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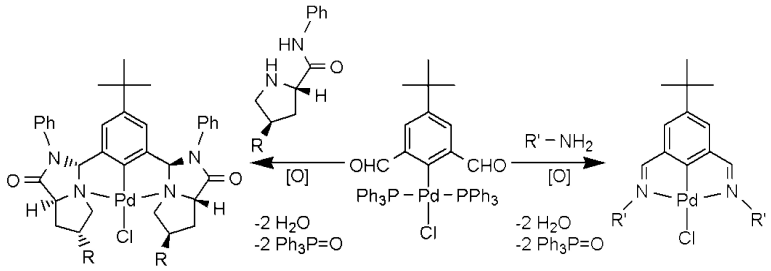

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NCN Pincer Palladium Complexes: Their Preparation via a Ligand Introduction Route and Their Catalytic Properties

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Abstract: A wide range of NCN pincer palladium complexes, [4-*tert*-butyl-2,6-bis(*N*-alkylimino)phenyl]-chloropalladium (alkyl = *n*-butyl, benzyl, cyclohexyl, *tert*-butyl, adamantyl, phenyl, 4-methoxyphenyl), were readily prepared from *trans*-(4-*tert*-butyl-2,6-diformylphenyl)chlorobis(triphenylphosphine)palladium via dehydrative introduction of the corresponding alkylimino ligand groups (ligand introduction route) in excellent yields (71−98%). NMR studies on this route for forming pincer complexes revealed the intermediacy of [4-*tert*-butyl-2,6-bis(*N*-alkylimino)phenyl]chlorobis(triphenylphosphine)palladium which is in equilibrium with the corresponding NCN pincer complexes via coordination/dissociation of the intramolecular imino groups and triphenylphosphine ligands. A series of chiral NCN pincer complexes bearing pyrroloimidazolone units as the *trans*-chelating donor groups, [4-*tert*-butyl-2,6-bis{(3*R*,7a*S*)-2-phenylhexahydro-1*H*-pyrrolo[1,2-*c*]-imidazol-1-on-3-yl}phenyl]chloropalladium, were also prepared from the same precursor via condensation with proline anilides in high yields. The catalytic properties of the NCN imino and the NCN pyrroloimidazolone pincer palladium complexes were examined in the Heck reaction and the asymmetric Michael reaction to demonstrate their high catalytic activity and high enantioselectivity.

Introduction

Organometallic pincer complexes containing terdentate monoanionic ligands composed of an anionic aryl carbon atom and two mutually *trans*-chelating donor sites at the 2,6-positions of the aromatic ring have been attracting widespread interest in catalysis and material science.[1] Various methods for the preparation of such compounds have been developed, and they can be mainly divided into four strategies: (1) direct cyclometalation, (2) oxidative addition, (3) transmetalation, and (4) transcyclometalation.[1a] All of these methods must involve a metalation reaction of the corresponding pincer ligands creating a new metal−carbon σ bond in the final step (hereafter, we will refer to these methods as "*metal introduction routes*," Scheme 1a). While the metal introduction route is the most straightforward process, a synthetic limitation has emerged as a serious problem. First, it appears difficult for the pincer ligands having sterically demanding groups as coordination sites to react with transition metals: Chung and co-workers reported that the *N*-benzyl aminal-type ligand was inert to palladation due to its bulkiness.[2] Another problem is that chemically unstable functional groups, such as imines, are not suitable for metalation, and substantial decomposition of the ligands under reaction conditions was observed.[3a] Furthermore, in the direct cyclometalation protocol via C−H activation, the regioselectivity of metalation is not controlled: in particular, palladation would prefer the 3,5-positions to the desired 1-position (Chart 1).[4] These problems therefore impose a restriction on research for pincer complexes bearing imine-donating groups; i.e., there are few articles describing the Rh,[5] Pd,[6] and Pt[3,7] complexes in contrast to the many reports for those with other coordinating groups.[1a]

Scheme 1. Synthetic Strategy for Pincer Complexes

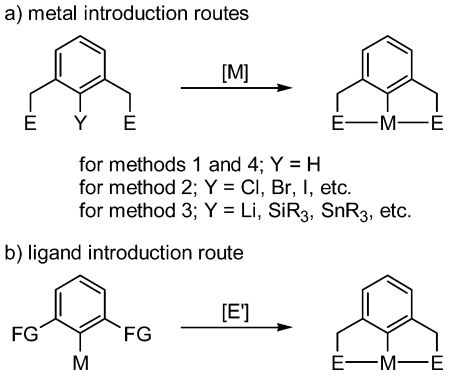
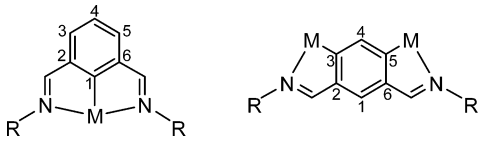


Chart 1



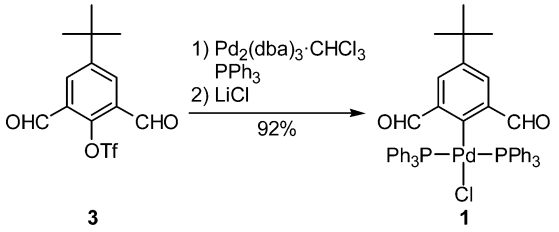
(1) For reviews on pincer complexes, see: (a) Albrecht, K.; van Koten, G. *Angew. Chem., Int. Ed.* **2001**, *40*, 3750. (b) van der Boom, M. E.; Milstein, D. *Chem. Rev.* **2003**, *103*, 1759. (c) Singleton, J. T. *Tetrahedron* **2003**, *59*, 1837. (d) Dupont, J.; Consorti, C. S.; Spencer, J. *Chem. Rev.* **2005**, *105*, 2527.

(2) Jung, I. G.; Son, S. U.; Park, K. H.; Chung, K.-C.; Lee, J. W.; Chung, Y. K. *Organometallics*, **2003**, *22*, 4715.

(3) (a) Fossey, J. S.; Richards, C. J. *Organometallics*, **2002**, *21*, 5259. (b) Fossey, J. S.; Richards, C. J. *Tetrahedron Lett.* **2003**, *44*, 8773.

(4) (a) Steenwinkel, P.; Gossage, R. A.; Maunula, T.; Grove, D. M.; van Koten, G. *Chem.—Eur. J.* **1998**, *4*, 763. (b) Fossey, J. S.; Richards, C. J. *Organometallics*, **2004**, *23*, 367.

Scheme 2



3 1

To overcome these problems, we planned to develop a new synthetic strategy based on a metalation-ligand-construction sequence, referred to as "*ligand introduction route*" (Scheme 1b). The site-controlled metalation of an aromatic ring before the introduction of the ligand moieties can overcome the inhibition of formation of the M−C bond by the bulky coordinating groups. The subsequent ligand construction at the 2,6-positions makes it easy to use sensitive donor groups.

Here we report the preparation of NCN pincer palladium complexes having imine or chiral pyrroloimidazolone moieties via the ligand introduction route. The complexation pathway of this new protocol was also investigated by variable-temperature NMR spectroscopy. In addition, the pincer complexes obtained here exhibited high catalytic activity and high stereoselectivity in the Heck reaction and in the asymmetric Michael reaction, respectively.

Results and Discussion

1. Preparation of *N*-Alkylimine Pincer Complexes - Ligand Introduction Route 1. Metalation of a functionalized aromatic ring prior to construction of coordinating groups is a prerequisite for our strategy. As the key precursor, the *trans*-(4-*tert*-butyl-2,6-diformylphenyl)chlorobis(triphenylphosphine)-palladium (**1**), in which the two formyl groups at the 2,6-positions of the anionic aromatic ligand can be converted into imino groups, was designed. The complex **1** was readily prepared in high yield starting with 4-*tert*-butyl-2,6-diformylphenyl trifluoromethanesulfonate (**3**) via oxidative complexation with Pd^0 in the presence of PPh_3, as shown in Scheme 2. The X-ray structure of **1** unambiguously shows that the aromatic ring is directly connected to the palladium atom, where the two formyl groups are located at both *ortho* positions (Figure 1).

With the precursor **1** in hand, we examined whether the ligand introduction route would indeed work. We were consequently pleased to find that a pincer palladium complex having imine functionalities was obtained using this strategy. Thus, the reaction of **1** with 5 equiv of cyclohexylamine in acetonitrile at reflux temperature under an O_2 atmosphere afforded the complex **2a** in 92% yield (Scheme 3). Since it was reported that a similar complex **4** was isolated in less than 15% yield,[6] this ligand introduction route would provide an effective synthetic method for the pincer complexes having imine donors. The X-ray structure of **2a** with selected bond lengths and angles is presented in Figure 2. The Pd−C(1) distance of 1.927(3) Å is significantly shorter than that of the precursor **1** (1.999(4) Å), which reflects the strong binding nature of the pincer ligand

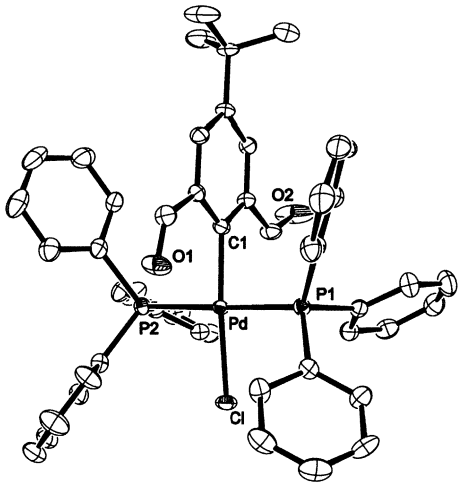
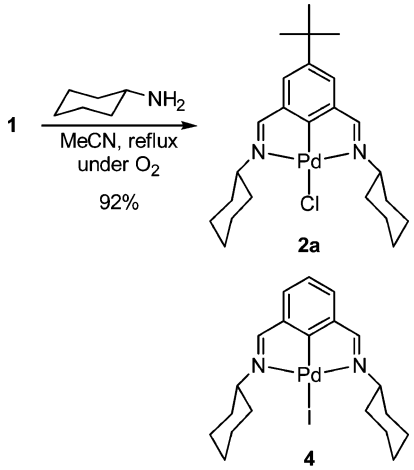


Figure 1. ORTEP drawing of the complex **1** with thermal ellipsoids at 50% probability levels. The solvated CH_3CN molecule and the hydrogen atoms are omitted for clarity. Selected bond distances (Å) and angles (deg): Pd−C(1) = 1.999(4), Pd−P(1) = 2.322(2), Pd−P(2) = 2.317(2), Pd−Cl = 2.378(2); P(1)−Pd−P(2) = 178.80(4), Cl−Pd−C(1) = 171.25-(11).

Scheme 3



caused by two additional intramolecular imine coordinations. Although the Cl−Pd−C(1) angle is 176.21(7)°, the N(1)−Pd−N(2) angle is 156.74(8)°, which indicates the distortion from the ideal square planar geometry due to the two fused five-membered rings. In the IR spectrum of **2a**, the band at 1601 cm^{-1} diagnostic of the coordinated C═N stretch[6] was observed instead of the carbonyl stretch at 1672 cm^{-1} of **1**. The iminyl protons and carbons appeared as singlets at 8.00 and 169.3 ppm in the ^1H and ^{13}C NMR spectra, respectively. The signal responsible for the *ipso* carbon connected to palladium was found at 179.2 ppm, which was shifted toward high frequency as compared to the starting material **1** (172.4 ppm). The absence of PPh_3 ligands was established by the lack of any resonance in the ^{31}P NMR spectrum.

Other primary amines were used in this ligand introduction route. Under the same reaction conditions, **1** reacted with benzylamine and butylamine to produce the pincer complexes **2b** (86% yield) and **2c** (98% yield), respectively (Scheme 4). The X-ray structures of both complexes are depicted in Scheme 4. For each complex, all the spectroscopic data and the elemental analysis were consistent with the expected structure (see Supporting Information).

(5) Hoogervorst, W. J.; Goubitz, K.; Fraanje, J.; Lutz, M.; Spek, A. L.; Ernsting, J. M.; Elsevier, C. J. *Organometallics*, **2004**, *23*, 4550.
(6) Vila, J. M.; Gayoso, M.; Pereira, M. T.; Torres, M. L.; Fernández, J. J.; Fernández, A.; Ortigueira, J. M. *J. Organomet. Chem.* **1996**, *506*, 165.
(7) (a)Hoogervorst, W. J.; Elsevier, C. J.; Lutz, M.; Spek, A. L. *Organometallics* **2001**, *20*, 4437. (b) Hoogervorst, W. J.; Koster, A. L.; Lutz, M.; Spek, A. L.; Elsevier, C. J. *Organometallics* **2004**, *23*, 1161.

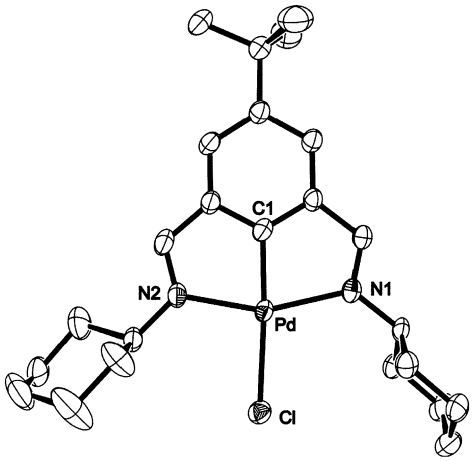
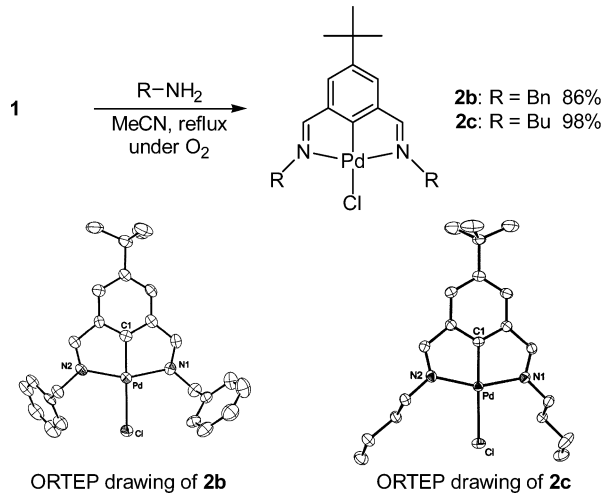
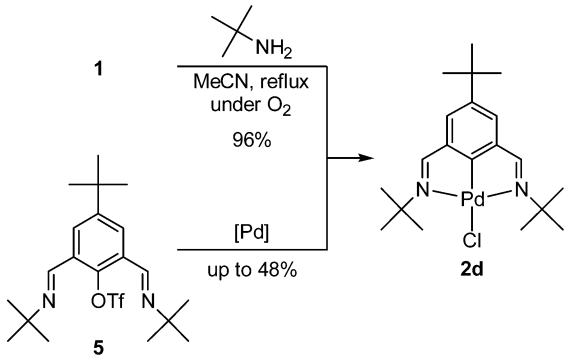


Figure 2. ORTEP drawing of one of the two independent crystal structures of the complex **2a** with thermal ellipsoids at 50% probability levels. One molecule of two independent molecules in a unit cell is presented. The solvated CH_3CN molecule and the hydrogen atoms are omitted for clarity. Selected bond distances (Å) and angles (deg): Pd−C(1) = 1.927(3), Pd−N(1) = 2.117(2), Pd−N(2) = 2.087(2), Pd−Cl = 2.4112(8); N(1)−Pd−N(2) = 156.74(8), Cl−Pd−C(1) = 176.21(7).

Scheme 4

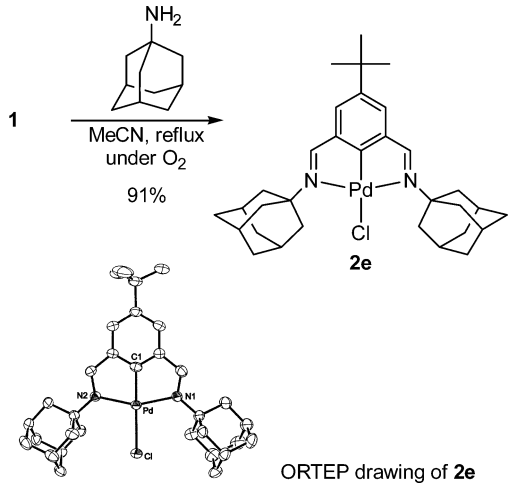


Scheme 5

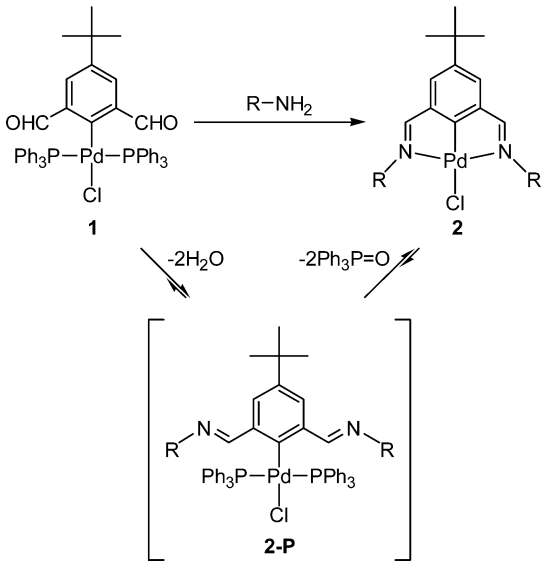


Using this method, we also built up a pair of *N-tert*-butylimino moieties on the aromatic ring of **1** to give the complex **2d** in 96% yield as shown in Scheme 5. The conventional synthetic route via oxidative addition to the corresponding ligand **5**, which was prepared from **3** and *tert*-butylamine, furnished only up to 48% of **2d** even with prolonged reaction time and higher temperatures (Scheme 5).

Scheme 6



Scheme 7. Proposed Pathway

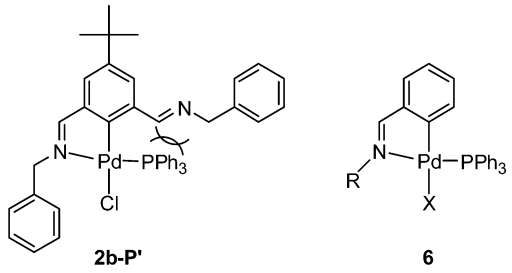


Complex **2e** having more bulky 1-adamantyl groups at both nitrogen atoms was obtained in 91% yield after 50 h (Scheme 6). The relatively long reaction time could be attributed to the steric hindrance of 1-adamantamine. The X-ray structure of **2e** elucidates the coordination of the *N*-(1-adamantyl)imino functionalities to the palladium center (Scheme 6). The structure of **2e** was also identified by NMR, IR, FAB-MS, and elemental analysis.

From these results, the ligand introduction route should be recognized as being an alternative synthetic protocol for pincer palladium complexes since it overcomes the problems of the known pincer complex formation (introduction of sterically demanding substituents onto the ligand sites, utilization of sensitive donor groups, and regioselectivity of metalation).

2. Variable-Temperature NMR Study. In the ligand introduction route, it was presumed that the pincer complexes were formed through condensation of the 2,6-formyl groups of **1** with primary amines and subsequent ligand exchange by the resulting imine functionalities constructing the Pd−N bonds (Scheme 7). Irreversible trapping of PPh_3 ligands liberated from a possible intermediate **2-P** by oxidation under an O_2 atmosphere might be an important step, since van Koten and co-workers reported quantitative replacement of the amine ligands in the

Chart 2



NCN pincer complex by PPh_3.[8] Therefore, recoordination of the phosphine ligands to Pd (dissociation−association equilibrium of PPh_3) would likely take place at the ligand exchange step.

To confirm our hypothesis, we carried out variable-temperature ^1H and ^{31}P NMR measurements for the isolated complexes **2b** and **2c** in the presence of 2 mol equiv of PPh_3. Figure 3a and 3b show the ^1H and ^{31}P NMR spectra of **2b** ranging from −40 to 80 °C, respectively. In the ^1H NMR spectrum at 80 °C, only a broad peak at 5.01 ppm ascribed to the benzyl protons of the complex **2b** is observed. Upon cooling, the resonance becomes broader. At 30 °C a new signal appears around 4.50 ppm, which increases gradually as the initial peak of **2b** decreases below that temperature. Finally, at −40 °C the new peak (at 4.42 ppm) becomes the major peak, accompanied by a tiny peak of **2b** (at 4.96 ppm). This behavior is reversible. From the two-dimensional ^1H EXSY NMR spectrum, it becomes obvious that these two peaks are interchangeable. In the ^{31}P NMR spectrum measured at 80 °C, there are no peaks except for a broad singlet which represents a free PPh_3 at −3.0 ppm. At 60 °C a new signal appears at 22.9 ppm. Upon cooling, the new signal increases gradually, whereas the PPh_3 signal decreases. At −40 °C the former exceeds the latter in intensity. Reheating to 80 °C restored the original spectrum, indicating the reversibility of this behavior. During these experiments a monophosphine-adduct **2b-P′** was not perceived at all, although the half-pincer Pd complexes **6** ($R = (CH_2)_3Si(OEt)_3$, X = Br;[9a] R = Ph, $X = OCOCF_3$[9b]) which possess one PPh_3 ligand at the trans position to the coordinated imine moiety were prepared and structurally characterized (Chart 2). The steric hindrance between the phosphine ligand and the noncoordinated imine moiety seemed to be the reason for the instability. These observations imply that the proposed equilibrium exists between **2b** and the corresponding bisphosphine complex **2b-P** (Figure 3). Fortunately, we were able to obtain single crystals of **2b-P** suitable for X-ray diffraction analysis by layering a hexane solution of an excess amount of PPh_3 onto a $CHCl_3$ solution of **2b**. The molecular structure of **2b-P** given in Figure 4 definitely shows coordination of two PPh_3 molecules to Pd dangling two *N*-benzylimino groups on the aromatic ring. NMR spectra of the single crystals measured at −40 °C indicated that the structure found in the solid-state was retained in solution (see Supporting Information). It is of great importance to note that the solution of **2b-P** exhibited the same reversible temperature-dependent dynamic behavior as shown in Figure 3. Thus, **2b-P** was an observable species at only lower temperatures, while the pincer complex **2b** and the free PPh_3 were generated at higher temperature. These results are compatible with our hypothesis that **2b** and **2b-P** are in equilibrium with each

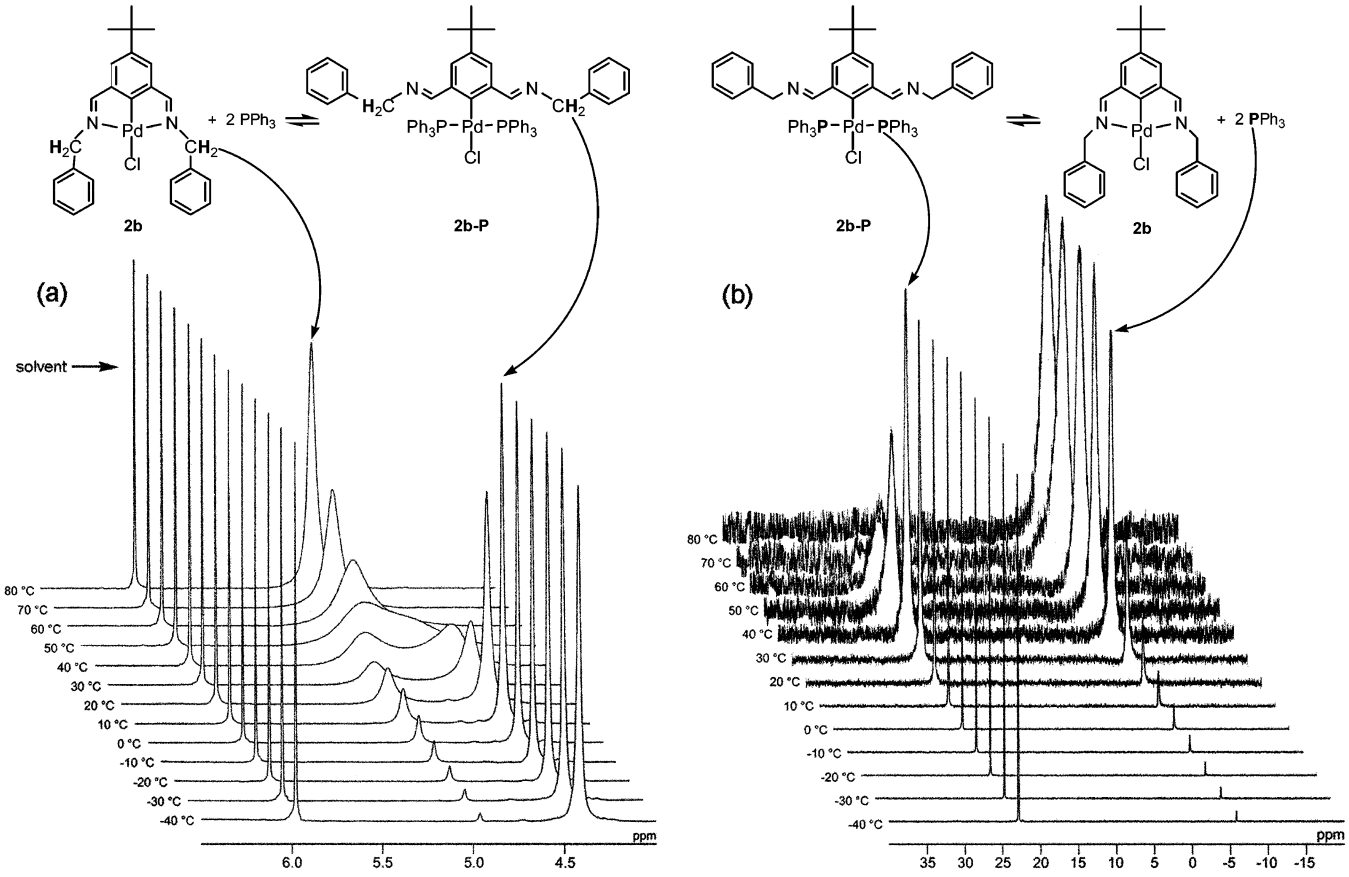


Figure 3. Variable-temperature (a) ^1H and (b) ^{31}P NMR spectra of complex **2b** in the presence of 2 mol equiv of PPh_3.

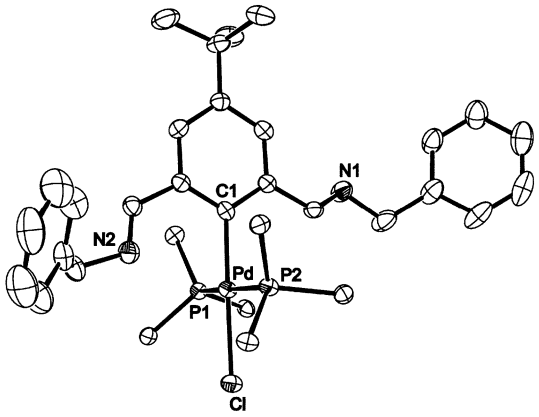
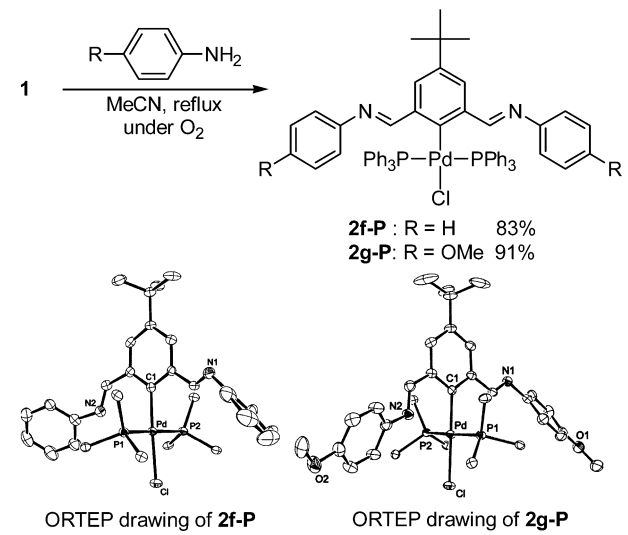


Figure 4. ORTEP drawing of complex **2b-P** with thermal ellipsoids at 50% probability levels. The carbon atoms of PPh_3 ligands except for the *ipso*-carbons and the hydrogen atoms are omitted for clarity. Selected bond distances (Å) and angles (deg): Pd−C(1) = 2.023(2), Pd−P(1) = 2.3344(7), Pd−P(2) = 2.3258(7), Pd−Cl = 2.4007(6); P(1)−Pd−P(2) = 174.16(2), Cl−Pd−C(1) = 177.15(5).

Scheme 8



other: the van't Hoff plots afforded the thermodynamic parameters ($\Delta H° = -90.5 \pm 2.9$ kJ mol^{-1}, $\Delta S° = -231 \pm 11$ J K^{-1} mol^{-1}). Complex **2c** displayed similar fluxional behavior (Figure 5): $\Delta H° = -63.0 \pm 2.1$ kJ mol^{-1} and $\Delta S° = -167 \pm 8.2$ J K^{-1} mol^{-1}. While the large negative entropy apparently reflects the convergent reaction of the three molecules, the negative enthalpy value is large enough to compensate for this disadvantage (Figures 3a and 5a, forward reaction). Hence, this relationship makes the postulated equilibrium during the reaction possible.

3. Preparation of *N*-Arylimine Pincer Complexes - Ligand Introduction Route 2. Because the ligand introduction route turned out to be an efficient preparation method for pincer complexes bearing *N*-alkylimine coordinating groups, aromatic amines were studied to develop the utility of this method. However, when aniline and *para*-anisidine were used as the amine, the desired pincer complexes were not produced but instead the corresponding PPh_3 adducts (Scheme 8). Thus, under the same conditions mentioned above, the reaction of **1** with aniline and *para*-anisidine gave *trans*-[4-*tert*-butyl-2,6-bis(*N*-phenylimino)phenyl]chlorobis(triphenylphosphine)palladium (**2f-P**) and *trans*-[4-*tert*-butyl-2,6-bis{*N*-(*p*-methoxyphenyl)imino}-phenyl]chlorobis(triphenylphosphine)palladium (**2g-P**) in 83% and 91% yield, respectively. Unequivocal confirmation of the

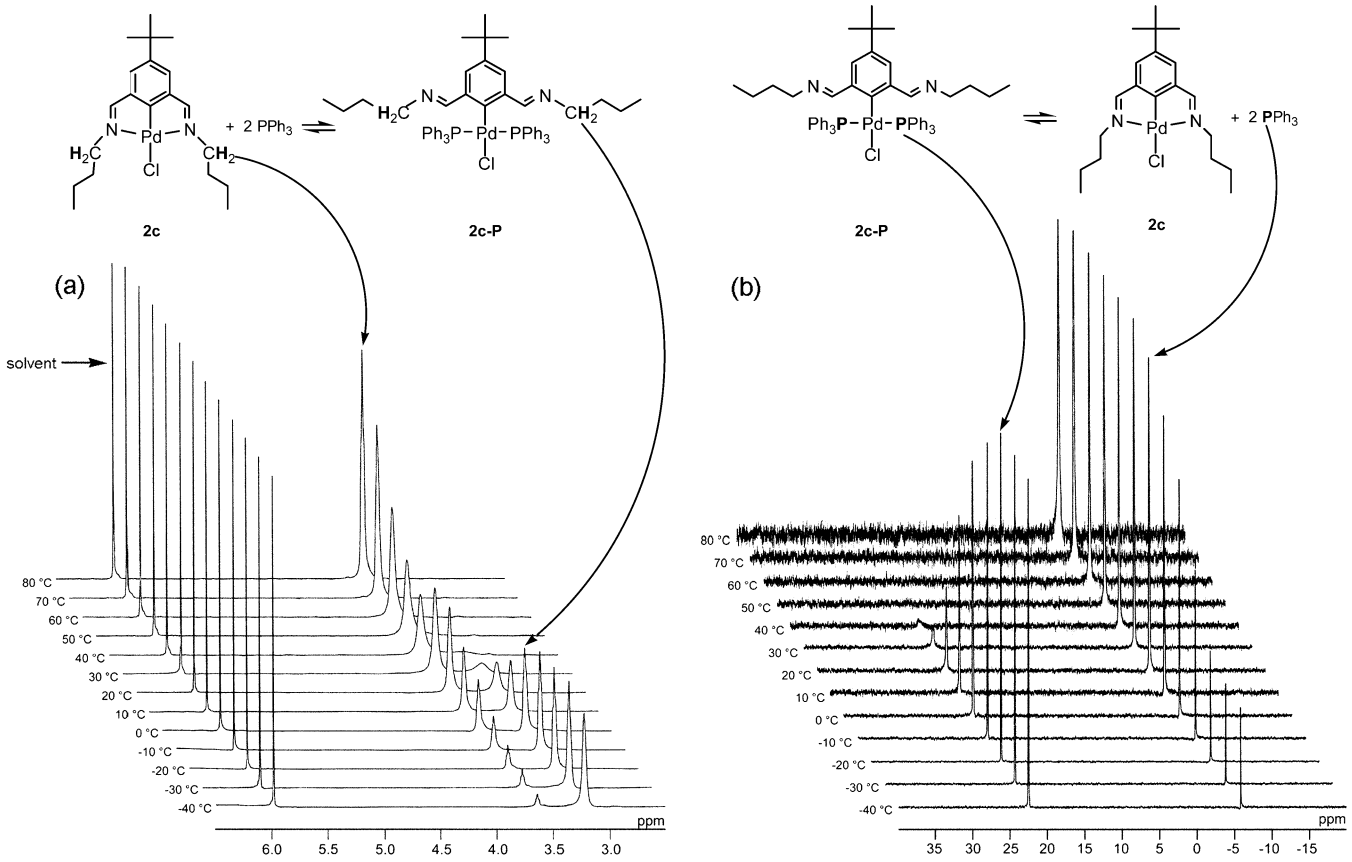
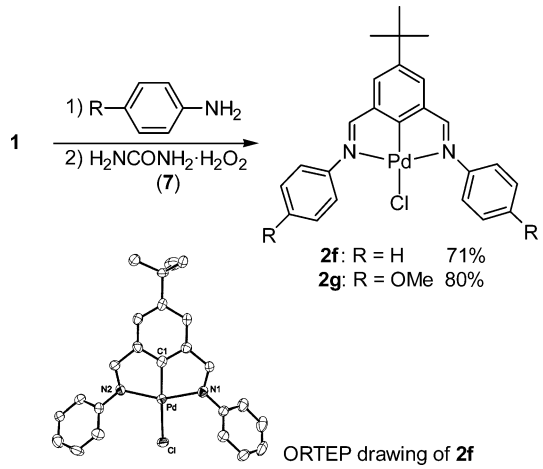


Figure 5. Variable-temperature (a) ^{1}H and (b) ^{31}P NMR spectra of complex **2c** in the presence of 2 mol equiv of PPh_3.

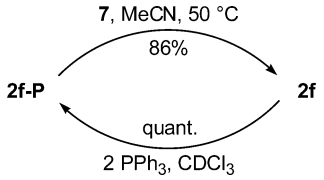
Scheme 9



proposed connectivity pattern of these complexes was obtained from X-ray structure analyses (Scheme 8: The carbon atoms of PPh_3 ligands except for the *ipso*-carbons are omitted for clarity). Prolonged reaction, however, did not convert these phosphine complexes into the desired pincer complexes. Presumably the lowered nucleophilicity of the resulting imines derived from the aromatic amines rather than those derived from the aliphatic amines keeps the PPh_3 ligands bonded to the Pd atom. Such a marked difference in reactivity is well correlated with the order of pK_a values of the conjugated acids of the amines: 9.33−10.77 for aliphatic amines, 4.63 for aniline, and 5.34 for *para*-anisidine. It is noteworthy that the structures of **2f-P** and **2g-P** are reminiscent of the intermediate **2-P** in the proposed reaction pathway of the ligand introduction route. As discussed above, the ligand introduction route seems to include equilibria between the pincer complexes **2** and the corresponding PPh_3 adducts **2-P** (Scheme 7). It follows then that the complexes **2f-P** and **2g-P** might be equilibrated with the desired pincer complexes; however gaseous oxygen was too weak to oxidize the trace amount of PPh_3 released from **2f-P** and **2g-P**. If a more powerful oxidizing agent had been employed in these reactions, the pincer complexes might have been obtained by shifting the equilibrium to the product side.

After screening several oxidizing agents, the urea hydrogen peroxide addition compound, $H_2NCONH_2{\cdot}H_2O_2$ (**7**), was found to be a suitable oxidant to produce the pincer complexes bearing the *N*-arylimine coordination groups. Thus, condensation of **1** with aniline and subsequent treatment of the resulting reaction mixture with **7** at 50 °C gave the complex **2f** in 71% yield (Scheme 9). Similarly, the pincer complex **2g** was obtained by using *para*-anisidine as the primary amine in 80% yield (Scheme 9). The X-ray structure of **2f** illustrated in Scheme 9 elucidates the expected η^3-N,C,N terdentate bonding mode of the ligand. As shown in Scheme 10, the formation of **2f** from the isolated complex **2f-P** by treatment with the oxidant **7** indicates that such phosphine complexes are actual intermediates in the ligand introduction route. The reversed transformation starting from the pincer complex is easy to predict.[8] NMR experiments, indeed, revealed that addition of 2 equiv of PPh_3 to **2f** led to a quantitative formation of **2f-P** (Scheme 10). Since it was

Scheme 10



reported that compound **7** did not oxidize the coordinated phosphines but instead the uncoordinated phosphines,[10] the PPh_3 ligand was oxidized after dissociation from the metal center at the ligand exchange stage. No detectable change was observed during the reaction of the formyl complex **1** with **7**, suggesting that the intramolecular interaction of the imines to the palladium center assisted the liberation of PPh_3. Consequently, the pincer complexes **2** were obtained by way of the imino phosphine complexes **2-P** in the ligand introduction route, where both the complexes were in equilibrium and the *ortho* imino groups played a key role (Scheme 7).

4. Catalytic Activities of the Imine Pincer Complexes - the Heck Reaction. A variety of pincer palladium complexes have been emerging as a new class of efficient catalysts for several coupling reactions such as the Heck reaction.[2,11] To test the catalytic abilities of the imino pincer palladium complexes **2** to promote the Heck reaction, we initially examined the reaction of iodobenzene (**8a**) with methyl acrylate (**9a**) (Table 1). The reaction proceeded smoothly when a combination of 1-methyl-2-piperidone (NMP) as the solvent and tributylamine (Bu_3N) as the base was used. Thus, the reaction of **8a** with **9a** was carried out in NMP in the presence of 1.4 mol equiv of Bu_3N and 1.0 mol % of the pincer complex **2a** at 100 °C for 2 h to give methyl *trans*-cinnamate (**10**) in 90% yield (entry 1). The other complexes **2b-f** exhibited similar catalytic activities under otherwise similar conditions (entries 2−6).

The reaction of **8a** and butyl acrylate (**9b**) was found to proceed very efficiently with only 1 mol ppm of the pincer catalyst **2c** by employing an NMP/H_2O mixture (7:3) as a solvent to give 90% isolated yield of butyl *trans*-cinnamate **11a** (entry 7). Using the reaction conditions (NMP + H_2O/Bu_3N/140 °C) identified above, various aryl halides were examined for the Heck reaction with acrylates in the presence of 1 mol ppm of the pincer palladium complex **2c**. Thus, the reactions of *ortho*-, *meta*-, and *para*-iodotoluenes (**8b**−**d**) with 1.4 equiv of **9b** were catalyzed by 1.0 mol ppm of the pincer palladium complex **2c** at 140 °C in NMP to give 83%, 88%, and 91% isolated yields of the Heck products **11b**, **11c**, and **11d**, where the turnover numbers (TONs) of the palladium catalyst were

(8) (a) Albrecht, M.; Dani, P.; Lutz, M.; Spek, A. L.; van Koten, G. *J. Am. Chem. Soc.* **2000**, *122*, 11822. (b) Rodriguez, G.; Albrecht, M.; Schoenmaker, J.; Ford, A.; Lutz, M.; Spek, A. L.; van Koten, G. *J. Am. Chem. Soc.* **2002**, *124*, 5127.

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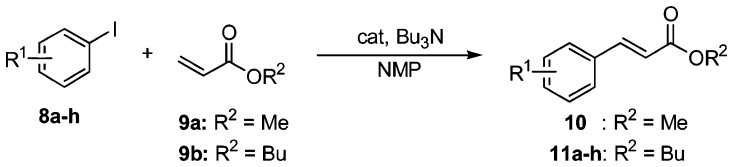
(11) For recent studies on the Heck reaction with pincer catalysts, see: (a) Ohff, M.; Ohff, A.; van der Boom, M. E.; Milstein, D. *J. Am. Chem. Soc.* **1997**, *119*, 11687. (b) Bergbreiter, D. E.; Osburn, P. L.; Liu, Y.-S. *J. Am. Chem. Soc.* **1999**, *121*, 9531. (c) Miyazaki, F.; Yamaguchi, K.; Shibasaki, M. *Tetrahedron Lett.* **1999**, *40*, 7379. (d) Morales-Morales, D.; Redón, R.; Yung, C.; Jensen, C. M. *Chem. Commun.* **2000**, 1619. (e) Gruber, A. S.; Zim, D.; Ebeling, G.; Monteiro, A. L.; Dupont, J. *Org. Lett.* **2000**, *2*, 1287. (f) Morales-Morales, D.; Cramer, R. E.; Jensen, C. M. *J. Organomet. Chem.* **2002**, *654*, 44. (g) Sjövall, S.; Wendt, O. F.; Andersson, C. *J. Chem. Soc., Dalton Trans.* **2002**, 1396. (h) Díez-Barra, E.; Guerra, J.; Hornillos, V.; Merino, S.; Tejeda, J. *Organometallics* **2003**, *22*, 4610. (i) Huang, M.-H.; Liang, L.-C. *Organometallics* **2004**, *23*, 2813. (j) Yao, Q.; Kinney, E. P.; Zheng, C. *Org. Lett.* **2004**, *6*, 2997. (k) Consorti, C. S.; Ebeling, G.; Flores, F. R.; Rominger, F.; Dupont, J. *Adv. Synth. Catal.* **2004**, *346*, 617.

Table 1. Heck Reaction of Aryl Iodides and Acrylates Catalyzed by Imino Pincer Complexes[a]



entry	aryl iodide	olefin	catalyst (mol %)	*T* (°C)	time (h)	product	yield[b] (%)
1	**8a** (R^1 = H)	**9a**	**2a** (1.0)	100	2	**10**	90
2	**8a**	**9a**	**2b** (1.0)	100	2	**10**	89
3	**8a**	**9a**	**2c** (1.0)	100	2	**10**	91
4	**8a**	**9a**	**2d** (1.0)	100	2	**10**	86
5	**8a**	**9a**	**2e** (1.0)	100	2	**10**	86
6	**8a**	**9a**	**2f** (1.0)	100	2	**10**	89
7[c]	**8a**	**9b**	**2c** (0.0001)	140	21	**11a**	90
8[c]	**8b** (R^1 = 2-CH_3)	**9b**	**2c** (0.0001)	140	21	**11b**	83
9[c]	**8c** (R^1 = 3-CH_3)	**9b**	**2c** (0.0001)	140	21	**11c**	88
10[c]	**8d** (R^1 = 4-CH_3)	**9b**	**2c** (0.0001)	140	21	**11d**	91
11[c,d]	**8e** (R^1 = 4-OCH_3)	**9b**	**2c** (0.0001)	140	48	**11e**	91
12[c,d]	**8f** (R^1 = 4-Cl)	**9b**	**2c** (0.0001)	140	48	**11f**	87
13[c,d]	**8 g** (R^1 = 4-$COCH_3$)	**9b**	**2c** (0.0001)	140	48	**11g**	80
14[c,d]	**8h** (R^1 = 4-CF_3)	**9b**	**2c** (0.0001)	140	48	**11h**	78

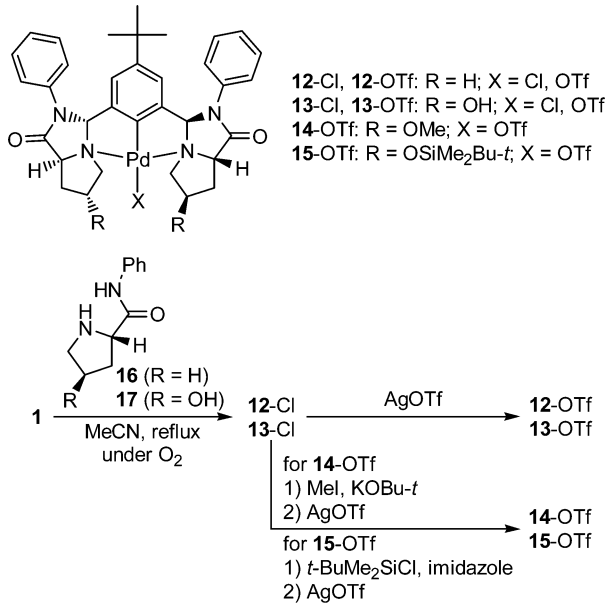
[a] All reactions were carried out in the presence of the pincer palladium complex and Bu_3N (1.4 equiv). [b] Isolated yield. [c] A mixture of NMP and H_2O (7:3) was used as a solvent. [d] Addition of 1 equiv of tetrabutylammonium bromide (TBAB).

830×10^3, 880×10^3, and 910×10^3, respectively (entries 8−10). Excellent TONs were also achieved in the reaction of the aryl iodides having electron-donating as well as electron-withdrawing substituents by adding 1equiv of tetrabutylammonium bromide (TBAB). The observed TONs in the reactions of *para*-iodoanisole (**8e**), *para*-chloroiodobenzene (**8f**), *para*-iodoacetophenone (**8g**), and *para*-(trifluoromethyl)iodobenzene (**8h**) affording **11e**, **11f**, **11g**, and **11h** were 910×10^3, 870×10^3, 800×10^3, and 780×10^3, respectively, demonstrating the wide substituent tolerance of this reaction system (entries 11−14).

The roles of H_2O and TBAB are not yet clear, but it has been reported that the combination of $Pd(OAc)_2$ and both the additives can be used as an effective catalyst for the Suzuki−Miyaura coupling of aryl chlorides in which the true active catalysts are Pd colloids stabilized by the ammonium salt.[12] Moreover, it has been proposed that the Pd^0 nanocluster species generated in situ from PCP[13] or SCS[14] pincer palladium complexes is likely to be the true active catalyst for the Heck reaction. Although the detailed mechanism of the present Heck reaction with the NCN pincer **2** is still unclear, an induction period was observed in the preliminary kinetic study of the reaction of **8a** and **9b** in good agreement with the profile of the pincer palladium catalysts.

5. Preparation of Chiral Pincer Complexes - Development of Ligand Introduction Route. We have recently reported that hexahydro-1*H*-pyrrolo[1,2-*c*]imidazolone serves as an effective chiral auxiliary.[15] These findings prompted us to prepare chiral pincer complexes having pyrroloimidazolone coordinating groups because the framework consists of a cyclic amino acid,

Scheme 11



a primary amine, and an *aldehyde*. In fact, the chiral pincer palladium complexes **12**−Cl and **13**−Cl were also prepared by the ligand introduction route (Scheme 11).[16] Thus, the arylpalladium complex **1** was treated with 5 equiv of the proline anilide **16** to give 98% yield of [4-*tert*-butyl-2,6-bis{(3*R*,7a*S*)-2-phenylhexahydro-1*H*-pyrrolo[1,2-*c*]imidazol-1-on-3-yl}phenyl]-chloropalladium (**12**−Cl). The structure of **12**−Cl was unequivocally established by X-ray diffraction study (Figure 6). Similarly, the analogue **13**−Cl was obtained in 87% yield by the reaction of **1** with the anilide **17** derived from *trans*-4-hydroxy-L-proline. As shown in Scheme 12, the corresponding pincer ligands showed little reactivity to palladium due to the steric bulkiness of the pyrroloimidazolone groups, similar to the preparation of complex **2d** (see above). The chloride ligands

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(13) Eberhard, M. R. *Org. Lett.* **2004**, *6*, 2125.
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(15) (a) Uozumi, Y.; Shibatomi, K. *J. Am. Chem. Soc.* **2001**, *123*, 2919. (b) Uozumi, Y.; Yasoshima, K.; Miyachi, T.; Nagai, S. *Tetrahedron Lett.* **2001**, *42*, 411. (c) Shibatomi, K.; Uozumi, Y. *Tetrahedron: Asymmetry* **2002**, *13*, 1769. (d) Uozumi, Y.; Tanaka, H.; Shibatomi, K. *Org. Lett.* **2004**, *6*, 281.
(16) Preliminary results have been published, see: (a) Takenaka, K.; Uozumi, Y *Org. Lett.* **2004**, *6*, 1833. (b) Takenaka, K.; Uozumi, Y *Adv. Synth. Catal.* **2004**, *346*, 1693.

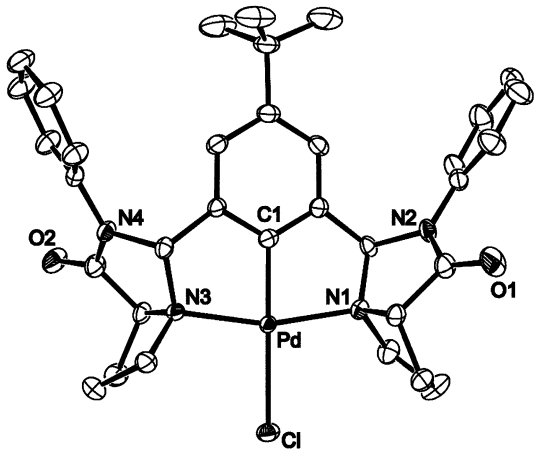
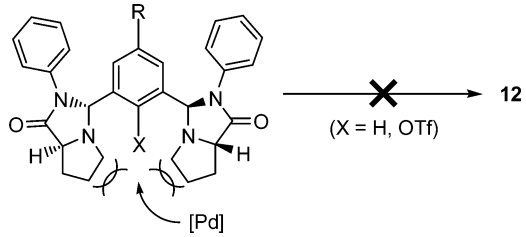


Figure 6. ORTEP drawing of complex **12**−Cl with thermal ellipsoids at 50% probability levels. The solvated toluene molecule and the hydrogen atoms are omitted for clarity. Selected bond distances (Å) and angles (deg): Pd−C(1) = 1.912(3), Pd−N(1) = 2.110(3), Pd−N(3) = 2.111(3), Pd−Cl = 2.437(1); N(1)−Pd−N(3) = 162.96(11), Cl−Pd−C(1) = 176.37-(10).

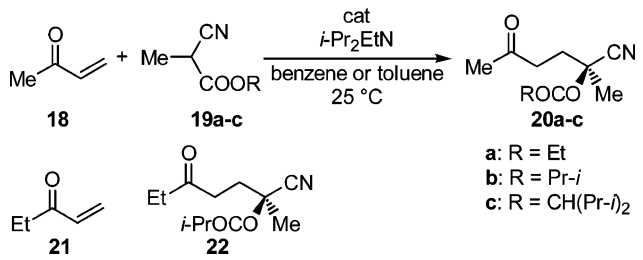
Scheme 12



of **12**−Cl and **13**−Cl were replaced with the more labile triflate ligand by treatment with silver triflate to give **12**−OTf and **13**−OTf in 95% and 94% yields, respectively. The pincer palladium complexes **14**−OTf and **15**−OTf having methoxy and silyloxy groups on their pyrrole rings were also prepared from **13**−Cl in 76% and 83% yields, respectively, via etherification followed by treatment with silver triflate.

To explore the enantiocontrolling potential of the chiral pincer palladium complexes, we elected to study the catalytic asymmetric Michael reaction of vinyl ketones and α-cyanocarboxylates as nucleophiles[17] which has attracted increasing attention since the products bear a quaternary carbon center with various functionalities.[18] The reaction of methyl vinyl ketone (**18**) with methyl 2-cyanopropionate (**19a**) was performed in benzene at 25 °C in the presence of 0.5 mol % of the chiral pincer palladium complex and 0.1 equiv of diisopropylethylamine to give the desired Michael adduct **20a**. Representative results are summarized in Table 2. Among the chiral pincer catalysts **12**−**15**, **13**−OTf bearing hydroxyl groups on the pyrrole rings turned out to be the best catalyst, giving **20a** with high enantioselectivity. Thus, the asymmetric Michael addition catalyzed by **13**−OTf afforded 81% ee (*S*) of the adduct ethyl 2-cyano-2-methyl-5-oxohexanoate (**20a**) in 89% yield (entry 2).

Table 2. Asymmetric Michael Addition of α-Cyanoesters to Vinyl Ketones Using Chiral Pincer Complexes[a]



entry	substrates	cat	time (h)	product	yield[b] (%)	% ee[c]
1	**18**/**19a**	**12**−OTf	3	**20a**	95	8
2	**18**/**19a**	**13**−OTf	4	**20a**	89	81
3	**18**/**19a**	**14**−OTf	3	**20a**	93	6
4	**18**/**19a**	**15**−OTf	4	**20a**	97	9
5	**18**/**19a**	**12**−Cl	144	**20a**	<2	
6	**18**/**19b**	**13**−OTf	4	**20b**	90	80
7[d]	**18**/**19c**	**13**−OTf	24	**20c**	93	80
8	**21**/**19b**	**13**−OTf	4	**22**	91	83

[a] All reactions were carried out in the presence of 0.5 mol % of the pincer palladium complexes and 0.1 equiv of *i*-Pr$_2$EtN at 25 °C in benzene or toluene unless otherwise noted. [b] Isolated yield. [c] Determined by GC analysis (Cyclodex CB). [d] 1.0 mol % of **13**−OTf was used.

The pincer complexes **12**−OTf, **14**−OTf, and **15**−OTf, which lacked hydroxyl groups, were much less stereoselective and only gave 8% ee, 6% ee, and 9% ee of **20a**, respectively (entries 1, 3, and 4). It is also interesting to note that the chemical yield of the product **20a** is strongly affected by the anionic ligand of the pincer complexes. Thus, the Michael addition did not take place with the complex **13**−Cl even after a reaction time of 144 h (entry 5), whereas, with **13**−OTf, the reaction gave a high yield of the product in 4 h. Isopropyl ester **19b** and diisopropylmethyl ester **19c** were subjected to the Michael addition under similar conditions to give 80% ee (*S*) of both **20b** and **20c** in 90% and 93% yields, respectively (entries 6 and 7). The highest stereoselectivity was obtained when the reaction was carried out with ethyl vinyl ketone (**21**) and **19b** in the presence of the chiral pincer catalyst **13**−OTf to give 91% yield of the heptanoate (*S*)-**22** with 83% enantiomeric purity (entry 8).

The structure of the pincer complex **13**−OTf which has hydroxyl groups on their pyrrole rings could not be determined by X-ray analysis because of the difficulty in obtaining adequate single crystals suitable for X-ray diffraction. Molecular modeling study of **13**−OTf indicates that the hydroxyl substituents on the pyrrole rings would play an essential role in the asymmetric induction. Thus, as can be seen from the schematic structure of **13**−OTf shown in Figure 7a, the hydroxyl groups on the pyrrole rings are situated in close proximity to the metal species in the regions of the second and fourth quadrants (from the viewpoint of metal side) where they would fix the enolate of the cyanoester and the vinyl ketone via hydrogen bonds to induce high enantioselectivity (Figure 7b).[17−19]

Conclusion

The ligand introduction route, in which a metal atom is introduced onto the aromatic ring prior to the construction of

(17) Naota, T.; Taki, H.; Mizuno, M.; Murahashi, S.-I. *J. Am. Chem. Soc.* **1989**, *111*, 5954.

(18) For asymmetric Michael addition of α-cyanoesters with chiral transition metal catalysts, see: Rh complexes: (a) Sawamura, M.; Hamashima, H.; Ito, Y. *J. Am. Chem. Soc.* **1992**, *114*, 8295. (b) Sawamura, M.; Hamashima, H.; Ito, Y. *Tetrahedron* **1994**, *50*, 4439. (c) Inagaki, K.; Nozaki, K.; Takaya, H. *Synlett* **1997**, 119. (d) Motoyama, Y.; Koga, Y.; Kobayashi, K.; Aoki, K.; Nishiyama, H. *Chem.*−*Eur. J.* **2002**, *8*, 2968. Pt complexes: (e) Blacker, A. J.; Clarke, M. L.; Loft, M. S.; Mahon, M. F.; Williams, J. M. J. *Organometallics* **1999**, *18*, 2867. Pd complexes: (f) Stark, M. A.; Jones, G.; Richards, C. J. *Organometallics* **2000**, *19*, 1282.

(19) Mechanistic studies on the catalytic Michael addition, see: (a) Murahashi, S.-I.; Naota, T.; Taki, H.; Mizuno, M.; Takaya, H.; Komiya, S.; Mizuho, Y.; Oyasato, N.; Hiraoka, M.; Hirano, M.; Fukuoka, A. *J. Am. Chem. Soc.* **1995**, *117*, 12436. (b) Naota, T.; Tannna, A.; Murahashi, S.-I. *Chem. Commun.* **2001**, 63 and references therein.

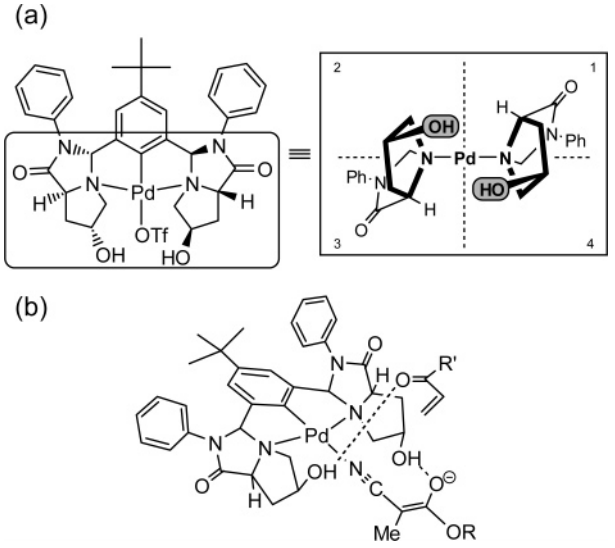


Figure 7. (a) Schematic structure of the complex **13**−OTf and (b) the plausible transition state of the Michael addition.

the ligand moieties, has been developed as a new synthetic methodology for pincer complexes. This concept has been applied to the preparation of NCN pincer palladium complexes bearing imine functionalities as coordinating sites. The three major problems found in conventional pincer formation, namely, introduction of sterically demanding donors, utilization of sensitive coordination groups, and regioselectivity of metalation, are no longer impediments using this strategy. The VT NMR experiments established the existence of an equilibrium between the pincer complexes and the corresponding PPh_3 adducts which are possible intermediates in the course of the reaction. It was also shown that the desired pincer complexes could be obtained by oxidative removal of the liberated PPh_3, thereby displacing the equilibrium. The ligand introduction route was also found to be an efficient method of preparation for the chiral pincer palladium complexes having pyrroloimidazolone coordination groups.

The imine pincer complexes obtained here displayed high catalytic activity in the Heck reaction of aryl iodides and butyl acrylate. Furthermore, the asymmetric Michael addition of α-cyanocarboxylates to vinyl ketones was catalyzed by the chiral pyrroloimidazolone pincer complexes with high enantioselectivity.

The application of the ligand introduction route to other transition metals as well as various functional groups is currently underway and will be reported in due course.

Experimental Section

General Procedure for the Preparation of Imino Pincer Palladium Complexes (Ligand Introduction Route 1).[20] The palladium complex **1** and the primary amine were suspended in MeCN. The suspension was refluxed under an O_2 atmosphere to give a clear yellow solution, which was then cooled to room temperature. The solvent was removed under reduced pressure, and the crude product was purified by column chromatography on silica gel, yielding the imino pincer palladium complex as a yellow solid.

General Procedure for the Preparation of Imino Pincer Palladium Complexes (Ligand Introduction Route 2). The palladium complex **1** and the primary amine were suspended in MeCN. The suspension was refluxed under a N_2 atmosphere to give a yellow solution, which was cooled to room temperature. The urea hydrogen peroxide addition compound (**7**) was added, and the reaction mixture was stirred at 50 °C. The solvent was removed under reduced pressure, and the resulting mixture was purified by column chromatography on silica gel to afford the imino pincer palladium complex as a yellow solid.

Equilibria Studies by NMR. The complex (**2b**; 10.5 mg, 20 μmol or **2c**; 9.0 mg, 20 μmol) and PPh_3 (10.6 mg, 40 μmol) were dissolved in 0.60 mL of tetrachloroethane-d_2. The ^1H and $^{31}P\{^1H\}$ NMR spectra were measured from −40 to 80 °C after reaching an equilibrium. At each temperature (for **2b**, −40 to 30 °C; for **2c**, −40 to 20 °C), the equilibrium constant, K_{eq}, was determined by the integration of the resonances assigned to the methylene protons attached to the N atom. Thermodynamic parameters were obtained from a plot of ln K_{eq} vs $1/T$, where the slope $= -\Delta H°/R$ and the intercept $= \Delta S°/R$, using Microsoft Excel.

General Procedure for the Heck Reaction. To a solution of Bu_3N (1.4 equiv) in a NMP/H_2O mixture (0.7 mL/0.3 mL) were added the aryl halide (1.0 equiv), butyl acrylate (1.4 equiv), and the catalyst **2** (as a 0.1 mM solution in NMP). The reaction mixture was heated at 140 °C for a specified period of time and allowed to cool to room temperature. The reaction mixture was then diluted with water, and the product was extracted three times with ether. The combined extracts were dried over Na_2SO_4. The organic phase was concentrated under reduced pressure, and the crude product was purified by silica gel column chromatography (eluent: hexane/EtOAc = 100/1), giving the desired product. CAS Registry numbers of the Heck products: **10**, 1754-62-7; **11a**, 52392-64-0; **11b**, 163977-61-5; **11c**, 173593-27-6; **11d**, 123248-21-5; **11e**, 121725-19-7; **11f**, 123248-22-6; **11g**, 173464-57-8; **11h**, 220466-27-3.

General Procedure for the Michael Reaction. To a solution of the catalyst (0.005 equiv) in either toluene or benzene (2.0 mL) were added the cyano ester (1.0 equiv), the Michael acceptor (1.5 equiv), and finally Hünig's base (0.1 equiv). The reaction mixture was stirred at 25 °C for an appropriate time. The solvent was removed, and the residue was purified by Kugelrohr distillation to give the desired product.

Acknowledgment. This work was supported by the CREST program sponsored by JST. We also thank the JSPS (Creative Scientific Research, No. 13GS0024; Grant-in-Aid for Scientific Research, No. 15205015) and the MEXT (Scientific Research on Priority Areas, Nos. 412 and 420) for partial financial support of this work.

Supporting Information Available: Full experimental details, spectral and analytical data for the products, and X-ray crystallographic data for **1**, **2a**, **2b**, **2c**, **2e**, **2f**, **2b-P**, **2f-P**, **2g-P**, and **12**−Cl in CIF format. This material is available free of charge via the Internet at http://pubs.acs.org.

JA052780N

(20) General experimental conditions, detailed procedures, and characterization of the products are given in the Supporting Information.