From Pyrroles to Isoindolines: Synthesis of a γ-Diimine Ligand for Applications in Palladium Coordination Chemistry and Catalysis

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The γ-diimine 1,2-(2,6-^{i}Pr$_2$-C$_6$H$_3$NC)$_2$-C$_6$H$_4$ (**2**) was synthesized by the reaction of phthalaldehyde with 2,6-diisopropylaniline. Depending on reaction conditions, **2** can cyclize to form the corresponding iminoisoindoline or isoindolinone. Unlike analogous α- and β-diimine complexes, reaction of the γ-diimine **2** with (MeCN)$_2$PdCl$_2$ results in a dinuclear complex, [(γ-diimine)PdCl(μ-Cl)]$_2$ (**5**), where the ligand does not coordinate to the Pd(II) center in a chelating fashion but instead adopts a monodentate coordination mode. On the other hand, reaction of **2** with Pd(OAc)$_2$ results in C−H activation and formation of the trinuclear Pd$_3$(OAc)$_4$-based palladacycle {1,2-(2,6-^{i}Pr$_2$-C$_6$H$_3$NC)$_2$-C$_6$H$_3$]Pd(μ-OAc)$_2$}$_2$Pd (**6**). The resulting palladium complexes were tested as precatalysts in Heck and Suzuki coupling reactions.

Introduction

α-Diimines based on 1,4-diazabutadienes of the general formula RN═CR′CR′═NR have received considerable attention in recent years due to their application as ligands in a wide variety of catalytic reactions. It was initial reports by Brookhart in the field of olefin polymerization and olefin/CO copolymerization using Ni(II) and Pd(II) complexes that have initiated the widespread interest in applications of these diimines as ligands.[1,2] Group 10 complexes with diazabutadiene ligands showed activities higher than those of the classical Ziegler catalysts and exhibited a greatly reduced susceptibility to poisoning by polar functionalities.[3] Pd(II) complexes of diimines have also been reported to be active catalysts for the Suzuki, Heck, Sonogashira, and Hiyama coupling reactions.[4]

This class of ligand has become increasingly popular, due to its ease of synthesis and outstanding steric and electronic tunability. The most common synthetic route to diimine ligands

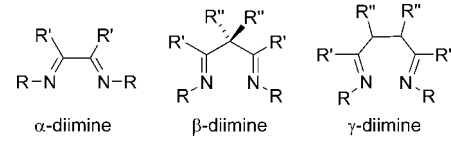
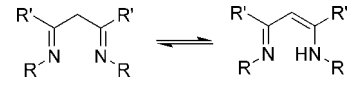


Figure 1

Scheme 1



is a simple condensation reaction of primary amines or anilines with diketones or dialdehydes, thereby producing a wide range of α- and β-diimines (Figure 1).

In 1997, β-diimine ligands analogous to Brookhart's α-diimines were synthesized and their reactivity was explored in the formation of group 10 complexes.[5] β-Diimines are usually best interpreted as β-diketimines, due to the acidic nature of the methylene protons (Scheme 1), and have been successfully employed as monoanionic ligands in a wide variety of reactions.[6]

β-diimine variations in which the acidic protons have been substituted by alkyl groups to form stable neutral ligands have

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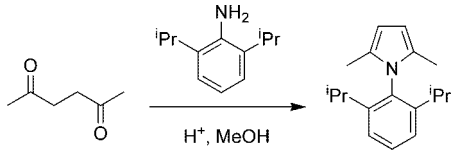
Scheme 2



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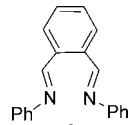
recently been reported.[6c,f,7] The corresponding Pd(II) complexes were found to be active precatalysts for C−C coupling reactions.[6c]

There is one report in the patent literature concerning the synthesis of a cobalt complex of **A**, which polymerizes ethylene in the presence of methylaluminoxane.[2,8] This represents the



A

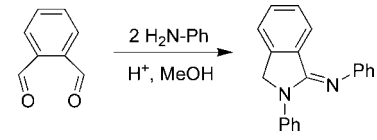
only report of a γ-diimine in the published literature. Analogous γ-diimines have, however, been proposed as intermediates in the synthesis of iminoisoindolines and isoindolinones.[9] We initially envisioned that the synthesis of γ-diimine compounds might be a general reaction leading to a new class of diimine ligands; however, intramolecular cyclization reactions have to date inhibited this notion. Herein we report the synthesis of a γ-diimine ligand and subsequent formation of Pd(II) complexes. Depending on the reaction conditions, cyclization of the γ-diimine can be induced to form either the corresponding iminoisoindoline or the isoindolinone. The resulting (γ-diimine)Pd^{II} complexes were tested as precatalysts for Suzuki and Heck coupling reactions.

Results and Discussion

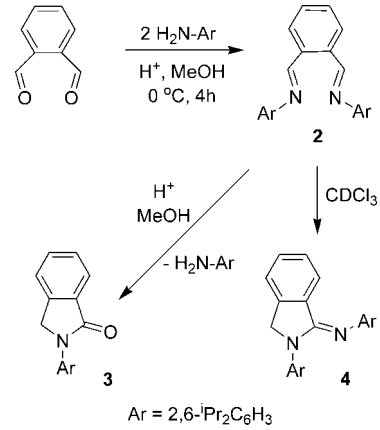
Synthesis of a γ-Diimine. Attempts to synthesize a γ-diimine ligand from a simple diketone such as 2,5-hexanedione and 2,6-diisopropylaniline in acidified methanol yielded only the pyrrole **1** via a Paal−Knorr synthesis as the sole product, regardless of stoichiometry (Scheme 2). The same pyrrole was recently synthesized employing metal triflates as catalysts.[10]

Use of a constrained dialdehyde such as phthalaldehyde should inhibit pyrrole formation, possibly allowing for isolation of the desired γ-diimine. As mentioned earlier, reactions of phthalaldehyde with primary amines have been known for several decades and usually result in formation of the corresponding iminoisoindoline or isoindolinone, depending on reaction conditions. While γ-diimines have been postulated as intermediates in the formation of iminoisoindolines or isoindolinones, only γ-diimine **A** has ever been isolated.[8,9]

Scheme 3



Scheme 4



Ar = 2,6-$^{i}Pr_2C_6H_3$

In our hands, all attempts to synthesize γ-diimine **A** were unsuccessful, yielding only the previously reported iminoisoindoline 1-(phenylimino)-2-phenylisoindoline, according to Scheme 3.[9a] It appears unlikely that the γ-diimine **A** was ever actually isolated, as it would be prone to rapid intramolecular cyclization to the corresponding iminoisoindoline. Increasing the steric bulk on the nitrogen positions via condensation with a bulky primary amine should, however, retard or inhibit intramolecular cyclization, allowing for isolation of a γ-diimine. Thus, a γ-diimine was prepared through the reaction of phthalaldehyde with 2,6-diisopropylaniline in methanol to yield the corresponding phthalaldimine 1,2-(2,6-$^{i}Pr_2$-$C_6H_3NC)_2$-C_6H_4 (**2**) as a yellow precipitate in 66% yield (Scheme 4). The remaining products in the filtrate consisted only of the isoindolinone **3** (30% yield) and 2,6-diisopropylaniline. ^{1}H NMR of **2** in $CDCl_3$ showed one singlet downfield at δ 8.78 integrating for two protons for the imine *H*C═N, while ^{13}C NMR showed one signal at δ 161.8 for the imine indicative of a C_{2v}-symmetric species in solution at room temperature. FT-IR spectroscopy showed a single C═N stretch at 1633 cm^{-1}.

The solid-state structure of **2** has been determined by X-ray diffraction (Table 1 and Figure 2). Unlike the proposed solution structure, the solid-state structure of **2** has C_s symmetry and crystallizes preferentially as rotamer **b** (Scheme 5), where one imine is rotated into a cisoidal orientation and the other imine adopts a transoidal orientation. The solution data indicates, however, that the barrier to rotation between the three possible rotational conformers depicted in Scheme 5 is low at room temperature, resulting in fast interconversion between the rotamers and an average structure with C_{2v} symmetry. While variable-temperature ^{1}H NMR spectra support the fluxional behavior of **2**, as seen in Figure 3, even at 183 K the static limit for rotational isomerization had not been reached and discrete rotational isomers were not observed. At 296 K one doublet at δ 1.08 for the methyl groups is observed, along with a sharp singlet at δ 8.78 for the imine protons. The ^{1}H NMR spectra at 183 K showed the methyl groups as two discrete broad resonances, while the signal for the imine protons exhibited line broadening.

Interestingly, if **2** is not isolated as a precipitate from the methanolic solution, it further reacts by redissolving back into

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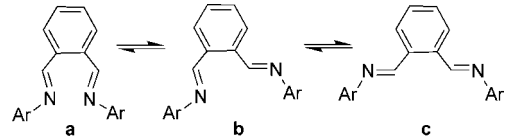
Table 1. Crystal Data and Refinement Parameters for Compounds 2−6

	2	**3**	**4**·DCl·$CDCl_3$	**5**·2$CHCl_3$	**6**·2CH_2Cl_2
formula	$C_{32}H_{40}N_2$	$C_{20}H_{23}NO$	$C_{33}H_{40}D_2Cl_4N_2$	$C_{66}H_{82}Cl_{10}N_4Pd_2$	$C_{74}H_{94}Cl_4N_4O_8Pd_3$
formula wt	452.66	293.39	608.49	1498.70	1628.53
color	yellow	colorless	colorless	orange	orange
cryst syst	orthorhombic	monoclinic	monoclinic	monoclinic	orthorhombic
space group	*Fdd*2	*C*2/*c*	$P2_1/m$	$P2_1/c$	*Pnn*2
a, Å	15.3632(15)	18.3891(6)	10.983(2)	12.5210(3)	13.101(3)
b, Å	41.9140(9)	14.9010(5)	14.196(3)	10.1820(2)	29.389(6)
c, Å	8.5520(9)	12.2811(4)	11.017(2)	27.5197(6)	10.898(2)
α, deg	90	90	90	90	90
β, deg	90	94.906(2)	106.04(3)	94.7006(8)	90
γ, deg	90	90	90	90	90
Z	8	8	2	2	2
ρ_{calcd}, Mg/m^3	1.092	1.162	1.224	1.423	1.289
temp, K	173(2)	173(2)	173(2)	173(2)	173(2)
F(000)	1968	1264	644	1536	1672
θ range, deg	3.65−25.02	3.52−26.37	2.40−27.48	2.29−27.48	2.80−25.35
final *R* ($I > 2\sigma(I)$)	R1 = 0.0848, wR2 = 0.1899	R1 = 0.0478, wR2 = 0.1090	R1 = 0.0642, wR2 = 0.1563	R1 = 0.0510, wR2 = 0.0809	R1 = 0.0444, wR2 = 0.1106
R (all data)	R1 = 0.0973, wR2 = 0.1981	R1 = 0.0743, wR2 = 0.1242	R1 = 0.0815, wR2 = 0.1658	R1 = 0.0949, wR2 = 0.0954	R1 = 0.0544, wR2 = 0.1167

Scheme 5



solution to form the corresponding isoindolinone **3** and 1 equiv of 2,6-diisopropylaniline. Thus, the yield of **2** decreases, favoring formation of isoindolinone **3** at longer reaction times. Isoindolinone **3** can be directly synthesized by reaction of phthaladehyde with 1 equiv of 2,6-diisopropylaniline at ambient temperature in 75% yield. *γ*-Diimine **2**, however, is stable in nonpolar organic solvents in the absence of protic acids for prolonged periods. ^{1}H NMR of the isoindolinone **3** in $CDCl_3$ showed a characteristic singlet at *δ* 4.56 for the two methylene protons. The solid-state structure of **3** has been determined by X-ray diffraction and is depicted in Figure 4 (Table 1). The structure of **3** has been previously communicated.[11]

Slow cyclization of *γ*-diimine **2** to form the corresponding iminoisoindoline **4** in quantitative yield is observed in $CDCl_3$ (Scheme 4). Presumably the reaction is catalyzed by trace DCl present in the solvent. Observation of **2** by ^{1}H NMR spectroscopy in $CDCl_3$ showed that, over the course of 12 h at 60 °C, 50% of the *γ*-diimine underwent cyclization to form the corresponding iminoisoindoline **4**. Heating for an additional 12 h resulted in quantitative cyclization of **2** to the iminoisoindoline (Figure 5). ^{1}H NMR spectra of **4** in $CDCl_3$ showed a characteristic singlet at *δ* 4.69 for the two methylene protons.

Prolonged exposure of iminoisoindoline **4** to $CDCl_3$ resulted in precipitation of the DCl salt of iminoisoindoline (**4**-DCl) as X-ray-quality crystals. The solid-state structure of **4**-DCl was subsequently determined by X-ray diffraction (Table 1 and Figure 6). The iminoisoindoline bicyclic ring is lying on a mirror plane. The two diisopropylphenyl moieties are bisected by the mirror plane and are thus perpendicular to the primary isoindoline ring.

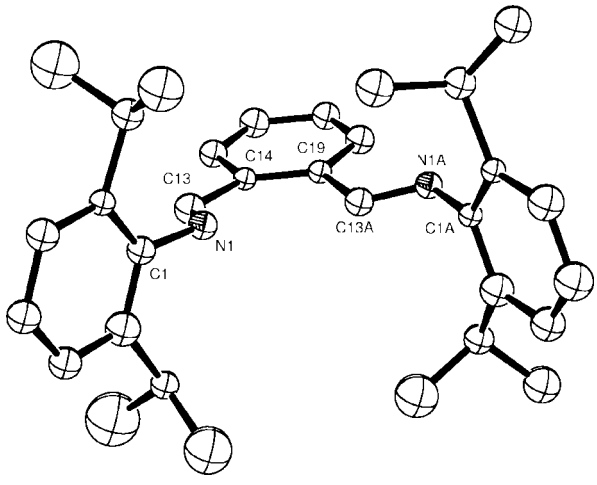


Figure 2. ORTEP plot of *γ*-diimine **2** at the 50% probability level. The hydrogen atoms have been omitted for clarity. Selected bond lengths (Å) and angles (deg): N(1)−C(13) = 1.250(15), N(1)−C(1) = 1.395(10), N(1A)−C(13A) = 1.280(13), N(1A)−C(1A) = 1.424(11); C(13)−N(1)−C(1) = 118.6(9), C(13A)−N(1A)−C(1A) = 120.1(9), N(1)−C(13)−C(14) = 125.8(9), N(1A)−C(13A)−C(19) = 120.4(9).

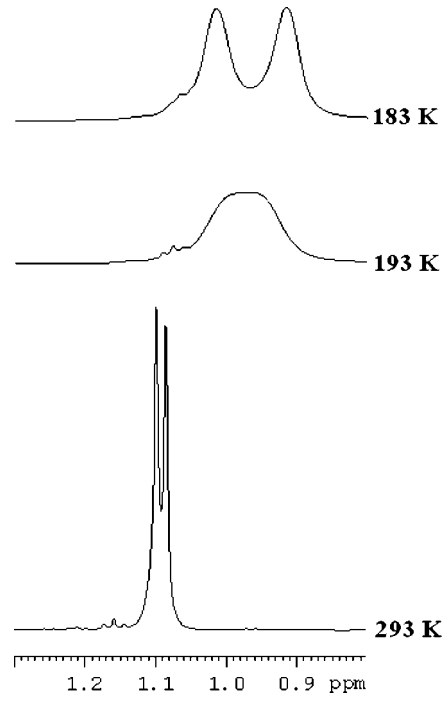


Figure 3. Variable-temperature ^{1}H NMR (CD_2Cl_2) study of *γ*-diimine **2** focusing on the methyl signals of the isopropyl groups (residual ether is observed immediately downfield of methyl resonances).

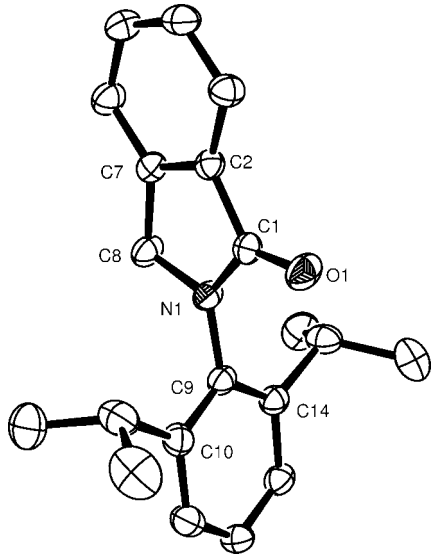


Figure 4. ORTEP plot of isoindolinone **3** at the 50% probability level. The hydrogen atoms have been omitted for clarity. Selected bond lengths (Å) and angles (deg): O(1)−C(1) = 1.223(2), N(1)−C(1) = 1.362(2), N(1)−C(9) = 1.362(19), N(1)−C(8) = 1.362(19); C(1)−N(1)−C(9) = 125.86(12), C(9)−N(1)−C(8) = 120.62(12), O(1)−C(1)−N(1) = 125.96(14).

(γ-diimine)Pd^{II} Complexes. Reaction of the γ-diimine ligand **2** with $(CH_3CN)_2PdCl_2$ in benzene afforded the dinuclear (γ-diimine)Pd^{II} complex [(γ-diimine)PdCl(μ-Cl)]$_2$ (**5**) as an orange solid in 47% yield (Scheme 6). The reaction also proceeded with [(cyclooctene)$PdCl_2$]$_2$ as the $PdCl_2$ source; however, no reaction was observed if (cyclooctadiene)$PdCl_2$ was employed. Complex **5** was air-stable both in noncoordinating solvents and in the solid state. The γ-diimine did not coordinate in a chelating mode but instead acted as a monodentate ligand with one imine remaining uncoordinated, as evidenced by ^{1}H, ^{13}C NMR, and IR spectroscopic studies. It is worthwhile to note that a reported (diphosphaalkene)Pd^{II} analogue showed the diphosphaalkene ligand coordinating in a bidentate fashion, forming a seven-membered ring.[12] ^{1}H NMR of **5** in $CDCl_3$ showed two characteristic singlets appearing downfield at δ 8.25 and 8.17, indicating that the two imine (*H*C═N) protons were no longer equivalent.

^{13}C NMR spectra showed that the chemical shift for the coordinated imine carbon (H*C*═N) had shifted downfield to δ 176.0 while the uncoordinated imine remained upfield at δ 161.8. Similarly, two C═N stretches were observed by FT-IR spectroscopy. One C═N stretch appeared at 1633 cm^{-1}, corresponding to the uncoordinated imine, while the other C═N stretch was observed at 1618 cm^{-1}, consistent with coordination of an imine nitrogen atom to an electrophilic metal center.The solid-state structure of **5** has been determined by X-ray diffraction and is depicted in Figure 7. The structure revealed that **5** is a dinuclear chloride-bridged complex with a slightly distorted square planar coordination geometry about each palladium atom. The environment around each palladium consists of two bridging chlorides, one terminal chloride, and a monodentate γ-diimine ligand with one of the ligand imine functionalities remaining uncoordinated. The ligand again preferentially adopts the same rotational conformer as that of the solid-state structure of the free ligand, thereby effectively inhibiting a bidentate coordination mode at the metal center.

Reaction of γ-diimine **2** with $Pd(OAc)_2$ in ether at ambient temperature for 16 h affords the air-stable five-membered palladacyclic species **6** as an orange solid (Scheme 6). In contrast to the reaction with $(MeCN)_2PdCl_2$ or [(cyclooctene)$PdCl_2$]$_2$, where no C−H activation of the ligand is observed, ortho cyclopalladation readily occurs when $Pd(OAc)_2$ is employed as the Pd(II) source. ^{1}H NMR of **6** showed two distinct singlets at δ 9.50 and 8.09 for the coordinated and uncoordinated imine protons (*H*C═N), respectively, as well as four bridging acetate ligands. The identity of the complex was further established by X-ray diffraction studies. Most interestingly, the complex possesses a rare $Pd_3(OAc)_4$ core, which results in an S-shaped complex (Figures 8 and 9). To our knowledge, this is the fifth example of a structurally characterized $Pd_3(OAc)_4$-containing complex.[13] The Pd−C distance of 1.949(6) Å is consistent with those in the previously reported $Pd_3(OAc)_4$-based complexes, as is the Pd−Pd distance of 2.9721(6) Å.

Catalysis. Cross-coupling reactions are powerful synthetic strategies to build carbon−carbon and carbon−heteroatom bonds.[14] Palladium -catalyzed Heck and Suzuki coupling reactions are among the most efficient methods to construct C−C bonds.[15] The development of coupling reactions for aryl chlorides has been a major research area in recent years, as aryl chlorides tend to be cheaper and much more widely available than the analogous bromides or iodides but are, however, much more difficult to activate.[16] Along these lines, several powerful systems have been developed for the activation of not only para-substituted aryl chlorides[16,17] but also hindered substrates such as ortho-substituted aryl halides, as shown by Buchwald's group,[18] and even alkyl halides, as reported by Fu's group.[19] While palladacycles have been around since 1965,[20] the first examples of palladacycles as precatalysts in the Heck and Suzuki

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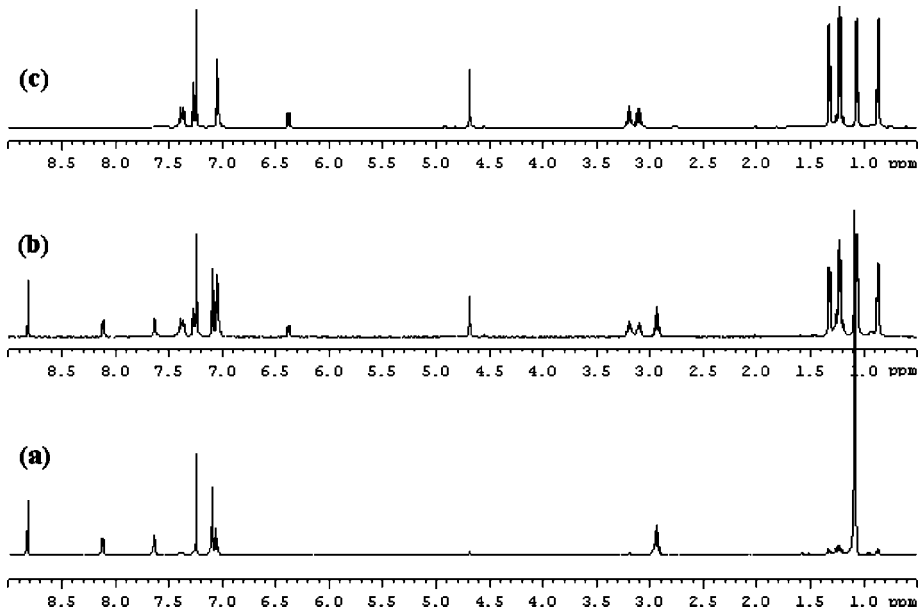


Figure 5. ^{1}H NMR ($CDCl_3$) spectra showing the cyclization of γ-diimine **2** to iminoisoindoline **4** at 60 °C: (a) γ-diimine **2** at $t = 0.25$ h; (b) 1:1 mixture of **2** and **4** observed at $t = 12$ h; (c) complete cyclization to **4** observed at $t = 24$ h.

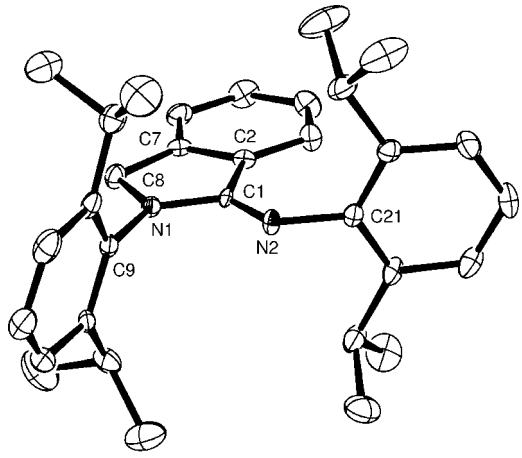
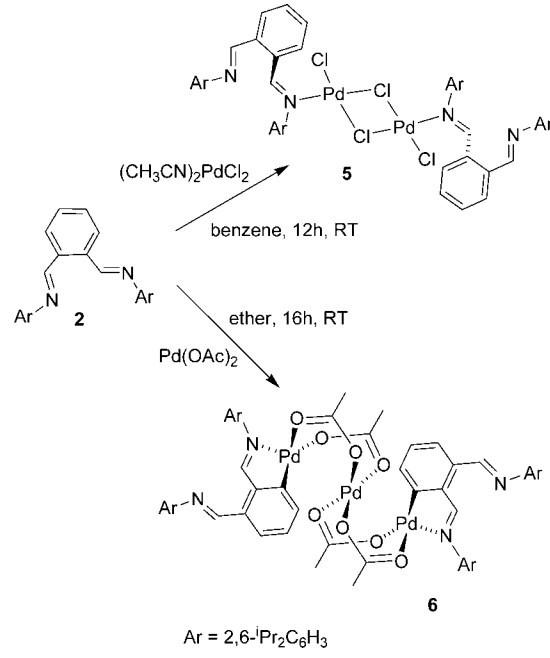


Figure 6. ORTEP plot of **4**-DCl·$CDCl_3$ at the 50% probability level. The hydrogen/deuterium atoms, chloride counterion, and solvent molecule have been omitted for clarity. Selected bond lengths (Å) and angles (deg): N(1)−C(1) = 1.345(3), N(1)−C(9) = 1.442(3), N(1)−C(8) = 1.469(4), N(2)−C(1) = 1.304(4); C(1)−N(1)−C(9) = 126.1(2), C(9)−N(1)−C(8) = 121.0(2), C(1)−N(2)−C(21) = 120.6(2), N(2)−C(1)−N(1) = 123.3(2).

Scheme 6



reaction were not reported until 1995.[21] Palladacyclic compounds currently rank among the best precatalysts for a variety of C−C coupling reactions.[21,22]

The catalytic activities of complexes **5** and **6** were investigated in the standard Heck coupling reaction of aryl halides with butyl acrylate (Table 2). Complex **5** showed catalytic activity similar to that of ligand-free $PdCl_2$, suggesting the ligand plays little, if any, role in the catalytic cycle. This is not unexpected, given the monodentate nature and poor σ-donating ability of the γ-diimine ligand. No activity was observed with aryl chlorides. Palladacycle **6**, on the other hand, was a comparatively exceptional precatalyst, even in the absence of stabilizing agents such as tetrabutylammonium iodide. Reactions were carried out in DMA at 145 °C in the presence of either CsOAc or Cs_2CO_3. The precatalyst was active for both activated and deactivated aryl bromides (Table 2). Palladacycle **6** also demonstrated activity for aryl chlorides; however, longer reaction times (24 h) were required. Palladacycle **6** was active for the coupling of butyl acrylate with 4-chloroacetophenone (18%) and 4-chlorobenzaldehyde (99%).

The catalytic activity of **6** was compared to that of $Pd(OAc)_2$, which is a known precatalyst. Under the conditions employed, $Pd(OAc)_2$ showed no activity for the coupling of aryl chlorides.

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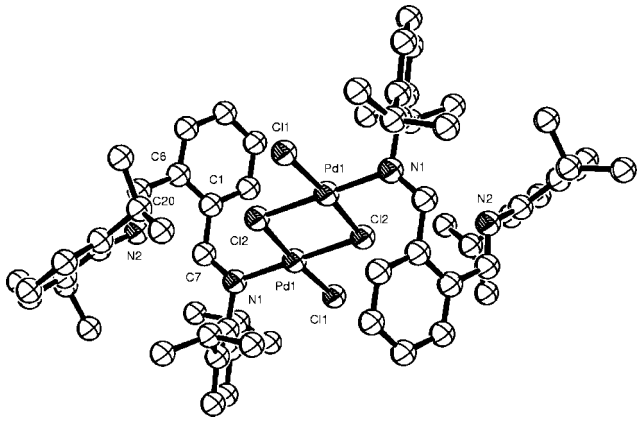

Figure 7. ORTEP plot of **5** at the 50% probability level. The hydrogen atoms have been omitted for clarity. Selected bond lengths (Å) and angles (deg): Cl(1)−Pd(1) = 2.2796(9), Cl(2)−Pd(1) = 2.3141(9), Cl(2)−Pd(1)′ = 2.3338(9), N(1)−C(7) = 1.276(4), N(1)−Pd(1) = 2.028(3), N(2)−C(20) = 1.259(5); C(7)−N(1)−Pd(1) = 122.6(2), N(1)−Pd(1)−Cl(1) = 90.79(8), Cl(1)−Pd(1)−Cl(2) = 91.15(3), N(1)−Pd(1)−Cl(2)′ = 93.50(8), Cl(2)−Pd(1)−Cl(2)′ = 84.63(3).

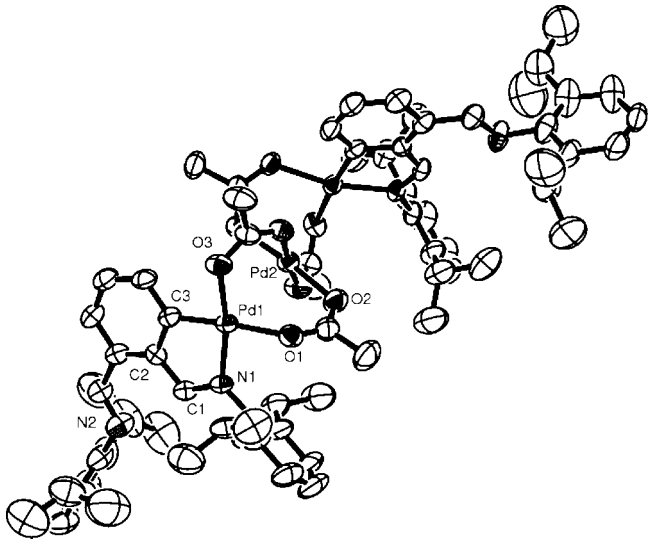

Figure 8. ORTEP plot of **6** at the 50% probability level. The hydrogen atoms have been omitted for clarity. Selected bond lengths (Å) and angles (deg): Pd(1)–C(3) = 1.949(6), Pd(1)–N(1) = 2.018(4), Pd(1)–O(3) = 2.057(4), Pd(1)–O(1) = 2.127(4), Pd(1)–Pd(2) = 2.9721(6); C(3)–Pd(1)–N(1) = 81.1(2), C(3)–Pd(1)–O(3) = 92.57(19), N(1)–Pd(1)–O(1) = 93.67(17), O(3)–Pd(1)–O(1) = 92.83(17).

Under different conditions, $Pd(OAc)_2$ has been reported to be active for the coupling of aryl bromides and aryl chlorides.[23]

The catalytic activity of complexes **5** and **6** were also tested in the Suzuki coupling reaction of aryl halides with phenylboronic acid, using Cs_2CO_3 or CsOAc as base and DMA as solvent at 80 °C (Table 3). As with the Heck reactions, while complex **5** was active for the catalytic coupling of aryl bromides, little or no activity was observed with aryl chlorides. Palladacycle **6** again demonstrated good activity for activated aryl chlorides, producing the target biphenyls in 73–86% conversions; however, lower conversions were achieved for deactivated aryl chlorides (entries 7 and 11 in Table 3).

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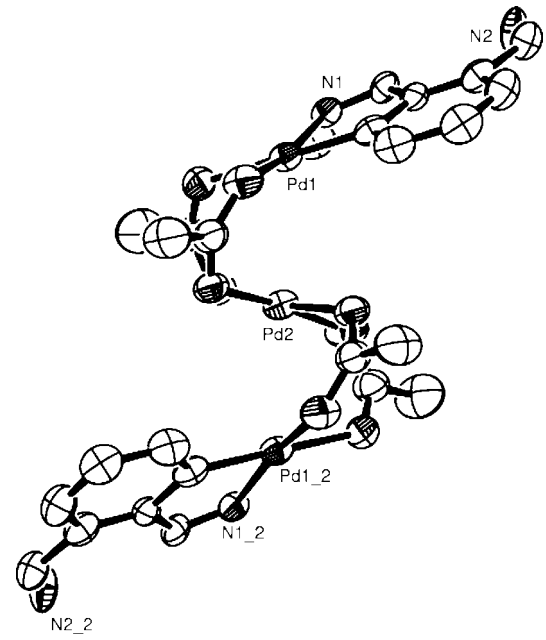


Figure 9. ORTEP plot of **6** at the 50% probability level, illustrating the S-shape derived from the $Pd_3(OAc)_4$ core. The 2,6-^{i}Pr$_2$-C$_6$H$_3$ groups and hydrogen atoms have been omitted for clarity.

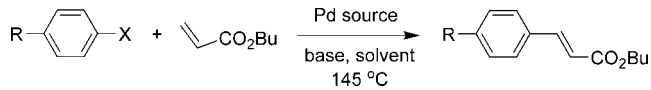
Conclusion

We have prepared and structurally characterized a bulky γ-diimine ligand and its corresponding Pd(II) complexes. Analogous γ-diimines are likely intermediates in the reaction of phthalaldehyde with primary amines to form the corresponding iminoisoindolines and isoindolinones due to rapid intramolecular cyclization reactions.[9] γ-Diimine **2** can, however, be isolated, due to the presence of bulky diisopropylphenyl groups which likely inhibit or retard cyclization reactions. Depending on the reaction conditions, cyclization of the γ-diimine can be induced to form either the corresponding iminoisoindoline or the isoindolinone. Unlike analogous α- and β-diimine complexes, the γ-diimine ligand does not coordinate in a chelating mode but instead adopts a monodentate coordination mode upon reaction with $PdCl_2$. On the other hand, reaction of γ-diimine **2** with $Pd(OAc)_2$ results in C−H activation of the ligand and formation of an air-stable palladacyclic species containing a rare $Pd_3(OAc)_4$ core. The resulting palladacyclic complex is an active precatalyst for the Suzuki and Heck coupling reactions when para-functionalized aryl chlorides and aryl bromides are employed. The non-palladacyclic analogue [(γ-diimine)PdCl(μ-Cl)]$_2$ is a relatively inferior precatalyst, exhibiting no activity for aryl chlorides. Due to intermolecular cyclization reactions, it is unlikely that γ-diimines will emerge as a new class of ligand comparable to α- and β-diimine analogues.

Experimental Section

General Information. Unless otherwise stated, all reactions were performed under N_2 or vacuum using standard Schlenk techniques or in an N_2-filled drybox. All reaction temperatures for catalytic reactions refer to the temperature of pre-equilibrated oil or sand baths. All melting points were recorded on a Gallenkamp melting point apparatus and are uncorrected. ^{1}H and ^{13}C{^{1}H} NMR spectra were recorded on a Bruker 500 MHz Avance spectrometer. Chemical shifts for ^{1}H and ^{13}C NMR are reported in ppm, referenced to the residual ^{1}H and ^{13}C resonances of $CDCl_3$ (^{1}H, δ 7.24; ^{13}C, δ 77.24). Coupling constants are given in Hz. Elemental analyses were performed on a Perkin-Elmer 2400 CHN elemental

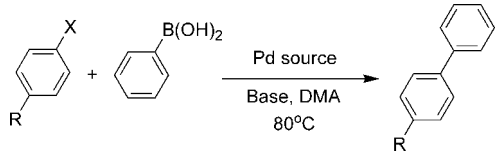
Table 2. Heck Cross-Coupling of Aryl Halides with Butyl Acrylate[a]



entry	R	X	base	time (h)	cat. (amt (mol %))	conversn (%)[b]	TON[c]
1	H	I	Cs_2CO_3	3	**5** (0.1)	>99	1000
2	H	Br	Cs_2CO_3	3	**5** (1)	50	50
3	COMe	Br	CsOAc	14	**5** (1)	97	97
4	CN	Br	CsOAc	14	**5** (3)	86	29
5	Me	Br	Cs_2CO_3	3	**5** (1)	66	66
6	COMe	Cl	CsOAc	42	**5** (3)	0	0
7	COMe	Br	CsOAc	14	$PdCl_2$ (1)	>99	100
8	H	Br	Cs_2CO_3	3	$PdCl_2$ (1)	48	48
9	COMe	Br	CsOAc	3	**6** (0.01)	>99	10000
10	COH	Br	Cs_2CO_3	3	**6** (0.1)	>99	1000
11	CN	Br	Cs_2CO_3	3	**6** (1)	88	88
12	OMe	Br	CsOAc	3	**6** (1)	65	65
13	Me	Br	CsOAc	24	**6** (1)	95	95
14	COH	Cl	Cs_2CO_3	24	**6** (1)	>99	100
15	COMe	Cl	CsOAc	6	**6** (1)	18	18
16	COMe	Cl	CsOAc	3	$Pd(OAc)_2$ (1)	0	0
17	COH	Cl	Cs_2CO_3	24	$Pd(OAc)_2$ (1)	0	0

[a] Reaction conditions: aryl halide (1.0 mmol), acrylate (2.0 mmol), base (2.0 mmol), Pd catalyst, solvent (DMA, 3 mL), 145 °C. [b] Determined by ^{1}H NMR on the basis of residual aryl halide.[26] [c] TON = turnover number ((mol of product)/(mol of catalyst)).

Table 3. Suzuki Cross-Coupling of Aryl Halides with Phenylboronic Acid[a]



entry	R	X	base	time (h)	cat. (amt (mol %))	conversn (%)[b]
1	H	I	Cs_2CO_3	3	**5** (1)	>99
2	H	Br	Cs_2CO_3	3	**5** (1)	94
3	Me	Br	Cs_2CO_3	3	**5** (1)	92
4	COMe	Br	Cs_2CO_3	3	**5** (1)	98
5	COMe	Cl	Cs_2CO_3	3	**5** (3)	3
6	H	Cl	Cs_2CO_3	3	**5** (3)	0
7	OMe	Cl	Cs_2CO_3	24	**6** (1)	8
8	COH	Cl	Cs_2CO_3	24	**6** (1)	73
9	COMe	Cl	CsOAc	24	**6** (1)	86
10	CN	Cl	Cs_2CO_3	3	**6** (1)	78
11	Me	Cl	Cs_2CO_3	24	**6** (1)	17

[a] Reaction conditions: aryl halide (1.0 mmol), phenylboronic acid (1.5 mmol), base (2 mmol), Pd catalyst, DMA (3 mL), 80 °C, 3 h. [b] Determined by ^{1}H NMR on the basis of residual aryl halide.[26]

analyzer. IR data were collected by diffuse reflectance spectroscopy. Reagents such as $PdCl_2$, $Pd(OAc)_2$, 2,6-diisopropylaniline, phthalaldehyde, and cyclooctene (COE) were purchased from Sigma-Aldrich Chemical Co. and used as received, except for 2,6-diisopropylaniline, which was distilled prior to use. $(CH_3CN)_2PdCl_2$[24] and $[(COE)PdCl_2]_2$[25] were synthesized according to literature procedures.

Synthesis of 1-(Phenylimino)-2-phenylisoindoline. A Schlenk flask was charged with phthalaldehyde (500 mg, 3.73 mmol), aniline (695 mg, 7.46 mmol), methanol (10 mL), and 2 drops of formic acid and stirred at ambient temperature for 12 h. The resulting precipitate was filtered, washed with methanol (3 × 20 mL), and then dried under vacuum to obtain a white solid (795 mg, 75%, mp 127.8–129.5 °C). ^{1}H NMR ($CDCl_3$, ppm): δ 8.01 (d, J = 6.0 Hz, 2H), 7.44 (d, J = 7.5 Hz, 1H), 7.38 (m, 3H), 7.31 (m, 2H), 7.04 (m, 3H), 6.99 (d, J = 6.7 Hz, 2H), 6.66 (d, J = 7.1 Hz, 1H), 4.94 (s, 2H). ^{13}C NMR ($CDCl_3$, ppm): δ 153.52, 150.87, 141.81, 140.59, 130.48, 129.34, 129.12, 127.53, 126.70, 123.33, 122.92, 122.44, 121.44, 120.18, 53.18. Anal. Calcd for $C_{20}H_{15}N_2$: C, 84.48; H, 5.67; N, 9.85. Found: C, 84.57; H, 5.62; N, 9.60. MS (TOF; m/z): calcd for $C_{20}H_{15}N_2$284.1313, found 285.1392 (M + 1). FT-IR (KBr): 1646 (C═N), 1590, 1498.

Synthesis of 2,5-Dimethyl-1-(2,6-diisopropylphenyl)pyrrole (1). A Schlenk flask was charged with 2,5-hexanedione (1.425 g, 0.0125 mol), 2,6-diisopropylaniline (6.65 g, 0.0375 mol), methanol (10 mL), and 1 drop of formic acid and the mixture stirred at ambient temperature for 12 h. The flask was then placed in a −30 °C freezer, where colorless needlelike crystals formed. The solvent was decanted and the resulting product washed with cold methanol and then dried under vacuum to yield a white powder of the title compound (2.03 g, 90%). ^{1}H NMR ($CDCl_3$): δ 7.39 (t, J = 7.7, 1H, C_6H_3), 7.61 (d, J = 7.7, 2H, C_6H_3), 5.92 (s, 2H, C_4H_2N), 2.35 (sept, J = 6.9, 2H, $CH(CH_3)_2$), 1.89 (s, 6H, $C_4H_2N(CH_3)_2$), 1.1 (d, J = 6.9, 12H, $CH(CH_3)_2$). ^{13}C NMR ($CDCl_3$): δ 147.8, 134.3, 129.3, 129.0, 124.0, 105.5, 28.0 ($CH(CH_3)_2$), 24.3 ($CH(CH_3)_2$), 12.9 (CH_3). Anal. Calcd for $C_{18}H_{25}N$: C, 84.65; H, 9.87; N, 5.48. Found: C, 84.41; H, 9.60; N, 5.45. EI-MS (m/z): calcd for $C_{18}H_{29}N$ 255.1987, found 255.1985.

Synthesis of the γ-Diimine 1,2-(2,6-^{i}Pr$_2$-C$_6$H$_3$NC)$_2$-C$_6$H$_4$ (2) and *N*-(2,6-Diisopropylphenyl)isoindolinone (3). A flask was charged with phthaldehyde (1.502 g, 11.2 mmol), 2,6-diisopropylaniline (14.1 g, 79.5 mmol), and methanol (15 mL) under a nitrogen atmosphere. Formic acid (0.4 mL) was added and the mixture stirred at 0 °C. A yellow precipitate appeared within 10 min of stirring. After 4 h of stirring, the precipitate was filtered, washed with methanol (3 × 10 mL), and dried under vacuum to yield **2** as a yellow powder (3.371 g, 66%). Yellow crystals were obtained from slow evaporation of ether at ambient temperature. The colorless filtrate was transferred back to the flask, where continued stirring was allowed for 12 h. Methanol and excess 2,6-diisopropylaniline were removed at 100 °C by vacuum distillation. Ether (10 mL) was added, and the flask was placed in a −30 °C freezer, whereupon colorless crystals of **3** were obtained (0.985 g, 30%).

1,2-(2,6-^{i}Pr$_2$-C$_6$H$_3$NC)$_2$-C$_6$H$_4$ (2). ^{1}H NMR ($CDCl_3$): δ 8.82 (s, 2H, C═NH), 8.11 (dd, J = 5.7, 3.4, 2H, C_6H_4), 7.63 (dd, J = 5.7, 3.4, 2H, C_6H_4), 7.07 (m, 6H, 2,6-^{i}Pr$_2$-C$_6$H$_3$), 2.94 (sept, J = 6.6, 4H, $CH(CH_3)_2$), 1.08 (d, 24H, J = 6.9, $CH(CH_3)_2$). ^{13}C NMR ($CDCl_3$): δ 161.8, 149.8, 137.5, 135.9, 131.5, 130.3, 124.7, 123.4,

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28.4 (*C*H), 24.9 (*C*H_3). Anal. Calcd for $C_{32}H_{40}N_2$: C, 84.90; H, 8.90; N, 6.18. Found: C, 84.30; H, 8.61; N, 6.02. Mp: 180.0−182.5 °C. FT-IR (KBr, cm^{-1}): 1633 (C═N). EI-MS (*m*/*z*): calcd for $C_{32}H_{40}N_2$ 452.3191, found 452.3185.

Alternative Synthesis of *N*-(2,6-Diisopropylphenyl)isoindolinone (3). A flask was charged with phthalaldehyde (0.526 g, 3.92 mmol), 2,6-diisopropylaniline (0.696 g, 3.92 mmol), formic acid (0.032 g, 0.695 mmol), and methanol (10 mL). After 19 h of stirring at ambient temperature, the flask was placed in a −30 °C freezer, whereupon colorless needlelike crystals formed. The solvent was decanted and the crystals dried under vacuum to yield a white powder of the title compound (0.861 g, 75%). Mp = 155.0–157.0 °C. ^{1}H NMR ($CDCl_3$): δ 7.98 (d, J = 7.5, 1H, C_6H_4), 7.61 (m, 1H, C_6H_4), 7.53 (d, J = 7.5, 1H, C_6H_4), 7.50 (d, J = 7.5, 1H, C_6H_4), 7.39 (t, J = 7.7, 1H, C_6H_3), 7.25 (d, J = 7.7, 2H, C_6H_3), 4.56 (s, 2H, CH_2), 2.76 (sept, J = 6.9, 2H, C*H*(CH_3)$_2$), 1.19 (d, J = 6.9, 12H, CH(CH_3)$_2$). ^{13}C NMR ($CDCl_3$): δ 168.8 (C═O), 147.8, 141.6, 133.0, 132.6, 131.8, 129.4, 128.5, 124.8, 124.3, 123.1, 54.0, 29.0 (*C*H), 24.7 (*C*H_3), 24.5 (*C*H_3). Anal. Calcd for $C_{20}H_{23}NO$: C, 81.87; H, 7.90; N, 4.77. Found: C, 81.70; H, 7.80; N, 4.76. FT-IR (KBr, cm^{-1}): 1694.8 (C═O). EI-MS (*m*/*z*): calcd for $C_{20}H_{23}NO$ 293.1779, found 293.1774.

Synthesis of *N*,*N*′-Bis(2,6-diisopropylphenyl)iminoisoindoline (4). A flask was charged with γ-diimine **2** (100 mg, 0.220 mmol) and chloroform-*d* (10 mL). After 48 h of stirring at 60 °C under an ambient atmosphere, the solution had changed from yellow to colorless. The solvent was removed under vacuum to yield a white powder (91 mg, 91%). The cyclization was observed to proceed considerably more slowly when the reaction was performed under nitrogen in place of air. ^{1}H NMR ($CDCl_3$): δ 7.37 (m, 3H), 7.26 (d, J = 2, 2H), 7.05 (m, 4H), 6.38 (d, J = 8.0, 1H), 4.69 (s, 2H, CH_2), 3.19 (sept, J = 6.8, 2H, C*H*(CH_3)$_2$), 3.10 (sept, J = 6.8, 2H, C*H*(CH_3)$_2$), 1.32 (d, J = 6.8, 6H, CH(CH_3)$_2$), 1.23 (d, J = 6.8, 6H, CH(CH_3)$_2$), 1.07 (d, J = 6.9, 6H, CH(CH_3)$_2$), 0.87 (d, J = 6.9, 6H, CH(CH_3)$_2$). ^{13}C NMR ($CDCl_3$): δ 155.0, 147.88, 146.26, 140.97, 139.21, 134.47, 131.42, 129.75, 128.56, 127.15, 126.44, 124.09, 122.64, 122.27, 55.22, 28.44, 27.44, 25.81, 24.17, 23.62, 23.52. FT-IR (KBr, cm^{-1}): 1644 (C═N). EI-MS (*m*/*z*): calcd for $C_{32}H_{40}N_2$ 452.3191, found 452.3185.

NMR-Tube Reaction for the Cyclization of γ-Diimine 2 to Iminoisoindoline 4. An NMR tube was charged with **2** (3 mg, 6.6 μmol) and $CDCl_3$ (0.6 mL) in air. The reaction was monitored over 24 h at 60 °C. During the course of the reaction, the solution changed from yellow to colorless. ^{1}H NMR spectra showed complete conversion of **2** to **4** after 24 h. Prolonged exposure of **4** to $CDCl_3$ over the course of 2 weeks resulted in precipitation of colorless crystals of the DCl salt of **4** (**4**-DCl).

Cyclization of γ-Diimine 2 To Form *N*-(2,6-Diisopropylphenyl)isoindolinone (3). A flask was charged with **2** (28.00 mg, 0.0619 mmol), methanol (15 mL), and 2 drops of formic acid. After the mixture was stirred for 24 h, the solution changed from yellow to colorless. Solvent was removed under vacuum, and ^{1}H NMR analysis showed the quantitative conversion of **2** to **4**, along with formation of 1 equiv of 2,6-diisopropylaniline.

Synthesis of [(γ-diimine)PdCl(μ-Cl)]$_2$ (5). A Schlenk flask was charged with **2** (0.168 g, 0.371 mmol), $(CH_3CN)_2PdCl_2$ (0.053 g, 0.204 mmol), and benzene (20 mL) under nitrogen. Within 0.5 h of stirring at ambient temperature, the yellow-green mixture became a red-brown homogeneous solution. After 16 h, the resulting yellow-brown precipitate was filtered and washed with cold benzene (3 × 10 mL) under air. The product was then crystallized by slow evaporation from $CHCl_3$ to give orange crystals of **5** (0.121 g, 47%). Mp: 181.5–182.0 °C dec. ^{1}H NMR ($CDCl_3$): 9.69 (d, J = 7.4 Hz, 2H), 8.25 (s, 2H, *H*C═N), 8.17 (s, 2H, *H*C═N), 8.04 (t, J = 7.5 Hz, 2H), 7.86 (m, 2H), 7.64 (d, J = 7.4 Hz, 2H), 7.17 (t, J = 7.5 Hz, 2H), 7.04 (d, J = 7.6 Hz, 4H, C_6H_3), 7.00 (br, 6H), 3.26 (m, 4H, C*H*(CH_3)$_2$), 2.57 (m, 4H, C*H*(CH_3)$_2$), 1.64 (br, 9H, CH(CH_3)$_2$). 0.88–0.80 (m, 39H, CH(CH_3)$_2$). ^{13}C NMR ($CDCl_3$): δ 176.0, 161.8, 148.8, 145.9, 142.8, 137.6, 135.8, 133.8, 132.9, 132.8, 131.9, 130.4, 128.7, 125.1, 124.6, 123.3, 28.9, 28.4, 23.9, 23.8. FT-IR (KBr, cm^{-1}): 1633 (free imine, C═N), 1618 (coordinated imine, C═N−Pd).

Synthesis of {1,2-(2,6-^{i}Pr$_2$-C_6H_3NC)$_2$-C_6H_3]Pd(μ-OAc)$_2$}$_2$Pd (6). A Schlenk flask was charged with **2** (657 mg, 1.45 mmol), $Pd(OAc)_2$ (362 mg, 1.45 mmol), and ether (20 mL) under nitrogen. After 16 h of stirring at ambient temperature, the resulting orange precipitate was filtered in air, washed with cold ether (3 × 10 mL), and dried under vacuum. Orange crystals of **6** were obtained from dichloromethane/hexanes (1:1) by slow evaporation at ambient temperature (504 mg, 24%). Mp: 206.5–208.5 °C dec. ^{1}H NMR ($CDCl_3$): 9.50 (s, 2H, *H*C═N), 8.09 (s, 2H, *H*C═N), 7.44 (dd, J = 6.3, 2.5 Hz, 2H), 7.30 (m, 4H), 7.19 (m, 4H), 7.05 (m, 8H), 4.17 (sep, J = 7.0 Hz, 2H, C*H*(CH_3)$_2$), 3.51 (sept, J = 7.0 Hz, 2H), 2.84 (sept, 4H, C*H*(CH_3)$_2$), 1.98 (s, 6H, OAc), 1.44 (d, J = 7 Hz, 6H, CH(CH_3)$_2$), 1.15 (d, J = 7 Hz, 6H, CH(CH_3)$_2$), 1.14 (s, 6H, OAc), 1.05 (d, J = 7 Hz, 12H, CH(CH_3)$_2$) 1.04 (d, J = 7 Hz, 18H, CH(CH_3)$_2$), 1.01 (d, J = 7 Hz, 6H, CH(CH_3)$_2$). ^{13}C NMR ($CDCl_3$): δ 184.1, 183.0, 177.7, 162.6, 161.0, 148.9, 144.6, 143.6, 143.0, 141.8, 137.5, 135.5, 134.7, 130.7, 130.0, 127.6, 124.6, 123.3, 123.3, 123.2, 66.1, 28.5, 28.2, 27.8, 26.2, 24.8, 23.8, 23.6, 23.5, 23.5, 23.0, 22.9, 22.8, 15.5. Anal. Calcd for $C_{72}H_{90}N_4O_8Pd_3$: C, 59.28; H, 6.22; N, 3.84. Found: C, 58.89; H, 6.44; N, 3.71. FT-IR (KBr, cm^{-1}): 1631 (free imine, C═N), 1580 (coordinated imine, C═N−Pd).

General Procedure for Heck Coupling Reactions. In a typical run, an oven-dried 25 mL two-necked flask equipped with a stir bar was charged with a known mole percent of catalyst and base (2.0 mmol). Under nitrogen, DMA (3 mL), aryl halides (1.0 mmol) and *n*-butyl acrylate (2.0 mmol) were added via syringe. The flask was then placed in a preheated sand bath at 145 °C. After the specified time the flask was removed from the sand bath and water (20 mL) added, followed by extraction with dichloromethane (4 × 10 mL). The combined organic layers were washed with water (3 × 10 mL), dried over anhydrous $MgSO_4$, and filtered. Solvent was removed under vacuum. The residue was dissolved in $CDCl_3$ and analyzed by ^{1}H NMR. Percent conversions were determined against the remaining aryl halide.[26]

General Procedure for Suzuki Coupling Reactions. In a typical run, an oven-dried 25 mL two-necked flask equipped with a stir bar was charged with a known mole percent of catalyst, base (2.0 mmol), and phenylboronic acid (1.5 mmol). Under nitrogen, DMA (3 mL) and aryl halides (1.0 mmol) were added via syringe. The flask was placed in a preheated sand bath at 80 °C. After the specified time the flask was removed from the sand bath and water (20 mL) added, followed by extraction with dichloromethane (4 × 10 mL). The combined organic layers were washed with water (3 × 10 mL), dried over anhydrous $MgSO_4$, and filtered. Solvent was removed under vacuum. The residue was dissolved in $CDCl_3$ and analyzed by ^{1}H NMR. Percent conversions were determined against the remaining aryl halide.[26]

X-ray Structure Determinations. Data were collected at −100 °C on a Nonius Kappa CCD diffractometer, using the COLLECT program.[27] Cell refinement and data reductions used the programs DENZO and SCALEPACK.[28] SIR97[29] was used to solve the

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structures, and SHELXL97[30] was used to refine the structures. ORTEP-3 for Windows[31] was used for molecular graphics, and PLATON[32] was used to prepare material for publication. H atoms were placed in calculated positions with U_{iso} constrained to be 1.5 times the U_{eq} value of the carrier atom for methyl protons and 1.2 times the U_{eq} value of the carrier atom for all other hydrogen atoms.

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Supporting Information Available: CIF files giving gull crystallographic data for compounds **2**, **3**, **4**·DCl·$CDCl_3$, **5**·$2CHCl_3$, and **6**·$2CH_2Cl_2$. This material is available free of charge via the Internet at http://pubs.acs.org.

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