Articles

Alkylpalladium N-Heterocyclic Carbene Complexes: Synthesis, Reactivity, and Catalytic Properties

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The dimers [*trans*-[(neopentyl)Pd(μ-Cl)(I^{t}Bu)]$_2$, **2**, and (*cis*-[(neopentyl)Pd(μ-Cl)(IPr)]$_2$, **3** (I^{t}Bu = 1,3-bis-*tert*-butylimidazol-2-ylidene, IPr = 1,3-bis-2,6-diidopropylimidazol-2-ylidene), have been synthesized from [Pd(neopentyl)(Cl)(1,5-COD)], and their reactivity toward a variety of nucleophiles has been evaluated. In particular, this study revealed that **2** can be readily cleaved by primary and secondary amines, affording stable transamination products, which are surprisingly resistant to deprotonation. Dimer **3** was subsequently used as a catalyst in a series of Buchwald−Hartwig amination reactions of aryl chlorides.

Introduction

Metal-catalyzed cross-coupling methodologies are extensively used in organic chemistry for the formation of carbon−carbon and carbon−nitrogen bonds.[1] Even though different metals have been used to mediate this process, the efficiency of palladium complexes has remained unsurpassed, and advances in palladium-catalyzed transformations are intrinsically related to the development of new ligands. Indeed electron-rich σ-donor ligands, such as bulky alkyl phosphines and N-heterocyclic carbenes (NHCs),[2] have considerably expanded the scope of aryl halide cross-coupling reactions to include aryl chlorides as standard substrates in Suzuki,[3] Negishi,[4] Heck,[5] Kumada,[6] or Buchwald−Hartwig amination[7] reactions. The use of alkyl halides in the same transformations has remained, until recently, much more challenging.[8]

The generation of well-defined Pd(II)-NHC precatalysts is an area of considerable activity. These complexes display improved air- and moisture-stability and contain the desired (1:1) ratio of NHC ligand:metal. The existence of easily displaceable ligands in the coordination sphere allows the generation, in solution, of the putative monoligated Pd^0-NHC active species. Nolan has explored this concept using (NHC)Pd(R-allyl)Cl

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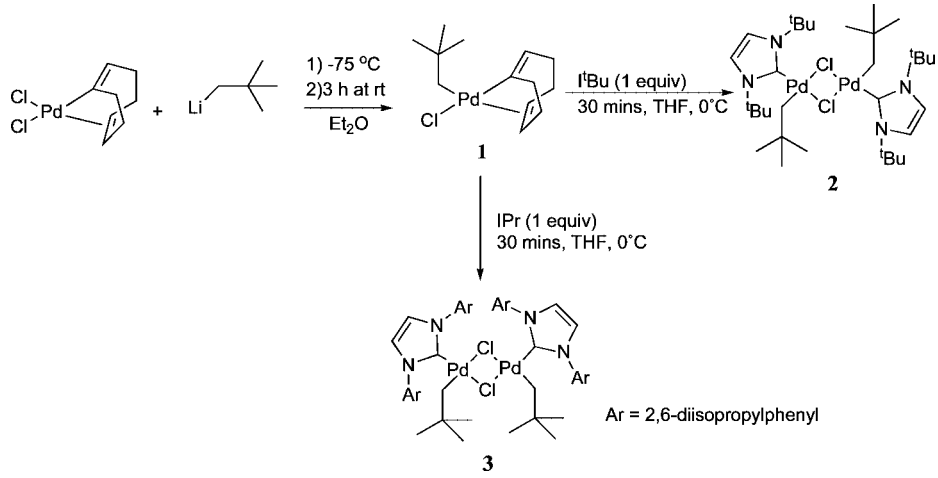
Scheme 1. Synthesis of Alkylpalladium N-Heterocyclic Carbene Complexes 2 and 3



complexes,[9] which proved to be extremely efficient catalysts in Suzuki−Miyaura and Buchwald−Hartwig reactions.[10]

Recently, we became interested in the development of new alkylpalladium N-heterocyclic carbene complexes, not least because their coordination sphere has the potential to generate, in solution, highly active catalytic Pd^0 species. Furthermore, these alkylpalladium N-heterocyclic carbene complexes may well also provide significant insight toward understanding the challenging cross-coupling reactions using alkyl halides,[11] in particular the still undeveloped alkyl-amination reaction. Herein we report the preparation of two alkylpalladium N-heterocyclic carbene complexes of the type $[Pd(alkyl)(\mu\text{-}Cl)(NHC)]_2$, their reactions with amines, phosphines, and NHCs, and their ability to catalyze a series of Buchwald−Hartwig amination reactions of aryl chloride; parts of this work have been briefly communicated.[12]

Discussion

In line with our ongoing efforts toward the isolation of alkyl halide oxidative addition (OA) and transamination products of Pd-NHC complexes, further investigations have been carried out on compounds **1**, **2**, and **3**, the synthesis of which was detailed in our previous work[12] and is summarized in Scheme 1.

The novel [Pd(neopentyl)(Cl)(1,5-COD)], **1**, resulting from the stoichiometric alkylation of $[Cl_2Pd(COD)]$, was prepared by a procedure analogous to that employed for the synthesis of [Pd(benzyl)(Cl)(1,5-COD)][13] and used in the preparation of complexes **2** and **3**, via displacement of the 1,5-COD ligand with the NHC. X-ray diffraction analysis was conducted on crystals of **1** obtained from a concentrated solution of pentane, kept at −20 °C for 3 days. The molecular structure of **1** is shown in Figure 1, together with selected bond lengths and angles, and **1** exhibits the expected square-planar geometry around the palladium center. The Pd−neopentyl bond length (Pd−C(9)) of 2.070(9) Å in **1** is comparable to that found (2.051 Å) for the benzyl ligand in [Pd(benzyl)(Cl)(1,5-COD)].[14] Addition of 1 equiv of ItBu (1,3-bis-*tert*-butylimidazol-2-ylidene) to **1** afforded exclusively the desired dimeric complex *trans*-$[Pd(I^t\text{Bu})(neopentyl)(Cl)]_2$, **2**, and following a similar procedure using IPr (1,3-bis(2,6-diisopropylphenyl)imidazol-2-ylidene) *cis*-$[Pd(IPr)(neopentyl)(Cl)]_2$ (**3**) was obtained in 80% yield. Unlike complex **2**, the neopentyl substituents in **3** do not adopt the *trans* geometry but prefer the *cis* orientation in the solid state, as confirmed by the X-ray structures of **2** and **3** previously communicated.[12]

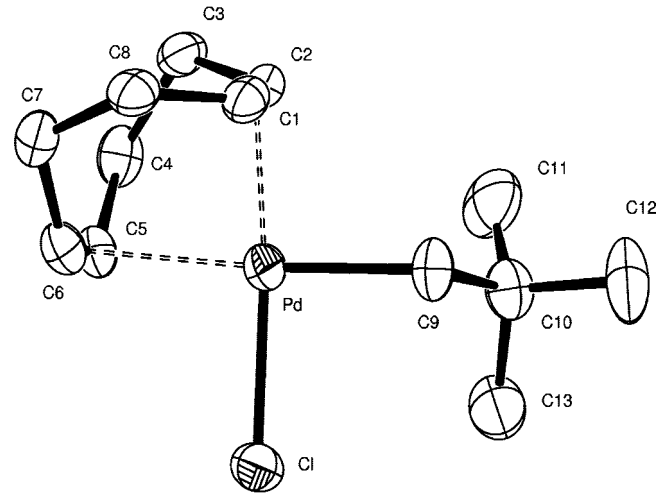


Figure 1. Molecular structure of **1**. Selected bond distances (Å) and bond angles (deg): Pd−C(1) 2.155(8), Pd−C(6) 2.457(9), Pd−Cl 2.332(2), Pd−C(9) 2.070(9); C(9)−Pd−Cl 91.4(3), M(1)−Pd−Cl 170.8(3), M(1)−Pd−M(2) 83.7(3), C(9)−Pd−M(2) 175.1(3). M(1) and M(2) are the midpoints of the C(1)−C(2) and C(5)−C(6) bonds.

The reactivity of dimer **2** toward the addition of a further equivalent of ItBu, ITMe (1,3,4,5-tetramethylimidazol-2-ylidene)

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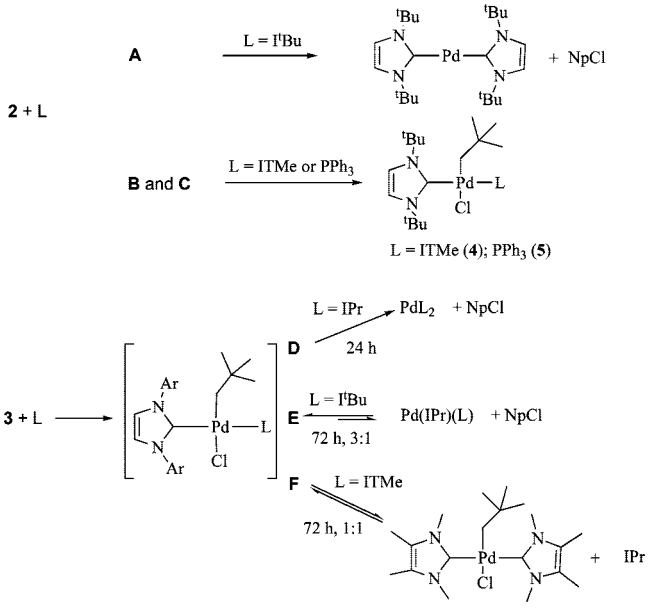
Scheme 2. Reactivity of Dimers 2 and 3 toward Nucleophiles



or PPh_3 (Scheme 2, reactions A, B, and C) was described in our previous communication.[12] The elimination of neopentyl chloride in reaction A in Scheme 2 is particularly noteworthy, as the reductive elimination of an alkyl halide from a palladium(II) moiety has, to the best of our knowledge, not been previously reported; Hartwig et al. have previously found that Pd[P(*o*-tolyl)$_3$](aryl)halide dimers reductively eliminate aryl halides in the presence of the strongly donating P(^{t}Bu)$_3$ ligand.[17] In general, the reductive elimination of alkyl halides is an uncommon process since the oxidative addition (inverse reaction) is thermodynamically favored. However, in the particular case of the oxidative addition of neopentyl chloride to **2**, the reaction is thermodynamically impeded even at high temperatures, as previously reported;[12] therefore, the reductive elimination in the presence of the bulky, strongly electron donating I^{t}Bu may be, to some extent, facilitated.

Further to the work described in our earlier communication,[12] the molecular structure of the phosphine complex **5** has been determined and is shown in Figure 2, together with selected bond lengths and angles. The mixed-ligand complex **5** exhibits a square-planar geometry around the palladium center, where the carbene ligand lies *trans* to the phosphine, on a plane perpendicular to the mean plane defined by Pd−C12−C1−Cl. Comparison with the analogous Pd(PPh$_3$)(IPr)(aryl)chloride complex **6** (Scheme 3), isolated by Marshall and Grushin,[15] reveals shorter palladium−phosphine (2.307(1) Å), Pd−Cl (2.404(1) Å), and palladium−carbene bond distances (2.057(2) Å) in **6**. The difference in bond lengths is probably due to the inferior σ-donating ability of the aryl group in **6**, compared to the neopentyl group of **5**, which makes the palladium center in **6** less electron rich. This increases the σ-bonding character of the palladium−phosphine bond in the latter, making this bond shorter than in **5**. In addition, the weaker *trans* effect induced by the aryl group may be responsible for the observed shorter palladium−chloride in **6**, while the increased bulk of I^{t}Bu compared to IPr (as measured by their relative $\%V_{Bur}$ (buried volume) in the DFT studies by Cavallo et al.[16]), along with the presence of a sterically demanding neopentyl group, makes the palladium−carbene bond longer in **5** than in **6**.

Different decomposition pathways were observed for the heteroleptic palladium complexes **4** and **5** and are shown in Scheme 3, with that of **6** included for comparison.[15] The

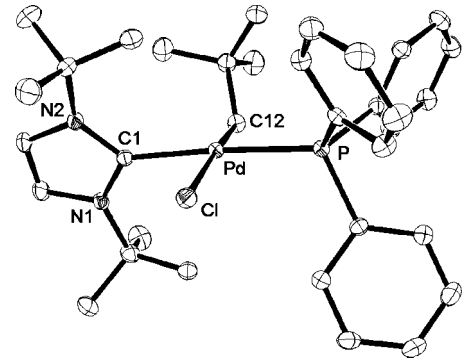


Figure 2. Molecular structure of **5**. Selected bond distances (Å) and angles (deg): Pd−(C1) 2.4554(7), Pd−C(12) 2.090(3), Pd−P 2.3211(8), Pd−Cl 2.4554(7) Å. C(1)−Pd−C(12) 90.92(11), C(1)−Pd−P 175.49(7), C(12)−Pd−P 92.36(8), C(1)−Pd−Cl 87.04(7), C(12)−Pd−Cl 174.01(8), P−Pd−Cl 89.38(2).

presence of an aryl group in **6**, as opposed to the alkyl substituent in **5**, promotes the reductive elimination pathway and formation of the corresponding arylated imidazolium salt, as reported by Marshall et al.[15] At 50 °C in C_6D_6, the neopentyl analogue **5** did not form the expected alkylated imidazolium salt, instead exhibiting clear signals in the ^{1}H NMR spectrum associated with the free carbene and a dimeric (or, less likely, a monomeric) phosphine complex still bearing a neopentyl group. The unusual reductive elimination of neopentyl chloride from **4** under the same conditions is therefore most probably the result of the presence of the ITMe ligand, both bulkier and a better σ donor than the PPh_3 ligand in **5**.

The reluctance of **4** and **5** to eliminate the neopentyl alkylimidazolium salt (Scheme 3) raises an interesting point for discussion. It is known that the reductive elimination of alkylimidazolium salt and precipitation of palladium(0) metal represents one of the potentially serious drawbacks of the application of NHC ligands in catalytic reactions involving alkyl halides as substrates. This deactivation process has been studied by Cavell and co-workers and reported in a series of publications,[17] in which the authors highlighted the fact that cationic palladium(II) species undergo alkyl-carbene reductive elimination at a much higher rate and at lower temperature than the corresponding neutral species. In fact, Pd(ITMe)$_2$(Me)Cl shows slight decomposition only at 120 °C,[18] in line with the lack of alkyl-carbene reductive elimination in **4** and **5**. Similar behavior was displayed by the Pd(I^{t}Bu)$_2$(tolyl)chloride complex previously reported from this laboratory: at high temperature (90 °C) free I^{t}Bu was observed by ^{1}H NMR spectroscopy, but no arylimidazolium salt deriving from reductive elimination was detected.[19]

Further studies were also conducted on the related compound **3** to allow comparison between the two dimeric species **2** and **3**. Indeed, treatment of dimer **3** with IPr, I^{t}Bu, and ITMe (reactions D, E, and F, Scheme 2) highlighted the ability of IPr (and, to a lesser extent, I^{t}Bu) to promote reductive elimination of neopentyl chloride (reactions D and E, Scheme 2). Addition of 5 equiv of IPr to **3** (reaction D, Scheme 2) led to quantitative formation of an intermediate species in 30 min, which was believed to be (IPr)$_2$Pd(neopentyl)chloride on the basis of the ^{1}H NMR spectrum. Subsequent full conversion to the known

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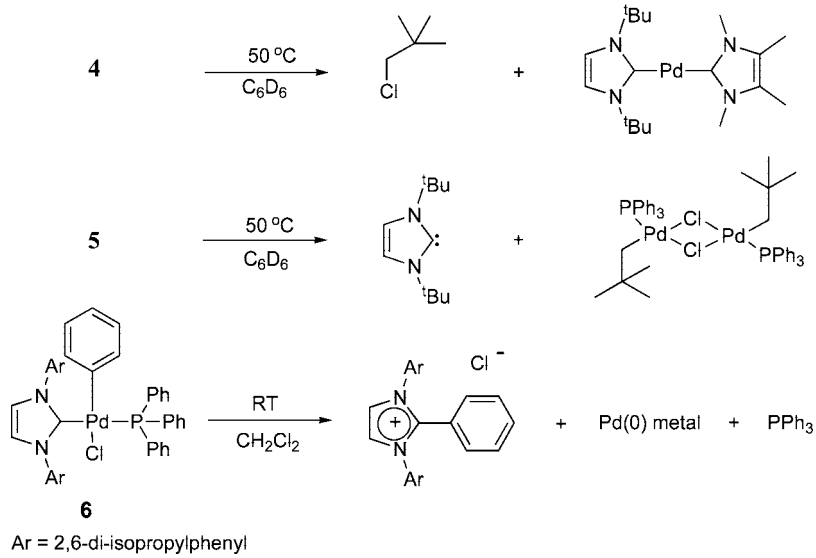
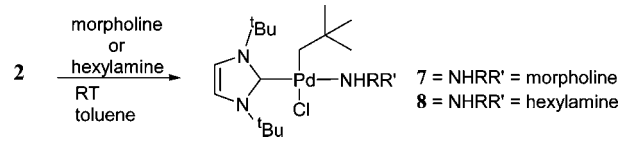
Scheme 3. Stability Evaluation of Complexes 4 and 5



Scheme 4. Preparation of Transamination Products 7 and 8



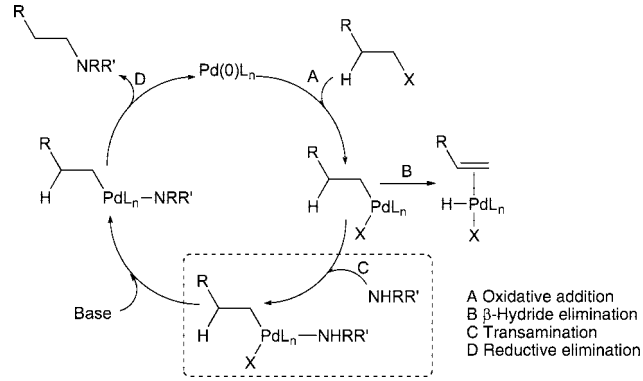
palladium(0) complex, $Pd(IPr)_2$,[20] and neopentyl chloride occurred in 24 h. In contrast, reaction of **3** with I^{t}Bu revealed a more stable (IPr)Pd(I^{t}Bu)(neopentyl)chloride species, which reductively eliminates neopentyl chloride to form (IPr)Pd(I^{t}Bu)[21] in only 3:1 ratio ((IPr)Pd(I^{t}Bu)(neopentyl)chloride:(IPr)Pd(I^{t}Bu)), as shown in reaction E of Scheme 2. Finally, the reaction of **3** with 5 equiv of ITMe (reaction F, Scheme 2) resulted in the displacement of the bulkier IPr to afford, in a 1:1 ratio ($Pd(ITMe)_2$(neopentyl)chloride:(IPr)Pd(ITMe)(neopentyl)chloride), the less sterically hindered $Pd(ITMe)_2$(neopentyl)chloride complex, which was found to be stable toward reductive elimination of neopentyl chloride at RT.

Dimer **2** is also readily cleaved by secondary (morpholine) and primary (hexylamine) amines, affording the [Pd(I^{t}Bu)(amine)(neopentyl)chloride] complexes, **7** and **8** (Scheme 4), respectively, which represent the transamination intermediates in a putative catalytic cycle for a palladium-catalyzed alkyl-amination reaction (Scheme 5).[22] The structure of **7** has been determined and previously communicated.[12]

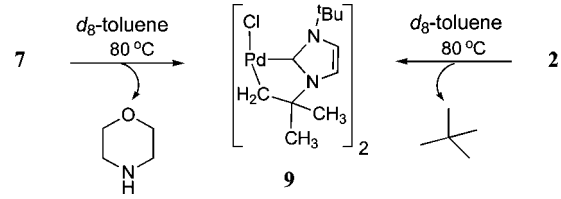
7 and **8** were found to be thermally stable at 50 °C; however when **7** was heated at 80 °C (Scheme 6), dissociation of free amine and formation of the (presumably dimeric) C−H activated product **9** and neopentane were observed by NMR spectroscopy. Complex **2** undergoes a similar C−H activation process, also observed in the reaction of $Pd(I^tBu)_2$ and neopentyl bromide at 75 °C, as previously reported.[12]

Despite the *cis*-geometry between the neopentyl and morpholine groups,[12] attempted deprotonation of the coordinated amines in either **7** or **8** by a variety of bases typically used in aryl-amination cross-coupling reactions (KO^{t}Bu, $NaOCEt_3$, LHMDS, and NaH) failed to yield the palladium amide complex

Scheme 5. Catalytic Cycle for Alkyl-Amine Cross-Coupling Reactions Mediated by Palladium Catalysts



Scheme 6. Surprising Stability of Transamination Product 7



or any alkyl-amine cross-coupling product. A likely explanation for this behavior is that the pK_a of the amine −NH is not significantly lowered to allow deprotonation, due to the increased electron density on Pd arising from the donating effects of the alkyl substituent and the I^{t}Bu ligand. These results indicate that alkyl-amination reactions may be complicated not only by β-hydride elimination but also by the formation of surprisingly stable transamination products.

Despite the stability shown by alkylpalladium complexes **2** and **3**, they were evaluated as potential catalysts for the Buchwald−Hartwig amination reactions. Complexes **2** and **3** were therefore tested in a series of preliminary reactions using different aryl chlorides, and indeed both catalysts afforded the desired cross-coupling products in high conversion even at room temperature (Table 1, entries 1−6). On the basis of these promising reactions, the catalytic system was optimized using chloroanisole and morpholine (Scheme 7). Among the conditions tested, dimer **3** proved to be the most efficient catalyst, allowing the cross-coupling reaction to occur at room temper-

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Scheme 7. Buchwald−Hartwig Amination Reaction Using Complexes 2 and 3

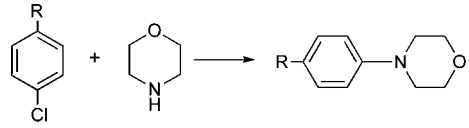
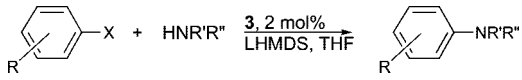


Table 1

entry	R	catalyst (mol %)	solvent	base	temperature (°C)	time (min)	yield (%)
1	COMe	**3** (4.5)	DME	$NaOCEt_3$	RT	1200	85
2	COOMe	**3** (4.5)	toluene	$NaOCEt_3$	50	60	90
3	OMe	**3** (4.5)	benzene	$NaOCEt_3$	80	20	100
4	OMe	**2** (4.5)	benzene	LHMDS	80	40	100
5	OMe	**2** (2.0)	toluene	LHMDS	90	90	34
6	OMe	**2** (2.0)	toluene	KO^tBu	90	90	27
7	OMe	**2** (2.0)	toluene	$NaOCEt_3$	90	90	37
8	OMe	**3** (2.0)	toluene	LHMDS	80	60	97
9	OMe	**3** (2.0)	toluene	LHMDS	80	60	99
10	OMe	**3** (2.0)	THF	LHMDS	RT	60	98
11	OMe	**3** (1.0)	THF	LHMDS	RT	60	84

Scheme 8. Scope of Optimized Buchwald−Hartwig Amination Reactions Using Complex 3



ature in 1 h (Table 1, entry 10). Despite the efficiency displayed by the different bases and solvents tested, the system LHMDS/THF was chosen to continue this study, as it allows a more practical synthetic protocol with no requirement to use a glovebox. In fact, a reaction was carried out outside the glovebox, using a solution of LHMDS in THF and, after 1 h at room temperature, the product was isolated in 84% with a catalyst loading of only 1 mol % (Table 1, entry 11).

Once optimized, the catalytic system was evaluated using several aryl halides and different amines (Scheme 8). Both bromo and chloro aryl compounds are suitable substrates in this protocol, affording the expected arylamines in high yields (Table 2). However, in several examples it was observed that steric effects can result in yield erosion (Table 2, entry 9). Regarding the range of amines used, the cyclic secondary amines displayed unsurpassed reactivity when compared with acyclic amines, which afforded a satisfying yield of cross-coupling products only at 40 °C (Table 2, entries 10 and 11).

Intriguingly, di-*n*-butylamine afforded a rather disappointing 42% yield of product under the standard protocol conditions (Table 2, entry 12), although by replacing the LHMDS base for KO^tBu, a much more efficient cross-coupling reaction was achieved, and 98% of arylated amine was isolated after 1 h at 40 °C (Scheme 9).

A possible explanation for this observation may reside in the steric constraints imposed by the amine volume, thus making deprotonation more difficult; another possibility is that the base may be ligated to the catalytically active species. The latter hypothesis suggests two possible mechanisms for the activation process of the precatalyst **2**. In the first, the activation of the precatalysts, **2** and **3**, proceeds through the mechanism depicted in Scheme 10: the three-coordinate palladium(alkoxide) intermediate reductively eliminates 3-ethyl(neopentyloxy)pentane, concurrently generating in solution the singly ligated, 12-electron Pd^0-I^tBu active catalyst species.

NMR experiments were run to acquire evidence to support the mechanism proposed in Scheme 10. The dimer **2** was reacted with an excess of $NaOCEt_3$ in d_6-benezene at RT, and instantly the color of the solution changed from bright green to deep red. Analysis of the ^1H NMR spectra identified a set of peaks belonging to a $OCEt_3$ moiety, along with another set of peaks assigned to a palladium I^tBu-ligated complex, whose integration gave a 1:1 ratio ($OCEt_3$:I^tBu). However, the absence of the distinctive peaks belonging to 3-ethyl(neopentyloxy)pentane, and the presence of peaks assignable to 2,2,5,5-tetramethylhexane, leads us to suggest the alternative activation mechanism presented in Scheme 11.

Cleavage of the Pd−neopentyl bonds in the intermediate species **20** reductively elimimates 2,2,5,5-tetramethylhexane (observed in the ^1H NMR study, *vide supra*) and affords the alkoxy-bridged dimer **21**. Palladium(I) complexes of this type, but with phosphine ligands and bromide or iodide bridge, have been found to be efficient precatalysts in aryl-amination reactions by Hartwig;[23] hence, there is a possibility that analogous species are involved in the activation of **2**. Ozerov et al. proposed a homolytic cleavage of the Pd−(n-C_8H_{17}) bond in **22** to generate the Pd−Pd bond in the resulting dimeric species, **23** (Scheme 12);[24] the latter theory was supported by the detection of the corresponding alkyl−alkyl product (n-$C_{16}H_{34}$) via GC-MS analysis of the reaction solution.

Similarly, formation and subsequent dimerization of the neopentyl radical via homolysis of the Pd−neopentyl bond in **20** (Scheme 11) would yield 2,2,5,5-tetramethylhexane, which was indeed detected in the reaction solution by ^1H NMR.

In conclusion, several alkylpalladium N-heterocyclic carbene complexes have been synthesized. The chloride-bridged dimers **2** and **3** can be readily cleaved by a variety of nucleophiles, including primary and secondary amines, which results in the isolation of surprisingly stable transamination products. These results highlight the fact that alkyl-amine cross-coupling reactions may be complicated not only by β-hydride elimination but also by the formation of stable transamination product. Complexes **2** and, in particular, **3** were also shown to be effective precatalysts for a series of Buchwald−Hartwig amination reactions of aryl chlorides. Based on ^1H NMR studies, a potential mechanism is proposed for the activation process of the precatalyst **2** in the latter.

Experimental Section

All glassware was oven-dried prior to use. Air-sensitive compounds were manipulated using standard Schlenk line techniques or in an inert atmosphere provided by an MBraun glovebox. Solvents were purified by predrying over sodium wire (except for chloroform), followed by heating at reflux over a suitable drying agent in a solvent still under an atmosphere of dinitrogen. The collected solvent was degassed and stored in an ampule under argon.

NMR solvents were purified by refluxing over a suitable drying agent, then vacuum transferred to an ampule and stored under dinitrogen in a glovebox.

$Pd(COD)Cl_2$,[25] neopentyl lithium,[26] I^tBu, and IPr[2a] were synthesized according to literature procedures. Morpholine and hexylamine (used in the reactions of Scheme 4) were purchased from Aldrich and dried over activated 3 Å molecular sieves, degassed, and vacuum transferred into ampules equipped with greaseless stopcocks. The aryl halides and amines used in the Buchwald−Hartwig amination reactions were distilled prior to use.

Synthesis of [Pd(1,5-COD)(neopentyl)(Cl)], 1. $Pd(COD)Cl_2$ (0.300 g; 1.05 mmol) was suspended in 20 mL of Et_2O and

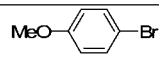
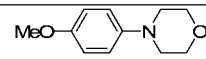
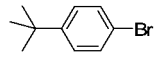
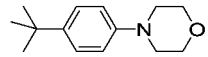
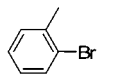
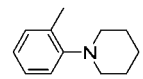
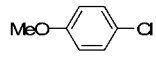
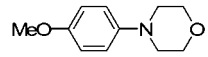
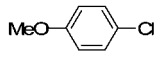
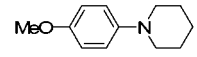
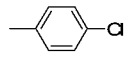
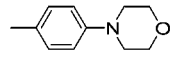
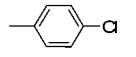
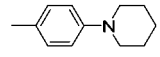
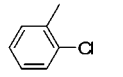
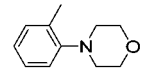
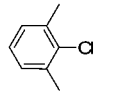
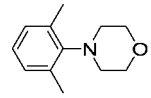
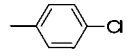
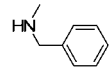
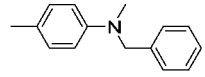
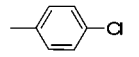
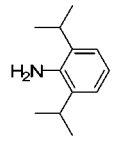
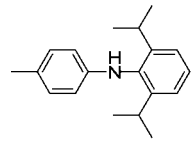
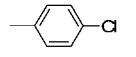
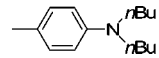
(23) (a) Hoper, M. W.; Utsunomiya, M.; Hartwig, J. F. *J. Org. Chem.* **2003**, *68*, 2861. (b) Hartwig, J. F. *Synlett* **2006**, *9*, 1283.

(24) Fafard, C. M.; Adhikari, D.; Foxman, B. M.; Mindiola, D. J.; Ozerov, O. V. *J. Am. Chem. Soc.* **2007**, *129*, 10318.

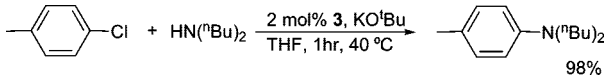
(25) Itoh, K.; Fukui, M.; Ishii, Y. *J. Organomet. Chem.* **1977**, *129*, 259.

(26) Beringer, F. M.; Nathan, R. A. *J. Org. Chem.* **1970**, *35*, 2095.

Table 2. Optimized Buchwald−Hartwig Amination Reactions Using Complex 3

Entry	Ar-X	Amine	Product	Product number	Temperature (°C)	Time (min.)	Yield (%)
1				**10**	RT	60	93
2				**11**	RT	30	95
3				**12**	RT	20	82
4				**10**	RT	60	98
5				**13**	RT	120	99
6				**14**	RT	30	99
7				**15**	RT	30	96
8				**16**	RT	60	92
9				**17**	RT	150	65
10				**18**	40	60	98
11				**19**	40	60	76
12				**20**	40	30	42

Scheme 9. Influence of Base in the Buchwald−Hartwig Amination Reaction.



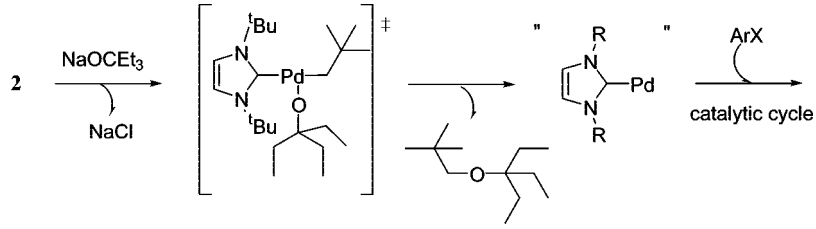
cooled to −75 °C in a acetone/IMS/dry ice bath. A solution of neopentyl lithium (0.090 g; 1 equiv) in 5 mL of Et_2O was added to the cold $Pd(COD)Cl_2$ suspension via cannula in small aliquots every 5 min until fully transferred in about $1^1/_2$ h. The dark reaction mixture was stirred at −75 °C for 1 h and allowed to gradually warm to room temperature and stirred for further 3 h. The reaction mixture was filtered through flamed-dried Celite, and the orange-yellow filtrate dried under vacuum to afford **1** in 48% yield (0.175 g; 0.5 mmol). The product was recrystallized from pentane at −20 °C.

^{1}H NMR (d_1-chloroform): δ 5.89 (q; 2H; $CH_2C\underline{H}{=}C\underline{H}CH_2$, $J_{(H-H)}$ 15 Hz); 5.15 (q; 2H; $CH_2C\underline{H}{=}C\underline{H}CH_2$, $J_{(H-H)}$ 12 Hz); 2.58 (m; 4H); 2.43 (m; 4H); 2.22 (s; 2H); 1.12 (s; 9H). $^{13}C\{^1H\}$ NMR (d_6-benzene): δ 125.1 (CH=CH), 99.9 (CH=CH), 35.8 ($\underline{C}(CH_3)_3$), 33.4 (CH_3), 30.6 (CH_2), 27.0 (CH_2-CH_2). MS (ES): *m*/*z* 285 (M^+ − Cl). Anal. Calcd for $C_{13}H_{23}ClPd$: C: 46.61, H: 7.17. Found: C: 46.50, H: 7.07. Crystal data: see Supporting Information.

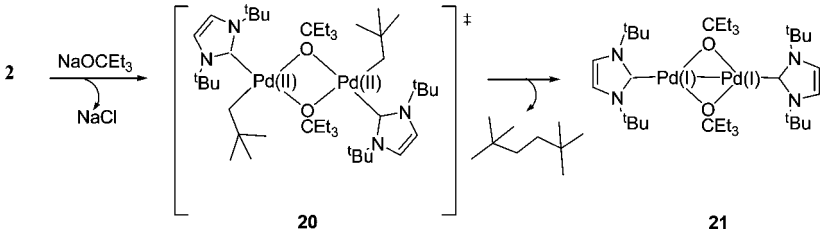
Synthesis of *trans*-[(I^tBu)Pd(neopentyl)(Cl)]$_2$, 2. To a solution of [Pd(1,5-COD)(neopentyl)(Cl)], **1** (0.175 g; 0.5 mmol), in 15 mL of THF cooled to 0 °C was added a solution of I^tBu (0.090 g, 1 equiv) in 5 mL of THF via cannula, and the reaction stirred at 0 °C for 30 min. A very fine gray solid ($I^tBuH^+Cl^-$) precipitated, which was allowed to settle, and the reaction mixture was filtered by cannula to afford a dark orange solution. The solvent was removed under reduced pressure, and the solid residue washed with pentane (2 × 10 mL) and Et_2O (1 × 15 mL) and dried under vacuum, yielding **2** as a white powder. A further batch of product was obtained by concentrating the Et_2O and pentane washings until precipitation was observed; the mixture was left at room temperature for 12 h to achieve complete precipitation of **2**, which was isolated by decantation and dried under vacuum. **2** was obtained in overall 75% yield (0.375 mmol; 0.147 g). Crystals suitable for X-ray diffraction were grown from Et_2O at −20 °C.

^{1}H NMR (d_6-benzene): δ 6.51 (s; 2H); 1.99 (s; 18H); 1.86 (s; 2H); 1.37 (s; 9H). $^{13}C\{^1H\}$ NMR (d_6-benzene): δ 170.4 (Pd−$C_{(carbene)}$); 118.7 (NCH=CHN); 59.2 ($\underline{C}(CH_3)_{(t\text{-Butyl})}$); 34.5 ($\underline{C}(CH_3)_{(neopentyl)}$); 32.8 ($CH_{3(neopentyl)}$); 32.3 ($CH_{3(t\text{-Butyl})}$); 31.0 ($CH_{2(neopentyl)}$). MS (EI): *m*/*z* 502 (M^+ − Cl, $CH_2(CCH_3)_3$ and I^tBu), 465 (M^+ − 2Cl, $CH_2(CCH_3)_3$ and I^tBu), 322 (M^+ − 2Cl,

Scheme 10. Possible Mechanism Proposed for the Activation Process of the Precatalyst 2



Scheme 11. Proposed Mechanism for the Activation Process of the Precatalyst 2.



Scheme 12. Proposed Homolytic Cleavage of the Pd−(n-C_8H_{17}) Bond in 12

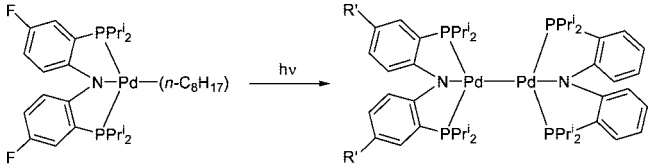


Table 3

solvent	drying agent	stored over
THF	potassium	4 Å molecular sieves
toluene	sodium	potassium mirror
pentane	potassium	potassium mirror
diethyl ether	sodium/potassium alloy	potassium mirror
chloroform	calcium hydride	4 Å molecular sieves

$2CH_2(CCH_3)_3$ and I^{t}Bu). Anal. Calcd for $C_{16}H_{31}N_2ClPd$: C: 48.87, H: 7.89, N: 7.12. Found: C: 48.73, H: 7.78, N: 7.07.

Synthesis of *cis*-[Pd(IPr)(neopentyl)(Cl)]$_2$, 3. The synthesis of **3** was conducted by following the same experimental procedure as that for **2**, with the exception that, following the addition of IPr (0.145 g, 1 equiv), no precipitate was observed. The reaction solution was stirred at RT and the solvent removed under vacuum, affording a yellow oil. Pentane (15 mL) was added and few seconds later a white solid precipitated. The solid was isolated by decanting the solution via cannula, washing the precipitate with cold pentane (3 × 5 mL), and drying under vacuum. The product was obtained as a white-gray powder in 80% yield. Crystals suitable for X-ray diffraction were grown from Et_2O at −20 °C.

^{1}H NMR (d_1-chloroform): δ 7.52 (t; 2H; $J_{(H-H)}$ = 8 Hz); 7.36 (d; 4H; $J_{(H-H)}$ = 16 Hz); 7.13 (s; 2H); 2.66 (septet; 4H; $J_{(H-H)}$ = 12 Hz); 2.29 (s; 2H); 1.44 (d; 12H; $J_{(H-H)}$ = 8 Hz); 1.17 (d; 12H; $J_{(H-H)}$ = 8 Hz); 0.73 (s; 9H). ^{13}C{^{1}H} NMR (d_1-chloroform): δ 187.8 (Pd−$C_{(carbene)}$); 146.5 ($C_{(aryl)}$); 134.6 ($C_{(aryl)}$); 130.7 ($CH_{(aryl)}$); 125.6 ($CH_{(aryl)}$); 124.6 (NCH═CHN); 31.8 ($\underline{C}H(CH_3)_2$); 31.2 ($\underline{C}(CH_3)_3$); 29.0 ($CH(\underline{C}H_3)_2$); 26.6 ($CH(\underline{C}H_3)_2$); 26.1 ($CH_{2(neopentyl)}$); 23.6 ($C(\underline{C}H)_3$). MS (ES): 996 (M^+ − aryl and $CH(CH_3)_2$), 960 (M^+ − aryl, $CH(CH_3)_2$ and Cl), 600 (M^+(monomer)). Anal. Calcd for $C_{32}H_{47}N_2ClPd$: C: 64.12, H: 7.84, N: 4.67. Found: C: 64.25, H: 7.74, N: 4.51.

General Procedure for the Reactions Shown in Scheme 2. 2 or **3** (0.03 mmol) was weighed in a glovebox and placed in a Young's tap NMR tube. Four equivalents of NHC or PPh_3, as indicated in Scheme 3, was added, followed by d_6-benzene (0.6 mL). The reactions were monitored by ^{1}H NMR on a regular basis.

Synthesis of [Pd(I^{t}Bu)(ITMe)(neopentyl)(Cl)], 4. To a mixture of **2** (0.050 g; 0.06 mmol) and ITMe (4 equiv; 0.030 g) was added C_6D_6 (0.6 mL). The ^{1}H NMR, recorded few minute after the starting of the reaction, showed that only the desired product was present in solution. The solution was transferred to a small Schlenck and the solvent removed under vacuum. The resultant white powder was washed with pentane (3 × 1 mL) and dried under vacuum to leave analytically pure **4** in 80% yield.

^{1}H NMR (d_6-benzene): δ 6.73 (s; 2H); 3.82 (s; 6H); 2.07 (s; 18H); 1.76 (s; 6H); 0.96 (s; 9H). ^{13}C{^{1}H} NMR (d_6-benzene): δ 184.7 (Pd−$C_{(carbene)}$); 181.0 (Pd−$C_{(carbene)}$); 124.0 (C═C); 118.1 (CH_2═CH_2); 58.8 ($\underline{C}(CH_3)_{(t\text{-Butyl})}$); 35.4 ($\underline{C}(CH_3)_{3(neopentyl)}$); 34.4 ($CH_{2(neopentyl)}$); 33.6 ($CH_{3(t\text{-Butyl})}$); 32.9 ($CH_{3(neopentyl)}$), 26.4 (N-$CH_3$); 8.8 ($\underline{C}H_3C$═$C\underline{C}H_3$). Anal. Calcd for $C_{23}H_{41}N_4Cl$: C: 53.40, H: 7.93, N:10.83. Found: C; 53.56, H: 8.09, N: 10.77.

Synthesis of [Pd(I^{t}Bu)(PPh$_3$)(neopentyl)(Cl)], 5. THF (15 mL) was added to a mixture of **2** (0.120 g; 0.15 mmol) and triphenylphosphine (4 equiv; 0.160 g) and the yellow reaction solution stirred at room temperature for 2 h, resulting in a color change from yellow to orange. The solvent was removed under vacuum, and the orange residue washed with pentane (3 × 5 mL) and dried under vacuum, to leave analytically pure **5** in 75% yield (0.150 g; 0.23 mmol). Crystals suitable for X-ray analysis were grown from toluene at −20 °C.

^{1}H NMR (d_6-benzene): δ 8.00−7.94 (m; 5H); 7.16−7.03 (m: 10H); 6.67 (s; 2H); 1.96 (s; 18H); 1.52 (s; 2H); 0.73 (s; 9H). ^{31}P{^{1}H} NMR: δ 27.37 ppm. ^{13}C{^{1}H} NMR (d_6-benzene): δ 176.0 (Pd−$C_{(carbene)}$); 135.9 ($CH_{(aryl)}$), 135.7 ($CH_{(aryl)}$), 134.0 ($CH_{(aryl)}$), 133.5 ($CH_{(aryl)}$), 129.7 ($CH_{(aryl)}$), 128.7 ($CH_{(aryl)}$), 128.7 ($C_{(aryl)}$), 128.5 ($C_{(aryl)}$), 119.6 (HC═CH); 59.9 ($\underline{C}(CH_3)_{(t\text{-Butyl})}$); 34.7 ($CH_{3(neopentyl)}$), 33.1 ($CH_{2(neopentyl)}$); 32.8 ($CH_{3(t\text{-Butyl})}$); 32.5 ($CH_{3(neopentyl)}$). MS (ES): m/z 655 (M^+), 399 (M^+ − PPh_3). Crystal data: see Supporting Information.

Synthesis of [Pd(I^{t}Bu)(neopentyl)(amine)chloride] Complexes, 7 and 8. 2 (0.08 g; 0.18 mmol) was dissolved in toluene (10 mL). The amine (morpholine 3.0 equiv, 27.0 μL or hexylamine 3.0 equiv, 38.0 μL) was introduced via syringe, and the reaction solution stirred at room temperature for 1 h. After that time the solvent and the excess amine were removed under reduced pressure. The residue was washed with pentane and the product dried under vacuum to afford, respectively, 84% (0.145 g) and 75% (0.132 g) yields of the palladium-amine adducts **7** and **8**.

7. ^{1}H NMR (d_1-chloroform): δ 7.12 (s; 2H); 3.83 (br d; 2H; $J_{(H-H)}$= 12 Hz); 3.74 (br s; 1H); 3.46 (br q; 4H; $J_{(H-H)}$ = 16 Hz); 2.91 (br d; 2H; $J_{(H-H)}$ = 12 Hz); 2.01 (s; 18H); 1.00 (s; 2H); 0.79 (s; 9H). ^{13}C{^{1}H} NMR (d_1-chloroform): δ 167.5 ($C_{(carbene)}$); 119.4 (NCH═CHN); 77.2 ($CH_{2(morpholine)}$); 68.4 ($\underline{C}(CH_3)_{(t\text{-Butyl})}$); 59.0

($\underline{C}(CH_3)_{3(neopentyl)}$); 48.1 ($CH_{2(morpholine)}$); 34.5 ($CH_{2(neopentyl)}$); 32.4 ($CH_{3(t\text{-}Butyl)}$); 32.1 ($CH_{3(neopentyl)}$). Anal. Calcd for $C_{20}H_{40}N_3OClPd$: C: 50.0, H: 8.33, N: 8.75. Found: C: 49.90, H: 8.24; N: 8.86.

8. ^1H NMR (d_1-chloroform): δ 7.14 (s; 2H); 2.30 (br t; 2H; NH_2; $J_{(H-H)} = 12$ Hz); 1.98 (s; 18H); 1.46 (br q; 2H; $J_{(H-H)} = 8$ Hz); 1.32 (s; 2H); 1.25 (m; 6H); 0.87 (m; 3H); 0.85 (s; 9H). $^{13}C\{^1H\}$ NMR (d_1-chloroform): δ 171.3 ($Pd-C_{(carbene)}$); 119.4 (NCH=CHN); 59.3 ($\underline{C}(CH_3)_{(t\text{-}Butyl)}$); 44.3 ($\underline{C}(CH_3)_{3(neopentyl)}$); 34.8 ($CH_{2(neopentyl)}$); 33.3 ($CH_{3(neopentyl)}$); 32.4 ($CH_{3(t\text{-}Butyl)}$); 31.9 ($CH_2$); 30.9 ($CH_2$); 23.0 ($CH_2$); 14.4 ($CH_3$). MS (ES): m/z 397 (M^+ − hexylamine). Anal. Calcd for $C_{22}H_{44}N_3PdCl$: C: 53.45, H: 8.90, N: 8.50. Found: C: 53.34, H: 9.10, N: 8.66.

General Procedure for the Buchwald−Hartwig Cross-Couplings (Scheme 8, Table 2). In a glovebox, to a round-bottom flask equipped with a magnetic stir bar was added the palladium precatalyst (2 mol %) and the base (0.456 mmol, 1.3 equiv), after which the flask was closed with a septum and taken out off the glovebox. Dry THF (0.5 mL), amine (0.421 mmol, 1.2 equiv), and aryl halide (0.351 mmol) were than sequentially added through the septum. The reaction mixture was then stirred at room temperature unless otherwise indicated. When the reaction reached completion (the disappearance of aryl halide was monitored by TLC), the volatiles were evaporated and the product was purified by flash chromatography on silica gel.

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Supporting Information Available: Details of structure determination for **1** and **5** and NMR data for Buchwald−Hartwig amination products in Table 2. This material is available free of charge via the Internet at http://pubs.acs.org.

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