Palladium Complexes with Tridentate Pincer Bis-Carbene Ligands as Efficient Catalysts for C−C Coupling

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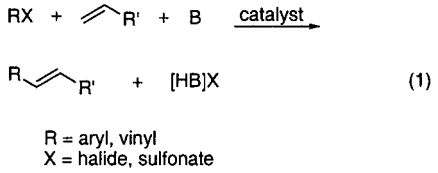
The synthesis and X-ray crystallographic characterization of a Pd complex (**3**) with a rigid C,N,C-tridentate pincer carbene ligand are described. At high temperatures (165 °C) it is an active and robust catalyst in the Heck reaction. Complex **3** gives some of the highest turnover numbers yet reported for coupling with aryl chlorides. Time dependence, reuse, and Heck reaction conditions are discussed for **3**. Data with F^- as base did not support Shaw's Heck mechanism. Suzuki and Sonogashira coupling reactions are also catalyzed by **3**. The palladium carbene complex **5**, containing an analogous C,N-bidentate ligand, is compared to **3** in terms of stability, catalytic activity, and reaction profile in the Heck reaction.

Introduction

Palladium complexes with pincer ligands are among the best Heck catalysts known.[1] PCP type ligands containing phosphonite donors can give especially high turnover frequency (TOF) and number (TON) for the Heck reaction: the olefination of aryl halides or sulfonates (eq 1).[2] However, aryl chlorides, the cheapest



and most readily available of the aryl halides, are still challenging substrates because they are relatively unreactive and, thus, desirable conditions such as low catalyst loadings, low temperatures, and short reaction times are hard to achieve. Successful aryl chloride activation has been carried out using Pd complexes with PCP pincer ligands,[2a] cyclometalated phosphines,[3] chelating bis-phosphines,[4] phosphites,[5] phosphonium salts,[6] bulky Lewis basic phosphines,[7] and cyclometalated sulfur and amine ligands.[8]

Recently, N-heterocyclic carbenes[9] were found to be versatile ligands in organotransition-metal catalysis.[10] Their palladium complexes are equal, and in some cases even superior, to the corresponding phosphine-containing catalysts.[11] Heck reactions with aryl chloride activation using carbene-containing Pd complexes have been shown in a preliminary communication from our group[12] and in the groups of Herrmann[11b,13] and Cavell.[11h] It therefore seemed useful to see whether pincer-type

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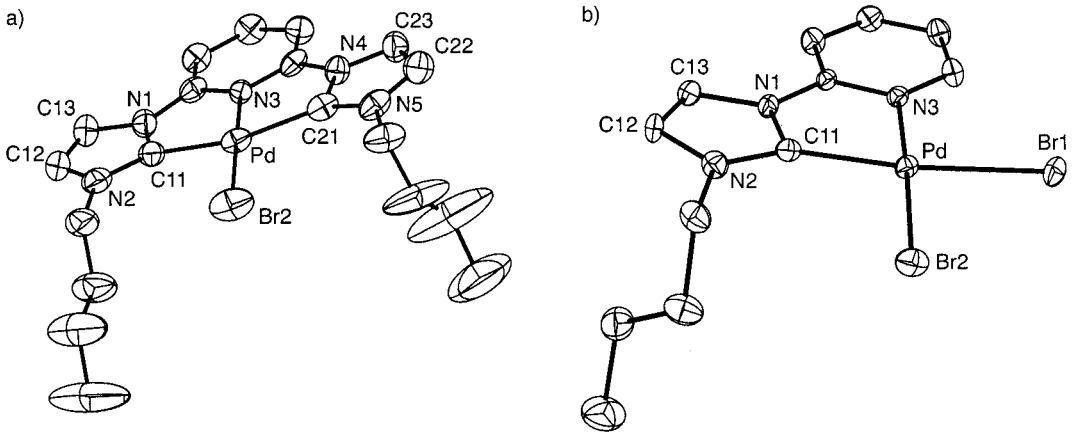
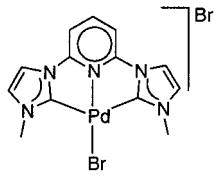


Figure 1. Molecular structures of **3** (a) and **5** (b).

ligands containing carbenes instead of phosphines or phosphonites would form palladium catalysts with enhanced or at least different properties.

Our preliminary results with the palladium complex **1**,[12] containing a rigidly tridentate C,N,C pincer bis-carbene unit and methyl wingtip groups, have shown effective catalysis of the Heck reaction. Disadvantages



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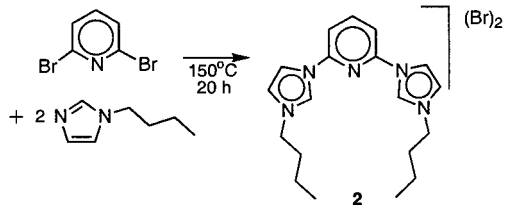
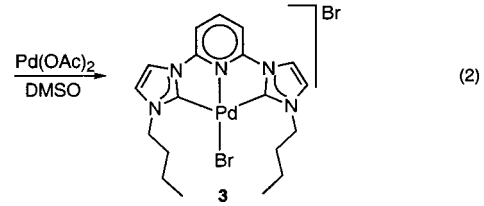
of **1**, however, are its low solubility in nonpolar solvents, which prevents its application in most other palladium-catalyzed reactions, and its high reaction temperature. We now report our efforts to solve the solubility issue, which at the same time has led to a catalyst with improved activity. Moreover, the stability of the pincer palladium complex allowed for more detailed studies of the reaction, leading to a few general conclusions regarding the controversial issue of the mechanism of the Heck reaction.[14]

Results and Discussion

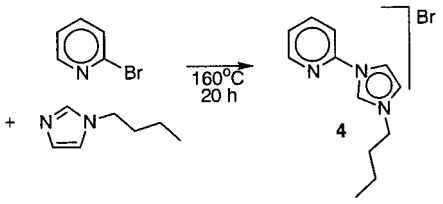
Synthesis of Pd Carbene Complexes. A likely reason for the low solubility of **1** is the planarity of the complex favoring intermolecular stacking in the solid state, possibly enhanced by metal−metal bonding. We hoped to disturb these interactions by using larger wingtip alkyl groups. A similar complex containing ethyl wingtip groups was synthesized, but its solubility was very similar to that of **1**. Ligand **2** containing *n*-butyl substituents was readily synthesized from commercial reagents, and its cyclometalation with $Pd(OAc)_2$ gave **3** in good yields (eq 2). Complex **3** is soluble in $CHCl_3$ but not in CH_2Cl_2 or acetone and appears to be thermally stable (decomposition above 245 °C). The NMR spectra suggest the core structure is very similar to that of complex **1**.

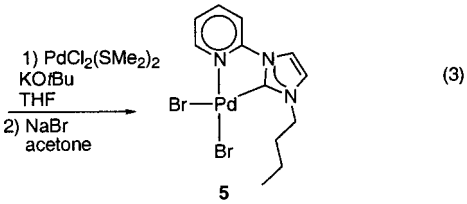




(2)

For reasons discussed later, **5**, a bidentate analogue of **3**, was synthesized from the mono-carbene precursor salt **4** (eq 3). An initial attempt at metalation via





(3)

oxidative addition led to coordination of two chelate ligands at the same metal center, but deprotonation of the imidazolium salt at low temperature followed by metalation with $PdCl_2(SMe_2)_2$ gave good yields. Perhaps because it has only one wingtip *n*-Bu group, **5** is only poorly soluble in chlorinated solvents and insoluble in hydrocarbon solvents. Polar solvents such as dmso and,

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Table 1. Selected Bond Lengths and Angles for the Palladium Complexes 1,[a] 3, and 5

	1 (L = C(21))	**3** (L = C(21))	**5** (L = Br(1))
	Bond Lengths (Å)		
Pd(1)−N(3)	1.979(4)	1.961(6)	2.062(5)
Pd(1)−C(11)	2.033(6)	2.021(10)	1.978(6)
Pd(1)−L	2.044(6)	2.025(10)	2.4816(8)
Pd(1)−Br(2)	2.4099(7)	2.3989(13)	2.4159 (8)
C(12)−C(13)	1.324(8)	1.310(16)	1.335(9)
C(22)−C(23)	1.321(8)	1.324(13)	
Pd···Pd	3.827(12)	3.511(18)	3.6585(9)
	Bond Angles (deg)		
C(11)−Pd(1)−L	158.5(2)	158.7(4)	172.5(2)
N(3)−Pd(1)−Br(2)	179.03(13)	177.0(2)	177.52(13)
N(3)−Pd(1)−C(11)	78.9(2)	78.6(3)	79.9(2)
N(3)−Pd(1)−L	79.6(2)	80.2(3)	93.10(13)
Br(2)−Pd(1)−C(11)	100.29(16)	100.9(3)	98.0(2)
Br(2)−Pd(1)−L	101.18(16)	100.4(3)	89.12(3)
N(1)−C(11)−N(2)	104.0(4)	102.4(9)	103.7(5)
N(1)−C(11)−Pd(1)	110.8(4)	111.5(6)	113.5(4)
N(2)−C(11)−Pd(1)	145.1(4)	146.1(9)	142.7(5)
N(4)−C(21)−N(5)	103.4(5)	102.5(8)	
N(4)−C(21)−Pd(1)	110.7(4)	110.6(6)	
N(5)−C(21)−Pd(1)	145.9(4)	146.9(8)	

[a] From ref 12 with adapted atom labeling.

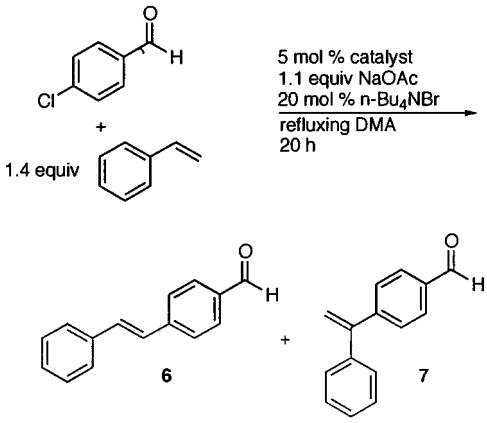
to a lesser extent, warm acetone were more useful. The ^{1}H NMR spectrum showed a characteristic low-field shift of the pyridine ortho proton (δ 9.78).

Structural Studies. The molecular geometries of **3** and **5** have been unequivocally confirmed by single-crystal structure analyses. The molecular structure of **3** (Figure 1a; selected bond lengths and angles listed in Table 1) shows the palladium in a distorted-square-planar conformation. The Pd−$N_{pyridine}$ and Pd−$C_{carbene}$ bond lengths are identical (within their esd's) with the structure reported for the methyl-substituted analogue **1** (see Table 1). As usual, the C−C distances in the imidazole units are short (ca. 1.32(1) Å), which points to enhanced C═C double-bond character. The pyridine ring and the palladium coordination plane are virtually coplanar (torsion angle C(11)−Pd(1)−N(3)−C(1) −1.3-(6)°), and the butyl groups point out of these planes. Remarkably, the closest contacts in **3** (Pd···Pd = 3.511-(18) Å) are significantly smaller than in **1** (Pd···Pd = 3.827(12) Å), which suggests aromatic stacking is the main interaction giving low solubility for **1**.

The molecular structure of **5** (Figure 1b) shows the expected C,N-bidentate coordination mode of the carbene ligand. The different Pd−Br bond lengths confirm the stronger trans influence of the carbene carbon (Pd−Br1 = 2.4816(8) Å) compared to the pyridine nitrogen (Pd−Br2 = 2.4159(8) Å). As expected, the rigidity of the ligand system is reduced in the bidentate system, which is reflected in a Pd−N3 bond length that is significantly longer in bidentate **5** than in tridentate **1** or **3**.

Heck Catalysis. The reaction between 4-chlorobenzaldehyde and styrene in refluxing dimethylacetamide (DMA, bp = 165 °C) was used as a standard reaction to compare the catalytic activity of methyl-substituted **1** and butyl-substituted **3** in Heck coupling (Table 2). Both reactions were carried out with 5 mol % of catalyst for 20 h. Catalysts **1** and **3** both show Heck activity with this activated aryl chloride; however, greater yields are obtained with **3**. Selectivity of the catalysts to form the *trans*-stilbene product (**6**) is good, although some *gem* olefin (**7**) is formed. The isomeric distribution (**6**/**7**) is

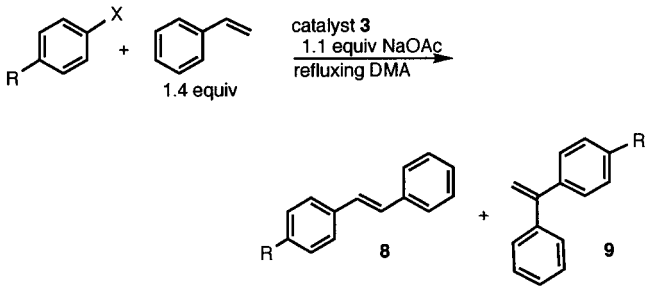
Table 2. Comparison of Heck Reaction Yields for the Reaction between 4-Chlorobenzaldehyde and Styrene with 1 or 3 as Catalyst



catalyst	**6**/**7** yield (%)[a]
1	69/6
3	88/7

[a] ^{1}H NMR yield using bis(ethylene glycol) dibutyl ether as standard.

Table 3. Activity of 3 with Different Substrates and Catalyst Loadings



entry	R	X	amt of **3** (mol %)	special conditions	reacn time (h)	**8**/**9** yield (%)[c]	TON[d]
1	CH_3	I	2×10^{-1}	*a*	0.25	86/13	495
2	CH_3	I	2×10^{-1}		4	83/15	490
3	CH_3	I	2×10^{-2}		7	84/13	4850
4	CH_3	I	2×10^{-3}		20	76/15	45500
5	OCH_3	Br	2×10^{-1}	*a*	0.25	87/11	490
6	OCH_3	Br	2×10^{-1}		1.5	85/11	480
7	CHO	Cl	2×10^{-1}	*a*	0.5	88/7	475
8	CHO	Cl	2×10^{-1}		22	74/6	400
9	CHO	Cl	2×10^{-2}	*a*	2	88/8	4800
10	CHO	Cl	2×10^{-3}	*a*	22	87/8	47500
11	CHO	Cl	5×10^{-4}	*a*	22	25/2	54000
12	CHO	Cl	2×10^{-4}	*a*	22	14/1	75000
13	$C(O)CH_3$	Cl	2×10^{-1}	*a*	0.5	90/8	490
14	OCH_3	Cl	2	*a*	40	6/0	3
15	CHO	Cl	2×10^{-1}	*a*,*b*	2	<5	

[a] With 20 mol % *n*-Bu_4NBr added vs ArX. [b] Reaction carried out at 145 °C. [c] ^{1}H NMR yield using bis(ethylene glycol) dibutyl ether as standard. [d] TON = (mol of product)/(mol of Pd).

unaffected by the difference in alkyl groups between **1** (Me) and **3** (*n*-Bu). No *cis*-stilbene product is detected (^{1}H NMR). With this information in hand, we decided to carry out the rest of the catalytic study with **3**.

Given that **3** shows activity for an aryl chloride substrate, it is not surprising that catalysis is also seen for the olefination of the more reactive aryl iodides and bromides (Table 3, entries 1−6). Reduction of catalyst loading to 2×10^{-3} mol % still gives good yields,

although with somewhat longer reaction times. The *trans*-stilbene is the major product, along with some 1,1-diarylethylene (**9**). The isomeric distribution is constant for a given substrate and not affected by catalyst loading or reaction time. Unexpectedly, reactions reach completion faster for a deactivated aryl bromide than for an unactivated aryl iodide (entries 2 and 6).

Alkylammonium bromides are often added to Heck reactions to facilitate the olefination of aryl chlorides. The olefination of 4-iodotoluene and 4-bromoanisole proceeds in the absence of *n*-Bu_4NBr (Table 3, entries 2 and 6), but can *n*-Bu_4NBr accelerate the reaction at low catalyst loading (2×10^{-1} mol % **3**)? Indeed, the rate of olefination markedly increased for both substrates, completion taking just 15 min (entries 1 and 5) without change in selectivity.

To extend the data in Table 2, we used lower catalyst loadings than the 5 mol % **3** used initially (Table 3, entries 7−12) with 4-chlorobenzaldehyde. Yields remain high even at a catalyst loading of 2×10^{-3} mol % **3**. The TONs of 47 500−75 000 obtained with 2×10^{-3}−2×10^{-4} mol % **3** (entries 10−12) are among the highest yet reported for aryl chlorides, although the temperatures previously used were lower.[3a,8b] Previous aryl chloride olefinations generally required high catalyst loadings or long reaction times for comparable conversions.[2a,3−8,11b,h,13] In addition, our yields are almost the same even in the absence of *n*-Bu_4NBr, but the reaction time is longer (entries 7 and 8).

Another activated aryl chloride, 4-chloroacetophenone, gave results similar to those for 4-chlorobenzaldehyde (Table 3, entry 13). Using 4-chloroanisole as a representative deactivated aryl chloride gave very low yields, even at high catalyst loading and long reaction time (entry 14).

Air Stability. Early on, we found that catalytic runs carried out with the careful exclusion of air and water provided the *same* rates, selectivities, and yields as those carried out without any special precautions. All catalytic reactions were then carried out without special effort to remove air and water and with the reflux condenser open to air. One might argue that solvent refluxing is efficiently degassing the system, thereby preventing the catalyst from being decomposed or otherwise altered by oxygen. Catalyst, solvent, and reagents can be heated 20 °C below reflux for 2 h in air, yielding less than 5% of the *trans*-stilbene product **8** (Table 3, entry 15). When the temperature is increased to reflux, the rate of catalysis increases and maximum conversion is reached after 0.5 h, just as in entry 7. Moreover, when diethylacetamide (DEA, bp 185 °C) is used as the solvent, catalytic Heck coupling is also observed at 165 °C: i.e., the reflux temperature of DMA. Regardless of whether catalysis with DEA is performed under air or an inert atmosphere, a moderate amount (60%) of *trans*-stilbene product is formed within 1 h. This is a lower yield than is found when using DMA as solvent (entry 7) but shows that the catalyst is still active. This difference in activity could be attributed to the decreased solvent polarity when changing from DMA to DEA.

Time-Dependent Reaction Profiles. Apart from the convenience of avoiding inert-atmosphere methods, using air-stable systems under atmospheric pressure also allows multiple samples to be taken from the reaction flask for analysis. Figure 2 shows the resulting time-dependent reaction profiles for the olefination of 4-chlorobenzaldehyde and 4-bromoanisole with catalyst **3**. The absence of an induction period is consistent with there being no slow initial catalyst reduction step. It has been suggested[13a] that *n*-Bu_4NBr can reduce the catalyst virtually instantaneously, leading to the absence of an induction period, but we do not observe an induction period, even for 4-bromoanisole, where there is no added *n*-Bu_4NBr. Elemental mercury selectively poisons heterogeneous catalysts,[15] and so we emphasize that, as we have seen previously,[12] Heck activity with **1** and **3** is entirely unaffected by added metallic Hg, lending support to a homogeneous mechanism.

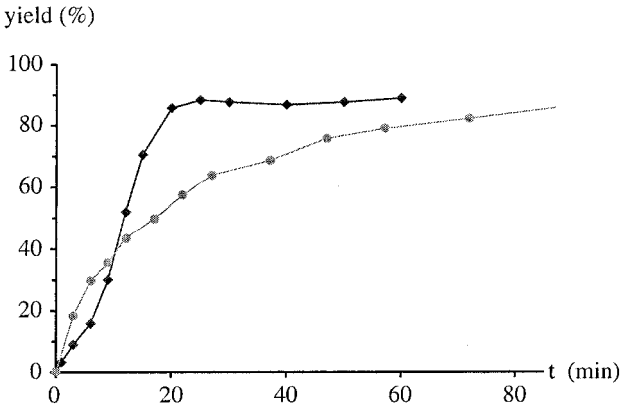


Figure 2. Reaction profiles for 4-chlorobenzaldehyde (♦) or 4-bromoanisole (●) and styrene with 2×10^{-1} mol % of **3**.

Interestingly, the reaction profile for the olefination of 4-chlorobenzaldehyde is sigmoidal, while the profile for 4-bromoanisole is not. As catalyst loading is reduced to 2×10^{-3} mol % for the reaction with 4-chlorobenzaldehyde, the sigmoidal shape of the curve is conserved, though it becomes less pronounced. The TOFs, determined at 50% trans product formation for reaction of 4-chlorobenzaldehyde with styrene at 2×10^{-1}, 2×10^{-2}, and 2×10^{-3} mol % **3**, increase with decreasing catalyst loading, i.e., 1250, 4000, and 6250 h^{-1}, respectively. A similar increase in catalyst efficiency at lower loadings has been reported by others.[16] They give strong kinetic evidence for dimer/monomer equilibria where only the monomer is active. At lower catalyst loading, the equilibrium is pushed toward the monomer. A similar equilibrium may exist in our system.

Reuse of Catalyst 3. Application of **3** in a repetitive process was probed with 4-bromoanisole (Table 4). On completion of the reaction pictured in Table 4, the mixture was cooled, additional aliquots of substrate and base were added, and reflux was continued without loss of activity. Six cycles were carried out, each time without addition of more catalyst or solvent. This necessarily dilutes the catalyst and substrates to some extent, but in independent experiments, we find that even a 5-fold dilution of a standard reaction hardly

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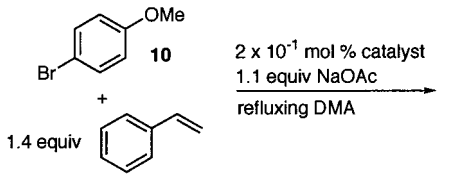
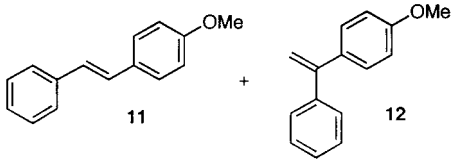
Table 4. Percentages of Aryl Halide and Products after Using 3 in Six Successive Heck Reaction Cycles[a]





cycle[b]	elapsed time since last cycle (h)	11	12	10
1	2[c]	86	12	2
2	2	77	8	13
3	4	86	9	5
4	12	88	8	4
5	3	76	7	13
6	7	79	8	7

[a] ^{1}H NMR yield using bis(ethylene glycol) dibutyl ether as standard; percentages of **10**, **11**, and **12** do not always add up to 100 because of integration error and reflect cumulative amounts at the end of each cycle. [b] For each cycle, the same amount of 4-bromoanisole, styrene, and NaOAc added as in original reaction. [c] Time elapsed since beginning of reaction.

affects the time needed to reach completion. This allowed us to use excess solvent at the very beginning so that only substrate and base would need to be added for each additional cycle. The fact that a reaction mixture retains full activity throughout several cycles provides evidence for the stability of the system and shows its potential use for recycling experiments. Table 4 shows that the longer a given cycle was left to react, the less 4-bromoanisole starting material was left, except for the last cycle, when activity was starting to decrease; therefore, activity is maintained whether or not the prior cycle has come to completion.

Reuse of **3** is also possible when a 5-fold excess of styrene is maintained for five catalytic cycles. The presence of excess styrene in a catalytic run does not stop catalysis but does slow the rate. When a 5-fold excess of styrene is used in a Heck reaction analogous to entry 6 of Table 3, 3 h is required to reach completion instead of 1.5 h when the standard 1.4 equiv of styrene is used. This decrease of rate can be seen when comparing the first two entries in Table 4. After the addition of a second 1.4 equiv of styrene, this amount plus the original excess prevented the second cycle from reaching completion in 2 h; i.e., 13% of **10** remained as opposed to only 2% after the first cycle.

Despite the activity observed for **3** with 4-bromoanisole throughout several cycles, no repetitive use of **3** was possible with 4-chlorobenzaldehyde.

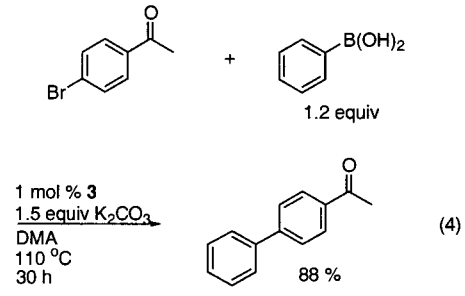
Fluoride as Base. Mechanisms other than the standard Pd(0)/Pd(II) cycle need to be considered. Others[2a,3,14] have invoked Pd(II)/Pd(IV) cycles to explain how pincer or phosphapalladacyclic Pd(II) complexes could achieve such high activity in the Heck reaction. Shaw's proposed mechanism[14a] involves attack of a coordinated olefin by a nucleophile (such as base or halide), generating an electron-rich metal center which is more prone to undergo oxidative addition. A crucial aspect of the proposal is that, after oxidative addition of the aryl halide, the nucleophile acts as a leaving group and is eliminated to regenerate the olefin. We reasoned that if NaF were used as the base, and Shaw's theory were correct, the nucleophilic fluoride attack at the olefin would generate a C−F bond which we expected would be too strong to be cleaved in preference to the alternate reductive elimination or β-hydride elimination, which would then lead to fluorine-containing products. We did not, however, detect any of these products by ^{19}F NMR.

Additional Stability and Activity Probes of 3. Conditions in which **3** deactivates include heating with either styrene or an aryl halide alone. Heating of **3** with 4-iodoacetophenone or 4-bromoacetophenone at 120 °C for 16 h leads to catalyst decomposition. Heating **3** with an excess of styrene at 100 °C for 20 h also leads to decomposition. Under normal catalytic conditions, an excess of styrene does not destroy **3**, but neither is all of the aryl halide consumed.

Use of bases other than NaOAc also leads to a less active system. Tributylamine, NaF, and Cs_2CO_3 were compared using the conditions of entry 7 in Table 3. Tributylamine allows for a maximum yield of 70% of **8** even after 23 h of reaction time, and a yield of only 36% of **8** is obtained with NaF after 19 h. Decomposition of starting materials is observed with the base Cs_2CO_3 after only 1 h.

If 20 mol % of *n*-Bu_4NCl or *n*-Bu_4NI is substituted for *n*-Bu_4NBr under the conditions of entry 7 in Table 3, the system again becomes less active. *n*-Bu_4NCl does give the same conversion as *n*-Bu_4NBr, but 1 h is required instead of 30 min. This reactivity is interesting in light of Jeffrey[17] finding that *n*-Bu_4NCl is more efficient than *n*-Bu_4NBr for room-temperature Heck couplings with $Pd(OAc)_2$ as catalyst. In addition, *n*-Bu_4NCl is more difficult to handle because it is much more hygroscopic than *n*-Bu_4NBr. Use of *n*-Bu_4NI gives only a 59% yield of **8** after 3 h.

Suzuki and Sonogashira Catalysis. Catalytic reactions other than Heck reactions were also probed. The Suzuki reaction between the activated aryl bromide 4-bromoacetophenone and phenylboronic acid yielded the substituted biphenyl in 88% yield (eq 4). With 2 ×

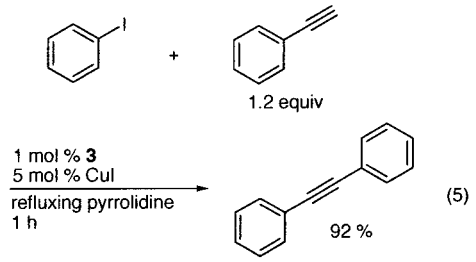


10^{-1} mol % of **3**, a yield of 70% is obtained in 30 h. Traditionally, solvents such as THF, dioxane, and toluene are used in the Suzuki reaction, but the solubility properties of **3** constrained us to using DMA. These

(17) Jeffery, T. *J. Chem. Soc., Chem. Commun.* **1984**, 1287−1289.

reactions were again unaffected by air, and the fact that DMA is not at reflux temperature during the reaction confirms that refluxing is not required to degas the system.

The Sonogashira reaction was also evaluated with **3** (eq 5). Iodobenzene and phenylacetylene can be coupled



(5)

in pyrrolidine (bp 87 °C) with CuI as cocatalyst. Yields are as low as 10% even after 19 h with 4-bromoacetophenone, however. Highly active substrates seem to be necessary for good yields with **3** in the Suzuki and Sonogashira reactions.

Heck Catalysis with 5. We synthesized the monocarbene complex **5** to investigate how its activity would differ from that of **3**. We postulated that **5** would promote catalysis at a lower temperature if a temperature of 165 °C was needed simply to promote loss of one of the carbenes of **3**. Using 2×10^{-1} mol % of **5** with 4-chlorobenzaldehyde, as in entry 7 of Table 3, yielded little product at 145 °C. At 165 °C, however, **5** gave product at the same rate as **3**. The sigmoidal reaction profile of **5** for this reaction with 4-chlorobenzaldehyde is also identical with that of **3**. This comparable activity between **3** and **5** contrasts with a prior report that a bidentate S,C-donor Pd chelate catalyst shows greater activity than a S,C,S tridentate pincer Pd catalyst analogue.[8a] The syntheses of **3** and **5** are comparable as far as ease and time required. The advantage to using **3**, however, is its greater stability vs **5**. Palladium black is seen upon reaction completion with **5** but not with **3**.

Conclusion

We report[12] a new and potentially useful ligand type, a C,N,C pincer bis-carbene complex of Pd(II) related to those very recently found by others.[11i] The complex shows excellent air and thermal stability at elevated temperatures and is an active catalyst for C−C coupling reactions. Complex **3** maintains activity with reuse and allows for markedly high TONs in the Heck olefination of activated aryl chlorides. Pd complexes with a C,N,C pincer ligand have stability advantages over a complex with a bidentate ligand analogue yet display activity similar to this analogue for a single catalytic cycle.

Experimental Section

General Considerations. The palladium complexes **1**[12] and $[PdCl_2(SMe_2)_2]$[18] were prepared according to literature procedures. All other reagents are commercially available and were used as received. All NMR spectra were recorded at room temperature on Bruker spectrometers operating at 400 or 500 MHz (^{1}H NMR) and 100 or 125 MHz (^{13}C NMR), respectively, and referenced to $SiMe_4$ (δ in ppm, J in Hz). Assignments are based either on distortionless enhancement of polarization transfer (DEPT) experiments or on heteronuclear shift correlation spectroscopy. Melting points are uncorrected. Elemental analyses were performed by Atlantic Microlab, Inc.; residual solvent molecules have been identified by ^{1}H NMR. GC/MS analyses were made on a HP-5971A MSD interfaced to a HP-5890 series II GC.

[CHNCH-Bu$_2$]Br$_2$ (2). A solution of 2,6-dibromopyridine (3.20 g, 13.5 mmol) and 1-butylimidazole (3.36 mg, 27.0 mmol) was stirred neat at 150 °C for 20 h. After cooling, the mixture was dissolved in $CHCl_3$ (50 mL) and Et_2O (250 mL) was added. The precipitate was collected, redissolved in $CHCl_3$, and precipitated with Et_2O. The crude product was purified by precipitation from MeOH/Et_2O to give an off-white NMR-pure solid. Yield: 5.94 g (91%). The product can be recrystallized from MeOH/Et_2O. ^{1}H NMR ($CDCl_3$): δ 12.00 (s, 2H, NC*H*N), 9.25 (s, 2H, imidazole *H*), 8.77 (d, 2H, $^3J_{HH} = 8.0$ Hz, pyridine *H*), 8.30 (t, 1H, $^3J_{HH} = 8.0$ Hz, pyridine *H*), 7.46 (s, 2H, imidazole *H*), 4.60 (t, 4H, $^3J_{HH} = 7.3$ Hz, NC*H*$_2$CH$_2$CH$_2$CH$_3$), 2.01 (quintet, 4H, $^3J_{HH} = 7.4$ Hz, NCH$_2$C*H*$_2$CH$_2$CH$_3$), 1.46 (sextet, 4H, $^3J_{HH} = 7.5$ Hz, NCH$_2$CH$_2$C*H*$_2$CH$_3$), 1.00 (t, 6H, $^3J_{HH} = 7.4$ Hz, NCH$_2$CH$_2$CH$_2$C*H*$_3$). ^{13}C{^{1}H} NMR ($CDCl_3$): δ 145.35 (N*C*HN), 145.23 (C_{ortho}), 136.75 (C_{para}), 122.95 (imidazole *C*), 120.88 (imidazole *C*), 115.45 (C_{meta}), 50.60 (N*C*H$_2$CH$_2$CH$_2$CH$_3$), 32.18 (NCH$_2$*C*H$_2$CH$_2$CH$_3$), 19.47 (NCH$_2$CH$_2$*C*H$_2$CH$_3$), 13.45 (NCH$_2$CH$_2$CH$_2$*C*H$_3$). Mp: 109−111 °C. Anal. Calcd for $C_{19}H_{25}Br_2N_5Pd$ (485.26) and H_2O: C, 45.34; H, 5.81; N, 13.92. Found: C, 45.06; H, 5.72; N, 13.81.

[PdBr(CNC-Bu$_2$)][Br] (3). A solution of **2** (485 mg, 1.0 mmol) and $[Pd(OAc)_2]$ (224 mg, 1.0 mmol) was stirred in DMSO (8 mL) for 3 h at room temperature and then for 12 h at 50 °C. Subsequently, the reaction mixture was heated to 155 °C for 1 h and cooled to room temperature. The solution was poured into CH_2Cl_2 (20 mL), and Et_2O was added (200 mL). The precipitate was washed three times by dissolving in $CHCl_3$ and precipitating with Et_2O, leaving 418 mg (71%) of the crude product as a yellowish solid. Analytically pure **3** was obtained by slow diffusion of Et_2O into a solution of **3** in $CHCl_3$, which afforded crystals that were also suitable for a single-crystal structure determination. ^{1}H NMR ($CDCl_3$): δ 8.66 (s, 2H, imidazole *H*), 8.49 (d, 2H, $^3J_{HH} = 8.0$ Hz, pyridin *H*), 8.33 (t, 1H, $^3J_{HH} = 8.0$ Hz, pyridine *H*), 7.17 (s, 2H, imidazole *H*), 4.62 (t, 4H, $^3J_{HH} = 7.5$ Hz, NC*H*$_2$CH$_2$CH$_2$CH$_3$), 1.82 (quintet, 4H, $^3J_{HH} = 7.5$ Hz, NCH$_2$C*H*$_2$CH$_2$CH$_3$), 1.42 (sextet, 4H, $^3J_{HH} = 7.5$ Hz, NCH$_2$CH$_2$C*H*$_2$CH$_3$), 0.96 (t, 6H, $^3J_{HH} = 7.4$ Hz, NCH$_2$CH$_2$CH$_2$C*H*$_3$). ^{13}C{^{1}H} NMR ($CDCl_3$): δ 166.54 (C−Pd), 150.10 (C_{ortho}), 146.66 (C_{para}), 123.63 (imidazole *C*), 119.06 (imidazole *C*), 110.13 (C_{meta}), 51.05 (N*C*H$_2$CH$_2$CH$_2$CH$_3$), 33.32 (NCH$_2$*C*H$_2$CH$_2$CH$_3$), 19.59 (NCH$_2$CH$_2$*C*H$_2$CH$_3$), 13.73 (NCH$_2$CH$_2$CH$_2$*C*H$_3$). Anal. Calcd for $C_{19}H_{25}Br_2N_5Pd$ (589.66): C, 38.70; H, 4.27; N, 11.88. Found: C, 38.44; H, 4.48; N, 11.83.

[CHN-Bu]Br (4). A solution of 2-bromopyridine (3.80 g, 24 mmol) and 1-butylimidazole (3.00 g, 24 mmol) was stirred neat at 160 °C for 20 h. After it was cooled, the mixture was dissolved in CH_2Cl_2 (20 mL) and Et_2O (100 mL) was added. The precipitate was collected, redissolved in CH_2Cl_2, and precipitated with pentane to give **4** as the monohydrate salt. Yield: 6.26 g (92%). ^{1}H NMR ($CDCl_3$): δ = 11.66 (s, 1H, NC*H*N), 8.56 (d, 1H, $^3J_{HH} = 8.0$ Hz, pyridine *H*-6), 8.49 (dd, 1H, $^3J_{HH} = 4.8$ Hz, $^4J_{HH} = 1.0$ Hz, pyridine *H*-3), 8.33 (t, 1H, $^3J_{HH} = 1.3$ Hz, imidazole *H*), 8.02 (dt, 1H, $^3J_{HH} = 8.0$ Hz, $^4J_{HH} = 1.0$ Hz, pyridine *H*-5), 7.62 (t, 1H, $^3J_{HH} = 1.3$ Hz, imidazole *H*), 7.43 (dd, 1H, $^3J_{HH} = 7.1$ Hz, $^4J_{HH} = 4.8$ Hz, pyridine *H*-4), 4.56 (t, 2H, $^3J_{HH} = 7.2$ Hz, NC*H*$_2$CH$_2$CH$_2$CH$_3$), 1.99 (quintet, 2H, $^3J_{HH} = 7.4$ Hz, NCH$_2$C*H*$_2$CH$_2$CH$_3$), 1.44 (sextet, 2H, $^3J_{HH} = 7.4$ Hz, NCH$_2$CH$_2$C*H*$_2$CH$_3$), 0.95 (t, 3H, $^3J_{HH} = 7.2$ Hz, NCH$_2$CH$_2$CH$_2$C*H*$_3$). ^{13}C{^{1}H} NMR ($CDCl_3$): δ 148.87 (N*C*HN), 145.89 (C_{ortho}), 140.56 (C_{para}), 135.66, 125.07, 122.26 (imidazole *C*), 118.80 (imidazole *C*), 115.01 (C_{meta}), 50.38 (N*C*H$_2$CH$_2$CH$_2$CH$_3$), 32.11 (NCH$_2$*C*H$_2$CH$_2$CH$_3$), 19.42 (NCH$_2$CH$_2$*C*H$_2$CH$_3$),

(18) Byers, P. K.; Canty, A. J.; Jin, H.; Kruis, D.; Markies, B. A.; Boersma, J.; Van Koten, G. *Inorg. Synth.* **1998**, *32*, 162−172.

13.41 ($NCH_2CH_2CH_2CH_3$). Mp: 68−70 °C. Anal. Calcd for $C_{12}H_{16}BrN_3$ (282.18) and H_2O: C, 48.01; H, 6.04; N, 14.00. Found: C, 48.09; H, 6.02; N, 14.00.

[PdBr$_2$(CN-Bu)] (5). To a solution of **4** (564 mg, 2.0 mmol) and $[PdCl_2(SMe_2)_2]$ (640 mg, 2.0 mmol) in THF (20 mL) was added KO*t*Bu (224 mg, 2.0 mmol) at −80 °C. This mixture was stirred for 12 h, while the reaction temperature was raised to room temperature. All volatiles were removed in vacuo, and the residue was suspended in CH_2Cl_2 (10 mL). After filtration, Et_2O (80 mL) was added to the filtrate and the precipitate collected and stirred in acetone (20 mL) in the presence of NaBr (1 g, 10 mmol) for 4 h. Filtration and evaporation of all the volatiles afforded **5** as a yellow solid (402 mg, 43%). Recrystallization from a saturated acetone solution at −20 °C gave analytically pure yellow crystals, which were also suitable for a single-crystal X-ray structure determination. ^{1}H NMR ($CDCl_3$): δ 9.78 (d, 1H, $^3J_{HH}$ = 5.8 Hz, pyridine *H*-6), 8.10 (dt, 1H, $^3J_{HH}$ = 8.0 Hz, $^4J_{HH}$ = 1.2 Hz, pyridine *H*-3), 7.54 (d, 1H, $^3J_{HH}$ = 1.6 Hz, imidazole *H*), 7.05 (d, 1H, $^3J_{HH}$ = 8.0 Hz, pyridine *H*-5), 7.39 (t, 1H, $^3J_{HH}$ = 6.6 Hz, pyridine *H*-4), 7.04 (t, 1H, $^3J_{HH}$ = 1.6 Hz, imidazole *H*), 4.80 (t, 2H, $^3J_{HH}$ = 7.6 Hz, $NCH_2CH_2CH_2CH_3$), 1.88 (quintet, 2H, $^3J_{HH}$ = 7.6 Hz, $NCH_2CH_2CH_2CH_3$), 1.44 (sextet, 2H, $^3J_{HH}$ = 7.5 Hz, $NCH_2CH_2CH_2CH_3$), 0.96 (t, 3H, $^3J_{HH}$ = 7.6 Hz, $NCH_2CH_2CH_2CH_3$). ^{13}C{^{1}H} NMR ($CDCl_3$): δ 152.64 (*N*CHN), 151.89 (C_{ortho}), 141.57 (C_{para}), 124.08, 122.92 (imidazole *C*), 115.01 (imidazole *C*), 110.71 (C_{meta}), 51.73 ($NCH_2CH_2CH_2CH_3$), 33.66 ($NCH_2CH_2CH_2CH_3$), 19.58 ($NCH_2CH_2CH_2CH_3$), 13.74 ($NCH_2CH_2CH_2CH_3$). Mp: >250 °C. Anal. Calcd for $C_{12}H_{15}Br_2N_3Pd$ (467.50): C, 30.83; H, 3.23; N, 8.99. Found: C, 31.13; H, 3.25; N, 8.96.

General Heck Procedure. Catalyst, NaOAc (180 mg, 2.2 mmol), aryl halide (2.0 mmol), styrene (320 μL, 2.8 mmol), DMA (5 mL), and bis(ethylene glycol) dibutyl ether (246 μL, 1.0 mmol, ^{1}H NMR standard) were added to a 35 mL round-bottom flask. The reaction vessel was attached to a reflux condenser and placed into an oil bath preheated to the desired temperature. Aliquots (100 μL) were removed after fixed times with a syringe and added to 10 mL of CH_2Cl_2. The organic layer was extracted four times with 10 mL portions of water and dried with $MgSO_4$. The mixture was then filtered and the CH_2Cl_2 removed in vacuo. The residue was dissolved in $CDCl_3$ and analyzed by ^{1}H NMR.

General Suzuki Procedure. Catalyst, K_2CO_3 (355 mg, 2.6 mmol), 4-bromoacetophenone (338 mg, 1.7 mmol), phenylboronic acid (247 mg, 2.0 mmol), DMA (5 mL), and bis(ethylene glycol) dibutyl ether (211 μL, 0.85 mmol, ^{1}H NMR standard) were added to a 35 mL round-bottom flask. The remainder of the reaction follows the general Heck procedure.

General Sonogashira Procedure. Catalyst **3** (10 mg, 17 μmol), aryl halide (1.7 mmol), phenylacetylene (220 μL, 2.0 mmol), pyrrolidine (5 mL), CuI (16.2 mg, 85 μmol), and bis(ethylene glycol) dibutyl ether (210 μL, 0.85 mmol, GC/MS standard) were added to a 35 mL round-bottom flask. The remainder of the reaction follows the general Heck procedure, except that yields were determinded by GC/MS.

Procedure for Continuous Use of 3. NaOAc (180 mg, 2.2 mmol), 4-bromoanisole (250 μL, 2.0 mmol), styrene (320 μL, 2.8 mmol), **3** (2.4 mg, 0.004 mmol), DMA (15 mL), and bis(ethylene glycol) dibutyl ether (246 μL, 1.0 mmol, ^{1}H NMR standard) were added to a 100 mL round-bottom flask. The reaction vessel was attached to a reflux condenser and placed into an oil bath preheated to the desired temperature. Aliquots (100 μL) were removed after desired times and worked up as described in the general Heck procedure. After an aliquot was removed, the round-bottom flask and reflux condenser were removed from the oil bath and cooled for 0.5 h. The reflux condenser was then removed so that NaOAc (180 mg, 2.2 mmol), 4-bromoanisole (250 μL, 2.0 mmol), and styrene (320 μL, 2.8 mmol) could be added. The condenser was reattached, and the round-bottom flask was placed back into the oil bath.

Table 5. Crystallographic Data for 3 and 5

	3	**5**
color, shape	yellow needles	yellow cube
empirical formula	$C_{19}H_{25}Br_2N_5Pd\cdot CHCl_3$	$C_{12}H_{15}Br_2N_3Pd$
fw	708.02	467.48
radiation, λ/Å	Mo Kα (monochr), 0.710 73	
T/K	293	183
cryst syst	triclinic	monoclinic
space group	$P\bar{1}$ (No. 2)	*C*2/*c* (No. 15)
unit cell dimens		
a/Å	10.5811(18)	14.1086(9)
b/Å	11.934(2)	11.8348(7)
c/Å	12.667(2)	17.4997(9)
α/deg	63.675(4)	90
β/deg	67.251(4)	99.540(4)
γ/deg	72.791(4)	90
V/Å^3	1307.0(4)	2881.6(3)
Z	2	8
D_{calcd}/g cm^{-3}	1.799	2.155
μ(Mo Kα)/mm^{-1}	4.091	6.838
cryst size/mm	0.35 × 0.12 × 0.09	0.10 × 0.12 × 0.14
total, unique no. of rflns	5618, 3192	8550, 3395
R_{int}	0.036	0.051
transmissn range	0.969−1.956	0.462−0.520
no. of params, restraints	280, 0	168, 0
R1,[a] wR2 or R_w,[b] *S*	0.0513, 0.1253, 0.983	0.034; 0.039, 0.89
resid. density/e Å^{-3}	−0.432 < 0.683	−0.73 < 1.24

[a] For **3** $R_1 = \sum||F_o| - |F_c||/\sum|F_o|$, for all $I > 4\sigma(I)$; for **5** for all $I > 3\sigma(I)$. [b] For **3** wR2 = $[\sum[w(F_o^2 - F_c^2)^2]/\sum[w(F_o^2)^2]]^{1/2}$; for **5** $R_w = [\sum w(|F_o| - |F_c|)^2/\sum wF_o^2]]^{1/2}$.

Structure Determination and Refinement of 3. Data for **3** were collected on a Bruker SMART CCD with a rotating anode (Mo Kα radiation, λ = 0.710 73 Å) and corrected for absorption (SADABS[19]). The structure was solved by direct methods and refined on *F*.[20] Non-hydrogen atoms were refined freely with anisotropic displacement parameters. Hydrogen atoms were refined at calculated positions riding on their carrier atoms. Weights were optimized in the final refinement cycles. Crystal data are given in Table 5.

Structure Determination and Refinement of 5. Data for **5** were collected on a Nonius KappaCCD (Mo Kα radiation) and corrected for absorption (SORTAV[21]). The structure was solved by direct methods (SIR92[22]) and refined against *F* of all reflections. Non-hydrogen atoms were refined freely with anisotropic displacement parameters. Hydrogen atoms were refined at calculated positions. Crystal data are given in Table 5.

Acknowledgment. We gratefully acknowledge financial support from the US DOE and NSF and the Swiss National Foundation (M.A.).

Supporting Information Available: Crystallographic details for **3** and **5**. This material is available free of charge via the Internet at http://pubs.acs.org.

OM010852N

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