1,1′-P/O-Ferrocenyl Ligands in Palladium-Catalyzed Suzuki Coupling of Aryl Chlorides

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Several new P/O-functionalized ferrocenyl ligands have been synthesized. They react with $Pd_2(dba)_3$ to promote the Suzuki cross-couplings of a range of arylboronic acids and aryl chlorides to give the desired biaryl products in high isolated yields. Different oxidative addition products were isolated and crystallographically identified. Their roles in the catalytic pathways are discussed.

Introduction

Ferrocenyl-based ligands functionalized by different donor atoms have a rich coordination and catalytic chemistry.[1] The hetero functionalities promote hemilability and coordinative flexibility of the ligand. They underpin the successes experienced by many P/P′-, P/N-, P/S- and even O/N-donating ferrocenes.[2] The P/O-ferrocenyl ligands remain rare, with a few notable exceptions, such as [(*rac*)-PPF-OMe],[3] (*S*)-(*R*)-bis-(PPFOMe),[4] and aryl-MOPFs,[5] which are remarkably active toward asymmetric Pd- and Ni-catalyzed amination of halides,[3a,b] Grignard reactions,[3c] Suzuki cross-couplings,[5a] and associated syntheses.[4,5b,c] A recent example is found in 1-(diphenylphosphino)-1′-methoxylferrocene toward Suzuki reactions of aryl bromides and arylboronic acids.[6] They compare well with the aromatic-based P/O ligands[7] that also showed promise in Suzuki syntheses[7a−d] and asymmetric Heck reactions,[7e] with MOP[7f,g] being among the best known in asymmetric metal-catalyzed reactions. The vastly different electronic and steric characters of the P and O donors, coupled with the conformationally flexible and coordinatively adaptive ferrocene backbone, make this an attractive system that could demonstrate the intricacies of ligand hemilability.[8] Recently we reported success in the use of the unsymmetrical [(1′-(di-*tert*-butylphosphino)ferrocen-1-yl)methyl]phenylimine[9] in supporting Pd(0) in Suzuki coupling[10] of aryl chlorides and arylboronic acids. Herein, we focus on the synthesis of some new 1,1′-phosphine-ether-functionalized ferrocenyl ligands and their catalytic efficiency toward C−Cl activation[10a,b] in Suzuki−Miyaura couplings. Through the detection or/and isolation of a number of key species in the catalytic process, we herein also demonstrate the rich underlying coordination chemistry.

Results and Discussion

The combinative use of strongly coordinating phosphine and weakly basic cyclic (di)ether as pendants on a ferrocene skeletal backbone is a key to our approach. Adapting known synthetic methods,[11] we synthesized and isolated the novel metalloligands **1a**, **1b**, and **2** in moderate yields (54−63%) (Scheme 1 and Figure 1). The advantages of the use of these ligands include their simple preparations and derivatization at the phosphorus and cyclic diether sites. To examine the role of hetero functionalities, we compared their activities with those of the related monophosphine **3**[12] and diphosphine **4** (Figure 1). A survey on a representative coupling of 4-chloroacetophenone with phenylboronic acid revealed a remarkable advantage of the presence of the ether pendant (Table 1). The isolated yield of the coupling

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(1) (a) Togni, A.; Hayashi, T. *Ferrocenes: Homogeneous Catalysis, Organic Synthesis, Materials Science*; VCH: Weinheim, Germany, 1995; Chapter 1. (b) Togni, A.; Haltermann, R. L. *Metallocenes*; Wiley-VCH: Weinheim, Germany, 1998. (c) Long, N. J. *Metallocenes: An Introduction to Sandwich Complexes*; Blackwell Science: Oxford, U.K., 1998.

(2) (a) Atkinson, R. C. J.; Gibson, V. C.; Long, N. J. *Chem. Soc. Rev*, **2004**, *33*, 313. (b) Gan, K. S.; Hor, T. S. A. *Ferrocenes: Homogeneous Catalysis, Organic Synthesis, Materials Science*; VCH: Weinheim, Germany, 1995. (c) Togni, A. *Angew. Chem., Int. Ed. Engl.* **1996**, *35*, 1475. (d) Dai, L.-X.; Tu, T.; You, S.-L.; Deng, W.-P.; Hou, X.-L. *Acc. Chem. Res.* **2003**, *36*, 659.

(3) (a) Wolfe, J. P.; Buchwald, S. L. *Tetrahedron Lett.* **1997**, *38*, 6359. (b) Marcoux, J.-F.; Wagaw, S.; Buchwald, S. L. *J. Org. Chem*. **1997**, *62*, 1568. (c) Hiyashi, T.; Hayashizaki, K.; Kiyoi, T.; Ito, Y. *J. Am. Chem. Soc*. **1988**, *110*, 8153.

(4) Ohmura, H.; Matsuhashi, H.; Tanaka, M.; Kuroboshi, M.; Hiyama, T.; Hatanka, Y.; Goda, K.-I. *J. Organomet. Chem*. **1995**, *499*, 167.

(5) (a) Josen, J. F.; Johannson, M. *Org. Lett.* **2003**, *5*(17), 3025. (b) Pederson, H. L.; Johannsen, M. *Chem. Commun.* **1999**, 2517. (c) Pederson, H. L.; Johannsen, M. *J. Org. Chem*. **2002**, *67*, 7892.

(6) Atkinson, R. C. J.; Gibson, V. C.; Long, N. J.; White, A. J. P.; Williams, D. J. *Organometallics* **2004**, *23*, 2744.

(7) (a) Bei, X.; Turner, H. W.; Weinberg, W. H.; Guram, A. S. *J. Org. Chem*, **1999**, *64*, 6797. (b) Bei, X.; Uno, T.; Norris, J. H.; Turner, W.; Weinberg, W. H.; Guram, A. S. *Organometallics* **1999**, *18*, 1840. (c) Kwong, F. Y.; Lam, W. H.; Yeung, C. H.; Chan, K. S.; Chan, A. S. C. *Chem. Commun*. **2004**, 1922. (d) Dai, W. M.; Li, Y.; Zhang, Y.; Lai, K. W.; Wu, J. *Tetrahedron Lett*. **2004**, *45*, 1999. (e) Dai, W. M.; Yeung, K. K. Y.; Wang, Y. *Tetrahedron* **2004**, *60*, 4425. (f) Hayashi, T. *Acta Chem. Scad*. **1996**, *50*, 259. (g) Hayashi, T. *Acc. Chem. Res*, **2000**, *33*, 354. (h) Dai, W.-M.; Zhang, Y. *Tetrahedron Lett*. **2005**, *46*, 1377.

(8) Braunstein, P.; Naud, F. *Angew. Chem., Int. Ed.* **2001**, *40*, 680.

(9) Weng, Z.; Teo, S.; Koh, L. L.; Hor, T. S. A. *Organometallics* **2004**, *23*, 4342.

(10) (a) Littke, A. F.; Fu, G. C. *Angew. Chem., Int. Ed.* **2002**, *41*, 4176. (b) Miura, M. *Angew. Chem., Int. Ed*. **2004**, *43*, 2001. (c) Suzuki, A. *J. Organomet. Chem*. **1999**, *576*, 147. (d) Miyamura, N.; Suzuki, A. *Chem. Rev*. **1995**, *95*, 2457.

(11) (a) Moulton, R. D.; Bard, A. J. *Organometallics* **1988**, *7*, 351. (b) Dong, T.-Y.; Lai, L.-L. *J. Organomet. Chem.* **1996**, *509*, 131. (c) Dong, T.-Y.; Lai, L.-L. *Synthesis* **1995**, 1231.

(12) For ferrocene-based monophosphine ligands in Suzuki cross-coupling of aryl chlorides, see: (a) Pickett, T. E.; Richards, J. C. *Tetrahedron Lett*. **2001**, *42*, 3767. (b) Liu, S. Y.; Choi, M. J.; Fu, G. C. *Chem. Commun.* **2001**, 2408. (c) Kataoka, N.; Shelby, Q.; Stambuli, J. P.; Hartwig, J. F. *J. Org. Chem.* **2002**, *67*, 5553. (d) Pickett, T. E.; Roca, F. X.; Richards, C. J. *J. Org. Chem.* **2003**, *68*, 2592.

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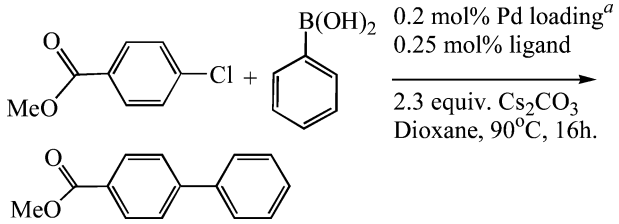
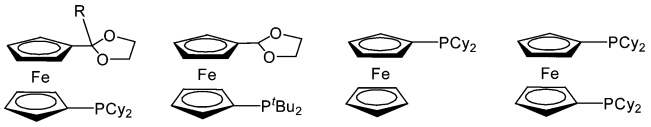
Table 1. Ligand Effect on the Suzuki Cross-Coupling Reaction of 4-Chloroacetophenone with Phenylboronic Acid



entry	ligand (L)	yield (%)[b]
1	**1a**	84
2	**1b**	100
3	**2**	100
4	**3**	trace[c]
5	**4**	26

[a] $Pd_2(dba)_3$. [b] Isolated yield. [c] GC yield; isolated yield of 59% when 5 mol % of $Pd(OAc)_2$ and 6 mol % of L are used.

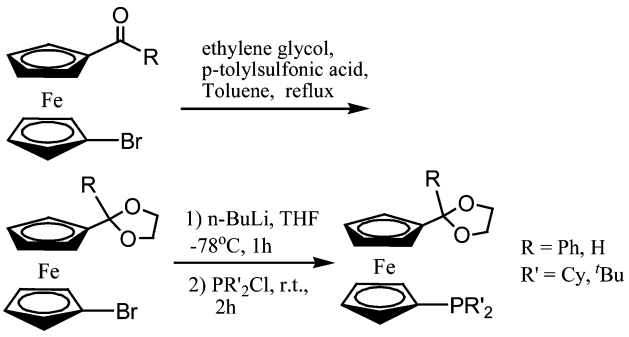


R = Ph, **1a** R = H, **1b** **2** **3** **4**

Figure 1. Different types of ferrocenyl ligands under survey.

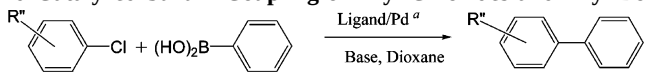
product is quantitative for **1b** and **2** and satisfactory for **1a**, whereas the controls (**3** and **4**) gave insignificant products. The simultaneous presence of a strong coordinating group (phosphorus) and a much weaker and restrictive donor (oxygen) gives the ligands (**1** and **2**) their hemilability and significantly increased the cross-coupling product yield, whereas **3** (monodentate) and **4** (bidentate chelate) are much less effective. These point to the delicate but important balance between coordination and noncoordination of the ligand as well as saturation and unsaturation of the metal. The activities of **1** and **2** are comparable to those of some P/O-ferrocenyl systems such as aryl-MOPFs, which catalyzed the Suzuki coupling of 4-chloroacetophenone with phenylboronic acid, giving up to 91% yield at 5 mol % of $Pd(OAc)_2$ and 6 mol % of the ligand under ambient conditions.[5a]

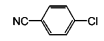
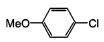
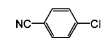
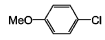
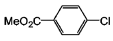
Scheme 1. Synthesis of a Phosphine−Cyclic(bi)ether Ferrocenyl Ligand



Ligand **1b** is our preferred choice, because it is less air sensitive than **2** and easier to handle experimentally. A typical catalytic screening toward a series of aryl substrates using $Pd_2(dba)_3$ and ligands **1** are conducted in 1,4-dioxane at 70−100 °C in the presence of CsF or Cs_2CO_3 (Table 2). Use of a base weaker than CsF, such as Cs_2CO_3, would generally result in lower yields. These findings are consistent with published results.[13] The contrast in the activities of **1a** and **1b** is exemplified in entries 6 and 12, which revealed that a simple

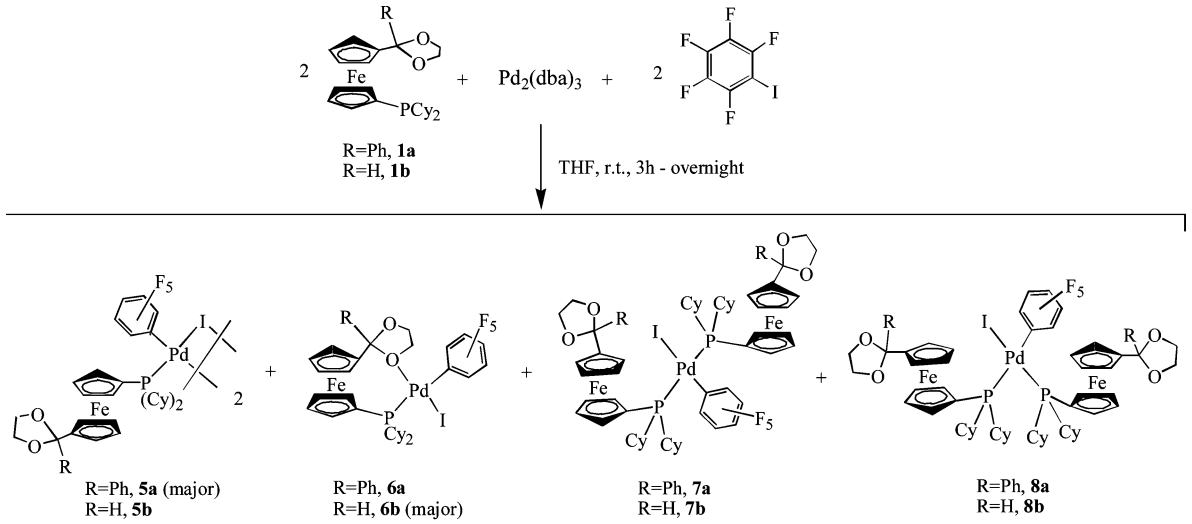
Table 2. Pd-Catalyzed Suzuki Coupling of Aryl Chlorides and Aryl Boronic Acids



Entry	Aryl chloride	Ligand	Base	Pd Loading/ mol% [b]	Temp./°C	Reaction Time/h[c]	% Yield[d]
1		**1a**	CsF	0.1	105	18	100
2		**1a**	CsF	1.0	105	24	84
3		**1a**	CsF	2.0	105	24	71
4		**1a**	CsF	1.0	105	24	96
5		**1a**	CsF	2.0	105	30	92
6		**1a**	CsF	2.0	105	24	97
7		**1b**	Cs_2CO_3	0.05	90	6	100
8		**1b**	Cs_2CO_3	0.5	90	16	100
9		**1b**	Cs_2CO_3	1.0	90	24	92
10		**1b**	Cs_2CO_3	1.0	90	30	96
11[e]		**1b**	Cs_2CO_3	1.0	90	24	100
12		**1b**	CsF	2.0	90	24	47

[a] $Pd_2(dba)_3$. [b] Pd:ligand = 1.0:1.1. [c] Not optimized. [d] Isolated yields. [e] *p*-Methoxylphenylboronic acid is used instead of phenylboronic acid.

Scheme 2. Different Oxidation Addition Products from the P/O Ligands



addition of a phenyl sidearm on the peripheral cyclic ether could turn a mediocre (47%) to near-quantitative yield toward a stable substrate such as 2-(chloromethyl)benzene. These somewhat unexpected differences between **1a** and **1b** and the atypical results found in the ortho-substituted aryl chlorides among the arylboronic acids prompted us to examine further the possible intermediates formed in these reaction mixtures. Although the catalytic mechanism of Suzuki-type coupling has been well researched[10a] and is outside the scope of our work, further structural information on the resulting complexes formed from these potentially hemilabile ligands would eventually lead to better catalyst design.

To meet the objective to trap and structurally characterize species that are mechanistically relevant, we have identified several oxidative addition products from stoichiometric reactions (Scheme 2).

All the complexes show oxidative addition of Pd^0, with $I-C_6F_5$ giving $[I-Pd-C_6H_5]$. Solution NMR analysis suggested that there is little perturbation at the cyclic ether moiety. X-ray single-crystal crystallographic analysis of **5a** confirmed this and further revealed a Pd(II) square-planar dimeric structure with a doubly bridging iodide. Ligand **1a** coordinates as a monodentate phosphine ligand with dangling ether (Figure 2 and Table 3). This gives rare crystallographic evidence that the oxidative addition step of a Pd(0)-catalyzed Suzuki coupling does not necessarily yield the commonly assumed mononuclear species. If a strongly coordinating chelating ligand (e.g. dppe, dppf, etc.) is absent or when the supporting monodentate phosphines (e.g. PR_3) are in short supply, the catalyst can be stabilized by a facile dimerization process. This takes advantage of the basicity of the halide from the substrate, thereby allowing the metal to

Table 3. Selected Bond Lengths and Angles of Complexes 5a, 5b, 7a, and 7b

	5a	5b	7a	7b
		Bond Lengths		
Pd(1)−I(1)	2.6577(6)	2.6710(6)	2.6535(4)	2.6452 (13)
Pd(1)−P(1)	2.2753(16)	2.2751(16)	2.3638(11)	2.354(2)
Pd(1)−C(1)	2.031(7)	2.046(7)		1.995(11)
Pd(1)−P(2)			2.3415(12)	
Pd(1)−C(32)			2.024(4)	
		Bond Angles		
P(1)−Pd(1)−I(1)	176.62(5)	177.88(5)	90.40(3)	91.56(7)
P(1)−Pd(1)−C(1)	91.34(17)	90.95(17)		88.44(6)
C(1)−Pd(1)−I(1)	86.88(17)	86.97(16)		180.00(1)
I(1)−Pd−I(1A)	87.06(19)	86.356(19)		
Pd(1)−I(1)−Pd(1A)	92.939(19)	93.644(19)		
P(1)−Pd(1)−I(1A)	94.62(4)	95.72(4)		
C(1)−Pd(1)−I(1A)	173.73(18)	173.32(16)		
C(32)−Pd(1)−P(1)				89.88(11)
C(32)−Pd(1)−P(2)			90.41 (11)	
C(32)−Pd(1)−I(1)			177.10 (13)	
P(2)−Pd(1)−P(1)			176.18(4)	
P(1A)−Pd−P(1)				176.87(13)

gain saturation and minimizing catalyst decomposition in the absence of a good coordinating solvent. When **1a** is replaced by ligand **1b**, the similar dimeric complex **5b** is isolated (Figure 3 and Table 3). Such dinuclear formation could be common among oxidative addition products.

Complex **6** corresponds to the expected mononuclear Pd(II) oxidative addition product with P/O chelation. The coordination of ether lacks crystallographic support but is inferred from the ^1H NMR shifts of the methylene protons neighboring the oxygen functions. Complexes **7a** and **7b** are also mononuclear but

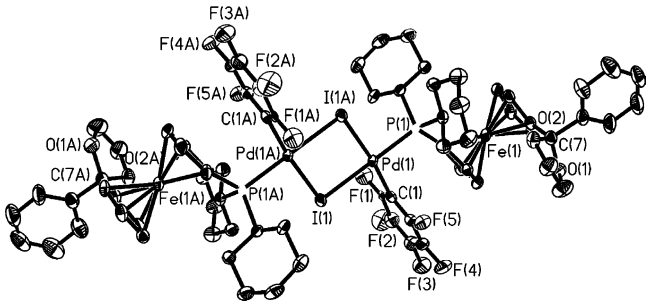


Figure 2. ORTEP representation of **5a** (40% probability ellipsoids and hydrogen atoms omitted for clarity).

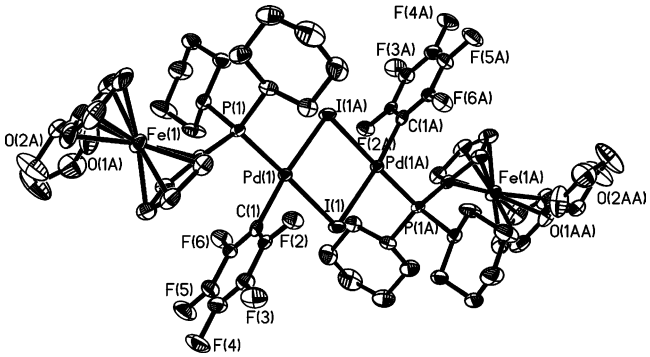


Figure 3. ORTEP representation of **5b** (40% probability ellipsoids and hydrogen atoms omitted for clarity).

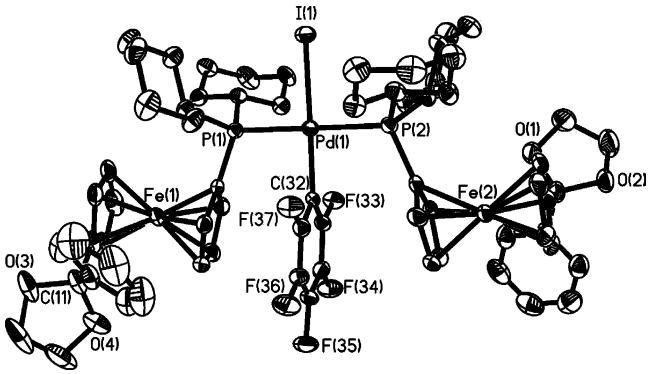


Figure 4. ORTEP representation of **7a** (40% probability ellipsoids and hydrogen atoms omitted for clarity).

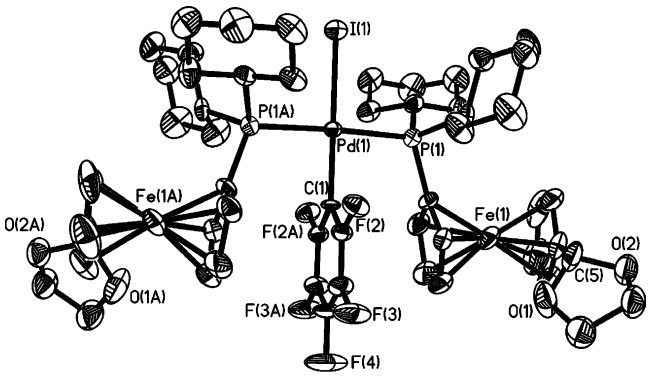


Figure 5. ORTEP representation of **7b** (40% probability ellipsoids and hydrogen atoms omitted for clarity).

without ether coordination or chelation. Instead, two units of **1** are coordinated as a unidentate P-only donor.

Complexes **7a** and **7b** form even under molar equivalence of Pd:**1**, although they are best prepared when ligand **1** is in excess. X-ray single-crystal crystallographic analysis confirmed a square-planar Pd(II) carrying two ligands of **1** with its dangling ether unit (Figures 4 and 5 and Table 3). The trans orientation of the two phosphines has significantly weakened the Pd−P bond from 2.2753(16) Å in **5a** to 2.3638(11) Å in **7a** and 2.2751(16) Å in **5b** to 2.354(2) Å in **7b**. The Pd−C_6F_5 links in **7a** (2.024(4) Å), **5a** (2.031(7) Å), and **5b** (2.046(7) Å) are consistent with weak Pd−C bonds.[14] The $C_5\cdots C_5$ ferrocenyl torsional twists for **7a** (124.1 and 84.7°) and **5a** (89.2°) are well short of an ideal anti twist (180°). This suggests that the ether moiety is not sterically obstructive to the phosphine coordination. The ferrocenyl twist is facile, which enables the ligand (**1a** or **1b**) to adapt to either chelating or unidentate mode to meet the saturation needs of the metal and, hence, catalyst.

There was no **5** or **8** detected (^{31}P NMR) when $Pd_2(dba)_3$, **1**, and C_6F_5I were mixed in C_6D_6, suggesting that the relative product formation is solvent dependent. In polar solvents (such as THF and dioxane) at room temperature, **7** exists in equilibrium with **8**. Complex **8a** could be isolated from a THF mixture at room temperature. Its catalytic role is demonstrated by its stoichiometric reaction with phenylboronic acid, which gives the desired hetero-biaryl product. Addition of free ligand **1** to complex **5** leads to bridge-cleavage reactions to yield **7** and **8**. In polar solvents, which favor the cleavage of the weak Pd−O link, **6** is unstable and readily dimerizes to **5**. The dinuclear **5** is less reactive than **6** toward reaction with phenylboronic acid; heating is generally required to facilitate the cross-coupling reaction. Complex **6** is much more reactive because of the facile Pd−O cleavage in a weak chelate.

Complexes **7** (**7a** and **7b**) are inactive toward biaryl cross-coupling in nonpolar solvents (e.g. toluene). Prolonged (overnight) reflux only yielded C_6F_5I and biphenyl, which suggests a competing homocoupling arising from disproportionation and hydrolytic deboronation.[15]

The above observations on the four different forms of oxidative addition products (**5**−**8**) help us contruct two different catalytic pathways via the dinuclear (route A) or geometric isometric (route B) forms (Scheme 3). Since the latter route stoichiometrically demands a 2-fold presence of ligand, one could in principle push the catalytic path toward route B from route A by increasing the ligand dosage. For **1a**, doubling the ligand dosage gives only a slight rise in TON (from ∼1000 to 2000). However, for **1b**, there is a ∼20-fold TON increase (from ∼2000 (max) to ∼44 600) for most of the electron-rich substrates when the ratio **1b**:Pd (in $Pd_2(dba)_3$) is raised from 1.2:1.0 to 2.4:1.0. This process is probably controlled by the cis-configured intermediate, **8b**. The higher ligand concentration, however, has little effect on the ortho-substituted electron neutral substrates. In fact, for *o*-chlorotoluene, the product yield would be significantly reduced to ∼10% (with respect to normal conditions, as in entry 2 in Table 2). This raises the possibility that different types of substrates would favor different mechanistic pathways.[16] The dimerization pathway (route A) goes through a more electrophilic metal, with only one phosphine, thus facilitating transmetalation with electron poorer substrates. On the other hand, the geometric isomerization pathway (route B) favors more the electron-rich aryl halides via *cis*-$RPd^{II}XL_2$ species, which isomerizes and equilibrates readily with the thermodynamically more stable trans form. The weakened Pd−X interaction would promote reductive elimination.[10b,c,17] When the experimental conditions do not favor route A, which is preferred by the ortho-substituted substrates, cross-coupling is thus suppressed.[18] There is also a steric influence on the pathways. When the oxidative addition product is sterically demanding, the dimeric complex **5** is the more stable form and is thermodynamically favored.[19] Thus, when isolated **5b** (1.0 mol % Pd) is added to a mixture of *o*-chlorotoluene, phenylboronic acid, and CsF, the cross-coupling product yield increases from 47% (Table 2 (entry 12)) to 55%. This lends support that route A is operative. These are simplistic generalizations with parallel pathways and competing reactions such as homocoupling, the latter of which is supported by the observed Pd black and biphenyl. Complex **5b** could also turn to **7b** upon

(13) See for example: (a) Walker, S. D.; Barder, T. E.; Martinelli, J. R.; Buchwald, S. L. *Angew. Chem., Int. Ed.* **2004**, *43*, 1871. (b) Wolfe, J. P.; Singer, R. A.; Yang, B. H.; Buchwald, S. L. *J. Am. Chem. Soc.* **1999**, *121*, 9550. (c) Littke, A. F.; Dai, C.; Fu, G. C. *J. Am. Chem. Soc.* **2000**, *122*, 4020. (d) Stambuli, J. P.; Kuwano, R.; Hartwig, J. F. *Angew. Chem., Int. Ed.* **2002**, *41*, 4746.

(14) (a) Galardon, E.; Ramdeedul, S.; Brown, J. M.; Cowley, A.; Hii, K. K.; Jutand, A. *Angew. Chem., Int. Ed.* **2002**, *41*, 1760. (b) Nishihara, Y.; Onodera, H.; Osakada, K. *Chem. Commun.* **2004**, 192.

(15) (a) Cammidge, A. N.; Crépy, K. V. L. *Tetrahedron* **2004**, *60*, 4377. (b) Cammidge, A. N.; Crépy, K. V. L. *J. Org. Chem.* **2003**, *67*, 6832. (c) Watanabe, T.; Miyaura, N.; Suzuki, A. *Synlett* **1992**, 207.

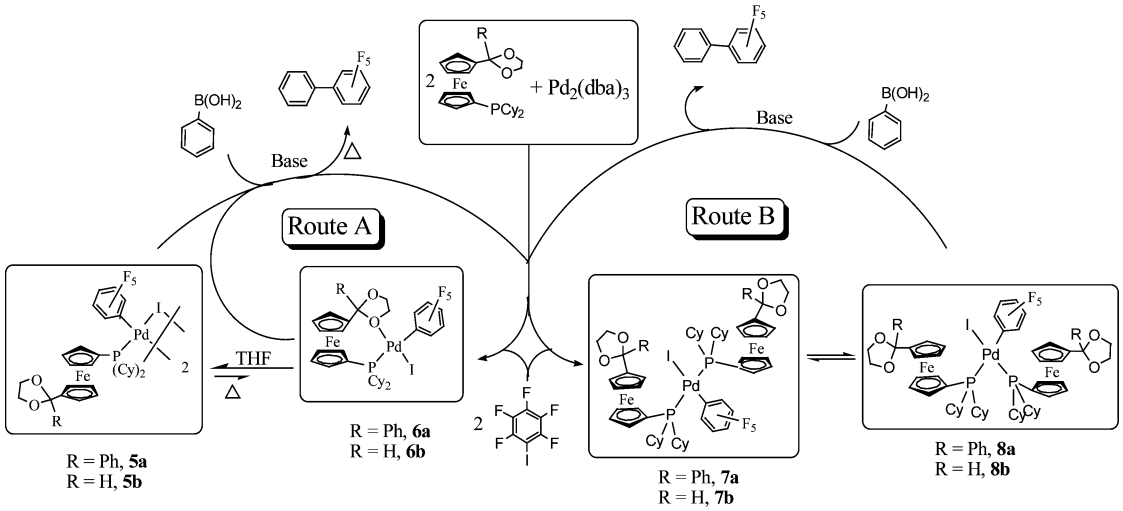
(16) (a) B−Landeros, F.; Hartwig, J. F. *J. Am. Chem. Soc.* **2005**, *127*, 6944. (b) Stambuli, J. P.; Incarvito, C. D.; Bühl, M.; Hartwig, J. F. *J. Am. Chem. Soc.* **2004**, *126*, 1184. (c) Goossen, L. J.; Koley, D.; Hermann, H. L.; Thiel, W. *Organometallics* **2005,** *24*, 2398.

(17) (a) Kastrup, C. J.; Oldfield, S. V.; Rzepa, H. S. *Dalton Trans.* **2002**, 2421. (b) Moore, J. W.; Pearson, R. G. *Kinetics and Mechanism*; Wiley: New York, 1981; p 304.

(18) (a) Kotha, S.; Lahiri, K.; Kashinath, D. *Tetrahedron* **2002**, *58*, 9633. (b) Goodson, F. E.; Wallow, T. I.; Novak, B. M. *J. Am. Chem. Soc.* **1997**, *119*, 12441.

(19) Echavarren, A. M.; Cárdenas, D. J. *Metal-Catalyzed Cross-Coupling Reactions*, 2nd ed.; VCH: Weinheim, Germany, 2004; Chapter 1.

Scheme 3. Different Catalytic Pathways of Heterocoupling via a Dinuclear Intermediate (Route A) and Mononuclear Geometric Isomers (Route B)



ligand addition, thus crossing route A to route B. Realistically, both pathways are operative and their dominance is governed sensitively by the choice of ligands and substrates, among others.

Conclusion

We have offered structural evidence that oxidative addition of Pd(0) in Suzuki coupling could proceed to yield several isolable products that could demonstrate geometric and nuclearity isomeric properties. They proceed to give the desirable cross-coupling products, the efficiency and effectiveness of which depend largely on the ligand design. Use of hemilabile P/O-ferrocenyl ligands potentially promotes a facile switchable protection and deprotection mechanism at the active metal center. It also adds stability to the metal through a direct dimerization process. The flexible coordination behavior inherent in a hybrid ligand system thus offers the metal several options to gain stability without compromising on its vital reactivitity. This is not achievable in a standard diphosphine system. These ideas should allow us to design better catalysts by the use of intelligent hemilabile ligands that could support different structural forms of the catalyst. When the catalyst can switch easily among different active forms, it should in principle cater to a range of different guest substrates and reaction conditions and, if needed, different catalytic pathways. Our research is driven by these desirable outcomes.

Experimental Section

1. General Considerations. All reactions were carried out using conventional Schlenk techniques under an inert atmosphere of nitrogen or under argon in an M.Braun Labmaster 130 inert gas system and dry deoxygenated solvents. Dry THF and hexanes were obtained by distillation from Na/benzophenone. Dry dichloromethane was distilled on CaH_2. Nuclear magnetic resonance spectra were recorded on a Bruker ACF 300 MHz FT NMR spectrometer operating at 300.14 MHz for ^{1}H, 75.43 MHz for ^{13}C, and 121.49 MHz for ^{31}P. Solvent peaks are used as an internal reference relative to TMS for ^{1}H and ^{13}C chemical shifts (ppm); ^{31}P chemical shifts are relative to an 85% H_3PO_4 external reference. Coupling constants are given in hertz. The following abbreviations are used: s, singlet; d, doublet; t, triplet; m, multiplet. Mass spectra were obtained on a Finnigan Mat 95XL-T spectrometer. Elemental analyses were performed by the in-house microanalytical laboratory. 1-Bromo-1′-(1-phenyl-2,5-dioxacyclopentyl)ferrocene and 1-bromo-1′-(2,5-dioxacyclopentyl)ferrocene were prepared by modifications of literature procedures.[11] $Pd_2(dba)_3$ was prepared according to literature procedures.[20] All other reagents and chemicals were obtained commercially and were used as received.

2. 1-(Dicyclohexylphosphino)-1′-(1-phenyl-2,5-dioxacyclopentyl)ferrocene (1a). To a solution of 0.205 g of 1-bromo-1′-(1-phenyl-2,5-dioxacyclopentyl)ferrocene (0.496 mmol) in dry THF was added *n*-BuLi (1.56 M, 0.32 mL, 0.50 mmol) dropwise at −78 °C, and the resultant solution was stirred for 1 h. Chlorodicyclohexylphosphine (0.1 mL, 0.53 mmol) was added and the resultant solution stirred and warmed to room temperature for 2 h. The resultant solution was filtered through Celite and the filtrate concentrated and chromatographed on silica gel under an argon atmosphere to give 0.184 g of **1a** as a yellow solid (yield: 0.302 mmol, 61%). ^{1}H NMR (C_6D_6): δ 7.80−7.22 (m, 5 H, Ph), 4.35 (t, J = 1.6 Hz, 2 H, Cp), 4.29 (t, J = 2.0 Hz, 2 H, Cp), 4.22 (quart, J = 1.6 Hz, 2H, Cp), 4.13 (t, J = 1.6 Hz, 2 H, Cp), 3.73−3.43 (m, 4 H, OCH_2CH_2O), 2.00 − 1.16 (m, 22 H, Cy). ^{31}P NMR (C_6D_6): δ −8.35. ^{13}C NMR (C_6D_6): δ 129.01, 128.68, 128.36 (Ph), 110.26 (Ph*C*O), 73.50, 73.35, 72.02, 71.99, 70.97, 69.57 (Cp), 65.61 (O*C*H_2*C*H_2O), 34.91, 34.68, 31.54, 31.51, 31.35, 28.48, 28.40, 28.35, 28.28, 28.27, 27.53, 27.50 (P*Cy*). MS (FAB): *m*/*z* 531 ([M + H])$^+$, 530 (M^+). Anal. Calcd for $C_{31}H_{39}FePO_2$: C, 70.18; H, 7.36. Found: C, 69.99; H, 7.37.

3. 1-(Dicyclohexylphosphino)-1′-(2,5-dioxacyclopentyl)ferrocene (1b). A 0.608 g portion of 1-bromo-1′-(2,5-dioxacyclopentyl)-ferrocene (1.81 mmol) was used, similar to the procedure for **1a**, giving **1b** as a yellow powder (yield: 0.522 g, 1.15 mmol, 63%). ^{1}H NMR (C_6D_6): δ 5.85 (s, 1 H, HCOO), 4.43 (t, J = 1.6 Hz, 2 H, Cp), 4.33 (t, J = 2.0 Hz, 2H, Cp), 4.27 (quart, J = 1.6 Hz, 2 H, Cp), 4.12 (t, J = 1.6 Hz, 2 H, Cp), 3.62−3.47 (m, 4H, OCH_2-CH_2O), 1.88−1.13 (m, 22 H, Cy). ^{31}P NMR (C_6D_6): δ −8.10. MS (FAB): *m*/*z* 455 ([M + H])$^+$, 454 (M^+). ^{13}C NMR (C_6D_6): δ 103.82 (HCO), 73.42, 73.27, 71.56, 71.05, 69.18 (Cp), 65.86 (O*C*H_2*C*H_2O), 34.84, 34.66, 31.54, 31.50, 31.49, 31.35, 28.51, 28.37, 28.27, 27.53 (P*Cy*). Anal. Calcd for $C_{25}H_{35}FePO_2$: C, 66.07; H, 7.70. Found: C, 66.05; H, 7.69.

4. 1-(Di-*tert*-butylphosphino)-1′-(2,5-dioxacyclopentyl)ferrocene (2). A 0.860 g portion of 1-bromo-1′-(2,5-dioxacyclopentyl)-ferrocene (2.56 mmol) reacted with chlorodi-*tert*-butylphosphine (0.43 mL, 2.56 mmol), similar to the procedure for **1a**, to give **2** as an orange-red oil (yield: 0.553 g, 54%). ^{1}H NMR (C_6D_6): δ 5.79 (s, 1 H, HCOO), 4.37 (t, J = 2.0 Hz, 2 H, Cp), 4.34 (t, J = 1.6 Hz,

(20) Ukai, T.; Kawazura, H.; Ishii, Y.; Bonnet, J. J.; Ibers, J. A. *J. Organomet. Chem.* **1974**, *65*, 253.

2 H, Cp), 4.29 (quart, $J = 1.6$ Hz, 2 H, Cp), 4.09 (t, $J = 1.6$ Hz, 2 H, Cp), 3.62−3.47 (m, 4 H, OCH_2CH_2O), 1.23,1.19 (d, 9H, CCH_3). ^{31}P NMR (C_6D_6): δ 27.5. ^{13}C NMR (C_6D_6): δ 103.72 (Ph*C*O), 74.84, 74.69, 71.57, 71.32, 69.85, 69.24 (Cp), 65.87 (O*C*H_2*C*H_2O), 33.61, 33.20, 31.86, 31.69, (P*t*-*Bu*). MS (FAB): *m*/*z* 403 ($[M + H]^+$), 402 $(M)^+$.

5.1. [(1a)Pd(I)(C_6F_5)]$_2$ (5a). Ligand **1a** (30 mg, 0.0633 mmol), $Pd_2(dba)_3$ (29 mg, 0.0317 mmol), and C_6F_5I (28 mg, 0.0945 mmol) were dissolved in THF, and the mixture was stirred for 5 h. The reaction mixture was filtered through a layer of Celite, and the solvent was removed. The dark brown oil was washed with hexane until a brown solid, **5a**, was left. This residual solid was redissolved in CH_2Cl_2 and overlayered with hexane to obtain dark brown crystals of **5a** (yield: 23.5 mg, 40%). ^1H NMR (C_6D_6): δ 7.82−6.90 (m, Ph), 4.00 (s, 4 H, Cp), 3.94 (s, 4 H, Cp), 3.78 (s, 8 H, Cp), 3.60−3.54 (m, 4 H, OCH_2CH_2O), 3.33−3.31 (m, 4 H, OCH_2CH_2O), 1.32−0.97 (m, 44 H, Cy). ^{31}P NMR (C_6D_6): δ 45.2. MS (FAB): *m*/*z* 1861 (M^+), 803 ($[^1/_2M - I]^+$). Anal. Calcd for $C_{74}H_{78}Fe_2P_2O_4F_{10}I_2 \cdot 3CH_2Cl_2$: C, 43.67; H, 3.97. Found: C, 43.23; H, 4.07. X-ray-quality single crystals of **6a** were grown from a CH_2Cl_2/hexane solution.

5.2. [(1b)Pd(I)(C_6F_5)]$_2$ (5b). Ligand **1b** (29 mg, 0.062 mmol) reacted with $Pd_2(dba)_3$ and C_6F_5I, similarly to the procedure described for **5a**. A dark brown solid of **5b** was obtained (yield: 8 mg, 15%). ^1H NMR (C_6D_6): δ 5.39 (s, 1H, HCOO), 4.10 (t, $J = 2.0$ Hz, 4H, Cp), 3.88 (s, 4 H, Cp), 3.76 (s, 8 H, Cp), 3.55−3.35 (m, 8 H, OCH_2CH_2O), 2.67−1.14 (m, 44 H, Cy). ^{31}P NMR (C_6D_6): δ 45.6. MS (FAB): *m*/*z* 727 ($[^1/_2M - I]^+$). X-ray-quality single crystals of **5b** were grown from a CH_2Cl_2/hexane solution.

6.1. [(1a)Pd(I)(C_6F_5)] (6a). Ligand **1a** (30 mg, 0.0633 mmol), $Pd_2(dba)_3$ (29 mg, 0.0317 mmol), and C_6F_5I (28 mg, 0.0945 mmol) were dissolved in THF, and the mixture was stirred for 1 h. The reaction mixture was filtered through a layer of Celite, and the solvent was removed. The orange oil was recrystallized in Et_2O to obtain a red solid of **6a** and traces of dba (yield: ca. 29.8 mg, 30%). ^1H NMR (C_6D_6): δ 7.80−7.03 (m), 4.48 (s, 2 H, Cp), 4.59 (s, 2 H, Cp), 4.44 (s, 2 H, Cp), 4.35 (s, 2 H, Cp), 3.68−3.41 (m, 4 H, OCH_2CH_2O), 2.14−1.12 (m, 44H, Cy). ^{31}P NMR (C_6D_6): δ 20.2. MS (FAB): *m*/*z* 931 ($[M + H]^-$), 803 ($[M - I]^+$). This compound was inevitably contaminated by dba, and hence, a satisfactory elemental analysis could not be obtained.

6.2. [(1b)Pd(I)(C_6F_5)] (6b). Ligand **1b** (45.6 mg, 0.101 mmol), $Pd_2(dba)_3$ (45 mg, 0.050 mmol), and C_6F_5I (50 mg, 0.170 mmol) were dissolved in THF, and the mixture was stirred for 1 h. The reaction mixture was filtered through a layer of Celite, and the solvent was removed. The dark brown oil was washed copiously with hexane to give a solid residue of **5b**. The washings were collected and evaporated to dryness to obtain a reddish brown solid, which was recrystallized in Et_2O to obtain the red solid **6b** and traces of dba (yield: ca. 63.7 mg, 70%). ^1H NMR (C_6D_6): δ 5.78 (s, 1 H, HCOO), 4.70 (s, 2 H, Cp), 4.54 (m, 4 H, Cp), 4.42 (s, 2 H, Cp), 3.73−3.41 (m, 4 H, OCH_2CH_2O), 2.00−1.12 (m, 22H, Cy). ^{31}P NMR (C_6D_6): δ 20.2. MS (FAB): *m*/*z* 727 ($[M - I]^+$). This compound was inevitably contaminated by dba, and hence, a satisfactory elemental analysis could not be obtained.

7.1. *trans*-[(1a)$_2$Pd(I)(C_6F_5)] (7a). Ligand **1a** (24 mg, 0.045 mmol), $Pd_2(dba)_3$ (11 mg, 0.012 mmol), and C_6F_5I (14 mg, 0.047 mmol) were dissolved in a minimum amount of toluene, and the mixture was stirred for 12 h. The toluene solution was then concentrated. The mixture was then left to stand in the freezer at −30 °C overnight. The resulting orange oil was then filtered through Celite. The orange filtrate was pumped, dried, and washed with hexane. The orange oil was recrystallized in CH_2Cl_2 and layered over hexane to obtain orange-red crystals of **7a** and yellow crystals of dba (yield: 28 mg, 80%). ^1H NMR (C_6D_6): δ 7.74−7.06 (m, 10 H, Ph), 4.30 (s, 4 H, Cp), 3.99 (s, 4 H, Cp), 3.91 (s, 4 H, Cp), 3.89 (s, 4 H, Cp), 3.67−3.66, 3.45−3.40 (m, 8 H, OCH_2CH_2O), 2.27−1.10 (m, 44 H, Cy). ^{31}P NMR (C_6D_6): δ 25.5. MS (FAB): *m*/*z* 1460 (M^+). This compound was inevitably contaminated by dba, and hence, a satisfactory elemental analysis could not be obtained.

7.2. *trans*-[(1b)$_2$Pd(I)(C_6F_5)] (7b). Ligand **1b** (23 mg, 0.048 mmol) reacted with $Pd_2(dba)_3$ and C_6F_5I according to a procedure similar to that for **7a**. A yellow oil of **7b** was obtained. ^1H NMR (C_6D_6): δ 5.46 (s, 1 H, HCOO), 4.15 (s, 4 H, Cp), 3.92 (s, 4 H, Cp), 3.84 (t, $J = 1.62$ Hz, 4 H, Cp), 3.75 (s, 4 H, Cp), 3.52−3.39 (m, 8 H, OCH_2CH_2O), 2.16−1.16 (m, 44 H, Cy). ^{31}P NMR (C_6D_6): δ 25.2. MS (FAB): *m*/*z* 1460 (M^+). This compound was inevitably contaminated by dba, and hence, a satisfactory elemental analysis could not be obtained.

8. *cis*-[(1a)$_2$Pd(I)(C_6F_5)] (8a). Ligand **1a** (20 mg, 0.042 mmol), $Pd_2(dba)_3$ (11 mg, 0.012 mmol), and C_6F_5I (28 mg, 0.0945 mmol) were mixed and stirred at room temperature in THF for 1 h. The resultant orange solution was filtered to remove the unreacted $Pd_2(dba)_3$. The orange filtrate was evaporated, dried, and redissolved in a minimum amount of Et_2O and left in the refrigerator (ca. −20 °C) overnight. The mixture was filtered, and the solid that was collected was dried and washed with a minimum amount of hexane to obtain the crude product **8a** as a red-orange oil (yield: ca. 20.1 mg). ^1H NMR (C_6D_6): δ 7.81−6.88 (m), 4.80 (s, 4 H, Cp), 4.69 (s, 4 H, Cp), 4.45 (s, 4 H, Cp), 4.39 (m, 4 H, Cp), 3.72−3.68 and 3.44−3.40 (m, 8 H, OCH_2CH_2O), 1.79−1.23 (m, 44H, Cy). ^{31}P NMR (C_6D_6): δ 30.0. MS (FAB): *m*/*z* 1460 (M^+). A satisfactory elemental analysis could not be obtained on the oily product.

9. NMR Studies. Experiments were performed at room temperature with 0.1 mmol of $Pd_2(dba)_3$ and 0.1 mmol of ligand in various solvents: C_6D_6, toluene, THF, and dioxane. After addition of the aryl iodide, the spectra of the mixture (in a solvent such as C_6D_6) were recorded at regular time intervals until no further changes were observed. Phenylboronic acid (1.3 equiv) and Cs_2CO_3 (1.5 equiv) were added to the mixture and monitored by ^{31}P NMR spectroscopy at regular intervals until there were no further changes or conversions.

10. General Procedure for Coupling Reactions of Aryl Chlorides with Boronic Acids. A typical procedure is given for the reaction represented in entry 2 of Table 2. Ligand **1a** (5 mg, 0.0110 mmol, 1.1 mol %), $Pd_2(dba)_3$ (5 mg, 0.005 mmol, 1 mol % Pd), phenylboronic acid (146 mg, 1.2 mmol), and CsF (2.3 mmol) were introduced into a flask filled with N_2 gas. 4-Chloroacetophenyl (154 mg, 130 μl, 1 mmol) was injected into the flask via a microsyringe, followed by addition of 1,4-dioxane. The mixture was stirred at 90 °C for 16 h, under an N_2 atmosphere. The solvent was then removed under reduced pressure, followed by addition of H_2O (10 mL) and Et_2O (10 mL). Extraction was repeated twice with Et_2O. The organic layer was collected and evaporated in vacuo to dryness. The crude product was purified by column chromatography on silica with hexanes/ethyl acetate as eluent to give 196 mg of 4-acetylbiphenyl as a solid, verified by GC/MS spectroscopy.

11. Crystal Structure Determinations. The crystals of **5a**, **5b**, **7a**, and **7b** were mounted on quartz fibers and X-ray data collected on a Bruker AXS APEX diffractometer, equipped with a CCD detector at −50 °C, using Mo Kα radiation (λ 0.710 73 Å). The data were corrected for Lorentz and polarization effects with the SMART suite of programs[21] and for absorption effects with SADABS.[22] Structure solution and refinement were carried out with the SHELXTL suite of programs.[23] The structures were solved by direct methods to locate the heavy atoms, followed by difference maps for the light non-hydrogen atoms. For **5a**, in the asymmetric unit there was half of the dimer and one dichloromethane. The

(21) SMART, version 5.1; Bruker Analytical X-ray Systems, Madison, WI, 2000.

(22) Sheldrick, G. M. SADABS, a Program for Empirical Absorption Correction; University of Göttingen, Göttingen, Germany, 2000.

(23) SHELXTL, version 5.03; Bruker Analytical X-ray Systems, Madison, WI, 1997.

Table 4. Crystal Data and Structure Refinement Parameters for Complexes 5a, 5b, 7a and 7b[a]

	5a·$2CH_2Cl_2$	**5b**·$2CH_2Cl_2$	**7a**·C_6H_{14}	**7b**
empirical formula	$C_{37}H_{39}F_5FeIO_2PPd{\cdot}CH_2Cl_2$	$C_{31}H_{35}F_5FeIO_2PPd{\cdot}CH_2Cl_2$	$C_{68}H_{78}F_5Fe_2IO_4P_2Pd{\cdot}C_6H_{14}$	$C_{56}H_{70}F_5Fe_2IO_4P_2Pd$
M_r	1015.73	1879.27	1547.42	1309.06
temp, K	223(2)	293(2)	223 (2)	243(2)
cryst color	dark brown	brown	orange	orange
cryst size, mm^3	0.30 × 0.20 × 0.10	0.28 × 0.08 × 0.06	0.14 × 0.08 × 0.06	0.08 × 0.06 × 0.03
cryst system	monoclinic	triclinic	triclinic	monoclinic
space group	$P2_1/c$	$P\bar{1}$	$P\bar{1}$	$C2/c$
a, Å	11.9657(8)	10.6130(5)	11.4379(4)	17.9960(15)
b, Å	16.0604(11)	12.0109(6)	17.5926(6)	19.5414(15)
c, Å	20.2335(14)	13.3195(7)	18.4657(7)	17.0394(15)
α, deg	90	90.4090(10)	75.9770(10)	90
β, deg	98.876(2)	95.3170(10)	76.1800(10)	114.753
γ, deg	90	94.3280(10	79.4350(10)	90
V, $Å^3$	3841.8(5)	1685.56(15)	3469.4(2)	5441.6(8)
Z	4	1	2	4
density, Mg/m^3	1.756	1.851	1.481	1.598
abs coeff, mm^{-1}	1.888	2.143	1.221	1.541
F(000)	2016	928	1588	2656
θ range for data collection, deg	1.63−27.50	1.93−25.00	1.84−27.50	1.62−25.00
index ranges	$-11 \le h \le 15$, $-20 \le k \le 15$, $-26 \le l \le 26$	$-12 \le h \le 12$, $-14 \le k \le 14$, $-15 \le l \le 15$	$-14 \le h \le 14$, $-22 \le k \le 22$, $-23 \le l \le 23$	$-21 \le h \le 21$, $-23 \le k \le 18$, $-20 \le l \le 15$
no. of rflns collected	26 142	18 450	36 447	15 772
no. of indep rflns	8828 (R_{int} = 0.0499)	5941 (R_{int} = 0.0447)	15 871 (R_{int} = 0.0546)	4788 (R_{int} = 0.1337)
max and min transmissn	0.8337 and 0.6013	0.8822 and 0.5853	0.9303 and 0.8476	0.9552 and 0.8866
no. of data/restraints/params	8828/24/460	5941/42/432	15 871/0/804	4788/0/323
final R indices ($I > 2\sigma(I)$)[a,b]	R1 = 0.0651, wR2 = 0.1683	R1 = 0.0512, wR2 = 0.1238	R1 = 0.0607, wR2 = 0.1150	R1 = 0.0771, wR2 = 0.1332
R indices (all data)	R1 = 0.0994, wR2 = 0.1901	R1 = 0.0656, wR2 = 0.1305	R1 = 0.0956, wR2 = 0.1274	R1 = 0.1521, wR2 = 0.1555
goodness of fit on F^2 [c]	1.045	1.063	1.021	1.010
largest diff peak and hole, e $Å^{-3}$	1.959 and −0.820	1.167 and −0.778	0.957 and −0.478	0.854 and −0.974

[a] $R1 = ||F_o| - |F_c||/|F_o|$. [b] $wR2 = [(\sum w(F_o^2 - F_c^2)^2)/(\sum w(F_o^2)^2)]^{1/2}$. [c] $GOF = [(\sum w(F_o^2 - F_c^2)^2)/(n - p)]^{1/2}$.

whole dimer was generated through the center of symmetry. For **7a**, the asymmetric unit contains one molecule of the title compound and one hexane. For **7b**, the asymmetric unit consists of half of the title molecule. Further details of the crystallographic information are provided in the Supporting Information. Crystal data and structure refinement parameters for **5a**, **5b**, **7a**, and **7b** are given in Table 4.

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Supporting Information Available: CIF files giving crystal data for complexes **5a**, **5b**, **7a**, and **7b**. This material is available free of charge via the Internet at http://pubs.acs.org.

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