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# *N*-Heterocyclic carbenes
# Part 26. *N*-Heterocyclic carbene complexes of palladium(0): synthesis and application in the Suzuki cross-coupling reaction ☆

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**Abstract**

Palladium(0) complexes of *N*-heterocyclic carbenes (NHC) are easily obtained starting from the free carbene and bis(tri-*ortho*-tolylphosphine)palladium(0) by ligand exchange. The complexes $[(R)\overline{N(H)C{=}C(H)N(R)C}]_2Pd$ of various 1,3-disubstituted imidazolin-2-ylidenes have been prepared by this method (R = mesityl, *t*-Bu, *i*-Pr, cyclohexyl). The activities of these complexes as catalysts for the activation of chloroarenes in the Suzuki cross-coupling reaction were evaluated. Turnover frequencies up to 552 (mol product × mol $Pd^{-1} \times h^{-1}$] were achieved without specific optimization of the system. 

*Keywords:* Palladium; *N*-Heterocyclic carbenes; Cross coupling; Carbon–carbon bond formation; Suzuki reaction

## 1. Introduction

Recently, the development of highly active palladium(0) catalysts for the activation of chloroarenes in Heck-type reactions has focused on sterically demanding, basic, monodentate phosphines [1–5]. *N*-Heterocyclic carbenes (NHC) are easily accessible, and due to their strong σ-donating character, resemble trialkyl phosphines [6]. This analogy was lately demonstrated for ruthenium(II) catalysts in olefin metathesis [7]. The versatility of NHC-ligands for palladium(II) pre-catalysts in Heck-type reactions has also been verified [8]. Furthermore, the application of NHC–palladium(0) olefin complexes in the Heck reaction with iodoarenes was demonstrated [9]. Recently, the use of imidazolium salts in combination with a palladium(0) source has emerged as being highly efficient for the Suzuki cross-coupling reaction [10]. As a consequence, homoleptic NHC–palladium(0) complexes were postulated as the catalytically active species and their preparation has become highly desirable. Herein, we report a convenient and general procedure to this type of complex. In addition, studies of the Suzuki cross-coupling reaction were performed (Table 1).

## 2. Synthesis

Despite the previous preparation of homoleptic nickel(0) and platinum(0) complexes of NHC by solution techniques, no such method was available for the corresponding palladium(0) complexes [11]. Only the co-condensation of the free 1,3-di-*tert*-butylimidazolin-2-ylidene (**1b**) and palladium vapor has led successfully to the desired homoleptic complex **3b** in 32% yield [12]. A more general and efficient method is to prepare these complexes by ligand exchange. The free NHC is added to a slurry of bis(tri-*ortho*-tolylphosphine)palladium(0) in toluene at room temperature upon which a clear yellow solution forms. The desired complexes **3** can be isolated analytically pure in over 60% yield after wash-

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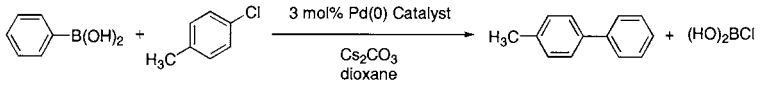
Table 1
Suzuki cross-coupling reaction [a]




| Entry | Catalyst | Additive (mol%) | $T$ (°C) | $t$ (min) | Yield (%) [b] |
|---|---|---|---|---|---|
| 1 | $Pd_2(dba)_3$ | $Im(mes)_2Cl(3)$ | 80 | 120 | 93 |
| 2 | $Pd_2(dba)_3$ | $Im(t\text{-}Bu)_2BF_4(3)$ | 80 | 120 | 0 |
| 3 | **3a** | | 80 | 120 | 0 |
| 4 | **3b** | | 80 | 60 | 68 |
| 5 | **3b** | | 40 | 120 | 0 |
| 6 | **3b** | | 80 | 10 | 55 |
| 7 | **3b** [c] | | 80 | 1 | 46 |
| 8 | **3c** | | 80 | 120 | 17 |
| 9 | **3d** | | 80 | 120 | 7 |

[a] One equivalent *p*-chlorotoluene, 1.5 equivalents phenylboronic acid, two equivalents $Cs_2CO_3$.
[b] GC-yield using diethyleneglycol-di-*n*-butylether as internal standard.
[c] Using 5 mol% **3b**.

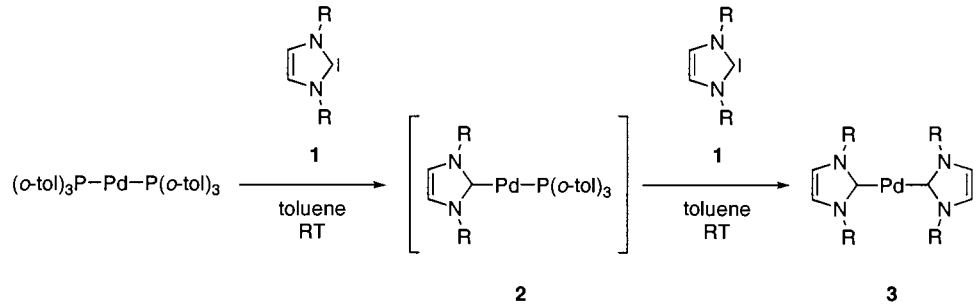
ing away the liberated tri-*ortho*-tolylphosphine P(*o*-tol)$_3$ with cold *n*-hexane. Monitoring the ligand exchange by $^{31}$P-NMR reveals full conversion in all cases after addition of an excess of NHC; loss of the desired product occurs during the work-up procedure. NMR data indicate that the reaction proceeds via step-wise exchange of the phosphine ligands (Scheme 1). In the case of 1,3-dimesitylimidazolin-2-ylidene (**1a**), the major species in solution after addition of one equivalent of the NHC are the free P(*o*-tol)$_3$ and a novel compound that can be assigned to a mixed phosphine–NHC complex **2**. Attempts to exchange ligands from tetrakis(triphenylphosphine)palladium(0) or bis(tricyclohexylphosphine)palladium(0) have resulted in lower yields and product mixtures.

In the $^{13}$C-NMR spectra, the carbene carbon signals are shifted approximately 20 ppm to higher field upon complexation to palladium(0). In comparison to related palladium(II) complexes, the signals are shifted about 30 ppm to lower field. Complex **3a** is stable with regard to the reaction conditions of the catalysis experiments (vide infra), whereas complexes **3b**–**3e** readily decompose to palladium black. All complexes, except for **3c**, are either slightly soluble or soluble in most organic solvents.

## 3. Catalysis

The Suzuki cross-coupling reaction has emerged as a powerful tool for the preparation of bis-arenes [13]. In mechanistic considerations of this reaction it is generally believed that 14-electron palladium(0) compounds are the catalytically active species. As NHC **1** have been shown to be highly activating ligands for this reaction [8b–d,10], the complexes **3** were supposed to constitute highly active catalysts for this reaction.

However, coupling of *p*-chlorotoluene and phenylboronic acid with **3a** as the catalyst was not achieved: Despite the high activity of the in situ system with the corresponding imidazolium salt and $Pd_2(dba)_3$ the preformed complex **3a** showed no activity at all (Entries 1 and 3). In contrast, with complex **3b** a high activity is observed, although the in situ system exhibits no activ-




Scheme 1. Reaction scheme for the preparation of the bis(NHC) complexes **3**. R = mes (**a**) (mes = mesityl), *t*-Bu (**b**), *i*-Pr (**c**), cyclohexyl (**d**). RT = room temperature.

ity with this corresponding imidazolium salt (Entries 2 and 4–7). Complexes **3c** and **3d** showed little activity (Entries 8, 9).

A detailed examination of the time-conversion characteristics of complex **3b** revealed an extraordinarily high turnover frequency (TOF) of 552 [mol product × mol $Pd^{-1} \times h^{-1}$] for the coupling of *p*-chlorotoluene (Entry 7 and Fig. 1). This is much higher than the TOFs obtained with any other system. For example, 3 mol% 1,3-dimesitylimidazolium chloride and $Pd_2(dba)_3$ achieve 24% conversion of *p*-chlorotoluene with phenylboronic acid after 10 min, whereas catalyst **3b** after 10 min has already almost reached maximum conversion at 55%. The difference in activity between the complexes **3a** and **3b** is accounted for either by the complex stability or by steric congestion on the metal center.

## 4. Conclusions

Homoleptic palladium(0) complexes of *N*-heterocyclic carbenes (NHC) are easily obtained under standard laboratory techniques by ligand exchange from bis(tri-*ortho*-tolylphosphine)palladium(0). These compounds are now available in a broad scope and on a large scale. Furthermore, a possible route to mixed phosphine–NHC complexes of palladium(0) has been sketched.

The 14-electron bis(NHC) complexes that were prepared have been evaluated in the Suzuki cross-coupling reaction. Compared to a mixture of the imidazolium salt and $Pd_2(dba)_3$, these complexes exhibit different activities. This observation suggests distinct mechanisms of activation in both cases. Despite the low stability of the very active complex bis(1,3-di-*tert*-butylimidazolin-2-ylidene)palladium(0) (**3b**), the reaction rate (TOF) is the highest observed for non-activated chloroarenes.

## 5. Experimental

### 5.1. General considerations

Chemicals were bought from Fluka and Aldrich. NMR spectra ($^1H$, $^{13}C$, $^{31}P$) were recorded on a Jeol JMX-GX 400 instrument. Elemental analyses were carried out by the Microanalytical Laboratory at the Technischen Universität München. CI-MS spectra were recorded on a Varian MAT 90 (150 eV, *i*-butane). GC–MS spectra were measured on a Hewlett–Packard gas chromatograph GC 5890 A equipped with a MS 5970 B mass-selective detector. The carbon–carbon-coupling products were identified by comparison of GC–MS data with authentic samples. The yields of catalysis experiments were generally determined by gas chromatography using diethyleneglycol-di-*n*-butylether as internal standard. All operations were carried out under argon. All solvents were carefully dried and degassed according to standard procedures [14].

### 5.2. Materials

$P(o\text{-tol})_3$ was prepared from the corresponding Grignard reagent and $PCl_3$ by literature methods [15]. Bis(tri-*ortho*-tolylphosphine)palladium(0) was prepared according to literature reports [16]. Imidazolium salts were prepared following published methods [17]. The free NHC **1** were prepared from the imidazolium salts by deprotonation with NaH in liquid $NH_3$ [18].

### 5.3. Preparation of bis(1,3-dimesitylimidazolin-2-ylidene)palladium(0) (3a)

Bis(tri-*ortho*-tolylphosphine)palladium(0) (1000 mg, 1.40 mmol) is suspended in 20 ml of toluene. To the slurry a solution of 1,3-dimesitylimidazolin-2-ylidene (**1a**) in 20 ml toluene is added (915 mg, 3.00 mmol). The mixture clarifies within 10 min upon addition and is stirred at ambient temperature for an additional 30 min. The solvent is evaporated in vacuo without heating and the light-yellow solid thus obtained is rinsed three times with 25 ml of cold hexane to wash away $P(o\text{-tol})_3$. After drying in vacuo the product is obtained as an analytically pure, light yellow solid. Yield: 651 mg, 0.91 mmol, 65%. $^1H$-NMR (400 MHz, $C_6D_6$): $\delta = 6.66$ (8H, s, arom.), 6.02 (4H, s, NCH=CHN), 2.27 (12H, s, *p*-$CH_3$), 2.05 (24H, s, *o*-$CH_3$). $^{13}C\{^1H\}$-NMR (100.5 MHz, $C_6D_6$): $\delta = 186.2$ (Pd–$CN_2$), 137.3 (arom.), 137.2 (double int., arom.), 136.0 (arom.), 125.1 (arom.), 123.5 (double int., NCH=CHN), 21.4 (*p*-$CH_3$), 18.6 (double int., *o*-$CH_3$). CI-MS *m*/*z* (%): 715 (100) [$M^+$], 320 (38), 304 (77) [$NHC^+$]. $C_{42}H_{48}N_4Pd$ (714.86): Calc. C 70.56, H 6.72, N 7.84. Found C 70.23, H 6.66, N 7.64%.

### 5.4. Preparation of bis(1,3-di-tert-butylimidazolin-2-ylidene)palladium(0) (3b)

The product is obtained in analogy to **3a** as a yellow solid. Yield: 400 mg, 0.85 mmol, 61%. $^1H$-NMR (400 MHz, $C_6D_6$): $\delta = 6.74$ (4H, s, NCH = CHN), 2.12 (36 H, s, $CH_3$). $^{13}C\{^1H\}$-NMR (100.5 MHz, $C_6D_6$): $\delta =$ 194.5 (Pd − $CN_2$), 113.9 (double int., NCH=CHN), 57.4 (double int., N$C(CH_3)_3$), 32.0 (double int., NC($CH_3$)$_3$). CI-MS *m*/*z* (%): 466 (100) [$M^+$], 285 (11) [$M^+$ − NHC], 180 (37) [$NHC^+$], 124 (53) [$NHC^+ - t$-Bu]. $C_{22}H_{40}N_4Pd$ (467.20): Calc. C 56.56, H 8.64, N 11.99. Found C 56.14, H 8.60, N 11.64%.

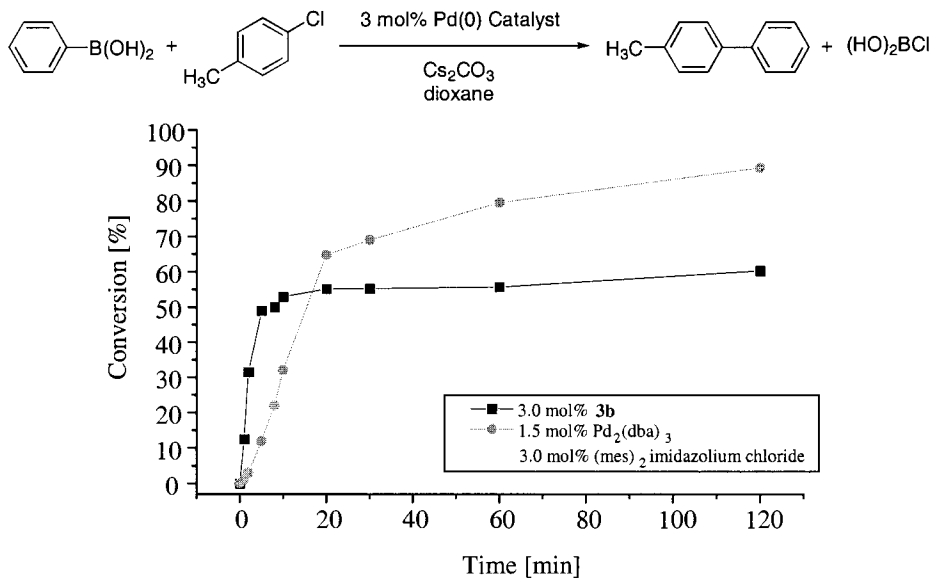



Fig. 1. Time vs. conversion diagram for the Suzuki cross-coupling reaction of *p*-chlorotoluene and phenylboronic acid using 3 mol% bis(1,3-di-*tert*-butylimidazolin-2-ylidene)palladium(0) (**3b**) vs. 1.5 mol% $Pd_2(dba)_3$/3 mol% dimesitylimidazolium chloride as the catalyst.

### *5.5. Preparation of bis(1,3-di-iso-propylimidazolin-2-ylidene)palladium(0) (**3c**)*

The product is obtained in analogy to **3a** as a yellow solid. Yield: 520 mg, 1.27 mmol, 91%. $^1$H-NMR (400 MHz, THF-$d_6$): $\delta = 6.81$ (4H, s (br), NCH=), 3.18–3.28 (4H, m, C*H*$(CH_3)_2$), 1.42 (6H, d, $CH_3$), 1.38 (6H, s (br), $CH_3$), 1.12 (6H, d, $CH_3$), 1.08 (6H, d, $CH_3$). $^{13}$C{$^1$H}-NMR (100.5 MHz, $C_6D_6$) not measured due to complex decomposition. CI-MS *m*/*z* (%): 411 (68) [$M^+ + H$], 281 (64), 258 (13) [$M^+ - NHC$], 207 (49), 152 (100) [$NHC^+$]. $C_{18}H_{32}N_4Pd$ (410.90): Calc. C 52.61, H 7.85, N 13.64. Found C 52.08, H 7.97, N 13.57%.

### *5.6. Preparation of bis(1,3-dicyclohexylimidazolin-2-ylidene)palladium(0) (**3d**)*

The product is obtained in analogy to **3a** as a yellow solid. Yield: 582 mg, 1.02 mmol, 73%. $^1$H-NMR (400 MHz, $C_6D_6$): $\delta = 6.50$ (2H, s (br), NCH=), 6.44 (2H, d, NCH=), 5.70–5.83 (2H, m, NCH(cy)), 5.36–5.55 (2H, m, NCH(cy)), 1.78–1.47 (16H, m, cy), 1.45–1.12 (16H, m, cy), 1.05–0.82 (8H, m, cy). $^{13}$C{$^1$H}-NMR (100.5 MHz, $C_6D_6$, characteristic signals): $\delta = 182.4$ (Pd–*C*$N_2$), 116.7 (NCH=), 116.5 (NCH=), 60.2 (NCH(cy)), 59.9 (NCH(cy)), 34.5, 34.1, 34.1, 26.5, 26.4, 25.8. CI-MS: *m*/*z* (%) 570 (17) [$M^+$], 337 (18) [$M^+ - NHC + H$], 267 (81), 233 (68) [$NHC^+ - H$], 164 (100), 149 (13) [$NHC^+ - C_6H_{11}$]. $C_{30}H_{48}N_4Pd$ (571.14): Calc. C 63.09, H 8.47, N 9.81. Found C 65.08, H 8.91, N 10.33%.

### *5.7. General procedure for the Suzuki cross coupling*

A Schlenk tube is charged with phenylboronic acid (122 mg, 1.50 mmol), $Cs_2CO_3$ (652 mg, 2.00 mmol) and complex **3** (0.03 mmol). The solids are degassed and purged with argon. At the reaction temperature, a pre-warmed solution of *p*-chlorotoluene (1.00 mmol, 126 mg, 120 μl) and diethyleneglycol-di-*n*-butylether (50 mg) in 3 ml 1,4-dioxane is added. The mixture is then stirred and maintained at the reaction temperature. After completion of the reaction, the solution is filtered at room temperature and an aliquot is examined by GC–MS.

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