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Evaluation of catalytic properties of aminocarbene species derived from the integration between 3-iminoisoindolin-1-ones and palladium-bound isonitriles in Suzuki–Miyaura cross-coupling

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ABSTRACT

A series of palladium aminocarbene complexes [PdCl{C(N=C($C_6R^2R^3R^4R^5$CON))=N(H)R^1}(C≡NR^1)] (**9**–**23**, 80–85% isolated yield) were obtained via the metal-mediated integration of one isonitrile in *cis*-[$PdCl_2$(C≡NR^1)$_2$] [R^1 = Cy **1**, *t*-Bu **2**, Xyl **3**, 2-Cl,6-Me-C_6H_3 **4**] and various 3-iminoisoindolin-1-ones [R^2–R^5 = H **5**; R^2, R^4, R^5 = H, R^3 = Me/R^2, R^3, R^5 = H, R^4 = Me **6** (isomeric mixture); R^2, R^5 = H, R^3, R^4 = Cl **7**; R^2–R^5 = F **8**]. New compounds **18**–**23** were completely characterized using (C, H, N), ESI^+–MS, IR, 1D (^{1}H, ^{13}C{^{1}H}) and 2D (^{1}H,^{1}H COSY, ^{1}H,^{13}C HMQC/^{1}H,^{13}C HSQC, ^{1}H,^{13}C HMBC) NMR spectroscopies.

The efficiency of all prepared aminocarbene species **9**–**23** in Suzuki–Miyaura cross-coupling reaction of aryl-bromides and iodides was evaluated, showing that complexes **9**, **14** and **21** manifest the highest activity furnishing the coupling product in 81–99% yield, and giving maximum turnover numbers (TONs) up to 7.6×10^4. Catalytic system employs non-dried EtOH as an environmentally benign solvent, K_2CO_3 as a base, and runs under air.

1. Introduction

Development of efficient cross-coupling catalytic systems depends predominantly upon design of appropriate metal catalysts and corresponding ligands [1,2]. At this point, the emergence of *N*-heterocyclic carbenes (*heterocylic* aminocarbenes, NHCs) as ancillary ligands in the place of commonly used phosphines, allows for better thermal and chemical stability of the catalysts, reduce the sensitivity of the system to air and humidity, preserving high catalytic activity [3–13]. Despite a widespread application of NHCs, a major disadvantage of these compounds regards their preparation, in particular, rather challenging synthesis of unsymmetrically substituted or chiral carbenes [14,15]. Furthermore, taking into account that the fine-tuning of the prepared metal–carbenes toward selected catalytic application is mostly achieved via the empiric variation of carbene structure, that, consequently, leads to a vast amplification of the synthetic protocol towards modified NHCs, the search for the alternative catalytic systems is being of high importance.

Acyclic aminocarbenes resemble *N-heterocyclic* species in terms of net electron-donor properties and steric flexibility [16], being, however, much less explored as catalysts. Complexes with acyclic aminocarbene ligands can be generated *via* an atom-efficient and modular protocol based on a stoichiometric nucleophilic addition to metal-bound isonitriles (Scheme 1) [16,17]. The vast majority of reported examples of the latter reaction concern the coupling of M-CNR species with amines/hydrazines (sp^3-N type nucleophiles) leading to complexes with acyclic diaminocarbene ligands (M-ADCs) [16]. Only recently, we have reported on first examples of the coupling between various imines (sp^2-N type nucleophile), such as benzophenone imine [18], 3-iminoisoindolin-1-one [19], or *N*-phenylbenzamidine [20], and metal-bound isonitriles, affording complexes containing novel types of aminocarbene ligands. For instance, when 3-iminoisoindolin-1-one (a stable heterocyclic imine) was used as a nucleophile, the formation of rare *chelating* acyclic aminocarbene species was observed (Scheme 2) [19]. Obtained compounds exhibit a superior chemical (towards air and humidity) and thermal (in a 20–120 °C range) stability as compared to the corresponding monodentate aminocarbenes [19], thus, being of potential interest for the catalytic applications.

Following our ongoing project on development of novel mild and efficient cross-coupling catalytic systems employing metal catalysts of novel types [20,21], we aimed to expand the series of palladium aminocarbene complexes by use of other

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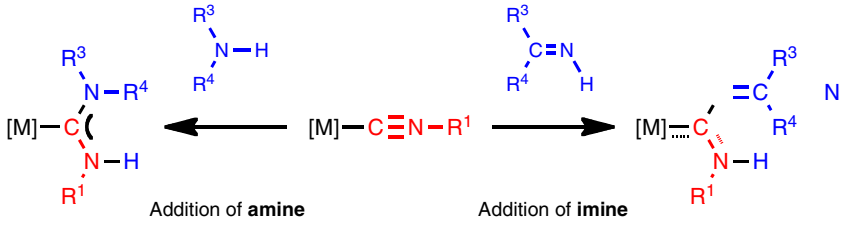


Scheme 1. Generation of M-ADC species via the addition of nucleophiles to metal-bound isonitriles.

3-iminoisoindolin-1-ones and isonitriles, and, to evaluate the catalytic efficiency of the thus prepared palladium–aminocarbenes in Suzuki–Miyaura coupling. The results of our studies are disclosed below.

2. Experimental

2.1. Materials and instrumentation

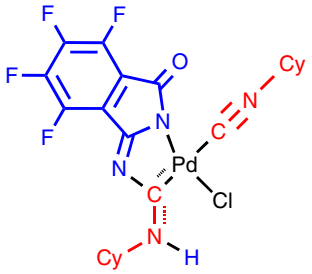
All solvents, $PdCl_2$, and all isonitriles were obtained from commercial sources and used as received apart from chloroform that was purified by conventional distillation over calcium chloride. The starting palladium-isonitrile complexes *cis*-[$PdCl_2(C{\equiv}NR^1)_2$] [R^1 = Cy **1**, *t*-Bu **2**, Xyl **3**, 2-Cl,6-Me-C_6H_3 **4**] [22–26] and various 3-iminoisoindolin-1-ones [R^2–R^5 = H **5**; R^2, R^4, R^5 = H, R^3 = Me/R^2, R^3, R^5 = H, R^4 = Me **6** (isomeric mixture); R^2, R^5 = H, R^3, R^4 = Cl **7**; R^2–R^5 = F **8**] [27], were prepared in accord with the published procedures. Known aminocarbene complexes **9**–**17** (Scheme 2) derived from the integration of **1**–**3** with 3-iminoisoindolin-1-ones **5**–**7**, were prepared as previously reported [19].

2.2. Preparation and analytical data for the palladium–aminocarbene complexes

2.2.1. Preparation of complexes ***18–23***

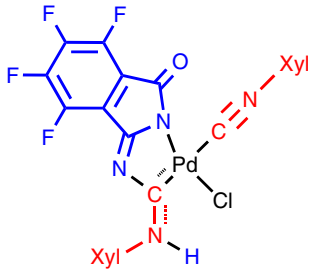
A slightly modified known procedure was employed [19]. Thus, a finely ground solid 3-iminoisoindolin-1-one (**5**–**8**) (0.1 mmol) was added to a solution of *cis*-[$PdCl_2(C{\equiv}NR^1)_2$] (0.1 mmol) in $CHCl_3$ (10 mL), and the resulting mixture was further refluxed for 4 h. After 4 h, the reaction mixture was filtered, and the filtrate was evaporated to dryness under a stream of nitrogen at room temperature, and washed with five 1-mL portions of cold (5 °C) Et_2O, and dried *in vacuo* at 20–25 °C. Yields of **18**–**23** were 80–85%.

2.2.2. [PdCl{C(N=C(C_6F_4CON))=N(H)Cy}(C≡NCy)] (***18***)



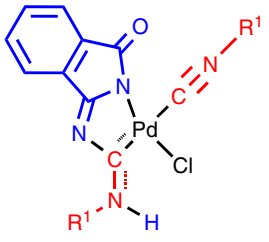
Anal. Calc. for $C_{22}H_{23}N_4ClF_4OPd$: C, 45.77; H, 4.02; N, 9.70. Found: C, 45.82; H, 4.00; N, 9.65%. ESI^+–MS, *m/z*: 595 $[M+H_3O]^+$. IR (KBr, selected bands, cm^{-1}): 3245 w *ν*(N–H); 2933 m, 2858 w *ν*(C–H); 2229 s *ν*(C≡N); 1723 s, 1601 m *ν*(C=O) + *ν*(C=N); 1553 s *ν*($C_{carbene}$=N); 730 s *δ*(C–H from aryls). ^1H NMR ($CDCl_3$, *δ*): 10.56 (s, br, 1H, NH), 4.50 (m, br, 1H, *H*CCy), 3.91 (m, br, 1H, *H*CCy), 1.94–1.79 and 1.47–1.44 (m, 20H, Cy). $^{13}C\{^1H\}$ NMR ($CDCl_3$, *δ*): 197.4 ($C_{carbene}$=N), 167.2 (C=O), 161.5 (C=N), 144.9, 143.9, and 141.3 (C–F aryls), 117.8, 116.1, (aryls), 56.0 and 53.9 (*H*CCy), 32.3, 31.9, 31.7, 24.7, 24.6, and 24.1 (H_2C–Cy).

2.2.3. [PdCl{C(N=C(C_6F_4CON))=N(H)Xyl}(C≡NXyl)] (***19***)



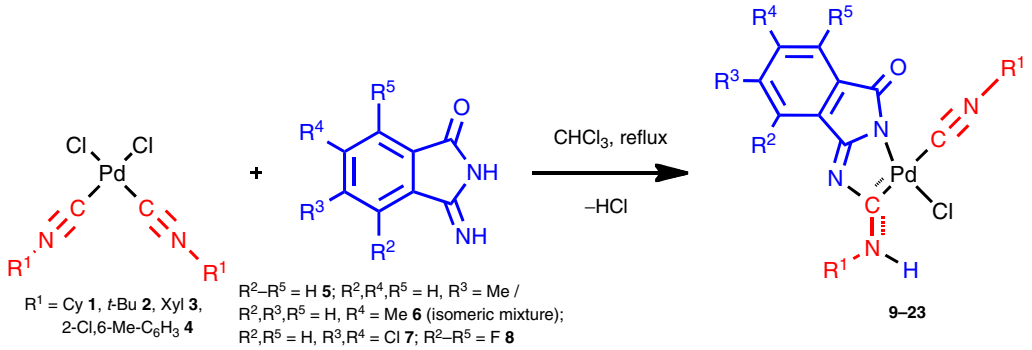
Anal. Calc. for $C_{26}H_{19}N_4ClF_4OPd$: C, 50.26; H, 3.08; N, 9.02. Found: C, 50.13; H, 3.12; N, 9.00%. ESI^+–MS, *m/z*: 620 $[M]^+$. IR (KBr, selected bands, cm^{-1}): 3246 m *ν*(N–H); 2931 s, 2857 m *ν*(C–H); 2229 s *ν*(C≡N); 1725 s, 1721 m, 1680 mw *ν*(C=O) + *ν*(C=N); 1554 vs *ν*($C_{carbene}$=N); 730 s *δ*(C–H from aryls). ^1H NMR ($CDCl_3$, *δ*): 10.38 (s, br, 1H, NH), 7.34–7.13 (m, 6H, aryls) 2.56, 2.49 and 2.28 (s, 12H, Me). $^{13}C\{^1H\}$ NMR ($CDCl_3$, *δ*): 200.0 ($C_{carbene}$=N), 181.3 (C=O), 167.2 (C=N), 136.6, 136.5, 136.3, and 135.2 (C–F aryls), 133.6, 131.0, 130.7, 130.1, 128.6, 128.4, 128.2, and 128.0 (aryls), 18.9 and 18.7 (Me).

2.2.4. [PdCl{C(N=C(C_6H_4CON))=N(H)(2-Cl,6-Me-C_6H_3)}(C≡N(2-Cl,6-Me-C_6H_3))] (***20***)



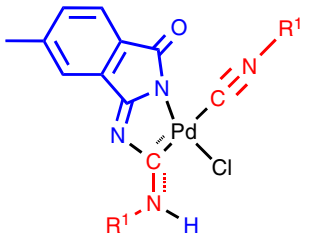
R^1 = 2-Cl,6-Me-C_6H_3

Anal. Calc. for $C_{24}H_{17}N_4Cl_3OPd$: C, 48.84; H, 2.90; N, 9.49. Found: C, 48.74; H, 2.82; N, 9.52%. ESI^+–MS, *m/z*: 553 $[M-Cl]^+$. IR (KBr, selected bands, cm^{-1}): 3201 mw *ν*(N–H); 2966 mw, 2926 mw *ν*(C–H); 2199 s *ν*(C≡N); 1735 s, 1673 s, 1607 s *ν*(C=O) + *ν*(C=N); 1522 vs *ν*($C_{carbene}$=N); 711 s *δ*(C–H from aryls). ^1H NMR ($CDCl_3$, *δ*): 10.27 (s, br, 1H, NH), 7.77 and 7.70 (m, 4H) (aryls from the isoindoline moiety), 7.60–7.48 (m, 6H, aryls), 2.59 and 2.32 (s, 6H, Me). $^{13}C\{^1H\}$ NMR ($CDCl_3$, *δ*): 202.5 ($C_{carbene}$=N), 188.6 (C=O), 173.6 (C=N), 139.5, 138.8, 136.9, 135.5, 134.4, 133.9, 132.3, 131.9, 130.8, 130.6, 129.3, 129.1, 128.8, 127.7, 127.3, and 124.4 (aryls), 22.9 and 19.3 (Me).



Scheme 2. Reaction of 3-iminoisoindolin-1-ones (**5**–**8**) with an isonitrile in *cis*-[$PdCl_2(C{\equiv}NR^1)_2$] (**1**–**4**) affording palladium–aminocarbene complexes (**9**–**23**).

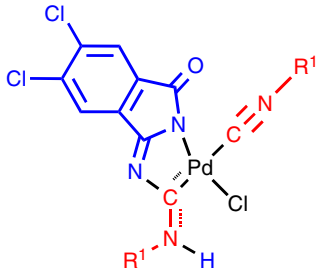
*2.2.5. [PdCl{C(N=C(C$_6$H$_3$(4-Me)CON))=N(H)(2-Cl,6-Me-C$_6$H$_3$)}(C≡N-(2-Cl,6-Me-C$_6$H$_3$))] (**21**)*



R^1 = 2-Cl,6-Me-C$_6$H$_3$

Anal. Calc. for $C_{25}H_{19}N_4Cl_3OPd$: C, 49.69; H, 3.17; N, 9.27. Found: C, 49.72; H, 3.02; N, 9.26%. ESI$^+$–MS, *m/z*: 569 [M−Cl]$^+$. IR (KBr, selected bands, cm^{-1}): 3233 mw *ν*(N–H); 2968 mw, 2922 mw *ν*(C–H); 2197 s *ν*(C≡N); 1751 s, 1720 s, 1674 s *ν*(C=O) + *ν*(C=N); 1521 vs *ν*($C_{carbene}$=N); 734 s *δ*(C–H from aryls). ^{1}H NMR ($CDCl_3$, *δ*): 10.23 (s, br, 1H, NH), 7.87–7.37 (m, 9H, aryls), 2.64 (Me from isoindoline moiety), 2.59, 2.32 (s, 9H, Me). $^{13}C\{^1H\}$ NMR ($CDCl_3$, *δ*): 202.4 ($C_{carbene}$=N), 188.7 (C=O), 173.5 (C=N), 144.9, 143.4, 139.5, 138.7, 136.8, 134.9, 134.0, 132.8, 131.8, 131.5, 130.7, 129.3, 129.1, 128.8, 127.7, 127.5, 127.4, and 127.3 (aryls), 22.9 (Me from isoindoline moiety), 21.7 and 19.4 (Me).

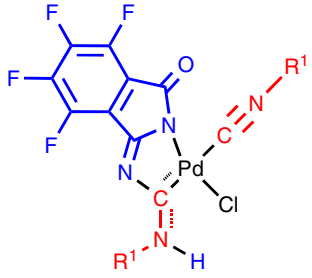
*2.2.6. [PdCl{C(N=C(C$_6$H$_2$(3,4-Cl$_2$)CON))=N(H)(2-Cl,6-Me-C$_6$H$_3$)}-(C≡N(2-Cl,6-Me-C$_6$H$_3$))] (**22**)*



R^1 = 2-Cl,6-Me-C$_6$H$_3$

Anal. Calc. for $C_{24}H_{15}N_4Cl_5OPd$: C, 43.64; H, 2.29; N, 8.50. Found: C, 43.34; H, 2.19; N, 8.28%. ESI$^+$–MS, *m/z*: 659 [M+H]$^+$. IR (KBr, selected bands, cm^{-1}): 3199 w *ν*(N–H); 2965 w, 2924 w *ν*(C–H); 2196 s *ν*(C≡N); 1775 m, 1721 m, 1686 m *ν*(C=O) + *ν*(C=N); 1527 vs *ν*($C_{carbene}$=N); 730 s *δ*(C–H from aryls). ^{1}H NMR ($CDCl_3$, *δ*): 10.35 (s, br, 1H, NH), 8.04, 7.96 (s, 2H, aryls from isoindoline moiety), 7.38–7.26 (m, 6H, aryls) 2.65 and 2.33 (s, 6H, Me). $^{13}C\{^1H\}$ NMR ($CDCl_3$, *δ*): 202.3 ($C_{carbene}$=N), 186.3 (C=O), 171.2 (C=N), 138.8, 138.3, 136.8, 136.6, 134.8 (aryls), 133.8, 133.1 (CH aryls from isoindoline moiety), 131.8, 130.9, 130.6, 129.3, 129.1, 128.8, 127.6, 127.4, and 126.0 (aryls), 19.3 and 19.1 (Me).

*2.2.7. [PdCl{C(N=C(C$_6$F$_4$CON))=N(H)(2-Cl,6-Me-C$_6$H$_3$)}(C≡N(2-Cl,6-Me-C$_6$H$_3$))] (**23**)*



R^1 = 2-Cl,6-Me-C$_6$H$_3$

Anal. Calc. for $C_{24}H_{13}N_4Cl_3F_4OPd$: C, 43.53; H, 1.98; N, 8.46. Found: C, 43.73; H, 1.89; N, 8.36%. ESI$^+$–MS, *m/z*: 626 [M−Cl+H]$^+$. IR (KBr, selected bands, cm^{-1}): 3200 mw *ν*(N–H); 3065 w, 2972 w *ν*(C–H); 2196 s *ν*(C≡N); 1730 s *ν*(C=O) + *ν*(C=N); 1533 s *ν*($C_{carbene}$=N); 741 s *δ*(C–H from aryls). ^{1}H NMR ($CDCl_3$, *δ*): 10.43 (s, br, 1H, NH), 7.38–7.23 (m, 6H, aryls) 2.62 and 2.30 (s, 6H, Me). $^{13}C\{^1H\}$ NMR ($CDCl_3$, *δ*): 201.5 ($C_{carbene}$=N), 182.4 (C=O), 167.1 (C=N), 139.5, 138.7, and 136.4 (C–F aryls), 133.4, 131.9, 131.8, 131.6, 130.9, 130.2, 129.6, 129.3, 129.1, 128.9, 127.7, 127.6, and 127.3 (aryls), 22.8 and 19.4 (Me).

2.3. General procedure for the Suzuki–Miyaura coupling

Selected base (2.0×10^{-4} mol, 1.5 equiv), aryl bromide (1.0×10^{-4} mol, 1.0 equiv) and phenylboronic acid (1.2×10^{-4} mol, 1.2 equiv) were mixed in a 5-mL round-bottom tube. Consequently, a solution of the precatalyst (1×10^{-8} mol) in non-dried EtOH (2 mL) was added, and the tube was closed with a septum and an aluminum crimp seal. The tube was placed in a preheated oil bath at 80 °C, stirred for 2.5 h, and then cooled down to 25 °C. The reaction mixture was evaporated to dryness under a stream of dinitrogen followed by addition of 1.0 equiv of 1,2-dimethoxyethane (NMR internal standard), and extraction of the reaction mixture with three 0.20-mL portions of $CDCl_3$. All fractions were combined and subjected to ^{1}H NMR monitoring. The product peak assignments were based on authentic samples or on the published data [28–31], while quantifications were performed upon integration of the selected peak of the product relatively to the peak of the standard. In some cases, the products were isolated by extraction of the residue after evaporation of the reaction mixture with

CH_2Cl_2, followed by column chromatography on silica gel (Fluka 40/60; 10:1 hexane/ethyl acetate, v/v).

3. Results and discussion

3.1. Synthesis and characterization of palladium–aminocarbene complexes

Synthesis of new (**18**–**23**) and known (**9**–**17**) palladium–aminocarbene complexes was accomplished under previously described experimental conditions [19]. Thus, the reaction between a palladium-bound isonitrile in *cis*-[$PdCl_2(C{\equiv}NR^1)_2$] (**1**, **3**, and **4**) and the 3-iminoisoindolin-1-ones (**5**–**8**) proceeds smoothly under reflux in $CHCl_3$ for 4 h (Scheme 2). Subsequent workup provides the carbene species [$PdCl\{\underline{C}(N{=}C(C_6R^2R^3R^4R^5CO\underline{N})){=}N(H)R^1\}(C{\equiv}NR^1)$] (**9**–**23**) in 80–85% isolated yields (Scheme 2, Table 1). The reaction between *cis*-[$PdCl_2(C{\equiv}N(t\text{-}Bu))_2$] (**2**) and **8** did not afford any isolable aminocarbene species. The authenticity of known species **9**–**17** was established upon comparison of the recorded ^1H NMR spectra with those previously reported by one of us [19], while new complexes **18**–**23** were completely characterized using (C, H, N), ESI^+–MS, IR, 1D (^1H, $^{13}C\{^1H\}$) and 2D (^1H,^1H COSY, ^1H,^{13}C HMQC/^1H,^{13}C HSQC, ^1H,^{13}C HMBC) NMR spectroscopies.

Complexes **18**–**23** gave C, H, and N elemental analyses consistent with the proposed formulations of the palladium–aminocarbene complexes [$PdCl\{\underline{C}(N{=}C(C_6R^2R^3R^4R^5CO\underline{N})){=}N(H)R^1\}(C{\equiv}NR^1)$], whereas the ESI^+–MS mass spectra display molecular ion peaks and/or a fragmentation corresponding to the loss of Cl's, *viz.* $[M{-}nCl]^+$ or the protonation $[M{+}H_3O]^+$ of the molecular ion. The IR spectra of **18**–**23** exhibit one strong $\nu(C{\equiv}N)$ stretching vibration in the range between 2196 and 2230 cm^{-1} suggesting the presence of one unreacted isonitrile ligand in **18**–**23**, while in the starting *cis*-[$PdCl_2(C{\equiv}NR)_2$] (**1**–**4**) complexes two overlapped stretches in the interval 2150–2250 cm^{-1} are normally detected [23]. In the C=N(H)R carbene moiety, very strong bands due to $\nu(C_{carbene}{=}N)$ appear in the range between 1521 and 1554 cm^{-1} as in the previously reported Pd-ADC species [19,21,22], while corresponding bands due to overlapped $\nu(C{=}O)$ and $\nu(C{=}N)$ vibrations from the iminoisoindolin-1-one moiety are found between 1624 and 1730 cm^{-1} [19,27].

The ^1H NMR spectra of the carbene complexes **18**–**23** display a broad peak in the range of δ 9.03–10.44 assigned to the M–$C_{carbene}{=}N(H)R$ proton, while the corresponding signal of the $C_{carbene}{=}NH$ carbon in the $^{13}C\{^1H\}$ spectra was found to resonate at *ca.* 200 ppm, *i.e.* approximately 80 ppm to lower field in comparison with the starting (isonitrile)M^{II} complexes (*e.g.* 115 ppm for C≡N in *cis*-[$PdCl_2(C{\equiv}NCy)_2$]). Complete ^1H and ^{13}C signal assignments were performed by interpretation of the gradient enhanced two-dimensional ^1H,^{13}C HMQC/^1H,^{13}C HSQC and ^1H,^{13}C HMBC NMR spectra.

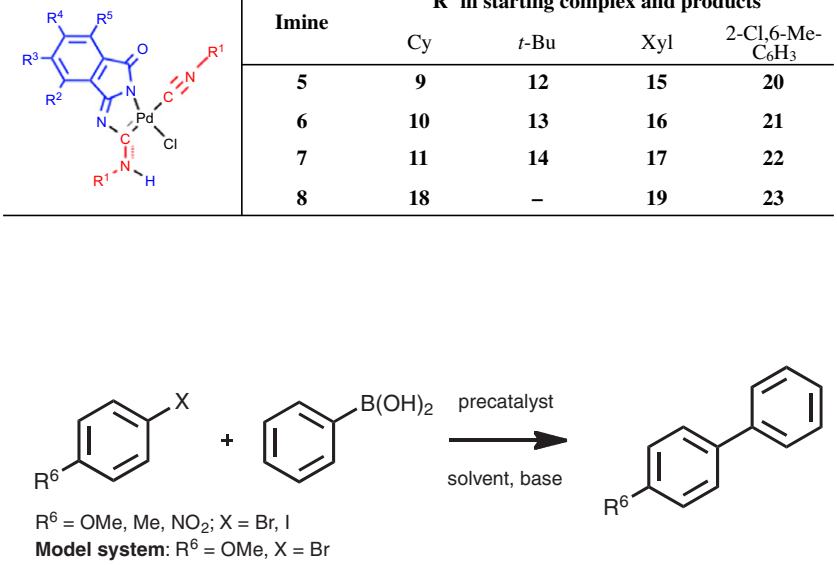
3.2. Catalytic studies

As a model system for the Suzuki–Miyaura coupling, we have chosen the commonly used reaction of 4-methoxy-bromobenzene (4-bromoanisole) with phenylboronic acid accomplishing 4-methoxybiphenyl (Scheme 3). Taking into account our preliminary data on optimization of the reaction conditions (performed for other Pd-aminocarbene species) [21], we opt to use ethanol as an environmentally benign solvent for our catalytic runs. In refluxing EtOH, the conversion of 4-bromoanisole is essentially complete after ca. 2.5 h, furnishing the target 4-methoxy-1,1'-biphenyl in ca. 84–92% yield (for precatalyst **9**). No visible catalyst decomposition (*i.e.* formation of the palladium black) was observed under these conditions.

It is known, that a type of base employed directly influences the catalyst activity in Suzuki–Miyaura cross-coupling reactions. Thus, different types of bases were screened and the results are summarized in Table 2. As can be inferred from an inspection of the obtained results, K_2CO_3 (Table 2, 92%, entry 4) is the most appropriate base for this catalytic system, while when K_3PO_4 (74%, entry 3) and Cs_2CO_3 (74%, entry 5) are applied, the yields are significantly decreased; KOH (13%, entry 2) and Et_3N (4%, entry 1) were not efficient. For further studies, K_2CO_3 has been chosen.

Table 1
Numbering of prepared palladium–aminocarbenes species.

Imine	R^1 in starting complex and products			
	Cy	*t*-Bu	Xyl	2-Cl,6-Me-C_6H_3
5	**9**	**12**	**15**	**20**
6	**10**	**13**	**16**	**21**
7	**11**	**14**	**17**	**22**
8	**18**	–	**19**	**23**



Scheme 3. Suzuki–Miyaura cross-coupling system employing 9–23 as precatalysts.

Table 2
Screening for an appropriate base for the model Suzuki–Miayura coupling system.

Entry	Base	Yield (%)
1	NEt_3	4
2	KOH	13
3	K_3PO_4	74
4	K_2CO_3	92
5	Cs_2CO_3	74

Base (2.0×10^{-4} mol, 2.0 equiv), 4-bromoanisole (1.0×10^{-4} mol, 1.0 equiv), phenylboronic acid (1.2×10^{-4} mol, 1.2 equiv); precatalyst **9** (1×10^{-8} mol); EtOH (2 ml).

Table 3
Screening of the catalytic efficiency for **9**–**23** in Suzuki–Miayura cross-coupling system.

Entry	Precatalyst	Yield (%)	Entry	Precatalyst	Yield (%)
1	**9**	92	9	**16**	63
2	**10**	75	10	**17**	58
3	**11**	73	11	**19**	52
4	**18**	46	12	**20**	62
5	**12**	73	13	**21**	81
6	**13**	64	14	**22**	77
7	**14**	86	15	**23**	60
8	**15**	54	16	–	4

4-Bromoanisole (1.0×10^{-4} mol, 1 equiv), phenylboronic acid (1.2×10^{-4} mol, 1.2 equiv), K_2CO_3 (2.0×10^{-4} mol, 2.0 equiv); selected precatalysts (1×10^{-8} mol); EtOH (2 ml).

The comparison of the catalytic activity for all prepared Pd-aminocarbene complexes **9**–**23** in the model Suzuki–Miyaura cross-coupling system was undertaken, and the results are summarized in Table 3. Thus, among all palladium species, complexes **9**, **14** and **21** manifest the highest activity furnishing the coupling product in 81–92% yield.

For the most efficient precatalysts **9**, **14** and **21**, we have verified the functional group tolerance – scope of the catalytic process. It was found that the various organobromides 4-$R^6C_6H_4Br$ bearing either electron-donor (R^6 = Me, OMe) or electron-withdrawing (NO_2) groups and organoiodide 4-$MeOC_6H_4I$, react with phenylboronic acid to give excellent yields of biphenyl species (Table 4), thus showing a valuable versatility of our catalytic system.

In order to estimate the catalytic efficiency, we also examined the effect of catalyst loading in the model catalytic system (Table 5). Yields up to 76%, and the TONs up to 7.6×10^4, were obtained with the catalyst loadings as low as 10^{-5} mol per mole of substrate. Moreover, we also evaluated the air/moisture stability of the catalytic system by performing some additional runs in dried EtOH and under dinitrogen, and observed no significant difference with those performed under air and in non-dried ethanol.

It is worth mentioning that understudied system is being highly efficient and green in a comparison with the other based on acyclic aminocarbenes [29–31]. Thus, we employ environmentally benign solvent (EtOH) in a place of toxic THF or toluene traditionally used for Suzuki–Miyaura coupling, as well as a cheap inorganic base (K_2CO_3). Our system also demonstrates high tolerance to air and humidity and requires low catalyst loading (less than 1×10^{-2} mol% of catalyst).

Table 4
Evaluation of the scope of the catalytic system with the selected precatalysts.

Entries	Aryl halide	Yields with the selected precatalyst (%)		
		9	**14**	**21**
1–3	4-$MeOC_6H_4Br$	92	86	81
4–6	4-MeC_6H_4Br	86	83	94
7–9	4-$NO_2C_6H_4Br$	91	98	95
10–12	4-$MeOC_6H_4I$	98	99	99

Aryl halide (1.0×10^{-4} mol, 1 equiv), phenylboronic acid (1.2×10^{-4} mol, 1.2 equiv), K_2CO_3 (2.0×10^{-4} mol, 2.0 equiv); selected precatalysts (1×10^{-8} mol); EtOH (2 ml).

Table 5
Effect of catalyst loading (for **9**, **14**, and **21**) in the Suzuki–Miayura cross-coupling system.

Entry	Precatalyst	Yield (%)
1	–	4
2	**9**	76
3	**14**	74
4	**21**	53

4-Bromoanisole (1.0×10^{-4} mol, 1.0 equiv), phenylboronic acid (1.2×10^{-4} mol, 1.2 equiv), K_2CO_3 (2.0×10^{-4} mol, 2.0 equiv); selected precatalyst (1×10^{-9} mol); EtOH (2 ml).

4. Final remarks

Within our studies we have widen the series of palladium–aminocarbene species derived from the metal-mediated integration between *cis*-[$PdCl_2$(C≡NR^1)] and 3-iminoisoindolin-1-one to twenty-four species, employing, among others, 2,3,4,5-tetrafluoro-3-iminoisoindolin-1-one and 2-chloro,6-methyl-phenylisonitrile as the previously unused coupling partners.

Prepared aminocarbene derivatives were evaluated as catalysts in Suzuki–Miyaura cross-coupling of aryl- bromides and iodides with phenylboronic acids, and we found that, catalytic systems based on **9**, **14**, and **21** exhibit highest efficiency in terms of yields/TONs (yields up to 91%, TONs up to 7.6×10^4 with 4-$MeOC_6H_4Br$ as a substrate) and run in non-dried EtOH as an environmentally safe solvent and under air. The reasons for the superior catalytic activity of **9**, **14**, and **21** as compared to other aminocarbene complexes from this study are not clear, and, in our opinion, can be justified by the achieved optimal balance between a sterical hindrance and an electronic distribution within the carbene species. Despite the fact that the conversion of aryl chlorides was not accomplished with the prepared precatalysts (see, for instance, examples for the transformation of those challenging substrates employing M-NHCs [2,9]), our catalytic scheme is being one of the mildest and most efficient Suzuki–Miyaura systems for transformation of aryl bromides based on acyclic aminocarbenes.

Further studies towards a development of efficient and green catalytic systems based on the novel types of carbene complexes, are currently under way in our group.

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References

[1] K. Sonogashira, Metal-catalyzed cross-coupling reactions, in: P.J.D. Stang, F. Diederich (Eds.), Metal-Catalyzed Cross-Coupling Reactions, Wiley, Weinheim, 1998, pp. 203–229.
[2] S.P. Nolan, O. Navarro, C–C bond formation by cross-coupling, in: A. Canty (Ed.), Comprehensive Organometallic Chemistry III, Elsevier, Oxford, 2007, pp. 1–38. and references therein.
[3] F. Glorius, Top. Organomet. Chem. 21 (2007) 1.
[4] K.S. Denk, P. Sirsch, W.A. Herrmann, J. Organomet. Chem. 649 (2002) 219.
[5] S. Díez-González, N. Marion, S.P. Nolan, Chem. Rev. 109 (2009) 3612.
[6] P. Arnold, S. Pearson, Coord. Chem. Rev. 251 (2007) 596.
[7] F.E. Hahn, M.C. Jahnke, Angew. Chem., Int. Ed. Engl. 47 (2008) 3122.
[8] S.T. Liddle, I.S. Edworthy, P.L. Arnold, Chem. Soc. Rev. 36 (2007) 1732.
[9] N. Marion, S.P. Nolan, Acc. Chem. Res. 41 (2008) 1440.
[10] F.E. Hahn, V. Langenhahn, T. Lügger, W.P. Fehlhammer, Chem.-Eur. J. 9 (2003) 704.
[11] F.E. Hahn, V. Langenhahn, T. Lügger, T. Pape, D.L. Van, Angew. Chem., Int. Ed. (2005) 3759.
[12] F.E. Hahn, V. Langenhahn, T. Pape, Chem. Commun. (2005) 5390.
[13] F.E. Hahn, C.G. Plumed, M. Münder, T. Lügger, Chem.-Eur. J. 10 (2004) 6285.
[14] A. Fürstner, M. Alcarazo, V. César, C.W. Lehmann, Chem. Commun. (2006) 2176.
[15] V. Cesar, S. Bellemin-Laponnaz, L.H. Gade, Chem. Soc. Rev. 33 (2004) 619.
[16] J. Vignolle, X. Catton, D. Bourissou, Chem. Rev. 109 (2009) 3333.
[17] R.A. Michelin, A.J.L. Pombeiro, M.F.C. Guedes da Silva, Coord. Chem. Rev. 218 (2001) 75.
[18] K.V. Luzyanin, M.F.C. Guedes da Silva, V.Yu. Kukushkin, A.J.L. Pombeiro, Inorg. Chim. Acta 362 (2009) 833.
[19] K.V. Luzyanin, A.J.L. Pombeiro, M. Haukka, V.Yu. Kukushkin, Organometallics 27 (2008) 5379.
[20] A.G. Tskhovrebov, K.V. Luzyanin, M.L. Kuznetsov, V.N. Sorokoumov, I.A. Balova, M. Haukka, V.Yu. Kukushkin, Organometallics 30 (2011) 863.
[21] K.V. Luzyanin, A.G. Tskhovrebov, M.C. Carias, M.F.C. Guedes da Silva, A.J.L. Pombeiro, V.Yu. Kukushkin, Organometallics 28 (2009) 6559.
[22] R.A. Michelin, L. Zanotto, D. Braga, P. Sabatino, R.J. Angelici, Inorg. Chem. 27 (1988) 85.
[23] F.M. Bonati, G. Minghetti, J. Organomet. Chem. 24 (1970) 251.
[24] B. Crociani, T. Boschi, U. Belluco, Inorg. Chem. 9 (1970) 2021–2025.
[25] R. Bertani, M. Mozzon, R.A. Michelin, Inorg. Chem. 27 (1988) 2809.
[26] R. Bertani, M. Mozzon, R.A. Michelin, F. Benetollo, G. Bombieri, T.J. Castilho, A.J.L. Pombeiro, Inorg. Chim. Acta 189 (1991) 175.
[27] K.V. Luzyanin, V.Yu. Kukushkin, M.N. Kopylovich, A.A. Nazarov, M. Galanski, A.J.L. Pombeiro, Adv. Synth. Catal. 350 (2008) 135.
[28] D. Kremzow, G. Seidel, C.W. Lehmann, A. Furstner, Chem.-Eur. J. 11 (2005) 1833.
[29] B. Dhudshia, A.N. Thadani, Chem. Commun. 6 (2006) 668.
[30] A.I. Moncada, S. Manne, J.M. Tanski, L.M. Slaughter, Organometallics 25 (2006) 491.
[31] A.I. Moncada, M.A. Khanb, L.M. Slaughter, Tetrahedron Lett. 46 (2005) 1399.