wolfe, J.P.; Singer, R.A.; Yang, B.H.; Buchwald, S.L. Highly active palladium catalysts for Suzuki coupling reactions. *J. Am. Chem. Soc.* **1999**, *121*, 9550–9561.
58. Thomas, A.; Anilkumar, G.; Nair, V. Photolytic double decarbonylation route to highly substituted indenes and benzene derivatives. *Tetrahedron* **1996**, *52*, 2481–2488.

59. Karami, K.; Rizzoli, C.; Salah, M.M. Synthesis and application of ortho-palladated complex of (4-phenylbenzoylmethylene)triphenylphosphorane as a highly active catalyst in the Suzuki cross-coupling reaction. *J. Organomet. Chem.* **2011**, *696*, 940–945.

60. Peña-López, M.; Ayán-Varela, M.; Sarandeses, L.A.; Sestelo, J.P. Palladium-catalyzed cross-coupling reactions of organogold(I) reagents with organic electrophiles. *Chem. Eur. J.* **2010**, *16*, 9905–9909.

61. Pal, A.; Ghosh, R.; Adarsh, N.N.; Sarkar, A. Pyrazole-tethered phosphine ligands for Pd(0): useful catalysts for Stille, Kumada and Hiyama cross-coupling reactions. *Tetrahedron* **2010**, *66*, 5451–5458.

62. Zhu, L.; Duquette, J.; Zhang, M. An improved preparation of arylboronates: Application in one-pot Suzuki biaryl synthesis. *J. Org. Chem.* **2003**, *68*, 3729–3732.

63. Wu, L.; Li, Z.-W.; Zhang, F.; He, Y.-M.; Fan, Q.-H. Air-stable and highly active dendritic phosphine oxide-stabilized palladium nanoparticles: preparation, characterization and applications in the carbon-carbon bond formation and hydrogenation reactions. *Adv. Synth. Catal.* **2008**, *350*, 846–862.

*Sample Availability*: Samples of the compounds 12a–q are available from the authors.

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