Modular Chelated Palladium Diaminocarbene Complexes: Synthesis, Characterization, and Optimization of Catalytic Suzuki−Miyaura Cross-Coupling Activity by Ligand Modification

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A general, two-step procedure is reported for the modular synthesis of a series of palladium complexes of chelating Chugaev-type diaminocarbene ligands via metal-templated addition of hydrazines to alkylisocyanides. This method afforded high yields of (dicarbene)palladium dihalide complexes with methyl, isopropyl, cyclohexyl, and *tert*-butyl substituents by addition of hydrazine to the corresponding alkylisocyanide, and analogous backbone-substituted complexes were prepared by palladium-templated addition of methylhydrazine to methylisocyanide. The complexes were fully characterized by IR, ^{1}H NMR, and ^{13}C NMR spectroscopies. X-ray crystallographic analyses of four (dicarbene)palladium dibromide complexes revealed structural similarities with complexes of imidizole-based N-heterocyclic carbenes (NHCs), characterizing these chelating ligands as strongly donating, resonance-stabilized diaminocarbenes. To examine whether these ligands are amenable to cross-coupling catalyst optimization via systematic ligand modification, a set of 10 (dicarbene)palladium dihalide complexes was tested as precatalysts in the Suzuki−Miyaura coupling of bromobenzene with phenylboronic acid. Substantial variations in catalytic activity were observed, and a backbone-substituted palladium dicarbene complex derived from methylhydrazine was identified as the most active precatalyst. Catalyst activities did not correlate with ligand sterics, and subtle electronic perturbation of carbene donor ability by the alkyl groups is proposed to be the origin of the differences in activity. The optimized catalyst was found to give high yields in Suzuki−Miyaura cross-couplings of electron-poor aryl chlorides and a range of aryl bromides, although elevated temperatures (120 °C) were necessary. Coupling reactions conducted open to air showed little formation of homocoupling byproduct and minimal loss of yield in most cases, identifying the optimized system as a rare example of an air-tolerant Suzuki−Miyaura catalyst. This study highlights the importance of a modular ligand design in fine-tuning the activity of a homogeneous catalyst.

Introduction

Access to new ligand types is a critical component of the design of novel homogeneous transition metal catalysts. Because drastic changes in catalytic activity can result from apparently minor modifications of ligand structure,[1] ligand designs that allow systematic variation of steric and electronic properties are particularly valuable. Notable examples of such modular ligand designs include salens, which have been structurally modified to optimize a range of synthetically useful catalytic asymmetric reactions,[2] and α-diimines,[3] which have been shown to engender substantial changes in the activity of late-metal olefin polymerization catalysts upon modular variation of ligand electronic properties.[4]

Since Arduengo's discovery of stable imidazol-2-ylidenes in 1991,[5] substantial efforts have focused on the design and catalytic application of diaminocarbene ligands,[6] primarily "N-heterocyclic carbenes" (NHCs) derived from imidazolium cations.[7] Diaminocarbenes function as exceptionally strong σ-donors to late transition metals, with binding energies exceeding those of the most basic phosphines by as much as 10 kcal/mol,[8] and they lack the electrophilic reactivity of Fischer-type carbenes.[6] The high catalytic activities achieved by a number of NHC-based catalysts have been attributed in part to this strong donor ability, in combination with the unique steric demands[8,9] and enhanced thermal stability[10] of these ligands compared with phosphines. Catalyst advances with particular promise for synthetic applications have been achieved using NHC ligands in ruthenium-catalyzed ring-closing olefin

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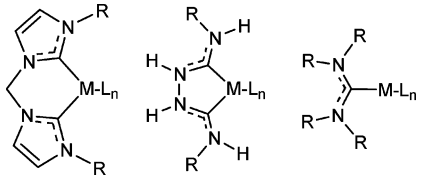

Figure 1. Chelating NHC (**A**) and Chugaev carbene (**B**) ligands, and a monodentate "open" diaminocarbene ligand (**C**).

metathesis,[10,11] palladium-catalyzed Suzuki−Miyaura cross-coupling,[12−17] nickel-catalyzed cycloaddition,[18] palladium-catalyzed aerobic alcohol oxidation,[19] and platinum-catalyzed hydrosilylation.[20] All of these examples employ monodentate NHC ligands, which can be readily modified at the nitrogen substituent but have otherwise limited potential for systematic variation.

Chelating dicarbene ligands offer greater modularity in principle, because the chelate backbone can be modified to vary bite angle or introduce chirality.[21,22] In practice, however, chelating carbenes (e.g., **A**, Figure 1) have not been as widely investigated in catalysis as monodentate NHCs,[23−25] perhaps due to a lack of general synthetic procedures for their attachment to metals. Metalation via the free dicarbene can be accomplished in some cases,[26,27] but problems can result from reaction of the strong base required to deprotonate the imidazolium precursor with acidic protons on linking groups.[28] The free carbenes are also very air-sensitive and are usually formed in moderate yields at best.[26,29] Chelating bis(NHC) ligands have been prepared by metal-mediated cleavage of tethered enetetramines in a few cases,[30] including an early report by Lappert and co-workers,[31] but this approach is limited by the need for a previously synthesized enetetramine precursor.[32] In situ treatment of a bis-imidazolium salt with a base in the presence of a metal precursor has also been employed,[33] but yields are variable, and in some instances the bis(NHC) coordination mode (i.e., bridging vs κ^2-coordination) has been difficult to control.[34] Direct reaction of metal acetates with imidazolium salts is an attractively simple metalation route, but it appears to be generally applicable only for palladium and often requires harsh temperatures for bidentate NHCs (130−170 °C).[21,35] This method has been reported to be effective at milder temperatures (refluxing THF) for benzannulated bidentate bis(NHC) ligands.[36] The silver-carbene transmetalation strategy introduced by Wang and Lin[37] has been successfully extended to chelating carbene ligands in a few cases,[22,28,38] but this method depends on the formation of a suitable silver carbene precursor and sometimes results in bis-(NHC)-bridged bimetallic complexes.[28] To realize the catalytic potential of chelating diaminocarbene ligands, additional synthetic approaches that are procedurally simple and amenable to modular variation would be advantageous.[39]

In our search for modular routes to chelating carbene ligands, we found an intriguing starting point in "Chugaev-type"

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carbenes (**B**, Figure 1),[40,41] a relatively unexplored class of chelate ligands prepared by metal-templated addition of hydrazines or other bifunctional nucleophiles to *cis*-coordinated isocyanides. These ligands are historically interesting because Chugaev's original platinum complexes[41] predate Fischer's seminal report of metal carbenes[42] by 49 years.[43] However, they were not recognized as carbene complexes until 1970, when spectroscopic studies by Rouschias and Shaw[44] and crystallographic studies by Burke, Balch, and Enemark[45] established their chelating structures. These ligands contain nitrogen-stabilized carbene moieties analogous to those in imidazole-based NHCs, suggesting that they might possess comparably strong donor properties that could be favorable for catalyst development. Indeed, the structurally similar "open" diaminocarbenes first prepared by Alder and co-workers (**C**, Figure 1)[46] have been shown to be even stronger donor ligands than NHCs.[47] The large variety of available metal-isocyanide complexes[48] suggests that this synthetic route could potentially be generalized to a range of catalytically important metals, and this is supported by reports of chelating Chugaev-type carbenes prepared from isocyanide complexes of Pt(II),[41,49−52] Pd(II),[45,53] Fe(II),[54] Ru(II),[55] and Au(III).[56] In addition, similar chelating carbene ligands have been synthesized from diamines such as 2,6-diaminopyridine[57] and 1,2-ethylenediamine,[58] indicating that the metal-templated synthetic strategy could possibly be extended to a range of structurally diverse bis-carbene ligands, including chiral examples. Assembly of chelating carbene ligands directly at the metal center could substantially reduce the number of synthetic steps needed to introduce desired structural elements.[59]

As an entry into modular dicarbene-ligated catalysts with potential catalytic utility, we have explored the synthesis of a series of palladium Chugaev carbene complexes derived from bulky alkylisocyanides. Reported examples of Chugaev-type carbene ligands have been prepared almost exclusively from methylisocyanide, with the exception of a platinum-bound example formed from *tert*-butylisocyanide[51,52] and two gold complexes derived from phenyl- and *p*-tolylisocyanides.[56] Palladium-NHC catalysts for the Suzuki−Miyaura cross-coupling reaction[12−17] have shown high activity and broad substrate scope comparable to those achieved by the best phosphine-based systems,[60−64] and therefore we viewed this reaction as ideal for testing our objective of optimizing catalytic activity through variation of the ligand structure. We have published a preliminary communication demonstrating that a palladium Chugaev carbene complex readily prepared from cyclohexylisocyanide is an effective precatalyst for Suzuki−Miyaura coupling of a range of aryl bromides, with the advantage of operating under air without significant loss of yield in many cases.[65] We now report a general, two-step procedure for the synthesis of a series of palladium complexes of Chugaev-type carbene ligands from alkylisocyanides. Preparation of a series of these chelating ligands from different isocyanides and hydrazines has not been previously reported for any metal. The reported method provides rapid access to a small catalyst "library" without the need for air-sensitive techniques. We find that ligand modification results in substantial changes in the activity of these complexes as Suzuki−Miyaura catalysts, and we have identified backbone-substituted Chugaev carbenes derived from methylhydrazine as the most promising for the formation of highly active, air-tolerant Suzuki−Miyaura catalysts. The convenient synthesis of this series of catalysts provides a promising starting point for the design of tunable catalysts containing modular, structurally diverse chelating carbene ligands.

Results

Syntheses. The two-step procedure we reported for the synthesis of a palladium Chugaev carbene complex from cyclohexylisocyanide[65] proved readily adaptable to commercially available isopropylisocyanide and *tert*-butylisocyanide. For comparison, we also used this method to prepare the previously reported methylisocyanide-derived complexes.[45,49]

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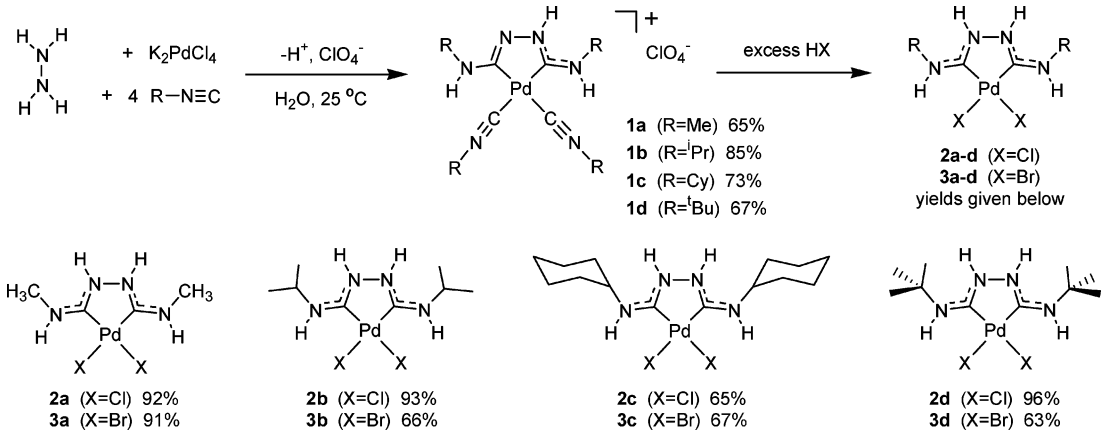
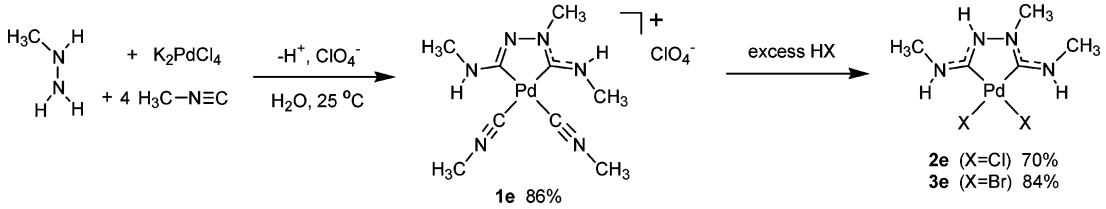
Scheme 1. Synthesis of Chelating Palladium Diaminocarbene Complexes from Hydrazine



Scheme 2. Synthesis of Palladium Diaminocarbene Complexes from Methylhydrazine



Aqueous solutions of $[Pd(CNR)_4]Cl_2$, prepared in situ by reaction of $PdCl_2$ with 4 equiv of alkylisocyanide in the presence of excess KCl, were treated with excess hydrazine hydrate to give yellow solutions of cationic complexes **1a**−**d** (Scheme 1). Complexes of this type, bearing two isocyanide ligands and a deprotonated form of the dicarbene ligand that is formally a carbene-imidoyl chelate, have been previously reported as the first species isolated in syntheses of platinum[49,50,52] and gold[56] Chugaev-type carbene complexes as well as the known palladium complex **1a**.[45,49] Precipitation of **1a**−**d** as yellow or orange solids was achieved by addition of excess $LiClO_4$. The only parameter that required significant adjustment in order to optimize yields was the amount of $LiClO_4$, which varied from 8 equiv for **1b** to 4 equiv for **1d**. The procedure for **1c** (R = Cy) differed slightly, as the chloride salt precipitated immediately upon addition of hydrazine. In this case the anion exchange was accomplished by washing the solid with aqueous $LiClO_4$. To obtain reproducibly pure products in subsequent transformations, it was necessary to recrystallize **1a**, **1b**, and **1d** from Et_2O/CH_3CN or Et_2O/CH_3Cl, and the reported yields (Scheme 1) are for recrystallized product for all complexes except **1c**. Attempts to use solutions of **1a**−**d** in subsequent reactions without isolation of the complex led to products with significant impurities.

(Dicarbene)palladium dihalide complexes were sought as potential Suzuki cross-coupling precatalysts. Both dichloride (**2a**−**d**) and dibromide complexes (**3a**−**d**) were readily prepared by addition of 3 M HCl or HBr, either directly to the solid compound (**1a**) or to an acetonitrile solution (**1b**−**d**) (Scheme 1). Reduction of solvent volume, followed by addition of Et_2O in all cases except **2a** and **3a**, allowed precipitation of analytically pure **2** and **3**, which were isolated in good to excellent yields. This procedure appears superior to the original syntheses of **2a**, for which solubility problems were cited and yields were not reported.[45,49] The use of larger alkyl isocyanides significantly improved the solubilities of these complexes. The parent Chugaev carbene complexes **2a** and **3a** dissolve with difficulty and only in polar aprotic solvents such as DMSO, DMF, and DMA, whereas the bulkier dihalide complexes are very soluble in these solvents and somewhat soluble in CH_3CN. The dibromide complexes are generally more soluble than the corresponding dichloride complexes.

A similar procedure using methylhydrazine and methylisocyanide led to palladium complexes **1e**, **2e**, and **3e** (Scheme 2), containing Chugaev carbene ligands with methyl-substituted backbones. The platinum analogues of **1e** and **2e** were previously reported by Balch and co-workers.[49,50] Attempts to prepare analogous complexes from methylhydrazine and bulkier alkylisocyanides failed, as the cationic complex **1** either did not form or could not be precipitated from solution. Efforts to prepare dicarbene complexes from 2,6-dimethylphenylisocyanide and hydrazine were also unsuccessful, leading to no apparent reaction in water or uncharacterizable solids in alcoholic solvents. Possible reasons for the failure to form carbene complexes in this case are the insolublity of the arylisocyanide in H_2O and the known preference for formation of the bis(isocyanide) palladium dihalide complexes over the tetrakis(isocyanide) palladium complexes when the less nucleophilic arylisocyanides are employed.[48a,59c] The latter effect could result in *trans* isocyanide ligands that are incapable of undergoing chelative hydrazine addition.[66]

Spectroscopic Characterization. The conversion of precursor complexes **1a**−**e** into dihalide complexes **2a**−**e** and **3a**−**e** is conveniently monitored by observing the disappearance of the two characteristic isocyanide C≡N stretching bands in the 2210−2260 cm^{-1} region of the IR spectra (Table 1). In addition, all of the dicarbene complexes exhibit two to four N−H stretches in the 3000−3500 cm^{-1} range and two or three bands corresponding to C═N stretching in the 1520−1600 cm^{-1} range. These assignments are consistent with IR spectral data reported for the original methylisocyanide-derived platinum Chugaev carbene complexes.[49]

The most distinctive features of the ^1H NMR spectra of the palladium dicarbene complexes are the ligand N−H resonances,

(66) (a) Hahn, F. E.; Lügger, T. *J. Organomet. Chem.* **1994**, *481*, 189−193. (b) Hahn, F. E.; Lügger, T.; Beinhoff, M. *Z. Naturforsch. B* **2004**, *59*, 196−201.

Table 1. Selected IR Spectral Data for Palladium Diaminocarbene Complexes[a,b]

compound	ν(NH)	ν(C≡N)	ν(C=N)
precursors (**1**)			
1a	3452, 3439, 3340	2251, 2241	1582, 1531
1b	3458, 3412, 3300	2230, 2218	1570, 1536
1c	3381, 3157	2220, 2210	1572, 1539
1d	3464, 3436, 3426	2225, 2210	1570, 1523
1e	3465, 3355	2255, 2243	1582, 1522
dihalides (**2**, **3**)			
2a	3362, 3205, 3142, 3085		1601, 1529
3a	3338, 3186, 3135, 3066		1597, 1530
2b	3327, 3194, 3119, 3089		1603, 1504
3b	3327, 3192, 3121, 3092		1598, 1516
2c	3320, 3177, 3115, 3074		1592, 1501
3c	3282, 3181, 3124, 3086		1586, 1510
2d	3323, 3309, 3274		1572, 1512
3d	3324, 3288, 3265, 3194		1571, 1513
2e	3317, 3293, 3256		1591, 1540, 1506
3e	3295, 3262, 3186		1593, 1544, 1508

[a] Collected from Nujol mulls, frequencies in cm^{-1}. [b] Full IR spectral data are compiled in the Supporting Information.

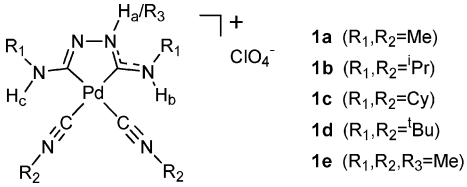
which appear in the δ 4.5−11.2 range (Table 2). For cationic complexes **1a**−**d**, room-temperature ^{1}H NMR spectra in CD_3CN or CD_2Cl_2 exhibit two broad N−H signals in a 2:1 ratio (e.g., **1b, 1d**, Table 2), suggesting a fluxional structure with averaged signals for the "terminal" N−H_b and N−H_c groups. For **1b**, cooling to −70 °C in CD_2Cl_2 revealed three broad but distinct N−H peaks, indicating that the H_b/H_c exchange is slowed at low temperature. Similar observations were reported for the platinum analogue of **1a**.[50] Given that the conjugate acid forms of Chugaev-type carbene ligands (e.g., **2**, **3**) are known to be subject to deprotonation at the "internal", hydrazine-derived N−H_a positions,[57] reversible protonation/deprotonation of the internal nitrogens is a likely mechanism for the observed N−H exhange (Scheme 3). This exchange occurs even in carefully dried CD_3CN or CD_2Cl_2, suggesting that it is catalyzed by minute traces of H_2O or acid. However, ^{1}H NMR spectra of **1a**−**d** acquired in undried DMSO-d_6 display three distinct N−H signals that are much less broad than those observed in other solvents, indicating slow N−H exchange. We postulate that the propensity of DMSO to form hydrogen bonds with the internal N−H groups of these ligands (vide infra) inhibits the exchange process. Methylhydrazine-derived complex **1e** cannot undergo the proposed exchange process, and it displays two N−H peaks in both CD_3CN and DMSO-d_6. No N−H exchange is evident for the palladium dihalide complexes **2a**−**e** and **3a**−**e**, which contain the protonated form of the dicarbene ligand. Two sharp N−H resonances are observed for all dihalide complexes except backbone-substituted complexes **2e** and **3e**, which show three signals. The upfield N−H signals appearing in the δ 7.6−8.1 range exhibit coupling to the R_1 α-protons for R_1 = Me, ^{i}Pr, and Cy, and therefore the downfield N−H signals (δ 9.9−11.2) are assigned as the internal N−H groups for all of the palladium carbene complexes.

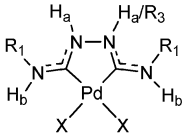
Two sets of alkyl ^{1}H NMR signals are observed for cationic complexes **1a**−**d**, corresponding to the dicarbene terminal alkyl groups (R_1) and the isocyanide alkyl groups (R_2). These signals do not split into four inequivalent sets even under conditions in which the N−H exchange is slowed (i.e., DMSO, other solvents at low temperature), suggesting that the ^{1}H chemical shift differences between R_1 or R_2 groups on opposite sides of complexes **1a**−**d** would be very small if the static structure depicted above Table 2 were attained. Consistent with this, the static complex **1e** displays only one peak for the isocyanide R_2 groups. For **1a**, the more upfield methyl resonance at δ 2.64 is ascribed to the dicarbene ligand by analogy with the reported platinum analogue.[50] This assignment is supported by the ^{1}H NMR spectrum of backbone-substituted analogue **1e**, which shows coupling between the two more upfield methyl peaks and the terminal N−H groups. However, a ^{1}H COSY experiment with isopropyl-substituted complex **1b** revealed cross-peaks between the more downfield ^{i}Pr C−H signal and the terminal N−H peak, establishing that the R_1/R_2 chemical shift assignments of **1b** are reversed relative to the methyl-substituted complexes. ^{1}H NMR assignments for the alkyl resonances of **1c** and **1d** are made assuming that the pattern observed for **1b** applies for alkyl groups larger than methyl. For the dihalide complexes **2a**−**e** and **3a**−**e**, the R_1 chemical shifts are between those observed for the dicarbene and isocyanide alkyl groups of the corresponding cation **1a**−**e** in most cases. For methylhydrazine-derived complexes **2e** and **3e**, the methyl resonance that does not show coupling to an N−H group is assigned to the backbone methyl group (R_3).

The fluxionality of cationic complexes **1a**−**d** is also apparent in their ^{13}C NMR spectra (Table 3). No signals for the carbene or imidoyl carbons are apparent in room-temperature spectra, and again only two sets of alkyl resonances are observed. However, a ^{13}C NMR spectrum of complex **1d** taken at −50 °C in CD_2Cl_2 exhibits sharp signals for the carbene and imidoyl carbons at δ 190.1 and 174.6 as well as two isocyanide resonances at δ 132.9 and 131.9. In addition, four sets of *tert*-butyl resonances can be discerned, indicating a static structure on the time scale of the ^{13}C NMR experiment. The solubilities of the other cationic complexes in CD_2Cl_2 are insufficient to obtain low-temperature ^{13}C NMR spectra. Backbone-substituted complex **1e** displays a static room-temperature ^{13}C NMR spectrum analogous to the low-temperature ^{13}C NMR spectrum of **1d**. The carbene and imidoyl resonances of **1d** and **1e** could not be definitively assigned, but comparison with the carbene shifts of complexes **2a**−**e** and **3a**−**e** makes it likely that the more upfield resonances (at δ 174.6 and 172.9, respectively) belong to the carbenes. The carbene ^{13}C chemical shifts of the dihalide complexes **2a**−**e** and **3a**−**e** (δ 176−183) are similar to the value of δ 186 reported by Herrmann and co-workers for an analogous chelating (bis-NHC)PdI_2 complex,[23] supporting the depiction of the Chugaev-type dicarbene ligands as possessing similar electronic properties and σ-donor abilities to imidazole-based chelating dicarbene ligands.[67]

Structural Characterization. An X-ray crystallographic analysis of cationic "precursor" complex **1b** (Figure 2) supports

Table 2. ^{1}H NMR Data for Palladium Diaminocarbene Complexes[a]

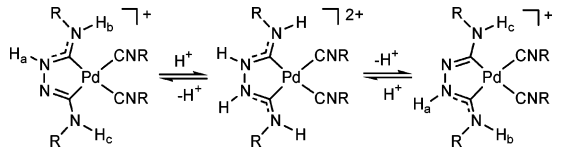




compound	solvent	NH	R_1	R_2, R_3
precursors				
1a	DMSO-d_6	10.05 (br s, 1H, H_a), 7.55 (br s, 1H, H_b), 5.56 (br s, 1H, H_c)	2.64 (br s, 6H)	3.52 (s, 6H)
1b[b]	CD_3CN	8.49 (br s, 1H, H_a), 5.10 (br s, 2H, $H_{b,c}$)	4.19 (sept, 2H, $^3J_{HH}$=6.4 Hz, C*H*), 1.45 (d, 12H, $^3J_{HH}$=6.4 Hz, CH_3)	3.70 (sept, 2H, $^3J_{HH}$=6.6 Hz, C*H*), 1.17 (d, 12H, $^3J_{HH}$=6.6 Hz, CH_3)
	CD_2Cl_2, 0 °C	7.90 (br s, 1H, H_a), 5.01 (br s, 2H, $H_{b,c}$)	4.26 (sept, 2H, $^3J_{HH}$=6.5 Hz, C*H*), 1.50 (d, 12H, $^3J_{HH}$=6.5 Hz, CH_3)	3.68 (sept, 2H, $^3J_{HH}$=6.6 Hz, C*H*), 1.21 (d, 12H, $^3J_{HH}$=6.6 Hz, CH_3)
	CD_2Cl_2, −70 °C	8.25 (br s, 1H, H_a), 5.99 (br s, 1H, H_b), 4.03 (br s, 1H, H_c)	4.21 (m, 2H, C*H*), 1.46 (br s, 12H, CH_3)	3.64 (m, 2H, C*H*), 1.14 (br s, 12H, CH_3)
	DMSO-d_6	10.15 (br s, 1H, H_a), 6.94 (br s, 1H, H_b), 4.78 (br s, 1H, H_c)	4.29 (br s, 2H, C*H*), 1.42 (d, 12H, $^3J_{HH}$=6.4 Hz, CH_3)	3.67 (br s, 2H, C*H*), 1.12 (br s, 12H, CH_3)
1c	DMSO-d_6	10.09 (br s, 1H, H_a), 6.79 (br s, 1H, H_b), 4.49 (br s, 1H, H_c)	4.04 (s, 2H, ipso C*H*), 1.0−2.2 (unresolved, 40H)	3.32 (s, 2H, ipso C*H*), 1.0−2.2 (unresolved, 40H)
1d	DMSO-d_6	9.86 (br s, 1H, H_a), 6.40 (br s, 1H, H_b), 4.52 (br s, 1H, H_c)	1.57 (s, 18H)	1.36 (s, 18H)
1e	DMSO-d_6	7.02 (br s, 1H, H_b), 5.61 (br s, 1H, H_c)	3.00 (d, 3H, $^3J_{HH}$=4.8 Hz), 2.56 (d, 3H, $^3J_{HH}$=4.8 Hz)	3.51 (unresolved, 6H), 3.08 (s, 3H, N_2CH_3)
dihalides				
2a	DMSO-d_6	10.97 (s, 2H, H_a), 7.80 (m, 2H, H_b)	2.83 (d, 6H, $^3J_{HH}$=5.1 Hz)	
3a	DMSO-d_6	11.08 (s, 2H, H_a), 7.77 (m, 2H, H_b)	2.83 (d, 6H, $^3J_{HH}$=5.4 Hz)	
2b	DMSO-d_6	11.12 (s, 2H, H_a), 7.57 (d, 2H, $^3J_{HH}$)=7.8 Hz, H_b)	3.78 (m, 2H, C*H*), 1.14 (d, 12H, $^3J_{HH}$=6.4 Hz, CH_3)	
3b	DMSO-d_6	11.17 (s, 2H, H_a), 7.59 (d, 2H, $^3J_{HH}$)=8.4 Hz, H_b)	3.79 (m, 2H, C*H*), 1.15 (d, 12H, $^3J_{HH}$=6.3 Hz, CH_3)	
2c	DMSO-d_6	11.15 (s, 2H, H_a), 7.71 (d, 2H, $^3J_{HH}$)=8.0 Hz, H_b)	3.53 (br s, 2H, ipso C*H*), 1.0−2.2 (20H, unresolved)	
3c	DMSO-d_6	11.21 (s, 2H, H_a), 7.74 (d, 2H, $^3J_{HH}$)=7.6 Hz, H_b)	3.55 (br s, 2H, ipso C*H*), 1.0−2.0 (20H, unresolved)	
2d	DMSO-d_6	10.37 (s, 2H, H_a), 8.05 (s, 2H, H_b)	1.32 (s, 18H)	
3d	DMSO-d_6	10.41 (s, 2H, H_a), 7.99 (s, 2H, H_b)	1.33 (s, 18H)	
2e	DMSO-d_6	10.74 (s, 1H, H_a), 7.97 (m, 1H, H_{b1}), 7.84 (m, 1H, H_{b2})	3.11 (d, 3H, $^3J_{HH}$=5.6 Hz), 2.81 (d, 3H, $^3J_{HH}$=5.2 Hz)	3.43 (s, 3H, N_2CH_3)
3e	DMSO-d_6	10.82 (s, 1H, H_a), 7.91 (m, 1H, H_{b1}), 7.79 (m, 1H, H_{b2})	3.11 (d, 3H, $^3J_{HH}$=5.2 Hz), 2.82 (d, 3H, $^3J_{HH}$=5.6 Hz)	3.44 (s, 3H, N_2CH_3)

[a] Spectra obtained at 400 MHz, 25 °C, unless otherwise noted. [b] Alkyl resonances of **1b** assigned on the basis of a ^{1}H COSY experiment (CD_3CN, 25 °C).

Scheme 3. Proposed N−H Exchange Mechanism for 1a−d



the designation of the ligand as a carbene-imidoyl chelate. Bond lengths between C(9) and neighboring nitrogens are nearly identical at 1.326(2) and 1.3294(19) Å to N(4) and N(5), respectively (Table 4), characterizing a resonance-stabilized diaminocarbene moiety. However, C(8) exhibits unequal carbon−nitrogen bond lengths consistent with a formally anionic imidoyl carbon, with the C(8)−N(3) distance of 1.3069(19) Å corresponding to a double bond and the C(8)−N(2) distance of 1.3588(18) Å representing a bond length intermediate between that of a single and a double bond. Significant π-delocalization in the ligand NCNNCN unit is indicated by these bond lengths as well as by the planarity of the chelate, which shows a mean deviation from planarity of only 0.073 Å within the N_4C_2Pd unit. The palladium−carbon bond lengths of the chelating ligand are similar at 2.0219(14) Å for Pd−C(8) and 2.0114(13) Å for Pd−C(9), suggesting no significant differences in the donor abilities of the two carbon atoms.

To identify any structural features of (dicarbene)palladium dihalide complexes that could potentially account for differences in their catalytic activities (vide infra), we obtained X-ray structures of complexes of all of the new ligands (Figure 3). Dibromide complexes **3b**−**e** were employed, because their superior solubility properties relative to dichlorides **2b**−**e** allowed the growth of higher quality crystals. Selected structural parameters of **3b**−**e** are compiled in Table 5, along with published data for the parent methylisocyanide-derived complex

(67) A possibly closer comparison in terms of carbene substitution pattern would be the NH,NR-substituted benzannulated heterocyclic carbenes reported by Hahn and co-workers,[59a−c] but no Pd-bound examples are known. Pt complexes of these ligands show carbene ^{13}C NMR signals at δ 167−169,[59c] but Pd-bound carbenes typically resonate significantly downfield of their Pt congeners.[23,33c]

Table 3. ^{13}C NMR Data for Palladium Diaminocarbene Complexes[a]

compound	solvent	Pd−*C*	R_1	R_2, R_3
precursors				
1a	DMSO-d_6	132.1 (MeN*C*)[b]	30.1	29.7
1b[c]	CD_3CN	133.7 (^{i}PrN*C*)[b]	50.7 (*C*H), 22.5 (*C*H$_3$, unresolved)	45.7 (*C*H), 22.5 (*C*H$_3$, unresolved)
1c	DMSO-d_6	not detected	53.0 (ipso), 31.9, 25.1, 24.3 (unresolved)	51.2 (ipso), 31.1, 24.3 (unresolved), 22.0
1d	CD_3CN	not detected	60.3 (*C*Me$_3$), 29.9 (*C*H$_3$)	54.9 (*C*Me$_3$), 28.9 (*C*H$_3$)
	CD_2Cl_2, −50 °C	190.1, 174.6 (carbene/imidoyl), 132.9, 131.9 (^{t}BuN*C*)	59.4, 59.3 (*C*Me$_3$), 29.7, 29.5 (*C*H$_3$)	54.7, 53.4 (*C*Me$_3$), 28.6, 28.3 (*C*H$_3$)
1e	DMSO-d_6	191.7, 172.9 (carbene/imidoyl), 133.0, 130.9 (MeN*C*)	34.0, 29.7	36.6 (N$_2$*C*H$_3$), 30.0 (CN*C*H$_3$), 29.7 (CN*C*H$_3$)
dihalides				
2a	DMSO-d_6	179.0	30.2	
3a	DMSO-d_6	179.0	30.6	
2b	DMSO-d_6	176.1	44.9 (*C*H), 21.8 (*C*H$_3$)	
3b	DMSO-d_6	175.9	45.3 (*C*H), 21.7 (*C*H$_3$)	
2c	DMSO-d_6	175.7	51.3 (*ipso*), 31.3, 24.7, 23.5	
3c	DMSO-d_6	175.7	51.3 (*ipso*), 31.2, 24.7, 23.5	
2d	DMSO-d_6	177.0	54.4 (*C*Me$_3$), 28.0 (*C*H$_3$)	
3d	DMSO-d_6	176.8	54.8 (*C*Me$_3$), 28.0 (*C*H$_3$)	
2e	DMSO-d_6	182.6, 175.8	34.2, 30.7	38.2 (N$_2$*C*H$_3$)
3e	DMSO-d_6	182.6, 175.7	34.2, 30.7	38.1 (N$_2$*C*H$_3$)

[a] Spectra obtained at 101 MHz, 25 °C, unless otherwise noted. [b] Carbene resonances not detected. [c] Alkyl resonances of **1b** assigned on the basis of a ^{1}H−^{13}C HMQC experiment (CD_3CN, 25 °C).

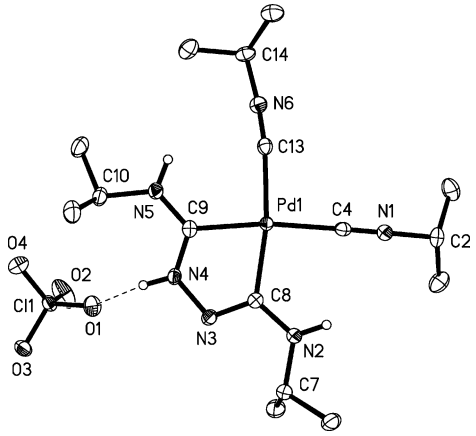


Figure 2. Molecular structure of **1b**, with thermal ellipsoids drawn at the 50% probablility level.

Table 4. Selected Bond Lengths (Å) and Angles (deg) for 1b

Pd−C(8)	2.0219(14)
Pd−C(9)	2.0114(13)
C(8)−N(3)	1.3069(19)
C(8)−N(2)	1.3588(18)
C(9)−N(4)	1.326(2)
C(9)−N(5)	1.3294(19)
N(3)−N(4)	1.4085(16)
Pd−C(4)	2.0195(15)
Pd−C(13)	2.0391(15)
C(4)−N(1)	1.140(2)
C(13)−N(6)	1.148(2)
C(8)−Pd−C(9)	77.87(6)
C(8)−Pd−C(4)	94.16(6)
C(9)−Pd−C(13)	92.79(6)
C(4)−Pd−C(13)	94.52(6)
N(3)−C(8)−N(2)	117.84(13)
N(4)−C(9)−N(5)	120.14(13)
sum of angles around C(8)	359.9(2)
sum of angles around C(9)	359.7(2)
C(7)−N(2)−C(8)−N(3)	−7.3(2)
C(7)−N(2)−C(8)−Pd	176.11(10)
C(10)−N(5)−C(9)−N(4)	5.8(2)
C(10)−N(5)−C(9)−Pd	179.36(11)
mean dev from plane N_4C_2Pd	0.073 Å

2a[53] for comparison. Crystallographic data for the carbene moieties of **3b**−**e** reveal structural similarities with imidazole-based NHC ligands. The Pd−$C_{carbene}$ bond lengths of 1.96−1.99 Å are very close to those observed in comparable *cis*-(bis-NHC)PdX_2 complexes (1.99−2.00 Å).[23,24] The $C_{carbene}$−N distances of 1.30−1.33 Å are indicative of resonance-stabilized diaminocarbenes. These distances are slightly shorter than the typical range of 1.34−1.37 Å for NHC ligands, implicating a high degree of π-delocalization within the chelate ligand. Substantial π-delocalization is also apparent from the small deviations from planarity (0.015−0.041 Å) observed in the N_4C_2Pd units of the complexes. The ligand geometry constrains the $C_{carbene}$−Pd−$C_{carbene}$ bite angles to approximately 80° for all of the complexes, although the sum of angles around Pd is still 360° in each case.

No substantial structural differences are evident among the hydrazine-derived carbene ligands of **2a** and **3b**−**d.** The dicarbene alkyl groups are oriented away from the palladium center, and they exert no apparent steric influence on the geometries of the ligand or the palladium coordination plane. As indicated by torsion angles (Table 5), the bulkier Cy and ^{t}Bu groups of **3c** and **3d** are rotated out of the ligand plane slightly more than the less bulky groups of **2a** and **3a**, but this is likely due to crystal-packing interactions rather than intramolecular steric interference. The only potential structural difference that can be discerned is a slight shortening of the $C_{carbene}$−$N_{terminal}$ distances for **3c** and **3d** (0.01−0.02 Å) relative to the other complexes, possibly resulting from a subtle electronic influence of the larger alkyl groups (vide infra). However, these distances are still within three standard deviations of the values for **3b** and **3e**, and therefore the available data do not permit meaningful analysis of such minor structural variations.

An unexpected structural feature of the methylhydrazine-derived complex **3e** is the *syn* configuration of the two methyl groups adjacent to C(4). Although no other metal dihalide complexes of the chelating ligand of **3e** have been structurally characterized, the structure of the platinum analogue of the cationic "precursor" complex **1e** has been reported, and it adopts an *anti* configuration of these two methyl groups presumably due to steric effects.[50] We have not been able to obtain X-ray quality crystals of **1e** to confirm its structure, but we have assumed the same configuration observed for the platinum congener (i.e., that shown in Scheme 2) given that Pd−C bond lengths are expected to differ little from Pt−C distances. The

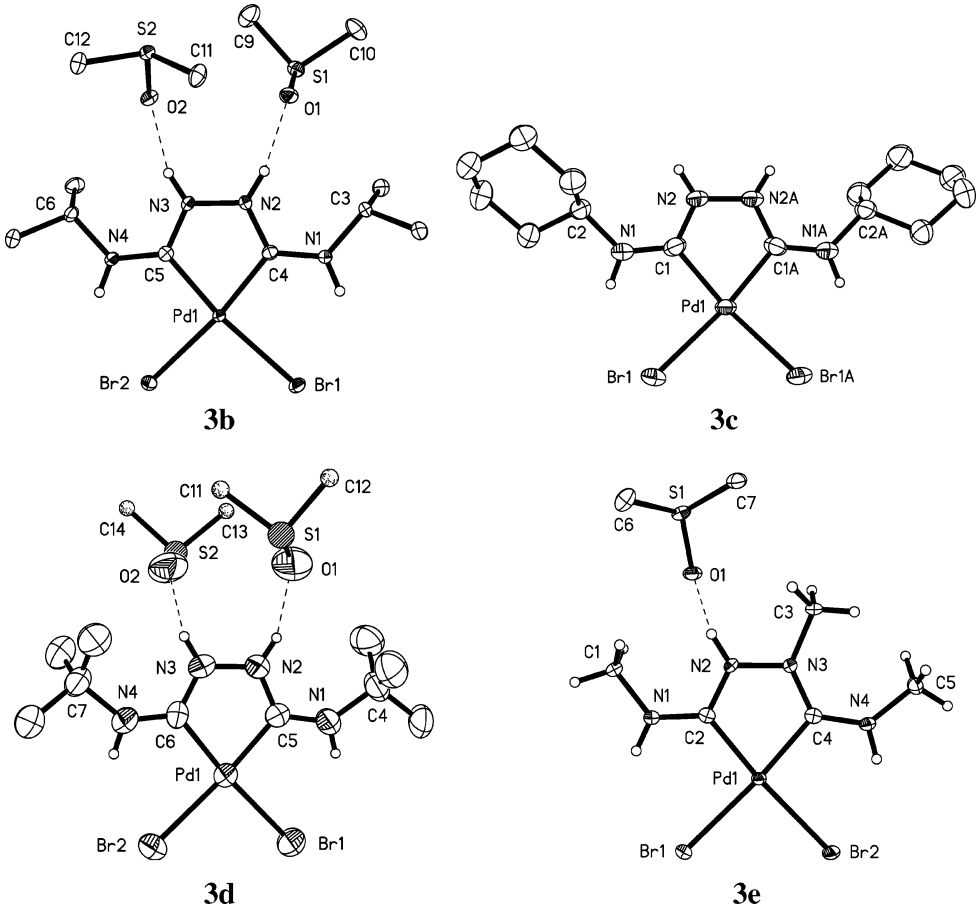


Figure 3. Molecular structures of **3b**−**e**, showing hydrogen bonding with solvent molecules. Thermal ellipsoids are drawn at the 50% probability level. For **3d**, the DMSO molecules were modeled as disordered, and only the dominant orientation is shown.

Table 5. Selected Bond Lengths (Å) and Angles (deg) for (Dicarbene)PdX_2 Complexes

	2a[a,b]	3b	3c[b]	3d	3e
			Distances		
Pd−$C_{carbene}$	1.948(5)	1.9721(15)	1.976(4)	1.969(8)	C(2): 1.962(2)
		1.9771(15)		1.970(8)	C(4): 1.991(2)
$C_{carbene}$−$N_{internal}$	1.309(6)	1.3293(19)	1.329(5)	1.330(10)	C(2): 1.329(3)
		1.3294(18)		1.330(11)	C(4): 1.332(3)
$C_{carbene}$−$N_{terminal}$	1.327(7)	1.324(2)	1.314(5)	1.302(10)	C(2): 1.323(3)
		1.319(2)		1.300(10)	C(4): 1.319(3)
N−N	1.395(8)	1.3942(17)	1.401(7)	1.401(10)	1.404(2)
Pd−X	2.387(1)	2.5029(3)	2.5127(5)	2.4933(12)	Br(1): 2.4930(4)
		2.5194(2)		2.5103(13)	Br(2): 2.4908(4)
			Angles		
C−Pd−C	79.5(3)	79.69(6)	79.8(2)	80.0(3)	80.23(9)
X−Pd−X	94.49(7)	93.446(7)	93.09(3)	91.36(4)	90.182(9)
sum of angles around Pd	360.0(4)	359.74(8)	360.1(3)	360.11(4)	360.0(1)
N−C−N(carbene)	118.2(4)	119.93(13)	120.5(4)	120.8(7)	C(2): 118.4(2)
		120.14(13)		121.6(8)	C(4): 123.79(19)
sum of angles around $C_{carbene}$	360.0(4)	360.0(2)	359.9(6)	359.8(11)	C(2): 360.0(2)
		360.0(2)		360.0(11)	C(4): 360.0(2)
other					C(3)−N(3)−C(4): 132.37(19)
					C(4)−N(4)−C(5): 132.54(19)
			Torsion Angles		
$C(R_1)$− N_{term}−$C_{carbene}$−$N_{internal}$	0[c]	−2.8(2)	−4.5	6.8(16)	C(2): −0.7(3)
		1.9(2)		−2.7(16)	C(4): 0.3(4)
$C(R_1)$− N_{term}−$C_{carbene}$−Pd	0[c]	176.67(10)	172.7	−167.9(8)	C(2): −179.36(15)
		180.00(11)		175.9(8)	C(4): −177.82(17)
			Mean Deviation from Plane (Å)		
N_4C_2Pd	0[c]	0.040	0.015	0.041	0.028

[a] Data taken from ref 53. [b] Two halves of molecule related by crystallographic 2-fold rotation axis. [c] Required by crystallographic symmetry.

preference for the *syn* isomer observed in **3e** indicates that the terminal methyl group is subject to greater steric repulsions from the bromide ligand than from the internal methyl group, whereas the repulsions from the internal methyl group are apparently more significant when an isocyanide ligand occupies the *cis* coordination site. Another possible explanation for the *syn*

Table 6. Hydrogen-Bonding Interactions in Palladium Carbene X-ray Structures

	D−H···A	*d*(D···A)	∠(DHA)
1b	N(4)−H···O(1)	2.9705(16)	150.9
3b	N(2)−H···O(1)	2.7808(17)	162.6
	N(3)−H···O(2)	2.7105(16)	158.7
3d	N(2)−H···O(1)	2.761(11)	141.0
	N(3)−H···O(2)	2.742(10)	138.9
3e	N(2)−H···O(1)	2.720(2)	141.0

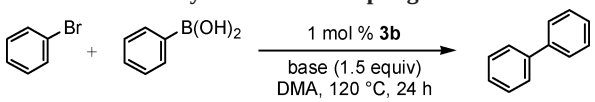
configuration of **3e** is that this geometry permits a favorable hydrogen bond-like interaction between the terminal N−H and Br(2). However, the long N···Br distances of **3e** (N(4)···Br(2) 3.2098(18) Å; N(1)···Br(1) 3.2903(18) Å) indicate that the H···Br interactions are weak at best[68] and unlikely to outweigh steric interactions.[69] Steric strain is apparent in the structure of **3e**, with the C(3)−N(3)−C(4) and C(5)−N(3)−C(4) angles distorted to 132.37(19)° and 132.54(19)°, respectively (Table 5). However, the carbene NCN unit is only slightly distorted, with a N(3)−C(4)−N(4) angle of 123.79(19)°, and the Pd−C and C−N distances are not signficantly affected. Thus, the donor ability of the ligand does not appear to be disrupted by the steric strain.

A common feature observed in the solid-state structures of the palladium carbene complexes is hydrogen bonding involving the acidic internal N−H groups. Precursor cation **1b** exhibits an unusual hydrogen bond with the ClO_4^- anion (Figure 2). The neutral dibromide complexes **3b**, **3d**, and **3e** all display hydrogen bonding with DMSO solvent molecules. Notably, DMSO was the only solvent that yielded X-ray quality crystals of these compounds. The structure of **3c**, which was obtained from a crystal grown from DMF, did not display any hydrogen-bonding interactions, but the structure of dichloride analogue **2c** previously reported by us contains hydrogen-bonding DMSO molecules.[65] The observed N···O distances (2.71−2.97 Å) and calculated N−H···O angles (139−163°) are within the normal ranges for hydrogen bonds (Table 6), although the hydrogen bond to ClO_4^- in **1b** is almost in the "weak" category.[68] The prevalence of these interactions in these structures suggests that hydrogen bonding plays an important role in solvation and crystal growth of Chugaev-type carbene complexes containing N−H groups.

Catalytic Suzuki−Miyaura Cross-Coupling Reactions. The preceding synthetic studies yielded a convenient and straightforward method for the preparation of a series of palladium dicarbene complexes with different alkyl substituents and halide ligands. Our goal was to exploit this synthetic flexibility to optimize the activity of Suzuki−Miyaura cross-coupling catalysts through ligand variation. Our preliminary studies of cyclohexyl-substituted catalyst **2c**[65] indicated that palladium Chugaev carbene complexes are promising candidates for the development of air- and moisture-tolerant Suzuki−Miyaura cross-coupling reactions. Given that drastic variations in catalytic activity have been observed in palladium Suzuki catalysts containing phosphine[60,70] or NHC[13,17] ligands upon variation of ligand substituents, we hypothesized that systematic screening of the palladium dicarbene catalyst "library" might allow identification of more active and/or air-stable catalysts.

Because catalyst activities in Suzuki−Miyaura cross-coupling reactions are often highly sensitive to the nature of the added base,[12,60,62] we first performed base optimization studies. Several commonly used bases were examined, using the prototypical coupling of bromobenzene with phenylboronic acid as a screening reaction (Table 7). Complex **3b**, with isopropyl substituents and bromides as labile ligands, was employed for these studies because initial screening identified it as a catalyst with moderately high activity. The most effective reagent was the mild base K_3PO_4 (Table 7, entry 4), which has also proved optimal in some of the most active palladium-phosphine[64] and palladium-NHC[17] Suzuki catalysts. Other mild bases such as K_2CO_3[71] and CsF[61] gave somewhat lower yields (Table 7, entries 1 and 3). The base of choice for in situ generated Pd−NHC catalysts is Cs_2CO_3,[12,13] but this was found ineffective in our system (Table 7, entry 2), as was the stronger base NaO^{t}Bu[62] (Table 7, entry 6). One possible explanation for the poor activity using stronger bases is that they could initiate catalyst decomposition by reaction with ligand NH groups. Very little cross-coupling occurred in the absence of base (Table 7, entry 7), reflecting that the base is an essential component of the catalytic system.

Table 7. Selection of Optimal Base for the Catalytic Suzuki−Miyaura Cross-Coupling Reaction[a]



entry	base	yield (%)[b]
1	K_2CO_3	69
2	Cs_2CO_3	34
3	CsF	73
4	K_3PO_4	81
5	$K_3PO_4 \cdot H_2O$	81
6	NaO^{t}Bu	45
7	none	4

[a] Reaction conditions: 0.017 mmol of **3b**, 1.7 mmol of PhBr, 2.04 mmol of $PhB(OH)_2$, 2.6 mmol of base, DMA, 120 °C, 24 h; reaction times not optimized. [b] Yields determined by ^{1}H NMR.

To probe the effect of ligand modification on catalytic activity, we screened the entire series of (dicarbene)palladium dihalide complexes obtained from our synthetic studies as precatalysts for the coupling of bromobenzene with phenylboronic acid (Table 8). Substantial variations in yield were observed, ranging from 31% to 95% at 24 h. No clear correlation between the size of the ligand substituents and catalytic activity was apparent among the hydrazine-derived complexes **2a−d** and **3a−d**. Precatalysts containing secondary alkyl substituents (^{i}Pr: **2b**, **3b**; Cy: **2c**, **3c**) displayed somewhat higher activity than the parent methyl-substituted complexes **2a** and **3a**, but a drastic drop in yield occurred with ^{t}Bu-substituted precatalysts **2d** and **3d**. Unexpectedly, the methylhydrazine-derived complexes **2e** and **3e** exhibited the highest activity among all the precatalysts tested. Our initially studied cyclohexyl-substituted catalyst **2c**[65] gave the best yields among the hydrazine-derived complexes. Little difference in activity was observed between precatalysts containing chloride versus bromide ligands in most cases, but the dichloride complexes gave slightly better yields in the most active systems.

Having identified **2e** as the most promising precatalyst, we investigated the functional group tolerance of this catalyst in Suzuki−Miyaura cross-couplings of aryl bromides and chlorides as well as its effectiveness in the presence of moisture and air. Optimal yields were obtained by increasing the amount of arylboronic acid from 1.2 equiv to 1.5 equiv and using a

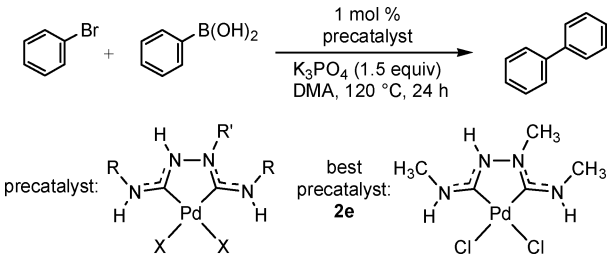
(68) Jeffrey, G. A. *An Introduction to Hydrogen Bonding*; Oxford University Press: New York, 1997; p 12.

(69) Similar N···Br distances were observed for complexes **3b**−**3d**; see Table S2 (Supporting Information) for relevant data.

(70) Kirchhoff, J. H.; Dai, C.; Fu, G. C. *Angew. Chem., Int. Ed.* **2002**, *41*, 1945−1947.

(71) Weissman, H.; Milstein, D. *Chem. Commun.* **1999**, 1901−1902.

Table 8. Optimization of Catalytic Suzuki−Miyaura Cross-Coupling Activity by Systematic Ligand Variation[a]



entry	precatalyst	R	R′	X	yield (%)[b]
1	**2a**	Me	H	Cl	74
2	**3a**	Me	H	Br	75
3	**2b**	^{i}Pr	H	Cl	80
4	**3b**	^{i}Pr	H	Br	81
5	**2c**	Cy	H	Cl	84
6	**3c**	Cy	H	Br	78
7	**2d**	^{t}Bu	H	Cl	34
8	**3d**	^{t}Bu	H	Br	31
9	**2e**	Me	Me	Cl	95
10	**3e**	Me	Me	Br	92

[a] Reaction conditions: 0.017 mmol of precatalyst, 1.7 mmol of PhBr, 2.04 mmol of $PhB(OH)_2$, 2.6 mmol of base, DMA, 120 °C, 24 h; reaction times not optimized. [b]Yields determined by ^{1}H NMR.

temperature of 120 °C. The solubility properties of **2e** necessitated the use of dimethylacetamide (DMA) as a solvent, and less polar solvents such as THF could not be used. Using 1 mol % of **2e** under these conditions, aryl bromides containing a range of functional groups underwent cross-coupling with phenylboronic acid in good to excellent yields (Table 9). Couplings of electron-poor (entries 1a−3a) and electron-neutral (entry 4a) aryl bromides generally gave 97−99% yield under N_2. Aryl bromides with electron-donating substituents were also well tolerated, with a 98% yield obtained for 4-bromotoluene (entry 5a) and an 89% yield obtained for 4-bromoanisole (entry 6a). The coupling of an ortho-substituted arylboronic acid was also successfully carried out (entry 7a). Conducting these reactions open to air in undried solvent led to identical or slightly lower yields in couplings of electron-poor or electron-neutral aryl bromides (entries 1b−4b), but substrates containing −Me or −OMe substituents showed significant drops in yield under aerobic conditions (entries 5b−7b). Because these substituents are prone to oxidation at elevated temperatures, it is likely that the oxidative stability of the substrate rather than that of the catalyst is the limiting factor in these cases. Overall, the yields obtained using catalyst **2e** in Suzuki−Miyaura cross-coupling reactions of aryl bromides are very similar to those previously reported by us for **2c**,[65] although **2e** provides better yields under air in some cases (entries 3b, 5b). However, **2e** does show substantial improvements in activity with activated aryl chlorides relative to **2c**. Catalytic cross-coupling reactions of 4-chloronitrobenzene, 4-chlorobenzonitrile, and 4-chloroacetophenone with phenylboronic acid provided yields of 92%, 93%, and 37% with **2e** (entries 8−10), whereas the same reactions using **2c** as a precatalyst gave respective yields of 79%, 25%, and 20%.[72] Like **2c**, precatalyst **2e** is ineffective in couplings of electron-rich aryl chlorides (entries 11, 12).

The amount of biphenyl homocoupling product was measured in all of the reactions in order to determine whether the use of aerobic reaction conditions resulted in increased byproduct formation (Table 9, last column). Homocoupling product can arise from "double transmetalation" of the arylboron reagent followed by biaryl reductive elimination,[73] and this side reaction might be increased if Pd(0) intermediates in the catalytic cycle[74] are diminished by aerobic oxidation to Pd(II). Indeed, substantial quantities of homocoupling product (up to 11%) have been observed in Suzuki−Miyaura cross-coupling reactions conducted under air.[75] Although larger quantities of homocoupling products were detected in aerobic Suzuki reactions catalyzed by **2e** compared with those performed under nitrogen, the largest amounts represented less than one catalytic turnover and only 1% of the total product. Thus, byproduct formation does not appear to be a significant problem in these aerobic Suzuki−Miyaura cross-coupling reactions.

Yield versus Time in Catalytic Suzuki−Miyaura Cross-Coupling Reactions. To gain further insights into the Suzuki−Miyaura cross-coupling activities of the most promising catalysts, the time course of the Suzuki coupling of bromobenzene with phenylboronic acid was monitored for precatalysts **2c** and **2e** (Figure 4). For both precatalysts, the reaction was essentially complete (97% yield) within 5 h. Importantly, no induction periods were observed for coupling reactions using either catalyst **2c** or **2e**, and **2e** displayed a small amount of product formation (3%) before heating. Induction periods can indicate that the catalytically active species is a palladium(0) colloid formed after initial decomposition of the ligated palladium precatalyst.[76] Such Pd(0) colloids are believed to be involved in a number of "ligandless" catalyst systems for Suzuki−Miyaura coupling.[77] The yield versus time plots for precatalysts **2e** and **2c** are quite similar, exhibiting maximum activity at the beginning of the reaction followed by gradual attainment of a plateau, in contrast to the sigmoidal plots reported for coupling reactions in which Pd(0) colloids are the catalytic species.[76] This is consistent with an active catalyst that forms immediately and contains an intact ligand. However, formation of palladium black was observed at ∼1.5 h for the reaction catalyzed by **2e**, corresponding to the time at which the yield reached ∼90% and began to level off. Thus, it is possible that colloidal palladium(0) formed by decomposition of **2e** is responsible for some of the activity in the later stages of the reaction. No palladium black formation was evident for catalyst **2c** within the 6 h reaction time.

Discussion

The synthetic results demonstrate that metal-templated addition of hydrazines to isocyanides can be used to prepare a series of alkyl-substituted palladium dicarbene complexes in high yields in only two steps, with the added advantages of employing aqueous solvent under air and not requiring a separate ligand synthesis. From the perspective of catalyst discovery, the primary benefit of this approach is that it provides rapid access to several variations of a modular ligand for catalytic evaluation. However, the reactions involving methylhydrazine

(72) The latter example (4-chloroacetophenone + phenylboronic acid) was not reported in ref 65.

(73) (a) Moreno-Mañas, M.; Pérez, M.; Pleixats, R. *J. Org. Chem.* **1996**, *61*, 1, 2346−2351. (b) Wong, M. S.; Zhang, X. L. *Tetrahedron Lett.* **2001**, *42*, 4087−4089. (c) Lei, A.; Zhang, X. *Tetrahedron Lett.* **2002**, *43*, 2525−2528.

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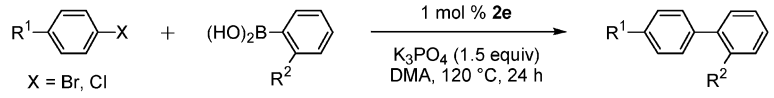
(77) (a) Reetz, M. T.; Westermann, E. *Angew. Chem., Int. Ed.* **2000**, *39*, 165−168. (b) Leadbeater, N. E.; Marco, M. *Org. Lett.* **2002**, *4*, 2973−2976. (c) Alimardanov, A.; Schmieder-van de Vondervoort, L.; de Vries, A. H. M.; de Vries, J. G. *Adv. Synth. Catal.* **2004**, *346*, 1812−1817. (d) Bhattacharya, S.; Srivastava, A.; Sengupta, S. *Tetrahedron Lett.* **2005**, *46*, 3557−3560.

Table 9. Functional Group Tolerance and Air/Moisture Tolerance of Suzuki−Miyaura Cross-Coupling Reactions Catalyzed by Optimized Catalyst 2e[a]



entry	aryl halide	R^2	product	atmosphere[b]	yield (%)[c]	homocoupling product (TON)[d]
1a	O_2N—Br	H	O_2N—	N_2	92 (92)	0.19
1b				air	90	0.45
2a	NC—Br	H	NC—	N_2	97	0.17
2b				air	97	0.27
3a	O(Me)—Br	H	O(Me)—	N_2	98 (91)	0.13
3b				air	98	0.49
4a	—Br	H	—	N_2	97	-
4b				air	92	-
5a	Me—Br	H	Me—	N_2	98	0.11
5b				air	76	0.51
6a	MeO—Br	H	MeO—	N_2	89	0.10
6b				air	62	0.69
7a	—Br	Me	—	N_2	87	nd[e]
7b				air	74	nd[e]
8	O_2N—Cl	H	O_2N—	N_2	92	0.18
9	NC—Cl	H	NC—	N_2	93	0.11
10	O(Me)—Cl	H	O(Me)—	N_2	37	0.072
11	Me—Cl	H	Me—	N_2	4	0.17
12	MeO—Cl	H	MeO—	N_2	4	0.023

[a] Reaction conditions: 0.017 mmol of precatalyst, 1.7 mmol of PhBr, 2.6 mmol of $PhB(OH)_2$, 2.6 mmol of K_3PO_4, DMA, 120 °C, 24 h. [b] Reactions under N_2 conducted in anhydrous DMA; reactions under air conducted open to atmosphere in undried DMA. [c] Yields determined by ^1H NMR; isolated yields in parentheses. [d] TON = moles biphenyl/moles catalyst; determined by GC. [e] None detected.

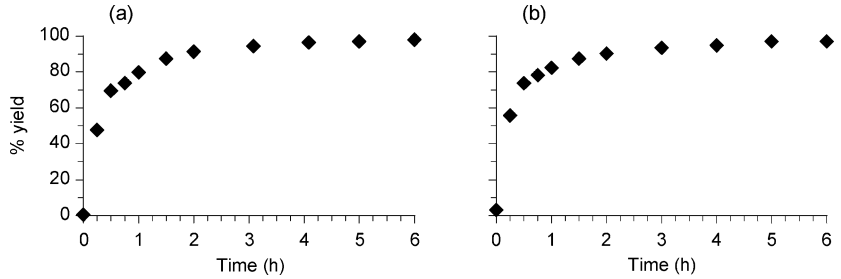


Figure 4. Yield versus time plots for Suzuki−Miyaura cross-coupling of bromobenzene with phenylboronic acid catalyzed by (a) **2c** and (b) **2e**.

suggest that this synthetic route is probably limited in its ability to provide carbene ligands with substantial steric bulk adjacent to the metal coordination sphere. Such bulk is thought to play an important role in catalytic cross-coupling reactions by increasing the rate of product-forming reductive elimination.[16] Whereas the methylhydrazine-derived precursor complex **1e** is expected to have an *anti* orientation of one terminal methyl group that directs it toward the palladium center, the corresponding dibromide complex does not retain this configuration, apparently due to steric interactions with a halide ligand. Similar steric interactions within the square coordination plane of palladium are a likely reason for the failure to form dicarbene complexes from reactions of methylhydrazine with bulkier alkylisocyanides.

Another possible limitation of these dicarbene ligands is the presence of acidic N−H groups. It is likely that these N−H functionalities are deprotonated to some degree in the presence of the base used under catalytic Suzuki−Miyaura conditions, and this might lead to decomposition and deposition of palladium black as observed in the later stages of reactions with catalyst **2e**. However, the lack of induction periods or sigmoidal yield versus time plots, which have been considered as evidence of catalysis by colloidal palladium in palladacycle Heck coupling systems,[76] supports catalysis by intermediates with intact though possibly deprotonated carbene ligands.

The substantial differences in catalytic Suzuki−Miyaura cross-coupling activity observed for the different palladium dicarbene complexes are difficult to rationalize on the basis of structural data. Ligand sterics are unlikely to be responsible, as the alkyl groups are directed away from the substrate binding sites, and the catalytic activities of the complexes do not correlate with alkyl group bulk. No other significant structural differences in the carbene moieties of the different complexes were apparent. Ligand electronic effects are a possible origin

of the differences in activity. The consensus mechanistic view is that increased σ-donation from ligands such as electron-rich phosphines[60−64] and NHCs[12−17] enhances Suzuki−Miyaura cross-coupling activity by boosting the rate of aryl halide oxidative addition and preventing ligand dissociation that could lead to catalyst destruction.[16] Increasing the size of an alkyl group is generally considered to increase the electron density at the substituted atom via the inductive effect.[78] Thus, larger alkyl substituents might be expected to result in more electron-rich and more strongly σ-donating carbene ligands. This is consistent with the higher activities of the precatalysts containing secondary alkyls (^{i}Pr, Cy) compared with the parent methyl-substituted complexes **2a** and **3a** (Table 8). However, *tert*-butyl-substituted complexes **2d** and **3d** do not fit this trend, as they exhibited the poorest catalytic activities. One effect that could counteract the inductive donation trend is the greater polarizability of a larger alkyl group.[79] This can result in a larger alkyl substituent effectively acting as an electron-*withdrawing* group in certain cases, particularly in reactions involving a buildup of negative charge such as gas-phase deprotonations of alcohols.[79,80] Such a charge buildup could occur in these catalytic systems if the dicarbene ligands are deprotonated. A plausible explanation for the trend in catalytic activities is that the donor abilities of the dicarbene ligands are influenced by opposing inductive and polarizability effects. In this scenario, inductive effects predominate for secondary alkyls, leading to greater σ-donation by the carbene moieties, whereas the polarizibility effect is dominant for *tert*-butyl groups, resulting in a more weakly donating ligand. The dicarbene ligands of the most active precatalysts, **2e** and **3e**, are more highly substituted than the other dicarbenes due to the backbone methyl group, and therefore they might be expected to have increased σ-donor ability. The ^{13}C NMR data for precatalysts **2a**−**e** and **3a**−**e** do not indicate substantial electronic differences among the carbene ligands, with a fairly narrow range of carbene chemical shifts observed (δ 176−183, Table 3). The striking outcome of this study is that substantial differences in the catalytic activity of the various complexes are observed despite the lack of distinguishing structural or spectroscopic features. This suggests that seemingly minor differences in ligand electronics can exert significant effects on the rates of key reactions in a catalytic cycle, and such effects are probably very difficult to predict.

Aside from their ease of synthesis, the primary advantage of the new palladium dicarbene catalysts over the majority of known Suzuki−Miyaura cross-coupling systems is their ability to operate effectively under air. Only a few palladium catalysts have been reported to perform Suzuki−Miyaura couplings under aerobic conditions.[71,75,81−85] Most of these examples employ chelating ligands,[82,85] primarily involving nitrogen donors.[71,75,81] To our knowledge, the only other example of a carbene-ligated Suzuki catalyst reported to function under air is a chelating pincer-type NHC complex.[82] Considering these precedents, it is probable that chelation of palladium by the bidentate diaminocarbene ligands enhances the stabilities of the catalysts under aerobic conditions, perhaps by preventing the formation of oxidatively unstable low-ligated intermediates. However, chelation may also limit the activity that can be attained by these catalysts, given that several studies of highly active Suzuki−Miyaura catalysts have suggested that formation of monoligated palladium intermediates[86] is required for high catalytic rates.[13,14,16,17,61,87] Thus, the room-temperature activity and high-yield couplings of unactivated aryl chlorides attained by these monodentate ligand-based systems may be out of reach for catalysts containing nonlabile chelate ligands such as the diaminocarbenes reported herein. This is in agreement with reported examples of Suzuki−Miyaura cross-coupling reactions employing chelated palladium(II)-NHC precatalysts, all of which require high temperatures (> 110 °C) and show limited activities with aryl chlorides.[24,82,88,89] Overall, the optimized catalyst **2e** compares favorably in terms of yields and substrate scope with other aerobic Suzuki−Miyaura catalysts. To the best of our knowledge, only four aerobic Suzuki−Miyaura systems have been reported to achieve high yields for aryl bromides containing a comparable range of functional groups,[71,83,85] and **2e** is free from the problem of significant homocoupling side product formation that has been observed in some aerobic Suzuki−Miyaura catalysts.[75]

Conclusion

A series of modular chelating diaminocarbene complexes of palladium have been prepared using a facile, procedurally simple synthetic method based on metal-templated addition of hydrazines to alkylisocyanides. Structural and spectroscopic data as well as Suzuki−Miyaura cross-coupling activities indicate that the new carbene ligands possess strong donor properties similar to those of imidazole-based N-heterocyclic carbenes. Systematic modification of the carbene substituents allowed rapid identification of a backbone-substituted palladium dicarbene complex as the most promising Suzuki−Miyaura cross-coupling catalyst. Although it does not exhibit the high catalytic activities in couplings of electron-rich aryl chlorides that have been attained by Suzuki−Miyaura catalysts containing monodentate carbene or phosphine ligands, this optimized catalyst has the advantage of maintaining high yields under air in many aryl bromide coupling reactions without significant byproduct formation. The catalyst optimization studies indicated that seemingly minor variations in ligand electronic properties can drastically affect catalytic activity, accentuating the importance of a modular ligand design that allows systematic variation of ligand substituents for rapid catalyst screening. Future studies will seek to extend this modular synthetic strategy to diaminocarbene ligands that do not contain acidic N−H groups as well as more

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structurally diverse examples derived from bulky or chiral diamine precursors.

Experimental Section

General Considerations. All syntheses were performed under air. Methylisocyanide was synthesized by a literature procedure.[90] Isopropylisocyanide (Strem, 99%), *tert*-butylisocyanide (Strem, 98%), cyclohexylisocyanide (Fluka, ≥98%), hydrazine hydrate (Acros), methylhydrazine (Aldrich, 98%), phenylhydrazine (Eastman, 97%), $PdCl_2$ (Alfa, 99.9%), KCl (Spectrum, reagent), and $LiClO_4$ (Aldrich, 95+%) were used as received. **CAUTION:** Perchlorate salts are potentially explosive, and they should be handled with care and in small quantities. Solvents used for syntheses and recrystallization: acetonitrile (EM Science), $CHCl_3$ (Pharmco), CH_2Cl_2 (Pharmco), Et_2O (Acros), DMSO (Fisher), and hexane (Pharmco) were of reagent grade and were used without purification. Water was purified by an E-pure system (Barnstead) and had a resistivity of ≥17.6 MΩ-cm. Suzuki−Miyaura substrates 4-bromoacetophenone (Aldrich), 4-bromonitrobenzene (Eastman), 4-bromobenzene (Aldrich), 4-chlorobenzene (Aldrich), and 4-chloronitrobenzene (Eastman) were purified by literature procedures[91] from samples that had been in use >4 years. All other aryl halides and arylboronic acids were purchased from Acros or Aldrich in the highest available purity and used as received. Anhydrous K_3PO_4 (Aldrich, 97%), $K_3PO_4 \cdot H_2O$ (Acros, c.p.), K_2CO_3 (Aldrich, anhydrous reagent), NaO^{t}Bu (Acros, 98%), CsF (Acros, 99.9%), and Cs_2CO_3 (Acros, 99.5%) were used as received. For Suzuki−Miyaura cross-coupling reactions, anhydrous DMA (Acros, septum-sealed bottle) was used as received for reactions under inert atmosphere, and undried DMA (Acros, 99+%) was used as received for aerobic reactions.

NMR spectra were recorded on a Varian Unity INOVA 400 MHz spectrometer. Reported chemical shifts are referenced to residual solvent peaks. NMR solvents were purchased from Cambridge Isotope Laboratories and were generally used as received. When dry NMR solvents were needed, they were dried over degassed 4 Å molecular sieves and then vacuum transferred into a glass ampule before use in the glovebox (CD_3CN, DMSO-d_6, DMF-d_7) or stored over P_2O_5 and vacuum transferred into a J Young NMR tube containing the sample (CD_2Cl_2). IR spectra were acquired from Nujol mulls on a Nicolet Protégé 460 FT-IR spectrometer. GC analyses utilized a Hewlett-Packard 6850 gas chromatograph with a 100% dimethylpolysiloxane capillary column (HP-1, Agilent Technologies, 0.25 mm i.d. × 30 m) and a flame ionization detector. For determination of concentrations by GC, multilevel calibration plots were performed with stock solutions of analytes and internal standard (diethylene glycol dibutyl ether) that approximated experimental concentrations. Elemental analyses were performed by Desert Analytics, Tucson, AZ.

Synthesis of $[Pd(C_4H_9N_4)(CNMe)_2][ClO_4]$ (1a). Methylisocyanide (213 mg, 5.18 mmol) was added to a stirred solution of K_2PdCl_4, prepared in situ from $PdCl_2$ (200 mg, 1.13 mmol) and KCl (336 mg, 4.51 mmol) in 20 mL of H_2O at room temperature. Excess hydrazine hydrate (1.0 mL, 15 equiv) was added to the resulting colorless solution of $[Pd(CNMe)_4]^{2+}$ to give a yellow solution. Dropwise addition of a saturated solution of $LiClO_4$ in H_2O resulted in the formation of an orange precipitate, which was collected by filtration, washed with water, and dried in vacuo over P_2O_5. The product was recrystallized by dissolution in a minimum amount of hot CH_3CN, followed by filtration and slow addition of Et_2O to give yellow-orange crystals (293 mg, 65%). Anal. Calcd for $C_8H_{15}N_6ClO_4Pd$: C, 23.96, H, 3.77, N, 20.95. Found: C, 24.10, H, 3.91, N, 20.77.

Synthesis of $[Pd(C_8H_{17}N_4)(CN^iPr)_2][ClO_4]$ (1b). Isopropylisocyanide (340 mg, 4.93 mmol) was added to a stirred solution of K_2PdCl_4, prepared in situ from $PdCl_2$ (217 mg, 1.22 mmol) and KCl (377 mg, 5.05 mmol) in 40 mL of H_2O at room temperature. Hydrazine hydrate (2.0 mL, 26 equiv) was then added to the resulting colorless solution of $[Pd(CNCy)_4]^{2+}$, affording a yellow solution. Excess $LiClO_4$ (1.043 g, 8 equiv) was added to the yellow solution to precipitate the product, which was collected by filtration, washed with water, and dried in vacuo over P_2O_5. Recrystallization of the product was achieved by slow diffusion of Et_2O into a $CHCl_3$ solution of the compound to yield yellow, needle-shaped crystals (533 mg, 85%). Anal. Calcd for $C_{16}H_{31}N_6ClO_4Pd$: C, 37.44, H, 6.09, N, 16.37. Found: C, 37.41, H, 6.35, N, 15.95.

Synthesis of $[Pd(C_{14}H_{25}N_4)(CNCy)_2][ClO_4]$ (1c). Cyclohexylisocyanide (400 mg, 3.68 mmol) was added to a stirred solution of K_2PdCl_4, prepared in situ from $PdCl_2$ (163 mg, 0.92 mmol) and KCl (274 mg 3.68 mmol) in 30 mL of H_2O at room temperature. Excess hydrazine hydrate (1.5 mL, 26 equiv) was added to the resulting colorless solution of $[Pd(CNCy)_4]^{2+}$ to give a yellow precipitate, which was collected by filtration, washed with aqueous $LiClO_4$ and water, and dried in vacuo over P_2O_5 (455 mg, 73%). Anal. Calcd for $C_{28}H_{47}N_6ClO_4Pd$: C, 49.93, H, 7.03, N, 12.48. Found: C, 50.32, H, 6.65, N, 12.48.

Synthesis of $[Pd(C_{10}H_{21}N_4)(CN^tBu)_2][ClO_4]$ (1d). *tert*-Butylisocyanide (305 mg, 3.63 mmol) was added to a stirred solution of K_2PdCl_4, prepared in situ from $PdCl_2$ (163 mg, 0.92 mmol) and KCl (274 mg, 3.67 mmol) in 30 mL of H_2O at room temperature. Hydrazine hydrate (1.5 mL, 26 equiv) was added to the resulting colorless solution of $[Pd(CN^tBu)_4]^{2+}$ to give a yellow solution. Excess $LiClO_4$ (391 mg, 4 equiv) was added to the yellow solution to precipitate the product, which was collected by filtration, washed with water, and dried in vacuo over P_2O_5. Recrystallization of the product was achieved by slow diffusion of Et_2O into a $CHCl_3$ solution of the compound to yield yellow crystals (352 mg, 67%). Anal. Calcd for $C_{20}H_{39}N_6ClO_4Pd$: C, 42.18, H, 6.90, N, 14.76. Found: C, 42.42, H, 7.20, N, 14.60.

Synthesis of $[Pd(C_5H_{11}N_4)(CNMe)_2][ClO_4]$ (1e). Methylisocyanide (100 mg, 2.45 mmol) was added to a stirred solution of K_2PdCl_4, prepared in situ from $PdCl_2$ (108 mg, 0.61 mmol) and KCl (190 mg, 2.54 mmol) in 8 mL of H_2O at room temperature. Excess methylhydrazine (65 μL, 2 equiv) was added to the resulting pale yellow solution of $[Pd(CNMe)_4]^{2+}$ to give an orange solution. Excess $LiClO_4$ (400 mg, 6 equiv) was then added to precipitate the product as an orange solid, which was collected by filtration, washed with cold water, and dried in vacuo over P_2O_5 (218 mg, 86%). Anal. Calcd for $C_9H_{17}N_6ClO_4Pd$: C, 26.04, H, 4.13, N, 20.24. Found: C, 25.86, H, 4.16, N, 19.86.

Synthesis of $Pd(C_4H_{10}N_4)Cl_2$ (2a). Compound **1a** (340 mg, 0.848 mmol) was dissolved in hot 3 M aqueous HCl, and the solution was then allowed to cool with stirring until a white precipitate formed. The solid was filtered, washed with water, and dried in vacuo over P_2O_5 (225 mg, 92%). Anal. Calcd for $C_4H_{10}N_4Cl_2Pd$: C, 16.48, H, 3.46, N, 19.22. Found: C, 16.55, H, 3.54, N, 19.07.

Synthesis of $Pd(C_4H_{10}N_4)Br_2$ (3a). Compound **1a** (332 mg, 0.828 mmol) was dissolved in hot 3 M aqueous HBr, and the solution was then allowed to cool with stirring until a white precipitate formed. The solid was filtered, washed with water, and dried in vacuo over P_2O_5 (287 mg, 91%). Anal. Calcd for $C_4H_{10}N_4Br_2Pd$: C, 12.63, H, 2.65, N, 14.73. Found: C, 12.8, H, 2.56, N, 14.47.

Synthesis of $Pd(C_8H_{18}N_4)Cl_2$ (2b). A 3 M aqueous solution of HCl was added dropwise to a CH_3CN solution (15 mL) of compound **1b** (260 mg, 0.506 mmol) until the solution became colorless. The volume of the solution was reduced until a white precipitate formed. Et_2O was added dropwise to complete precipitation of the solid, which was collected by filtration, washed with

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Table 10. Crystal Data and Structure Refinement Details

	1b	3b	3c	3d	3e
chem formula	$C_{16}H_{31}ClN_6O_4Pd$	$C_8H_{18}Br_2N_4Pd\cdot 2C_2H_6SO$	$C_{14}H_{26}Br_2N_4Pd$	$C_{10}H_{22}Br_2N_4Pd\cdot 2C_2H_6SO$	$C_5H_{12}Br_2N_4Pd\cdot C_2H_6SO$
fw	513.32	592.74	516.61	620.79	472.53
cryst syst	orthorhombic	triclinic	monoclinic	monoclinic	triclinic
space group	$P2_12_12_1$	$P\bar{1}$	$C2/c$	$P2_1/c$	$P\bar{1}$
cryst size (mm)	0.32 × 0.18 × 0.14	0.32 × 0.12 × 0.10	0.42 × 0.18 × 0.07	0.3 × 0.3 × 0.3	0.12 × 0.10 × 0.06
color, habit	yellow needle	colorless needle	colorless plate	colorless parallelepiped	colorless prism
growth method	slow diff ether/$CHCl_3$	slow diff ether/DMSO	slow diff ether/DMF	slow diff ether/DMSO	slow diff ether/DMSO
diffractometer	Bruker APEX	Bruker APEX	Bruker APEX	Syntex P21	Bruker APEX
temp (K)	103(2)	103(2)	296(2)	293(2)	103(2)
unit cell dimens					
a (Å)	8.0840(5)	10.8099(8)	26.2920(12)	11.698(2)	7.5348(10)
b (Å)	13.8728(9)	11.3178(9)	7.6568(3)	11.767(2)	9.0018(12)
c (Å)	20.2548(13)	11.3765(9)	9.6383(4)	21.873(6)	10.5540(14)
α (deg)	90	74.7190(10)	90	90	83.427(2)
β (deg)	90	62.9710(10)	107.610(3)	121.70(2)	88.080(2)
γ (deg)	90	62.2700(10)	90	90	81.682(2)
volume (Å^3)	2271.5(3)	1095.04(15)	1849.38(14)	2561.6(9)	703.55(16)
Z	4	2	4	4	2
abs correction	multiscan	multiscan	multiscan	psi-scan	multiscan
μ (mm^{-1})	0.967	4.698	5.324	4.021	7.134
θ range (deg)	2.01 to 28.32	2.01 to 28.30	3.25 to 28.30	2.05 to 28.00	1.94 to 28.35
index ranges	$-10 \le h \le 10$ $-18 \le k \le 18$ $-26 \le l \le 27$	$-14 \le h \le 14$ $-14 \le k \le 14$ $-14 \le l \le 14$	$-25 \le h \le 34$ $-8 \le k \le 10$ $-12 \le l \le 12$	$0 \le h \le 15$ $-15 \le k \le 0$ $-28 \le l \le 24$	$-10 \le h \le 10$ $-11 \le k \le 11$ $-13 \le l \le 14$
no. reflns collected	27 748	13 623	6130	6427	14 048
no. indep reflns [R_{int}]	5444 [0.0143]	5148 [0.0161]	2261 [0.0211]	6148 [0.0826]	14 048 [0.0000]
R indices ($I > 2\sigma(I)$)	R1 = 0.0149 wR2 = 0.0394	R1 = 0.0173 wR2 = 0.0452	R1 = 0.0411 wR2 = 0.0878	R1 = 0.0616 wR2 = 0.1664	R1 = 0.0445 wR2 = 0.1208
R indices (all data)	R1 = 0.0151 wR2 = 0.0395	R1 = 0.0179 wR2 = 0.0455	R1 = 0.0476 wR2 = 0.0894	R1 = 0.1282 wR2 = 0.2197	R1 = 0.0463 wR2 = 0.1219

Et_2O, and dried in vacuo (164 mg, 93%). Anal. Calcd for $C_8H_{18}N_4Cl_2Pd$: C, 27.64, H, 5.22, N, 16.12. Found: C, 27.97, H, 5.17, N, 15.75.

Synthesis of $Pd(C_8H_{18}N_4)Br_2$ (3b). A 3 M aqueous solution of HBr was added dropwise to a CH_3CN solution (10 mL) of compound **1b** (243 mg, 0.473 mmol) until a colorless solution was formed. The volume of the solution was reduced until a white precipitate formed. Et_2O was added dropwise to complete precipitation of the solid, which was collected by filtration, washed with Et_2O, and dried in vacuo (137 mg, 66%). Anal. Calcd for $C_8H_{18}N_4Br_2Pd$: C, 22.01, H, 4.16, N, 12.84. Found: C, 22.37, H, 4.46, N, 12.60.

Synthesis of $Pd(C_{14}H_{26}N_4)Cl_2$ (2c). A 3 M aqueous solution of HCl was added dropwise to a CH_3CN solution (15 mL) of compound **1c** (0.201 g, 0.298 mmol) until a pale yellow solution was formed. The volume of the solution was reduced until a white precipitate formed. Et_2O was added dropwise to complete precipitation of the solid, which was collected by filtration, washed with Et_2O, and dried in vacuo (83 mg, 65%). Anal. Calcd for $C_{14}H_{26}N_4Cl_2Pd$: C, 39.31, H, 6.13, N, 13.10. Found: C, 39.72, H, 6.11, N, 13.14.

Synthesis of $Pd(C_{14}H_{26}N_4)Br_2$ (3c). A 3 M aqueous solution of HBr was added dropwise to a CH_3CN solution (15 mL) of compound **1c** (109 mg, 0.162 mmol) until a pale yellow solution was formed. The volume of the solution was reduced until a white precipitate formed. Et_2O was added dropwise to complete precipitation of the solid, which was collected by filtration, washed with Et_2O, and dried in vacuo (60 mg, 72%). Anal. Calcd for $C_{14}H_{26}N_4Br_2Pd$: C, 32.56, H, 5.07, N, 10.84. Found: C, 33.01, H, 5.04, N, 10.60.

Synthesis of $Pd(C_{10}H_{22}N_4)Cl_2$ (2d). A 3 M aqueous solution of HCl was added dropwise to a CH_3CN solution (25 mL) of compound **1d** (400 mg, 0.702 mmol) until a colorless solution was formed. The volume of the solution was reduced until a white precipitate formed. Et_2O was added dropwise to complete precipitation of the solid, which was collected by filtration, washed with Et_2O, and dried in vacuo (253 mg, 96%). Anal. Calcd for $C_{10}H_{22}N_4Cl_2Pd$: C, 31.97, H, 5.90, N, 14.92. Found: C, 31.97, H, 5.85, N, 14.52.

Synthesis of $Pd(C_{10}H_{22}N_4)Br_2$ (3d). A 3 M aqueous solution of HBr was added dropwise to a CH_3CN solution (25 mL) of compound **1d** (400 mg, 0.702 mmol) until a colorless solution was formed. The volume of the solution was reduced until a white precipitate formed. Et_2O was added dropwise to complete precipitation of the solid, which was collected by filtration, washed with Et_2O, and dried in vacuo (204 mg, 63%). Anal. Calcd for $C_{10}H_{22}N_4Br_2Pd$: C, 25.86, H, 4.77, N, 12.06. Found: C, 25.98, H, 4.74, N, 11.85.

Synthesis of $Pd(C_5H_{12}N_4)Cl_2$ (2e). Compound **1e** (100 mg, 0.241 mmol) was dissolved in hot 3 M aqueous HCl, and the resulting solution was allowed to cool with stirring until a white precipitate formed. The solid was filtered, washed with water, and dried in vacuo over P_2O_5 (51 mg, 70%). Anal. Calcd for $C_5H_{12}N_4Cl_2Pd$: C, 19.66, H, 3.96, N, 18.34. Found: C, 19.77, H, 3.83, N, 18.07.

Synthesis of $Pd(C_5H_{12}N_4)Br_2$ (3e). Compound **1e** (89 mg, 0.214 mmol) was dissolved in hot 3 M aqueous HCl, and the resulting solution was allowed to cool with stirring until a white precipitate formed. The solid was filtered, washed with water, and dried in vacuo over P_2O_5 (72 mg, 85%). Anal. Calcd for $C_5H_{12}N_4Br_2Pd$: C, 15.23, H, 3.07, N, 14.20. Found: C, 15.14, H, 2.90, N, 13.85.

X-ray Crystallographic Analyses. Crystal data and refinement details for all X-ray crystallographic analyses are presented in Table 10. X-ray diffraction data for **1b**, **3b**, **3c**, and **3e** were collected on a Bruker APEX diffractometer with a CCD detector using combinations of φ and ω scans. Data integration employed the Bruker SAINT software package.[92] For **3d**, data were obtained on a Syntex P21 point-detector instrument using $\theta/2\theta$ scans, and data reduction employed REDUCE (UCLA crystallographic package). All X-ray diffraction experiments employed graphite-monochromated Mo Kα radiation ($\lambda = 0.71073$ Å). Structures were solved by direct methods

(92) *SAINT-plus*, Version 6.29; Bruker AXS: Madison, WI, 2001.

and refined by full-matrix least-squares on F^2 using the SHELXTL suite.[93] Non-hydrogen atoms were assigned anisotropic temperature factors, with hydrogen atoms included in calculated positions (riding model). For **3d**, the hydrogen-bound DMSO molecules were modeled as disordered, with the sulfur atoms occupying two possible positions for each DMSO. The occupancy factors of the sulfurs in the dominant orientations refined to values of 0.838 and 0.895 for the two different DMSO molecules.

General Procedure for Catalytic Suzuki−Miyaura Cross-Coupling Reactions. Base (2.57 mmol, 1.5 equiv), aryl halide (1.7 mmol), and arylboronic acid (2.04−2.57 mmol, 1.2−1.5 equiv) were added to a flask, followed by addition of a solution of the precatalyst (0.017 mmol) in DMA (5 mL). For reactions performed under N_2, all manipulations were done in a drybox, anhydrous DMA was employed, and the flask was sealed with a Teflon stopcock. For aerobic reactions, all manipulations were done on the benchtop, wet DMA was used, and the flask was connected to a reflux condenser open to air. The flask was placed in a preheated oil bath at 120 °C and stirred for 24 h. After cooling the reaction mixture, 100 μL of diethylene glycol dibutyl ether (GC and NMR internal standard) was added to the flask. A 200 μL aliquot of the reaction mixture was then added to 10 mL of CH_2Cl_2. The organic layer was extracted four times with 10 mL portions of water and then dried over $MgSO_4$, and the CH_2Cl_2 was removed in vacuo. The residue was dissolved in $CDCl_3$ and analyzed by ^{1}H NMR spectroscopy. The product peak assignments were based on authentic samples or on published data.[63,94] In some cases the product was isolated and purified by extraction of the whole reaction mixture with CH_2Cl_2, followed by silica flash chromatography (4:1 hexanes/ethyl acetate). In some reactions, the amount of homocoupling product was determined by GC analysis of the CH_2Cl_2 extract.

Yield versus Time for Suzuki−Miyaura Cross-Coupling Reactions. In a glovebox, K_3PO_4 (478 mg, 2.25 mmol), bromobenzene (158 μL, 1.5 mmol), and phenylboronic acid (2.25 mmol, 1.5 equiv) were added to a threaded vial containing a stir bar, followed by addition of diethylene glycol dibutyl ether (GC internal standard, 40 μL) and a solution of the precatalyst (0.015 mmol) in anhydrous DMA (3 mL). The vial was sealed with a screw cap containing a PTFE-silicone septum and stirred briefly at room temperature to mix the reagents. The vial was then placed in a preheated oil bath at 120 °C. Aliquots (5 μL) of the reaction mixture were removed after fixed times with a syringe and added to 50 μL of CH_2Cl_2. These mixtures were filtered through a glass microfiber plug and analyzed by GC.

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Supporting Information Available: Tabulated full IR spectral data for reported compounds; tabulated structural data for possible intramolecular N(H)···Br interactions in **3b**−**e**; crystallographic data for **1b**, **3b**, **3c**, **3d**, and **3e** in CIF format. This material is available free of charge via the Internet at http://pubs.acs.org.

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(93) *SHELXTL*, Version 6.14; *SHELXS* (structure solution, 1990); *SHELXL* (structure refinement, 1997); *XP* (Version 5.1, graphics); Bruker AXS: Madison, WI, 2000.

(94) Okamoto, K.; Akiyama, R.; Kobayashi, S. *Org. Lett.* **2004**, *6*, 1987−1990.